NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of percutaneous radiofrequency ablation of renal cancer

Renal cancer is cancer of the kidney. Percutaneous radiofrequency ablation of renal cancer involves placing one or more electrode-needles through the skin into the kidney. The electrodes are placed within the tumour and produce heat, with the aim of destroying the cancer cells.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2010.

Procedure name

- Percutaneous radiofrequency ablation of renal cancer

Specialty societies

- British Association of Urological Surgeons
- British Society of Interventional Radiology
- Royal College of Radiologists

Description

Indications and current treatment

Renal cancer is the eighth most common cancer in men and the fourteenth most common in women in England and Wales; in 2004, there were 5745 newly diagnosed cases. Most patients are diagnosed following the

development of symptoms – typically haematuria or loin pain. However, some patients are diagnosed as part of investigation of incidental renal abnormalities detected at imaging studies. Patients with genetic syndromes that predispose them to kidney tumours may undergo surveillance by repeat ultrasound scans.

The standard treatment for renal cancer is total or partial nephrectomy (open or laparoscopic). One of a range of non-resectional ablative procedures such as cryoablation and radiofrequency ablation may be selected for some smaller tumours.

What the procedure involves

Percutaneous radiofrequency ablation of renal cancer is carried out with the patient under either local anaesthesia and sedation or general anaesthesia. One or more electrodes are inserted percutaneously into the tumour, using ultrasound, computer-assisted tomography (CT) or magnetic resonance imaging (MRI) guidance. Radiofrequency energy, consisting of an alternating electrical current in the frequency of radiowaves, is passed through the electrode producing heat at the tip of the needle electrode which coagulates and destroys the tumour tissue in the target area. If the tumour is close to the bowel, hydrodisplacement is often used. Sterile water is instilled percutaneously under image guidance to displace the bowel away from the tumour. Percutaneous radiofrequency ablation can be repeated if necessary.

Percutaneous radiofrequency ablation may be particularly indicated in patients with small tumours (for example, less than 4 cm), those who are poor surgical candidates or have multiple comorbidities, a solitary kidney, renal insufficiency or unresectable tumours. Radiofrequency ablation may also be a viable treatment option for patients in whom renal preservation is desired, such as those with von Hippel-Lindau disease, a hereditary form of renal cancer.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to percutaneous radiofrequency ablation of renal cancer. Searches were conducted of the following databases, covering the period from their commencement to 9 September: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with renal cancer.
Intervention/test	Percutaneous radiofrequency ablation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on a meta-analysis of 47 studies including 1375 tumours and approximately 1008 patients from 3 non-randomised comparative studies, 5 case series and 5 case reports[1–14]. There will be considerable overlap of patients between the meta-analysis and the individual studies listed in table 2.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A. Only case series with more than 20 patients have been included unless they describe a complication that has not been reported elsewhere in the overview.

Table 2 Summary of key efficacy and safety findings on percutaneous radiofrequency ablation of renal cancer

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
Kunkle DA (2008)[1] **Meta-analysis (prospective and retrospective non-randomised comparative studies and case series)** USA Search date: October 2007 Study population: patients with clinically localised, sporadic renal tumours **n = 1375 renal tumours (775 RFA, 600 cryoablation [47 studies])** Mean age (weighted by sample size): 67 years Sex: not reported Median tumour size: 2.6 cm Study selection: meta-analysis was limited to series that analysed clinically localised (not further defined), sporadic renal tumours. Series that included only patients with hereditary or metastatic RCC were excluded. Technique: Of all RFA procedures, 94% were performed percutaneously and the other 6% laparoscopically. Cryoablation was performed percutaneously in 23% of cases, and surgically in 77% (of which 12% were open and 65% were laparoscopic). **Mean follow-up: 19 months** Conflict of interest/source of funding: none declared	Number of tumours analysed: **1375 (600 cryoablation, 775 RFA)** **The RFA procedures were predominantly percutaneous, whereas the cryoablation procedures were predominantly surgical – see first column 'Technique'.** Pre-ablation biopsy: • RFA = 62% (482/775) • Cryoablation = 82% (494/600), p<0.0001 ***Repeat ablations*** • RFA = 8.5% (66/775) • Cryoablation = 1.3% (8/600), p<0.0001 ***Local tumour progression*** (defined as radiographic or pathologic evidence of residual disease after initial treatment , regardless of time to recurrence) • RFA = 12.9% (100/775) • Cryoablation = 5.2% (31/600), p<0.0001 ***Progression to metastatic disease*** • RFA = 2.5% (19/775) • Cryoablation = 1.0% (6/600), p=0.06 *91% (43/47) of studies were included in regression analysis:* The higher incidence of local tumour progression was found to be correlated significantly with treatment by RFA on univariate analysis (p = 0.001) and on multivariate regression analysis (p = 0.003). The incidence of malignant pathology, incidence of unknown pathology, mean patient age, and mean tumour size were not associated with local recurrence in either the univariate or multivariate analyses. No significant differences were observed with regard to the incidence of metastases.	No safety outcomes were reported.	**Study population issues**: • The major problem with interpreting the comparative efficacy of the two procedures compared in this study is that the approach was usually percutaneous in the RFA group, whereas it was usually surgical in the cryotherapy group. • Overall, 54% of lesions were pathologically confirmed RCC and 13% were benign. Histology was unknown or indeterminate for 34% of lesions. There were statistically significantly more lesions of unknown or indeterminate pathology in the RFA group (40% vs 24%). • No statistically significant differences were observed between the groups with regard to age, tumour size, or duration of follow-up. **Other issues:** • The authors note that the natural history of small renal tumours shows some variability (growth rates of 0.09–0.86 cm per year). The indolent nature of certain small renal masses must be considered when analysing the treatment efficacy of ablative technologies.

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
Hegarty NJ (2006)[2] **Non-randomised comparative study** USA Recruitment period: 1997 onwards Study population: patients with localised, small (≤ 4 cm) enhancing solid renal mass seen on preoperative CT **n = 233 patients** (72 percutaneous RFA vs 161 laparoscopic cryoablation); **260 tumours (81 vs 179)** Mean age: 66 years Sex: 67% male (48/72) (for RFA) Median tumour size: 2.5 cm (for both groups) Patient selection criteria: localised, small (≤ 4 cm) enhancing solid renal mass seen on preoperative CT in patients with comorbidities that would render them high-risk for open or laparoscopic partial nephrectomy. Few anterior or medial tumours were selected for RFA because of proximity to adjacent viscera. If patients were suitable for laparoscopy, they were offered laparoscopic cryotherapy in preference to percutaneous RFA. Technique: RFA performed with local anaesthesia and sedation, with CT guidance. Laparoscopic cryotherapy was done using either transperitoneal or retroperitoneal approach. A cryoprobe was placed into the centre of the tumour under ultrasound guidance. Fine needle biopsy was done in both groups prior to ablation. **Median follow-up (years): RFA = 1, cryotherapy = 3**	Number of patients analysed: **233 (72 vs 161); 260 tumours (81 vs 179)** Follow-up assessment was by MRI scans at day 1 and 3, 6, 12, 24, 36, 48 and 60 months after the procedure, along with protocol kidney biopsy of the treatment site after 6 months. The presence or absence of enhancement and pattern of enhancement were noted. ***Radiologic imaging evidence of residual renal tumour (areas suspicious for renal tumour persisting beyond the first day scan) :*** • Percutaneous RFA = 3.7% (3/81) • Laparoscopic cryoablation = 1.7% (3/179) In the cryoablation group, 2 patients underwent laparoscopic nephrectomy and the third showed no evidence of enhancement on MRI 3 years after repeat cryoablation. In the RFA group, 2 patients underwent further RFA with no evidence of residual tumour on follow-up MRI. The other patient was assessed as stable as seen on serial CT scanning. An additional 7.4% (6/81) of tumours in the RFA group showed recurrent or residual disease on follow-up imaging or protocol biopsy. ***Cancer specific survival at follow-up*** • Percutaneous RFA =100% (median 1-year follow-up) • Laparoscopic cryoablation = 98% (median 3-year follow-up) 3 patients in the RFA group developed metastases during the follow-up period (all were alive at end of follow-up). 9 patients treated with cryoablation died with a median follow-up of 35 months (4 from metastatic renal carcinoma and 5 from causes other than renal malignancy). All 4 patients who died from renal cell carcinoma had been treated for at least 1 other RCC tumour before cryoablation and none of them showed signs of residual disease on serial MRI investigations	Number of procedures: 82 RFA, 164 cryoablation 'Major' complications: • Percutaneous RFA = 0% (0/82) • Laparoscopic cryoablation = 1.8% (3/164) (new-onset congestive heart failure, myocardial infarction, haemothorax requiring thoracotomy) 'Minor' complications associated with percutaneous RFA (9.8% [8/82]): • 3 perirenal hematoma (no treatment required) • 2 retroperitoneal haematoma (1 required blood transfusion) • 2 perirenal abscess (1 required percutaneous drainage) • 1 upper pole hydrocalycosis (resolved with ureteral stenting) 'Minor' complications associated with laparoscopic cryoablation (4.9% [8/164]): • 1 urine leak (resolved with ureteral stenting) • 1 obstructed solitary kidney (resolved with ureteral stenting) • 1 pneumothorax (chest drain inserted) • 1 perirenal fluid collection (drained percutaneously) • 4 blood transfusions	This study is included in the meta-analysis above[1]. **Follow-up issues**: • No losses to follow-up were described. **Study design issues**: • Laparoscopic cryoablation was performed from 1997 onwards. Percutaneous RFA was introduced in 2003, for the treatment of selected patients with small renal tumours. • Retrospective study. **Study population issues**: • The two groups were comparable in terms of mean age, body mass index, American Society of Anesthesiologists (ASA) score, mean tumour size on preoperative CT and mean preoperative serum creatinine levels. • However, less than 10% of tumours in the RFA group were anterior, compared with 39% of tumours in the cryoablation group. • There were more patients with solitary kidneys in the RFA group than in the cryoablation group (49% vs 24%). **Other issues:** • There is a discrepancy in the number of RFA patients with recurrent or residual disease on follow-up (5 or 6).

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Conflict of interest/source of funding: none declared	(paper did not state whether the tumours were in the same or contralateral kidney). No significant differences were seen between preoperative and postoperative renal function measured with serum creatinine levels.		

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Weight CJ (2008)[3] **Non-randomised comparative study** USA Recruitment period: 1997 – 2006 Study population: patients with small renal lesions **n = 264 patients** (88 percutaneous RFA vs 176 laparoscopic cryoablation); **301 tumours (109 vs 192)** Median age: 68 years Sex: 68% male (74/109) (for RFA) Median tumour size: RFA = 2.5 cm, cryotherapy = 2.4 cm Patient selection criteria: none described. Patients scheduled to undergo percutaneous RFA generally underwent biopsy with fine needle aspiration and those scheduled for cryoablation underwent intraoperative biopsy. 8% (9/109) tumours in the RFA group and 24% (47/192) of tumours in the cryotherapy group were benign. Technique: RFA performed with local anaesthesia and sedation, with CT guidance and using Starburst(® FLEX ablation electrode. Laparoscopic cryotherapy was done under general anaesthesia, using either transperitoneal or retroperitoneal approach. A cryoprobe was placed into the centre of the tumour under ultrasound guidance. **Follow-up: 6 months** Conflict of interest/source of funding: not reported	Number of patients analysed: **264 (88 vs 176); 301 tumours (109 vs 192)** Follow-up assessment was by radiographic imaging (post-contrast CT or subtraction imaging MRI) on postoperative day 1, at 3, 6 and 12 months and annually thereafter. Radiographic success was defined as no evidence of central or nodular enhancement after treatment. Routine biopsy of the treated site was performed immediately after the 6-month scan. ***Radiographic success at 6 month :*** • Percutaneous RFA = 85% (62/73) • Laparoscopic cryoablation = 90% (125/139) ***Pathological success (lack of malignant/atypical cells on post-ablation biopsy or radical nephrectomy)*** • Percutaneous RFA = 65% (24/37) • Laparoscopic cryoablation = 94% (91/97) Follow-up biopsies were not completed for 66% (72/109) of tumours in the RFA group and 49% (95/192) of tumours in the cryotherapy group. Reasons included anticoagulant therapy, loss to follow-up, solitary/remnant/chronic renal insufficiency, recurrence, benign pretreatment biopsy, death before 6 months. In the RFA group, 12 of the 13 patients with positive follow-up biopsy had a malignant or 'favour malignant' diagnosis on pretreatment biopsy. One patient was diagnosed as having a benign pretreatment biopsy. In the cryoablation group, 3 out of 6 patients with positive follow-up biopsies had a negative pretreatment biopsy.	No safety outcomes were reported.	**Follow-up issues**: • 8 tumours in the RFA group and 23 tumours in the cryotherapy were lost to follow-up. • Follow-up biopsies were only available for 44% (134/301) of tumours. **Study design issues**: • Laparoscopic cryoablation was performed from 1997 onwards. Percutaneous RFA was introduced in 2002. **Study population issues**: • Significantly more tumours were centrally located in the RFA group compared to those in the cryoablation series (39% vs 16%, p <0.0001). • There were more indeterminate pathological results on pre-ablation biopsy in the percutaneous RFA group, compared with the laparoscopic cryoablation group (35% vs 20%, p = 0.0052). This may reflect inadequate sampling, because of percutaneous as opposed to operative biopsies in the two groups; or true differences in the proportion of tumours with indeterminate pathology in the two groups (less likely). **Other issues:** • The authors note that the clinical significance of the presence of viable cells in the absence of radiographic enhancement is not clear and longer follow up is needed to

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
	Correlation of pathological and radiographic results		determine if these patients are at higher risk of local or systemic progression.

	RFA n = 36	Cryoablation n = 97	p value
No enhancement	25	60	0.42
Negative biopsy	19	60	0.0004
Positive biopsy	6	0	
Positive peripheral enhancement	4	26	0.054
Negative biopsy	2	24	0.021
Positive biopsy	2	2	
Positive central enhancement	7	11	0.22
Negative biopsy	2	7	0.15
Positive biopsy	5	4	

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Onishi T (2007)[4]

Non-randomised comparative study

Japan

Recruitment period: 2004–6

Study population: patients with T1a renal cell carcinoma

n = 37 (20 percutaneous RFA vs 17 laparoscopic radical nephrectomy)

Mean age (years): RFA = 62.3, surgery = 53, p = 0.008
Sex: 73% male (27/37)

Patient selection criteria: eligibility criteria for RFA were single kidney (n = 7), renal dysfunction (n = 3), general anaesthesia risk (n = 5), double cancer (n = 2, not stated if both cancers were in the same kidney), refusal of open or laparoscopic surgery (n = 3). Pathological diagnosis was confirmed by biopsy.

Technique: RFA performed with local or epidural anaesthesia.

Follow-up: 24 weeks

Conflict of interest/source of funding: none declared</td>
<td>Number of patients analysed: 37 (20 vs 17)

Mean difference in HRQoL values from baseline
<table>
<tr><th></th><th></th><th>RFA</th><th>Laparoscopic radical nephrectomy</th></tr>
<tr><td>Physical functioning</td><td>1 week*
24 weeks</td><td>7.5
12.5</td><td>-22.5
-2.5</td></tr>
<tr><td>Role-physical functioning</td><td>1 week*
24 weeks</td><td>1.0
15.0</td><td>-21.0
-12.5</td></tr>
<tr><td>Bodily pain</td><td>1 week
24 weeks</td><td>-6.0
6.0</td><td>-15.0
-2.5</td></tr>
<tr><td>General health</td><td>1 week
24 weeks</td><td>3.0
6.0</td><td>-6.0
-7.5</td></tr>
<tr><td>Vitality</td><td>1 week
24 weeks</td><td>1.0
12.5</td><td>-10.0
-2.5</td></tr>
<tr><td>Social functioning</td><td>1 week
24 weeks</td><td>1.0
14.0</td><td>-6.0
12.5</td></tr>
<tr><td>Role-emotional functioning</td><td>1 week*
24 weeks</td><td>-7.5
10.0</td><td>-22.5
-7.5</td></tr>
<tr><td>Mental health</td><td>1 week
24 weeks</td><td>1.0
13.0</td><td>-6.0
12.0</td></tr>
</table>
* The scores of physical functioning, role-physical functioning and role-emotional functioning were significantly lower in the surgery group at 1 week compared with baseline (p = 0.006, p = 0.028 and p = 0.036 respectively).</td>
<td>The authors note that ‘no major surgical and postoperative complications such as organ injury, ileus and severe infection, were seen.’</td>
<td>Follow-up issues:
• Data were collected at baseline and at 1, 4, 12, and 24 weeks after surgery. No losses to follow-up were described.

Study design issues:
• Consecutive patients
• HRQoL was assessed using the Medical Outcomes Study 36-Item Short Form (SF-36). A higher score indicates a better level of QoL.
• The aim of the study was to assess the changes in HRQoL during the postoperative follow-up period.

Study population issues:
• Patients in RFA group were statistically significantly older than those in surgery group (62 years vs 53, p = 0.008).
• There were no significant differences between the groups with regard to tumour size and body mass index.
• The baseline HRQoL scores for physical functioning, role physical functioning, vitality, and mental health were significantly lower in the RFA group compared with the surgery group.
Other issues:
• The means of differences of values from baseline were presented graphically in the paper. Therefore , the figures in the tables are approximate.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
Gupta A (2009)[5] **Case series** USA Recruitment period: not stated Study population: patients with clinically localised enhancing renal masses **n = 151 patients; 163 tumours** Mean age: 65.0 years (range 37.1–87.7) Sex: 64% (97/151) male Mean tumour size: 2.5 cm (range 1.0–5.4) Patient selection criteria: patients with clinically localised disease and at least one post-procedure follow-up imaging study. Patients with tumours > 4 cm were not usually offered RFA unless their age or comorbidities made them poor candidates for surgical interventions. Definitive pathology was available for 80% (130/163) of tumours and 55.6% (84/151) patients had confirmed RCC. Technique: all procedures were performed under general anaesthesia with contrast-enhanced CT guidance. RF energy was applied using a RITA model generator (RITA medical systems) and a Starburst XL probe or Cool-tip™ probe (Valleylab). **Median follow-up: 18 months (range 1.5–70)** Conflict of interest/source of funding: none	Number of patients analysed: **151; 163 tumours** All patients underwent contrast-enhanced CT or MRI scans at 4 to 6 weeks, 3 to 6 months, and every 6 to 12 months thereafter. Incomplete ablation was defined as any enhancement on the scan or a positive biopsy, at 4 to 6 weeks. Local recurrence was defined as any new enhancement after a non-enhancing 4 to 6 week scan, or lesion growth. ***Complete ablation at first session*** **= 97% (158/163)** Four patients had enhancement on the postoperative CT scan and one patient had a positive postoperative biopsy. The mean size of lesions that were incompletely treated was 3.4 cm. ***Local recurrence diagnosed during follow-up*** = 3.3% (5/151) ***Metastatic disease diagnosed during follow-up*** = 1.3% (2/151) Masses that were in the central region and were endophytic had the highest risk of recurrence (16% [4/25] vs 2% [3/138]). Relative risk of developing any recurrence was 6.3 (95% CI 1.4 to 28.1, p = 0.016) for interpolar endophytic lesions as compared with other lesions. The risk of recurrence increased with increasing size of the mass, but this was not statistically significant. 5 patients died during follow-up, 2 due to metastatic RCC. Two patients died because of congestive heart failure and one because of metastatic prostate cancer. The first patient who died because of renal cancer had	**Complications** No complications were reported.	**Study design issues**: • The aim of the study was to assess intermediate-term outcomes of percutaneous RFA when using contrast-enhanced CT imaging and general anaesthesia. • A small subset of 7 patients underwent biopsy of the ablation zone at 4 to 6 weeks. • Survival analysis and multivariate analysis of prognostic factors were performed.

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
	also undergone contralateral nephrectomy for RCC. It was suspected that she had unrecognised metastases at the time of RFA. The second patient underwent RFA using only ultrasound and non-contrast-enhanced CT guidance (as opposed to contrast-enhanced CT). Renal insufficiency precluded use of contrast medium. Metastatic RCC was diagnosed 1 year after RFA treatment. Overall 1-year recurrence-free survival (defined as no evidence of radiographic recurrence independent of tumour pathology) probability = 97%. Overall 3-year recurrence-free survival probability = 92%. **Analysis of patients with confirmed RCC** (84 patients, 91 masses) Mean tumour size = 2.7 cm ***Complete ablation at first session* = 96% (87/91)** ***Local recurrence diagnosed during follow-up*** = 4.8% (4/84) ***Metastatic disease diagnosed during follow-up*** = 2.4% (2/84) 1-year recurrence-free survival probability = 96.1% 3-year recurrence-free survival probability = 86.7% The risk of recurrence for interpolar endophytic cancers was 4 times the risk of other cancers (95% CI 0.8 to 20, p = 0.09)		

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
Breen DJ (2007)[6] **Case series** UK Recruitment period: 1999 onwards Study population: patients with renal tumours **n = 97 patients; 105 tumours** Mean age: 71.7 years (range 36–89) Sex: 67% (65/97) male Mean tumour size: 3.2 cm (range 1.1–6.8) Patient selection criteria: patients unfit for major surgical intervention, or for whom the surgeon deemed that resection would be problematic due to tumour location, multifocal disease, or in the setting of a solitary kidney. The decision to treat was based on established CT criteria. Although most tumours were small, 12 were larger than 4 cm. Technique: most procedures were performed under conscious sedation although general anaesthesia was used for larger-volume or multifocal treatments (n = 38). A combination of ultrasound and CT guidance was used for 62 tumours. In the remaining 43, ultrasound guidance alone was used. In the case of two larger tumours, embolisation was performed prior to RFA. Two RFA systems were used: Tyco/Radionics (Boulder, USA) and Starburst, RITA Medical Systems (Mountainview, USA). **Mean follow-up: 16.7 months (range 1–76)** Conflict of interest/source of funding: not reported.	Number of patients analysed: **97; 105 tumours** Active follow-up with 6-monthly CT surveillance. Follow-up assessment was by contrast-enhanced CT reported by one of the two operators. Treatment adequacy was determined by the area of non-enhancement with respect to the tumour mass. Residual tumour was defined as enhancing tumour remnants within the volume of the lesion. ***79% (83/105) tumours were completely treated at a single sitting***. ***Overall technical success = 90.5% (95/105)*** In 5 elderly patients with residual tumour at CT, a clinical decision was made not to re-treat. In one case of subtotal treatment, the patient proceeded to nephrectomy. 14 tumours were re-treated (12 under CT guidance) and one patient was awaiting re-treatment at the time of reporting. A statistically significant association was seen between tumour size ≤ 3 cm and complete treatment at a single session (p = 0.007, odds ratio 3.99) No statistically significant association was seen with regard to imaging modality, tumour location within the kidney or the type of probe used for RFA. ***Metastatic renal cancer = 2.1% (2/97)*** Of 13 deaths, 1 was due to disseminated metastatic disease in a patient with von Hippel-Lindau disease who had previously undergone a contralateral nephrectomy for renal cell carcinoma. Six patients died of unrelated causes and the cause of death was unknown for the remaining 6 patients. One further patient developed lung metastases three months after RFA. There were no other cases of metastatic disease and no local recurrences.	**Complications (120 treatment episodes)** • Profuse but self-limiting haematuria = 0.8% (1/120) • Thermal injury to duodenum that required laparotomy and repair = 0.8% (1/120) (patient had a scoliotic deformity and a renal haematoma had complicated the procedure) • Moderate hydronephrosis due to a proximal ureteric stricture approximately 4 months post-RFA = 0.8% (1/120) (treated by temporary placement of ureteric stent) • Pneumothorax in a patient with a marked kyphoscoliotic deformity = 0.8% (1/120) (treated by chest tube drainage) • Calyceal leak and subsequent urinoma, treated by percutaneous drainage and placement of temporary ureteric stent = 0.8% (1/120) (patient had scoliosis) The authors note that 3 of the 5 complications occurred in the setting of marked scoliotic deformity.	Data from the same study centre is included in the meta-analysis above[1]. **Follow-up issues**: • No losses to follow-up were described. **Study design issues**: • Biopsies were not routinely performed prior to ablation.

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
Gervais DA (2005)[7] **Case series** USA Recruitment period: 1999 onwards Study population: patients with renal cell carcinoma **n = 85 patients; 100 tumours** Mean age: 70 years (range 22–88) Sex: 68% (58/85) male Mean tumour size: 3.2 cm (range 1.1–8.9) Patient selection criteria: one or more of the following: comorbid conditions precluding surgery or rendering surgery high risk, age > 80 years, life expectancy of more than 1 year but less than 10 years, solitary kidney, multifocal renal cell carcinoma such as in patients with von Hippel-Lindau disease or familial renal cell carcinoma. 90% (90/100) of tumours were biopsy-proven renal cell carcinoma. Technique: RFA was performed under sedation. Repeat ablation sessions were scheduled as needed. The majority of sessions were performed with CT guidance. Two RFA systems were used: Cool-tip™, Valleylab and StarBurst, RITA medical systems. Mean follow-up: 2.3 years (range 3.5 months–6 years) Conflict of interest/source of funding: not reported	Number of patients analysed: **85; 100 tumours** Active follow-up with CT or MRI at 1 month, 3 months and 6 months. Subsequent imaging follow-up at 6 to 12 month intervals. ***Complete tumour necrosis by imaging criteria*** = 91% (77/85) of patients; 90% (90/100) of tumours In an additional patient, there was no enhancement before ablation, so the absence of enhancement was not a reliable sign. In the remaining 7 patients, residually enhancing viable tumour was seen after 1–4 ablation sessions. All tumours < 4 cm were completely ablated. No tumours > 5.5 cm were completely ablated. Multivariate analysis showed that both small size (p < 0.0001; odds ratio 12.5) and non-central location (p = 0.0049; odds ratio 5.6) were independent predictors of success. 6 patients died within 2 years of ablation from another primary cancer (n = 4) or complications of cirrhosis (n = 2). Of the 80 patients without preexisting metastatic disease or contralateral renal cell carcinoma, none developed new metastatic disease over this period. ***Local progression = 1.2% (1/85)*** (detected at 14 months after RFA and treated with repeat RFA) ***Metastases = 3.5% (3/85)*** (two patients had pre-existing metastatic disease before RFA) 3 patients developed new renal tumours (1 with von Hippel-Lindau disease). The rate of the rise in blood creatinine levels after RFA remained the same as the rate of rise before ablation.	**Complications** • Haemorrhage = 5.9% (5/85) (1 required transfusion and stent placement for ureteral obstruction, 1 required transfusion, 2 required bladder catheter placement for bladder outlet obstruction and the remaining patient had conservative management for mild transient ureteral obstruction). • Asymptomatic posterior abdominal wall enhancing mass, diagnosed as benign inflammation at surgical excision = 1.2% (1/85) • Ureteral stricture = 1.2% (1/85) (treated with nephrostomy and ureteral stent placement) • Urinoma and ureteral injury = 1.2% (1/85) (treated with percutaneous drainage and nephroureteral catheter placement) • First- and second-degree burns at a grounding pad site = 1.2% (1/85) • Transient neuropathic pain along the distribution of the lumbar plexus = 2.4% (2/85) There were no cases of bowel perforation or tumour seeding. One patient with a solitary kidney required dialysis 3 months after RFA for renal failure of unknown cause.	Data from the same study centre is included in the meta-analysis above[1]. **Study design issues**: • Retrospective study. • The images obtained after ablation were interpreted by consensus of two experienced radiologists. Enhancement of any portion of the tumour was considered residual viable tumour, and the absence of enhancement was considered complete necrosis and thus completely ablated tumour. **Study population issues**: • Four patients had limited non-progressive metastatic disease treated with immunotherapy, radiation or surgery, at entry to study.

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
Zagoria RJ (2007)[8] **Case series** USA Recruitment period: 2000–2006 Study population: patients with biopsy-proven renal cell carcinoma **n = 104 patients; 125 tumours** Mean age: 70 years (range 30–89) Sex: 66% (69/104) male Mean tumour size: 2.7 cm (range 0.6–8.8) Patient selection criteria: no imaging evidence of metastatic disease or local spread to the renal vein on pretreatment CT or MRI scan; at least one imaging follow-up with CT or MRI with and without contrast. All patients were considered to be at substantially increased risk for developing complications during and after renal surgery due to comorbidities or syndromes with multifocal renal cell carcinoma. At least one tumour in each patient was confirmed as renal cell carcinoma by biopsy. Technique: RFA was performed under conscious sedation. Repeat ablation sessions were scheduled as needed. One RFA systems was used: Cool-tip™, Valleylab. Mean follow-up: 13.8 months (range 1–75.8) Conflict of interest/source of funding: study was partially supported by ValleyLab Inc. The first author is an unpaid consultant for Valleylab Inc.	Number of patients analysed: **104; 125 tumours** Active follow-up with CT or MRI at 1–3 months and at regular intervals thereafter. Lack of contrast enhancement was considered as no evidence of disease. Presence of enhancement was interpreted as residual tumour. ***Tumour-free status*** = 93% (116/125) (109 single sessions, 7 patients had a second session) 12 patients had residual tumour detected on the first postoperative scan. In 4 patients, the residual disease was detected at the second scan after 3 to 12 months. Tumours in the medial half of the kidney had marginally worse disease-free survival compared with tumours in the lateral position (p = 0.05) Tumour size was highly significantly associated with achieving tumour-free survival (p<0.001). After a single ablation session, tumour-free survival was achieved in 100% (95/95) of tumours ≤ 3.6 cm versus 47% (14/30) of tumours > 3.7 cm. As a tumour increased 1 cm in size, the likelihood of residual tumour increased 2.19 times (95% CI 1.74 to 2.76). Of the 16 initial treatment failures, 7 were successfully retreated with percutaneous RFA or cryoablation. ***Metastatic disease after treatment*** = 1.9% (2/104) (One patient had prostate and thyroid cancer as well as renal cancer and the source of the lung metastases was undetermined. Pulmonary nodules were present before the RFA treatment. The second patient had residual tumour after RFA and multiple pulmonary nodes were seen on a chest CT scan 11 months later).	**Complications** • Small pneumothorax = 1.9% (2/104) (no treatment required) • Large perirenal haematoma = 1.0% (1/104) (required transfusion) • Apnoea during RFA procedure = 1% (1/104) (the patient was resuscitated with naloxone and later discharged after an uneventful period of observation) • Pneumonia 3 days after RFA = 1% (1/104) (treated with antibiotics) • Severe neuropathic pain a few days after RFA = 1% (1/104) (spontaneously resolved 3 months after RFA procedure) **Long-term complications (> 30 days after RFA)** • Ureteral strictures with concomitant hydronephrosis = 1.9% (2/104) (both patients declined any further intervention)	This study is included in the meta-analysis above[1]. **Follow-up issues**: • One patient (1%) was described as being lost to follow-up. **Study design issues**: • Retrospective study. • The effects of location, type and size of tumours on disease-free survival time were assessed by Cox regression analysis.

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
Levinson AW (2008)[9] **Case series** USA Recruitment period: 2000–2003 Study population: patients with solitary small renal masses **n = 31 patients; 31 tumours** Mean age: 71.7 years (range 47–91) Sex: 77% (24/31) male Mean tumour size: 2.1 cm (range 1.0–4.0) Patient selection criteria: Only renal masses less than 4 cm in size were eligible for RFA. 18 patients with a documented familial syndrome that predisposed them to renal masses, or known metachronous, synchronous or metastatic lesions were excluded from the study. None of the included patients were considered to be a good surgical candidate secondary to medical comorbidities or advanced age.CT guided biopsy of the tumour was done Immediately before RFA. Technique: 85% of RFA procedures were performed under conscious sedation. CT guidance was used. The RITA medical systems electrode was used. Mean follow-up: 61.6 months (range 41–80) Conflict of interest/source of funding: not reported	Number of patients analysed: **31; 31 tumours** Persistent enhancement on initial follow-up imaging was considered incomplete treatment (primary treatment failure). All such patients underwent biopsy and were offered repeat RFA. Enhancement or enlargement on subsequent imaging after an initial negative imaging study was considered tumour recurrence. ***Primary treatment failure*** = 3.2% (1/31) (patient was retreated with RFA and was disease-free after 76 months of follow-up) ***Tumour recurrence*** = 9.7% (3/31) (discovered at 7, 13 and 31 months after RFA respectively; managed by repeat RFA, cryoablation and laparoscopic radical nephrectomy, respectively) No patients had metastasis or died of disease during follow-up. 29% (9/31) of patients died during follow-up from causes other than renal cell carcinoma. Mean serum creatinine increased from 1.05 mg/dl at baseline to 1.19 mg/dl at last follow-up (p = 0.06). Actuarial disease specific survival at 80 months = 100% Actuarial metastasis-free survival at 80 months = 100% Actuarial recurrence-free survival at 80 months = 89.2% Actuarial overall survival at 80 months = 62.7% **Patients with pathologically confirmed renal cell carcinoma (n = 18)** Actuarial disease specific survival at 57 months = 100% Actuarial metastasis-free survival at 57 months = 100% Actuarial recurrence-free survival at 57 months = 79.9% Actuarial overall survival at 57 months = 58.3%	**Complications (34 treatment sessions)** • Premature termination of treatment because of pain = 8.8% (3/34) (patients were offered repeat ablation under general anaesthesia) • Aspiration pneumonia 3 days after RFA procedure = 2.9% (1/34) (patient with known severe pulmonary compromise died at home) • Asymptomatic perirenal haematoma = 11.8% (4/34) (managed conservatively with no sequelae) • Pain from iatrogenic liver burn on day 5 (required readmission) = 2.9% (1/34) • Over-sedation requiring reversal with naloxone = 2.9% (1/34)	Data from the same study centre is included in the meta-analysis above[1]. **Follow-up issues**: • No losses to follow-up were described. **Study design issues**: • Routine post-RFA biopsy was not performed. **Study population issues:** • Only 18 patients had pathologically confirmed RCC. The authors note that two patients who had original negative biopsies were later confirmed to have had RCC. **Other issues:** • The authors note that the increase in serum creatinine levels is likely to be within the realm of normal renal function deterioration during years in a cohort with multiple comorbidities, including advanced age, diabetes, hypertension and coronary artery disease.

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Chen SH (2007)[10] **Case report** USA Recruitment period: not stated Study population: patient with biopsy confirmed RCC **n = 1** Age = 48 years Sex = male Tumour size = 2.9 cm Technique: Starburst Xli probe (Rita Medical) used under combined ultrasound and CT guidance. **Follow-up: 12 months** Conflict of interest/source of funding: not reported	**Ureteropelvic junction obstruction resulting in nephrectomy** Comorbidities included chronic renal insufficiency (baseline creatinine 1.6 mg/dl), multivessel coronary artery disease, and previous laparotomies for a gunshot wound and thoracic aortic aneurysm repair. Approximately 2 months after RFA, the patient complained of intermittent left flank pain. A large urinoma was found and percutaneously drained. Retrograde pyelography showed complete stenosis of the left ureter at the level of the ureteropelvic junction. The patient underwent left nephrectomy. Histopathologic analysis showed viable high-grade RCC amid extensive tissue necrosis. The lumen of the proximal ureter was obliterated. During the next 12 months, the patient demonstrated stable renal function and no radiological evidence of residual tumour or metastatic disease.		
Roach H (2006)[11] **Case report** UK Recruitment period: not stated Study population: patient with solitary RCC **n = 1** Age = 78 years Sex = female Tumour size = 2.5 cm Technique: Conscious sedation and ultrasound guidance was used. Follow-up: not reported Conflict of interest/source of funding: not reported	**Life-threatening delayed haematuria requiring transcatheter embolisation** Comorbidities included diabetes mellitus, acromegaly, prosthetic mitral valve requiring full anticoagulation, previous subarachnoid haemorrhage, ischaemic heart disease and osteoarthritis. Macroscopic haematuria was noted immediately after the procedure. Approximately 42 hours after RFA, the patient became profoundly hypotensive and tachycardic and experienced torrential haematuria. After transfusion, CT showed a vessel actively bleeding into the collecting system of the right kidney. Transcatheter embolisation was performed and the patient made a satisfactory recovery. The authors noted that the tumour had a central component.		

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation

Study details	Key efficacy findings	Key safety findings	Comments
De Arruda HO (2006)[12] **Case report** Brazil Recruitment period: not stated Study population: patient with anterior renal mass suggestive of RCC **n = 1** Age = 32 years Sex = female Tumour size = 2.5 cm Technique: Conscious sedation and ultrasound guidance was used. Starburst XL (RITA Medical Systems) probe was used. Follow-up: 6 months Conflict of interest/source of funding: not reported	**Renoduodenal fistula** The procedure was without incident but 3 different cutaneous punctures were needed before starting RFA. The patient was readmitted after 5 days with nausea, vomiting and abdominal discomfort. CT with double contrasts showed a fistula between the pelvis and the duodenum. A cystoscopy and gastroduodenoscopy were performed. Enteral feeding was necessary for 21 days. The pelvic urinary fistula remained for 3 months and then the ureteral catheter was removed. At 6 months, CT showed that the tumour was growing again and an open nephrectomy was performed. Pathology confirmed a clear cell carcinoma.		
Bhayani SB (2005)[13] **Case report** USA Recruitment period: not stated Study population: patients with renal tumours **n = 3** Age = one patient was 80 years old, the ages of the other two were not stated Sex = one male, two not reported Tumour size = one was 2.2 cm, the other two were not described Technique: not described Follow-up: 8 months Conflict of interest/source of funding: not reported	**Neuromuscular complications** Case 1: 80-year old man underwent percutaneous RFA for 2.2 cm renal tumour. Immediately after procedure, he developed laxity of the flank musculature. A CT scan showed slight laxity of the transverse abdominis and oblique muscles as they insert at the iliac crest, which progressively became more pronounced on subsequent imaging. The abnormality remained at 8 months of follow-up. Two additional patients experienced transient flank paraesthesia and sensory deficit on the lateral abdominal wall that started with 24 hours of the procedure. In both cases, the symptoms at resolved at 3 months of follow-up.		**Study population issues:** • These 3 patients were identified from a series of 48 patients who underwent percutaneous RFA.

Abbreviations used: CI, confidence interval; CT, computed tomography; HRQoL, health-related quality of life; MRI, magnetic resonance imaging; QoL, quality of life; RCC, renal cell carcinoma; RFA, radiofrequency ablation			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Schneider J (2010)[14] **Case report** USA Recruitment period: not stated Study population: patients with renal cell carcinoma **n = 2** Age (years) = 62 and 71 Sex = male Technique: not described Follow-up: 8 months and 11 months Conflict of interest/source of funding: not reported	**Chyluria (resulting from an abnormal connection between the lymphatic and urinary collecting system)** Case 1: 62-year-old man underwent percutaneous RFA for renal mass confirmed cytologically as renal cell carcinoma. Eight months later, new fat-fluid levels were seen within a haemorrhagic renal cyst and within the urinary bladder, consistent with chyluria. The patient had no urinary complaints and was treated conservatively. Case 2: 71-year-old man underwent RFA (method of approach not stated) for cytologically confirmed clear cell renal cell carcinoma. CT scan performed 11 months later showed a new fat-fluid level in the bladder indicating chyluria that was not present on preablation CT scans. The patient remained asymptomatic and was treated conservatively.		

Efficacy

Residual or recurrent tumour

A meta-analysis of 47 studies (non-randomised comparative studies and case series) including 1375 tumours with a mean follow-up of 19 months, reported local tumour progression in 13% (100/775) of tumours in the radiofrequency ablation (RFA) group (predominantly using a percutaneous approach) and 5% (31/600) of tumours in the cryoablation group (predominantly using a surgical approach) ($p < 0.001$). Progression to metastatic disease was described in 2% (19/775) of tumours in the RFA group and 1% (6/600) of tumours in the cryotherapy group ($p = 0.06$)[1].

In a non-randomised comparative study of 233 patients, 11% (9/81) of tumours in the percutaneous RFA group and 2% (3/179) of tumours in the laparoscopic cryotherapy group were judged to have residual or recurrent tumour on follow-up MRI scans[2]. Another non-randomised comparative study reported radiographic success of 85% (62/73) for percutaneous RFA and 90% (125/139) for laparoscopic cryoablation at 6 months. Negative biopsies were reported for 65% (24/37) of tumours in the RFA group and 94% (91/97) of tumours in the cryotherapy group[3]. The study reported that there was a poor correlation between radiographic imaging and pathological analysis.

Three case series of 15, 104 and 97patients reported that 79% (83/105), 87% (109/125) and 97% (158/163) of tumours respectively were completely ablated at the first session of percutaneous RFA, as evidenced by contrast-enhanced CT or MRI scans[5,6,8]. Two other case series reported primary treatment failure in 3% (1/31) and 8% (7/85) of patients respectively[7,9].

In 1 case series, local recurrence was reported in 3% (5/151) of patients after a median follow-up of 18 months[5]. A second case series reported local recurrence in 10% (3/31) of patients at 7, 13 and 31 months, respectively, after RFA[9]. In a third case series of 85 patients, 1 patient had a local recurrence diagnosed by contrast-enhanced CT scan 14 months after RFA[7].

Survival

In a non-randomised comparative study of 233 patients, cancer-specific survival was 100% in the percutaneous RFA group with a median follow-up of 1 year and 98% in the laparoscopic cryotherapy group with a median follow-up of 3 years[2].

In a case series of 151 patients, 3-year recurrence-free survival probability was 92% for all patients and 87% for those 84 patients with confirmed renal cell carcinoma[5]. In a case series of 31 patients, disease-specific survival at 80 months was 100%, recurrence-free survival was 89% and overall survival was 63%[9].

Quality of life

One non-randomised comparative study of 37 patients showed that there was no reduction in quality of life for patients in the percutaneous RFA group at 1 week after the procedure and there was a trend towards improved quality of life in comparison to baseline over the 24-week follow-up period. Patients in the laparoscopic surgery group, however, had a significant reduction in several quality of life scores at 1 week postoperatively[4].

Safety

One case series reported haemorrhage in 6% (5/85) of patients[7].Haematoma was reported as a complication in 3 studies, with rates of 1% (1/104), 6% (5/82) and 12% (4/34) of procedures[8,2,9]. One case report described a case of life-threatening delayed haematuria requiring transcatheter embolisation[11].

Three case series reported ureteric stricture development after 1% (1/120), 1% (1/85) and 2% (2/104) of procedures[6,7,8]. Two case series including a total of 182 patients each reported 1 case of urinoma[6,7]. A case report described a case of ureteropelvic junction obstruction resulting in nephrectomy[10].

In a case series of 97 patients, 1 case of thermal injury to the duodenum that required laparotomy was reported[6].

A case report described a patient with renoduodenal fistula diagnosed 5 days after the RFA procedure[12]. A cystoscopy and gastroduodenoscopy were performed.

Another case report described 3 patients with neuromuscular complications out of a series of 48 patients undergoing RFA treatment[13]. One of these patients developed permanent flank laxity and the other 2 had transient paraesthesia.

Validity and generalisability of the studies

- One of the main limitations of the studies is the use of loss of CT lesion enhancement as a surrogate of successful tumour destruction. One study reported that 6 patients with no enhancement seen on radiographic imaging had a positive biopsy[3].
- Patient characteristics such as tumour location and tumour size varied among the studies. This is important when assessing the generalisability of results. Two studies only included patients with tumours of size 4 cm or smaller and both medially and more peripherally located tumours[2,9]. The authors of one study highlight the variable natural history of small renal masses[1].

- In 1 non-randomised comparative study, the median follow-up was only 1 year for the RFA group, compared with 3 years for the cryotherapy group[2].
- The sample populations were heterogenous in both comparative studies. The authors of 1 of the studies note that there was considerable selection bias between the 2 treatment groups[2,4].
- The technique used for RFA and method of imaging varied between studies.
- Only 4 studies reported that biopsies were routinely performed prior to ablation[2,4,7,8].

Existing assessments of this procedure

The Canadian coordinating office for health technology assessment (CCOHTA) published a report on radiofrequency ablation in the treatment of kidney cancer in February 2006[15]. The report concluded that 'radiofrequency ablation is an option for the treatment of small tumours, and in cases where surgery is contraindicated. Its safety and efficacy compare favourably with those of other approaches. The persistence of residual tumour is a disadvantage of earlier versions of the technology. The use of more powerful radiofrequency generators may reduce such persistence, but definitive evidence is unavailable. Experience with this application of the technology is limited. Longer follow-up of patients is required to provide an adequate comparison with nephrectomy'.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Percutaneous radiofrequency ablation of renal cancer. NICE interventional procedures guidance 91 (2004). Available from www.nice.org.uk/Guidance/IPG91
- Percutaneous radiofrequency ablation for primary and secondary lung cancers. NICE interventional procedures guidance 185 (2006). Available from www.nice.org.uk/Guidance/IPG185
- Radiofrequency ablation of hepatocellular carcinoma. NICE interventional procedures guidance 2 (2003). Available from www.nice.org.uk/Guidance/IPG2

- Radiofrequency ablation for the treatment of colorectal liver metastases. NICE interventional procedures guidance 327 (2009). Available from www.nice.org.uk/Guidance/IPG327
- Cryotherapy for renal cancer. NICE interventional procedures guidance 207 (2007). Available from www.nice.org.uk/Guidance/IPG207
- Laparoscopic nephrectomy (including nephroureterectomy). NICE interventional procedures guidance 136 (2005). Available from www.nice.org.uk/Guidance/IPG136

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr M Aitchison (British Association of Urological Surgeons).

Professor A Adam, Dr D Breen, Dr U Patel (Royal College of Radiologists).

- Three Specialist Advisers consider the procedure to be established practice and 1 considers it to be novel and of uncertain safety and efficacy.
- Theoretical adverse events include haemorrhage, ureteric stricture, bowel perforation, perirenal haematoma, pelvicalyceal injury, pain due to intercostal nerve damage and haematuria.
- The key efficacy outcomes are radiologic confirmation of tumour devascularisation, imaging follow-up to confirm tumour involution at 2 and through 5 years, and overall and disease-free survival.
- There is some concern about the possibility of inadequate tumour destruction.
- One Specialist Adviser noted that there is uncertainty about efficacy in tumours 4 cm or greater in diameter.
- Training and experience in interventional radiology is necessary.
- One Specialist Adviser noted that there is currently no accepted standard way to assess the success of RFA.

- One adviser commented that the procedure was only suitable for highly selected patients and that a uro-oncology multidisciplinary team should be involved with patient selection.
- Two advisers thought that the procedure would have a minor impact on the NHS, one thought it would have a moderate impact and one thought that the potential impact was major.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme were unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- The indication in the title is renal cancer but some of the studies included in this overview did not routinely biopsy the tumour prior to ablation.
- There are several different ablation systems and techniques. Some radiofrequency generators are more powerful than others.

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6. Breen DJ, Rutherford EE, Stedman B et al. (2007) Management of renal tumors by image-guided radiofrequency ablation: experience in 105 tumors. Cardiovascular & Interventional Radiology 30: 936–42.

7. Gervais DA, McGovern FJ, Arellano RS et al. (2005) Radiofrequency ablation of renal cell carcinoma: part 1, Indications, results, and role in patient management over a 6-year period and ablation of 100 tumors. American Journal of Roentgenology 185: 64–71.

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14. Schneider J, Zaid UB, Breyer BN et al. (2010) Chyluria associated with radiofrequency ablation of renal cell carcinoma. Journal of Computer Assisted Tomography 34: 210–2.

15. Hailey D. (2006) Radiofrequency ablation in the treatment of kidney cancer [Issues in emerging health technologies issue 80]. Ottawa: Canadian Coordinating Office for Health Technology Assessment.

Appendix A: Additional papers on percutaneous radiofrequency ablation of renal cancer

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Ahrar K, Matin S, Wood CG et al. (2005) Percutaneous radiofrequency ablation of renal tumors: technique, complications, and outcomes. Journal of Vascular & Interventional Radiology 16: 679–88.	Case series. 29 patients.	4 major complications (3 gross haematuria and urinary obstruction, 1 persistent anterior abdominal wall weakness). Complete ablation = 96%	Small case series.
Arima K, Yamakado K, Kinbara H et al. (2007) Percutaneous radiofrequency ablation with transarterial embolization is useful for treatment of stage 1 renal cell carcinoma with surgical risk: Results at 2-year mean follow up. International Journal of Urology 14: 585–90.	Case series. 31 patients. Mean follow-up = 2 years	Tumour enhancement was eliminated after two RFA sessions in all tumours. Recurrence rate of RCC after successful RFA was 2.8%.	Small case series.
Arzola J, Baughman SM, Hernandez J et al. (2006) Computed tomography-guided, resistance-based, percutaneous radiofrequency ablation of renal malignancies under conscious sedation at two years of follow-up. Urology 68: 983–7.	Case series. 23 patients. Mean follow-up = 2 years	16 (80%) had successful ablation with a single treatment, 4 had initial failure, and 3 were lost to follow-up. Overall cancer-free survival rate = 90% (18/20) at a mean follow-up of 24 months.	Small case series.
Bandi G, Hedican S, Moon T, et al. (2008) Comparison of postoperative pain, convalescence, and patient satisfaction between laparoscopic and percutaneous ablation of small renal masses. Journal of Endourology 22: 963–7.	Non-randomised comparative study 93 patients (percutaneous RFA = 15)	Compared with laparoscopic cryoablation, percutaneous RFA was associated with earlier return to non-strenuous activity, strenuous activity and work.	Small number of patients in percutaneous RFA group.
Carey RI, Leveillee RJ. (2007) First prize: direct real-time temperature monitoring for laparoscopic and CT-guided radiofrequency ablation of renal tumors between 3 and 5 cm. Journal of Endourology 21: 807–13.	Case series. 37 patients. Mean follow-up = 11 months	100% (37/37) patients achieved complete necrosis at the initial session. There were two radiographic failures at 9 months and 30 months that required a second treatment (95% radiographic success rate).	Laparoscopic and CT-guided RFA were reported together.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Clark TW, Malkowicz B, Stavropoulos SW et al. (2006) Radiofrequency ablation of small renal cell carcinomas using multitined expandable electrodes: preliminary experience. Journal of Vascular & Interventional Radiology 17: 513–9.	Case series. 22 patients. Mean follow-up = 11 months	Technical success in targeting and ablation was 100%. Recurrence = 4.5% (1/22)	Small case series.
del Cura JL, Zabala R, Iriarte JI et al. (2010) Treatment of renal tumors by percutaneous ultrasound-guided radiofrequency ablation using a multitined electrode: effectiveness and complications. European Urology 57: 459-465.	Case series n = 58 (65 tumours) Mean follow-up = 26.5 months	Therapeutic success = 91% (59/65) Complications = 13% of procedures (5% major)	Small case series
Doody O, Given MF, Harper M, et al. (2008) Rendezvous technique following thermal ureteric injury after radiofrequency ablation in a solitary kidney. Journal of Vascular and Interventional Radiology 19: 1112–4.	Case report. 1 patient	Ureteric stricture secondary to thermal injury after RFA.	Case report of a complication already mentioned in table 2.
Fotiadis NI, Sabharwal T, Morales JP et al. (2007) Combined percutaneous radiofrequency ablation and ethanol injection of renal tumours: midterm results. European Urology 52: 777–84.	Case series. 27 patients. Mean follow-up = 19 months	96% (27/28) tumours were completely ablated with either one (21 tumours) or two treatment sessions (6 tumours). No local recurrence or metastases.	Small case series.
Ganguli S, Brennan DD, Faintuch S et al. (2008) Immediate renal tumor involution after radiofrequency thermal ablation. Journal of Vascular & Interventional Radiology 19 (3) 412–8.	Case series. 66 patients. Follow-up = 1month.	Renal tumours decrease in size immediately after treatment with RF thermal ablation.	Small case series with short follow-up.
Gervais DA, Arellano RS, McGovern FJ, et al. (2005) Radiofrequency ablation of renal cell carcinoma: part 2, lessons learned with ablation of 100 tumors. American Journal of Roentgenology 185: 72–80.	Case series. 85 patients.	Clinically significant urine leak = 1% (1/100) There were no bowel complications.	Patient outcomes from the same study cohort are included in table 2.
Gervais DA, McGovern FJ, Arellano RS et al. (2003). Renal cell carcinoma: clinical experience and technical success with radio-frequency ablation of 42 tumors. Radiology 226: 417–24.	Case series. 34 patients Mean follow-up = 13.2 months	Complete ablation = 86% (36/42) tumours 3 haematomas, 1 urethral stricture	Small case series (included in table 2 of overview for original guidance)
Hiraoka K, Kawauchi A, Nakamura T et al. (2009) Radiofrequency ablation for renal tumors: Our experience: Original Article. International Journal of Urology 16: 869-873.	Case series n= 40 Median follow-up = 16 months	Complete response = 85% (34/40) 1 recurrence Complications = 4% (3/77) of procedures	Small case series

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Johnson DB, Solomon SB, Su L et al. (2004) Defining the complications of cryoablation and radio frequency ablation of small renal tumors: a multi-institutional review. Journal of Urology 172: 874–7.	Case series. 271 patients. (including all percutaneous and laparoscopic ablative treatments)	11% (30/271) complications occurred (5 major and 25 minor), and 1 death (0.4%). Overall 87% (26/30) of the complications were directly attributable to the ablation procedure. The most common complication was pain or paraesthesia at the probe insertion site.	Article reported complications for all kinds of ablation together (percutaneous and laparoscopic cryotherapy and radiofrequency ablation).
Kunkle DA, Egleston BL, Uzzo RG. (2008) Excise, ablate or observe: the small renal mass dilemma – a meta-analysis and review. Journal of Urology 1227–33.	Meta-analysis. 6471 renal masses (including 5037 treated by partial nephrectomy)	Relative risk of local recurrence: • Partial nephrectomy = 1.00 • Cryoablation = 7.45 • RFA = 18.23 Relative risk of metastatic progression: • Partial nephrectomy = 1.00 • Cryoablation = 1.24 • RFA = 3.21 • Active surveillance = 0.11	A meta-analysis by the same author is included1.
Kutikov A, Kunkle DA, Uzzo RG. (2009) Focal therapy for kidney cancer: a systematic review. Current Opinion in Urology 19: 148–53.	Systematic review. Primary analysis of 82 patients delayed for 6 months or more before treatment.	Given the excellent results reported for active surveillance of small renal masses in selected patients, the extent to which focal ablation alters the natural history has not yet been established. Only 4% (3/82) of patients with an enhancing renal mass ≤ 4 cm were upstaged at resection after a 6-month treatment delay.	Study summarises results from other meta-analyses.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Long L, Park S. (2009) Differences in patterns of care: reablation and nephrectomy rates after needle ablative therapy for renal masses stratified by medical specialty. Journal of Endourology 23: 421–6.	Systematic review. 620 patients Mean follow-up = 20 months	24 studies were included. Reablation rates: • RFA = 7.4% • Cryoablation = 0.9% ($p < 0.05$) Salvage nephrectomy: • RFA = 1.1% • Cryoablation = 2.4% (p = ns) Cancer specific success = 95%	A meta-analysis with a later search date is included1.
Lucas SM, Stern JM, Adibi M, et al. (2008) Renal function outcomes in patients treated for renal masses smaller than 4 cm by ablative and extirpative techniques. Journal of Urology 179: 75–80.	Non-randomised comparative study. 86 patients (RFA) Median follow-up = 22 months	Nephron sparing surgery preserves renal function in comparison to radical nephrectomy.	Laparoscopic and CT-guided RFA were reported together.
Matsumoto ED, Watumull L, Johnson DB et al. (2004) The radiographic evolution of radio frequency ablated renal tumors. Journal of Urology 172: 45–8.	Case series. 64 tumours. Median follow-up = 14 months.	97% (62/64) RFA lesions demonstrated an absence of contrast enhancement on CT scan.	Laparoscopic, percutaneous and open RFA reported together.
Matin SF, Ahrar K, Cadeddu JA, et al. (2006) Residual and recurrent disease following renal energy ablative therapy: a multi-institutional study. Journal of Urology 176: 1973–7.	Case series 63 patients	Residual or recurrent disease occurred in 16% (53/340) of patients undergoing percutaneous RFA. The majority of cases were detected with 12 months of treatment.	The study focuses on patients with recurrent or residual disease after treatment.
Mayo-Smith WW, Dupuy DE, Parikh PM et al (2003). Imaging-guided percutaneous radiofrequency ablation of solid renal masses: techniques and outcomes of 38 treatment sessions in 32 consecutive patients. AJR180:1503–8.	Case series 32 patients Mean follow up = 9 months	26/32 tumours (81%) showed no evidence of recurrence at follow-up after one treatment session. 2 patients had transient hypertension 2 patients had haematomas	Small case series (included in table 2 of overview for original guidance)

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Pavlovich CP, Walther MM, Choyke PL et al. (2002) Percutaneous radio frequency ablation of small renal tumors: initial results. Journal of Urology 167:10–5.	Case series 21 patients Follow up =2 months	19/24 tumours (79%) showed no signs of recurrence at 2 month follow-up. 5 cases optimal temperature was not reached. 4 patients experienced pain and numbness, 1 haematoma.	Small case series (included in table 2 of overview for original guidance)
Prevoo W, van den Munckhof MP, Meinhardt W et al. (2010) Radiofrequency ablation of kidney tumours in patients with a solitary kidney. Clinical Radiology 65: 230-236.	Case series n = 13 Mean follow-up = 9 months	Technical success = 75% at 1 month Complete response after follow-up = 69% (11/16) tumours.	Small case series
Salagierski M, Salagierski MS, Salagierska-Barwinska A. (2010) Radiofrequency ablation in kidney tumour management: a method of real-time monitoring. Scandinavian Journal of Urology & Nephrology 44: 84-90.	Case series n = 42 Mean follow-up = 24 months	90% (38/42) successful treatments 2 major and 2 minor complications	Small case series
Schirmang TC, Mayo-Smith WW, Dupuy DE et al. (2009) Kidney neoplasms: renal halo sign after percutaneous radiofrequency ablation–incidence and clinical importance in 101 consecutive patients. Radiology 253: 263-269.	Case series n = 101 patients Mean follow-up = 25 months	Renal halo sign developed in 75% (79/106) of ablated tumours.	Focuses on incidence of renal halo sign.
Stern JM, Svatek R, Park S, et al. (2007) Intermediate comparison of partial nephrectomy and radiofrequency ablation for clinical T1a renal tumours. BJU International 100: 287–90.	Non-randomised comparative study 77 patients (40 RFA) Mean follow-up = 30 months	Actuarial disease-free probability: • Partial nephrectomy = 95.8% • RFA = 93.4% (p = 0.67)	RFA included percutaneous and laparoscopic.
Stern JM, Gupta A, Raman JD, et al. (2009) Radiofrequency ablation of small renal cortical tumours in healthy adults: renal function preservation and intermediate oncological outcome. BJU International 104: 786–9.	Case series 63 patients Median follow-up = 34 months	Renal preservation rate = 97%	Small case series.
Su L, Jarrett TW, Chan DY et al. (2003) Percutaneous computed tomography-guided radiofrequency ablation of renal masses in high surgical risk patients: preliminary results. Urology 61: 26–33.	Case series 29 patients Mean follow up = 9 months	33/35 (94%) renal lesions required only a single treatment session. 2 patients had disease recurrence. 8 haematomas, 1 abdominal pain (burn)	Small case series (included in table 2 of overview for original guidance)

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Turna B, Kaouk JH, Frota R et al. (2009) Minimally invasive nephron sparing management for renal tumors in solitary kidneys. Journal of Urology 182: 2150-2157.	Non randomised comparative study n = 101 Follow-up = 2 years	Overall survival: • Laparoscopic partial nephrectomy = 91% • Cryoablation = 89% • RFA = 84% Disease-free survival: • Laparoscopic partial nephrectomy = 100% • Cryoablation = 70% • RFA = 33% p < 0.0001	Larger non-randomised comparative studies are included.
Varkarakis IM, Allaf ME, Inagaki T et al.(2005) Percutaneous radio frequency ablation of renal masses: Results at a 2-year mean followup. Journal of Urology 174: 456–60.	Case series. 46 patients. Mean follow-up = 28 months	Local recurrence = 6.5% (3/46) Larger (greater than 3.0 cm) central tumours represent unique technical challenges, making these tumours more prone to recurrence.	Small case series.
Veltri A, Garetto I, Pagano E, et al. (2009) Percutaneous RF thermal ablation of renal tumours: is US guidance really less favourable than other imaging guidance techniques. Cardiovascular and Interventional Radiology 32: 76–85.	Non-randomised comparative study. 71 patients	Tumour-specific 2-year survival = 92% (ultrasound guidance) and 90 – 96% in CT-guided series. Ultrasound guidance was not less favourable than other guidance techniques.	The study focuses on ultrasound guidance in comparison with other guidance techniques.
Wah TM, Irving HC (2009) Acute tubular necrosis following radiofrequency ablation of a renal cell carcinoma. Cardiovascular & Interventional Radiology 32: 591–2.	Case report n = 1	Acute tubular necrosis in a solitary kidney after RFA.	Case report.
Wingo MS, Leveillee RJ (2008) Central and deep tumours can be effectively ablated: radiofrequency ablation outcomes with fiberoptic peripheral temperature monitoring. Journal of Endourology 22: 126 –7.	Case series 131 patients	Enhanced RFA with peripheral temperature monitoring resulted in an improved single treatment success rate and boosted operator confidence in the management of endophytic, central, or hilar renal tumours.	Laparoscopic and percutaneous RFA reported together.

Appendix B: Related NICE guidance for percutaneous radiofrequency ablation of renal cancer

Guidance	Recommendations
Interventional procedures	***Current guidance for review:*** **Percutaneous radiofrequency ablation of renal cancer. NICE interventional procedures guidance 91 (2004).** 1.1 Limited evidence suggests that percutaneous radiofrequency ablation (RFA) of renal cancer brings about reduction of tumour bulk and that the procedure is adequately safe. However, the evidence of its effect on symptom control and survival is not yet adequate to support the use of this procedure without special arrangements for consent and for audit or research. 1.2 Patient selection is important and the procedure should normally be limited to patients who are unsuitable for surgery. The procedure should only be offered after assessment by a specialist multidisciplinary team, which should include a urologist and an interventional radiologist. 1.3 Clinicians wishing to undertake percutaneous radiofrequency ablation of renal cancer should take the following actions. • Ensure that patients offered it understand the uncertainty about the procedure's efficacy and provide them with clear written information. Use of the Institute's *Information for the Public* is recommended. • Audit and review clinical outcomes of all patients having radiofrequency ablation of renal cancer. 1.4 Controlled research into the long-term clinical outcomes will be useful in reducing the current uncertainty. The Institute may review the procedure upon publication of further evidence. **Percutaneous radiofrequency ablation**

	for primary and secondary lung cancers. NICE interventional procedures guidance 185 (2006) 1.1 Current evidence on the safety and efficacy of percutaneous radiofrequency ablation for primary and secondary lung cancers shows that there are no major safety concerns with this procedure. There is evidence that the treatment can reduce tumour bulk; however, this evidence is limited and is based on heterogeneous indications for treatment. The procedure should therefore be used only with special arrangements for consent, audit and clinical governance. 1.2 Clinicians wishing to undertake percutaneous radiofrequency ablation for primary and secondary lung cancers should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, use of the Institute's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG185publicinfo). • Audit and review clinical outcomes of all patients undergoing percutaneous radiofrequency ablation for primary and secondary lung cancers. 1.3 Patient selection should be carried out in the context of a multidisciplinary team, usually including a thoracic surgeon, an oncologist and a radiologist. This procedure should be used in patients for whom surgery is inappropriate or who are unwilling to undergo surgery. 1.4 Further research will be useful in relation to survival and quality-of-life outcomes, and in establishing the potential role of this procedure as either curative or palliative treatment. **Radiofrequency ablation of**

	hepatocellular carcinoma. NICE interventional procedures guidance 2 (2003) 1.1 Current evidence of the safety and efficacy of radiofrequency ablation (RFA) for hepatocellular carcinoma appears adequate to support use of the procedure, provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 It is recommended that: • patient selection should be carried out by a multidisciplinary team that includes a hepatobiliary surgeon • the procedure should be monitored by CT or ultrasound. **Radiofrequency ablation for the treatment of colorectal liver metastases. NICE interventional procedures guidance 327 (2009)** 1.1 Current evidence on the safety and efficacy of radiofrequency (RF) ablation for colorectal liver metastases is adequate to support the use of this procedure in patients unfit or otherwise unsuitable for hepatic resection, or in those who have previously had hepatic resection, provided that normal arrangements are in place for clinical governance, consent and audit. 1.2 Patient selection should be carried out by a hepatobiliary cancer multidisciplinary team. **Cryotherapy for renal cancers. NICE interventional procedures guidance 207 (2007)** 1.1 Current evidence suggests that cryotherapy for renal cancer ablates tumour tissue and that its safety is adequate. However, the evidence about its effect on long-term local control and survival is not yet adequate to support the use of this procedure without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake cryotherapy for renal cancer should ensure

	that patients understand the uncertainties about its effect on quality of life and long-term survival, and provide them with clear written information. Use of the Institute's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG207publicinfo). 1.3 The procedure should only be offered after assessment by a specialist multidisciplinary team, which should include a urologist, an oncologist and an interventional radiologist. 1.4 Controlled studies into the long-term clinical outcomes will be useful. Clinicians are encouraged to collect long-term data and should enter all patients with renal cancer treated with cryotherapy into the British Association of Urological Surgeons Cancer Registry (www.baus.org.uk). The Institute may review the procedure upon publication of further evidence. **Laparoscopic nephrectomy (including nephroureterectomy). NICE interventional procedures guidance 136 (2005)** 1.1 Current evidence on the safety and efficacy of laparoscopic nephrectomy (including nephroureterectomy) appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Patient selection is important when this procedure is being considered for the treatment of malignant disease. Long-term follow-up data are lacking, and clinicians are encouraged to collect data on rates of recurrence in patients with malignant disease.

Appendix C: Literature search for percutaneous radiofrequency ablation of renal cancer

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	09/09/09	Issue 3, 2009	0
Database of Abstracts of Reviews of Effects – DARE (CRD website)	09/09/09	N/A	0
HTA database (CRD website)	09/09/09	N/A	0
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	09/09/09	Issue 3, 2009	0
MEDLINE (Ovid)	09/09/09	1950 to August Week 4 2009	37
MEDLINE In-Process (Ovid)	09/09/09	September 08, 2009	27
EMBASE (Ovid)	09/09/09	1980 to 2009 Week 36	77
CINAHL (NLH Search 2.0 or EBSCOhost)	09/09/09	N/A	0
BLIC (Dialog DataStar)	09/09/09	N/A	0

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Catheter Ablation/
2	(Radiofrequency* or Radio-frequency* or Radio frequency*).tw.
3	1 and 2
4	((Radiofrequency* or Radio-frequency* or Radio frequency*) adj3 Ablation*).tw.
5	RFA.tw.
6	or/3-5
7	Carcinoma, Renal Cell/
8	Kidney Neoplasms/
9	(Renal* adj3 (Neoplasm* or Cancer* or Carcinoma* or Adenocarcinom* or Tumour* or Tumor* or Malignan* or Lump* or Masses* or Sarcoma* or Metastasis*)).tw.

10	(Kidney* adj3 (Neoplasm* or Cancer* or Carcinoma* or Adenocarcinom* or Tumour* or Tumor* or Malignan* or Lump* or Masses*or Sarcoma* or Metastasis*)).tw.
11	or/7-10
12	6 and 11
13	Cool-Tip RF.tw.
14	Boston scientific RF.tw.
15	RITA RF.tw.
16	or/12-15
17	Animals/
18	Humans/
19	17 not (17 and 18)
20	16 not 19
21	limit 20 to ed=20090101-20090804