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Image-Guided Percutaneous Ablation of Renal Tumors

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1. Introduction

Renal tumors account for more than 50,000 new cases annually in the United States with a rising incidence (Chow et al., 1999). This is mainly because of an increase in diagnosis due to widespread use of cross-sectional imaging (Pantuck et al., 2001). Renal cell carcinoma constitutes 4% of all adult malignancies (American Cancer Society, 2008) and about 70 to 80 percent of patients presenting with localized limited-stage disease (Luciani et al., 2000; Janzen et al., 2003). Nephron-sparing surgery remains the gold standard treatment for small renal tumors. Although operative resection has been shown to be effective for treatment of small renal tumors and for preservation of renal function, it does have morbidity and mortality risks (Fergany et al., 2000; Gill et al., 2007; Breda et al., 2009). Early laparoscopic renal cryoablation results have shown technical feasibility and offer a less invasive technique for destroying small renal tumors (Spaliviero et al., 2004). Image-guided percutaneous ablation of small renal tumors is less invasive, incurs less damage to uninvolved noncancerous renal tissue and is becoming a viable alternative to nephron-sparing surgery (Hui et al., 2008; Gontero et al., 2010).

2. General concepts of percutaneous image-guided ablation

Ablation refers to the destruction of tissue in its original location without the removal of the treated tissue. A resection refers to the removal of tissues from the body. Cross-sectional imaging modalities enable the operator to safely target the tumor through the skin without the need for incisions (percutaneous). The most common imaging guidance modalities are ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). Energy is applied to the tumor via placement of needle-like devices called probes or applicators. The energy deposition results in irreversible damage to the tissues in its field; this area is called the ablation zone. Ablation procedures are usually performed by interventional radiologists and/or urologists (the operating physician). It can be performed in an outpatient setting. The most important factors in determining the outcome of an ablation are tumor size and location of tumor within the kidney. The best results are achieved in tumors less than 4 cm in diameter (Boss et al., 2005; Miki et al., 2006). The least challenging tumor location is posterior exophytic and the most challenging locations are central hilar and anterior. Central tumors carry a higher risk for bleeding, a higher risk of damage to hilar structures such as collecting system and

vessels, and have a higher recurrence rate due to thermal sink effect. The thermal sink effect refers to the phenomenon whereby the thermal energy deposition to a tumor during ablation is dissipated by the blood flow in the vessels abutting the tumor. Depending on the location of an anterior tumor, it may be approachable percutaneously. However, treatment of these tumors may require a trans-renal or trans-hepatic approach. All tumors less than 3 cm can be treated in one session and the need for more than one ablation session increases with tumor size larger than 3 cm (Boss et al., 2005). Ablation of a 5 to 10 mm margin around the tumor is ideal to minimize the risk of recurrence.

3. Ablation modalities

The choice of percutaneous ablation modality is based on the availability of equipment, the operating physician’s experience with a particular device and limitations based on anatomy and patient body habitus.

3.1 Radiofrequency ablation and cryoablation

Radiofrequency ablation (RFA) and cryoablation are the two most commonly used ablation modalities (Gervais et al., 2000; Joniau et al., 2010; Atwell et al., 2008). RFA destroys tumors by denaturing and hydrolyzing tumor proteins by heating them to temperatures above 60°C, whereas cryoablation destroys tumors by the formation of intracellular ice crystals which disrupt cell membranes by cooling them to temperatures generally below -20°C. Pathologically, both processes result in coagulation necrosis in the center and apoptosis in periphery of the treated tissues. , Both modalities are minimally invasive, as the thermal energy is applied by placing one or more probes into tumors. Each has unique technical features, and neither of the two has clearly been proven to be superior to the other (Maybody & Solomon, 2007; Mouraviev et al., 2007)(Table 1).

Radiofrequency Ablation	Cryoablation
Typical ablation: 20-30 minutes	Typical ablation: 30-40 minutes
Less bleeding	More bleeding
More pain (greater need for general anesthesia)	Less pain (moderate sedation)
Ablation zone not visible during ablation <ul style="list-style-type: none">Higher recurrence ratesHigher likelihood of repeat ablation	Ablation zone visible during ablation <ul style="list-style-type: none">Lower recurrence ratesLower likelihood of repeat ablation
Larger ablation zone per applicator (requires fewer applicators)	Smaller ablation zone per applicator (requires more applicators)
CT monitoring during ablation difficult (artifacts)	CT monitoring during ablation possible
Interferes with pacemakers	No interference with pacemakers
More likely to damage the collecting system	Less likely to damage the collecting system (Janzen et al. 2005)
Less control over individual applicators	More control over individual applicators
Grounding pads (risk of skin burn)	Cumbersome equipment

Table 1. Comparison of main technical features of radiofrequency ablation and cryoablation in percutaneous image-guided ablation of renal tumors

3.2 Other ablation modalities

Microwave is a heat-based modality which involves deploying microwave energy (300-3000 MHz) from a non-tined probe (antenna) into a tumor causing oscillation of ions. This creates heat resulting in coagulative necrosis. Advantages include faster ablation times and less susceptibility to thermal heat-sink effect (Simon et al., 2005).

Laser is another heat-based ablation modality that deposits laser energy into the tumor via tiny flexible fiber optic conduits. Laser energy raises the tissue temperature and causes coagulative necrosis. Laser ablation has been successfully performed in renal tumors (Dick et al., 2002), and can be done under CT or MRI guidance. The flexibility of the fiber outside of the patient is an advantage when working in a CT or MRI gantry. Relative small ablation zones mandate multiple probe placements with laser ablation.

Irreversible electroporation (IRE) is a non-thermal ablation modality that causes apoptotic cell death by creating permanent microscopic pores in cell membranes when cells are exposed to specific electrical fields. This modality is much faster than other minimally invasive ablation techniques. Another advantage of IRE is that it is not affected by thermal sink phenomenon (Rubinsky et al., 2007). Preliminary animal and human experience is promising (Deodhar et al., 2011). Due to the stimulation of skeletal muscle by the electric field in IRE, the need for general anesthesia with paralytic agents remains a challenge to widespread use of the technique.

High-intensity focused ultrasound (HIFU) is a noninvasive heat-based ablation modality. It causes coagulation necrosis by focusing a high-intensity ultrasonic beam onto a small volume of target lesion. Respiratory movements and overlying ribs are major problems with the use of HIFU in renal tumors (Marberger et al., 2005; Klatte et al., 2009).

4. Imaging guidance

Percutaneous image-guided ablation can be performed under ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) guidance. The tumor should be well visualized on the imaging modality planned for the procedure. The advantages of ultrasound are its "real-time" capability and lack of ionizing radiation. Ultrasound can be used for accurate placement of probes before switching to CT or MRI for further monitoring. However, imaging with ultrasound is highly operator dependent and may be compromised in certain settings, such as patients with a large body habitus, the presence of abundant bowel gas, and when the tumor is near a focal loop of bowel that needs to be avoided. Another setback to ultrasound is the degradation of landmarks during ablation. In cryoablation, image degradation is caused by acoustic shadowing on the far side of the ice ball, and in RFA it is produced by micro bubbles.

CT is the most commonly used imaging modality for guidance (figure 1). It is not as operator dependent as ultrasound and is widely accessible to most operators. Its wide field of view is excellent to cover the critical organs and structures that need to be avoided. CT scanning is much less sensitive to body habitus than is ultrasound and CT images are not affected by bowel gas. If CT is chosen as image guidance method, the target lesion should ideally be visible on a non-contrast examination. Percutaneous ablation can be performed using a conventional CT scanner or a CT scanner with real-time fluoroscopic capability. Imaging monitoring with CT during active ablation with RFA is prone to significant artifacts due to interference of RF energy with the CT scanner. Cryoablation can be monitored by CT imaging during active ablation.

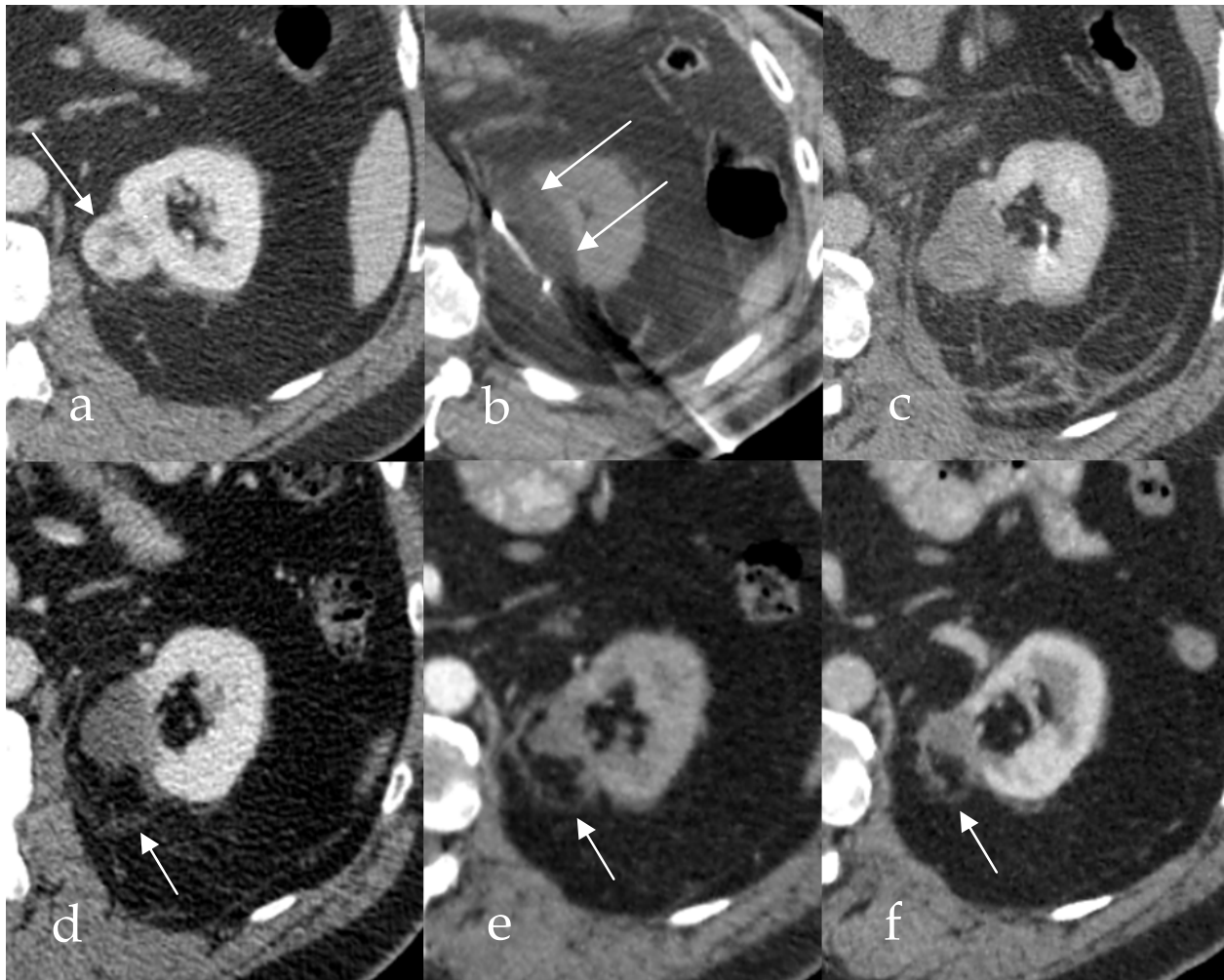


Fig. 1. (a) 62-year-old patient with an incidentally discovered left renal cortical mass (arrow). Separate session biopsy showed conventional clear cell renal cancer. (b) Cryoablation was performed in prone position. This picture is rotated to simulate supine position for ease of comparison. The edge of ice ball is clearly visible in renal parenchyma (white arrows). (c) Contrast enhanced CT image one day after ablation shows lack of enhancement in the ablation zone which covers tumor and an intended margin of renal parenchyma. Follow up contrast enhanced CT images at 3 months (d), 15 months (e) and 30 months after ablation (f). The tumor and adjacent ablated renal parenchyma continuously get smaller in size. A halo at the edge of ablation zone (white arrows) is visible.

MRI is the least commonly used imaging modality for percutaneous ablation. It provides excellent soft tissue resolution with multi planar imaging capability (figure 2). Lack of ionizing radiation is a safety advantage of MRI. MR fluoroscopic sequences can be used for real-time targeting of tumor. MR thermometry can assess cytotoxic tissue temperatures noninvasively. Image-guided percutaneous ablation can be performed using a dedicated interventional magnet, a conventional solenoid magnet, or an open magnet. The ice ball is visualized as a zone of decreased signal intensity on T1- and T2-weighted images. MRI-compatible ablation equipment is available to perform both RFA and cryoablation under MRI guidance (Boss et al., 2005; Miki et al., 2006).

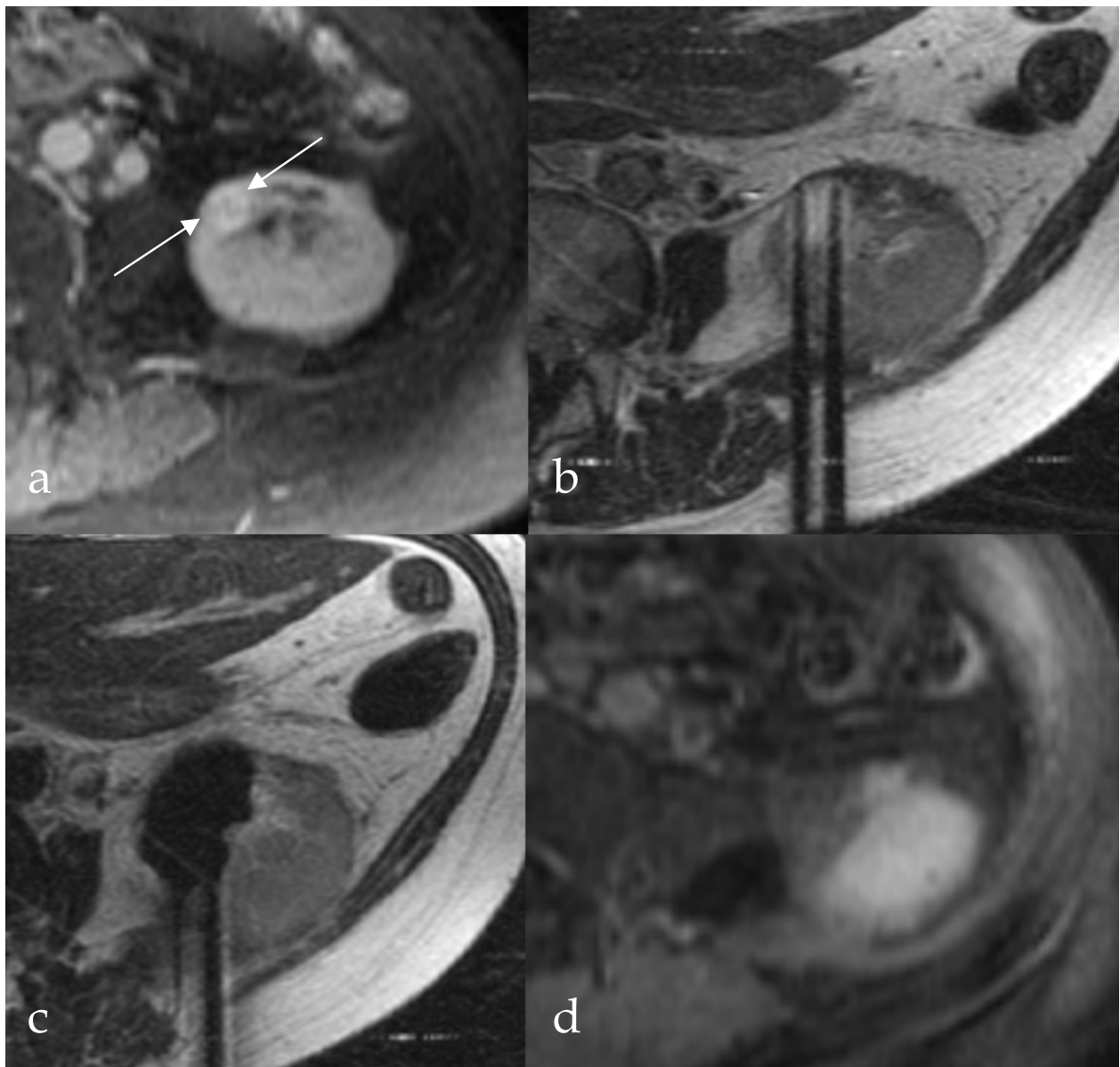


Fig. 2. 77-year-old patient with renal cell cancer of the left kidney (arrows). (a) Contrast enhanced T1 weighted MR scan demonstrates an enhancing tumor in the lower pole of the left kidney. Biopsy confirmed renal cell carcinoma. (b) Two cryoprobes are placed in the tumor under T2 weighted MR guidance. (c) During cryoablation, a low signal “ice ball” encompasses the lesion. Images c and d are rotated to simulate supine position for ease of comparison. (d) Contrast enhanced T1 weighted MRI 3 months after cryoablation demonstrates non-enhancement of the tumor and ablation zone, and shrinkage of the residual mass.

5. Indications and patient selection

Image-guided percutaneous ablations are especially ideal in patients who do not want to undergo surgery, elderly patients with significant medical co-morbidities that preclude them from surgery, patients with renal insufficiency, solitary kidney, transplanted kidney, and multi-focal tumors or patients with diseases such as von Hippel Lindau, which

predisposes them to develop multiple renal tumors. Documentation of renal cell carcinoma by needle biopsy is mandatory, as up to 25% of renal masses smaller than 3 cm are benign (American Cancer Society, 2008). Ideally, biopsy should be performed in a session separate from ablation. Tumors should be isolated to kidney with no evidence of vascular invasion or metastases. The best results are anticipated from tumors smaller than 4 cm in diameter, although larger tumors have been successfully ablated. The decision to perform percutaneous ablation is best made as a cooperative multidisciplinary agreement between an interventional radiologist and a urologist.

5.1 Pre procedural evaluation

Before the procedure, a physical exam should be performed, and the patient's medical history should be reviewed. Informed consent is required, and patients must understand that percutaneous ablations are relatively new procedures. Patients are informed about the possibility of retreatment and follow up imaging studies. Allergies to contrast media, antibiotic medications, or anesthetic drugs should also be noted. Laboratory blood tests should include hematocrit, platelet count, prothrombin time, and international normalized ratio (INR), partial thromboplastin time (PTT), and creatinine with calculation of an estimated glomerular filtration rate (eGFR). A platelet count of more than 100,000 per mL, INR of less than 1.5, and normal PTT would ideally be met prior to the procedure. Patients should not be acutely coagulopathic.

Warfarin, aspirin, and clopidogrel should ideally be stopped at least 7 days before the procedure. The operating physician should consult the referring physician prior to withholding anticoagulation medication. In patients with strict warfarin requirements, special arrangements can be made so that ablation is performed using a "heparin window," in which warfarin is held and patients are systemically anticoagulated with heparin until the time of procedure. Patients are instructed to abstain from eating for 6 hours prior to ablation so they are able to receive intravenous moderate sedation or general anesthesia. They may take other routine oral medications with small sips of water. Modification of the insulin regimen in diabetics should be considered during the food restriction period prior to the procedure. Nephrology consultation may be needed prior to ablation in patients with chronic renal insufficiency (estimated GFR less than 60 mL/min).

6. Ablation procedure

The patient should be placed in a comfortable position (prone, supine, lateral decubitus, or with slight elevation of one side) that also facilitates the procedure. Intravenous midazolam and fentanyl are the most commonly used medications for moderate sedation. The drug dosage is titrated for patient comfort and is monitored with telemetry and pulse oximetry by a sedation nurse or anesthesia team. Alternatively and based on institutional policies, percutaneous ablations may be performed under general anesthesia with endotracheal intubation. If desired, a biopsy of the lesion can be performed in the same session prior to the ablation. A challenge with same day biopsy is that bleeding associated with the biopsy may obscure the tumor and potentially affect outcome.

The procedure plan should be outlined by the operating physician before the procedure. The number of probes used for a particular tumor depends on the equipment used and the size of tumor. Placement of more than one probe is often required to cover the entire tumor

and the desired rim of surrounding parenchyma. The length of devices extending outside of the patient and their connecting cords, as well as patient positioning and the angle of probe placement, all have major practical implications and should all be planned in advance. Frequently, the injection of intravenous contrast medium during the procedure can help visualize relatively inconspicuous lesions. Smaller doses of iodinated contrast (50 mL) are usually sufficient for CT visualization and can allow for a repeat bolus later in the procedure if necessary. Similarly, there are circumstances when sonographic or MRI contrast agents may be useful.

Adjacent critical structures may be damaged when they are located within the target region. Occasionally, a second percutaneous needle can be inserted and carbon dioxide, water, air, or balloons may be placed to separate bowel, for instance, from the target tumor (Farrell et al., 2003; Kam et al., 2004; Gervais et al., 2005b). It is important not to use saline for hydro dissection in RFA cases, as saline conducts current and may damage organs. Nonionic 5% dextrose in water should be used instead. Certain patient positioning maneuvers or the operating physician's hands may also be used to move away bowel loops from the tumor. Retrograde ureteral stents can be used to circulate warm or cold fluid during the ablation period to provide some protection to the ureter (Cantwell et al., 2008). The probe can also be used as a lever to move the kidney away from adjacent structures (Park & Kim, 2008). If a transpleural approach is inevitable, it can be pursued and any pneumothorax that develops may be treated accordingly. Alternatively, an iatrogenic pneumothorax or hydrothorax can be created to avoid potential damage to the lung.

Unless a tined RFA probe is used, most probes have no tines and produce an oval zone of ablation. After adequate positioning of the probe(s) is complete, the tumor is ablated once or more according to the suggested manufacturer protocol. If the patient's renal function allows, a contrast-enhanced CT or MRI scan may be performed after removing all probes. This will allow for an immediate assessment of the adequacy of the ablation. MRI-guided ablations can also be immediately assessed by MR thermometry. Certain areas with suboptimal ablation can then be immediately re-treated during the same session. At a minimum, it is usually helpful to do a noncontrast scan of the treatment area following removal of probes to assess for complications.

An advantage of cryoablation over heat-based ablation modalities is its relative painlessness (Allaf et al., 2005). This may be of importance for patients who cannot undergo general anesthesia or receive deep moderate sedation due to medical comorbidities.

In contrast to heat-based ablation modalities, the ice ball can be clearly seen with CT (Littrup et al., 2007; Solomon et al., 2004), MRI (Silverman et al., 2005), and ultrasound imaging (Gill et al., 2000). This imaging characteristic allows the operator to ascertain coverage of the tumor more confidently and also to better protect certain nearby critical structures. Because of this feature, cryo ablated lesions tend to have less residual tumor (Marin et al., 2006).

Intravenous contrast is not necessarily needed immediately following cryoablation to verify proper coverage of tumor by the ablation zone. This is a significant advantage for patients with renal insufficiency. The outer edge of the ice ball that is visualized is not cytotoxic. The cytotoxic part of an ice-ball is contained a few millimeters inside the visible edge.

Unlike the heat-based ablation modalities, freezing does not cauterize or coagulate vessels within the ablation zone. Hence, patients may be at slightly higher risk of bleeding during or immediately following cryoablation. For this reason, patients with borderline coagulation status should have laboratory abnormalities more vigorously corrected. One relative

limitation of current cryoablation probes is the size of the ablation zone created by a single probe as compared with the same size RFA probe. In general, each 2 mm probe creates an approximately 2 cm diameter of necrosis (Permpongkosol et al., 2007). For this reason, insertion of multiple simultaneous probes is commonly needed to cover the entire tumor and desired margin of surrounding parenchyma. A simple rule-of-thumb is to position the probes about 1 cm from the margin of the tumor and 1 to 2 cm apart from each other, giving priority to the periphery of the tumor (Solomon et al., 2004). It is important to remember that all available cryoablation probes currently have an extension cord attached to them. This cord contains tubing for gases, and in certain versions, temperature sensor wiring as well. The weight of the cord produces torque during and after placement of the probe. When planning for cryoablation, it is important to make sure the trajectory of each probe has enough purchase inside the patient so they are not constantly pulled or deviated by the torque produced by the cord. When positioning the patient for the procedure, it is critical to remember to provide enough space between the patient and gantry so that the equipment does not contact the gantry during the procedure. Additionally, the operating physician will have far more freedom to make fine adjustments during the procedure without having to take the patient out of the gantry repeatedly.

7. Treatment outcomes

Technical success rates of 97 to 100 percent are reported with RFA and cryoablation (Atwell et al., 2008; Boss et al., 2005; Gervais et al., 2005a). In a series of 616 patients, the incidence of residual or recurrent tumor was 13.4 percent with a single radiofrequency ablation and 3.9 percent with a single cryoablation (Gervais et al., 2000). In this series, the overall incidence of residual or recurrent tumor after repeated ablation therapy in all patients was 4.2 percent (Gervais et al., 2000). The overall 2-year survival rate was 82.5 percent, including patients who died of unrelated causes, and the metastasis-free survival rate was 97 percent at 2 years (Gervais et al., 2000). Five-year local and distant tumor-free rate after RFA has been reported at 94 percent (McDougal et al., 2005). Similar success rates are reported with cryoablation, but the mean follow-up time period is shorter at 1 to 2 years (Littrup et al., 2007).

8. Complications

The rate of major complications from percutaneous ablation of renal tumors is about 2 to 6 percent (Atwell et al., 2008; Boss et al., 2005; Johnson et al., 2004). Complications include hemorrhage, pneumothorax, and bowel and nerve injury. In contrast to other heat-based ablation modalities, cryoablation does not cauterize blood vessels within the ablation zone. Therefore, hemorrhage at the ablation zone after removal of probes appears to be slightly more common when compared with heat-based ablation modalities. Hemorrhage after cryoablation is most often self-limited and responds to conservative management. Damage to the renal collecting system and the neighboring structures such as nerves and bowel are among other reported complications.

9. Patient follow up

If the patient's renal function allows, the ablated tumor should be evaluated by CT or MRI without and with intravenous contrast at 1, 3, 6, 12, 18, and 24 months after ablation. Early

post ablation studies show the ablation zone as a non-enhancing area surrounded by a thin smooth rim of enhancement (Smith & Gillams; 2008). This rim is considered a physiologic response to thermal ablation and disappears within 3 months (Merkle et al., 2005). Ideally, the ablation zone should include the entire tumor and the expected 5 to 10 mm noncancerous rim; (figure 1 c, d; figure 2 d). The ablation zone appears T1 hyper intense and T2 hypo intense (Uppot et al., 2009; Kawamoto et al, 2009). The ablation zone continues to decrease in size over time (Merkle et al., 2005) (figure 1 d, e, f). Complete disappearance of cryoablated tumors over time has been reported (Gill et al., 2005). A thin curvilinear hyper attenuating rim or halo on CT imaging, which is hypo intense on T1-weighted images, is commonly seen parallel to the tumor extending to the perinephric fat (figure 1 d, e, f). This halo may persist for several months after treatment (Uppot et al., 2009; Kawamoto et al, 2009). Nodular or irregular enhancement within the ablation zone and enlargement of ablation zone is considered suspicious for residual tumor or recurrence (Kawamoto et al, 2009). These areas may be biopsied and if positive for malignancy they can be treated by ablation.

10. Conclusion

Image-guided percutaneous ablation is a viable option for patients who cannot undergo surgery because of medical co morbidities. Experience with these ablation modalities is promising.

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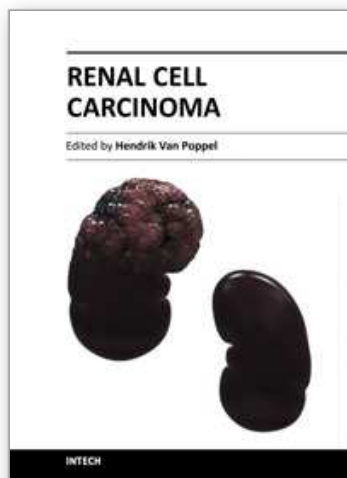
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Renal Cell Carcinoma

Edited by Dr. Hendrik Van Poppel

ISBN 978-953-307-844-1

Hard cover, 144 pages

Publisher InTech

Published online 16, December, 2011

Published in print edition December, 2011

Surgical and medical oncologists have been unable to decrease renal cell carcinoma mortality for uncertain reasons, although a lot of progress has been made in diagnosis and imaging, recognition of different genetic and pathological entities, management of localized disease and in the research on new drug treatments for advanced stages of the disease, potentially combined with surgery. The purpose of this book, which tackles a number of separate interesting topics, is to provide further insight into the disease and the management of early and advanced renal cell carcinoma. The volume is divided into different parts; the first part covers the characterization of renal masses and the second part covers rare distinct pathological entity. In the management section, active surveillance, partial nephrectomy and radiofrequency ablation are presented. A separate chapter reviews the management of Von Hippel Lindau disease, and finally, conventional and aberrant signaling pathways are explored.

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