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MulticentRe rEal World outcomes of IrReversible Electroporation for complex small kiDney cancers (REWIRED)

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Abstract

Purpose Image-guided ablation (IGA) of central, endophytic and hilar tumours close to vital structures remains a major clinical challenge. This study evaluates real-world outcomes of irreversible electroporation (IRE) for small renal mass (RCCs) deemed unsuitable for surgery or conventional thermal ablation.

Material and methods This retrospective analysis utilised a prospectively maintained database from three specialist centres (USA, UK, Spain) for patients undergoing percutaneous IRE (NanoKnife® 3.0 System, Angiodynamics) for biopsy-proven RCC between May 2015 and October 2024. Patients were selected via multidisciplinary team discussion, typically due to tumour proximity to vital structures, solitary kidneys, significant comorbidities, or prior interventions.

Results 68 patients (mean age 66.9 years; SD 12.3) with 71 tumours were included. Mean tumour size was 2.83 cm (SD 1.39) and median RENAL Nephrometry score was 9 (IQR 6–9). Primary technique efficacy was 77.5% (55/71), with a local control rate of 95.8% (68/71). Technical success rate was 100%. Two major adverse events (2.8%; ureteric injury and haematuria) were observed. Mean eGFR change was -7.5 ml/min/1.73m^2, with 10.0% of cases seeing a > 25% reduction. At 59-month mean follow-up (SD 35), 5-year Local Tumour Progression-Free Survival was 84.4% (95% CI 71.8–91.7%). The trifecta outcome (primary efficacy, no major adverse events, and < 25% eGFR decline) was achieved in 68.6% of cases.

Conclusion According to the results of the current study, IRE is safe and effective in managing tumours near vital structures that are unsuitable for surgery or other ablation modalities. Further studies comparing IRE to other modalities are warranted.

Level of Evidence Level 4, Case Series

Keywords Image-guided ablation, Renal cancer, Irreversible electroporation, Small renal mass

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Background

Small renal masses (SRMs) have traditionally been managed through partial nephrectomy (PN) or radical nephrectomy (RN). However, in the past decade, image-guided ablation (IGA) has emerged as a promising alternative for managing SRMs. While level 1 evidence is not available, a systematic review and meta-analysis of cohort studies comparing PN and IGA revealed comparable long-term recurrence-free survival (RFS), cancer-specific survival (CSS), and metastasis-free survival (MFS). Additionally, IGA was associated with significantly fewer complications and a smaller decline in renal function post-operatively [1]. IGA is therefore commonly utilised in patients at high risk of complications (i.e. significant comorbidities or frailty), solitary kidneys, and recurrent hereditary renal cell carcinomas (RCCs) [2]. Both American Urological Association (AUA) and European Society for Medical Oncology (ESMO) have advocated IGA as an alternative to PN in managing SRMs < 3 cm [3, 4]. Similarly, the National Comprehensive Cancer Network (NCCN) guidelines recommend the Ablative Technique as the primary treatment for T1a renal cancer, in conjunction with partial nephrectomy, active surveillance, and radical nephrectomy for selected patients [5].

IGA is traditionally performed using thermal energy such as radiofrequency, cryoablation (CRYO) or microwave (MWA). However, thermal ablative therapies are associated with high risk of collateral damages and adverse events [6, 7], notably ureteric stricture, haemorrhage or damage to the collection system, especially in endophytic tumours. Despite introduction of counter strategies such as pre-ablation ureteric stent insertion [7], cold pyeloperfusion [8], or hydrodissection [9], the adverse events rate of cryoablation in completely endophytic or hilar tumours are up to 10%, with sub-optimal long-term RFS of only 74.2% at 5 years [10, 11]. Furthermore, the percentage of patients achieving "trifecta" (defined as having negative surgical margin or primary technical success, post-operatively ≤ 10% decrease in estimated glomerular filtration rate (eGFR) and absence of urological complications) were only 58.8% in percutaneous thermal ablation group, compared to 65.3% in PN group for completely endophytic tumours [12]. This emphasises the limitation of both IGA and PN in managing completely endophytic tumours with critical distance to vital structures and the need of a strategy to mitigate risk of injuries and complications.

Irreversible electroporation (IRE) is a non-thermal ablative technology novel to treating RCCs. It utilises high voltage electrical impulses which lead to irreversible nanopores in cellular membranes. The formation of these irreversible nanopores disrupts cellular homeostasis, leading to increased membrane permeability, loss of intracellular contents, and ultimately, activation of apoptotic signalling cascades [13]. This technology has been shown to preserve structures rich in collagen, such as ureters, vessels, and bile ducts, adjacent to the ablation zone [14]. This non-thermal technology is also thought to minimise the "heat sink" effect and possibly increases the effectiveness of ablation [14]. The first IRE treatment of RCC was published by Pech et al. in 2011 [15] and has been adopted mostly as a problem-solving technique, where other IGA or surgical techniques were deemed unsuitable due to high risk of collateral damage. An analysis of 30 patients with a median of 37-months follow-up had revealed a primary efficacy rate of 73.3%, and a secondary efficacy rate of 97%, with local RFS of 91% at 3-years follow-up [16]. The same study also observed good preservation of renal function with only one major adverse event of a proximal ureteric injury.

To date, the evidence of IRE in renal tumours are limited in single centre series with small number of patients with relatively short follow-up duration [17]. This study aims to be the first to report over 9 years' experience in a multicentre setting to evaluate the safety and efficacy of IRE in managing complex renal masses which were deemed unsuitable for other IGA or surgical management.

Methods

This study is performed according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [18] where applicable. All procedures performed in studies involved human participants and are in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Twenty-six of the included patients in this study had previously been reported in 2021 [16]. This study represents a further follow-up of this group of patients.

Study design

This is a retrospective review of all patients undergoing image-guided IRE for SRMs at three international expert tertiary centres in the UK, the US, and Spain (Supplementary Appendix 1) from May 2015 to October 2024.

Patient selection

All consecutive patients undergoing image-guided IRE for localised RCC (T1N0M0) at each individual centre during the study period were included in the study. There were no other inclusion or exclusion criteria to the study population, hence no patients were excluded from the analysis (Supplementary Fig. S2). All patients had received confirmatory percutaneous biopsies for RCC

prior to treatment, apart from patients with presumed histology due to pattern of disease or hereditary RCCs. As IRE is a problem-solving technique, there were no set criteria for when IRE is offered to a patient. All cases were discussed thoroughly at local tumour boards and multidisciplinary team as per local standard of care. If the tumour were deemed unsuitable for PN or RN by urologists (for example due to anatomy, or renal function), or unsuitable for conventional IGA by interventional radiologists (for example due to distance to vital structure), suitability of IRE will be discussed and offered to the patient if appropriate.

Treatment

The full description of the IRE procedure at the institution was previously described [16]. As experience with this novel technology increased, in selected patients deemed high-risk for intra-operative ureteric injury, a retrograde ureteric stent was placed pre-operatively to prevent ureteric injury. IRE was performed with the NanoKnife® 3.0 System (Angiodynamics, Latham, NY, USA) and NanoKnife® monopolar probes (15 cm, 19G) under ultrasound or computed tomography (CT) guidance with or without navigation assistance by four interventional radiologists across the three sites, all with over 10 years of experience in IGA. General anaesthesia with deep neuromuscular blockade was used for all patients to ensure total muscle paralysis. The number of electrodes were determined by the size and location of the tumour to ensure full coverage of the ablative margins as per manufacturer guidance. A test run of 20 pulses per electrode pair was performed prior to treatment to determine the electrical conductivity across electrodes and to allow for adjustments of the interelectrode voltage to ensure current delivered was between 20 and 40 A. All SRMs were treated with designated voltage which was delivered at 90 pulse per electrode pair with cardiac gating during the pulsation (100 ms at 1 Hz). All patients were monitored overnight post-IRE treatment. Examples of the IRE treatments are shown in Figs. 1 and 2.

Follow up

All patients received a contrast-enhanced CT immediately after the procedure to ensure the ablation zone encompasses the entire tumour. All patients are followed up as per local standard of care [16, 19] using CT or MRI at the discretion of the treating clinician and local protocols. Follow-up consisted of a minimum of CT or MR imaging of the kidneys at 1 month, 3 months and 6 months post-procedure for local tumour progressions, then with annual full body CT Thorax, abdomen and pelvis to assess for distant metastases.

Clinical features, variables, covariates and data acquisition

All sites collected patients' clinical features include age, sex, treatment date, follow-up details, histopathological outcomes, tumour complexity as measured by R.E.N.A.L. Nephrometry score [20], comorbidities, adverse events and pre-/post-operative renal function.

Outcomes

The outcomes of this study are defined according to the 2014 standardisation of image-guided tumour ablation terminology and reporting criteria [21], as well as the 2021 SIO and DATECAN consensus guidelines [22].The primary outcome of the study is primary technique efficacy, defined by complete treatment response at the first follow-up imaging study (1 month post-procedure), with the zone of ablation encompassing the entire tumour and no evidence of residual enhancing tumour at the treated area on CT or MRI following the initial IRE [21, 22]. Secondary outcomes include technical success, defined by complete treatment of tumour according to protocol and was completely covered by the ablation zone immediately following the procedure [21, 22], secondary technique efficacy rate for IRE (complete treatment response after undergoing successful repeat IRE following identification of residual unablated tumour), local control (complete treatment response after undergoing successful repeat treatment using other IGA modalities) [22], adverse event rate (as defined by the Clavien-Dindo Grade [23]), change in renal function as measured by eGFR (CKD-EPI [24]) and serum creatinine, local tumour progression free survival (LTPFS), overall survival (OS), cancer specific survival (CSS) and metastasis free survival (MFS). Local tumour progression was defined as (1) presence of focal diffuse restriction on diffusion-weighted imaging in the case of MRI, (2) gradual increase in ablation zone on follow-up image in cases of both MR or CT imaging, or (3) new area(s) of enhancement in the zone of ablation after at least one imaging study had shown complete lack of enhancement in the treated area on both MR or CT imaging. Metastatic disease was defined as extra-renal disease on imaging confirmed or have suspected kidney origin. Cancer-specific death was defined as any death from renal cancer. Additionally, a composite outcome of achievement of "trifecta" for IGA was used, as described previously in literature as (1) composing of < 25% drop in eGFR reduction from baseline post-operatively, (2) no major perioperative adverse events and (3) achieving primary technique efficacy [25].

Data analysis

Statistical analyses were performed using STATA/MP 18.0 (STATA Corp.). Baseline characteristics of

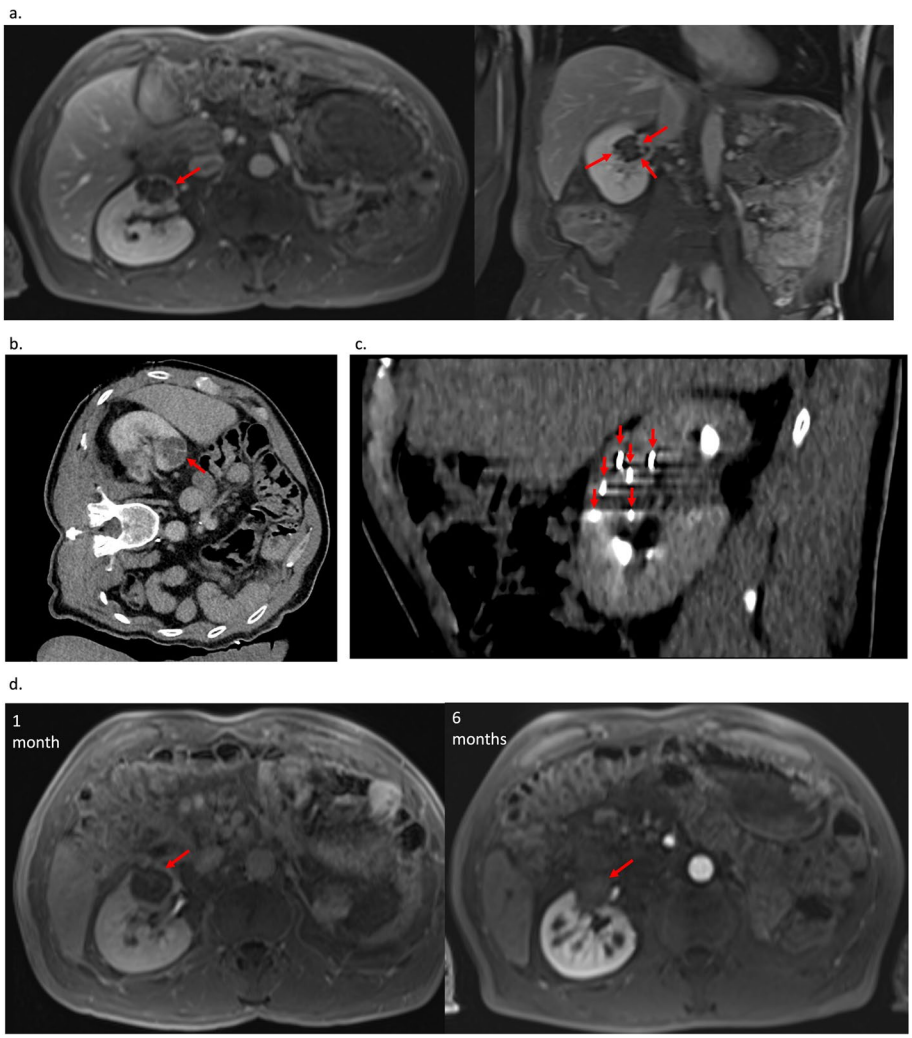

Fig. 1 **a** Axial and coronal view contrast enhanced T1 weighted MRI showing a part cystic and peripherally enhancing lesion in the anterior right kidney (Arrows). **b** Intra-operative contrast enhanced CT for IRE planning showing the right anterior partly cystic renal mass (Arrow). The patient is in a lateral position supported by a conformable mattress with the right side up. **c** Intra-operative CT (Sagittal view) showing 6 IRE needles (arrows) bracketing the tumour. **d** Post-treatment axial MRI at 1 month showing the low signal ablation zone (arrow) encompassing the tumour and then involution of this area at 6 months with no residual enhancement to suggest residual disease

included patients were summarised using descriptive statistics. Primary efficacy rate, secondary efficacy rate, local control, adverse event rates, and achievement of "trifecta" were reported proportionally with percentages and associated 95% confidence intervals (95% CI). Pre- and post-operative renal function is summarised using mean and standard deviations, alongside mean change in renal function pre- and post-operatively. Unpaired t-tests were used to assess mean differences between renal function pre- and post-operatively. Patients with > 25% or < 25% drop in renal function are described proportionally. Exploratory logistic regression models were used to explore the relationship between pre-operative factors and outcomes. Survival outcomes are measured from the time of treatment to time of event and reported by percentages at 1, 3, 5 and 7-years accordingly with respective 95% CIs, alongside Kaplan–Meier Graphs. Patient with missing data were excluded from the specific analysis(s) where required. A sensitivity analysis was conducted to ascertain that only the effects of IRE are included in the survival analysis. For the sensitivity analysis, patients with residual disease requiring further thermal ablation (CRYO, MWA), excluding IRE, were right-censored at the time of further treatment to ensure that the effects of IRE are accurately captured.

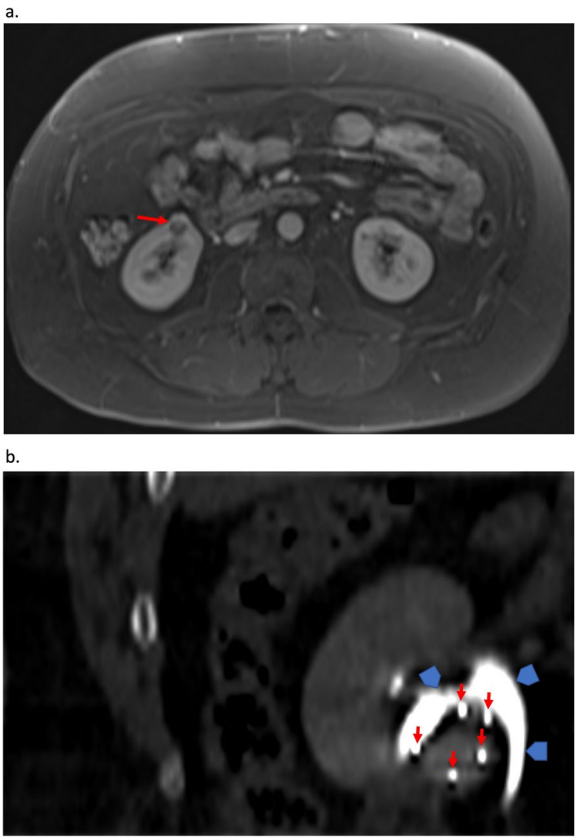

Fig. 2 **a** Axial view contrast enhanced T1 weighted MRI showing a right anterior cortical renal mass (arrow) with close proximity to small bowel interiorly and difficult access for conventional cryoablation. **b** Coronal intra-operative CT shows the position of the 5 IRE needles (red arrows) within the right anterior renal mass close to the renal collecting system, renal pelvis and proximal ureter (blue arrow heads)

Results

A total of 68 patients with 71 renal tumours undergoing 71 ablation sessions were included in the analysis; a breakdown of the number of patients for each site is included in Supplementary Appendix 1. A flow diagram of the study process is included in Supplementary Appendix 2.

Baseline characteristics of included patients

Baseline characteristics of all included patients are outlined in Table 1. Mean (SD) age at treatment was 66.9 (± 12.3). Tumour characteristics of all treated tumours are outlined in Table 1. Median R.E.N.A.L nephrometry of included tumours were 9 (IQR 6–9). Forty-one (57.7%) of all tumours were entirely endophytic. Thirty-five (49.3%) of all tumours were hilar tumours, touching the renal artery or vein. Fifteen (21.1%), 16 (22.5%), 37 (52.1%), 19 (26.8%) tumours are of < 1 mm distance from the colon, ureter, renal artery or vein and collecting

Table 1 Baseline characteristics of included patients

	Characteristic (N = 68)
Age at treatment	
≤ 49	6 (8.8%)
50–69	13 (19.1%)
70–79	21 (30.9%)
≥ 80	28 (41.2%)
Sex	
Female	15 (22.1%)
Male	53 (77.9%)
Von Hippel Lindau Syndrome	
No	60 (88.2%)
Yes	8 (11.8%)
Birt-Hogg-Dube Syndrome	
No	67 (98.5%)
Yes	1 (1.5%)
Pre-existing renal Impairment	
No	56 (82.4%)
Yes	12 (17.6%)
Diabetes Mellitus	
No	44 (64.7%)
Yes	24 (35.3%)
Solitary Kidney	
No	49 (72.1%)
Yes	19 (27.9%)
Mean Creatinine (μmol/L; SD)	98.3 (33.0)
Mean eGFR ($mL/min/1.73m^2$; SD)	81.1 (24.1)
Chronic Kidney Disease*	
No	52 (77.6%)
Yes	15 (22.4%)
Modality§	
Ultrasound guidance only	2 (2.8%)
CT Guidance only	48 (67.6%)
Ultrasound and CT Guidance	19 (26.8%)
Ultrasound guidance and CT guidance with navigation system	2 (2.8%)
Size of lesion§	
1–1.9 cm	12 (16.9%)
2–2.9 cm	29 (40.8%)
3–3.9 cm	24 (33.8%)
4–4.9 cm	2 (2.8%)
≥ 5.0 cm	4 (5.6%)
Mean size of lesion in cm (SD)	2.83 (1.39)
Laterality§	
Right	36 (50.7%)
Left	35 (49.3%)
R.E.N.A.L nephrometry score§	
4	8 (11.3%)
5	5 (7.0%)
6	7 (9.9%)
7	6 (8.5%)
8	9 (12.7%)
9	24 (33.8%)
10	12 (16.9%)

SD Standard Deviation, *eGFR* estimated glomerular filtration rate, *CT* Computed tomography, *cm* centimeter

* *n* = 67 due to missing data; §n = 71 due to tumour level characteristic

system, respectively. Other vital structures < 1 mm from the tumours include the IVC (1 [1.40%] tumour), liver (1 [1.40%] tumour), small bowel (2 [2.80%] tumour), spleen (1 [1.40%] tumour), and splenic artery (2 [2.80%] tumours). Overall, 66 (93.0%) of all tumours were < 1 mm distance from vital structures. Pre-operative biopsy histologies are outlined in Table 2.

Operative characteristics

Image-guided approaches of included cases are outlined in Table 1. The mean number of electrodes inserted was 4.56 (± 1.31). Mean anaesthesia time was 107.4 (± 50.3) minutes. Mean hospital stay duration is 1.60 (± 1.40) days.

Technical success and technique efficacy

Technical success was achieved in 71/71 (100%; 95% CI 94.9%–100%) of treated tumours and ablation sessions. Primary technique efficacy was achieved in 55/71 (77.5%; 95% CI 66.0% – 86.5%) tumours (Table 3). Primary technique efficacy rates were found to decrease significantly as tumour sizes increase (OR: 0.94, 95% CI 0.89–0.99, p = 0.034). Especially, tumours more than 3.5 cm are significantly less likely to achieve primary technique efficacy (OR 0.29, 95% CI 0.09–0.95 p = 0.041). R.E.N.A.L nephrometry score, completely endophytic tumours and distance to vital structure such as ureter, colon, and the collecting system were not found to be associated with worsening primary technique efficacy. Of the 16 patients with residual disease at first follow-up, 13 (18.3% of the total cohort) patients received further IGA. Two (2/13; 15.4%) underwent further IRE, nine (9/13; 69.2%) underwent further CRYO, and one (1/13; 7.7%) underwent further MWA. One patient (1/13; 7.7%) underwent both IRE and CRYO salvage therapy for residual disease. The mean duration from initial treatment to repeat treatment was 3.1 months (SD: 3.31). Secondary technique efficacy rate of IRE was achieved in 57/71 patients (80.3%; 95% CI 69.1–88.8%). When combined with other IGA modalities, 68/71 patients achieved local control (95.8%; 95% CI 88.1–99.1%) after only one extra session of IGA in addition to IRE session. One patient was found to have residual disease on first follow-up imaging but unfortunately succumbed to a haemorrhagic stroke prior to further treatment. Similarly, another patient was found to have residual disease on first follow-up imaging but had unfortunately succumbed to presumably old age prior to further treatment.

Table 2 Grade and histology of all included patients

Grade*	
1	23 (41.1%)
2	24 (42.9%)
3	9 (16.1%)
4	0 (0%)
Histology^	
Clear Cell	47 (75.8%)
Papillary	10 (16.1%)
Eosinophil	2 (3.2%)
Chromophobe	3 (4.8%)

* $n = 56$ due to missing histology data

^ $n = 62$ due to missing histology data

Table 3 Procedural outcome of all treated patients

Technical Success	
Not Achieved	0 (0%)
Achieved	71 (100%)
Primary Technique Efficacy	
Not Achieved	16 (22.5%)
Achieved	55 (77.5%)
Repeat treatment with IGA	
No	58 (81.7%)
Yes	13 (18.3%)
Modality used in repeat treatment	
IRE	2 (15.4%)
CRYO	9 (69.2%)
MWA	1 (7.7%)
IRE + CRYO	1 (7.7%)
Duration to from first treatment to repeat treatment (months)	
Mean	3.1
SD	3.31
Secondary Technique Efficacy (IRE)	
Not Achieved	14 (19.7%)
Achieved	57 (80.3%)
Local Control (All IGA Modalities)	
No	3 (4.2%)
Yes	68 (95.8%)

IGA Image-guided ablation, *CRYO* Cryoablation, *MWA* Microwave ablation, *IRE* Irreversible electroporation, *SD* Standard Deviation

Adverse events

A breakdown of adverse events according to the Clavien-Dindo Grade are outlined in Table 4. A total of 11 (15.5%; 11/71; 95% CI 8.0%–26.0%) adverse events were observed. Two Grade 3 major adverse events (2/71; 2.8%; 95% CI 0.3%–9.9%) were due to one permanent ureteric injury requiring long-term ureteric stenting [26] and one incidence of haematuria which completely resolved after stent removal. The size of the treated tumours, R.E.N.A.L Nephrometry score, endophytic tumours and distance to vital structure such as ureter, bowel, and the collecting system were not found associated with worsening adverse events rates (p > 0.05).

Table 4 Peri-operative outcomes of all treated patients

	Pre/post-operative outcomes
Mean pre-operative creatinine in µmol/L (SD)	98.3 (33.0)
Mean post-operative creatinine in µmol/L (SD)	109.4 (37.7)
Mean percentage creatinine change pre- and post-operatively (SD)	12.3% (19.3%)
Mean pre-operative eGFR in ml/min/1.73 m^2 (SD)	81.1 (24.1)
Mean post-operative eGFR in ml/min/1.73 m^2 (SD)	73.6 (24.1)
Mean percentage eGFR change pre- and post-operatively (SD)	− 8.6% (13.3%)
> 25% drop in eGFR (clinically significant*§)	
0	63 (90.0%)
1	7 (10.0%)
Clavien–Dindo classification adverse events	
0	60 (84.5%)
I	9 (12.7%)
II	0 (0%)
IIIa	2 (2.8%)
≥ IIIb	0 (0%)

SD standard deviation, *eGFR* estimated glomerular filtration rate

* Patients with > 25% drop in eGFR, but which remains > 90 are not considered clinically significant

§ $n = 70$ due to missing data

Renal function outcomes

Mean difference in eGFR pre- and post-operatively was −7.5 ml/min/1.73m^2 (95% CI 4.8–10.3 ml/min/1.73 m^2, $p < 0.001$; Table 4). Mean difference in creatinine pre- and post-operatively was 11.1 µmol/L (95% CI 6.6–15.6), $p < 0.001$: Table 4). Mean percentage drop of eGFR post-operatively was 8.6% (± 13.3%). The mean percentage increase in creatinine post-operatively was 12.3% (± 19.3%). Seven (10%) patients developed a larger than 25% drop in eGFR, which was deemed clinically significant. The size of the treated tumours, R.E.N.A.L Nephrometry score, and endophytic tumours were not found associated with increasing clinically significant decrease in renal function ($p > 0.05$).

Survival outcomes

Mean follow-up duration of the cohort is 59 (± 35.0) months. No patients were lost to follow-up. Local tumour progression was observed in 10/71 (14.1%; 95% CI 7.0%–24.4%) tumours. Local tumour progression free survival (LTPFS) was 95.6% (95% CI 86.9%–98.6%) at 1 year, 88.5% (95% CI 77.2%–94.4%) at 3 years, and 84.4% (95% CI 71.8%–91.7%) at 5 years and 81.1% (95% CI 66.7%–89.7%) at 7 years (Fig. 3). Patients were managed with repeat IRE, CRYO or nephrectomy.

Five of the 68 (7.35%; 95% CI 2.43% – 16.3%) patients developed metastatic disease. MFS was 96.9% (95% CI 88.1–99.2%) at 1 year, 93.3% (95% CI 83.0–97.4%) at 3 years, and 91.0% (95% CI 79.3–96.2%) at 5 and 7 years (Fig. 4). Three of the 68 patients succumbed to RCC at 24, 72 and 83 months post-treatment, respectively. This suggests a CSS of 100% (95% CI 94.7%–100%) at 1 year, 98.0% (95% CI 86.9—99.7%) at 3 years and 5 years, and 93.6% (95% 74.4–98.5%) at 7 years (Fig. 5).

A total of 13/68 (19.1%; 95% CI 10.6–30.5%) patients died during the study period, suggesting an OS of 93.9% (95% CI 84.6–97.7%) at 1 year, 90.4% (95% CI 79.8-95.6%) at 3 years, 88.0% (95% CI 76.2–94.2%) at 5 years and 75.2% (95% CI 58.2—86.1%) at 7 years (Fig. 6).

Sensitivity analyses were performed by right-censoring patients who had residual disease requiring further thermal ablation, thereby isolating the specific therapeutic effects of IRE. At 1-year post-treatment, the LTPFS, MFS, and CSS, rates were 93.3% (95% CI: 83.1–97.4%), 96.3% (95% CI: 86.0–99.1%), and 100% (95% CI: 94.7–100%), respectively. At the 3-year interval, the LTPFS rate was 86.8% (95% CI: 73.9–93.6%), the MFS rate was 92.0% (95% CI: 80.0–97.0%), and the CSS rate decreased to 97.7% (95% CI: 84.6–99.7%). At 5 years, the LTPFS rate was 81.8% (95% CI: 67.4–90.2%), the MFS rate reached 89.2% (95% CI: 75.5–95.4%), and the CSS rate remained constant at 97.7% (95% CI: 84.6–99.7%). At 7-years, the estimated rates for LTPFS, MFS, and CSS were 77.4% (95% CI: 60.6–87.8%), 89.2% (95% CI: 75.5–95.4%), and 91.9% (95% CI: 68.2–98.2%), respectively. The full results and associated Kaplan–Meier graphs of this sensitivity analysis are reported in Supplementary Appendix 3.

Achievement of "Trifecta"

Forty-eight cases (68.6%; 95% CI 56.4–79.1%) achieved "trifecta" for ablation status. The size of the treated tumours, R.E.N.A.L Nephrometry score, and endophytic tumours were not found associated with worsening achievement of "trifecta" status.

Discussion

IRE was first performed for RCC by Pech et al. [15]. Since then, IRE has been employed as a problem-solving technique in mostly complex tumours which are otherwise not suitable for thermal ablation or partial nephrectomy. This study aimed to report mid-term outcomes of IRE in this population.

IRE is a technically challenging procedure even in experienced interventional radiologist's hands, the parallel placement of IRE electrodes poses a significant technical challenge. Despite that, our study observed a 100%

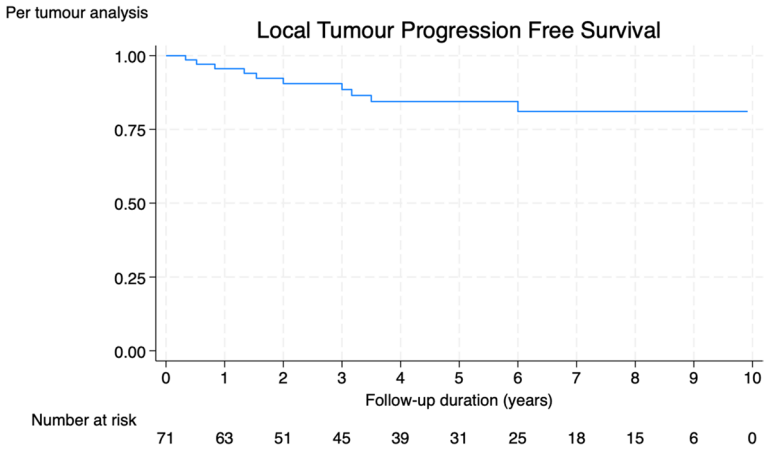

Fig. 3 Kaplan-Meier Graph outlining Local Tumour Progression Free Survival (Per Tumour analysis)

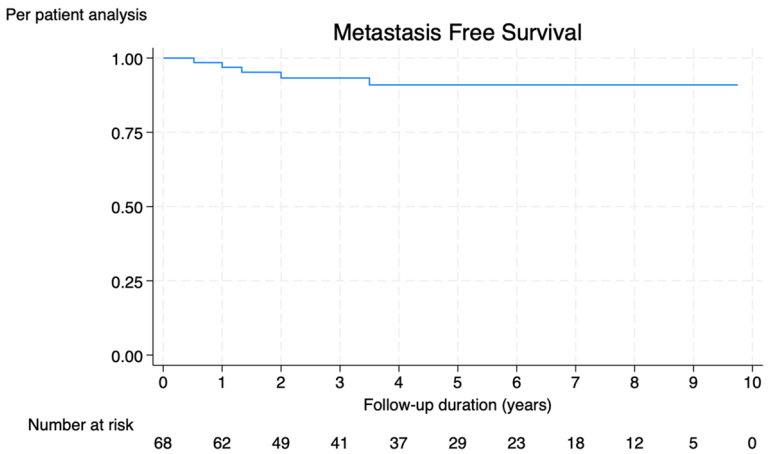

Fig. 4 Kaplan-Meier Graph outlining Metastasis Free Survival (Per Patient Analysis)

technical success, similar to 90% in prospective series reported by Buijs et al. [27]. Our study observed a primary technique efficacy of 77.5%, while slightly lower than other series, such as 93% in series by Canvasser et al. [28] and 91.7% in series by Dai et al. [29], it is noteworthy that our study addressed larger and more complex tumours. In particular, mean tumour size in both Canvasser et al. [28] and Dai et al. [29] was 2 cm, compared to almost 3 cm in our study. Similarly, median R.E.N.A.L. nephrometry score was 5 in both Canvasser et al. [28] and Dai et al. [29] compared to 9 in our study. As shown in our study, increasing tumour size is directly correlated with reduced primary technique efficacy, specifically in tumours larger than 3.5 cm. Furthermore, the slightly lower primary technique efficacy is not translated to worsened long-term oncological outcomes. IRE remain to demonstrate promising mid- to long-term oncological durability in our series, with LTPFS of 84.4% observed at 5-years, which is similar to 81% at 5-years observed in series by Dai et al. [29] and 83% at 2-years in Canvasser et al. [28].

Although our cohort included patients deemed less suitable for thermal ablation modalities due to tumour locations, several studies have reported outcomes of CRYO in completely endophytic renal masses. Jensen et al. [10] reported a 93% primary technique efficacy, while Murray et al. [11] reported an 87% primary technique efficacy rate, which is comparable to our study's 77.5% primary technique efficacy rate, especially considering the larger tumour sizes (mean 3 vs 2.5 cm) and proximity to complex tumours (94% vs 21%) in our cohort compared to Murray et al. [11]. Similar local RFS rates were observed across the two studies (Jensen et al. [10] of 74.2% at 5-years and Murray et al. [11] of 75% at

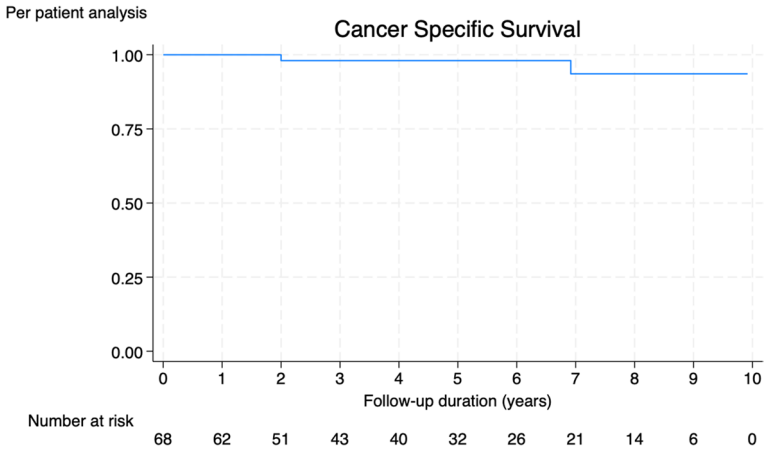

Fig. 5 Kaplan-Meier Graph outlining Cancer Specific Survival (Per Patient Analysis)

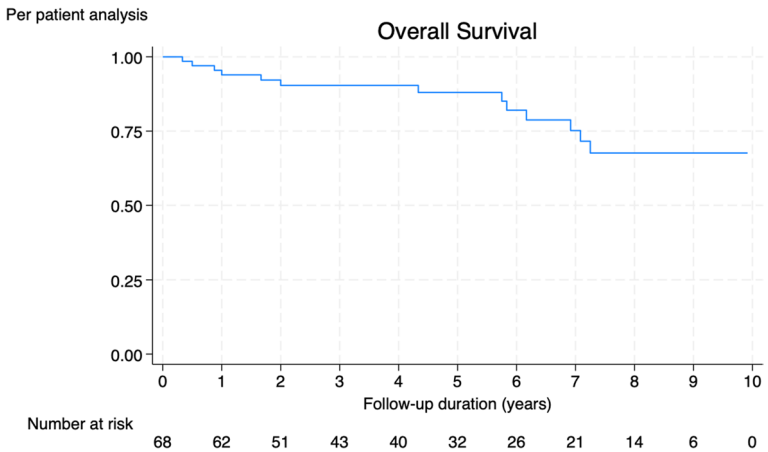

Fig. 6 Kaplan-Meier Graph outlining Overall Survival (Per Patient Analysis)

5 years) and our study showed a slightly higher LTPFS of 84.4% at 5 years and 81.1% at 7-years. Similarly, although not directly comparable to our cohort, a systematic review and meta-analysis of PN in completely endophytic and hilar tumours demonstrated a recurrence rate of 1.9%, which is significantly lower than CRYO and IRE studies [30].

To ensure the results of the survival analysis are solely attributed to IRE, a sensitivity analysis was performed by censoring patients who had further sessions of thermal ablation at the time of treatment in the case of residual unablated tumour. This revealed a similar LTPFS of 81.8% (95% CI 67.4–90.2%) at 5-, and 77.4% (95% CI 60.6–87.8%) at 7 years.

Our study observed two grade 3 adverse events, which were related to haematuria and ureteric injury, both managed by ureteric stenting. However, both Canvasser et al. [28] and Dai et al. [29] reported no grade 3 or above adverse events. This could once again be a result of the larger and more complex nature of the tumours treated in this cohort. From our experience, the ureteric injury may have been caused by the electrical current surge from the generator, leading to thermal injury [7, 31]. It is crucial to ensure that the IRE electrode closest to the vital structure is set as the anode so that electrical pulses are fired away from the anode and the vital structure, avoiding thermal injury which could be due to electrical current surge from the generator [7]. In selected cases, the authors now opt for a pre-operative retrograde ureteric stent placement to reduce the risk of ureteric injuries. Furthermore, given the need for precise and parallel placement of electrodes, it is important to evaluate the potential benefit of navigation systems in facilitating accurate needle placement. However, this remains inconclusive due to the limited number of cases (n = 2) using navigation in this study.

Compared to studies investigating the use of CRYO in completely endophytic masses, our study reported a slightly lower rate (2.8%) of major complications, with Jensen et al. [10] and Murray et al. [11] observing a 9.8% and 10% major complication rate, respectively. When comparing to robotic PN, a large multicentre series has suggested a 17.5% Clavien-Dindo grade 3 or above complication rate, significantly higher than IGA series reported [32]. This suggests a possible improved adverse events profile of IRE compared to CRYO or PN in complex tumours. However, further prospective studies are required to confirm this speculation.

While our study revealed a significant drop in eGFR post-operatively, mean difference was clinically insignificant (− 7.5 ml/min/1.73m^2, 8.6%), this is similar to findings from the series by Canvasser et al. [28] (mean difference −6 ml/min/1.73m^2) and Diehl et al. [33] (mean difference −2.75 ml/min/1.73m^2). These results are also similar to other thermal ablation modalities, including CRYO (mean difference −6.2 ml/min/1.73 m^2) [34] and RFA (mean difference − 7 ml/min/1.73 m^2) [35]. These contrast the results of robotic PN cohorts, which reported a mean difference of −15.5 ml/min/1.73 m^2 in eGFR post-operatively [12]. This contributes to the ongoing safety profile in renal function for IGA.

Our study utilised a modified "trifecta" composite outcome, defined by (1) composing of < 25% drop in eGFR reduction from baseline post-operatively, (2) no major perioperative adverse events and (3) achieving primary technique efficacy [25]. This is in order to allow similar comparison to the "trifecta" known in partial nephrectomy [36], which is typically defined as (1) no significant drop in renal function or warm ischaemia time of < 25, (2) no major complications, and (3) negative surgical margin. Our study identified a "trifecta" achievement rate of 68.6%, which is significantly higher than a large multicentre series reporting achievement of "trifecta" in 45.4% of patients with completely endophytic tumours undergoing robotic-assisted PN [32].

Furthermore, a notable study by Pandolfo et al. [12] compared robotic PN with thermal ablation (RFA, CRYO or MWA) and found that thermal ablation achieved comparable oncological and safety outcomes to PN in cases of completely endophytic tumours. Our study included slightly larger tumours, with a mean diameter of 3 cm versus 2.6 cm in Pandolfo et al., and similar tumour complexity, with both studies reporting a median R.E.N.A.L. nephrometry score of 9. Notably, our study demonstrated a higher achievement rate of the "trifecta" compared to the study by Pandolfo et al. (68.6% vs 58.8%) for thermal ablation. This finding may reflect the superior efficacy of IRE in achieving optimal outcomes compared to conventional thermal ablation techniques. It is necessary to provide further prospective evidence to definitively establish the superiority of IRE over conventional thermal ablation techniques.

This study represents the largest series to date evaluating the long-term efficacy and safety of IRE for complex RCC unsuitable for other treatment modalities. Our findings provide further evidence supporting the use of IRE as a valuable treatment option in this challenging patient population. The study is not without its limitations, including the retrospective nature of the study, as well as the absence of strict selection criteria for the use of IRE, given the study's pragmatic nature. The result of this study is also only generalisable to the particular population included in our cohort. Furthermore, the study is limited by the lack of a centralised imaging review, variations in follow-up imaging modalities (CT and MRI), and potential inter-operator variability among the four operators across three centres. Finally, given the lack of a contemporaneous comparator, dedicated studies with propensity-matched tumour characteristics are needed to directly compare the performance of IRE with CRYO and establish the definitive role of IRE in managing complex tumours.

Conclusion

In the management of renal masses located in close proximity to vital structures, IRE emerges as a safe and effective problem-solving technique. It presents a viable alternative to thermal ablation and surgical management, which may not be ideal in such cases. However, more prospective data are necessary to establish the comparative efficacy of IRE with surgery or thermal ablation and to further validate its long-term outcomes. Additionally, head-to-head comparisons of IRE with other techniques are required to definitively establish its role in managing renal masses.

Supplementary Information

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Supplementary Material 1: Appendix 1: Study design.

Supplementary Material 2: Appendix 2: Patient selection and analysis flowchart.

Supplementary Material 3: Appendix 3: The full sensitivity analysis and associated Kaplan–Meier graphs.

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None.

Authors' contributions

Conceptualization: TMW, GN, JMA. Methodology: TMW, VWSC. Investigation: VWSC, HHLN, AM, EMR, PEG. Formal analysis: VWSC. Writing: VWSC, HHLN. Review and Editing: TMW, AM, EMR, PEG, GN, JMA. Supervision: TMW, GN, JMA. All authors read and approved the final manuscript.

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Data availability
The data supporting the findings of this study are not publicly available due to privacy and ethical restrictions regarding identifiable patient details. Requests for access to de-identified data may be considered by the corresponding author upon reasonable request and subject to institutional approval.

Declarations

Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required. Institutional Review Board (IRB) approval was also not required.
Informed consent was obtained from all individual participants included in the study.

Consent for publication
For this type of study, consent for publication is not required.

Competing interests
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References

1. Chan VW, Abul A, Osman FH, Ng HH, Wang K, Yuan Y, Cartledge J, Wah TM. Ablative therapies versus partial nephrectomy for small renal masses - A systematic review and meta-analysis. Int J Surg. 2022;97:106194. https://doi.org/10.1016/j.ijsu.2021.106194. Epub 2021 Dec 24. PMID: 34958968.
2. Osman FH, Chan VW, Breen DJ, et al. Oncological and peri-operative outcomes of percutaneous cryoablation of renal cell carcinoma for patients with hereditary RCC diseases—an analysis of European multi-centre prospective EuRECA registry. Cancers (Basel). 2023. https://doi.org/10.3390/cancers15133322.
3. Campbell S, Uzzo RG, Allaf ME, et al. Renal mass and localized renal cancer: AUA guideline. J Urol. 2017;198(3):520–9.
4. Powles T, Albiges L, Bex A, et al. Renal cell carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆ Ann Oncol. 2024;35(8):692–706.
5. Motzer RJ, Jonasch E, Agarwal N, et al. NCCN Guidelines® Insights: kidney cancer, Version 2.2024. J Natl Compr Canc Netw. 2024;22(1):4–16
6. Wah TM, Irving HC, Gregory W, Cartledge J, Joyce AD, Selby PJ. Radiofrequency ablation (RFA) of renal cell carcinoma (RCC): experience in 200 tumours. BJU Int. 2014;113(3):416–28.
7. Ng H, Chan VW-S, Cartledge J, et al. Iatrogenic ureteric stricture post image guided renal cryoablation in a patient with von Hippel-Lindau syndrome. Radiol Case Rep. 2021;16(8):1980–4.
8. Wah TM, Koenig P, Irving HC, Gervais DA, Mueller PR. Radiofrequency ablation of a central renal tumor: protection of the collecting system with a retrograde cold dextrose pyeloperfusion technique. J Vasc Interv Radiol. 2005;16(11):1551–5.
9. Weiss J, Garnon J, Cazzato RL, et al. Percutaneous hydrodissection for thermoprotection during cryoablation of periureteric and pyeloureteric junction renal cell carcinomas. Abdom Radiol. 2021;46(3):1179–87.
10. Jensen CG, Dybdahl M, Valtersson J, et al. Percutaneous image-guided cryoablation of endophytic renal cell carcinoma. Cardiovasc Intervent Radiol. 2024;47(4):453–61.
11. Murray CA, Welch BT, Schmit GD, et al. Safety and efficacy of percutaneous image-guided cryoablation of completely endophytic renal masses. Urology. 2019;133:151–6.
12. Pandolfo SD, Beksac AT, Derweesh I, et al. Percutaneous ablation vs robot-assisted partial nephrectomy for completely endophytic renal masses: a multicenter trifecta analysis with a minimum 3-year follow-up. J Endourol. 2023;37(3):279–85.
13. Deodhar A, Monette S, Single GW Jr., et al. Renal tissue ablation with irreversible electroporation: preliminary results in a porcine model. Urology. 2011;77(3):754–60.
14. Lee EW, Loh CT, Kee ST. Imaging guided percutaneous irreversible electroporation: ultrasound and immunohistological correlation. Technol Cancer Res Treat. 2007;6(4):287–94.
15. Pech M, Janitzky A, Wendler JJ, et al. Irreversible electroporation of renal cell carcinoma: a first-in-man phase I clinical study. Cardiovasc Intervent Radiol. 2011;34:132–8.
16. Wah TM, Lenton J, Smith J, et al. Irreversible electroporation (IRE) in renal cell carcinoma (RCC): a mid-term clinical experience. Eur Radiol. 2021;31(10):7491–9.
17. Hilton A, Kourounis G, Georgiades F. Irreversible electroporation in renal tumours: a systematic review of safety and early oncological outcomes. Urologia (Oxf). 2022;89(3):329–37.
18. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med. 2007;147(8):573–7.
19. Chan VW-S, Osman FH, Cartledge J, et al. Long-term outcomes of image-guided ablation and laparoscopic partial nephrectomy for T1 renal cell carcinoma. Eur Radiol. 2022;32(9):5811–20.
20. Kutikov A, Uzzo RG. The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. J Urol. 2009;182(3):844–53.
21. Ahmed M, Solbiati L, Brace CL, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria–a 10-year update. Radiology. 2014;273(1):241–60.
22. Puijk RS, Ahmed M, Adam A, et al. Consensus guidelines for the definition of time-to-event end points in image-guided tumor ablation: results of the SIO and DATECAN initiative. Radiology. 2021;301(3):533–40.
23. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205–13.
24. A new equation to estimate glomerular filtration rate. Ann Internal Med. 2009;150(9):604–612
25. Pandolfo SD, Loizzo D, Beksac AT, et al. Percutaneous thermal ablation for cT1 renal mass in solitary kidney: a multicenter trifecta comparative analysis versus robot-assisted partial nephrectomy. Eur J Surg Oncol. 2023;49(2):486–90.
26. Ng H, Wang K, Cartledge J, et al. Ureteric injury after image-guided ablation of renal cell cancer with irreversible electroporation. J Vasc Interv Radiol. 2021;32(2):322–4.
27. Buijs M, Zondervan PJ, de Bruin DM, van Lienden KP, Bex A, van Delden OM. Feasibility and safety of irreversible electroporation (IRE) in patients with small renal masses: results of a prospective study. Urol Oncol. 2019;37(3):183.e181-183.e188.
28. Canvasser NE, Sorokin I, Lay AH, et al. Irreversible electroporation of small renal masses: suboptimal oncologic efficacy in an early series. World J Urol. 2017;35(10):1549–55.

29. Dai JC, Morgan TN, Steinberg RL, Johnson BA, Garbens A, Cadeddu JA. Irreversible electroporation for the treatment of small renal masses: 5-year outcomes. J Endourol. 2021;35(11):1586–92.
30. Gao H-w, Ma X, Xiao C-h, Pan Y-y. Robot-assisted partial nephrectomy for technically challenging renal tumors (completely endophytic and hilar): a systematic review and meta-analysis of perioperative, oncological, and functional outcomes. J Robot Surg. 2025;19(1):144.
31. Wagstaff PG, de Bruin DM, van den Bos W, et al. Irreversible electroporation of the porcine kidney: Temperature development and distribution. Urol Oncol. 2015;33(4):168.e161-167.
32. Carbonara U, Simone G, Minervini A, et al. Outcomes of robot-assisted partial nephrectomy for completely endophytic renal tumors: a multi-center analysis. Eur J Surg Oncol. 2021;47(5):1179–86.
33. Diehl SJ, Rathmann N, Kostrzewa M, et al. Irreversible electroporation for surgical renal masses in solitary kidneys: short-term interventional and functional outcome. J Vasc Interv Radiol. 2016;27(9):1407–13.
34. Pietersen PI, Stougaard S, Keeley FX Jr., et al. Renal function after CT-guided cryoablation of small renal tumours in patients with solitary kidney: an analysis of European Multinational Prospective EuRECA Registry. Cardiovasc Intervent Radiol. 2024;47(5):583–9.
35. Curry D, Pahuja A, Loan W, Thwaini A. Radiofrequency ablation of small renal masses: outcomes, complications and effects on renal function. Curr Urol. 2018;11(4):196–200.
36. Hung AJ, Cai J, Simmons MN, Gill IS. "Trifecta" in partial nephrectomy. J Urol. 2013;189(1):36–42.

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