

# Percutaneous Radiofrequency Ablation of Small Renal Tumors Using CT-Guidance

## A Review and Its Current Role

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**Purpose:** To provide key evidence-based strategies to improve outcomes of radiofrequency ablation and limit recurrences of small renal tumors.

**Materials and Methods:** The literature was searched via OvidSP MEDLINE from 1997 to current using MeSH terms. All levels of evidence and types of reports were reviewed.

**Results:** We comprehensively reviewed technical issues, mechanisms, imaging criteria, ablative success, enhancement within one month, contraindications, oncological efficacy, morbidity rates, and follow-up strategies.

**Conclusion:** The technique is safe and effective. Tumors < 2.5 cm are statistically most likely to remain disease-free. Anterior tumors are contraindicated. Strict follow-up is needed to detect failures, most of which occur within 3 months and can be easily salvaged with repeat radiofrequency ablation. Homogeneous enhancement within 1 month is not necessarily a failure, and tends to disappear after 4 to 6 weeks. Multi-disciplinary meetings must occur to discuss each case prior to treatment.

**Keywords:** percutaneous, radiofrequency ablation, renal cell carcinoma, computed tomography

## INTRODUCTION

**S**mall renal tumors (SRT) are increasingly detected as incidental findings because of the widespread use of abdominal imaging, such as computed tomography (CT) and ultrasonography (US). An enhancing SRT may be either benign or malignant.

The patient and physician have many treatment options available, including active surveillance, open or minimally-invasive surgery, or ablative techniques, such as radiofrequency ablation (RFA) and cryoablation (CA). Percutaneous RFA plays a role in clinical T1a renal cell carcinoma (RCC) in patients unfit for surgical excision because of medical comorbidity, and in those with hereditary multiple RCC syndromes or those with a high risk of chronic kidney disease in whom nephron-sparing surgery (NSS) is favored.

Renal cell carcinoma comprises 2% to 3% of human adult cancers, with an incidence that has risen from 7.4 to 17.6 per 100 000 from 1975 to 2006 in the United States, corresponding to a mean annual increase in incidence of 3%.<sup>(1)</sup> There are 50 000 new cases of RCC per year in the United States.<sup>(2)</sup> As is the case with other urological malignancies, the treatment of a SRT suspected of being RCC depends on stage, grade, and patient's factors.

The metastatic potential of SRT rises with increasing tumor size from 1.2% of 2 to 3 cm RCC metastasizing to 3.9% of 3 to 4 cm RCC metastasizing.<sup>(3,4)</sup> The histological grade and biological natural history can be difficult to establish. Although biopsy can help, it may lead to false-negative results. An Australian study examined pathological outcomes of 499 nephrectomies over 15 years and discovered that Fuhrman grade 3 RCC and the papillary RCC subtype were increasingly seen over time,<sup>(5)</sup> and that benign tumors were less frequently seen at final pathology.

Zlotta and colleagues in 1997 first described RFA as a possible treatment modality for a SRT.<sup>(6)</sup> The treatment options for a clinical stage T1a RCC depend on patient choice after the treatment options have been discussed.<sup>(7)</sup> Surgical excision by either open or minimally-invasive techniques is the gold standard for a healthy patient who is keen on intervention. Oncological outcomes have been shown to be equivalent comparing radical nephrectomy versus partial surgery (NSS).<sup>(8,9)</sup>

Active surveillance can fail due to patient's anxiety, and also relies on a strict imaging follow-up protocol involving either CT, US, or magnetic resonance imaging (MRI). Issues of radiation exposure and intravenous contrast media may complicate such an approach. Radiofrequency ablation plays a role in populations who are either unfit for, or refuse major surgery, or when NSS is preferable, as in hereditary or multiple RCC syndromes, chronic kidney disease, and a solitary kidney.

The percutaneous technique is minimally invasive and can be performed as an outpatient procedure. Computed tomography guidance allows for accurate tumor localization and immediate assessment of tumor response to treatment, and the prompt identification of complications.

Level 4 evidence case series of percutaneous-RFA have reported complete ablation rates of above 90% at 3 to 27 months follow-up.<sup>(10-17)</sup> In a survey of trends of the treatment of SRT in academic American centers using ablative technology, 55% used RFA while 79% used CA.<sup>(18)</sup>

## MATERIALS AND METHODS

A literature search was performed using OvidSP MEDLINE from 1997 to current, using the keywords of "radiofrequency ablation, percutaneous, computed tomography-guided, and renal cell carcinoma". Results were filtered based on relevancy to percutaneous CT-guided RFA of renal tumors to include review articles, any available level 1 to 4 evidence series, reports of technique, and morbidity. Cryoablation reports were excluded as were articles describing the use of RFA in open or minimally-invasive surgery. Oncological efficacy data were tabulated.

## RFA PROCEDURE TECHNIQUE

A combined urology and interventional radiology approach is required to decide on appropriate cases. Coagulation profile and blood group and hold are required. Conscious sedation is used for the most part, otherwise general anesthesia is used. An initial planning CT scan guides exact patient positioning. The patient position depends on tumor location and the relationship of adjacent viscera to the kidney.

A fine needle aspiration biopsy for cytology is performed immediately preceding RFA. The electrode is inserted

along the same tract, and the tract ablated at the completion of the procedure to reduce the risk of seeding.<sup>(15)</sup> The diameter of the probe tines is matched to the diameter of the tumor. Therefore, the probe tines cover an additional 5 to 10 mm margin of renal tissue beyond the circumferential margin of the tumor. Computed tomography guidance confirms the probe's position and accounts for motion. The number of probe tines that are deployed depends on the diameter or size of the lesion. Deploying more tines allows for increased coverage and enhanced ablative effect. Dependent upon the tumor size and density and the number of probe tines being used, the impedance and temperature settings can be adjusted by the operator. Larger lesions may require overlapping or repeated RFA sessions to achieve a complete ablative response.

An immediate post-RFA CT scan is performed to assess adequate tumor destruction, and to exclude immediate procedure-related complications. After an observation period of 4 hours, the patient is discharged. The follow-up CT scan protocol is 6 weeks, then at 3, 6, 12, and 18 months, and then annually.<sup>(11)</sup>

### MECHANISM OF TUMOR DESTRUCTION

Radiofrequency ablation produces thermal injury on tumor cells. The thermal energy produces ionic agitation and frictional heating. A minimum critical temperature of 48 to 50 °C is required for cellular damage. Temperatures reaching 80 to 100 °C produce irreversible protein denaturation, cell membrane damage, and coagulation necrosis.<sup>(19)</sup> The extent of thermal damage depends on treatment time in a linear fashion and temperature rise in an exponential fashion.<sup>(20)</sup> Radiofrequency delivers a high frequency (460 to 500 kHz) alternating current into the tumor via the electrode (also called a tine), delivered from a power generator (250 W).<sup>(21,22)</sup> The energy is transferred via electrodes that are insulated along their course except at their active 2 to 5 cm tip.

The tumor core is vaporized at temperatures nearing 100 °C, whereas the surrounding concentric zones of tumor are ablated by convective heating. One single electrode will generally ablate a tumor less than 3 cm in diameter; however, this depends upon the variability in tissue density.

Larger and denser tumors require overlapping ablations with repositioning of the electrode tines and longer treatment sessions. Radiofrequency is limited by tissue charring and carbonization, which increases impedance to the RFA current.<sup>(19,23)</sup>

### TECHNICAL CONSIDERATIONS

There are different types of RFA energy delivery systems.<sup>(21)</sup> The 'Impedance Based' system delivers energy based on a predetermined level of tissue impedance. The problem with this method is that even if a preset level of impedance is reached, this may not correlate with what is needed to reach adequate levels of tissue coagulative necrosis, and treatment may fail.

The 'Heat Based' system delivers energy based on a preset temperature level. Usually the temperature is set to 70 to 100 °C for a duration of 5 to 12 minutes. The problem with this method is that the temperature at the tip of the electrode may be higher than the actual temperature within the tumor tissue, again accounting for treatment failure. This reiterates the importance of the post-treatment CT scan to assess tissue destruction and then the long-term follow-up imaging to rule out tumor recurrence.

Electrode tips can be either 'wet' or 'dry'. A wet electrode tip is one which is cooled by infusing a saline solution into the peri-tumor tissue before and during the RFA session.<sup>(21,23)</sup> This decreases tissue resistance and allows for larger tumors to be treated. The problem with a wet electrode technique is that it may cause CT imaging artifact and compromise the accuracy of the immediate post-RFA CT scan. A dry electrode is more prone to cause peri-electrode charring that increases resistance, which in turn limits the energy transfer from the central tumor zone to the peripheral zone. Another consideration is the protection of adjacent viscera during treatment, including the colon, spleen, duodenum, inferior vena cava, ureter, body wall muscle, pancreas, and pleura.

One reported technique is the instillation of water or 5% dextrose solution to 'volume displace' the at risk structure away from the treatment zone.<sup>(24-27)</sup> A separate puncture is made between the tumor and the viscera, and the solution is instilled into the peri-nephric space.

Another technique is to instill carbon dioxide gas (1.2 L at 1 atmosphere pressure) within the peri-nephric space to push the at risk structure aside.<sup>(28)</sup> The urinary collecting system is also at risk of thermal damage, which may lead to urinoma, ureteral perforation, or stricture.

Retrograde cold pyelo-perfusion, using 5% dextrose infusing up the ureter into the collecting system via a retrograde ureteral catheter has been described.<sup>(28,29)</sup> A flow rate of 60 mL per minute is suggested.

### CT-GUIDANCE

Computed tomography guidance is the preferred method with a sensitivity and specificity of helical CT in assessing renal tumors of 100% and 90%, respectively.<sup>(30)</sup> A pre-treatment CT scan is performed to assess tumor size and location and the surrounding viscera, and to plan the path of electrode insertion. Intermittent ‘real-time’ CT can be performed to assess tumor response, seen on CT imaging as vacuolation, cavitation, and Hounsfield unit (HU) density change. Computed tomography gives accurate information about electrode position and movement during treatment. The post-RFA CT identifies any problems, such as hematoma, pneumothorax, bowel injury, and vascular injury.

Computed tomography may however be contraindicated in certain populations, such as young women, pregnancy, and iodinated contrast allergy. Here there is a role for US or MRI. Ultrasonography may not be as accurate as CT because gas bubbles, which form during RFA, appear hyperechoic and distort the US image. Magnetic resonance imaging with gadolinium is well-suited for RFA because it produces high quality definition of soft tissues and anatomic planes. In addition, the T2-weighted acquisition times of 2 seconds allows for real-time monitoring of RFA.<sup>(19,31)</sup> Furthermore, MRI provides an accurate account of ablative success, seen as a signal loss in T2-weighted images. Magnetic resonance imaging can be used during pregnancy and iodinated contrast allergy.

### DEFINING COMPLETE ABLATIVE SUCCESS

There is an absence of standardized criteria to define RFA success. In the immediate term, success is divided into technical and clinical, whereas in the long-term, it is defined as

recurrence-free survival (RFS). Immediate technical success requires (i) ‘impedance roll-off’, which suggests that an adequate level of tissue ablation has taken place during treatment, and (ii) immediate CT evidence of tissue change, including CT evidence of loss of tissue density, tumor vacuolation, and cavitation.<sup>(32,33)</sup>

At the earliest follow-up CT, at the 6 week mark, there should be no appreciable contrast enhancement of the treated tumor, which is no increase in HU density greater than 10 HU between the non-contrast and contrast scans.<sup>(14,34)</sup> There should also be no enlargement of the tumor bed or RFA treatment zone at long-term follow-up (after several months).<sup>(10,11)</sup> Earlier than 4 to 6 weeks, there may be post-treatment effect visualized on a contrast-enhanced CT that may be confused with failure. These changes eventually disappear and should not be evident at a 1-month scan.<sup>(35)</sup> Furthermore, another study has shown that the post ablation beds of SRT < 3 cm can show a slight increase in volume on follow-up CT scans within the first 1 to 2 months post-RFA. However, this eventually scars down and the post ablation bed becomes smaller at long-term follow-up.<sup>(36)</sup>

Failure is therefore defined as persistent contrast enhancement of the tumor using the 10 HU cut-off and/or enlargement of the tumor bed after RFA treatment beyond the 1 month point. It is not infrequent that a repeat treatment session is required after the 1 month mark, within the follow-up period, generally for persistent contrast enhancement, and this should be considered a failed RFA treatment. It is possible to visualize scar tissue within the treatment bed on follow-up scans, which is not to be confused with true treatment failure. Scar tissue will have a differing HU density than surrounding renal tissue; however, it should not enhance like a recurrent tumor would be expected to.<sup>(19)</sup>

One study reported on contrast-enhanced CT findings within the ablation zone immediately after the RFA session (day 0), and compared this to CT scans 1 and 6 months post-treatment. At day 0, 78% of tumors (28 of 36) showed a clinically significant mild homogeneous contrast enhancement (> 10 HU) within the ablation zone.<sup>(35)</sup> However, at the 1 and 6 month scans, no tumor exhibited any significant contrast enhancement. This means that early enhancement (< 1 month) post-RFA will eventually disappear at follow-

up (usually after 1 month), and does not mean RFA has failed.

Post-RFA biopsy of the ablation zone, as a method of confirming the absence of residual disease, is typically not performed. Since heat fixes tissue, the post-RFA histology may appear like there is cancer still present. However, when a cell viability stain is performed, this confirms that the cells are in fact dead.<sup>(37)</sup> In summary, the interventional radiologist and urologist need to follow the post-ablation bed carefully with contrast-scans, especially during the first 3 months post-RFA. There are predictable imaging patterns that guide the interpretation of successful RFA.

## INDICATIONS AND CONTRAINDICATIONS FOR RFA

Indications can be divided into patient's and tumor's factors.<sup>(13,18,22,32)</sup> It is important to choose a suitably sized and located tumor in order to maximize the chance for a successful RFA session. This is particularly relevant when a urology unit begins to offer RFA to patients, and undergoes a learning curve. The ideal tumor's factors are: 1) Size  $\leq$  2.5 cm; 2) Exophytic, lateral, or posterior location; 3) Solid neoplasm, without cystic component; and 4) Favorable peri-renal anatomy.

It has been shown that size  $>$  3 cm is prognostic of recurrence.<sup>(38,39)</sup> This suggests that especially during the learning phase, the urologist and radiologist should choose smaller tumors. In one series reporting initial experience with RFA, 2 patients who recurred had tumor sizes of 3.2 cm and 4 cm (in diameter), and one was mixed endophytic/exophytic.<sup>(40)</sup> Another series had excellent oncologic outcomes using RFA for cystic RCC (total of 9 patients). However, it is generally felt that a cystic RCC does not respond to RFA well because the fluid component adversely affects the convective thermal energy transfer from the central to peripheral zone of the tumor.<sup>(41)</sup> Unfavorable tumor's factors therefore include: 1) Size  $>$  2.5 cm; 2) Anterior location; 3) Endophytic; 4) Close to the collecting system; and 5) Cystic RCC.

The patient's factors that make RFA a preferred treatment option include: 1) Unfit for or refuses surgical excision; 2) Requires nephron-sparing, as in renal insufficiency, chronic

kidney disease, or solitary kidney; and 3) Multiple RCC syndrome, or high risk of developing RCC in the future.

The patient's factors that preclude RFA include a coagulation disorder, gross obesity (precluding electrode placement), or noncompliance with follow-up protocol.

## ONCOLOGICAL EFFICACY

Several series, as listed in Table, have shown an overall recurrence-free rate of  $>$  90%, at median follow-up periods greater than 24 months.<sup>(17,38,41-43)</sup> Radiofrequency ablation has become a popular treatment alternative in elderly or comorbid patients. Such a patient cohort may not tolerate a partial nephrectomy, and particularly may not tolerate the morbidity of a partial nephrectomy. The RFA series listed in Table are CT-guided renal RFA series.

Radiofrequency ablation can also be used via a laparoscopic technique. In one large series of 208 patients receiving either percutaneous or laparoscopic RFA, the percutaneous approach was used for posterior or laterally positioned tumors, whereas tumors located anteriorly or medially, or in close proximity to the bowel were managed by laparoscopic RFA.<sup>(17)</sup>

It is not uncommon for certain tumors to recur either early on in follow-up (within 3 to 6 months) or later (after 24 months). Recurrence occurs in less than 10% of the time. Recurrence is dealt with differently, either by additional RFA sessions, with success, or by radical nephrectomy or partial nephrectomy in other cases. Most RFA recurrences can be salvaged by repeat RFA, and this is one advantage of RFA over CA.

Tumor size and location have been shown to be independent predictors of success.<sup>(13,38,49)</sup> Anterior tumors are in bad locations and tend to recur, and are linked to a higher rate of adjacent organ damage.<sup>(51)</sup> Tumors smaller than 2.5 cm are less likely to recur, as are exophytic, lateral, or posterior tumors. In one study, there was a statistically significant correlation ( $P = .001$ ) between higher 3 and 5-year disease-free survival and tumor size  $<$  3 cm. Their difference in 5-year disease-free survival rates for tumors that were  $<$  3 cm compared to  $>$  3 cm was 91% and 79%, respectively.<sup>(52)</sup> For tumors  $>$  3 cm, the recurrence rate was 20%.

Peripheral tumors are surrounded by peri-nephric fat, which

**Oncological results of percutaneous CT-guided renal RFA series.\***

First Author	Year	n	Size (mean), cm	Age (mean), y	FU (mean), mon	RFS, %	Pre-RFA biopsy
Nitta <sup>(44)</sup>	2012	22	2.4	73	18	85	NA
Kim <sup>(41)</sup>	2011	49	2.4	58.6	31.7	94	13/49
Tracy <sup>(17)</sup>	2010	172	2.4	64	27	97	172/172
Ferakis <sup>(38)</sup>	2010	31	3.9	61	61	90	NA
Hiraoka <sup>(39)</sup>	2009	40	2.4	73	16	85	34/40
Levinson <sup>(42)</sup>	2008	31	2.1	71.7	61.6	90	31/31
Park <sup>(45)</sup>	2008	9	2.5	50	8	100	NA
Raman <sup>(43)</sup>	2008	19	2.3	62	27	100	19/19
Watkins <sup>(10)</sup>	2007	11	3.5	74	8	82	8/11
Sabharwal <sup>(11)</sup>	2006	11	1.95	72	11	78	11/11
Hegarty <sup>(46)</sup>	2006	72	2.5	67	12	100	72/72
Arzola <sup>(33)</sup>	2006	23	2.7	74	24	90	23/23
Park <sup>(47)</sup>	2006	46	2.4	63.5	25	96.8	41/46
Ahrai <sup>(48)</sup>	2005	29	3.5	65	10	96	29/29
Matsumoto <sup>(34)</sup>	2005	63	2.5	62	19	98	63/63
Gervais <sup>(49)</sup>	2005	85	3.2	70	27	90	85/85
Mayo-Smith <sup>(15)</sup>	2003	32	2.6	76	9	81	18/32
Pavlovich <sup>(16)</sup>	2002	21	2.4	39	2	79	NA
McGovern <sup>(50)</sup>	1999	1	3.5	84	3	100	1/1
Zlotta <sup>(6)</sup>	1997	3	2 to 5	NA	NA	NA	3/3

\*CT indicates computed tomography, RFA, radio frequency ablation; FU, follow-up; and NA, not available.

is insulating and tends to enhance the coagulative effects of RFA current. Central tumors suffer from a ‘heat-sink’ effect. This is when the RFA energy is dispersed because of the tumor’s proximity to either larger vessels or the collecting system. Vessels and the collecting system do not have the same insulating properties as fat, and RFA heat energy is lost to these structures. Furthermore, it has been suggested that benign lesions, such as oncocytoma, may have better efficacy because they are less vascular, and therefore, suffer from less heat-sink effect.<sup>(53)</sup>

Most patients require one RFA session; however, a minority requires an additional RFA session to salvage early failures.<sup>(38)</sup> The indication is for those tumors with persistent enhancement after 4 to 6 weeks. The treatment times within one RFA session depends on tumor size, with larger lesions requiring several overlapping RFA sessions in order to completely cover the entire tumor area.

A pre-RFA biopsy is generally used to confirm RCC. How-

ever, the exact histological subtype of RCC is not always possible to determine, and at times the biopsy is inconclusive. Certain authors use biopsy only if they are uncertain of the nature of the tumor on CT imaging, or to exclude a metastatic lesion to the kidney.<sup>(41)</sup> One author confirmed the lack of viable cancer cells within the ablation zone at one year post-RFA by performing a biopsy of the tumor bed using an 18-gauge Tru-Cut needle, with 4 passes into each tumor.<sup>(43)</sup> They confirmed histological tumor absence in 100% of cases. One author reported on RFA of 9 patients with cystic RCC, either Bosniak III or IV lesions, with 100% RFS at 8 months median follow-up.<sup>(45)</sup> In general, cystic RCC is seen as a contraindication to RFA.

One earlier series described a mean age of 39 years, where in 21 patients with either von Hippel-Lindau or hereditary papillary RCC were treated with RFA.<sup>(16)</sup> One study compared either laparoscopic or percutaneous RFA with either open or laparoscopic partial nephrectomy for clinical T1a

RCC. Of 40 RFA and 37 partial nephrectomy, there were local recurrences in 2 RFA and 1 partial nephrectomy (mean follow-up of 30 and 47 months, respectively).<sup>(54)</sup>

There is reproducible level 4 evidence (Table) that RFA is effective in rendering the patient disease-free. Ongoing reporting of longer term outcomes is required to monitor a durable RFS. Radiofrequency ablation is also safe with minimal morbidity.

## MORBIDITY

Reported morbidity rates are between 0 to 11%.<sup>(17,39,41,46,49)</sup>

There is no standardized reporting of morbidity among series. However, morbidity can be divided into major that requires intervention and minor, which resolves with conservative management. The Clavien Classification of surgical complications should be used to standardize morbidity reporting.<sup>(55)</sup> It is conceivable that any structure adjacent to the RFA zone may be injured.

Mortality is very rare; however, it has been reported.<sup>(56)</sup>

The cause of death is aspiration pneumonia post procedure. Any form of adverse cardiorespiratory or cerebrovascular outcome is possible, especially since the patient cohort is elderly and comorbid.

The more frequent minor complications include hematoma (peri-nephric or retroperitoneal) not requiring transfusion (5%), hematoma requiring transfusion (1%), neuromuscular complications, including flank pain and/or paresthesia (< 2%), and wound infection.<sup>(57,58)</sup> Other more problematic complications include urinoma (< 1%), ureteral stricture (< 1%), thermal injury to the duodenum (< 1%), reno-duodenal fistula (< 1%), life-threatening hematuria (< 1%), and splenic or liver injury, pancreatic injury, hilar vascular injury or dissection, and colonic or bowel perforation (all < 1%).<sup>(59)</sup> Furthermore, pneumothorax, renal-pleural fistula, and appendicular perforation are reported. Post-procedure pneumonia can occur. Also delayed ureteropelvic junction obstruction is seen. Chronic pain or paresthesia at the skin site or in the distribution of the genitofemoral nerve is seen. Skin tract metastasis has been reported.<sup>(15)</sup> Damage to a segmental arterial branch can cause segmental renal infarction.<sup>(60)</sup> With these morbidities in mind, the operative morbidity is higher after partial nephrectomy, ranging from

14% to 26%.<sup>(60)</sup>

## RECOMMENDATIONS

Percutaneous CT-guided RFA is efficacious and safe as an option for treating an SRT. Its role is in comorbid patients unfit for the gold standard surgical excision. A strict post-RFA CT imaging follow-up protocol is required to identify recurrences, most of which can be salvaged with repeat RFA. Risk factors for recurrence include tumor size > 2.5 cm and anterior tumors. Ideal tumors are < 2.5 cm, exophytic, and posterior or lateral. The evidence for oncological efficacy is level 4, and in the absence of randomized evidence, we rely on series which report long-term disease-free survival rates.

Failure rates are expected to be higher during the learning curve of units, which begin to offer renal RFA. Strong collaboration between the urologist and interventional radiologist through a multi-disciplinary meeting is mandatory to discuss each case and decide whether the tumor meets suitability selection criteria. This will help reduce morbidity and maximize oncological efficacy.

## CONFLICT OF INTEREST

None declared.

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