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Technical Report

Radiofrequency ablation of kidney tumours in patients with a solitary kidney

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Introduction

Renal cell carcinoma (RCC) is a relatively rare tumour accounting for 3% of malignancies in adults.[1] The widespread dissemination of high-quality imaging has led to increasing detection of small, early-stage RCCs in asymptomatic patients.[2–4] For many decades total nephrectomy has been the reference standard treatment, with a 5-year survival rate of 88%.[1,5,6] Partial nephrectomy is considered to be equivalent for small, low-stage RCCs ($T_1 < 4$ cm), indicating that renal-sparing procedures can be curative in selected patients.[1,7,8]

Some patients are not ideal candidates for invasive surgical resection because of serious comorbidities.[5] These patients can be offered renal-sparing minimally invasive image-guided radiofrequency ablation (RFA).[9] In RFA, a high-frequency alternating current is emitted through a probe placed centrally within the target tissue.[10] Deposition of radiofrequency energy results in frictional heating of electrons in cells surrounding the tip of the probe causing protein denaturation and cell death.[10]

Since 1997, RFA has been used to treat renal tumours in non-surgical candidates, i.e., patients with serious comorbidities or marginal renal function.[11,12] The reported efficacy of RFA for treatment of renal tumours defined as no residual enhancement during follow-up computed tomography (CT) or magnetic resonance imaging (MRI), ranges from 79 to 100%.[13–17] The size and location of the tumour within the kidney are important outcome predictors with the highest chance of survival provided by total ablation of lesions <4 cm located peripherally in the kidney.

A special group of patients with RCC consists of patients with a congenital or acquired solitary kidney. These patients cannot undergo radical nephrectomy without subsequent need for dialysis or transplantation. Partial nephrectomy is sometimes performed depending on tumour location, but usually leads to diminution of functional nephrons as renal artery clamping is often necessary..[5] RFA offers a minimally invasive treatment alternative. Studies focusing on local tumour control and impact on renal function of RFA in patients with a solitary kidney are limited.[18]

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The purpose of this study is to report our clinical experience with percutaneous image-guided RFA of RCC in patients with a solitary kidney. Furthermore the efficacy of this novel technology in terms of total tumour ablation and survival will be evaluated.

Materials and methods

Patients

From September 2005 to September 2008, 13 patients with a mean age of 67 years (range 47–80 years) with tumours in a solitary kidney underwent percutaneous CT-guided RFA at our Institution. The majority of patients ($n = 12$) had a history of contralateral nephrectomy because of RCC. One patient had a congenital solitary kidney. Patients were offered RFA because of advanced age, significant medical comorbidity, advanced symptomatic disease, or refusal of conventional therapy. Patients were treated with curative intent. Patients were evaluated by a multidisciplinary team consisting of a radiologist, a urologist, and an oncologist to determine each patient's suitability for RFA and to ensure that all surgical alternatives had been considered. Informed consent was obtained from all patients. Procedures were performed in a routine clinical care setting and, therefore, Medical Ethics Committee approval was not required.

Ten patients had one tumour, and three patients were diagnosed with two kidney tumours, resulting in a total of 16 tumours. The mean tumour diameter was 3.9 cm (range 2.4–6.3 cm). Tumours were classified into three groups: exophytic (>50% of tumour volume outside the renal capsule), intraparenchymal (<50% of tumour volume outside the renal capsule) or central (tumour extended into the renal pelvis). Six kidney tumours were classified as exophytic (38%) and 10 classified as intraparenchymal (62%). There were no central tumours.

Renal masses had a presumptive diagnosis of malignancy based on imaging (CT or MRI). Out of 16 tumours, five had additional pathological confirmation of the diagnosis from imaging-guided biopsy. The results from the biopsies were RCC in four cases and metastasis of an adenocarcinoma in one case. Baseline characteristics are listed in Table 1.

Pre-procedural assessment consisted of dedicated contrast-enhanced CT for tumour evaluation, physical examination, and preoperative screening by an anaesthesiologist and laboratory screening.

RFA

During RFA, an alternating current that oscillates in the range of high frequency (200–1200 kHz) passes down from the electrode tip into the surrounding tissue causing ionic agitation resulting in frictional heat. At tissue temperatures higher than 55 °C nearly immediate coagulation of tissue is induced with irreversible damage to mitochondrial and cytosolic enzymes of the cells.[19]

The RFA procedure was performed with a Cool-tip ™ RF ablation system (Valleylab, CA, USA) including a 500 kHz RF generator attached to a Cool-tip ™ electrode ($n = 8$), or a RF 3000 system (Radiotherapeutics, CA, USA) connected to a LeVeen monopolar multi-array electrode ($n = 9$). An overview of the equipment and set-up used for percutaneous CT-guided RFA of kidney tumours in our institution is provided in Fig. 1.[20]

A RFA session was defined as one visit to the Radiology Department when a renal mass was treated with RFA, thus a patient could undergo more than one radiofrequency treatment in a single session. RFA was performed as an inpatient procedure in all patients by an experienced interventional radiologist. Patients received prophylactic antibiotics (1500 *mg* cefuroxime *i.v.).* After induction of regional anaesthesia (*thoracic epidural at Th 10/11 or Th 11/12)* patients were placed in the Siemens Somaton Sensation open (wide bore) 24 section CT machine (Erlangen, Germany) gantry in the prone position and tumour localization was performed supported by CT guidance and fluoroscopy. The choice of RFA system and electrode were at the discretion of the primary operator, taking into account tumour size and location. Based on imaging, direction, and

Table 1
Baseline table

Patient	Sex	Age	Cause of solitary kidney	Number of tumours	Tumour size (cm)	Tumour location	Right/Left	Pathological confirmation
1	M	74	RCC	1	3.2	Exophytic	L	–
2a	M	73	RCC	2	5.1	Exophytic	L	–
2b	M	4.1	Exophytic	L	–			
3	V	69	RCC	1	6.2	Intraparenchymal	R	Metastasis of adenocarcinoma
4a	M	78	RCC	2	6.3	Exophytic	L	RCC
4b	M	3.3	Intraparenchymal	L	RCC			
5	M	71	RCC	1	2.6	Exophytic	R	–
6	V	78	RCC	1	2.4	Intraparenchymal	R	–
7	M	80	RCC	1	4.2	Intraparenchymal	R	–
8	M	73	Congenital	1	4.0	Exophytic	R	–
9	V	47	RCC	1	3.0	Intraparenchymal	R	–
10	V	62	RCC	1	2.6	Intraparenchymal	R	RCC
11a	M	52	RCC	2	5.9	Intraparenchymal	R	–
11b	M	5.0	Intraparenchymal	R	–			
12	M	51	RCC	1	2.5	Intraparenchymal	L	RCC
13	M	64	RCC	1	2.5	Intraparenchymal	L	–

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Fig. 1 Overview of the equipment and set-up used for percutaneous CT-guided RFA of kidney tumours.

position of the needle and the number of needles used were determined. All RFA procedures were performed percutaneously. Because each tumour was treated with the intention of providing at least a 0.5 cm tumour-free margin, overlapping compound CT-guided ablations were performed by repositioning the needle to ablate the entire tumour, if required, based on the size and geometry of the lesion. In all cases, the required temperatures and a successful roll-off (signalling the clinical endpoint of treatment) were reached.

Response evaluation

All patients stayed for a minimum of an overnight admission. Patients underwent a follow-up regimen, consisting of laboratory studies and serial renal-protocol contrast-enhanced CT examinations at 1, 3, 6, and 12 months and semi-annually thereafter. In cases of renal function impairment contrast-enhanced MRI was used instead of CT. Imaging was only executed earlier than 1 month after the procedure when required based on clinical assessment. No post-procedural biopsies were performed.

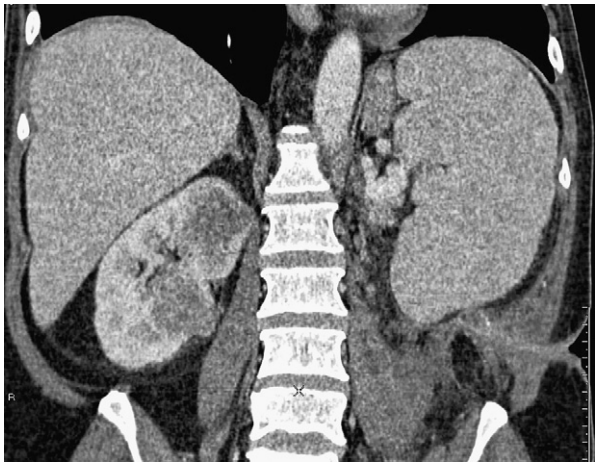

Fig. 2 A 52-year-old man with two tumours before treatment.

Fig. 3 A 52-year-old man with two tumours 1 month after treatment.

Technical success was defined as absence of enhancement in any area of tumour on images from the 1-month follow-up study, residual disease was defined as persistent enhancement in an area or areas of tumour after ablation as determined on the 1-month follow-up study, and recurrent disease was defined as new tumour enhancement after at least one imaging study had demonstrated complete eradication of enhancement (i.e., technical success).[21] Additionally, in this study, any increase in tumour size during follow-up was considered equal to tumour enhancement and treated similarly when evaluating technical success and determining residual disease and recurrent disease. If residual or recurrent disease was detected on imaging after ablation, repeat ablation sessions were scheduled as needed and appropriate. Complete response was defined as the absence of tumour enhancement and absence of increase in size on contrast-enhanced CT after treatment. Examples of CT images before and after RFA are provided in Figs. 2 and 3. Complications occurring during the procedure or in the first month after the procedure were classified as early complications, thereafter they were classified as late complications.

Results

The 16 renal tumours were treated with a total of 17 RFA sessions. During five sessions, two tumours were treated in patients with a double tumour. Patients were available for evaluation at a mean follow-up of 9 months (range 1–25 months). At the 1 month contrast-enhanced CT follow-up examination, 12/16 tumours showed no sign of enhancement indicating a technical success of 75%.

Four tumours (from two patients with a double tumour each) were treated with additional RFA sessions due to residual disease, resulting in successful treatment and complete necrosis in three of these four tumours.

During follow-up, four of the 12 tumours that were initially treated with technical success showed recurrent disease after a mean follow-up period of 6 months (range 3–12 months) and were not treated with additional RFA sessions. Finally, total tumour ablation (i.e., complete response) was obtained in 11/16 (69%) tumours. Results are provided in Table 2.

The average hospital stay was 1.9 days (range 1–4 days). Anuria, elevated creatinine (a rise from 128 pre-procedural

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Table 2
Results

Patient	RFA session	1-Month follow-up (residual disease)	3-Month follow-up (recurrent disease)	Follow-up imaging (months)	Total ablation	Survival
1	1	−	n.a.	6	No	Lost to follow-up
2a	1	+	−[a]	25	No	25
	2	−	+		No	
	3	−	−		Yes	
2b	1	+	−[a]		No	
	2	−	−		Yes	
3	1	−	n.a.	1	Yes	Lost to follow-up[b]
4a	1	+	n.a.	21	No	21
	2	+	n.a.		No	
	3	+	−	2	No	
4b	1	+	n.a.		No	
	2	−	−		Yes	
5	1	−	−	9	No	Died 10 months post-RFA
6	1	−	−	13	Yes	13
7	1	−	−	12	Yes	11
8	1	−	−	7	Yes	7
9	1	−	−	9	Yes	9
10	1	−	−	6	Yes	6
11a	1	−	+	3	No	3
11b	1	−	+		No	
12	1	−	n.a.	1	Yes	1
13	1	−	n.a.	2	Yes	2

[a] Residual disease
[b] Hospital dismissal end 2006, died afterwards

to 308 mmol/l), nausea, and vomiting were reported in one patient as major early complications. Subcapsular haematoma ($n = 2$), urinoma ($n = 1$), and haematuria ($n = 1$) were noticed as minor early complications. Late complications included renal insufficiency ($n = 2$), acute tubular necrosis ($n = 1$), and renal vein thrombosis ($n = 1$). The average increase in serum creatinine 1 and 3 months post-RFA was 14% (mean 149 mmol/L, range 104–232) and 32% (mean 173 mmol/l, range 105–323), respectively, compared to pre-RFA levels (mean 131 mmol/l, range 81–230).

No procedure related deaths were observed. Two patients died during follow-up. One patient died 10 months after RFA because of pulmonary metastases. For the other patient date and cause of death was unknown. One patient was lost to follow-up.

Discussion

An overview of available studies regarding RFA in solitary kidneys is provided in Table 3.[5,12,18,22–24] Compared with the present results these studies mention higher success rates. However, clearly, the population in the present study was a high-risk population who wished to avoid haemodialysis. Besides, in the present study the average tumour size (3.9 cm) was higher than in any of the comparable studies and patients with double tumours were included in the cohort. In several cases multiple RFA sessions were foreseen in advance in order to treat the patients. Two patients with double tumours (5.1 and 4.1 cm, 6.3 and 3.3 cm) underwent three RFA sessions each; this sessions were undertaken as in line with the conservative approach to treatment in these patients in order to preserve renal function.

Earlier studies concluded that tumour size is an independent significant predictor of complete necrosis after a single ablation session.[5,17,23] In the present study, tumours that were finally ablated with success (mean size 3.6 cm) were smaller than tumours that showed residual tumour (mean size 4.6 cm). This study underlines the generally accepted fact that the success of RFA in treating RCCs is related to tumour size and that 4 cm is a suitable cut-off value. However, patients who have solitary kidneys and have tumours >4 cm are usually treated in this way to prevent dialysis.

Studies have shown that complications of RFA in the treatment of RCCs are usually clinically insignificant and that the rate of serious complications is very low.[5] In this study anuria, elevated creatinine (308 mmol/l), nausea, and vomiting were reported in one patient as major early complications. This case of acute renal insufficiency was well treated with a one session of dialysis. Late complications in this study are comparable to complications mentioned in Table 3.

In 69% of the tumours in this study diagnosis was based on imaging without biopsy. Other studies have demonstrated that needle biopsy of renal lesions is inaccurate.[25] During follow-up, various studies suggest a close correlation between imaging and tumour necrosis.[22,26] Therefore, in this study no needle biopsies were undertaken during follow-up.

Although this study underlines that RFA provides promising results for this patient group, follow-up periods are inadequate to demonstrate long-term survival.

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Table 3
Summary of published results

Study	Number of patients	Type of lesions (biopsy-confirmed)	RFA system	Follow-up period	% Total ablation (after one or more RFAs)	Complications
Krambeck *et al.*, 2008	26	Biopsy performed in 25% of lesions: 86% showed RCC and 14% were non-diagnostic.	Two RFA devices, RITA XL electrode (RITA Medical Systems, Mountain View, CA) or the Cool-tip ™ electrode (Valleylab, Boulder, CO), were used. The majority were treated with the Cool-tipTM electrode.	3–47 months (mean 25)	100%. 1 patient lost to follow-up, 3 patients did not have a contrast enhanced CT or MRI for evaluation, for the remaining patients no local tumor progression was noted.	No major acute complications noted. Perirectal and peritoneal drop metastases noted in 1 patient 9 months after most recent RFA. 1 patient with pre-existing renal insufficiency prior to RFA underwent a native nephrectomy and renal transplant for imminent renal failure. At last follow-up, 17% of patients had died, with 1 death from RCC progression.
Syvanthong *et al.*, 2006	12	Biopsy performed in 83% of patients: RCC in 90% of these patients and oncocytic neoplasm in 10%.	All radiofrequency ablation procedures were performed with a Cool-Tip system (Radionics).	1–6 months (mean 2.9)	100%. During follow-up, none of the patients had evidence of residual or recurrent tumour at the radiofrequency ablation site.	None of the 12 patients had complications during the procedure.
Jacobsohn *et al.*, 2007	16	Biopsies were taken during procedure: RCC was diagnosed in 75% of patients with de novo localized disease.	Percutaneous RFA was performed using a 200-W, impedance-based device (Tyco Healthcare, Valleylab, Boulder, Colo) in combination with a Cooltip RFA electrode.	1–45 months (mean 15.3)	100%. No recurrence in zone of ablation. (One patient showed recurrence in kidney outside the zone of ablation.)	Major acute complications in 4 patients after percutaneous RFA: 3 cases of clot obstruction that were readily treated with ureteral stenting and 1 case of perinephric haemorrhage.C hronic complications occurred in 2 patients: 1 patient, with history of partial nephrectomy, underwent ureteral stenting. 1 patient developed renal failure 4 months after percutaneous RFA and underwent nephrectomy elsewhere.
Mylona *et al.*, 2008	18	Biopsies performed in 28% of cases and in these cases RCC was diagnosed.	The RFA-system used was with expandable needle electrode with 7 or 9 arrays [RITA Medical Systems (Mountain View, CA, USA)]. The selection of the electrode was based on tumour size.	12–72 months (mean 31.2)	83%. In 1 patient there was persistent enhancement after the 2nd RFA; no 3rd RFA done due to irreversible coagulopathy. 2 other patients had local recurrence after initial successful treatment.	No major complications were observed. In 2/24 RFA sessions (8.33%), a minor subcapsular haematoma was noticed without haematuria. 3/18 patients (16.7%) complained of mild pain at the ablation site, which regressed with analgesics. Survival ranged from 12 to 72 months (mean 31.2 months). 2 patients died 17 and 28 months after RFA because of heart attack and car accident. 3/18 patients died of their disease.
Salagierski *et al.*, 2006	14	Lesions were not confirmed by biopsy.	Monopolar Cool-tip Tyco (Tyco-Valleylab, Boulder, CO, USA) (n=12) or bipolar Celon Olympus (Medical and Industrial Equipment, Southend-on-Sea, Essex, UK) (n=2).	Minimal follow-up period of 3 months.	100%. No local recurrences, with the exception of 1 metastasis to an ipsilateral adrenal gland, have been observed.	There were no major complications. There has been no need for definitive renal replacement therapy in any of the cases.

(*continued on next page*)

Table 3 (*continued*)

Study	Number of patients	Type of lesions (biopsy-confirmed)	RFA system	Follow-up period	% Total ablation (after one or more RFAs)	Complications
Raman *et al.*, 2008	16	Preoperative biopsy was diagnostic of RCC in 75% of cases.	RITA model 1500 RF generator (RITA Medical Systems, Mountain View, CA) with a 14-gauge Starburst XL probe.	Mean followup of 30.7 months (range 1.5 – 660)	94%. One patient had severe baseline renal insufficiency with progression to end -stage renal disease 2.5 years following RFA and underwent a radical nephrectomy.	In the acute setting, there were no major complications, and four patients developed minor complications (haematuria, ileus, subcapsular haematoma and paresthesia). Two patients developed chronic complications (dialysis-dependency and hydrocalyx).

Comparable studies demonstrate maximum follow-up periods of approximately 30 months.[5,24] There is still a lack of data regarding long-term outcome after RFA in patients with solitary kidneys.

In conclusion, in patients with a tumour in a solitary kidney percutaneous RFA is sometimes performed in cases that otherwise would not be considered as candidates due to tumour size or location to avoid haemodialysis. The present study shows that CT-guided RFA is technically feasible and safe in these cases with a technical success rate of 75%. The procedure has an early complication rate of 31%, a late complication rate of 25%, and results in successful tumour ablation in 69% of tumours. These figures present results in a complicated group of patients treated to avoid haemodialysis.

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