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Radiofrequency-Assisted Laparoscopic Partial Nephrectomy: Clinical and Histologic Results

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Abstract

Purpose: To evaluate a surface conductive radiofrequency (RF) coagulation instrument (Tissuelink FB3.0) in laparoscopic and open partial nephrectomy (PN) in hereditary kidney cancer. The lesion depth and viability in the pathologic specimens from a surgical series and an acute porcine model were characterized under conditions of vascular perfusion and occlusion.

Materials and Methods: A total of 19 patients underwent 20 laparoscopic and open procedures with the device. Data were acquired on tumor number, size, operative time, blood loss, length of stay, renal function, complications, pathologic diagnosis, and surgical-margin status. Renal lesions were created in pigs with the device, ultrasonic shears, and a standard electrocautery for specified time intervals and operative energy settings. These lesions were analyzed for depth, diameter, and tissue viability.

Results: In 20 separate (14 laparoscopic; 6 open) procedures in 19 patients, a total of 112 tumors were removed (range 1–31 tumors per procedure). The median operative time, blood loss, and length of stay were 310 minutes, 250 mL, and 4 days, respectively. There were no positive surgical margins. Median preoperative and postoperative creatinine concentrations were similar (1.0 *v* 1.0 mg/dL). The average treatment margin depth was 3 mm. In the porcine experiments, the treatment depth in the unclamped vascular model was significantly less in than the clamped model (4.0 ± 1.7 mm *v* 7.0 ± 1.6 mm; $P < 0.05$). Lesion depth and diameter increased with treatment time. Viability depth correlated well with the depth of the visible thermal lesions (Pearson correlation 0.989).

Conclusions: This RF energy device can provided adequate and uniform hemostatic control without hilar clamping during laparoscopic and open PN for hereditary renal tumors. Gross measures of renal function after surgery appeared clinically unchanged. Coagulation depth is dependent on both tissue perfusion and time in the porcine model.

INTRODUCTION

Minimally invasive nephron-sparing techniques are emerging as an alternative to open partial or radical nephrectomy in patients with small kidney tumors. Adapting these approaches to patients with genetically derived kidney-cancer syndromes presents a challenge, as most affected individuals will have bilateral and multiple renal lesions. Several groups have used

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ablative techniques with some success in these patients, yet the procedure of laparoscopic partial nephrectomy (LPN) for multiple tumors has been slower to develop, in large part because of perceived issues with prolonged whole-organ ischemia. Although ischemic damage can be controlled to some extent by various cooling techniques, the long-term effects of vascular occlusion (VO) on renal function in the laparoscopic setting have not been well studied.[1-3] An LPN performed without VO offers the least chance of renal dysfunction secondary to whole-organ ischemia.

Radiofrequency (RF) tissue coagulation has been used for *in-situ* tumor ablation and as an aid to renal and hepatic wedge resection. The RF-ablated areas undergo direct thermal cellular damage, as well as delayed ischemic injury as a result of microvascular destruction secondary to thermal contraction of perivascular collagen.[4,5] Percutaneous RF ablation of small renal tumors is currently an experimental minimally invasive procedure that is well tolerated with short-term data that support its efficacy in selected patients.[6-8] However, real-time evaluation of lesion size and the extent of adjacent tissue damage cannot be done well with this method. Furthermore, the proximity of tumor to critical structures (i.e., ureter, collecting system, renal pedicle) may create a risk of significant morbidity.[9,10]

The recent introduction of a commercial hand-held surface-conductive RF coagulation instrument (FB3.0 Tissuelink, Dover, New Hampshire) for hemostatic coagulation may limit blood loss. Its adaptation for nephron-sparing surgery (NSS) has been reported previously.[11-13] However, its use in performing PN for multiple tumors in hereditary kidney cancer and the effects of VO have not been described. We report our initial experience with open and laparoscopic partial nephrectomy using this device in the setting of multiple renal lesions in hereditary and sporadic kidney cancer. The characteristics of lesion depth in human pathologic specimens and in an acute porcine model with and without VO also are described.

MATERIALS AND METHODS

Operative surgical series

Nineteen patients (20 renal units) underwent procedures with the device between August 2002 and September 2003. Fourteen laparoscopic and six open procedures were performed. All patients had a preoperative CT or MRI scan confirming enhancing solid renal lesions or suspicious complex cysts. Electrical grounding pads were placed according to the manufacturer's guidelines. Data were acquired on tumor number and size, surgical procedure, length of procedure, blood loss, transfusion requirement, length of stay, complications, pathologic diagnosis, and surgical margin status under a research protocol approved by the Institutional Review Board. Serum creatinine values were obtained within 2 weeks prior to surgery and at follow-up a minimum of 3 months after surgery.

The device was used intraoperatively to obtain a coagulative margin in normal tissue around each lesion. An operator-controlled drip of room-temperature normal saline emerges from the tip of the device to dissipate the heat and prevent tissue carbonization. Lesions were sharply excised circumferentially through the area of coagulation until bleeding, uncoagulated tissue was encountered, as has been described.[11] Repeat treatment of the underlying tissue was performed until hemostasis was achieved and lesions were removed completely. Initial energy settings of 30 W were used and increased in increments of 10 W to a maximum of 80 W to obtain hemostasis. The saline drip was slow enough to allow adequate heating without electric arcing or carbonization. In cases where the renal collecting system was entered, suture closure was performed. The pathologic margin between normal and coagulated tissue in addition to the surgical margin was assessed from the excised specimen. Cautery artifact did not obscure the pathologic evaluation of tissue-margin status or tumor histology, as determined by a pathologist. Additional hemostatic measures including sealants were not used routinely.

Porcine model

Studies were performed on eight live anesthetized animals (14 renal units) under a research protocol approved by the Institutional Animal Care and Use Committee in accordance with National Institutes of Health Guidelines for Animal Care. The instrument was evaluated in three clinically relevant settings: cortical-surface lesions (CL), cut-surface treatment (CS), and continuous focal treatment (CTmax; Fig. 1). Treatments with an ultrasonic coagulating device (Laparosonic; Ethicon, Cincinnati, OH) and a handheld bovie electrocautery also were performed in the CL group. Lesions were excised, transected, and measured to determine the treatment depth and diameter. Viability study using tetrazolium-red staining was performed on a randomly selected subset of 20 lesions, as previously described.[14]

For CL treatment, kidneys were exposed by open surgical technique, and multiple circular 1-cm lesions were created with the device using room-temperature 0.9% saline (drip rate 4 mL/min) for 15, 30, 45, and 60 seconds at a power setting of 30 W (Fig. 2). A standard operative energy generator (Force 5; Valley Lab, Boulder, CO) was used for all treatments. Comparison lesions were created using the alternative coagulation devices. The blunt, non-cutting edge of the ultrasonic scalpel was placed against the kidney surface, and treatment at energy level 7 was provided for 30, 45, and 60 seconds. The metal tip of a bovie electrocautery was placed in contact with the renal surface, and 30 and 100 W of coagulation energy was applied for 30 and 60 seconds. Kidneys in both experimental arms were treated with and without VO.

Animals undergoing CS treatment were utilized as a model of clinical use in human PN. Hemi-transection and wedge resection was performed and treatment applied to the cut surface until durable hemostasis was achieved for >30 minutes. Energy levels of 30 to 80 W were used as necessary to obtain hemostasis. The same procedure was performed in a VO model. Kidneys were allowed to perfuse for a minimum of 30 minutes before they were harvested. Lesions were sectioned, treatment depths were measured, and the tissue was fixed for histologic analysis.

Continuous circular (1-cm) treatment of the kidney surface was applied starting at an energy setting of 10 W and increasing by 10 W every 30 seconds to a maximum energy of 100 W for a total of 5 minutes. This was performed to determine a maximum depth of treatment with the device, as might be expected if attempting to perform a crude form of RF lesion ablation. After 30 minutes of post-treatment tissue perfusion, the kidneys were harvested and the lesions excised for measurements of split lesion depth, diameter, and viability using tetrazolium-red staining.

RESULTS

Operative series

Altogether, 20 procedures were performed using the device, yielding 112 tumors (Table 1). One patient underwent staged bilateral laparoscopic NSS. One patient with a history of familial renal cancer undergoing NSS also underwent planned ipsilateral partial adrenalectomy using this device. Renal tumors ranged from 0.3 to 6.0 cm in diameter (mean 2.0 cm). All planned laparoscopic cases were completed without conversion to open NSS. The median operative times and blood losses were 310 minutes (range 50–540 minutes) and 325 mL (range 50–2000 mL). The median length of stay (LOS) was 4 days for the entire cohort (range 2–16 days) and 2 days for the laparoscopic group. Median follow-up of 27.5 months (range 3–38.3 months) has not shown any local recurrences. Mean preoperative and postoperative serum creatinine concentrations were 1.0 mg/dL (0.6–1.5 mg/dL) and 1.1 mg/dL (0.7–1.6 mg/dL), respectively ($P = 0.6$). Two patients received blood transfusions.

The median depth of coagulation necrosis was 4 mm. The median width of the surgical margin was 3 mm (range 1–5 mm). No positive surgical margins were encountered. Three patients developed postoperative complications. One patient had an early urine leak that resolved after 2 weeks of percutaneous drainage and decompression with a ureteral stent. One patient in the laparoscopic group who had chronic intermittent atrial fibrillation had spontaneous atrial fibrillation and required systemic anticoagulation. A second patient developed a pulmonary embolus on day 2 after laparoscopic NSS and also received anticoagulation. This patient developed an ipsilateral perinephric hematoma and contralateral pyelonephritis that resolved completely with conservative medical therapy.

Porcine model

CL group—A total of 110 lesions were studied in 8 kidneys. The treatment depth in the unclamped vascular model was less than in the VO model at all time intervals ($P < 0.05$ to $P < 0.001$) (Fig. 3). Corresponding treatment depths using the Harmonic Scalpel averaged 2.0 mm at both 30 and 60 seconds in the VO kidney model and 1.0 and 1.5 mm in the unclamped kidney model at the same time intervals.

Lesion diameter increased with the treatment time. The mean cross-sectional treatment diameter measured 8.8, 11.0, 12.4, and 13.0 mm for the unclamped and 9.9, 13.2, 15.8, and 15.2 mm for the VO model at 15, 30, 45, and 60 seconds, respectively. The differences in the lesion diameter between the unclamped and VO conditions were statistically significant at the 30- and 45-seconds treatment time (Fig. 4; $P < 0.002$ and 0.001, respectively). The lesion diameter produced using the Harmonic Scalpel averaged 3.0, 3.0, and 4.0 mm in the unclamped and 7.0, 7.0, and 6.3 mm in the VO model at 30, 45, and 60 seconds, respectively.

The lesions produced using the electrocautery at 30 W were consistently 1.0 mm in depth and 1.0 mm in diameter at 15, 30, 45, and 60 seconds in both the unclamped and VO kidneys. Lesions produced at 100 W were 2.0 mm in depth and 3.0 mm in diameter for both the unclamped and the clamped model. Gross measured treatment depth of all lesions obtained in the study correlated well with viability depth (Pearson correlation 0.989; $P < 0.001$), as measured by tetrazolium-red staining (Fig. 2).

CS group—The median treatment depth at multiple sites across each lesion in the unclamped model was 4.0 mm *v* 7.0 mm in the clamped model ($P < 0.001$).

CTmax group—The maximum depth of lesion achieved with the treatment over 5 minutes was 8.0 mm in the unclamped and 15 mm in the VO model. Viability depth, as measured by tetrazolium-red staining, correlated with the depth of the visible thermal lesion.

DISCUSSION

Nephron-sparing surgery as a treatment for renal cancers is driven in part by the rise in the detection of small incidental lesions. In some centers, screening of hereditary renal cancer kindreds has led to earlier diagnosis in patients with multiple tumors of defined natural history and malignant potential. Management algorithms in these cases are suited to minimally invasive approaches because of the predictable behavior of renal tumors <3 cm.[15]

Surgical removal of solid enhancing renal masses remains the standard of care. In NSS, preservation of renal function is a secondary, although significant, goal. Open techniques using VO may ultimately result in significant functional loss in 3% to 12% of patients.[15,16] Limiting the time of warm ischemia to <30 minutes appears to have the greatest impact on functional recovery, perhaps best estimated in models such as NSS in solitary kidneys and in experience

with bilateral renal hypoperfusion in humans.[17,18] Performing tumor excision without VO would be expected, therefore, to decrease the risk of global renal injury.

The Tissuelink™ device has been used safely to perform wedge resection for renal, hepatic, and pulmonary lesions without requiring VO.[11-13,19,20] The rapid adaptation of this device to clinical use for NSS in patients has provoked interest in exploring the capabilities of this instrument and other similar technologies. Although it has been used for solitary renal lesions, its safety and efficacy in multiple renal lesions has not been investigated, making impossible comparison of this series with other small series. As demonstrated in this study, the device can create various depths of coagulative effect, depending on the way it is used. We attempted to establish the range of capabilities in both the patient setting and an experimental porcine model under a spectrum of clinically relevant conditions.

The clinical results demonstrated adequate margin control and no radiographic recurrence at a median follow-up of 27.5 months. Functional changes, as reflected by the serum creatinine concentration, were negligible. The drawbacks of this study include combining open and laparoscopic surgical groups. The selection bias between these groups made statistical comparison difficult to interpret; however, a review of the data demonstrates that the tumor size, operative time, and LOS were similar (Table 1). Blood loss, although a notoriously inaccurate clinical parameter, was considerably higher for the open-surgery group, likely reflecting the selection of patients with more extensive and complex renal involvement for open procedures. This study also assumed that the treatment margin on the specimen side was similar to what would be expected at the *in situ* margin, which may be incorrect. Although a coagulative margin of 4 mm was confirmed in the perfused porcine model, direct correlation between the porcine and human tissues may be inaccurate.

We had three complications in our operative series. One patient developed postoperative urinary extravasation after open partial nephrectomy during which collecting-system entry and intraoperative suture closure were performed. The patient was managed with percutaneous drainage and a ureteral stent for 2 weeks. The known rate of this complication, 2% to 17% during from partial nephrectomy series, is similar to what we found, but further study is required.[21] However, use of this device near the collecting system did not appear to increase the risk of urinary complications or cause difficulties in management when they did occur.

The depth of treatment effect with RF is dependent on both the treatment time and kidney perfusion. Maximum lesion depth in the unclamped kidney reached a plateau of 5.3 mm at 45 seconds, whereas in the VO model, thermal tissue coagulation averaged 7.0 mm at 45 seconds and continued beyond 7.5 mm by 60 seconds (Fig. 3). Also, VO produced a significant increase in the depth of treatment, from a median of 4.0 mm to 7.0 mm in the CS group. Tissue viability assessment using tetrazolium-red staining confirmed that the lesion dimensions matched those of the visible treatment effect.

Tissue heating, as described by the Pennes bioheat equation, results from the balance between the heat generated by the energy source and the heat lost from thermal conduction and thermal convection or tissue perfusion. Heat losses secondary to tissue perfusion may limit the extent of tissue destruction. These data indicate that limiting the heat-sink effect with VO can produce a significant increase in lesion size and should be taken into consideration when using RF energy during NSS. Notably, conventional bovie electrocautery is not sensitive to perfusion effects because of the charring and carbonization effects that coagulate tissue immediately, creating a thin zone of high impedance, insulating against further energy deposition.

Given the ablative treatment depth seen with the device, its use to obtain additional surgical-margin control can be speculated on. The use of this instrument for this purpose would appear to provide greater depth than either conventional electrocautery or harmonic coagulation

devices and deserves further study. Additional possible uses include the treatment of small surface lesions or as an “insurance burn” along a margin or surface of questionable histology.

CONCLUSIONS

Surface-conductive RF coagulation using the Tissuelink device provided adequate and predictable hemostatic control without hilar clamping during laparoscopic and open NSS for hereditary multiple renal lesions with good renal-function outcomes. Coagulation depth is both perfusion and time dependent in a porcine model. An understanding of the extent of treatment effects is important for appropriate and effective use in treating renal lesions, particularly in cases where vascular clamping is necessary. Treatment efficacy and safety with the use of this device in renal tissue were not endpoints of this study and cannot be assessed by an interpretation of the data.

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ABBREVIATIONS USED

CL, cortical-surface lesions
CS, cut-surface treatment
CT, computed tomography
CTmax, continuous focal treatment
EBL, estimated blood loss
LPN, laparoscopic partial nephrectomy
LOS, length of stay
MRI, magnetic resonance imaging
NSS, nephron-sparing surgery
PN, partial nephrectomy
RF, radiofrequency
VO, vascular occlusion

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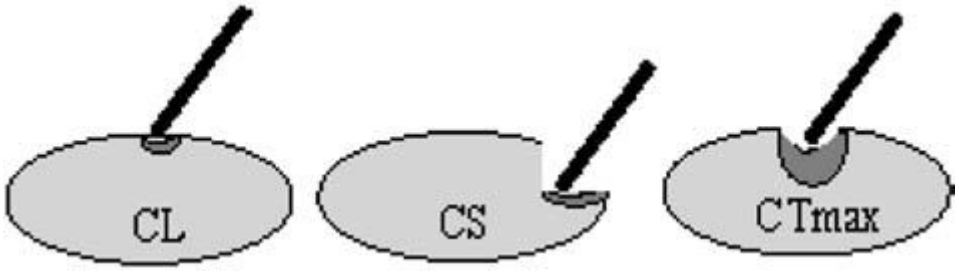

FIG. 1.

Schematic of three treatment conditions from porcine model: timed cortical lesion (CL), cut surface until hemostasis (CS), and continuous treatment for 5 minutes to maximum depth (CTmax). Treatments were applied with and without VO.

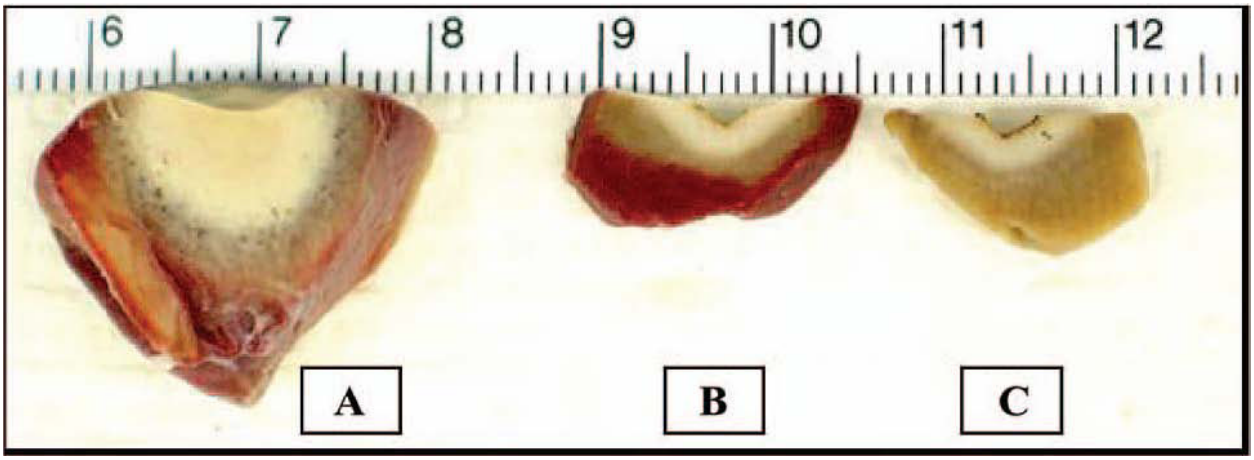

FIG. 2.

Clamped porcine kidney with tetrazolium-red stain for tissue viability. Lesion A was treated for 45 seconds at 30 W with the Tissuelink device. Lesions B (tetrazolium stained) and C (unstained) were treated with the Harmonic Scalpel for 45 seconds. Depth of effect was measured perpendicularly from center of contact point on cortical surface to margin of desiccated tissue.

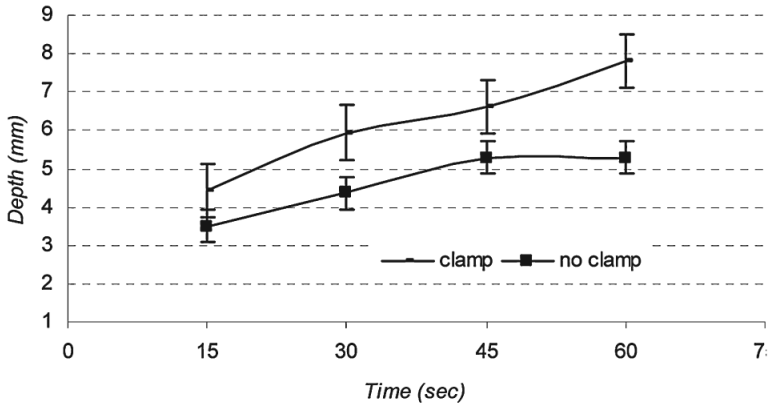

FIG. 3.
Effect of treatment time and vascular clamping on depth of treatment effect.

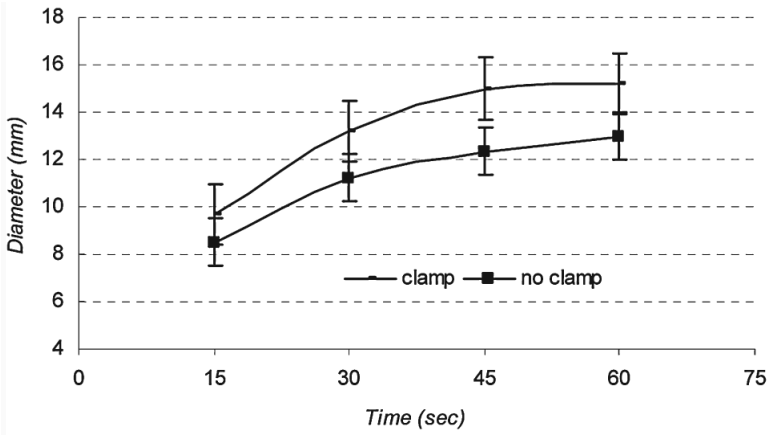

FIG. 4.
Effect of treatment time and vascular clamping on cross-section diameter of treatment area.

Table 1

Patient Characteristics and Results

Tumor pathology	*No. of patients*	*Mean age*	*Hereditary*	*No. tumors*	*Mean tumor size*	*No. lap.*	*Mean OR time (min)*	*EBL (mean)*	*LOS (median)*
Conventional clear	8	45.7	6	59	1.7	4	223	990	7
Papillary	2	51.0	1	12	2.6	2	240	150	2
Oncocytoma	4	63.8	0	11	2.3	4[a]	348	388	5
Chromophobe	2[b]	43.5	2	20	1.9	1	330	1100	5
Hybrid (chromo/onco)	0[b]			6	1.2				
Benign cyst	2	44.0	0	1	1.9	2	305	200	2
Adrenal met (clear cell)	1	54.0	0	2	1.5	1	420	200	2
Total	19[a]	50.6	8	112	2.0	14[a]	306	540	4

[a] One patient with bilateral oncocytomas underwent two laparoscopic procedures for staged LPN.

[b] One patient with Birt-Hogg-Dube syndrome had mixed tumor histology, including chromophobe and chromophobe/oncocytoma lesions. This patient is listed as having a chromophobe tumor.