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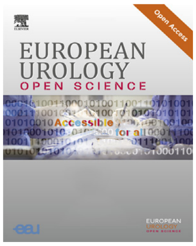

Surgery in Motion: Open Science

Robot-assisted Partial Nephrectomy Using Intra-arterial Renal Hypothermia for Highly Complex Endophytic or Hilar Tumors: Case Series and Description of Surgical Technique

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Abstract

Background: In partial nephrectomy for highly complex tumors with expected long ischemia time, renal hypothermia can be used to minimize ischemic parenchymal damage.

Objective: To describe our case series, surgical technique, and early outcomes for robot-assisted partial nephrectomy (RAPN) using intra-arterial cold perfusion through arteriotomy.

Design, setting, and participants: A retrospective analysis was conducted of ten patients with renal tumors (PADUA score 9–13) undergoing RAPN between March 2020 and March 2023 with intra-arterial cooling because of expected arterial clamping times longer than 25 min.

Surgical procedure: Multiport transperitoneal RAPN with full renal mobilization and arterial, venous, and ureteral clamping was performed. After arteriotomy and venotomy, 4°C heparinized saline is administered intravascular through a Fogarty catheter to maintain renal hypothermia while performing RAPN.

Measurements: Demographic data, renal function, console and ischemia times, surgical margin status, hospital stay, estimated blood loss, and complications were analyzed.

Results and limitations: The median warm and cold ischemia times were 4 min (interquartile range [IQR] 3–7 min) and 60 min (IQR 33–75 min), respectively. The median rewarming ischemia time was 10.5 min (IQR 6.5–23.75 min). The median pre- and postoperative estimated glomerular filtration rate values at least 1 mo after surgery were 90 ml/min (IQR 78.35–90 ml/min) and 86.9 ml/min (IQR

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62.08–90 ml/min), respectively. Limitations include small cohort size and short median follow-up (13 [IQR 9.1–32.4] mo).

Conclusions: We demonstrate the feasibility and first case series for RAPN using intra-arterial renal hypothermia through arteriotomy. This approach broadens the scope for minimal invasive nephron-sparing surgery in highly complex renal masses.

Patient summary: We demonstrate a minimally invasive surgical technique that reduces kidney infarction during complex kidney tumor removal where surrounding healthy kidney tissue is spared. The technique entails arterial cold fluid irrigation, which temporarily decreases renal metabolism and allows more kidneys to be salvaged.

1. Introduction

If technically feasible, nephron-sparing surgery through partial nephrectomy (PN) is the standard treatment for fit patients with T1-T2 renal masses [1]. The main goals of PN include complete tumor excision and minimal injury to the healthy renal parenchyma, while avoiding complications [2].

Robot-assisted PN (RAPN) has increasingly been adopted as it allows safe tumor resection and kidney reconstruction with similar oncological outcome and less morbidity for the patient than open surgery [3]. The main predictors for postoperative kidney function include the patients' preoperative kidney function, preserved renal parenchyma volume, and warm ischemia time. Classically, maximal warm ischemia times of 20–25 min are targeted [4–8]. Recent high-level evidence has also shown that the clinical impact of warm ischemia time is futile when staying below these thresholds [9]. However, Antonelli et al [10] found statistically significant renal function impairment on renal scintigraphy at 6 mo postoperatively when clamping times exceeded 10 min. This indicates that, at least in the first 6 mo, warm ischemia negatively influences renal metabolism and function. Nonetheless, the effect is subclinical and not noticeable while assessing global renal function with a healthy baseline renal function and normal contralateral kidney.

In highly complex cases such as completely endophytic, hilar, or multiple unilateral tumors, clamping time during PN may easily exceed the 25 min threshold, which may induce chronic kidney disease.

Several studies have investigated different renal hypothermia application methods. In open PN, ice slush can be positioned around the kidney. In minimally invasive surgery (apart from kidney transplantation [11]), ice slush application is rather cumbersome and therefore not widely adopted [5,12–14]. Alternative cooling techniques have been described for laparoscopic PN, including cold saline surface irrigation [15], ureteral retrograde cooling [16], and intra-arterial perfusion [17,18]. Little evidence exists comparing different cooling techniques with no clear superior method [19]. Marberger and Eisenberger [20] reported better postoperative GFR outcomes using intra-arterial cooling (IAC) than an ice slush technique. The advantages of the intra-arterial approach for renal hypothermia include a rapid, stable, and homogenous decrease in kidney temperature; removal of any blood left in the kidney; prevention of intravascular coagulation; and improvement of intraoperative visibility [21,22].

Both Marberger and Eisenberger [20] and Liu et al [18] used an endovascular femoral access with catheterization of the renal artery by an interventional radiologist. Femoral intra-arterial access before abdominal surgery is time consuming and logistically demanding, and requires intrarenal administration of nephrotoxic contrast agents. Alternatively, the renal artery and vein can be incised and catheterized transperitoneally during surgery. This technique has been described by Gschwend et al [23] and Steffens et al [22] in open surgery, by Simon et al [24] laparoscopically in a porcine model, and by Herrmann et al [25] laparoscopically in two patients. Previously, we successfully used this

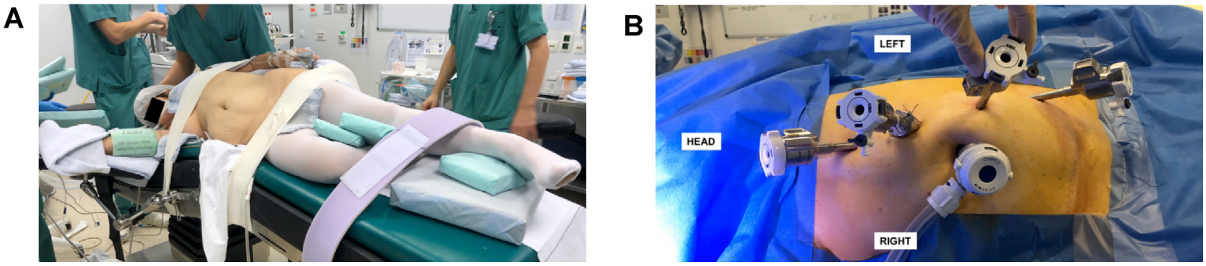

Fig. 1 – Patient positioning and trocar placement for RAPN with intra-arterial cooling. (A) Standard patient positioning for a left-sided procedure, with the patient positioned in the right lateral flank position, strapped to the operating table at the thoracic and ischial level. Extraposterior support is placed at the pelvic level and underneath the ipsilateral scapula. Special care is taken for head positioning as well as to avoid traction on the brachial plexus. (B) Trocar placement for the same left-sided procedure. Camera ports were inserted using the Hasson [38] technique. Other ports were inserted under direct vision.

technique for establishing cold ischemia in total intracorporeal robot-assisted kidney autotransplantation (tiRAKAT) [26,27].

Here, we describe our initial experience of applying transperitoneal intra-arterial renal cooling using arteriotomy during RAPN for highly complex small renal masses. We provide a step-by-step description of our technique. To our best knowledge, this is the first patient series of robotic transperitoneal IAC for localized kidney cancer.

2. Patients and methods

2.1. *Design, setting, and participants*

This study focused on patients treated with intra-arterial renal hypothermia between March 2020 and March 2023 in three different tertiary setting hospitals.

Ten patients were treated for complex renal tumors (PADUA 9–13) through RAPN. All cases were referred as second to fourth opinion and previously advised for radical nephrectomy as clamping times above 25 min were to be expected.

Apart from radical nephrectomy, the following other therapies were considered: active surveillance, radiofrequency ablation, open PN with cold ischemia, and autotransplantation with ex vivo tumor resection [28].

None of the patients preferred active surveillance. Radiofrequency ablation was not pursued either due to risk of vascular injury given the hilar or endophytic tumor location, as well as the possible risk of a heat sink effect, or due to too large a tumor mass. Classical PN with full arterial clamping was discarded due to expected prolonged clamping times well exceeding 25 min [29].

Patients were deemed eligible for RAPN with IAC when they had a single renal artery, without early branching or abundant arterial calcifications on the anticipated position of the arteriotomy. Given the anatomical complexity, virtual three-dimensional (3D) models were created by segmenting arteries, veins, parenchyma, tumor, and possible cysts using Mimics Innovation Suite (Materialise, Leuven, Belgium) in a systematic 3D model–making method [30].

All surgeries were performed using the Intuitive Xi platform (Intuitive Surgical, Sunnyvale, CA, USA). The technique was initiated and performed in eight cases by a highly experienced robotic and renal transplant surgeon (K.D., 843 robotic procedures, including 42 R[A]KAT and 297 RAPN cases) [31]. Subsequently, a second experienced robotic surgeon (T.Q., 1386 robotic procedures including 249 RAPN cases) performed one case while proctored by the former surgeon (K.D.) and a subsequent case independently.

2.2. *Surgical procedure*

2.2.1. *Patient positioning*

Patients were positioned in our standard setup for RAPN as depicted in Figure 1A, with port placement as depicted in Figure 1B. All procedures were performed under low pneumoperitoneum pressure of 8 mmHg, using AirSeal (ConMed Corp, Utica, NY, USA) [32].

2.2.2. *Hilar dissection*

After reclining the descending colon (for left RAPN) or performing Kocher's maneuver (for right RAPN), Gerota's fascia is incised and the renal artery and vein are identified, mobilized, and wrapped with vessel loops. The kidney capsula is exposed, and the kidney is entirely mobilized until it is attached only through the hilum. Incomplete mobilization may cause residual arterial or venous flow into the kidney through small collateral branches, compromising effective cooling and a bloodless tumor enucleation. Fatty tissue in the "golden triangle" between the ureter, the lower pole of the kidney, and the hilum is maintained to protect vascular supply to the proximal ureter (Fig. 2A) [33]. The left gonadal vein and/or adrenal vein is clipped when necessary. In case of endophytic lesions, the tumor is delineated through robotic drop-in ultrasound assistance (BK Medical, Burlington, MA, USA). For completely endophytic tumors, the course of renal vessels and the urinary collecting system is taken into account to identify the most practical and safest access. The 3D model is visualized through the TilePro window (Intuitive Surgical) to assist as depicted in Figure 2B or overlaid through augmented reality [34].

2.2.3. *Intra-arterial cooling*

A thru-lumen Fogarty catheter (Edwards Lifesciences, Irvine, California, USA) is inserted transcutaneously into the abdominal cavity using the Seldinger technique [35]. Bulldog clamps and sutures for renorrhaphy are introduced intracorporeally to minimize ischemia times.

Bulldog clamps are placed on the renal artery, on the renal vein, and on the proximal ureter and its vascular sheath. Renal arterial clamping initiates the warm ischemia time. Ureteral and venous clamping is performed to avoid venous backflow, which also occurs through the ureteral golden triangle.

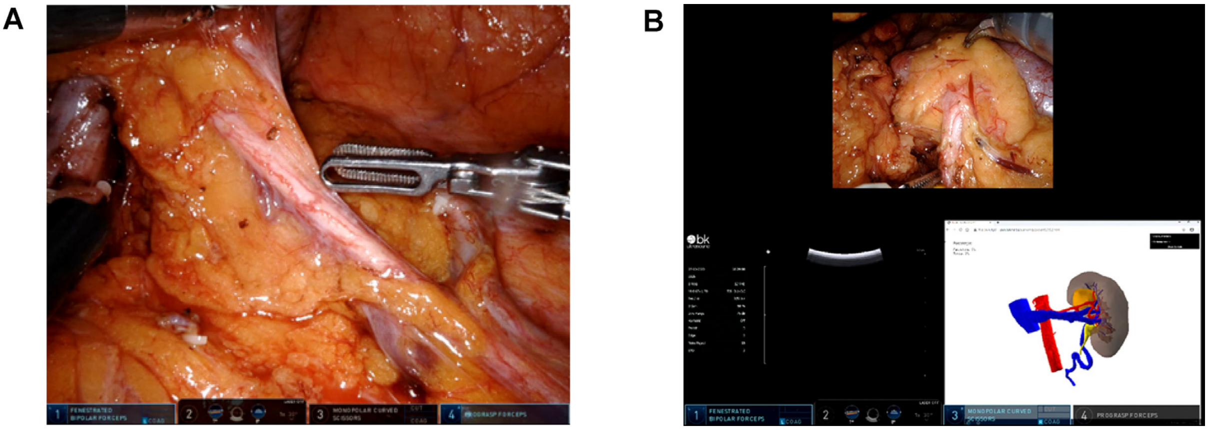

Fig. 2 – Complete kidney mobilization and tumor identification. (A) Retained fatty tissue to preserve ureteral perfusion. (B) Integration of the three-dimensional model into the operative flow to help in tumor delineation and surgical approach.

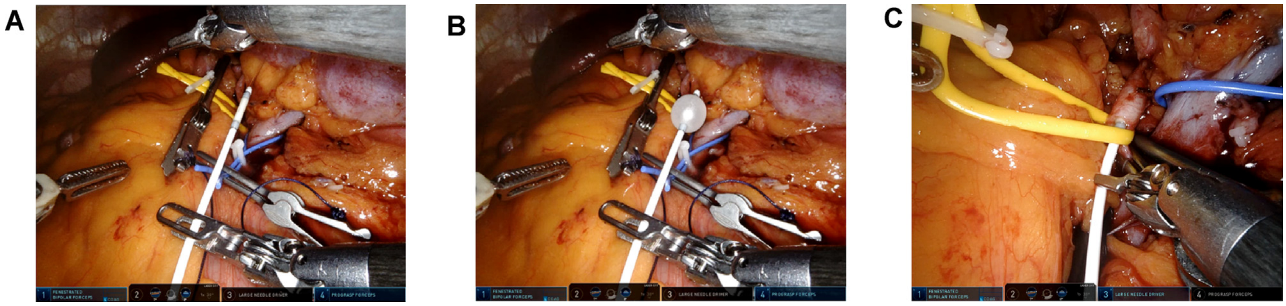

Fig. 3 – Transcutaneous introduction and catheterization of 6 Fr Fogarty thru-lumen catheter. The catheter is tested for functionality (A) by flushing and (B) by inflation before commencing the arteriotomy and (C) inserting the catheter to administer heparinized sodium chloride.

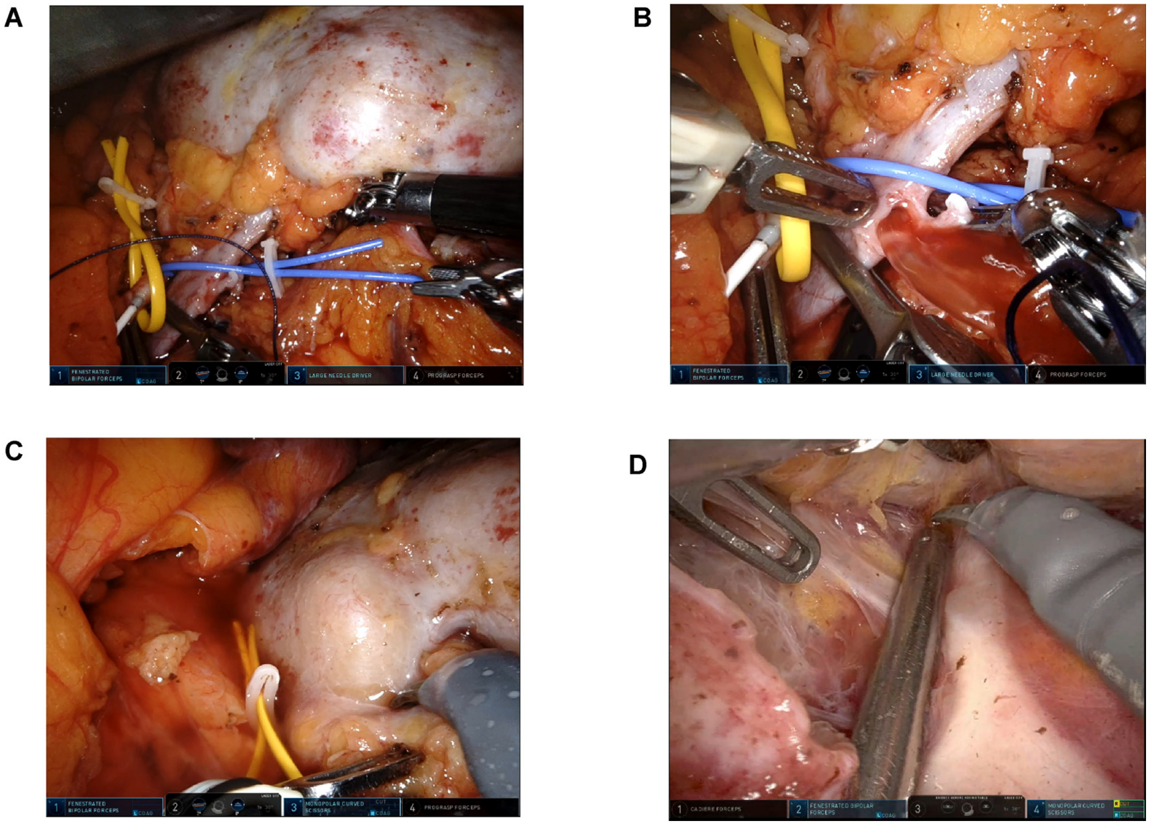

Fig. 4 – Application of intra-arterial cooling through arteriotomy. (A) Pale kidney after flushing with heparinized saline at 4°C. (B) Clear effluent from the renal venotomy, which implies that switching to nonheparinized saline at 4°C is possible. (C) How the tumor gently delineates itself from the underlying tissue due to a more yellowish appearance is depicted here. (D) How ureteral clamping facilitates tumor dissection and enucleation is demonstrated here. The temporarily hydronephrotic renal calyces are better objectifiable, as can be seen on the right side of the suction device. The tip of the suction is compressing a minor calyx on its left side.

Renal artery and vein are incised using Pott's scissors. On the left, the gonadal vein can also be incised instead. Figure 3 depicts the testing of the Fogarty catheter before arteriotomy and subsequent arterial introduction. The 4–6 Fr Fogarty catheter is inserted into the renal artery and inflated with just enough saline (usually 0.1 or 0.2 ml) to block the catheter in the arterial lumen but avoiding intima rupture. Pulling the arterial vessel loop can further help prevent backflow from the arteriotomy. A 4°C heparinized isotonic saline solution (10 IU/ml) is injected, which initiates the cold ischemia time. The heparinized solution should prevent or dissolve possible intrarenal microthrombi. Following the cooling administration, the kidney usually decolors rapidly. Proper cold ischemia is achieved when observing clear effluent from the incised renal vein (Fig. 4A and 4B). The effluent was aspirated continuously, and its temperature was measured at 20°C during the first cases [26].

2.2.4. *Tumor enucleation and renorrhaphy*

Once cold ischemia is in place, the cooling solution is switched to a nonheparinized 4°C saline solution and tumor enucleation is started. Tumor enucleation is facilitated due to the color difference between healthy parenchyma and the lesion (Fig. 4C). Apart from backflow, ureteral clamping can also assist in tumor enucleation and recognition of the collecting system (injury) due to the temporary ensuing hydronephrosis (Fig. 4D).

After resection, the tumor specimen is inspected and placed in an endobag for removal. The tumor bed is inspected, and any significant leaking vessels are selectively sutured with a Prolene 5/0 suture. Opened urinary collecting system is closed with a running PDS 5/0 suture (Ethicon Inc., Johnson & Johnson Corp, Cincinnati, OH, USA). This is followed by a classic internal renorrhaphy using Monocryl 3/0 suture and external renorrhaphy using Vicryl 1 suture with the sliding hem-o-lok technique [36]. In hilar tumors, adjacent vessels may impede proper renorrhaphy. In these cases, the kidney defect is filled with a Surgifoam absorbable gelatin sponge that is compressed and tied inside a Surgicel absorbable hemostat (Ethicon Inc., Johnson & Johnson Corp). It is held in place by one or two overlying sutures in the kidney parenchyma.

2.2.5. *Reperfusion*

After renorrhaphy, the cooling perfusion is stopped, initiating rewarming ischemia time. The incisions on the renal artery and vein are closed using a running Gore-Tex 6-0 suture (W.L. Gore and Associates Inc., Flagstaff, AZ, USA). Before final closure, the vessels are vented with a heparinized saline solution. Bulldog clamps are removed from the ureter, vein, and artery in this order. The kidney is reperfused, and the resection zone is inspected once more for hemostasis. Additional external renorrhaphy sutures or hemostatic agent application may be performed. The global renal parenchymal reperfusion and turgor is assessed and double checked using intravenous indocyanine green (ICG) administration through near infra-red fluorescence technology (Firefly; Intuitive Surgical) and through the robotic drop-in ultrasound probe.

After specimen extraction and incision closure, a single abdominal drain is placed and removed on the first postoperative day if no urinary leakage or abundant bleeding is present.

2.2.6. *Postoperative evaluation*

Postoperative renal monitoring was performed for the first cases through renal ultrasound. This ultrasound assessed proper revascularization and was performed in the postanesthesia recovery unit. Thromboembolic prophylactic stockings are applied perioperatively and continued until the patient is completely ambulatory. Low-molecular-weight heparin is administered in prophylactic dosage starting 8 h postoperatively and continued during 10–20 d depending on the patient's risk of thromboembolic events. The patient is mobilized on the 1st postoperative day and is discharged when he or she is pain free and self-reliant.

During follow-up, kidney function was assessed through estimated glomerular filtration rate (eGFR) and creatinine levels.

3. Results

Figure 5 depicts the 3D models of all cases.

Table 1 depicts patient demographics and surgical outcomes. We generally note stable kidney function, with one significant drop for patient 8 who was converted to radical nephrectomy.

The median warm ischemia time (time between clamping and initiation of saline irrigation) was 4 min (interquartile range [IQR] 3–7 min). The median cold ischemia time was 60 min (IQR 33–75 min). The median rewarming ischemia time was 10.5 min (IQR 6.5–23.75 min). The median hemoglobin drop on the 1st postoperative day was 2.7 g/dl (IQR 2.7–3.3 g/dl). The median length of stay was 4 d (IQR 4–4 d). The median preoperative eGFR and serum creatinine levels were 90 ml/min (IQR 78.35–90 ml/min) and 0.79 mg/dl (IQR 0.69–1.00 mg/dl), respectively. The median postoperative eGFR and serum creatinine levels were, respectively, 75.95 ml/min (IQR 54.7–87.2 ml/min) and 0.89 mg/dl (IQR 0.82–1.20 mg/dl) on postoperative day 1, and 86.8 ml/min (IQR 57.1–90 ml/min) and 0.81 mg/dl (IQR 0.71–1.06 mg/dl) during follow-up of at least 1 mo after surgery. When pooling renal function (eGFR) of the eight cases that had a contralateral healthy kidney in situ, the mean eGFR decreased from 87.68 to 83.49 ml/min during follow-up of at least 1 mo, where for the two single kidney cases, the mean eGFR even increased from 42.0 to 45.65 ml/min.

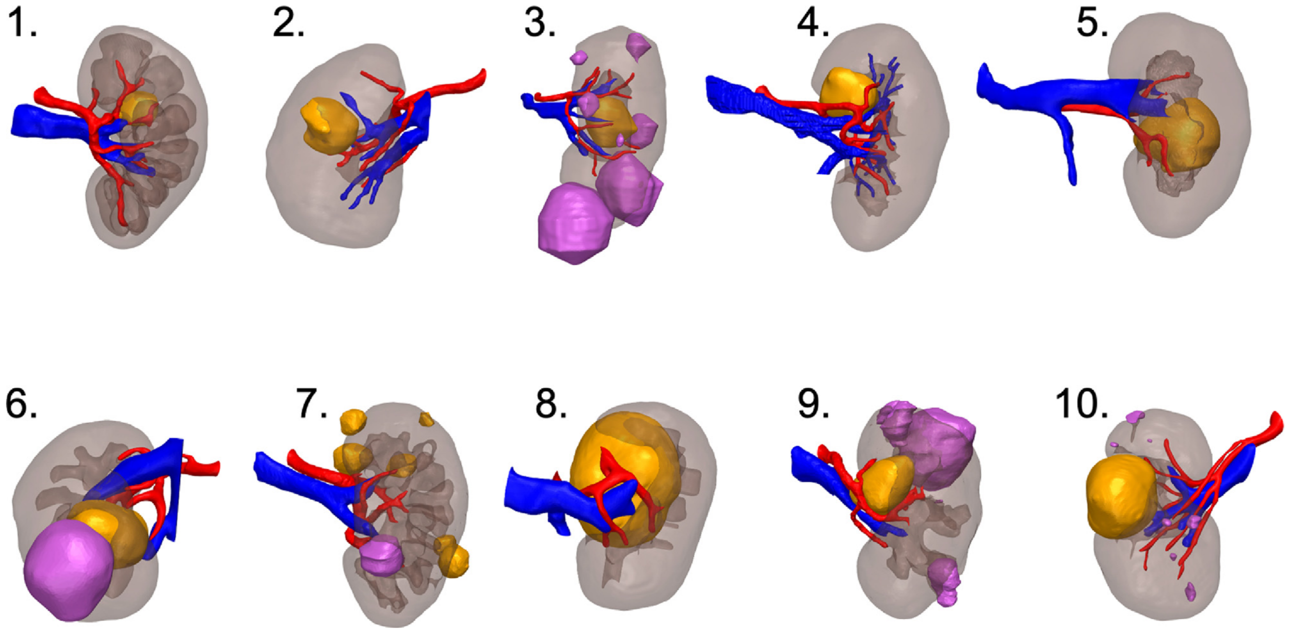

Fig. 5 – Overview of the different renal lesions with corresponding patient number (Table 1). Tumors are depicted in orange, renal cysts in purple, the arterial tree in red, and the venous tree in blue. All arteries and veins were truncated at the respective levels of the aorta and vena cava. Case 10 depicts the anatomy after cytoreduction through neoadjuvant therapy.

Table 1 – Patient characteristics for intra-arterial RAPN cases[a]

Patient number	1	2	3	4	5	6	7	8	9	10
Gender	F	F	F	F	M	F	M	F	F	F
Age (yr)	29	49	66	58	44	54	58	49	70	57
BMI (kg/m^2)	19.04	26.16	22.79	23.94	23.77	26	28.7	24.5	31.4	21,9
Indication	DE	DE	IH	IH	DE	DE	6 lesions, including 1 DE	DE + IH	IH + nonfunctional contralateral kidney	Partially endophytic lesion in solitary kidney
Side	L	R	L	L	L	R	L	L	L	R
LS (mm)	15	26	35	31	51	67	T1 = 19 T2 = 13 T3 = 18 T4 = 13 T5 = 8 T6 = 14	80	41	43
PADUA score	12	11	12	10	13	13	T1 = 7 T2 = 7 T3 = 6 T4 = 6 T5 = 6 T6= 9 AVG = 7	13	9	11
CT (min)	180	190	300	180	306	216	259	254	153	330
Warm ischemia time (min)	4	4	4	3	2	3	4	9	13	8
Cold ischemia time (min)	32	23	65	36	72	96	55	76	24	81
Rewarming ischemia time (min)	40	23	24	24	10	11	5	5	6	8
Number of calyces opened during UCS repair	1	2	None	None	2	2	1	3	1	3
Hemostatic agent	Surgicel at hilus	None	Surgifoam + Surgicel fibrillar	TachoSil	Spongostan + Surgicel at hilus	Floseal	Floseal	TachoSil	Floseal	None
EBL (ml)	150	130	600	100	300	200	400	1200	200	800
Hb drop postop day 1 (g/dl)	–2.2	–0.2	–4.0	–1.4	–3	–3.3	–2.7	–4.2	–2.4	4.6
Histotype	Reninoma	ccRCC	OCC	OCC	ccRCC	ccRCC	pRCC	chRCC	chRCC	ccRCC
pT	NA	pT1a	NA	NA	pT3a	pT1b	pT1a m R0	pT2a	pT1a R1	ypT0
Preop eGFR/creat	90/0.83	90/0.65	92/0.7	82.4/0.79	90/0.64	90/0.68	77/1.05	90/0.78	36/1.43	48/1.45
Postop day 1 eGFR/creat	78.5/0.97	71.5/0.94	73.4/0.83	78.8/0.82	90/0.74	90/0.73	96/0.83	49.1/1.28	26/1.87	26.7/2.01
Postop eGFR/creat	86.8/0.89 (3 mo)	90/0.72 (12 mo)	87/0.72 (12 mo)	77/0.64 (6 mo)	90/0.64 (6 mo)	90/0.71 (6 mo)	90/0.92 (6 mo)	57.1/1.13 (1 mo)	36/1.46 (12 mo)	55.3/1.1 (1 mo)
Length of stay (d)	4	4	4	4	4	4	4	5	3	6

AVG = average; BMI = body mass index; ccRCC = clear cell renal cell carcinoma; chRCC = chromophobic renal cell carcinoma; creat = creatinine (mg/dl); CT = console time; DE = deep endophytic lesion; EBL = estimated blood loss; eGFR = estimated glomerular filtration rate (ml/min); F = female; Hb = hemoglobin; IH = intrahilar lesion; L = left; LS = lesion size; M = male; NA = not applicable; 1 mo = 1-mo postoperative; 3 mo = 3-mo postoperative; 6 mo = 6-mo postoperative; 12 mo = 12-mo postoperative; OCC = oncocytoma; preop = preoperative; postop = postoperative; pRCC = papillary renal cell carcinoma; R = right; RAPN = robot-assisted partial nephrectomy; UCS = urinary collecting system.

[a] The last two columns in grey depict cases of unique kidneys.

Patient 7 had multiple bilateral tumors. First, left-sided RAPN for six lesions including one endophytic lesion was performed using IAC.

Patient 8 required conversion to radical nephrectomy due to excessive bleeding from the resection bed during the reperfusion phase despite selective suturing and second renorrhaphy. Apart from patient 8, no intraoperative complications were withheld.

Patient 10 received neoadjuvant axitinib-pembrolizumab treatment with radiological tumor reduction from 80 to 43 mm for a biopsied clear cell renal cell carcinoma (ccRCC) International Society of Urological Pathology grade 2. This patient previously underwent contralateral radical nephrectomy for ccRCC. One mostly endophytic lesion was resected using IAC, six suspicious satellite lesions were subsequently resected off-clamp as cold ischemia time had attained 81 min, and the IAC was thought to be suboptimal as the renal vein effluent still contained some blood, indicating remaining partial renal perfusion (arterial inflow or venous backflow) despite main artery occlusion. Final pathology did not withhold the remaining tumor (all ypT0). The patient received a blood transfusion postoperatively (2 units of packed cells).

All patients completed 90 d of follow-up. The median follow-up was 13 mo (IQR 9.1–32.4). Patient 2 experienced hematuria 2 wk postoperatively: a pseudoaneurysm was diagnosed for which segmental embolization was performed (Clavien-Dindo grade 3b [37]). Patient 9 received empirical postoperative ciprofloxacin due to fever. No other complications were noted beyond 30 d for all patients.

We note one positive surgical margin (patient 9). No sign of recurrence was withheld up to 13 mo of follow-up. All other surgical margins were negative.

4. Discussion

We show that transperitoneal applied IAC has several advantages. First, it extends the scope of robot-assisted nephron-sparing surgery in small but anatomically difficult located lesions or multiple tumors due to safe prolonged clamping times.

Second, due to flushing and cold ischemia, tumor visualization and enucleation become increasingly achievable, also for challenging tumor locations. In classical arterial clamped procedures, continuous blood loss may still hamper visualization and cause inadvertent damage to healthy parenchyma, blood vessels, or the urinary collecting system. It may also lead to positive surgical margins. This oozing and blood loss can originate from aberrant unidentified arterial vessels, venous backflow from both venous and ureteral systems, and intra/extrarenal venous anastomosis. One way to tackle the oozing is full renal mobilization in combination with arterial, venous, and ureteral clamping. However, this would increase operative time to similar ranges as our proposed approach. A less invasive and more time-efficient alternative might involve ICG administration after clamping. Similarly, complete kidney surface inspection for ICG necessitates complete mobilization, does not provide subsurface information for deep endophytic tumors, and does not inform on venous backflow adequately. Lastly, even under perfect fully clamped conditions, remnant blood can still be present inside the parenchyma as it is not flushed and can obscure initial enucleation.

Third, applying cold irrigation through arteriotomy has several advantages compared with the endovascular arterial cooling approach. Operative time was not reported by Liu et al [18] who used a transfemoral renal arterial access, but their approach required patient transfer between two operative rooms and two subsequent procedures with patient movement and repositioning. Endovascular balloon dislocation [18] is very unlikely in our approach as catheters are positioned under direct endoscopic sight and thus can easily be repositioned. We note similar average kidney temperature during cooling (19.3°C vs 20.0°C in our approach). We note longer average cold ischemia times (56 min on average compared with 39.5 min) in our case series, however with higher nephrometry scores (PADUA 12 compared with PADUA 8–11) and in a smaller cohort. It might be advocated that the relative benefit for IAC due to prolonged clamping increases for highly complex lesions.

Our proposed operative strategy also has several limitations. First, the proposed technique requires expert robotic surgery skills in both oncology and vessel manipulation such as in renal transplantation. In all cases, bench surgery with autotransplantation [28] or radical nephrectomy was considered a backup strategy.

Second, this technique is not eligible for every complex renal lesion due to constraints on the arterial tree. Renal arteriotomy requires a sufficiently long renal arterial trunk to insert the Fogarty catheter and deploy the balloon, and hence would not be the proposed approach in case of early arterial branching. The use of multiple Fogarty catheters for multiple arteries is also feasible as we already experienced in tiRAKAT, although not in this IAC RAPN series. Care should be taken with heavily calcified vessels as arteriotomy and intra-arterial manipulation might dislodge plaques or cause intima rupture with subsequent thrombosis. This should be considered a contraindication for IAC.

Third, when compared with radical nephrectomy, the operative time and bleeding risk increase, due to the extensive arterial tree manipulation and the complexity of the lesions. In our cohort, we report one intraoperative bleeding requiring radical nephrectomy and one postoperative bleeding requiring interventional radiological coiling. It should be noted that radical nephrectomy should always be considered the safest alternative when expecting long ischemia times in complex masses, especially while a contralateral healthy kidney is in place with good baseline renal function. In comparison, the procedure we describe has a higher complication rate, which was illustrated by one patient who needed embolization for a postoperative pseudoaneurysm. The benefit of saving the kidney should be weighed against the increased complication risk for each individual case.

Fourth, we did not add a comparative arm to investigate the protective effect of cold ischemia when compared with standard warm ischemia. Identification of ten matched cases proved to be impossible as such cases with expected long ischemia times were previously typically addressed with radical nephrectomy. Given the small sample size of ten patients, a differential outcome in one single matched case could also easily alter the results.

5. Conclusions

In this patient series, we demonstrated, to our best knowledge, the first feasibility study of RAPN using intra-arterial renal hypothermia with arteriotomy. In selected patients and when performed by expert robotic surgeons, this approach allows for more precise surgery in a bloodless field. The most clinically relevant setting for this technique might be patients with highly complex renal masses and comprised renal baseline function and/or a solitary kidney when prolonged ischemia times are expected.

***Author contributions*:** Pieter De Backer had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: De Backer, Quackels, Mottrie, Decaestecker.
Acquisition of data: De Backer, Vangeneugden, Quackels, Decaestecker.
Analysis and interpretation of data: De Backer, Vangeneugden, Van Praet, Mottrie, Dekuyper, Decaestecker.
Drafting of the manuscript: De Backer, Vangeneugden.
Critical revision of the manuscript for important intellectual content: Van Praet, Berquin, Dekuyper, Quackels, Mottrie, Decaestecker.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2023.10.004.

References

[1] Ljungberg B, Albiges L, Abu-Ghanem Y, et al. European Association of Urology guidelines on renal cell carcinoma: the 2022 update. Eur Urol 2022;82:399–410.
[2] Hung AJ, Cai J, Simmons MN, Gill IS. “Trifecta” in partial nephrectomy. J Urol 2013;189:36–42.
[3] Ingels A, Bensalah K, Beauval JB, et al. Comparison of open and robotic-assisted partial nephrectomy approaches using multicentric data (UroCCR-47 study). Sci Rep 2022;12:18981.
[4] Porpiglia F, Fiori C, Bertolo R, et al. The effects of warm ischaemia time on renal function after laparoscopic partial nephrectomy in patients with normal contralateral kidney. World J Urol 2012;30:257–63.
[5] Becker F, Van Poppel H, Hakenberg OW, et al. Assessing the impact of ischaemia time during partial nephrectomy. Eur Urol 2009;56:625–34.
[6] Lane BR, Gill IS, Fergany AF, Larson BT, Campbell SC. Limited warm ischemia during elective partial nephrectomy has only a marginal impact on renal functional outcomes. J Urol 2011;185:1598–603.
[7] Rod X, Peyronnet B, Seisen T, et al. Impact of ischaemia time on renal function after partial nephrectomy: a systematic review. BJU Int 2016;118:692–705.
[8] Thompson RH, Lane BR, Lohse CM, et al. Every minute counts when the renal hilum is clamped during partial nephrectomy. Eur Urol 2010;58:340–5.
[9] Antonelli A, Cindolo L, Sandri M, et al. Is off-clamp robot-assisted partial nephrectomy beneficial for renal function? Data from the CLOCK trial. BJU Int 2022;129:217–24.
[10] Antonelli AD, Cindolo L, Sandri M, et al. The role of warm ischemia time on functional outcomes after robotic partial nephrectomy: a radionuclide renal scan study from the clock randomized trial. World J Urol 2023;41:1337–44.
[11] Menon M, Sood A, Bhandari M, et al. Robotic kidney transplantation with regional hypothermia: a step-by-step description of the Vattikuti Urology Institute-Medanta technique (IDEAL phase 2a). Eur Urol 2014;65:991–1000.
[12] Gill IS, Abreu SC, Desai MM, et al. Laparoscopic ice slush renal hypothermia for partial nephrectomy: the initial experience. J Urol 2003;170:52–6.
[13] Taylor JS. Kidney cooling in partial nephrectomy. Evaluation of a technique. Urology 1975;5:456–60.
[14] Canda AE, Ozkan A, Arpali E, et al. Robotic assisted partial nephrectomy with cold ischemia applying ice pieces and intraoperative frozen section evaluation of the mass: complete replication of open approach with advantages of minimally invasive surgery. Cent European J Urol 2020;73:234–5.
[15] Kijvikai K, Viprakasit DP, Milhoua P, Clark PE, Herrell SD. A simple, effective method to create laparoscopic renal protective hypothermia with cold saline surface irrigation: clinical application and assessment. J Urol 2010;184:1861–6.
[16] Crain DS, Spencer CR, Favata MA, Amling CL. Transureteral saline perfusion to obtain renal hypothermia: potential application in laparoscopic partial nephrectomy. JSLS 2004;8:217–22.
[17] Janetschek G, Abdelmaksoud A, Bagheri F, Al-Zahrani H, Leeb K, Gschwendtner M. Laparoscopic partial nephrectomy in cold ischemia: renal artery perfusion. J Urol 2004;171:68–71.
[18] Liu F, Yuan H, Li X, Ma X, Wang M. Application of hypothermic perfusion via a renal artery balloon catheter during robot-assisted partial nephrectomy and effect on renal function. Acad Radiol 2019;26:e196–201.
[19] Hruby S, Lusuardi L, Jeschke S, Janetschek G. Cooling mechanisms in laparoscopic partial nephrectomy: are really necessary? Arch Esp Urol 2013;66:139–45.
[20] Marberger M, Eisenberger F. Regional hypothermia of the kidney: surface or transarterial perfusion cooling? A functional study. J Urol 1980;124:179–83.
[21] Yin M, Currin RT, Peng X-X, Mekeel HE, Schoonhoven R, Lemasters JJ. Different patterns of renal cell killing after warm and cold ischemia. Ren Fail 2002;24:147–63.
[22] Steffens J, Humke U, Ziegler M, Siemer S. Partial nephrectomy with perfusion cooling for imperative indications: a 24-year experience. BJU Int 2005;96:608–11.

[23] Gschwend JE, de Petriconi R, Maier S, Kleinschmidt K, Hautmann RE. Continuous in situ cold perfusion with histidine tryptophan ketoglutarate solution in nephron sparing surgery for renal tumors. J Urol 1995;154:1307–11.

[24] Simon J, Meilinger M, Lang H, Hautmann RE, de Petriconi R. Novel technique for in situ cold perfusion in laparoscopic partial nephrectomy. Surg Endosc 2008;22:2184–9.

[25] Herrmann TRW, Kruck S, Nagele U. Transperitoneal in situ intraarterial cooling in laparoscopic partial nephrectomy. World J Urol 2011;29:337–42.

[26] Van Praet C, Lambert E, Desender L, Van Parys B, Vanpeteghem C, Decaestecker K. Total intracorporeal robot kidney autotransplantation: case report and description of surgical technique. Front Surg 2020;7:65.

[27] Breda A, Diana P, Territo A, et al. Intracorporeal versus extracorporeal robot-assisted kidney autotransplantation: experience of the ERUS RAKT Working Group. Eur Urol 2022;81:168–75.

[28] Verbakel I, Wirtz M, De Backer P, et al. Pushing boundaries in extracorporeal robot-assisted kidney autotransplantation (eRAKAT): bench surgery for an oncologic partial nephrectomy in a patient with a solitary kidney. A joint meeting of the EAU Section for Urotechnology and the EAU Section of Urolithiasis. Vol. 39, biblio.ugent.be; 2022. p. S44–5.

[29] Nahar B, Bhat A, Parekh DJ. Does every minute of renal ischemia still count in 2019? Unlocking the chains of a flawed thought process over five decades. Eur Urol Focus 2019;5:939–42.

[30] De Backer P, Vermijs S, Van Praet C, et al. A novel three-dimensional planning tool for selective clamping during partial nephrectomy: validation of a perfusion zone algorithm. Eur Urol 2023;83:413–21.

[31] Decaestecker K, Van Parys B, Van Besien J, et al. Robot-assisted kidney autotransplantation: a minimally invasive way to salvage kidneys. Eur Urol Focus 2018;4:198–205.

[32] West A, Hayes J, Bernstein DE, et al. Clinical outcomes of low-pressure pneumoperitoneum in minimally invasive urological surgery. J Robot Surg 2022;16:1183–92.

[33] Streeter EH, Little DM, Cranston DW, Morris PJ. The urological complications of renal transplantation: a series of 1535 patients. BJU Int 2002;90:627–34.

[34] De Backer P, Van Praet C, Simoens J, et al. Improving augmented reality through deep learning: real-time instrument delineation in robotic renal surgery. Eur Urol 2023;84:86–91.

[35] Sternbach G. Sven Ivar Seldinger: catheter introduction on a flexible leader. J Emerg Med 1990;8:635–7.

[36] Benway BM, Wang AJ, Cabello JM, Bhayani SB. Robotic partial nephrectomy with sliding-clip renorrhaphy: technique and outcomes. Eur Urol 2009;55:592–9.

[37] Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.

[38] Hasson HM. Open laparoscopy: a report of 150 cases. J Reprod Med 1974;12:234–8.