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Title: Initial Assessment of the Efficacy of Irreversible Electroporation (IRE) in the Focal Treatment of Localised Renal-Cell Carcinoma (RCC) with Delayed-Interval Kidney Tumour Resection (IRENE Trial – an Ablate-and-Resect Pilot Study)

Author: Johann J. Wendler, Maciej Pech, Frank Fischbach, Julian Jürgens, Björn Friebe, Daniel Baumunk, Markus Porsch, Simon Blaschke, Daniel Schindele, Sandra Siedentopf, Jens Ricke, Martin Schostak, Jens Köllermann, Uwe B. Liehr

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ORIGINAL ARTICLE

Title:
Initial assessment of the efficacy of irreversible electroporation (IRE) in the focal treatment of localised renal-cell carcinoma (RCC) with delayed-interval kidney tumour resection (IRENE trial – an ablate-and-resect pilot study)

Authors:
Johann J. Wendler¹#, Maciej Pech²#, Frank Fischbach²#, Julian Jürgens²#, Björn Friebe²#, Daniel Baumunk⁶*, Markus Porsch⁵, Simon Blaschke¹, Daniel Schindele¹, Sandra Siedentopf³, Jens Ricke⁷#, Martin Schostak¹*, Jens Köllemann⁴**, Uwe B. Liehr¹#^

^The last two authors contributed equally to this work.

Affiliations:
Study group IRENE trial featured by AKFM-DGU* and DAfMT#, Germany.
¹Dept. of Urology, Otto von Guericke University of Magdeburg, Germany;
²Dept. of Radiology, Otto von Guericke University of Magdeburg, Germany;
³Dept. of Pathology, Otto von Guericke University of Magdeburg, Germany;
⁴Dept. of Pathology, Sana Medical Center Offenbach, Germany;
⁵Urological practice, Magdeburg, Germany;
⁶Urological practice, Stuttgart, Germany;
⁷Dept. of Radiology, Ludwig Maximilians University of Munich, Germany.

Contact information corresponding author:
Dr. med. Johann J. Wendler
Leipziger Str. 44, 39120 Magdeburg, Germany
Department of Urology, University of Magdeburg
Email: johann.wendler@med.ovgu.de
Fon: 00493916715036; Fax: 00493916715094

Abstract
**Objectives:** To assess the efficacy of irreversible electroporation (IRE) ablation of pT1a renal-cell carcinoma (RCC) in the first prospective, monocentric Phase 2a pilot ablate-and-resect study (IRENE trial). It has been postulated that focal IRE can bring about complete ablation of soft-tissue tumours with protection of healthy peritumoral tissue and anatomical structures.

**Methods:** The first seven study patients, with biopsy-proven pT1a RCC (15–39mm) underwent IRE. Percutaneous computed-tomography-guided IRE was performed with electrocardiographic triggering under general anaesthesia and deep muscle paralysis with 3–6 monopolar electrodes positioned within the renal tumour. 28 days later the tumour region was completely resected to confirm tumour destruction pathologically. Individual results for these patients are displayed, described and discussed.

**Results:** Technical feasibility was attained in all patients, but electrode placement and ablation were complex, with a mean overall procedure time of 129min. There were no major complications. Partial kidney resection was performed in five patients and, in two, radical nephrectomy because of central tumour location and ablation areas. Resections revealed by TNM classification no residual tumour as complete ablation in four cases (ypT0V0N0Pn0R0), and microscopic residual tumour cells as incomplete ablation in the other three (ypT1aV0N0Pn0R1).

**Conclusions:** Renal percutaneous IRE appears to be a safe treatment for pT1a RCC but requires substantial procedural effort. Resection specimens of the ablation zone revealed a high rate of microscopic incomplete ablation four weeks after IRE. According to these initial study results curative, kidney-sparing ablation of T1a RCC appears possible, but needs technical improvement to ensure complete ablation.
Key words
Irreversible electroporation, renal-cell carcinoma, kidney tumour resection, IRENE study.

1. Introduction

Focal therapy of small renal-cell carcinoma (RCC) has the goal to achieve total destruction of the tumour tissue with minimising the damage to the surroundings [1,2,21,25,26]. For irreversible electroporation (IRE), it has been postulated that complete ablation of soft-tissue tumours with protection of the healthy peritumoral tissue is possible [3,4,5,6]. IRE is mostly investigated for percutaneous ablation of prostate and pancreatic cancer, cholangiocarcinoma, hepatic and pulmonal malignancies and small renal masses. However, there is still a lack of clinical data for its application in renal cell carcinoma (RCC) [7,8,9,10,11]. Most IRE studies have been based on computed tomography (CT) or magnetic resonance (MR) radiological or inconsistent post-biopsy assessment only [10,11]. With this pilot ablate-and-resect study [12,9,30], we present detailed histopathological resection data of IRE-treated RCC to evaluate the ablation efficacy and accuracy of percutaneous focal IRE, in RCC, using the NanoKnife™ system.

2. Patients and methods

2.1 Study design and approval

This pilot study was planned to achieve histological data (primary objective) of percutaneous CT-guided IRE treated localized RCC followed by delayed ablation
zone resection four weeks after IRE (primary endpoint), according to previous animal swine studies of RCC in normal kidneys. The resection was performed to assess histological changes of the IRE ablation area within the tumour and the surrounded tissue (primary objective). The protocol of this GCP-compliant, prospective, monocentric, non-randomised, uncontrolled, non-blinded, single-arm Phase 2a interventional pilot study (“IRENE” – IRreversible Electroporation of kidney tumours before partial NephrEctomy; ClinicalTrials.gov NCT01967407 (10/2013), WHO ICTRP DRKS00004266) has been published separately [12]. Approval according to German medical product law (MPG) was granted by German Federal Institute for Drugs and Medical Devices (BfArM) [CIV-12-4-006021] and the Ethics Committee of Magdeburg University [73/2012]. Informed consent was obtained from all subjects in this study. The study was planned to include up to 20 patients with an interim analysis after the first ten recruited patients. According to plan, ten patients were recruited into the study. For two of these, the study biopsy showed that their disease was not RCC, so they were not IRE treated and were withdrawn from the study. A third patient could not be treated for technical reasons (persistent boot failure of the NanoKnife generator) and was also withdrawn before IRE.

2.2 Procedures

Before IRE treatment, CT-guided coaxial core biopsies were taken from all tumours for initial histological assessment and selection of patients. For IRE treatment, we used the NanoKnife™ IRE electroporator (AngioDynamics Inc., Latham, NY, USA; firmware V3.29, software V2.2.0.23) and NanoKnife™ monopolar probes (15 cm, 19G). The electrodes were positioned under CT guidance (Aquillion™ prime CT scanner, Toshiba Inc., Tustin, CA, USA) and on the basis of individual treatment-
planning data (ProcedureManager-2_2_0_23 for Windows™, AngioDynamics). Before each ablation a test run (10 pulses per electrode pair) was performed to determine conductivity. IRE (70–90µs, 450–1300 pulses per target, 1.8–3kV, 28–50A, at least two rounds per electrode pair) was performed with ECG triggering under general anaesthesia and deep muscle paralysis with 3–6 monopolar electrodes positioned within the renal tumour (see Table 1). Intraprocedural IRE modification was performed after immediate evaluation of post-IRE ablation graphs by interelectrode voltage modulation, separate electrode-pair ablation and IRE electrode placement [13,24]. After 28 days, open lumbar or transperitoneal resection of the complete ablation region (partial renal resection or nephrectomy if necessary) was performed, to allow better assessment of the organ and its surroundings.

### 2.3 Imaging

Contrast-enhanced, diffusion-weighted MRI (1.5T scanner, gadobutrol: 0.1ml/kg Gadovist 1.0mmol/ml; Bayer, Leverkusen, Germany) of the kidneys was carried out 1 day before and 2, 7 and 27 days after IRE. Contrast-enhanced sequences ‘arterial’, ‘portal-venous’, ‘venous’ and ‘urographic’ (late venous phase) were carried out (T1w-2D-GRE (Scout), T2w-SShTSE, T2w-FS-TSE, T2w-RT-TSE, DWI (b=0/500), T1w-GRE, T1w-FS-3DGRE transversal, T1w-FS-3DGRE coronal). Infiniti PACS software (INFINITT PACS, INFINITT Europe GmbH, Germany) was used for evaluation.

### 2.4 Histopathological analysis

The resection specimens were fixed in buffered 4% formaldehyde solution for at least 24h followed by complete sectioning of the ablation area including a border of macroscopically inconspicuous kidney tissue in 0.4cm-thick slices. The ablation area
was measured two-dimensionally. Thereafter, the specimens were completely embedded in paraffin in standard tissue cassettes after topographic assignment based on macrophotography. Each tissue block was used to prepare 3µm-thick sections, and these were stained with HE for morphological assessment in 500µm steps with one unstained section each for transmission microscopy. The extent of histologically demonstrable damage was determined by a regression grade (RG) [9]. Additional immunohistological staining of the tumour region with proliferation marker Mib1 (Dako; Santa Clara, CA, USA; dilution 1:100) at least still rudimentary basic structure was performed to determine viability or irreversible cell death. In each specimen, the complete ablation area, the tumour area and non-affected renal tissue on each slide was outlined manually. The maps from each subject were scanned with a digitising pad (Bamboo One™) using image-manipulation software (GIMP 2.8.14), inspected serially in the computer and the volume was determined; volume was calculated as the sum of tumour areas multiplied by the section thickness (0.4 cm) and by a factor of 1.5 to take account of formalin-induced tissue shrinkage.

3. Results

3.1 IRE treatment

Seven patients, who had biopsy-proven RCC pT1a cN0cM0 with a mean tumour size of 22mm (range 15–39mm), underwent lumbar percutaneous CT-guided IRE with the NanoKnife™ system (Table 1). In 6 patients one IRE ablation in one session and in 1 patient for 2 IRE ablations in one session (total, 8 ablations; Table 1) were performed. The mean planned IRE treatment zone was 17.3cm³ (8 ablations; range 8.2–45.6cm³). Because of the proximity between the kidney (and renal tumour) and
the adjoining colon, an expandable balloon was placed in between to move the colon out of the IRE ablation field, thus avoiding possible perforation. Technical feasibility was attained in all patients, but electrode placement and ablation was complex, with a mean overall procedure time of 129 min (range 53–203min) and an anaesthesia time of 165min (range 91–317min).

3.2 **MR imaging**

The analysis of the MRI of the tumour texture and renal parenchyma and its correlation to the histological results have to be published separately.

3.3 **Side effects**

There were no major or residual procedure-related complications. Minor complications included slight self-limiting gross hematuria (in 7/7 patients), perirenal haematomas (2/7) and temporary post-puncture pain, treated by drugs (7/7) – Clavien-Dindo grade I and II [27]. Renal function after IRE was retained in all cases, with no urinary leakage or retention, no renal infarction and no significant change in creatinine level. After a mean follow-up time of 25 months (range 15–36), no evidence of local recurrence or metastasis was seen.

3.4 **Resection and histological analysis**

Four weeks after IRE, a residual tumour contour within in the ablation area was macroscopically by MR imaging persistent in all cases, and was similar to the initial tumour size. Partial kidney resection was performed in 5 of the 7 patients. Two patients had a centrally located RCC adjacent to the hilum or renal pelvis (P3 and P5). Despite the relatively small tumour sizes, these two nephrectomies had to be
performed to obtain a complete resection of the tumour and ablation zone analogous to the study protocol, whereas the unfavourable location and central expansion near the hilum made a partial resection not feasible in surgeon’s indication. Intrasurgical examination at resection showed severe local perirenal/ peritumoral adhesions due to a local inflammatory unspecific reaction resulting from puncture and/or IRE. Complete macroscopic coverage of the tumour by the IRE ablation field was achieved in 100% of cases. In each of the seven cases investigated, IRE induced massive damage to the tumour tissue. Macroscopic analysis showed sharply demarcated, approximately ellipsoidal, haemorrhagically altered IRE ablation zones. The peritumoral damage zones had spread to peritumoral renal tissue and in some cases to perirenal fatty tissue. The ablation IRE zone was larger than expected in 3/7 cases.

Microscopic analysis showed the tumour focus within the ablation zone with strong treatment effects (regression grade III–IV; strongest effect = IV [9]) with almost complete tumour destruction by extended, homogeneously eosinophilic coagulation necrosis. Alongside the tumour-related histological changes, all cases showed zonal structuring of the ablation region, as described earlier in detail [9]. In the centre, an amorphous necrosis zone of the coagulation-necrosis type was seen. Next to this, there was a necrosis zone of variable width, also of the coagulation-necrosis type, in which ghost structures of the tissue affected could still be discerned (e.g. tubules, glomerules, fat). Some dystrophic areas of calcification and resorptive chronic-inflammatory changes could also be seen, sometimes with the formation of foreign-body giant cells. In sections where the ablation zone included the renal pelvis and papillae, both structures showed necrosis with urothelial sloughing and incipient regeneration. Adjacent to this zone, there was a gradual transition to a zone of
granulation tissue associated with frequent, in part luminal occlusive intimal hyperplasia of small- and medium-sized arterial renal vessels. Adjacent to this, unaffected renal parenchyma was found. Within or closed to the necrotic tumour only, a small focus of preserved residual tumour texture was detected in five of the seven patients. (Table 1). In three of these five cases the microscopic tumour texture residues showed only minor regressive changes (grade 3 of 4) with a mean volume of $0.11 \text{cm}^3$ (range 0.009–0.280). (Table 1). According to Mib-1 staining, it had proliferative activity in two of these three cases (ypT1a R1 according TNM classification) and intermediate or uncertain viability in the third (ypT0-1a R0-1 according TNM classification), (Table 1). [28;29]. One of these three cases showed intratumoral microscopic skip-lesions (in-field residual tumour) and in two of the three cases a microscopic tumour residue appeared at the edge of the ablation zone (out-of-field/field-margin residual tumour). According to the TNM classification, resection revealed ypT0V0N0Pn0R0 in four cases as complete ablation. In the other three due to microscopic residual tumour cells was found as incomplete ablation (Table 1) [28;29].

4. Discussion

Diehl et al. [10] treated 7 SRM (range 15-18 mm) with percutaneous IRE in 5 patients with a solitary kidney. A progressive, significant decrease in contrast-enhanced MR signal intensity of the ablated area was seen at follow-up, suggesting a treatment response rate of 100% at a mean follow-up of 6.4 months (range 3–11). The study was limited to an unknown SRM entity, and did not include histological evaluation after ablation [10].
Canvasser et al. [11] reported ‘suboptimal oncological efficacy’ and imaging features after IRE of 42 SRM (10-36 mm), observed by CT or MRI immediately, 6 weeks, 6 months and 12 months after percutaneous IRE ablation. CT/MR imaging after IRE ablation demonstrated an area of non-enhancement in the treatment zone that became involuted over about 6 months. Three cases showed incomplete ablation with a margin of residual enhancing tumour consistent with viable malignancy; the patients proceeded to salvage therapy. One patient showed local recurrence after one year. This study was limited to a mixed entity of malignant (20 RCC) and benign or unknown SRMs; no histological evaluation after ablation was performed [11].

In contrast to these studies we present the first results of resection following IRE of human biopsy-proven pT1a RCC [23]. These histologies represented “snapshots” taken four weeks after IRE, with procedure-specific findings. The histological remodeling process of necrosis, vessels and inflammation of the ablated area seemed to be not completed. Previous animal studies of renal IRE in healthy swine suggested a favourable follow-up of 4 weeks, although knowing to have no tumour model [5;6]. On that concept this subsequent clinical pilot study in human RCC was based. Although the choice of a different interval between IRE and histological analysis could of course influence this result, the optimum interval between IRE and histological assessment is at present still unclear.

In the context of initial results it was discussed whether the basic histological structures of papillary and cystic RCC cause incomplete ablation due to reduced tissue connectivity and homogeneity [9]. Nevertheless, the results presented here demonstrate complete ablation of 1/2 papillary and 1/1 cystic clear-cell RCC, so that no conclusion of different IRE ablation responses for specific RCC subtypes can be drawn.
Complete coverage of the tumour by the IRE ablation field was possible, but microscopic residual tumour areas could be found in 3/7 cases. The ablation quality and success with a homogenous, complete IRE ablation with no in-field or out-of-field residual tumour areas could not be predicted certainly. On the basis of this initial analysis, we conclude that complete ablation of T1a RCC in different locations, and renal preservation also in case of centrally located tumours, is possible with IRE. The nephrectomy was performed in the 2 cases because of central tumour location and ablation areas. As opposed to this, these two patients revealed a functional kidney after central IRE ablation that would not have required nephrectomy out of the study protocol. Our study demonstrated that IRE might be useful for ablation of centrally located renal tumours showing severe tumour destruction with protection or regeneration of the urine-collecting system [30]. This fact may point out the advantage of IRE application over surgical resection and thermal ablation techniques in centrally located kidney tumours.

The rate of residual tumour or incomplete ablation is also dependent on the follow-up tool. Resection histology may evaluate microscopic cancer cell areas more effective and therefore in a higher rate than imaging, especially in specimen with remodelling process after ablation. The issue of residual tumour cells is common to all ablation and radiation methods and not specific for IRE [19,20,22,26]. It should be considered that IRE studies with imaging and biopsy control only may fail to detect microscopic tumour residues or recurrences [19,20,22]. That fact may explain the higher rate of microscopic incomplete ablation of 43% in our study. However, the ablation success is also dependent on the ablation technique and its feasibility. Despite that, each of the known ablation modalities has a unique working principle and biophysics underlying the ablative effect, which largely determines the clinical indication for its
application and the specific histological presentation [31]. Similarly, after radio-
frequency ablation (RFA) residual tumour areas are seen that possess a residual
viability immediately and one week after ablation [16,17]. The primary ablation
success of RFA and cryoablation (CA) of SRM is about 90-100% depending from the
tumour size and location. Several studies reported a local recurrence rate of pT1a
RCC between 2-12% for RFA and 3-17% for CA within the first 5 years [21,32]. Small
case studies of laparoscopic HIFU of SRM showed incomplete ablation between 42-
75 % in resection specimen [21,32]. Following IRE of liver tumours, for comparison,
29% showed recurrent tumour after six months [18].

Meta-analyses of patients with positive surgical margin after nephron-sparing surgery
of RCC have suggested that small tumour residues lack prognostic relevance [14,15].
Therefore, a surveillance strategy seems preferable to surgical or ablative re-
intervention. That fact is also based on the known low progression rate of 0.13
cm/year and low dissemination rate of 1.1 % for pT1a RCC [33]. Finally, the detection
of residual tumour or local recurrence after ablation offers the possibility of a
repetition of the ablation. Microscopic, dubious tumour residues remaining in the non-
viable ablation region four weeks after IRE must be assessed in the light of this.

According to these study experiences, the intended curative IRE ablation of located
RCC sized below 4cm is feasible, but makes a high procedural demand (especially
the aimed CT-guided IRE electrode placement and the intra-interventional 2D
treatment planning control) and was not reliable reproducible. Maybe, the application
of MR imaging usable IRE electrodes, a combination of 3D-navigated IRE electrode
placement and treatment planning of IRE, as well as the development of clinical
applicable high frequency IRE (HF-IRE) for muscle relaxation-free and anaesthesia-
free IRE ablation could adopt a broadly utilization.
Limitations

The strength of our pilot study according to German medical product law (MPG) was to obtain first histological resection analyses of the IRE tumour ablated area of biopsy-proven renal cell carcinoma in all patients. But the procedures in this study place a substantial burden on the patients, because of the two-stage intervention principle, with general anaesthesia for IRE ablation and again for delayed resection. Moreover, the specimens had to be obtained by open surgery. A factor that also made it difficult to recruit a larger patient collective. Hence, our study is limited statistically by the small number of patients. The results do not lead to a recommendation of specific changes in IRE ablation parameters. Finally, it does not seem likely that further recruitment, to reach the originally planned total of 20 patients, would lead to different results, so that termination of the study is under consideration.

5. Conclusions

According to these limited and initial study results, renal percutaneous IRE using the NanoKnife appears to be a safe treatment for small renal masses (SRM), including centrally located tumours with kidney preservation. The intended curative IRE ablation of located RCC sized below 4cm may be feasible, but makes a high procedural demand and was inconstant and not reliable reproducible. We observed by histological resection analysis a high rate 43% of microscopic residual cancer cells within the IRE ablation zone in a short follow-up setting of 4 weeks. Percutaneous NanoKnife IRE still needs further technical improvement and evaluation in trials to ensure complete ablation by this still experimental and not reliable method. It needs
to be improved before offering it to patients as an option for cure. Larger studies of renal IRE of biopsy-proven RCC pT1a with MR imaging and biopsy follow-up according to current recommendations are needed, to draw consistent conclusions [22].

**Compliance with ethical standards**

The authors declare that they have no conflict of interest. All procedures performed and the conduct of the study as a whole were in accordance with the 1964 Helsinki declaration and its later amendments and comparable ethical standards.

**References**


**Figure 1:** Patient 6 – example of incomplete ablation: (a), Initial MRI representation of the tumour before IRE: cortical RCC with 2.4 cm from the ventrolateral lower pole to mid-level of the right kidney, imaged by MRI before IRE. (b) NanoKnife IRE planning and representation of the calculated ablation zone (red-brown) in relation to the tumour (yellow). (c) Computer-tomographic 2D transversal representation of the IRE electrodes in the kidney tumour: (d) MRI representation of the tumour 27 days after IRE. (e) Partial kidney resection with macroscopic tumour contour 28 days after IRE, fixed and cut open. (f) A microscopic tumour residue at the edge of the tumour (solid blue area) resulting from incomplete coverage of the tumour in ablation (blue-hatched area) and the ablation zone (violet line). (h) Viable microscopic tumour residue (dashed line with #) in the edge zone of the ablation area (out-field) with fibrotic peritumoral border (area § between the solid lines) and bordering, completely necrotic tumour (asterisk). (i) Viable tumour residue marked by Pancytokeratin antibodies AE1/AE3 (arrows).

**Figure 2:** Patient 7 - example of complete ablation: (a) Initial MRI representation of the tumour: cortical RCC 1.8 cm from the lower pole dorsomedical to the left kidney, before IRE. (b) NanoKnife IRE planning and representation of the calculated ablation zone (red-brown) in relation to the tumour (yellow). (c) Computer-tomographic 2D transversal representation of the IRE electrodes in the kidney tumour (d) MRI representation of the tumour 27 days after IRE. (e) Partial kidney resection with tumour contour 28 days after IRE, fixed and cut open, with tumour contour (#), peritumoral ablation zone (asterisk) and healthy parenchyma outside the ablation zone. (f) Complete ablation without microscopic tumour residue (blue-hatched area) in the ablation zone (violet line). (g) The border (black line) between completely
necrotic tumour (#) and necrotic tumour-free parenchyma (asterisk), seen by HE staining. (h) Magnified detail of completely necrotic tubules (§) and a non-viable glomerule (asterisk) from the ablation zone. (i) For comparison, unchanged viable parenchyma (glomerule and tubules) in the adjacent tissue. (j) Vessel with fresh, partly organised thrombus (asterisk) from the edge zone of the necrosis.
Tab.1: Patient, treatment and resection parameters.

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<td>3 / 3</td>
<td>triangular</td>
<td>4 / 6</td>
<td>square</td>
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<tr>
<td>Tip exposure</td>
<td>2.5 cm</td>
<td>1.5 cm</td>
<td>2.0 cm</td>
<td>2.0 cm</td>
<td>2.0 and 2.5 cm (pull-back)</td>
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<td></td>
<td>Planned treatment zone (cm) / (cm³)</td>
<td>2.4 x 2.9 x 3.5 / 12.7</td>
<td>2.5 x 2.5 x 8.2</td>
<td>3.5 x 4.0 x 22.0</td>
<td>3.0 x 3.0 x 2.9 / 13.7</td>
<td>2.7 x 2.7 x 10.3 and 4.4 x 4.4 x 4.5 / 45.6</td>
<td>3.0 x 3.3 x 15.6</td>
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<tr>
<td></td>
<td>Pulse length</td>
<td>90 µs</td>
<td>90 µs</td>
<td>90 µs</td>
<td>90 µs</td>
<td>70, 80, 90 µs</td>
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<td>Pulses</td>
<td>1300</td>
<td>450</td>
<td>1320</td>
<td>840</td>
<td>570 + 880</td>
<td>450</td>
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<tr>
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<td>Current min./max.</td>
<td>30 / 49 A</td>
<td>30 / 42 A</td>
<td>30 / 49 A</td>
<td>25 / 49 A</td>
<td>22 / 50 A</td>
<td>28 / 50 A</td>
</tr>
<tr>
<td></td>
<td>Voltage min./max.</td>
<td>1800 / 2800 V</td>
<td>2200 / 2640 V</td>
<td>1960 / 3000 V</td>
<td>2160 / 3000 V</td>
<td>1800 / 2800 V</td>
<td>1850 / 2600 V</td>
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<tr>
<td></td>
<td>Intervention / Anaesthesia</td>
<td>131 / 193 min</td>
<td>126 / 162 min</td>
<td>163 / 208 min</td>
<td>123 / 194 min</td>
<td>203 / 317 min</td>
<td>53 / 91 min</td>
</tr>
<tr>
<td>Surgery</td>
<td>P1</td>
<td>P2</td>
<td>P3</td>
<td>P4</td>
<td>P5</td>
<td>P6</td>
<td>P7</td>
</tr>
<tr>
<td></td>
<td>Initial / presurgical eGFR</td>
<td>107 / 106 ml/min</td>
<td>86 / 88 ml/min</td>
<td>70 / 73 ml/min</td>
<td>67 / 63 ml/min</td>
<td>78 / 72 ml/min</td>
<td>48 / 47 ml/min</td>
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<tr>
<td></td>
<td>Resection type;</td>
<td>Partial</td>
<td>Partial</td>
<td>Nephrectomy;</td>
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<td>Partial</td>
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<table>
<thead>
<tr>
<th>access</th>
<th>resection; open lumbar</th>
<th>resection; open lumbar</th>
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<th>resection; open abdominal</th>
<th>open lumbar</th>
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<tbody>
<tr>
<td>Surgery / Ischaemia</td>
<td>185 / 16 min</td>
<td>175 / 19 min</td>
<td>115 / 0 min</td>
<td>190 / 18 min</td>
<td>130 / 0 min</td>
<td>140 / 21 min</td>
<td>185 / 35 min</td>
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<tr>
<td>Pathology</td>
<td>P1</td>
<td>P2</td>
<td>P3</td>
<td>P4</td>
<td>P5</td>
<td>P6</td>
<td>P7</td>
</tr>
<tr>
<td>Ablation zone (cm) / (cm³)</td>
<td>2.5 × 2.0 × 1.3 / 3.4</td>
<td>3.0 × 2.5 × 2.0 / 7.9</td>
<td>4.2 × 1.4 × 1.2 / 17.2</td>
<td>2.8 × 2.2 × 2.0 / 3.5</td>
<td>4.2 × 2.8 × 3.5 / 19.2</td>
<td>2.9 × 2.5 × 3.5 / 4.5</td>
<td>4.6 × 2.2 × 3.0 / 8.4</td>
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<tr>
<td>Tumour shape (cm) / (cm³)</td>
<td>1.6 × 1.5 × 1.2 / 1.6</td>
<td>1.6 × 1.7 × 1.1 / 1.6</td>
<td>1.5 × 1.4 × 1.2 / 1.3</td>
<td>1.2 × 0.8 × 1.0 / 0.2</td>
<td>3.0 × 2.4 × 4.0 / 9.7</td>
<td>3.0 × 2.2 × 2.0 / 2.0</td>
<td>1.3 × 1.2 × 1.0 / 0.2</td>
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<td>complete</td>
<td>complete</td>
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<tr>
<td>Residual ablated tumour texture</td>
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<td>0.045 cm³; in-field</td>
<td>1.185 cm³; in-field</td>
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<td>0.009 cm³; out-field/margin</td>
<td>0.03 cm³; out-field/margin</td>
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<td>Regression</td>
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<td>0 %</td>
<td>0 %</td>
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<td>1 %</td>
<td>1 %</td>
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<td>uncertain</td>
<td>non-viable</td>
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<td>non-viable</td>
<td>viable</td>
<td>viable</td>
<td>non-viable</td>
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<tr>
<td>TNM (IRE)</td>
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<td>complete, ypT0 V0 L0 Pn0 R0</td>
<td>complete, ypT0 V0 L0 Pn0 R0</td>
<td>complete, ypT1a V0 L0 Pn0 R1</td>
<td>incomplete, ypT1a V0 L0 Pn0 R0</td>
<td>complete, ypT1a V0 L0 Pn0 R1</td>
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<td>TNM (OP)</td>
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<td>R0</td>
<td>R0</td>
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<td>R0</td>
<td>R0</td>
<td>R0</td>
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</tbody>
</table>

UP, upper pole; MP, mid-pole, LP, lower pole; cc, clear-cell. Active tip (exposure) plus postulated ablation field in depth 2 × 0.5 cm. Volumes are calculated for ellipsoidal tumour: \( V = \frac{4}{3} \pi a \times b \times c. \)