# Review of the efficacy and safety of radiofrequency ablation for the treatment of small renal masses

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## Abstract

**Background:** Small renal masses are increasingly being discovered incidentally on imaging performed for another reason. The standard of care for these masses involves excision by open or laparoscopic techniques. Recently, ablative techniques such as radiofrequency ablation (RFA) and cryoablation have taken a more prominent role in the treatment algorithm for these masses. We sought to evaluate the efficacy and safety of radiofrequency ablation in the treatment of renal tumours.

**Methods:** We conducted a review of the literature. There was no language restriction. We obtained studies from the following sources: the Cochrane Library, PubMed, EMBASE, LILACS and Current Controlled Trials.

**Results:** We identified no clinical trials in the literature. Thus we described the results from case series and retrospective studies with a reasonable sample size (number of reported patients in each study > 65). Most patients undergoing RFA had T1a disease with a mean tumour size of about 3 cm. Radiofrequency ablation was usually performed percutaneously with image guidance. Reported follow-up was short and ranged from 1 to 30 months. Most series used radiographic response as a surrogate for cancer control. The rates of local recurrence of the tumour were as high as 13.0% (average 8.5%) and were slightly higher than those associated with cryoablation and partial nephrectomy. Complications included hemorrhage, ureteral strictures and loss of a renal unit.

**Conclusion:** Our review demonstrates that RFA is a suitable and promising therapy in patients with small renal tumours who are considered to be poor candidates for more involved surgery. However, clinical trials with long-term data are needed to establish the oncological efficacy.


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## Résumé

**Contexte :** De petites masses rénales sont de plus en plus souvent découvertes de façon fortuite lors d'épreuves d'imagerie commandées pour une autre raison. Les soins standard pour ces masses incluent une excision par chirurgie ouverte ou par laparoscopie. Dernièrement, des techniques comme l'ablation par radiofréquence (ARF) et la cryoablation ont pris plus d'importance dans l'algorithme de traitement. Nous examinons l'efficacité et l'innocuité de l'ablation par radiofréquence dans le traitement des tumeurs rénales.

**Méthodologie :** Une revue de la littérature a été effectuée, sans restriction de langue. Des articles ont été obtenus des sources suivantes : la Bibliothèque Cochrane, PUBMED, EMBASE, LILACS et Current Controlled Trials.

**Résultats :** Comme aucun essai clinique n'a pu être cerné dans ces bases de données, nous décrivons les résultats d'études de cas et d'analyses rétrospectives avec populations de taille raisonnable (nombre de patients pour chaque étude > 65). La vaste majorité des patients ayant subi une ARF présentaient une tumeur T1a de taille moyenne d'environ 3 cm. L'ARF était habituellement effectuée par voie percutanée et guidée par imagerie. Le suivi était court, allant de 1 à 30 mois. La plupart des études sérielles avaient recours à la réponse radiographique comme paramètre de substitution de la maîtrise du cancer. Les taux de récidive locale de la tumeur atteignaient 13.0 % (moyenne 8.5%), et étaient en général légèrement plus élevés que les taux notés avec la cryoablation et la néphrectomie partielle. Les complications signalées étaient les suivantes : hémorragie, sténose urétérale et perte d'une unité rénale.

**Conclusion :** Le présent article montre que l'ARF est une technique convenable et prometteuse chez les patients porteurs de petites tumeurs rénales considérés comme de mauvais candidats pour une intervention plus lourde. Cependant, il est impératif d'effectuer des essais cliniques à long terme afin d'établir dans un avenir rapproché l'efficacité oncologique de cette technique.


## Introduction

In Canada, the incidence of renal cancer is 4500 new cases per year, with 1500 patients dying of the disease.[1] Small renal masses are increasingly being discovered incidentally on imaging performed for another reason.[2–4] The natural history of these incidentally discovered masses remains unclear. When surgically excised, 70%–80% are proven to be renal cell carcinomas and the rest are benign.[5–8]

When technically feasible, the standard of care for these masses has been partial nephrectomy. Local and distant oncological control has been well established with surgical excision.[9] In the last 10 years, a minimally invasive approach with laparoscopy has largely supplanted open surgery. The question of whether in situ ablative technologies[10,11] can replace excision for the treatment of small renal tumours remains unanswered. The reported advantages of ablative approaches over extirpative techniques include reduction

of perioperative morbidity, shorter hospital stay and faster recovery time. The main advantage of ablative techniques, however, would be to offer treatment to patients who are otherwise not candidates for invasive extirpative techniques.[12,13]

Several ablative technologies have been investigated, including cryoablation (CA), radiofrequency ablation (RFA), microwave,[14] high-intensity focused ultrasonography,[15,16] laser interstitial thermotherapy,[17] microwave thermotherapy and radiosurgery.

Radiofrequency ablation is a minimally invasive treatment for localized cancer in which a small needle attached to a device that delivers radiofrequency energy is inserted into a tumour to destroy the cancerous tissue while the patient is sedated or under general anesthesia. The procedure is usually performed percutaneously with image guidance using computed tomography (CT) or ultrasonography and the tumour is destroyed by heating to temperatures exceeding 60ºC.[18]

Radiofrequency ablation has been licensed by Health Canada and used for many years in the treatment of cardiac abnormalities, trigeminal neuralgia and osteoid osteomas; more recently, it has been used in the treatment of neoplasms in the liver, kidney, prostate, bone and soft tissues, and other areas.[19] The role of RFA in the treatment of renal neoplasms is still being investigated with several series reporting short-term outcomes.

We sought to examine the state of knowledge of RFA in the treatment of renal tumours. We reviewed the efficacy of this technology in terms of oncological control and prevention of local recurrence and metastasis. We also examined complications and safety concerns as they relate to RFA.

## Methods

There was no language restriction. We obtained studies from the following sources: Cochrane Central Register of Controlled Trials (Central, The Cochrane Library, issue 3, 2008), US National Library of Medicine (PubMed; 1966–2008), Excerpta Medica database (EMBASE; 1980–2008), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS; 1982–2008) and Current Controlled Trials to identify all studies about RFA in patients with renal cell carcinomas.

We searched the databases using a comprehensive search strategy for kidney cancer and RFA using medical subject headings (MeSH) and key words, including an exhaustive list of synonyms (Appendix 1). We adapted the search strategy for each database to achieve more sensitivity. We also examined the bibliographic references in relevant review articles for eligible trials.

We were interested in the following clinical outcome measurements: cancer specific survival, radiographic success, tumour recurrence, local tumour progression or distant metastases, need for repeat ablation, complications, adverse events reported and renal function.

## Results

Our search in the electronic databases identified 1428 titles. After screening by title and then abstract, we obtained full paper copies for 71 studies that were potentially eligible for inclusion in the review. Of these, we did not identify any randomized controlled trials. We identified several case series and retrospective studies and 1 controlled clinical trial. Thus we included the case series and retrospective studies with a reasonable sample size ($n > 65$), and the controlled clinical trial in our review.

Table 1 summarizes the characteristics of published studies on RFA. Most patients undergoing RFA had T1a disease with a mean tumour size of about 3 cm. RFA was usually carried out percutaneously with image guidance. However, if the tumour was endophytic or otherwise not accessible percutaneously, laparoscopy could be carried out to expose the kidney and the tumour. Reported follow-up was short and ranged from 1 to 30 months.

Table 2 outlines the clinical outcomes and complications reported in the RFA studies we examined. Most series used radiographic response as a surrogate for cancer control. We considered lack of contrast enhancement, decrease in size of the tumour or lack of growth on serial imaging to be signs of complete and successful ablation. The rates of local recurrence of the tumour were as high as 13.0% (average 8.5%) and were slightly higher than those associated with cryoablation and partial nephrectomy.

Although RFA is generally well tolerated with a favourable complication profile, it is not an innocuous procedure. Serious complications can occur, including hemorrhage, ureteral strictures and loss of a renal unit.

## Discussion

The goal of RFA is to destroy tissue by heat using radiofrequency energy. The procedure involves delivering an alternating electrical current at high frequency causing agitation of ions, which in turn results in heat. It has been shown that heating tissue to 55°–60°C for 5 minutes results in irreversible

**Table 1. Noncontrolled, controlled and retrospective studies on radiofrequency ablation for renal tumours**

| Study | Design | Comparative group(s) | No. of patients | No. of tumours | Mean tumour size or range, cm | Tumour type | | Type of RFA | Follow-up, mo |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Exophytic | Parenchymal, central or mixed | | |
| Ganguli et al.[20] | Retrospective study | NA | 66 | 72 | 2.7 | 47 | 25 | Percutaneous | 1 |
| Lucas et al.[5] | Retrospective comparative study | RN or PN | RFA 86<br>PN 85<br>RN 71 | NR | RFA 2.34<br>PN 2.6<br>RN 3.16 | NR | | NR | RFA 22.0‡<br>PN 24.0‡<br>RN 45.5‡ |
| Weight et al.[21] | Retrospective comparative study | LC | RFA 88<br>LC 176 | RFA 109<br>LC 192 | RFA 2.5<br>LC 2.4 | NR | | Percutaneous | 6 |
| Wingo and Leveillee[22] | Case series | NA | 131 | 146 | 1.0–5.3 | 41 | 105 | Percutaneous and laparoscopic | 29§ |
| Bensalah et al.[23] | Retrospective comparative study | Laparoscopic PN | RFA 38<br>LPN 50 | NR | RFA 2.3<br>LPN 2.6 | NR | | Laparoscopic | RFA 15§<br>LPN 25§ |
| Breen et al.[24] | Case series | NA | 97 | 105 | 3.2 | 86 | 19 | NR | 16.7§ |
| Stern et al.[25] | Retrospective comparative study | Open or laparoscopic nephron-sparing surgery PN | RFA 40<br>PN 37 | NR | RFA 2.41<br>PN 2.43 | NR | | Percutaneous and laparoscopic | RFA 30§<br>PN 47§ |
| Zagoria et al.[26]* | Case series | NA | 104 | 125 | 2.7 | 94 | 31 | Percutaneous | 13.8§ |
| Hegarty et al.[27] | Retrospective comparative study | LC | RFA 72<br>LC 161 | RFA 81<br>LC 179 | RFA 2.51<br>LC 2.56 | NR | | Percutaneous | RFA 12<br>LC 36 |
| Matin et al.[28] | Retrospective comparative study | CA | RFA 410<br>CA 206 | RFA 466<br>CA 230 | 0.9–8.9 | 39% | 61% | Percutaneous and laparoscopic | 24.2§ |
| Gervais et al.[29] | Retrospective study | NA | 85 | 100 | 3.2 | 67 | 33 | Percutaneous | 28 |
| Matsumoto et al.[30]† | Retrospective study | NA | 91 | 109 | 2.4 | NR | | Percutaneous and laparoscopic | 19 |
| Wah et al.[31] | Controlled clinical trial | CG (biopsy of focal renal lesions) | RFA 17<br>CG 20 | RFA 11<br>CG NR | 3.1 | NR | | Percutaneous | |
| DiMarco et al.[32] | Case series | NA | 66 | 91 | 2.0 | 53 | 38 | NR | 9.0§ |

CA = cryoablation; CG = control group; LC = laparoscopic cryoablation; LPN = laparoscopic partial nephrectomy; NA = not applicable; NR = not reported; PN = partial nephrectomy; RFA = radiofrequency ablation; RN = radical nephrectomy.
*Uzzo 2007 study is a duplicate publication of Zagoria et al.[34]
†A 2006 study by Park has the same participants as the study by Matsumoto and colleagues.[23]
‡Median.
§Mean.

cellular damage, and heating to more than 70°C causes cell death and tissue coagulation.[33,34] Temperature-based RFA machines (e.g., RITA Medical Systems, Inc.) use temperatures as high as 105°C during treatment. One drawback to RFA is that, unlike cryoablation, it is not possible to monitor the ablated area via imaging in real time. It is therefore difficult to ensure that the entire surface area of a tumour receives the same amount of heat.

Our review demonstrates that although promising, the evidence behind RFA remains immature. Prospective and randomized trials are lacking. Reported follow-up is too short, with most studies reporting a follow-up of 2 years or less and all studies reporting a follow-up less than 3 years. The natural history of small renal masses is not well defined, but one review demonstrated a growth rate of 0.28 cm/year with a metastatic rate of 1% after 34 months of follow-up.[35] This seems to indicate that the reported follow-up for most RFA series is too short to draw any meaningful conclusions about oncological efficacy.

Most RFA studies equate a successful ablation with radiological response. However, imaging changes after RFA are not always predictable. Tumours ablated with RFA do not consistently

**Table 2. Clinical outcomes and complications of each included study (part 1 of 2)**

| | Outcome | | Complication | |
|---|---|---|---|---|
| Study | Clinical outcome studied | Occurrence, % | Major | Minor |
| Ganguli et al.[20] | Average percentage decrease in tumour size | 21 | Ureteral injury; large perinephric, retroperitoneal, and pelvic hemorrhage | Second-degree burn; small perinephric or subcapsular hematomas |
| Lucas et al.[5] | 1) Renal function — GFR < 60 mL/min/1.73 $m^2$ | RFA 89.47<br>PN 88.88<br>RN 100 | NR | NR |
| | 2) Local recurrence | RFA 6.97<br>PN 2.35<br>RN 0 | NR | NR |
| Weight et al.[21] | 1) Radiographic success | RFA 85<br>CA 90 | NR | NR |
| | 2) No malignant cells on biopsy | RFA 65<br>CA 94 | NR | NR |
| Wingo and Leveillee[22] | Successfully managed with a single RFA session | 92.7 (data from endophytic tumours) | Lower extremity paresthesia | Hematuria, retention, flank bruising |
| Bensalah et al.[23] | 1) Hospital length of stay, d | RFA 1.5 | Ureteric stricture (requiring a nephrectomy) | |
| | | LPN 2.9 | Urinary leak; delayed bleeding (requiring bladder clot evacuation and stenting) | Acute urinary retention, perirenal hematoma |
| | 2) Recurrences | RFA 2.63<br>LPN 0 | | |
| Breen et al.[24] | 1) Tumours completely treated | 79.04 | Moderate hydronephrosis and clyceal leak (subsequent urinoma) | Hematuria, renal hematoma |
| | 2) Overall technical success rate | 90.47 | | |
| Stern et al.[25] | 3-year recurrence-free survival rate | RFA 93.4 | UPJ obstruction (subsequently had a nephrectomy) and pneumonia | Asymptomatic lower-pole hydrocalyx and temporary probe-site numbness |
| | | PN 95.8 | Flank-site hernia | Ileus |

*Continued on next page*

regress in size. In addition, a peritumour halo may form with fat infiltration. Successfully treated tumours do usually demonstrate a lack of enhancement on CT scans.[30] It remains unclear whether radiological response is an adequate surrogate for cancer control. Histopathological confirmation of complete ablation is also not completely reliable owing to sampling error and the high false-negative rate of percutaneous biopsies.[36] Three studies performed a complete histopathological examination of tumours treated with RFA after either a radical or partial nephrectomy. Rendon and colleagues[37] found persistent cancer in 5%–10% of tumour volume. Matlaga and colleagues[38] found 2 of 10 tumours to be incompletely ablated, and Michaels and colleagues[39] found 4 of 5 tumours to be incompletely ablated.

## Conclusion

This review demonstrates that RFA is a suitable and promising therapy in patients with small renal tumours (< 4 cm) who are considered to be poor candidates for more involved surgery. Long-term data on oncological control is lacking. Longer follow-up and more rigorous head-to-head trials

**Table 2. Clinical outcomes and complications of each included study (part 2 of 2)**

| | Outcome | | Complication | |
|---|---|---|---|---|
| Study | Clinical outcome studied | Occurrence, % | Major | Minor |
| Zagoria et al.[26] | Completely ablated tumour | 93 | Large perinephric hematoma; pneumonia; severe neuropathic pain and ureteral strictures with concomitant hydronephrosis | Small pneumothoraces, perirenal hemorrhage, apnea, tachycardia, flank pain |
| Hegarty et al.[27] | 1) Radiological evidence of tumour recurrence or persistence of disease | RFA11.1 | There were no major complications | Perirenal hematoma; retroperitoneal hematoma; perirenal abscess and upper pole hydrocalicosis |
| | | CA 1.8 | Myocardial infarction; congestive heart failure and hemothorax | Urine leak; obstructed solitary kidney; pneumothorax; perirenal fluid collection and blood transfusion |
| | 2) Cancer-specific survival | RFA 100<br>CA 98 | | |
| Matin et al. [28] | Overall residual or recurrent disease | RFA 13.4<br>CA 3.9 | NR<br>NR | NR<br>NR |
| Gervais et al.[29] | Complete tumour necrosis by imaging criteria | 90 | Hemorrhage requiring RBC transfusion and stent placement; asymptomatic posterior abdominal wall enhancing mass; ureteral stricture; urinoma and ureteral injury | Hemorrhage not requiring transfusion; inflammatory track mass; skin burns and transient neuropathic pain |
| Matsumoto et al.[30] | Successful ablation of the tumour | 98 | Lower-pole infarct, urine leak and UPJ obstruction | Leg and arm neuropathy; pneumonia; prolonged pain; postoperative narcotic reaction and hydrocalix |
| Wah et al.[31] | Occurrence of fever and flulike symptoms | RFA 82<br>CG NR | Flu-like symptoms; pneumonia; pain; | Lifestyle interference with general activities and work activities |
| DiMarco et al.[32] | Successful ablation of the tumour | 95 | UPJ obstruction; chronic lumbar plexopathy pain; wedge shaped renal infarct; major hemorrhage | NR |

CA = cryoablation; CG = control group; GFR = glomerular filtration rate; LPN = laparoscopic partial nephrectomy; NR = not reported; PN = partial nephrectomy; RBC = red blood cells; RFA = radiofrequency ablation; RN = radical nephrectomy; UPJ = uretero–pelvic junction

are needed to determine the exact role of RFA in the treatment algorithm of small renal masses.

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**Appendix 1. Summary of the bibliographic search strategies for type of clinical situation and intervention of interest**

((Kidney Neoplasm) OR (Renal Neoplasms) OR (Renal Neoplasm) OR (Kidney Neoplasms) OR (Cancer of Kidney) OR (Kidney Cancers) OR (Renal Cancer) OR (Renal Cancers) OR (Cancer of the Kidney) OR (Kidney Cancer) OR (Kidney Cancers) OR (Renal masses) OR (Renal cell carcinoma)) **AND** ((Radiofrequency ablation) OR (Catheter ablation) OR (Electric Catheter Ablation) OR (Electrical Catheter Ablation) OR (Radiofrequency Catheter Ablation) OR (Transvenous Catheter Ablation) OR (Transvenous Electric Ablation) OR (Transvenous Electrical Ablation) OR (Percutaneous Catheter Ablation) OR (Percutaneous Radiofrequency ablation) OR (Radio frequency) OR Radio-frequency OR (Radiofrequency thermal ablation) OR (Minimally invasive therapy) OR (Tumor ablation) OR (CT-guided percutaneous radiofrequency ablation))