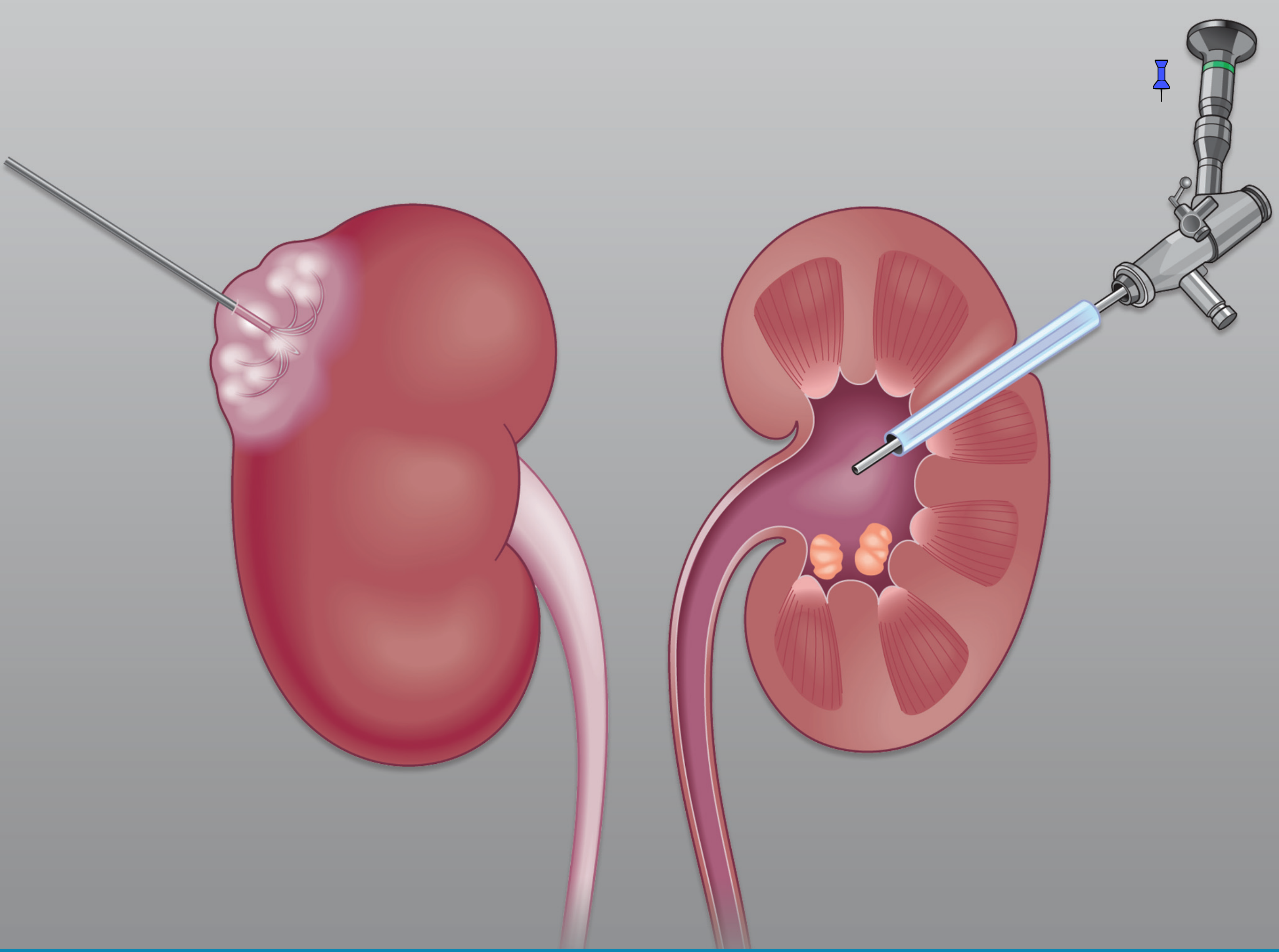

Percutaneous Renal Surgery

Edited by Manoj Monga and Abhay Rane

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Percutaneous Renal Surgery

To our parents:

Uma and Trilok Monga
Snehalata and Murali Rane

Percutaneous Renal Surgery

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This edition first published 2014 © 2014 by John Wiley & Sons, Ltd

Registered Office
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Library of Congress Cataloging-in-Publication Data

Percutaneous renal surgery / [edited by] Manoj Monga, Abhay Rane.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-118-27873-4 (hardback : alk. paper) – ISBN 978-1-118-67090-3 – ISBN 978-1-118-67092-7 (pub) – ISBN 978-1-118-67093-4 (pdf) – ISBN 978-1-118-67095-8 (mobi)
I. Monga, Manoj, editor of compilation. II. Ran?, Abhay, editor of compilation.
[DNLM: 1. Kidney Diseases–surgery. 2. Kidney–surgery. 3. Nephrostomy, Percutaneous–methods. 4. Urologic Surgical Procedures–methods. WJ 368]
RD575
617.4′61059–dc23
2013007101

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Cover image: ©John Wiley & Sons Ltd.
Cover design by OptaDesign.co.uk

Set in 9/12pt Minion by SPi Publisher Services, Pondicherry, India

1 2014

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Preface

As medical students, we learn that the kidney receives 20% of the cardiac output. The thought of making a 1 cm hole in the kidney and relying on the forces of nature for hemostasis is understandably met with trepidation. Yet, the foresight, innovation, and courage of our predecessors have paved our path towards minimally invasive percutaneous approaches to renal diseases.

In this book we explore both the novel developments in percutaneous renal surgery and percutaneous ablative techniques, recognizing that the overlap in anatomical considerations, radiological and surgical skill sets, instrumentation and technique present an opportunity for collaboration and synergy.

Manoj Monga
Abhay Rane

About the Companion Website

This book is accompanied by a companion website:

www.wiley.com/go/monga/percutaneous

The website includes 10 video clips.

I

SECTION 1

Introduction

1

CHAPTER 1

Percutaneous Renal Access: A Historical Perspective

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Introduction

Percutaneous nephrolithotomy (PCNL) has evolved to become the preferred minimally invasive approach for treating large-burden renal stones. This approach has replaced open renal surgery for stones. It has also evolved into a treatment option for treating noninvasive urothelial tumors of the upper urinary tract. Current percutaneous access techniques involve fluoroscopic or ultrasound guidance with a small-gauge needle for initial access. In selected cases, computed tomography (CT) guidance or blind access by anatomical landmarks may be indicated. The complications of PCNL are minimal and the associated morbidity is far less than for open renal surgery.

History

In 1865 at the Great Ormond Street Hospital, a case report by Thomas Hillier of therapeutic percutaneous renal decompression in a 4-year-old boy with congenital obstruction of the ureteropelvic junction was the first such case of percutaneous nephrostomy [1]. Through the course of the following 5 years, he performed multiple nephrostomies to relieve the recurring abdominal distension from the obstructed kidney. However, there was no suitable trocar available with which to create a permanent nephrocutaneous fistula. The child subsequently died at the age of 8 after a febrile illness.

The history of modern percutaneous renal surgery began with the first image-guided renal biopsy performed in 1944 by Nils Alwall by means of needle aspiration using a simple radiograph and retrograde pyelogram to localize the kidney with the patient in the sitting position. The procedure was performed at the University of Lund, Sweden. While the initial procedure was performed in 1944, the experience was not published until 1952 [2]. Subsequent series of percutaneous renal biopsy had the patient positioned prone, and the kidneys were localized using landmark distances between the vertebral spinous processes and the 11th and 12th ribs, and palpation for kidney movement [3].

The next reported description of percutaneous renal access was in 1955. Goodwin, Casey, and Woolf presented their experience at Harbor General Hospital of the University of California, Los Angeles, in 16 patients with hydronephrosis managed with percutaneous nephrostomies for drainage. All cases were performed under local anesthesia [4]. This technique followed as a natural extension of their initial report of percutaneous antegrade pyelography [5]. The authors noted in their technique that the procedure should be limited to patients with severe hydronephrosis since it was easier to puncture a larger hydronephrotic sac. The punctures were made with 12–14 gauge needles. It is of interest to note that the authors fashioned polyethylene tubings with several additional lateral holes to increase urinary drainage, allowing 2–4 inches of that portion of the tubing to coil in

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

the renal pelvis. These early modifications are now the standard design of pigtail nephrostomy tubes that are currently available.

In 1975, Stables published a case series in which he described a technique to convert a standard temporary percutaneous nephrostomy to prolonged or permanent nephrostomy drainage with Foley catheters [6]. This was thought to be of benefit in the management of obstructive nephropathy in cases where the primary lesion was not readily amenable to surgical repair. In a larger series and review of the literature, Stables described the application of the percutaneous nephrostomy in supravesical urinary obstruction, urinary fistulas, and renal calculi [7]. He reported a success rate of over 90% with percutaneous nephrostomies, with major complications limited to 4% and minor complications to 15%. This represented a significant advance because open nephrostomy had been associated with such complications as uremia, hemorrhage, infections, sepsis, and at times difficult access to the renal pelvis.

In another series, Hellsten et al. reported performing percutaneous nephrostomy in 32 patients. Of these, eight patients were for permanent drainage and 24 for temporary drainage. Malignant obstruction of the distal ureter was the most common indication [8]. Access to the renal pelvis was obtained with the aid of fluoroscopy and/or ultrasound. Change to larger catheters was achieved using the Seldinger technique. The most common complication reported was hemorrhage in five patients. Percutaneous nephrostomy has thus remained in use for temporary or permanent drainage of the urinary tract for various indications including infections, obstruction or neoplasm.

Percutaneous nephrolithotomy

In 1976, Fernstrom and Johannson reported on the first percutaneous image-guided nephrolithotomy [9]. The tract was dilated coaxially with graded plastic dilators over the course of a few days. The tract was then used for renal manipulation using grasping tools and Dormia baskets after allowing the tract to mature. Following shortly thereafter in 1979, Smith et al. from the University of Minnesota reported on their experience [10]. By 1984, they reported results from their first 100 patients [11]. Interestingly, the complication rate decreased to 5% as their experience with the procedure grew, with a reported stone-free rate of 91% for the most recent patients in that series. One year later in 1985, the same group reported on a further 400 patients. This time, the stone-free rate had improved to 99% for patients with renal stones and 94.5% for ureteral stones [12]. Their results compare very favorably to stone-free and complication rates from more modern PCNL series.

Percutaneous transitional cell carcinoma resection

In 1984, Orihuela, Crowley, and Smith from the Long Island Jewish Medical Center in New York extended the techniques for percutaneous renal access to the treatment of upper tract urothelial carcinomas. Two years later, they became the first to report their experience at the annual meeting of the American Urological Association in 1986 [13]. The initial series of patients was a highly selected group suitable for renal-sparing surgery for solitary kidney, bilateral synchronous disease, renal insufficiency, poor surgical risk for open surgery or biopsy evidence of a solitary low-grade superficial tumor. The authors' technique involved an initial resection through a percutaneous nephrostomy, followed by a second-look procedure 2–28 days later to assess the completeness of the initial resection and to remove any residual tumors. Of note, with this initial series of patients, the authors used adjuvant topical therapy through the nephrostomy tube with mitomycin C and bacillus Calmette–Guerin (BCG). Subsequently, the same group published results on their experience with their first nine patients [14]. Other authors emulated the technique and reported similar success [15].

Percutaneous endopyelotomy

The percutaneous renal access technique was also adapted to treatment of the obstructed ureter. With percutaneous renal access, the ureteropelvic junction is easily accessible and made endoscopic incision feasible, avoiding the need for open surgery. In 1983, Whitfield et al. described a procedure of percutaneous incision of the ureteropelvic junction using a modification of the Davis intubated ureterostomy technique. The authors reported a success rate of 64% with their technique [16]. In 1984, Smith reported on the various adaptations of the nephrostomy tract to renal surgery [17]. He demonstrated that the nephrostomy tract permits antegrade insertion of ureteral stents, ureteral dilation, and insertion of ureteral catheters to which other instruments such as stone baskets, steel stylets, etc. could be attached, thus facilitating controlled stone manipulation, ureteral meatotomy, and retrograde stent insertion. He adapted the technique reported by Whitfield et al. and termed it endopyelotomy. In 1986, Badlani et al. reported on their initial experience in the treatment of ureteropelvic junction obstruction using this modified technique in 31 patients with a cold knife direct-vision urethrotome inserted through a percutaneous nephrostomy tract [18]. A success rate of 87.1% was reported by the authors. Notably, eight of these patients were undergoing endopyelotomy after previous failed open pyeloplasty.

Other applications

The next application of the nephrostomy tract was the attempt to dissolve stones by chemolysis. The instillation of acetylcysteine together with sodium bicarbonate through a nephrostomy tube into the renal pelvis was highly effective for dissolving cystine stones. Subsequently, renacidin was used to dissolve struvite stones. Blaivas et al. attempted chemical dissolution of residual stone fragments in 12 instances via nephrostomy tube irrigation [19]. Solutions containing either hemiacidrin or sodium bicarbonate were used for struvite and uric acid stones respectively, with a 75% success rate (complete dissolution of stones) reported. Pfister and Dretler also reported a considerably higher success rate in the management of renal and ureteral calculi with chemolytic drug irrigation through a percutaneous nephrostomy catheter [20]. Struvite, apatite, and carbonate stones were dissolved with an acidic solution (hemiacidrin, Suby solution G) and cystine stones were dissolved with an alkaline agent (Tham-E, acetylcysteine). A success rate of 85% in more than 150 stones cases was reported. This was particularly advantageous in medical conditions (cardiac, metabolic) where oral alkalinization with sodium bicarbonate or potassium citrate may be contraindicated. However, it took about 3–4 weeks of continuous irrigation to dissolve a stone. Chemolysis has since fallen out of favor due to the excellent outcomes from percutaneous nephrolithotomy.

Conclusion

The evolution of percutaneous renal access became the highway. The early innovations in minimally invasive urological surgery have evolved into what has today become the standard of care for many urological diseases. Those experiences propelled minimally invasive urology in great leaps and bounds. Not long after the early days of percutaneous renal surgery, in 1991 Ralph Clayman, one of the early pioneers, performed the first laparoscopic nephrectomy [21]. That endeavor has driven the evolution of urological surgery to a craft that is accomplished primarily through minimally invasive techniques.

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2

CHAPTER 2

Interventional Imaging and Radiation Safety

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Introduction

Medical imaging plays an essential role during the diagnosis, treatment, and follow-up of patients undergoing percutaneous renal surgery. As minimally invasive surgery has employed smaller and less invasive techniques for renal surgery, surgeons have increasingly relied upon interventional imaging to provide the information regarding anatomical relationships and pathology which previously could be directly seen or felt during open surgery. These imaging modalities have allowed surgeons to gain percutaneous access to the kidney for stone treatment, treat upper tract transitional cell carcinoma (TCC) in an endoscopic manner and perform percutaneous renal ablative surgery for small renal tumors. However, this increased reliance upon medical imaging during diagnosis, treatment, and follow-up has increased the radiation exposure received by patients. It is important that the surgeon performing minimally invasive renal surgery is facile with interventional imaging, knowledgeable regarding basic radiation physics and fully appreciates the differences between imaging modalities. Finally, the surgeon must use this knowledge to select diagnostic, therapeutic and follow-up imaging in a manner that will provide the optimal outcome and patient safety while minimizing the radiation exposure to the patient, surgeon, and staff.

Basic radiation physics

A fundamental understanding of the biological effects of radiation in the patient is essential in order to optimally utilize diagnostic and therapeutic imaging. The term "absorbed dose" refers to the amount of energy deposited per unit mass and is a way to determine the probability of biological effect (Box 2.1). Absorbed dose is measured in units of gray (Gy) or milligray (mGy). One gray is equal to 1 joule per kilogram of tissue (J/kg). Entrance skin dose refers specifically to the measure of radiation dose absorbed by the skin where the x-ray beam enters the patient. Finally, organ dose describes the amount of radiation to the organs of a patient [1, 2].

The two types of biological effects observed in patients following radiation exposure include immediate deterministic effects and delayed stochastic effects. Deterministic effects typically have a short latency period and are characterized by nonlinear dose–responses with a threshold dose (> 0.1 Gy) [3]. At lower doses, these deterministic effects (i.e. erythema and epilation) will completely resolve but above 10 Gy permanent damage may result [4].

The stochastic effects of radiation include the development of secondary malignancies. Unlike deterministic effects, there are no data to support a threshold below which stochastic effects will not occur [3]. The development of secondary malignancies is thought to be due to misrepair

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

Box 2.1 Radiation sources and recommendations

Radiation conversions

1 mGy	100 mrad
1 mSv	100 mrem
1 mGy*	1 mSv*
1 rad*	1 rem*
1 Gy	100 roentgen
10 mSv	1/1000 develop cancer; 1/2000 fatal cancer [107]
100 mSv	1% increase in cancer in a population [108]
1 Sv	Onset of early radiation effects [109]
2 Sv	Threshold for early death [109]
4 Sv	50% chance for survival [109]

Environmental exposures

Natural background radiation per year	2.72 mSv [110]
Cosmic radiation per year	0.28 mSv [110]
Radiation from airport scanners (50 kVp)	0.9 uSv [111]
Airplane flight from New York to London	0.1 mSv [112]
Within 3 km of Hiroshima detonation	50–100 mSv [112]
237 onsite Chernobyl workers at meltdown	1–16 Sv [113]

Medical imaging exposures

KUB	0.7 mSv [47]
Chest x-ray 2 view	0.05–0.24 [47]
Voiding cystourethrogram	0.2–8.5 mSv [114]
Intravenous pyelogram	3–9 mSv [56,115]
Noncontrast CT abdomen or pelvis (1 phase)	10 mSv [112]
CT urogram	14.8–36.1 mSv [56,116]
Nuclear renal scan DTPA	1.8 mSv [47]
Nuclear renal scan MAG 3	2.6 mSv [47]
Nuclear renal scan DMSA	3.3 mSv [47]
Bone scan	6.3 mSv [47]
PET scan	14.1 mSv [47]
Low-dose CT abdomen and pelvis	2.1 mSv [117]
Ultra low-dose CT abdomen and pelvis	0.95 mSv [112]
Percutaneous cryoablation	120 mSv [118]

Exposure recommendations

Maximum occupational radiation exposure	20 mSv/year averaged over 5 years with no more than 50 mSv in any one year [119]
Allowable exposure to the lens of the eye/yr	150 mSv [119]
Hands and feet/yr	500 mSv [119]

*= when discussing x-rays, gamma rays, and beta radiation.
CT, computed tomography; DMSA, dimercaptosuccinic acid; DTPA, diethylene triamine pentaacetic acid; KUB, kidney, ureter and bladder; MAG 3, mercaptoacetyltriglycine 3; PET, positron emission tomography.

of damaged DNA that results in a genetic transformation. This damage is directly correlated with the total radiation absorbed by organs and tissues [5]. Since intentionally exposing patients to high levels of radiation would be unethical, much of our understanding of radiation's stochastic effects is inferred from the effects observed in atomic bomb survivors. However, since atomic bomb survivors also received neutrons, protons, and other radioactive materials for which the biological effects are not as well characterized, this may not be the most accurate comparison [6,7].

At the present time the linear no-threshold model is felt to best represent the risk for stochastic injury following radiation damage. It has been documented that solid cancer rates will increase by 35% per Gy for men and 58% per Gy for women after exposure at age 30 if they live to 70 years of age [8]. The likelihood that exposing patients to ionizing radiation will result in cancer is dependent upon how much radiation they absorb, the type of radiation they are exposed to, and the sensitivity of the organ exposed.

Humans receive radiation from a variety of natural and iatrogenic sources (see Box 2.1). During the diagnosis, treatment, and follow-up of patients undergoing percutaneous renal surgery, patients may receive substantial radiation exposure. Most of this imaging is essential to allow safe and effective patient treatment. However, it has been estimated that of the 80 million computed tomography (CT) scans performed annually, 20–40% may be unnecessary [9]. Medical imaging currently contributes to approximately 50% of overall radiation exposure in the United States compared to 15% in 1980 [9]. It was recently estimated that 29,000 tumors may result from the 70 million CT scans performed in the United States in 2007 alone and this may account for 2% of US cancers [10]. In 2010, the Food and Drug Administration (FDA) issued a White Paper calling for a reduction in the radiation exposure received by patients during medical imaging and specifically recommended reductions in radiation from CT, fluoroscopy, and nuclear medicine imaging [11].

Percutaneous renal surgery for stones

Preoperative imaging

The treatment of large renal stones with percutaneous nephrostolithotomy (PCNL) begins by obtaining an appropriate characterization of the preoperative stone volume and location, anatomical relationships and at least indirect information to suggest the presence of adequate renal function. Although a plain abdominal radiograph (KUB), intravenous pyelogram (IVP), nuclear renography, and renal ultrasound (US) are sometimes used, CT imaging is the most commonly employed modality in the evaluation of staghorn calculi. CT acquires images rapidly, is nearly universally available, and provides important anatomical relationships. CT imaging can also create three-dimensional (3D) reconstructions to assist in tract site planning [12], although the benefits of the 3D reconstructions are not uniformly accepted [13]. Furthermore, in some patients with complicated anatomy, the nephrostomy tube may have to be placed using CT guidance [14].

Figure 2.1 Plain abdominal x-ray demonstrating full bilateral staghorn calculi.

Although magnetic resonance imaging (MRI) provides excellent soft tissue imaging, its use in the evaluation of staghorn calculi has been limited due to poor visualization of stones, high cost, long acquisition time, and degradation with motion artifact [15,16]. Ultrasound is able to accurately detect renal calculi, determine parenchymal thickness and access for hydronephrosis without ionizing radiation. A KUB is also routinely performed to give an overview of the stone size and location, and to determine whether the stone is radiopaque (Figure 2.1). A nuclear renogram may be helpful to access renal function in staghorn patients, particularly in those with long-standing hydronephrosis, parenchymal thinning or prior interventions [17].

Imaging for establishing nephrostomy tract

The most common imaging modality employed intraoperatively in the treatment of staghorn calculi is fluoroscopy. Appropriate utilization of fluoroscopy during PCNL provides an important understanding of anatomical and spatial relationships that leads to a decrease in the complexity and improved procedure safety. The cinematic images are particularly helpful for advancing the guidewire past the stone into the ureter prior to tract dilation [18].

Computed tomography-guided percutaneous access to the kidney can also be employed. It is slower and more cumbersome than nephrostomy placement under fluoroscopy but may be helpful in identifying a retrorenal colon and the location of the lung, pleura, liver, and spleen in upper pole access. Some of the indications for CT-guided percutaneous access include spinal dysraphism, morbid obesity, and abnormal anatomy [19–21]. The success of CT-guided percutaneous nephrostomy tube placement approaches 100% and may minimize the risk of major complications like bowel and visceral injury [22,23].

The use of US guidance during nephrostomy tube placement has some potential advantages compared to fluoroscopy and eliminates the need for ionizing radiation. US may result in shorter procedure times, fewer punctures, real-time visualization of surrounding structures, easier identification of posterior and anterior calyces and the ability to visualize and avoid the lung, pleura, and bowel [24]. Using ultrasound, successful nephrostomy placement has been reported in 91–100% of patients [25–27]. Major complications occurred in about 5% of patients [27].

Radiation implications of percutaneous stone surgery

The imaging used and the manner in which that imaging is employed may have significant effects upon the radiation exposure for patients during PCNL. Lipkin and colleagues used a validated phantom model to determine the effective dose during PCNL. The effective dose for left and right PCNL was 0.021 mSv/s and 0.014 mSv/s, respectively. These corrections were multiplied by the median fluoroscopy time of 386.3 and 545 sec for left and right PCNL, respectively. The effective dose received by the patient was 8.11 mSv on the left and 7.63 mSv on the right [28].

The fluoroscopic radiation exposure received by the patient is dependent upon patient factors, fluoroscopy settings, and the specifics of the machine. Newborns have a 3× higher risk of developing cancer compared to adults due to their longer life expectancy and greater susceptibility to the effects of ionizing radiation [29,30]. A patient of medium build may typically receive a skin entrance dose of 30 mGy/min [31]. Obesity increases radiation exposure due to poor radiation penetration and the x-ray source being closer to the patient [32]. An obese patient may receive a dose as high as 10–50× that of an individual with normal build [33,34].

There are several radiation reduction strategies that can be employed during the diagnosis, treatment, and follow-up of stone patients, including avoiding ionizing imaging, spacing out imaging intervals, and the use of intraoperative behavioral and technical modifications. Alternative imaging strategies may include the use of US to place the nephrostomy tube and to monitor stone fragmentation. Behavioral changes include shorter pedal activations, use of last image hold, maintaining appropriate distance from the radiation source, and monitoring and recording fluoroscopy time. There are also technical modifications to reduce radiation exposure, including maintaining an optimal fixed and intentionally lowered kVp and mA instead of using automatic brightness control settings, use of a laser guided C-arm, use of pulsed instead of continuous fluoroscopy, and the use of shielding and collimation.

Early C-arm machines provided only real-time images and if the foot pedal was not depressed, there was no screen image. Last image hold allows the physician to scrutinize the last image and develop an appropriate management plan without exposing the patient to additional doses of radiation [35]. Although some steps during percutaneous nephrolithotomy, such as placing the guidewire past an obstructing stone, may require dynamic fluoroscopy, most tasks can be effectively performed by viewing a static image. This maneuver may reduce radiation exposure by up to 60% [36].

Perhaps the most intuitive behavioral method of reducing radiation exposure is to reduce the amount of time that the fluoroscopy pedal is depressed [37]. Using shorter rather than longer periods of continuous fluoroscopy will reduce radiation exposure. By only obtaining images that are necessary for the surgery, the overall exposure is reduced. Substituting visual and tactile cues for fluoroscopic cues may significantly reduce radiation exposure [38]. An example of this technique is confirming placement of a safety guidewire by comparing its length to the original wire instead of employing fluoroscopy.

Surgeon monitoring and recording of activation times have been shown to result in a 24% reduction in fluoroscopy [39]. Also, employing the inverse square law between exposure and distance during fluoroscopy can lower radiation exposure to the patient, urologist, and ancillary staff. If the distance from the source is doubled, the radiation exposure decreases by a factor of 4. The fluoroscopy machine should always be used with the spacer at the source to prevent the operator from moving the source too close to the patient. All operating room members should work at the greatest distance from the source that allows the safe performance of their clinical duties.

There are also several easily implemented technical modifications that can reduce the radiation exposure during PCNL. In a review of 96 patients by Lipkin and colleagues, it was found that using air instead of contrast for the nephrostogram reduced the radiation exposure from 7.67 mSv to 4.45 mSv ($p = 0.001$). This reduction was thought to be due to the automatic brightness control (ABC) mode increasing settings to preserve image quality in response to dense contrast [40,41].

Another technique to reduce radiation exposure during PCNL is through intentional alteration of the fluoroscopy machine settings prior to the procedure. Fluoroscopy machines are routinely operated using ABC settings where the machine automatically adjusts the mA and kVp to provide optimal image quality based upon the density of objects within the field of interest [42]. One highly effective method for reducing radiation exposure is to maintain the kVp while decreasing the mA using fixed manual settings [43]. During fluoroscopy, guidewire and nephroscope position, stone fragmentation and nephrostomy position can all be determined using a relatively low-quality image. Use of intentionally lowered fixed settings also prevents the “whited out” image which can occur using automated settings if the C-arm sensor encounters dense structures such as the bar on the fluoroscopy table or a dense region of contrast [44]. These settings can be placed at the lowest level that will provide adequate image quality for the task at hand.

Another alteration that can be applied to the fluoroscopic machine is the use of pulsed rather than continuous fluoroscopy. In continuous fluoroscopy, x-rays are continuously created and captured on a video camera display at a rate of 30 frames/sec [45]. In contrast, the operator can manually adjust the number of frames/sec in pulsed fluoroscopy. It has been documented in the literature via phantom models that pulsed fluoroscopy at rates of 15, 10, 7.5, and 3.75 frames/sec were associated with radiation reduction of 22%, 38%, 49%, and 87%, respectively [46].

Collimation and shielding are other technical strategies for reducing the amount of radiation by restricting the radiation solely to the area of interest. Collimation occurs at the level of the machine and can be used to narrow the amount of radiation exposure escaping the machine, thereby reducing the x-rays to the areas of interest. In contrast, shielding is routinely placed between the x-ray source and the patient. Similar to collimation, shielding limits the radiation exposure to the area of interest and may reduce exposure by 80% [47,48].

In addition to taking measures to protect the patient, the surgeon should also be aware of methods to improve the safety for themselves and their staff. In an internet study, Elkoushy and colleagues reported that only 68% of surgeons wore thyroid shields and 34.3% reported wearing dosimeters. Only 17.2% reported wearing lead-impregnated glasses and 9.7% used lead-impregnated gloves [49]. The reasons for noncompliance included unavailability, carelessness and denial, lack of knowledge of the hazards of radiation, inadequate knowledge of radiation protective measures, and discomfort of heavy lead aprons. Thyroid shielding should be utilized as the radiation exposure may be decreased by 23-fold [50]. Even though the National Council on Radiation Protection and International Commission on Radiological Protection reported that the lowest cumulative lens dose resulting in cataracts is 2 Gy, other evidence suggests that even centigray doses may cause cataracts [51], highlighting the importance of lead glasses.

A study performed by King and colleagues demonstrated that by using a disposable sterile bismuth drape the amount of scatter radiation to the surgeon was reduced 12-fold to the eyes, 25-fold to the thyroid and 29-fold to the hands. Yang and colleagues demonstrated that a 0.5 mm lead equivalent vinyl-coated sheet fastened to the operating table acting as a curtain to protect the surgeon decreased the radiation exposure 71–96% [52].

Interventional imaging and radiation safety for upper tract transitional cell carcinoma

Upper tract TCC accounts for approximately 12% of the diagnosed upper tract urothelial cancers [53]. Traditionally, hematuria patients underwent a cystoscopy and IVP [54]. More recently, the IVP has been replaced by a three-phase CT urogram (CTU) including noncontrast, early arterial and delayed phases (Figure 2.2). CT urography is more sensitive (93.5% versus 80.4%) and more specific (94.8% versus 81%) than IVP in the diagnosis of upper tract TCC [55], but is associated with greater radiation exposure. Nawfel and colleagues found a mean exposure of 14.8 mSv in eight CT urography patients compared to 9.7 mSv in 11 patients undergoing IVP [56].

Magnetic resonance urography (MRU) has also been reported for the diagnosis and follow-up of upper tract TCC. MR imaging provides better tissue contrast resolution, greater ease of evaluation of vascular structures, and better identification of perivascular lymph nodes, and can provide greater information with regard to tissue properties than CT scan [57–59]. Typically, TCC has lower signal intensity than the high signal intensity urine on T2-weighted images and thus allows identification of the tumor in a dilated collecting system [60]. Conversely, TCC is essentially isointense with renal parenchyma on T1- and T2-weighted images. Hence, gadolinium is often required for accurate delineation and assessment of tumor extent [61].

A study performed by Jung and colleagues found that MRU had an 88% sensitivity and a 100% specificity for detection of ureteral tumors [61]. This is comparable to the 87% sensitivity and 98% specificity of CTU [62–64]. Therefore, MRU is a viable alternative to using ionizing radiation when evaluating patients for upper tract TCC. MRU may also be ideal in patients with an iodine allergy or in younger and healthier patients concerned about radiation exposure.

The process of obtaining percutaneous access to the kidney to manage upper tract TCC is similar to the process for obtaining percutaneous access to the kidney to manage staghorn calculi, except that the access is placed to allow inline treatment of the TCC without placing access directly through the tumor [65]. Compared to treatment of staghorn calculi, most of the treatment for endoscopic management of upper tract TCC is via direct visualization and therefore these patients tend to receive less radiation exposure. In addition, patients with upper tract TCC have a peak incidence in the seventh decade of life and often present with significant medical comorbidities. Although many of the same radiation principles discussed in the section on treatment of large renal stones are also applicable in this patient population, concerns for radiation-related morbidity are much less [66,67].

Figure 2.2 CTU demonstrating a right filling defect in the renal pelvis due to upper tract TCC.

Intraoperatively, endoluminal ultrasound (EUS) may provide a promising new staging tool for upper tract TCC that does not require ionizing radiation. Matin and colleagues reviewed 15 patients being evaluated for suspected upper tract urothelial carcinoma. Six out of seven patients treated with nephroureterectomy were appropriately staged with EUS. In this study, the positive predictive value of endoluminal ultrasonography was 66.7% and the negative predictive value was 100% [68].

Similarly, the postoperative follow-up of upper tract TCC patients should be dictated by the provision of optimal follow-up and should not be overly concerned with radiation exposure. A wide variety of methods for follow-up of the upper tract have been reported including IVP, CT urogram, MR urogram, and endoscopic surveillance. The method selected for follow-up should be influenced by the availability and expertise at the treating institution. Similarly, follow-up interval and method should be dictated by the tumor biology and patient comorbidity [69–79].

Interventional imaging and radiation safety for percutaneous renal mass ablation

The incidence of renal cell carcinoma in the United States has risen over the last 30 years [80,81]. This increase has been attributed to increased utilization of CT and US in the evaluation of abdominal symptoms as well as an increase in risk factors, such as obesity and hypertension [82,83]. Many patients who are poor surgical resection candidates are amenable to percutaneous ablative therapies.

When treated using percutaneous ablative techniques, patients with renal masses typically undergo multiple imaging tests in the pre-, intra, and postoperative periods. Therefore, it is important for the physician to understand the advantages and disadvantages of each imaging modality. While the clinical effect of radiation exposure in the older patient with multiple comorbidities may be minimal, reducing radiation exposure in younger, healthier patients with potential long-term survival is important.

Preoperative imaging of the small renal mass

Ultrasonography has the advantage of delivering no ionizing radiation, being relatively inexpensive, and is useful for differentiating solid and cystic lesions. However, ultrasound lacks the ability to provide detailed anatomical images, is operator dependent, and is inferior to CT in the identification of renal masses < 2.5 cm [84].

Magnetic resonance imaging is a reasonable alternative to CT in the evaluation of renal masses, particularly in patients with known iodine contrast allergy. Additionally, advances in MRI technology may help differentiate between oncocytomas and renal cell carcinoma and differentiate amongst the other histological subtypes of renal cell carcinoma [85]. Disadvantages of MRI include higher costs, the risk of nephrogenic systemic fibrosis with gadolinium administration in patients with renal failure, and decreased patient tolerance due to claustrophobia and anxiety [86].

Computed tomography provides exceptional image quality and is currently the imaging method most widely used in the evaluation of renal masses. A major limitation, however, is the exposure to ionizing radiation and the possible subsequent increased risk of malignancy [87]. In an effort to reduce radiation exposure, Graser and colleagues utilized single-phase dual-energy CT. Radiation dose was reduced by nearly 50% while maintaining diagnostic accuracy of >95% for the evaluation of renal masses [88].

Use of the preoperative imaging modality to be employed during the ablation will allow the surgeon to predict the tumor appearance at the time of ablation. Understanding the advantages and disadvantages of each imaging modality will help guide the clinician in developing a management plan to maximize treatment success while minimizing patient risk.

Intraoperative radiation safety

Percutaneous ablative therapy of renal masses requires image guidance for probe placement and, in the case of cryoablation, active monitoring of treatment effect. As with preoperative imaging, CT, MRI or ultrasound can be employed, each with modality-specific advantages and disadvantages. Currently, CT is the imaging technique most widely used during percutaneous ablative therapy [89]. It provides rapidly acquired images with high resolution and the ability to characterize anatomical relationships. CT without contrast is usually adequate to guide probe placement and treatment. The major disadvantage with CT is patient exposure to ionizing radiation. Although there are currently no published reports comparing radiation exposure between the varying percutaneous ablative therapies, fewer CT scans are typically obtained during radiofrequency ablation (RFA) compared to cryoablation. This is due to the greater number of probes that are typically needed for cryotherapy and the resultant need for increased CT imaging used during probe placement. Additionally, repeated scans are needed for active monitoring of ice ball growth during cryotherapy (Figure 2.3a). In contrast, active image monitoring of RFA is not useful [90] (Figure 2.3b). In a retrospective review, Leng and colleagues reported a mean effective dose of approximately 120 mSv in 42 patients undergoing CT-guided cryoablation of a renal mass [91] (Figure 2.4).

Several techniques can be implemented to minimize radiation exposure when using CT for image guidance during percutaneous ablation. First, the extent of intraoperative CT images should be limited to 1 cm above and below the tumor and imaging should be performed within the same phase of respiration to assure accuracy in slice position. This reduces unnecessary imaging of tissue out of the treatment field. Additionally, while there are

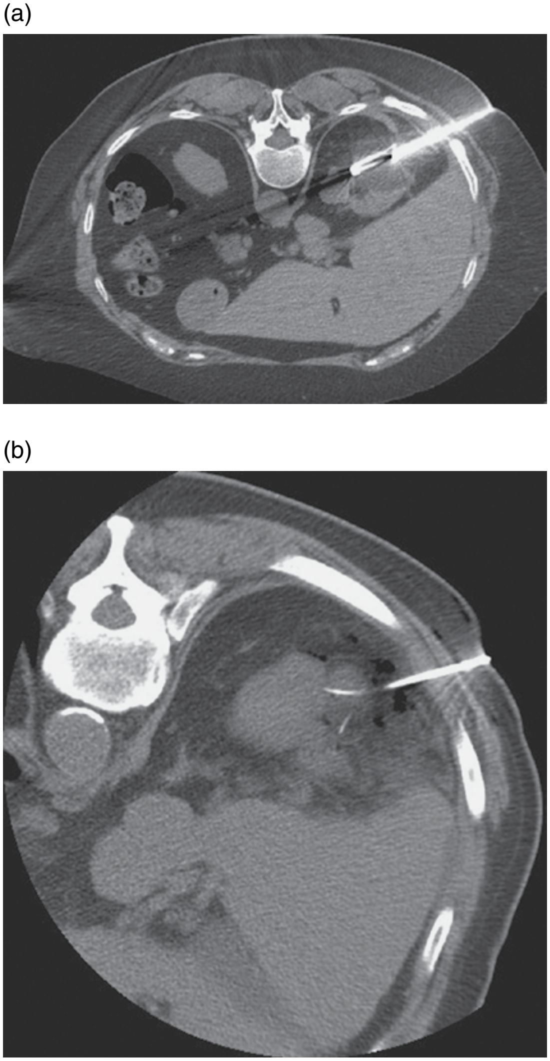

Figure 2.3 (a) Using cryotherapy active monitoring of the iceball with CT ensures adequate treatment of the mass and avoidance of injury to surrounding structures. (b) Using RFA, no benefit is obtained from real-time monitoring of ablation.

no published reports of reduced radiation protocols in patients undergoing CT-guided ablation, image quality with reduced radiation settings may prove adequate for intraoperative monitoring [92]. Leng and colleagues utilized validated noise addition software to simulate reduced radiation dose exposure during acquisition of CT images obtained during monitoring of ice ball progression. They found that >94% of images were adequate for ice ball monitoring at a 50% reduction in radiation dosage [93]. Finally, the operating physician should continually monitor the images acquired, ensuring appropriate slice selection including only essential portions of the anatomy while using the lowest energy possible to obtain adequate images. Implementing these techniques will aid in keeping radiation exposure “as low as reasonably achievable.”

Magnetic resonance imaging is an attractive alternative to CT for intraoperative image-guided percutaneous treatment of renal masses due to the avoidance of ionizing radiation. Silverman and colleagues reported their experience with MR-guided cryoablation of 26 small renal masses in 23 patients. Twenty-three of the 26 tumors were completely treated in a single session at a mean follow-up of 14 months [94]. Active monitoring of the ice ball was accomplished with a rapidly acquired T2 image where the margin is clearly seen as a dark signal void. Image acquisition times ranged from 20 to 60 sec during monitoring of ice ball growth and total procedure time was between 3 and 4 h. In this study, gadolinium-based contrast was injected intravenously prior to ablation for patients who did not yet have a preoperative MRI of the abdomen. Limitations include the need for gadolinium, increased cost and the limited availability of open MR suites equipped to provide anesthesia in close proximity to strong magnetic forces.

Boss and colleagues have evaluated the use of MR-guided RFA using both a 0.2 T and 1.5 T MRI system [95,96]. Utilizing the 0.2 T MRI, 11/12 patients were successfully treated in a single session, with one recurrence found at 13-month follow-up. When using a 1.5 T MRI system, the authors noted improved image quality, faster acquisition time, and the ability to more clearly identify postablative low signal intensity consistent with coagulative necrosis. The mean operative time was approximately 5 h in their initial pilot study using the 0.2 T MRI and ranged from 3 to 4 h in the study using the 1.5 T MRI.

Although ultrasound lacks the anatomical detail of CT and MRI, it is widely available and has been shown to be adequate for image guidance for percutaneous ablative therapies. Bassignani and colleagues reported their experience in three patients who underwent US-guided percutaneous renal cryoablation of four masses [97]. There were no perioperative complications and follow-up imaging 6–7 weeks following cryoablation demonstrated no enhancement in any lesion. Veltri and colleagues

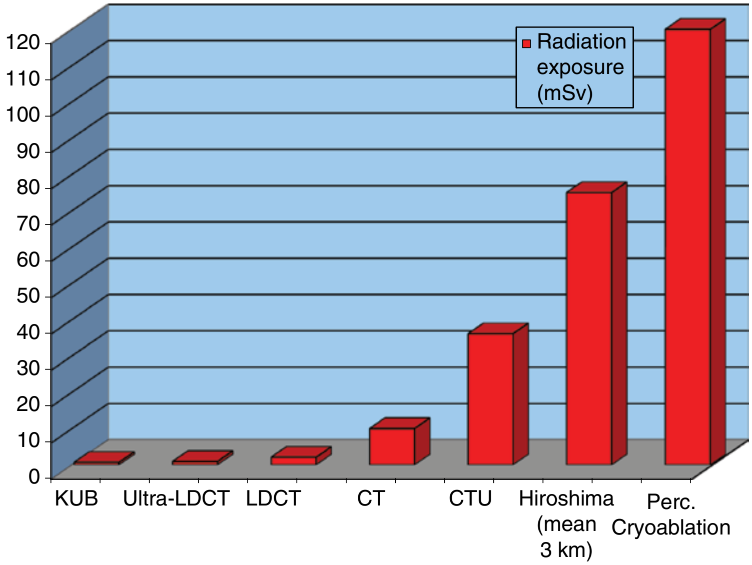

Figure 2.4 Bar graph comparing radiation exposure of several common diagnostic and therapeutic imaging modalities. CT, computed tomography; CTU, computed tomography urogram; KUB, kidney, ureter and bladder; LDCT, low-dose computed tomography.

reviewed 71 US-guided RFA patients and found at a mean 24-month follow-up that there was successful treatment in 89.7% of patients with a major complication rate of 4.6% [98]. However, due to the inferior image quality compared to CT and MRI, ultrasound guidance for percutaneous ablation is typically reserved for small, exophytic, peripheral masses. McGahan and colleagues retrospectively reviewed 56 patients who underwent either ultrasound alone in 27 patients or combined ultrasound and CT in 29 patients undergoing RFA. With appropriate selection, there was no statistically significant difference in complications or treatment success between the two groups [99]. A potential benefit of US-guided percutaneous ablation is reduced operative time due to real-time imaging and the ability to remain at the bedside throughout the procedure. In contrast, CT-guided ablative therapy requires leaving the bedside during image acquisition to avoid radiation exposure to the surgeon.

To date, there are no published reports directly comparing operative times between differing image-guided percutaneous ablative therapies. When ultrasound is utilized during cryoablation of renal masses, the growing ice ball is identified as an echodense interface with dark posterior shadowing. However, some centers have reported inferior accuracy of ice ball monitoring compared to CT and MRI [100].

Deciding which intraoperative imaging modality to utilize is dependent on patient and tumor characteristics, as well as operator expertise and available resources. Hinshaw and colleagues have reported excellent treatment success in 30 patients who underwent percutaneous cryoablation of renal masses using a combination of US and CT image guidance [101]. By combining imaging techniques, it may be possible to optimally capitalize on the advantages of each respective imaging modality and minimize the shortcomings.

Postoperative radiation safety

Currently, there are no widely accepted guidelines for postablative imaging follow-up. It is important to be familiar with the characteristic appearance of renal masses following ablation, as without knowledge of a patient's history, they may be erroneously interpreted as an untreated or an enlarging mass. Following RFA, the ablative zone often appears as a residual mass with a bull's eye (or halo sign) on CT and MRI, even in the absence of residual tumor [102]. Following cryoablation, a peripheral rim of enhancement may persist for months in the absence of residual tumor [103]. Residual or recurrent tumor is typically noted to have a nodular or crescentic enhancement on contrast-enhanced CT or MRI images. In a retrospective review of 172 cryoablative procedures, Tsivian and colleagues found that resolution of postablative contrast enhancement was significantly less when the residual lesion enhanced by >35 Hounsfield units (HU) on CT imaging [104]. Also, lesions that enhance after having previous negative enhancement are not likely to spontaneously resolve [104].

In an effort to reduce patient radiation exposure, low-dose CT scans may be used for monitoring the ablated lesion, although the accuracy of specific radiation reduction protocols has not yet been reported. Alternatively, MRI or US can be used in postablative follow-up of renal masses. As with CT, peripheral enhancement is frequently seen on postablative MRI, yet this is poorly correlated with presence of residual tumor [102]. MRI criteria for recurrence include peripheral rim enhancement, increased lesional size or nodular enhancement [105].

Meloni and colleagues compared contrast-enhanced ultrasound with contrast-enhanced CT and MRI in 27 patients following percutaneous RFA of small renal masses [106]. They found a 96% (27/28) concordance between imaging modalities, with a single progression not identified with ultrasound in a hypovascular lesion. They concluded that, with contrast-enhanced CT and MRI as the reference, contrast-enhanced ultrasound had a sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of 96.6%, 100%, 100%, 95.8%, and 98.1% respectively in the monitoring of postablative renal masses. Currently, contrast enhanced ultrasound is not yet available in the United States.

Technological advances have increased the available options for image-guided percutaneous treatment of small renal masses. Likewise, advances in imaging technology have allowed dramatic improvement in percutaneous therapy. Understanding the advantages and disadvantages of each imaging modality will enable the treating physician to develop a treatment and imaging algorithm that maximizes treatment success and minimizes radiation exposure to the patient and the operating room personnel.

Conclusion

Diagnostic, therapeutic, and follow-up medical imaging plays an integral role in the management of large staghorn calculi, upper tract transitional cell carcinoma, and small renal masses. As procedures become less invasive, the reliance upon medical imaging continues to increase. It is the surgeon's responsibility to become familiar with the unique advantages and disadvantages of each imaging modality. The knowledge of how radiation interacts with the patient and the amounts of radiation associated with each of these imaging studies may allow the surgeon to utilize imaging safely and appropriately in order to assure the optimal patient outcome.

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SECTION 2

Percutaneous Management of Large Renal Calculi (Percutaneous Nephrolithotomy)

3

CHAPTER 3

Epidemiology of Large Renal Stones and Utilization Patterns of Percutaneous Nephrolithotomy

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Introduction

Patients with large or complex renal calculi represent a distinct subpopulation of individuals afflicted with urolithiasis. Stones may become large because of delayed presentation, rapid growth or conducive anatomy. The etiology of branched, or staghorn, calculi was once believed to be almost exclusively infectious [1,2]. However, although infection stones do have rapid growth potential, modern series have established that more than half of staghorn calculi are actually metabolic in nature, a finding that alters our preconceived notions about the etiology and epidemiology of this condition [3–5].

Percutaneous nephrolithotomy (PCNL), first reported in 1976 [6], has largely supplanted open surgery to constitute first-line therapy for large and/or staghorn calculi [7]. Consequently, analysis of PCNL series offers valuable insights into the etiology and epidemiology of large stones, although admittedly PCNL utilization does not precisely mirror the incidence of large renal stones because this modality is additionally used to treat stones of any size that fail shock wave lithotripsy (SWL), lower pole renal calculi and stones in patients with anomalous kidneys. Furthermore, PNCL utilization rates vary regionally and temporally. Factors that influence the decision to perform PCNL can be broadly categorized as “clinical” or “economic.” Clinical factors include stone (stone size, location, and composition) and patient (body habitus, renal anatomy, medical conditions) characteristics that largely comprise the basis for indications for PCNL. However, economic factors also play an important role in treatment decisions when clinical factors are less definitive. This chapter addresses the epidemiology of large renal calculi and analyzes the determinants of PCNL utilization to treat patients harboring these stones.

The large renal stone

Epidemiology

The epidemiology of large renal stones cannot be extrapolated from series of patients with stones in the general population, as these series more accurately reflect patients with smaller stones and those with a metabolic etiology. The population of patients with large stones typically have rapidly growing stones associated with unique stone compositions, live in unique geographic areas and may be more likely to have underlying metabolic or genetic conditions or anatomical anomalies. Unfortunately, there is a paucity of epidemiological data examining presentation patterns of patients with large renal calculi, in part

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

because there are no specific diagnostic codes by which these patients can be identified from national datasets or electronic medical records. Our best estimate is to identify patients from case logs, published series or national datasets using CPT codes for PCNL.

In one of the largest published contemporary PCNL series, Duvdevani and colleagues reported patient characteristics associated with 1585 consecutive PCNL procedures performed over 15 years [4]. Mean patient age was 53.2 years (range 4–89 years) and 67% of patients were men [4]. Lee and colleagues also found a similar mean age (53 years) and slight preponderance of male patients (53%) in their older series of 500 PCNLs [8]. Abnormal upper tract anatomy, particularly when associated with obstruction, appears to be more prevalent in patients treated for large stones. Duvdevani and colleagues reported a 25% incidence of anatomical anomalies in their PCNL series, including calyceal diverticulum (4.9%), ureteropelvic junction obstruction (4.3%), horseshoe kidney (2.6%), ureteral duplication (1.8%), and urinary diversion (1.8%) [4].

On the other hand, in published series restricted exclusively to patients with staghorn calculi, there has been a predilection for women. In two series each analyzing 44 patients with staghorn calculi, women comprised 61% [9] and 52% [10], respectively. Viprakasit and colleagues examined 48 patients with staghorn calculi, among whom 80% were women [3]. In this series, gender differences were further analyzed with regard to stone composition (infection versus metabolic). Interestingly, women accounted for 83% (17 of 21) of infection stones but only 41% (11 of 27) metabolic stones, suggesting that the relatively high prevalence of staghorn calculi in women is due to a higher prevalence of infection stones.

Stone composition: a reflection of etiology

Stone composition provides valuable information because it can provide insight into the etiology and epidemiology of large renal calculi [11]. Although the most common stone compositions are calcium oxalate (60%) and mixed calcium oxalate/hydroxyapatite (20%) [12], large stones are more likely to contain struvite, calcium phosphate, cystine or uric acid [5].

Historically, staghorn calculi were thought to be most commonly composed of struvite [1,7,13], implying an increased risk in the specific patient population susceptible to recurrent urinary tract infections, e.g. those with urinary tract obstruction, chronic indwelling catheters, urinary diversion, and neurogenic voiding dysfunction [1,14]. Recent PCNL series, however, have revealed that more than 50% of contemporary staghorn calculi are metabolic in origin. In the Duvdevani series [4], the prevalence of each stone composition, in decreasing order, was calcium oxalate monohydrate (26.5%), calcium phosphate (14.1%), and uric acid (13.6%). Struvite comprised only 8% of stones and cystine 5.7%. In the subgroup of patients with staghorn calculi, however, struvite was indeed the most common composition (21.5%), although calcium oxalate stones ran a close second (19.2%), followed by uric acid (14.8%), calcium phosphate (11.8%), and cystine (9.2%) [15].

Viprakasit and colleagues reviewed 48 patients undergoing PCNL for 52 staghorn calculi and found that 56% of staghorn calculi had a metabolic etiology, while only 44% were infection related (either struvite or calcium carbonate apatite). In their study, the most common metabolic stone was calcium phosphate (31% of the entire cohort) [3]. In the high-risk population of patients with neurogenic bladders, Matlaga and colleagues found that most large renal calculi were not infectious despite the higher predilection for urinary tract infections in this group of patients. Among 32 patients with either spinal cord injury or meningomyelocele, 37.5% of stones were infection related while 62.5% were metabolic [5] (Table 3.1).

The high prevalence of struvite stones among large calculi is primarily due to their rapid growth (and regrowth) potential. As little as 4–6 weeks may be sufficient time to develop a staghorn calculus that involves the entire renal collecting system [14]. The declining prevalence of struvite in contemporary series may be a function of increased aggressiveness on the part of urologists to achieve a stone-free state [10] and better management and control of recurrent urinary tract infections [5]. However, even in the 1980s, it was recognized that up to 50% of patients with staghorn calculi had a metabolic component [9]. Among infectious staghorn calculi, some cases may result from secondary infection of a metabolic stone nidus [10].

Other stone compositions may also be associated with growth to a large size. Uric acid stones can grow rapidly under conducive conditions of an overly acidic urinary environment [16]. In PCNL series, the prevalence of uric

Table 3.1 Stone composition of large renal stones in recent PCNL series.

	Duvdevani et al. [4]	Soucy et al. [15]	Viprakasit et al. [3]	Matlaga et al. [5]
Time period	1990–2005	1990–2005	2005–2010	2002–2005
No. patients	1338	505	48	32
Inclusion criteria	Consecutive cases	Staghorn stones	Staghorn stones	Patients with neurogenic bladder
Stone composition				
Infection	8% (Struvite)	21.5% (Struvite)	44% (Struvite or calcium carbonate apatite)	37.5% (Struvite or calcium carbonate apatite)
Calcium oxalate	26.5% (COM) 5.2% (COD)	19.2% (Calcium oxalate)	8%	2/32 (COM)
Uric acid	13.6%	14.8%	12%	1/32
Cystine	5.7%	9.2%	6%	–
Calcium phosphate	14.1%	11.8%	16%	8/32 (Brushite, hydroxyapatite)
Mixed metabolic stones	–	23.5%	–	9/32

COD, calcium oxalate dihydrate; COM, calcium oxalate monohydrate.

acid stones varies from 13.6% to 21% [3,4,15]. Cystine stones also have a predisposition to grow to large size under appropriate urinary conditions, but only in patients with a genetically inherited defect in renal tubular reabsorption of dibasic amino acids, leading to excretion of poorly soluble cystine in the urine [13]. Although cystine stones comprise only 1% of all renal calculi, they are overrepresented in PCNL series, comprising 5.7% of all stones in the Duvdevani series [4] and up to 10% of staghorn calculi [3,15]. As an autosomal recessive inherited disease, cystinuria has a distinct epidemiological pattern with no gender predilection [17]. The most common age of stone presentation is between 20 and 30 years [13]. Cystinuria has a wide range of incidence worldwide but is more common in Caucasians. Newborn screening programs, which may overestimate the incidence because of the inclusion of heterozygotes, estimate frequencies ranging from 1:2000 in England to 1:15,000 in the United States [13,18].

Calcium phosphate stones comprise a disproportionately high percentage of large renal stones in modern series [3]. These stones arise under conditions of high urine pH arising from nutritional or hereditary causes [3,19]. However, calcium oxalate stones are also more prevalent among large stones than previously believed, perhaps as a result of the obesity epidemic in the United States [20]. In obese patients, insulin resistance and the metabolic syndrome may play an underlying role in the pathogenesis, predisposing to both uric acid and calcium oxalate stones [21–23].

Characteristics of large renal stones treated with percutaneous nephrolithotomy

Percutaneous nephrolithotomy is the procedure of choice for large and/or complex renal calculi, but the procedure is also used to treat noncomplex stones that fail other forms of treatment. Although not all PCNL series represent treatment of large or complex stones and not all large stones are treated with PCNL, analysis of PCNL series can provide insight into the characteristics of large stones. In one large contemporary PCNL series comprising 1338 consecutive patients at a single tertiary center, complete, partial, and nonstaghorn renal calculi comprised 14.5%, 23.5%, and 62% of cases respectively, and the mean stone burden was 941 mm^2 [4]. In another large series of 500 consecutive PCNLs, only 9.2% of procedures were performed for complete staghorn stones [8]. Duvdevani and colleagues [4] and Lee and coworkers [8] found no predilection for large stones to form on one side or the other. PCNL was performed for stones in the left kidney in 48% and 54% of cases respectively, while bilateral PCNL was performed in 15.9% and 1.6% of cases respectively. Typically, PCNL can be accomplished through a single percutaneous tract. Duvdevani and associates utilized a single tract in 92% of 1338 PCNL cases [4]. In another series, however, 16% of 509 staghorn calculi treated with PCNL required multiple tracts, increasing to 53% among patients with complete staghorn calculi [15]. Up to five percutaneous accesses in a single kidney have been reported for treatment of a complex stone [4].

Table 3.2 Percutaneous nephrolithotomy (PCNL) utilization trends.

	Pearle et al. [24]	Pearle et al. [24]	Kerbl et al. [25]	Morris et al. [26]	Strope et al. [27]	Lee et al. [30]
Dataset	US CMS	US CHCPE dataset	US Medicare data from the HCFA	US Healthcare Cost and Utilization Project	Florida SASD and SID	Australian Medicare
PCNL utilization	*1992–1998: 3–4%	*1994–2000: 5–6%	*1988: 6% *2000: 6.7%	^1988: 1.2 ^2002: 2.5	^1998: 5.5 ^2004: 6.7	*1995: 6% *2010: 3.5%

* Percentage of stone cases.
^ Number of PCNL cases per 100,000 residents.
CHCPE, Center for Health Care Policy and Evaluation (commercially insured individuals); CMS, Centers for Medicare and Medicaid; HCFA, Health Care Financing Administration; SASD, State Ambulatory Surgery Database; SID, State Inpatient Database.

Trends in percutaneous nephrolithotomy utilization

Current utilization patterns (Table 3.2)

Despite widespread utilization of SWL and ureteroscopy (URS) to treat renal and ureteral calculi [24], PCNL remains the most effective treatment for large and/or complex renal calculi. As part of the Urologic Disease in America Project, Pearle and colleagues found that the distribution of surgical procedures for stone disease remained stable between 1992 and 1998 in both the Medicare population and among commercially insured individuals [24]. PCNL consistently comprised 3–4% of stone procedures in Medicare beneficiaries and 5–6% in the commercially insured population compared with SWL and URS, which comprised 51–54% and 40–41% respectively during this time period. Open surgery declined from 4.3% in 1992 to 1.6% in 1998 and has arguable been completely supplanted by less invasive treatment modalities. The absolute number of PCNLs performed in 1998 was 844 per 100,000 procedures. Kerbl and colleagues, in a review of the Health Care Financing Administration dataset, also found that PCNL utilization remained relatively stable at 4–6% of procedures between 1992 and 2000. They did note, however, that over time PCNL has been used more selectively for large renal stones: in 1988 only 36% of cases (745 of 2068) were performed for stones >2 cm in size, while in 2000 stones in this size category accounted for 62% (1661 of 2678) of cases [25].

There is evidence, however, that more recently PCNL utilization has been slowly increasing. According to the Nationwide Inpatient Sample (NIS) dataset, among 12,948 patients undergoing PCNL during the time period 1998–2002, the number of PCNL procedures doubled from 1.2 to 2.5 per 100,000 US residents ($p < 0.0001$) [26]. In contrast, open surgical procedures decreased by 83%, from 1980 cases in 1992 to 332 cases in 1998. Using data from the Florida State Ambulatory Surgery Databases and State Inpatient Database, which are compendiums of datasets collected as part of the Healthcare Cost and Utilization Project (HCUP), Strope and colleagues identified 107,417 patients undergoing stone surgery in Florida between 1998 and 2004 [27]. PCNL accounted for 22% more inpatient procedures in 2004 than in 1998 (6.7 versus 5.5 per 100,000), although the difference did not quite reach statistical significance ($p = 0.07$).

In order to better examine the practice patterns of individual urologists, Bird and colleagues conducted a survey of practicing members of the North Central Section of the American Urological Association (AUA) [28]. With a response rate of 51%, they found that a mean of five and median of two PCNLs are performed per urologist per year. The disparity between the mean and median number of PCNLs performed suggests that a minority of urologists performs the majority of PCNLs. Nevertheless, 73.4% of urologists responded that they felt comfortable performing PCNL, although only 11% of urologists who perform PCNL routinely obtain their own percutaneous access. It is important to keep in mind, however, that responding urologists may be those more likely to perform PCNL and therefore introduce a selection bias.

Utilization patterns vary geographically, by country and region. The European Society of Urological Technology (ESUT) queried 695 certified urologists and urology residents regarding their PCNL practice [29]. The majority of respondents (79.3%) were chief or staff urologists, while the remainder (20.7%) comprised urology residents. Overall, 69.6% of respondents reported performing PCNLs, with a surprising mean of 16.8 PCNL procedures per month, although this group also likely overrepresented urologists and trainees who perform the procedure. Geographic variability was noted among this group, as PCNL was performed more commonly among respondents from Eastern Europe and non-European countries than in those from northern and southern European countries ($p = 0.017$). Using the Australia Medicare dataset, which excludes public healthcare patients, Lee and Bariol evaluated the distribution of stone procedures performed between 1995 and 2010 [30]. Unlike the trend seen in the US, they found a 42% reduction in the proportion of PCNL procedures performed, from 6% in 1995 to 3.5% in 2010. The authors theorized that this trend is due to a downward "stage migration" in stone diagnosis resulting from the widespread use of highly sensitive computed tomography (CT), which is likely to identify stones when they are smaller and therefore amenable to less invasive treatment modalities. However, the proportion of SWL procedures also declined, while ureteroscopy procedures increased substantially, representing 32.6% of procedures in 1994 and 69.7% of procedures in 2000.

Factors affecting percutaneous nephrolithotomy utilization

A variety of clinical and socioeconomic factors influence the decision of whether or not to perform surgery and which procedure to perform for renal calculi. Although one might expect that PCNL utilization would reflect the prevalence of patients with stones meeting the accepted surgical indications for PCNL, i.e. patients with large stones and/or complex renal anatomy or distal obstruction, actual utilization patterns often reflect other factors, such as physician training and experience, patient socioeconomic status, and regional economic pressures. Purely clinical determinants of utilization, such as stone size and anatomy, are addressed in other chapters.

Physician factors

Generation of training

Recently trained urologists have been shown to be more likely to perform PCNL than older urologists. Matlaga utilized case logs obtained from the American Board of Urology for urologists undergoing certification (2004–2008) or recertification (2003–2007) to evaluate trends in the distribution of surgical stone procedures [31]. Based on a sample of nearly 3000 urologists, Matlaga determined that 6.8% of recently trained urologists (those undergoing initial certification) performed PCNL compared to only 4.5% and 2.6% of urologists undergoing their first and second recertification, respectively. He concluded that younger urologists have a different treatment paradigm for the management of large renal calculi than their older counterparts and likely have more experience with PCNL based on their recent completion of residency training. For the same reason, ureteroscopy was the most common procedure performed by the initial certification cohort (52%) while SWL was the most commonly performed procedure in the second recertification group (60.5%). A survey of members of the Minnesota Urological Society likewise found that patients with staghorn and lower pole renal calculi were more likely to be treated by PCNL or URS rather than by SWL [32].

Physician training

While recent training in PCNL tends to increase PCNL utilization, remote training engenders higher utilization than no training. In a survey of members of the North Central Section of the AUA, urologists who admitted they were not comfortable performing PCNL commonly cited inadequate training as the reason (39%). The inability to obtain percutaneous access did not preclude performing PCNL, as the majority of urologists reported using interventional radiologists to obtain access prior to PCNL [28]. In another survey of urologists who graduated between 1981 and 2001 ($n = 48$, response rate 77%), Lee and colleagues found that only 27% of urologists trained in percutaneous access continued to perform it compared to 11% of those not trained who currently perform PCNL ($p = 0.33$). Commonly stated reasons for not performing the access were that radiologists had better equipment (61%) or better skills (44%), or that it required extra time (50%) [33].

Not surprisingly, obtaining appropriate percutaneous renal access is considered the most difficult step in PCNL, rendering access the greatest technical barrier to utilization. In one study evaluating the learning curve for PCNL, "competence" was determined to be achieved after 60 cases, while "excellence" required over 100 cases [34]. Another study likewise found that mean operating time for a novice surgeon plateaued at 92 min after 60 cases. Fluoroscopy time and radiation dose, however, did not plateau until 115 cases, a milestone that the authors felt reflected reaching "excellence." These volumes may only be attainable by trainees at large academic centers [34]. Finally, in a study of 103 patients undergoing PCNL with either interventional radiologist-obtained access or urologist-obtained access, more complications (28% versus 8% respectively, $p = 0.02$) and a lower stone-free rate (61% versus 86% respectively, $p = 0.01$) were recorded with radiologist-obtained access compared with urologist-obtained access [35], providing further support for urologist training in percutaneous renal access.

Practice setting: academic versus private

The treatment of large stones by PCNL is more likely to occur at academic medical centers than in the community. Between 1998 and 2001, PCNL comprised 30% of all surgical stone procedures at Wake Forest University, a far greater proportion than was identified in national datasets by the Urologic Diseases in America Project [24,36]. This finding was further corroborated by findings from the Nationwide Inpatient Sample dataset evaluating 12,948 patients undergoing PCNL which revealed that the vast majority of PCNLs (94%) were performed at urban hospitals, which often represent teaching hospitals [26]. Indeed, this study demonstrated that over the past 10 years there has been a migration of PCNL cases into teaching centers; the proportion of PCNL procedures performed at teaching hospitals increased from 50% during 1988–1990 to 63% during 2000–2002.

Patient factors

The decision to perform PCNL in patients with large renal stones may also be affected by patient age, gender, socioeconomic status, patient preference, and geographical location.

Age and gender

Although historically kidney stones have more commonly afflicted men than women [37], the gender gap is closing [24, 38]. PCNL also shows a gender predilection for men over women, but the ratio is less pronounced. In a series of 1338 patients undergoing PCNL, the ratio of treatment of men to women was 1.29 to 1 (893 men and 692 women) [26]. Using the NIS dataset, among 12,948 patients undergoing PCNL between 1988 and 2002, gender differential was negligible, with women comprising 49.7% of PCNL recipients. The unexpected similarity in utilization among genders may provide further evidence that renal stone disease is increasing in women [27], or it may simply reflect disparity in the gender distribution of large and complex stones.

Large renal calculi have been observed in patients of all ages. In one large series, patients from 4 to 89 years old were treated with PCNL, although the mean age was 53.2 years. In the NIS, the majority of patients undergoing PCNL were between 39 and 67 years of age (54.4%), although 24% of PCNLs were performed in patients aged 67 years and older [26]. A recent retrospective review indicates that older age does not preclude PCNL utilization [39]. McCarthy and colleagues compared 102 patients <80 years and 26 patients ≥80 years who were treated for large renal calculi and found that PCNL was performed in 23% of patients ≥80 years but in only 9% of patients <80 years. The younger patients were most commonly treated with SWL, which was rarely used in the older group (35% versus 8%, $p < 0.01$). However, in this retrospective review, the reasons for intervening surgically for patients with stones were not assessed, and the disparity in PCNL utilization may reflect a reluctance to treat older patients with stones unless the stones are particularly large, which would favor PCNL utilization in this group.

Socioeconomic status

There is a paucity of data regarding the influence of socioeconomic status on PCNL utilization. Among the 12,948 patients undergoing PCNL between 2000 and 2002 from the NIS, 54% of patients treated had private insurance, 27% had Medicare, and 19% were identified as having "other" funding [26]. It is unknown whether race or cultural backgrounds affected utilization. The majority of patients in this dataset were white (57.3%), while 6.3% were black and 6.8% were Hispanic (data were missing in 24.6%).

Geographic location

Typical metabolic stones occur more commonly in hot, arid climates [37]. However, geographic variability is evident not only in the prevalence of stone disease but also in the practice patterns of stone treatment. A survey of urologists in Europe revealed significant differences in PCNL utilization according to region, with PCLN less commonly performed in western and northern Europe compared with southern European locations [29].

Percutaneous nephrolithotomy utilization also varies over time as regional practice patterns evolve. Morris and colleagues analyzed changes in PCNL utilization between the time periods 1988–1990 and 2000–2002 in the four geographic regions of the US (Midwest, South, Northeast, and West) [26]. They identified an increase in the proportion of total PCNLs performed nationally in the Midwest (from 14.7% to 25.5%) and South (from 34.1% to 39.8%), as well as an increase in the total number of PCNLs performed nationwide. During 2000–2002, the Northeast and West accounted for only 19.2% and 15.5% of PCNLs, respectively, performed nationally. The authors contend that community acceptance and the spread of technology might have occurred more readily in the Midwest and South and could have contributed to these trends.

Economic factors

The economic burden of treating large stones can only be roughly estimated by the cost of PCNL. Unfortunately, cost studies typically compare the cost of different treatment modalities rather than specifically evaluating the cost of treating different-sized stones.

In a retrospective, nonrandomized study comparing PCNL and URS for the treatment of 39 patients with large (2–3 cm) calculi, costs were estimated using local Medicare reimbursement rates and the need for secondary procedures with each treatment modality [40]. By this analysis, the estimated cost of PCNL was significantly greater than URS ($19,845 versus $6675, $p < 0.0001$) because patients treated with PCNL were more likely than those treated with URS to undergo secondary procedures (1.6 procedures versus 1.1 procedures, $p = 0.003$), despite a significantly higher stone-free rate in the PCNL group (89% versus 47% respectively, $p = 0.01$). Due to the biased retrospective study design, it is likely that patients undergoing PCNL were treated with the intention of obtaining stone-free status and thus had higher costs associated with secondary procedures to reach this goal. As such, the relative cost burdens of URS and PCNL for the treatment of large renal stones remain unclear.

Economic considerations will undoubtedly influence the utilization of PCNL into the future. The cost of retreatment significantly affects cost-effectiveness, which in turn is affected by individual practitioner success rates and the degree of tolerance for residual stones. We predict that the larger the stone, the greater the likelihood that PCNL is the most cost-effective option.

Conclusion

Large epidemiological studies examining the prevalence and characteristics of patients with large renal calculi are needed to further define this unique subpopulation of stone-forming patients. Although infection stones have traditionally been thought to comprise the majority of staghorn calculi, metabolic stones account for a high proportion of patients with large stones. However, it remains unclear why some calcium-based stones grow to large size, while others do not. Because large and/or complex stones are often best treated with PCNL, PCNL series provide the best insight into the epidemiology of large stones, although there are numerous external factors that influence utilization patterns and confound these extrapolations.

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4

CHAPTER 4

Evolution of Evidence-Based Outcomes for Percutaneous Nephrolithotomy

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Introduction

Since the first report of stone extraction through a nephrostomy tract in 1976 [1], percutaneous nephrolithotomy (PCNL) has become the preferred treatment for large or staghorn renal calculi [2]. PCNL is a common procedure, now performed worldwide. The Clinical Research Office of the Endourological Society (CROES) PCNL Global Study reported the results of 5803 PCNLs performed in a 1-year period, at 96 centers in five continents [3], and subanalyses will be highlighted throughout this chapter. This chapter will review and evaluate the evidence supporting various PCNL practices using the Oxford Centre for Evidence-Based Medicine Levels of Evidence (Table 4.1). Table 4.2 summarizes the evidence discussed throughout the chapter.

Choice of treatment

Urologists and stone patients have a variety of treatment options, ranging from observation to shock wave lithotripsy (SWL) to ureteroscopy (URS) to PCNL to laparoscopic or robot-assisted lithotomy to, rarely, open surgery. There are a number of situations where PCNL provides the optimal balance of excellent outcomes and stone-free rates (SFR) with minimal morbidity.

Stone burden

Large stone burden, measured by cumulative stone area, estimated stone volume or by other means, is the primary reason for choosing PCNL over other treatment modalities. In a large subanalysis of the CROES PCNL Global Study, PCNL outcomes for large nonstaghorn renal calculi varied with stone size [4]. An increase in stone size was associated with higher rates of fever and blood transfusion and lower SFR, as determined by the local imaging protocol. A smaller case series of 238 patients supported the association of increased stone surface area with lower SFR, rates of complications and secondary procedures, longer mean operative times, and the need for multiple tracts [5].

Despite these concerns, the advantage of PCNL over URS and SWL is more pronounced with larger stone burdens. Bryniarski et al. randomized 64 patients with renal pelvic stones >2 cm to PCNL or semi-rigid URS with laser [6]. The SFRs after a single treatment were superior post-PCNL (93.75 versus 75%, $p = 0.03$), with similar transfusion rates, though the mean hemoglobin drop was larger post-PCNL [6]. Two retrospective studies compared PCNL to URS for renal stones, one for intermediate-sized (1–2 cm) [7] and one for large (2–4 cm) stones [8]. A third study compared PCNL, URS, and SWL for intermediate-sized stones (100–300 mm^2) [9]. For intermediate-sized

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

Table 4.1 Summary of the Oxford Centre for Evidence-Based Medicine's levels of evidence, for studies addressing therapy/prevention or etiology/harm.

Level of evidence	Study description
1a	1a systematic review (SR) (with homogeneity) of randomized controlled trials (RCTs) ("-" if study has worrisome heterogeneity)
1b	Individual RCT (with narrow confidence interval)
1c	All or none study, where all patients died before the treatment became available, but some now survive on it; or when some patients died before the treatment became available, but none now die on it
2a	SR (with homogeneity) of cohort studies
2b	Individual cohort study (including low-quality RCT, e.g. <80% follow-up)
2c	"Outcomes" research; ecological studies
3a	SR (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case series (and poor-quality cohort and case-control studies)
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

stones, the success rates favored PCNL (95.3% for PCNL versus 87.8% for URS versus 60.4% for SWL, $p<0.001$) [9] but equalized amongst the three modalities when a second SWL was considered [9], with similar complication rates. For larger stones, superior SFRs and similar complication rates were encountered after single treatments with PCNL and URS, in a case–control retrospective analysis [8].

Stone configuration: staghorn versus nonstaghorn

Staghorn calculi are commonly treated by PCNL. One difficulty with assessing the literature is the variability in the definitions of complete and partial staghorn stones. Desai et al. compared the outcomes in the CROES PCNL Global Study for staghorn versus nonstaghorn calculi [10]. Patients with staghorn calculi (27.5%) required higher rates of multiple tracts (16.9% versus 5.0%, $p=0.0001$), though most tracts were lower calyceal in both groups. Staghorn patients experienced higher rates of transfusion, perforation and fever, though the preoperative urine culture was more commonly positive in the staghorn group. The SFR was lower for staghorns (56.9% versus 82.5%, $p=0.0001$), and the operative duration and hospital stay were longer.

There are numerous case series of PCNL for staghorn calculi, with the largest consisting of 509 patients [11]. One study randomized patients to staged or simultaneous PCNL for bilateral staghorn calculi ($n=99$) [12]. All tracts were infracostal and all procedures were tubeless, with a stent. Compared to staged procedures separated by 4 weeks, simultaneous PCNL was associated with comparable rates of bleeding and complications, but superior pain scores, analgesic use, operative time, and length of stay [12]. In a large ($n=413$) but nonrandomized, study, multitract PCNL for staghorn calculi was associated with a higher SFR and higher transfusion rate than single tract [13].

While staghorn calculi increase the complexity and morbidity of PCNL, other endourological treatments have inferior outcomes and SFRs, particularly for struvite stones. SWL monotherapy for staghorns has been described, most recently by Heretis et al. [14]. Though 69% of the 16 patients with staghorn stones treated on the Doli S EMSE 220 F-XP electromagnetic lithotriptor became stone free, all patients underwent stenting, two developed pyelonephritis, two required URS for steinstrasse, and up to six SWL sessions each were required [14]. The 2004 American Urological Association (AUA) guidelines for the treatment of staghorn calculi recommended that PCNL be the first treatment utilized for most patients and that if combination therapy with SWL is undertaken, PCNL should be the last modality [15]. SWL monotherapy is not recommended in most patients but should be considered an option for small-volume staghorn calculi in patients with normal collecting system anatomy [15]. However, only four treatment modalities were considered (PCNL, combination PCNL and SWL, SWL monotherapy, and open surgery), but not URS. Recent series of URS for staghorn calculi [16,17] showed inferior single-treatment SFRs, and staged and multiple treatments were common. The mean number of treatments was higher in the staghorn group (2.2 for partial and 3.45 for complete) than URS for single renal calculi (1.6) [16]. PCNL remains the gold standard for the treatment of staghorn calculi.

Stone location

The lower pole is the most common calyceal site for stones treated by PCNL [4], with excellent outcomes. The Lower Pole I randomized trial was the first to demonstrate the superiority of PCNL to SWL for all lower pole stones, particularly for those >10 mm in size [18]. One case series [19] showed excellent SFRs of at least 95% in 144 patients with lower pole stone(s) that had already failed SWL.

A Cochrane Database systematic review compared SWL versus PCNL or URS for renal stones [20]. Three small randomized controlled trials (RCTs) involving 214 patients were included, though the results could not be pooled. Two RCTs compared PCNL to SWL and one compared SWL to URS. Two of the three RCTs addressed lower pole stones, including Lower Pole I [18]. The authors concluded that, based on only a few studies of low methodological quality, SWL is less effective for lower pole kidney stones than PCNL but not significantly different from URS. Hospital stay and treatment duration were shorter with SWL. More recently, a retrospective, nonrandomized study compared URS to PCNL for lower pole stones measuring 15–20 mm [21]. Of the 79 patients, the single-treatment SFR was similar with PCNL and URS and the transfusion rate was higher after PCNL (7.1% versus 0%) [21]. However, more RCTs are required to investigate the relative effectiveness and complications of SWL, PCNL, and URS for renal stones, particularly in the lower pole.

Stone composition and density

A search failed to reveal studies examining the effects of stone composition on PCNL outcome. However, stone density, measured in Hounsfield units (HU) on unenhanced computed tomography (CT), was predictive of PCNL outcomes [25]. Logistic regression analysis of 179 PCNL treatments found that stone size, radiopacity, and HU value were predictors of PCNL success. Stone density less than 677.5 HU increased the likelihood of treatment failure by 2.65 times, whereas staghorn composition increased the likelihood by 5.68. Examining how stone density or composition affects PCNL outcomes warrants further evaluation.

Patient factors: Body Mass Index

Multiple studies have evaluated how obesity affects PCNL outcomes, by retrospectively stratifying patients by Body Mass Index (BMI). Tomaszewski et al. demonstrated that the length of hospital stay and stone-free, complication and hemorrhage rates were independent of BMI [22]. Similar results were found in studies by Bagrodia et al. [23] and Koo et al. [24]. The direct costs were no different in the obese group in an American study [23] and one study found no relationship between BMI and the operative duration or analgesic use [24].

The higher complication rates seen in obese patients undergoing abdominal, cardiothoracic, and orthopedic surgery [23] have not been demonstrated post PCNL by these retrospective studies. However, obesity may affect the positioning used, which was not addressed in these three studies. URS may play a role in the super-obese and morbidly obese, in whom prone or lateral positioning can be challenging.

Special cases

The safety and efficacy of PCNL have been demonstrated in a number of special stone cases, including pediatric patients, anomalous kidneys, solitary kidneys and following open stone surgery (OSS). A full discussion of these circumstances is beyond the scope of this chapter, but Table 4.2 summarizes the levels of evidence available.

Surgical planning

Many of the techniques discussed in this section are described in a step-by-step fashion in Chapter 6.

Antibiotics

There have been few studies that define the risk of infection following PCNL [26], with no clear-cut evidence. The European Association of Urology (EAU) Guidelines on Urological Infections cites Level 2b evidence supporting the consideration of factors such as stone size, location, length of procedure, bleeding, and surgeon experience when choosing an antibiotic regimen. These guidelines recommend antibiotic prophylaxis for all patients, for a short course, with intravenous antibiotics suggested at the time of operation [26]. Recommended

Table 4.2 Summary of levels of evidence for PCNL outcomes.

Setting	Variable	Best level of evidence	Study	Study design	Findings/comments
Stone Burden	**Stone size**	2b	Xue et al. 2012 [4]	CROES PCNL global study	Larger stone size associated with decreased SFR and increased complications, including transfusions and fever
Choice of PCNL	**PCNL vs. semirigid URS**	2b	Bryniarski et al. 2012 [6]	RCT: PCNL vs semi-rigid URS for renal pelvic stones >2 cm	Better SFR with PCNL, with similar transfusions rates but greater hemoglobin drop
	PCNL vs. flexible URS	3b	Chung et al. 2008 [7] Akman et al. 2011 [8]	Retrospective comparison of outcomes for intermediate and large stones; matched-pair analysis for large stones	Better SFR with PCNL, but studies were small
	PCNL vs. flexible URS vs. SWL	2b	Wiesenthal et al. 2011 [9]	Retrospective comparision for intermediate-sized stones	Allowing for a second SWL treatment, the success rates of the 3 treatments were comparable
Stone configuration	**Staghorn vs. non-staghorn**	2b	Desai et al. 2011 [10]	CROES PCNL global study	Higher rates of multiple tracts, complications, operative time and length of stay, and lower SFR in staghorn patients
	Staged vs. simultaneous PCNL for bilateral staghorns	2b	Wang et al. 2011 [12]	Patients randomized to staged or simultaneous PCNLs for bilateral staghorns	Simultaneous: comparable rates of bleeding and complications, with better pain scores, analgesic use, operative time and length of stay
Stone Location	**Lower pole stones**	1a -	Srisubat et al. 2009 [20]	Cochrane review comparing SWL, PCNL and URS for renal stones. 2 of 3 RCTs were exclusively for lower pole stones	SWL less effective than PCNL for lower pole stones, but not significantly different from URS
Patient Factors	**BMI**	2b	Tomaszewski et al. 2010 [22] Bagrodia et al. 2008 [23] Koo et al. 2004 [24]	Retrospective, with patients stratified into BMI groups	Complication and efficacy rates of PCNL were independent of BMI
Stone Composition	**Stone density**	2b	Gucuk et al. 2012 [25]	Retrospective, with logistic regression analysis of factors associated with PCNL failure	Stone density of <677.5 Hounsfield units increased the likelihood of treatment failure by 2.65 times
Pediatrics	**Younger vs. older children**	2b	Dogan et al. 2011 [61]	Retrospective: outcomes in younger (<5 years) vs older (>5 years) children	With same tract sizes, younger group had smaller stone burdens and fewer tracts required. The SFR was higher in the younger group, and complication rates were similar

	Adult-sized sheaths in children	4	Nouralizadeh et al. 2009 [62]	Retrospective series: single 26 F sheath in children <5	Acceptable complication rate (15%) and SFR (79%)
	Renal morphology and function post-PCNL	2b	Wadhwa et al. 2007 [63]	Prospective nonrandomized study of PCNL vs SWL in patients <13 years, with US, nuclear renograms, glomerular filtration rate at baseline, 3 and 6 months	None developed new renal scars, hypertension, proteinuria or alteration in renal size at 3 and 6 months
Anomalous Kidneys	**Anomalous vs. normal kidneys**	2b	Osther et al. 2011 [64]	CROES PCNL global study	3.6% of PCNLs were in anomalous kidneys: horseshoe > malrotated > ectopic. Prone and upper pole (supracostal) punctures were more common in the anomalous group. Complication and stone-free rates similar to PCNL in normal kidneys
	Totally tubeless in anomalous kidneys	2b	Aghamir et al. 2008 [65]	RCT: TT vs standard (nephrostomy and ureteral stent) in anomalous kidneys	Similar types of anomalies in each group. TT associated with improved pain, shorter length of stay and quicker convaslescence
Solitary Kidneys	**Solitary vs. non-solitary**	2b	Bucuras et al. 2011 [66]	CROES PCNL global study	Solitary group had higher cardiovascular risk and ASA scores. Higher rates of transfusion and renal dysfunction in solitary group. Complication and stone-free rates were less favorable in the solitary group
	Solitary with longer follow-up	4	Akman et al. 2011 [67]	Case series	With mean follow-up of 18.7 months (6-60 months) renal function stabilized or improved in 90%
Previous Open Stone Surgery (OSS)	**OSS vs. no OSS**	2b	Gupta et al. 2011 [68] Falahatkar et al. 2009 [69]	Retrospective: previous ipsilateral OSS vs no OSS	Previous surgery associated with comparable mean operative times and rates of transfusion, complication and success. OSS may be associated with a greater number of attempts at access, and a slightly longer time
	Totally tubeless in patients with previous OSS	2b	Lojanapiwat et al. 2010 [70]	Retrospective: TT vs standard PCNL (with nephrostomy) in patients with previous OSS	TT tubeless equally safe and effective in patients with previous OSS
Antibiotics	**Immediately preoperatively**	2b to 3	EAU Guidelines [26] AUA's Best Practice Policy Statement [27]	Level 2b or 3 studies cited	"Short course" antimicrobial prophylaxis for all patients prior to PCNL, with IV administration immediately preoperatively
	Prolonged preoperative course	2b	Mariappan et al. 2006 [29]	Prospective cohort with 7 day-course of oral ciprofloxacin pre-PCNL vs historical control without. All patients received IV gentamicin (5 mg/kg) preoperatively	For patients with dilated pelvicalyceal systems and/or stones >/= 20 mm, 7 days of cipro (250 mg po bid) decreased urosepsis risk

(*continued*)

Table 4.2 (*continued*)

Setting	Variable	Best level of evidence	Study	Study design	Findings/comments
Patient Positioning	**Prone vs. supine**	1a	Liu et al. 2010 [30] Wu et al. 2011 [31]	Meta-analyses. Each included the same 2 RCTs and 2 case-control studies, and Wu meta-analysis included 27 case series	No differences in SFR, complications, or failed access. Case series portion showed slightly lower transfusion rate in the supine group, though there were fewer complex stones in this group. Operative time shorter for supine
	Prone vs. supine	2b	Valdivia et al. 2011 [32]	CROES PCNL global study	Prone: shorter operative time (in contrast to the metaanalyses), greater rates of upper pole and multiple access, higher SFR, no differences in transfusions (when comparing sites performing one position only)
Technique for Access	**Fluoroscopic: bull's-eye vs. triangulation**	2b	Tepeler et al. 2012 [33]	RCT: bull's-eye vs triangulation in prone PCNL	Similar outcomes, complications and fluoroscopic and access times
	Ultrasonic vs. fluoroscopic	2b	Basiri et al. 2008 [34] Karami et al. 2010 [35]	"Pseudo-randomized" studies: ultrasonic vs fluoroscopic access attained by radiologist	Ultrasonic access took longer but used less fluoroscopic time. Similar complication and success rates. Fluoroscopic techniques not described
	Urologist vs. radiologist	2b	Watterson et al. 2006 [36]	Retrospective: patients treated by one surgeon with urologist-achieved access vs PCNLs by separate surgeon with access obtained exclusively by radiologist	PCNLs with access obtained by a urologist had higher SFRs and lower rates of access-related complications. In one series, only 1/3 of accesses were used for PCNL
Tract Development	**Number of tracts**	2b	Hegarty et al. 2006 [39]	Case-control study, with patients with multiple tracts matched to patients with single tracts. Patients with multiple tracts had higher stone burdens	Single-tract PCNL had lower transfusion rate (though higher preoperative hemoglobin) and similar complication rate. For patients with large stone burdens, PCNL monotherapy with multiple tracts is safe and effective treatment
	Single smaller vs. larger tract	2b	Cheng et al. 2010 [41]	RCT of 16 F vs 24 F tracts	Lower transfusion rates and longer operative times with small tracts. In the smaller tract group, SFRs were similar, except in patients with multiple calyceal stones who had lower SFRs
	Multiple small tracts vs. single large	2b	Zhong et al. 2010 [42]	RCT of patients with staghorn stones randomized to either multiple mini-tracts (16 F) or standard tracts (26 F) (only 12% were multiple)	Longer operative time and higher rates of stone clearance with multiple, smaller tracts. Similar rates of complications, including transfusions

	Method of tract dilation	2b	Yamaguchi et al. 2011 [44]	CROES PCNL global study: balloon vs metal telescopic and serial Amplatz dilators combined	Method of tract dilation not associated with rates of bleeding or transfusion on multivariate analysis
	Gradual vs. one-step tract dilation	1b	Aminsharifi et al. 2011 [46]	Randomized to gradual (Alken dilators) or one-step (Amplatz), up to 28 F	Though one-step dilation was quicker and required less fluoroscopic time, it may be more traumatic. On 4-week DMSA scans, the overall renal uptake was lower with one-step dilation, and there were more new scars in this group
Lithotripsy	**Modality**	1b	Chew et al. 2011 [47] Lehman et al. 2008 [48]	Randomized studies comparing 2 pneumatic lithotripters (Stonebreaker and Lithoclast) and the lithoclast alone or combined with ultrasound	Lithotripsy modalities appear to be similar with respect to SFR and complications but may differ in terms of efficiency and cost
Postoperative Drainage	**Tubeless vs. total tubeless vs. standard**	1a	Amer et al. 2012 [51] Yuan et al. 2011 [53] Ni et al. 2011 [54]	SR (Amer): 11 RCTs and 13 nonrandomized comparative studies with level of evidence of 1b to 2b 2 metaanalyses of RCTs (Yuan and Ni)	Pain, length of stay, and convalescence better with tubeless. SFR and morbidity rates were comparable. No increase in intrathoracic complications in supracostal access. TT similar to tubeless in select patients
Tract Closure	**Comparison of methods**	2b	Aghamir et al. 2006 [55] Singh et al. 2008 [56] Li et al. 2011 [57]	Small RCTs including various methods: deep fascial stitch, FloSeal, Spongostan, Surgicel	In RCTs with a no closure group, closure was not beneficial for bleeding. Spongostan had lower rates of urinoma and Surgicel did not. Small study sizes, no sample size calculations. Unclear if closure needed

BMI, Body Mass Index; IV, intravenous; PCNL, percutaneous nephrolithotomy; RCT, randomized controlled trial; SFR, stone-free rate; SWL, shock wave lithotripsy; TT, totally tubeless; URS, ureteroscopy; US, ultrasound.

agents include trimethoprim ± sulfamethoxazole, a cephalosporin (second or third generation), aminopenicillim/betalactamase inhibitor, or fluoroquinolone. The AUA's Best Practice Policy Statement on Urologic Surgery Antimicrobial Practice cites Level 2b and 3 evidence to recommend prophylaxis for all patients, for up to 24 h [27]. Antimicrobials of choice include cephalosporins or an aminoglycoside with either metronidazole or clindamycin [27].

In selected patients, extended courses of prophylactic antibiotics may be beneficial. Mariappan et al. demonstrated that renal pelvic urine culture and sensitivity (C&S) was a better predictor of potential urosepsis after PCNL than midstream urine C&S [28]. Patients with either infected renal pelvic urine (predicted by pelvicaliectasis) or an infected stone (predicted by stone(s) ≥20 mm) had a four times greater risk of urosepsis. These findings prompted a prospective trial examining the impact of 1 week of ciprofloxacin on upper tract infection and urosepsis post PCNL [29]. Fifty-two patients at risk for infected stones or pelvic urine received 1 week of ciprofloxacin before PCNL, regardless of the midstream urine C&S. Outcomes were compared to 46 historical control patients. All patients received intravenous (IV) gentamicin preoperatively. One week of ciprofloxacin decreased the relative risk of upper tract infection and urosepsis by 2.9 (95% confidence interval [CI] 1.3–6.3, $p = 0.004$). Though this approach is not currently discussed in any guidelines, further study with a multicentered RCT is warranted.

Patient positioning

The optimal patient position for PCNL has been widely debated, and there are increasing reports of novel positions with purported strengths and weaknesses. The conventional prone position will be described later in this text, as well as the supine, lateral and prone-flexed positions.

Liu et al. published the first prone versus supine metaanalysis [30], consisting of two RCTs and two case–control studies. Three of the four studies were assessed as high quality. SFR was comparable between the groups: 83.5% supine versus 81.6% prone (95% CI 0.68–1.98, $p = 0.59$). Operative time was shorter supine (mean difference = −24.84 min, 95% CI −34.45 to −15.23, $p < 0.00001$), with no differences in the transfusion, fever, and complications rates. Wu et al. later published another metaanalysis [31] that added 27 case series, including 1469 supine and 4837 prone renal units, to the Liu et al. metaanalysis. From the case series, the supine position was associated with a similar SFR (84.9% versus 83.5%, $p = 0.271$) and slightly lower transfusion rate (2.7% versus 4.5%, $p = 0.002$) than prone, though there were more staghorn and multiple calculi in the prone group (45.8% versus 31.7%).

In the CROES PCNL Global Study, 80.3% PCNLs were performed prone [32]. Numerous baseline differences between the groups included fewer males, older patients, higher rates of previous SWL, and higher American Society of Anesthesiologists (ASA) scores in the supine group, though stone burden and rates of staghorn stones were similar. Contrary to the metaanalyses, operative time was shorter prone (82.7 versus 90.1 min, $p < 0.0001$), regardless of the method of tract dilation. When supine, upper pole access was less common (4.0% versus 11.4%), with higher rates of lower pole (74.8% versus 63.8%) and multiple (4.1% versus 9.0%) accesses. SFR was significantly lower in the supine position (70.2% versus 77.0%, $p < 0.0001$), while the rates of several complications were also lower (transfusion, fever, and failed procedures). In a subanalysis comparing centers performing only supine ($n = 538$) or prone ($n = 1675$) procedures, the supine group was still found to have a lower SFR and longer operative time, but similar rates of blood transfusion.

Though the CROES study provides the largest comparison, global practices and reporting are heterogeneous and the lack of randomization allows selection bias. The metaanalyses show similar stone-free and complication rates in supine and prone procedures. However, larger RCTs would be required to detect differences in more rare complications. It remains unclear which position is associated with a shorter operative duration.

Access technique

Renal access can be attained through a variety of techniques, by either a urologist or radiologist. Three RCTs compare access techniques. Tepeler et al. randomized 80 patients undergoing prone PCNL to either triangulation or bull's-eye fluoroscopic access, and found similar fluoroscopy and operative times [33]. In a "pseudo-randomized" study involving 100 patients, fluoroscopic (technique not described) and ultrasound (US) accesses (18 gauge Chiba needle in a 3.5 MHz probe with a needle holder) were compared [34]. Once the wire was in the chosen calyx, the remainder of the procedure was carried out fluoroscopically. The ultrasonic group had similar rates of successful access to the targeted calyx. Though the access time was longer for the ultrasonic group (11 versus 5.5 min, $p = 0.0001$), the duration of radiographic exposure, as expected, was shorter (0.69 versus 0.95 min, $p = 0.0001$). Another "pseudo-randomized" trial, involving 60 patients, compared purely ultrasonic access in the flank position and fluoroscopic access (techniques not described) in the prone position [35]. Renal access was successfully attained in all patients but mean access and operative times were longer in the ultrasound group. In all three studies comparing access techniques, the success and complication rates were similar between the groups [33–35].

In these three studies, access was obtained by a urologist. However, Watterson et al. showed a higher complication rate when access was obtained by an interventional radiologist [36]. Consecutive prone PCNLs were retrospectively compared: 54 patients were treated by a single urologist after access was obtained by an interventional radiologist, and 49 patients were treated by a second single urologist who gained access himself. Despite larger stones and a higher rate of multiple tracts, the urologist access group had superior SFR and rates of access-related complications. Aslam et al. retrospectively compared 134 PCNLs, in which access was performed in 23% by an interventional radiologist [37]. The rates of failed access were low, at 5.8% in the urologist group and 0% in the radiologist group (no p-value). However, the rates of access-related complications were not compared and there was considerable selection bias. A retrospective study found that only 36.8% of the tracts performed by interventional radiology were ultimately used for PCNL [38]. Access attained by a radiologist might be associated with more complications and the urologist may be in a better position to select the preferred calyx for entry.

Number of tracts

One case–control study matched 20 patients with multiple tracts to patients with single tracts (1:1) [39]. Patients with multiple tracts had larger stone burdens and a median of three tracts (range 2–6). Transfusion rates were higher with multiple tracts (20% versus 0%, $p < 0.01$), though the preoperative hemoglobin was lower; complication rates were comparable. PCNL monotherapy with multiple tracts is safe and effective for patients with large stone burdens.

Aron et al. published a case series of multitract PCNL (2–5 tracts) for complete staghorn calculi, involving 121 renal units [40]. All wires were placed at the start of the procedure, with tracts dilated to 34 F when needed. All patients had upper pole access, 76% of which were supracostal. Complications included transfusion (17%), pseudo-aneurysm (2%), septic shock (1%), and hydrothorax (3%). Including second-look nephroscopies in 16% of renal units, PCNL monotherapy had a complete clearance rate of 84%.

Multitract PCNL can be effective for complex stone disease, but with greater morbidity.

Tract size

The widths of the tract and working sheath have been postulated to affect the outcomes of PCNL, and new nonstandardized terms such as "mini-perc" and "minimally invasive perc" have appeared. Three prospective studies have examined the influence of tract size on PCNL outcome.

Cheng et al. randomized patients to mini-PCNL ($n = 72$) versus standard PCNL ($n = 115$) [41]. Patients with multiple tracts, conversion to standard PCNL or histories of ipsilateral PCNL were excluded. Dilation was performed with telescoping metal dilators, to 16 F for mini-tracts and 24 F for standard tracts. There were no differences in analgesic use, length of stay, pleural complications, fever or prolonged urinary leak. Mini-PCNL was associated with a lower transfusion rate (1.4% versus 10.4%, $p < 0.05$), but longer operative times. Though the SFRs were similar for staghorn and simple calculi, mini-PCNL was less effective than standard PCNL for patients with multiple calyceal stones. A major limitation was the lack of intention-to-treat analysis, as 52 mini-PCNL patients were excluded after conversion to standard due to low efficiency of fragmentation.

Another study explored whether multiple mini-tracts or fewer standard tracts were preferable for the treatment of staghorn calculi. Zhong et al. randomized 54 patients to mini-PCNL or standard PCNL [42]. Mini-PCNL tracts were "gradually dilated" to 16 F, while the standard PCNL used 26 F tracts. All mini-PCNL patients had 2–4 tracts, while 88% in the standard PCNL group had a single tract. The use of multiple smaller tracts was associated with higher stone clearance rates and no increase in the rate of complications, though PCNL took longer when compared to the use of fewer, larger tracts.

Li et al. evaluated the invasiveness of a standard versus smaller tract by measuring acute phase markers of tissue trauma [43]. In this nonrandomized study, the mini-PCNL group ($n = 93$) underwent tract dilation to 14–18 F using fascial dilators, and telescoping Alken metal dilators were used in the standard PCNL group ($n = 72$) to dilate to 30 F. There was an increase in all of the markers, except IL-10, with no differences between the mini- and standard PCNL groups [43]. Though a PCNL with a 14–18 F tract was associated with less bleeding than 30 F, the operative time was longer and the amount of tissue trauma was comparable.

A subanalysis of the CROES PCNL Global Study showed higher transfusion rates with larger sheaths [44]: 12.1% for 32–34 F versus 5.9% for 27–30 F versus only 1% for 18 F or smaller. However, this observational study did not account for confounders such as differences in access techniques that may affect the rates of bleeding.

Tract dilation

Balloon dilators are the most costly dilation method, while Amplatz dilators and Alken telescoping metal dilators dilate with tangential shearing forces. Amplatz dilators have traditionally been used serially or, more recently, with one-step dilation.

In the CROES PCNL Global Study, balloon dilation was associated with longer operative times (median 94 versus 60 min, $p < 0.0001$) and higher rates of bleeding and transfusion (9.4% versus 6.7%, $p < 0.0001$) than telescopic metal and serial Amplatz dilators combined [44]. However, on multivariate analysis, the method of tract dilation was no longer significant. To examine the impact on renal function, Unsal et al. randomized 75 patients to balloon, metal or Amplatz dilators, though 25 patients were lost to follow-up [45]. All tracts were dilated to 28–30 F, and six patients required two tracts. On quantitative single-photon emission computed tomography (QSPECT), new cortical defects were found in nine cases (18%) 3–6 months after PCNL. Thirteen patients had a change in renal function from baseline, with increases or decreases occurring with all types of dilation. This study was limited by its sample size, short follow-up, and lack of statistical reporting.

Aminsharifi et al. randomized patients to either gradual (with Alken telescopic metal dilators) or one-step dilation to 28 F to evaluate the effect of renal function [46]. Though 70 patients were randomized, 22 were excluded for failed first access, multiple accesses, residual fragments or ancillary procedures. The mean access time and the duration of radiation were longer with gradual dilation. A decrease in overall renal uptake (47.7% versus 50.1%, $p = 0.001$) and new scars (48.3% versus 11%, $p = 0.007$) were more common in the one-step group on ^{99m}Tc-DMSA scans performed 4 weeks post PCNL. Limitations of this study include the small sample size, lack of a balloon dilation arm, and brevity of follow-up.

Lithotripsy modality

Several comparative studies of different lithotripsy modalities in PCNL have been reported. The Canadian StoneBreaker Trial was a multicentered RCT comparing the efficacy of the LMA Stonebreaker™ (SB) (Laryngeal Mask Airway [LMA] Company, Switzerland) versus the Swiss Lithoclast® (LC) (Electro Medical Systems [EMS], Switzerland) ($n = 77$) [47]. Both are pneumatic lithotrites, with the LC using compressed air, controlled by a foot pedal, to produce a "jackhammer" effect. The SB is a cordless, hand-held device using compressed CO_2 cartridges. Lithotripsy time was shorter with the SB (mean 11.19 versus 16.88 min, $p = 0.0139$) with a higher rate of stone fragmentation (6.46 versus 3.59 mm^2/sec). There were no differences in SFR, stone composition or complications [47].

Lehman et al. randomized patients to combined ultrasonic and pneumatic lithotrite (Swiss Lithoclast Ultra, EMS, Switzerland) versus ultrasonic lithotrite (LUS-1, Olympus, Center Valley, PA) ($n = 30$) [48]. No differences were found in the mean times for stone fragmentation or retrieval, operative time or SFR. Ultrasound-only lithotripsy may be advantageous from a cost perspective over the combined unit [48].

One small ($n = 74$) retrospective study compared the LC alone or in combination with an ultrasonic lithotripter [49]. It was found that adjunctive ultrasound was associated with a decrease in overall operative time and blood loss.

Zhu et al. compared four lithotripsy modalities used when treating proximal ureteral stones with severe hydronephrosis with PCNL [50]. Retrospectively, the outcomes of 192 patients treated with LC, a combination pneumatic and ultrasonic lithotrite called the Swiss Lithoclast Master (Electro Medical Systems, Switzerland)

and holmium:YAG laser at either low power or high power were compared. The LC was the slowest (118 min) and the Swiss LC Master the fastest (81 min). The "low" power setting was faster than the "high" (85 versus 110 min). Length of hospital stay, SFR, and mean blood loss were similar. There were higher rates of stricture formation associated with "high" power laser (15.8% versus combined rate of 2.6% in the remaining patients, $p < 0.001$). Although various lithotripsy modalities appear safe, differences may exist in terms of lithotripsy efficiency.

Method of postoperative drainage

Classically, postoperative decompression is performed with a nephrostomy tube, ureteral stent, and bladder decompression. Numerous reports have challenged this approach. For clarity, "tubeless" will refer to a ureteral stent without nephrostomy tube, while "totally tubeless" (TT) will describe a PCNL with neither ureteral stent nor nephrostomy.

A recent systematic review examined the safety of standard versus tubeless PCNL [51]. Eleven RCTs and 13 nonrandomized studies were included due to the small sample size in most RCTs [51]. Groups included standard (with tube), tubeless (with stent), and TT. Unfortunately, heterogeneity of tube size and type, technique and patient groups precluded metaanalysis. Stone size comparison was hindered by the use of different types of measurements but in the largest comparative study in the review, the stones were larger in the standard group than the tubeless group. Pain levels, analgesic requirements, length of stay, and convalescence times were all significantly lower in the tubeless groups. The morbidity and SFR did not differ between the tubeless and tubed groups. A cost benefit favoring the tubeless approach was suggested in two studies. Additionally, there were no reports of increased intrathoracic complications in any of the five studies with supracostal access. One study showed the tubeless approach to be acceptable in patients with renal anomalies, such as horseshoe kidney. Large, multicenter RCTs would be useful in confirming the findings of this systematic review, and determining the role of TT PCNL.

Etemadian et al. performed an RCT not included in this review, that examined the role of tubeless PCNL in patients with intraoperative bleeding, though the degree was not specified [52]. Tract dilation was performed in a one-step method to 30 F, and 200 patients were randomized to either tubeless or a 24 F nephrostomy. All patients had Foley and ureteral catheters. The transfusion rate did not differ between the groups but was high overall (25% versus 20%, $p = 0.233$). The only difference noted was a shorter length of hospitalization, reinforcing the safety of tubeless PCNL, even with bleeding.

Two separate metaanalyses of only RCTs have been reported, unlike the Amer systematic review that included nonrandomized studies. Yuan et al. included 14 RCTs with 776 patients [53]. Standard PCNL was divided into two subgroups: small (4–10 F) and large (14–24 F) nephrostomy tubes. Two of the studies were high quality and the remainder moderate [53]. No differences were found in the stone-free, fever, and transfusion rates between the standard and tubeless groups. The tubeless group was superior in terms of analgesic requirements, length of stay, and urinary leakage [53]. No differences were found between the small tube group and the tubeless group for analgesic requirements or urine leakage, though the authors attributed this to the small size of the small-tubed cohort. TT patients were not analyzed.

Ni et al. also performed a metaanalysis of RCTs, 10 of which compared tubeless to standard PCNL ($n = 643$) and three of which compared tubeless to small-bore tube (8.2–9 F, $n = 109$) [54]. Of the 13 studies, only two were not included in the Yuan metaanalysis. Again, tubeless PCNL involved less analgesia, a shorter hospital stay and quicker recovery time, even relative to the small-bore tubed group, while no differences were observed in the transfusion or complication rates. A TT subgroup analysis involving four studies showed similar advantages to tubeless PCNL when compared to standard PCNL.

Though many of the RCTs were small, the tubeless approach was beneficial in terms of pain, recovery, and length of stay, without an increase in bleeding and other complications. However, larger, well-designed randomized studies are needed to help identify the settings in which nephrostomy drainage, tubeless or the TT approach would be most appropriate.

Role of tract closure

With tubeless PCNL becoming more common, various methods of tract closure have been described in an effort to avoid excessive bleeding and urinary drainage. However, many of the tubeless procedures in the metaanalyses did not include tract closure. Aghamir et al. randomized 20 patients undergoing TT PCNL into tract closure with Surgicel (oxidized cellulose, placed using the nephroscope prior to complete sheath removal) versus the control group of no closure [55]. No differences were found in the hemoglobin drop or urinary extravasation, detected by US on postoperative day 2 or the number of wet dressings. Singh et al. randomized 50 tubeless PCNL patients to either no tract closure or Spongostan®, an absorbable gelatin sponge [56]. A rolled sheet was placed in the tract and sutured to the skin with silk. Though the operative time was longer, the group with absorbable gelatin experienced less pain and lower analgesic requirements, with smaller urinomas on ultrasound and a shorter duration of urinary leakage. No bleeding differences were noted between the groups.

One randomized trial compared two methods of tract closure to a control group (with 10 F nephrostomy tube) [57]. Either a deep fascial stitch (O PDS) or a gelatin matrix hemostatic sealant (FloSeal, Baxter Medical, Freemont, CA) was used, after tracts had been balloon dilated to 30 F. No differences were found in the operative time, length of stay, hemoglobin drop or stone clearance rate. However, the FloSeal patients had significantly higher pain scores at 1 week that resolved by 1 month, though the narcotic use was similar.

These small studies establish the safety of various methods, but it is not yet clear whether there is any benefit of closing or sealing the tract in tubeless PCNL.

Postoperative considerations

Determination of treatment outcomes

The literature surrounding stone surgery can be difficult to compare due to the heterogeneity in the definitions of "stone free" and "success." Altunrende et al. highlighted that, though termed "clinically insignificant" residual fragments (CIRFs), these asymptomatic, noninfectious fragments ≤4 mm have been shown to progress commonly [58]. Of 38 patients with post-PCNL CIRFs followed for at least 2 years, over 25% had a symptomatic episode and over 20% had a radiological increase in size [58]. Deters et al. found that nearly one-third of 239 articles addressing stone surgery did not define "stone free," with the remainder using definitions that varied widely [59]. Although CT is the most accurate imaging modality to assess for residual stones, 28% of studies used KUB (kidney ureter bladder x-ray) alone, while 22% used KUB with US. Another study found that residual fragments were included in the definition of "stone free" in 12%, while "success" included residual fragments ranging from <1 to <7 mm, with only a quarter of these determinations being based on CT [60]. Standardization of reporting could enable more meaningful comparisons of treatment modalities and outcomes.

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5

CHAPTER 5

Patient Selection and Informed Consent

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Patient selection

The primary objective for stone management should be focused on maximal stone clearance with lowest possible patient morbidity. With the advent of minimally invasive surgery, endourological procedures have eventually replaced open surgery for the management of large kidney stones. Since its first description more than seven decades ago [1], the indications for percutaneous nephrolithotripsy (PCNL) have greatly expanded. Technological advances, surgeon experience, economic awareness, and patient education have all contributed to a versatile array of indications that are dependent on stone, patient, and health provider factors. Even though these factors are so often intermixed, for simplicity they will be described separately here.

Due to its more invasive nature, as a general rule, patients with stones deemed unlikely to pass spontaneously and who are predicted to have a poorer outcome if treated with shock wave lithotripsy (SWL) or ureteroscopy (URS) are considered for PCNL.

Stone factors

These include several aspects, including stone burden, composition, and location.

Stone burden

This is often considered as the most discriminative factor [2]. Stone burden is an estimation of size and number. The most accurate stone burden determination is computed from a three-dimensional computed tomography (CT) reconstruction [3]. However, given the cost, complexity, radiation exposure and in some jurisdictions limited availability of this technology, stone burden is most often alternatively expressed as mm^2 and is determined by multiplying the horizontal and vertical dimensions of each stone computed from conventional two-dimensional imaging [4]. If multiple stones exist, these measurements are aggregated. In general, as stone burden increases, PCNL becomes more efficient than SWL or URS in achieving optimal stone-free rates [5]. Patients with stones larger than 2 cm are best treated with PCNL (Grade B recommendation) [6]. Larger stones that occupy the renal pelvis and extend into one or more of the calyces are designated staghorn stones. According to the American Urological Association (AUA) guidelines, PCNL should be the first treatment used for most patients with staghorn stones [7]. In the exceptional very large and complex stone burdens where a combined approach is deemed necessary, PCNL should be used as the primary procedure. SWL may only be considered as an adjunct procedure for inaccessible

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

stones to minimize access tracts. A secondary nephroscopy may be later considered to allow rapid stone clearance following SWL [8].

Percutaneous nephrolithotripsy as primary therapy resulted in significantly higher stone-free rates (SFR) (78%) than SWL (54%), open surgery (71%), or even combined SWL-PCNL approaches (66%) and was hence associated with significantly lower stone recurrences. In addition, PCNL had the advantage of requiring significantly fewer additional procedures [7].

Most management controversies are, however, related to nonstaghorn stones less than 2 cm in diameter. Although PCNL may still offer a better SFR for stones 1–2 cm, it is associated with higher complication rates and thus less invasive procedures like SWL or URS are typically primarily considered [9]. Nevertheless, since URS is frequently associated with stent insertion, counterbalancing its perceived benefits, PCNL may still offer a possible advantage over URS for smaller stone dimensions in selected cases [10].

Stone composition

Stone chemical composition directly correlates with its hardness [11]. Cystine, brushite, and calcium oxalate monohydrate stones are examples of hard stones. On the other hand, matrix stones are considered soft and gelatinous stones. Both ends of the spectrum provide a weak acoustic interface for SWL and are hence resistant to fragmentation. Additionally, if fractured, harder stones tend to produce larger stone fragments [12].

Percutaneous nephrolithotripsy is usually considered the mainstay of treatment for SWL-resistant stones, especially when larger than 1.5–2 cm. For smaller stones, PCNL may be reserved for those who fail SWL or URS [13,14].

The possibility of predicting stone composition pretreatment often presents a challenge to the practicing urologist. Medications [15], recurrent urinary tract infections (UTI), previous stone composition, urinalysis, and imaging [11] are helpful tools. A smooth-edged homogeneous stone that has a Hounsfield unit density (HU) greater than 1000 may correlate with harder consistency [16]. Unfortunately, the overlap in HU and the frequent mixed stone composition make it more problematic to accurately identify stone composition. Dual-source CT has been recently reported as a useful tool to distinguish certain stone structures [17].

Stone location

Lower pole stones

As a result of their dependent location, management of lower pole calyceal stones, especially those <2 cm, continues to provoke controversy [18]. Randomized prospective studies [19,20] have demonstrated that PCNL for lower pole calculi is consistently more successful than SWL. PCNL success is independent of stone size, with SFR for stones <1, 1–2 or >2 cm noted to be 100%, 93%, and 86% respectively. When compared to SWL, PCNL was associated with significantly higher overall SFR (95% versus 37%), lower retreatment rates (9% versus 16%), a decreased requirement for auxiliary procedures (2% versus 14%) and no significant difference in overall complications. On the other hand, hospital stay was significantly longer for the PCNL group (2.66 versus 0.55 days). When stratified by stone size, patients with stones greater than 1 cm treated by PCNL had significantly higher SFR when compared to those treated by SWL (91% versus 21%) [19]. Similarly, patients with stones 10–25 mm in the lower calyx when treated by PCNL had significantly higher SFR than those treated by URS (71% versus 37%) [21].

An added advantage to PCNL may be further accentuated by the fact that retained stone debris in the lower calyx, even when considered nonsignificant, is still associated with significantly higher symptomatic recurrence, stone events, and intervention rates within 1–2 years [22]. Acknowledging the limitations of SWL, investigators have attempted to identify if predictive factors for SWL treatment failure exist and hence favor PCNL. Other than gravity, it has been suggested that calyces with longer and/or narrower infundibula, drained by multiple infundibula and/or having an acute infundibulo-pelvic angle may all contribute to a poorer stone clearance [23,24].

Overall, given the more invasive nature of PCNL, lower pole calyceal stones smaller than 1 cm are typically primarily managed by SWL. However, if such stones demonstrate a harder consistency (>1000 HU on noncontrast CT), URS may be a better alternative. PCNL is often considered the best management option for all lower calyceal stones larger than 1 cm or for smaller stones that fail either SWL or URS [19,25].

Bilaterality

Large stone burden bilaterally presents a particular challenge. Typically, for bilateral stones, PCNL is performed as a staged procedure. The most symptomatic side, the kidney at greatest risk of functional deterioration and the more complex stone burden and configuration usually dictate the initial procedure side. The contralateral procedure can be performed from a few weeks to a few months later with timing dependent on symptoms and degree of obstruction. Alternatively, a synchronous bilateral PCNL can be successful in selected cases, with comparable SFR and postoperative pain [26]. Bilateral synchronous PCNL was associated with a significant decrease in operative time, blood loss, transfusion rates, and hospital stay when compared to staged procedures [26,27]. The decision to simultaneously pursue the contralateral side should be made following a comprehensive clinical judgment and only when the first stage of the procedure is accomplished safely, within a reasonable time and the patient is clinically stable intraoperatively with no excessive bleeding. Bilateral simultaneous PCNL performed by experienced surgeons is a well-tolerated, safe, efficient, expeditious, and cost-effective approach [26,27].

Renal anatomical anomalies

Stones in calyceal diverticula

The preferred management option for treating stones in calyceal diverticula is still under debate. It is, however, generally accepted that the ideal approach to prevent stone recurrence is through stone clearance along with a concomitant obliteration of the diverticulum. Diverticula with a narrow neck, noncommunication with the collecting system, harboring a large stone burden >2 cm or in an anterior location can present a specific challenge. In many cases, a percutaneous approach offers the optimal means to achieve resolution of both the stone(s) and the diverticulum simultaneously [28,29]. If identified, a stenotic infundibulum can be dilated or incised or alternatively, a neoinfundibulotomy can be created and the diverticulum can then be ablated [30]. A less invasive ureteroscopic retrograde approach has been advocated for treating stones in calyceal diverticula, yet because of retained stone fragments or an unidentifiable ostium, a secondary PCNL was required in almost half of the cases. When compared to URS, PCNL was shown to have significantly better outcomes. It was associated with higher SFR (78% versus 19%), diverticular resolution (61% versus 18%), and overall symptom-free rates (86% versus 35%) [31].

Fusion abnormalities

Horseshoe kidney is the most common renal fusion anomaly and is often associated with vascular and collecting system anatomical abnormalities [32]. These anomalies may predispose to an increased risk of renal stone formation and ureteropelvic junction obstruction (UPJO) [33]. Stone clearance may be substantially affected by the calyceal orientation and/or the presence of associated distal obstruction [34]. For stones larger than 1.5 cm and/or in the presence of impaired drainage, PCNL is considered the preferred primary approach [35,36]. URS in these circumstances is technically challenging [34]. PCNL offers the advantage of adequately treating both the urolithiasis and, if present, the UPJO.

Percutaneous nephrolithotripsy performed in horseshoe kidneys is more technically demanding and was linked to increased fluoroscopy use, longer operative times, and prolonged hospitalization [36]. An upper pole, posteriorly oriented calyceal access is the preferred approach in horseshoe kidneys, as it provides access to the remaining dependent calyces and those in the isthmus, the UPJ, and the ureter with minimal torque and thus less bleeding [32]. Furthermore, since horseshoe kidneys are displaced inferiorly and medially, upper pole access is usually performed subcostally and is less likely to be associated with thoracic complications [35,37]. On the other hand, this displacement is often associated with a retrorenal colon and may predispose to colonic injury.

With proper planning, careful attention to technique and free use of flexible nephroscopy, PCNL is considered a safe and effective option for the management of stones larger than 1.5–2 cm in horseshoe kidneys with no additional morbidity [36].

Ectopic kidneys

Nonrandomized, observational, retrospective studies have shown that PCNL of ectopic kidneys demonstrated a better overall SFR when compared to SWL or URS, with significantly lower retreatment rates [38,39]. Due to the adjacent location of the kidney to other visceral structures, a carefully planned percutaneous CT-guided renal access tract may be established prior to the procedure or alternatively, an intraoperative laparoscopic assistance may be required [39].

Ureteropelvic junction obstruction and distal obstruction

Urolithiasis is commonly associated with UPJO [40]. Through a percutaneous approach, a careful examination of the UPJ can be performed. Both a nephrolithotomy and a concomitant endopyelotomy can be successfully accomplished with low morbidity [41]. Stone extraction is much easier through this antegrade approach which may be favored over a retrograde URS.

Previous interventions

Previous shock wave lithotripsy

Percutaneous nephrolithotripsy following unsuccessful SWL has been associated with subjective nonspecific nephroscopic findings including bruised calices and presence of white membranes in the pelvicalyceal system. Furthermore, since shattered stone fragments post SWL may be located in numerous calyces, PCNL following SWL has been associated with the requirement for several percutaneous accesses [42] and significantly longer operative times [43]. In the hands of experienced surgeons, PCNL can be safely and effectively performed following an unsuccessful SWL [42,43].

Previous open renal surgery

It has been suggested that the resultant inflammation and subsequent scarring may potentially make needle and guidewire placement more demanding [43]. Furthermore, the resultant pelvicalyceal system distortion may possibly decrease stone clearance. Bowel displacement following open surgery may require additional planning for puncture placement to avoid bowel perforation [44]. Alternatively, fixation of the kidney caused by scar tissue may limit its movement, facilitating calyceal targeting and puncture [45]. Currently, despite the fact that PCNL may become more technically challenging in some of these patients, PCNL is still considered safe, requiring no technical modification, with no additional morbidity and similar stone-free rates following open renal surgery [43,45].

Interventions restricting retrograde ureteric access

When previous bladder or ureteric surgery hampers retrograde access, PCNL becomes an attractive option even for smaller stones. Examples of such procedures include surgeries associated with ureteral reimplantation (due to stricture disease or correction of vesicoureteral reflux), kidney transplantation and/or ileal ureter [10].

Urinary diversion

In addition to restricting retrograde access, urinary diversions are often associated with higher frequency of stone formation [46]. Struvite stone occurrence is higher in this patient group, thus making URS and SWL less reliable in achieving a stone-free status [47]. PCNL is often considered the treatment of choice and sometimes the only reliable treatment for patients with a urinary diversion and having a larger or more complex stone burden [48]. Liberal use of second-look nephroscopy allows the achievement of unequivocal stone-free status, decreasing further stone recurrences. Caution should be exercised in this patient population as PCNL has been found to be associated with a higher risk of postoperative infection and sepsis [48]. It is recommended that patients should therefore be admitted preoperatively for 24 h of intravenous broad-spectrum antibiotics prior to the procedure. With proper planning and experience, patients with urinary diversions can be treated as safely and effectively by PCNL as nondiverted patients [48].

Encrusted foreign bodies

Stones formed on retained foreign bodies, such as stents, sutures or leftover debris from broken instruments, may not only potentially reach large dimensions, but may also impede retrograde access and/or become impossible to retrieve [49]. PCNL may provide a successful management alternative in these circumstances if retrograde URS fails. It offers the advantages of both managing the stone and retrieving the retained foreign body, thus preventing further stone recurrence [10].

Patient factors

Obesity

Stone patients with a Body Mass Index (BMI) over 30 kg/m^2 present a considerable challenge. SWL table or gantry weight limits, suboptimal imaging resolution and increased skin-to-stone distance (SSD) significantly limit the possible use of SWL in such circumstances [50,51]. BMI positively correlates with SSD in upper tract calculi. When the target stone is beyond the set maximum focal distance of the shock wave lithotripter, the effectiveness of shock waves significantly declines. SSD >10 cm has been shown to independently predict inferior SFRs following SWL with a sensitivity of 87% and a specificity of 85% (odds ratio 0.32, 95% confidence interval 0.29–0.35) [52]. PCNL offers an attractive management alternative in obese patients with stones that cannot be efficiently treated with flexible URS or SWL. Various studies have suggested that, other than instrument size modifications, the cost and outcomes of PCNL were not affected by patient BMI [50,53]. Additionally, the feasibility of performing PCNL under local sedation and awake endotracheal intubation as well as supine and lateral decubitus positioning provides an alternative in this patient population. A recent prospective multicenter study has shown that PCNL may safely be performed in obese patients with acceptable morbidity. It may, however, be associated with longer operative duration, inferior SFR, and higher rates of reintervention [50].

Skeletal anomalies

Percutaneous nephrolithotripsy offers an advantage over URS when patients with skeletal anomalies cannot be placed in the lithotomy position. Moreover, some anomalies may interfere with patient positioning and coupling for SWL [54]. Unfortunately, severe skeletal anomalies may likewise limit positioning for PCNL. A preoperative CT-guided access to the kidney may be necessary in some cases.

Diabetes mellitus

Given the potential severe complication of diabetes, rendering these patients stone free in a single session tends to favor the liberal use of PCNL in this population. Despite the fact that diabetes mellitus predisposes patients to potentially higher perioperative complications, PCNL is not associated with higher morbidity in patients with diabetes when compared to those without and has excellent SFR [55].

Uncorrected coagulopathy

Patients' coagulation profiles should be assessed. Any anticoagulant medication should be discontinued at the appropriate time before surgery. If anticoagulation therapy cannot be discontinued, URS is an option [56]. PCNL performed in the presence of bleeding diathesis may be life threatening [57].

Pregnancy

Despite anecdotal reports of successful PCNL during the 14th week of gestation [58] or radiation-free PCNL [59], PCNL generally should not be considered during pregnancy and should be postponed until after delivery due to the general anesthetic requirements, the prone positioning, and the use of ionizing radiation. A ureteral stent or ultrasound-guided nephrostomy tube drainage should alternatively be considered for larger stone burden [60].

Other factors

Age

Age should not be considered as a deterrent limiting or rejecting the use of PCNL [61,62]. Patient selection should be similar to other age categories providing no specific contraindications exist. In selected pediatric cases, owing to the smaller caliber of the ureter limiting the use of retrograde URS, PCNL may be indicated for renal stones with a smaller cut-off size (>15 mm) when compared to the adult population [63]. The successful use of PCNL in the pediatric population has been facilitated by significant technical advances. PCNL is safe and efficacious in both extremes of ages [61,62]. It may, however, be associated with a higher transfusion rate in the elderly [64].

Occupation

Even when asymptomatic, stones in high-risk occupations, such as airline pilots, are associated with significant days of work loss and the accompanying economic consequences [65]. PCNL is often the most efficient in this select cohort [10].

Healthcare provider factors

The role of surgeon factors in determining PCNL patient selection remains unclear [66]. Physician-, hospital-, and healthcare system-specific factors may influence a specific treatment choice. Training background, experience, surgeon schedule accessibility, institution type, equipment availability, cost, reimbursement, and personal surgeon preference may play important roles in treatment selection. Academic, fellowship trained endourologists and urologists in practice for <5 years were found to have a tendency to perform PCNL more frequently [67].

Informed consent

As with any surgical procedure, a patient's agreement and authorization for PCNL therapy are fully dependent on clear communication and a comprehensive discussion with the urologist regarding diagnosis, treatment options and the relative risks and benefits associated with each treatment modality. It is inappropriate to withhold treatment alternatives based on surgeon's experience or equipment availability [68]. Patients should always be entitled to have a second opinion and/or referral to a more experienced endourologist. The patient should be given sufficient time during his/her clinic appointment and all his/her questions should be answered. All communications should be clearly documented by the urologist. This clear communication is both the ethical and legal obligation of the treating urologist [69].

Refinements in PCNL techniques over the past decades have yielded higher SFR and led to significant decrease in morbidity. SFR should, however, be examined prudently since the timing of SFR determination varies among studies and is not universally strictly assessed by CT scans and therefore true SFRs are different from those often reported in the literature [70]. In high-volume centers, with experienced endourologists, the overall SFRs at hospital discharge and at 3 months postoperatively were 78% and 91% respectively [71]. A recent multicenter observational prospective study has shown that PCNL was associated with an overall 76% SFR, with 85% of the patients not requiring any additional treatment for stones. Total complication rates following PCNL vary considerably and are reported as between 15% [71,72] and 83% [73–77]. This variability is likely a reflection of a difference in surgical techniques, surgeon experience, and patient populations. Significant complications are, however, infrequent. Only 3.6% of patients had grade III and 0.5% > grade IV Modified Clavien Score [71,72].

Early recognition of complications and their prompt management may significantly reduce associated morbidity. For descriptive purposes, complications will be divided according to whether they are related to the surgical technique or other general operative complications.

Surgical-related complications

Surgeons with modest experience and poor techniques were associated with higher complication rates. Improving surgeons' experience significantly reduced complications rates from 61% to 37% [2].

Complications will be divided into access-related and stone retrieval-related complications.

Complications related to establishing access

Bleeding

Since the kidney is considered an extremely vascular organ, venous bleeding that does not require blood transfusion may be associated with PCNL [73]. Bleeding requiring blood transfusion is considered the most common significant complication following PCNL [78]. Transfusion rates have been reported from 0.8% [71] to 45% [79].

Severe persistent bleeding intraoperatively may impede proper visualization. In this case, the procedure should be aborted and a nephrostomy tube placed [80]. A subsequent procedure should be planned after clearing of the gross hematuria, typically from a few days to a few weeks later [78]. Significant postoperative bleeding may be controlled with clamping of the nephrostomy tube to tamponade bleeding vessels. If persistent, a Kaye (Cook Urological, Spencer, IN) tamponade balloon catheter can be placed and left for 2–4 days [81]. If bleeding persists, a selective embolization should be performed by an interventional radiologist [73]. When there is a significant drop in hemoglobin, while urine remains clear, a perinephric hematoma should be suspected [78].

Late bleeding occurring several weeks postoperatively is most often secondary to an arteriovenous fistula or a pseudo-aneurysm and almost universally requires angiography and embolization [73]. Significant bleeding requiring angiographic embolization is reported to be as low as 0.6–1.4% [77,82]. In more severe cases, bleeding requiring an emergency partial or total nephrectomy is fortunately an uncommon occurrence (<0.5%) [83].

Adjacent organ injury

Lung and pleural injury

The overall risk for pleural injury is reported to be 1% [84] to 4.5% [77,85]. This risk may significantly increase to up to 13.6% with supracostal access [86]. Pneumothorax (1%), hydrothorax or hemothorax (4%) may necessitate chest tube insertion [86]. Thoracoscopy or thoracotomy is rarely needed [73]. Nephropleural fistula may occur in 2% [87]. Fistulae usually resolve after placement of a ureteral stent [88]. Lung parenchymal injury is unusual [83]. Routine intraoperative fluoroscopy or postoperative chest x-ray is recommended.

Colonic injury

Risk factors include congenital renal fusion or ectopic anomalies, previous open surgery, a left-sided procedure, old age, distended colon or low-weight individuals [89]. Risk of colon perforation is estimated to be <1% [73,77,89]. If extraperitoneal perforation occurs, conservative management is usually successful [90]. A nephrotomy tube is placed in the colon and the kidney is drained by a ureteral stent. Broad-spectrum antibiotics should be started and patients are placed on low-residue diet. Contrast is injected 7–10 days postoperatively through the colostomy tube and in the absence of documented nephron-colonic fistula, the tube can be removed. Alternatively, intraperitoneal colon perforation is associated with peritonitis and serious infective complications requiring immediate open surgical repair [73].

Duodenal injury

This is a rare complication that may follow a right renal pelvic or lower collecting system perforation [91]. Open surgical repair is indicated in large perforations or cases associated with peritonitis. In less severe cases, conservative management may be considered [78]. Antibiotics, nasogastric and nephrostomy tube placements along with parenteral hyperalimentation may be attempted [78].

Liver and splenic injuries

Splenic injury is rare in left subcostal punctures [73]. The risk increases with the existence of splenomegaly or if the puncture is performed during inspiration (13%) [92]. Minor tears may be managed conservatively but in the presence of extensive bleeding, an urgent open splenectomy may be life saving [93]. Liver injury has been associated with cases of right supracostal punctures during inspiration (14%) [92]. The presence of hepatomegaly increases the risk. A nephrostomy tube may be left in place for 7–10 days along with a retrograde ureteral stent to prevent renobiliary fistula.

Chyluria

Perforation of the collecting system associated with disruption of renal lymphatics may lead to chyluria [94]. Management consists of total parenteral hyperalimentation, somatostatin, and stent insertion to enhance urinary drainage [95]. Refractory cases may require a laparoscopic renal pedicle lymphatic interruption [96].

Physician obtaining access

When compared to interventional radiologists, urologists performing percutaneous renal access were associated with fewer access-related complications and higher SFRs [97].

Complications related to stone retrieval

Sepsis

Sepsis has been reported to occur in 0.6–1.4% of PCNL patients [74]. Infection may be introduced exogenously while obtaining access to the kidney or may result from endogenous exposure to either infected urine or following fragmentation of an infected stone. Duration of surgery, irrigation fluid volume and pressure, and renal insufficiency are significant risk factors for bacteremia and sepsis [73].

Positive preoperative urine cultures have been shown to be associated with significant postoperative morbidity. Even in the presence of sterile preoperative cultures, stone fragmentation during treatment may release bacteria and/or preformed endotoxin and lead to subsequent urosepsis. Stone or renal pelvic cultures are considered the best predictors for post-PCNL urosepsis rather than bladder urine cultures as it has been demonstrated that voided urinary cultures do not necessarily correlate with stone cultures [98]. It is therefore recommended to use an antibiotic that possesses sensitivity to both urinary cultures and urease-producing stone organisms [78]. One week of routine preoperative oral quinolone was found to significantly reduce the risks of infection [99].

Patients who are hemodynamically stable and adequately drained can be observed and do not require bacteriological cultures, especially if they had negative preoperative urine cultures and were maintained on pre- and postopertive prophylactic antibiotics [100]. In the event of finding purulent material intraoperatively, the PCNL procedure should be postponed. The collecting system should be drained via a nephrostomy tube, urine should be cultured and appropriate postoperative IV antibiotic therapy should be instituted. Intensive care therapy, fluid resuscitation, forced diuresis, pressors, and steroid administration may be required [73]. PCNL management should not be considered until complete resolution of the infection has occurred [78].

Extravasation

Extravasation caused by perforation of the collecting system has been documented in up to 7% of cases undergoing PCNL [101]. Extravasation may lead to fluid overload with resultant hypoxemia and hypertension. In cases with hemodynamic alterations secondary to severe intraoperative extravasation, the procedure should be stopped, a nephrotomy tube inserted and serum electrolytes monitored [102]. Most perforations, however, are minor and heal with antegrade ureteral stent placement. Less than 1% may require surgical repair [101]. Postoperative urinomas usually resolve spontaneously but may become infected and lead to flank pain, fever, ileus, and/or respiratory compromise [103]. Adequate percutaneous drainage of the urinoma and the collecting system may be required with proper antibiotic coverage [78].

Extrarenal stone migration

This is usually associated with collecting system perforation and is of no clinical significance as long as the urine and the stone are not infected [104]. Trials to retrieve the stone are usually associated with extending the perforation.

Retained foreign bodies

These can cause infections, new stone formation, and granulomatous reactions. These foreign bodies can be removed by retrograde URS but if this is unsuccessful, a percutaneous approach may be necessary [105].

Infundibular stenosis

This occurs in <2% of PCNL patients [106]. Previous studies have demonstrated that infundibular stenosis may be independently associated with large stone burden, extended procedure and/or prolonged postoperative nephrostomy tube drainage [106]. If asymptomatic, management is usually conservative and associated with no renal deterioration. Alternatively, an endourological management may be considered [78].

Ureteral stricture

Ureteral stricture occurs in <1% of PCNL patients. The proximal ureter and UPJ are most susceptible to stricture [83]. Causes may include operative trauma, stone impaction, and/or infection [107]. Patients may be managed endourologically but if this is unsuccessful, a laparoscopic or open technique may be needed [78].

Ureteral avulsion

This occurs in <0.2% of PCNL patients and has most frequently been related to basketing of large impacted stones [108]. Management usually involves either a temporizing nephrostomy tube or immediate surgical repair [78].

Nephrocutaneous fistula

This is a rare condition that is almost always associated with distal obstruction secondary to residual stone fragments, stricture, edema, blood clot, and/or retained foreign body [109]. Managing the distal obstruction usually prompts healing of the fistula. Electrocautery of the tract is rarely necessary [78].

Air embolism

Air embolism is extremely uncommon and may result from injection of air into the collecting system to visualize a posterior calyx [110]. It has also been reported following an alteration in the air flow of ultrasonic lithotriptors [78].

Other complications

Hypothermia may result from anesthesia-related vasodilation, prolonged operative procedures, low operative room temperature, exposed body surfaces, absence of body warmers and use of unwarmed irrigants. Hypothermia may lead to impaired platelet function, altered drug clearance, shivering, myocardial infarction, and/or arrhythmias [111].

Deep vein thrombosis (DVT) and pulmonary embolism may occur in 1–3% [102,108]. DVT can be prevented by the liberal use of thromboembolic deterrent (TED) and sequential compression pneumatic stockings along with early postoperative ambulation. These stockings may be more effective when worn prior to administration of muscle-paralyzing drugs during anesthesia. Pharmacological prophylaxis of DVT and inferior vena cava filter may be considered preoperatively in high-risk patients [78].

Musculoskeletal and nerve injuries: patient positioning may be associated with cutaneous trauma, brachial plexus injury, shoulder dislocation, lower limb peripheral nerve injury, breast, face and/or dental trauma. These injuries can be prevented by proper padding of pressure points [112]. Management is usually conservative and full resolution occurs over time. Physiotherapy and neurology consult may be required in severe or persistent cases.

Renal function deterioration and the development of renal scars following PCNL are still debated. While some studies have failed to demonstrate any change in renal function and in the development of renal scars following PCNL [113], others have documented a scar in up to <4% of the renal cortical mass along with renal function deterioration [114]. Patients with hypertension, staghorn stones, solitary kidney, recurrent stones, neurogenic bladder or urinary diversion experienced an increased risk of worsening renal function [115]. An acute renal loss following an intractable hemorrhage has been reported in <0.3%. Long-term risk of renal loss may occur in 1.6% [68].

Mortality is extremely uncommon and has been reported to be <0.2% [116]. Potential causes of death are myocardial infarction, pulmonary embolism, anesthetic allergy, hypothermia, sepsis, and severe hypovolemia [78].

Conclusion

Percutaneous nephrolithotripsy plays an important role in the management of complex large renal calculi. Currently, patients undergoing PCNL are expected to have excellent SFR outcomes with minimal morbidity. The success of PCNL is validated by improved surgical instruments and techniques. When performed by experienced endourologists, PCNL has extremely low complication rates.

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6

CHAPTER 6

Instrumentation and Surgical Technique: Percutaneous Access

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Informed consent

Before proceeding with percutaneous access, the patient must be informed of all aspects of the procedure. In the same way that the technique of percutaneous access has evolved, so has its associated complications. Complications associated with percutaneous nephrolithotomy (PCNL) have become fewer and major complications have become infrequent. The most common complication is bleeding. This can most often be controlled with conservative maneuvers and on rare occasions may require angioembolization (<1%) [1]. The rate of reported blood transfusions ranges from 6% to 18% [2–5]. The rate of fever and urine extravasation ranges from 1.8% to 10.5% and 1.8% to 7.2% respectively [3–5]. As stated earlier, more significant complications are uncommon and include septicemia (0.3–4.7%) and colonic perforation (0.06–0.8%) [3, 4]. Pleural injury is rare (0.0–3.1%) and usually only occurs when an upper pole puncture is attempted [3,4]. Other rare complications include injury to the spleen, liver or duodenum [3,6].

Preoperative preparation

With the increasingly widespread access to cross-sectional abdominal imaging, all patients should undergo a noncontrast abdominal computed tomography scan (NCCT) prior to surgery. NCCT is important for percutaneous tract planning and to rule out anatomical malformations. Also, preoperative imaging helps to identify hepatosplenomegaly or the presence of retrorenal colon so that these organs can be avoided during tract placement.

As with any surgical procedure, the patient's surgical risk needs to be evaluated. More specifically, the patient's cardiac as well as pulmonary function needs to be adequate for this procedure, especially since the majority of PCNL procedures are done in the prone position. This is of particular importance in the obese patient and may require further testing and/or the involvement of other medical specialties.

All patients should receive preoperative antibiotics. Patients who are known to harbor struvite stones should begin culture-specific (if possible) antibiotic treatment at least 2 weeks in advance of PCNL. Similarly, if the patient has a positive preoperative urine culture, 2 weeks of culture-specific antibiotic treatment is instituted. Randomized clinical trials have demonstrated a lower risk of systemic inflammatory response syndrome with an empirical 1-week course of quinolones prior to PCNL. If there is no suspicion of struvite stones and if the preoperative urine culture is negative, it is our practice to prescribe 2 weeks of antibiotics [7,8].

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Figure 6.1 Appropriate prone patient positioning.

Patient positioning

Fluoroscopically guided percutaneous access requires the opacification of the renal collecting system. Most commonly, radiographic contrast is injected using cystoscopically placed ureteral catheters. The cystoscopic portion can be performed in both the dorsal lithotomy position and the prone position with flexible cystoscopy. Once the ureteral catheter is in place, a Foley catheter is also placed before the patient is positioned prone. Once in the prone position, the ipsilateral upper extremity (shoulder) to the stone-containing kidney is placed in 90° of abduction and the contralateral upper extremity is tucked at the side to allow the C-arm of the fluoroscopic machine to be positioned as close to the patient as possible. The neck of the patient is positioned as close to the neutral position as possible and a chest roll is positioned to facilitate ventilation. Finally, all pressure points including the face and extremities are carefully padded (Figure 6.1).

Instrumentation

- 18 gauge diamond tip needle
- 0.035 inch hydrophilic nitinol core glidewire
- 8 F fascial dilator
- 0.0035 inch straight and J removable core wire
- Amplatz super-stiff wire
- 8/10 coaxial dilator
- 5 F Cobra tipped angiographic catheter (Figure 6.2)
- 30 F balloon dilator
- Amplatz 30 F working sheath

Step-by-step technique

When performing percutaneous access using radiographic guidance, one of two techniques can be used: eye of the needle or triangulation. Either technique can be used in most situations depending on the surgeon's preference and experience. In specific situations such as when an upper pole calyx is being approached subcostally, the triangulation technique is preferred as positioning the C-arm to perform an eye of the needle technique in this situation may be difficult. It is the authors' belief that triangulation is a more versatile technique. For a lower pole puncture, the access should be done one fingerbreadth lateral and one fingerbreadth below the tip of the 12th rib. For an upper pole puncture, the access should be done between the 11th and 12th ribs just lateral to the paraspinal muscles.

Eye of the needle

As with most percutaneous techniques, fluoroscopy is used to perform this method of access. After the patient is positioned as stated above, the C-arm is placed at the

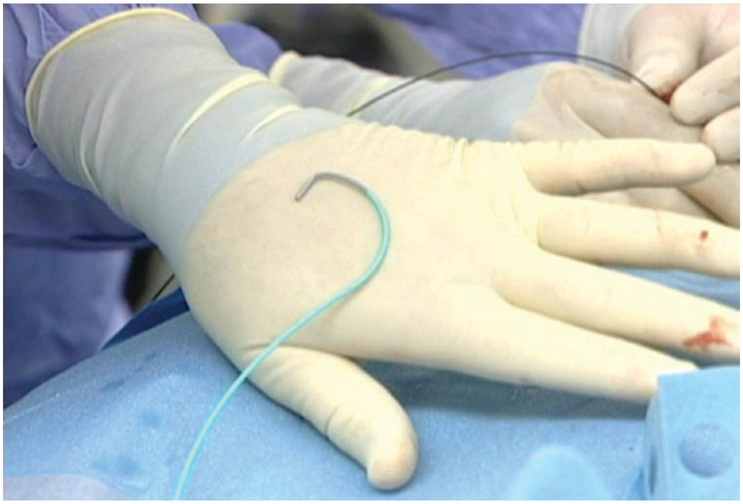

Figure 6.2 5 F Cobra tipped angiographic catheter.

Figure 6.3 Fluoroscopic view of needle tip, needle and targeted calyx in percutaneous eye of the needle puncture.

30º position and the 18 gauge diamond tip access needle is positioned so that the needle tip, needle and targeted calyx are all inline with the C-arm (i.e. bull's-eye) (Figure 6.3). In essence, the surgeon is looking straight through the needle into the calyx of interest, hence the term "eye of the needle." Using a hemostat, the needle is advanced in 1–2 cm increments using fluoroscopy between movements to maintain the proper positioning. Rotating the C-arm to a vertical position monitors needle depth. Once the needle tip appears to be within the calyx, fluid (urine or contrast) should be aspirated to confirm proper location.

Triangulation (Video Clip 6.1)

With the use of biplanar fluoroscopy, the correct orientation and optimal calyx can be determined. The ideal point of entry into the collecting system is through a fornix, in the axis of the calyx.

Once the targeted calyx is identified under fluoroscopic guidance, the C-arm is used to determine the proper location of the ideal access site. The C-arm is moved back and forth between two positions, one that is parallel and one that is oblique to the line of puncture. With the C-arm in the parallel position, adjustments are made in the mediolateral direction (right/left). With the C-arm in the oblique position, adjustments are made in the cephalad/caudad direction (up/down). It is crucial to only make adjustments in one direction at a time and to respect the different orientations as they pertain to the C-arm position. The best way for the surgeon to keep the needle steady is to rest his/her arm on the patient's torso while making needle adjustments. In order to decrease radiation to the surgeon, the C-arm is angled away from the line of puncture with the image intensifier angled towards the head of the patient.

As soon as the proper orientation is obtained, ventilation is suspended (in full expiration) and an 18 gauge diamond tip needle is advanced towards the targeted calyx with the C-arm in the oblique position (Video Clip 6.2). Before the renal capsule is penetrated, the position of the needle is checked with the C-arm in the parallel position. After proper positioning is confirmed, the needle is advanced into the renal collecting system with the C-arm back in the oblique position. Needle adjustments after it has penetrated the renal capsule are discouraged as this may displace the kidney and alter the position of the desired calyx.

Once the target calyx has been identified with the aspiration of urine, the next step is to introduce a glidewire via the needle into the renal collecting system. Ideally, when this wire is introduced under fluoroscopic guidance, it is advanced down the ureter (Video Clip 6.3). However, this is not always possible due to renal anatomy and/or the presence of renal stones. Therefore, the wire is coiled in the renal pelvis and an 8 F fascial dilator is passed into the calyx. Once the 8 F dilator is removed, a 5 F Cobra tipped angiographic catheter is used in an attempt to maneuver the glidewire down the ureter (Video Clip 6.4). Once down the ureter, the glidewire is exchanged for an Amplatz super-stiff wire. The glidewire should not be used as a working wire as it is very easily displaced. Next a 8/10 Frcoaxial dilator is introduced into the collecting system. Once this is in place, the 8 F is removed and a second safety wire, usually a 0.035 inch straight removable core wire, is placed down the ureter. Finally, a balloon dilation is performed and a 30 F working sheath is placed into the targeted calyx (Video Clip 6.5). Care should be taken to avoid overadvancement of the working sheath as this can cause trauma to the collecting system and bleeding.

Subsequent to the removal of all renal calculi, usually a 10 F coup loop is placed in the renal collecting system. Ideally this is placed in the upper pole. Also, if a secondary PCNL is planned, a 5 F ureteral catheter is placed down the ureter to facilitate the secondary procedure. If multiple accesses were required, a circle nephrostomy tube is preferred as it is very hard to displace and its material (silicone) decreases the discomfort of the patient.

Intraoperative trouble-shooting

During percutaneous access, all steps should be performed in the exact same sequence every time. This minimizes complications and maximizes efficiency. On occasion, problems do arise that require slight modifications in the technique. One such problem occurs when the initial wire cannot be placed down the ureter. In this scenario, a super-stiff wire should be coiled into the renal pelvis. The next step is to use the 8/10 F coaxial dilator and to then place a 0.035 inch J-tipped removable core guidewire instead of a straight removal core wire into the renal pelvis. After balloon dilation and the placement of a 30 F working sheath, a wire should be secured down the ureter under direct vision using a rigid nephroscope or a flexible nephroscope if necessary.

Postoperative follow-up

Once the PCNL is terminated and if an upper pole puncture was performed, intraoperative fluoroscopy should be performed to rule out hydropneumothorax and/or significant pulmonary effusions. This is done so that they can be treated while the patient is still under anesthetic sedation. If intraoperative fluoroscopy is normal, then a formal chest x-ray should only be performed if the patient becomes symptomatic [9].

Following the initial percutaneous access and removal of renal calculi, it is the authors' belief that all patients should undergo a noncontrast CT scan of the abdomen. This is used not only to identify possible residual calculi but also to look for any unforeseen complications such as pulmonary effusion or renal hematoma formation. Gnessin et al. demonstrated that post-PCNL CT scans can be useful in diagnosing postoperative complications [10]. In this study patients undergoing post-PCNL CT scans were less likely to be readmitted because of missed complications. The CT scan should be done the day after the PCNL so that if residual calculus is found it can be treated while the patient still has percutaneous access. If the postoperative CT scan shows minimal residual calculi, the secondary PCNL can then be performed under sedation without endotracheal intubation. If, however, the CT scan shows considerable residual calculi, the secondary PCNL should then be performed with intubation. Alternatively, high-magnification intraoperative rotational fluoroscopy can be used (if available) in order to identify fragments 4 mm or greater [11]. Using this technique, fragments less than 4 mm can be missed. However, Raman et al. demonstrated that a second-look flexible nephroscopy is not cost-effective for residual fragments less than 4 mm compared to observational management [12].

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7

CHAPTER 7

Instrumentation and Surgical Technique: Tract Dilation and Endoscopes

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Percutaneous nephrolithotomy (PCNL) can be a difficult multistep procedure. Other authors in this textbook have highlighted upper tract access. In this chapter we discuss techniques of upper tract dilation and their outcomes as well as describing both rigid and flexible nephroscopes commonly used in PCNL.

Upper tract dilation

Once access to the renal collecting system has been obtained, the access tract must be dilated to allow for endoscopes and instruments to pass into the collecting system and safely remove the kidney stone. The two main categories for tract dilation are sequential dilation and balloon dilation (Table 7.1). Sequential dilation can be performed with Amplatz malleable dilators or metal coaxial dilators. Each method has its merits. In this portion of the chapter we discuss dilation of the nephrostomy tract and the various methods of achieving endoscopic access into the kidney.

Informed consent

Prior to any procedure, the patient must be made aware of all risks that they may be subject to, both common and significant. Informed consent is reviewed in Chapter 5 of this textbook. Complications that tract dilation may contribute to include hemorrhage and/or hematuria which may result in blood transfusion (5–25%), angioembolization (<1%), nephrectomy (extremely rare), collecting system perforation (up to 20%), sepsis (<5%), pleural effusion (<5%), and development of a urinoma (<1%) [1–3]. Complication rates related to dilation are discussed in detail in this chapter.

Preoperative preparation

A well-prepared surgery is a successful surgery. An approach to management of the stone must be planned prior to the operating room (OR). Key points from the history, physical examination, and preoperative imaging that are considered in planning include recognition of body habitus and skeletal deformity, positioning requirements of the patient, relative location of adjacent organs and any aberrant anatomy, the presence of renal parenchymal scarring, prior difficult tract dilations/perforations, calyceal anatomy, and the size/location of the stone burden. The planned entry calyx should be identified and the length of tract required should be measured using available preoperative radiography. The required lithotripters and endoscopes should be checked to ensure they are functioning properly and must be readily accessible during the operation. Preoperative imaging should be readily available for viewing in the operating room.

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Table 7.1 Methods of tract dilation in percutaneous nephrolithotomy.

Method	Product	Maximum diameter (mm)	Length (cm)	Comments	Advantages	Disadvantages
Balloon dilators	Cook Ultraxx™	30 F (10 mm)	10–15	20 ATM burst pressure	Radial Compressive force	Disposable Cost
	Bard X-Force™	24–30 F (8–10 mm)	15	30 ATM burst pressure	Less major perforation	Higher fail rate in scarred system
	Boston Scientific NephroMax™	30 F (10 mm)	12	17 ATM inflation pressure	Less blood loss in initial use	
Sequential dilators	Cook Amplatz renal dilator™	12–30 F (4–10 mm)	20	11-piece set, malleable	Malleable (Amplatz) Reusable (Alken)	Rigid (Alken) Disposable (Amplatz)
	Alken coaxial metal dilator™	12–36 F (4–11.3 mm)	30	4 F increments	Less ilation time (Alken) Higher success in scarred system	11-step dilation (Amplatz) Use of high axial force

Patient positioning

Most percutaneous nephrolithotomies are performed in the prone position but can also be performed in supine or decubitus positions. Positioning is dependent upon patient factors, stone factors, and surgeon comfort. All three methods are safe and efficacious. They have similar stone-free rates, complication rates, incidence of postoperative fever and blood transfusion rate with variance in operative time [4]. The specifics of each method are discussed in sections 6.3 and 6.4 of this text.

Instrumentation

Malleable sequential dilator sets

The Amplatz dilator system (Figure 7.1a,c) is a set of malleable polyurethane cylinders that can be used in a sequential fashion to gradually dilate a nephrostomy tract over a guidewire. By dilating in incremental steps, very little force is required to insert each dilator. The commonly utilized Cook™ set consists of 14 dilators. The initial three dilators consist of thinner radiopaque dilators that range from 6 F to 10 F which fit over a 0.038 inch diameter guidewire to dilate up to accommodate and place an 8 F radiopaque tetraflouroethylene (TFE) double-tapered catheter. The next set consists of 11 radiopaque tapered dilators that are passed sequentially over the 8.0 F radiopaque TFE double-tapered catheter until the target diameter of the tract is reached. Lastly, a working sheath is advanced over the target dilator that is then removed, leaving the stiff guidewire in place. Radiopaque TFE sheaths are supplied for the four largest dilators (24–30 F, 16 cm length). For obese patients a 24 cm length access sheath can be used to accommodate the extra distance to reach the kidney.

Advantages of serial dilation include tract dilation in the setting of significant perinephric or renal scarring. Disadvantages of these disposable items include the increased axial force required for tract dilation, which may result in kinking of the working guidewire or perforation of the medial wall of the renal pelvis. In addition, mobile kidneys, often seen in the setting of thin patients with minimal perinephric fat or obesity with abundant perinephric fat, can present a challenge with this technique. In an attempt to decrease operative time and cost, a single-step technique using one 28 F Amplatz dilator has been reported as safe by multiple authors [4–6].

Metal dilators

Rigid metal dilators, such as the Alken dilators, are a telescopic set of stainless steel rods that gradually increase in diameter (Figure 7.1b). Over the working guidewire, a guide rod with a blunted ball tip is passed into the collecting system. Each telescopic segment increases by 4 F until a final 30 F diameter is reached. Advantages of these reusable metal dilators include reduced cost and the potential for reduced time for tract dilation. The guide rod design reduces the potential for overinsertion of each dilator and the risk of collecting system perforation. In a paper by Ozok et al., Alken metal dilators were compared to the Amplatz serial dilation method and were found to be nearly equivalent in OR time, with a slight trend towards fewer transfusions and perforations [7]. For a full comparison of Alken versus Amplatz dilators see Table 7.3.

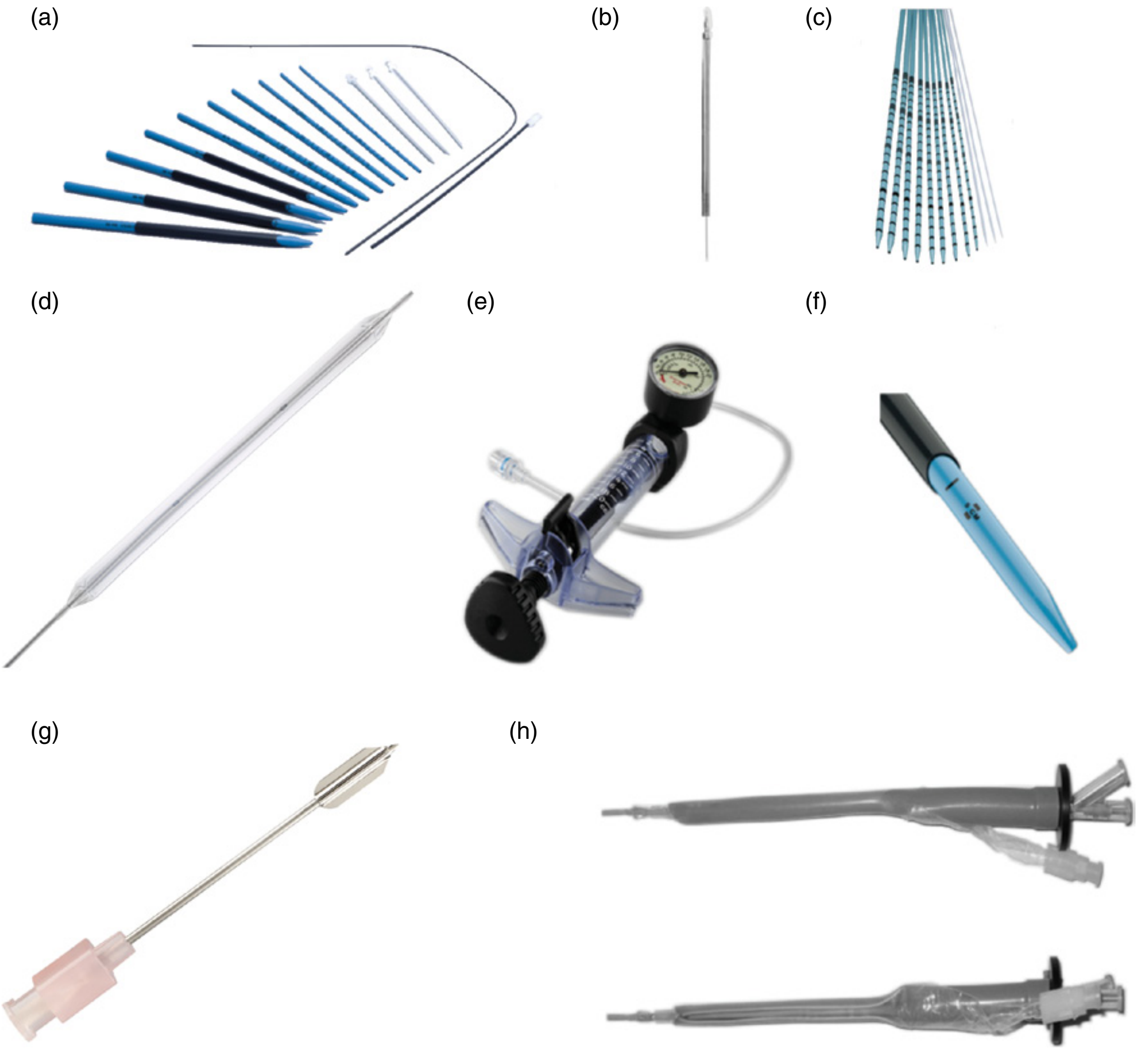

Figure 7.1 (a) Amplatz renal dilator set. (b) Telescopic metal dilator, Storz©. (c) Amplatz renal dilator set, Boston Scientific. (d) Ultraxx™ nephrostomy balloon, Cook®. (e) Nephrostomy balloon inflation device, Cook®. (f) Amplatz dilator. (g) Fascial incising needle, Cook®. (h) Radially expanding single-step access sheath dilator with access sheath (*top*) and without (*bottom*). (Parts d-f permission for use granted by Cook Medical Incorporated, Bloomington Indiana).

Balloon dilators

The single-step balloon dilator set consists of an inflation device and a nephrostomy balloon with a sheath that fits over a 0.038 inch guidewire. Balloons that are 15 cm in length range from 18 to 30 F in diameter. The ideal balloon has a short radiopaque tip so that its position within the collecting system can be confirmed prior to inflation. Opacification of the collecting system prior to balloon dilation with contrast agents is helpful. Furthermore, the balloon should be inflated with dilute contrast to ensure its visibility on fluoroscopy. Kinking or "waisting" is sometimes seen with tight fascia, scar tissue, an inadequate sized skin incision or an adjacent rib. The balloon should be inflated to the nominal pressure and to the point where there are no kinks and no pinching of the balloon. Once the balloon is straight and rigid, the access sheath should advance smoothly over the balloon until in position in the collecting system. The largest comparison of Amplatz dilation to balloon dilation comes from the Clinical Research Office of the Endourological Society

(CROES) group which reported that balloon dilation took longer and had a higher transfusion rate in the long term, but had better outcomes in initial use when compared to Amplatz [3]. Unfortunately, no comparison data on collecting system perforations were presented.

Access sheaths

Access sheaths maintain a previously dilated nephrostomy tract. The sheath protects the abdominal wall and maintains tract patency while the endoscopes are passed in and out of the collecting system. Most access sheaths are 26–30 F and can easily be back-loaded over the last dilator once the desired tract diameter is achieved. Access sheath lengths of 14–30 cm are available and are tailored to the needs of each individual case. Also, they can be made of opaque or clear material to alter the visualization in the collecting system. Most access sheaths are beveled and easily rotate to facilitate complete evaluation of the areas adjacent to the sheath tip without losing access.

Radially expanding single-step nephrostomy dilator

The radially expanding single-step nephrostomy dilator (RESN) (Figure 7.1h) is composed of four components: an 8 F woven sleeve, an inner stylet, a 30 F tapered fascial dilator, and an access sheath. After a working wire has been placed and the skin incision made, the 8 F woven sleeve and stylet are advanced under fluoroscopic guidance. The stylet is removed once the collecting system is reached. Next, the tapered fascial dilator and back-loaded access sheath are advanced through the woven sleeve to dilate the tract. The woven sleeve expands and the sheath is advanced into position and secured. The fascial dilator is then removed, allowing the passage of endoscopes. Initial studies show this method to be safe and effective [8] with the potential for decreased axial force compared to Amplatz dilation.

Pathway access sheath

The pathway access sheath (PAS) is similar to the RESN in that it allows for tract dilation and placement of the access sheath in a single step, but utilizes balloon dilation rather than a one-step tapered dilator [9]. The working sheath of the PAS sits on the outside of the noninflated balloon and following balloon inflation, the working sheath is set in place to 30 F and the balloon is then deflated and removed. It obviates the requirement for insertion and advancement of a working sheath over an inflated balloon. Pathak and Bellman were able to demonstrate that this method was significantly faster than the standard two-step technique (3 min versus 5 min 42 sec, $p < 0.01$) [9]. However, the clinical significance of this time is likely minimal. It is a promising method to decrease force on the kidney as it avoids having to advance the sheath over the balloon, which can put significant axial strain and shearing forces on the system, which is one of the major advantages of the balloon system.

Outcomes

The decision to use one tract dilation method over another takes into account surgeon preference, cost, equipment availability, and patient-specific factors, to name a few. Arguing for one technique over another remains challenging when faced with low failure rates of tract dilation and low complication rates. The most commonly analyzed parameters in studies comparing techniques include hemorrhage/transfusion rates, operating room time, renal function loss, and collecting system perforation rates, as demonstrated in Table 7.3. Unfortunately, other described complications of PCNL such as sepsis, pleural effusion, renal pseudo-aneurysm, and urinoma have rarely if ever been documented in previously reported tract dilation technique series.

Hemorrhage

Hemorrhage is a constant concern in PCNL due to both patient-specific and technical risk factors [2,10]. Controversy exists with respect to the choice of tract dilation method and the risk of hemorrhage (Table 7.2). Proponents of balloon dilation often quote the Davidoff and Bellman study that demonstrated a significant decrease in transfusion rates with balloon dilation (10%) compared to Amplatz dilation (25%) [10]. However, the multiinstitutional consortium reporting to the CROES studied the difference in operating times and bleeding complications in balloon dilation and serial dilation in over 5000 patients and found conflicting evidence. CROES reported that although the bleeding rate, transfusion rate, and operation time were greater in the serial dilation group, this was only in the initial experience and these findings were reversed after 100 cases [3] (Table 7.3). Associated variables that were significant for bleeding complications in their study

Table 7.2 Balloon dilation versus serial dilation.

Study	Dilation method	n	OR time (min)	Transfusion rates (%)	Perforations (%)
Davidoff & Bellman [10]	Amplatz	100	118 +/– 46.6	25	–
	Balloon	50	108.8 +/– 41.4	10	–
Safak et al. [11]	Amplatz	30	116.4 +/– 23.7	17	16.60
	Balloon	95	106.8 +/– 41.4	13.70	0.0
Armitage et al. [1]	Amplatz	222	–	3.2	–
	Balloon	245	–	0.8	–
Amjadi et al. [8]	Alken dilators	14	–	5.9	–
	Amplatz single step	17	–	5.9	–
Wezel et al. [12]	Alken dilators	100	100	2	5
	Balloon	100	80.5	8	14
Frattini et al. [6]	Alken	27	–	1.8	–
	Amplatz single step	26	–	0	–
	Balloon	25	–	15	–
Gönen et al. [19]	Amplatz	30		16.6	
	Balloon	43		13.7	
Yamaguchi et al. [3]	Amplatz	3260	60	4.9	–
	Balloon	2277	94	7.0	–
Ozok et al. [7]	Amplatz	67	103.3 +/– 46.5	13.4	3
	Alken dilators	121	99.1 +/– 44.4	11.6	2.5

Table 7.3 Bleeding complications and median operating times by study center volume.

		Balloon dilation (n = 2277)	Serial dilation (n = 3260)
Low volume (<25 procedures/yr)	Bleeding rate	7.9%	12.9%
	Blood transfusion rate	4.8%	8.1%
	Operating time (min)	105	108
Medium volume (25–100 procedures/yr)	Bleeding rate	8.8%	11.6%
	Blood transfusion rate	4.5%	4.5%
	Operating time (min)	98	80
High volume (>100 procedures/yr)	Bleeding rate	10.4%	3.6%
	Blood transfusion rate	10.1%	4.8%
	Operating time (min)	90	55

Adapted from Yamaguchi et al. [3].

included operating time, stone burden, anticoagulation therapy, and larger size of access sheath.

Perforation

Significant renal pelvis perforation during PCNL can occur either at the time of tract dilation or during intracorporeal lithotripsy. The most concerning time for major perforation is during aggressive dilation. Safak et al. demonstrate that the Amplatz system provides a much higher risk of medial renal pelvic perforation when compared to balloon dilation (16.6% versus 0%, n = 125) [11]. However, total perforation rate, including minor peripheral perforations, is approximately equal when other studies are taken into consideration (see Table 7.2) [7,11,12]. Renal pelvis perforation is not always reported in dilation technique papers and likely both methods are safe when used carefully.

Renal function

Tract dilation has been shown to have moderate short-term effects on renal function with minimal effect in the long term [13]. Animal studies reveal that recovery can occur as early as 72 h [13]. Clinical studies demonstrate that any initial deterioration resolves within

2 weeks and some studies found improvement in renal function immediately following the PCNL due to relief of the obstructing stone [14,15]. Interim loss of renal function was not related to balloon versus Amplatz dilation in a randomized porcine model that monitored intraoperative renal function [13]. Renal function and scarring were measured with serum creatinine and DMSA following balloon dilation, metal dilation, and Amplatz dilation and results showed no significant difference between groups with minimal change in renal function [16].

Step-by-step technique

Once the appropriate method of tract dilation has been decided upon, the same approach must be used for all, with certain key steps.

1 *Guidewires*: dilation is always performed over a guidewire. Under fluoroscopy, the guidewire should be advanced into the collecting system, and preferably down the ureter into the bladder to optimize wire stabilization. However, if this is not possible, the wire should be coiled with adequate redundancy into the renal pelvis to minimize the chance of displacement (ideally it should be as far away from the calyx of puncture as possible, i.e. the upper pole for lower pole punctures). A 0.035–0.038 inch diameter stiff guidewire functions as the working guidewire as it minimizes any bending or kinking during passage of the deflated balloon. A second safety guidewire is strongly recommended to ensure that access is not lost. This is generally an inexpensive, atraumatic guidewire that easily passes down the ureter.

2 *Incision*: once the guidewire(s) are in place, a skin incision (~1–1.5 cm) just slightly larger than the diameter of the access sheath is made adjacent to the guidewire. Care is taken to avoid cutting the wire by starting on the wire and using a scalpel to incise away from the wire. An angled tip hydrophilic catheter can be placed over the safety guidewire to minimize possible trauma to the ureter.

3 *Dilation*: once the incision is made, the dilator is advanced over the stiff guidewire under fluoroscopic guidance. With fluoroscopy, care is taken not to insert the dilator beyond the minimum necessary distance. Over advancement of the dilator can put pressure on the back wall of the collecting system and risk perforation. If serial dilation is being used, the distance that the first dilator is inserted is marked so as to not surpass this point on serial dilations. Upon inserting and removing dilators, careful attention must be paid to not displace the guidewire.

4 *Access sheath*: once the tract is dilated to its desired French size, a working sheath is placed over the dilator and the dilator is removed so that endoscopy and intracorporeal lithotripsy may begin.

Intraoperative trouble shooting

Unable to dilate

Failure to dilate a tract can be caused by scarring from prior surgery, a previous retroperitoneal process, presence of an adjacent rib, an incomplete skin incision, a mobile kidney or thick musculocutaneous fascia [17]. When difficulty with dilation occurs, it is worth ensuring that the skin incision has been made to the appropriate length and that the balloon is inflated to the nominal pressure. Next check with fluoroscopy to see if there is an adjacent rib that is blocking the route. If the rib is too close and the working sheath cannot be advanced, serial dilators may be necessary but care must be taken not to injure any subcostal nerves or arteries, or a separate puncture site may have to be chosen in a different location.

If the failure to dilate is limited by fascia, renal capsule or scarring of these layers, multiple options are available. A commonly employed method is to consider changing to another tract dilation method. Joel et al. reported a balloon dilation failure rate of 25% in the setting of prior renal surgery compared to 8% in renal units without prior surgery [17]. The authors reported that 15/16 of the failed balloon dilations were resolved by changing to Amplatz serial dilation. Other options prior to changing to another tract dilation method include passing a hemostat down the guidewire to determine the level of the resistance followed by gently dilating the tract with the hemostat. An additional method for treating resistance at the fascial level is passage of a fascial incising needle over a guidewire. The fascial incising needle is an 18 gauge, 5–10 cm long needle which fits over a 0.038 F guidewire and has a 4.5–10 mm wide, pointed tip (Figure 7.1g). It is passed over the guidewire to incise through any scar tissue, then withdrawn outside the skin, rotated 90° and then inserted again to form a cruciate incision. This should be performed under fluoroscopy with careful attention to past pointing. If these adjunct maneuvers still do not help with dilation, a new access tract or alternative approach via retrograde or open surgery may be required.

If the problem is related to soft tissue only, the balloon dilator is a very reliable method when inflated to its nominal/maximal pressure. There are only minor differences between balloon dilators from different companies. A randomized trial comparing compressive forces between balloons found that the Bard and Cook products most reliably achieved their expected diameter under a set load when compared to the Boston Scientific model [18]. This may be due to the maximal inflation pressure of 17 ATM, which is lower than the other balloons.

Perforation

Perforations are fortunately uncommon. They can be divided into peripheral calyceal perforations and perforations of the renal pelvis. Generally, the renal pelvis perforations occur at the medial wall near the ureteropelvic junction and are much more severe. Continuing with the procedure may result in exacerbating the perforation and extending the tear down to the ureteropelvic junction. Large tears mandate cessation of the procedure, especially in the setting of significant hemorrhage, prolonged procedures with the potential of excessive loss of fluid into the retroperitoneum and concern about stone extrusion through the perforation with continued lithotripsy. Postoperative renal drainage is essential with attention to ensure the stent or nephrostomy curl is away (and not outside the perforation). More minor perforations should not delay the operation and the case can proceed. The surgeon should take care not to exacerbate the perforation and again, a stent or nephrostomy tube should be placed postoperatively to optimize urine diversion and tract healing.

An ideal location for the coil of the stent or nephrostomy tube is in a peripheral calyx well away from the site of perforation. Having the stent coil sit outside the collecting system will result in failure of the collecting system to heal and increased risk of a urinoma. These stents should be repositioned under fluoroscopy with contrast to highlight the system and ensure the coil is sitting within it.

Hemorrhage

Hemorrhage can be concerning as it decreases visualization and if severe and persistent can result in hemodynamic instability. The degree of bleeding is often difficult to gauge intraoperatively due to the large amounts of irrigation required during nephroscopy. Also, bleeding can occur into either the collecting system or the retroperitoneum, the latter being more difficult to recognize. Therefore, clear communication with the anesthesiologist is essential. Often, bleeding from a friable, inflamed urothelium or minor venous bleeding from tract dilation will gradually resolve and not impair the operation. Having your access sheath fully advanced and ensuring adequate irrigation will allow the procedure to proceed safely.

More significant venous bleeding can impair visualization and result in significant blood loss causing hemodynamic instability and requiring transfusion if not addressed. The reduced visualization can result in cessation of the procedure and require a nephrostomy tube. Manual pressure on the flank for 5–15 min with clamping of the nephrostomy tube will tamponade moderate venous bleeding. Additional measures to control significant bleeding include reinsertion and inflation of the balloon dilator, use of a clamped malecot or Councill catheter, or a tamponade balloon (e.g. Kaye tamponade balloon™, Cook). Interventional radiology should be contacted if bleeding persists or if features of an arterial bleed become more apparent.

Arterial bleeding can be significant and is indicated by pulsatile bleeding, bright red color or failure to respond to the above standard techniques to tamponade bleeding. Urgent renal angiography and selective embolization follow these temporizing measures. Although surgical repair is described as an option for management of post-PCNL arterial bleeding, this would be limited to patients who are too unstable to transfer to interventional radiology, transfers between hospitals or failure of multiple embolization procedures to control ongoing bleeding.

Loss of access

The presence of a safety wire in every case remains the best security measure to prevent this unfortunate event. A much more common and simple problem is access sheath displacement. Direct visualization of the guidewire will help guide the rigid nephroscope back towards the access site into the collecting system. The sheath can then be advanced over the nephroscope back into the collecting system. Failure of this technique may necessitate redilating the tract over the safety guidewire and reinserting the access sheath.

If a safety wire was not used or became dislodged and there is no remaining access to the collecting system, repeating the access will likely be required (see Chapter 6). Once access has been regained, we suggest placing a safety wire prior to dilation to avoid repeating this complication.

Balloon malfunction

Although a rare occurrence, causes of balloon malfunction include overinflation or accidental iatrogenic puncture during insertion. If this occurs, manufacturers suggest removing the damaged balloon catheter and using a new balloon or switching to a different method of tract dilation. Care must be taken not to inflate over the maximal rated burst pressure of each balloon as this can cause damage to the parenchyma along the tract.

Endoscopes

Rigid endoscopes

Differences in rigid nephroscopes revolve around scope diameter, scope length, size of working channel, advances in optics, and the option of an offset eyepiece with an end-on working channel to allow passage of rigid instruments (Figure 7.2a). Rigid nephroscopes use a series of lenses along the tunnel to relay an image to the eyepiece where it is magnified. Rigid nephroscopes most commonly employ a direct vision, 0° lens. Magnification depends on the diameter of the distal end-viewing lens. As a result, rigid endoscopes that are a larger French size provide superior optics over smaller diameter French endoscopes or semi-rigid/flexible fibrotic endoscopes. Some newer rigid nephroscopes have fibrotic vision with comparable visualization.

Rigid nephroscopes usually have either a right-angle offset position of the eyepiece or a 30° angled eyepiece (Figure 7.2b). This allows for a working channel that is straight, as opposed to the angled ports seen more commonly in cystoscopes. The straight access sheath allows for passage of rigid lithotripters and graspers. Video cameras and monitors optimize visualization by magnifying the image and providing binocular vision, allowing the surgeon to work in a more ergonomic position. Furthermore, a monitor allows the assistant to anticipate steps and increases teaching opportunities.

Unfortunately, if the nephroscope is torqued, the image may become fragmented from the lens-mirror system losing alignment. Now, flexible fiberoptics is implemented in flexible and semi-rigid endoscopes.

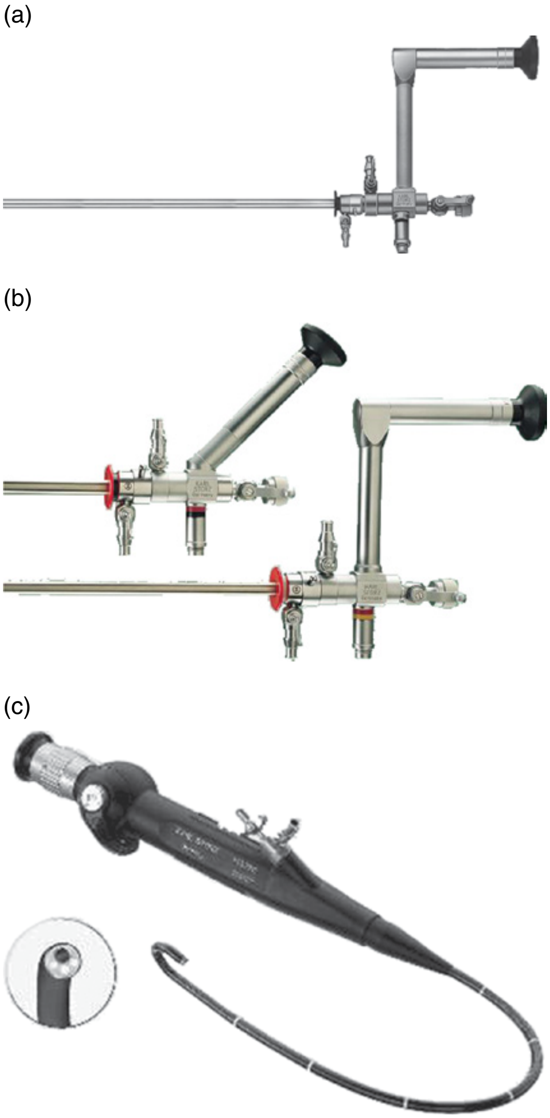

Figure 7.2 (a) Rigid nephrosocope (15 cm long, 17 F sheath size, 10.6 F working channel and 0° angle of view), Storz©. (b) Comparison of rigid nephroscopes: (*top*) wide-angle straight forward telescope with angled eyepiece, (*bottom*) wide-angle straight forward telescope with parallel eye piece, Storz©. (c) Flexible nephroscope (37 cm long, 16 F sheath size, 6.5 F working channel, 120° deflection and 0° angle of view), Storz©.

Flexible endoscopes

Flexible endoscopes (see Figure 7.2c) implement fiberoptic technology to transmit light in a nonlinear plane. Each scope uses three flexible fiberoptic bundles:

two bundles transmit light along with a solitary, glass imaging bundle. Each bundle is composed of thousands of fibers and the final image is a composite of images from the individual fibers. This reconstructed image can give a "honeycomb" appearance that has a decreased resolution when compared to a rigid endoscope.

Flexible endoscopes have the ability to flex in two directions at one or two positions (two points of flex give an S-curve). There is a sequence of pulleys and cables that stem from the tip and are attached to a working lever in the handle. Rotation of the handpiece allows for movement of the viewing lens in planes not amenable to the deflection applied by the pulley system. The fibers are pliable and can bend to a certain extent. However, there is a point at which excessive curvature results in fracture of the light fibers. The point of fracture is dependent upon the quality of fibers and their diameter, which vary among endoscopes. Since there are thousands of fibers, damage to one fiber does not affect the image. However, many fractured fibers caused by wear on the scope do result in distortion of the final image.

The working channels of flexible endoscopes are approximately 7 F and allow for simultaneous irrigation and passage of guidewires, flexible lithotripters (electrohydraulic or laser fibers), graspers, and basket extractors. The maximum size of instruments is approximately 5 F to allow for irrigation while an instrument is loaded.

Digital imaging is increasingly popular in flexible scopes. This involves an electronic charged couple device (CCD) or complementary metal oxide semi-conductor (CMOS) which relays a digital image from the distal viewing piece of the scope through a single, pliant fiber to the monitor. This allows for a lighter handpiece, fewer cables (only one digital cable as opposed to separate camera and light cables), and better optics. The durability of these in the real world is currently under investigation.

Conclusion

There are many techniques that can be used to dilate a tract for PCNL. They are safe and effective when used carefully and properly. There are multiple indications in addition to surgeon comfort for each method. Complications can occur as with any branch of surgery but the risks can be reduced with the proper selection and careful execution of each method.

Acknowledgment

Thank you to Olga Arsovska for her help on this chapter.

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8

CHAPTER 8

Instrumentation and Surgical Technique: Intracorporeal Lithotrites

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Introduction

Percutaneous nephrolithotomy (PCNL) was first described by Fernström and Johansson in 1976 when they successfully extracted a stone from the kidney. Since then it has developed into a highly effective method for the treatment of large stones in the renal collecting system, with a low overall complication rate due to continual refinements in both the surgical technique and the equipment used [1]. While some stones may be small enough to remove with a simple grasping forceps, many stones treated percutaneously are not. Therefore, one of the most critical steps of the procedure is the effective fragmentation and evacuation of the target stones using intracorporeal lithotripters. Whether the PCNL is performed prone, supine or in another modified position, effective intracorporeal lithotripters are needed.

Intracorporeal lithotrites can be broadly separated into two categories, rigid and flexible. Rigid lithotrites include the ultrasonic and pneumatic devices, whereas the flexible lithotrites include electrohydraulic (EHL) and the holmium:YAG (yttrium-aluminum-garnet) laser. Ultrasonic and pneumatic (rigid) lithotrites are typically used to fragment the majority of the stones during PCNL, whereas the flexible lithotrites are reserved for stones that lie outside the linear path of the rigid instruments. Utilizing the less efficient but flexible lithotrites avoids the need to create additional percutaneous tracts to access stray stones [2]. The rigid lithotrites all have a handpiece that generates the energy, and a probe to deliver the energy and fragment the stone when direct contact occurs.

Pneumatic lithotripters

A pneumatic lithotrite uses ballistic energy to propel a rigid, solid probe that contacts the target, leading to mechanical fragmentation similar to a pneumatic jackhammer. The controlled bursts of compressed air are generated either from a main clean air line in the hospital or from portable compressed air tanks, and transferred to the handpiece. A foot pedal is used to trigger the device and subsequently propel the probe. Advantages of this method include a decreased risk of thermal injury to the urothelium, since no heat is generated, and a low risk of ureteral perforation even with prolonged contact. For optimal usage, the stones should be pinned down against the urothelium to limit movement of the stone away from the probe. The disadvantages of pneumatic lithotripters include a relatively high rate of retropulsion, and like the ultrasonic lithotrite, the rigid nature of the technology requires direct visualization of the stone through a straight working channel. Unlike the ultrasonic lithotrite which

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

has the option of suction irrigation, after pneumatic lithotripsy the stone fragments have to be removed separately. This can be done by using a grasping forceps or by switching to ultrasonic lithotripsy with suction [3].

Swiss LithoClast®

The Swiss LithoClast (EMS, Nyon, Switzerland) is a pneumatic lithotripter that may be used with a variety of rigid probes ranging in size from 0.8 to 3.0 mm. Probe size is selected based on the working channel size of the endoscope and the size of the stone target. The device is activated by the foot pedal once direct contact with the stone is achieved. Short bursts are used to fragment the stone. Care should be taken to limit contact with the urothelium despite the large margin of safety with this device. Denstedt and associates demonstrated in a study using female Duroc-Hampshire pigs that even with direct contact of the bladder and ureteral urothelium with the activated probe, there was no extravasation on retrograde pyeloureterography. Focal hemorrhage and edema were, however, noted. This appeared to be self-limited as at 6 weeks post procedure histological analysis revealed no evidence of fibrosis [4]. In a subsequent clinical study, Yinghao and associates reported outcomes in 145 patients who had ureteral stones treated with the Swiss LithoClast. They reported five perforations in these 145 cases, suggesting that extreme care must be used with this device [5].

In an effort to improve the versatility of the Swiss LithoClast, the Lithovac® (EMS, Nyon, Switzerland) was developed. To improve efficiency, this device allowed for suction with the goal of reducing stone migration and increasing contact time with the stone. Haupt reported the ability to remove fragments up to 2 mm in size with the probe in place and up to 3.5 mm in size with the probe removed [6]. However, clinical studies revealed that the device was subject to clogging which ultimately limited its effectiveness and adoption [7].

Cook LMA StoneBreaker®

The Cook LMA StoneBreaker (Cook Medical, Bloomington, IN) is a self-contained portable pneumatic lithotripter. It has a small cartridge of high-pressure carbon dioxide gas which serves as the compressed air source. It does not require an electrical source but is limited to around 80–100 shocks per cartridge. Given that the device does not require a central source of compressed air and has no electrical connections, it is highly portable [8]. It also functions well as a potential back-up device for use if the surgeon’s primary lithotrite were to fail. Initial reports demonstrated that the StoneBreaker was safe and effective for use in the ureter with high fragmentation rates and no reported urothelial trauma [9]. A more recent study randomized patients undergoing PCNL to either the StoneBreaker or the Swiss LithoClast. Although ballistic lithotrites were used to fragment the stones, a grasper or an ultrasonic lithotripter was used to clear the fragments. The study concluded that the StoneBreaker had faster stone fragmentation time, reduced lithotripsy time, and lower set-up time compared to the Swiss LithoClast. Stone-free rates, device-related failures, and damage to the mucosa were similar between the two groups, suggesting that the StoneBreaker is a viable alternative to the Swiss LithoClast [10].

Swiss LithoBreaker®

An alternative to the gas cartridge-powered impulse generation used in the StoneBreaker is to employ electromechanical impulse generation. EMS recently introduced the Swiss LithoBreaker (EMS, Nyon, Switzerland), which uses rechargeable batteries to provide power. This device works on a similar principle to the pneumatic devices but is entirely powered by batteries, providing additional portability and maneuverability as well as decreasing running costs. It is anticipated that the device will deliver significantly more impulses before exhaustion of the batteries compared to the LMA StoneBreaker and its replaceable carbon dioxide cartridges. Future studies comparing the two devices are required to determine their relative efficacy.

Ultrasonic lithotripters

Karl Storz Endoscopy of Tuttlingen, Germany, developed the “Aachen model” that formed the basis for current ultrasonic lithotripters. While the technology has been refined since the early devices were developed, the principles remain the same; a current is passed through the piezoceramic crystals which convert the electric energy into mechanical energy to generate ultrasonic waves. The waves are of an acoustic frequency that is above the threshold of human hearing. These acoustic waves travel from the handpiece through the probe to vibrate the tip, which in turn comes into contact with the stone and causes mechanical fragmentation. Direct contact with the stone is needed for this to occur. Fragmentation does not occur secondary to heat or shock wave generation. The ultrasound probe has a hollow lumen which not only allows suction aspiration of the stone fragments, but the evacuated fluid also cools the piezoceramic crystals as it runs through the handpiece, providing optimum operating temperatures [3]. Probes are available in a variety of sizes ranging from 2.5 F to 6.0 F. The smallest probes do not have a central lumen and thus do not allow for suction evacuation of fragments.

Several animal studies have tested the safety of ultrasonic lithotripsy. Terhorst evaluated this by applying the activated probe directly on the urothelium of rabbit bladders and determined that only edema of the mucosa occurred. Similarly, testing in a canine model revealed minimal histological changes with direct contact [11]. However, if the device malfunctioned and the continuous suction irrigation failed, then the probe may overheat and cause thermal damage to the tissue. Therefore, operating room staff should regularly monitor that the suction is operating adequately and alert the surgeon to any problems.

Ultrasonic lithotripters require solid contact with the target stone to work effectively. Stones generally need to be pinned down or held in place during contact to maximize efficiency, although smaller fragments may be successfully held against the tip of the probe with suction alone. For harder stones, such as calcium oxalate monohydrate and calcium phosphate brushite, we typically fragment the stone into pieces that are just small enough to fit through our nephroscope sheath and then remove them with a two-prong grasping forceps. For softer stones, such as magnesium ammonium phosphate, we tend to clear the bulk of the stone entirely with the ultrasonic device, relying on the suction to evacuate all the small fragments. It is important to keep the device activated with the suction on as much as possible near the stone to maintain negative pressure and reduce the risk of stone migration.

Dual ultrasonic and ballistic lithotripters

One of the more recent developments in intracorporeal lithotripsy for percutaneous stone surgery has been the advent of dual-modality lithotripters. These are a combination of a traditional ultrasonic component coupled with a ballistic component. The goal of these devices is to gain the benefits of both devices in one design and therefore improve the efficiency of stone fragmentation and clearance.

Figure 8.1 The Gyrus ACMI CyberWand generator. Two attachments are seen, one for the foot pedal and another for the handpiece.

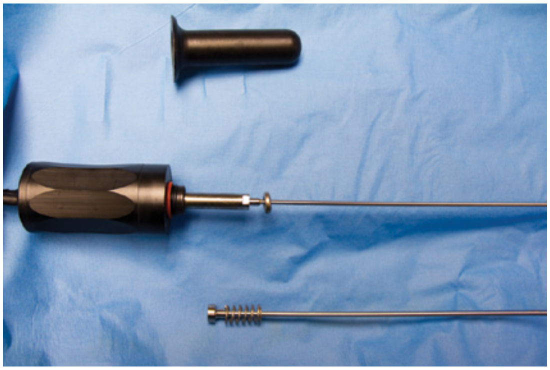

Figure 8.2 Components of the CyberWand handpiece. The inner probe with the free ring is attached to the handle. The outer probe with the spring is shown unattached below.

CyberWand®

The CyberWand (Gyrus ACMI, Southborough, MA) (Figure 8.1) is a dual ultrasonic and ballistic intracorporeal lithotripter that contains two probes (Figure 8.2). The inner probe vibrates at 21,000 Hz and has a hollow central lumen for suction. It functions similarly to a traditional single probe ultrasonic lithotripter. It also has a second outer probe that is set back about 1 mm from the tip of the inner probe (Figure 8.3). The outer probe can be activated separately and vibrates at a much slower rate,

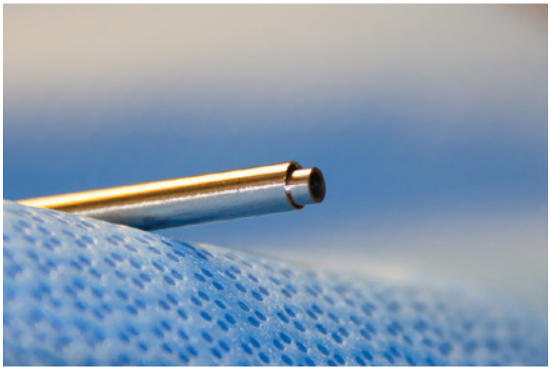

Figure 8.3 The contact points of the outer and inner probes of the CyberWand handpiece are seen here. The outer probe is set back roughly 1 mm from the inner probe, allowing the inner ultrasound probe to make maximal contact with the stone.

Figure 8.4 The CyberWand's foot pedal system. The pedal on the left activates only the inner ultrasonic probe (small stone). The pedal on the right activates both the inner and outer probes (large stone).

approximately 1000 Hz, and creates a ballistic motion that strikes the stone, causing mechanical fragmentation [3,8]. The foot controller for the CyberWand has two pedals. One activates only the inner ultrasound probe, whereas the other activates both the inner and outer probes (Figure 8.4). The inner probe is connected directly inline to the suction tube, facilitating removal of stone fragments. Due to the rigid probe design, direct inline contact must be made with the stone for fragmentation to occur.

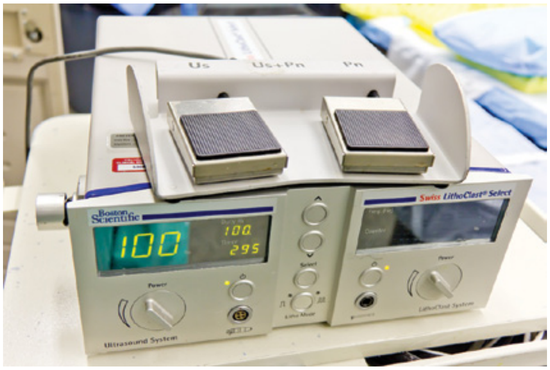

Figure 8.5 Swiss LithoClast Select. As printed on the foot pedal, the surgeon has the ability to selectively activate both the ultrasound (Us) and pneumatic (Pn) modalities.

Figure 8.6 The Swiss LithoClast Select handpiece.

Lithoclast Master/Select®

The Lithoclast Master (EMS, Nyon, Switzerland) (in North America, Lithoclast Ultra/Select [Boston Scientific, Natick, MA]) (Figures 8.5, 8.6) is a combination ultrasonic and pneumatic lithotripter. The two modalities may be used in tandem or activated independently. A dual foot pedal allows for individual control of both the ultrasonic and pneumatic components. When set up in dual-modality mode, the pneumatic probe runs through the hollow lumen of the ultrasonic probe, allowing both modalities to contact the target. The tip of the pneumatic probe is positioned just short of the end of the ultrasonic probe. This allows for the ultrasound probe to make good initial contact with the stone. When the pneumatic probe is activated, the tip projects out past the ultrasound probe and drills into the stone, resulting in mechanical fragmentation. It then retracts back to allow for maximum ultrasound contact with the target. The pneumatic frequency can be adjusted from 2 to 12 Hz. The operator can also remove the pneumatic portion and convert the device to a pure ultrasonic lithotripter.

A recent redesign of the handpiece, now called the "Vario" handpiece, improved on the design of the suction channel and the piezoceramic crystals. The previous model had the suction port coming off the handpiece at a 90° angle which resulted in frequent clogging. The Vario handpiece has less of an acute angle to prevent obstruction. The suction channel operates in a straight configuration in "pure" ultrasound and at a 45° angle in combination ultrasonic/pneumatic modes. The Vario handpiece also underwent a change to the tuning of the transducer frequency. The frequency was changed from 23.2 to 26.4 kHz in an effort to improve power output with the goal of less heat build-up and longer probe life [3].

Several studies have tested the performance of this dual ultrasonic/pneumatic device. In a bench study using model stones, Hofmann and associates determined that using the lithotripter in combination ultrasonic/pneumatic modes resulted in a 25–200-fold shorter fragmentation time than using the modalities individually. Furthermore, the time to reach disintegration of 50% of the stone burden was reduced nearly in half [12]. In another study using Bego stone phantoms, Auge and associates demonstrated that combination ultrasonic/pneumatic lithotripsy was significantly more effective for both fragmentation and stone clearance than ultrasonic or pneumatic lithotripsy used alone. The fragment sizes generated in combination mode were also smaller than when used in single-modality modes [13].

Several clinical trials have validated the results of the initial bench studies. Hofmann and associates reported their experience during 68 procedures, which included 35 complete staghorn stones. They reported a 66% stone-free rate after the first session but did note two collecting system perforations thought to be secondary to the lithotripsy probe [12]. Another study performed by Pietrow and associates randomized 20 patients undergoing PCNL to either ultrasonic or combination ultrasonic/pneumatic lithotripsy. While the procedure was deemed successful in both arms, the time to complete stone fragmentation and extraction was approximately 50% less in the combination arm. No significant complications were reported in either arm and at 3-month follow-up the stone-free rate was similar between the two groups. The primary advantage of the combination mode was the increased rate of stone fragmentation and clearance [14].

In another clinical trial, 30 patients undergoing PCNL were randomized to either combination ultrasonic/pneumatic lithotripsy or pure ultrasonic lithotripsy. Lehman and associates concluded that the combination mode was faster for fragmentation of hard stones (calcium oxalate monohydrate, calcium phosphate, cystine) but slower for softer stones. Stone retrieval times, mean operating time, mechanical failure rate, and blood loss were similar between the two groups [15]. The faster clearance time in the pure ultrasonic arm may be related to the larger suction channel that is created by removing the pneumatic probe. This allows for more rapid clearance of the soft stone based on Poiseuille's Law for laminar flow where the flow rate is proportional to four times the power of the radius.

Several authors have reported on how different settings and techniques used with the Lithoclast Master can change its performance characteristics. Kuo and associates in an *in vitro* study evaluated different pneumatic (1, 4, 8, and 12 Hz) and ultrasonic (40%, 70%, and 100%) settings and their impact on penetration into a U-30 gypsum stone phantom. They determined that the fastest penetration was achieved with the maximum setting of 12 Hz for the pneumatic probe and 100% power for the ultrasound. At maximum settings, it was determined that 79% of the penetration was achieved from the pneumatic component [16]. In another *in vitro* study, Goldman and associates evaluated the effect of both probe pressure and rotation on the efficiency of the Lithoclast Master. They determined that in pure ultrasound mode, a pressure of 1000 g, versus 400 g and 2000 g, with 90° of rotation resulted in maximum efficiency with this device. Similarly, in dual ultrasonic/pneumatic mode, 1000 g of pressure produced the best results. Interestingly, pneumatic frequencies of 6 Hz and 12 Hz performed similarly, but both outperformed the 3 Hz setting. Of note, the pure ultrasound mode with 1000 g of pressure and 90° of rotation at 2 Hz outperformed all settings tested for the dual ultrasonic/pneumatic modes [17].

Comparison of ultrasonic lithotripters

In 2001 Liatsikos and associates, in an *in vitro* study, compared a series of commercially available ultrasonic lithotripters including the ACMI USL 2000, Storz Calcuson 27610020, Wolf 2270004, and Olympus LUS (LUS-1) [18]. Plaster of Paris stone phantoms of different hardness were utilized for the testing. The Storz Calcuson tested with the best efficiency and had the fastest time to complete fragmentation. The Wolf, ACMI USL, and Olympus LUS were the second, third, and fourth best performers. The Olympus LUS suffered from several technical problems including overheating of the probe and incomplete stone fragmentation and has subsequently been replaced by the newer LUS-2.

In another *in vitro* study, Haupt and Haupt evaluated a series of ultrasonic lithotripters where the penetration ability of the probes was evaluated with a fixed weight of 300 g on the handpiece [19]. The Storz 27085k, Wolf 2167.01, ACMI USL 2000, and a prototype EMS design were tested. The EMS ultrasonic lithotripter demonstrated statistically significantly the best overall performance for all stone compositions tested with the exception of the very soft Moldablaster stone phantoms, where all devices performed equally [19].

In a similar study using a fixed weight to apply pressure to the handpiece, Kuo and associates used Ultracal-30 gypsum cement stone phantoms to test the Olympus LUS-1, Olympus LUS-2, ACMI USL 2000, Storz Calculus, and Wolf 2271.004 ultrasonic lithotripters [16]. The primary outcome measure was the time required for the probe tip to drill through the stone phantom. The Olympus LUS-2 had the fastest time recorded but was not statistically significantly faster than the ACMI USL 2000. The Storz Calculus, Olympus LUS-1, and Wolf 2271.004 were all less efficient in that order.

Comparison of Lithoclast Master and CyberWand

Kim and associates compared the performance of the Lithoclast Master (prior to the introduction of the second-generation Vario handpiece) with the CyberWand [20]. Using a fixed weight test set-up with gypsum stones, they determined that the CyberWand outperformed the Lithoclast Master with a mean fragmentation time of 4.8 versus 8.1 sec when averaged over 10 trials. In a related study, Goldman and colleagues determined that the CyberWand more rapidly removed stone mass compared to the Lithoclast Master [17]. Louie and associates evaluated the Lithoclast Master with the second-generation Vario handpiece and the CyberWand in a cystolithopaxy model [21]. Both harder Bego and softer U-30 stone phantoms were tested. A single surgeon was tasked with both fragmenting the stone phantom and then clearing all the fragments using the suction channel of the probes. For the softer U-30 stones, the CyberWand, operated in dual ultrasonic and ballistic (large stone setting) mode, was significantly faster than the Lithoclast Master. For the harder Bego stone phantoms, the CyberWand did not perform well and suffered from multiple probe failures and was not able to fragment and clear all the stone. The Lithoclast Master was able to clear the stone and was therefore the better performing device. A subsequent redesign of the CyberWand probe has since occurred but has not been tested with this set-up to date.

In a clinical study, Lehman and associates compared the Olympus LUS-1 with the Lithoclast Master in a prospective randomized trial of 30 patients undergoing PCNL [15]. The Lithoclast Master was more efficient for harder calcium oxalate monohydrate and calcium phosphate stones, while the Olympus LUS-1 was more efficient for the softer struvite and uric acid stones. The larger suction channel of the LUS-1 may have allowed it to clear the stone more efficiently. The LUS-1 had device-related problems in 47% of the procedures versus only 23.1% with the Lithoclast Master.

Krambeck and associates compared the CyberWand to the Olympus LUS-2 in a randomized, controlled, multicenter clinical trial [22]. The primary outcome was the time to total removal of the targeted stone and was not statistically significantly different between the two groups. The stone-free rates were also similar between the two groups (CyberWand 60.0%, LUS-2 62.1%). The device malfunction rate was higher in the CyberWand (32.0%) compared to the LUS-2 group (15.6%). Since the study was completed, a revised CyberWand probe design has been introduced.

Currently we utilize both the CyberWand and the Lithoclast Select (Lithoclast Master with second-generation Vario handpiece) for PCNL. For these procedures, we start with the Lithoclast Select in pure ultrasound-only mode and do not initially load the pneumatic probe. With the Vario handpiece, we have found that most stones can be easily fragmented with just the ultrasound used alone. By not employing the pneumatic probe, the size of suction channel is maximized, leading to rapid clearance of the stone fragments through the hollow lumen. It is vital that the suction be running continuously when the probe is activated. This limits the migration of fragments, cools the handpiece, and keeps the piezoelectric crystals performing in their optimal temperature range. If the stone is very large and resistant to ultrasonic fragmentation, then the pneumatic probe is loaded. We recommend running the pneumatic probe at a low frequency (2–4 Hz) so that it simply provides assistance to the fragmentation process and still allows the ultrasound to make contact with the stone. Running the pneumatic at a higher frequency will result in a primary pneumatic effect with limited impact by the ultrasound. Once the stone has been adequately fragmented, the pieces can either be cleared with a grasping forceps or suction evacuated. If suction evacuation is chosen, then the pneumatic probe should first be removed to maximize the suction channel.

When we utilize the CyberWand, our technique is slightly different. The smaller lumen of the ultrasound probe does not appear to clear fragments as quickly and is subject to clogging, as noted by Krambeck and associates in their clinical trial [22]. Therefore, we typically run it in dual ultrasonic/ballistic mode (large stone setting) and quickly fragment the stones in pieces just small enough to fit through the 30 F nephrostomy sheath. The fragments are then systematically cleared with a two-prong grasping forceps.

Occupational noise exposure

The CyberWand, when in the dual mode with both the inner ultrasonic and outer ballistic probes activated, has been noted to be quite loud. This led to a study investigating the risk of occupational noise exposure during endourological procedures. The CyberWand was compared to a standard single-probe ultrasonic lithotripter, the Olympus LUS-2. The noise level generated by the CyberWand was 93 dB (range 85–102) and the Olympus LUS-2 was 65 dB (range 62–68). Hearing protection would be recommended with the CyberWand based on US Department of Labor Occupational Health and Safety Administration (OHSA) and Canadian Centre for Occupational Health (CCOH) recommendations if the device were used in dual mode for greater than 90 min a day to prevent hearing loss [23].

Electrohydraulic lithotripter

The electrohydraulic lithotripter (EHL) was the first intracorporeal lithotrite used to fragment kidney stones, introduced in 1975. An electric current is passed between two electrodes separated by an area of insulation, creating a spark. The spark in turn causes vaporization of water surrounding the electrode, creating a cavitation bubble that creates a shock wave during expansion. This shock wave is not focused and as such the stone must be placed with precision at the location of the shock wave [24]. Unlike the ultrasonic and pneumatic lithotrites, the EHL is very flexible and can be used to perform intracorporeal lithotripsy throughout the urinary system with a flexible or rigid cystoscope, ureteroscope or nephroscope (Figures 8.7, 8.8).

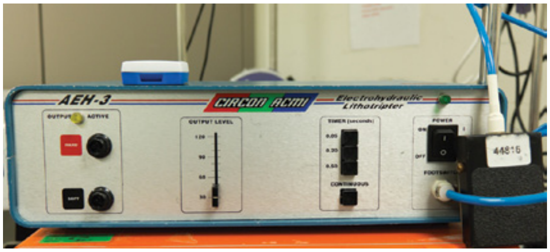

Figure 8.7 Example of an EHL lithotripter, the Circon ACMI AEH-3 with foot pedal.

Figure 8.8 Another example of an EHL lithotripter, the Wolf 2137.50.

However, since the introduction of the holmium: YAG (yttrium-aluminum-garnet) laser, the role of the EHL has been marginalized as it is not as versatile as the holmium:YAG laser. While the holmium:YAG laser can fragment stones of all composition, the EHL can have difficulty fragmenting very hard stones such as calcium oxalate monohydrate [25, 26]. Perhaps the biggest disadvantage of the EHL is its capacity to damage the urothelium [27], with the proposed mechanism relating to damage caused by the rapidly expanding cavitation bubble.

We currently limit the use of the EHL during PCNL to stones in the kidney that cannot be reached with a flexible nephroscope and either a tipless nitinol stone basket or a holmium:YAG laser optical fiber. In this situation we employ a 1.9 F flexible EHL probe and activate it near the stone at the lowest energy settings, taking care not to place the probe near the urothelium. The cavitation bubble may either fragment the stone or displace it to a location that can then be reached with the stone basket. We discourage use of the EHL in the confined space of the ureter.

Holmium:YAG laser

The holmium:YAG laser is the most commonly used intracorporeal lithotripter at the present time and has displaced other modalities of lithotripsy during retrograde procedures [28]. The photothermal mechanism of this laser vaporizes the crystalline matrix of all compositions of kidney stones, including hard cystine and calcium oxalate monohydrate stones [29–31]. The laser is used primarily to treat stones after access to the urinary system is obtained endoscopically in a retrograde fashion (cystoscopy and ureteroscopy). Its main function during PCNL is to treat stone fragments that cannot be reached with a rigid nephroscope, such as when they are in the calyx parallel to the access track or when they are lodged in the upper ureter. The laser optical fiber can easily be passed through the working channel of a flexible nephroscope and still allow for deflection and irrigation. The advantage of laser over EHL is its decreased rate of retropulsion and its capacity to be absorbed by water within a few millimeters of the fiber, leading to minimal tissue penetration and a wide margin of safety [32]. The main variability with the laser is the fiber size, which ranges in core sizes from 150 to 1000 μm, with somewhat larger total diameters (Figure 8.9) [33]. Smaller fibers are typically more flexible and also provide better irrigation flow, but they may not be as robust and are more prone to fiber tip degradation [34]. Larger fibers are typically more robust but are less flexible and may place more strain on the delicate flexible endoscopes. The larger diameter will also reduce flow based on Poiseuille's Law.

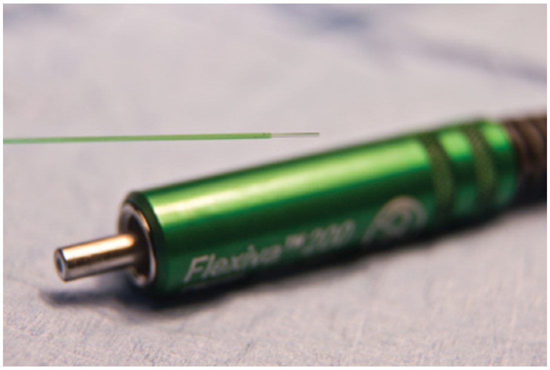

Figure 8.9 The main variability with the laser is the fiber size, which ranges in core size from 150 to 1000 μm. Shown here is the connecter and optical tip of a 240 μm laser fiber.

While not our primary lithotripter for PCNL cases, we always ensure that the holmium:YAG laser is available for all cases. As discussed, it may be employed to reach stones in an adjacent calyx that the rigid scope cannot enter, but may also be utilized to fragment stones that have migrated during the procedure such as down the ureter.

Intraoperative trouble-shooting for rigid intracorporeal lithotripters

Several common problems may occur with ultrasonic and dual ultrasonic pneumatic lithotripters. The most common reason for failure is that the probe is not secured tightly to the handpiece and the probe fails to resonate when the piezoelectric crystal is activated. Keeping a probe wrench sterile and on the operating field allows the surgeon or their assistant to quickly tighten the probe if it was either not set up properly or became loose during the procedure.

Fragment migration can be a problem if the suction tubing is not correctly connected or if the suction device is not turned on. The surgeon should check that the suction is functioning well prior to initiating fragmentation of the stone, to limit fragment migration. The surgeon should also periodically check that the suction is continuing to flow well during the procedure, as suction failure can also lead to probe overheating, decreased efficiency and possibly premature handpiece failure. Poor suction can also lead to an increased rate of clogging of the ultrasound. Clogging may occur in the probe, the handpiece, the suction tubing or the canister. Handpieces where the suction connects at a 90° angle are particularly prone to clogging and should be checked when suction pressure is reduced.

Most probes have a limited lifespan. The number of uses should be tracked and the probes disposed of once the upper limit has been reached. Failure to do so may lead to a higher rate of intraoperative probe failures.

Conclusion

Both rigid and flexible intracorporeal lithotripters are essential devices needed to perform successful percutaneous stone surgery. The new generation of dual-mode ultrasonic/ballistic lithotripters gives the surgeon powerful and efficient tools to fragment and clear the stone burden rapidly. The holmium:YAG laser remains the flexible intracorporeal lithotripter of choice based on its ability to fragment stones of all compositions and its wide margin of safety.

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9

CHAPTER 9

Instrumentation and Surgical Technique: Step-by-Step Percutaneous Nephrolithotomy: Prone

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Introduction

Percutaneous access for removing renal stones was first performed by Fernström and Johannson in 1976 [1]. Since its initial description, advances in endoscopy, fluoroscopy, and intracorporeal instrumentation have established prone percutaneous nephrolithotomy (PCNL) as the first-line therapy for staghorn calculi and complex stones [2]. No other position for PCNL has been more extensively reviewed. Choosing the optimal access site is the first critical step in performing the procedure safely and efficaciously. All strategies should maximize the use of rigid instruments, minimize morbidity, and allow for any adjunctive procedures when necessary. This chapter will address the preoperative planning, the intraoperative instrumentation, and techniques of prone PCNL, and postoperative management of these patients in a stepwise fashion.

Informed consent

Over the last three decades, the role of PCNL in the treatment of complex calculi has expanded (Box 9.1). In 2005, the American Urological Association Nephrolithiasis Clinical Guidelines Panel reaffirmed PCNL as the gold standard in the management of staghorn calculi [3].

Informed consent for PCNL begins with a discussion regarding all associated risks, benefits, alternatives, and complications. Potential intraoperative and postoperative events should be mentioned. Common events include temporary insertion of a bladder catheter and/or ureteral stent/nephrostomy tube needing later removal, and transient hematuria. Occasional events may be multiple puncture sites and low-grade postoperative temperatures, incomplete removal of all calculi, postoperative sepsis, the need for secondary procedures, and severe kidney bleeding requiring transfusion. Rare events include embolization or nephrectomy, and injury to visceral organs including the lungs, bowel, spleen or liver. Renal insufficiency, severe infection requiring prolonged antibiotics and drainage, and absorption of irrigant causing fluid overload or metabolic derangements are also categorized as rare events. Patients should be informed that PCNL is generally an inpatient procedure, requiring a brief hospitalization of 1–3 days. Consent for possible blood transfusion should also be obtained, although the need for transfusion is uncommon (2–10%) [4].

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Box 9.1 Indications for percutaneous nephrolithotomy in the treatment of complex stones

Renal anatomy

- Lower pole calculi >1 cm
- Surgical intervention of ureteropelvic junction obstruction in setting of concomitant large or multiple calculi
- Horseshoe, pelvic, transplant kidneys
- Calculi in calyceal diverticulum

Stone characteristics

- Staghorn calculi
- Nonstaghorn renal calculi >2 cm
- Large, impacted proximal ureteral calculi
- Extracorporeal shock wave lithotripsy/ureteroscopy failures
- Calcium oxalate monohydrate, brushite, cystine stones

Preoperative preparation

Preoperative imaging of the kidneys, ureters, and bladder with plain abdominal films, intravenous pyelogram (IVP) or noncontrast computed tomography (CT) can be used to identify the number and location of stones and detail the anatomy of the collecting system. Currently, noncontrast CT is the imaging of choice not only for its sensitivity in calculi detection but also for its ability to visualize renal vascular anatomy, calyceal locations, and any visceral organs that are adjacent to the kidney. Ectopic kidneys, malrotated or fused kidneys, retrorenal colon, and splenomegaly can be easily visualized with CT and may guide intraoperative planning during PCNL. This is especially important in patients with morbid obesity or physical deformities since renal anatomy may be distorted. Since a retrograde pyelogram is typically performed at the time of surgery, a preoperative IVP is usually unnecessary. Preoperative IVP, however, can be helpful when the diagnosis of a calyceal diverticulum or ureteral stricture is in question.

Preoperative evaluation should also include routine pulmonary and cardiac evaluation for elderly patients. Prone positioning during PCNL has been associated with a decrease in cardiac index and decreased pulmonary capacity due to limited abdominal and chest wall movement [5]. However, Edgcombe et al. have reported that with proper padding, pulmonary capacity may actually be greater in the prone position than in supine [6]. Thus, minor impairment in pulmonary function does not necessarily preclude patients from prone PCNL.

As urinary calculi can contain bacteria, preoperative urinalysis and urine culture are imperative. In its best practice policy, the American Urological Association supported the use of periprocedural antimicrobial prophylaxis for all cases of percutaneous renal surgery [7]. A nonrandomized study by Darenkov et al. also demonstrated a postprocedure urinary infection rate of 40% if antimicrobial prophylaxis is not used compared with 16.7% if prophylaxis is used [8]. In situations with colonized externalized urinary catheter, nephrostomy tube or an infected calculus, it may not be possible to eradicate the infection completely before the percutaneous procedure. However, it is still critical to suppress the bacterial count before intervention. Urine cultures should be obtained in all patients. If positive, sensitivity profile should be checked, and urine culture should be treated with a 5–7-day course of appropriate antibiotics. Patients with an indwelling external tube or previous infections are treated with empirical antibiotics until the date of surgery even if cultures show mixed flora. All patients receive broad-spectrum coverage on the day of surgery tailored to the sensitivity profiles obtained preoperatively. In noninfected patients we use a combination of ampicillin/gentamicin or vancomycin/gentamicin in patients with penicillin allergy.

Patient positioning

The patient's back in the prone position provides a large surface area for multiple access sites and a stable horizontal working surface. In our hands, PCNL routinely begins with the placement of a retrograde ureteral catheter or occlusion device in supine position before placing the patient prone, although others place these in the prone position using spreader bars. Our prone position is illustrated in Figure 9.1. Frequent and judicious use of padding is important to avoid neuromusculoskeletal complications such as nerve compression or stretch injury, ocular or facial injuries, and rhabdomyolysis [9]. Secure the head in a neutral position that allows access to the mouth. We have found that a padded helmet with mirror platform (ProneView®, Union City, CA) (Figure 9.2) works best in achieving this goal. Ensure that there is not undue pressure on the facial bones, nose, and ears. Bolsters are placed from the shoulder to the iliac crest on each side to facilitate ventilation and let the

Figure 9.1 Patient positioning during prone PCNL. Bolsters are placed at the level of the shoulder and the iliac crest to facilitate ventilation and let the abdominal contents fall anteriorly. The retrograde contrast (indigo carmine is added in this case) syringe is placed at the ipsilateral side.

Figure 9.2 Padded helmet with mirror platform (ProneView®, Union City, CA) used during prone PCNL. The helmet reduces pressure on the facial bones, nose, and ears, and keeps the neck in the neutral position. The mirror platform allows anesthesiologists to easily monitor the endotracheal tube position, and may help prevent any kinking or displacement of the tube during the case.

abdominal contents fall anteriorly. When the patient is turned from the supine to the prone position, anesthesiologists should always participate in this maneuver, securing the endotracheal tube and avoiding its dislodgment. The knees, ankles, and feet are also padded, supported, and secured. Place the ipsilateral arm above the head to get it out of the operative field, with the shoulder and elbow at right angles with the use of generous padding. Position the contralateral arm in a similar fashion. Rest the lateral aspects of the chest on rolled blankets or other bulky foam or gel bolsters to allow for chest and abdominal wall expansion. Provide support under the ankles to take pressure off the feet, and pad the knees and feet. The Foley catheter is placed between the legs, and the retrograde injection syringe is placed at the side of the patient.

Prepare the ipsilateral flank in a sterile manner with cleansing alcohol followed by povidone-iodine skin or chlorhexadine gluconate scrub. We currently use an endourology drape with a plastic side pouch for the collection of irrigant fluid. Finally, hypothermia from anesthetic vasodilation, exposed body surface, and high volume of room-temperature irrigant can be prevented by placing an air warmer in contact with the patient's body surface and by using warmed saline. Be aware that prone positioning might not be possible in patients with extreme obesity or spinal deformity.

Instruments

The instruments used for percutaneous nephrolithotomy at our hospital are listed in Box 9.2. The equipment listed can be used for any stone burden, whether simple or complex, because multiple accesses can easily be performed. If multiple punctures are necessary, additional

Box 9.2 Instruments used for prone percutaneous nephrolithotomy at New York Presbyterian Hospital, Columbia University School of Medicine

Intraoperative, rotating C-arm
Lingeman PCNL drape
16 F flexible cystoscope/nephroscope
7 F flexible ureteroscope
16–24 F foley
Coaxial retrograde occlusion device
2-0 Silk suture/tie
18 gauge × 11.5 cm percutaneous access needle
22 gauge needle
Ultrasonic or pneumatic lithotrite
Holmium laser fiber (200 or 365 μ fiber)
Nitinol basket
Balloon dilator with 20 or 30 F sheath
10 F fascial dilator
15 scalpel blade
26 F (outer sheath) offset nephroscope
Heavy-duty PTFE J-tip 0.038-in × 80 cm guidewire
Amplatz super-stiff 0.038-in × 145 cm guidewire or
0.035-in × 145 cm glidewire

wires and access sheaths (20–30 F) may be needed; all other equipment can be reused throughout the procedure. Mini-PCNL, as described in the literature, does not necessarily require specialized smaller diameter equipment, but can be readily performed with current intracorporeal lithotrites. Our modified technique will be further discussed in this chapter in detail.

In the operating room, we attempt to minimize radiation exposure to the patient and surgeon. Direct and scatter radiation is absorbed by the patient, surgeon, and operating room personnel in addition to the image intensifier. Currently, our C-arm has a 9-inch image intensifier that is placed above and as close to the patient as possible, which produces good focal resolution with much less scatter radiation. In addition, during access, the needle is advanced with a hemostat clamp or needle holder to further minimize radiation exposure.

We use an 11.5 cm, 18 gauge diamond-tipped trocar needle. Longer needles have a more flexible shaft, making it harder to directly puncture the desired calyx, especially in obese patients. A beveled needle should never be used because it skives away from the intended target.

The selection of wires during PCNL is critical in achieving atraumatic access. We use an 80 cm heavy-duty J-wire that safely coils in the collecting system. We have found that the Amplatz super-stiff J-wire is too floppy for efficient manipulation. We do not necessarily attempt to guide the wire into the ureter if it is difficult to do so, but rather attempt a good position in the calyx or renal pelvis. In the setting of large stones or complex calyces, angled glidewires or a straight tip glidewire can be used to access the ureter during initial access using a Kumpe catheter as a guide when needed. The glidewire is exchanged for a Teflon-coated wire, which is a more secure working wire. A dual-lumen catheter or 8–10 coaxial set can be used to introduce a safety wire.

A complementary set of rigid nephroscopes and flexible nephroscopes aids in PCNL of kidneys with complex calyceal anatomy. We prefer to maximize the use of rigid nephroscopy, as this expedites the overall procedure. The tract is dilated to 30 F and a 26 F nephroscope is used for staghorn calculi or heavy stone burden. For children and for patients with a lower stone burden or tight calyces without hydronephrosis, a modified mini-PCNL is performed by dilating to 20 F. The same nephroscope is used but without its outer sheath. For obese patients, horseshoe kidneys, and severely hydronephrotic collecting systems requiring upper pole access, a longer offset rigid nephroscope is used.

The use of both rigid and flexible nephroscopy allows for the examination of all calyces to optimize stone-free status. All attempts are made to maximize use of the rigid nephroscope and flexible endoscopy is performed when the limit of the rigid scope has been reached. We use flexible nephroscopy in all PCNL cases; calyces that are not accessible with rigid nephroscopy can be entered. In our hospital, we use the 16 F flexible scope in conjunction with 7.5 F ureteroscope to access all calyces and ureters if necessary.

Step-by-step technique

Step 1: retrograde ureteral access

Our PCNL begins with the patient in the supine position using a flexible cystoscope to establish retrograde ureteral access. For women, the perineum is accessed by abducting the hips with the knees bent in a frog leg position. This provides better access to the external urethral meatus. A guidewire is then guided into the ipsilateral ureter and advanced under fluoroscopic imaging toward

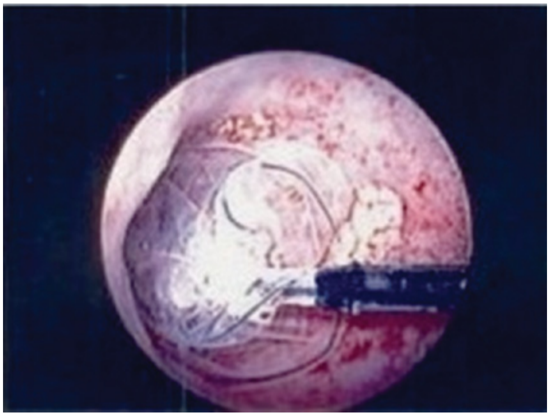

Figure 9.3 Coaxial retrograde occlusion device (Percsys, Palo Alto, California) used to distend and opacify the renal collecting system. This instrument also prevents the antegrade migration of calculi during stone extraction.

the upper tract collecting system. The flexible cystoscope is subsequently removed and an open-ended ureteral catheter or a coaxial Accordion™ occlusion device (Percsys, Palo Alto, CA) is positioned over the guidewire in the renal pelvis. The occlusion device is deployed at the ureteropelvic junction (UPJ) to preclude dislodgement of stone fragments down the ureter during the intracorporeal lithotripsy procedure (Figure 9.3). The guidewire is removed and the catheter is used to inject contrast material or air to delineate the contour of the collecting system during the percutaneous access. A Foley catheter is inserted alongside the ureteral catheter or the occlusion device to ensure bladder decompression during the procedure. The Foley catheter and the occlusion device are then secured to each other with a 2-0 silk tie to prevent migration. When the patient is fully secure in the prone position, the tie is cut to allow retrograde manipulation if necessary.

Step 2: antegrade percutaneous renal access

Despite the recognition that percutaneous renal surgery starts with appropriate renal access, the majority of urologists refer this critical first step to radiologists. A 2003 review of stone management patterns showed that only 11% of urologists obtain their own percutaneous access [10]. Even if the political patterns drive this trend, it is still important for urologists to be engaged in both the selection of access and the technique. The access site should be aligned with the orientation that would be least likely to injure the renal vasculature. Because the posterior calyces are usually oriented so that the long axis points to the avascular Brödel's line, a posterolateral puncture into a posterior calyx traverses this avascular plane. Also, the posterior calyx is the shortest path to access the renal collecting system. Of note, the C-arm must have an excursion of at least 20° and image storage so that the image can be saved for comparison during the access.

Sometimes, anterior calyceal access may be required for some stones or for anterior calyceal diverticula but it should be used only if posterior calyceal access is not possible. Anterior calyceal access also provides less security because it may not be possible to advance a guidewire into the renal pelvis. In general, direct puncture of the renal pelvis should be avoided because it carries a higher risk of injury to the posterior branch of the renal artery. The more medial the puncture, the greater the risk of injury to large branches of the renal vessels. Moreover, the path of this type of puncture provides no stability for the nephrostomy tube, because it lacks parenchymal support [11].

Injection of contrast material through the retrograde catheter will delineate the calyces of interest. Sometimes, air may be injected instead to provide an air pyelogram to identify the posterior calyces since air is lighter than urine or contrast material and therefore identifies posterior calyces first with the patient in the prone position. In the case of stones in multiple calyces or complete staghorn calculi, an air pyelogram may also outline the collecting system satisfactorily without interfering with subsequent evaluation of residual stones or fragments due to retained or extravasated contrast material.

Bull's eye technique

First, with the C-arm in the vertical position, the collecting system is surveyed and the appropriate calyx is identified. The ideal puncture site provides the shortest tract to the calyx from below the 12th rib. Examination with the C-arm at 90° defines the medial vertical plane for entry into the calyx. The C-arm is then rotated approximately 30° toward the surgeon. This places the axis of the C-arm in the same central posterior plane of the kidney, providing a direct end-on view of the posterior calyces. After the calyx has been identified, the overlying skin site is marked with a hemostat. An 18 gauge percutaneous access needle is advanced in the plane of the fluoroscope beam with the C-arm in the 30° position. The appropriate direction for needle advancement can be assessed by the presence of a "bull's eye" on the fluoroscopic screen. This image is visible only when the needle hub is aligned directly on the needle shaft; this denotes that the plane of the needle is directly parallel to that of the x-ray beam. If the axis of the needle advancement is not in the same plane as the axis of the C-arm beam, a portion of the needle shaft will be visible. The needle is then advanced in 1–2 cm increments toward the calyx. Use of a hemostat or needle holder is recommended to minimize the radiation exposure to the surgeon. Again, the needle should approximate the avascular line of Brödel, as this transparenchymal route avoids the hilar vessels and seals the nephrostomy tract from urine leakage [12].

Finally, the depth of needle penetration is monitored by rotating the C-arm back to the vertical position. With the C-arm back at 90°, the tip of the needle at the predetermined calyx can be seen and adjusted as needed. For example,the needle is too deep if it appears to be past the calyx on the fluoroscopic screen. Periodically, the correct direction of needle advancement should be monitored prospectively by alternating the C-arm positions to determine the correct axis and depth. The inner obturator is removed, and urine efflux confirms needle placement in the collecting system.

Triangulation technique

One of the more frequently used techniques for access to a superior calyx is triangulation [13] (Video Clip 9.1). The C-arm is positioned over the patient in the vertical, 90° position. A retrograde distension outlines the calyces, and the skin over the desired calyx is marked with a hemostat while the C-arm is maintained in the vertical position. Just as in the bull's eye technique, this plane defines the medial extent of needle penetration for access to the desired calyx. The C-arm is then rotated 30° toward the surgeon for an end-on view of the posterior group of calyces (Figure 9.4b). With the C-arm at 30°, the skin site over the calyx is marked lateral to the first site. The surgeon uses this point on the skin surface to move in a vertical line inferiorly until a site 1–2 cm below the 12th rib is reached. This third site is marked and serves as the site of needle entry (Figure 9.4a). From this point, the needle is advanced to the junction of the vertical plane and the 30° plane (Figure 9.4c). Access is achieved at the junction of all three axes, hence the term *triangulation* [11].

The bull's eye sign does not exist with this approach; the needle advancement is based on the surgeon's appreciation of two-plane fluoroscopic dimensions of the needle tip and position of the calyx. It is also critical to be familiar with the perception of the angle of advancement of the needle as it relates to the depth of penetration along the medially defined plane described previously. This approach is technically more demanding and requires more experience with percutaneous punctures. In the situation of a malrotated calyx, commonly seen with ectopic and horseshoe kidneys, lateral views of IV urograms may be required to differentiate between the posterior and anterior groups of calyces. Moreover, the skin puncture site may be more medial.

The above techniques take advantage of the subcostal approach since the risk of hydrothorax and hemothorax is increased when percutaneous access to the calyces is performed above the 12th rib [14]. In a situation where direct percutaneous access to an upper pole calyx is necessary, the surgeon needs to be familiar with the intercostal approach. Many urologists favor this approach for gaining access to the upper pole and suggest that it provides direct and optimal access to most staghorn calculi, even though it carries a slight and acceptable increase in risk of pulmonary complications. This is performed by visualizing the upper pole at the 30° rotation toward the surgeon, and puncturing into the calyx in the presence of a bull's eye on the fluoroscopic screen, above the 12th rib. Fluoroscopy can be used to check for lung markings if an intercostal or supracostal puncture is performed. Ogan et al. showed that all clinically significant pneumothoraces can be imaged intraoperatively, thus not even requiring postoperative chest x-rays [15]. In addition, any pleural fluid can be easily aspirated prospectively while the patient is still intubated.

Step 3: dilation of the access tract

Once the correct needle position is verified by aspiration of urine or air, a 0.038-inch floppy-tip stiff J-shaped guidewire is advanced across the UPJ or coiled within the renal pelvis. The needle is then removed, and an approximately 1 cm transverse incision is made at the wire site. Following the initial puncture, we prefer a J-tipped stiff polytetrofluoroethylene (PTFE) guidewire that easily coils in the calyx or renal pelvis. The wire should be stiff enough to support dilation without kinking. Ideally, it should be placed in the ureter to the level

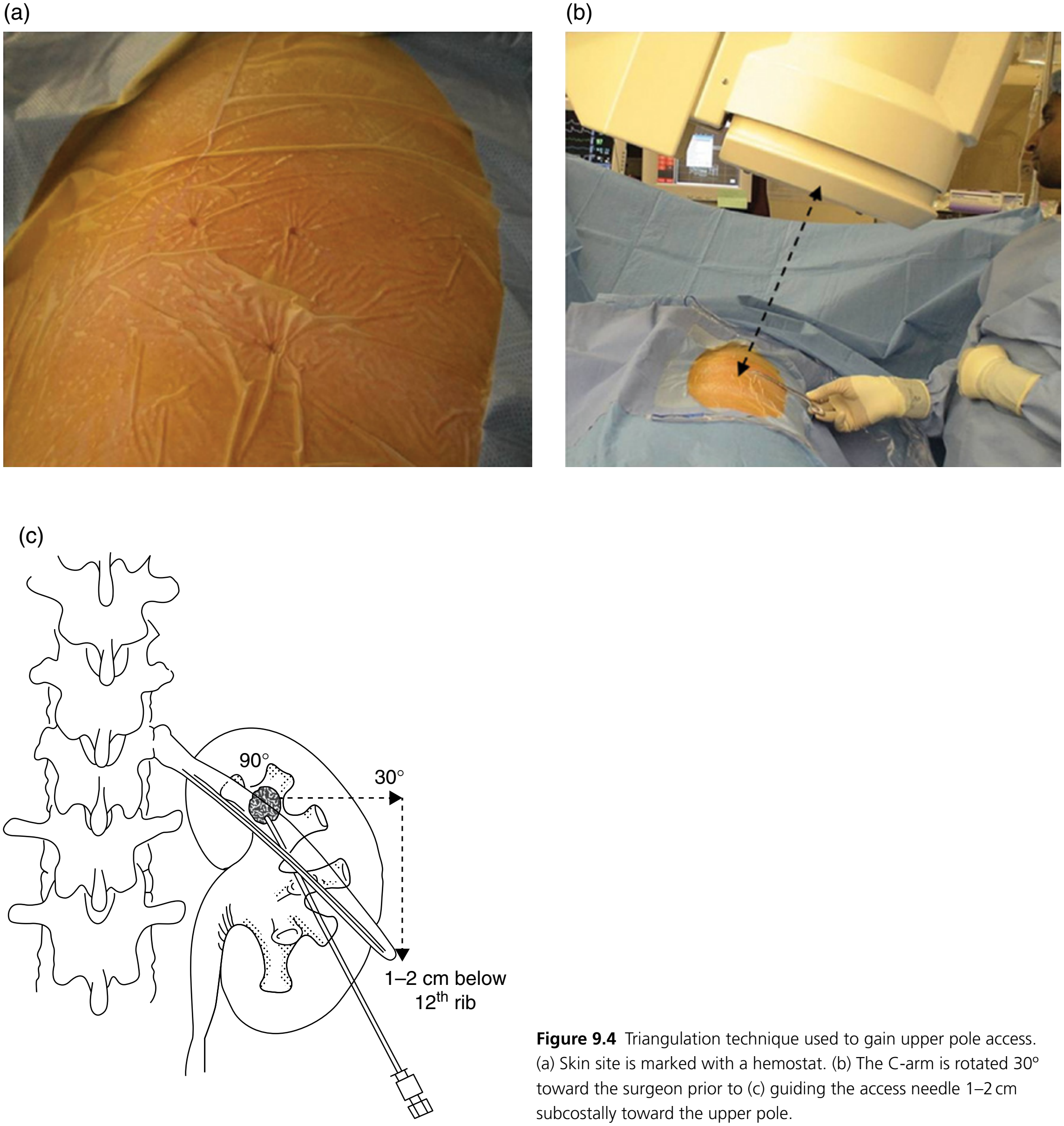

Figure 9.4 Triangulation technique used to gain upper pole access. (a) Skin site is marked with a hemostat. (b) The C-arm is rotated 30° toward the surgeon prior to (c) guiding the access needle 1–2 cm subcostally toward the upper pole.

of the bladder to avoid dislodgment during tract dilation. Sometimes, passage of the wire into the bladder is not feasible because of obstruction within the collecting system, cases of impacted ureteral calculus or UPJ narrowing. The final diameter of the tract should exceed the nephroscope size by 2–4 F, allowing continuous flow. The three most commonly used devices are high-pressure balloons, Amplatz dilators (plastic), and the coaxial Alken dilator set (metallic).

Balloon dilators are the mostly frequently used dilation devices for PCNL at our hospital. Balloon dilation can establish the tract in a single step, avoiding the need for serial dilations. In addition, balloons produce lateral compressive forces rather than angular shearing forces, and therefore theoretically generate less bleeding and trauma. Nevertheless, there is controversy in the literature regarding the effects of the various dilating techniques on the risk of bleeding. High-pressure balloons are available with diameters of 20–30 F. Limitations include higher costs and suboptimal dilation in the setting of dense fascial tissue planes or retroperitoneal scar tissue.

The radiographic marker at the tip of the balloon is positioned just inside the calyx. Passing the balloon tip beyond the calyx or stone may result in infundibular tears or urothelial injury from the impaction of the stone. As the balloon is inflated, a characteristic "waist" appears in areas of high resistance, such as the renal capsule or a previous operative scar. With persistent inflation, the balloon expands fully and the waist disappears, and a 24 F or 30 F Teflon working sheath is advanced over the balloon in a rotating fashion.The sheath should be advanced to the end of the balloon, not the end of the catheter. The balloon is then deflated and retrieved from the tract.

The Amplatz serial dilator set includes a long 8 F Teflon "snake" catheter that is tapered to fit over a 0.038-inch guidewire, and a series of progressively larger, tapered polyurethane dilators that are passed over the snake catheter and the guidewire. The dilating catheters range in diameter from 12 to 30 F in increments of 2 F. The outer sheaths are designed to advance in a coaxial fashion over the blue polyurethane dilators and are available in 24–34 F sizes. Each sheath has an outer diameter that exceeds the inner diameter by 4 F; thus, the 34 F sheath is designed to slide over the 30 F dilator. Because of its flexibility, the snake catheter can be manipulated into the ureter, sliding over the guidewire and protecting and stabilizing it to prevent kinking during progressive dilation. The nephrostomy tract can either be dilated in a step-wise fashion in 2 F increments, or some sizes can be skipped. It is important to note that the dilators must be advanced over the working guidewire until they enter the calyceal lumen. Aggressive insertion may result in pelvicalyceal tears and should be avoided. Fluoroscopically, the distal end of the dilators should not be advanced beyond the UPJ. This is especially critical when nephrostomy tract dilation is performed to treat large renal stones. The dilators should be advanced only to the peripheral edge of the stone, as further advancements can cause calyceal or infundibular tears [16].

Step 4: stone extraction

Once the tract has been stabilized, the working channel scope is advanced to address the stone burden. For staghorn calculi, we prefer the ultrasonic lithotrite to both fragment and suction out the stone fragments. A pneumatic or combined pneumatic/ultrasonic lithotripter can also be employed in the case of durile stones. Cho et al. demonstrated that the combination of ultrasonic and pneumatic lithotripsy had a significantly lower operative time compared to the ultrasonic approach alone, regardless of stone composition [17]. Residual stone fragments are removed with graspers or suction. During stone fragmentation, we take special care not to disperse fragments, since this may displace fragments into inaccessible calyces and significantly increase operative time. Excessive torquing of the rigid scope should be limited since it can lead to calyceal or infundibular tear. Our initial placement of an occlusion device prevents antegrade migration of stone fragments, which also decreases total operative time [18]. If some calyces are not accessible due to a narrow infundibulum, the rigid scope can be used without the outer sheath.

Intraoperative stone culture and upper tract urine cultures are obtained from patients at risk for urosepsis. Although a positive preoperative urine culture can tailor perioperative antibiotic choice, Gönen et al. demonstrated the importance of pelvic urine culture and stone culture during PCNL in guiding antibiotic therapy [19]. In their prospective review of 198 patients undergoing PCNL, Korets et al. examined the relationship between organisms cultured from the blood in patients with sepsis and organisms cultured preoperatively, from the renal pelvis at the time of surgery and from stones themselves. In their series, they concluded that both renal pelvis urine cultures and stone cultures correlated with organisms causing sepsis, and in a multivariate analysis, they found that a stone burden of $10\,\text{cm}^2$ or greater was a significant predictor of systemic inflammatory response syndrome postoperatively [20]. Thus, we recommend collecting renal pelvic urine and stone cultures for all patients with a large stone burden, especially those requiring multiple access sites.

Recently, we assessed the efficacy, safety, and morbidity of a modified PCNL technique that allows for the use of standard PCNL equipment and lithotripters through a tract that is smaller (24 F) than traditional PCNL (30 F) but larger than reported for mini-PCNL

(14–18 F). This novel technique utilizes the nephroscope without the outer sheath, providing excellent irrigation flow and visualization during rigid nephroscopy. In patients with stone burdens greater than 2 cm, both mean operative time and estimated blood loss were lower for groups with this modified technique, while achieving 100% stone-free status at the end of the procedure. Thus, this technique could be used in conjunction with the traditional instruments to efficiently remove renal calculi.

We are extremely aggressive about stone clearance. Flexible nephroscopy using a flexible cystoscope is always performed to visualize calyces inaccessible to rigid nephroscopy [21]. Pressurized irrigation fluid is sometimes necessary to improve visualization, especially if ureteroscopes are used. The entire collecting system should be examined, and instillation of contrast can also help with systematic visualization of all calyces. We prefer to remove fragments or multiple stones using stone baskets, but if too large, a holmium laser can be used for fragmentation. Laser fibers of 365–500 microns are the most efficient for a flexible cystoscope.

Step 5: nephrostomy placement/drainage (Figure 9.5)

The final step in PCNL is the establishment of nephrostomy drainage. Traditionally, percutaneous drainage of the collecting system has been routine after percutaneous renal procedures in order to tamponade bleeding, prevent urinary extravasation, and allow renal healing, pelvicalyceal system drainage, and access for possible second-look procedures [3]. Some urologists promote "tubeless" PCNL and have not routinely placed nephrostomy tubes after PCNL in an effort to decrease postoperative pain and analgesic use, reduce the length of hospital stay, and speed the return to regular activities [22]. For our nephrostomy tubes, we use latex Foley catheters with self-retaining balloon capacities of 5 mL. Balloons should always be inflated with water with a touch of contrast to ensure proper placement. We have found that this does not jeopardize the balloon deflation since our nephrostomy tubes are usually kept only overnight. At our institution, we verify lack of infection, stone-free status, lack of obstruction, and lack of tract or collecting system bleeding prior to performing tubeless PCNL [23].

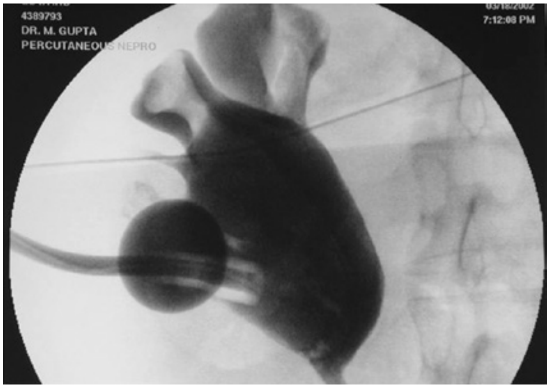

Figure 9.5 Nephrostomy tube placed at the end of THE procedure. The balloon is inflated in the calyx used to enter the collecting system. An antegrade nephrostogram is then performed to confirm placement.

Intraoperative tips/trouble-shooting

When placement of the guidewire down the ureter is not feasible, positioning it in a calyx that is distant from the initial nephrostomy tract prevents its dislodgment during dilation. The guidewire may not pass into the renal pelvis because of the impacted stone and is then coiled within the punctured calyx. Dilation in this case must be performed very gently because the guidewire can easily be displaced from the collecting system.

How do we achieve direct upper pole access without puncturing above the 12th rib? In a situation of single access, the occlusion device can be used to apply gentle caudal traction and displace the kidney downward and below the costal margin during the initial access approach. In a case of multiple accesses, this is achieved by placing an Amplatz sheath through a central or lower pole calyx and rotating the back of the dilator cranially, which causes caudal displacement of the kidney that can be viewed fluoroscopically. A second distinct puncture is then performed directly into the upper pole.

Sometimes retrograde opacification of the pelvicalyceal system is not possible due to the obstruction of ureteral lumen, or the ureteral catheter cannot be placed. In this case, puncturing onto a stone, intravenous urography or ultrasound-guided puncture can be used for access. In a rare situation, blind access may be necessary. The renal pelvis is situated approximately 1–1.5 cm lateral to the L1 vertebral body. When this bony landmark is identified on fluoroscopy, a perpendicular skin puncture is made with a 22 gauge "skinny" needle, lateral to the psoas muscle and just below the level of the 12th rib. One potential concern with this needle is that it is not diamond shaped, and it tends to deflect easily. Thus, the puncture must be directly posterior. If these steps are followed, access to the pelvicalyceal system can be normally achieved, especially if the system is hydronephrotic. Once urine can be aspirated from the renal pelvis, contrast material can be instilled to outline the upper collecting system and calyceal puncture is performed as described previously.

Perforation of the pelvicalyceal system, hemorrhage, extravasation, and trauma to the renal capsule can occur during nephrostomy tract dilation. In order to avoid this, the tract must always be performed under fluoroscopic observation. If excessive force is used during the insertion of the dilators, the renal pelvis may be perforated despite the ureteral catheter stabilizing the pelvicalyceal system. When the renal pelvis is perforated, there is a possibility of extravasation of irrigation fluid into the retroperitoneum. In this situation, continue with the procedure only if the calculus can be removed expeditiously. The procedure should be aborted in the setting of any large, residual stone burden or excessive bleeding. Excessive bleeding can be managed by selective inflation of a Council balloon catheter [24].

Postoperative care

Pain control after PCNL is paramount in convalescence. We perform intercostal block, using 0.25% marcaine, at the end of all cases. The intercostal neurovascular bundles of the 11th and 12th ribs, as well as the access site, are injected with local anesthetic. Care is taken not to inject an excessive amount, since it can lead to intercostal muscle paralysis and postoperative bulge. In addition, patients with normal renal function and good hemostasis receive a bolus of ketorolac (15 mg or 30 mg) at the conclusion of the procedure while still under anesthetic in the operating room. In our experience, this regimen maximizes postoperative pain relief and decreases narcotic use in the postoperative period. Most patients are admitted for overnight observation. In nontubeless patients urinary catheters and/or nephrostomy tubes are removed the following morning prior to discharge.

Conclusions

Percutaneous nephrolithotomy in the prone position has been the standard technique in the treatment of complex renal and proximal ureteral calculi. With proper calyceal access, calculi of most sizes can be successfully treated. All strategies should maximize the use of rigid instruments, minimize morbidity, and allow for any adjunctive procedures when necessary.

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CHAPTER 10

Instrumentation and Surgical Technique: Step-by-Step Percutaneous Nephrolithotomy: Supine

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Introduction

Since the first description of supine position percutaneous nephrolithotomy (PCNL) by Valdivia and associates, the interest in this approach for PCNL is ever increasing [1]. The drawbacks of traditional prone position PCNL include the need to change position for retrograde catheterization, which may at times be challenging in morbid obesity and cardiorespiratory compromise. In addition, in the prone position, the hands of the urologist are in the field of fluoroscopy, thus increasing the radiological hazards [2]. The advantages of the supine position are comfortable positioning for the patient and the surgeon, and a significant amount of time is saved in positioning the patient. In the supine position, it is hypothesized that the intrarenal pressure is lower compared to prone positioning because the tract is horizontal and inclined downward; as a result the stone fragments exit spontaneously through the working sheath. The chances of the fragments migrating in the ureter are minimal, as the calyces are dependent in relation to the pelvis. The drawbacks of the supine position include inability to puncture the upper pole calyx and the pelvis tends to be collapsed in supine position and hence nephroscopy is difficult.

In this chapter we describe the indications, procedural steps with special reference to unusual situations such as ectopic kidney, fused kidney and transplant kidney, and relevant literature in the context of this approach for PCNL.

Indications for supine percutaneous nephrolithotomy

A few workers have performed supine PCNL as an alternative to the prone position [3]. We feel supine PCNL offers definitive advantages in the following conditions.

- Renal pelvic calculi and/or concomitant ureteric calculi in morbidly obese and other high-risk patients [4].
- Renal pelvic calculi and/or concomitant ureteric calculi in patients with skeletal deformities such as kyphoscoliosis related to osteogenesis imperfecta which precludes prone position.
- PCNL in special situations such as ectopic kidneys and urolithiasis in transplant kidneys [5,6].

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

Informed consent

Informed consent should be obtained from the patient, detailing the procedure; in addition, the possibility of performing the procedure in the traditional prone position should be explained to the patient. The possible complications, which include life-threatening hemorrhage, infection and possibility of residual stones, should be noted. In addition, the consent should mention the possible need to stage the procedure, if required. The patient needs to be informed about the accepted stone-free rates, complication rates, and morbidity as reported in the literature.

Instrumentation

Guidewires and glidewires

The preferred size of glidewire is 0.035 inch. A J-tip curved wire 0.038 in × 145 cm × 3 mm (Cook Urological Inc., Spencer, IN) will help in preventing trauma to the renal pelvic mucosa. A "fixed core" straight tip 0.035 in × 145 cm wire (Cook Urological Inc., Spencer, IN) is used in the ureter. The surgeon should not force the straight tip wire as this tends to damage the mucosa.

The glidewire is the preferred wire for ureteric catheterization. Prior to percutaneous access, the glidewire can maneuver across obstructions and narrow ureters, though it tends to slip because of the hydrophilic coating. All glidewires should be parked securely in the adapters. The J-tip wire is used occasionally to "push" an impacted upper ureteric calculus in the kidney. The "J" of the wire helps in pushing the stone in the pelvis.

Once access is gained, the choice of wire is a matter of surgeon preference. We prefer to use either a J-tip guidewire or a glidewire. The glidewire does not kink and should be preferably passed into the ureter or a distant calyx. The J-tip guidewire has a tendency to kink during dilation.The guidewire or super-stiff guidewire is preferred if the procedure is being performed on a previously operated renal unit.

Ureteric catheter

The ureteric catheter has several advantages which are listed later. An open-ended ureteric catheter, either 5 F or 6 F, is used through a cystoscope sheath. A cystoscopy helps to assess the bladder and the lower tract. The ureteric catheter is fixed to the Foley catheter.

Puncture needles

The puncture needles that are available include a two-part 18 gauge stainless steel puncture needle (Cook Urological Inc., Spencer, IN) and the three-part needle (18 gauge × 20 cm; Bard/Angiomed Ltd, Covington, GA). An echo-reflective needle, the Echotip™ (Cook Medical, Bloomington, IN), is helpful if ultrasound-guided puncture is contemplated, as the echo-reflective characteristic facilitates identification of the needle tip with the ultrasound.

Tract dilators

Dilators available include Amplatz dilators, telescopic dilators, and balloon dilators. The Amplatz dilator set is available as a catheter (8 F) which is 84 cm long (Cook Urological Inc., Spencer, IN) and serial dilators which range in size from 12 to 30 F in increments of 2 F. The dilators are 20 cm and 30 cm in length. Apart from providing stability to the entire assembly, the 8 F dilator helps in preventing kinks in the wire. Once the tract is dilated, a coaxial sheath is used which serves as a conduit from the skin to the pelvicalyceal system. The external sheath secures access to the kidney and allows the repeated introduction and withdrawal of endourological equipment. The Amplatz dilators provide a low-pressure system which makes the procedure safe. The sheaths range in size from 28 to 34 F and the outer diameter exceeds the inner diameter by 4 F; thus, the 34 F sheath is designed to slide over the 30 F dilator.

Telescopic dilators (Karl Storz Endoscope,Tuttlingen, Germany) have a central rod with a knob at the tip. The rod has a diameter of 6 F and the knob a size of 9 F. The serial metal dilators pass over the rod similar to a radio antenna.

The available balloon dilators are Nephromax (Boston Scientific, Natick, MA), Ultraxx (Cook Urological Inc., Spencer, IN), Omega NV (Cook Urological Inc., Spencer, IN), and X-Force (Bard Urological, Covington, GA). The balloon length varies from 12 to 15 cm and the outer balloon diameter ranges from 6 to 10 mm.We prefer to use the 10 mm balloon. The balloon dilators dilate by radial compression of the renal parenchyma, which theoretically reduces the possibility of guidewire slippage and kinking. The operator should be cautious while using the balloon dilators in a compact calyx with large stone, as in such situations the tract is likely to be underdilated. In these situations the metallic dilators are useful.

Telescopes

The nephroscopes are either offset or straight lens. The size of the nephroscope depends on the size of the Amplatz to be used. The lens is either 25° or 30°. The size ranges from 12 F to 26 F. The size of the working channel differs according to the size of the nephroscope.

Retrieval baskets and forceps

The forceps available are either "triflange" (three jaws) or "biflange" (two jaws). Grasping forceps (Karl Storz Endoscope, Tuttlingen, Germany) for stone fragments have fenestrated jaws and spring handles; the length is 31 cm. The advantage of biflange forceps is that it can be used in small calyces; the triflange requires a bigger space to open.

Energy sources

The available energy sources include lasers (holmium: yttrium aluminum garnet[YAG]), pneumatic lithotripter, and combinations of ultrasonic and pneumatic devices. The pneumatic lithotripsy and combination devices remain the mainstay in the armamentarium, the latter being more efficacious and faster in fragmenting hard stones.The holmium:YAG laser acts as a useful adjunct when a flexible nephroscope is used for accessing calyces in a distant calyx not accessible by a rigid nephroscope. This is of importance in the supine position while accessing the upper pole with a flexible nephroscope.The ability of the holmium:YAG laser to fragment stones in dust has expanded its application in fragmentation of soft stones. The holmium:YAG laser can be used with smaller sized nephroscopes, thus limiting the size of the tract.

Technique

Ureteric access

A retrograde ureteropyelography (RGP) is done with a 5 F or 6 F ureteric catheter. The ureteric catheter is placed with either a rigid or flexible cystoscope.

Ureteric access with a catheter serves the following purposes.

- It helps in "repositioning" an upper ureteric stone into the kidney, thus enabling its removal through a percutaneous tract in a supine position.
- In the event that the stone does not get "pushed' into the kidney, the ureteric access helps to pass a flexible ureteroscope and/or an access sheath into the pelvis for disintegration of the stone.
- The ureteric catheter helps to distend the renal pelvis, which helps in achieving renal access with either fluoroscopy or ultrasound guidance.
- The ureteric catheter acts as a medial guide during dilation of the percutaneous tract.
- The ureteric catheter is used for instillation of saline and/or contrast during the procedure.

Position

At our center, during a supine PCNL, the patient is placed at the edge of the table in the dorsal lithotomy position with the lower limbs placed in stirrups, maintaining hip joint flexion at 45° on the ipsilateral side and 30° on the contralateral side. A soft bolster (towel, serum bag, or custom-made bolster) is placed below the ipsilateral flank so that the posterior axillary line faces 45° to the horizontal. The ipsilateral arm crosses the chest. The arms are not extended excessively to avoid any neuropraxis. Depending on the physique of the patient, the size of the bolster can vary. In contrast to the prone position, the surgeon operates in a sitting position. The operating table should be at the level of the surgeon's shoulder. The ultrasound and endovision equipment is kept at the surgeon's eye level.

Combined approach: the modified supine position

In the combined approach, the patient is placed in a supine position with the leg on the ipsilateral side of the stone in extension and the other in flexion; this position helps in gaining retrograde access. The ipsilateral arm is crossed on the chest and the region next to the stone is elevated by 20°. One surgeon performs cystoscopy and RGP, the other achieves percutaneous access guided by either ultrasound or fluoroscopy [7].

Figure 10.1 Ultrasound-guided access is achieved with an ultrasound probe and a puncture attachment. One hand of the surgeon holds the probe steady while the puncture guide directs the needle in the desired calyx.

Complete supine position

Once a ureteric catheter is placed, the patient is placed in supine position for percutaneous access without any bolsters. This offers the potential advantages of better urethral access, less patient handling, no need for drape change, ability to perform simultaneous PCNL and ureteroscopic procedures, and better control of the airway during procedures, thus reducing overall operative time [3].

Renal access

The choice of access is a matter of surgeon preference. Either ultrasound or fluoroscopy or a combination of both may be used. An ultrasound-guided access has been reported to be safe in transplant kidneys and ectopic kidneys in supine position [5,6,8]. The proven advantages of ultrasound as a modality to gain access include shorter exposure to radiation, potential to avoid visceral injury and less need for contrast [9]. The disadvantages of this method include the need for additional equipment and expertise for gaining access. In obese patients, due to poor ultrasound penetrability of the tissues, ultrasound-guided puncture may not be successful. A 3.5 MHz probe, preferably with a puncture attachment, is utilized (Figure 10.1). An ultrasound-guided access is achieved if the needle is seen throughout the access path. The electronic dotted line will show any visceral organ (spleen, liver, and bowel) in the way of the needle trajectory.

At our center, ultrasound access is the method of choice. We prefer the posterior axillary line approach with the patient in a 45° supine oblique position because this position places the posterior calyx and the desired tract in a straight line. In addition, it provides enough space for the surgeon to move the probe in the posterior midline. As one moves the probe towards the axillary line, the first calyx to be seen is the posterior calyx, while as one moves further, the anterior calyx becomes evident. The Echotip needle is useful as it casts a shadow along the path due to the serrations on the shaft of the needle, which make it echo-reflective. The access point on the skin is on the posterior axillary line. Correct access is confirmed by egress of clear fluid from the needle hub. The position is further confirmed with injection of contrast.

Tract dilation

Tract dilation is done by the surgeon under fluoroscopic guidance in either a sitting or standing position. It is performed with either a single-step screw dilator or telescopic dilators. Depending on the size of stone and width of infundibulum, the size of the Amplatz sheath is chosen. The surgeon should orient himself/herself to the position of the calyces in supine position. An antero-medial movement of the kidney during dilation is noticed with the supine position, sometimes making the procedure more difficult [10]. Nephroscopy is one of the

Figure 10.2 During supine PCNL, the surgeon sits while the patient lies supine at the edge of the table. The Amplatz sheath is directed horizontally and towards the floor and as a result the intrapelvic pressure remains low.

most challenging steps in supine PCNL. The challenges include, first, the need to work in a collapsed collecting system, resulting in limited space for nephroscopy in the collecting system, and second, the upper calyx in most of these cases is difficult to access, which becomes significant in situations such as a migrated stone in the upper calyx following intracorporeal lithotripsy – such fragments need to be tackled with flexible instrumentation.

The choice of nephroscope is important from the maneuverability standpoint; nephroscopes with offset light cables and optics are likely to impair the mobility of instruments because of the possibility of collision with the operating table [7]. Nephroscopy is best done with the surgeon sitting. In this position the lie of the Amplatz is horizontal and the relative position of the calyces is less dependent and hence the intrapelvic pressure is low, which enables easy egress of irrigation fluid and broken fragments (Figure 10.2).

In situations with simultaneous ureteric and renal calculi, an initial attempt is made to push the stone into the renal pelvis but if this is not successful, a retrograde ureteroscopic fragmentation is done. In a combined approach, when an associated impacted upper ureteric stone cannot be pushed successfully, a ureteroscope is negotiated into the upper ureter and the stone fragmented. Bolsters are removed after antegrade renal access has been achieved. Flexible nephroscopy is employed for retrieving fragments which have migrated into the upper calyx [4] (Figure 10.3). It has been argued that flexible nephroscopy is a mainstay in this approach to renal stones because of its ability to avoid multiple access and related morbidity. It also helps in identifying residual stones or stones migrated into inaccessible calyces, thus ensuring “on-table” clearance of stones [11]. The decision to postoperatively drain the kidney depends on the level of hemostasis, possibility of extravasation, and residual stones. The decision is dictated by the intraoperative findings and the surgeon’s discretion [7].

Visceral injury in supine percutaneous nephrolithotomy

As described by Hopper, colonic injuries are less frequent in the supine position due to the more anterior displacement of the colon [12]. PCNL in prone position is associated with a 0.3–0.8% chance of a visceral injury, but the incidence of colonic injury in supine position PCNL is still lower; this may be related to shifting of intraperitoneal organs in prone position and this being accentuated by placement of bolsters in prone position. This fact has been proved in a study by Azhar and associates in which the skin-to-stone distance, angle of the percutaneous

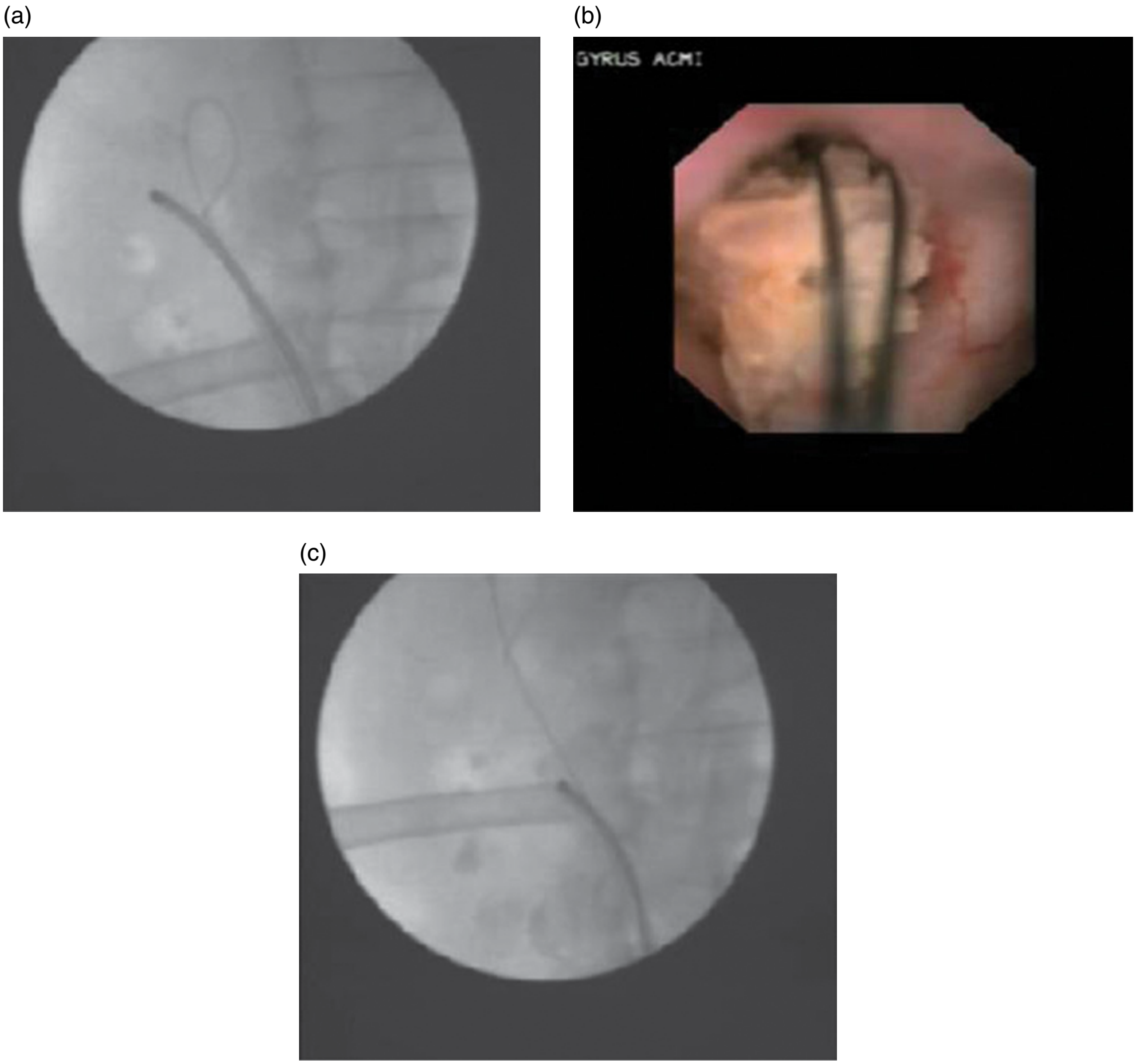

Figure 10.3 The use of flexible instruments is important in supine PCNL as it helps to reduce the number of tracts needed to change the position. (a) Multiple calyceal stones: a single middle calyceal tract was created and the majority of stones were cleared through this tract. (b) A flexible ureteroscope is negotiated in supine position. (c) The stones are "passed" to a nephroscope positioned in an Amplatz sheath for retrieval.

tract to the anterior posterior axis and the visceral organ-to-tract distance were measured. The authors concluded that in prone position, skin-to-stone distance and visceral organ-to-tract distance were shorter. The measurements were done on a preoperative supine (without bolsters) and a prone (with bolsters) noncontrast computed tomography (CT) scan [13].

Supine percutaneous nephrolithotomy in special situations

Ectopic and L-shaped kidneys

Stones in an ectopic kidney can be tackled in the supine position using ultrasound- or laparoscopic-

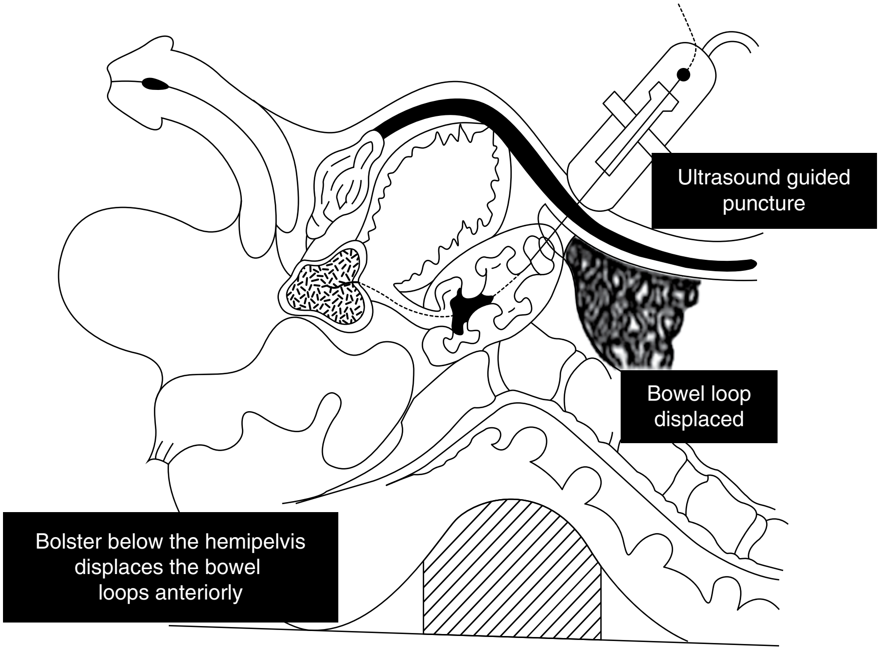

Figure 10.4 The principles of ultrasound-guided PCNL in an ectopic position, which include ultrasound guided-puncture, displacement of bowel loops with the probe and strategic placement of bolsters.

guided access. We prefer ultrasound-guided access. The procedure is done with the patient under general anesthesia. After retrograde catheterization, the pelvicalyceal system is opacified, the side-to-side mobility of the kidney is assessed, and the ability to displace the kidney close to the abdominal wall by contralateral pressure is determined. A supine oblique position with a bolster under the ipsilateral hemipelvis is preferable. A slight tilt of the table to the opposite side displaces the bowels. A mechanical bowel preparation with a low enema is given before surgery, The desired calyx of entry is localized using ultrasound guidance. Pressure on the ultrasound probe itself displaces any intervening loops of bowel away from the puncture line to the targeted calyx, following which, the calyx is punctured (Figure 10.4). Dilation is performed using telescopic metal dilators under fluoroscopic control.

The salient features of our technique is the relative displacement of bowel and kidney while making the puncture. The operating urologist, using ultrasound guidance, makes the initial puncture. Contralateral pressure is applied to displace the kidney closer to the abdominal wall. The bowels are displaced away from the line of puncture by the pressure of the transducer probe itself. Simultaneous fluoroscopic and sonographic localization helps in selecting the lateralmost calyx for puncture, giving a short, straight, direct tract to the desired calyx. Punctures in the supine position are made through the iliac fossa considering the position of the targeted calyx [6].

L-shaped and fused kidneys in the pelvis

Figure 10.5 illustrates supine PCNL in a patient with L-shaped kidney. The patient was planned for bilateral PCNL in supine position with a slight tilt on the right side. An assistant gave gentle traction to the L-shaped kidney (decreasing the distance of the calyx from the kidney) from the medial border towards the lateral aspect and ultrasound was used to gain

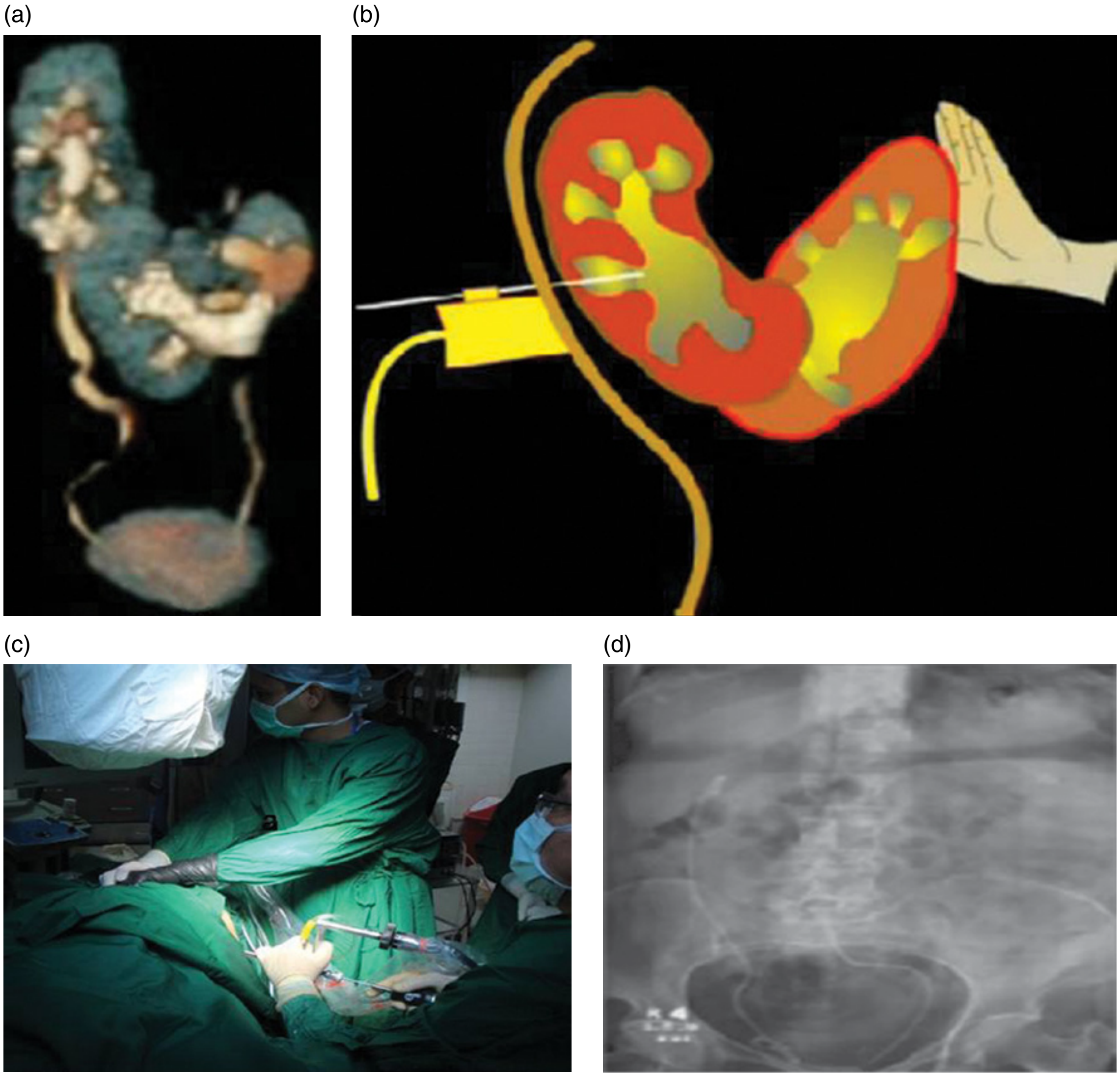

Figure 10.5 (a) L-shaped fused kidney in a ectopic pelvic position; the patient was planned for supine PCNL. (b,c) Supine position was achieved and the kidney was pushed towards the anterior abdominal wall by an assistant, who is wearing lead gloves.The "push" given by the assistant helped in positioning the kidney near the abdominal wall. (d) Complete clearance of calculi on x-ray.

access to the middle calyx of the right kidney. The major bulk of the stones was thus cleared with separate punctures for the lower calyx and upper calyx. After clearing the right renal moiety, a Y tract was made by removing the lower calyx nephrostomy and placing it on the superior calyx of the left kidney (laterally directed just inferior to the right kidney). Through this access tract, the majority of the staghorn calculus was cleared with an extra-long nephroscope. Salient features of this technique included ultrasound-guided puncture, strategic planning with three-dimensional reconstruction (positioned laterally away from the surgeon), and judicious use of flexible nephroscopy (see Figure 10.5).

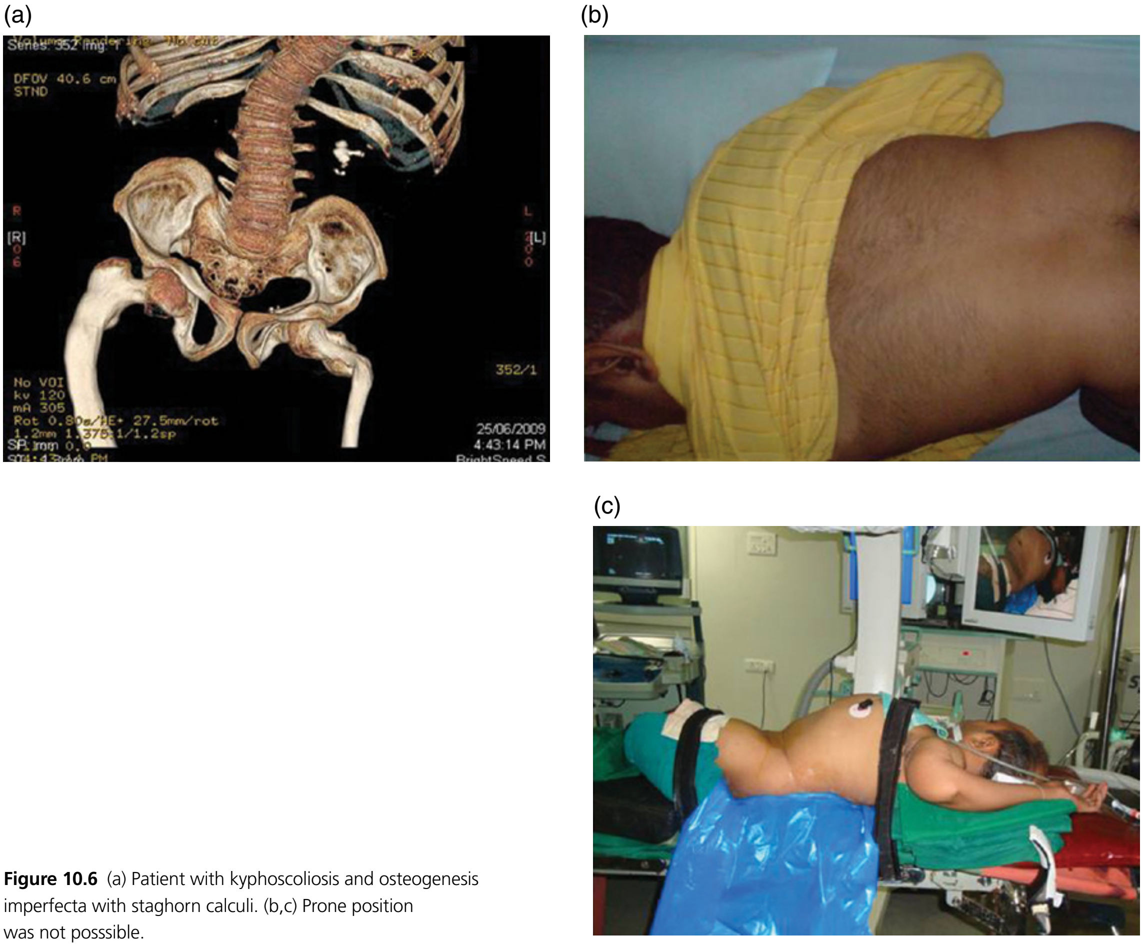

Figure 10.6 (a) Patient with kyphoscoliosis and osteogenesis imperfecta with staghorn calculi. (b,c) Prone position was not posssible.

In patients with kyphoscoliosis and skeletal deformities, positioning the patient in prone position is challenging and supine PCNL is a viable option. Figures 10.6 and 10.7 depict a similar case.

Stones in a renal allograft

Large stones in a renal allograft need clearance with PCNL. PCNL in an iliac fossa transplant needs to be done in a supine position because of the position and lie of the kidney. The allograft lies superficial in comparison to a normally placed kidney.Thus technically the renal access is easier but in such situations ultrasound-guided access is preferable as it would show the intervening bowel and Doppler mode would show the relation of the kidney to the vasculature. The access point should be lateral as a more medial access would bring the risk of intraperitoneal transgression. It would also be prudent to gain upper pole access in such situations as this would make manipulations into the upper ureter and the renal pelvis easier if required; in addition, upper pole access would decrease the chance of injury to the bladder, ureter, and major vascular structures.

Francesca et al. report a case of a staghorn calculus in a 45-year-old female recipient of a renal allograft [5]. The positioning of the patient is crucial. The patient should be kept in a supine position with a bolster under the ipsilateral flank with a slight tilt on the opposite side. Upper pole access was gained and a balloon dilator was used for dilating the tract up to 30 F.

There may be concerns regarding the density of scar tissue and difficulties in dilating the tract [14]. To

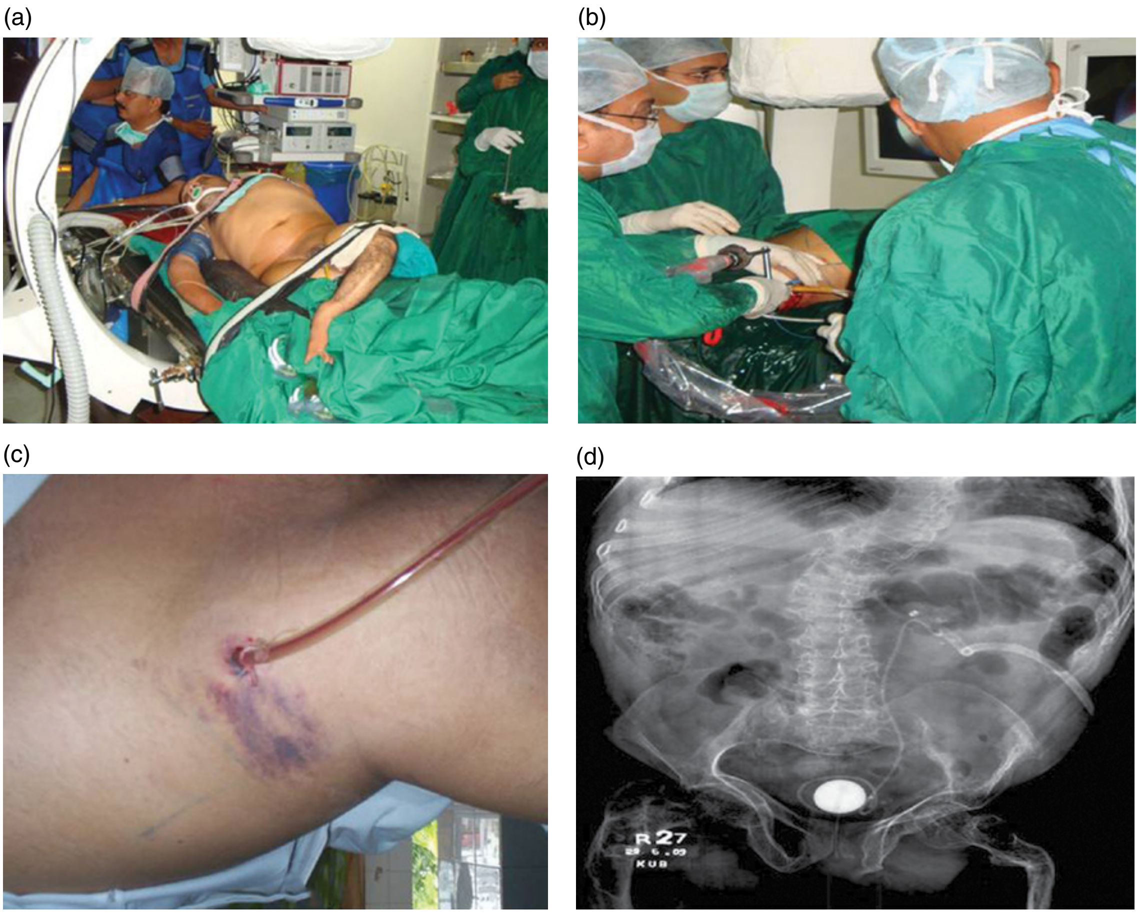

Figure 10.7 In this case supine PCNL was performed. (a,b) Care taken with positioning. (c) Postoperatively, a nephrostomy was retained and (d) a radiograph showed complete clearance.

overcome the morbidity of larger instruments and working sheaths in these patients, del Pizzo et al. used a modification of an O'Brien suprapubic peel-off sheath for PCNL in these patients, which helped by decreasing the size of the nephroscopes [15].

Outcome for supine percutaneous nephrolithotomy

In their metaanalysis of four studies, Liu et al. [16] found that there was no significant difference between PCNL in supine and prone position with regard to stone-free rate, which was 83.5% and 81.6% respectively. They also observed that supine PCNL had a shorter operative time. De Sio and associates [17] and Shoma and coworkers [18] reported higher complication rates in supine position, whereas Falahatkar et al. [3] and Amon et al. [19] reported more complications in prone position. In their metaanalysis, Liu et al. [16] found similar complication rates irrespective of position for PCNL. There was no statistically significant difference in transfusion rate and fever rate between supine and prone position in the metaanalysis by Liu et al. [16].

In their study comparing Valdivia and prone position in PCNL, Amon et al. [19] reported one incidence of colonic injury and to date this is the only incidence of colonic injury published.

Conclusion

Supine PCNL is a viable alternative for management of renal calculi in a subgroup of patients with urolithiasis which includes simultaneous renal and ureteric calculi, high-risk, and obese patients. Supine PCNL offers the known advantages of being anesthesia friendly, shorter hospital stay, lesser exposure of surgeon to radiation, and less chance of colonic injury. The disadvantages of this approach include inability to access the upper calyx and less maneuverability.

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11

CHAPTER 11

Instrumentation and Surgical Technique: Step-by-Step Percutaneous Nephrolithotomy: Prone-Flexed/Lateral

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Percutaneous nephrolithotomy (PCNL) can be performed with the patient in a variety of positions. This chapter will first describe the prone-flexed position, which is the preferred approach at our center, followed by the lateral-flexed position, which is our preference for obese patients.

Although preoperative preparation was discussed in Chapter 5 (Patient Selection and Informed Consent), patient- and stone-related factors must be considered when deciding if it is safe to proceed under a general anesthetic (GA) in the surgeon's preferred position. PCNL is usually performed under GA but in morbidly obese patients, in whom there is concern that ventilation will be difficult, successful PCNL has been described under local anesthetic [1] or intravenous sedation [2].

Patient positioning

Urologists around the world are taught various methods of performing a PCNL. Once they become comfortable with a specific technique, they tend to become advocates and promote that approach. Ideally, one would learn the various techniques described in this book, and choose the most suitable procedure and position for a specific case.

Prone-flexed

The prone-flexed position for PCNL is a simple modification of the prone position that we have been using as our standard position for 10 years. In the prone-flexed position (Figure 11.1), the anesthetized patient is placed prone on a radiolucent operating table, with the endotracheal tube and face protected by appropriate padding. The patient is flexed at the waist by 40–60° and at the knees by 30°. Patients are positioned with the iliac crest at the level of the break in the table. Alternatively, bolsters or a modified mattress may be placed at the waist to achieve this flexion, with the knees flexed on pillows. A padded chest bolster is placed slightly inferior to the axillae to facilitate ventilation. Pressure points are padded and the arms are extended above the head. Both elbows are flexed with the shoulders abducted 90°. Care is taken to avoid excessive external rotation of the shoulders to avoid brachial plexus injury.

There has been much debate about the advantages and disadvantages of various positions for percutaneous surgery, which is beyond the scope of this chapter. However, the prone-flexed position, which is our standard position, has several advantages.

1 Flattening of the normal lumbar lordosis, which:
  - drops the buttocks to give improved access (over the prone position) for lower pole tracts. This allows more

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Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

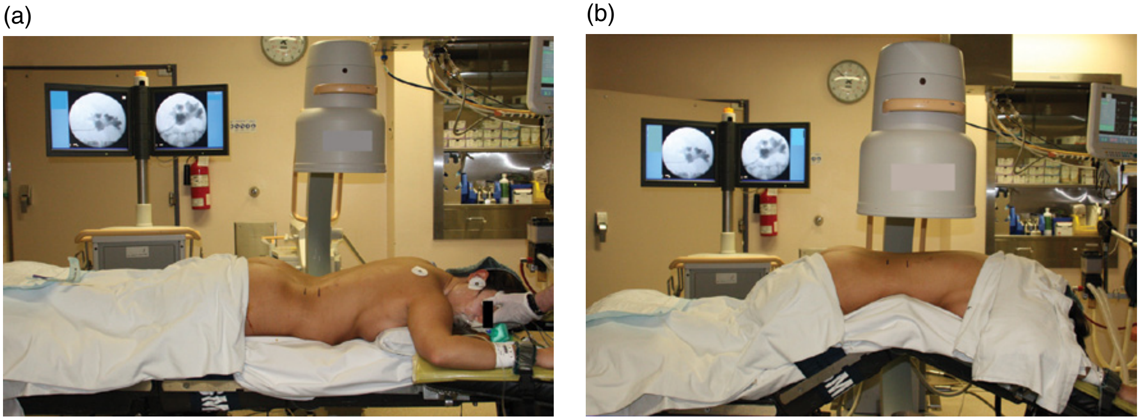

Figure 11.1 (a) Patient in traditional prone position. (b) Same patient in prone-flexed position. Note the widening of the working space and flattening of the lumbar lordosis, which drops the buttocks and allows improved lower pole access.

angulation of the nephroscope, which may otherwise be restricted by the buttocks

- allows a wider range of motion of the nephroscope with upper pole access, for a more direct view down the axis of the kidney.

2 Widening of the space between the 12th rib and posterior iliac crest, which increases the working space for PCNL [3].

3 Shortening of the skin-to-calyx distance for upper or lower pole access, compared to the prone position [3].

4 Displacement of both kidneys inferiorly relative to the ribs, with the left kidney becoming more inferior than the right. When prone-flexed versus prone position was compared with computed tomography (CT) scans of a group of patients, it was predicted that there would be 45.5% fewer supra-11th rib punctures if access was performed in the most superior calyx [3]. With the prone-flexed position requiring fewer supracostal accesses, the risk of pleural complications is diminished.

5 Widening of the angle between the upper pole calyx and the spleen (on the left) and the liver (on the right), when compared to prone and supine, making injury to these organs less likely during upper pole access [3].

6 Patient comfort. With the patient prone, the lumbar spine has a slight lordosis and the neck is extended. In the prone-flexed position, the spine and neck are flexed, which is the more comfortable "fetal position."

We have examined triphasic CT scans of patients performed for the evaluation of gross hematuria, with each phase in a different position (supine, prone, and prone-flexed). This has documented the improved angles and distances described above [3].

There are advantages shared with the traditional prone position, such as easier access to the upper pole for the treatment of staghorn stones and stones in multiple lower pole calyces. Most supine procedures are performed through a lower pole access.

Most of the disadvantages of the prone-flexed position are shared with the standard prone position, including:

- longer operative time due to patient repositioning after GA induction, which is performed with the patient supine
- respiratory or cardiovascular changes that may preclude PCNL while the patient is prone or prone-flexed. Although airway pressures are increased with the patient prone, and further increased to a minor degree with the patient flexed, at no time have we found the prone-flexed position to increase the difficulty of ventilation that would be improved by conversion to the prone position. When prone, the most universal cardiovascular finding is a decrease in the cardiac index (CI). A major contributor is inferior vena cava obstruction, with a resultant decrease in venous return, from pressure on the abdomen that can be exacerbated in the obese patient [4]
- the most consistent respiratory finding is a relative increase in the functional residual capacity (FRC) when moved from supine to prone [4]. However, the FRC was lower in obese patients when supine than in nonobese supine [5]. Interestingly, obese patients (Body Mass Index [BMI] >30) have been shown to have increases in lung

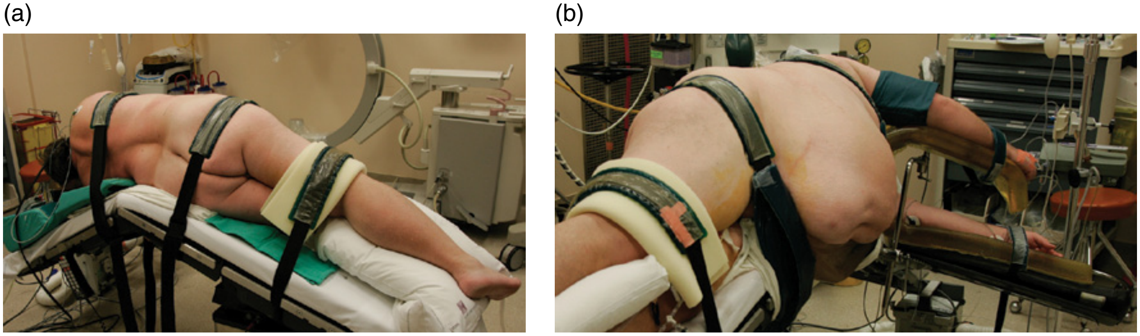

Figure 11.2 (a) Obese patient in lateral-flexed position, seen from behind. (b) Note the pannus that falls laterally, away from the puncture site of the PCNL.

volumes, lung compliance, and oxygenation when turned prone [5]. From a respiratory standpoint, the prone-flexed position is usually well tolerated, as seen in our reported series of 318 consecutive PCNLs in the prone-flexed position [6]. However, the mean BMI was 27.8 ± 6.0, so the population as a whole was not obese

- theoretical risk of postoperative visual loss (PVL). This is a rare complication that has mostly been reported after prolonged spinal surgery in the prone position [7]. To our knowledge, it has been reported, as a transient complication, in only one patient after PCNL [8]
- poorly tolerated by morbidly obese patients who may have to be repositioned to the lateral-flexed position
- prone and prone-flexed positioning may not be feasible in patients with spinal deformities such as kyphoscoliosis.

When it is anticipated that a specific patient may not tolerate the prone or prone-flexed position from a respiratory or anesthetic perspective, PCNL in the lateral-flexed position is usually the best option.

Lateral decubitus and lateral-flexed

Percutaneous surgery in the morbidly obese need not be as challenging as it would first appear. There are patients whose weight makes it difficult to ventilate for any reasonable length of time while supine, and even more so when prone. However, once positioned laterally, the weight of the abdomen and pannus falls laterally (Figure 11.2), taking pressure off the diaphragm and vena cava and reducing ventilation pressures. Our preference is to flex the table, as one would for a flank incision, so the space between the 12th rib and the posterior iliac crest widens. The rolls of fat and pannus hang over the side of the table and may require additional support. There is usually significantly less fat over the back, and it is often possible to feel the ribs without difficulty. An upper pole puncture lateral to the paraspinal muscles gives the shortest tract to the collecting system and, even with morbidly obese patients, one is often surprised that a standard-length sheath and nephroscope are all that is required. This is especially noticeable with upper pole punctures, as the upper pole is closer to the posterior abdominal wall than the lower pole and less mobile, since it is more densely attached to Gerota's fascia.

The position is identical to the lateral-flexed position for open renal surgery through a flank incision. An axillary role and appropriate padding are used. There are numerous advantages to the lateral decubitus or the lateral flexed position.

1 Useful in patients who cannot tolerate prone or prone-flexed surgery, including the morbidly obese and those with severe skeletal deformities (e.g. kyphoscoliosis).
2 Can be performed safely under local anesthetic alone in patients who are not good candidates for GA [1].
3 The anatomical relations and position are familiar to all urologists who perform open or retroperitoneoscopic renal surgery.
4 Allows a large working space for PCNL instruments, particularly in the lateral-flexed position.
5 Allows simultaneous nephroscopy and retrograde ureteroscopy, if necessary.
6 Facilitates more comfortable and ergonomic angles for the instruments than when the patient is postioned prone or prone-flexed.

Some limitations to the lateral decubitus and lateral-flexed positions include the following.

1 Difficulty in using the bull's-eye fluoroscopic technique for access (described below). In the lateral position, the C-arm image intensifier cannot be rotated sufficiently, and complete lateral orientation of the C-arm would also expose the urologist to more radiation [1]. The triangulation fluoroscopic technique, used routinely by some urologists, should be used (described below). Many urologists are not familiar with the triangulation technique, and fluoroscopy can be limited by poor penetration in the morbidly obese. In these situations, ultrasound-guided access can also be used, either intraoperatively or preoperatively, but may require the assistance of an interventional radiologist.

2 Increased operative time due to the need for repositioning after anesthetic induction.

Instrumentation

Most of the instruments used in our standard, prone-flexed approach to PCNL can also be used for the lateral-flexed approach. A radiolucent operating table is needed, with either the capability to flex at the waist or a bolster (padded foam or a modified mattress) for 40–60° waist flexion, and a C-arm image intensifier.

Step-by-step technique

A retrograde pyelogram (RPG) is the initial step. It is our preference to perform this immediately after induction of anesthesia while the patient is still supine, as this is the simplest way to demonstrate the posterior calyces. However, it can be performed once the patient is repositioned prone. To start, a magnified scout film of the affected kidney is taken and either stored on the image intensifier or printed. With flexible cystoscopy, the ureteric orifice is cannulated with a 5 F Flexitip (Cook Medical, Bloomington, IN) ureteral catheter, with a terminal side hole to facilitate the aspiration of urine. Radiographic contrast is introduced and followed up the ureter with the C-arm, to exclude an undiagnosed ureteral stone. Contrast is observed flowing into the kidney and pooling in the dependent posterior calyces, as it is denser than urine. Full delineation of the posterior calyces is one advantage of performing the RPG while the patient is supine. Posterior calyces filled with urine may be difficult to opacify in the prone position and may remain invisible fluoroscopically.

The ureteral catheter is passed up into the renal pelvis and all the urine is aspirated. The collecting system is filled with undiluted contrast, which gives a complete picture of the collecting system and fills all the calyces. If any urine is left in the collecting system, the posterior calyces may become invisible when the patient is prone, as it floats atop the denser contrast. Further magnified images (an anterior-posterior and left and right 30° oblique) of the full collecting system are all captured, and saved for later review. In this way one can develop a mental three-dimensional image of the collecting system and plan the most appropriate site for puncture. In the anterolateral view, the posterior calyces are seen from the side and appear longer. In the anteromedial view, the posterior calyces move more medially and are viewed end-on and appear shorter or rounder (Figure 11.3).

After the RPG, a 0.038 inch guidewire is passed into the collecting system, and a ureteropelvic junction (UPJ) occlusion balloon (Cook Medical, Bloomington, IN) is passed over the guidewire and positioned with the tip in the renal pelvis. The balloon, filled with up to 1.0 cc of water, is seen as a filling defect in the contrast. It is positioned at the UPJ or upper ureter as dictated by the size and position of the stone. This is then secured to a Foley catheter with tape. The UPJ occlusion balloon is connected to contrast infusion, which distends the pelvis and calyces, while the balloon prevents contrast drainage from the system. The distended calyceal system facilitates access and, when access is performed, contrast flowing briskly out of the access needle confirms successful puncture. Our practice is to wrap the ureteral occlusion and Foley catheters in a sterile towel, to allow sterile access later for the retrograde placement of a ureteral stent with an attached tether.

The patient is then repositioned in either the prone-flexed or the lateral-flexed position. The positions are described in an earlier section.

Step-by-step technique: prone-flexed position

Once repositioned and prepared, a sterile neurosurgical drape is placed, with the adhesive film centered over the area to be accessed and drainage tubing attached to the

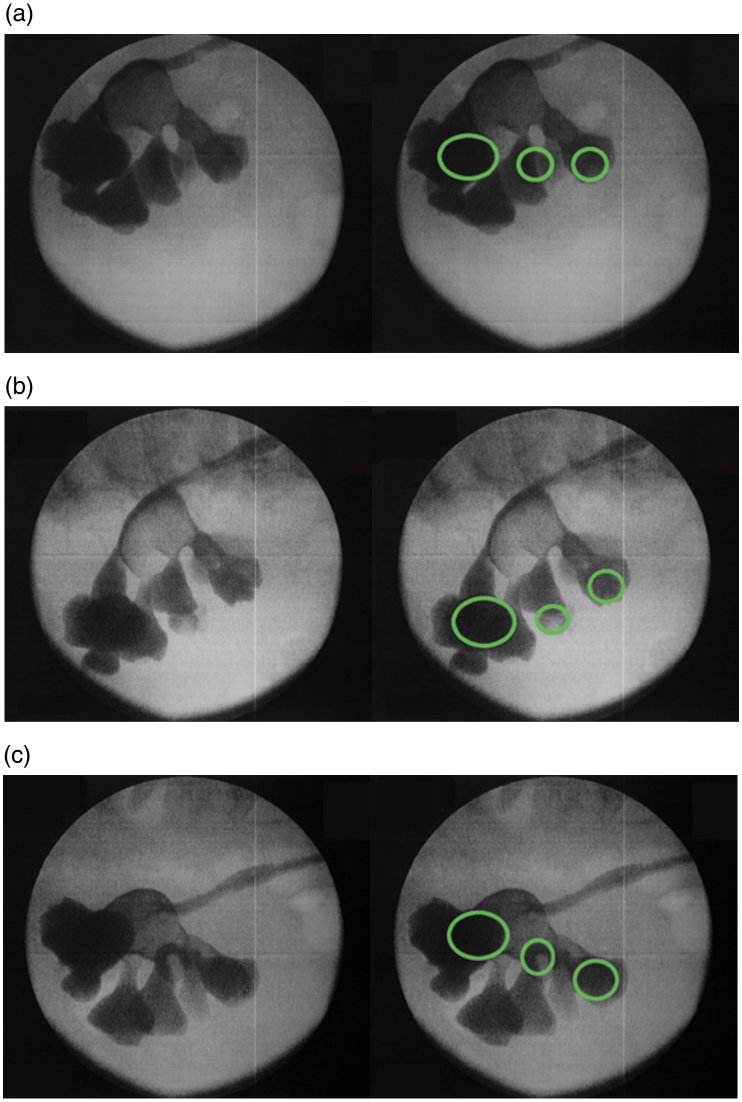

Figure 11.3 Example of retrograde pyelogram (RPG) images performed with the patient supine. A scout film is not shown. On the right-sided images, the posterior calyces are shown with green circles. (a) Antero-posterior (AP) RPG, performed with the C-arm vertical. While supine, the posterior calyces are dark. (b) Anterolateral RPG, performed with the C-arm rotated towards the surgeon. With the patient supine, posterior calyces are seen from the side and appear longer and more lateral versus AP. (c) Anteromedial RPG, performed with C-arm rotated away. With the patient supine, the posterior calyces are viewed end-on, appearing shorter, rounder, and more medial.

pouch. The surgeon reviews the saved anterior-posterior (AP), anteromedial, and anterolateral RPG images and chooses the most appropriate posteriorly oriented calyx for access. With the patient prone, the C-arm can be used to confirm the orientation of a calyx. The relative movement of a posterior calyx is opposite to when the patient is positioned supine: it will lengthen and move laterally when the C-arm is rotated away from the surgeon (i.e. anteromedial), and shorten and move medially when it is rotated towards the surgeon (i.e. anterolateral).

The ideal access will allow complete removal of all stones with rigid instruments, through a single tract, while minimizing the risk of associated morbidities. For example, an infracostal puncture through a lower calyx

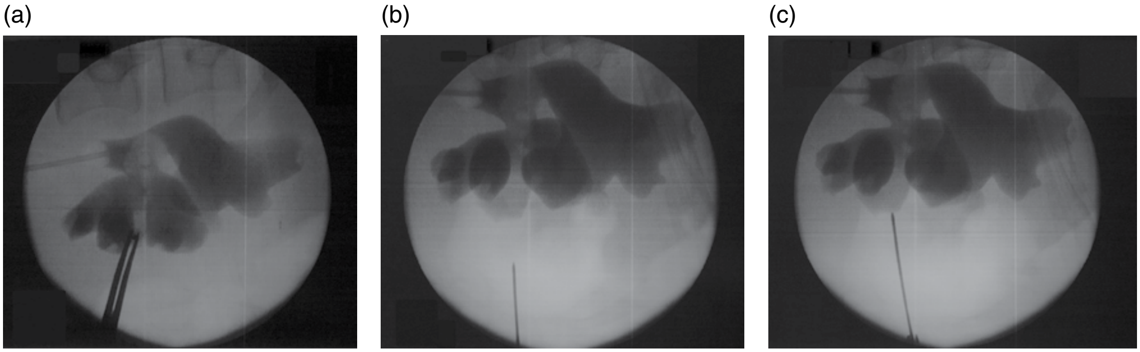

Figure 11.4 Bull's-eye targeting of a posterior calyx on fluoroscopy. (a) With the patient positioned prone-flexed, the C-arm is oriented so the x-ray beam follows the axis of a posterior infundibulum as closely as possible. Typically, this would be with the C-arm head angled 30° toward the surgeon. For upper and lower calyces, slight C-arm angulation towards the head (for upper calyces) or towards the foot (for lower calyces) gives a tract more in line with the axis of the kidney. With the C-arm stationary, looking at the calyx end-on, an 18 gauge diamond tip trocar needle is fluoroscopically aligned such that the needle tip overlies the center of the calyx. With the needle shaft held by a Kelly clamp or other device, to keep the surgeon's hand out of the image, the entire needle is aligned in a bull's-eye fashion: only the knob of the needle's obturator will be seen rather than the needle itself. The surgeon advances the needle in increments, during expiration, checking periodically to ensure the needle remains correctly aligned in a bull's-eye orientation. For supracostal punctures, the needle should be advanced only during full expiration, to ensure the lung is maximally displaced from the needle tract. (b) The needle depth relative to the calyx can be assessed by rotating the C-arm away from the surgeon, approximately 60–90° from the original position. In this case, the needle needs to be advanced several more centimeters. Before it is advanced, the C-arm is repositioned as in (a) to confirm that the needle is aimed right for the calyx in a bull's-eye orientation. (c) After further needle advancement during expiration, the needle is almost in the targeted calyx on this view with the C-arm rotated away from the surgeon.

eliminates the risk of pleural complications, but will make it difficult to access the upper calyces with a rigid instrument. On the other hand, access through an upper calyx enables access to the renal pelvis, UPJ, and the lower calyces via a more obtuse angle. An upper pole access frequently, however, results in a supracostal tract with a higher chance of pleural complications and possible intercostal nerve injury. Regardless of the calyx chosen, we use the bull's-eye fluoroscopic technique (Figure 11.4) to obtain percutaneous access.

An 18 gauge diamond tip trocar needle with a sliding depth marker (Cook Medical, Bloomington, IN) is used, held in a Kelly forceps to keep the hands out of the x-ray beam. The depth of the needle is checked in the AP and oblique views and once the needle has punctured the calyx, one feels a slight "give" as the needle advances more easily. Removal of the obturator will result in free flow of contrast out of the needle. An extra-stiff guidewire is advanced through the needle under fluoroscopic guidance, until a sufficient portion is within the collecting system to avoid inadvertent wire displacement during tract dilation. Ideally, the wire is advanced down the ureter, but coiling the floppy portion of the wire in an upper or lower calyx is acceptable. Prior to needle removal, the needle depth is marked with the sliding plastic depth marker.

The skin incision is widened horizontally to approximately 1 cm. Serial dilation is performed with fascial dilators (6, 8, 10 F) over the wire, which are passed to the same depth as the needle's depth marker. The dilators are fluoroscopically confirmed to have passed into the calyx. A 35 cm, 10 F dual-lumen catheter (Cook Medical, Bloomington, IN) is then passed over the wire, to permit passage of a second safety wire (Bentson) into the collecting system, which is secured to the drapes with drape tape.

Balloon dilation of the tract is addressed in detail in Chapter 7 (Tract Dilation and Endoscopes). An Amplatz working sheath with a 30 F inner diameter is advanced over the inflated balloon, in a twisting fashion, until it appears to be within the calyx on fluoroscopy. We start with a 20 F urethroscope with a 0° lens to confirm that the sheath is well positioned, as the irrigant flow and visualization are superior to the 26 F offset nephroscope. Lithotripsy techniques were discussed in Chapter 8 (Intracorporeal Lithotrites).

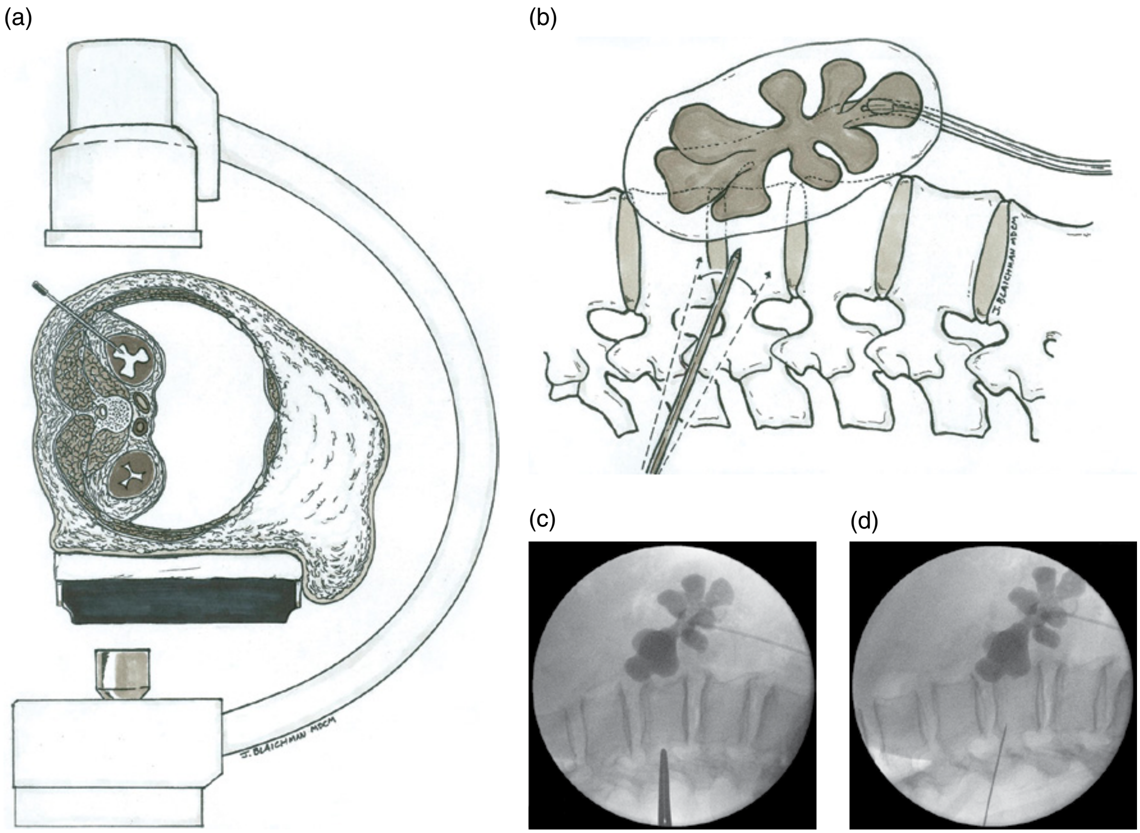

Figure 11.5 Triangulation fluoroscopic technique for access to a posterior calyx in the lateral-flexed position. The C-arm image intensifier is positioned vertically, perpendicular to the floor. (a) Cross-sectional illustration depicting the relative positions of the kidney, spine, and access needle. (b) Illustration of the fluoroscopic view with the C-arm in this position. Posterior calyces are directed towards the surgeon. Movement of the hand in the cranial-caudal plane will move the needle in the left-right plane. (c) With the calyces distended with contrast, the posterior calyx previously chosen for puncture is identified, as seen on this fluoroscopic image. This calyx should be directed towards the surgeon. A point on the skin is chosen, one to two fingerbreadths lateral to the paraspinal muscles and in line with the calyx in the cephalad/caudal plane. This site can be moved more cephalad or caudal if a rib is in the way, or if one wishes to angle the tract superiorly into a lower pole calyx. In this case, the skin puncture site was moved more cephalad since the chosen point was over the rib. Once the exact skin puncture site has been chosen, a small incision is made. (d) The needle is inserted and aimed directly at the chosen calyx under fluoroscopic guidance. Note should be made of the natural oblique axis of the kidney in these images, making access to the upper pole calyx relatively straightforward, whereas access to the lower pole, in the obese patient, may not be possible.

Step-by-step technique: lateral-flexed position

Once the patient is positioned as described above, access can be achieved with either ultrasound or fluoroscopy. Ultrasonic access is beyond the scope of this chapter, and is not our preferred approach. When performing fluoroscopy-guided access in the lateral-flexed position, supine RPG and UPJ occlusion balloon insertion are performed in a similar fashion to that described in the prone-flexed section.

With the patient in the lateral-flexed position, the C-arm cannot be rotated sufficiently for the bull's-eye technique. For an end-on view of the needle, the C-arm beam would have to be parallel to the floor with radiation directed at the operator. Instead, the triangulation fluoroscopic technique is used, which involves positioning the C-arm image intensifier vertically (Figure 11.5) and obliquely, towards the feet (Figure 11.6). Once the needle has punctured the targeted calyx, the remainder of the access proceeds as described in the prone-flexed section.

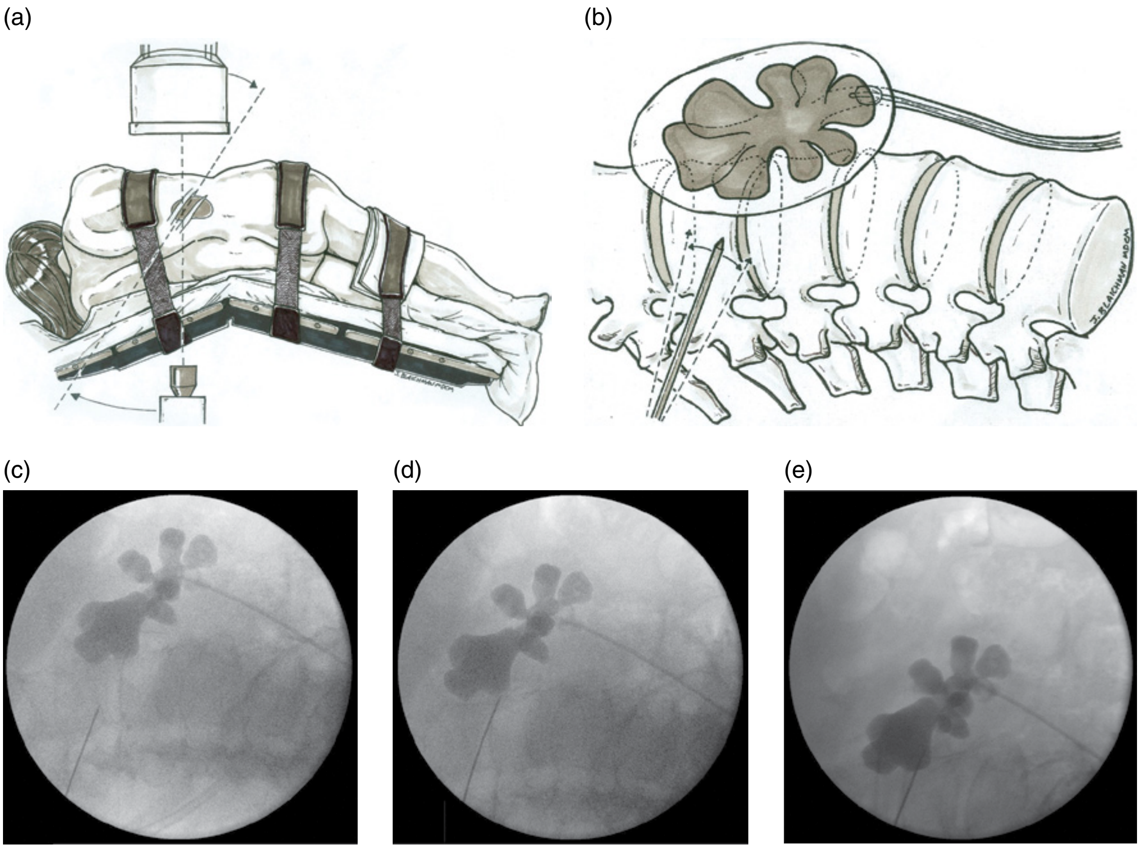

Figure 11.6 Triangulation fluoroscopic technique for access to a posterior calyx in the lateral-flexed position. The C-arm image intensifier is repositioned 45° from the vertical position towards the feet, for an oblique view. (a) Once the needle has been inserted 2–3 cm with the C-arm in the vertical position, the C-arm is rotated obliquely towards the feet so the x-ray beam penetrates at a 45° angle to the initial view. This gives a side view of the needle, rather than a view from above. (b) When the needle is viewed from the side, elevation (towards the ceiling) or lowering (towards the floor) of the hand holding the needle will adjust its tip in the anterior-posterior plane, relative to the kidney. (c) With the needle angle adjusted, in the vertical then the oblique planes, to aim directly at the calyx, the needle is advanced under fluoroscopic guidance. (d) The needle is advanced in a step-wise fashion during expiration, checking the direction in the two planes until the calyx is entered. Here, seen in the oblique plane, the needle is about to enter the calyx. (e) The needle has entered the collecting system.

Step-by-step technique: final steps

For all supracostal approaches, the ipsilateral lung field is examined fluoroscopically prior to concluding the procedure, to ensure there is no pneumo- or hydrothorax. The choice of drainage tubes and/or stents is surgeon specific, and will be discussed in Chapter 15 (Tube or Tubeless). However, our preference is to leave a ureteral stent without a nephrostomy tube. Although the stent can be placed in an antegrade fashion, it is our preference to insert this in a retrograde fashion, and a tether attached to the stent is left protruding from the urethra. A sterile towel is used to wrap the UPJ occlusion balloon and Foley catheters, prior to positioning the patient. At the end of the procedure, the UPJ occlusion balloon is cut to deflate the balloon and a guidewire is advanced through it up into the kidney. The UPJ occlusion balloon is removed and a short ureteral access sheath (e.g. 35 cm, 12/14 F) or an 8/10 F coaxial dilator can be advanced fluoroscopically to the level of the bladder neck, which is landmarked by the contrast-filled Foley balloon. The access sheath or dilator helps to maintain sterility of the ureteral stent as it is advanced over the wire into the desired position, under direct visual and fluoroscopic guidance. The working sheath is then removed, with direct pressure applied to the site for 2–3 min. We do not use sealants for the tract. Once hemostatic, the skin is closed with absorbable sutures and a sterile dressing is applied.

Intraoperative trouble-shooting

Related to positioning

Prone-flexed

If the anesthetist is having trouble ventilating the patient:

- ensure the bolster is under the upper chest at the level of the axillae
- ask the anesthetist to ensure that the endotracheal tube is not kinked and that excessive secretions are not the cause of the problem
- reduce the amount of table flexion, though it is rare to have to do this
- if returning the patient to the flat prone position does not solve the problem, consider using the lateral-flexed position, especially in obese patients.

Lateral-flexed

If the patient is well secured to the table with all pressure points padded, no problems should be anticipated with respect to positioning.

Related to procedure

1 Inability to opacify the collecting system during a RPG (e.g. from an impacted UPJ stone).

- Use alternative wires/catheters to bypass the stone. Examples include the Sensor wire (Boston Scientific, Natick, MA), with its hydrophilic tip, or the BiWire (Cook Medical, Bloomington, IN). The wire may be buttressed with a ureteral catheter for better purchase (e.g. 5 F Flexitip or a Kumpfe catheter).
- Use a 21 gauge spinal needle aimed at, and inserted directly down onto, the stone. Once urine is aspirated, a pyelogram can be performed by instilling contrast through the needle. A second puncture can then be made with the regular needle into a chosen calyx.
- Ultrasound-guided access for hydronephrotic systems.

2 After reviewing the previous RPG and choosing a calyx, the calyx may no longer be visible in the prone-flexed position. Being less dense, the urine may have floated atop the contrast and filled the posterior calyces, making them invisible.

- The UPJ occlusion balloon should be aspirated, with the introduction of more contrast.
- If unsuccessful, a small amount of air or CO_2 (<5 cc) can be injected via the ureteral occlusion catheter. The bubbles can be seen, on fluoroscopy, as filling defects floating up into the posterior calyces.

3 An inability to successfully enter the chosen calyx can be overcome by various strategies.

- Consider leaving the needle in position, to avoid contrast extravasation, and attempt a new approach with a second needle.
- Advance the needle slowly, using the bull's-eye technique, while checking the needle's position intermittently in two planes. The oblique plane is not at right angles to the needle, so the needle may actually be short of the target and require further advancement.
- If there is an inability to pass a wire into the collecting system due to an impacted stone, try a new wire (Sensor or fully hydrophilic BiWire). If unsuccessful, a new calyx should be targeted.
- If the path to the chosen is obstructed by a rib:
  - pick an alternative calyx, or
  - rotate the C-arm laterally towards either the head or feet, at right angles to the C-rotation, in order to look above or below the rib. However, it is important to consider the future direction of the nephroscope to reach the stone. For example, one should avoid angling the needle up in a superior direction to access an upper calyx, if it will be necessary to work down the axis of the kidney towards the lower pole. The torque required to do this could split the renal parenchyma and cause bleeding.

4 Inability to clear stone(s) with one tract.

- If it is not possible to access some of the stones with the flexible instruments through the tract, consider:
  - placing another tract
  - retrograde ureteroscopy and lithotripsy. The ureteral occlusion catheter can be exchanged to a ureteral access sheath, over an extra-stiff guidewire, through which ureteroscopy can be performed. This may performed in the prone-flexed position or, even more simply, in the lateral-flexed position
  - planning for an ancillary procedure, such as ureteroscopy or shock wave lithotripsy.
- If the need for multiple tracts is anticipated, based on the initial images, consider making multiple needle punctures with placement of a regular Bentson

guidewire in each, prior to dilation of the first tract. Each tract should be dilated only if it is needed. When the tract is needed, dilation is started by changing to an extra-stiff guidewire. If one waits until the PCNL is under way to attempt a second tract, it can be difficult to distend the collecting system and opacify the calyx. However, provided the chosen calyx is accessible, one can use a flexible nephroscope to visualize the targeted calyx and then pass the needle directly onto the tip of the scope, using the bull's-eye technique.

5 Discussion of the management of PCNL complications is beyond the scope of this chapter.

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12

CHAPTER 12

Instrumentation and Surgical Technique: Step-by-Step Percutaneous Nephrolithotomy: Endoscopic Guidance

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Percutaneous renal surgery is frequently employed to treat large renal and proximal ureteral calculi, ureteropelvic junction obstruction, and selected upper collecting system tumors. According to the American Urological Association (AUA) guidelines for staghorn calculi, percutanous nephrolithotomy (PCNL) is the treatment of choice for its relatively low morbidity and high stone-free rates [1]. With regard to the management of ureteral calculi, the AUA guidelines recommend a percutaneous antegrade approach for large (>15 mm) impacted proximal ureteral stones, in conjunction with renal stone removal, in patients with a urinary diversion, and in patients in whom retrograde access has previously failed [2]. For optimal outcomes during PCNL procedures, precise access to the collecting system is required in order to achieve high efficacy and low morbidity. The technique of percutaneous renal access has evolved continuously since its inception 50 years ago [3]. This chapter reviews our technique for endoscopic-assisted percutaneous nephrolithotomy (EA PCNL).

Since its initial description by Fernström and Johansson in 1976 [4], PCNL has virtually dominated the field of surgical management of renal lithiasis for the management of large renal calculi [5]. Although percutaneous renal surgery has been established as the treatment of choice for patients with large renal stones [6], the imaging technique for establishing percutaneous access has remained essentially unchanged through the years. Fluoroscopy- or ultrasonography-guided establishment of the percutaneous tract has been the standard for more than 50 years, despite the well-recognized risks and limitations of this approach. Undoubtedly, fluoroscopy-guided percutaneous renal surgery can be technically demanding and at times ineffective in cases of a nondilated system, large stone burden, aberrant anatomy, and in patients who are either obese or have had previous renal surgery. Difficulty in reaching the desired calyx or the need for multiple punctures may result in a higher risk of intraoperative bleeding, urinary tract perforation, or unsuccessful stone removal [7].

Evolution of retrograde percutaneous access

The concept of retrograde access into the collecting system to improve the safety of establishing a percutaneous tract for stone extraction was first introduced in the 1980s. Hunter and associates [8] and Lawson and

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

colleagues [9] described their techniques for retrograde access independently. Retrograde access was initially thought to represent a safer and possibly easier technique to establish a tract as, in theory, the surgeon would be going from known (i.e. inside the kidney) to unknown (i.e. the retroperitoneal track). In addition, access to the calyx of interest could be precisely determined, because the puncture would begin in the calyx and proceed outward.

Toward this end, the Hawkins–Hunter and Lawson techniques were introduced as alternative methods of establishing a nephrostomy tract for percutaneous stone surgery [8,9]. The Lawson technique for retrograde access, which proved to be the more popular of the two, used a deflecting guidewire and ureteral catheter handled by the operator. The guidewire and ureteral catheter were advanced to the renal pelvis under fluoroscopic control to puncture the selected calyx for percutaneous access. The percutaneous tract was created from the inside out. The original technique and its subsequent modifications were reported to achieve successful establishment of percutaneous tracts in 89–100% of cases [10–14]. There were problems with this technique, however, which ultimately precluded its widespread adoption. These problems included the inability to bypass an impacted stone and the creation of long and serpentine percutaneous tracts due to the inability to control the puncturing rocket wire once it left the confines of the guiding catheter [15,16].

The next step in retrograde access and retrograde intrarenal surgery paralleled the development of highly functional flexible ureteroscopes [17].The smaller size, flexibility, improved active and passive deflection [18], and durability [19] of the new-generation ureteroscopes have enabled urologists to explore all renal calices in upward of 98% of patients [20]. Given a 3.6 F working channel and the miniaturization of the holmium laser fiber down to approximately 270 microns along with further downsizing of stone baskets, adequate irrigation flow could be assured. Reasonable irrigation and functional small-caliber instruments allowed for maintenance of visibility while stones could be adequately fragmented and extracted [21,22].

Further advances in retrograde access came with the resurgent interest in highly lubricated ureteral access sheaths. An initial experience with the reintroduced ureteral access sheath was reported in 2002, where both 10/12 F and 12/14 F access sheaths were studied in a cadaveric model. In this study, the authors compared intrarenal pressures when the ureter was empty or when it contained an access sheath, 6 F ureteral catheter, or occlusion balloon catheter. The use of the ureteral access sheath dramatically decreased intrarenal pressure while increasing irrigation to the renal pelvis [23]. Further study revealed that during the application of a ureteral access sheath with ureteroscopic irrigation pressures of 200 cmH_2O, the intrarenal pelvic pressures never exceeded 30 cmH_2O, and never exceeded 20 cmH_2O while using the larger 12/14 F or 14/16 F ureteral access sheaths [24]. In addition to reducing intrarenal pressures, placement of an access sheath can be beneficial by facilitating rapid, repeated, and atraumatic access to the upper tract. Accordingly, the safe repeated passage of the endoscope both minimizes ureteral trauma and endoscope damage, which can provide long-term cost savings [25,26]. The sheath is now a widely accepted tool that enables passage of small stone fragments and debris, improves irrigant drainage, and maintains low intrarenal pressures during endoscopic procedures [27,28].

In 2003, a case series using a combined antegrade and retrograde approach for PCNL utilizing a ureteral access sheath confirmed that the application of the access sheath was safe and effective for PCNL of large renal stones, thus paving the way for EA PCNL [29]. The EA PCNL technique capitalized on the advantages previously demonstrated by using an access sheath for PCNL procedures and moved this concept to a new level by using direct endoscopic vision to facilitate the needle puncture, tract dilation, and sheath placement. Upon initial application of the EA PCNL technique, it became immediately clear that it had tremendous advantages. The procedure enabled precise placement of the nephrostomy needle and made the dilating balloon and PCNL sheath placement precise to the millimeter. The EA PCNL technique for percutaneous access was initially reported by us in 2006 [30]. Using this technique in over 100 patients now at the University of California, Irvine, we have been able to eliminate both the common problem of having the 30 F sheath fall short of the collecting system, necessitating additional tract manipulation, and the less common, but more disconcerting, situation of injury to the anterior wall of the calyx secondary to "past-pointing" with passage of the dilator or sheath too deeply into or through the collecting system. Our rate of pulmonary complications (hemo/hydrothorax and pneumothorax) has also declined despite our routine use of supracostal upper pole access. The technique has also allowed less experienced members of our surgical team to more easily and safely deploy the nephrostomy needle percutaneously.

Technique

Patient preparation

Patients are positioned prone with their legs abducted on spreader bars to allow simultaneous access to the affected flank and to the perineum (Figure 12.1). Two padded rolls are typically used beneath the lower chest/upper abdomen, and special care is taken to secure the neck, shoulders, and upper extremities in a neutral position. Both areas, flank/perineum, are prepared and draped. Access to the urethral meatus is critical, and the patient is positioned such that the meatus is easily accessible. In male patients, it is important to position the patient far enough down on the table such that the phallus lies entirely free of the operating table.

Instrumentation necessary for this approach is detailed in Box 12.1.

Box 12.1 Instrument set for endoscopy-guided percutaneous renal access

Fluoroscopy-compatible operating room table with spreader bars
Fluoroscopic C-arm
Flexible cystoscope (16 F standard)
Flexible ureteroscope (7.5 F tip and 7.5 F shaft if using a 9.5/11 F ureteral access sheath)
Rigid nephroscope (26 F offset lens)
Flexible nephroscope (16 F)
Video tower set-up with light source and monitor
Standard surgical tray (with #11 scalpel blade and Kelly clamps)
8/10 F coaxial dilator introducer set (2)
Side arm sealing adapter
5 mm fascial incising needle
Ureteral access sheath – size and length dependent upon patient's sex and size of ureteroscope to be used
0.035 inch 150 cm nitinol guidewire
0.035 inch 145 cm super-stiff guidewire (2)
0.035 inch 150 cm floppy-tip guidewire
0.035 inch 260 cm floppy-tip exchange guidewire
18 gauge 15 cm nephrostomy needle
30 F nephrostomy dilating balloon with 30 F sheath
12 F Foley catheter
Ominpaque contrast (Iohexol 300 mg/mL) – can be used as full strength or diluted with saline
10 cc syringe; 20 cc syringe; three-way stopcock and irrigation extension tubing, which can be used in circuit with endoscopic irrigation for ease of aspiration or instillation of contrast via the scope channel

(N.B: guidewires should only be opened upon request of the surgeon)

Figure 12.1 Patient is positioned prone on spreader bars ensuring access to the urethra and flank at all times during the case.

Ureteral access

A flexible cystoscope equipped with a 0.035 inch floppy-tip hydrophilic or nitinol guidewire is passed with the patient lying in the prone position as described above; the ipsilateral affected ureteral orifice is identified and the guidewire is advanced up the ureter under fluoroscopic control into the renal pelvis.

After removal of the flexible cystoscope, an 8/10 F coaxial dilator sheath system (Boston Scientific, Natick, MA or Cook Urological, Bloomington, IN) is advanced over the guidewire; the 8 F catheter is removed and an adapter is placed on the 10 F sheath to perform retrograde pyelography. The adapter is removed and a 0.035 inch super-stiff guidewire (working guidewire) is passed through the 10 F sheath. The 10 F sheath is withdrawn and the floppy-tip or nitinol guidewire is coiled and fixed to the drapes with a Kelly clamp; this guidewire will serve as the safety guidewire. A 12 F Foley catheter is passed into the bladder to provide bladder drainage throughout the procedure. Next, a suitably long (35 cm for females and 55 cm for males) and appropriately sized (usually 9.5/11 F, 10/12 F, 11/13 F, or 12/14 F diameter) ureteral access sheath is passed over the working guidewire until its distal tip rests at the ureteropelvic junction. If the patient has been prestented, a 14/16 F access sheath can often be atraumatically deployed.

The working guidewire is removed and the ureteroscope is advanced into the renal pelvis through the access sheath. Via the working channel of the flexible ureteroscope, double-contrast nephrography (dilute contrast followed by 2–5 cc of air) is done to map the calyceal system and identify the calyx of choice, because the air will naturally move to the posterior calyces with the patient in the prone position. In cases where the infundibulum of the desired calyx is obstructed by a large calculus, ureteroscopic holmium laser lithotripsy is performed to carve a channel through the stone to allow the ureteroscope to be advanced into the desired calyx.

Percutaneous access

Typically, an upper pole posterior calyx is selected for the puncture. Calyceal puncture is performed under fluoroscopic control with the fluoroscope in a 30° cephalocaudal or 90° anterior-posterior position to move the puncture site away from an underlying rib. A small skin incision is made over the selected calyx. An 18 gauge nephrostomy needle is advanced toward the tip of the ureteroscope which is stationed in the desired calyx. The ureterosope provides a densely radiopaque target for guiding the needle. The advancement of the needle is monitored fluoroscopically with initial anterior-posterior views to position the needle hub over the tip, over the selected calyx and the tip of the ureteroscope. The needle is initially advanced 4–6 cm into the flank to fix its trajectory.

Figure 12.2 Combined fluoroscopic and endoscopic view ensuring precise needle entry into the calyx of choice.

Next, the C-arm is rotated in an arc to a 25–30° posterolateral-oblique position to monitor the advancement of the needle toward the calyx and the tip of the ureteroscope. The actual insertion of the nephrostomy needle into the collecting system is monitored under both fluoroscopy and direct ureteroscopic vision (Figure 12.2). The advancement of the needle as it punctures the calyx is monitored to ensure that the needle is not inadvertently advanced too deeply, thereby perforating the anterior wall of the calyx. The needle's obturator is removed and a 0.035 inch nitinol guidewire is passed through the needle and is directed down the ureter alongside the access sheath; alternatively, it can be coiled in the renal pelvis. This is also monitored under ureteroscopic and fluoroscopic control.

We find that through-and-through access provides the greatest safety and security. The guidewire can generally be passed into the access sheath; alternatively a basket can be deployed through the ureteroscope and opened just beneath the nephrostomy needle such that when the guidewire is passed, it traverses the open basket. The basket can then be closed and the ureteroscope, closed basket, and guidewire are delivered via the urethral end of the ureteral access sheath. Note that, if doing this in a tall or overly large male patient, a 260 cm exchange guidewire should be employed instead of the standard 145 cm length guidewire. The guidewire is delivered via the urethral end of the access sheath. The access sheath can then be withdrawn and passed again over the original safety guidewire, because the antegrade flank to urethral meatus through-and-through guidewire now can act as the new safety guidewire. A Kelly clamp can be placed on both the flank and urethral end of this guidewire, thereby securing it. Note that, when a through-and-through guidewire is secured, one does not need a separate percutaneous or ureteral safety guidewire as this one guidewire serves both purposes.

After the antegrade guidewire has been deployed, a #11 blade is used to enlarge the incision to 10–15 mm. The nephrostomy needle is removed and a 5 mm fascial incising needle is advanced over the guidewire parallel to the skin incision and the adjacent rib, thereby creating a 5 mm fascial incision. An 8/10 F dilator sheath introducer is then passed over the nitinol guidewire just into the collecting system to facilitate passage of a second (working) guidewire; this is performed under ureteroscopic vision. The 8 F dilator is removed and a 0.035 inch super-stiff floppy-tip guidewire is passed into the renal pelvis and coiled or passed into the ureter. At this point, if a through-and-through guidewire has not been established, then the original nitinol guidewire can be exchanged for a floppy-tip guidewire as the latter can be more easily kept in place. The 10 F sheath is removed and the floppy-tip guidewire is sutured to the flank to serve as a safety guidewire.

Tract dilation is performed under both endoscopic vision and fluoroscopic control. A 30 F dilating balloon is advanced over the working guidewire just until the tip of the balloon is ureteroscopically seen to enter the calyx (Figure 12.3). The nephrostomy tract is dilated by inflating the balloon under direct ureteroscopic vision and fluoroscopic control. Next, the 30 F working sheath which had been backloaded over the balloon is advanced until it has visually entered the desired calyx. The 30 F sheath is rotated under ureteroscopic guidance until all of its leading edge is circumferentially visible within the collecting system (Figure 12.4). This deployment technique allows for millimeter precision, and minimal trauma to the surrounding intrarenal collecting system. The balloon dilator is deflated and withdrawn. The ureteroscope can now be removed to allow maximum drainage of fragments and irrigation through the access

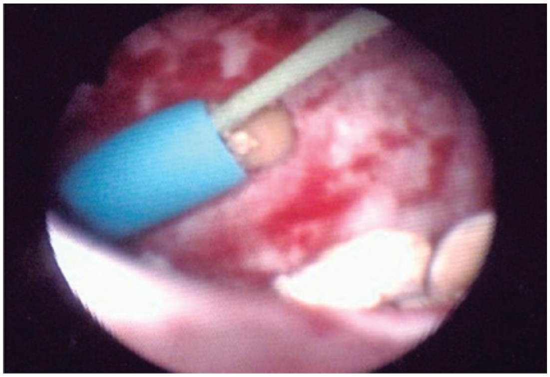

Figure 12.3 Placement of the 8/10 F coaxial dilator sheath system over the guidewire; the 8 F catheter is removed and an adapter is placed on the 10 F sheath to perform retrograde pyelography. Combined fluoroscopic and endoscopic vision ensures there is no unrecognized injury to the anterior collecting system.

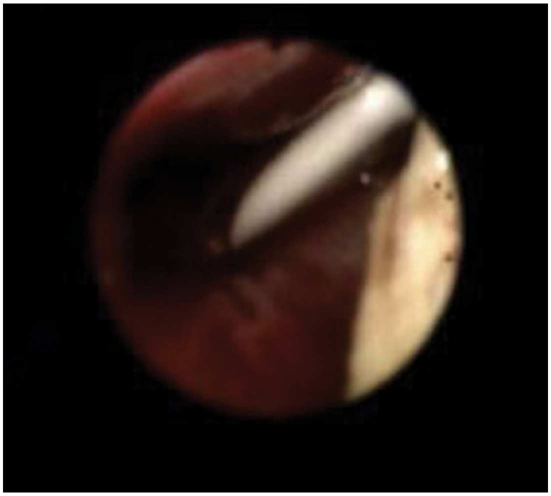

Figure 12.4 Endoscopic view showing percutaneous placement of balloon dilator under direct endoscopic vision ensuring precise tract dilation.

Figure 12.5 The tip of the ureteral access sheath is positioned just above the ureteropelvic junction to allow maximum drainage of fragments and irrigation through the access sheath during the nephrolithomy.

sheath, the tip of which should be positioned just above the ureteropelvic junction (Figure 12.5).

The rigid nephroscope is introduced through the 30 F sheath. If not performed earlier, at any point during the procedure, a 260 cm exchange guidewire can be advanced retrograde through the ureteral access sheath up to the renal pelvis, grasped with the nephroscope rigid forceps, and removed through the 30 F sheath to establish through-and-through flank-to-urethra access. In this case, the same maneuver as previously described can be done to remove and replace the ureteral access sheath, thereby insuring that the safety guidewire resides outside the sheath, allowing for maximal flow of irrigant and stone fragments down the ureteral access sheath.

Role in urological practice

Endoscopy-assisted percutaneous renal access was first successfully reported as a salvage procedure by Grasso and colleagues in 1995 [16]; they described seven patients for whom previous attempts at fluoroscopy-guided renal puncture had failed and among whom this approach worked well. Kidd and Conlin [31] later reported three cases in which through-and-through access was achieved with endoscopically guided percutaneous puncture and use of the ureteroscope. Both these techniques involved fluoroscopically guided percutaneous puncture with simultaneous direct vision using an actively deflectable, flexible ureteroscope to identify a specific calyx through which the tip of the intrusive needle and its antegrade guidewire were ureteroscopically snared and withdrawn out the urethra. The majority of the 10 patients from these two studies presented with a staghorn and/or diverticular calculi and were obese. However, in both reports, the endoscopic guidance was used only as a second-line salvage approach after the standard imaging technique had failed or proved problematic. It is also important to mention that in both these techniques, the ureteral access sheath was not used and as such the flexible ureteroscope was only used to monitor the percutaneous puncture and assist in establishing through-and-through wire access.

The combination of this approach with the ureteral access sheath was first applied by one of the authors at the Southwestern University in Dallas in 2005 [30]. The application of the ureteral access sheath took the procedure to the next level by allowing not only precise percutaneous access but also monitoring of guidewire placement, tract dilation and placement of the 30 F Amplatz sheath under direct vision at all times while keeping intrarenal pressures low at all times during the procedure due to outflow through the ureteral access sheath. The success of that initial case resulted in the technique being applied by one of the authors to all subsequent PCNLs at the University of California, Irvine, beginning in May 2005. Our initial results using this technique for 11 PCNL cases were promising [29]. Our cumulative experience with this technique in more than 100 patients now has confirmed that using both fluoroscopic and ureteroscopic guidance enables safe and precise placement of the nephrostomy needle into the desired posterior calyx and facilitates safe and accurate tract dilation and sheath placement. Moreover, in cases in which the targeted calyx is occupied by a large stone or a branch of a staghorn calculus, prepuncture reduction of the stone bulk with ureteroscopy ensures proper and complete entry of the sheath into the collecting system, thereby precluding extravasation of irrigant into the retroperitoneum, excessive manipulation of the tract with possible pleural injury, and loss of stone fragments into the retroperitoneum. This is especially beneficial in cases of large branched stones that are occupying several calyces where, using conventional PCNL, multiple tracts would be needed for complete stone clearance.

The number of access tracts appears to correlate with greater risk for parenchymal injury, increased blood loss, and higher transfusion rates [32–34]. In a report by Borin [34], endoscopy-guided access aided in reducing the number of punctures and tracts used for PCNL for staghorn calculi, with beneficial results in blood loss, pain, and less postoperative risk of fever and sepsis. Furthermore, some of the most dangerous complications of PCNL occur because of unrecognized perforation of the anterior collecting system. Even in very experienced hands, perforation of the collecting system has been noted in up to 7.9% of cases [35]. Collecting system perforation can lead to parenchymal injury and bleeding and, in some cases, even to injury to the colon or duodenum.

The combined EA PCNL technique provides a solution to preventing this potential problem from occurring. Apart from ensuring the safe establishment of the percutaneous tract, the combined use of antegrade and retrograde manipulations into the collecting system helps to ensure optimum stone clearance in cases of large staghorn calculi, because access to almost all renal calyces can be readily attained with the new-generation flexible ureteroscopes combined with an upper pole percutaneous access. Accordingly, the entire collecting system can be surveyed, and calculi in peripheral calyces, which would potentially need a second access tract, are accessed and treated [36,37]. The use of a ureteral access sheath facilitates the extraction of stone fragments and helps reduce intrapelvic pressure while maintaining irrigation flow [27,38]. Retrograde irrigation may further facilitate needle access by dilating the targeted collecting system [37]. Also, the presence of an access sheath facilitates antegrade flexible ureteroscopy from the tract to the ureter at the end of the procedure to identify and manage any missed ureteral stones or fragments as the sheath is being withdrawn.

Endoscopy-guided percutaneous renal access may be the answer to the problem of the steep learning curve of PCNL, which remains perhaps the most complicated stone surgery technique to teach. This translates into approximately 24 procedures needed for a resident to obtain proficiency in PCNL [39]. According to another study, surgical competence in PCNL, measured by fluoroscopy and operative times, is not achieved until after 60 cases [40]. The steepness of the PCNL learning curve is further emphasized by the fact that only 11% of US urologists obtain their own renal access [7]. Of note, this same study revealed that the rate of access-related complications was significantly higher when radiologists were obtaining the percutaneous tract. Therefore, combining the endoscopic skills inherent in all urologists with developing fluoroscopic skills for the establishment of renal access may help more urologists to become comfortable and proficient with percutaneous renal access. The shortcoming of this approach when applied to all PCNL cases is that it may add to operative time and cost. When we reviewed and compared our experience of 51 endoscopically assisted (E) to 70 standard access (S) PCNL cases [41], we discovered that operative time tended to be slightly longer, 19 min ($p = 0.1$), with the endoscopic approach. In the same series, estimated blood loss for the endoscopic group was 158 mL versus 211 mL for the standard group ($p = 0.03$), while postoperative transfusion rates were 7.8% in the endoscopic group versus 21.4% for the standard group ($p = 0.05$). Of note, more patients in the endoscopic group presented with a nonhydronephrotic system (27.1% versus 11.7%, $p = 0.04$). Although not statistically significant, there was a trend towards increased retreatment rates in the standard group (36% versus 24%, $p = 0.19$). Thus, the added cost of an additional few minutes of operating room time during the initial procedure may be counterbalanced by the 33% fall in second-look procedures and a more than 50% drop in transfusions.

Pulmonary complications after PCNL remain a significant source of morbidity. Using a supracostal approach while performing PCNL carries a higher risk of pulmonary complications than lower pole access [42]. According to a study done by Sukumar and colleagues [43], although the supracostal approach for PCNL is used when the predominant distribution of stone material is in the upper calyces or above the level of the 12th rib, in practice, this approach is often avoided for fear of potential chest complications. In a study done by Munver and coworkers [44], a comparison was made between a supracostal approach (supra-11th or -12th) and a subcostal approach. In 300 patients undergoing PCNL, 202 underwent a subcostal approach with one intrathoracic complication (0.5%), 72 underwent a supra-12th approach with one intrathoracic complication (1.3%), and 26 underwent a supra-11th approach with six intrathoracic complications (23%). This vividly demonstrated the increased morbidity with the more cephalad access.

We have analyzed the data in 111 patients at our institution (June 2005 to January 2010) using the endoscopic-guided percutaneous access and have found a significant decrease in the percentage of pulmonary complications when compared to other series in the literature [45]. A single needle stick was sufficient to gain precise access to the desired calyx in 84% of our patients. Upper pole access was obtained in 93% of our patients; 5% had lower pole and 2% had interpolar calyceal access. Overall, 96% of our patients required only a single access tract. Supracostal access was obtained in 75%. Postoperative chest radiographs revealed no abnormal findings in 72% of patients, atelectasis in 14%, pneumothorax in 3%, and effusion in 11% patients. Only two patients required a chest tube for drainage of effusion.

Comparison of our results to the current literature from eight large combined series of patients undergoing PCNL reported in *Campbell's Urology*, 9th edition, shows that despite a much higher number of supracostal accesses in our series (75%) versus 30% in the combined series, the incidence of pleural complications requiring treatment was significantly less (1.8% versus 4.1%).

Conclusion

Percutaneous renal surgery has proven to be a paradigm of how combining refined endoscopic techniques and advanced flexible endoscope technology results in an effective management solution. Recent developments are based on the surgical fundamental of optimal visualization, with an emphasis on control and precision to minimize surgical morbidity and complications.

As renal access techniques have progressed from a retrograde approach to a percutaneous approach with simultaneous endoscopic and fluoroscopic guidance, we have witnessed improved safety and efficacy in treating some of the most challenging upper tract pathology. In an effort to optimize outcomes, urologists performing these procedures need to consider all the equipment that is currently available, and the best combination of technologies to apply to each procedure. In this chapter we described how the arsenal of guidewires, endoscopes, ureteral catheters/dilators, and ureteral access sheaths can be utilized for obtaining and maintaining renal access throughout a procedure, but the story does not end here. The future will be in the development of sophisticated training programs so that urologists, both novice and expert, continue to obtain percutaneous renal access in an optimal manner. Ultimately, needle targeting will be the domain of computer-driven robots. However, until this time, EA PCNL provides the urologist with augmented control and effective access for large renal stone removal.

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13

CHAPTER 13

Instrumentation and Surgical Technique: Step-by-Step Percutaneous Nephrolithotomy: Mini-Percutaneous Nephrolithotomy

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Introduction

Percutaneous nephrolithotomy (PCNL) is recommended as standard therapy for kidney stones >20 mm, while shock wave lithotripsy (SWL) or flexible ureterorenoscopy (URS) is recommended for smaller renal calculi [1,2]. However, the stone clearance of lower pole calculi after SWL is limited, thus leading to an extended indication for PCNL even for stones 10–20 mm in many centers [3]. This trend has been further promoted by the introduction of so called mini-PCNL or mini-perc, which is postulated to be less invasive compared to standard PCNL due to the miniaturized instruments. It was first described by Jackman et al. for percutaneous nephrolithotomy in infants [4]. The use in adults has been subsequently described by several groups in the last few years [5–8].

Up to now, the term "mini-PCNL" has not been standardized, leading to the fact that sheath diameters below 20 F are defined as miniaturized. In fact, Jackman described a technique using an 11 F access tract, while Nagele et al. use 18 F and Lahme et al. 15 F [3,4,8]. The idea of using miniaturized instruments was based on the assumption of lower morbidity due to reduced tract dilation and less renal trauma. However, the reduced sheath diameter causes disadvantages as irrigation flow is limited and more extensive stone fragmentation is necessary, leading to prolonged operation times. Furthermore, no clear advantage in terms of less morbidity in comparison to conventional PNL has yet been demonstrated and some authors deny a benefit of mini-PCNL procedures [9]. Therefore, the role of mini-PCNL in the treatment of renal stones is still under debate.

In our department, we use mini-PCNL for solitary calyceal or renal pelvic stones up to 2 cm, whereas larger or complex stones are treated with conventional PCNL. Mini-PCNL is therefore rather an alternative to SWL or flexible URS in the treatment of nephrolithiasis < 2 cm.

Informed consent

Generally the informed consent for mini-PCNL is consistent with that of conventional PCNL. It should include information about the alternative treatment options for renal stones, SWL and flexible URS, including their pros

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and cons in comparison to mini-PCNL. Furthermore, information about conventional PCNL should be included and the differences from the mini-PCNL technique outlined.

In detail, the informed consent should include the following topics/risks.

- Increased stone-free rate after a single procedure in comparison to SWL and flexible URS
- Need for reintervention in cases of stone persistence
- Possible need for urine drainage via a nephrostomy or ureteral catheter postoperatively
- Urinary tract infection, fever, and urosepsis
- Bleeding with the rare need for transfusion
- Severe bleeding with the very rare need for superselective embolization or emergency nephrectomy
- Injury of adjacent organs (bowel, lung, spleen, liver)
- Injury of ureter resulting from balloon occlusion catheter.

Preoperative preparation

All patients need thorough preoperative imaging, including plain abdominal film and intravenous urography or computed tomography, to determine the exact stone size and localization. Furthermore, outlining the anatomy of the renal collecting system gives crucial information in the planning phase of the procedure, e.g. which calyx to choose for access. Also, preoperative ultrasound imaging is advisable to determine if the planned access to the kidney can be achieved or if anatomical abnormalities, e.g. interposition of colon, prevent safe puncture of the desired target calyx. Ideally, the urologist who will perform the procedure should do the preoperative ultrasound examination.

Laboratory tests should include a dipstick urine analysis and preoperative urine culture. Existing urinary tract infections should be treated with appropriate antibiotics, ideally for several days before surgery. However, urine cannot always be completely sterilized, especially in patients with infection-associated stones.

Blood analysis should include electrolytes, red and white blood count, serum creatinine, and coagulation status. Untreated coagulation disorders or anticoagulative medication are regarded as contraindications for percutaneous stone surgery.

Besides imaging, the preoperative diagnostic work-up should include a general physical examination of the patient to reveal any severe comorbidities. Other specific preparations of the patient before surgery are usually not necessary.

Patient positioning

Generally, the operating room should include a fluoroscopy unit (C-arm or fixed unit) and, in our technique, an ultrasound scanner, ideally with a needle-guide adapter. As the procedure is most often performed under general anesthesia, the required anesthesiological facilities have to be available.

At the beginning of the procedure, the patient is positioned in lithotomy position to allow cystoscopy and placement of the balloon occlusion catheter. Afterwards, the patient is turned into prone position for the puncture of the collecting system and percutaneous intervention. Although this is our preferred positioning, alternative positions have been described for PCNL, including supine, prone-flexed or oblique supine [10–12]. Generally all described positions can also be used for mini-PCNL.

Instrumentation

The instrumentation for mini-PCNL includes the following.

- Fluoroscopy unit
- Video-endoscopy
- Ultrasound scanner with needle-guide adapter
- Balloon occlusion catheter 5 F
- Foley catheter 18 F for bladder drainage and fixing the occlusion catheter
- Sterile coverings
- Puncture needle
- Contrast dye
- A set of guidewires (floppy-tip guidewire, glidewire, Lunderquist wire)
- Metal single-step dilator 16.5 F
- Amplatz sheath 18 F
- Mini-nephroscope 14 F
- Holmium:YAG laser and 220 μm or 365 μm fiber
- If necessary, nephrostomy tube 16 F or double-J catheter
- Optional: thrombin matrix (e.g. Floseal, Baxter) for access tract closure.

Step-by-step technique

Generally the intervention is performed under antibiotic prophylaxis. Ideally, manifest urinary tract infections should be treated with appropriate antibiotics according to the urine culture for several days before the intervention.

For puncture, we follow the Mannheim technique [13]. The patient is first placed in the lithotomy position. A cystoscope is introduced into the bladder and an overview cystoscopy is performed. Afterwards, a balloon ureter catheter is introduced in the orifice and a retrograde pyelography is performed. The balloon catheter is advanced into the renal pelvis or proximal ureter and blocked with 1–2 mL air under fluoroscopic control. A Foley catheter is placed and the balloon catheter is fixed to the Foley catheter.

The patient is then turned into the prone position, but alternative positions (supine, prone-flexed, oblique supine) are also possible. To facilitate access to the target calyx, the renal collecting system is filled with a mixture of contrast agent and methylene blue dye via the balloon catheter.

In our technique, the puncture is performed under simultaneous fluoroscopic and sonographic guidance. Depending on stone localization, a target calyx is identified. The ideal approach is a transpapillary puncture of the calyx with a straight access to the renal pelvis. By combining fluoroscopy and ultrasound, a three-dimensional view of the kidney and the collecting system is achieved in real time. Furthermore, in contrast to sole fluoroscopic imaging, adjacent organs such as bowel, liver, spleen or lung can be identified and an accidental injury avoided. The use of a needle-guide adapter facilitates the puncture greatly. The puncture and dilation process are demonstrated in Video Clip 13.1.

After identifying the ideal puncture site, a small skin incision is performed and the needle is advanced to the desired calyx under continuous sonographic control. In addition, short fluoroscopic pulses can be used to confirm the advance to the correct calyx (Figure 13.1). After reaching the calyx, the correct puncture is verified by the blue color of the methylene blue dye/contrast agent outflow.

Figure 13.1 Puncture of renal collecting system via lower calyx.

Once the correct position of the needle tip is ascertained by contrast agent injection, a floppy-tip guidewire is advanced into the collecting system under fluoroscopic control. If possible, it should be positioned in the renal pelvis. The tract is initially dilated with a 9 F polytetrafluoroethylene (PTFE) dilator. If the puncture was performed correctly, the dilator passes easily into the renal pelvis with no resistance. After removal of the plastic dilator, a metal 16.5 F single-step dilator is used for further dilation. It is also advanced over the guidewire under fluoroscopic control (Figure 13.2). To avoid kinking of the guidewire, the dilator is pushed using rotating movements with careful pressure. Intermittent short fluoroscopic pulses are used to control the advance into the renal pelvis. A second wire can be passed as a safety wire through the dilator. Next, the 18 F mini-nephroscope Amplatz sheath is introduced over the dilator and advanced into the collecting system (Figure 13.3).

After removing the dilator, the 14 F mini-nephrosope is introduced through the Amplatz sheath (Figure 13.4). The continuous inflow of irrigation fluid through the nephroscope and outflow through the sheath provide

Figure 13.2 Dilation with metal single-step dilator over previously placed guidewire.

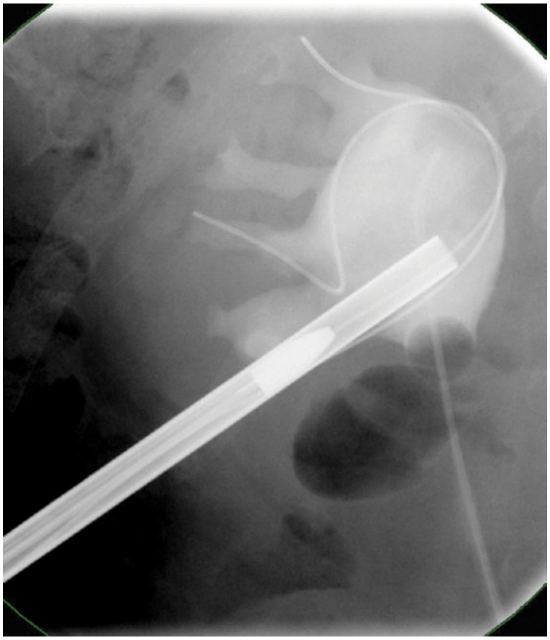

Figure 13.3 Advancing the mini-nephroscope sheath over the dilator.

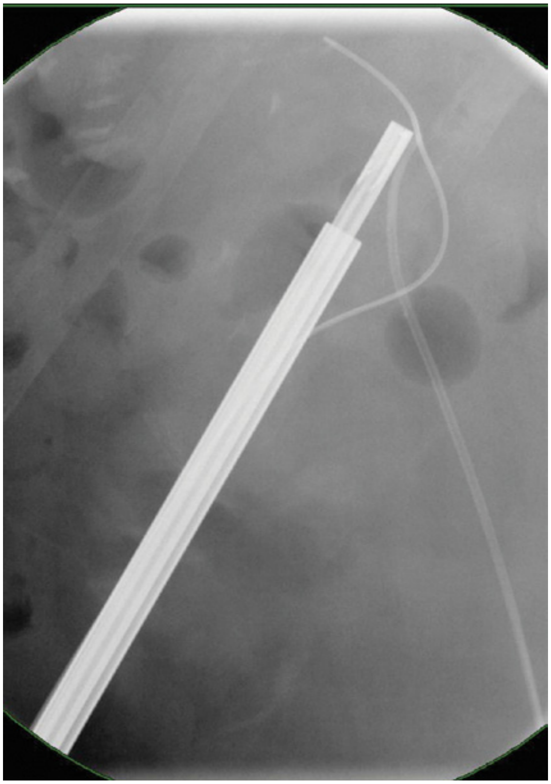

Figure 13.4 Introduction of mini-nephroscope through the sheath.

a good visibility and low intrarenal pressure. This is important to prevent pyelotubular and pyelovenous reflux with consecutive septicemia, especially in patients with infection stones.

After visualization of the stone, a holmium:YAG laser is used for lithotripsy. We use mainly 365 nm fibers for stone disintegration, but 600 nm fibers can also be used as higher energy levels can be transmitted through them, allowing more rapid disintegration of larger stones. Generally two lithotripsy concepts are possible. The first option is to use the laser to pulverize the stone. The resulting fragments are small enough to be washed out by the irrigation flow between the nephroscope and the sheath. To achieve this, a low-energy/high-frequency setting should be chosen for the laser. The other option is to disintegrate the stone into larger pieces which can be either extracted with a basket or forceps or washed out passively by slowly pulling back the nephroscope into the sheath. If this is done correctly, the

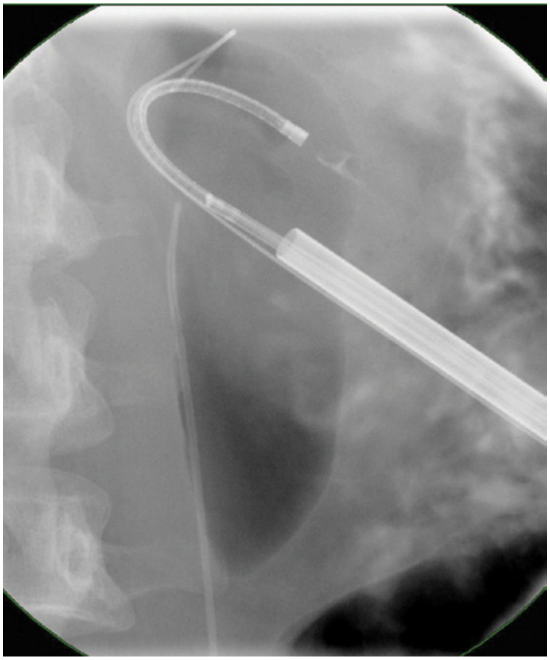

Figure 13.5 A flexible ureterorenoscope can be passed via the sheath to reach other calyces.

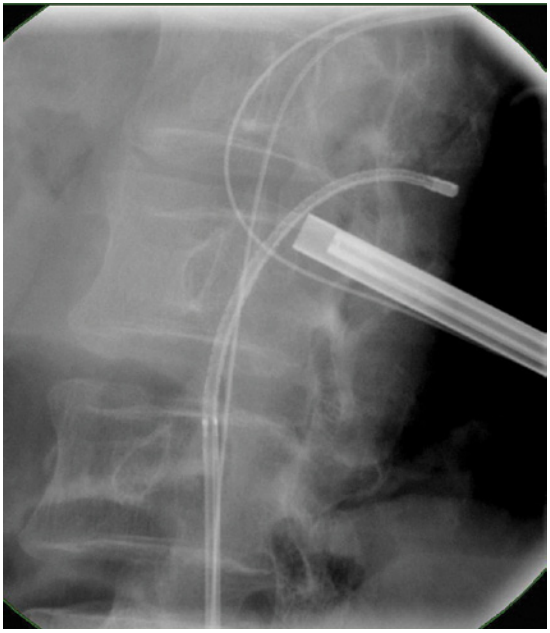

Figure 13.6 In cases of larger stone burden the percutaneous access can be combined with a retrograde flexible ureterorenoscopy.

stone fragment will follow the instrument as it is propelled by the outflow of the irrigation fluid. By completely removing the nephroscope, the stone fragment is washed out and falls out of the sheath. This technique is demonstrated in Video Clip 13.2. In any case, stone material should be retrieved and sent for analysis.

If stones or fragments cannot be reached with the rigid nephroscope, a flexible cystoscope or ureterorenoscope can be introduced via the Amplatz sheath (Figure 13.5). With these usually all locations in the renal collecting system and the complete ureter can be reached. Again, the holmium laser is used for stone disintegration and the fragments can be removed with a nitinol basket. Another possibility to reach inaccessible stones is to create a second or third access tract. Especially in patients with a large stone burden or staghorn stones, this can be advantageous as the use of flexible instruments can be time consuming. A third option is to perform a simultaneous retrograde flexible ureterorenoscopy and translocate the stone into the renal pelvis where it can be fragmented and extracted via the percutaneous tract (Figure 13.6).

At the end of the procedure complete stone clearance is verified endoscopically and radiologically. Contrast dye should be injected via the nephroscope sheath to display the complete collecting system and to rule out residual fragments (Figure 13.7).

Several exit strategies for finishing the intervention exist. In cases of significant bleeding or residual stones, a 16 F nephrostomy can be placed in order to provide urine drainage or to secure the percutaneous tract for a repeat intervention. Alternatively, urine drainage can be secured by the antegrade placement of a double-J catheter after removal of the balloon occlusion catheter. However, the double-J and especially the removal may cause further morbidity and patient discomfort. To prevent this and to secure urine drainage in the first days, we usually leave the deflated balloon catheter in place until the urine is clear. After 1 or 2 days, it can be removed together with the Foley catheter. A totally tubeless approach in which both a nephrostomy and a ureteral catheter are omitted is the last option but this carries the risk of

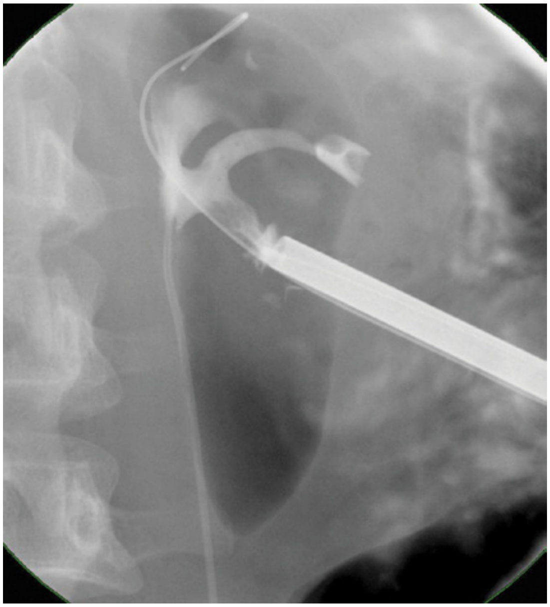

Figure 13.7 At the end of the procedure the deflated balloon ureter catheter can be left in place to secure urine drainage.

secondary obstruction and the need for intervention. If no nephrostomy tube is placed, the percutaneous access tract can be sealed using thrombin matrix (e.g. Floseal, Baxter, Deerfield, IL) to prevent bleeding or urine extravasation. However, a clear advantage in terms of less bleeding has not been demonstrated yet. In contrast, in a small series access tract closure with thrombin matrix seemed to result in an initial increase of postoperative pain [14].

Intraoperative trouble-shooting

Puncture

As the puncture is probably the most crucial step during the procedure, it should be planned exactly. Holding the puncture needle over the skin, the ideal angle of puncture of the target calyx can be determined under fluoroscopy. If the puncture follows this axis, which can be marked on the skin, the chance of a transpapillary puncture is high. The ultrasound adds the third dimension to the image and identifies adjacent organs.

Dilation

In patients with a firm fascia or with scarring due to previous interventions, the wire may deviate and consecutively kink during the dilation process. In these cases it is advisable to exchange the guidewire for a Lunderquist wire, which has a stiffer medium part and therefore a lower risk of deviation during dilation. However, care must be taken not to perforate the renal pelvis with the wire.

Nephroscopy

After introducing the nephroscope, several situations are possible: in the easiest case, the wall of the access calyx or the renal pelvis is visualized. In this case, the instrument is moved to the stone and disintegration may commence. “White-out” is a situation in which the nephroscope has direct contact to the wall of the collecting system, so that only a white area appears on the monitor. In this case, the instrument has to be retracted until the collecting system can be visualized. In the “red-out” situation, the collecting system is filled with blood clots, so that the monitor shows only a red area. In this more complicated situation, first, the correct localization in the collecting system has to be verified, either endoscopically by moving the instrument and visualization of the wall or by injecting contrast dye and verifying correct localization under fluoroscopic control. In the mini-PCNL technique, no ultrasound probe can be used, so the evacuation of blood clots is more difficult compared to conventional PCNL, where clots can be aspirated with the probe easily. However, blood clots can be extracted with forceps or a suction pump (e.g. borrowed from the anesthesiologists).

In cases in which part of the stone burden cannot be reached, e.g. in parallel calyces, a flexible nephroscope or ureterorenoscope can be used to reach the stone. The holmium laser can be used to fragment the stones and a basket is utilized for stone extraction. In this way, multiple accesses can be avoided in most cases. In rare cases, when stones cannot be reached with flexible instruments, a second access tract may become necessary. An alternative is to combine retrograde flexible ureterorenoscopy and mini-PCNL. The ureterorenoscope can be used to pull stones into the renal pelvis, where they can be extracted through the percutaneous tract.

Exit strategy

At the end of the procedure several options are available. A nephrostomy can be placed if a significant residual stone burden is present to secure the access tract for a second-look intervention. A second indication for a nephrostomy is bleeding to ensure urine drainage. In cases of significant venous bleeding, the nephrostomy can be clamped temporarily to control the bleeding. In this way most bleedings terminate and the nephrostomy can be opened again.

In uncomplicated cases, a nephrostomy is not necessary. In these patients either a double-J stent can be placed antegradely to secure urine drainage into the bladder, or the deflated balloon ureter catheter can be left in place. The double-J catheter can be removed after a week, whereas the balloon catheter can be removed together with the Foley catheter 1 or 2 days after the procedure. In this way, an auxiliary intervention to remove the double-J stent can be avoided.

A last option for uncomplicated cases is to omit both a nephrostomy and a ureteral stent and perform the procedure in a totally tubeless fashion. However, this approach bears the risk of an acute hydronephrosis, so that the placement of a double-J stent may become necessary.

Postoperative follow-up

Although reports on mini-PCNL as an outpatient procedure exist, we prefer to perform the intervention on an inpatient basis. The postoperative follow-up includes general monitoring of vital parameters and a lab test on the day after the operation. The prophylactic antibiotic treatment is usually continued for 2–3 days. Complete stone clearance is confirmed on a plain x-ray or, in selected cases (e.g. nonradiopaque stones), with computed tomography. An ultrasound examination of the kidney is performed to exclude the development of a hematoma or urinoma.

The Foley catheter is left *in situ* for 1–2 days, depending on the amount of gross hematuria. In cases in which the deflated balloon catheter was left attached to the Foley catheter, it is removed simultaneously. In cases where a double-J stent was placed, it can be removed usually after 1 week. If a nephrostomy was placed, it remains until the repeat percutaneous intervention or until the urine outflow is clear.

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14

CHAPTER 14

Instrumentation and Surgical Technique: Step-by-Step Percutaneous Nephrolithotomy: Multiple Access

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Introduction

Percutaneous nephrolithotomy (PCNL) is an effective method of removing large-volume renal stones. While many procedures can be accomplished with one percutaneous access, some patients with large stones and/or complex collecting system anatomy may necessitate a multi-access approach. Patient preparation, equipment utilized, technical aspects of this approach, potential complications, and method of patient follow-up are reviewed in this chapter.

The reported utilization of multiple accesses during PCNL varies, and this may be influenced by the stone size and collecting system features. Ganpule and Desai reported using a multi-access approach in 500 out of 725 (69%) staghorn stone PCNL cases [1]. The high percentage of multi-access cases in this series may have been influenced by this group's reliance on utilization of rigid nephroscopy for stone clearance. Results from a prospective multinational database managed by the Clinical Research Office of the Endourological Society (CROES) demonstrated that, of 1166 patients with staghorn stones, 16.9% underwent multi-access PCNL [2]. In contrast, only 5% of 3869 patients with nonstaghorn stones were subjected to this approach.

Patient preparation

Patient preparation is one of the foundations of success for multi-access PCNL. A thorough history and physical examination are conducted. The patient must be in satisfactory medical condition. Routine preoperative blood testing should include complete blood count, serum electrolytes, glucose, calcium, blood urea nitrogen (BUN), and creatinine. Coagulation studies are not routinely obtained but should be done in patients with liver disease, a history of easy bleeding or bruising, and in those who have recently taken anticoagulants [3]. Patients are instructed to stop anticoagulants, nonsteroidal antiinflammatory drugs, antiplatelet agents, and supplements such as fish and flaxseed oil prior to surgical intervention. Urine culture is mandatory and, if infected, the patient is treated with a 1-week course of a broad-spectrum, culture-specific antibiotic because of the known discordance between voided urine and stone culture [4]. The administration of a quinolone antibiotic such as ciprofloxacin during the

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

Figure 14.1 Reconstruction from noncontrast computed tomography demonstrating a large complex right staghorn stone and multiple left renal calculi.

week before surgery in patients with sterile urine should be considered, as it may reduce the risk of systemic inflammatory response syndrome (SIRS) or sepsis [5].

Computed tomography (CT) should be obtained in all patients, as it defines stone burden, relationships with surrounding structures, and collecting system anatomy if intravenous contrast is administered. Three-dimensional reconstructions can be generated to define the spatial relationships of the stone and the collecting system (Figure 14.1). While retrograde pyelography is performed at the time of the procedure, it may be necessary beforehand in cases where a decision needs to be made whether to proceed with anatrophic nephrolithotomy or multi-access PCNL. It is also important to determine function of the targeted renal unit, as nephrectomy may be indicated if function is absent or extremely limited. This can be estimated with a contrasted CT scan or more accurately with nuclear renography.

Informed consent

A thorough discussion of risks, benefits, and treatment alternatives is undertaken. Potential complications that should be mentioned in this encounter include bleeding with the need for blood transfusion, urinary tract infection (UTI), sepsis, injury to adjacent structures (including bowel, spleen, liver, pleura, and lung), ureteral injury, injury of the collecting system, deterioration of renal function, loss of kidney, failure of the procedure, potential need for further stone-removing procedures, anesthetic risks, ureteral stricture, and infundibular stenosis.

Box 14.1 Instrumentation for multi-access PCNL

Catheters

- Straight ureteral catheters
  - 5F
  - 6F
- Angled angiographic catheters
  - Slightly angled
    - 5F 65cm
  - More angulated (Cobra)
    - 5F 65cm
- Coaxial catheters
  - 8–9F 20cm

Dilating devices

- 30F balloon with sheath
- Amplatz coaxial dilating set
- Individual Amplatz dilators and sheaths
- 24–30F sheath
- Lengths 16cm and 25cm

Lithotripters

- Pneumatic
- Ultrasound
- Pneumatic/ultrasound
- Dual ultrasound (Cyberwand®)
- Holmium laser

Needles

- Amplatz needleholder
- Two-part trocar needle
  - 18 gauge 20cm
  - 18 gauge 25cm
- 22 gauge Chiba tip needle 20cm

Endoscopes and cameral system

- Digital or high-definition imaging preferred
- Rigid cystoscope
- Flexible cystoscope/nephroscope
- Rigid nephroscope
  - Standard
  - Extra long
- Flexible ureteroscope

Nephrostomy tubes

- Council catheters 16–20F
- Coiled nephrostomy tube 8–14F
- Malecot catheter 18–24F
- Reentry Malecot catheter 16–24F

Guidewires

- Hydrophilic (straight and angled)
- Stiff guidewire
- Super-stiff guidewire

Baskets and graspers

- Nitinol baskets
- Grasping devices
  - Rigid
  - Flexible

Instrumentation

The operating theater must be properly supplied with the equipment needed for this procedure, and the patient should not be anesthetized if it is not available. This includes both disposable and reusable devices. The equipment utilized is listed in Box 14.1.

Anesthesia

While PCNL can be done under regional or local anesthesia with intravenous sedation, general anesthesia with oral endotracheal intubation is preferred. A blood specimen is obtained for type and screening for possible transfusion if the patient has a normal blood count. However, if the patient is anemic, blood is typed and crossed for a prescribed number of units based on the hemoglobin and hematocrit levels.

Pneumatic compression devices are placed on the patient's lower extremities to limit the risks of thromboembolic complications.

Step-by-step technique

After induction of general anesthesia, the typical patient is placed in the dorsal lithotomy position, the perineum and genital area are prepped with antibacterial solution, and sterile draping is undertaken. Cystoscopy, retrograde pyelography of the targeted renal unit, and placement of an externalized stent are performed. The stent is placed so that contrast can be introduced into the collecting system at the time of access. A Foley catheter is inserted, and the stent is affixed to it with an 0 silk suture. Some surgeons perform the aforementioned procedures with the patient in the prone position, using a special platform which eliminates the need for repositioning. Transstomal flexible endoscopy is performed in patients with ileal or colon conduits in an attempt to identify the ureteral orifice for stent cannulation and placement. If this is not possible, a loopogram is performed by inserting a Foley catheter into the stoma and instilling contrast via gravity under fluoroscopic guidance. If the targeted collecting system is opacified, the catheter is occluded, and it is unclamped after initial access is obtained.

The prone position is preferred, as the supine position limits the ability to establish multiple accesses and facilitates upper pole access. The patient is carefully positioned on chest rolls oriented either vertically or horizontally. The latter is preferred in those with a large panniculus. Pressure points are carefully padded. A prone-flexed position with the head flexed down 30° and the legs flexed upward 15° can be used if upper pole access is anticipated, as this increases the distance between the posterior-superior iliac crest and 12th rib, and it displaces the kidney inferiorly. This may permit infracostal access of the upper pole collecting system in many cases, thus limiting morbidity associated with a supracostal approach. In addition, this position flattens the flank and limits interference during instrument manipulation by the buttock with a lower pole access [6].

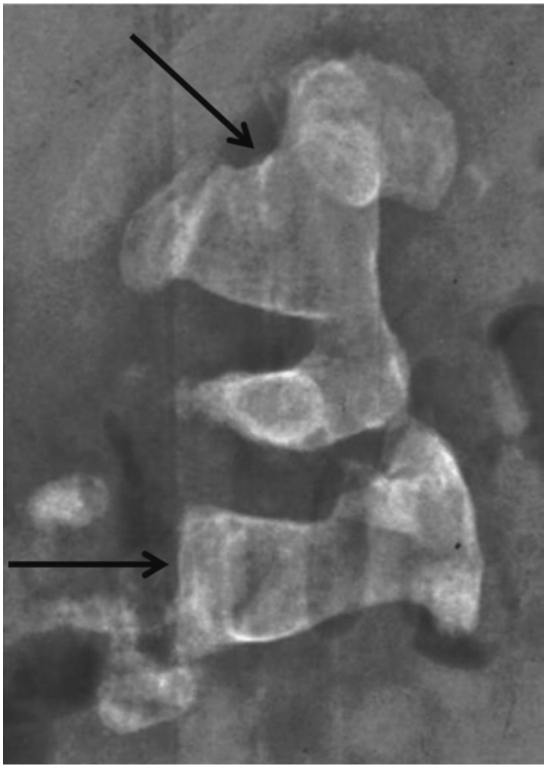
Figure 14.2 Two accesses utilized to remove staghorn stone.

A strategy for access is synthesized based on stone volume, anatomy of the collecting system, and unique patient characteristics. The initial access should provide the most direct route to the highest volume of stone. Sometimes other access points can be predicted at the start of the case and can be done simultaneously; however, in the majority of cases, the other accesses are done after removing as much stone in an expeditious manner through the initial point of entry. Figures 14.2, 14.3, 14.4, and 14.5 show cases where two, three, and four accesses

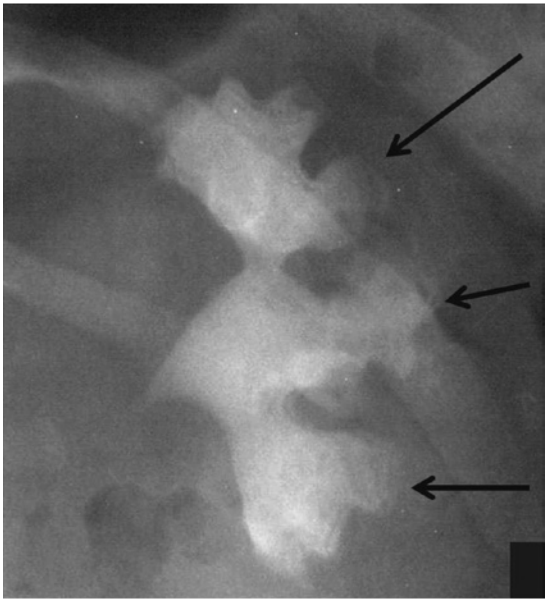

Figure 14.3 Three accesses utilized to remove staghorn stone.

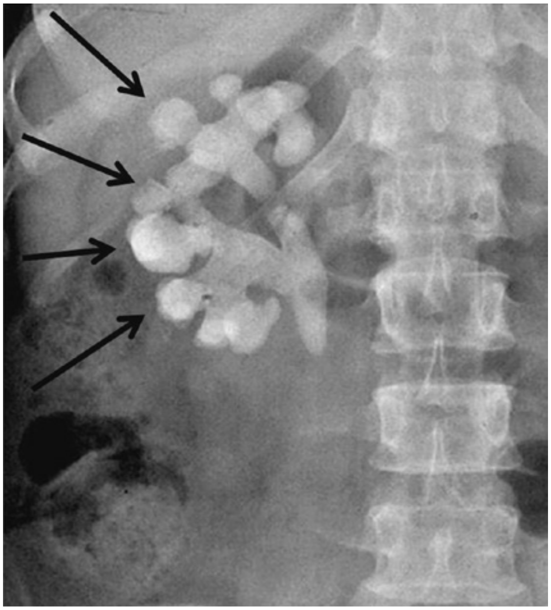

Figure 14.4 Four accesses utilized to remove staghorn stone.

were utilized. We have utilized as many as 15 accesses to remove complex branched stones. Upper pole access may be a preferable initial route in many cases, as it is typically well aligned with the renal axis, and the majority of the collecting system can be reached with a rigid or flexible nephroscope.

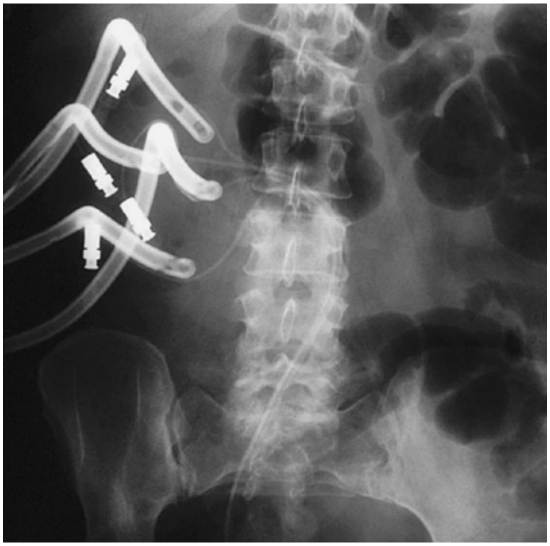

Figure 14.5 Four percutaneous nephrostomy tubes in place after four access percutaneous nephrostolithotomy.

Access is usually monitored with fluoroscopic imaging, but ultrasonograpy can also be utilized to limit ionizing radiation exposure. The collecting system is typically opacified first using the aforementioned approaches for retrograde instillation of contrast. If the latter is not possible, the patient can be given intravenous contrast if not contraindicated. When this is not possible, a 22 gauge Chiba needle can be directed on to a stone with fluoroscopy (if the calculus is radiopaque) or with ultrasonography (if the stone is radiolucent). Contrast can then be instilled through this needle to opacify the collecting system. If the patient has a large branched radiopaque stone, it may be possible to identify the optimal point of entry without contrast instillation based on the anatomy of the stone. The initial access is through a posterior calyx, as this typically allows manipulation of guidewires into the renal pelvis and down the ureter.

The collecting system is accessed with an 18 gauge needle. A 1–2 mm transverse incision is made in the skin through which the needle is directed into the desired posterior calyx. This can be done using the bull's eye/eye of the needle technique, triangulation, or ultrasonography. The needle stylet is removed, and urine/contrast will typically drain out and confirm entry into the collecting system. This may not occur when stone fills the entire targeted calyx. In this instance, the needle can be gently manipulated to feel for the grittiness of the stone to confirm proper entry. A hydrophilic guidewire is inserted through the needle sheath and directed into the renal pelvis. This and all subsequent maneuvers involving guidewires, catheters, sheaths, and dilating devices should be conducted under fluoroscopic guidance.

The track can initially be enlarged using short dilators (6–8 F) inserted over the guidewire. A slightly curved 5 F angiographic catheter with a radiopaque tip is manipulated into the renal pelvis and used to guide the wire down the ureter and into the bladder. After this, the catheter is passed over the wire and into the bladder. The wire is removed and replaced with a super-stiff guidewire, and the angiographic catheter is removed. Insertion of a second guidewire, usually a stiff guidewire, is desired for the initial access. This is passed down the ureter and into the bladder using a short 8–9 F coaxial sheath. The latter is used as a working guidewire, and the super-stiff wire is used as a safety wire. If it is determined that other accesses will be needed through different skin incisions, this can be undertaken at this time using the aforementioned techniques or after stone removal through the first tract is completed. A safety guidewire is typically not placed for these accessory accesses. If the wire cannot be manipulated down the ureter, it is curled in the renal pelvis or targeted calyx if the latter is not achievable. A stiff guidewire is usually used for the additional accesses.

Dilation of the tract is performed next. The previously made incision is enlarged to 1 cm and a Vanderbilt clamp is used to spread the tissue in the tract. We prefer using a 30 F balloon for dilation. Before this is used, the short hollow tube in which the balloon is housed is removed and reinserted over the device with the fluted end directed toward the balloon. This facilitates reconstitution of the balloon, allowing it to be used for other accesses. The balloon is inserted over the working guidewire and directed to the peripheral aspect of the targeted calyx. After inflation, a sheath is passed over the balloon and manipulated into the outer edge of the calyx. Other methods of dilation can be used if preferred by the surgeon, such as an Amplatz coaxial device or reusable metallic dilators.

Rigid nephroscopy using sterile saline as an irrigant is then performed, and visualized stone is removed. This is typically done with a lithotripsy device which has vacuuming/suctioning capabilities (ultrasound, pneumatic/ultrasound, dual ultrasound). A pneumatic-only device can be used for dense stones but is not recommended for soft stones due to fragment dispersal and migration. The resultant fragments in such cases can be removed with a rigid grasping device. We prefer a two-prong over a three-prong device. After all visible stone is removed with the rigid instrument, flexible nephroscopy is undertaken to inspect the peripheral and other stone-containing portions of the collecting system. Smaller stones seen in these areas can be removed using a stone basket or flexible grasping device. Larger stones can sometimes be manipulated into the renal pelvis with the aforementioned instruments and then removed using rigid nephroscopy and a rigid lithotripsy device. Some of the peripheral stone can be fragmented using a holmium laser and removed with a basket or flexible grasping device or manipulated into the central collecting system for rigid extraction. The remaining stone which cannot be accessed, fragmented, or removed expeditiously will then need to be approached using another access.

If the other accesses have already been established, dilation and stone removal are undertaken using the aforementioned techniques. The size of access sheaths used for these additional tracts is based on stone size and collecting system anatomy. When the additional accesses have not been obtained, this is undertaken with subsequent dilation and stone removal. It may be possible to use the initial incision for the additional accesses if the targeted stone-containing calyx is adjacent to the original entry or if the triangulation technique is employed. The original access sheath is removed, but the guidewires are left in place. It may be necessary to access anterior stone-containing calyces and in such cases, the wire is curled in the targeted calyx with subsequent dilation and stone removal.

Nondilated access is a technique that may be utilized if stones in a peripheral calyx cannot be reached with rigid or flexible nephroscopy (Figure 14.6). The targeted calyx is entered using fluoroscopic or ultrasonic guidance. Saline may be infused through the needle sheath to displace the stone(s) into the central collecting system for subsequent removal. Methylene blue

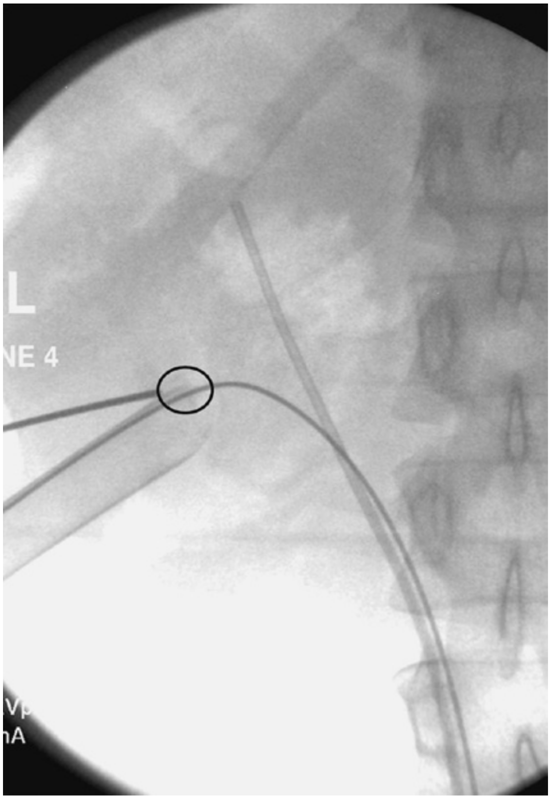

Figure 14.6 Nondilated access where a needle is directed into a stone-containing calyx (highlighted by circle) and attempts were made to manipulate the stone into the central portion of the collecting system with probing and irrigation.

mixed with sterile saline can also be injected into the targeted calyx to facilitate location of this area during nephroscopy. A guidewire may be manipulated into the central portion of the collecting system or down the ureter. This guidewire can be used to assist in locating the targeted calyx (Figure 14.7). It can also be grasped and pulled out of an established working tract. A flexible nephroscope or ureteroscope can be backloaded on the wire and manipulated fluoroscopically into the targeted calyx for stone removal. If the guidewire is passed down the ureter, it can be manipulated out of the urethra with the aid of an angiographic catheter. This wire can be used for retrograde passage of a flexible ureteroscope and stone removal (Figures 14.8, 14.9).

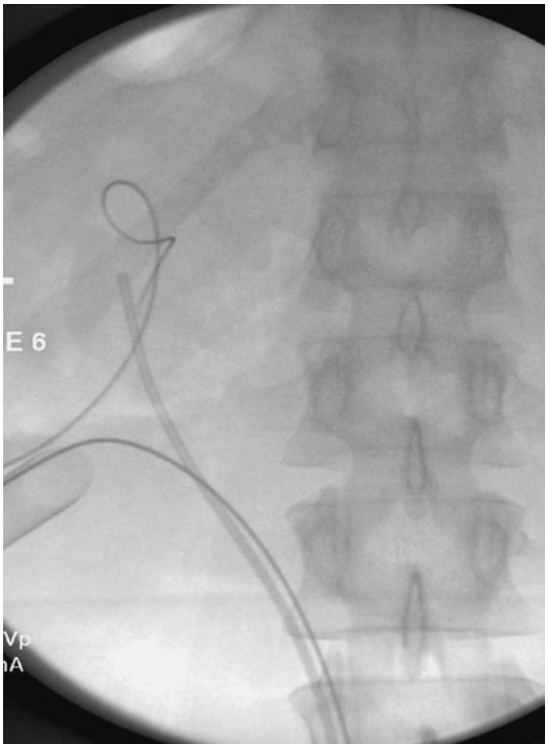

Figure 14.7 Nondilated access where a guidewire is manipulated into the collecting system. This facilitates location of the stone-containing calyx with flexible nephroscopy.

After stone removal is complete or if it is decided to terminate the procedure with the intention of performing further stone-removing procedures (staged approach), nephrostomy tube drainage is recommended. However, successful tubeless multi-access procedures have been reported by some groups [7–9]. The latter approach should not be taken if the need for another PCNL is anticipated, active bleeding is present, extravasation is evident, or hydrothorax/pneumothorax is suspected. Various types of nephrostomy tubes can be utilized, and the choice is influenced by the anatomy of the collecting system, the patient’s body habitus, the presence of active bleeding, and the potential use of the tract as a port of entry for future PCNL. Options include coiled nephrostomy tubes, straight (Foley) catheters, standard Malecot catheters, or reentry Malecot catheters. At least one nephrostomy tube should be inserted through the traversed posterior calyx with the end positioned in the renal pelvis

Figure 14.8 This image demonstrates non-dilated access where a small upper pole calyx was entered with a needle through which a guide wire was manipulated down the ureter and out the urethra.

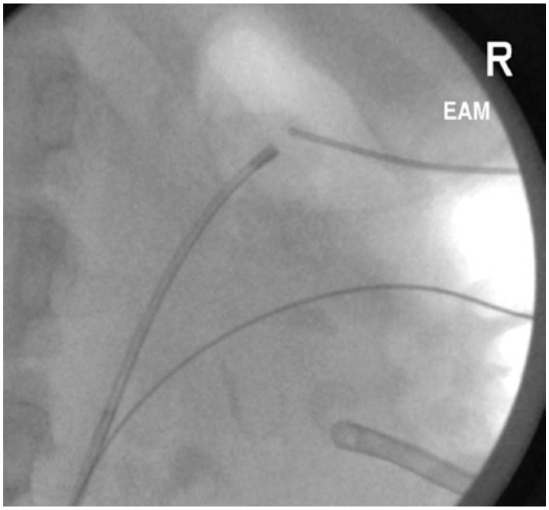

Figure 14.9 A flexible ureteroscope was passed over the wire (shown in Figure 14.8) and up the ureter to the stone-containing calyx permitting stone removal.

if possible. We favor the utilization of a coiled nephrostomy tube and typically insert one 8–10 F in size. This is preferably done through an infracostal site, as this limits pain. A 5 F angiographic catheter may be placed over the safety guidewire and manipulated down the ureter and into the bladder if future procedures are anticipated, as this may facilitate subsequent reentry into the collecting system. If there is active bleeding at this site, a larger tube or a tamponade catheter can inserted. Nephrostomy tubes in the other tracts are not needed if all stone is thought to have been removed, active bleeding is absent, and utilization of the tract for future procedures is not anticipated.

Intraoperative trouble-shooting

Certain problems may arise during these procedures which can usually be easily remedied. If a guidewire cannot be manipulated out of the initially targeted calyx, it may be an anterior calyx and another port of entry should be selected. When the wire can be manipulated into the renal pelvis but not down the ureter, it can be curled in the central collecting system after which the tract is dilated and stone is removed. A guidewire can be manipulated up the ureteral stent and into the renal pelvis where it can be grasped and brought out of the nephrostomy tract. This provides secure through-and-through access.

When active bleeding is present after tract dilation and working sheath placement, the end of the sheath may be exterior to the targeted calyx. Bleeding will typically subside if the tube is repositioned under fluoroscopic guidance. Flexible nephroscopy can also be utilized for repositioning of the sheath. If the tube is positioned properly but high-volume bleeding persists, inflating the dilating balloon in the tract for 10 min will typically cause bleeding to subside. If it does not, one should suspect that an intralobar or segmental artery has been lacerated. A tamponade catheter can be placed and the patient should undergo renal arteriography and possible selective arterial embolization by an interventional radiologist. If persistent low-volume bleeding occurs during stone removal, it may be prudent to insert a nephrostomy tube and terminate the procedure before the patient requires a blood transfusion. The tract can be left to mature and, usually 5–7 days later, stone removal can be undertaken safely and successfully.

It may be impossible to fluoroscopically visualize a stone-containing calyx for initial, subsequent, or additional access due to the density of the stone or the patient's body habitus. Ultrasound-guided access may be helpful in this setting. Flexible nephroscopy or retrograde flexible ureteroscopy can be employed to demonstrate the calyx, and the tip of the scope may be targeted with the access needle.

When the stone is not visible on initial rigid nephroscopy, flexible nephroscopy may be utilized to reposition the sheath and provide better alignment with the rigid scope. Redilation and sheath repositioning may be needed. Reaccessing the kidney through the originally targeted calyx or another one may ultimately be required. The utilization of flexible nephroscopy with fluoroscopic guidance and contrast instillation through the endoscope may facilitate the identification of peripheral stone-containing calyces.

Perforation of the renal pelvis may occur during access, dilation or stone removal. If this is encountered, it is best to place a nephrostomy tube and terminate the procedure. It may be difficult or impossible to manipulate a nephrostomy tube into a diminutive renal pelvis. In such cases, a straight tube can be positioned in the renal pelvis or just peripheral to this area. Attempts at placing Malecot-type catheters or coiled nephrostomy tubes in this setting may result in further violation of the renal collecting system and inadequate drainage.

Fluoroscopy of the chest should be done at the termination of the procedure or if problems with ventilation arise intraoperatively. This is undertaken to assess for hydrothorax or pneumothorax and, if present, a chest tube should be placed. The position of the tip of the endotracheal tube should be checked to determine if a right main stem intubation has occurred, as this may result in deflation of the left lung, mimicking a pneumothorax. Repositioning of the endotracheal tube will typically correct this problem.

Follow-up

Noncontrast CT is obtained prior to removal of drainage tubes to assure complete stone removal. CT should also be entertained if stone is known to be present but location is uncertain (as this facilitates secondary interventions) or if the clinical status of the patient suggests a major complication such as injury to surrounding viscera/structures. Nephrostomy tubes are generally removed 3–5 days after complete stone removal is confirmed radiographically, and this is generally done in the outpatient clinic. A stone culture should be considered, as a significant number of patients with a negative preoperative urine culture may have pathogens in the stone and be at risk for septic events [4]. This provides earlier bacteriological data if the latter complication ensues. Stone compositional analysis is also advised, as the majority of these patients have either pure metabolic stones or mixed metabolic and infection stones [10]. Twenty-four hour urine testing and preventive medical therapy are recommended for those with metabolic stone components. Those with infection stone components need to be monitored carefully for recurrent infection and may be candidates for antibiotic prophylaxis. A functional study of the kidney such as nuclear renography is recommended 3–4 weeks after nephrostomy tube removal.

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15

CHAPTER 15

Instrumentation and Surgical Technique: Step-by-Step Percutaneous Nephrolithotomy: Tube or Tubeless Percutaneous Nephrolithotomy

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Introduction

Percutaneous renal surgery (PRS) is widely utilized to treat a variety of urological conditions, from stone disease to upper tract urothelial cell carcinoma. Percutaneous nephrolithotomy (PCNL) has become the preferred treatment method for large and/or complex renal and proximal ureteral calculi during the last 30 years after its first introduction in a larger cohort in 1981 [1]. Nephrostomy tube placement at the end of the operative procedure was considered the standard of care until 1997, when Bellman et al. first introduced the concept of tubeless PCNL, demonstrating few operative complications, lower cost, shorter hospital stay, lower analgesia requirements, and a quicker return to normal activities [2]. Since that time a rapidly growing number of studies have explored various aspects of tubeless PCNL to determine the indications and limitations of this approach.

In this chapter we review the evidence which can be found from evaluating the literature from May 1997 to May 2012 regarding the technique of tubeless PCNL and provide recommendations on its potential application. In addition, we will highlight the main differences to the classic approach (using a nephrostomy tube at the end of the procedure) regarding informed consent, preoperative preparation, patient positioning, instrumentation, step-by-step technique, intraoperative trouble-shooting, and postoperative follow-up. This chapter also reviews the spectrum of complications that can occur during and after PRS. Diagnosis, treatment, and preventive measures are presented.

Definition of tubeless percutaneous nephrolithotomy

Tubeless PCNL has been defined in a variety of ways. Most authors define tubeless as not placing a nephrostomy tube at the end of the procedure. However, in the majority of the techniques previously reported, surgeons have left some sort of drainage, most commonly an open-ended ureteral catheter (tubeless, stentless PCNL)

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

Box 15.1 Comparison of percutaneous nephrolithotomy approaches [35]

NT (large caliber)	US [2–12]
NT (small caliber)	US [5,13–15]
No control	US [16–20]
NT	UC [21,22]
No control	UC [7,23–26]
US	UC [7,18,27]
NT	Totally tubeless [14,28–31]
No control	Totally tubeless [32,33]
NT versus US	Totally tubeless [34]

NT, nephrostomy tube; UC, ureteral catheter (open-ended); US, ureteral stent (double-J).

or internal double-J stent (DJ). Some studies have reported a totally tubeless approach during which no internal or external drainage tubes are left. In most of the studies, the tubeless or totally tubeless group is compared to a control group with a nephrostomy tube (NT) (Box 15.1).

This confusion regarding a precise definition of tubeless PCNL makes comparison between different studies quite difficult. For the purposes of this review, the term "tubeless PCNL" refers to a procedure where a NT is omitted from the end of the procedure and either a urethral catheter (UC) or urethral stent (US) is left for drainage. Totally tubeless refers to a procedure where no drainage tubes other than a Foley catheter are left at the conclusion of surgery.

Advantages of tubeless versus standard percutaneous nephrolithotomy

Despite varying exclusion criteria and limitations, the advantages of tubeless versus standard PCNL have been reported in several studies and in some recently published metaanalyses [2,3,5,10,14,16,23,31,33–38]. Additionally, complication rates are comparable in tubeless and standard PCNL with placing of a nephrostomy tube. A summary of reported complications is given in Table 15.1. The most commonly reported postoperative complications are urinary tract infection and bleeding requiring blood transfusion, however there was no statistical difference found between the tubeless and standard PCNL groups [31,35,37]. Intraoperative stone free rates for tubeless PCNL have been reported to be between 71.4 and 100 %, with a mean of 89% [3,6,7,11,14–20, 22–25,29,30,33]. These rates were even better than the average overall stone free rate of 78% which has been recently reported by Armitage et al from a large prospective PCNL data registry in the UK (24 % of these procedures were performed without NT or tubeless and stentless). This rate dropped in postoperative imaging to 68% on average. This registry included 987 patients: the data demonstrates that there is no difference in complication rates between tubeless and standard PCNL but the tubeless procedure did lead to a significant reduction in median length of stay(3d vs 5 d; $p<0.0001$) [31]. In this cohort, 138 patients (14%) were performed totally tubeless with no difference in bleeding complications to the other groups. The most common auxiliary procedure after tubeless PCNL is shock wave lithotripsy; reported re-intervention rates are between 1.3% and 16% [35]. These results are consistent with the conclusions of recently published meta- analysis showing no difference in efficacy but shorter hospital stay and lower analgesic requirements as well as lower urinary leakage [35,37,38]. With regard to operative time, there is some discrepancy in outcomes with some reports demonstrating no difference and a few studies reporting a significantly shorter operative time with the tubeless approach [9,21,38]. Tubeless PCNL can reduce medical expenses per patient.

Use of hemostatic agents in tubeless percutaneous nephrolithotomy

Certain techniques have been applied to tubeless PCNL to minimize blood loss and the risk for transfusion. Many people still believe that a NT prevents bleeding and urinary leakage and allows renal healing by facilitating hemostasis [2]. To avoid significant hemorrhage and urinary extravasation after premature NT removal within 24–48 h postoperatively, placement of an NT is advocated [45]. Therefore many authors were looking for an alternative method of sealing of the nephrostomy tract. Jou et al. perform electrocauterization of bleeding points along the nephrostomy tract and inside the collecting system [46]. They found that cautery leads to a

Table 15.1 Complications following tubeless percutaneous nephrolithotomy (PCNL).

Complications	Tubeless PCNL	Standard PCNL
Pulmonary embolus [10]	1.5	-
Hydrothorax [8,10,23,32,36]	0.7–4	1.4–3.3
Pseudo-aneurysm or arteriovenous fistula requiring embolization [10,13,17,34,36,39]	1.1–8	1.4
Bleeding requiring transfusion [3,4,7–11,13, 19–24,26,27,29,30,32–34,36,39,40]	0–11.9	3.1–12
Splenic injury [36]	0.22	0.25
Ileus [20]	0.7	-
Urinoma/leakage [4,7,23,36,39–42]	0–4.1	0.3–3.9
Pleural effusion [10,11,27,34]	1.5–4.3	0
Urinary tract infection [4,7,9–11,14,16,21,23,24, 29,32,40–44]	1.1–15	3.1–11.4

significantly lower transfusion rate and were able to obtain a bloodless tract in 33.7% of patients. When bleeding persists, the authors advocate leaving a nephrostomy tube in place.

Hemostatic fibrin glue can be placed in the nephrostomy tract to aid in hemostasis. Mikhail et al. reported retrospectively in 2003 [47] and Shah et al. prospectively in 2006 the use of Tisseel® vapor heated sealant (Baxter AG, Vienna, Austria) [48]. They compared patients who underwent tubeless PRS with Tisseel placed in the tract at the end of the case to those without Tisseel. Both found no significant difference in the change in hematocrit between the two groups. Care must be taken to avoid injecting the Tisseel into the collecting system, as it can form a solid clot which could possibly obstruct the collecting system [49]. Patients with continued bleeding at the end of the case should have a NT left in place to control bleeding.

FloSeal® (Baxter Healthcare, Irvine, CA) (a gel matrix thrombin) has been used in the NT tract whenever persistent bleeding after removal of the NT occurs [13]. Others used FloSeal in cases of brisk bleeding from the nephrostomy tract but conclude nevertheless that the best way of stopping any tract bleeding is manual compression and turning the patient into the supine position as soon as possible with a bulky compression tape [50]. Mandhani et al. utilized an absorbable gelatin (Spongostan®, Johnson and Johnson, Somerville, NJ), which was placed in the nephrostomy tract before closing the skin with a silk suture [18]. This porcine, water-insoluble gelatin is absorbed in 3–5 weeks. Although Singh et al. could not demonstrate a reduction of bleeding using Spongostan, they advocated its use on a routine basis to avoid complications after the tubeless procedure [51]. Since studies have failed to prove a significant reduction in the incidence of postoperative hemorrhage, the use of hemostatic agents in the tract remains controversial.

Okeke et al. reported using cryoablation in the nephrostomy tract after tubeless PCNL to avoid bleeding [52]. In their study group of 30 consecutive patients, they inserted a 2.4 mm cryoprobe in the tract and a 10 min freeze-thaw cycle was applied at a temperature of −20°C. They showed significantly shorter hospital stay and fewer episodes of delayed bleeding and urinary extravasation compared to the standard PCNL group. A contraindication to the use of cryoablation in the tract is supracostal access, given the risk of breaching the thoracic cavity.

One recently published study in animals demonstrated that sealants may only reduce the risk for early urinary tract leakage after tubeless PCNL. Lipkin et al. performed the tubeless access in 19 renal units in 10 farm pigs [53]. Ten units were used as control group and the percutaneous tracts of nine units were injected with the fibrin sealant (FS) Evicel® (Johnson and Johnson, Somerville, NJ) (5 units) and hemostatic gelatin matrix (HGM) Surgiflo® (Johnson and Johnson, Somerville, NJ) (4 units) and checked at various time intervals to determine their absorption and tract closure rates. Fibrin sealant remained in the tract at the 30th postoperative day (pathologically proven). In two renal units out of the control group, there was imaging evidence of urinary extravasation on postoperative day 1. No leakage was observed in the groups with the sealants. The authors concluded that the use of hemostatic agents may reduce the risk of early urinary extravasation, but they may persist in the tract for up to 30 days.

Supracostal access

Some authors suggest that using a tubeless approach for supracostal access in PCNL should be avoided because of an increased risk of hydrothorax/pneumothorax in the absence of a nephrostomy tube [54]. On the other hand, placing a nephrostomy tube over a rib can cause significant discomfort. Others have reported no increased risk for intrathoracic complications and decreased morbidity in patients undergoing tubeless PCNL who had a supracostal access [8,11]. These studies support the tubeless approach for supracostal access, demonstrating lower rates of complications, specifically bleeding, and decreased pain with less need for analgesia in patients who are left without a nephrostomy tube.

Special considerations

Tubeless percutaneous nephrolithotomy in children

A few small studies have analyzed the outcome of tubeless PCNL in comparison with standard PCNL in children. Khairy Salem et al. compared 20 children between the ages of 4 and 14 years who received just an open-ended ureteral stent to 10 children treated with a NT at the end of the procedure (control group) and found no difference in complication rates [55]. Aghamir et al. recently reported results of a prospective randomized trial in 23 patients under the age of 14 with renal stones [56]. In 13 children, the approach was performed totally tubeless, while 10 patients underwent standard PCNL with a NT left at the conclusion of the procedure. The incidence of complications, transfusion rate, analgesic use, hemoglobin drop, operation time, and hospital stay were compared. The patients who underwent a totally tubeless procedure had decreased hospital stay and analgesic use with no difference in complications. Tubeless PCNL appears to be safe in properly selected cases in the pediatric population and may have reduced morbidity and hospital stay compared to standard PCNL.

Tubeless percutaneous nephrolithotomy in obese patients

One recent study reports no difference in outcomes according to Body Mass Index (BMI) for tubeless PCNL [20]. Fifty-five overweight patients (BMI 25–30 kg/m^2), 28 obese (BMI 30–40 kg/m^2) and five morbidly obese (BMI 40 kg/m^2 or greater) underwent tubeless PCNL and no correlations between outcomes and BMI could be demonstrated.

Bilateral tubeless percutaneous nephrolithotomy (simultaneous)

Simultaneous bilateral tubeless PCNL has been reported [9,57–60]. These small series suggest that bilateral tubeless PCNL is safe and feasible with decreased postoperative morbidity. With knowledge that prolonged operative time significantly increases morbidity, we would recommend simultaneous tubeless PCNL only in a highly selected patient group who may not be able to tolerate two separate general anesthetics.

Informed consent

We use the same consent form as for the classic approach with a nephrostomy tube in our institution. Patients should be counseled for the modifications of the procedure, noting the advantages (mentioned above) and disadvantages. It is important to counsel patients that even if the intention is to perform a tubeless PCNL, there is still a chance that a nephrostomy tube may be placed. The final decision as to whether the nephrostomy tube is placed is made at the end of the procedure. The complications of the procedure are the same but it is important to mention that if there are residual fragments necessitating a second percutaneous procedure, a new access will need to be obtained.

Preoperative preparation

There is no difference in the preoperative preparation for tubeless PCNL compared to a classic approach with a nephrostomy tube. Routine preoperative labs should be obtained as described elsewhere for standard PCNL. A preoperative urine culture should also be obtained. In general, it is our practice to obtain a preoperative noncontrast computed tomography (CT) or intravenous pyelogram to aid in planning the nephrostomy tract access.

Patient positioning

Prone positioning

At our institution all PCNL procedures are performed in the prone position if either a tubeless approach is intended or a nephrostomy tube is placed at the end of the procedure. After cystoscopic placement of a retrograde open-ended 6 F ureteral catheter in the lithotomy position, the patient is placed in the prone position. Padding is placed under the chest, pelvic brim, knees, and feet to prevent any injury during the procedure. After performing an air pyelogram, access is gained via a posterior, anatomically favorable calyx. In our institution, the distribution of calyces (lower/mid/upper) utilized for PCNL access is equally divided.

Supine positioning

Tubeless PCNL can also be performed with patients in the supine position. Rana et al. reported in a study of 184 patients that the tubeless approach was feasible and safe in the supine position [61]. Using their technique, only 3% of the patients required a NT because of intraoperative adverse events, namely hemorrhage, perforation of the collecting system or purulent discharge. Their overall complication rate was not increased compared to prone tubeless PCNL and they achieved a stone-free rate of 84%.

Instrumentation

No notable change of instruments is needed for the tubeless approach.

Step-by-step technique

We routinely obtain percutaneous renal access at the time of surgery using fluoroscopy. A retrograde air pyelogram is performed through the previously placed 6 F open-ended catheter with injection of approximately 5 mL of air. Air is used as it preferentially fills the posterior calyx and does not obscure the view of the stone [62]. An 18 gauge trocar needle is used to obtain access to the selected posterior calyx.

The remainder of the procedure is performed with the same sequential steps that include establishing percutaneous access, dilation of the tract, and stone manipulation with fragmentation and extraction regardless of whether the procedure is to be performed tubeless or not. All these steps and techniques of percutaneous access, dilation of the tract and stone extraction with fragmentation are addressed elsewhere in this volume. Once stone fragmentation and removal are complete, the collecting system is completely examined with flexible nephroscopy. Fluoroscopy is also used to determine if there are residual fragments.

At this point, the decision to perform the surgery tubeless or to leave a nephrostomy tube is made. It is our practice to leave a nephrostomy tube in cases of collecting system injury, significant residual stone burden necessitating a second-look procedure, significant bleeding, and altered urinary tract anatomy (i.e. patients with urinary diversions). In general, for patients undergoing tubeless PCNL, we leave the 6 F open-ended ureteral catheter in place overnight secured to a 16 F Foley catheter (a tubeless, stentless PCNL). A DJ stent is left in place in cases where a large proximal ureteral stone is treated and in cases of access above the 11th rib. Nephrostomy tube placement at the end of the procedure is covered elsewhere in this text. Here we describe our technique at the conclusion of the procedure for performing tubeless PCNL.

For patients who are left with just the 6 F ureteral catheter, at the conclusion of the procedure the safety wires and percutaneous access sheath are removed. Manual pressure is held over the percutaneous tract for 5 min. A 3-0 Vicryl suture is used to reapproximate the subcutaneous tissue. A 4-0 Monocryl suture is used to close the incision in a subcuticular fashion. The incision is dressed with gauze and Tegaderm™ (3M, St Paul, MN).

In patients in whom it is preferable to leave a DJ stent, one of the guidewires is backloaded into the rigid nephroscope. The 6 F ureteral catheter is removed under vision. The DJ stent is then placed over the wire through the nephroscope under vision. Fluoroscopy is used to confirm that the proximal end of the stent is in the bladder. The wire is removed and fluoroscopy is again used to confirm an appropriate curl in the bladder. The distal curl (in the kidney) is confirmed under vision. The remaining safety wire and the percutaneous access sheath are removed. The remainder of the procedure is performed as outlined above, beginning with manual pressure.

Intraoperative trouble-shooting

It is recommended that a nephrostomy tube be placed when more than two access tracts are needed for the PCNL procedure. In cases of a significant perforation of the collection system, we recommend placement of a NT. When there is increased risk for pleural injury (supra-11th rib puncture) we recommend leaving a DJ stent and sometimes a NT. For cases in which there is significant intraoperative bleeding, the procedure should be suspended and a NT should be left in place. On rare occasions, if brisk bleeding is noted from the nephrostomy tract, 5 mL of FloSeal gelatin matrix can be instilled followed by manual compression as described by Yoon and Bellman [50].

Postoperative follow-up

Patients are kept in hospital overnight in our observation unit. A Foley catheter draining the bladder is left in place. For patients who were left with just a ureteral catheter, the Foley and ureteral catheters are removed the morning of the first postoperative day. Patients with a DJ stent typically have their Foley removed on postoperateive day 1, as well. Intravenous antibiotics are continued for 24 h after the procedure. Patients are seen for a postoperative visit 2 weeks after surgery. The DJ stent is removed with a flexible cystoscope in the clinic 1–2 weeks after surgery. Imaging is typically obtained at a 3-month visit with either an intravenous pyelogram or noncontrast CT scan.

Postoperative trouble-shooting/ auxiliary procedures after tubeless percutaneous nephrolithotomy

The need for auxiliary procedures after tubeless PCNL varies depending on which study is referenced, but is typically from 1.6% to 16% [3,4,8–11,13,17,19–22,26,39,41]. A recent metaanalysis demonstrated equivalent stone-free rates, blood loss/transfusion and postoperative fever and lower rates of postoperative urine leakage and analgesic requirements, as well as operative time and hospital stay for the tubeless approach compared to leaving a nephrostomy tube [38]. Ancillary procedures after tubeless PCNL have been addressed by Brusky et al. [63]. Fifteen percent of a total of 125 patients undergoing tubeless PCNL needed auxiliary procedures, including shock wave lithotripsy (15/19 patients, 79%), second PCNL (11%), ureteroscopy (5%), and internal DJ stent placement (5%).

Conclusion and recommendations

Tubeless PCNL is a safe and effective procedure for treatment of renal calculi. Results from multiple studies have demonstrated similar, if not lower complication rates for the tubeless approach compared to standard PCNL. Moreover, regarding cost, length of hospital stay, postoperative pain, and recovery time, tubeless PCNL appears to be superior to a nephrostomy tube. In cases where there is not significant bleeding, collecting system perforation, infection or the need for a second-stage PCNL, tubeless PCNL should be strongly considered. In our institution more than 85% of all PCNL procedures are performed tubeless (with a temporary open-ended ureter catheter or DJ stent).

The following criteria may be useful as a guideline in deciding when to leave a nephrostomy tube.

1 Success has recently also been shown in tubeless PCNL cases with supracostal access and for larger stone burdens but these scenarios still require further investigation in larger cohorts to prove their safety [31,35,37,48].

2 When a large perforation of the collecting system is recognized, the procedure should be terminated and a nephrostomy tube left in place.

3 Tubeless PCNL is not recommended if significant intraoperative bleeding occurs.

4 In complicated procedures it is favorable to place a NT at the end of surgery.

5 If there is a chance of intrathoracic violation, it is recommended to keep an internal ureteral stent and NT in place.

6 A NT should be left in place in patients with residual stone requiring a staged procedure. A recently published metaanalysis indicated no significant difference in stonefree rates between tubeless procedures and standard PCNL with a big tube. Nevertheless, the data suggested a slightly better stonefree rate for tubeless procedures [38]. The ideal indications for the tubeless procedure or contraindications to it have yet to be documented in well-designed, large, randomized controlled trials.

The rate of stone clearance when performing tubeless PRS has been reported to range from 71.4% to 100% [31,35,37].

Acknowledgments

Andreas Neisius is supported by a Ferdinand Eisenberger grant (ID NeA1/FE-11) from the Deutsche Gesellschaft für Urologie (German Society of Urology).

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CHAPTER 16

Instrumentation and Surgical Technique: Postoperative Imaging Following Percutaneous Nephrolithotomy

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Introduction

Percutaneous nephrolithotomy (PCNL) constitutes first-line therapy for patients with large, complex or staghorn calculi, those with stones and complex intrarenal anatomy, and those who have failed shock wave lithotripsy or ureteroscopy. The goal of preoperative imaging is to define the location and extent of the stone burden, to delineate the relational anatomy of the kidney and to demonstrate pelvicalyceal anatomy in order to facilitate safe, efficient, and efficacious percutaneous renal access and stone removal. Intraoperative imaging is essential to guide percutaneous renal puncture and to monitor the establishment of safe, secure access to the collecting system, as well as to assure endoscopic inspection of the entire collecting system, thereby promoting complete stone removal. Finally, postoperative imaging confirms complete stone removal or identifies residual stone fragments (RFs), assures anterograde urinary drainage, and identifies potential complications. A thorough understanding of the role and selection of postoperative radiographic imaging after PCNL is necessary for safe and effective PCNL and constitutes the topic of this chapter.

The importance of residual fragments

Although the goal of any surgical stone procedure is complete stone removal, the optimal treatment modality eliminates the entire stone burden with the fewest procedures and the least morbidity. If stone fragments remain after treatment, they may be associated with growth, migration, obstruction or infection [1,2]. Residual stones of an infectious composition are particularly susceptible to continued growth and recurrent infection. However, despite aggressive attempts to removal all stone fragments, including multiple accesses and liberal use of flexible nephroscopy, upwards of 70% of patients who undergo PCNL for large renal calculi are left with RFs after the initial procedure [3,4]. Accurate diagnosis and an understanding of the fate of these residual stone fragments are essential in order to appropriately counsel patients regarding the need for secondary procedures including flexible nephroscopy (SLFN), ureteroscopy or shock wave lithotripsy (SWL) versus expectant management.

The shock wave lithotripsy literature provides insight into the natural history of posttreatment

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

residual fragments because this treatment modality relies on spontaneous passage of generated fragments to achieve a stone-free state. The concept of "acceptable" small residual fragments originated because the noninvasiveness of SWL was thought to offset the fact that patients may not be rendered stone free. However, careful analysis of outcomes of patients with small (< 4 mm) residual fragments revealed that these fragments often do not remain quiescent [5,6]. Osman and colleagues reported that 21% of 173 patients with ≤4 mm RFs after SWL required retreatment at a mean follow-up of 4.9 years [7]. Streem and coworkers retrospectively analyzed 160 patients with ≤ 4 mm RFs and found that 43% of patients became symptomatic and/or required intervention at a mean follow-up of 26 months [5]. Khaitan and colleagues observed that 59% of 75 patients left with <4 mm residual fragments after SWL required intervention [8]. Finally, El-Nahas and colleagues followed 154 patients with RFs for a mean of 31 months and reported that during that period, 49% of patients had a "clinically significant outcome," i.e. required surgical intervention or pain medication [9].

In contrast, however, Buchholz and associates followed 44 patients with ≤5 mm fragments after SWL for a mean of 30 months and found that only 12.5% of the 94 total fragments identified on follow-up plain radiographs remained at the end of the study period and only 2.1% appeared to have grown [6]. Furthermore, despite a third of RFs residing in the proximal ureter, no patient reported associated pain. Consequently, the authors concluded that salvage procedures to remove RFs were not justified.

Although it seems likely that fragments remaining after any surgical procedure demonstrate a similar natural history, the literature is heavily weighted toward the natural history of RFs after SWL. However, small fragments left after SWL are justified by the minimally invasive nature of the procedure. On the other hand, PCNL is the most "invasive" of the minimally invasive procedures, and a higher premium is placed on a stone-free state to justify the added risk. Furthermore, the ease with which residual fragments can be accessed through the existing nephrostomy tract encourages efforts to achieve a stone-free state. Raman and colleagues reviewed a series of 527 PCNL patients with a minimum follow-up of 6 months and identified 42 patients with RFs (median size 2 mm) by computed tomography (CT) who did not undergo second-look flexible nephroscopy (SLFN) [10]. Overall, 43% of patients experienced a stone-related event, defined as interval growth of the fragment or need for emergency department visit, hospitalization, or additional surgical intervention, at a median time of 32 months. Among these patients, 61% required a secondary procedure including five ureteroscopies, two PCNLs, two SWLs, one stent placement, and one nephrectomy for a patient who refused less invasive surgery. On univariate analysis, stone size > 2 mm, cumulative stone burden, and location in the renal pelvis or ureter were associated with a future stone event. When adjusting for other prognostic factors, only dominant fragment size > 2 mm and pelviceal/ureteral location were independent predictors of a stone-related event on multivariate analysis.

Ganpule and Desai also evaluated the outcome of patients with RFs detected by plain radiography and ultrasonography post PCNL [11]. Among 187 patients, 45% spontaneously passed their RFs at a mean of 24 months, although there is no mention in the report of associated pain or obstruction. RFs <25 mm^2 and those located in the renal pelvis were associated with the highest likelihood of spontaneous passage. Of note, no RF > 100 mm^2 in size passed spontaneously.

Not only do residual fragments pose a risk for future patient morbidity, but they are also associated with economic consequences. In a pooled analysis of 678 patients with ≤4 mm post-SWL or post-PCNL RFs, 40% of patients experienced a stone-related event and 57% of those patients subsequently required surgical intervention [12]. By applying a decision tree model to this pooled group of patients, the cost associated with expectant management of RFs was determined. The cost of expectant management correlated with the size of the RF: the mean cost of observation for a ≤ 4 mm RF was $1743 versus $4674 for observation of > 4 mm RFs [12]. On the other hand, the cost of SLFN was estimated at approximately $2500, leading to the conclusion that SLFN is cost-effective for RFs > 4 mm in size but not for RFs ≤ 4 mm. The significant clinical and economic impact of residual fragments after PCNL underscores the need for accurate diagnosis of RFs post PCNL in order to appropriately counsel patients regarding the risks of observation versus secondary intervention.

Diagnosis of residual fragments

Historically some practitioners routinely performed SLFN after initial PCNL to assess and remove RFs and assure a stone-free state because imaging was less accurate than direct inspection for identifying RFs. However, this practice resulted in unnecessary procedures in at least 32% of patients [4]. As such, a less invasive means of accurately diagnosing RFs is desirable and cost-advantageous. Reliable assessment of the presence of RFs after intervention is paramount not only for individual patient decision making but also for uniform and accurate comparison of the outcomes of stone procedures.

Kidney, ureter, bladder plain abdominal radiographs and renal tomography

Approximately 80% of stones are radiopaque, with calcium oxalate monohydrate and brushite the most readily visualized, followed by calcium apatite and calcium oxalate dihydrate. Cystine and struvite stones are faintly opaque, and uric acid stones are radiolucent [13]. The target stone is determined to be radiopaque or radiolucent preoperatively by plain radiography or nephrotomography, or intraoperatively by fluoroscopy. The advantages of plain radiography or nephrotomography for the identification of RFs include rapid acquisition, ubiquitous availability, low radiation exposure, and relatively low cost. However, if the stone was not visualized on initial plain radiographs, RFs are unlikely to be identified postoperatively with this imaging modality. The sensitivity of plain radiography and nephrotomography is limited by the presence of overlying stool and bowel gas, bone (ribs, transverse processes), nephrostomy tubes or stents, retained contrast, small stone size, and nonrenal calcifications.

Studies have shown that the sensitivity and specificity of plain radiography for the detection of renal and ureteral calculi are 58–62% and 67–69%, respectively [14–17]. Denstedt and colleagues compared the sensitivity of plain abdominal radiography and renal tomography in patients undergoing PCNL, using flexible nephroscopy as the gold standard for identifying RFs [18]. Among 29 patients who underwent PCNL, 19 were deemed stone free by plain radiographs. However, five of these patients were found to have RFs when imaged with nephrotomography, thereby decreasing the overall stone-free rate from 66% by KUB to 48% by nephrotomography. On mandatory “final-look” nephroscopy, an additional five patients (17%) initially thought to be stone free by plain films and nephrotomograms were found to have RFs, further lowering the stone-free rate to only 31% [18]. Thus, plain abdominal radiography overestimated stone-free rate by 34% and nephrotomography by 17%. The authors concluded that only flexible nephroscopy can reliably assess and ensure a stone-free rate.

Computed tomography

In 1998, Gaucher and colleagues included a relatively new imaging modality, helical CT, in their postoperative algorithm to assess residual stone burden after SWL or PCNL [19]. In a prospective study of 31 patients (40 renal units), plain radiography, nephrotomography, ultrasonography, and helical CT were each performed postoperatively to identify RFs. The sensitivity of each imaging modality, in decreasing order, was 100% for CT, 89% for nephrotomography, 82% for plain abdominal radiography and 68% for ultrasonography. Indeed, CT had a 100% detection rate for millimeter stones (Figure 16.1). These authors concluded that CT offered the most reliable means of diagnosing postoperative RFs.

The increasingly widespread use of CT and the superior sensitivity of axial imaging compared to plain radiographs for the diagnosis of renal calculi led other investigators to study the potential role of CT in the evaluation of patients post PCNL. Waldmann and colleagues reviewed 121 patients (124 renal units) who were imaged by CT within 12–36 h after PCNL and found that 59% of patients were stone free and 41% had retained calculi 1–3 mm in size that were observed, removed via second-look flexible nephroscopy, or treated with subsequent SWL [20]. Notably, CT was presumed to be the “gold standard” for detecting residual fragments and no other imaging modality or flexible nephroscopy was compared with CT.

Pearle and colleagues prospectively evaluated 31 patients (41 renal units) with large and/or complex renal calculi who were imaged with plain radiography and nonenhanced CT scan and underwent compulsory flexible nephroscopy after initial PCNL [4]. RFs were identified at SLFN in 67.5% of renal units (28 of 37). The sensitivity and specificity of plain film radiography were 46% and 82% compared with 100% and 62% for CT, respectively, using SLFN as the referent standard. The false-positive results with CT were attributed to Randall’s

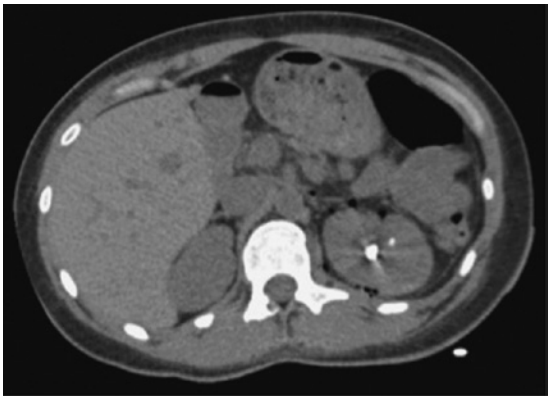

Figure 16.1 Nonenhanced helical CT scan obtained on postoperative day 1 after PCNL demonstrating a 2 mm residual fragment. The high-attenuation central density is the nephrostomy tube.

plaques, submucosal stones, or tiny irretrievable stone fragments. In addition, the cost savings associated with selective use of SLFN based on positive CT findings were estimated to be greater than $100,000 per 100 patients because fewer patients were undergoing reoperation. The authors concluded that an unnecessary procedure could be avoided in approximately 20% of patients if only those with a positive CT undergo SLFN. This study confirmed the central role of CT in the accurate diagnosis of post-PCNL residual fragments.

Several studies have specifically assessed the utility of CT compared with other imaging modalities in the management of radiopaque stones. Park and colleagues prospectively compared early postoperative antegrade nephrostogram to 1-month KUB and CT scan for detection of residual fragments in a series of 50 patients with preoperatively verified radiopaque stones [3]. Stone-free rates according to antegrade nephrostogram, KUB, and CT were 74%, 62%, and 21%, respectively. In a subgroup analysis of 22 patients with stones detected on CT but not KUB, 45.5% of patients had stones > 4 mm in size (mean 7.4 mm), revealing that even relatively large, radiopaque stones may escape detection on plain film radiography. In another prospective study, 100 renal units with 55 radiopaque and 45 radiolucent stones were subjected to post-PCNL imaging with plain radiographs (KUB), ultrasonography, nephrotomography and helical CT [21]. Among patients with radiolucent stones, sensitivities were 100%, 11%, 22%, and 22% ($p < 0.05$) for CT scan, KUB, nephrotomography and ultrasonography, respectively. Among patients with radiopaque stones, 100% of RFs were detected by CT, 63% by KUB, 74% by nephrotomography, and 49% by ultrasonography. The authors also noted that detection rates for stones >5 mm were 100% for CT, 86% for KUB, 95% for nephrotomography, and 57% for ultrasonography. Consequently, they concluded that KUB and/or nephrotomography are sufficient to identify "clinically significant residual fragments" [21].

The use of CT for the detection of residual fragments after PCNL is not without limitations. Randall's plaques or submucosal stones cannot be clearly distinguished from accessible collecting system stones and may result in false-positive studies that lead to unnecessary secondary procedures, incurring additional cost and morbidity. Furthermore, CT is associated with significant radiation exposure. A multicenter study demonstrated that up to 20% of patients diagnosed with a first-time stone received doses of ionizing radiation over the 12 months after diagnosis that exceeded recommended occupational exposure limits [22]. A significant portion of excessive radiation levels was attributable to the widespread use of CT. Low-dose CT (<30 mA), which has an effective radiation dose of ≤4 mSv, has been shown to maintain >90% sensitivity and specificity for ureteral stones and may be effective in the setting of post-PCNL imaging. Poletti and colleagues compared the sensitivity of low-dose CT (30 mA) with standard dose (180 mA) in a group of 125 patients suspected of having renal colic [23]. The sensitivity of low-dose CT for the detection of ureteral calculi was 93%. Among 85 patients with renal calculi and a Body Mass Index (BMI) <30, the sensitivity of low-dose CT was only 76% overall but increased to 97% in patients with stones ≥3 mm in size. Zilberman and colleagues evaluated the utility of low-dose CT in the ambulatory setting and found that it was effective for identifying stones, particularly if they were large or located in the kidney [24]. Although low-dose CT scan has not been specifically evaluated in the post-PCNL setting, it is likely that this modality will reliably identify most residual calculi in patients with a BMI <30.

Other treatment parameters in addition to dose influence the sensitivity of CT in detecting residual fragments post PCNL. The size of the scanning interval or image slice also affects sensitivity and specificity. Data acquisition based on thin sections potentially provides higher quality images. However, in order to keep radiation exposure low, scan parameters must be used that result in a low signal-to-noise ratio, leading to a poorer quality image. Memarsadeghi and colleagues attempted to identify the ideal section setting (1.5 mm, 3 mm, or 5 mm) while standardizing radiation exposure levels to a safe range (11.4 mGy) for stone detection [25]. Although detection rates were comparable for 1.5 and 3 mm slices, 5 mm slices led to significantly more missed stones. Notably, all stones that failed to be detected on 5 mm slices were <3 mm in size. While the cut point for "clinically significant" fragments remains to be determined, CT imaging using 3 mm sections is advisable.

The accuracy of CT in determining stone size is not uniform for all dimensions. Indeed, urologists and radiologists have been accused of relying more on an "educated guess" than actual measurements based on imaging studies for determining stone size [26]. In a survey of 435 radiologists and urologists in the United Kingdom, 10–59% of respondents admitted to using an estimate of calculi size rather than actual measurements based on imaging. In this study, physicians consistently underestimated an 11 mm stone at 9.6 mm [26]. On the other hand, several investigators have found that CT consistently overestimates the longitudinal measurement of stones compared with KUB. Typically, the craniocaudal dimension of a stone is obtained by multiplying the number of axial images in which a stone is visible by the slice thickness. Van Appledorn and colleagues found a 30–50% overestimation of size on CT compared to plain film radiography. Likewise, Narepalem and colleagues found good concordance between KUB and CT for the transverse dimension of stones, but the craniocaudal dimension was overestimated on CT by an average of 0.8 mm [27]. The potential oversizing or undersizing of RFs based on CT scan and the subsequent decision to intervene may have important clinical consequences, as size is a determinant of outcomes in the natural history of residual fragments [10].

In summary, several factors must be taken into account in the selection of postoperative imaging for the detection of residual fragments after PCNL, including sensitivity/specificity, effective radiation dose, cost and convenience. CT scan has the highest sensitivity for stone detection, but it is associated with the highest cost and radiation exposure of the commonly utilized imaging modalities. The use of low-dose CT may mitigate the harmful radiation effects while maintaining high sensitivity and specificity. Although there is no reliable stone size, location, or characteristic that accurately predicts which fragment will remain clinically silent or which will lead to problems, a natural history study identified stone size >2 mm and location in the renal pelvis as factors predictive of a stone-related event. As such, stones with those characteristics, as well as fragments associated with infections stones (because of the higher risk of continued stone growth and infection) should prompt secondary intervention with flexible nephroscopy [1]. Ultimately, however, the decision to proceed with additional treatment is a cooperative decision between the surgeon and patient.

Antegrade nephrostogram

Ureteral stone fragments, blood clots, and edema can lead to distal obstruction after PCNL. Endoscopic inspection of the ureter and/or intraoperative antegrade nephrostogram at the conclusion of PCNL ensures antegrade drainage, absence of ureteral fragments and a well-positioned nephrostomy tube. Although a satisfactory intraoperative antegrade nephrostogram does not guarantee that fragments will not subsequently migrate down the ureter or that edema will not develop, it does lessen the likelihood of occurrence. For patients with a nephrostomy tube in place after the procedure, if antegrade nephrostogram on postoperative day 1 demonstrates urinary extravasation or poor or absent antegrade drainage, the nephrostomy tube should remain in place [28]. Although some groups advocate a trial of capping the nephrostomy tube prior to removal, drainage around the tube may decompress the collecting system and can lead to a false sense of security that there is sufficient antegrade drainage. Khan and colleagues reviewed 124 patients who underwent PCNL with an occlusion balloon catheter who were not imaged postoperatively with an antegrade nephrostogram [29]. In all patients, the nephrostomy tube was capped on the second postoperative day, with subsequent tube removal if they remained asymptomatic. Although two patients underwent nephrostogram for suspected perforation (neither demonstrated extravasation), no patient was readmitted with pain after discharge. The authors concluded that use of an occlusion balloon catheter to prevent migration of fragments and a capping trial to assure antegrade drainage are sufficient measures to identify/avoid postoperative obstruction. Of note, there is no published comparison of the safety of antegrade nephrostogram and prompt tube removal versus a capping trial and observation before tube removal.

Prolonged urine leakage (>24 h) is not uncommon, with an incidence of 5–16% [30,31]. Prolonged leakage of noninfected urine can be managed conservatively with Foley catheter drainage to prevent reflux if a stent is present and either frequent dressing changes or placement of an ostomy appliance at the nephrostomy site if a stent is not in place. However, persistent leakage or infection may require placement of a ureteral stent and comprises a Clavien Grade III complication [32]. In a series of 1407 PCNLs, Binbay and colleagues reported a 4.3% incidence of prolonged urine leakage requiring stent placement, despite finding adequate drainage on antegrade nephrostogram prior to tube removal [30]. The authors identified large or complex stone burden, residual stones, and need for adjunctive treatment as factors predictive of prolonged urine leakage requiring stent placement. They suggested that intraoperative stent placement be considered in the case of complex procedures in which there is a high suspicion of residual fragments.

In a prospective study of 50 patients (51 renal units) with radiopaque renal calculi who underwent routine antegrade nephrostogram on postoperative day 2 after PCNL, the nephrostomy tube was removed if no stones were identified in the ureter, regardless of antegrade drainage. Among these patients, 14 (27%) underwent nephrostomy tube removal despite evidence of distal obstruction not due to ureteral calculi. Prolonged urinary leakage (>24 h) occurred in eight patients from the entire cohort, including five of 14 (36%) with obstruction on antegrade nephrostogram and three of 37 (8%) without obstruction ($p = 0.02$). Of note, none of the patients with obstruction on nephrostogram versus one patient without obstruction required stent placement for prolonged urinary leakage. Although the authors recommended routine postoperative anterograde nephrostogram to identify the presence of residual fragments, urinary extravasation, and distal obstruction, they admitted that obstruction on antegrade nephrostogram correlates only with prolonged urine leakage but not the need for stent placement [31].

No randomized trial has compared the findings of intraoperative with postoperative nephrostogram. Furthermore, most clinicians would likely consider urinary leakage for up to 48 h acceptable, which would change the outcomes of the above study. Moreover, in that study the authors failed to document whether patients experienced pain after nephrostomy tube removal, which would also dictate the need for intervention. Our practice is to obtain a limited unenhanced CT of the abdomen and antegrade nephrostogram (Figure 16.2) on the first postoperative day after PCNL and to remove the tube and discharge the patient home if there are no residual stones or obstruction.

Evaluation of hydrothorax

Supracostal access associated with PCNL risks violation of the pleural space and accumulation of urine, irrigation fluid or blood. With access above the 12th rib, there is a 0–12% incidence of pleural complications [33–40], increasing to upwards of 23% for access above the 11th rib [38]. Expeditious diagnosis and treatment of pleural complications may prevent sequelae such as respiratory compromise or empyema. Moreover, intraoperative diagnosis of pleural fluid allows placement of a thoracostomy tube while the patient is still anesthetized (Figure 16.3). Because the pleural fluid that accumulates during PCNL is composed primarily of irrigant, it can be adequately drained with a small-caliber (8-10 F) thoracostomy tube that is placed under direct fluoroscopic guidance utilizing the same familiar equipment required for percutaneous renal access [41].

Hydrothorax can be diagnosed intraoperatively by fluoroscopy or postoperatively by chest radiograph or CT. Ogan and associates prospectively compared the sensitivity of intraoperative fluoroscopy, chest x-ray obtained in the postanesthesia care unit (PACU) and unenhanced abdomen CT that included the lung bases on postoperative day 1 in 89 consecutive patients (100 renal units) undergoing PCNL [42]. Hydropneumothorax after initial PCNL was detected fluoroscopically in one case (1%), by chest radiograph in eight patients (8%), and by CT in 38 patients (38%). The sensitivity of fluoroscopy and chest x-ray using CT as the gold standard was 3% and 21%, respectively. An additional two patients were diagnosed with hydrothoraces postoperatively, one by fluoroscopy at the time of second-look flexible nephroscopy and one by chest x-ray after developing symptoms. Drainage was required in two patients intraoperatively and in five patients postoperatively after developing symptoms despite a negative PACU chest x-ray. The authors concluded that routine postoperative chest x-ray is unnecessary and intraoperative fluoroscopy is sufficient to detect a clinically significant

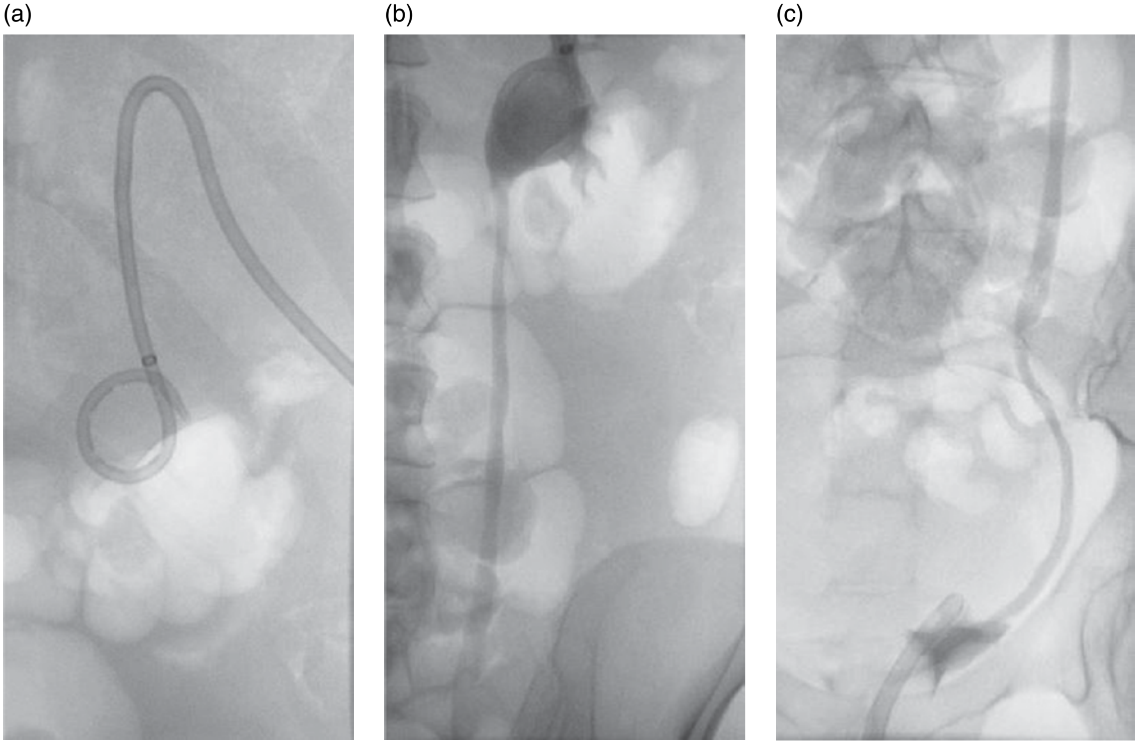

Figure 16.2 Antegrade nephrostogram. (a) Fluoroscopic scout film demonstrating a nephrostomy tube positioned in the collecting system. (b) Opacification of the collecting system and proximal ureter. (c) Drainage of contrast into the bladder.

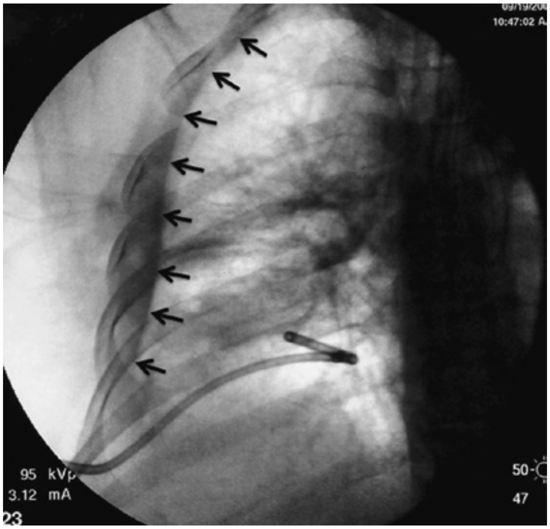

Figure 16.3 Intraoperative fluoroscopic image of the right chest after PCNL showing hydrothorax and 10 F thoracoscopy tube in the pleural space. Arrows indicate the demarcation between pleural fluid and lung.

hydrothorax, but that postoperative symptoms should prompt further imaging. Of note, despite the high rate of radiographically detected pleural fluid (38% by CT scan), only 7% actually required intervention, a rate of intervention validated in other studies [43].

In a retrospective review of 214 PCNL procedures, two patients reportedly developed hydropneumothoraces [44]. In one patient the hydrothorax was suspected intraoperatively because of poor ventilation and air exchange and confirmed by fluoroscopy and chest x-ray. The other patient had a normal PACU chest x-ray but was diagnosed on postoperative day 3 when he developed respiratory symptoms. These authors concur that routine postoperative chest x-ray is unnecessary for the detection of a clinically significant hydropneumothorax but that a high index of suspicion should be maintained postoperatively because pleural fluid can accumulate in a delayed setting.

In summary, chest fluoroscopy should be performed at the conclusion of PCNL to detect pleural fluid and guide thoracostomy tube placement. However, even in the face of negative intraoperative imaging, the development of pulmonary/respiratory symptoms postoperatively should prompt the use of chest imaging to identify a hydrothorax.

Additional considerations

This chapter has addressed the use of routine postoperative imaging after PCNL. However, the development of other complications, such as bleeding, collecting system perforation (2%) or urinoma (1%) or colonic or splenic injury (<1%) should prompt the use of selective imaging such as CT or renal arteriogram that are aimed at identifying and potentially providing guidance for treatment of specific complications.

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17

CHAPTER 17

Instrumentation and Surgical Technique: Step-by-Step Antegrade Ureteric Stenting

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Insertion of a ureteric stent is an "everyday" procedure for urologists. Done for a wide variety of indications, it is most frequently performed in a retrograde manner via the cystoscope. The technique is well established. The selection of guidewires, the stent diameter, design, and length are determined by the underlying pathology, patient habitus, and personal preference of the urologist.

The same procedure can be performed in an antegrade manner in a selected cohort of patients and may become necessary for a variety of reasons. The ureteric orifice may be inaccessible due to invasion by malignancy [1]. Ureteric obstruction may be too severe to allow the passage of a guidewire into the renal pelvis for a successful retrograde stent insertion [2,3]. Such clinical situations require insertion of a nephrostomy tube prior to stenting.

Insertion of a nephrostomy tube becomes necessary when upper tract obstruction is supravesical. Acute renal failure due to bilateral ureteric obstruction that cannot be relieved by retrograde stenting is a common indication for bilateral nephrostomy tube insertion. This may become imperative if the patient is acutely ill and cannot be anesthetized for the insertion of a JJ stent. Unilateral decompression of a ureter with a nephrostomy tube is necessary when the obstruction is severe or complicated by sepsis or the patient has a solitary functioning kidney. Other clinical settings when a patient needs insertion of a nephrostomy prior to JJ stent insertion are ureteric trauma (frequently iatrogenic) [4–7], ureteric fistulas [8], and ureteric obstruction in the presence of urinary diversion.

Another indication for antegrade stenting of the ureter is following endopyelotomy for pelvi-ureteric junction (PUJ) obstruction performed via a percutaneous route.

The insertion of a ureteric stent can be performed when renal function has improved and sepsis settled [9]. Insertion of a JJ stent in an antegrade manner is a useful technique in these clinical settings. It can be performed under sedation in a radiology suite in selected patients [10,11].

Principles and prerequisites

Although the technique of antegrade stenting can be considered to be a simple reversal of the conventional retrograde technique, there are important differences. Insertion of a JJ stent is usually performed a few days after insertion of a nephrostomy tube. However, it can be performed as a primary procedure.

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

Patient preparation

It is essential to optimize the patient's condition before undertaking stenting. Renal function should be as normal as possible. Sepsis should be fully treated. Prophylactic antibiotic cover should be administered at least 1 h before the procedure. The choice of antibiotic will be determined by the urine culture from the nephrostomy urine. Hemogram and coagulation screen should be performed. Long-acting anticoagulation medication should be reversed and antiplatelet medications discontinued.

A written consent should be obtained from the patient. It is important to ensure that a premenopausal female patient is not pregnant as the procedure is performed under fluoroscopic guidance.

Consideration should be given to the patient's age, comorbidity, and willingness to undergo the procedure under local anesthesia. This is more significant if bilateral stenting is to be performed. A general anesthetic may be more appropriate in some patients in these settings.

The operating surgeon/radiologist should be aware of the underlying pathology, patient comorbidity, and previous surgical procedures on the urinary tract, especially urinary diversions.

The decision to remove or reinsert the nephrostomy tube after successful stent insertion should be made before commencing the procedure.

Equipment

The procedure can be performed in a radiology suite or a fully equipped endourology theater with an image intensifier. A wide range of guidewires, standard access catheters, angled tip catheters, stents of various lengths, and diameter should be available. Stepped and tapered as well as balloon dilators should also be available in case a tight ureteric obstruction requires dilation before stenting.

Patient position

The patient is usually kept in a tilted supine position with the ipsilateral flank slightly raised. Bolsters containing radiopaque materials should be avoided. The operating table should have the facility of a side tilt as the patient may need to be brought into a supine position during the procedure. This is often necessary in patients with ileal conduits as access to the stoma can be difficult. The patient should be in a lithotomy position if a combined procedure (rendezvous) is planned.

Analgesia and sedation

Patient monitoring is essential before sedating the patient. The task of monitoring vital signs should be delegated to a specific member of the team. Suitable sedation is given along with a prophylactic antibiotic. The choice of sedative is determined by local protocol, the experience of the operator in handling these medications combined with patient factors. Intravenous midazolam is a suitable agent that can be used in titrated doses. A general anesthetic is preferred for the rendezvous procedure.

Technique

An antegrade study is performed via the nephrostomy tube (Figure 17.1). This helps to get the surgeon oriented to the anatomy of the renal pelvis, the location of the PUJ in relation to the tip of the nephrostomy tube, and the direction of the ureter. It also reveals the exact position of the nephrostomy tube. The latter is usually performed by another member of the team in an emergency setting and therefore may not be placed in the most convenient location. It is useful to make a note of the direction and length of the tract of the nephrostomy tube as a tortuous and long tract may cause buckling of the stent during insertion.

The nephrostomy tube is unlocked (Figure 17.2). It is important to familiarize oneself with the locking and unlocking mechanism of the tube as there are significant variations between manufacturers. The guidewire will not advance if the tube remains locked, nor will it be possible to remove the nephrostomy tube.

A suitable guidewire is inserted into the renal pelvis (Figure 17.3). A floppy tip wire with a moderately stiff shaft is the best as it allows manipulations within the pelvis. A straight tip 0.035 inch Zebra wire (Boston Scientific, Natick, MA) is the personal preference of the author. Terumo (Terumo Medical, Somerset, NJ), ZIPwire and Sensor (both Boston Scientific) and Roadrunner (Cook Medical, Bloomington, IN) are suitable alternatives.

Figure 17.1 Antegrade study.

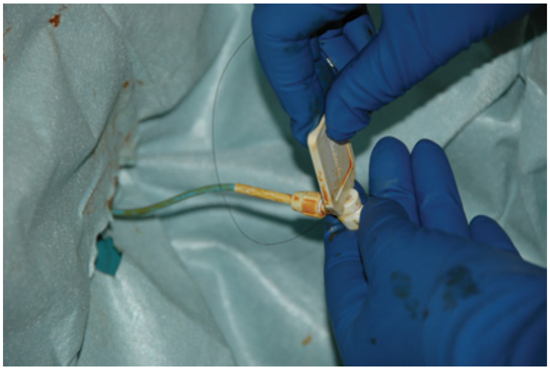

Figure 17.2 Unlocking of the nephrostomy tube.

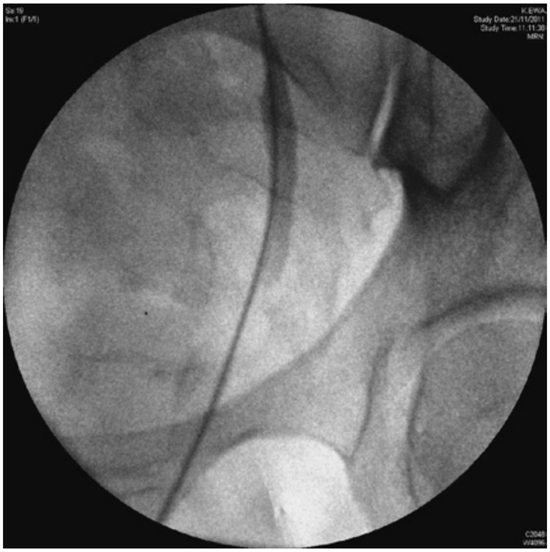

Figure 17.3 Successful insertion of guidewire.

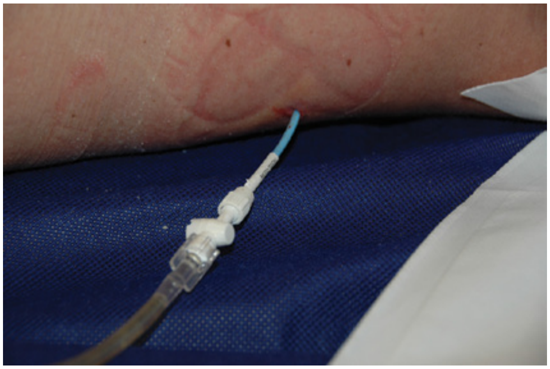

Figure 17.4 Nephrostomy too medial.

Getting the wire down the PUJ is the vital step of the procedure. This can be difficult. Various tricks have been described.

Several centimeters of the guidewire are inserted in the renal pelvis. The nephrostomy tube is gently withdrawn until it becomes straight. The tip of the guidewire can be directed to the PUJ with the help of a rotating movement of the nephrostomy tube. This can be difficult in patients with a baggy renal pelvis. Nephrostomy sited too medially (Figure 17.4) or in the lower calyx in a patient with "high take-off" of the ureter (high location of the PUJ) are common scenarios which complicate insertion of the wire into the ureter. The following variations can be tried.

Changing the guide ire to a slippery and hydrophilic type is a useful first step. A Terumo or Zip-wire have a floppy tip and are small enough to negotiate tight corners. These wires can be inserted and maneuvered with ease but care needs to be exercised as they can fall out easily with a resultant loss of access. Zebra, Sensor, Amplatz or Road-runner wires can be used as alternatives. All these wires are hydrophilic and must be kept wet during the procedure to get the maximum benefit of this feature.

Figure 17.5 Cook angled tip catheter.

Figure 17.6 Boston angled tip catheters.

Angled tip stiff catheters (Figures 17.5, 17.6) can be used to direct the tip of the guidewire into the PUJ. A Torcon Blue Biliary manipulating catheter (Cook Medical, Bloomington, IN) (see Figure 17.5) is the personal preference of the author. However, many other devices are available that can serve the purpose. The catheter should have adequate stiffness in the shaft. The length and the angle of the tip are variable. Selection is made to suit the anatomy of the PUJ. The devices used in vascular surgery are often too long and unsuitable. Bending the tip of the needle has been described to help achieve the same [12].

Once the PUJ is entered, the guidewire is advanced down the ureter. The antegrade study performed while commencing the procedure will guide the surgeon to get the wire past the obstruction. It may be necessary to perform further imaging if the guidewire fails to advance. A 6 F ureteric catheter is passed over the wire to perform an antegrade study. A long and tortuous ureter, tight obstruction, deviation of the ureter due to extraluminal compression, and extravasation of urine following trauma are the usual obstacles that prevent successful advance of the guidewire. Change to a smaller guidewire (such as 25 F) and the use of angled tip catheter are some alternatives that may help to get past a difficult section of the obstructed ureter.

The guidewire is advanced into the bladder. This can be confirmed by inserting a 6 F ureteric catheter over the wire and injecting of contrast.

A suitable stent is chosen. The diameter, stiffness, and the length will be determined by the height of the patient and the underlying pathology. It is essential to familiarize oneself with the stent features as the radiopaque marker positions vary from stent to stent. The stent is mounted over the wire and is advanced into the renal pelvis. The guidewire must remain straight and the tip should be maintained in the bladder. Intermittent fluoroscopy should be used to check the position of the wire to prevent accidental withdrawal. It is vital to have an assistant during the procedure.

A purpose-built variable-width stent (e.g. 7/14 F) with its wide section sited at the PUJ is selected after the endopyelotomy procedure.

Once the tip of the stent enters the bladder, a pusher is used to advance it further till the marker is seen in the bladder, thus ensuring that the curl has gone past the ureteric orifice. The wire is withdrawn into the ureteric stem of the stent and the distal coil is checked again.

A decision needs to be made about maintaining the nephrostomy tube after a successful stent insertion before the guidewire is removed completely. Drainage through a JJ stent may not be adequate and retaining a nephrostomy tube as a fail-safe back-up is a sensible option. It can be clamped and removed when the stent has adequately stabilized renal function.

A variation of technique should be used before removal of the guidewire if a nephrostomy is to be reinserted. The stent pusher is reinserted over the guidewire. The tip of the pusher should be in contact with the tip of the renal end of the JJ stent (Figure 17.7). This “joint” should be positioned in the renal pelvis. This can be confirmed by using fluoroscopy as the metal tip of the pusher can help locate its tip. The guidewire is slowly withdrawn under fluoroscopic control. The stent will curl away when the wire leaves its lumen (Figure 17.8). The wire is now advanced back into the renal pelvis and the pusher is withdrawn. A fresh nephrostomy tube is inserted into the

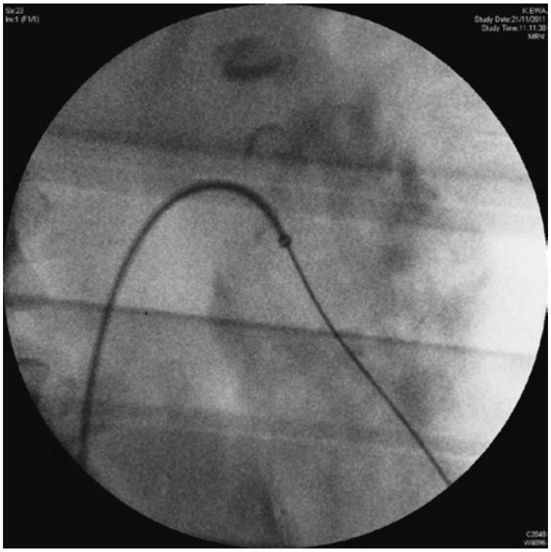

Figure 17.7 JJ stent and pusher over wire.

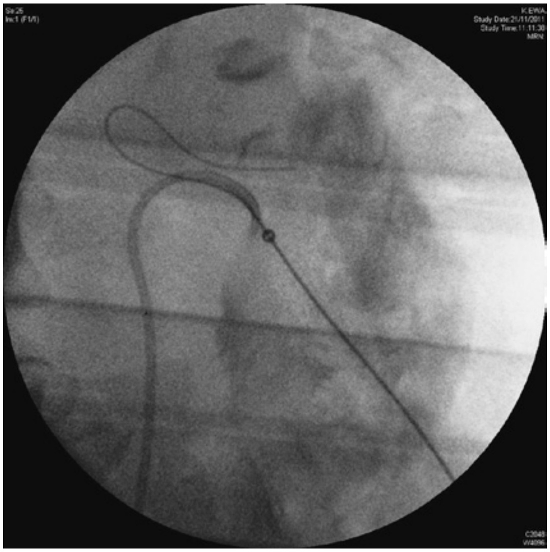

Figure 17.8 JJ stent separating from the guidewire.

renal pelvis over the wire (Figure 17.9). The guidewire is removed when the positions of the proximal end of the JJ stent and the nephrostomy tube are confirmed to be satisfactory (Figures 17.10, 17.11).

In conventional antegrade stenting, the guidewire is removed under fluoroscopic control. It is essential to ensure that the renal end of the JJ stent is curled in the renal pelvis and not left in the tract as this may lead to a urinary leak.

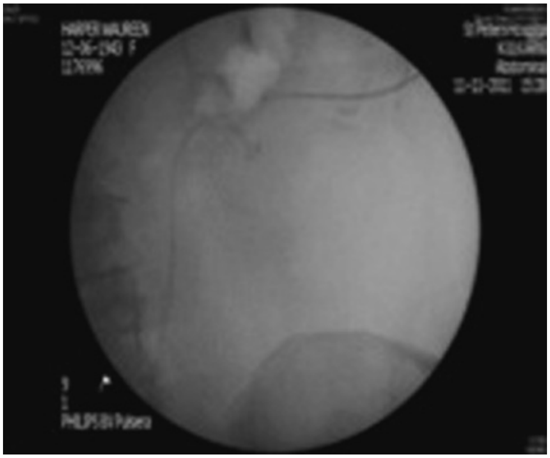

Figure 17.9 Nephrostomy reinserted.

Rendezvous stenting

One of the pitfalls of antegrade stenting is the lack of control of the distal end of the stent. There is a distinct possibility of inadvertent failure to enter the bladder and to leave the distal end of the JJ stent curled in the lower end of the ureter. A cystoscopic confirmation is definitive proof of correct stenting.

The other problem one may encounter is failure of progression and inability to advance the guidewire past a tight obstruction or a disrupted ureter due to severe trauma (Figure 17.12) [13,14]. These problems can be overcome by a combined procedure – the rendezvous technique. This essentially involves two teams working simultaneously to achieve successful passage of a guidewire from the skin to the meatus or the stoma (Figure 17.13). The use of a ureteroscope from below to help the team working from the renal end has been shown to improve success. It not only guides both the teams, but also irons out the curvature of the ureter. Once the site of obstruction is reached [15], a guidewire can be placed by either team. This procedure is almost obligatory in patients with ileal conduits, especially if the ureteroileal anastomosis has been done with the Bricker technique as this makes retrograde access difficult.

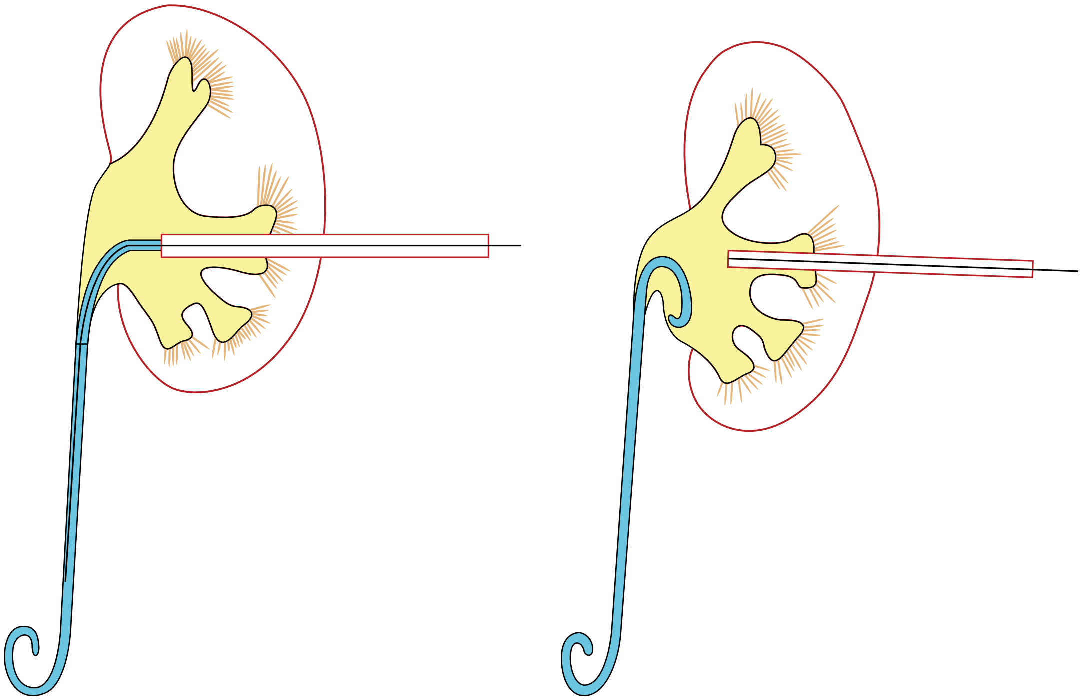

Figure 17.10 Technique of retaining guidewire in pelvis after stent insertion.

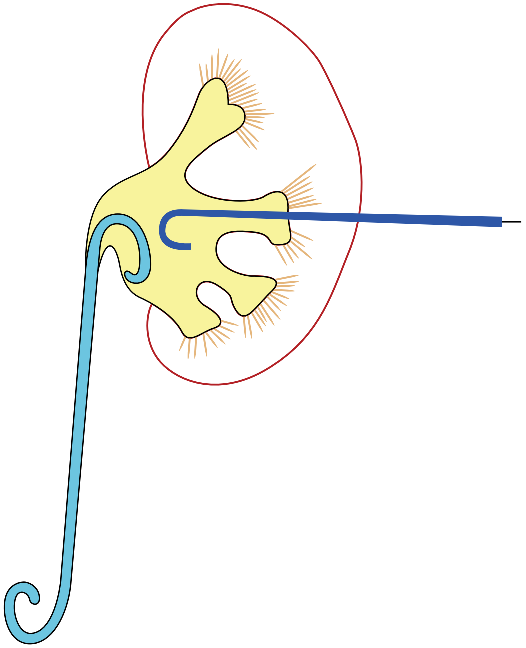

Figure 17.11 Reinsertion of nephrostomy.

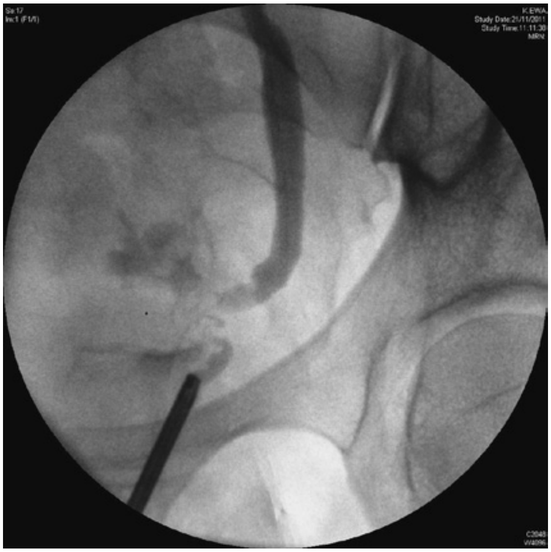

Figure 17.12 Ureteric injury: retrograde study demonstrates traumatized ureter with extravasation.

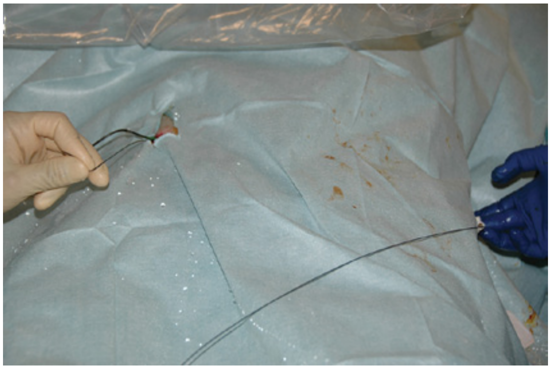

Figure 17.13 Placement of a through-and-through guidewire.

Special situations

Renal anomalies and solitary kidney

Renal anomalies such as duplex, ectopic, horseshoe and pelvic kidneys need special consideration due to the variations in the anatomy. It is advisable to reinsert the nephrostomy tube after stenting when the patient has a solitary functioning kidney.

Invasion of ureteric orifice

Involvement of the ureteric orifice due to pelvic malignancy may be impossible to negotiate during antegrade stenting. It may be prudent to consider a rendezvous type of procedure in such patients. A guidewire can be advanced down to the bladder in an antegrade fashion. Cystoscopic resection of the tumor invading the ureteric orifice is guided by the position of the guidewire tip located with fluoroscopy. The guidewire is retrieved after careful resection and the stent inserted in a conventional manner.

Ureteric injuries

Patients with ureteric trauma and subsequent extravasation of urine (see Figure 17.12) can be difficult as the guidewire has a tendency to enter the traumatized wall of the ureter. This can be more difficult if the separation of the two ends of the traumatized ureter is significant or the entire circumference of the ureter has been damaged.

The use of two ureteroscopes from either end aided by cautious use of methylene blue can help to overcome this problem. The nephrostomy tract is dilated to a size large enough to accommodate a fiberoptic ureteroscope. The latter is advanced to the superior end of the tear. A semi-rigid or a fiberoptic ureteroscope is inserted from below, intending to "rendezvous" and get a guidewire past the traumatized segment. Successful stent insertion may resolve the problem (Figure 17.14).

Figure 17.14 IVU after removal of JJ stent in the same patient.

Ileal conduits

Ureteric strictures in patients with ileal conduits can be difficult to manage. The left ureter is more commonly affected. Ischemia due to its long and tortuous route behind the rectosigmoid results in this complication. These strictures can also be caused by recurrence of the underlying malignancy or late development of ureteric tumors.

Stenting of a stenosed ureter in this group of patients needs full evaluation of the conduit as well as upper tracts. Cross-sectional imaging with a CT scan, a contrast study through the ileal conduit (a loopogram) as well as renography are essential. Insertion of a nephrostomy tube in the obstructed kidney followed by an antegrade study will also help to plan the procedure. Knowledge of the type of ureteroileal anastomosis (Wallace or Bricker) is important.

Figure 17.15 Pyelogram to help insertion of guidewire.

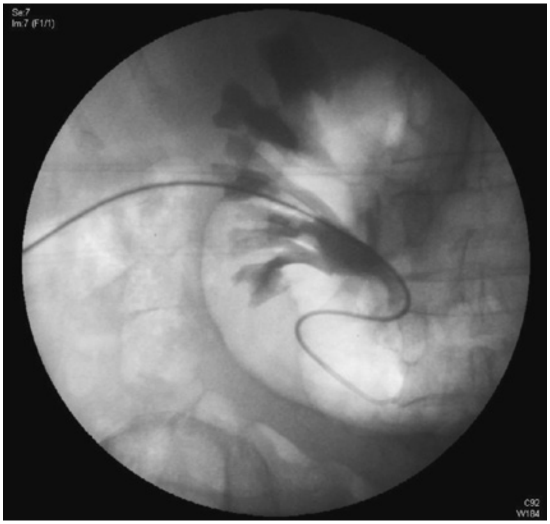

Figure 17.16 Advancement of ureteric catheter down the ureter.

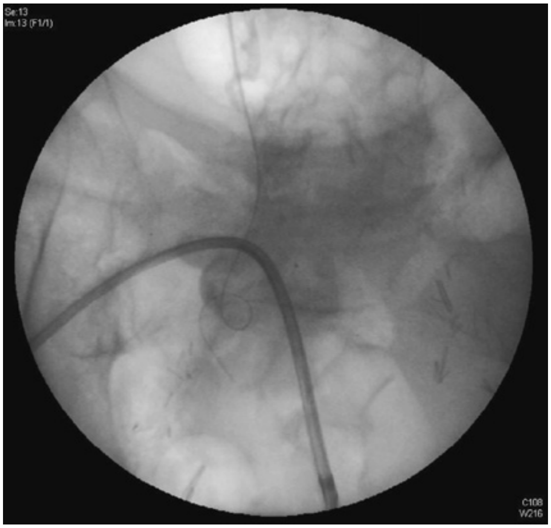

Figure 17.17 Advancement of guidewire.

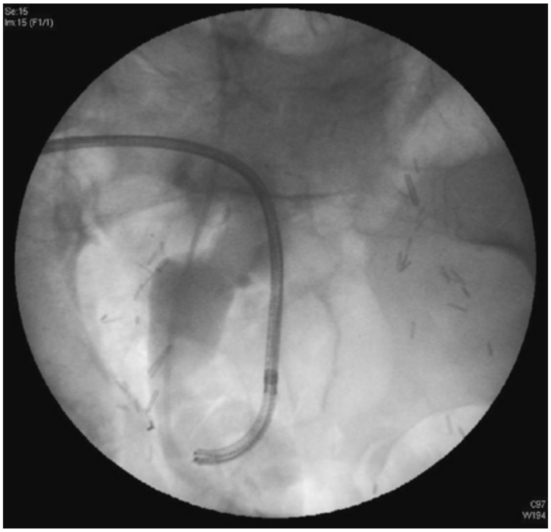

Figure 17.18 Rendezvous with a flexible endoscope.

The guidewire should be introduced from above through the nephrostomy. It should be guided down the ureter after imaging the upper tract as dilated ureters are often tortuous and the bends can be difficult to negotiate (Figures 17.15, 17.16). The use of fiberoptic scopes from below via the ileal conduit is advisable as this would aid retrieval of the guidewire (Figures 17.17, 17.18, 17.19). Single J (cystectomy stent) stents should be used in preference to double J. The caudal end of a double J stent will remain inside the conduit which will be inaccessible for future stent changes. A cystectomy stent can easily be changed by inserting a guidewire up its lumen (Figure 17.20).

Other conditions

Insertion of a stent during pyeloplasty can be performed in either a retrograde or antegrade manner. The selection of the technique depends largely on the experience of the surgeon, especially if a laparoscopic approach is used [16].

Figure 17.19 Retrieval of the guidewire with a fiberoptic endoscope.

Figure 17.20 Two single J stents inserted in an ileal conduit.

Chronic inflammatory processes of the ureter such as tuberculosis result in multiple strictures at various levels of the ureter. Balloon dilation followed by a stent is preferable to open correction. A combined approach may be necessary in patients with tight stenoses [17,18].

Pitfalls and dangers

It is important to be aware of the complications of this technique. It is possible for the guidewire to perforate the wall of the ureter. The stent will follow the wire and remain outside the lumen. This complication can occur at any level and may be missed. It is more likely to develop in the lower third of the ureter (Figures 17.21, 17.22, 17.23, 17.24).

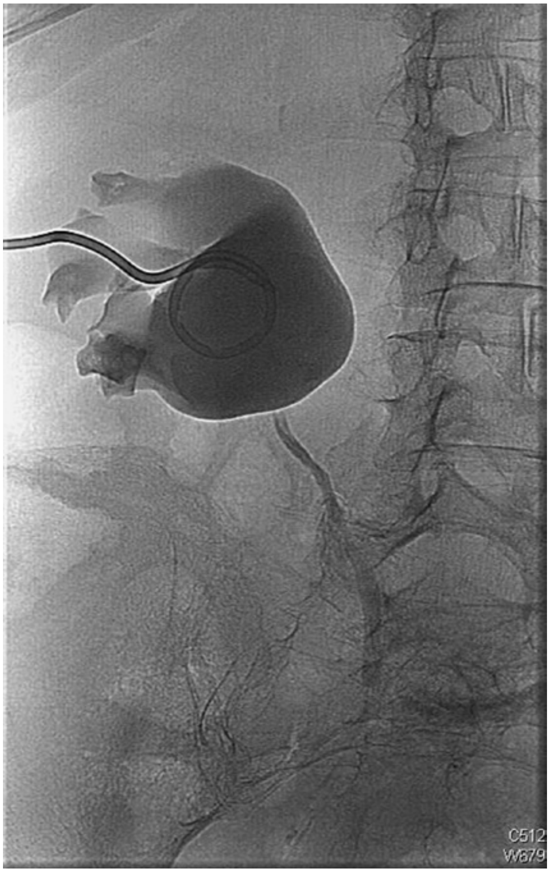

Figure 17.21 Antegrade pyelogram.

Exchange of guidewires and access catheters is necessary in complicated ureteric strictures. The risk of accidental loss of access due to inadvertent withdrawal of the nephrostomy can be salvaged if the guidewire is maintained in the system. The slippery guidewires can accidentally fall out and therefore must be secured during maneuvers. It is advisable to use a 10 F dual-lumen catheter (Figure 17.25) and insert a second wire to prevent this accident if the procedure is difficult.

Removal of the nephrostomy tube from the renal pelvis after a stent insertion needs attention. The coil of the nephrostomy tube and the upper turn of the JJ stent can get entangled. Inadvertent upward migration of the JJ stent can easily occur (Figure 17.26).

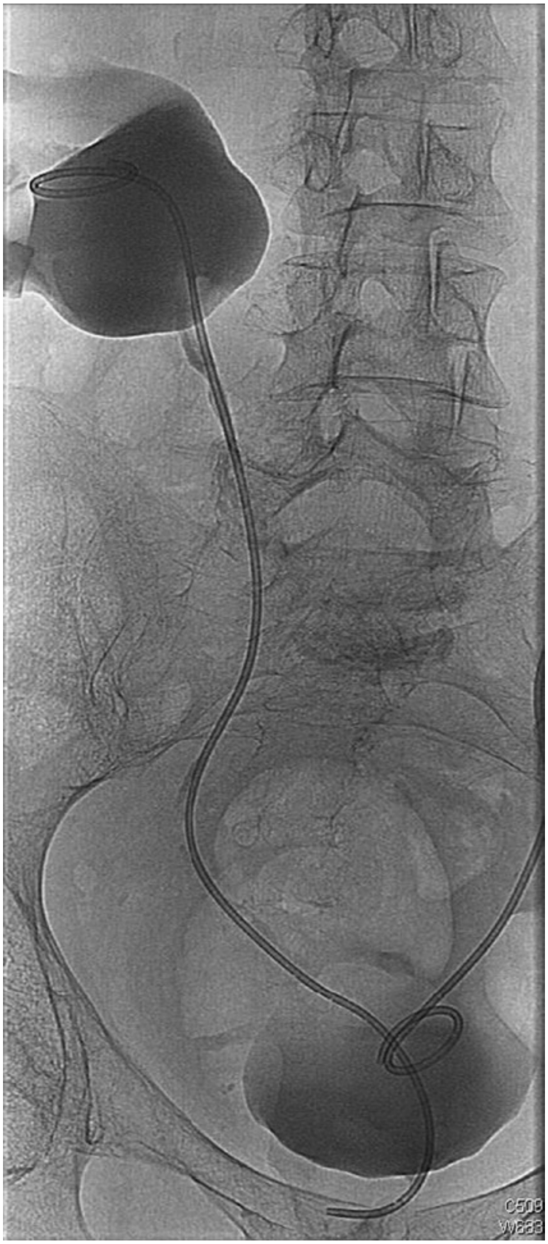

Figure 17.22 Incorrectly placed JJ stent – distal end in vagina.

Conclusion

Antegrade stenting of an obstructed ureter can be a technical challenge due to many factors. Success can be improved with careful planning, use of appropriate guidewires and access catheters. Alternative plans need to be considered in the event of obstacles encountered during the procedure. Complex clinical scenarios should be anticipated. Consideration should be given to a combined (rendezvous) procedure under general anesthetic to improve success, especially in bilateral ureteric obstruction.

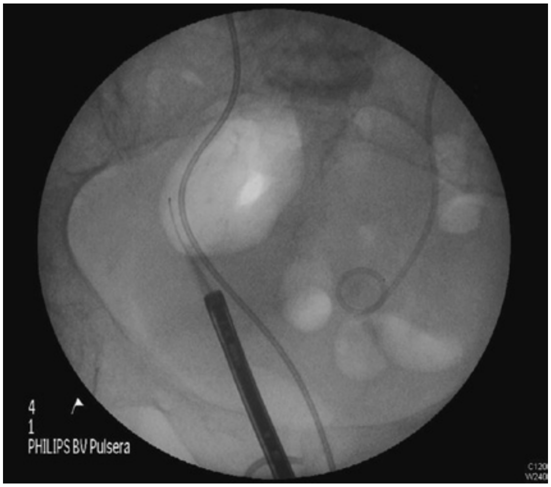

Figure 17.23 Incorrect antegrade placement of a JJ stent in the vagina. Retrograde catheter in the distal ureter.

Figure 17.24 Both stents in correct positions.

The debate about who should undertake this procedure continues. Many centers expect their radiology colleagues to undertake the antegrade stenting while urologists

Figure 17.25 Dual-lumen catheters.

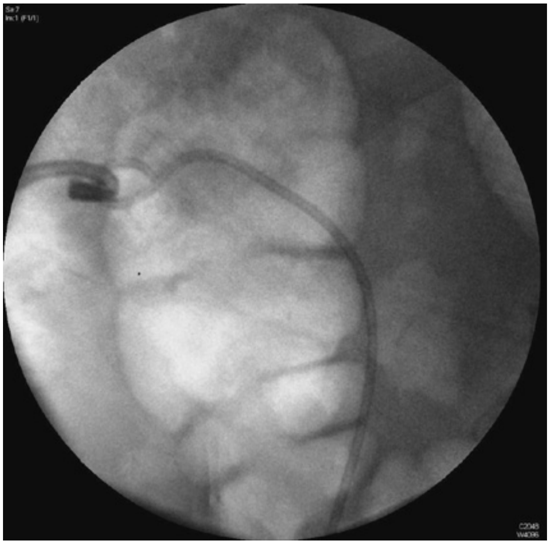

Figure 17.26 Accidental locking of the nephrostomy tube and the JJ stent during removal.

restrict themselves to the retrograde procedure. The rendezvous procedure needs two teams with skills to perform steps necessary from either end – perhaps a urologist and a radiologist.

It is helpful for urologists to become familiar with the technique of antegrade stenting as it is a natural extension of the established retrograde technique. Ability to undertake antegrade or rendezvous stenting gives the surgeon the flexibility of switching over to these techniques if conventional retrograde procedure proves difficult.

Acknowledgments

The author wishes to thank Boston Scientific and Cook for their permission to use the images of devices and Dr Elizabeth Bellamy for her artwork and help.

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SECTION 3

Percutaneous Management of Transitional Cell Cancer (Percutaneous Resection of Tumor)

18

CHAPTER 18

Epidemiology of Disease (Upper Tract Transitional Cell Cancer)

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Overall incidence and trend

Transitional cell carcinoma of the upper urinary tract (upper tract TCC), involving the renal pelvis or ureter, is relatively uncommon. In general terms, it represents around 5% of urothelial cancers and up to 10% of kidney cancers [1,2]. The most commonly used and accepted staging classification for upper tract TCC is the TNM (Box 18.1) [3]. Historically, it has been difficult to obtain data on specific trends in worldwide incidence, not only due to its infrequency but also because most cancer registries do not separate renal "pelvic" tumors from renal "cortical" tumors. However, the incidence tends to be increasing [2,4–6].

Cancer registries from the United States regularly publish their incidence and survival rates, using the Survival, Epidemiology, and End Results (SEER) program from the National Cancer Institute. This tends to represent 26% of the US population [7]. Using this database, Munoz and Ellison compared upper tract TCCa rates from 1973 to 1996 [2]. The overall incidence of upper tract TCC slightly increased over this period, as ureteral TCC increased from 0.69 to 0.73 per 100,000 person-years, but renal pelvic TCC stayed unchanged. Raman et al. analyzed the same SEER database to compare the incidence in 1973 to 2005 [6]. The overall incidence increased further from 1.88 in 1973, to 2.06 cases per 100,000 person-years. Again, ureteral TCC became more prevalent over this period (0.69 to 0.91/100,000), but renal pelvic TCC slightly reduced (1.19 to 1.15) [6].

Large series documenting trends in upper tract TCC incidence in Europe are limited. In Denmark, the overall incidence from 1943 to 1988 increased from 0.2 to 2.1 cases per 100,000 person-years [2]. More recently, using the Dutch national histopathology registry, PALGA, the trend in epidemiology of upper tract TCC between 1995 and 2005 was compared [5]. The overall incidence increased from 2.1 to 2.4 cases per 100,000 person-years.

The two other regions worthy of note are Taiwan and the Balkan countries. In Taiwan, the south west in particular, upper tract TCC incidence is high, representing 20–25% of all TCCs diagnosed [8]. Although not conclusive, this has been attributed to the unusually high arsenic content of the wells used for drinking water [8]. Balkan endemic nephropathy (BEN) is a familial chronic tubulointerstitial disease, which occurs in adults living in Balkan countries. It is associated with increased risk of upper tract TCC but interestingly, not bladder TCC, which tends to be of low grade, and can be multiple or bilateral at presentation [9]. Its pathophysiology is still uncertain, although exposure to Chinese herbs containing *Aristolochia fangchi* has been proposed [10]. This plant contains aristolochic acid which has nephrotoxic and carcinogenic effects [11].

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Box 18.1 TNM classification for upper tract transitional cell carcinoma

T Primary tumor
TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
  Ta Noninvasive papillary carcinoma
  Tis Carcinoma *in situ*
T1 Tumor invades subepithelial connective tissue
T2 Tumor invaded muscle
T3 (Renal pelvis) Tumor invades beyond muscularis into peripelvic fat or renal parenchyma (Ureter) Tumor invades beyond muscularis into periureteric fat
T4 Tumor invades adjacent organs or through the kidney into perinephric fat

N Regional lymph nodes
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in a single lymph node 2 cm or less in the greatest dimension
N2 Metastasis in a single lymph node more than 2 cm but not more than 5 cm in the greatest dimension or multiple lymph nodes, none more than 5 cm in greatest dimension
N3 Metastases in a lymph node more than 5 cm in greatest dimension

M Distant metastasis
M1 No distant metastasis
M2 Distant metastasis

Source: Leslie H Sobin, Mary K Gospodarowicz and Christian Wittkeind. TNM Classification Malignant Tumours. (2009) Published by John Wiley & Sons Ltd.

Tumor location and stage at presentation

Most cases of upper tract TCC involve the renal pelvis. Data from 1363 patients undergoing nephroureterectomy (NU) for upper tract TCC demonstrated that 64% were located in the renal pelvis [12]. However, recent data from the Dutch histopathology registry report it only as 51.3% [5].

In comparison to bladder TCC, upper tract TCC tends to be of higher stage and grade at presentation. Around 70% of patients have high-grade disease, and 45% are at least T2 at diagnosis [13]; 25% will have lymphovascular invasion, and a similar proportion will be found to have coexisting carcinoma *in situ* (CIS) and lymph node metastases [12,13]. In the US, however, there has been a more recent trend towards upper tract TCC presenting at an earlier stage, with *in situ* tumors increasing from 7.2% to 31% from 1973 to 2005 [6]. The proportion presenting with distant disease remained the same (around 9%). In contrast, European patients are increasingly likely to present with Grade 3 and/or muscle-invasive disease, compared with a decade ago [5].

Bilateral disease at presentation is very uncommon, with incidence rates of less than 2%. In a series of 936 patients diagnosed with upper tract TCC between 1971 and 1998, only 15 had synchronous disease, 11 with bilateral pelvic TCC, two bilateral ureteral TCC, and two combined pelvic and ureteral TCC [14]. Over this period, the incidence decreased, largely attributed to the reduced use of the analgesic agent phenacetin.

Age, sex, and race

The peak incidence of upper tract TCC is 70–80 years of age. In the US, the mean age at diagnosis has increased from 68 years between 1973 and 1984, to 73 years between 1997 and 2005 [6]. In a smaller cohort of 130 patients, the mean age was less, at 64 years [12]. Furthermore, using histopathological specimens as a means of national data detection of upper tract TCC, the mean age was 68 years (25–96) in The Netherlands [5]. Those with hereditary risk factors tend to present earlier (see later).

Men are more than twice as likely to develop upper tract TCC than women [12,15]. In the US, there were estimated to be 40,250 new cancers of the kidney and renal pelvis in men, and 24,500 cases in women in 2012 [7]. Women are more likely to present with more advanced stage and grade of disease [16], although men are now also increasingly likely to develop Grade 3 or muscle-invasive disease [5].

Regarding race, in the US whites are twice as likely to develop upper tract TCC as African Americans [15]. However, there is a 30% higher mortality rate in black non-Hispanic people [6].

Smoking and occupational exposure

Tobacco smoking is the most common risk factor for upper tract TCC [17]. Smoking exposure increases the relative risk from 2.5 to 7 [18], which is also related to frequency of smoking and duration of use. Ex-smokers remain at increased risk of upper tract TCC, having twice the risk of those who have never smoked [19]. Aromatic amines that are present in cigarette smoke are metabolized to the potent carcinogen N-hydroxyalanine [20].

Exposure to aromatic hydrocarbons present in certain dyes, rubber, petroleum, coal, and chemicals is also responsible for upper tract TCC development, still seen in some industrialized countries [21]. The relative risk ranges from 4 to 5.5, with a latency period of 15–20 years [21,22].

Analgesic abuse

The most common analgesia associated with upper tract TCC is phenacetin, although its use as an analgesic has been discontinued for over 20 years. This is due to its carcinogenic properties, thought to be from its association with the development of renal papillary necrosis, particularly in the presence of smoking or infection [23].

Other environmental risk factors

Frequent consumption of coffee (more than seven cups a day) has been reported to increase the relative risk of upper tract TCC by 1.8 [24]. However, no studies have since been able to confirm this finding. The regular use of laxatives has been associated with increased upper tract TCC risk, although the exact mechanism for this is unknown [18].

Hereditary cases of upper tract transitional cell carcinoma

Hereditary nonpolyposis colorectal cancer (HNPCC), or Lynch syndrome, is an autosomal dominant inheritance disorder, predisposing affected individuals to various malignancies other than colorectal cancer [25]. Specifically, they have a 6% lifetime risk of developing upper tract TCC, a risk 22 times greater than the general population [26]. Suspicion for this syndrome should be raised in those diagnosed with upper tract TCC under the age of 60 years, especially if there is a positive family history of HNPCC [25]. Patients can then be diagnosed through various DNA tests such as microsatellite instability analysis (MSI), immunohistochemistry, and DNA sequencing [25]. Subsequent close monitoring for colonic and extracolonic malignancies should be offered, as well as genetic counseling.

Metachronous upper tract transitional cell carcinoma

The development of contralateral upper tract TCC following nephroureterectomy is rare. Incidence rates vary from 1% to 6% [27–30]. Higher rates are seen in Balkan nephropathy and Taiwan blackfoot disease [31]. The only current predictor of contralateral metachronous upper tract TCC is previous history of bladder TCC [29,30]. Patients with concurrent bladder TCC have a 4 times greater risk of developing disease compared to those without disease [30]. Patients tend to have poor survival, largely due to progession of the bladder cancer [29].

The risk of metachronous upper tract TCC in patients diagnosed with bladder TCC ranges from 2.4% to 8.5%, and depends on a number of factors [32–34]. The incidence is highest in those with superficial bladder TCC with high risk of progression and recurrence [34]. In patients cystectomized for bladder TCC, again superficial disease carries a higher risk of metachronous upper tract TCC than invasive bladder cancer (11.1% versus 3.1%) [34]. Other risk factors include bladder TCCs that are high grade, multifocal, or recurrent, associated CIS, and long prior history of superficial disease [35–37].

Metachronous bladder transitional cell carcinoma

Bladder TCC recurrence after surgery for upper tract TCC is common, occurring in around 15–50% patients

[38–40]. The risk of recurrence is lifelong, but it tends to occur in the first few years. Currently, the only identified independent risk factor for this development is prior history of bladder TCC. Patients therefore require close bladder surveillance following surgery for upper tract TCC for at least 5 years [41].

Prognosis

The all-stage 5-year cancer-specific survival probability for upper tract TCC treated with radical nephroureterectomy has been reported as 73% [42]. Given the age and comorbidities of this patient population, overall survival is considerably lower, with 41–46% of deaths in the 5 years after diagnosis being noncancer related [43,44]. The surgery itself is not without complications, with analysis of the SEER database for procedures between 1988 and 2006 showing a 90-day mortality rate of 4.4% following nephroureterectomy [45].

The most important prognostic factors are the stage and grade of the tumor in the pathology specimen. Results from the 1363 patients treated in a study by the Upper Tract Urothelial Carcinoma Collaboration show 5-year cancer-specific survival probabilities of around 91% (pT1), 75% (pT2), 54% (pT3), and 12% (pT4), although many of the pT4 patients had a recurrence at that time, leading to a 7-year survival of only 6% [42]. The same data showed 5-year cancer-specific survival probabilities from low- and high-grade tumors as 89% and 63% respectively [42].

For low-grade lesions treated endoscopically, rather than with nephroureterectomy, 5-year cancer-specific survival has been reported as similar, at 89% for extirpative surgery and 87% for ureteroscopy [46], suggesting that this is a reasonable management strategy in low-risk disease. This study also showed a median overall survival of 29 months (range 6–52) in a small group of patients undergoing palliative ureteroscopic tumor ablations for symptom control [46].

Other pathological characteristics can be used as prognostic indicators, although their effects are small once stage and grade are accounted for. Lymphovascular invasion on the nephroureterectomy specimen has been shown to be a poor prognostic indicator in those with node-negative disease or those in whom a lymphadenectomy has not been performed [47]. In a study by Remzi et al., it was demonstrated that 72% of tumors had a papillary rather than sessile architecture on presentation, and that papillary tumors had an improved cancer-specific survival and lower recurrence rates [48]. Extensive tumor necrosis defined as >10% of tumor area on microscopy has been investigated and was associated with poorer outcomes in two large studies, although in only one was it an independent risk factor once other pathological characteristics were taken into account [49,50].

Preoperative hydronephrosis has been shown to be a poor prognostic risk factor for ureteric tumors [51,52]. Brien et al. showed it as a significant predictor of muscle-invasive disease (pT2 or greater) with hazard ratio (HR) 12.0 or nonorgan-confined disease (pT3 or N1 or greater) with HR 5.2 after adjusting for biopsy grade, cytology, gender, age, and tumor site [51]. Ng and colleagues showed an association with metastasis and cancer-specific death [52]. When adjusted for stage, there is no outcome difference between ureteric or pelvicalyceal system tumors in terms of survival [53,54] or recurrence, including bladder recurrence [55].

Increased age is associated with worse outcomes following surgery. Age >60 was associated with worse overall survival and age >80 with worse cancer-specific survival, even after controlling for standard pathological variables [56]. There was no effect on disease recurrence. Gender is no longer considered to be an independent risk factor for poor outcome. Analysis of SEER data suggested that women were more likely to present with pT3 tumors, but there was no survival difference once this was accounted for [16]. Another study found no difference in either survival or pathological characteristics between genders [56].

Of increasing importance is the need for accurate prognostic information to judge suitability for endoscopic management of upper tract TCC, and for appropriate counseling of patients. Grasso et al. showed that for those with low ureteroscopic biopsy grade treated in this manner and who had intensive endoscopic follow-up, local recurrence was essentially inevitable, but progression to more extensive disease requiring nephroureterectomy occurred in only 15% [46]. A model has been developed using ureteroscopic biopsy grade, urine cytology, and hydronephrosis on preoperative imaging to predict pT2 or greater disease on the nephroureterectomy specimen. Although not a study of the outcomes of endoscopic treatment, this type of disease would be unsuitable for this management. Absence of all three risks had a 100% negative predictive value for muscle-invasive disease. Abnormality of 1–3 variables had a positive predictive value for muscle-invasive disease of 24%, 46%, and 89% respectively [51]. On multivariate analysis, hydronephrosis was the strongest predictor (HR 12) followed by high-grade disease (HR 4.5). Positive cytology was not an independent predictor of muscle-invasive disease [51].

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19

CHAPTER 19

Evidence-Based Outcomes for Percutaneous Management of Upper Tract Urothelial Carcinoma

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Urothelial carcinoma (UC) of the upper tracts represents nearly 5–10% of all upper tract tumors [1]. The majority, approximately 75%, of patients with this disease present with tumor confined within the renal pelvis [2] (Figures 19.1, 19.2). Although radical nephroureterectomy historically has been the standard treatment, a number of surgical approaches exist for the treatment of upper urinary tract UC, including a percutaneous approach. The percutaneous approach to upper tract UC was first described by Tomera and colleagues in the early 1980s [3] but percutaneous entry into the renal collecting system was described as early as the 1950s with later modifications made in the 1960s [4]. Years later, percutaneous access to the collecting system for nephrolithotomies and endopyelotomies was described in the late 1970s and early 1980s, respectively [5,6]. The eventual application of this approach to upper tract UC by Tomera was likely inevitable given the search for more conservative treatment options for upper tract UC [7].

Traditionally, measures to save the ipsilateral renal unit in upper tract UC, including the percutaneous approach, are employed when patients are poor candidates for radical open surgery. Historically, a patient was considered a poor candidate for a variety of reasons, including possessing significant comorbidities, presenting with bilateral upper tract disease burden, being at an increased risk for disease (such as with Balkan nephropathy), having poor renal function or a solitary renal unit [8]. Additionally, the percutaneous approach is advisable in upper tract recurrences after cystectomies for bladder UC. Over time, the indications for definitive endoscopic approaches have broadened to include any patient with low-volume, low-grade and low-stage disease willing to adhere to the strict surveillance protocol after endoscopic resection. Generally patients are selected for definitive percutaneous resection after an initial retrograde resection reveals a small burden of less than 1.5–2 cm of low-grade disease [9].

With respect to UC grading, the most common classification system used previously was based on the World Health Organization (WHO) system of 1973 that classified UC into three grades. In 2004, the WHO altered its system based on scientific advances to distinguish between only low- and high-grade UC disease [10,11]. Therefore, both grading systems are included herein, dependent on the year of publication of the cited article.

Due to the overall rarity of the disease and the even smaller subset of patients who have undergone percutaneous resection of their upper tract UC, there is on the whole a limited amount of data available. There is a complete paucity of Level 1 data for the treatment of UC via this approach, and the majority of such data and inferences can be gained from several detailed retrospective reviews.

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

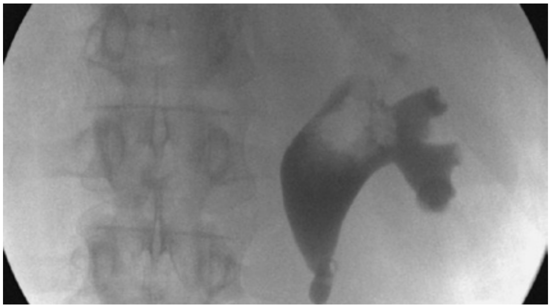

Figure 19.1 Retrograde pyelogram revealing large renal pelvic UC.

Figure 19.2 Computed tomograph revealing large renal pelvic UC.

Following Tomera's initial work, one of the earliest series regarding percutaneous resection was presented by Smith and colleagues [12]. A recurrence rate of 45% was found in a total of 14 patients treated over the course of 3 years. Three of these patients underwent immediate nephroureterectomy for inadequate initial resection, and an additional three patients out of five recurrences eventually underwent nephroureterectomy as well. Thereafter, a number of very small series were published, each with 1–4 patients who were treated with promising results [13]. Support then began to grow for the percutaneous resection of renal pelvic UC in low-grade (Grade 1 and 2) disease [12].

With the feasibility of this approach growing secondary to improved equipment and promising results, Jarrett and colleagues accrued a larger number of patients and published their findings in 1995 [14]. They treated 11 women and 23 men from 1984 to 1993, with a mean age of 66 years and with follow-up data ranging from 9 months to 9 years. Indications for percutaneous intervention included bilateral disease, solitary kidney, renal insufficiency, and elective selection by the patient. Of 34 patients with 36 treated renal units, six patients underwent immediate nephroureterectomy, and overall only two were lost to follow-up. Nine patients were found to have Grade 1, 12 patients had Grade 2, and 13 patients had Grade 3 disease. As expected, the authors found that recurrence rates increased with tumor grade. Only 18% of patients with Grade 1 disease had evidence of recurrence, while 33% with Grade 2 and 50% with Grade 3 disease had recurrence. Furthermore, no patients with Grade 1 or 2 disease succumbed to their UC, but four of the 10 patients with Grade 3 disease treated solely with the percutaneous approach died of their disease [14].

Shortly after Jarrett and colleagues published their results, Patel and colleagues made their series available [15]. A total of 26 patients underwent percutaneous tumor resection with follow-up data ranging from 12 to 108 months. Of these, 12 patients met "absolute criteria" for percutaneous resection with a solitary kidney or bilateral disease. The remaining 14 had "relative indications" including small-volume disease or disease considered unlikely to metastasize due to low grade and low stage. Overall, local recurrences occurred in six patients (23%), and bladder or ureteral metachronous or synchronous recurrences occurred in 11 patients (42%). Similar to Jarrett's early findings, increased local recurrence rates were seen in Grade 1 and Grade 2 lesions of 18% and 27% of patients respectively. A single Grade 3 lesion was identified, but this patient died in the perioperative period after thiotepa percutaneous installation. Therefore no inferences regarding recurrence in this patient could be made. Notably, increased tumor size and multifocality increased local recurrence rates from 12.5% to 40% and from 7% to 46%, respectively. Furthermore, their estimated 3-year local recurrence-free survival rate was 86%, with five patients (19%) eventually requiring nephroureterectomy. As in many early series, there was great concern regarding tumor seeding of the access tract, and consequently all but one patient had his or her percutaneous access tract radiated at the time of surgery or in follow-up, and none developed an access tract recurrence. This was one of the few series ever to take such measures.

Clark and colleagues then published their data with a mean follow-up period of 20.5 months (range 1.7–75.5) regarding 18 renal units in 12 men and five women at a mean age of 72.2 years (range 50–86) [16]. All treated renal units underwent 6-weekly courses of BCG treatment at least 2 weeks after percutaneous resection, and second- and third-look nephroscopies were performed in all. Of the 18 renal units, 83.3% had pTa disease, 11.1% had pT1 disease, 5.6% had pT2 disease, and no pT3 or carcinoma *in situ* (CIS) disease was found. Grade 1, Grade 2, and Grade 3 disease was found in 33.3%, 44.4%, and 22.2% of the patients, respectively. Ipsilateral recurrences occurred in 28% and 50% of patients with Grade 1–2 or 3 disease respectively. Two patients eventually required nephroureterectomy, and three died with evidence of metastatic UC. Of the three patients with metastatic disease, one had an unknown history of previous resections but two had a history of CIS or pT2–3 disease treated elsewhere in the urinary tract. The authors arrived at a similar conclusion to previously published series that an increased risk of recurrence occurs with increased grade of UC when treated via a percutaneous endoscopic approach.

With refinement of the percutaneous approach and a better understanding of urothelial upper tract disease, the relative indications for this treatment began to expand and more patients began to have upper tract resection as definitive treatment [17]. This was heavily supported by a study from Lee and colleagues in 1999, which compared survival rates between the percutaneous approach and the standard open radical nephroureterectomy [18]. After a mean follow-up of 39 months, they found no difference in survival rates for Grade 3 disease and no difference in disease-free intervals for Grades 1 and 2 disease. The authors strongly supported the application in Grades 1 and 2 disease, but recommended the standard open approach for Grade 3 disease. With the literature clearly supporting percutaneous resection in appropriately selected patients, willingness to broaden the indications for this approach grew. This was made apparent in later studies in which many patients who underwent percutaneous treatment had relative indications [19].

A clear broadening of the indications for percutaneous management of upper tract UC was illustrated by Palou and colleagues [20]. In their retrospective review, 47.1% of 34 patients at a mean age of 64.5 years were treated for elective reasons. Grade 1, 2 or 3 lesions were identified in 20.6%, 61.8%, and 14.7% of subjects respectively. More than half or 55.9% of these patients did receive adjuvant treatment with BCG or mitomycin C. Fifteen recurrent lesions were identified at a median of 24 months with nine patients requiring radical nephroureterectomy. Forty-two percent of these recurrences had Grade 1 or 2 initial lesions and 60% had Grade 3 disease. Fortunately, a review of the literature shortly before this study highlighted that with strict follow-up, recurrent disease does not have a direct impact on survival [17]. In this review Jabbour and Smith highlighted that Grade 1 disease was associated with a 0–27% recurrence rate and 100% survival, as opposed to Grade 2 disease which had a slightly higher recurrence rate (27–40%) but an 80–100% survival rate. Palou and colleagues found that 3.6% of patients with Grade 1 or 2 lesions succumbed to their upper tract UC compared to 20% of those with Grade 3 lesions [20]. The cancer-specific survival and overall survival rates were 93% and 71%, respectively. Like most series regarding upper tract UC treated via an endoscopic approach, there were too few patients in this study to reach statistical significance when searching for risk factors for recurrence. A few trends were identified, however, regarding increased risk for recurrence. Tumor location within the renal pelvis, multifocal disease, a history of bladder CIS and grade, to a lesser degree, were identified as risk enhancers.

Comfort with this approach and acknowledgment of the ability to percutaneously treat patients with upper tract UC continued to increase. This was evident in a Palou and colleagues series in which no second- or third-look nephroscopies were performed. Furthermore, they highlighted that the only real indication for multiple-look nephroscopies was an inadequate or partial initial resection. Without any access tract recurrences, the need for measures such as access tract irradiation, as described by Patel or Woodhouse and colleagues, was regarded as unnecessary [15,21].

More recently, Roupret and colleagues published their findings regarding 24 patients at a mean age of 70 years who underwent percutaneous UC resection [22]. Ten of these patients underwent resection for relative indications, and an additional five underwent resection after failed retrograde attempts. Additionally, only 14 of these patients underwent ureteroscopy with biopsy prior to definitive percutaneous resection. It appears that this was likely due to failed retrograde attempts or to the fact that ureteroscopy prior to percutaneous resection was not standard protocol early in the series. Of the 24 patients, 17 (70.8%) were found to have low-grade disease. A total of eight (33%) local recurrences occurred at a median time of 17 months, three (12.5%) of which were after an initial resection of low-grade disease. Fifty percent of these local recurrences occurred in the bladder. After a median follow-up of 62 months, they revealed a disease recurrence rate of 68% and a 5-year survival rate of 79.5%. A total of five (20.8%) patients eventually underwent radical nephroureterectomy, all of whom had high-grade disease. Consistent with previous reports, only clinical stage and tumor grade on univariate analysis correlated with recurrence or disease-free survival. Unlike previous series, only three of the 24 patients received adjuvant topical treatment with mitomycin C. During their follow-up schedule which included computed tomography and direct-look cystoscopy and ureteroscopy every 6 months for 3 years, only two patients, one of whom had pT2 and one of whom had pT3 disease, were found to have distant metastases of their UC at a median follow-up of 26 months. Both of these patients died within 3 years of their initial percutaneous resection. This work continued to support the notion that clinical stage and grade are the most important factors regarding survival, but other risk factors have been suggested.

Some differences do exist between upper and lower tract UC, one of which is the presence of invasion. More than 50% of upper tract UC is invasive at the time of diagnosis, compared to only 10–15% of bladder UC [2,23,24]. When focusing on the upper tracts only, even more distinctions have been made regarding disease location and prognosis. It has been postulated that the region in which upper tract UC occurs affects patient prognosis, and that a higher location of UC correlates with a poorer outcome. If true, this portends a poor prognosis for patients with UC, as UC within the renal pelvis or calyceal system occurs nearly twice as often as UC within the ureter [25].

A variety of etiologies has been suggested for this potential difference in prognosis. A commonly held theory is based on the anatomical differences between the thin muscular layer of the upper ureter and pelvis and the thick, muscular distal ureter and bladder. This may account for the overall poorer prognosis of invasive upper tract UC compared to invasive bladder UC [26–29]. This could also account for the higher progression rates for renal pelvic UC versus more distally located ureteral UC after endoscopic resection [30–33]. Van der Poel and colleagues arrived at this conclusion in 2005 after retrospectively reviewing a series of 149 patients treated for upper tract UC, including 12 treated endoscopically [34]. Although they concluded that location did correlate with patient prognosis, with more proximal UC having more invasive disease, UC located within the renal pelvis had to be excluded from the analysis to arrive at this conclusion with statistical significance. Raman and colleagues arrived at a similar conclusion in 2010 in a group of patients with upper tract UC treated with radical nephroureterectomy [25].

However, this belief that location affects prognosis is not widely accepted. One year prior to van der Poel's work, Park and colleagues presented their data that described renal pelvic tumors as in fact having a better prognosis than ureteral UC, with the latter showing greater rates of distant metastasis and local recurrence [31]. A retrospective review of the SEER database in 2000 also suggested that when adjusted for disease stage at diagnosis, location did not affect survival. This has been supported in other studies as well [35].

Notably, in 2011 Milojevic presented a thoughtful retrospective review of 133 patients with upper tract UC and did not find any correlation between location and overall patient prognosis. Patients in his review with renal pelvic UC did present with higher grade disease that was more advanced, similar to previous studies' findings [35]. When adjusted for tumor grade and pathological stage, however, location itself did not correlate with recurrence or overall survival. Therefore, it appears that renal pelvic tumors do present with higher grades and stages possibly due to the lack of obstructive disease, but that its location in and of itself does not correlate with a poorer prognosis. This supports the application of percutaneous resection of upper tract UC in patients with low-grade and pathological stage disease.

Location is not the only prognostic factor regarding upper tract UC that has been disputed over the years. Female gender was previously thought to portend a poorer prognosis in upper tract UC treated with radical nephroureterectomy [36–39]. Although women with upper tract UC are more likely to present at more advanced stages than men, large studies suggest gender has no role in prognostication when adjusted for stage [37]. However, advanced age, tumor grade and stage, multifocality, and lymphovascular invasion are still considered independent risk factors for poorer survival [40–43].

Adjuvant topical therapies with BCG or chemotherapeutic agents such as mitomycin C, interferon, adriamycin or thiotepa have been used in the treatment of upper tract

UC in a fashion similar to bladder UC [44]. They have been applied via double pigtail stents or ureteral catheters, but nephrostomy tubes are more often employed in this setting as conduits for application. Unlike in UC of the lower tract, there is no agreed-upon regimen for adjuvant chemotherapy or immunotherapy for noninvasive upper tract UC treated via endoscopic or percutaneous approaches [45,46]. Although no consensus exists, some series have suggested the efficacy of adjuvant treatments in both low-grade upper tract and bladder UC [46,47].

Over the years the usage of adjuvant treatment has varied. Most series employed topical BCG or mitomycin C as adjuvant treatment, and rarely has thiotepa been applied [15,48]. This is likely due to the lack of clear guidelines regarding the timing of and indications for adjuvant treatment. This is secondary to the rarity of the disease process and the even fewer number of patients undergoing endoscopic treatment. The majority of studies regarding adjuvant treatment are small retrospective studies with short follow-up periods.

Small series have used topical mitomycin C with varied results ranging from a reduction in residual tumor burden to an absence of statistically significant change in recurrence rate [45,49]. Goel and colleagues experienced leakage around the nephrostomy sites leading to symptomatic complications such as local skin irritation in the majority of the 10 patients treated in this manner. They note that although outcomes are variable and no formal guidelines have been crafted regarding adjuvant treatment, it is best to use topical treatment until long-term studies disprove any benefit [19]. Most series have utilized BCG as the topical adjunctive agent of choice.

Although smaller studies described a reduction in recurrence rates in Grade 1 disease with adjuvant BCG treatment [50], one of the largest retrospective studies with long-term follow-up in this patient population did not show any evidence of improved long-term survival. Similar findings have been described in other much smaller series [14,20,47,51,52]. In the largest study thus far, a total of 89 renal units were treated with percutaneous resection, with 56.2% receiving adjuvant BCG treatment at a mean age of 70.9 years and with mean follow-up of 61.1 months. No statistical differences regarding stage or grade of disease existed between the BCG and non-BCG treated groups. When stratified by grade and stage, disease recurrence, time to recurrence, long-term renal preservation, and progression of disease were not significantly different between treatment groups. Therefore, no benefit was found with adjunctive immunotherapy [53]. This contradicts previous reports in which some benefit was seen in patients with Grade 2 disease [53,54]. This is likely due to the smaller sample size and shorter follow-up in the earlier series. Another small series supports these earlier findings with a reduction in recurrence from 50% to 23% with topical BCG application in Grade 2 and 3 tumors. These smaller series offer conflicting data, and no consensus has been reached regarding adjuvant topical treatments. However, the majority of patients are still managed in a similar manner to those with bladder UC. It is clear that large randomized multicenter trials are still needed to clearly define the utility of adjuvant topical treatment for upper tract UC.

Although the utility of BCG application is debatable, most agree regarding its potential complications, the most common of which is fever [55]. In appropriately selected patients, severe adverse outcomes such as sepsis and death are rare [14]. As with topical adjuvant treatment, life-threatening complications are rarely experienced during the percutaneous procedure itself.

Overall potential complications associated with percutaneous resection of upper tract UC are similar to any surgical approach involving minimal invasive access to the kidney, such as with percutaneous nephrolithotomy. Uncommon complications include perforation, hemothorax or hydrothorax, persistent bleeding requiring embolization, renal failure, ureteropelvic junction (UPJ) stricture, and malignant seeding of the access tract [14–16]. Although often cited as a significant risk, few studies have described access tract recurrences, and those that have represent less than 1% of the patients treated. Furthermore, these few patients were frequently treated early in various series and were often managed with an indwelling nephrostomy tube to alleviate an obstructed system [53,56–58]. Measures such as continuous-flow nephroscopes, low-pressure irrigation, and not leaving an indwelling nephrostomy tube in the presence of UC were deemed key to preventing tract seeding. Goel and colleagues completely excised the old nephrostomy tract in all six patients (25%) who eventually required nephroureterectomy, and histopathological analysis did not reveal any tumor seeding of the tract. Furthermore, no access tract recurrences occurred in the remaining patients after 64 months of follow-up [19].

Table 19.1 Percutaneous treatment of upper tract urothelial carcinoma.

Series	Patients	Recurrence %	DSS %	Follow-up (months)
Jarrett et al. [14]	34	33	87	9–111
Clark et al. [16]	17	33	83	1.7–75
Lee et al. [18]	49	12	–	6–150
Patel et al. [15]	26	23	91	1–100
Jabbour & Smith [17]	54	38	84	11–168
Liatsikos et al. [50]	69	36	84	11–168
Goel et al. [19]	22	55	69.2	24–132
Palou et al. [20]	34	44.2	94.1	3–131
Roupret et al. [22]	24	33	79.5	18–188

DSS, Disease-specific survival.

Unlike access tract recurrences, bleeding necessitating transfusions is commonly described throughout all published series. Bleeding during or following percutaneous resection of upper tract UC, significant enough to require blood transfusions, reportedly occurs in 11–37% of treated patients [16,17,50]. Jarrett and colleagues experienced a transfusion rate as high as 50% [14]. Importantly, they found a correlation with grade and stage. Since higher grade and stage lesions required deeper resections, the likelihood of significant bleeding increased [14]. Additionally, fulguration of the resection base has been shown to significantly reduce the need for blood transfusions, with a reduction in one study from 37% to 12% after the application of laser fulguration [17].

Appropriate patient selection is key, as 5-year survival rates decline significantly from 60–90% in T1 or CIS disease to roughly 5% in T3 or worse disease [59]. Most would now agree that grade, stage, and multifocality directly correlate with patient outcome, and the application of percutaneous resection in low-grade, low-stage and low-volume UC is therefore appropriate in the majority of patients willing to adhere to a strict follow-up schedule. Patient adherence to strict postresection surveillance is key. The largest retrospective series to date have shown recurrence rates ranging from 23% to 41% and the eventual need for radical nephrourertectomy in 11–42% of patients [14–16,20,22] (Table 19.1). Furthermore, those patients found to have high-grade disease do more poorly than those with low-grade disease, and patients with a high stage (pT3 or greater) do poorly regardless of the surgical approach. Although those with pT3 or greater UC do poorly whatever the approach, radical nephroureterectomy is still advocated for these patients to provide the highest likelihood of complete eradication of disease. The percutaneous approach to upper tract UC has increased in popularity since its early application by Tomera and will likely continue to do so with improved instrumentation, technique, and patient outcomes.

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CHAPTER 20

Patient Selection and Informed Consent

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Introduction

The best oncological treatment for most cases of upper urinary tract transitional cell carcinoma (TCC) remains nephroureterectomy, whether performed open or laparoscopically. However, with advances in upper urinary tract endoscopic techniques and instrumentation, we are extending the principles of endoscopic management of transitional cell carcinoma from the bladder to the upper urinary tract. This includes ureteroscopic and percutaneous techniques. The choice of the most appropriate therapy for patients with upper tract transitional cell carcinoma can be challenging. In this chapter, we will examine the factors affecting the selection of appropriate patients for percutaneous management of upper urinary tract transitional cell carcinoma, and the risks involved to perform an informed consent of our patients.

Patient selection

Nephroureterectomy versus endoscopic treatment

Many patients treated endoscopically for upper urinary tract transitional cell carcinoma are those in whom nephroureterectomy would be difficult or dangerous. A common indication for a nephron-sparing endoscopic approach is patients with a solitary kidney (functional or anatomical) or renal insufficiency. This includes situations such as prior nephrectomy, congenital solitary kidney, or significant chronic kidney disease. Patients with both kidneys present but a creatinine clearance of less than 30 mL/min would likely need renal replacement therapy such as dialysis or transplantation if nephroureterectomy is performed. This condition is becoming more common given the increasing incidence of obesity and subsequent diabetes [1]. Bilateral upper tract transitional cell carcinoma is a similar situation where preservation of functional renal tissue is a priority. Endoscopic treatment can be a very good option for many of these patients, when preservation of renal function is a priority. This of course must be balanced against oncological outcome.

Another common reason for choosing an endoscopic approach to upper tract transitional cell carcinoma is in those patients with significant medical comorbidities in whom a nephroureterectomy would carry significant risk of morbidity and/or mortality. Patients with significant cardiac, pulmonary, vascular or other conditions that would increase their perioperative risk of a nephroureterectomy might be better served by an endoscopic approach. However, with advances in laparoscopic techniques for nephroureterectomy, these perioperative risks are lessening and this situation may be less common than when nephroureterectomy was performed only via an open approach.

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Rather than rely upon our general assessment of the overall health of the patient, the use of a grading system can help guide our determination of the patient's suitability for surgery. In 1961, Dripps and colleagues published their research on the role of anesthesia in surgical mortality that became the basis for the Dripps–American Surgical Association classification system [2]. This became a widely used tool to classify surgical risk and was the forefather of our modern-day surgical risk calculators. In addition to the assessment of cardiac risk, modern risk stratification tools include other important factors such as odds of stroke, infection, and death [3–5]. Although there are no specific risk calculators designed for nephroureterectomy or percutaneous treatment of TCC, use of these nonspecific tools can help inform our preoperative risk assessment.

Finally, patients who present with metastatic disease, and little chance of cure, may benefit from an endoscopic treatment to decrease local problems such as hemorrhage.

With successful application of an endoscopic approach to patients with upper tract transitional cell carcinoma for the indications given above, greater oncological confidence has been gained. The endoscopic approach is now used in otherwise healthy patients (who would be candidates for nephroureterectomy) who have low-grade, low-volume disease. Patients are often initially diagnosed with ureteroscopic inspection and biopsy and if the appearance is favorable, the tumor is ablated. If the pathological examination shows that the patient is an acceptable candidate for continued minimally invasive endoscopic management, a nephron-sparing approach can be presented to the patient as a management option. Endoscopic management of patients with low-grade disease has proven to be a reasonable option, without compromise of patient survival [6–10]. If the tumor is multifocal, unresectable, high grade or invasive, the patient should proceed to nephroureterectomy if they are a good surgical candidate.

Regardless of the indication, patients who undergo endoscopic treatment, whether percutaneous or ureteroscopic, must be willing to have vigilant follow-up. Recurrence of tumors of the upper urinary tract treated endoscopically can be expected in at least 40% of patients with renal pelvic tumors and 25% of those with ureteral tumors [6,11,12]. Therefore, careful and frequent endoscopic inspection and treatment are required to prevent progression following nephron-sparing endoscopic management.

Ureteroscopy versus percutaneous treatment

Tumors of the upper urinary tract can be approached endoscopically in a retrograde or antegrade fashion. In general, a ureteroscopic approach is used for low-volume tumors. The ureteroscopic approach is preferred as it is less morbid with fewer risks. Most tumors in the upper urinary tract can be reached with modern flexible ureteroscopes. Access to the lower pole is less of a problem than with previous generation flexible ureteroscopes [13]. Ureteroscopic biopsy is possible using the 3 F diameter cup biopsy forceps, and can give adequate tissue for tumor grading [14]. Tumor staging is more difficult, but tumor grade and stage have been shown to correlate strongly enough that grade may be used as a surrogate for tumor stage for treatment decisions. The holmium laser allows safe treatment of the tumors in the "what you see is what you get" method. Tumors can be safely treated down to the appropriate depth with precision.

The percutaneous approach to the treatment of upper tract TCC was first described by Tomera et al. in 1982 [15] and can be used for tumors located in the proximal ureter and renal pelvis. A percutaneous approach may be necessary for larger tumors of the upper ureter or kidney and for those that cannot be adequately accessed in a retrograde approach. Although now less common with advances in flexible ureteroscope design, the lower pole calyces in some patients may not be adequately accessible ureteroscopically, and a percutaneous approach might be necessary. Another anatomical situation creating difficult access is prior urinary diversion (common in this population following cystectomy for lower urinary tract transitional cell carcinoma). This includes ileal conduit, neobladder, and continent cutaneous diversion. Although ureteroscopy can be performed in these situations, occasionally retrograde access to the ureter may not be possible, necessitating an antegrade approach.

There are other advantages with the percutaneous approach. Percutaneous access to the intrarenal collecting system permits the use of rigid instruments such as a resectoscope. More efficient removal of larger volumes of tumor is possible using the resectoscope compared to ablation with the holmium laser through the ureteroscope. Deeper biopsies can also be obtained, with a greater ability to accurately stage the tumors. Enhanced visibility is also possible with greater irrigation capabilities of the larger scope and sheath used percutaneously. Additionally, the nephrostomy tract can be maintained for immediate postoperative nephroscopy and administration of topical adjuvant therapy if needed. Combined antegrade and retrograde approaches can be considered in patients with multiple tumors.

Due to the low incidence of upper tract transitional cell carcinoma, and limited indications for percutaneous treatment, there are relatively few reports examining results with percutaneous management of upper tract transitional cell carcinoma. One study comparing 50 patients who underwent percutaneous management with 60 patients who underwent nephroureterectomy for transitional cell carcinoma during a 13-year period found no significant difference in overall survival [16]. As expected, patients with low-grade disease did well regardless of modality and patients with high-grade disease did poorly after either percutaneous management or radical nephroureterectomy. Most urologists would agree that percutaneous management is acceptable in patients with low-grade (Grade 1) disease regardless of the status of the contralateral kidney, provided the patient is committed to lifelong endoscopic follow-up. Patients with Grade 3 disease will likely fair poorly regardless of treatment chosen, but good surgical candidates should undergo nephroureterectomy to maximize cancer therapy [17].

The use of percutaneous management for patients with Grade 2 disease and a normal contralateral kidney still remains an area of controversy. A retrospective evaluation of 24 patients found a disease-specific survival of 95% overall, including 100% for stage Ta and 80% for stage T1 lesions [18]. This study shows that acceptable results can be obtained with conservative treatment of noninvasive Grade 2 disease. In another study of 84 patients, Okada et al. found that tumor grade strongly predicted outcomes after percutaneous treatment with an overall recurrence rate of 27% [19].

In summary, the most common indications for percutaneous treatment will be patients with large-volume, low-grade disease or tumor not accessible ureteroscopically. With more invasive lesions, the potential for disease progression and worse outcomes is significant enough that nephroureterectomy should still be considered the standard of care. Box 20.1 summarizes the most common situations in which consideration of an endoscopic and percutaneous approach to treating these patients would be reasonable.

Box 20.1 Factors to consider for endoscopic and percutaneous treatment of upper tract transitional cell carcinoma

Consider endoscopic treatment

Risk of renal failure:
  Solitary kidney
  Chronic kidney disease
  Bilateral tumors
Palliative treatment in metastatic disease
Poor candidate for open or laparoscopic surgery
Low-grade tumor

Consider percutaneous treatment

High-volume, low-grade tumor
Inability to access tumor ureteroscopically:
  Lower pole tumor
  Urinary diversion

Informed consent

Risks related to endoscopic management

The greatest risk related to endoscopic management rather than nephroureterectomy is tumor recurrence. Higher grade tumors will have enough of a risk of tumor progression that except in unusual circumstances, the patients will be better served with a nephroureterectomy. In patients treated endoscopically, the patient and urologist should expect recurrence of tumor and plan on its detection and treatment.

There were early concerns regarding the risk of ureteroscopic spreading of tumor due to the increased intrarenal pressures produced during irrigation and possible lymphatic migration of tumor. These concerns were addressed in two separate studies. In 1994, Kulp and Bagley reported that they found no local recurrence or evidence of local spread of tumor in 13 patients who underwent ureteroscopy (1–4 times) prior to nephroureterectomy [20]. In 1999, Hendin et al. reported their experience with ureteroscopic evaluation prior to nephroureterectomy [21]. They compared 48 patients who underwent ureteroscopic evaluation prior to nephroureterectomy to 48 patients who had not had prior ureteroscopy. There was no significant difference in tumor stage, grade or patient characteristics. They found no difference between the two groups in recurrence rates, time to recurrence or mortality after nephroureterectomy.

Ureteroscopy seems to be safe for the evaluation and treatment of patients prior to nephroureterectomy.

Risks related to percutaneous approach

Although percutaneous techniques can be utilized, and allow resection of large amounts of tumor, the ureteroscopic approach is preferred because it avoids the risk of seeding the percutaneous tract and retroperitoneum with tumor. The lack of a "closed" urothelial system and the use of irrigation fluid permits the spread of transitional cell carcinoma cells into the surrounding, nonurinary tract tissues. Extravasation of irrigation fluid during percutaneous nephrolithotomy is relatively frequent, but usually of little consequence. The easy implantation of transitional cell carcinoma cells is well known and makes this risk particularly concerning. This risk of tract seeding is small but has been reported [22–28]. Additionally, seeding of laparoscopic trocar sites at the time of laparoscopic cystectomy or lymph node dissection for transitional cell carcinoma has also been reported [29–31]. It is difficult to estimate the risk of this after percutaneous resection of intrarenal transitional cell carcinoma, as it is very small, but it should be discussed with the patient as a possible complication. Efforts to minimize this risk include the use of low-pressure irrigation, visually ensuring the proper placement of the sheath tip inside the collecting system throughout the case, and avoidance of pleural or collecting system injury. If injury of the pleura, collecting system or surrounding organs is noted, and extravasation suspected, the procedure should be terminated immediately.

Establishment of the percutaneous tract also has inherent noncancer-related risks, and the procedure usually requires inpatient admission. The risks of hemorrhage requiring transfusion, pneumothorax, hydrothorax, injury to the collecting system, extravasation of urine or irrigation fluid, and injury to bowel or other nearby organs have all been reported [32,33]. The risk of hemorrhage appears to be higher when resecting tumor percutaneously, and may be related to the volume and stage of the tumor. Although this can be managed conservatively, at times angioembolization may be required. The risk of injury to the collecting system, with possible scarring and obstruction at the ureteropelvic junction (UPJ) or infundibula, is higher than during percutaneous nephrolithotomy due to the use of electrocautery and resection of tumor. Tumor that is circumferential in an infundibula or at the UPJ should be resected in a staged manner. This will help avoid circumferential tissue damage from ablation or resection that might lead to stenosis.

Pleural injury with resulting pneumothorax, hemothorax or hydrothorax is relatively common in percutaneous

Table 20.1 Recurrence and complications after percutaneous treatment of upper urinary tract transitional cell carcinoma.

Study (1st author)	Year	n	Local recurrence (%)	Complications (%)
Tasca [44]	1992	10	5 (50)	1 (10) death 4 months later
Plancke [40]	1995	10	1 (10)	Not reported
Fuglsig [35]	1995	26	8 (31)	3(12) total: 1 tract seeding, 2 hemorrhage
Patel [39]	1996	26	9 (35)	7 (27) total: 3 hemorrhage, 1 fistula, 1 death (thiotepa related)
Martinez-Pineiro [37]	1996	18	2 (11)	7 (33) total: 1 colon perforation, 3 renal pelvic perforations, 1 TUR syndrome; 1 hydrothorax
Clark [34]	1999	17	6 (33)	2 (12) total: 1 hemorrhage, 1 UTI
Goel [36]	2003	20	12 (65)	4 (20) total: 2 nephrectomies (1 for hemorrhage, 1 for stricture), 2 requiring dialysis
Suh [43]	2003	14	14 (100)	6/31 (19): including transfusion, pneumothorax, fungal UTI, fluid overload
Palou [38]	2004	34	15 (44)	2 (6) total: 1 hemorrhage requiring nephrectomy, 1 stricture
Roupret [42]	2007	24	3 (13)	7 (30) total: 3 transfusions, 3 requiring dialysis, 1 colon perforation
Rastinehad [41]	2009	89	30 (33)	Not reported

TUR, transurethral resection; UTI, urinary tract infection.

nephrolithotomy [32,33]. The risk of pleural injury increases with higher, supracostal access. We prefer upper pole access for percutaneous nephrolithotomy as it results in more direct access to the majority of the collecting system. However, to avoid the risk of tumor spillage in the chest, pleural injury should be avoided. For this reason, it is best to perform lower pole access when an upper pole approach would require a supracostal access site. Results and complications with percutaneous treatment are presented in Table 20.1.

Conclusion

The choice between open or laparoscopic nephroureterectomy, ureteroscopic or percutaneous management of upper tract transitional cell carcinoma is a complicated decision process. Factors including the patient's perioperative risks, tumor grade and stage, the natural history of the disease, the risks of tumor recurrence and progression, and additional risks associated with percutaneous surgery need to be weighed carefully. Although there are no randomized trials to guide us, there are published data, presented here, to help this decision process, and help us counsel our patients appropriately.

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CHAPTER 21

Percutaneous Treatment of Upper Tract Urothelial Carcinoma

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Introduction

Upper tract urothelial carcinoma (UTUC) is a tumor that affects the lining of the urinary tract from the calyces to the distal ureter, and comprises 5% of all urothelial tumors and 5% of all renal tumors [1]. Typically it affects one kidney – bilateral disease is rare and occurs in only 2–4% of cases [2]. The biological make-up and tumor appearance of UTUC are highly similar to bladder urothelial carcinoma. Both present most commonly with gross hematuria but despite some similarities, the two differ vastly in several areas. Firstly, UTUC is extremely rare. In the United States, UTUC affects only 3000 cases each year, limiting the ability to conduct well-powered studies or acquire good-quality evidence for various possible treatment approaches. Secondly, UTUC is often located in an uncommon region, creating difficulty for traditional treatment methods. UTUC of the renal pelvis or calyces can only be reached using a small-caliber ureteroscope, which could not manage the disease properly if the tumor is bulky or found in a difficult location. Due to these limitations, approaching UTUC with percutaneous treatment is sometimes the most appropriate option.

Indications

The definitive treatment for UTUC is nephroureterectomy with bladder cuff excision. However, the complications are extensive, including morbidity and mortality associated with loss of renal unit, renal insufficiency, and long-term hemodialysis. With the advancement of endourological techniques, endoscopic management via ureteroscopic or percutaneous methods has been increasingly advocated. The indications for nephron-sparing treatment include patients with solitary kidney who would otherwise be on dialysis after extirpative treatment, those with bilateral disease, and those with medical comorbidities that preclude a major operation. With healthy patients with two normal kidneys, a nephron-saving procedure is also valid for those with low-volume and low-grade (Grade 1) disease.

Contraindications to endoscopic management include high-grade disease and tumors that are unresectable endoscopically. However, there have been cases in which patients suffering from high-grade or -stage disease have declined a nephroureterectomy. In these situations, percutaneous resection can be used for symptomatic relief of gross hematuria rather than for cure of the cancer [3].

The conservative treatment approach to UTUC includes percutaneous and retrograde ureteroscopic methods. Comparing the two, the ureteroscopic approach is generally used for ureteral tumors and low-grade, low-volume (<1.5 cm) urothelial tumors in the kidney. Though the advantage is decreased morbidity, this method is limited by the procedure's use of

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small instruments and reduced ability to treat large volumes of tumor [4]. Percutaneous treatment is preferred in cases of bulky disease, and for kidneys or calyces that cannot be accessed ureteroscopically. Cases with difficult retrograde ureteroscopic access include patients whose tumor in a lower pole calyx is hard to reach with a flexible scope, or patients who have had cystectomy and urinary diversion. However, use of the percutaneous approach allows larger instruments that can remove a higher burden of tumor in the renal collecting system in a shorter amount of time. Furthermore, it allows staging of the cancer, something the ureteroscopic approach is unable to do. The established nephrostomy tube tract can be maintained for postoperative administration of topical adjuvant therapy. Despite the advantages, with any kind of endoscopic approach, the patient must be aware that anything short of nephroureterectomy will have an associated higher recurrence rate. The patient is committed to a lifetime of follow-up with endoscopy and imaging.

Techniques

Prior to obtaining access

After induction of general anesthesia, flexible cystoscopy is done in the supine position and an open-ended catheter is placed to the renal pelvis. A standard Foley catheter is then placed, and the ureteral catheter is secured to the Foley with a silk tie. The patient is then placed in the prone position. Care is taken to pad feet, knees, chest, and face. Air or contrast is injected through the ureteral catheter to define the anatomy of the collecting system and create hydronephrosis to facilitate puncture [5].

Percutaneous access

The approach to access prior to nephrostomy tube placement depends on the location of the tumor. It is important to note that a well-positioned tract is essential to the success of the procedure, and this should be done by the operative urologist, or a radiologist in consultation with the urologist. The ideal tract is one that allows access the tumor without being directly on it. Tumors in the renal pelvis are best accessed by an upper or midpole stick, while tumors in the calyces are best approached with direct puncture distal to the tumor [6]. More than one stick may be required to completely access the entire tumor burden.

To begin the procedure, a long cannulated biopsy needle is used for access under biplanar fluoroscopic guidance. A hydrophilic-coated guidewire is passed into the renal pelvis, and either serial (Amplatz) or balloon dilation is performed under radiographic guidance. A large-diameter sheath (30 F) is used to maintain a low-pressure system [7].

Normal saline is our irrigation of choice. However, some authors use glycine 1.5% while others prefer sterile water to lyze tumor cells that may reimplant elsewhere [8]. However, a potential risk is the hypernatremia that may result.

Treatment

The entire collecting system is studied thoroughly. All tumors are identified with rigid and flexible nephroscopy. Many techniques have been described. First of all, a cutting loop from a standard resectoscope can be used to remove the tumor. Alternatively, a cup biopsy forceps can be used through the nephroscope to debulk the tumor. If a tumor is difficult to reach with a rigid scope, a flexible endoscope can be used, and the tumor can be removed with a platinum flatwire or Segura basket. Once the basket is around the tumor, it should not be closed completely to allow the specimen to rest between the tines and prevent dropping of the resected tissue. In any case, all samples sent for pathology, and if possible, the base of the tumor should be sent separately for staging purposes. The remaining tumor and base are fulgurated with electrocautery or neodymium:YAG laser (20–30 watts). The laser should be used with caution, especially at the ureteropelvic junction and the ureter because of its deeper penetration and association with high rates of stricture. Electrocautery is done using a Bugbee electrode or resectoscope loop. One paper recommended using a roller ball electrode which may assist in the smaller available space and different folds of the collecting system [9]. The roller ball may also prevent any potential loop resection through the thin pelvic urothelium into the renal vasculature.

Jarrett et al. [7] and Clark et al. [3] describe a protocol in which the patient returns for a second look 3–7 days after the initial procedure, and in some cases a “third look” (Figure 21.1). A staged procedure should especially be considered in cases of high-volume

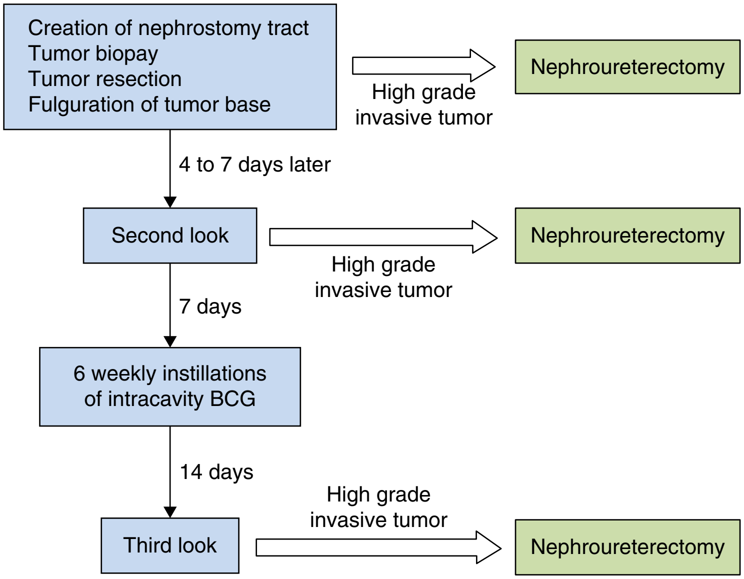

Figure 21.1 An algorithm for treatment of upper tract urothelial carcinoma. (Source: Jarrett TW, Sweetser PM, Weiss GH, Smith AD. 1995 [7]).

disease. However, some authors believe that a second or third look is not necessary if one is confident that there is a complete resection in low-grade tumors [5]. Whenever a high-grade tumor is identified, a nephroureterectomy should be strongly considered. In contrast, Boorjian et al. have shown that attempts at endoscopic management prior to an extirpative procedure with an average of 6 months delay did not adversely affect survival, although most patients in the series had low-grade disease [10].

Use of adjuvant topical agents after treatment

After complete percutaneous resection of tumor, a smaller, 8 F nephrostomy tube can be left to allow instillation of adjuvant topical agents. Prior to use of the tube, a nephrostogram is done to ensure proper position of the nephrostomy tube and to rule out extravasation [3]. Therapy is given for 1–3 weeks after the percutaneous procedure. The agent is instilled by gravity to prevent excessive intrarenal pressure which may cause systemic absorption and bacterial sepsis (Figure 21.2). Typically, 81 mg BCG is given with each instillation weekly for 6 weeks. The chemotherapy regimen consists of 40 mg of mitomycin C [5]. Safety has been proven when using either BCG or mitomycin, but there has been no clear proven efficacy [11,12].

Follow-up

Patients who elect to undergo endoscopic management are reevaluated every 3–6 months, and more frequently if there are concerns about incomplete tumor resection or if a patient becomes symptomatic. Follow-ups should include a urine cytology, cystoscopy, retrograde urography, loopogram or retrograde ureteroscopy. Long-term follow-up recurrence is not uncommon, and may be dealt with using endourological maneuvers. In a pooled study of 288 patients, the total recurrence rate was 37% [17]. Patients need to be committed to long-lasting, rigorous surveillance of the upper urinary tract [13].

Complications

The procedure is generally well tolerated. (see Table 21.1). Cutress et al. found overall complication rate of percutaneous treatment is 27% [17]. The major complication is blood loss, which is related to both percutaneous access as well as depth of resection [14]. Persistent or prolonged arterial bleeding may require embolization. Other complications include urinary tract infection, perforation, secondary ureteropelvic junction obstruction and those

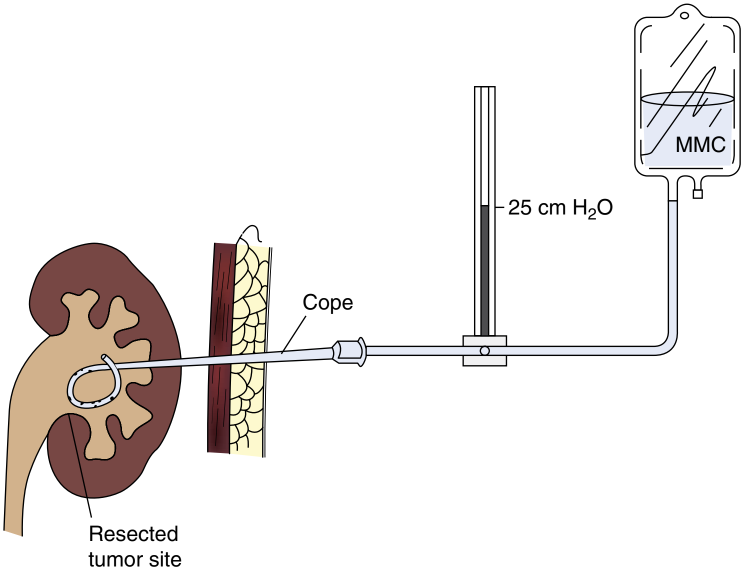

Figure 21.2 Topical immunotherapy or chemotherapy is delivered through a Cope loop nephrostomy tube. Therapy instilled by gravity prevents excessive intrarenal pressures. High pressures have been linked to complications of systemic absorption and sepsis. MMC, mitomycin C. (Source: Wein AJ. 2012 [1]).

related to upper pole access such as pleural injury. The incidence of these is low [8].

Risk of tumor tract seeding

There are case reports of nephrostomy tract tumor seeding, most resulting from percutaneous nephrostomy drainage of an obstructed system. Likewise, in two reports [15,16], there was tumor recurrence in the percutaneous tract after percutaneous treatment of UTUC. Treuthardt et al. reported a patient who had high-grade bladder cancer and previously had a cystectomy [15]. Huang et al. reported a case of a high-grade pT3b ureteral tumor which was accessed percutaneously and subsequently had a nephroureterectomy 1 month later [16]. However, in the pooled study [17], the incidence of seeding of urothelial carcinoma was 0.3% (1/236) overall, making this event extremely rare. Therefore, using established protocols and indications, the risk of tumor seeding is low, although the treating urologist should be aware of the potential risk of tumor seeding through the tract.

Results

Most available studies were published in previous decades. With the development of more advanced flexible ureteroscopes, retrograde access has become technically less complicated and increasingly prevalent. Percutaneous treatment continues to be recommended, and is especially important for tumors that are too large or are locations too awkward for the traditional ureteroscopic approach. In the literature, studies focused on the percutaneous approach tend to be small because of the rarity of the disease, with a mean study size of 24 patients [17]. They often do not reflect outcomes of noninvasive UTUC as the study population had significant medical comorbidities. Overall survival in the pooled percutaneous study is 79% at a follow-up of 37 months (Table 21.1). In the pooled study, the total recurrence rate in the upper tract is 37% (106/288). Disease-specific mortality rate is 11% [17].

Overall, studies of percutaneous treatment tend to have slightly worse outcomes than retrograde ureteroscopic methods. This is largely due to the overall indication that percutaneously treated tumors tend to be larger with worse clinical sequelae. Metastatic progression has been reported sporadically and is intimately connected to the grade of the disease. Higher grade tumors (2–3) may best be treated with nephroureterectomy [6]. There is also one report of patients with low-grade disease managed endoscopically whose disease progressed to high grade, with metastases to the liver [18]. While this is

Table 21.1 Literature review of outcomes of patients who underwent percutaneous treatment of UTUC, for which 26% of the patients had an imperative indication. Overall mortality was 21%. Disease-specific mortality (DSM) was 11%. Total recurrence rate is 37%. Overall complication rate is 27%, with the majority due to bleeding that required transfusion. (Source: Cutress ML, Stewart GD, Zakikhani P, Phipps S, Thomas BG, Tolley DA. 2012 [17]).

Study	***N* (1%)**	**Grade distribution [G1/G2/G3]**	**Prior UC bladder, *n* (%)**	**Follow-up, months**	**UT-recur., *n* (%)**	**Bl-recur., *n* (%)**	**OM, *n* (%)**	**DSM, *n* (%)**	**RNU rate, *n* (%)**	**Progression, *n* (%)**	**Failed endo management, *n* (%)**	**Complications, *n* (%)**
Tasca et al., 1992 [21]	10	[1/5/-]	ND	mean 19	5/10	ND	1/10	0	3/10	ND	3/10	ND
Fuglsig et al., 1995 [22]	26,27 RU(27)	ND	14(54)	mean 21	8 (31)	ND	1 (4)	0	9 (35)	2 (8)	9 (35)	2 (8) haemorrhage, 1 (4) tumour seeding Along percutaneous nephrostomy tract
Plancke et al., 1995 [23]	10 (10)	[6/3/1]	1 (10)	mean 28	1/10	1/10	1/10	0	1/10	0	1/10	None (0/10)
Patel et al., 1996 [24]	26 (42)	[11/11/1]	7 (27)	mean 45	9 (35)	11 (42)	8 (31)	2 (8)	5 (19)	2 (8)	6 (23)	7 (27) overall complications; 3 (12) haemorrhage and 1(4) death from adjuvant thiotepa
Martinez-Pineiro et al., 1996+ [25]	18	ND	24/54 (44)+	mean 31	2 (11)	ND	11/44 (25)+	4/44 (9)+	1 (6)	ND	3 (17)	7 (33) overall; 4 renal/colonic perforations; 1(6) hydrothorax; 1(6) TUR syndrome
Clark et al., 1999 [26]	17.18 RU (82)	[6/8/4]	11 (65)	mean 24	6 (33)	ND	6 (35)	3 (18)	2 (12)	≥3 (33) mets	-	2 (12) blood transfusion; 1 (6) UTI
Goel et al., 2003 [27]	20 (15)	[LG15/HG5]	1 (5)	mean 64	13 (65)	3 (15)	ND	5 (25)	10 (50)	7 (35)	10 (50)	1 (5) emergency RNU for haemorrhage, 1 (5) RNU for stricture, 2 (10) ESRF with dialysis
Suh et al., 2003 [28]	14 (86)	[LG8/HG6]	40/58 (69)+	mean 21	14/14	ND	3/14	2/14	5/14**	1/14 mets	8/14	6/31 (19) overall; 1 (7) transfusion, 1 (7) Pneumothorax, 1 (7) fluid overload, 1 (7) fungal UTI
Palou et al., 2004 [29]	34 (47)	[7/21/5]	27 (79)	mean 51	15 (44)	ND	9 (26)	2 (6)	9 (26)	ND	-	1 (3) emergency RNU for haemorrhage, 1 (3) stricture; 14 BCG, 5 MMC
Roupret et al., 2007 [30]	24 (38)	[LG17/HG7]	4 (17)	median 62	3 (13)	4 (17)	5 (21)	4 (17)	5 (21)	4 (17)	-	3 (13) blood transfusion; 3 (13) ESRF with dialysis; 1 (4) colonic perforation
Rastinehad et al., 2009 [31]	89 (29)	[LG50/ HG39]	17 (19)	mean 61	30 (33)	ND	42%+	ND	12 (13)	18 (20)	-	ND
	n (l%)	Grade distribution [G1/G2/G3]	Prior UC bladder	Follow-up, months	UT-rec, *n* (%)	Bl-rec, *n* (%)	OM, *n* (%)	DSM, *n* (%)	NU rate, *n* (%)	Progression, *n* (%)	Failed Endo Management, *n* (%)	Complications, *n* (%)
Overall	288 (26)	[36/47/11] [LG90/ HG57]	68/220 (31)	19-64	106/288 (37)	19/80 (24)	34/161 (21)	28/248 (11)	62/288 (22)	33/195 (17)	40/124 (32)	64/236 (27) overall; 37/218 (17) transfusion; 5/256 (2) ESRF with dialysis; 2/189 (1) emergency RNU/ embolisation for bleeding; 1/236 (<1) tract seeding

very unusual, it highlights the importance of proper surveillance and the potential of disease progression even in low-risk patients.

It is difficult to compare results with nephroureterectomy because there are no randomized head-to-head comparison studies. Secondly, the indications are different; one study showed that those who underwent endoscopic management tend to be less healthy than those who underwent nephroureterectomy [19]. Nevertheless, others have shown that the results are highly dependent on the pathological grade of the tumor [20]. For low-grade disease with little invasive potential, percutaneous treatment and nephroureterectomy have similar disease-specific outcomes. In their study of 110 patients, Lee et al. also found that even in Grade 2 disease, a more aggressive entity, the outcome was still equivalent regardless of therapy selection (disease-specific survival 53.8 ± 7.2 versus 53.3 ± 9.7 months) [4]. However, with Grade 3 cancer, the results are not comparable and anything less than a nephroureterectomy presents a higher risk of recurrence, metastasis, and worsening disease-specific survival.

Conclusion

Percutaneous treatment of upper tract urothelial carcinoma is an established method that has many advantages. In a well-selected patient, it offers a minimally invasive nephron-sparing treatment. However, patients must be aware of and committed to lifelong surveillance of the upper urinary tract.

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IV

SECTION 4

Percutaneous Ablation of Renal Cell Cancer (Thermal and Nonthermal)

22

CHAPTER 22

Epidemiology and Biology of Small Renal Masses

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Epidemiology of small renal masses

The incidence of renal cell carcinoma (RCC) has been steadily increasing in the United States, with an estimated 64,770 new cases in 2012 [1]. Of these cases, a significant proportion will be ≤4 cm in diameter and thereby characterized as small renal masses (SRM). The detection of SRM has accounted for the greatest increase in RCC with a 285% increase of tumors <2 cm and a 244% increase of 2–4 cm tumors between 1983 and 2002 [2]. With this increase, up to 70% of patients with RCC will present with an SRM [2]. The noted increase in the diagnosis of SRM is largely attributed to the routine use of cross-sectional imaging to evaluate abdominal symptomatology and for surveillance of other disease processes. Figure 22.1 provides two prototypic examples of incidentally detected SRM, both suspicious for RCC. Increased prevalence of etiological factors such as obesity and hypertension has also been implicated in the increased incidence of SRM [3].

Although the average age at diagnosis has remained relatively constant over time at 62–63 years, a significant proportion of patients will be diagnosed during the eighth decade of life, with 26% of patients ≥70 years [4]. Given the advanced age at diagnosis, many patients will present with substantial medical comorbidities. In a series by Berger and colleagues, over 75% of patients had at least one preexisting medical comorbidity. Severity of medical comorbidities has been noted to be mild in 37%, moderate in 25%, and severe in 13% of patients [5]. In another series, 24% of patients had a Charlson comorbidity score of 2 or greater, with the most common medical comorbidities being hypertension (58%) and diabetes mellitus (17%) [6]. Most importantly, the prevalence of chronic kidney disease (CKD), stage 3 or greater, in patients presenting with renal tumors at multiple centers is reported to be above 20% [7,8].

The increase in the incidental detection of SRM has lead to a paradigm shift in management strategies. Given the heterogeneous population of patients presenting with SRM, based on age and medical comorbidities, not all patients will be well suited for any single treatment. This is especially true in elderly patients and those with multiple medical comorbidities who wish to avoid the potential complications of extirpative treatment. While partial nephrectomy (PN) remains the standard of care, alternative treatments have gained acceptance and are now utilized in select patients. Thermal ablation (TA) and active surveillance (AS) are now accepted as appropriate treatment options in carefully selected patients with SRM. When deciding the best treatment strategy, both patient and tumor factors should be considered, including tumor biology, role of renal mass sampling (RMS), potential impact on renal function, and the relative effectiveness of available treatments.

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

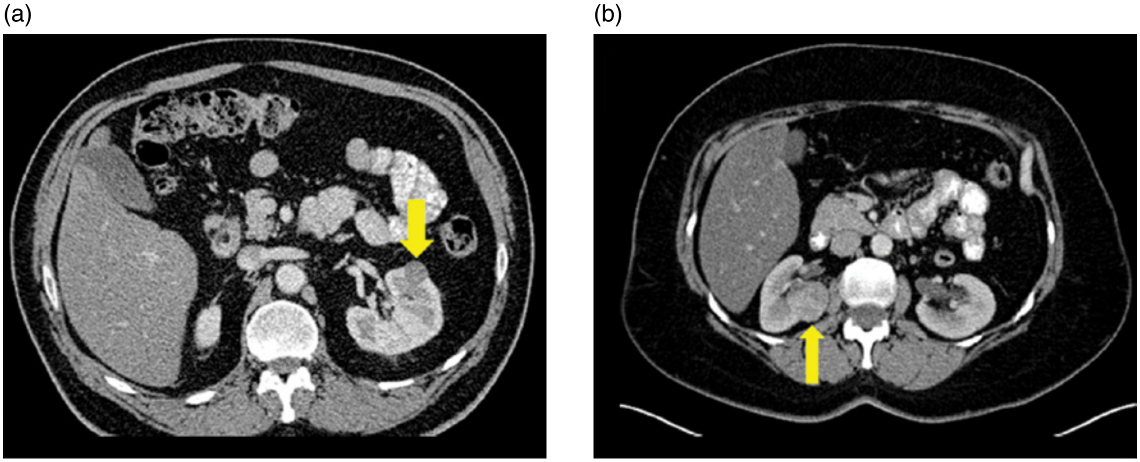

Figure 22.1 Computed tomography images of SRM, which are defined as enhancing renal masses ≤4 cm in diameter. Tumor size and location visualized on cross-sectional imaging can have a significant impact on counseling and treatment options. (a) A 2 cm exophytic left SRM (*yellow arrow*) amenable to PN, although AS and TA are also viable options dependent on patient age, comorbidities, and preference. (b) A 3.5 cm SRM (*yellow arrow*) located within the posterior hilar region of the right kidney with a normal contralateral kidney. The endophytic location of this tumor adds to the surgical complexity, although PN is still the reference standard for this patient. TA is less appealing due to tumor size and location, and AS is also a less attractive option in this patient due to increased tumor size that correlates with more aggressive tumor biology.

Tumor biology and natural history of small renal masses

Treatment of SRM should be tailored to the biology of the disease, recognizing that about 20% of SRM are benign, and only about 20–30% have a potentially aggressive phenotype [9]. Overtreatment can lead to unnecessary morbidity while undertreatment may result in otherwise preventable cancer-related mortality. This balance regarding the treatment of renal tumors is especially relevant as metastatic RCC is rarely curable while many SRM prove to be indolent when undergoing AS. Two factors that warrant special attention when examining the tumor biology of SRM are the incidence of benign histology and the clinical behavior of SRM during AS.

Based upon nephrectomy series, it is now well established that a significant proportion of SRM suspicious for RCC are benign, with the majority being oncocytomas and atypical (fat-poor) angiomyolipomas. In single institutional series, 8–26% of SRM are benign upon pathological evaluation [10–12]. Furthermore, the finding of malignant disease is significantly associated with increasing tumor size. Tumors <1 cm are noted to harbor benign disease in 38–46% cases [10,12], with a 17% increase in malignancy with each 1 cm increase in tumor diameter [10]. Nuclear grade of malignant tumors has also been associated with tumor size, with smaller tumors more likely to be low grade and indolent [13]. In addition to tumor size, patient age, gender, and smoking history have been significantly associated with the finding of benign histology. Based upon these associations, Lane and colleagues created a preoperative prognostic nomogram to predict the findings of benign versus malignant renal tumors among a population of patients managed with PN for clinical T1 lesions [9]. The nomogram performed modestly with a concordance index of 0.644 for predicting benign disease. Overall, approximately 20% of the tumors in this series were benign, and 20–30% were high grade or locally invasive (stage T3a). Interestingly, there was a significant interaction between age and gender in predicting benign histology, with young females and elderly males being the most likely to have benign tumors, although even in these populations RCC remained predominant.

Active surveillance has greatly expanded our understanding of the natural history of SRM, demonstrating that most SRM exhibit a relatively indolent clinical course. Tumor growth rates and the incidence of disease progression during AS have revealed that many patients can safely be observed, and have established AS as a

Table 22.1 Summary of selected active surveillance series.

Series	Number of patients	Duration of follow-up (months)	Average tumor size (cm)	Growth rate (cm/year)	% Progressing to metastatic disease
Crispen et al. [17]	154	31	2.0	0.29	1.3%
Mason et al. [44]	82	36	2.3	0.25	1.2%
Rosales et al. [15]	212	35	2.8	0.34	1.9%
Sui et al. [45]	41	30	2.0	0.27	2.4%
Abouassaly et al. [46]	110	24	2.5	0.26	0%

preferred management strategy for patients with limited life expectancy. Several AS series have demonstrated that the majority of SRM grow slowly with average growth rates of 0.13–0.34 cm/year [14,15]. Interestingly, a significant proportion of the tumors do not demonstrate interval growth. Kunkle and colleagues reported that 33% of tumors did not demonstrate interval growth during an average follow-up of 29 months [16]. Average tumor size for this cohort was 2.0 cm. This finding is supported by Jewett and colleagues who noted that 36% of tumors remained unchanged or decreased in size during an average of 28 months of follow-up [14]. Conversely, a small subset of tumors undergoing AS demonstrates accelerated growth rate, correlating with a small but finite risk of disease progression. Tumor growth of >1 cm/year is uncommon, being noted in only 5.8–6.7% of tumors [15,17]. Disease progression to metastatic status during AS has been noted in approximately 2% of patients, although follow-up remains limited in many of these series. In a pooled analysis, Smaldone and colleagues reported that patients exhibiting disease progression during AS were significantly older (75 versus 66 years of age), had larger tumors at presentation (4.1 versus 2.3 cm), and faster tumor growth rates (0.8 versus 0.3 cm/year) compared to patients without disease progression [18].

Table 22.1 summarizes the important findings of several selected AS series. These observations may explain the minimal impact that definitive therapy of SRM has on overall survival in most population-based studies [19].

Renal mass sampling

With the known incidence of benign histology in patients presenting with SRM, renal mass sampling (RMS) via percutaneous biopsy and/or aspiration has been advocated to help guide treatment decisions. However, RMS does have limitations that have restricted routine use in the past. Potential limitations include nondiagnostic results, inaccuracy of diagnostic results, and procedure-related complications.

Nondiagnostic biopsies are the greatest limitation of RMS and have been noted in 8–15% of patients in recent series [20]. These biopsies are the result of inability to target the tumor, lack of tumor tissue in the biopsy specimen, or inability of the pathologist to make a definitive diagnosis based on the tumor tissue provided. Options following a nondiagnostic biopsy include repeat biopsy, AS, or proceeding to definitive treatment without histological confirmation of malignancy. Repeat biopsies following a nondiagnostic biopsy are reported to produce adequate tissue for diagnosis in 83–100% of cases, much higher than one might have expected. The outcome of these patients was recently reported by Leveridge and colleagues in a series of 58 patients who underwent an initial nondiagnostic biopsy [21]. The majority, 55%, of these patients underwent AS. Of the remaining patients, 20% underwent repeat biopsy of which 80% of the tumors were malignant and 9% underwent surgical excision of which 60% were malignant. The yield of repeat biopsy was very similar to that of the initial biopsy, demonstrating that repeat biopsy can provide considerable utility. These findings suggest that an initial nondiagnostic biopsy does not appear to adversely affect patient outcomes or limit future treatment.

In the past, major limitations of RMS were low accuracy in diagnosing malignant disease and the frequent occurrence of false-negative biopsies. However, the accuracy of biopsy in differentiating benign from malignant disease is now greater than 96% in contemporary series in which adequate tissue is obtained [22]. Most importantly, false-negative rates are now below 1% in most series.

Despite this improvement in the accuracy of RMS, concern about false-negative biopsies appears to be one of the most important reasons why urologists do not routinely perform biopsies. In a survey by Barwari and colleagues, over 80% of respondents stated that the risk of a false-negative biopsy was an important reason for not performing RMS [23]. This underscores the need for improved education about the encouraging results and utility of RMS in the modern era.

Renal mass sampling can also provide useful data about nuclear grade and histological subtype of malignant lesions. While the ability to accurately determine nuclear grade and histological subtype is not as critical as determining the presence of benign versus malignant disease, these tumor features can be utilized in assessing biological potential and ultimately influence treatment decisions. The ability to accurately assign tumor grade on biopsy is comparatively diminished at 43–76% [24,25], although most discordant cases are only off by one grade. However, the concordance of histological subtype RCC between biopsy and surgical specimens is higher and ranges from 86% to 100% [20,26]. Although the accuracy of RMS has greatly improved, advances in the molecular analysis of biopsy specimens may further enhance information provided in the future [22].

Postbiopsy complications are uncommon, occurring in only 1–5% of patients, and can include hematoma, infection, pain, pseudo-aneurysm, pneumothorax, injury to adjacent organs, and tumor seeding of the biopsy tract [27]. The majority of complications are minor, with only 0–7% requiring emergency room evaluation or hospital admission, and loss of the kidney and other severe complications are now extremely rare [28]. The low rate of complications in contemporary series is likely attributable to improved image guidance and techniques employed to decrease postbiopsy bleeding and tumor tract seeding. Needle tract seeding appears to be relatively rare, with less than 10 cases reported in the literature. Centrally located, infiltrative renal masses often correlate with high-grade urothelial carcinoma and represent one relative contraindication to RMS, because they are at increased risk for needle tract seeding. Most studies suggest that RMS does not appear to have an impact on the feasibility of future extirpative therapy [20].

In order for RMS to be clinically useful, evidence demonstrating the impact on treatment decision making is needed. Traditionally, the indications for RMS were limited to patients in whom renal involvement from nonrenal malignancies was suspected [26]. However, given the increased accuracy of RMS, the indications may expand to include patients presenting with SRM. Contemporary series report that RMS altered 41–69% of patient treatment decisions [26,29]. Specific alterations in treatment were outlined by Tan and colleagues in a series of 204 patients presenting with SRM. In this series, the use of RMS was significantly associated with increased Body Mass Index (BMI), tumor location, and high complexity nephrometry score [28]. Patients with biopsies demonstrating benign, indeterminate, or favorable histology were more likely to undergo AS. Additionally, patients undergoing RMS were more likely to undergo radical nephrectomy (RN). These results suggest that biopsy results were being used to guide treatment decisions.

Despite RMS having the potential to provide valuable data to aid in patient counseling, acceptance into routine practice has been slow to develop. In a survey by the American Urological Association examining the evaluation and treatment of SRM, suspicion of nonurological malignancy, significant medical comorbidities, and patient age were the most common reasons for obtaining a biopsy. However, only 8% of respondents reported obtaining a biopsy on a routine basis [30]. In a second survey by the Endourological Society, only 9% of respondents obtained biopsies on a routine basis and 73% of respondents never or rarely obtained biopsies [23]. The most common reasons for not performing biopsies were that they would not change in management, concern about false negatives, and risk of complications. When biopsy was performed, important reasons included tumors in solitary and transplanted kidneys, metastatic renal cancer, and presence of bilateral tumors.

Based on the known incidence of benign disease, improved accuracy of biopsies, and the emerging evidence supporting TA and AS, the use of RMS has the potential to expand. While the previous indications for biopsy would remain, RMS utilized to improve risk stratification may help guide treatment decisions in patients with competing medical conditions who may be candidates for multiple types of treatment. Figure 22.2 provides a utility-based evaluation and management strategy for SRM incorporating RMS in select patients, which is currently practiced at our centers.

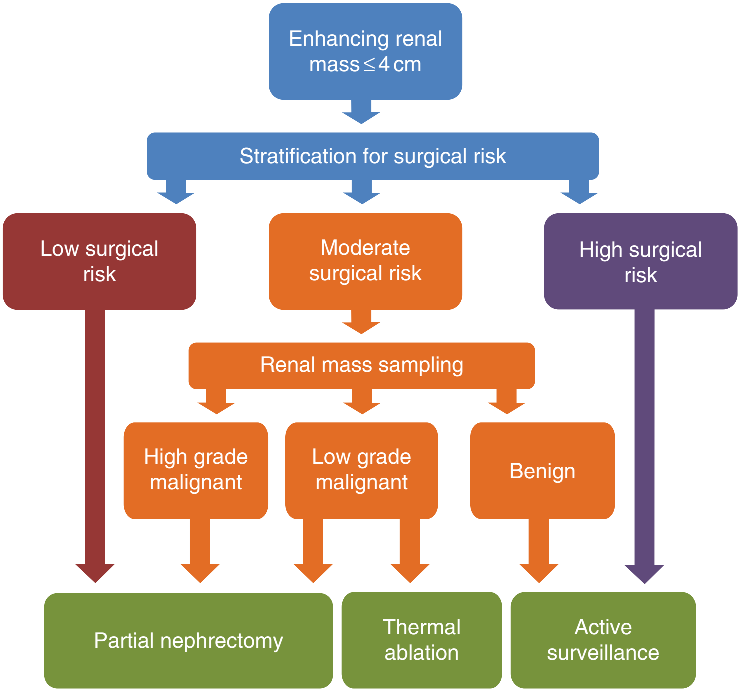

Figure 22.2 Potential algorithm for the evaluation and management of SRM that incorporates a utility-based approach to RMS. Following identification on cross-sectional imaging, surgical candidacy is assessed. PN is the primary recommendation for patients with low surgical risk, while AS is recommended as the initial treatment for patients with high surgical risk or limited life expectancy. Patients at moderate surgical risk and with reasonable life expectancy, for whom a variety of options can be considered, can be further stratified with RMS.

Functional impact of small renal mass treatment

The increased detection of SRM has been associated with an increase in treatment with the primary goal of reducing cancer-specific mortality [19]. However, as outlined above, a significant proportion of SRM harbor benign disease and many behave in an indolent manner during AS. For these reasons careful consideration must be given to the impact of treatment on overall health and renal function. Several retrospective series have suggested that PN is associated with increased overall survival compared to RN in the treatment of SRM, in part related to improved renal function and a reduction in morbid cardiovascular events [31,32]. This potential link between PN, better renal function, and improved survival, when compared to RN, is now engrained in our mindset, although the latter aspect of this paradigm has recently been challenged. Certainly, the ability of PN to preserve renal function relative to RN cannot be challenged.

In an early report by Lau and colleagues, 10-year survival from renal insufficiency defined as serum creatinine >2.0 was 88% in PN patients versus 78% in RN patients [33]. In a more recent series defining chronic renal insufficiency as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 cm^2, only 20% of PN patients developed chronic renal insufficiency compared to 65% of RN patients [34]. PN has also been associated with decreased need for postoperative hemodialysis compared to RN [31]. Similar to PN, the use of TA has also been noted to maintain renal function. In a series of 54 patients undergoing radiofrequency ablation, the average decrease in GFR was only 2 mL/min/1.73 cm^2 and no patients presenting with an eGFR >60 mL/min/1.73 cm^2 developed chronic renal insufficiency during follow-up of 34 months [35]. Similar results have been noted with cryoablation of renal tumors with few patients developing chronic renal insufficiency following treatment [36].

However, the results of a recent phase 3 randomized trial comparing elective PN with RN have cast doubt on the link between PN and improved survival in the management of localized renal tumors [37]. A normal contralateral kidney was required for entry into this study, and maximum tumor size was 5.0 cm. Median follow-up was 9.3 years. Surprisingly, 10-year overall survival rates were 76% following PN compared to 81% following RN.

The most common cause of death in the population was cardiovascular, with cardiovascular deaths occurring in 9.3% of PN patients and 7.3% of RN patients. RCC-related death was uncommon (<4%) in both cohorts consistent with the limited biological potential of most SRM. Unfortunately, the trial closed early due to poor accrual and a comprehensive evaluation of renal functional outcomes was not provided. Further limitations of the trial included a cross-over rate of 10% between assigned and received treatments, and possible variability in the PN procedure because multiple surgeons were involved.

Despite the importance of this randomized trial and lack of survival benefit noted, it has limitations as outlined above, and many surgeons still advocate a nephron-sparing approach in the treatment of SRM, given the large body of literature that has indicated the importance of optimizing renal function on a long-term basis. This also reflects a strong belief that RN represents gross overtreatment of most SRM, with both PN and RN providing similar oncological outcomes for this patient population. One interpretation of the randomized trial is that it clearly blunts the strong impetus towards PN in our field and should be taken into account when managing some patients with clinical T1b or T2 tumors or those with potentially infiltrative characteristics on imaging. In these settings, RN should be strongly considered but enthusiasm for RN for most SRM remains low, and RN should definitely be avoided if possible whenever it will lead to CKD.

Nephron-sparing approaches, including PN, TA, and AS, remain vitally important for several reasons. As stated above, a significant proportion of patients presenting with SRM have preexisting renal insufficiency and may be at risk for the adverse sequelae of CKD if RN is performed. Additionally, patients presenting with solitary kidneys, a poorly functioning contralateral kidney, or bilateral renal tumors are best treated with nephron-sparing approaches. In the end, most experts in this field still strongly believe that SRM in particular are best managed with nephron-sparing approaches in an effort to preserve renal function and avoid gross overtreatment.

Management of small renal masses and role of thermal ablation (Table 22.2)

Radical nephrectomy (RN) was once considered the standard of care for all renal masses, with PN being reserved for patients with absolute indications for nephron-sparing surgery. However, with increased experience and success in patients with absolute indications for nephron-sparing surgery, PN became increasingly utilized in all patients with SRM. This change in practice is supported by equivalent oncological outcomes when comparing PN and RN in this patient popultation [33,38]. Both of these modalities provide local control in 97–99% of patients with SRM, with only very occasional local recurrences [39]. For PN, such local recurrences are often found away from the tumor bed, likely representing multicentric tumor occurrence. Morbidity with PN is higher than after other treatment modalities due to the need for renal reconstruction, and can include urine leak and postoperative bleed. However, most such complications are manageable and associated with favorable long-term outcomes. Surgical excision, whether by PN or RN, remains the gold standard for local tumor control for SRM.

The established oncological efficacy of PN has led to the rapid development and implementation of alternative nephron-sparing techniques. Strategies involving TA have gained popularity based on ease of application and minimal treatment-associated morbidity. Several modalities

Table 22.2 Score card for small renal mass treatment options.

	Treatment modality			
	Radical nephrectomy	Partial nephrectomy	Thermal ablation	Active surveillance
Oncological efficacy	+	+	+/-	-
Functional preservation	-	+	+	+
Pathological assessment	+	+	+/-	-
Morbidity	+/-	+/-	+/-	+

of TA have been evaluated, including radiofrequency, cryotherapy, microwave, laser, high-intensity focused ultrasound, and radiosurgical ablation [40]. Of these modalities, the greatest experience has been with cryotherapy and radiofrequency ablation, and the other modalities are still best considered experimental. In addition to PN and TA, AS of SRM has become an option based upon the observed indolent behavior of most renal tumors as described above.

Due to the paucity of clinical trials comparing treatment modalities for SRM, most analyses of the comparative effectiveness of the individual treatment modalities have been based on pooled analysis of multiple retrospective series. Selection bias is a clear limitation in this literature, and differences in patient age and tumor size and location are commonly observed. In addition, duration of follow-up is highly variable between the various modalities. Nevertheless, certain findings appear to be real and are strongly supported by the current database. One such finding pertains to the incidence of local recurrence after TA, which appears to be higher than after surgical excision. In the American Urological Society guidelines analysis of the management of clinical T1 renal masses, the local recurrence rates after cryoablation and radiofrequency ablation (RFA) were 9.4% and 13.0%, respectively, compared to 1.9% and 2.0% after open RN or PN, respectively [39]. This occurred despite the fact that TA modalities were used to treat smaller tumors (2.5 and 2.8 cm mean tumor size for cryoablation and RFA, respectively, versus 3.3 cm and 4.6 cm mean tumor size for open PN and RN respectively) and had substantially shorter follow-up (20 and 23 months mean follow-up for cryoablation and RFA, respectively, versus 56 and 59 months mean follow-up for open PN and RN, respectively). In reality, when such confounding factors have been taken into account, the relative risks of local recurrence after cryoablation and RFA have been estimated to be about 8- and 18-fold higher than after surgical excision, respectively [41]. Many of these local recurrences can be salvaged with repeat ablation, but as with all cancers, there will always be some risk associated with tumor persistence or recurrence after incomplete or inadequate initial therapy.

The TA literature has suffered from a variety of other limitations in addition to short duration of follow-up, as reviewed by Kang and colleagues [42]. For instance, biopsy data at the time of TA are lacking in 18–43% of series [29], allowing many benign tumors to be included in the analysis and potentially underestimating cancer recurrence rates.

Other ongoing controversies about TA have included concerns about the accuracy of radiographic criteria for success, with some biopsies showing apparent tumor persistence or recurrence despite loss of enhancement, and difficulty of surgical salvage related to extensive fibrosis that can be associated with TA failures [43]. More recent studies suggest substantially improved results with TA, particularly for tumors <2.5 cm in size. More prolonged follow-up is also now available in some series, although this is still best characterized as intermediate rather than long term, and most such series still suggest suboptimal tumor control when compared to the gold standard of surgical excision. With further experience, the ideal and potential indications for TA are now coming into focus and provide a clear vision that TA remains a vital component in our armamentarium for the management of patients with SRM. The following chapters will provide more detailed analyses about TA and current perspectives about some of the controversies that have arisen during its development over the past 15 years.

With the increased incidence of SRM and wide range of treatment options, in 2009 the American Urological Society created guidelines for the management of clinical T1 renal masses [39]. This includes patients with SRM, which correspond to index patients 1 and 2 in this document, specifically patients with clinical T1a renal masses and good health or major comorbidities and increased surgical risk, respectively (Figure 22.3) [39]. In this context, standards, recommendations, and options are presented, with successively decreasing enthusiasm based upon the strength of the literature supporting each modality. The guidelines define PN as a reference standard that should be considered in all patients with an SRM when technically feasible, particularly in healthy patients who are at relatively low surgical risk. However, RN remains an alternative standard when PN is not feasible, although renal functional considerations may preclude RN. AS should be considered in all patients, but is a recommendation for index patient 2, best reserved for those with limited life expectancy or those who are unfit for surgical intervention. TA also can be considered an option in all patients but was further recognized as a recommendation in patients with major comorbidities and increased surgical risk who desire proactive management.

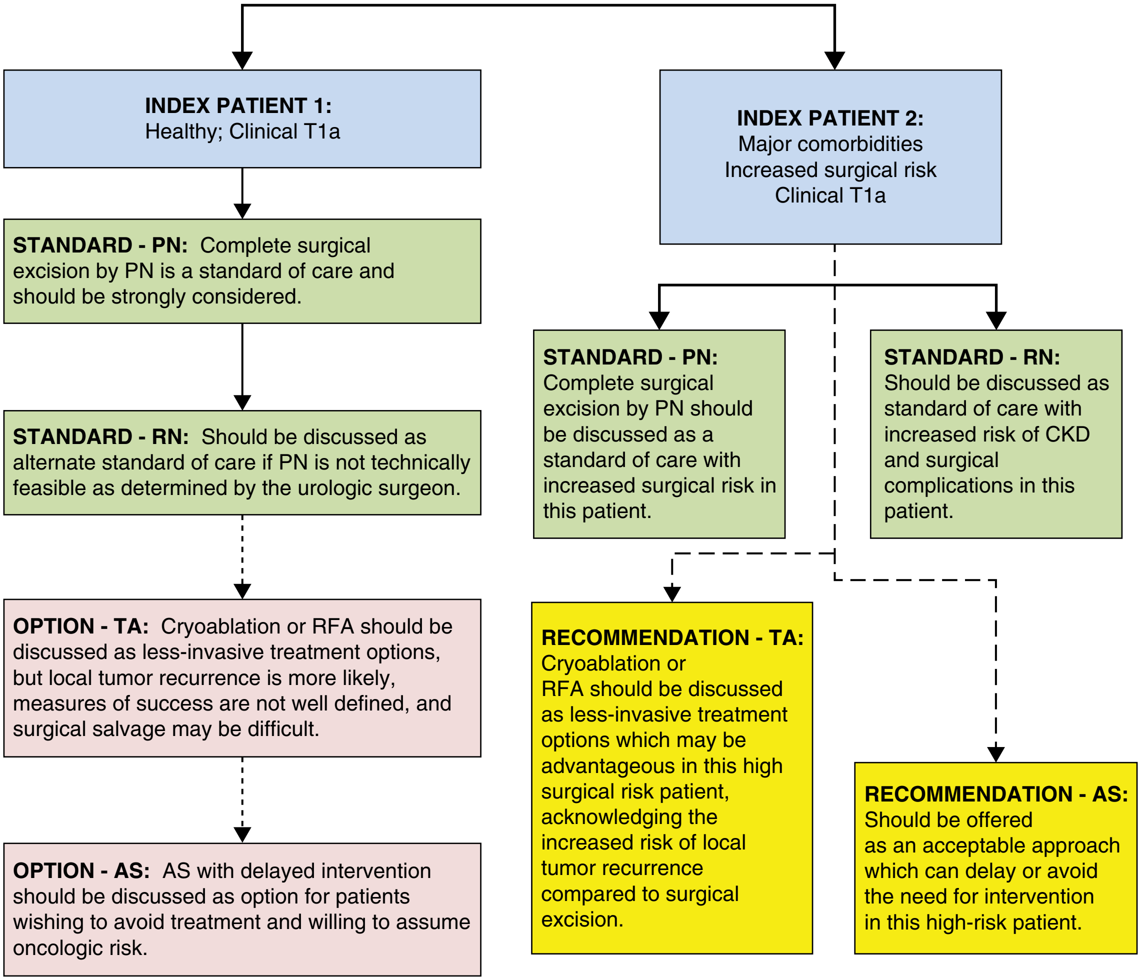

Figure 22.3 American Urological Association guidelines for treatment of SRM (clinical T1a renal tumor). Patient counseling should include discussion of the potential for benign disease and the risks and benefits of all available treatment options. Treatment alternatives are then stratified based on patient health status and life expectancy. Standards, recommendations, and options are presented with successively decreasing enthusiasm based on the strength of the literature supporting each modality. (Source: Adapted with permission from Campbell SC, Novick AC, Belldegrun A, et al. 2009 Copyright © American Urological Association Inc. [39]).

Further research is already beginning to alter our perspectives about these guidelines and various aspects of this will be highlighted in subsequent chapters.

Conclusion

The tumor biology of SRM represents a spectrum that includes extremes such as benign histologies and potentially aggressive RCC, with many indolent tumors occupying the space in between. A wide variety of treatment options is now available, ranging from AS to surgical excision, further complicating patient counseling and decision making. RMS has great potential to provide improved risk stratification in the future, particularly when combined with molecular profiling. Treatment should be individualized based on tumor biology, renal functional considerations, the efficacy and potential morbidity of each treatment modality, and patient comorbidities and preferences. An important role for TA has been established for the management of SRM despite a literature that has several limitations, and further studies will be needed to define the optimal indications and true oncological efficacy of this modality.

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23

CHAPTER 23

Evolution of Evidence-Based Outcomes for Percutaneous Management

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Introduction

Percutaneous ablation of renal masses is now considered as a management strategy, particularly with the recent increase in incidentally detected small renal masses. Percutaneous ablation was developed to provide a treatment alternative to patients with high surgical risk, preexisting renal dysfunction including solitary kidneys, or multiple bilateral renal masses. As percutaneous ablation has become more commonplace there has also been increasing interest in extending the application of these treatment methods to younger and healthier patients. Continued adaptation of percutaneous techniques for ablation of renal masses will require proof that outcomes of percutaneous ablation are comparable to those for extirpative surgery, currently considered the gold standard for management of small renal masses [1,2]. It is our aim to review the evidence-based outcomes for percutaneous ablation techniques with respect to oncological efficacy, safety, renal function, and financial considerations.

Clinical data for percutaneous ablation techniques, particularly with cryoablation (CA) and radiofrequency ablation (RFA), have now matured to the point where conclusions can begin to be drawn about the value of these procedures. In this chapter we will analyze these data to determine the oncological effectiveness, complication rates, preservation of renal function, and cost-effectiveness.

Oncological outcomes

Interpretation of oncological outcomes for ablation of renal masses requires consideration of several issues: the relative novelty of the procedure, the lack of standardization in indications for the procedure, and the different ablation modalities. Validation of oncological outcomes including local recurrence, metastasis rates, cancer-specific survival, and overall survival is dependent on the availability of data that encompass the time course of expected recurrence. Because most recurrences for stage T1–T2 renal cell carcinoma occur within 5 years [3], outcomes data should be of at least this length to make conclusions about oncological efficacy.

Furthermore, attention must be paid to tumor characteristics including tumor size and location (i.e. peripheral or central), patient characteristics, and ablation technique as these are likely to affect oncological outcomes. Because ablation techniques were first applied to older patients and those with comorbidities who were not otherwise amenable to surgical extirpation, there is a

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well-recognized selection bias that needs to be considered in interpretation of outcomes data using these patient populations.

Another potential bias arises from the fact that a preablation biopsy is not done for many renal masses, meaning that the true nature of the ablated renal mass is not well defined [4]. Studies evaluating oncological outcomes of ablative therapies rarely control for this, while it is known that approximately 20% of these small renal masses are likely benign. This potential bias may make ablative therapies appear more effective than they actually are. In addition, there is a lack of histopathological confirmation of tumor cell death as very few studies report postablation biopsies. Even in the setting of a negative biopsy, there is no way to determine margin status in contemporary studies. Instead, lack of contrast enhancement and shrinkage of the ablation site on postablation imaging have been used as surrogate endpoints for successful ablation.

The adequacy of these endpoints is debatable as at least one study reported a substantial degree of residual tumor viability in biopsies of renal ablation sites despite no contrast enhancement on imaging [5]. Furthermore, shrinkage of the ablation site may or may not be present post ablation and assessment of the ablation site boundaries can be difficult to differentiate from postablation fibrosis and perinephric stranding [6,7].

Taking all of these factors into account, it is difficult to draw definite conclusions on the relative oncological efficacy of ablation versus more time-honored techniques such as partial nephrectomy and nephrectomy. However, an analysis of available information does provide perspective on its effectiveness to date.

In order to examine oncological efficacy, we have separated oncological failures into local recurrences and metastatic disease. We will examine local recurrence first.

Local recurrence

In terms of local recurrence, there is controversy about what constitutes a local recurrence versus an incomplete ablation. Without the pathological analysis inherent in partial and radical nephrectomy, it has been difficult to come to a standard definition for what constitutes local recurrence versus incomplete ablation. Some series report local recurrence (and thus primary treatment failure) as any radiographic enhancement at the tumor ablation site at any time following initial treatment. Other series consider persistent enhancement (other than small areas of rim enhancement, especially on magnetic resonance imaging) to be incomplete ablation and an indication for immediate reablation.

Cryoablation

Individual series report local recurrence rates following percutaneous cryoablation (PCA) ranging from 5% to 10%. Finley et al. reported persistent enhancement during follow-up imaging in one of 19 patients, resulting in a primary failure rate of 5.3% [8]. However, in this study, only 67% of tumors had a biopsy diagnostic for renal cell carcinoma. Atwell et al. performed a retrospective review of 91 patients with 93 tumors undergoing PCA [9]. Biopsies were performed on 73 of the tumors and of these, seven were nondiagnostic and 14 were consistent with oncocytoma. Persistent enhancement was appreciated in four tumors at 3 months, yielding a primary failure rate of 5.1%. Additionally, there was a single tumor recurrence at 14 months. Excluding the oncocytomas, the local cancer control rate was 94% (74/79 tumors) following a single PCA treatment, though this rate included the seven nondiagnostic masses.

In another retrospective analysis of 99 lesions with mean tumor size 2.1 ± 0.7 cm and treated by PCA by Mues et al., nine (9.1%) were incomplete ablations as evidenced by persistent contrast enhancement within the first 6 months following treatment [10]. All nine lesions (none of which had pathological diagnoses) were treated with PCA a second time, after which only one lesion had persistent enhancement (1.1%). In a smaller series of 20 lesions (mean renal tumor size 2.2 cm) treated by PCA, two (10%) patients had persistent enhancement consistent with incomplete ablation, but had no evidence of disease after retreatment with mean follow-up of 12 months [11].

Radiofrequency ablation

For renal masses treated by RFA, local recurrence rates in single series are similar. Success of initial ablation in a series reported by Ferakis et al. was 90%, with 35 of 39 tumors showing no enhancement when measured by computed tomography (CT) scan or magnetic resonance imaging (MRI) 4 weeks after percutaneous RFA (PRFA) [12]. Similarly, in a series of 31 patients treated by PRFA for renal masses less than 4 cm, Levinson et al. reported a 3.2% rate of primary treatment failure (1 of 31) and three recurrences between 7 and 31 months, resulting in a recurrence-free survival rate of 90% [13].

Tracy et al. reported initial treatment success of 97% in a series of 243 renal masses (average tumor size 2.4 cm) treated by RFA, with incomplete ablations of seven renal masses [14]. Seventy-nine percent (179 of 243) of tumors were biopsy-proven renal cell carcinoma (RCC) with nine local recurrences in the 179 biopsy-proven RCCs, yielding a 90% recurrence-free survival rate at 5 years. The earliest local recurrence was at 3 months and no patient developed local recurrence after 36 months. Seventy-one percent (172/243) of the RFAs were done percutaneously and 28% were done laparoscopically, but outcomes comparing approaches were not reported. It is not clear if the technical approach to RFA is important in local recurrence, but it may be as tumor location is critical to selection of the approach. Tumors in an anterior or central location or near adjacent organs are more likely to be treated by laparoscopic RFA (LRFA) and posterior or lateral tumors were mostly treated by PRFA [15,16].

Lesion size may be predictive of increased risk of recurrence following RFA. Zagoria et al. reported on a series of 41 patients (48 biopsy-proven RCCs) treated by PRFA with median follow-up of 56 months [17]. The overall recurrence rate was 12%, but median treated lesion size for patients with recurrences was 5.2 cm and there were no recurrences for masses less than 4 cm at 61 months follow-up. Median time until recurrence was 7 months and as early as 1.3 months, suggesting that recurrence was more likely due to residual tumor and inadequate initial treatment rather than truly recurrent RCC. In the report by Ferakis et al., each recurrence in the entire cohort of 39 renal tumors treated with PRFA was in a patient with a tumor at least 4 cm in size [12]. The recurrence rate for masses larger than 4 cm was 50% (4 of 8) with no recurrences for masses smaller than 4 cm. Central (versus peripheral) tumor location was also associated with increased risk of recurrence [12]. Best et al. found a significantly higher rate of recurrence and thus lower disease-free survival (DFS) rate in patients with masses 3 cm or larger (96% 3-year DFS for masses <3 cm versus 79% 3-year DFS for masses 3 cm or larger) [15]. As we learn more about tumor features such as size and centrality that affect outcomes, the use of indices such as the RENAL nephrometry score is likely to become more common.

Comparative studies

In an attempt to summarize this large volume of disparate date, Kunkle and Uzzo performed a metaanalysis comparing outcomes of CA and RFA of renal masses [18]. This showed local tumor progression in 31 of 600 lesions (5.2%) treated by CA (mean tumor size 2.6 cm) and in 100 of 775 lesions (12.9%) treated by RFA (mean tumor size 2.7 cm) [18]. Repeat ablation was required in 1.3% lesions treated by CA and 8.5% of lesions treated by RFA required retreatment. A percutaneous approach accounts for only 23.2% of CAs (laparoscopy and open surgery account for the other cases) but 93.7% of the RFAs in this analysis, which may explain the slightly lower local recurrence rate for CA.

A recent multiinstitutional retrospective analysis comparing ablation of renal masses by PCA or PRFA showed a slightly higher local recurrence rate of 11% (4/41) for RFA compared to 7% (4/70) for PCA, although the difference was not statistically significant [19]. In this study, all lesions were biopsied, 5% (6 of 111) were nondiagnostic, 83% (92/111) were clear or papillary RCC, and 12% (13/111) were benign.

In another large metaanalysis by the group from Fox Chase, local recurrence was seen in 4.6% of lesions treated by CA (mean tumor size 2.6 cm, mean follow-up 18.3 months) and 11.7% of lesions treated by RFA (mean tumor size 2.7 cm, mean follow-up 16.4 months), compared to 2.6% treated by partial nephrectomy (PN) (mean tumor size 3.4 cm, mean follow-up 54 months) [4]. Compared to PN, the relative risk of recurrence for lesions treated with CA was 7.45, and for RFA it was 18.23. Taken together, these data suggest that although local recurrence rates for ablation techniques approach that of PN, they may be slightly higher for ablation techniques.

Long-term survival

Cryoablation

Several groups report 100% short-term cancer-specific survival and low (1.2%) rate of progression to metastasis following PCA with short-term median follow-up between 11 and 18 months [4,8,11]. Although early short-term efficacy appears promising, the absence of postablation pathological confirmation of tumor cell death must be kept in mind. Furthermore, the expected rate of metastasis from small renal masses even under observation is very low [20], so these short-term results are not able to support any significant conclusions about the oncological efficacy of CA. The series with the longest follow-up after PCA is from Johns Hopkins and retrospectively evaluated 141 patients with 154 tumors with a mean follow-up of 36.1 months [21]. Five-year recurrence-free survival in this cohort was 95.6%, and 5-year cancer-specific survival (CSS) and overall survival (OS) were 98% and 77.7%, respectively. These results suggest that encouraging oncological outcomes are likely to hold up throughout at least intermediate-term results. One limitation of this study, however, is that only 34% of the tumors treated by PCA were biopsy-proven RCC and oncological outcomes may be different in a population of exclusively biopsy-proven RCC.

Though laparoscopic CA (LCA) and PCA differ in the way they target renal lesions, results from long-term studies for LCA may provide insight into potential longer-term outcomes with PCA. Two of the LCA series provide intermediate outcomes up to 8 years [22,23]. Aron et al. report a 92% CSS rate at 5 years, an 83% CSS rate at 10 years, an 84% overall survival rate at 5 years, and a 14% recurrence rate in 55 patients with biopsy-proven RCC with a median follow-up of 93 months [22]. Guazzoni et al. showed CSS of 100% and OS of 93% in 44 patients who had LCA at mean follow-up of 61.3 months [23]. Because only the surgical approach differs and the ablation technology is similar, it is hoped that similar results will be recapitulated as the collective experience with PCA grows.

Radiofrequency ablation

Long-term oncological outcomes for PRFA are also limited by series with short follow-up, limited patient size, or lack of pathological diagnoses. Levinson et al. showed 100% disease-specific and metastasis-free survival, 79.9% recurrence-free survival, and 58.3% overall survival in a cohort of 18 biopsy-proven RCC (median tumor size 2.0 cm) who underwent PRFA with mean follow-up of 57.4 months [13]. The overall survival is likely low as a result of patients being treated at a time (2000–2003) when RFA was used primarily for patients who were not considered surgical candidates. Tracy et al. evaluated 208 patients, of which 160 were patients with biopsy-proven RCC, who underwent either laparoscopic or percutaneous RFA (mean tumor size 2.4 cm). At a mean follow-up of 27 months, the 160 patients with biopsy-proven RCC had 90% recurrence-free survival, 95% metastasis-free survival, and 99% cancer-specific survival. The 5-year overall survival was 85% [14]. Zagoria et al. evaluated 41 patients with RCC treated by percutaneous RFA (median lesion size 2.6 cm) and recurrence-free survival was 88%, disease-free survival 83%, and overall survival 66% [17]. Overall, these studies show promising results, but the limitations mentioned must be considered.

The most robust study to date, from Psutka et al., analyzed oncological outcomes from 185 patients with biopsy-proven T1 RCC treated by PRFA (median tumor size 3 cm) with median follow-up of 6.4 years [24]. Five-year recurrence-free survival (RFS) was 95.2%, 5-year metastasis-free survival was 99.4%, cancer-specific survival was 99.4%, and overall survival was 73.3%. Compared to patients with T1b tumors, patients with T1a tumors had slightly better recurrence-free survival, metastasis-free survival, and cancer-specific survival rates, but there was no difference in overall survival. These results are encouraging as they demonstrate that excellent cancer control of stage T1 RCC can be achieved with PRFA in a center with proficiency in this technique.

Comparative studies

To truly determine oncological efficacy of percutaneous ablative techniques for treatment of RCC, prospective randomized studies are needed for comparison of outcomes with extirpative surgery, the current gold standard. Studies of this nature are lacking, but a retrospective cohort comparison suggests that RFA and PN appear to have equivalent oncological outcomes for treatment of solitary biopsy-proven cT1a RCC at 5 years [16]. RFS was 91.7% for RFA versus 94.6% for PN, CSS was 97.2% versus 100%, and 5-year OS was 97.2% versus 100%. The cohort treated by RFA was significantly older (63.8 versus 54.8 years, $p = 0.0001$) with a higher American Society of Anesthesiology score than those treated by PN, supporting the use of RFA in an older patient population but potentially limiting a broader application of these data. Another group reports 100% 5-year CSS for patients undergoing either radical nephrectomy (RN) or RFA, although interpretation of this study is limited as less than 24% of the masses treated with RFA were biopsied [25]. These studies suggest that RFA is likely to be an effective minimally invasive ablative technique for management of patients who desire or need oncological control of at least 5 years, particularly patients who are older or have more comorbid conditions. Because there are no published data longer than 5 years, it is still not clear whether ablative techniques will continue to have oncological outcomes equivalent to PN for younger, healthier patients with longer life expectancy.

When looking at a larger, population-based cohort from the Surveillance, Epidemiology and End Results database, Choueiri et al. found no differences in CSS or OS between patients with T1 RCC who underwent thermal ablation (n = 578 who underwent RFA or CA), PN (n = 4402) or RN (n = 10,165) [26]. The significance of these data may be limited as it pertains specifically to percutaneous ablation, however, due to short median follow-up of 21 months, inability to differentiate between percutaneous and laparoscopic thermal ablation approaches, and bias toward thermal ablation for several factors including smaller tumors and older patients.

Complications

Much of the rationale for supporting the use of renal ablative therapies for small renal masses stems from the belief that these treatments afford fewer morbidities and complications than extirpative surgery. One early multi-institutional retrospective study reviewed the cumulative ablative experience of four high-volume ablation centers and found an overall complication rate of 11.1% (30/271) [27]. Patient selection was mixed and included both CA and RFA done both percutaneously and laparoscopically. Major complications occurred in 1.8% (5/271) and minor complications in 9.2% (25/271) of the entire cohort. No subset analysis was done to differentiate between percutaneous and laparoscopic CA, but scrutiny of the data indicates a 13.7% overall complication rate for CA with an incidence of 12.2% minor complications (17/139) and 1.4% major complications (2/139; one transfusion, one conversion to open). For RFA (both percutaneous and laparoscopic), the overall complication rate was 8.3% (11/132) with one death due to aspiration pneumonia. The major complication rate for RFA was 2.3% (3/132; one ileus, one ureteropelvic junction obstruction, one urine leak) and the minor complication rate was 6.1% (8/132). The most common minor complication for both CA and RFA was pain or paresthesia at the probe site (5.2% or 14/271), most of which was self-limited. The complication rate appeared to decrease over time in this cohort, suggesting that lower complication rates could be expected as the techniques become more commonly used.

In a single-institution study of 573 percutaneous ablation procedures from the Mayo Clinic between 2000 and 2010, including 254 percutaneous RFAs and 311 PCAs, the overall complication rate was 11% of which slightly more than half (38/66) were Clavien-Dindo Grade 2–4 complications [28]. Complication rates were higher for central tumors and larger tumors and did not significantly differ between CA and RFA. Retroperitoneal bleeding (4.8%) and hematuria (2.6%) were the most common complications with cryoablation and were managed with angiographic embolization or red blood cell transfusion. Bleeding complications were associated with advanced patient age, increased tumor size, number of probes, and central location of the tumor. They may be due to a transient coagulopathy which occurs during the CA process. Rare complications following CA include pulmonary embolus (1%), nerve injury (0.6%), infection (0.6%), pneumothorax (0.3%), skin freezing (0.3%), and seeding of the cryoprobe tract (0.3%).

The most common complication with RFA was nerve injury (3.9%), including pain, paresthesia or numbness to the genitofemoral nerve, intercostal or lumbar nerve distributions. In these cases, the ablation zone extended into the body wall or psoas muscle. Most patients had resolution of nerve deficits within 6 months. Ureteropelvic junction strictures developed in 2% of patients. Bleeding complications are less common with RFA (1.2%), possibly due to coagulation associated with RFA. Less common reported complications following RFA include urine leak (0.4%), abscess (0.4%), and pneumothorax (0.4%).

As groups have gained experience with percutaneous ablation techniques, strategies to avoid complications have been suggested, including prophylactic transfusion for patients at risk of anemia with blood loss and use of CA rather than RFA for tumors near the ureter. Additionally, injecting fluid around the psoas or body wall may decrease the risk of nerve injury associated with RFA.

Tsivian et al. compared complication rates between PCA (n = 123) and LCA (n = 72) and found that the overall complication rate trended higher for PCA (21.1% versus 13.9%, p = 0.253) [29]. While the overall number of complications was higher, the number of severe complications was smaller (Clavien Grade 3–4; 0.8% versus 8.3%; $p = 0.011$) and it was instead mild complications (Clavien Grade1–2) that were more numerous in the percutaneous group (20.3% versus 5.6%; $p = 0.001$). Still, the surgical approach (percutaneous versus laparoscopic) was not a significant predictor of complications on multivariate analysis ($p = 0.941$). Similar complication rates have been reported for PCA by other groups as well, but with smaller cohorts [8,10,11].

A separate retrospective chart review determined the complications associated with PCA in treatment settings when the cryoprobe ice ball was in contact with or overlapped the renal sinus [30]. In this study, 67 centrally located tumors underwent PCA with ice ball progression either abutting or overlapping the renal sinus in all cases. There were no collecting system injuries, urine leaks or hemorrhagic complications. The authors did report a single hemorrhagic complication that occurred in the PCA of a noncentrally located tumor. Mean follow-up was short at approximately 9 months.

Overall, both PCA and RFA appear to have a low complication rate, particularly for major complications.

Preservation of renal function

Another potential advantage of ablative therapies is improved renal functional preservation compared to surgical approaches because of the avoidance of ischemia and preservation of normal renal parenchyma. In general, most series report that renal function remains essentially unchanged following CA or RFA [10,31,32], even up to several years after treatment [33].

Despite studies showing few differences in cohort estimated glomerular filtration rate (eGFR) after ablation of renal masses, there is likely a small subset of patients who will develop clinically significant chronic kidney disease (CKD) after renal tumor ablation. In a retrospective cohort review of 62 patients undergoing LCA and PCA for small renal masses, 11% (4/45) of patients developed "*de novo*" stage III CKD (eGFR <60 mL/min/1.73 m^2) at a mean of 11.4 months post ablation [34]. In this population, the patients who developed new CKD had significantly lower preoperative eGFR (71 versus 98.4 mL/min/1.73 m^2, $p = 0.03$) and larger tumors (2.94 versus 2.19 cm, $p = 0.04$). There is also a minority of patients who will develop CKD following RFA, although when compared to RN or PN, significantly more patients who were treated with RFA (laparoscopic or percutaneous) maintain an eGFR greater than 60 mL/min for at least 3 years (95% for RFA versus 71% and 40% for PN and RN, respectively) [35]. Maintenance of eGFR greater than 60 mL/min/1.73 m^2 is important clinically as GFR less than 60 mL/min/1.73 m^2 equates to stage 3 CKD which is known to increase the risk of hospitalization, cardiovascular events, and death [36].

When either PCA or PRFA is used in patients with preexisting CKD (pretreatment eGFR <60 mL/min) there appears to be minimal change in renal function, regardless of ablation technique, for at least 1 year following ablation [37,38]. A recent retrospective cohort of 48 patients with CKD (eGFR <60 mL/min/1.73 m^2) undergoing thermal ablation (22 PCA, 26 PRFA) showed statistically unchanged eGFR at 1 month and 12 months post ablation [38]. In subgroup analysis for the 18 PCA patients followed for 12 months, there was no difference between mean baseline eGFR and eGFR at 12 months (42.1 versus 44.4 mL/min/1.73 m^2, $p = 0.19$). Similarly for the patients who had PRFA, there was no difference in eGFR at 12 months post ablation (40.4 versus 37.8 mL/min/1.73 m^2, $p = 0.09$). A subgroup analysis of patients with ablated tumors larger than 4 cm also showed no significant change in eGFR compared to preablation levels.

Length of hospital stay and postoperative convalescence

Some of the most appealing aspects of percutaneous ablation to patients are shorter hospital stay, less postoperative pain, and a more rapid recovery. In a retrospective study comparing LCA ($n = 58$), PCA ($n = 20$) and PRFA ($n = 15$) [11], PCA showed statistically significant improvement in mean length of hospital stay of 1.1 versus 2.5 days ($p = 0.007$), mean time to return to nonstrenuous activities of 3.1 versus 8.1 days ($p = 0.007$), and mean return to complete recovery of 13.5 versus 27.5 days ($p = 0.05$) compared to LCA. There was also a nonsignificant trend toward lower median opioid usage (5 versus 19 mg morphine equivalents) for PCA compared to LCA. PRFA showed improvements in return to nonstrenuous activities (2.9 versus 8.1 days; $p = 0.009$), return to strenuous activity (10.5 versus 22.1 days,

$p = 0.007$), and return to work (4.0 versus 17.5 days, $p = 0.05$). There was no difference in convalescence parameters between PCA and PRFA. These cohorts were well matched, except that mean renal mass size was slightly larger for the LCA patients compared to PCA or PRFA patients (2.2 versus 2.6 cm), and for PCA required more cryoprobes on average (1.5 versus 1.1, $p = 0.04$). Other studies show an even greater advantage in shorter length of hospital stay for percutaneous ablation when the ablation is done under local anesthesia, avoiding a general anesthestic [10].

Cost-effectiveness

Because of shorter hospital stay, percutaneous ablation techniques have the potential to impart significant cost savings compared to open or laparoscopic surgical procedures. In contrast, adoption of new medical technologies can be associated with higher costs of healthcare delivery. Several groups have performed cost-analysis studies, demonstrating a significant net saving in percutaneous ablation of renal masses by either CA or RFA.

Using a model based on cost estimates from 317 actual cases, Link et al. studied perioperative costs for treatment of a small renal mass by open PN, laparoscopic PN, LCA, and PCA [39]. Total costs were $8264, $6734, $6743, and $3109, respectively. Anesthesia costs, CT usage, operative time, consumables, hospitalization, transfusion expenses, CT scanner fees, and biopsy costs were factored into the model. PCA was approximately 38–46% the cost of other modalities, with a potential cost saving of $3625–5155 per ablation. More than 70% of the cost of PCA was attributable to cryoprobe consumables, while approximately 70% of the cost of the other treatment modalities was attributable to hospitalization and operative time expenses.

Another single-institution cohort study compared 23 LCA with 13 PCA [40]. All LCA were performed by surgeons and all PCA were performed by a single interventional radiologist. This group calculated the total costs and those associated with anesthesia, operating room (OR), hospital admission, surgeon charges, radiologist fees, radiology department fees, disposables, and pathology laboratory fees. Median cost of PCA was only 23% of the cost for LCA ($6861 versus $29,617), with the bulk of the difference attributable to hospital admission and operating room costs. Only two of the 13 patients undergoing PCA were admitted to the hospital postoperatively. In this study, Medicare information was also assessed and LCA collected a substantially larger amount on average at $14,346 per case while PCA collected only $4134.

Cost analysis comparing PRFA to LRFA, robot-assisted laparoscopic PN and RN found that the median cost for PRFA is 35–48% of the total costs for LRFA, robot-assisted laparoscopic PN, or RN for costs incurred over an initial 6-month treatment period [41]. Another cost analysis showed PRFA to be 57–64% the cost of open PN or LPN [42]. The significant cost saving for PRFA is also largely due to lower operating room fees and shorter hospital stay as many percutaneous RFA procedures can be done on an outpatient basis [41, 42]. Imaging fees are consistently higher for ablation techniques but not enough to offset the otherwise significant cost savings.

One limitation to these studies is the lack of information and cost analysis on postoperative complications and potential secondary ablative or surgical procedures or potential costs for long-term surveillance imaging. One Markov decision model was used to analyze the cost-effectiveness of RFA including risk of local recurrence. This study found that RFA was preferred over partial nephrectomy when post-RFA local recurrence was up to a 48% higher annual probability than for partial nephrectomy for a societal willingness-to-pay threshold of $75,000 per quality-adjusted life-year.

Consistently, percutaneous treatment has been found to be more cost-effective than laparoscopic or open approaches, even taking into account a slightly higher rate of local recurrence and possible need for a second percutaneous procedure.

Alternative techniques

High-intensity focused ultrasound, laser interstitial thermotherapy, microwave thermoablation, pulsed cavitational ultrasound, chemoablation, and radiosurgery are all potential percutaneous treatments of renal cell carcinoma but little outcomes information exists on these treatments. Hopefully future work will better define their utility relative to the more established cryo- and radiofrequency ablation.

Conclusion

Despite more than 15 years since percutaneous ablation for renal masses was originally reported, the overall quality of evidence is poor and consists almost exclusively of single-arm observational case reports or series. Most of these studies are marred with methodological flaws such as low patient numbers, selection bias, limited duration, and incomplete follow-up [43]. Notwithstanding the lack of robust data, the last decade has seen a considerable increase in the adoption of renal ablative techniques and the number of studies published about these therapies. Though of low quality, available evidence is encouraging for properly selected patients, especially those with high surgical risk with small renal masses. There is a clear need for randomized, prospective trials comparing ablative and surgical modalities, but these studies have not yet been done. Despite this, percutaneous ablation has been established as an effective treatment for small renal masses with a favorable complication profile and relative low cost.

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CHAPTER 24

Patient Selection and Informed Consent

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Introduction

The diagnosis of renal cell carcinoma (RCC) has increased over the last two decades, not only due to an increased incidence of the disease but also secondary to the widespread use of abdominal imaging [1–4]. This change in practice has led to earlier detection of RCC, which is now commonly diagnosed when it is small and localized [5]. Partial nephrectomy is regarded as the standard treatment for clinical T1 renal masses in current guidelines [6,7]. Long-term oncological outcomes are equivalent to radical nephrectomy, with the advantage of improved renal function preservation [8]. Radical nephrectomy is also classified as standard, though it should be mainly considered in tumors not amenable for nephron-sparing surgery [6,7]. Nevertheless, partial or radical nephrectomy may not be suitable for all patients.

Percutaneous ablation may be a reasonable option for patients in whom a major surgical procedure is undesirable or contraindicated. Potential advantages of percutaneous ablation include its low invasiveness, short procedural and recovery time, low complication rate, short hospital stay, maximal renal function preservation, and lower costs in comparison to surgical resection. Cryoablation and radiofrequency ablation (RFA) are the modalities of percutaneous ablation most studied in the clinical setting [7]. Other techniques of renal tumor ablation, such as high-intensity focused ultrasound (HIFU), laser interstitial thermotherapy, microwave thermotherapy, and chemoablation are not yet widely available. They are mostly under protocol investigation or in preclinical phases [5]. Because renal ablation does not involve tumor excision, a strict follow-up protocol is crucial for these patients, in order to detect prematurely any eventual recurrence [9].

Patient selection

Reported indications for ablative techniques include incidental small cortical masses in the elderly, patients who have hereditary syndromes with an increased risk of developing multifocal tumors, patients with a solitary kidney, patients with chronic kidney disease (CKD), and patients who do not want to undergo a major surgery. However, percutaneous ablation is not suitable for all renal masses. Tumors most amenable for percutaneous ablation are small and located in the posterior cortex. Tumors larger than 3 cm or located in the hilum, close to the ureter or the central collecting system are generally less suitable for percutaneous ablation. Clinical instability and irreversible coagulopathies are absolute contraindications to the procedure. Some of the most common indications for percutaneous ablation are discussed below.

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

High surgical risk

Patients with a clinical T1a renal mass (preferably <3 cm) who have a poor surgical and/or anesthetic risk profile constitute the major group for whom percutaneous ablation should be considered [10]. The low morbidity of percutaneous ablation and the outpatient nature of this procedure make it an interesting option for these patients. However, the current American Urological Association's guideline for management of the clinical T1 renal mass still considers partial or radical nephrectomy as the standard treatment even for high surgical risk patients due to concerns with a possible increased risk of recurrence with ablative techniques. According to the guideline, active surveillance is also an acceptable recommendation and should be offered to high-risk patients. Some authors disagree and believe that active surveillance and ablation should be regarded as the standard in this subset of patients [11]. In our opinion, this should be thoroughly discussed with the patient, who should be encouraged to actively participate in the decision process. The best approach will depend on whether the patient prefers to assume a greater risk of morbidity/mortality to have a higher chance of cure with surgery or an increased risk of cancer recurrence, but with lower morbidity. This is discussed further ahead in the section on informed consent below.

Solitary kidney

Solitary kidney is the classic example of an imperative indication for a nephron-sparing approach in order to avoid dialysis. Partial nephrectomy is still the preferred approach for such cases due to the more established oncological control associated with satisfactory functional outcomes. However, ablative therapy has also been reported and it provides renal function preservation at least as good, if not better than partial nephrectomy [12].

Chronic kidney disease

Similar to what happens with patients with a solitary kidney, it is imperative to maximize renal function preservation of patients who have CKD, to avoid deterioration to end-stage kidney disease.

Multiple tumors in patients with hereditary syndromes

Percutaneous ablation may be indicated for patients with familial syndromes who are at high risk of developing multiple tumors over time, such as those patients with von Hippel–Lindau (VHL), Birt–Hogg–Dubé and hereditary leiomyomatosis and papillary renal cell carcinoma syndromes. Up to 40% of patients with VHL will develop ipsilateral or bilateral multifocal renal tumors at a young age. Chronic renal failure and metastasis are among the major causes of death in these patients [13]. The management of VHL can be challenging, as a delicate balance must be achieved between the avoidance of tumor progression and the prevention of end-stage renal disease. With promising oncological outcomes and minimal surgical trauma, percutaneous ablation techniques might be an attractive treatment option for VHL patients [13–17].

Refusal of major surgery

Occasionally, no matter how well informed about the most recommended practices, some young and healthy patients may still refuse a major surgical procedure. In general, but particularly in such cases, it is important for the physician to certify that the patient understood well all the available treatment options and that the patient is fully capable of making such decision. Due to the possibility of a relatively less complex procedure, with a typical same-day discharge, some of these patients might still consider active treatment with percutaneous ablation. Most percutaneous ablation procedures are done under sedation with local anesthesia, which can be another attractive feature for these patients. Active surveillance is also an option for patients who reject surgery.

Previous kidney surgery

Patients who have had previous nephron-sparing surgery or any operation in the same kidney affected by the tumor may have an increased risk of complications during repeat partial nephrectomy, due to the distortion of the anatomy caused by scarring and adhesions [18]. In such cases, percutaneous ablation may be a valid option.

Informed consent

The informed consent process has been definitively incorporated into the medical routine. Though it can often be time-consuming, it is a practice of the utmost importance for the protection of patients, healthcare professionals, and hospitals. Informed consent should not be considered as a mere formality. Instead, it must be perceived as a communication process in which the patient receives a comprehensive explanation about his or her condition, treatment options and available alternatives, as well as risks and possible complications.

The informed consent document should be handed to the patient as early as the visit when the procedure is planned or scheduled, which should be done well in advance before the actual date. This is important to give the patient time to reflect about and assimilate the information newly received, ask additional questions that may arise during this period, and get all the information he/she wants from different sources. At the end of this process, the patient will likely feel much more comfortable with his/her final decision and then can be considered fully informed. During this period, the physician should document all discussions and information provided in the patient's chart. For legal purposes, the documentation of the whole information process is more valuable than the signed piece of paper itself. A simple signature collected just before the procedure does not prove that the informed consent process was adequately followed and may have its validity questioned [19].

The informed consent process must consider the patient's circumstances, capacity, and concerns, such as their level of understanding, impairment or disability, as well as their cultural and language characteristics. Some of the most important points to communicate to the patient are:

- nature and severity of the patient's condition
- what the proposed treatment entails
- who will be the responsible for the procedure
- anticipated risks and benefits, including the odds that the benefit may not be accomplished
- common side-effects and potential long-term physical, mental, emotional, social, sexual or other outcome which may be affected by the planned procedure
- the level of doubt regarding the diagnosis and outcomes
- whether the procedure is experimental or not
- if applicable, the estimation of costs associated with the procedure
- their right to refuse treatment, and withdraw their consent at any time
- alternative options, as well as the expected outcome of not having any treatment at all.

In order to be considered capable of giving valid consent, the patient must be able to:

- understand the information received, which includes risks and benefits of the procedure and its alternatives, as well as the possible consequences of his/her decision
- retain that information
- make a judgment based on that information
- communicate the decision clearly.

If the patient is considered not capable of making a decision, it may be appropriate to have input from other professionals, such as a psychiatrist. Eventually, obtaining a legal opinion may be required. Even though the informed consent process may seem burdensome, it is much simpler than facing a lawsuit [19].

Although percutaneous ablation is a less invasive procedure than partial or radical nephrectomy, it is not free of complications. Obviously, it is not possible to mention in the informed consent all the possible complications that may occur following any specific procedure. However, it is common sense that the most frequent complications should be clearly stated. Serious and life-threatening complications should also be discussed and included in the consent form. Although rare, such complications are more likely to cause litigious issues [19]. Recently, Atwell et al. evaluated complications after 573 percutaneous RFA (44%) and cryoablation (56%) procedures done over a period of 10 years, in a large retrospective study [20]. They observed a complication rate of 9.8% and 13.2% for RFA and cryoablation, respectively. Larger size and central location were associated with higher complication rates ($p < 0.001$ for both). The chance of a complication increased by a factor of 1.5 for each 1 cm increase in size. The odds of a complication increased by a factor of 2.4 for central tumors compared to peripheral tumors. The grade, as assessed by the Clavien-Dindo classification, was 1 in 52% and 37%, 2 in 12% and 24%, 3 in 36% and 32%, and 4 in 0% and 7% of the complications occurred in the RFA and cryoablation groups, respectively. The most common complications related to cryoablation were hemorrhage/anemia and hematuria. In the RFA group, the most frequent complications were urinary tract and nerve injuries, mostly manifested as transient paresthesia or pain.

There is no predefined period during which consent continues to be valid. If there is no change in the patient's circumstances, it remains valid until the patient withdraws consent. Changes may include improvement or worsening of the patient's condition, novel treatment options after the time when the consent was signed, or any review of the treatment's goals, due to changes on the disease stage.

Informed consent for research

The use of percutaneous ablation for the treatment of renal tumors is relatively recent if compared to more established techniques, such as partial and radical nephrectomy. Although cryoablation and RFA are already widely known for the treatment of renal masses, other modalities such as HIFU, microwave thermotherapy, and laser interstitial thermotherapy are mainly under evaluation for the same purpose. Whenever a treatment is under protocol investigation, it obviously needs to be first evaluated and approved by an institutional review board (IRB), which reviews both the research protocol and the specific consent form to be used in the research.

Generally, the consent form used for research purposes follows the same principles previously described. However, there are additional aspects that must be included in research-related consent forms. The patient must receive clear information in plain language about the reasons why the specific research is being performed, why the patient was invited to participate, potential benefits and risks associated with the research treatments, and the planned follow-up visits. Similarly, the research informed consent must be discussed well in advance before the treatment protocol starts. The patient must understand his/her guaranteed right to withdraw from the research at any time and still have the option to receive standard treatment. Although all IRBs in the United States are regulated by the Food and Drug Administration and Department of Health and Human Services, each institution may have specific requirements in its application process.

Recently, Brehaut et al. evaluated objectively the informed consent documents of 139 trials registered in ClinicalTrials.gov, obtained from study investigators [21]. Using the International Patient Decision Aids Standards (IPDAS), a set of empirically derived, consensus-based standards for good decision making, they concluded that existing informed consent documents do not meet validated standards for encouraging good decision making. Specifically, they identified that consent documents could be greatly improved regarding how to present outcome probabilities, clarifying and expressing values, structured guidance, and using evidence [21]. In order to assess comprehension of study information and satisfaction, Enama et al. randomized 111 subjects to one of two IRB-approved consents: either a standard or a concise form, which had 63% fewer words on average. All other features of the consent process were similar. They concluded that there are no significant differences in study comprehension or satisfaction whether using a standard or a concise consent form [22]. Simplifying the whole consent process, while still keeping its main characteristics and acceptable standards, might be helpful to maintain adherence to recommended practices and to minimize risks of protocol violations.

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CHAPTER 25

Instrumentation and Technique: Cryotherapy

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Introduction

Over the last several decades, the widespread use of abdominal imaging has led to a significant increase in the number of incidentally discovered renal cortical neoplasms (RCN) [1–3]. It is estimated that over 64,000 new cases of RCN will be detected in the United States in 2012 [4] and the majority of these will be discovered in the elderly population. However, until the 1990s, the historical standard treatment of all RCNs was the open radical nephrectomy. In 1990, Clayman and colleagues performed the first laparoscopic radical nephrectomy (LN) followed by the first laparoscopic partial nephrectomy (LPN) by Howard Winfield in 1992. Soon thereafter, numerous authors reported immediate advantages such as reduced intraoperative blood loss, reduced postoperative pain, shortened hospital stay, and an expedited convalescence which resulted in the acceptance of renal laparoscopy.

More recently, the long-term sequelae of radical nephrectomy, including renal insufficiency, negative cardiovascular effects, and shorter overall survival, have become evident [5–8]. The detrimental effects of diminished renal function support the importance of preserving nephrons if feasible to optimize patients' long-term outcomes. The excellent oncological outcome of partial nephrectomy in selected patients and an improved understanding of tumor biology led to a shift to nephron-sparing surgery. As a result, the American Urological Association (AUA) released new guidelines for the treatment of RCN in 2009. These guidelines proclaimed partial nephrectomy as the gold standard for all T1 (≤7 cm) masses, when surgically feasible [9].

In the last decade, ablative therapies such as cryoablation (laparoscopically and percutaneously) and radiofrequency ablation have begun to gain traction as nephron-sparing alternatives to partial nephrectomy. While various other ablative therapies such as microwave therapy, interstitial laser therapy, and high-intensity focused ultrasound do exist, they are currently considered experimental and are still under investigation for efficacy and safety.

Herein we will focus on the details of cryoablation including patient selection, informed consent, preoperative preparation, patient positioning, intraoperative step-by-step technique, trouble-shooting, and postoperative follow-up.

Patient selection

The small renal mass dilemma

Prior to the AUA guidelines, in 2008, Kunkle and coworkers first coined the phrase "the small renal mass dilemma." The authors were referring to the confusing array of treatment options available for small RCNs [10].

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

As the number of incidentally discovered RCNs increased, so did the number of treatment options available to the patient such as partial and radical nephrectomy (open, laparoscopic, robotic), ablative therapies, and active surveillance (AS). The wide array of available options and the limited available data significantly complicated the decision-making process for both the physician and the patient.

Recent publications of large intermediate-term AS series helped to define the natural course of RCNs. Rosales and coworkers demonstrated in the largest worldwide single-center AS series that most small renal masses grow slowly (0.27 cm/year) and show a low metastatic rate of 1.9% (4/212 patients) [11]. Likewise, in a recent review Graversen and colleagues showed a similar growth rate of 0.31 cm/year, a metastatic potential of 1.4% (12/874 patients), and a cancer-specific mortality of 0.34% [12]. These findings were supported by several smaller series with comparable annual growth rates of 0.3 cm/year and an equally low metastatic potential [13–17]. Furthermore, a higher growth rate seems to be related to a higher tumor grade and an increased risk of metastatic progression. These findings were supported by Rosales and colleagues whose data indicated that tumors with a more aggressive pathology presented a almost two-fold increased growth rate compared to the average small RCN (sRCN) [11]. Additionally, 20% of the sRCN show a benign pathology with a further 50–60% depicting only low-grade features [9,18–20].

Indications and contraindications for percutaneous cryotherapy

Currently, nephron-sparing extirpative surgery remains the gold standard for all T1a and T1b tumors. However, partial nephrectomy remains associated with a significant morbidity, and is therefore not suitable for the elderly or patients with poor health. Herein lies an essential issue, as it is the patient with significant comorbidities who is at higher risk for complications from invasive surgery but who will still require a form of active treatment for their renal mass that is the ideal candidate for ablative therapy.

Ablative techniques such as cryoablation and radiofrequency ablation (RFA) become attractive alternatives in these patients due to the decreased invasiveness and morbidity [21]. In addition, recent promising long-term data and improvements in technique and instrumentation have made ablative cryotherapy available to younger, healthier and well-informed patients, who wish to avoid the risks and the extended convalescence associated with extirpative renal surgery.

The biggest challenge for a successful ablative treatment is tumor size. Atwell and coworkers described their experience of percutaneous cryoablation (PCA) and lesions >3 cm [22]. In this series, the mean tumor size was 4.2 cm (range 3.0–7.2 cm) and technical success was achieved in 95% of the procedures. They described only one Grade 3 adverse event in this series. However, in a recent retrospective analysis for laparoscopic cryoablation (LCA), Lehman and colleagues reported a greater complication rate (0% versus 62%) and a longer hospital stay (1.65 versus 3.52 days) by stratifying RCN into small (<3 cm) and large (>3 cm) lesions [23].

Finally, in our experience percutaneous cryoablation is a poor treatment modality for tumors >3 cm due to higher local recurrence rates and higher complication rates, and should only be offered to patients with posterior located renal masses.

Informed consent

Informed consent is a mandatory component of any conversation between a physician and patient when discussing any type of invasive or noninvasive treatment strategy. The consent should be based on a complete disclosure of relevant facts needed to make the decision intelligently and includes alternatives, risks, and benefits. Alternatives pertaining to consent for percutaneous cryoablation include active surveillance, alternative ablative therapies such as radiofrequency ablation, and extirpative approaches. The discussion of extirpative approaches should include both laparoscopic and open approaches as well as partial and radical options. The risks and benefits of each option should be extensively discussed with the patient.

Preoperative patient preparation

Patients who are considering percutaneous cryoablation should be evaluated by an interdisciplinary team consisting of urologists, interventional radiologists and, in some instances, oncologists. The standard work-up begins with the history and physical examination. Given that percutaneous cryoablation is often an option employed in patients with significant comorbidities, a careful medical evaluation is a vital component of the work-up. A complete medication list including the use of complementary and alternative medications is also essential and the patient should be counseled on the importance of discontinuing any blood-thinning agents sufficiently prior to the procedure. Whenever appropriate, medical consultation to evaluate the patient's candidacy for surgery should be undertaken.

Essential laboratory studies include complete blood count, comprehensive metabolic panel (creatinine, calcium, alkaline phosphatase), coagulation studies (prothrombin time and partial thromboplastin time), and urine culture. High-quality preoperative imaging is vital in the planning process and usually consists of contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI). High-quality imaging is important to optimize treatment and staging. Low-quality imaging has the potential to compromise outcomes. Anatomical considerations to take into account include tumor size and location in relation to the upper or lower pole or the kidney, and the location of the renal hilum and collecting system (especially the ureter). Additionally, the exophytic or endophytic nature of the tumor, cystic or solid nature of the lesion, abnormalities of shape or contour, and degree of enhancement should also be taken into account.

The role of definitive histopathological diagnosis prior to definitive treatment of renal masses is a source of debate. To date, pre-procedure percutaneous biopsy of renal masses has had a limited role, especially when taking into consideration tumor targeting and sampling error which may result in equivocal findings [24]. Due to all of these issues, preprocedural biopsy rarely changed the treatment course when extirpative measures were the only option available. In most situations, cryoablation is a suitable option solely based on high-quality cross-sectional imaging and preprocedural biopsies are rarely indicated. However, renal biopsy is increasingly being performed at the time of ablation in order to strive for definitive diagnosis to help guide follow-up. In cases where the patient's decision to have ablation versus active surveillance or ablation versus extirpation remains equivocal, knowing the histopathology prior to treatment may help guide definitive management. We are increasingly using pretreatment biopsy in our management of small RCNs.

Principles of ablation

In an effort to optimize the efficacy and minimize the complications of ablation, the surgeon should have a comprehensive understanding of the technology being applied. Knowing the benefits and limitations of each energy modality used in ablation can also help determine the exact technology which will suit the patient's needs.

The current cryoablation systems produce tissue destruction by rapid decreases in temperature at the probe tip by taking advantage of the Joule Thompson principle [25,26]. These systems use highly pressured liquid argon which expands into a gaseous state near the tip of the probe across a small orifice. The resulting expansion and phase change cause extreme cooling near the tip of the cryoprobe which induces ice ball formation. Ice ball shape and dimension depend on the probe design and local tissue properties. Contemporary cryoablation technology includes a wide array of probes that have different diameters and are associated with variable sized and shaped ice balls.

There are several mechanisms known to be responsible for tissue destruction with cryoablation. Cryoablation technologies result in rapid tissue cooling with associated extracellular and intracellular ice crystal formation. The ice formation itself causes a massive mechanical disruption of the cell membrane, including extreme changes in ionic composition and pH, followed by microcirculatory failure and protein denaturization. These are the well-recognized primary mechanisms of tissue destruction associated with cryoablation technologies [25]. The local microcirculatory failure causes thrombosis, coagulation necrosis, and apoptosis. Additionally, the decreasing temperature intensifies the extracellular osmotic force, resulting in dehydration and cellular crenation followed by uniform cellular death within the ablated tissue.

A key issue to understanding cryoablation is that the temperature distribution of the ice ball is not homogeneous. Isotherms range from −140°C to −190°C at the tip of the cryoprobe to −3°C at the outer margin of the ice ball [27]. Cellular death generally occurs at temperatures below −20°C, but the tissue death is inconsistent until the temperature falls below −40°C [28]. The temperature gradient within ice balls creates three zones of tissue response to the cryoablation process (Figure 25.1). The most

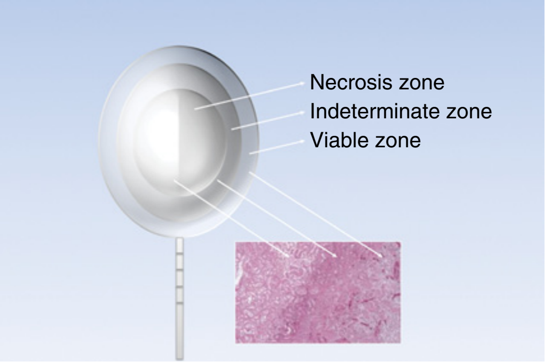

Figure 25.1 Ablation zones.

central portion of the ice ball produces a zone of total necrosis. Total necrosis occurs reliably from the cryoprobe out to where the −40°C isotherm is located. Just outside the zone of necrosis is the intermediate zone which consists of the −40°C to −20°C isotherms. The intermediate zone is characterized by both viable and necrotic elements. Finally, the outer area where isotherms are above −20°C is characterized by mostly viable tissue. As the −20°C isotherm is within 3.1 mm of the outer margin of the ice ball, it is critical to extend the ice ball 1 cm beyond the tumor edge to guarantee a uniform ablation of the renal lesion [29]. After completing the freeze cycle, helium or an RFA heating element is used to actively thaw the probe. Typically, two freeze-and-thaw cycles are employed for each lesion.

Patient positioning

Patients are usually placed in the prone or lateral decubitus position. There are no studies comparing the efficacy of these positions. However, this is where the importance of an interdisciplinary approach is vital. The interventional radiologist and urologist each bring various viewpoints and expertise to the positioning process.

As the patient is only moderately sedated during the procedure, care must be taken to ensure the comfort of the patient with adequate padding. Patient comfort is also important to minimize patient motion during the procedure. Patient movement can prolong the procedure needlessly, and has the potential to cause significant complications.

Instrumentation

- Philips 256-slice Brilliance ICT scanner (Philips Healthcare, Andover, MA)
- 14 gauge BD Angiocath™ (BD, Franklin Lakes, NJ)
- 18 gauge Temno® II Biopsy Needle (10 or 20 mm sample notch, 9/11/15/20 cm) (Cardinal Health, Dublin, OH)
- Galil Medical Precise Cryoablation Unit (Galil Medical Incorporation, Arden Hills, MN):
  - 17 gauge IceRod Plus (straight/90°)
  - 17 gauge IceBulb (straight/90°)
  - 13 gauge IceEDGE (90°)

Step-by-step technique

In an effort to optimize outcomes, percutaneous cryoablation requires the close collaboration of an interventional radiologist and a urologist. While the interventional radiologist provides expertise in targeting and imaging, the urologist contributes with experience in the treatment of renal malignancies and with hands-on anatomy drawn from surgical experience.

As already mentioned, percutaneous cryoablation is recommended for posterior located masses that can be easily approached from the posterolateral flank. The treatment of tumors located in a more anterior position will often require traversing a significant amount of renal parenchyma. The loss of the additional renal tissue is inadvisable.

One hour prior to surgery, a single dose of cefazolin calculated by patient weight is administered. Due to the minimally invasive nature of percutaneous cryoablation, we perform the operation under conscious sedation with local anesthesia. Other institutions recommend general anesthesia for better respiration control and patient comfort.

After the patient is positioned in a prone position on a CT or a MRI scanner, a preliminary scan is performed. Using the data from the initial scan, a percutaneous marker is deployed on the expected primary access site, and the location of this site relative to the tumor is confirmed with a second noncontrast scan. The new study images are then compared to the preoperatively obtained contrast images. If tumor borders cannot be clearly delineated, a repeat CT scan with half bolus of intravenous contrast can be performed to accurately identify deep and lateral margins of the tumor.

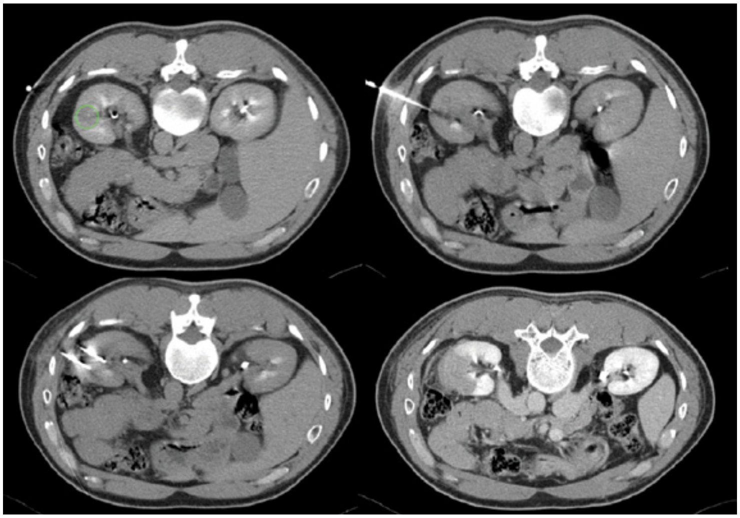

Figure 25.2 Different steps of cryoablation. (*Top left*) Target lesion. (*Top right*) Kidney biopsy. (*Bottom left*) Cryo-needle positioning. (*Bottom right*) Postablation image.

For needle positioning, the probes should pass percutaneously and enter the mass at a perpendicular angle whenever possible. Cryoablation probes as a rule do not ablate beyond the tip of the probe, as the ablation zone extends laterally. As such, the probes should be positioned 5 mm beyond the deepest margin of the tumor when possible to prevent inadequate ablation (Figure 25.2). Tangential probe deployment is feasible, but makes accurate targeting of the lesion more challenging in our experience. Therefore, the accurate skin entry point and tract should be established prior to probe placement.

A 14 gauge BD Angiocath is used for establishing the correct angle of deployment for tumor access. Once the Angiocath is directed properly, a biopsy needle is placed through it and advanced into the tumor under image guidance. Several core biopsies of the mass are performed using an 18 gauge Temno II Biopsy Needle (10 or 20 mm sample notch, 9/11/15/20 cm). We perform biopsies and then have cytology performed by a pathology team in order to confirm that neoplastic tissue has been successfully obtained. After confirming successful biopsy, the first cryoprobe is deployed through the same Angiocath.

The number and configuration of cryoprobes deployed are dependent on the patient's tumor characteristics. The majority of tumors are ablated with three IceRod Plus cryoablation probes deployed in an equilateral triangle configuration approximately 1–1.5 cm apart. Smaller tumors (<1.5 cm) are occasionally ablated with a single needle. In these cases, we often use the 13 gauge IceEDGE which has a slightly larger diameter and larger ablative capacity. For very endophytic tumors, we deploy IceBulb probes which have a short ablation zone, and can be used to avoid damage to the renal parenchyma being traversed. The IceBulb is also useful for very thin patients when damage to the body wall is a concern.

In cystic masses, the probes are positioned within the lesion's outer margin in order to assure both a central overlap of the ice balls and a marginal ablation. In contrary to our technique with solid masses, the probes are placed beyond the outer edge of the mass, avoiding spillage of cyst fluid. In these cases, we do often defer biopsy as the tissue yield is rather poor. If there is a significant solid component to the cystic mass (e.g. Bosniak IV cyst), a biopsy is sometimes considered.

Probe placement should take place only one probe at a time, in order to avoid confusion and guarantee accurate placement. After precise deployment of cryoablation probes, we perform an active freeze. The freeze cycle is continued until the ice ball extends beyond the tumor in all dimensions as seen on a noncontrast CT scan. After the first freeze cycle, we perform an active thaw for 5 min and then activate a second freeze cycle. Typically, the second freeze cycle is much shorter as the heatsink effect of vessels is very much diminished. After the second freeze, we perform an active thaw just long enough to allow for atraumatic removal of the cryoablation probes. With the probes removed, the ice ball is allowed to passively thaw. Approximately 10–15 min after the probes have been removed, the ice ball has typically completely melted. We then perform a half contrast dose-enhanced CT scan to confirm that the area of the tumor and a surrounding margin of normal tissue have been ablated. The CT scan is performed approximately 60 sec after contrast injection to optimize parenchymal assessment (see Figure 25.2). If there is any evidence of residual enhancement within the lesion or near the margin, we deploy additional cryoablation probes prior to terminating the procedure and repeat the same dual-freeze technique.

Management of complications

Generally, complications with percutaneous cryotherapy are less common compared to laparoscopic cryotherapy and to extirpative nephron-sparing modalities. While rare, the most frequent complication during or after percutaneous cryotherapy is ice ball fracture and resulting bleeding. The bleeding event is mostly managed conservatively with observation and transfusion. In case of bleeding persistence, selective embolization is typically the first technique employed to control the bleeding. Open or laparoscopic exploration would be considered if embolization were to fail. However, this has never been required in our experience to date.

An extremely rare complication of percutaneous ablation is urine leakage as a result of the involvement of the collecting system [30–33]. The intrarenal collecting system is very resilient to cryoablation. Indeed, the urothelium has been shown to normalize after cryoablation within just a few days [34]. While the intrarenal collecting system does respond well to cryoablation, the renal pelvis and ureter do not and will scar and stenose if ablated. As such, it is imperative to avoid cryoablation of the renal pelvis (outside the renal parenchyma) and the ureter during any ablation procedure.

Another uncommon complication of percutaneous cryoablation is skin or nerve damage. Despite reaching freezing temperatures, the skin and subcutaneous tissues rarely experience damage. In patients with microvascular compromise (e.g. peripheral vascular disease, diabetes mellitus, etc.), care should be taken to avoid extensive freezing of the skin. Occasionally, the cryoablation process results in cutaneous nerve injury. The vast majority of these are short-lived and self-resolving, but they can cause the patient significant discomfort due to anesthesia, paresthesia, or pain in the distribution of the affected cutaneous nerves.

Postoperative follow-up

In current percutaneous cryoablation practice, most patients are admitted for overnight observation and laboratory evaluation. Laboratory tests are conducted immediately post procedure in the recovery room as well as on the morning of postoperative day 1. They include complete blood counts (CBC) and comprehensive metabolic panel. Some patients are treated as outpatients. If the procedure is uncomplicated and little or no hematoma is noted around the kidney, we will perform laboratory evaluation with a CBC after the procedure. If the patient is feeling well 3 h later and a repeat CBC shows no evidence of bleeding, we consider discharge of patients who live in the region of our facility. Patients who travel are all observed overnight to assure that they do not experience any problems. After discharge, we contact patients 1 week later to inquire about their condition and to share the histopathology results of the biopsy. Patients are seen for evaluation approximately 4–6 weeks after the procedure. Repeat contrast-enhanced imaging is performed 3 months after the procedure for evidence of residual tumor. Any degree of enhancement in the ablation zone should be considered an incomplete ablation. The converse is true and an ablation zone that does not demonstrate enhancement likely does not contain viable tumor [35]. Residual tumor or recurrence is rare. When it does occur, there are several options available, including immediate retreatment with partial nephrectomy or repeat ablation, or even continued observation.

It is of paramount importance to distinguish between ablation zone enhancement and persistence of viable tumor within the lesion. There are several causes of enhancement, such as inflammation and increased metabolic activity among tumor cells during the ablation [36,37]. Hegarty and coworkers showed a decrease of peripheral enhancement of more than 20% during 3-month follow-up imaging to less than 5% at 1-year follow-up for LCA [38]. In our experience, it is typical to distinguish an incomplete ablation from peripheral enhancement by careful evaluation of the pre- and postprocedure images. As such, we believe that a 3-month evaluation is of great value.

Our current practice for a patient with *bona fide* enhancement on the 3-month postoperative imaging is surveillance. We recommend a repeated CT or MRI scan every 3–6 months until the lesion has declared itself to be completely ablated or a failure. If complete ablation results, the patient is put on a standard surveillance protocol.

In patients with persistent enhancement beyond 1 year or a significant, more peculiar-appearing lesion during observation, we highly recommend repeat ablation or a laparoscopic/robotic partial nephrectomy.

Conclusion

Renal percutaneous cryotherapy is an emerging technique that provides a true minimally invasive approach to therapy for renal masses. The procedure is well tolerated even under mild sedation with limited complications. In conjunction with a knowledgeable interventional radiologist, excellent oncological outcomes can be attained. Long-term multiinstitutional studies are needed to provide definitive outcomes and ideal follow-up protocols.

Disclosure

Dr Landman is primary investigator for the TRACE registry sponsored by Galil Medical Inc.

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26

CHAPTER 26

Instrumentation and Technique: Hyperthermal Ablation: Radiofrequency and Microwave Ablation

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Introduction

Due to the routine use of ultrasound for screening and the advent of precise imaging modalities such as computed tomography (CT) scans and magnetic resonance imaging (MRI), the detection of small renal masses (SRM) has increased [1]. Radical nephrectomy, the traditional treatment for renal malignancies, would be an overtreatment for these small tumors. Moreover, there is growing evidence in recent studies that documents oncological and functional outcomes in favor of nephron-sparing surgery (NSS) [2,3]. The current American Urological Association (AUA) guidelines recommend NSS for clinical T1 renal masses if feasible [4].

Current literature shows that warm ischemia time (WIT) in nephron-sparing surgery has an inverse relationship with posttreatment renal function. It is in light of the deleterious effect of ischemia employed in NSS that ablation modalities which do not employ ischemia should be considered appropriate first-line treatment for SRM. To date, however, there is still no randomized controlled trial comparing hyperthermal ablation (radiofrequency ablation and microwave ablation) and partial nephrectomy (PN) in the treatment of SRM. Although both treatment modalities have the same indications, present guidelines have relegated hyperthermal ablation as the recommended treatment for patients “unfit” for extirpative surgery. But with the geometric increase in the number of studies attesting to the efficacy of this treatment modality, a paradigm shift in the treatment of SRM is on the horizon.

This chapter will outline the instrumentation and technique of two hyperthermal ablation modalities: radiofrequency ablation (RFA) and microwave ablation (MWA), which have the common goals of complete ablation of tumor, preservation of normal parenchyma, and minimal morbidity.

History

The concept of poking needles into the human body to heal ailments can be traced back to ancient times. The Chinese have reaped the benefits of an elaborate body of knowledge that was charted by their ancestors as they

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

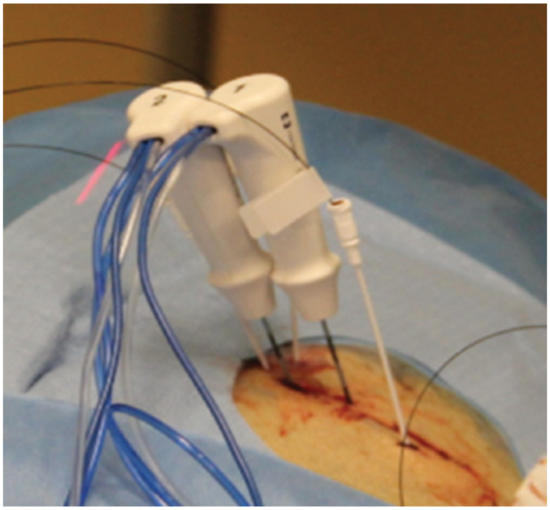

Figure 26.1 Cooltip ablation probes for RFA.

developed the ancient art of acupuncture. Then the development of western medicine from the time of Galen in ancient Greece started putting a premium on what can be seen by the naked eye, hence initiating the scientific drive to pursue what is empirical. From this lineage sprang surgery, evolving from crude and primitive dissection of the human body to refined aseptic modern techniques. The rapid technological advancement in medicine fueled by the lofty goal of eradicating disease through the least invasive means has compelled our scientific journey to come to a full circle. Today needle ablative treatment modalities, which in general utilize a form of therapeutic energy interaction between the needle and the surrounding tissues, are part of our armamentarium to combat a kaleidoscope of diseases (Figure 26.1).

How radiofrequency ablation works (Figure 26.2)

The capability of hyperthermal ablation to eliminate target tumor tissues is dependent on four factors: the power supplied to the probe, the geometry of the probe, the temperature attained during treatment, and the total length of time for which ablation is conducted. The local milieu and tissue characteristics are vital to the ability to achieve sizeable ablation zones. Nonetheless, tumor cell death or ablation is the end result of cellular changes which are dependent on time and temperature. High temperatures in excess of 100°C cause instantaneous cell death by disruption of cellular architecture. Depending on the temperature and time duration, heat induced by hyperthermal ablation can also cause vaporization and carbonization as well as damage to essential cellular structures such as the DNA or RNA. Low temperatures (<45°C), on the other hand, require a greater amount of time (several minutes to hours) to inflict irreversible cellular damage. In *in vitro* studies, Bhowmick and colleagues assessed the efficacy of thermal therapy in both benign and malignant prostate tissues [5,6]. Irreversible thermal injury was achieved at 45°C in 60 min, 55°C in 5 min, and 70°C in 1 min.

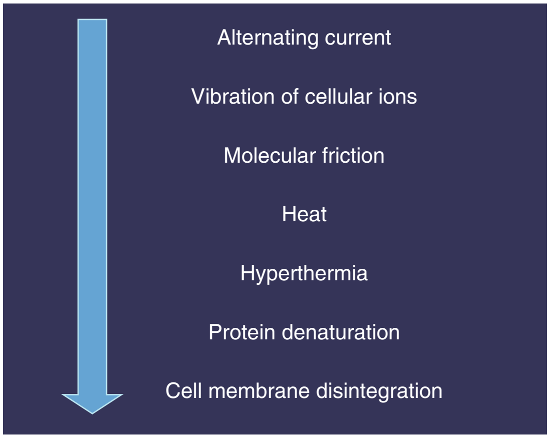

Figure 26.2 Mechanism of hyperthermal ablation.

Lower temperatures induce a gradual infliction of injury by first causing deactivation of enzymes involved in vital cellular functions while maintaining microscopic cellular architectural integrity. This is followed by swelling, blebbing, and finally coagulation necrosis, the deterioration process taking hours to complete. Coagulation necrosis is pathognomonic of cell death via hypoxia and ablation. Its morphological features are basically caused by the denaturation of intracellular protein and autolysis or enzymatic digestion from the body's own immune system. It is due to this protracted process of cellular withering that there are no detectable changes in cells immediately and 1 month after ablative treatment [7,8].

Gross examination of the ablation zone reveals coagulation necrosis in the form of a well-delineated circular blanched and yellowish-tan colored tissue (Figure 26.3). Histology as seen through standard light microscopy is characterized by a hazy nuclear chromatin, increased eosinophilia, hemorrhage, and loss of cellular integrity. Further examination under an electron microscope reveals an almost complete obliteration of the ultrastructural details of the cytoplasmic organelles as well as prominent cytoplasmic granularity [9]. Within a month the cellular changes brought about by the body's reaction to inflammation settle down and the four distinct zones of ablation become grossly and microscopically evident [10,11]: zone 1, carbonization on the point of puncture of the needle; zone 2, area of complete necrosis; zone 3, area of inflammation and hemorrhage or incomplete cell death; zone 4, normal renal parenchyma (Figure 26.4). Within a few months the ablation zone shrinks and eventually fibroses [12].

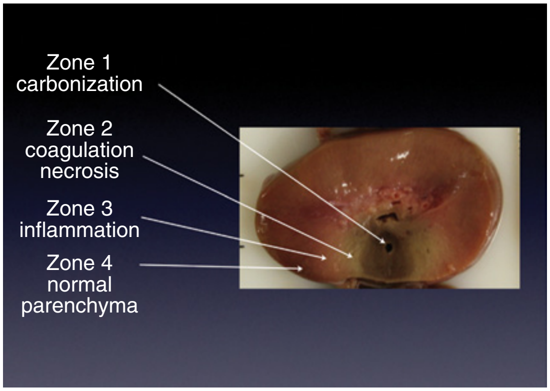

Figure 26.3 Gross specimen of RFA-treated porcine kidney showing necrotic tan-colored central ablation zone surrounded by a dark red zone of thrombosis which is then followed by a flesh-colored zone of edema.

The appropriate method of histological examination of the treatment zone remains a controversial issue. Marcovich and colleagues compared the use of hematoxylin and eosin (H&) staining to that of nicotinamide adenine dinucleotide (NADH) staining in evaluating post -RFA porcine renal tissues [11]. H&E revealed only focal findings with areas of parenchyma that appeared intact. In contrast, there were no skip areas noted in the NADH specimens and the treated sections appeared as well-delineated areas of ablation. Bastide et al. carried out the same experiments in humans [13] using Matlaga's protocol [10]. In a series of 10 patients who underwent RFA and then immediate partial nephrectomy, H&E and NADH staining revealed complete ablation in 50% of the specimens. However, the utility of this information could not be fully realized since postablation biopsy is not routinely recommended.

Radiofrequency blation

The first recorded use of radiofrequency energy in medicine can be traced back to 1960 when Aronow described its use to destroy neural tissues to alleviate

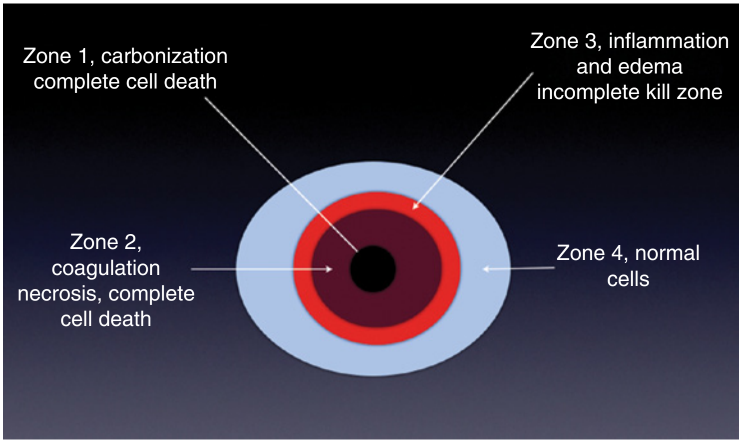

Figure 26.4 Schematic diagram of the zones of ablation. Zone 1, carbonization; Zone 2, coagulation necrosis; Zone 3, inflammation; Zone 4, normal parenchyma.

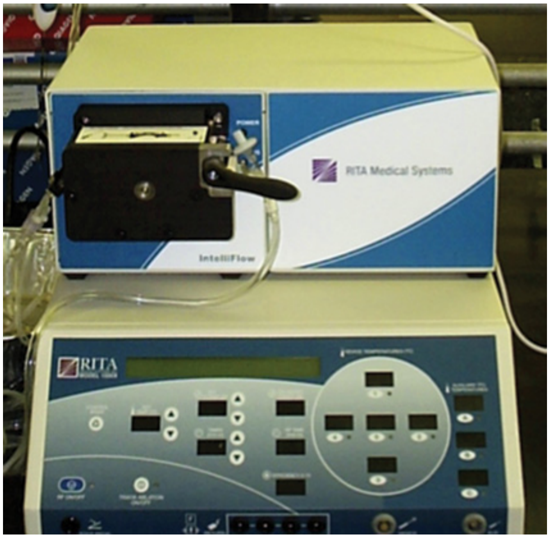

Figure 26.5 RITA Starburst system.

pain [14]. It was not until the 1980s that the use of RFA for treatment of metastatic liver lesions was explored and then finally two decades later Zlotta et al. described the effect of RFA in renal tumors [15,16]. However, it is the study Mcgovern et al. that is credited as the first application of RFA technology with the intent to treat renal cell carcinoma [17]. Since then, numerous studies have been published documenting the feasibility and safety of RFA in treating renal tumors. Hence, the use of RFA in treating SRM has grown exponentially, paralleling the increased utility of NSS for the same indication. In a survey conducted by Bandi et al. examining the general trend of the use of ablative treatment modalities in addressing SRM in academic centers in the United States, the authors discovered that 93% of university-based urologists specializing in minimally invasive treatments employed needle-ablative technology for SRM [18].

Fundamental concepts in radiofrequency ablation

In RFA, a monopolar alternating current with a frequency range of 375–480 kHz and a power of up to 250 W is created in the generator and then delivered to the tumor tissue via insulated monopolar or bipolar probes with a diameter of 1.6–2.5 mm and an effective contact length of 2–5 cm [9]. The current triggers vibration of cellular ions, activating the cascade of molecular friction, heat production, hyperthermia, protein denaturation and finally cell membrane disintegration (see Figure 26.2). Radiant energy from the generator is converted to heat by the tissue impedance to the high current density at the needle surface. Heat therefore does not come from the probe itself but rather is a byproduct resulting from the ions rubbing against each other [19].

Instrumentation

Radiofrequency ablation systems can either be temperature based or impedance based.

Temperature-based systems measure tissue temperature at the tip of the probe only and do not measure the temperature of the surrounding tissues. Their application endpoint is achieving a certain temperature and maintaining it over a specified time period. An example of this system is the radiofrequency interstitial tissue ablation (RITA) system (Angiodynamics, Queensbury, NY) (Figure 26.5). Its 1500 or 1500x radiofrequency generator models are capable of generating power of up to 250 W at frequencies of up to 460 KHz. It delivers a preset power to the probe until the average temperature of the tines located at the probe tips reaches the target temperature. This average temperature is then maintained for a specified time which is dictated by the size of the ablation zone.

Impedance systems measure tissue impedance or the tissue's resistance to the alternating current at the probe tip. A predetermined impedance signifies completion of the ablation cycle. Examples of this system include the Covidien Cooltip™ RFA system (Boulder, CO) (Figure 26.6), Covidien E-series Cooltip™ RFA and the Boston Scientific RF 3000® or LeVeen system (Mansfield, MA) (Figure 26.7). The E-series is not commercially readily available in the United States. The Covidien Cooltip RFA system generates up to 200 W of power at frequencies of up to 480 KHz. It makes use of a sterile chilled water cooling system to prevent carbonization at the probe tip. It also has a switching controller that allows up to three probes or one cluster to be used simultaneously. Its single probe use runs in 12-min cycles while multiple probe deployments are run in 16-min cycles. Both have a safety feature of a 15-sec shut-off after a rise of 30 ohms is

Figure 26.6 Covidien system.

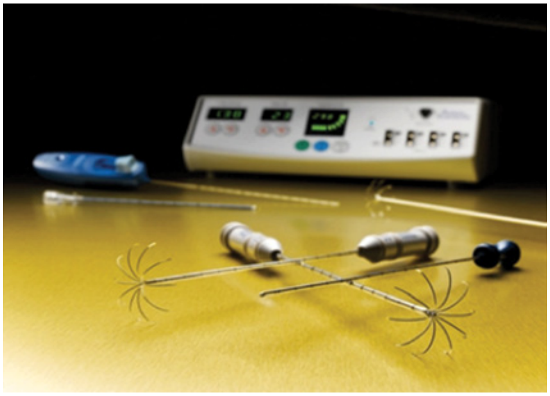

Figure 26.7 Boston Scientific RF 3000 system.

detected from the baseline impedance. However, multiple minopolar probes do not emit RF current simultaneously. At the start of ablation with multiple probes, current is emitted from the first probe until 30 sec have elapsed or the tissue impedance rises 30 ohms above baseline. RF current is then emitted from the second probe under the same conditions. This continues from one probe to the next until the end of treatment. The Boston Scientific RF 3000 or LeVeen system can generate power of up to 200 W at frequencies of up to 460 KHz. The power gradually increases at 10 W per minute until an impedance roll-off is encountered. Its final endpoint is delivering a total power output of 100–130 W.

Another way of classifying RFA devices is differentiating between wet and dry RFA. RFA energy can be delivered with a needle into the tissue directly, a process known as dry RFA. Alternatively, it can be delivered via ionic solutions and this process is called wet RFA [20, 21]. In dry RFA systems, the electrical circuit is established between the probe tip and the grounding pads (Figure 26.8). Thermal heating is intimately concentrated near the needle tip. Due to the narrow electrical streamlines and the high current density in the applicator tip, the highest temperatures are achieved only in areas a few millimeters away from the needle tip. Coagulative necrosis is induced through conduction. In this method, carbonization or charring and vaporization or tissue boiling close to the needle tip increase impedance, thus limiting the zone of ablation. Wet RFA avoids carbonization at the needle tip through constant saline infusion. Pereira et al. documented the larger ablation zones created by perfused and cooled-tip electrodes [22].

Lastly, RFA devices can be differentiated by their probe designs. They can either be single-point probes or umbrella-shaped, multitine electrodes. The RITA and LeVeen systems make use of Christmas tree or multitine electrodes (Figure 26.9). Since it is a temperature-based system, the RITA probe has thermistors embedded in five of the nine electrodes on its probe tip. The Cooltip system makes use of a single-point probe that is intrinsically perfused by chilled saline. It also has a thermocouple that measures the temperature of the probe (Figure 26.10). Pereira's study outlined the differences in these three systems and concluded that the Cooltip system has a larger zone of ablation, the 12-tine probes produce a more spherical lesion and nine-tine electrodes have better reproducibility [22].

Technical considerations

The indications for percutaneous RFA are the same as those for NSS (Box 26.1). As mentioned earlier, it has found a niche as the treatment of choice for patients with SRM who are poor candidates for extirpative surgery. Its popularity stems from the fact that

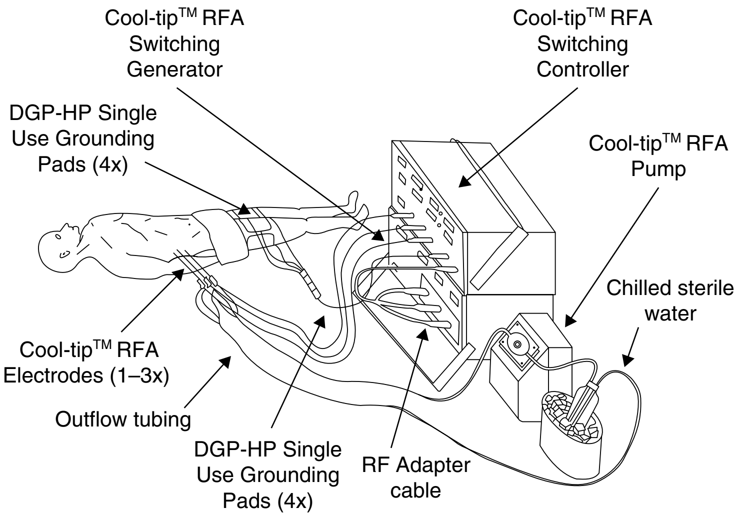

Figure 26.8 Electrical circuit diagram.

Figure 26.9 Multitine electrode.

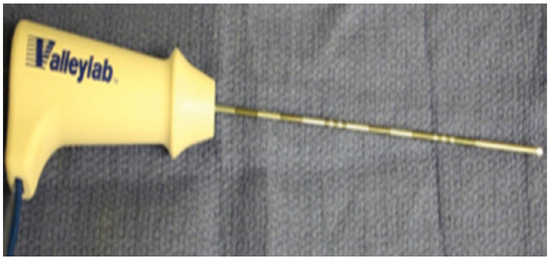

Figure 26.10 Single-point probe.

advancements in medical technology have led to an increase in the population's life span as well as incidental detection of renal masses on routine screening. Because these aging patients with SRM are also saddled with comorbidities, the low invasiveness of RFA makes it second only to the conservative approach of active surveillance in the roster of treatment options. Due largely to the American culture's proactive approach to diseases, RFA has emerged as these patients' preferred treatment.

Percutaneous RFA may also be employed in patients with metastatic disease necessitating only palliative symptom control and avoidance of dialysis. Its use has also been reported in patients with peculiar anatomy, e.g. horseshoe kidneys [22]. Its successful use in the treatment of benign renal masses such as angiomyolipomas has also been studied [23,24]. Gervais et al. noted that tumor size and location are strong predictors of ablation outcome in RFA [25]. Tumors <3 cm achieve complete ablation in just one session whereas, tumors >5 cm in size require repeated cycles to achieve the desired ablation. This observation has been verified by Best et al. in their recent publication demonstrating that RFA provides excellent and durable outcomes in patients with tumors smaller than 3 cm [26]. As for location, percutaneous RFA is best employed in

Box 26.1 Indications and contraindications

Indications

- Bilateral renal tumors
- Multiple tumors in VHL patients
- Solitary kidneys with SRMs
- SRM patients not fit for surgery
- SRM patients with renal impairment
- Patient choice
- Post partial nephrectomy recurrence

Contraindications

A. Absolute contraindication
  Uncontrolled bleeding diathesis

B. Relative contraindications
  1. Patients on anticoagulation
  2. Confounding anatomical factors
     a. pleura open up after positioning
     b. proximity of bowel, ureter or adrenal
     c. cystic tumors
     d. proximity of large vessels
  3. Absence of appropriate imaging
  4. Inexperienced surgeon

SRM, small renal mass; VHL, von Hippel–Lindau.

posteriorly or laterally located tumors. It has also been noted to be less successful in centrally located hilar tumors where the "heatsink" effect of proximal vessels drastically reduces its effectiveness [27].

Contraindications for percutaneous RFA include proximity of the bowels or ureter within 1 cm of the ablation zone. Confounding anatomical factors such as hindrance of needle placement by the liver, spleen or lungs are also contraindications to this treatment approach. Adherence of the lesion to the body wall and diaphragm, which brings with it the high likelihood of thermal injury to muscle and nerves, also prohibits the use of percutaneous RFA (see Box 26.1). For patients excluded from percutaneous RFA due to these anatomical factors, the laparoscopic approach is recommended. Laparoscopic manipulation of these confounding anatomical variables prevents thermal injury to these adjacent structures.

Technique

Imaging plays a major role in RFA. As outlined by Leveillee and Ramanathan, this modality is a four-stage process [28]. In each stage, imaging plays a vital role in attainment of successful outcome. RFA can be performed using CT scan, MRI, and ultrasound. A comparison of the utility of these imaging devices in RFA has been summarized by Leveillee and Ramanathan [28].

In the preoperative assessment stage, a good history and physical examination is warranted. A CT renal mass protocol is requested in order to evaluate the tumor thoroughly. Patients with renal insufficiency can alternatively undergo an MRI with gadolinium enhancement. Baseline laboratory values for metabolic and coagulation panels should be obtained. It is in this stage that a good rapport is established. The patient is then asked to read and sign a clear and concise informed consent form.

The urologist reviews the preoperative scan and outlines tumor size, characteristics, and anatomical relationships. Based on these findings, he/she then collaborates with the interventional radiologist and anesthesiologist to plan the flow of treatment. It is at this point that probe type, point of insertion, and RFA system to be used are determined.

Percutaneous RFA can be carried out under either general anesthesia or conscious sedation. Several studies have documented the feasibility of conducting percutaneous RFA as an outpatient procedure [29,30]. Using sedation, percutaneous RFA can be done successfully in carefully screened patients with tumors <4 cm in size. Intravenous sedation purportedly has the advantage of decreased morbidity from general anesthesia. However, we advocate the use of general anesthesia to allow complete respiratory control during probe placement, ensuring accurate tumor targeting and hence maximizing the chances of successful ablation. The use of general anesthesia also optimizes patient tolerance [31].

Intraoperative guidance again utilizes precise imaging modalities. The popularity of CT over MRI and ultrasound was documented by Bandi et al. in their survey [18]. Their results revealed that 70% of academic urologists who perform percutaneous RFA prefer to use CT as their primary imaging modality to facilitate RF needle insertion. Several studies have described the effectiveness and limitations of using the other imaging modalities [32–34]. Using the CT scan, the urologist has the option to use intravenous contrast provided that the patient has a normal serum creatinine. We do not recommend routine use of IV contrast, especially if this has been done preoperatively with satisfactory results. However, if this needs to be done, it should only be performed once during the entire treatment session. Contrast absorption requires several hours of clearance. Postablation CT may reveal mild enhancement of the lesion which may be mistaken for incomplete ablation [35].

Contrast enhancement facilitates accurate localization of the tumor as well as identification of adjacent vital structures. Close proximity of these structures to the targeted lesion warrants maneuvers to increase their distance from the tumor. Park et al. described how to use the needle probe itself as a lever to increase the distance between the tumor and intestines [36]. Ginat et al. presented other alternative maneuvers such as using angioplasty balloons to facilitate bowel displacement [37]. Other investigators have described the use of hydrodissection and pneumodissection to insulate adjacent vital structures [38,39]. However, a simple move such as changing the patient's position may also produce the same result. We advocate the use of paper grid templates during this targeting and intraoperative planning stage (Figure 26.11) to facilitate marking the point of entry of the needle probes.

Once a clear path to the target area has been identified, the patient is usually relegated to a prone or full flank position. Standard antiseptic preparation of the operative area and aseptic technique are employed. For lack of real-time visual monitoring, we advocate the use of peripheral thermometry as a substitute [40]. Under CT scan, guidance nonconducting 18 gauge sheaths are placed in the tumor's periphery at a distance of 5 mm from the tumor margin. The fiberoptic temperature sensors (Lumasense, Santa Clara, CA) are then inserted inside the Huey (percutaneous) or TLA sheaths (laparoscopic) (Figure 26.12). A preablation biopsy of the tumor is performed using a spring-loaded core type needle. At least three cores of biopsies should be taken to ensure specimen adequacy for a definitive histopathological diagnosis. The ablation probe, again under CT guidance, is inserted to the predetermined direct path towards the tumor center. Needle advancement is halted once the deep margin of the tumor is reached by the probe tip. For Christmas tree or umbrella needles, the tines are deployed according to the manufacturer's algorithm. With the Covidien Cooltip RFA system, its single probe runs a 12-min treatment cycle. A three-cluster probe or multiple probe kits are available for larger tumors. When peripheral temperature fibers are utilized, target temperature is usually set at 60°C. The generator box itself has no independent temperature shut-off mechanism (Table 26.1).

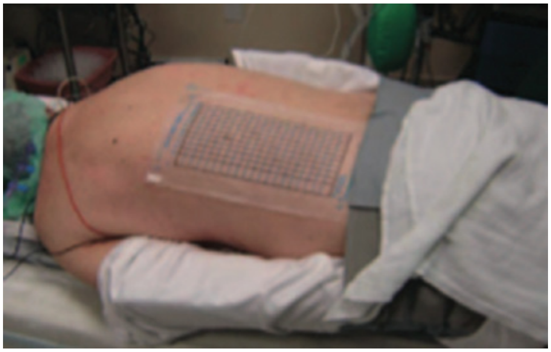
Figure 26.11 Localization grid.

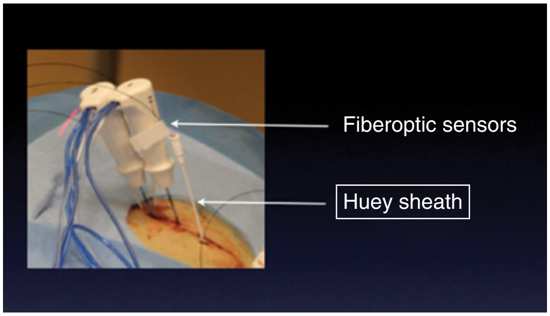

Figure 26.12 Fiberoptic temperature sensor inside the Huey sheath.

The surgeon must take a proactive role and deliberately pursue attainment of the target temperature through manipulation and alternating of the RF probes. Additional treatment cycles may be done to ensure complete ablation of the tumor. For tumors greater than 3 cm, it is recommended to do several overlapping ablations with repositioning of the applicator. This is because augmenting the distance between needles in the multiprobe approach in order to induce an increase in ablation diameter is actually hindered by electrical shadowing of treatment spheres created by each applicator [9]. It is from this concept that the multipass technique is extrapolated. Bird et al. employed reinsertion of the ablation probe into the tumor at different angles so as to address "cold areas" not sufficiently ablated during the first pass [41].

Table 26.1 Treatment algorithm based on Covidien's published algorithm for the Cool-tip RFA system.

Electrode	Exposure (cm)	Duration (min)	Mean volume (cm³)
Single	2	6	7.9
Single	3	12	21.4
Cluster	2.5	12	48.9
Multiple switching	3	16	93.7
Multiple switching	4	16	111.8
Multiple switching	4	25	164.4

The use of MRI as the guidance system of choice requires custom-made, magnetically inert RFA probes. Despite this minor drawback, several investigators still advocate its use because of the perceived "real-time" monitoring that it allows [42]. Complete ablation is seen as a zone of low signal intensity on T2-weighted images. In an independent study, Davenport et al. have proven the reproducibility of this observation [43]. Sterret et al. expounded on the identification of residual tumor in the MRI as isointense or hyperintense areas outside the halo emitted by the zone of inflammation and hemorrhage [44]. These incompletely treated sections can then be ablated through repositioning of the needle. Multiple assessments without the use of contrast and repeated ablation can then be performed until complete destruction of the tumor is achieved.

After the treatment session is over the probe tract is "cauterized" as the ablation probe is removed. This maneuver is suggested to prevent tumor seeding and bleeding of the needle tract [45]. A posttreatment CT scan is done to check for pneumothorax or perirenal hematoma. A study by Ganguli et al. showed that immediately post treatment, renal tumors shrink by an average of 21% [46].

Tracy and Cadeddu outlined how they conduct RFA using the RITA system [47]. They usually approach patients with posterior tumors through a prone position, varying the patient's position to best expose the tumor for access by the probe. An initial plain CT is done after positioning to check that there is an unobstructed path for the probe-to-tumor trajectory. After verification of the clear path and subject to the patient's renal function, a second scan with IV contrast is done. A 20 gauge Chiba needle is used to bore an access towards the tumor's central rim. The position of the finder needle is verified by another scan, then once the correct position is confirmed, the 14 gauge Starburst XL probe is advanced to the rim of the tumor. The tines are deployed to delineate an ablation zone about 5–10 mm beyond the tumor edges. This is verified by another CT scan, then 2–3 specimens of the mass are taken using am 18 gauge Trucut biopsy. The system's 1500 RF generator creates up to 150 W of power, achieving an average temperature of 105°C. The temperature is monitored through sensors embedded in five of the nine tines. Once the desired temperature is reached, treatment is achieved by carrying out ablation for a duration based on an algorithm as follows: 2 cm tine deployment, 5 min; 2–3 cm, 7 min; and more than 7 cm, 8 min. A 30-sec cool-down period is observed and then a second ablation with the same parameters is done. The tract is then ablated by gradually withdrawing the tines at a temperature of 70°C. A posttreatment CT is done to check for completeness of the ablation.

Table 26.2 Follow-up protocol.

Date	Diagnostics
1–3 months	Computed tomography (CT) scan, renal mass protocol
6 months	CT scan, renal mass protocol Chest x-ray
Annually	CT scan, renal mass protocol
Thereafter × 4	Chest x-ray, liver function tests (LFT)
Thereafter × 5	CT scan, renal mass protocol Annual chest x-ray and LFTs

The last stage of the treatment process is follow-up. At every clinic visit, an adequate posttreatment history and physical examination should be done. A chest x-ray as well as serum creatinine should be requested. Imaging studies should be done at recommended intervals (Table 26.2).

Success is defined as the absence of tumor growth and enhancement. Any enhancement within the ablation zone detected through CT scan or MRI 6 weeks after ablation is considered a residual tumor and hence an incomplete ablation. These are typically found in the periphery owing to the normally spherical shape of the ablation lesion. Recurrence, on the other hand, is the appearance of enhancement within the ablation zone after a normal 6-week imaging. Recurrences are not confined to the periphery and may appear anywhere in the ablation zone.

Treatment outcomes

There is controversy in defining a successful treatment in RFA as some surgeons consider successful treatment as those that have no residual tumor after a complete ablation. Hence, they do not count treatment failures as recurrences but only consider them when enhancement persists despite reablation of the tumor. As expounded by Faddegon and Cadeddu, the rate of local recurrence depends on definition [48]. If persistent enhancement after a single ablation is considered a recurrence then local recurrence-free survival ranges from 33% to 88%. Despite this contention, however, a lot of mid- and long-term studies have been published that have adopted the strict single ablation rule to define treatment success that shows the efficacy of RFA to be comparable to the gold standard of treatment of SRM which is partial nephrectomy. In a cohort of 70 patients, Stern et al. showed that disease-free survival at 3 years between partial nephrectomy and RFA was 95.8% and 93.4% respectively [49]. Our own study comprising 291 patients who underwent RFA treatment of SRM had a disease-free survival of 99% at 20.6 months of median follow-up [50]. In a study of 124 patients, Karam et al. had a recurrence-free survival of 94.6% at 3 years [51]. All these new additions to the literature point to the increasing role of renal ablation as a possible first-line treatment for small renal tumors across the board in all patients and not just as an alternative treatment for the geriatric and surgically unfit population.

Microwave ablation

A similar modality that uses heat to eradicate tumor is microwave ablation (MWA). It first became known to urologists for the treatment of the prostate, specifically, transurethral microwave thermotherapy [52]. MWA was used in its early stages for ablation in the treatment of cardiac arrhythmias [53]. As time progressed, the technology has been utilized in the treatment of solid organ masses including liver, lung, bone, kidney, adrenal, uterus, breast, and thyroid [54–58]. Microwave energy has also been used in a nonablative format for intraoperative coagulation, hemostasis, and cutting. Most experience with MWA was gained from its use in ablation of liver masses, and it has been used most widely in China and Japan.

Ablation of the kidney is considered more difficult compared to liver due to the distinct heterogeneity within the kidney. The multiple layers of the kidney result in varying compositions of water, electrolytes, and blood vessels, affecting how the energy is absorbed [59]. MWA may be more suitable for the kidney, because of the high water content and increased blood flow present in the kidney compared to other organs such as the liver [60]. Wright et al. showed that MWA is less susceptible to the heatsink effect as seen with RFA [61].

Radiofrequency ablation has the flexibility to be utilized for open, laparoscopic, and percutaneous surgery. MWA is similar to RFA but with some additional benefits. MWA has been shown to have consistently higher intratumoral temperatures, larger ablation volumes, shorter procedure times, easier ability to use multiple simultaneous probes, does not require grounding pads, and may provide improved treatment of cystic lesions [59,62–65]. Other benefits of thermal ablation over traditional extirpative surgery include reduced perioperative morbidity/decreased pain, shorter hospital duration, earlier return to normal activities, preservation of normal renal function, and the ability to treat patients who are poor surgical candidates [2].

Fundamental concepts in microwave ablation

Medical applications of microwave radiation generally refer to the electromagnetic spectrum of frequencies between 900 MHz and 2.45 GHz, although the full spectrum ranges from 300 MHz to 300 GHz. MWA, like RFA, works by heat diffusion. When microwave energy is applied, the electromagnetic energy is absorbed by the surrounding tissue as it propagates from the antenna probe tip. The charged electromagnetic energy waves rapidly alternate, causing water molecules to rapidly realign and alternate as well. The rapid shifting, approximately 2–5 billion times per second, is due to the dipolar make-up of water molecules, meaning water molecules have positive and negative sides. The alternation creates kinetic energy and is transformed into heat, leading to coagulation necrosis and cell death [66,67].

The amount of penetration and the amount of heat produced by the electromagnetic energy are related to the water content of the target tissue [62,68]. One of the main benefits of MWA that differentiates it from RFA is that microwaves propagate through all types of tissue, including desiccated, charred, and water vapor, which may be formed during the ablation [67]. MWA allows for active tissue heating that is not affected by charring like RFA. Heating also occurs by direct conduction through the tissue from the antenna probe. Tissue heterogeneity within the ablation zone may result in some variability in the microwave propagation and ablation size [59]. Intralesional temperatures >60°C cause rapid irreversible cellular damage [68]. Histological changes are generally measured the same as in RFA, using H&E for general cell appearance and NADH to evaluate for cell death.

The Evident™ MW ablation system (Figure 26.13) uses a 915 MHz generator with a maximum recommended output of 45 W coupled to a 13 gauge water-cooled microwave antenna (Covidien, Mansfield, MA). The system more popular in China and Japan is the KY2000 MW ablation system (Kangyou Medical Instruments, Nanjing, China) which consists of a water-cooled shaft 15 gauge antenna connected to a microwave generator capable of producing 1–100 W of power at 2.45 GHz.

The number of companies producing microwave systems has grown rapidly in the last several years (Figure 26.14). Many of these other devices have now received Food and Drug Administration 510(k) marketing clearance, including the AveCure™ system (MedWaves, San Diego, CA), which uses a 902– 928 MHz generator at 10–32 W and 12–16 gauge noncooled antennae, offering temperature or power control; the MicrothermX® (BSD Medical, Salt Lake City, UT), which uses a 915 MHz generator at up to 180 W (60 W maximum per channel) and up to three 14 gauge internally cooled antennas; and the Certus 140™ (NeuWave Medical, Madison, WI), which uses a 2.45 GHz generator at up to 140 W, with up to three 17 gauge gas-cooled antennae. Also offered are the HS Amica™ system (HS Hospital Service, Rome, Italy), which uses a 2.45 GHz generator at up to 100 W, with 14-17 gauge water-cooled antenna; and the Acculis Accu2i™ pMTA system (Microsulis Medical, Denmead, United Kingdom), which uses a 2.45 GHz generator at up to 100 W, with a 15 gauge water-cooled antenna [69].

Figure 26.13 The Evident™ MW ablation system.

Indications and contraindications

Currently, MWA shares its selection criteria with RFA and is utilized in a highly selected group of patients, not only selecting small, enhancing renal masses <4 cm but patients with advanced age and multiple comorbidities. Other possible patient targets include patients with baseline renal insufficiency and those with multiple masses related to hereditary predisposition (i.e. von Hippel–Lindau disease). Relative contraindications to ablation include larger tumors (>4 cm), central or hilar tumors (due to risk of ureteral or vascular injuries), acute illness or infection, hemodynamically unstable and poor life expectancy. The only absolute contraindication is an uncorrected coagulopathy [2].

Technical considerations

Microwave ablation is still being studied and as such there are no standardized protocols for its use. Hope et al. used porcine models and a 915 MHz generator to identify optimal ablation parameters [70]. They felt that 45 W at 10 min produced the optimal ablation diameter in the shortest amount of time. They were limited at longer time intervals by the larger ablation zone sizes because they could no longer perform accurate size measurements. Conversely, Laeseke found the application of 90 W for

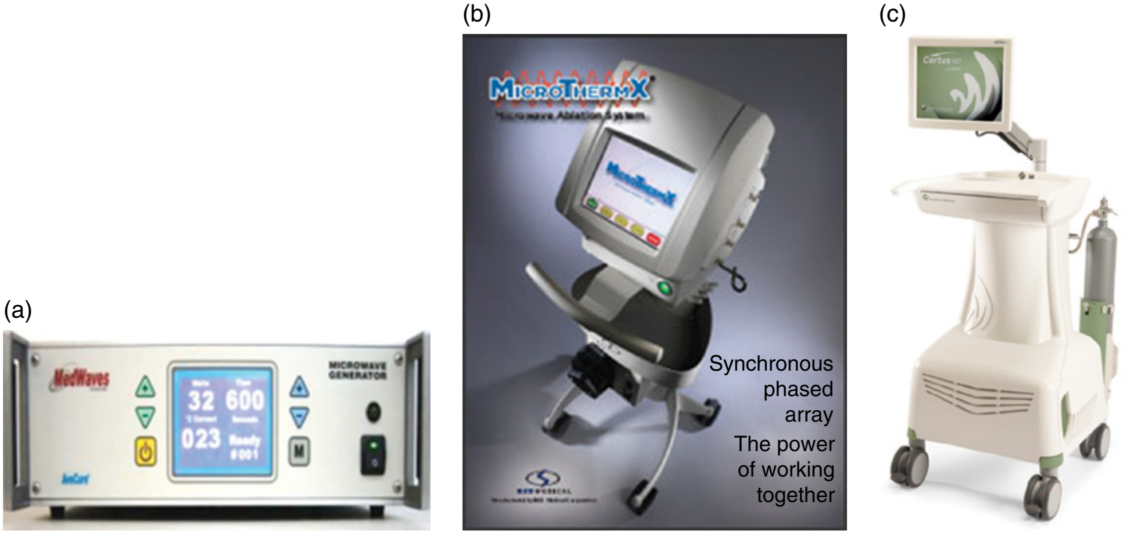

Figure 26.14 (a) AveCure™. (b) MicroThermX®. (c) Certus 140™.

12 min yielded larger ablation diameters [60]. This larger ablation size may be secondary to Laeseke using a different frequency generator – 2.45 GHz compared to the 915 MHz used by Hope. Sommer et al. showed that ablations performed with temperature control versus power control had fewer system failures but comparable ablation zones [71]. He et al. found that the internally cooled antenna performed better than the noninternally cooled version in liver models [72]. They noted that there was less charring around the antenna and more spherical ablations. In another study, ablation zones were compared with and without renal blood flow intact, and although MWA is less affected by the heatsink effect, there was a significantly larger ablation zone when the blood flow was interrupted [73]. Triaxial ablations were found to be significantly larger when using MWA antennas compared to RFA [60].

In RFA, the use of temperature probes around the perimeter of the ablation zone has been shown to reduce overtreatment of normal tissue and reduce the risk of damage to nearby structures [40]. Moore et al. found asymmetrical ablations around the collecting system [59], postulating that when the ablation zone is close to the collecting system, water/urine may absorb the microwave energy to a greater degree than the surrounding tissue, dampening the energy field and reducing ablation zone size.

Complications

The goal of ablation is to destroy malignant tissue while minimizing the damage to normal parenchyma. Types of complications are similar to RFA. The most commonly observed complication is pain or paresthesia at the operative site which is usually self-limited. Other reported complications include perinephric hematomas, transient hematuria, ureteropelvic junction obstruction, liver and pancreatic injury, and postprocedure ileus [2,74]. Complication rates range from 0% to 38% in reported human studies [75–77]. Optimal patient selection can minimize complications when tumor location, size, depth, and proximity to hilum are considered.

There was a report of carcinomatosis in a rabbit model which used VX-2 tumor, a highly aggressive rabbit epidermoid tumor with high metastatic potential [78]. In this study, MWA resulted in the highest number of cases with carcinomatosis when compared with RFA and cryotherapy. The authors attributed this response to the boiling effect of heat-based therapies causing the release of interstitial liquids around the probe. These results have not been reported in any clinical trials with human patients with renal cell carcinoma (RCC).

Treatment outcomes

Markers of successful thermal ablation include the absence of continued growth or contrast enhancement.

Persistent enhancement at 3-month follow-up suggests incomplete ablation. However, absence of enhancement within the ablation zone with enhancement on follow-up imaging or continued growth suggests tumor recurrence [2]. Liang et al. reported 12 patients who underwent percutaneous ablation for RCC and at median follow-up of 11 months, no residual tumor or recurrence was observed [76]. Guan et al. performed a prospective randomized trial comparing laparoscopic/percutaneous MWA to open/laparoscopic PN [79]. They amassed 102 patients, finding estimated blood loss, complications, and postoperative decline of renal function were significantly less in the MWA group compared to the PN group. Also, they reported 3-year recurrence-free survival in patients with RCC of 90.4% for MWA and 96.6% for PN, and this was not statistically significant. Clark et al. performed a trial to identify the presence of skip lesions within the ablation zone, by performing MWA before nephrectomy [64]. They performed MWA on 10 patients, all of whom had RCC, and complete tumor kill was achieved with the absence of skip lesions. Castle et al. performed laparoscopic/percutaneous MWA on 10 patients and reported a 38% recurrence rate [75]. Bai et al. performed retroperitoneal laparoscopic MWA on 23 tumors and reported that initial ablation was successful in 94.4% of patients [77]. They also found no recurrences at a median follow-up of 20 months and an 18.2% complication rate. Muto et al. reported that unclamped laparoscopic MWA and enucleation in a series of 10 patients with RCC showed extensive coagulation necrosis without skip lesions and no complications [63].

Much like RFA, follow-up after MWA is crucial to monitoring for recurrence. The same follow-up protocol is generally used for both RFA and MWA. Serial biopsy has been suggested as a way to augment the method of follow-up for patients who have an ablation performed [77].

Future outlook

Research into the conjoint use of nanoparticles and hyperthermal ablation is being carried out to see whether this combination therapy will augment the efficacy of thermoablative treatments [80]. In parallel to this, a growing number of studies aimed at harnessing the immune-modulating properties of thermal ablation are being carried out [81]. These initiatives aim to establish the full potential of thermoablative therapy.

Conclusion

Needle-ablative hyperthermal therapy is here to stay. We are currently witnessing an exponential increase in the number of scientific papers that attest to its efficacy and safety. With the development of advanced imaging modalities that allow real-time monitoring and improved tumor targeting, hyperthermal ablation's present status as an alternative treatment for patients with advanced ages and significant comorbidities is bound to be upgraded to that of a first-line treatment for small renal tumors.

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27

CHAPTER 27

Instrumentation and Technique: High-Intensity Focused Ultrasound

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Introduction

Ultrasound is a sound wave at frequencies above the threshold for human hearing – approximately 20 KHz. It is produced via the reverse piezoelectric effect where an electrical current is applied to a piezoceramic material (often piezoceramic zirconate titanate) at the resonant frequency of the material. The alternating electrical current produces material vibrations which emit a pressure wave which is transmitted through the surrounding gas, liquid or solid. By focusing the ultrasound (US) wave, using an appropriately shaped transducer or adjacent lens, a small focal point is produced where the pressure can become very high. The incident ultrasound is attenuated by tissue to varying degrees, resulting in the transfer of energy from the propagating pressure wave in heat. A rapid temperature rise results which, if sufficiently high, results in cell death. The tissue lying in front of the focus is unharmed as the beam as the intensity is relatively low and therefore heating modest (Figure 27.1).

High-intensity focused ultrasound (HIFU) was historically proposed as a treatment for benign prostatic hyperplasia. However, clinical results proved unsatisfactory. Advances in the quality of diagnostic ultrasound and computed tomography (CT) led to development of energy ablative therapies for renal cancer, eliminating the need for extirpative surgery. Extracorporeal renal HIFU can be undertaken entirely without incision or tumor puncture, resulting in zero risk of tumor seeding, hemorrhage or urinary leakage.

Early clinical trials established proof of concept [1–3]. Three-year follow-up data are now available although currently renal HIFU should be regarded as experimental. Treatments should only be conducted in centers with the appropriate expertise. Ideally, treatments should be undertaken within a clinical trial or in units where careful data collection and audit are undertaken.

High-intensity focused ultrasound stands apart from other energy ablative therapies, such as radiofrequency ablation and cryotherapy, because the treatment is entirely noninvasive. However, general anesthesia is invariably required and careful discussion of the inherent risks and alternative treatment options should take place before HIFU is undertaken.

Informed consent

The process of obtaining informed consent for renal HIFU should follow the standard principles of consent for a surgical procedure under general anesthesia or sedation. The process should begin with a thorough review of the medical records, cross-sectional imaging, staging investigations, and any biopsy histology. The side of the tumor should be confirmed from this review and should be directly confirmed with the patient. This

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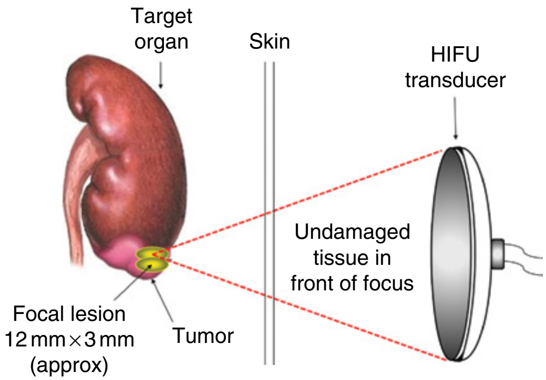


Figure 27.1 Schematic of an extracorporeal HIFU treatment demonstrating the focusing of the beam to a small focal point in the target tumor without damage to the prefocal tissues.

confirmation should then lead to marking of the site with indelible pen *prior* to transfer to the procedure room.

It should be carefully explained to the patient that the purpose of renal HIFU is to cause thermal ablation (destruction) of the entire tumor. This includes ablation of a small margin of normal kidney to ensure an appropriate "surgical" margin. The benefits of renal HIFU over surgical excision – shorter hospital stay, less pain, no skin incision, no tumor puncture, no risk of hemorrhage or urine leakage – should be emphasized. The benefits of active management over a surveillance protocol should also be discussed – risk of disease progression and metastasis under surveillance. A discussion on alternative ablative therapies is also appropriate although a satisfactory explanation is difficult as comparative studies do not currently exist. Renal HIFU follow-up data are limited and HIFU has been used considerably less than radiofrequency ablation or cryotherapy. However, it avoids the risk of tumor puncture, parenchyma hemorrhage, blood transfusion, and urinary leakage that may occur with these methods.

The general risks of surgery and anesthesia should be discussed, including the risks of myocardial infarction, stroke, deep vein thrombosis, and pulmonary embolism. However, the likelihood of these events occurring during renal HIFU is low.

The key risks of renal HIFU are those associated with thermal damage to the skin, abdomen, and structures surrounding the target tumor. Some degree of skin and abdominal wall pain over the treatment site is invariable in renal HIFU. It should be explained that mild pain, easily managed with oral nonopioid analgesia, is expected. Moderate pain occurs in approximately 10% of cases and may require oral opioid analgesia in the perioperative period. Severe pain requiring intravenous opioid analgesia is rare. A mild skin burn, best described as superficial sunburn, is commonly seen following renal HIFU. Skin erythema and edema are the characteristic clinical signs. Skin blistering may occasionally occur. Full-thickness skin burns are rare but may occur if skin cooling and regular inspection during treatment are not undertaken.

The risk of inadvertent injury to surrounding structures should be discussed although this is rare and is expected to occur in less than 1% of cases. Thermal damage to bowel resulting in peritonitis is a serious, life-threatening complication which may require intravenous antibiotics and surgical repair. Injury to other vital structures such as major blood vessels and pleura is very rare.

Complete tumor ablation is not always possible in a single sitting of renal HIFU, particularly if tumor imaging is poor. This should be discussed and the possible need for a repeat treatment should be explained if postoperative cross-sectional imaging suggests subtotal ablation. There are no additional risks associated with repeat HIFU provided any skin and abdominal wall injury has resolved.

Preoperative preparation

It is essential to ensure that satisfactory cross-sectional imaging is available before renal HIFU is commenced. Contrast-enhanced CT or magnetic resonance imaging (MRI) is appropriate and the choice should be based on local expertise. However, the ability to view imaging in the transverse, sagittal and coronal planes is essential. A pretreatment biopsy is now often considered a sensible approach prior to embarking on ablative treatment – a significant percentage of small tumors may be benign [4].

It is vital that the tumor visualization is confirmed using the imaging modality integrated into the clinical HIFU device. This may be ultrasound or MRI depending on the type of device used. It is not adequate to confirm visualization using standard clinical ultrasound or MR machines; the imaging may be different on the integrated device and the tumor may be less easy to see. This is especially true with ultrasound-guided HIFU where the water stand-off between the probe and the abdominal wall leads to a significant loss of spatial and contrast resolution. We recommend that this process is undertaken at a pretreatment screening visit rather than on the planned day of treatment. At this visit, the optimal patient position can be determined to avoid additional wasted time during anesthesia. Informed consent can also be taken at this visit.

Laboratory blood analysis should be undertaken prior to treatment. Renal function, full blood count, and a clotting assessment should be undertaken. Anemia and renal failure are not absolute contraindications to renal HIFU but require monitoring during the perioperative period. Aspirin and other antiplatelet agents, such as clopidogrel, may be continued. It is not known whether renal HIFU can be undertaken in those who are anticoagulated using drugs such as warfarin or heparin. However, it is our recommendation, in the absence of medical literature, that these medications are stopped before treatment. A normal international normalized ratio (INR) should be confirmed before treatment is undertaken.

Women of child-bearing age should have a negative pregnancy test before renal HIFU. Treatment of pregnant women is not reported and pregnancy should thus be considered an absolute contraindication to renal HIFU.

Infection in the skin and abdominal wall is very rare following renal HIFU. Urinary infection is also very rare. Prophylactic antibiotics are therefore not indicated.

A preoperative electrocardiogram (ECG) should be undertaken in appropriate patients although this is not mandatory for renal HIFU. Six hours (2 h for clear fluids) of preoperative starvation is mandatory to ensure the stomach is empty prior to anesthesia. No other specific preoperative preparation is indicated. Other investigations such as echocardiography or lung function tests may be indicated depending on patient comorbidity but are not essential for renal HIFU.

Patient positioning

The patient should be positioned such that the tumor overlies the therapeutic transducer when it is positioned at its central point. This ensures that the maximum displacement of the transducer is possible in all directions during treatment. It is helpful to position the patient as much as possible prior to anesthesia. This includes placement of any straps and padding that are used to support the patient. Depending on the device used, this may not be possible. Using our ultrasound-guided HIFU device, we position the patient and induce anesthesia with the patient on the treatment bed itself. A padded board is used to support the patient over the water reservoir which is subsequently removed when the positioning straps are secured. This process minimizes patient lifting and reduces the time taken to position the patient for treatment.

The patient should be positioned in the right lateral position for renal HIFU to the right kidney, and in the left lateral position for left-sided tumors. Depending on the location of the tumor within the kidney, a semi-prone (more anterior tumors) or semi-supine (more posterior tumors) position may be more appropriate. This should be determined using preoperative imaging and the device imaging at the prescreening visit. In general, a semi-supine approach is usually favored – this optimizes the acoustic field and minimizes the risk of bowel injury. Extreme care should be taken when treating anteriorly or laterally placed tumors where bowel lies immediately adjacent to the tumor.

Considerable attention should be paid to obtaining the ideal patient position. It is easier to move the patient before treatment has commenced – doing so after treatment requires a repeat of the treatment planning process, including marking of the tumor boundaries, because the imaging will change with patient movement. When a satisfactory position has been achieved, this should be held securely using the equipment supplied with the HIFU device – often this is straps which are secured to fixed points on the machine.

After positioning, any body parts which may be prone to pressure damage should be carefully protected with gel pads. The feet, hips, elbows, and head in particular require attention during renal HIFU. A pneumatic calf compression device should also be used to minimize the risk of perioperative deep vein thrombosis (DVT).

A urinary catheter is generally not required and is not recommended. However, if the procedure is expected to be very lengthy then insertion of a catheter may be prudent.

Instrumentation

Almost all the equipment required for renal HIFU is incorporated in the clinical device itself. The diagnostic imager (MR or US) is fully integrated with the therapeutic head,

Table 27.1 Summary of transducer characteristics used in our renal HIFU clinical trials.

Transducer	Frequency (MHz)	Focal length (f) (mm)	Outer diameter (D) (mm)	f-number f/D	Dimensions of focus (mm)	
					FWHM (transverse)	FWHM (axial)
20010A3 JC	0.84	128	150	0.85	1.9	15.0
20099-44 JC-200	0.95	135	202	0.67	1.2	9.5

FWHM, full width half maximum.

and the software for both imaging and treatment is purpose designed and fully integrated. There is little additional equipment required for renal HIFU other than that required for standard general anesthesia. We strongly recommend the use of a patient-warming blanket – body temperature can drop significantly as a wide surface area of the abdomen is submerged in cold water during the treatment.

Some clinical HIFU devices may have a choice of therapeutic transducer – these often vary in physical dimension, focal beam size, focal length, and driving frequency. The choice of transducer is also a trade-off between the maximum depth of treatment (determined by the focal length), the size of the focus (determined by the physical dimensions and the drive frequency), and the amount of prefocal attenuation of ultrasound (determined by the drive frequency). The distance between the skin and furthest point of a renal mass is typically 5–10 cm – the transducer should therefore have a focal length of at least this distance. In our experience, the ideal driving frequency is 0.8–1.0 MHz. Frequencies higher than this are too readily attenuated to allow sufficient energy to be delivered through the prefocal skin, muscle, and perinephric fat. Frequencies lower than 0.8 MHz have a large focus which limits the focal intensity and the ability to successfully ablate the tumor. For reference, the transducer characteristics that we have used to treat renal tumors are shown in Table 27.1.

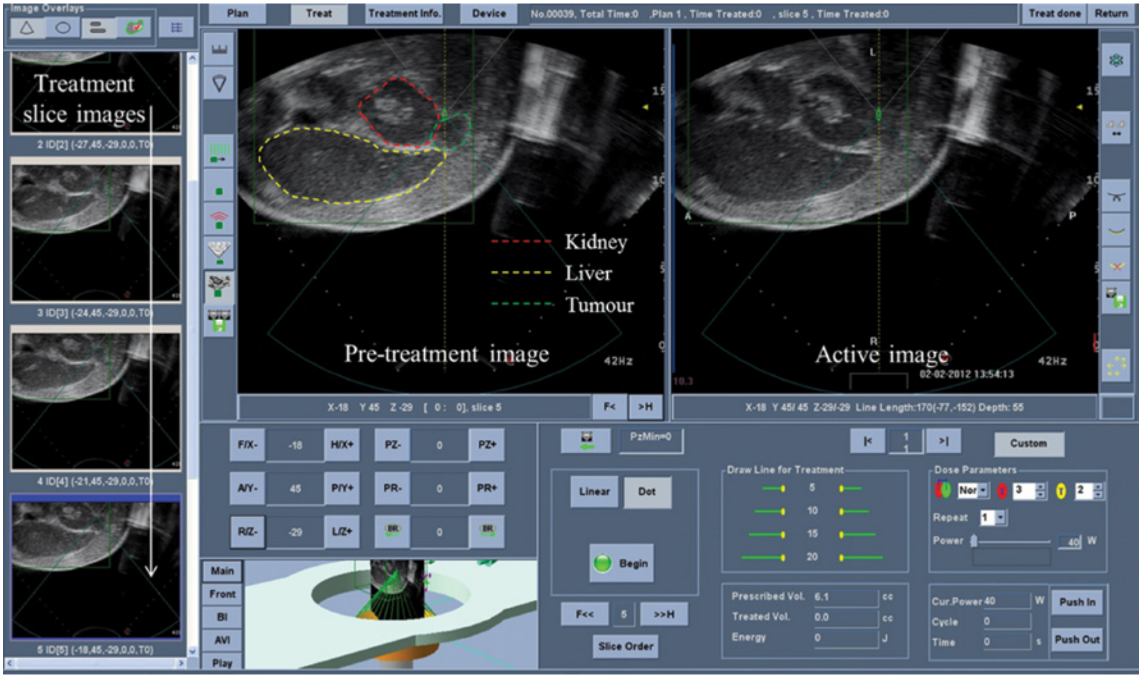
Step-by-step technique

The treatment technique used in renal HIFU depends to a large extent on the clinical device used. The imaging modality and integrated device control software are purpose built for each device. However, a number of key principles are common to all clinical HIFU devices.

The first step in successful renal HIFU is obtaining adequate tumor visualization. This process is intrinsically linked with patient positioning, which often needs modifying to obtain optimal image quality. This step can be time-consuming and may take up to 1 h. It is essential to visualize all tumor boundaries, normal kidney, and any surrounding structures. In particular, it is important to ensure that the acoustic window is not obscured by the overlying ribs which prevent adequate focal energy deposition and result in significant pain due to rib heating.

Once the tumor is adequately imaged, it should be divided into treatment slices, as demonstrated in Figure 27.2. This process is particular to the device being used. However, given the typical focal dimensions of HIFU transducers, it is usual to use a 3 mm slice separation to ensure that intervening tumor is not missed. The tumor boundaries should be carefully outlined using the device software, ensuring that the entire tumor is incorporated with a thin margin of surrounding normal tissue.

Once the tumor contours have been adequately outlined, treatment can begin. We recommend the early administration of a single dose of intravenous steroid (e.g. 100 mg hydrocortisone) to minimize edema of the abdominal wall which serves to degrade diagnostic imaging and limit therapeutic energy delivery to the focus. The initial phase of treatment requires a dose escalation ramp to determine the ideal acoustic output parameters. A central location within the tumor is chosen and the acoustic output is set at its lowest setting. A 2–3 sec HIFU is undertaken and the imaging is observed for a response to suggest thermal ablation. With ultrasound-guided HIFU, an increase in grayscale at the site of the focus, known as a hyperecho, is



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X-18 Y 45 Z-29 [0: 0], slice 5

X-18 Y 45/ 45 Z-29/-29 Line Length:170(-77,-152) Depth: 55

F/X-	-18	H/X+	PZ-	0	PZ+
A/Y-	45	P/Y+	PR-	0	PR+
R/Z-	-29	L/Z+		0	

Nor 3 2

Repeat 1

Power 40 W

Prescribed Vol. 6.1 cc
Treated Vol. 0.0 cc
Energy 0 J

Cur.Power 40 W
Cycle 0
Time 0 s

Figure 27.2 Screenshot of the JC-200 HAIFU Tumor System device (Chongqing, China) control software demonstrating pretreatment and active imaging. The treatment slices are shown on the left-hand side with the transducer movement and acoustic output control shown at the bottom.

indicative of thermal ablation [5]. With MRI-guided HIFU, thermometry data will be displayed with an indication of whether ablative temperatures have been reached. This process may be automated with MRI-guided HIFU devices.

When the appropriate treatment parameters have been satisfactorily determined, HIFU treatment can begin. With certain HIFU devices, notably MRI-guided machines, the treatment process is semi-automated, using closed feedback loop algorithms to achieve the desired focal temperature rise. With ultrasound-guided HIFU, the process is more operator dependent. The tumor is "painted" with contiguous HIFU exposures using either a side-by-side pulse mode or a continuous linear track mode, as shown in Figure 27.3. The duration and overlap of the HIFU pulses may be automatically determined or be open to manual control. Under manual control, a minimum one-third overlap of adjacent pulses is essential to prevent missed areas of tumor. Pulse duration should be adjusted depending on hyperecho feedback; 2–3 sec exposures are typical. The operator must ensure that the entire tumor is covered in the course of the treatment. It is recommended to begin with the most distally located tumor and then move proximal towards the therapeutic transducers. This helps to maintain the quality of tumor imaging which would otherwise be obscured by ablation of more proximal tissues.

The skin overlying the tumor should be examined at regular intervals – we recommend every 30 min. It should be visually inspected and palpated for evidence of erythema, blistering, edema, and overt tissue damage. Mild erythema and edema are invariable; more significant burns should prompt the immediate cessation of treatment. It is vital to ensure that the circulating water within the treatment reservoir is maintained at a low temperature – approximately 5–10°C is recommended to minimize the risk of skin burns.

Once the entire tumor has been treated, general anesthesia can be reversed. A careful skin inspection should be undertaken during transfer from the device and a cold compress applied if any skin burn is evident. The patient should then be transferred to the recovery

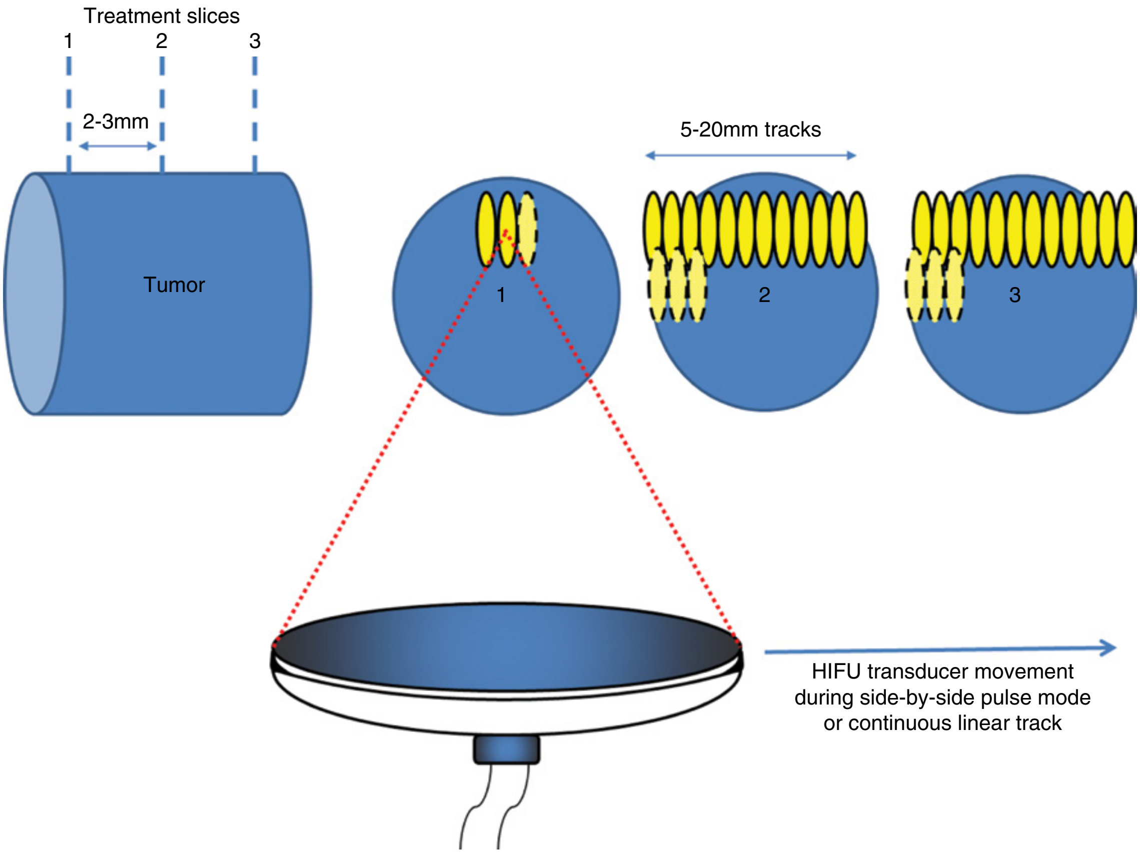

Figure 27.3 Schematic of a renal HIFU treatment using a JC/JC-200 ultrasound-guided device. 2–5 sec HIFU exposures are placed adjacent to one another to "paint" out the entire tumor. Distal tumor is treated first to limit image degradation due to ablation of prefocal tissues.

room for routine observation. No specific interventions are required in the immediate postoperative period. Appropriate analgesia should be administered when required – usually this is oral nonopiate analgesia but rarely intravenous opiate may be required. We recommend that patients stay overnight for observation but this is not mandatory if appropriate social support is available on discharge.

Intraoperative trouble-shooting

The most common difficulties encountered with renal HIFU are due to poor tumor imaging. This is most notable with ultrasound-guided devices although imaging may also be challenging with MRI-guided devices. HIFU treatment should not begin unless the tumor margins and surrounding structures are clearly visible. However, it is common for these boundaries to become blurred during HIFU as prefocal tissue damage causes loss of both contrast and spatial resolution. We recommend periodic cessation of HIFU treatment to allow cooling – this may lead to an improvement in imaging. In addition, it may be possible to reposition the patient to allow treatment from a different angle through untreated tissue.

The rib cage may impede HIFU treatments significantly, particularly with upper pole renal tumors which are harder to ablate successfully. With ultrasound-guided HIFU, imaging reveals a strong acoustic shadow behind the rib, rendering tumor visualization impossible. With MRI-guided HIFU, the tumor will still be clearly visible in the presence of overlying ribs but HIFU will not pass through the rib cage and treatment will result in rib damage and significant pain. Caution should be exercised when treating renal tumors where ribs lie in the acoustic field. It is advisable to adjust the patient position to move the propagation path away from the rib rather than attempt transcostal treatment.

The respiratory excursion of the kidney can be significant, particularly in the obese patient. This can make renal HIFU treatment difficult as the focal point moves during an exposure and prevents ablative temperature rises. Ventilation with low tidal volumes may limit this excursion. However, the use of a dual-lumen endotracheal tube is strongly recommended. This technique allows ventilation of lung contralateral to the tumor whilst the ipsilateral lung is unventilated. There are two benefits of this: first, respiratory excursion of the kidney is eliminated or significantly reduced and second, varying the insufflation of the ipsilateral lung can move the kidney into an improved position, particularly if it lies directly behind a rib.

A lack of intraoperative feedback on treatment efficacy may be encountered, most often during ultrasound-guided HIFU. Hyperecho changes appear on B-mode imaging when tissue temperatures approach 100°C – boiling bubbles strongly scatter the incident ultrasound beam, resulting in strong echoes which cause the image bright-up. *In situ* temperature rises to this level are *not* required to cause tissue ablation – a rise to 60°C is sufficient to cause immediate cell death. Therefore, there is a significant window in which tissue ablation may occur in the absence of hyperecho feedback to confirm ablation. At present, there are no alternative clinically available methods for monitoring US-guided HIFU. We recommend selecting the minimum power required to produce an image bright-up when the dose escalation ramp is conducted in an easily visible part of the tumor. The same power should subsequently be used throughout the remaining tumor even in the absence of significant hyperecho change so as to prevent overtreatment. Newer methods of monitoring HIFU are under development which will help to improve real-time feedback [6].

Mild skin injury is inevitable during extracorporeal renal HIFU. This should be carefully monitored during treatment with direct inspection and palpation. A cold compress should be applied to any areas of erythema following HIFU. In addition, skin blistering may also appear during or immediately after treatment. This is self-limiting. The occurrence of a full-thickness skin burn should prompt immediate treatment cessation. Burn excision is usually required and primary closure is usually possible provided the skin defect is not too large.

Postoperative follow-up

Clinical

Following an uncomplicated renal HIFU treatment, patients can be safely discharged the same day provided their pain is controlled with simple oral analgesia and they have an adult to stay with them for at least 24 h. Renal HIFU treatments can be lengthy (2–4 h) and therefore we recommend a single overnight stay for monitoring and pain assessment. The majority of patients experience only mild pain which requires nonopioid analgesia. Opioid analgesia should be reserved for those with moderate and severe pain and this is invariably temporary. Regular assessment for skin burns should be undertaken and a cold compress applied to any areas of erythema or blistering. Regular assessment of pulse, blood pressure, temperature, and oxygen saturations should be undertaken – any significant abnormality should prompt an urgent assessment for evidence of bowel injury.

A laboratory assessment of full blood count, renal profile, and inflammatory markers on the first postoperative day is recommended following renal HIFU but is not mandatory. A transient rise in white cell count and inflammatory markers is commonly seen; a mild dilutional anemia may occur and renal function is rarely affected [2].

Patients should be discharged with advice on appropriate over-the-counter analgesia and contact details in case of complications. We currently undertake a clinical review at 2 weeks following renal HIFU; this can be undertaken at the time of follow-up imaging. No further clinical follow-up specific to HIFU is required but all patients should continue to have regular clinical oncological follow-up as determined by local protocols – as a minimum this should be 6-monthly for the first year and then annually until 5 years.

Radiological

Similar to other renal ablative therapies, the optimum time for postoperative imaging follow-up is not known. An early (<24 h) posttreatment scan may show reduced enhancement if feeding blood vessels have been destroyed but thermal ablation in the tumor may not be evident at this stage. We therefore do not advocate early imaging as it does not affect management at this stage. Currently we undertake formal contrast-enhanced cross-sectional imaging at 2 weeks after treatment. At this stage, tumor ablation is evident and any residual regions of tumor enhancement will be visible. The cross-sectional imaging modality should be the same as that used for preoperative imaging to allow a direct comparison. Ideally, this should be examined by the same radiologist with experience in ablation imaging. MRI allows a better assessment of any prefocal damage that may have occurred in the abdominal wall or perinephric fat.

Follow-up imaging at 2 weeks should be used to determine future management. Persistent central tumor enhancement should be considered to represent viable tumor, indicating treatment failure [7]. However, a smooth, symmetrical, thin ring of peripheral enhancement is commonly seen following ablative treatment and is due to fibrosis occurring at the boundary of the zone of ablation [8]. This should not be considered to represent residual viable tumor. If residual viable tumor is suspected on the basis of residual tumor enhancement, consideration should be given to repeat HIFU or alternative treatment. This should be discussed carefully with the patient and a range of options should be provided. Repeat HIFU can be undertaken straight away and should be no more complicated than the primary procedure. There are no published reports on the use of alternative ablation modalities following renal HIFU but radiofrequency ablation or cryotherapy could be considered. Surgical resection, as either partial or radical nephrectomy, should be discussed; in our experience, surgery is no more difficult compared with that in an untreated patient. However, often the perinephric fat is hard and firmly fixed to the tumor due to thermal ablation – it should be carefully removed to avoid tumor puncture [7].

If early follow-up imaging suggests complete ablation then patients should undergo repeat imaging at regular intervals. For the first year, this should occur every 3 months. Thereafter, a follow-up protocol of 6-monthly or annual scans should be undertaken depending on prior imaging results. Regular imaging should continue to at least 5 years; in the absence of long-term studies of renal HIFU, it is not known whether continued follow-up after this time is required.

The only published study of renal HIFU with intermediate follow-up contained limited patient numbers. Fifteen of 17 patients in a clinical trial were treated; two treatments were abandoned due to intervening bowel in the acoustic field [7]. After 2 weeks, definite MRI evidence of ablation was seen in 7/15. Fourteen of these patients went on to have 6-month imaging; one had surgical resection. Of those 14, four had continued irregular enhancement suggestive of residual tumor and therefore underwent additional treatments. The remaining 10 patients were followed for a mean of 36 months; tumor involution was seen in all patients with central loss of enhancement and a mean 30% decrease in tumor cross-sectional area.

Conclusion

High-intensity focused ultrasound is a truly noninvasive energy ablative therapy for renal cancer which is associated with low morbidity, is repeatable and acceptable to both patient and clinicians alike. Devices are either ultrasound or MRI guided and the treatment technique varies according to each device. In general terms, it is necessary to cover the entire tumor with HIFU thermal lesions to ensure complete ablation. Major complications are rare but minor side-effects such as skin burns and pain are common. Currently treatment is limited by poor-quality imaging and a lack of effective intraoperative feedback on the progress of treatment. As a result, HIFU should be considered an experimental, minimally invasive therapy for renal cancer and should only be undertaken within clinical trials or in centers where careful audit of results is performed and analyzed.

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28

CHAPTER 28

Instrumentation and Technique: Laser

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Introduction

With increased detection of small renal masses, a minimally invasive treatment option that could be performed percutaneously under image guidance using a technology that is widely available can be very useful. The technology and technique must effectively destroy tumor cells with minimal patient morbidity. Laser technology is easily and widely available in many hospitals and has potential for the above application. There are several animal studies evaluating different types of lasers, both in the form of interstitial tissue ablation (ILA) and laser resection of kidney tissue. Also, there are clinical studies that have evaluated the safety and efficacy of percutaneous laser interstitial ablation to treat renal malignancy under magnetic resonance imaging (MRI) guidance [1,2]. Currently, laser application to treat renal tumors is investigational. Further evaluation is warranted, including the ability for real-time accurate monitoring of the laser ablation process, confirmation of adequate kill zone and methods to increase the size of the treatment ablation area.

For clinical stage 1 renal mass, currently available energy-based treatment options include cryoablation and radiofrequency ablation (RFA). With the above treatment modalities, complete tumor ablation is suboptimal when compared to surgical excision. With the need to achieve complete tumor ablation with no renal ischemia in a hemostatic environment by a minimally invasive method, several novel treatment modalities are in evolution. These include interstitial laser ablation (ILA), radiosurgery, microwave thermotherapy and high-intensity focused ultrasound. Currently, these technologies remain investigational. As laser technology is commonly available in hospitals worldwide, extending its application to treat a renal mass seems logical.

Laser technology for renal ablation

The laser effect on tissues is mainly thermal. Tissue interaction is dependent on the laser's wavelength, the power density delivered to the tissues, the wave modulation, and the exposure time. At 60 °C, there is coagulation of tissue and at 100 °C there is carbonization. And at 300 °C, there is melting of tissue or vaporization. Another effect, plasma-induced ablation, occurs at much higher temperatures.

Different types of lasers for ablation of kidney tissue and for partial nephrectomy have been described. These include the diode laser, holmium laser, KTP green light laser, Nd:YAG, thulium, and CO_2 lasers. Interstitial laser ablation of kidney involves delivery of energy through the placement of a specialized laser fiber directly into the lesion. Laser light is converted into heat >55 °C which causes tissue necrosis. For ILA of kidney, Nd:YAG and diode lasers have been used. Interstitial laser was described in 1983 by Bown to treat inoperable tumors of lung, stomach, and esophagus [3]. Holmium laser and

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green light laser (532 nm wavelength) used to perform partial nephrectomy without hilar clamping have been reported with inadequate hemostasis and unclear tumor margin [4,5]. Also, a solid-state thulium laser (wavelength 2013 nm) for partial nephrectomy (open or laparoscopic) in 16 patients has been reported by Gruschwitz and Mattioli in separate studies [6,7]. They report that a 2013 nm solid-state thulium fiber could coagulate vessels up to 1.5 mm. The estimated blood loss was approximately 156 mL for laparoscopic and 260 mL for open partial nephrectomy. With thermal injury, the deep margin can be difficult to assess for tumor, especially on a frozen section.

Experimental studies

Much of the reported use of laser ablation of kidneys has been in animal models. Lofti and co-authors investigated the acute tissue effects of contact Nd:YAG interstitial laser energy in porcinejkidneys under laparoscopic guidance [8] They developed a model to test the feasibility of using interstitial laser energy, administered under laparoscopic guidance, to ablate porcine normal renal tissue. Utilizing a synthetic sapphire interstitial Nd:YAG contact probe, minimal tissue effects were observed using total energies between 120 and 240 J. At energies of 480 J (8 W/60 sec), there was predominantly coagulation necrosis of the renal parenchyma. At 720 J (12 W/60 sec), there was tissue vaporization surrounded by a zone of coagulation necrosis approximately 1.5 cm across. This preliminary investigation demonstrated that the interstitial Nd:YAG contact laser probe can be used for both controlled coagulation necrosis and vaporization of renal parenchymal tissue.

Gettman and co-authors described the safety and efficacy of interstital laser coagulation through a laparoscopic approach with and without hilar occlusion in a porcine model [9]. They used a 600 μm bare-tip silicon diode laser fiber inserted 0.5 cm into the lower pole of each kidney at laser energy (wavelength 805 nm) applied for 15 min at 6 W. The hilum was clamped in one of the kidneys. The animals were sacrificed immediately and at 2 weeks or 4 weeks. The lesions were evaluated microscopically, including nicotinamide adenine dinucleotide (NADH) staining to assess cell viability. Acutely, there was cellular inflammation; chronic lesions demonstrated coagulative necrosis with progressive fibrosis. As also previously reported by Lofti et al., the authors noted that NADH staining showed residual viable cells in the treatment zone of survival animals, which is concerning. The mean size of the treatment zone in nonoccluded kidneys was 2.4 × 2.1 × 2.0 cm.The hilar occlusion group had lesion sizes of 4.0 × 3.3 × 2.8 cm and 3.3 × 3.5 × 2.0 cm in the 2-week and 4-week groups, respectively. Also, the hilar occlusion group resulted in slightly larger but statistically insignificant lesions. They reported on complications such as subcapsular hematoma, extension of laser coagulation zone into the psoas muscle, perinephric urinoma, and gross hematuria.

Another study using a new generation diffuser tip diode laser was reported by LaGrange and colleagues [10]. They used a temperature-adaptive diode laser (Indigo Optima®) at a wavelength of 800–850 nm in the hope of increasing the size of the treatment zone with the diffuser tip laser. Bilateral lower pole ILA of normal porcine kidneys via an open approach was performed. They evaluated the treatment zones in the acute (Figure 28.1) and also in the chronic group (45 days survival) of animals. The treatment time was increased for each pig from 4 to 8 to 12 min at a temperature-adaptive mode of 100 °C. The acute lesions were elliptical, measuring 18 × 9 mm and 17 × 9 mm at 4 min, 25 × 6 mm and 18 × 15 mm at 8 min, and 22 × 18 and 19 × 12 mm at 12 min. Unlike the previously reported studies, the authors found no viable cells with NADH staining and the treatment lesions were smaller than expected (Figure 28.2). The average dimension of the zone of nonviable cells was approx 1.4 × 0.8 cm.in acute animals and 1.25 × 0.7 cm in chronic animals. The lesions in the above animal studies produced by ILA were uniform in size and reproducible.

Of note, all the reported animal studies are in normal kidneys; there are no data on the effect of ILA in a cancer model. As suggested by LaGrange and co-authors, it would be interesting to study a cancer model such as the VX-2 kidney cancer model described by Nakada and colleagues [11]. Here, tumor cells are implanted under the renal capsule in New Zealand white rabbits, which produces an aggressive tumor with predictable course of metastatic spread. Also of note, there are no reported studies of renal laser application by a percutaneous approach.

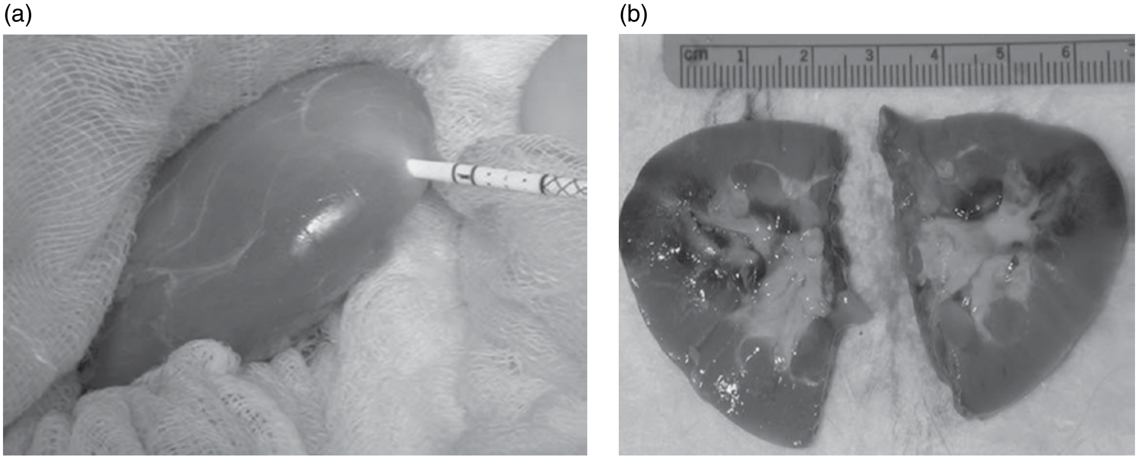

Figure 28.1 (a) Laser ablation in process in a porcine kidney. (b) Laser-ablated lesions (acute) in a bivalved kidney lower pole.

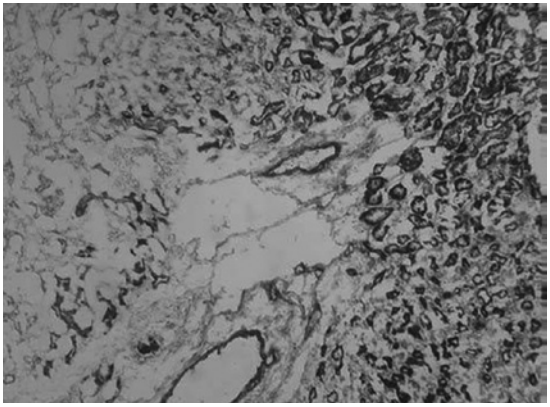

Figure 28.2 Acute lesion with NADH stain showing robust staining of normal kidney on right, mild staining of transition zone, and no staining of treatment zone on left.

Clinical studies

Although ablative therapies such as cryoablation and radiofrequency ablation have shown promise of efficacy, long-term oncological follow-up is not yet available. Surrogate outcome measures to detect for tumor recurrence, such as radiographic demonstration of loss of contrast enhancement or renal biopsy, have come into question occasionally.

For laser ablation of a renal mass, an interstitial laser with controllable ablation size which could be delivered by a percutaneous approach with real-time intraoperative monitoring of the lesion is optimal. Currently, there is no such system available.

There are a handful of reports related to the use of laser in the management of renal malignancy. De Jode and associates performed percutaneous ILA of renal tumors [1]. This is the first description of a percutaneous MR-guided laser ablation technique using real-time MR monitoring in the therapy of primary renal carcinoma. Laser therapy was delivered using a Nd:YAG source via a water-cooled applicator system. Thermal lesions were monitored in real time using a color thermometry sequence. Open MRI enables almost "real-time" placement of laser fibers in the tumor, with the patient under sedation or general anesthesia, with almost real-time thermal mapping of ablation, allowing continuous adjustment of the probe site and easy patient monitoring for sedation and pain. The above authors used laser (20–25 W for ≤20 min) in three patients with inoperable renal tumors, ranging from 2.5 cm to 5.5 cm (mean 3.6 cm). No perioperative complications were noted. Two patients required secondary treatments, and the remaining patient died of metastatic renal cell carcinoma (RCC).

The same group from London reported further on nine patients (range 56–81 years) with renal tumors [2]. Seven patients had biopsy-proven primary renal cell carcinoma, one patient had a secondary from contralateral renal cell carcinoma and one had oncocytoma with flank pain. Patients underwent percutaneous laser thermoablation (LTA) under MRI guidance in a 0.5 T

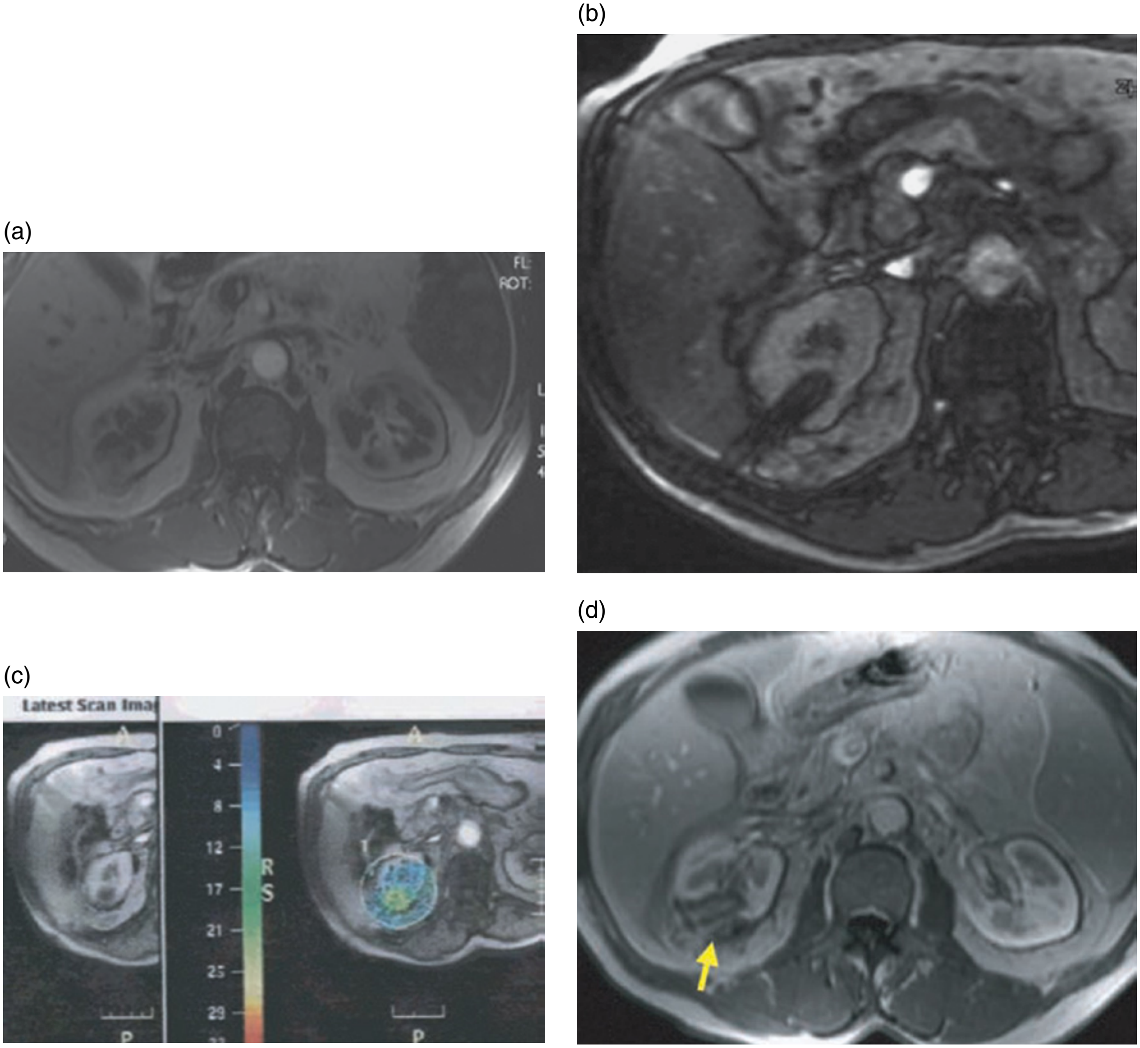

Figure 28.3 Images taken in a 75-year-old woman with right RCC. (a) Gadolinium-enhanced MRI before LTA shows that 85% of the tumor enhances. (b) A real-time image shows the needle *in situ* just before laser fiber insertion into the tumor. (c) Gray and color scale thermal maps, updated every 4 sec, showing the temperature within the tumor as heat is applied. (d) Six weeks after LTA, gadolinium-enhanced MRI shows that 21% of the tumor now enhances. (Source: de Jode MG, et al. 1999 [1]).

open magnet. Laser energy was applied at 25 W for 10–30 min in one or two applications of laser energy per session. Thermal ablation was monitored using a continuous-subtraction, colorization software algorithm, "real-time image processing" (RTIP). Irreversible tissue necrosis occurs at tissue temperatures of >55 °C, indicated by a persistent green area developing in the thermal map. The size of the thermal lesion corresponds to the area within the region of interest which is persistently green. Depending on the size of the tumor, the laser fiber delivery system was withdrawn 2–3 cm and further laser energy applied, with a maximum of two applications of laser energy per treatment session (total time for applying the laser energy of 30 min). Real-time color thermal mapping was used to monitor tumor ablation, and the follow-up was with gadolinium-enhanced MRI at 6 weeks and (where appropriate) 3–4 months after the procedure (Figure 28.3). Tumor volume and percentage tumor enhancement before and after ablation were compared. The percentage of tumor ablated on real-time T1-weighted thermal maps was compared with that on gadolinium-enhanced follow-up MRI. The mean follow-up was 16.9 (3–32) months after the first ablation. The mean tumor size did not change significantly but the mean percentage of viable tumor decreased significantly from 73.7% before to 29.5% after ablation. Thermal maps correlated moderately well with follow-up MRI in predicting the extent of tumor ablation (Pearson correlation coefficient 0.55).

There were two minor complications, including a perirenal hematoma that resolved with conservative management. There was one major complication, where one patient developed bradycardia, which responded rapidly to intravenous atropine but necessitated a short admission to the high-dependency unit.

The mean (range) maximum tumor diameter before treatment was 3.7 (2.0–6.0) cm. As mentioned before, the mean percentage enhancement decreased significantly from 73.7% before to 29.5% after LTA. Notably, the initial gadolinium-enhanced MRI after LTA (at 4–6 weeks) showed a characteristic inflammatory rim around the ablation zone which was not seen on subsequent films (≥3–4 months). The mean tumor volume destroyed for each burn was 5.4 mL. The authors in this pilot study concluded that MRI-guided LTA of renal tumors was safe, well tolerated by the patients, and significantly reduced enhancing tumor volume by a mean of 45%. LTA has several advantages over other ablative therapies: it is optimally suited to MRI guidance as it does not cause any field interactions (unlike RFA); there is little risk of laser fiber charring; the fibers are autoclaved and reused, and thus it is economical. Disadvantages of LTA include that although in theory a 3 cm diameter lesion is produced by a single ablation, many procedures may be needed to fully treat a tumor. In the above study, there was no histopathological correlation by biopsy to confirm the presence of residual tumor.

Holder et al. (unpublished, presented at the Radiological Society of North America meeting, November 2000) conducted bare-tipped laser ablation in eight patients with small RCCs immediately before nephrectomy. T1-weighted in-phase gradient echo imaging in a 1.5 T MRI system was used to guide needle placement in the tumor. No thermal mapping was used during the procedure. Immediately afterward, postcontrast fat-saturated T1-weighted gradient echo MRI was used to identify the size of the (hypointense) ablation zone, but this correlated poorly with pathological measurements of cell death. However, the appearances immediately after ablation might differ from those at 4–6 weeks and this factor may have contributed to the inaccuracy of MRI in assessing tumor necrosis. In the present study, the aim of each treatment session was to fully or partially ablate the tumor, depending on time constraints (30 min of ablation was the arbitrary upper limit) and patient tolerance, including accounting for patient movement. Including preliminary image acquisition, the entire procedure lasted 1.5 h, which all patients have so far found acceptable. As the procedure can be repeated with relative ease, the authors report it is not imperative to ablate the entire tumor in one treatment. The advantages are that it is well tolerated by the patients, involving only one night of inpatient stay, and the entire procedure can be monitored by MRI with no risk to the patient or operator (in contrast to a CT-monitored procedure).

In the cryoablation and RFA series, the percutaneous approach, although less invasive, reportedly had higher incomplete tumor ablation rates compared to the laparoscopic approach. However, as the percutaneous approach is less invasive, treatment can be repeated though this is not ideal. Percutaneous renal core biopsy is encouraged in patients undergoing thermal ablative therapies, including laser ablation, along with imaging studies to confirm the absence of viable tumor cells.

Lasers have also been used to ablate upper tract transitional carcinomas through an endoscopic approach by either a retrograde or antegrade percutaneous approach. Currently, holmium:YAG and neodymium:YAG lasers are used for ablation of these tumors but the procedure can be cumbersome. Anusionwu and co-authors reported the first use of diode laser technology (1470 nm) for the ablation of renal pelvic urothelial tumor 5 mm in size (Anusionwu et al., AUA 2012, Atlanta, video presentation 407). The laser fiber used was a 1470 nm diode laser that is 400 μm in diameter. The depth of penetration is 500 υm and both side-fire and end-fire fibers are available. The tumor was ablated in a 65-year-old man with low-grade transitional cell carcinoma of the renal pelvis with good hemostasis.

Conclusion

Percutaneous interstitial laser ablation for renal tumor has the potential to provide a reproducible area of tumor destruction with real-time monitoring of the ablative process under image guidance. It is currently investigational. Further evaluation of interstitial laser ablation is required, including the capability for real-time accurate monitoring of the laser ablation process by imaging, confirmation of adequate kill zone, and methods to increase the size of the treatment ablation area. Following further confirmation of adequate kill zone in experimental studies, percutaneous renal core biopsy should also be part of the evaluation process in patients undergoing thermal ablation in addition to the imaging studies to assess for any residual tumor to confirm the absence of viable cells within the laser-ablated treatment zone.

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29

CHAPTER 29

Instrumentation and Technique: Irreversible Electroporation

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Background and preclinical data

With the increasing incidence of small renal masses, there is a growing interest in minimally invasive surgery for treatment of these lesions. As covered elsewhere in this text, radiofrequency ablation (RFA) and cryoablation (CA) have shown both short-term and intermediate-term success in terms of surgical morbidity and oncological outcomes [1–4]. However, these techniques can be limited to the treatment of specific tumors due to anatomical factors that may affect the success of thermal ablation, namely centrally located tumors [5,6]. These tumors, because of their proximity to the renal hilum, are often close to large vasculature as well as the renal collecting system, such that ablation may lead to urothelial disruption or incomplete ablation secondary to "heatsink."

"Heatsink" is a well-described phenomenon that occurs secondary to countercurrent exchange of heat through large blood vessels that are in immediate proximity to the target ablation zone or within a target lesion. These areas of high flow "steal" heat (RFA) or cold (cryotherapy) from the target lesion, resulting in inadequate treatment in these zones [7]. In fact, the presence of vessels ≥3 mm in diameter near the tumor that must be ablated is a strong independent predictor of incomplete thermal tissue destruction [8]. Clinically, heatsink affects both the delivery of energy as well as the ability of that energy to lead to cell death, which may result in incomplete thermal ablation [9,10].

Another concern of thermal ablation is damage that may occur to the renal collecting system, resulting in calyceal stricture, urinary extravasation, and irreparable ureteral damage, all of which have been well documented in the literature. Overall, the majority of complications do not appear to be significantly different between cryotherapy and RFA, as there have been several reports of urinary fistula or collecting system injury following radiofrequency ablation [11,12] and cryoablation [13]. Involvement of the urinary tract in the ablation zone may present as minor hematuria, hematuria with significant clots, or obstruction of urinary drainage due to urothelial damage. Retrograde renal cooling during radiofrequency ablation may protect the urothelium, though this technique is rarely used in clinical practice [14]. Permanent urothelial damage may present as either calyceal obstruction or ureteral obstruction if damage occurs at the ureteropelvic junction (UPJ) or distally [12]. In extreme cases, damage to the urinary tract may result in perirenal urinoma formation or cutaneous urinary fistula.

Irreversible electroporation, first described by Neumann and colleagues in the 1980s in an *in vitro* gene transfer experiment [15], is a novel method for ablation of living tissue that is unique in that the process is nonthermal, offering potential advantages over radiofrequency ablation and cryoablation. Electroporation is a process whereby nanoscale pores are generated within cellular membranes as a consequence of an electric field across the

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.

cell and can be either reversible or lethally irreversible, depending on the magnitude of electricity applied [16]. When appropriately modulated, irreversible electroporation (IRE) is able to ablate a substantial and reproducible amount of tissue without inducing a thermal effect [17].

Irreversible electroporation is produced through a series of electrical pulses delivered by a single (bipolar) or multiple (monopolar) electrodes. Electrical fields surrounding the electrodes create a field with magnitude that decreases from the electrodes outward toward the tissue, such that fields near the electrodes undergo irreversible electroporation, while those slightly beyond the target zone may undergo reversible electroporation [18]. Regardless of reversibility, the electric charge delivered by IRE leads to increased cell membrane permeability, opening a pathway for ion transport that ultimately leads to cell death while preserving extracellular matrix, tissue scaffolding, ductal structures, and large blood vessels [17,19,20].

Due to its ability to avoid pitfalls of thermal ablation, there is a great deal of interest in applying IRE to ablation of renal tumors. While IRE has been shown to be effective in ablating liver and prostate tissue, these results cannot be immediately applied to the kidney, which is substantially different from these organs given the vigorous arterial blood supply, complex renal collecting system, and presence of urinary solutes. The efficacy of IRE ablation of renal parenchyma was first described by our group in 2011 [21]. Using IRE bipolar and monopolar electrodes (Angiodynamics, Queensbury, NY), we performed 24 laparoscopic ablations on porcine kidneys with four endpoints for histological analysis (immediate, 1 h, 7 days, and 14 days after ablation). Hematoxylin and eosin (H&E) staining and nicotinamide adenine dinucleotide (NADH) staining (for cellular viability) showed initial grossly hemorrhagic lesions, which decreased progressively to small white scars over the 14-day period (Figure 29.1). Histopathological evaluation revealed diffuse tubular desquamation, eosinophilia, swelling of cells, and absence of cellular viability immediately following IRE treatment (Figure 29.2). These changes evolved to diffuse cellular necrosis and early peripheral granulation by 7 days and chronic inflammation, cellular contraction, and fibrosis by day 14. In addition to its effect on the parenchyma, IRE appeared to provide some urothelial sparing with initial ulceration followed by signs of early repair and viability at 14 days.

Other authors subsequently confirmed the above findings using image-guided percutaneous placement of IRE electrodes followed by imaging correlated with histology. Deodhar et al. utilized computed tomography (CT)-guided placement of monopolar electrodes, followed by contrast-enhanced CT immediately, 7 days, and 21 days following treatment [19]. CT scans of the IRE lesions were characterized by nonenhancing hypodense ablation zones immediately post treatment, focal hyperdensities within otherwise hypodense ablation zones at 1 week, and no identifiable ablation zone by 3 weeks in the majority of animals. Additionally, there were no cases of urinary extravasation or evidence of collecting system injury in any of the cases, confirming the potential connective tissue-sparing effects of IRE. Wendler et al. evaluated magnetic resonance imaging (MRI)-guided percutaneous ablation using MRI and intravenous urography (IVU) [22]. Both MRI and histological analysis demonstrated localized necrosis at 7 days with progressive scarring by 7 days and intense scar contraction by 28 days. Again, there was no evidence of urothelial injury, with unaltered morphology of the renal calyces, pelvis, and ureter on IVU.

In addition to the interest in nonthermal IRE's (NTIRE) ability to spare connective tissue structures, there is also significant interest in its ability to be used in juxtaposition to large vessels and in the central portion of the highly perfused renal parenchyma. In order to evaluate the effects on vasculature, Wendler et al. performed conventional dynamic digital subtraction angiography (DSA) to evaluate large vessels and high-resolution x-ray in mammography technique to evaluate microvascularity before, during, and after NTIRE of porcine kidneys perfused *ex vivo*. They found no extravasation or disruption of the terminal vascular bed of the renal parenchyma, which is in contrast to several prior reports using cryoablation, RFA, and microwave treatments [23].

In addition to monopolar and bipolar IRE, an alternative platform combining NTIRE and thermal IRE (TIRE) (Ethicon Endosurgery, Cincinnati, OH) was recently evaluated in a porcine model to determine any potential benefit to a hybrid system [24]. In NTIRE, temperatures are kept <50 °C, while temperatures are allowed up to 90 °C in TIRE, theoretically allowing the physician to target peripheral tumors with TIRE and more central tumors with NTIRE. The authors found that while both modalities were able to ablate normal renal

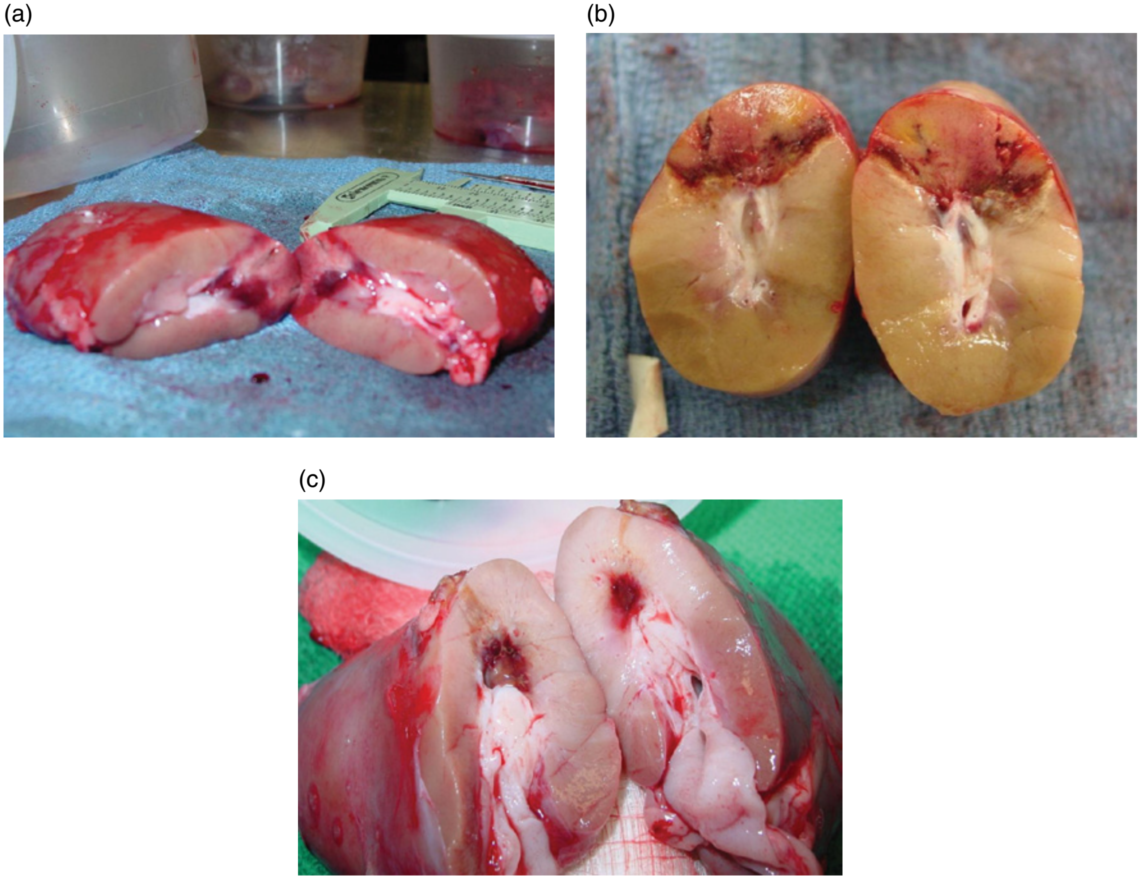

Figure 29.1 Gross images following IRE treatment in three porcine kidneys in the acute (1 h), subacute (7 days), and chronic (14 day) periods. (a) Acute changes 1 h following IRE are characterized by a central ischemic scar with surrounding hemorrhage. (b) By 7 days after the ablation, there is evidence of hemorrhage resolution with scarring and atrophy of the involved parenchyma. (c) At 14 days, the lesion has decreased significantly in size and is replaced by a small area of scar.

parenchyma with no viable cells based on NADH staining, NTIRE lesions were smaller with fewer inflammatory and hemorrhagic changes, while TIRE lesions were larger and characterized by coagulative necrosis. Interestingly, retrograde pyelography performed at the time of the ablation revealed urinary extravasation in one-third of animals in both the NTIRE and TIRE ablation groups. However, extravasation of contrast stopped completely by 24 h in both of the animals treated with NTIRE, while it persisted to 24 h and beyond 21 days in the two animals treated with TIRE. In addition, all chronic animals (7 and 21 days) in the TIRE group displayed irregularities in calyceal contour and in some cases complete calyceal obliteration, as compared to the NTIRE group in which normal anatomy was preserved in all animals. The authors felt that acute urinary extravasation in this study likely occurred as a result of direct puncture into the collecting system as insertion was performed visually, rather than with image guidance as reported elsewhere [19].

Clinical data

With mounting evidence of the potential benefits of IRE for renal tumor ablation, Pech et al. carried out the first human trial of IRE in 2011 [25]. The study, designed as a phase 1 trial evaluating safety of the technology rather than efficacy, was carried out in six patients with tumors

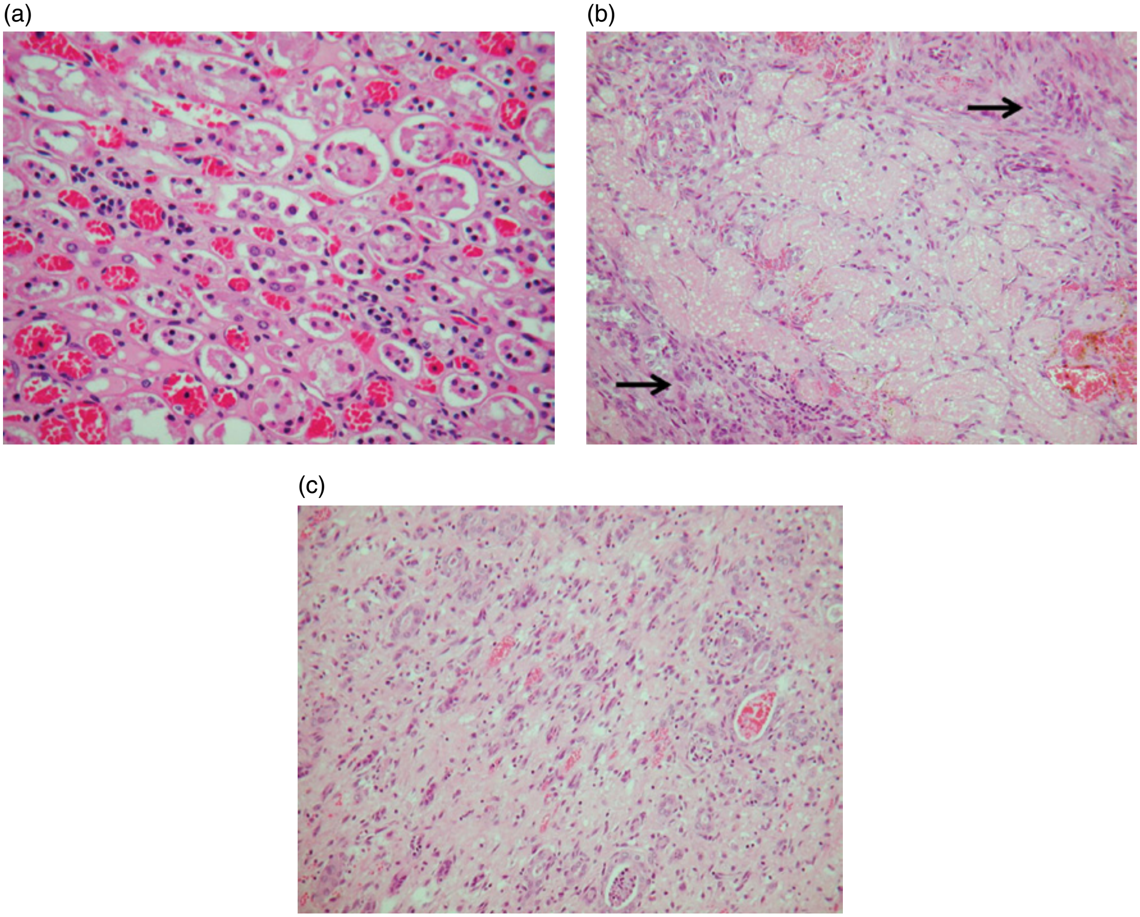

Figure 29.2 H&E stained porcine parenchyma (×100) at (a) 1 h after IRE, characterized by tubular eosinophilia and nuclear pyknosis consistent with early apoptosis. (b) Seven days after IRE there is diffuse necrosis, minimal inflammation, early scar tissue, and early granulation tissue (*arrows*). (c) Fourteen days after IRE, there is primarily chronic inflammation with more advanced granulation tissue and early fibrosis.

2.5–3.5 cm scheduled for extirpative surgery (partial or radical nephrectomy). Electrodes were placed under ultrasound guidance with a target treatment size of 30 × 15 mm and delivered using cardiac synchronization. All patients tolerated the procedure well with no changes identified during the procedure with regard to pulse rate, mean blood pressure, central venous pressure (CVP), creatine kinase muscle and brain (CK-MB), troponin-T or changes in ST segment on electrocardiogram (ECG). One patient did experience intraoperative supraventricular extrasystole, but this completely resolved postoperatively with no ECG changes identified during the postoperative monitoring phase. Ablated lesions were examined acutely 15 min after treatment with H&E staining only, which showed cellular swelling, but is inadequate at assessing postablative cellular viability.

General surgical considerations

As with other ablative technologies, there are few strict contraindications to renal mass ablation, including an uncorrected coagulopathy and the patient's overall medical condition. Patients should have preoperative coagulation studies (prothrombin time/partial thromboplastin time) and should be held from all medications that may alter platelet activity, including aspirin and clopidogrel. As NTIRE is not a coagulative technology, patients are likely at similar risk of bleeding complications as those undergoing cryotherapy and RFA. In contrast to percutaneous cryoablation and RFA, patients undergoing IRE must be under general anesthetic, as complete muscular relaxation is required to prevent muscular contraction from the high-voltage pulses generated during treatment.

General contraindications to laparoscopic surgery apply to laparoscopic ablation, including multiple intraabdominal adhesions, history of peritonitis, bowel distension, and severe chronic obstructive pulmonary disease (COPD). Laparoscopy should be considered the primary approach for all patients with anterior lesions and for those with lesions located within close proximity to other intraabdominal organs, as intraoperative dissection allows for an increased margin for safely avoiding adjacent structures. A needle-spacing device is available that can be used to place the electrodes at an appropriate distance extracorporeally, while intracorporeal distance can be confirmed with a small suture cut to the desired length.

Both irreversible and reversible electroporation lead to increased cell membrane permeability, leading to an increase in ion transport which may lead to cardiac arrhythmias and defibrillation [26–29], depending on the voltage applied and the distance from the heart to the target treatment area [27,30]. Because of the potential risk of inducing cardiac dysrhythmia, current algorithms incorporate cardiac synchronization, whereby pulses are delivered during the absolute refractory period of the cardiac rhythm (i.e. during the QRS complex). Because of these risks, all patients undergoing IRE should have a preoperative ECG and cardiac evaluation in order to rule out underlying cardiac abnormalities due to the potential for cardiac dysrhythmias from high-voltage pulses.

Figure 29.3 Nanoknife IRE generator from Angiodynamics (Queensbury, NY). Note the six inputs on the front of the machine for insertion of individual IRE electrodes.
(Source: Used by permission, AngioDynamics).

Instrumentation and technology

Currently IRE electrodes (Angiodynamics, Queensbury, NY) are available in both monopolar and bipolar configurations (Figure 29.3). Monopolar IRE probes are intended to be inserted at the periphery of the target tissue. Once in the appropriate position, an electrical pulse is transmitted between the probes, with the electrical field directly proportional to the supplied voltage and inversely proportional to the distance from the probe. Each monopolar probe is covered with a protective sheath, such that the exposed portion of the probe (the portion which can be used to transmit energy) can be set at 1 mm increments from 0 to 40 mm.

The IRE generator, which can accommodate up to six probes, can be set for variable pulse number (10–100), pulse amplitude (100–3000 V), and pulse length (20–100 μsec). Once activated, the generator delivers a "test pulse" to assure adequate coupling between probes. Energy is then delivered based on a predetermined protocol with each ablation cycle occurring between pairs of electrodes, leading to an ellipsoid ablation. If more than two probes are placed, ablation carries on between pairs of probes until all tissue is treated within the target zone. According to the company's recommendations, two monopolar probes placed 15 mm apart with a deployed length of 2 cm, voltage of 2500 V, pulse length of 100 μsec, and 90 pulses should generate a lesion 25 mm in length, 30 mm deep, and 17 mm in width, with an approximate volume of 8340 mm^3.

Bipolar IRE probes generate energy between two portions of an exposed electrode (7.5 mm) on a single probe that are separated by an intermediate insulator of similar length. Energy is transmitted between these two coupling points along a single probe. When inserted 2.5 cm into the tissue, with energy applied at 2750 V with pulse length of 100 μsec and 90 pulses, the bipolar device should create a zone of ablation that is 29 mm in depth and 17 mm in diameter, with an approximate volume of 3929 mm^3 (assuming the shape of a prolate spheroid). While the length of the ablation is fixed due to probe configuration, the diameter can be altered by either lowering the voltage or shortening the duration of each pulse.

Informed consent

Patients undergoing IRE should be counseled on the potential short-term and long-term complications of renal tumor ablation [31], including bleeding, infection, damage to surrounding structures (spleen, liver, bowel, etc.), pneumothorax (for percutaneous ablation), urine leak, and cardiac dysrhythmias. Additionally, patients should be made aware that while intermediate- and long-term results appear favorable for radiofrequency ablation and cryoablation, there are very few clinical data with IRE validating its use even in the short term, not to mention the intermediate or long term and, therefore, clinical application currently should be reserved for investigation only.

Positioning and step-by-step technique

Positioning for percutaneous and laparoscopic IRE is similar to that previously described for other ablative techniques [32]. Briefly, for CT-guided percutaneous IRE, after induction of anesthesia and complete muscular blockade as confirmed by absence of response on twitch monitor, the patient is positioned on the CT table in order to best expose their tumor for placement of the percutaneous electrodes. Once positioned appropriately, an initial CT scan confirms a clear path to the kidney tumor. If positioning appears appropriate and the patient's creatinine clearance permits, intravenous contrast is administered and the scan is repeated in order to further delineate the lesion. Using measurements and calculated angles from this "scout" image, individual probes may be placed as needed around the periphery of the target tumor. An external spacer should be utilized to approximate an accurate distance between probes (this can be confirmed on subsequent imaging). Ultrasound guidance may be of assistance for placement of multiple probes. After CT confirmation of probe placement, ablation is carried out using NTIRE according to a predetermined algorithm based on the size of the patient's tumor. Once the probe has been removed, a contrast CT scan can be performed in order to confirm complete tumor ablation.

For laparoscopic IRE, the patient is positioned in the modified flank position at 30–45° and strapped to the table using 2 inch cloth tape. The kidney is accessed in a standard laparoscopic fashion and the perinephric fat is dissected away from the kidney in order to fully expose the lesion. A laparoscopic ultrasound probe is brought through the inferior laparoscopic port in order to confirm the lesion characteristics, including size and depth of penetration. Once the lesion has been exposed, the IRE probes may be positioned around the border of the lesion (with a 0.5–1 cm margin) through separate stab incisions along a perpendicular orientation to the tumor surface. Depth of electrode insertion may be confirmed with ultrasonography, while distance between tines can be confirmed with an appropriately cut piece of 0 silk suture.

Postoperative follow-up

There is no currently accepted follow-up regimen for patients undergoing IRE due to the paucity of clinical information. Our current preferred practice for follow-up of renal ablation using RFA is an initial contrast-enhanced renal protocol CT scan at 6 weeks to look for persistent disease, followed by CT scan every 6 months for 3 years and then yearly looking for tumor recurrence. In contrast to RFA and cryoablation, lesions treated with IRE may resolve more rapidly, allowing for earlier declaration of success and earlier detection of subsequent recurrences [19]. Patients with stage T1a renal cell carcinoma should also be followed with annual physical exam, laboratory evaluation, and chest radiographs.

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CHAPTER 30

Instrumentation and Techniques in Renal Radiosurgery

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Informed consent

In broaching the topic of renal stereotactic radiosurgery (SR) with patients, the clinician performing the procedure should disclose and discuss the following: the patient's diagnosis; the nature and purpose of the proposed procedure; alternative treatments, including no treatment; and the associated risks and benefits of each of these options. While robotic SR is approved by the US Food and Drug Administration for use anywhere in the body where clinically indicated, the field of radiosurgery for the treatment of renal cell carcinoma (RCC) is still in its infancy and should be considered largely investigational at present.

Renal SR involves the *extracorporeal* delivery of fractionated ablative radiation to the target lesion, over the course of several days, avoiding the need for general anesthesia. Its purpose is two-fold: to preserve renal parenchyma and to achieve oncological control comparable to conventional therapies, while avoiding the surgical and/or anesthetic morbidity associated with nephron-sparing surgery and other ablative technologies (including cryoablation and radiofrequency ablation).

Traditionally, RCC has been regarded as a relatively radioresistant tumor using conventional radiotherapy [1–5]. The efficacy of SR for localized and/or metastatic RCC seems promising based on short- to intermediate-term outcomes of small series and early clinical trials [6–11]. However, its "off protocol" application outside the auspices of a clinical trial should be approached cautiously with full disclosure to patients of its yet unproven benefit and/or harm.

Despite the very low rates of toxicity seen thus far with renal SR in our phase 1 trial, confirmation of its safety and efficacy awaits the results of ongoing phase 1/phase 2 and perhaps future phase 3 clinical trials. Organs at risk (OAR) include the treated kidney itself, especially the renal medulla, and occasionally the bowel. From our own intermediate-term data (median follow-up, 30 months), dose escalation to 48 Gy in four fractions has been completed without dose-limiting toxicities, that is, Grade 3 or worse gastrointestinal/genitourinary toxicity as defined by Common Terminology Criteria of Adverse Events (CTCAE version 4) (unpublished data). Acute side-effects include transient Grade 1–2 nausea, fatigue, skin rash, and local pain. Intermediate-term side-effects include Grade 1–2 renal toxicity with exacerbation of chronic renal insufficiency. The need for posttreatment dialysis has not been reported.

Preoperative preparation

A unique renal mass treatment plan is designed preoperatively for every patient. It involves using three-dimensional (3D) reconstructions of the patient's anatomy generated from contrast-enhanced cross-sectional imaging studies (computed tomography [CT]

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and/or magnetic resonance imaging [MRI]) to characterize the target lesion from surrounding OAR and to guide treatment beam positioning. Once acquired, the 3D images are transferred to a treatment planning system. The clinical target volume (CTV), which is usually equivalent to the gross tumor volume (GTV), is defined, and a uniform 5–10 mm margin is added to the CTV circumferentially to obtain the planning target volume (PTV). The margin of error included in the PTV allows for radiosurgical leeway, taking into account CTV movements, set-up deviations, and a good surgical margin. The remaining healthy kidney, excluding the CTV, and surrounding uninvolved tissues are defined as a separate volume, the OAR.

The goal of treatment beam positioning is to create a highly conformal dose distribution within the irregular PTV. Each beam is described by a vector that links the origin of the beam, i.e. the linear accelerator (LINAC), known as the source point or node, to its desired destination, a defined location within the PTV, known as the direction point. Using the nonisocentric beam generation mode, a candidate beam set is automatically generated, semi-randomly linking thousands of direction points within the PTV to one of up to 133 possible nodes along the path set of the robotic manipulator. For dose calculation planning, the Monte Carlo algorithm is used. The candidate beam set is generated and its dose distribution is calculated. The relative weight of each beam is further optimized using a sequential optimization algorithm to select optimal beam weights, beam directions, and field sizes. The physicist tailors the candidate beam set to each patient to avoid radiation exposure to the OAR. After being approved by both the surgeon and the radiation oncologist, the final treatment plan is sent to the treatment delivery system (Figure 30.1).

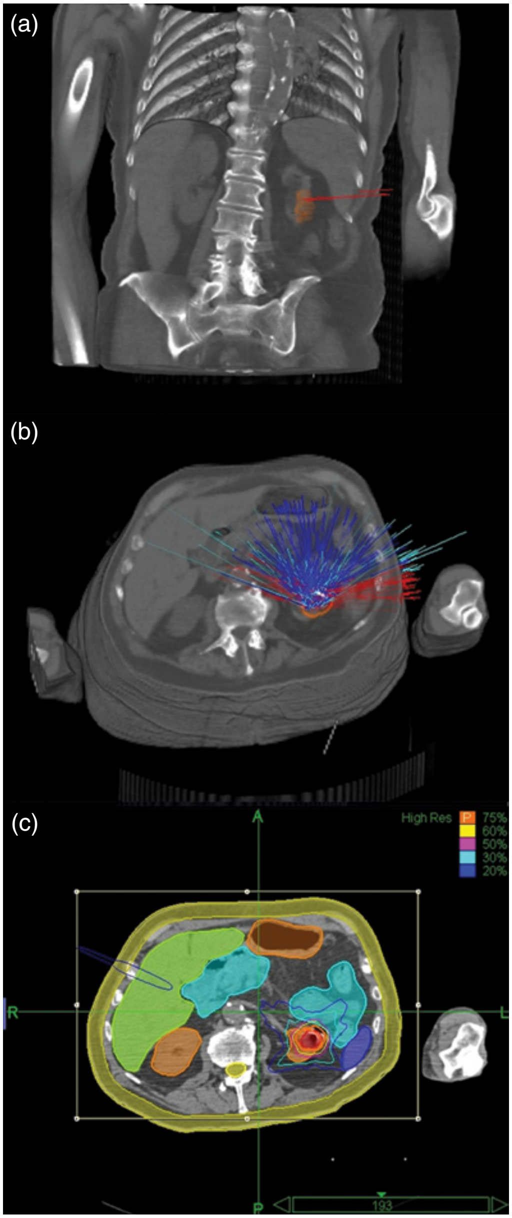

Figure 30.1 A renal mass treatment plan generated using a nonisocentric candidate beam set. The preprocedural coronal CT image (a) localizes the left inferior pole renal mass for radiosurgical treatment planning. (b) In this particular case, 141 beams originate at 56 nodes, and each beam carries a variable intensity, indicated by its relative length. (c) The highly conformal dose distributions avoid the OAR (*shaded structures*) while delivering isodoses to the GTV as shown (by the outlines): 32 Gy (prescription), 24 Gy (orange), 19 Gy (yellow), 16 Gy (magenta), 10 Gy (aqua), and 6 Gy (blue). The conformality index of the prescription isodose is 1.62.

Patient positioning

The key to positioning for renal SR is ensuring comfortable and consistent patient immobilization. In plain clothes, patients are positioned supine with arms outstretched above their heads. Patients are placed atop a vacuum cushion (SecureVac™, Bionix, Toledo, OH) which is nested within a rigid Stereotactic Body Frame (Elekta Corporation, Stockholm, Sweden). Once the patient is positioned, negative pressure is applied to the vacuum cushion, which conforms to the patient's body and limits movement. The vacuum cushion is saved and reused in its filled form for all subsequent planned treatments. An abdominal compression device may be employed to limit the respiratory motion of the target if necessary. While current advances in SR technology, including continuous image guidance, dynamic motion targeting, and intelligent patient positioning, may decrease the need for complete immobilization, the authors prefer to limit patient motion as much as possible.

Instrumentation

Several radiosurgery systems exist that are suited to treat organs, like the kidney, that move with respiration, including the CyberKnife® VSI™ System (Accuray Incorporated, Sunnyvale, CA), the Novalis® System (BrainLab AG, Heimstetten, Germany), and Tomotherapy® (Tomotherapy Incorporated, Madison, WI). The CyberKnife, currently used by the authors, uses a lightweight 6 MV linear accelerator mounted to a highly maneuverable KR240-2 (Series 2000) robotic manipulator (Kuku Roboter GmbH, Augsburg, Germany) to deliver highly collimated beams of radiation in almost any direction. Secondary collimation is achieved with one of 12 fixed circular collimators that can be changed manually or automatically by the Xchange® Robotic Collimator Changer (Accuray) or with a single variable aperture collimator, like the Iris™ Variable Aperture Collimator (Accuray). An x-ray imaging system, including two diagnostic x-ray sources mounted to the ceiling and two flat panel x-ray detectors fixed in the floor, monitor the location of bony landmarks, implanted fiducials, and soft tissue targets throughout the treatment. A stereo camera system mounted on a boom arm from the ceiling monitors the location of light-emitting diodes (LEDs) placed on the patient's skin. Processing the information obtained from the x-ray tracking system and the stereo camera system, the Synchrony® Respiratory Tracking System (Accuray) directs the robotic manipulator to track renal tumors as they move with respiration. Further advances, like the RoboCouch™ Patient Positioning System (Accuray), allow for automatic real-time positioning and repositioning of the patient with 6° of freedom during treatment (Figure 30.2).

Step-by-step technique

(Video Clip 30.1)

Once the patient is secured in a fixed position, the tumor is grossly aligned relative to the LINAC by adjusting the treatment table. Real-time tumor localization is achieved by the juxtaposition of digitally reconstructed radiographs (DRRs) from the 3D patient model on live images obtained from the x-ray imaging system based on the position of known radiopaque fiducial markers. This amalgam 3D reconstruction is automatically generated and guides initial treatment beam alignment with the PTV. Image acquisition, target localization, and fine alignment corrections occur dynamically throughout the treatment at 30–60 sec intervals. Based on small positional changes detected on the most recently acquired image pair, the image guidance system determines the additional translational and rotational corrections required to precisely align the treatment beam and relays these corrections to the robotic manipulator, which in turn adjusts the LINAC accordingly. Since renal target lesions move with respiration, an additional motion-tracking system (Synchrony) is employed. Synchrony correlates LED (external body surface) movement detected by the stereo camera system with internal fiducial (tumor) movement seen on fluoroscopy, enabling treatment beams to follow the target in real time while the patient breathes freely. During treatment, the robotic manipulator moves in sequence through the preselected nodes, and at each node, it automatically reorients the LINAC for treatment beam delivery.

Intraoperative troubleshooting

Capable of producing a highly potent radiobiological dose, SR is ideally suited for treating even relatively radioresistant tumors like RCC. Due to the high dose of radiation delivered per fraction, the radiation tolerance of surrounding normal tissues must be considered so as to avoid severe toxicity. Especially true for renal tumors, tumor motion must be accounted for during treatment planning and delivery to ensure safe and effective SR administration. While the robotic manipulator automatically corrects for small patient movements, large translations and rotations put a hold on the treatment. Since motion interruptions can significantly delay treatment

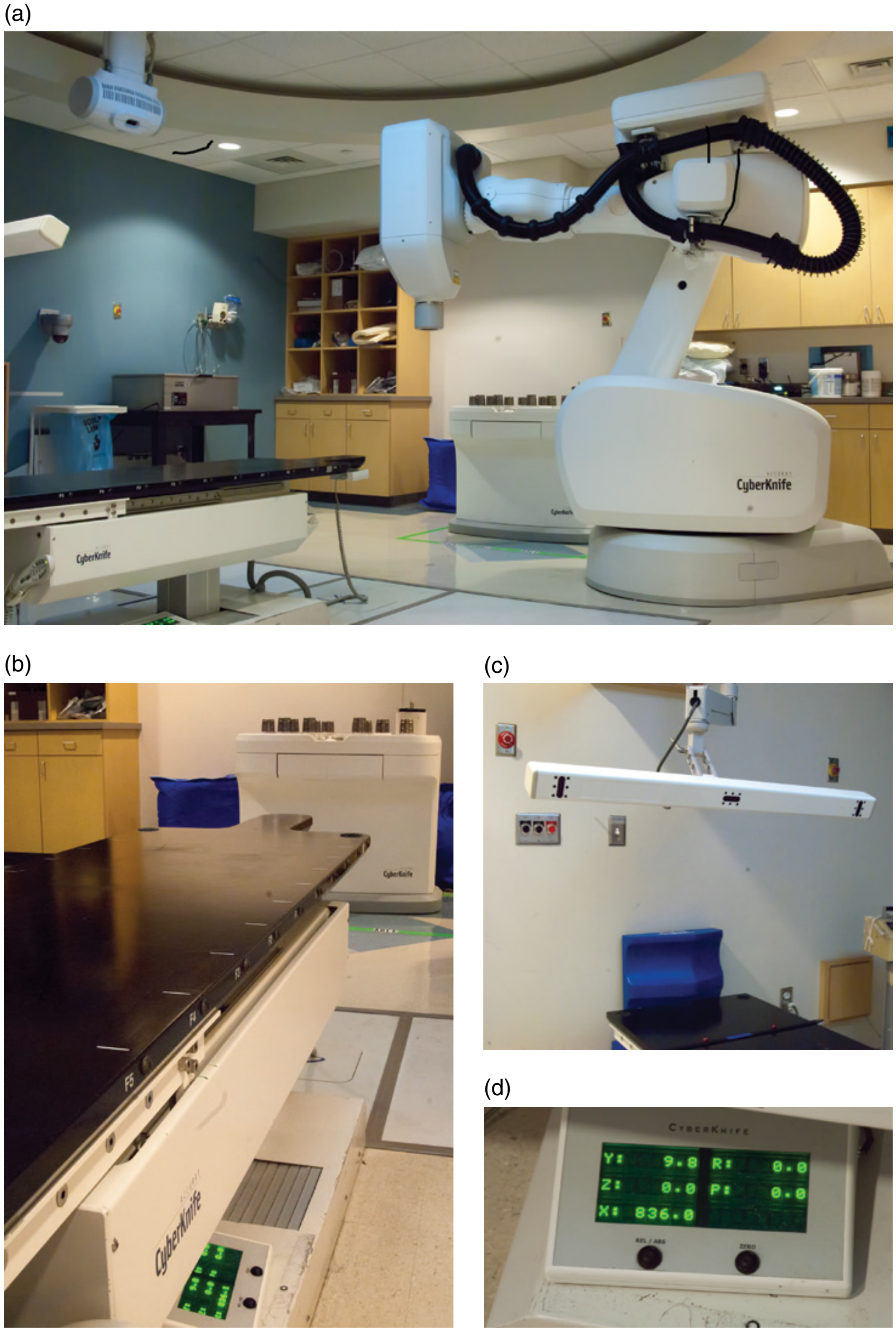

Figure 30.2 The CyberKnife System (a) constitutes a LINAC mounted on a robotic manipulator that precisely delivers radiation under the continual x-ray guidance provided by two diagnostic x-ray sources mounted on the ceiling (one source seen in the upper left-hand corner) and two flat-panel x-ray detectors installed flush with the floor. Before each treatment, the x-ray image guidance system aligns the patient on an adjustable five-axis treatment table (b, d) based on the tumor location as defined by radiopaque fiducial markers. The stereo camera system (c), which is out of full view on the far left-hand side of (a), is shown in better detail here. It detects the movement of LEDs placed on the patient's chest, allowing for real-time tracking of renal tumors with respiration while minimizing the radiographic imaging exposure. (Photos courtesy of Gary Coffey).

due to time-consuming manual repositioning, it is the authors' preference to spend a significant amount of time at the beginning of the procedure to ensure satisfactory patient positioning.

Posttreatment follow-up

The authors recommend a close patient follow-up regimen immediately following renal SR. Clinical examinations, including blood chemistry analysis and CT or MRI imaging, are routinely performed at 3–6-month intervals for the first 2 years. As part of our clinical trials, patients receive a 6-month posttreatment biopsy to ensure efficacy, as contrast-enhanced axial imaging does not necessarily correlate with histopathological examination following renal tumor ablation [12,13]. Intervals between clinical examinations are extended to 6–12 months in patients without recurrences or with stable disease for more than 2 years.

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CHAPTER 31

Instrumentation and Technique: Renal Histotripsy

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Controlled acoustic cavitation

Histotripsy is an experimental focused ultrasound modality in which tissues and cellular structures are homogenized with intense pulses of acoustic energy [1–5]. Acoustic energy is generated by applying a voltage change to piezoelectric elements. The conformational change creates a pressure wave which can be focused to generate intense pressures (compressive and rarefactive) at the geometric focus.

Ultrasound energy can produce a range of biological effects, depending upon the form of energy delivery (intensity, duration, pulsed or continuous waveform, etc.) and intrinsic characteristics of the affected tissue. As acoustic amplitude increases, the pressure generated also increases. Acoustic intensity is proportional to the square of pressure amplitude and is often used to characterize the applied force from a focused transducer.

Low-intensity ultrasound, as is typically used for diagnostic imaging, results in minimal biological effects and no tissue damage. At higher acoustic intensities (greater than 300 W/cm^2) when energy is applied continuously or as long pulses, temperature elevation can occur as a result of ultrasound-induced frictional heating. High-intensity focus ultrasound (HIFU) is based on this process and leads to coagulative necrosis of the targeted tissues [6–9]. At even greater acoustic intensities (i.e. 2000 W/cm^2), cavitation (formation of microbubbles) can also be observed [1–3,10–12]. As the pressure becomes sufficiently low during the rarefactive phase of the pressure wave, vapor accumulates and dissolved gases come out of solution, forming microbubbles. These microbubbles do not immediately dissolve back into solution with the next positive pressure phase. Rather, they oscillate in response to subsequent ultrasound pulses, expanding when ambient pressure is low and shrinking when pressures are high.

It is important to understand that several forms of cavitation exist. Microbubbles can exhibit "stable cavitation" (perpetual oscillation) or "unstable cavitation" (Figure 31.1) where initial bubble expansion exceeds a threshold rate and energy stored during the expansion phase is released synchronous with a compressive phase of the ultrasound pulse. This results in violent collapse of the bubbles [13].

Pyrotherapy, a form of therapeutic ultrasound in which intense continuous application of ultrasound energy resulted in both thermal and cavitational effects, was previously explored [14]. Ultimately, this approach was abandoned when cavitation appeared to be unpredictable and too difficult to control [9,10]. Based on this experience, contemporary therapeutic ultrasound research has primarily focused on optimizing thermal effects below the cavitational threshold [6–8,15–17].

However, our research group has pursued the idea that cavitation can be controlled by delivering intense, short (<50 μsec) pulses of ultrasound energy at a low

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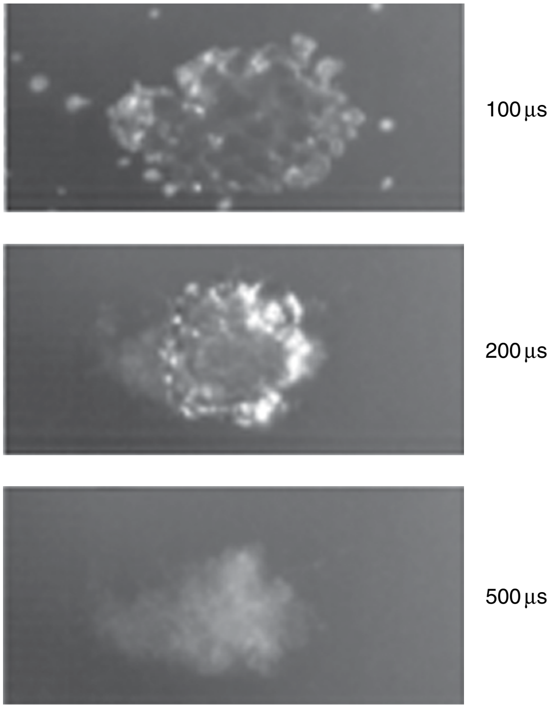

Figure 31.1 High speed photographs of histotripy bubble clouds 100, 200, and 500 microseconds after a histotripsy pulse. The microbubbles are observed to enlarge, coalesce, and then collapse with only tiny nuclei remaining.

time-averaged power. This strategy minimizes thermal effects, effectively isolating cavitational activity [18–22]. Each ultrasound pulse creates a highly dynamic but localized cloud of microbubbles. The subsequent oscillation and violent collapse of these bubble clouds reduce tissue to a homogenate of subcellular particles. This form of therapeutic ultrasound has been named “histotripsy” to emphasize the nonthermal, mechanical mechanism of action.

Tissue homogenization

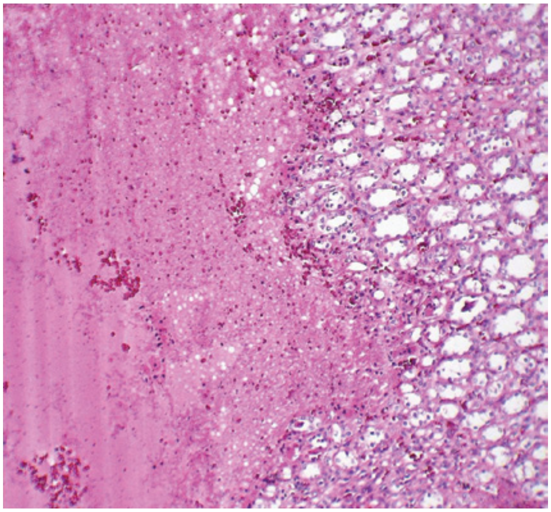

Figure 31.2 H&E-stained slide of rabbit renal tissue encompassing the edge of the targeted zone. On the right are normal-appearing tubules. On the left, histotripsy has reduced the tissue to a fine homogenate of subcellular material. Note the sharpness of the margin between homogenized and normal-appearing tissue.

After histotripsy treatment (Figure 31.2), cellular structures and architectural features are homogenized to a slurry of subcellular debris [2]. This effect was initially demonstrated in *ex vivo* porcine kidneys submerged in a tank of degassed water. Thermocouples were placed at target points within the cortex of the kidney. The histotripsy bubble cloud was then swept through a 3 × 3 grid of closely spaced points incorporating the location of the thermocouple tips. A number of parameter sets (varying intensity, pulse repetition frequency, number of pulses per point, and duty cycle) were utilized to span the acoustic spectrum and replicate energy delivery seen with diagnostic ultrasound, HIFU, and histotripsy. After treatment, the kidneys were sectioned and treated target volumes were examined macroscopically and morphologically classified as disrupted, desiccated, or mixed [18].

Treated volumes characterized as disrupted (where liquefied material spilled out of a cavity after sectioning) were associated with a temperature rise no greater than 27 °C indicative of nonthermal cavitational tissue homogenization. Temperature increases of greater than 40 °C were associated with desiccated tissue lesions consistent with thermal coagulative necrosis. When plotted in parameter space, the various parameter sets clustered based on the morphological appearance of the lesion produced (Figure 31.3). These results demonstrate that a range of acoustic parameters exists capable of producing mechanical tissue homogenization without thermal coagulative necrosis [18].

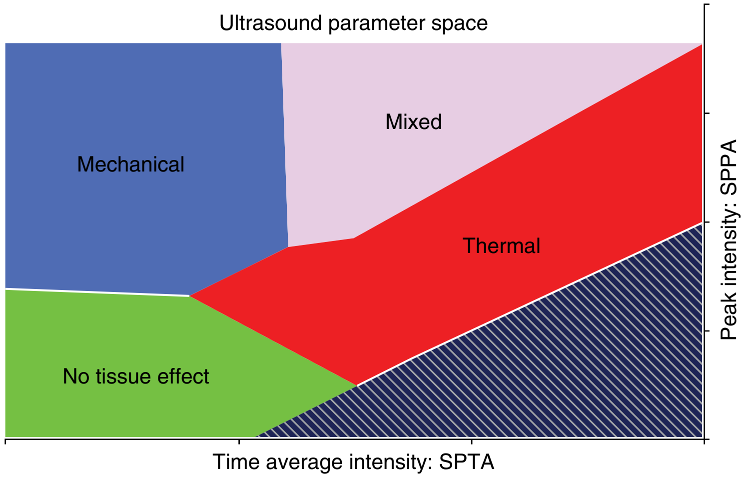

Figure 31.3 A plot of time averaged intensity (SPTA) versus peak intensity (SPPA). Histotripsy occupies the blue zone where mechanical effects predominate without substantial thermal contribution. HIFU corresponds to the red zone and diagnostic ultrasound to the green zone.

Ultrasound feedback

The microbubbles produced by histotripsy, which homogenize tissue, are also excellent acoustic reflectors. They appear as hyperechoic (bright) foci on diagnostic ultrasound images [2,12] and indicate the presence of cavitational activity (tissue homogenization). They can be used as a feedback mechanism for target localization and real-time monitoring of tissue change and treatment progression (Figure 31.4, Video 31.1). This form of real-time image feedback is directly linked to the tissue ablative process of histotripsy and is difficult to achieve with thermal ablation modalities.

During histotripsy treatment, the dynamic activity of microbubbles produces a temporally changing (twinkling) appearance on diagnostic ultrasound. High-quality real-time B-mode ultrasound images are achievable during histotripsy treatment with only occasional scan line corruption since therapeutic pulses are applied at low duty cycle [23]. Tissue homogenized with histotripsy appears hypoechoic (dark) compared to surrounding tissue on ultrasound images. Other forms of ultrasound backscatter data have also been examined and show promise as indicators of degree of tissue homogenization [24,25].

Histotripsy dose–bioeffect relationship

Histotripsy is a stochastic process, in that bubbles develop at nucleation sites randomly distributed throughout the focal volume (i.e. the zone where the rarefactive pressure is sufficiently negative to induce bubble formation and growth). Progressive acoustic pressure pulses induce and maintain cavitation activity, which leads to bubble collapse and local zones of tissue homogenization. These zones of damage enlarge and coalesce as additional acoustic pulses are applied, ultimately covering the entire focal volume.

Figure 31.4 Ultrasound image of the left kidney (*center*) of a rabbit undergoing histotripsy treatment. The cavitation bubble cloud appears as a bright cluster near the superficial surface of the kidney. See also Video Clip 31.1.

To explore the relationship between dose and bioeffect, histotripsy was applied to single focal volume (3 × 3 × 10 mm) located within normal renal cortical tissue of an *in vivo* rabbit model. “Doses” of 10, 100, 1000, 10000 or 26000 pulses of ultrasound energy were applied to each targeted volume from a 750 kHz piezoelectric transducer (Figure 31.5) [2]. Scattered pockets of extravasated blood were apparent within the 3 × 3 × 10 mm ellipsoid focal volume after 10 pulses (Figure 31.6). A greater number of hemorrhagic areas of larger size were noted within the same sized ellipsoid focal volume after 100 pulses. Surrounding each area of hemorrhage, a two-tiered pattern of cellular injury was noted, spanning 200 microns [2].

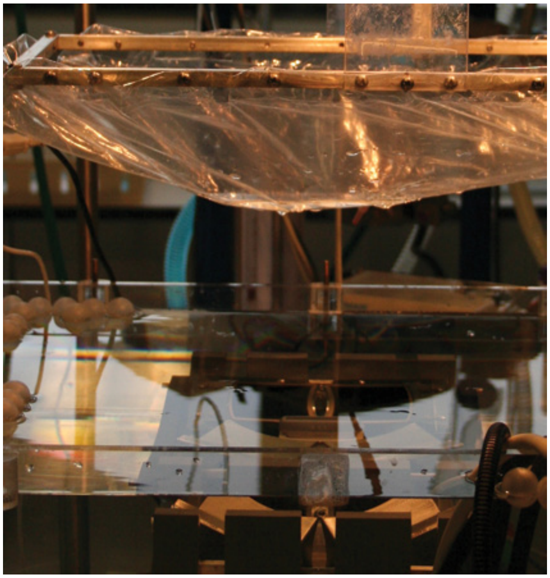

Figure 31.5 Rabbit histotripsy is performed by placing an anesthetized rabbit with its shaved flank down on the plastic sling. The rabbit is then lowered partially into a tank of degassed water. Histotripsy is delivered from a therapeutic transducer system at the bottom of the tank aiming upwards. An 11 MHz imaging probe aligned with the therapy beam is used to colocalize the bubble cloud with the targeted tissue.

An elliptical cavity with liquefied core and smooth boundaries was observed after 1000 pulses (see Figure 31.6). The homogenate was histologically characterized as hemorrhage and acellular material thought to represent cytoplasm and fractionated cellular material. The few islands of recognizable parenchymal structure within the large confluent areas contained only mortally damaged cells. With application of more than 1000 pulses, the size of the homogenized zone did not expand. However, the boundary of the confluent acellular region became more uniform with a narrower zone of peripheral damage [2].

Histotripsy thresholds and renal structures

The threshold for histotripsy damage appears to differ based on tissue type and architectural structure. To investigate this observation, histotripsy was applied to porcine kidneys *in vitro* by placing individual focal volumes 2 mm apart within a 5 × 5 grid. When this strategy was utilized on cortical tissue, complete homogenization resulted. Following histotripsy of a similar volume that encompassed renal cortex, medulla, and collecting system, the collecting system was found to be intact and undamaged,

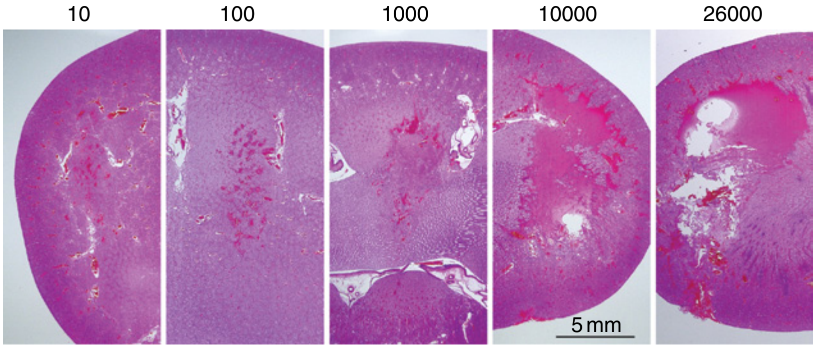

Figure 31.6 Application of a few pulses of histotripsy results in random foci of damage (hemorrhage) within the targeted volume. As additional pulses are applied, these foci enlarge and increase in number, ultimately coalescing. By 100 pulses pockets of homogenate in addition to hemorrhage are apparent within the focal volume.

while the cortical tissue was homogenized and medulla tissue exhibited pockets of hemorrhage containing small zones of tissue homogenate [26].

Although further characterization of tissue thresholds is needed, these findings suggest a number of potential treatment strategies. Natural anatomical boundaries that are more resilient to cavitational effects could serve as borders confining the treatment effect. In addition to the ability to utilize certain anatomical features as safety margins, histotripsy can be made extremely precise by modulating the acoustic beam and further controlling the microbubble population within the target volume – a technique called active protection [27].

Hemostasis with histotripsy

In a rabbit model, renal histotripsy produced only minimal perinephric hematoma and hematuria. Furthermore, in canine studies only mild gross hematuria was observed without clots or change in hematocrit when prostate histotripsy was performed to create a transurethral resection of prostate (TURP)-like defect. These observations prompted a study in nine canine subjects anticoagulated with warfarin (international normalized ratio 1.2–11.3). Aggressive histotripsy was performed on the prostate [28] and did not produce clinically significant hematuria, blood clots, or a drop in hemoglobin. This suggests that the mechanical process of tissue homogenization by histotripsy may also activate the coagulation cascade directly or induce signaling mechanisms via fractionation of structural and cellular components.

Chronic histotripsy effects

The tissue effects produced by histotripsy are different from the coagulative necrosis seen with thermal ablative modalities. To better understand the chronic effects of this form of tissue ablation, renal histotripsy was performed in rabbits. The kidneys were harvested 1–60 days after treatment and examined. Within the targeted volume of renal tissue, small hemorrhage was apparent acutely (days 0–2), followed by tubular dilation (days 7–60), and evolution of surface contour defects suggestive of lesion contraction (days 21–60) (Figure 31.7). By day 60 there was near complete absence of scar formation, suggesting that the acellular material generated by histotripsy is completely reabsorbed [29]. This is distinct from the tissue response normally seen with thermal ablation modalities. Following renal radiofrequency of small renal masses in humans, the ablated tissue did not substantially reabsorb or shrink when monitored for 2 years [30]. After cryoablation, only 32% of ablated lesions had shrunk to a radiographically undetectable size on follow-up imaging by 2 years [30].

Histotripsy of malignant tissue

Based on the exciting results achieved with transcutaneous histotripsy ablation, it is natural to consider applying histotripsy for ablation of tumors. However, it is important to carefully examine the effects of delivering acoustic energy to malignant tissues. Some have postulated that histotripsy, by mechanically disrupting

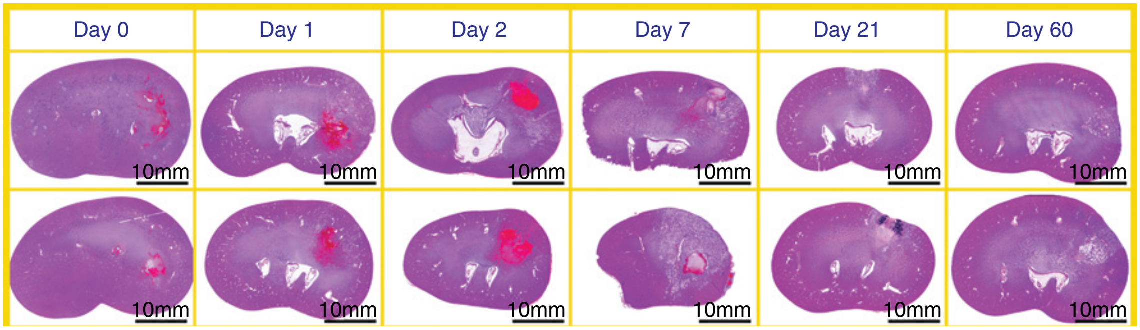

Figure 31.7 Following histotripsy treatment, an initial acute inflammatory response was followed by rapid resorption of histotripsy homogenate. By 3 weeks a contour defect was evident, indicative of loss of the treated volume of tissue.

the cellular attachments and structure of tumors, may increase the potential for metastasis. This is in contrast to HIFU, which is predominantly a thermal coagulation modality, and has been reported to not increase risk for metastatic dissemination of tumor [31,32].

In order to fully understand the literature on ultrasound and tumor metastasis, it is necessary to rank order ultrasound modalities based on the extent of mechanical tissue damage they produce in targeted tissue. Ordered from least to most destructive, diagnostic ultrasound (DUS) is followed by "pulsed HIFU" and high-amplitude ultrasound (HAUS). These are followed by shock wave lithotripsy (SWL), "mechanical HIFU," and then histotripsy.

Diagnostic ultrasound produces no tissue damage and does not result in an increase in metastases even in the presence of ultrasound contrast agent [33,34]. The purpose of pulsed HIFU or HAUS, which utilize acoustic intensities above the cavitational threshold, is to alter cellular properties (loosen intercellular connections and sonoporate cell membranes) without destroying the cells in order to facilitate drug or genetic uptake. Hancock et al. evaluated metastatic activity following pulsed HIFU in a murine melanoma breast cancer model. Although no statistically significant increase in metastasis was found, qualitatively the metastatic burden appeared greater in the pulsed HIFU group [35]. In another study, Miller and Dou compared DUS and HAUS exposures with and without presence of ultrasound contrast agent in subcutaneously injected melanoma B16-D5 tumors in a murine model [34]. In these studies, ultrasound contrast agent was directly injected into the tumor to increase the likelihood of cavitation events. The number of lung metastases was statistically greater in HAUS-exposed animals than in those who received DUS. However, the extent of tissue effect within the targeted tumor was not assessed. It is likely that these exposures produced little cellular and architectural destruction of the primary tumor.

With SWL, where treatments are generally limited to several thousand pulses, cavitation is responsible for hemorrhage and limited cellular damage. A number of experiments were described in the literature which did not report an increase in metastatic rate with SWL application to tumor models [36–39]. However, a study by Oosterhoff et al. [40] and a more recent investigation by Miller et al. [41] have both provided contradictory evidence suggesting an increased metastatic rate with SWL administration. In Miller's study, subcutaneous melanoma tumor was grown in a mouse model and then injected with ultrasound contrast agent or gas. Subsequent SWL produced a statistically significant increase in lung metastases compared to control [41].

Mechanical HIFU uses moderately intense output pressures that are sufficient to induce some mechanical tissue disruption in conjunction with low-level tissue heating. In studies assessing effects of mechanical HIFU in a murine melanoma model, the gross pathological appearance of the treated tumor appears to approximate the tissue destruction seen with histotripsy. Xing and colleagues concluded that mechanical HIFU treatment did not increase the rate of metastasis either with immediate or two-day delayed amputation of affected tumor-bearing limbs [42]. Interestingly, they provide evidence of an immunological mechanism that further reduced the metastatic rate in the group with delayed limb amputation [42,43].

Considering each of the previously discussed cavitation modalities, it is clear there is much variability in the form of ultrasound energy and cavitation dose applied. Furthermore, as many of the experimental results appear contradictory, it is not possible to draw broad conclusions regarding cavitation activity and metastatic risk. Although tissue destruction with histotripsy can be complete and homogeneous, the possibility also exists that histotripsy might facilitate metastatic spread of tumor. To investigate this experimentally, a study applying histotripsy to aggressive VX-2 tumor was conducted in a rabbit model [44]. Twenty rabbits were treated with histotripsy (day 13 after implantation) while eight served as controls. All rabbits underwent left nephrectomy (day 14) and then were euthanized (day 19). Homogenized tumor was seen in all treated nephrectomy specimens. Whole-mount, coronal lung sections were viewed to calculate number and density of metastases. Viable tumor was present in all 28 lungs examined. Histology confirmed fractionation of tumor in all treatment rabbits. There was not a statistical difference in total lung metastases or metastatic density when comparing treated and control rabbits [44]. However, further investigation is needed to validate these results in the VX-2 model and to assess metastatic rates in less aggressive tumors treated with histotripsy.

Some forms of cavitation-based ultrasound therapy have been associated with increased rates of metastases in certain studies of highly aggressive tumors. It is plausible that modalities which produce nonlethal and temporary disruption of cellular connections without extensive cellular death of malignant tissue may facilitate entry of malignant cells into the vascular system and possibly increase metastatic rates. In the case of pulsed HIFU and HAUS, acoustic intensity is not sufficient to produce homogeneous cellular death. With SWL and high-energy shock wave, intensities are much greater but the number of pulses generally applied results in limited injury and sporadic cell death within the focal region. A relationship between dose (number of pulses) and tissue damage was elucidated in one study in which higher cavitation dose was associated with greater growth delay of implanted Dunning prostate cancer tumors in a rat model, as well as greater hemorrhage, tissue disruption, and necrosis [45]. With histotripsy and mechanical HIFU, both acoustic intensity and total number of pulses (tens of thousands) produce extensive cellular destruction and homogenization. Experimental tumor studies with these modalities *in vivo* have not demonstrated a statistically or clinically significant increase in metastatic rate [44]. Although histotripsy appears to be promising as a focal therapy, further additional studies in tumor models are needed prior to clinical use of histotripsy for treatment of malignancy.

Conclusion

Histotripsy holds great promise as a unique nonthermal ultrasound ablative modality that may be well suited for focal treatment of renal masses as well as other urological diseases. Benchtop and animal research have revealed a number of unique properties of histotripsy, including real-time feedback by ultrasound monitoring of cavitation bubbles, hemostasis, and rapid resorption of debris from tissue homogenization. Further research into histotripsy effects on malignant tissues as well as confirmation of the favorable safety profile seen in preclinical work are necessary before histotripsy can be applied for treatment of human renal cell carcinoma.

Acknowledgments

The development and exploration of histotripsy as described in this chapter were supported by the following grant awards and foundations: NIH R01 DK087871, NIH R01 CA134579, NIH K08 DK081656, AUA Foundation/Astellas Rising Star in Urology Award, Wallace H. Coulter Translational Partners Grant Program, Kidney and Urology Foundation of America.

Disclosure

William W. Roberts MD is an inventor of intellectual property associated with histotripsy and founder of HistoSonics, Inc. As such, he has equity, royalty, and consulting interests in HistoSonics, Inc.

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Abbreviations; PCNL, percutaneous nephrolithotomy; RCC, renal cell carcinoma; TCC, transitional cell cancer/carcinoma.

Percutaneous Renal Surgery, First Edition. Edited by Manoj Monga and Abhay Rane.