

Renal Cell Carcinoma

Fry, freeze, electrocute, or...?

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More than 65,000 patients will be diagnosed with renal cell carcinoma (RCC) in the United States this year.¹ RCC is the most common malignant renal neoplasm and accounts for 2% to 3% of all malignancies in the United States.² The proliferation of cross-sectional imaging techniques (CT and ultrasound) for abdominal disease and symptomatology has led to increased diagnosis and awareness of incidental RCC. Incidental RCCs tend to be smaller and lower stage with an advantageous survival profile when compared to patients with regional or distant metastases.³

In part due to increased detectability and survivability of incidental RCC, the American Urological Association and the European Association of Urology have put forth guidelines for the treatment of localized RCC. Specifically, the American Urological Association consensus guidelines for treatment of T1 renal masses highlight nephrectomy (nephron sparing or radical) as standard of care, with thermal ablation reserved for patients with increased operative risk or extensive comorbidities.⁴ While acknowledged, the European Association of Urology guidelines do not include thermal ablation in the treatment algorithm of localized RCC due to a paucity of high-quality data in the available literature.³

Despite initial difficulties with mainstream acceptance, thermal ablation has emerged as a safe and effective means of local tumor eradication in select patient cohorts. Moreover, continuous technologic innovation and improvement have equipped proceduralists with increasingly effective tools for ablation procedures. Specifically, radiofrequency ablation (RFA), cryoablation, and microwave ablation (MWA) have emerged as common thermal treatment modalities for small renal tumors, with irreversible electroporation (IRE) also showing promise as a nonthermal alternative.

RADIOFREQUENCY ABLATION

RFA is likely the most established and well-studied means of percutaneous renal thermal ablation, with multiple studies showing durable tumor control. RFA utilizes high-frequency alternating electric current to heat tissue to lethal temperatures (approximately

55°C), while balancing the adverse effects of local tissue impedance.⁵

RFA is a safe and highly effective treatment for small renal masses measuring < 3 to 4 cm, with numerous studies demonstrating efficacy > 95%.⁶⁻¹⁰ In a study including 143 patients (median follow-up, > 6 years), Psutka et al showed 96% recurrence-free survival for patients with T1a RCC treated with RFA.¹¹ Of the patients with recurrent tumors, half were re-treated with RFA, with five of the six salvage treatments providing long-term control.

These successful long-term outcomes after RFA have been shown to be similar to partial nephrectomy (PN). One study showed similar recurrence-free survival between RFA and PN (91.7% vs 94.6%) and similar cancer-specific survival (97.2% vs 100%).¹² Such similar outcomes have been demonstrated elsewhere, showing RFA and PN to both be efficacious in managing small renal masses.¹³

Whereas RFA has well-documented safety and effectiveness in treating small renal masses, oncologic efficacy in treating large renal masses (> 3 to 4 cm) is mixed. Local progression and incomplete treatment rates > 20% have been reported after RFA of larger renal tumors.^{11,14} Importantly, many of these lesions can be re-treated successfully, but Best and colleagues suggest that RFA of renal masses > 3 cm may achieve long-term disease control in no more than 80% of patients.¹⁴ In addition to size considerations, central tumors may be better treated with an alternate ablative technique due to heat sink and risk of urothelial injury.^{9,10}

Major complications after RFA occur at low rates (5% to 6%) and have been reported less frequently than with cryoablation, PN, and radical nephrectomy.^{4,15} In particular, hemorrhagic complications can be mitigated due to heat-induced vascular coagulation. Although RFA may diminish hemorrhagic complications, it does present a risk to adjacent nervous and urothelial structures. Damage to sensory or motor nerves may result in secondary deficit, although such deficits are often transient. Urothelial injury and subsequent stricture can represent a potentially devastating postprocedural complication that may necessitate surgical management. Recently, the

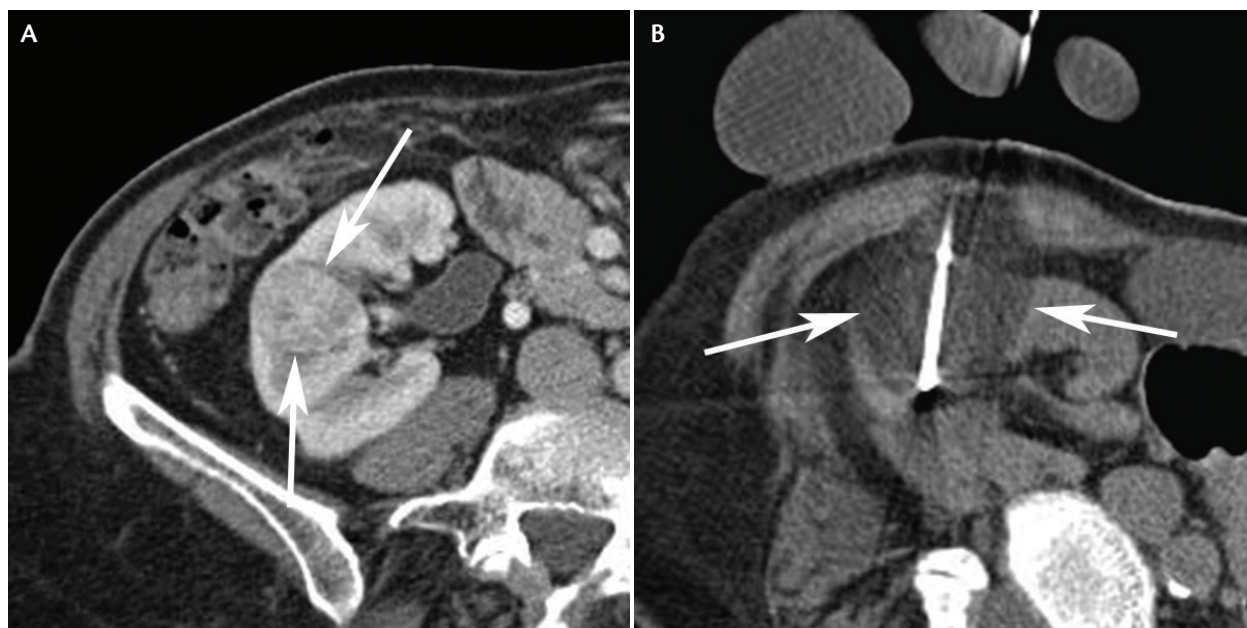


Figure 1. CT with intravenous contrast in an 87-year-old woman with an incidental 2.7-cm centrally located mass in her right kidney (arrows) (A). A CT scan obtained during the cryoablation procedure shows a hypodense iceball (arrows) extending from one of two cryoprobes placed during treatment (B).

ABLATE algorithm has been devised to assist proceduralists in expert preprocedural planning based on multiple potential lesion-related pitfalls, including location within the kidney and adjacency to the ureter.¹⁶

CRYOABLATION

Tumor destruction using extreme cold temperatures has been used for centuries. Renal cryoablation has its origins in the operating room, where large first-generation cryoprobes required open exposure to the kidney and aggressive control of bleeding during treatment. During the past 15 years, small-caliber, argon-based cryoprobes have allowed the percutaneous application of lethal cold temperatures to renal masses, resulting in effective tumor eradication.

In contrast to the heat-based ablation techniques, the iceball generated during cryoablation is well depicted by cross-section imaging techniques, including CT and MRI (Figure 1). Such monitoring allows a high level of confidence in tumor treatment with potentially less risk of thermal injury to nontarget structures, such as the bowel. Allowing for the gradient of truly lethal temperatures associated with specific types of cryoablation probes, the goal of treatment is to extend the iceball 3 to 5 mm beyond the tumor margin to generate 100% cell death at temperatures below -20°C .

Outcomes of percutaneous cryoablation are quite favorable, with several studies showing recurrence-free survival rates of 97% to 99%.¹⁷⁻²⁰ In a landmark study

by Thompson et al comparing outcomes after PN, RFA, and cryoablation, local recurrence-free survival for T1a (≤ 4 cm) renal masses treated with percutaneous cryoablation was 97% at 3 years.¹³ Although the duration of patient follow-up was much shorter for those treated with cryoablation, this oncologic result was the same as for those treated with PN. The authors concluded that if the results were validated elsewhere, “an update to clinical guidelines would be warranted.”

The synergy of multiple cryoprobes does allow treatment of relatively large masses, including T1b (4 to 7 cm) tumors and even T2 (> 7 cm) tumors, although the complication rates are much higher in treating such masses. The Mayo group showed that the outcomes after cryoablation of T1b renal masses was not significantly different compared to those treated with cryoablation.¹³ Specifically, an update showed 96% recurrence-free survival at 3 years for patients treated for T1b RCC.²¹ Other investigators have also shown that size does not appear to be related to treatment failure.^{22,23} In some cases, staged treatment of such large tumors may be reasonable.¹⁹

As one might expect, the aggressive treatment required for successful treatment of such tumors is associated with an increased risk of complications. Bleeding is the most common complication of cryoablation, occurring in 3% to 5% patients.^{15,18} Major bleeding complications after cryoablation have been shown to be associated with tumor size and number of cryoprobes.¹⁵ Prophylactic embolization of larger tumors prior to definitive cryo-

ablation should be considered in some patients. One needs to also consider the select patient group treated with ablation, including those with tenuous comorbidities less capable of responding to the physiologic stress of tumor treatment. For this reason, multidisciplinary management may be warranted in many patients to help optimize overall patient outcomes during the peri-procedural period.

In addition to bleeding and medical events often related to underlying patient comorbidity, other complications associated with cryoablation include hematuria, nerve injury (resulting in sensory or motor deficit), infection, bowel injury, venous thromboembolism, and pneumothorax.

MICROWAVE ABLATION/IRREVERSIBLE ELECTROPORATION

Microwave ablation (MWA) is a newer heat-based modality that allows hotter and faster ablations than RFA. This technique is gaining popularity in renal ablation because it allows larger ablations and less thermal sink effects than RFA, which should improve outcomes for ablation of larger and central renal masses. MWA also allows cauterization of the needle tracts, so there should be fewer bleeding complications compared to cryoablation. However, because it is very hot and fast, there is an increased risk of urothelial injury, and the size and shape of the ablation zones can be less predictable, although this is less of an issue with second-generation MWA systems.

There is mounting evidence to support the use of MWA for renal ablation. For example, Yu et al recently showed 98% technical success and 92% 3-year recurrence-free survival in treatment of 49 RCC, and there were no technical failures or recurrences identified for patients treated with tumors < 4 cm.²⁴ The University of Wisconsin has also recently reported 100% technical success and no tumor recurrence during a mean 8-month follow-up when using MWA to treat 55 T1a RCCs.²⁵

Irreversible electroporation (IRE) is the newest modality to be considered for renal ablation. IRE is a nonthermal ablation method that uses ultra-short, high-intensity electrical pulses to cause irreversible disruption of cell membranes and subsequent cell death. One significant potential advantage of IRE over thermal-based ablation systems is that it should be less likely to cause damage to the adjacent urothelium, vessels, and nerves. Renal IRE is still considered investigational, but several human trials are now underway.

CONCLUSION

Thermal ablation of renal masses has successfully evolved over the past 15 years to establish itself as an effective means of tumor treatment. While historically reserved for patients with contraindications to surgery, we should

expect to see a greater role of thermal ablation in conventional renal tumor management algorithms. For the radiologist, it is important to recognize the strengths and weaknesses associated with the different ablation modalities in order to optimize patient and tumor-specific outcomes. ■

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