Partial Nephrectomy Without Renal Ischemia Using an Electromagnetic Thermal Surgery System in a Porcine Model

Chien-Hui Ou, Wen-Horng Yang, Hung-Wen Tsai, Tung-Jen Lee, Szu-Yin Chen, Sheng-Chieh Huang, Yi-Yuan Chang, Gwo-Bin Lee, and Xi-Zhang Lin

OBJECTIVE To test the feasibility of partial nephrectomy using needle arrays under alternating current (AC) electromagnetic field without renal artery clamping.

METHODS We performed an experimental study for partial nephrectomy without renal artery clamping in a porcine model, comparing a new thermal surgery system consisting of an AC electromagnetic field generator and stainless steel needle arrays (using 10 pigs) vs an ultrasonic Harmonic Scalpel (on 8 pigs). Two cm of the upper pole of the kidneys were resected, and then the feasibility, operation time, blood loss, biochemical parameters, pathology, and complications were observed for 14 days.

RESULTS There was no difference by weight in the mean percentage of kidney removed between the 2 groups (8.1 ± 3.4% vs 12.7 ± 5.5%). The estimated blood loss for the partial nephrectomy with electromagnetic thermal surgery system was significantly less compared to the ultrasonic Harmonic Scalpel (53.0 ± 73.0 vs 188.8 ± 49.3 mL). Transection time was shorter with the electromagnetic thermal surgery system (10 vs 12 minutes). Bleeding from the cut surface after partial nephrectomy was noted in 2 pigs (electromagnetic surgery group) and 8 pigs (control group); all the bleeding was controlled with additional monopolar electrocoagulation and sutures. No urinoma was identified in either group when a second laparotomy was performed 2 weeks later.

CONCLUSION Our study of a partial nephrectomy in a porcine model demonstrates that the heat generated by the electromagnetic thermal surgery system is sufficient to coagulate renal parenchyma and to seal off the blood vessels without pedicle clamping. UROLOGY 81: 1101−1107, 2013.

Partial nephrectomy has become the standard of surgical procedures for small (<4 cm) and selected moderately sized (<7 cm) renal masses. This procedure provides excellent local tumor control, equivalent to that of radical nephrectomy for T1 tumors, while preserving residual renal function that can prevent or delay chronic renal function insufficiency.[1] Unfortunately, partial nephrectomy is still an underused technique because of its technical complexity and higher risk for postoperative complications.[2]

Traditionally, cold scissors or energy-based devices, such as bipolar cautery (LigaSure) and ultrasonic Harmonic Scalpel, have been used to incise the renal parenchyma. The renal pedicle is typically occluded temporarily during partial nephrectomy with a period of ischemia to reduce blood loss and to achieve a bloodless field for the tumor bed.[3] However, it raises the risk of ischemic injury. A deterioration of renal function after operation has been reported, and if the operation time is prolonged, the ischemia can cause permanent renal function impairment.[4-6] Often, when the renal pedicle has been temporarily clamped and renal parenchyma were incised with traditional hemostatic tools, bleeding from the cut surface of the remnant kidney usually requires additional monopolar cautery, argon beam coagulation, sutures, Surgicel, or fibrin glue application.[2,3] An ideal energy-based device for partial nephrectomy should be able to coagulate bleeding surfaces and simplify the procedure without the need for renal artery clamping. Using such a device would eliminate ischemic time and simplify the procedure, thereby facilitating the adoption of partial nephrectomy.

We have recently developed a new electromagnetic thermal therapy system at our university that may serve

Financial Disclosure: *The authors declare that they have no relevant financial interests.*

This study was supported by the National Cheng Kung University of Taiwan. We also thank the Metal Industry Research Institute co-funding grant #10010030.

From the Department of Urology, College of Medicine, National Cheng Kung University, Tainan, Taiwan; Department of Pathology, College of Medicine, National Cheng Kung University, Tainan, Taiwan; Department of Internal Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan; and Department of Power Mechanical Engineering, National Tsing Hua University, Hsinchu, Taiwan

Reprint requests: Xi-Zhang Lin, M.D., Department of Medicine, College of Medicine, National Cheng Kung University and Hospital, 138 Sheng-Li Road, Tainan 704, Taiwan. E-mail: linxz@mail.ncku.edu.tw

Submitted: July 17, 2012, accepted (with revisions): December 26, 2012

0090-4295/13/$36.00
http://dx.doi.org/10.1016/j.urology.2012.12.036

these purposes. This technology consists of a high-frequency alternating current (AC) electromagnetic field generator, a coil, and specially-designed needle arrays. This system can generate enough heat to seal off vasculature in the liver and spleen to achieve a bloodless resection.[7-9] In this study, we evaluated the feasibility of performing a partial nephrectomy without temporary clamping of the renal pedicle in a porcine experimental model. We compared the operation time, amount of blood loss, and postoperative renal functions by using ultrasonic Harmonic Scalpel vs using the electromagnetic thermal surgery system.

MATERIAL AND METHODS

Electromagnetic Thermal Surgery System

Our system was co-developed by our university, including the Industry and Technology Research Institute. It was described in previous articles[7-9] and has been periodically improved. The most recent version is NCKU-ITRI-1. The system consists of a high-frequency electromagnetic generator (dimensions of 41.5 cm × 19 cm × 39 cm), an extension cord (80 cm in length) connected to induction coils, a user interface, a water cooling system, and a temperature feedback control system to maintain the tissue at a constant temperature. A schematic diagram of the electromagnetic thermal therapy system is shown in Figure 1. The input voltage is 220 V, 60 Hz, with a power consumption of 15 kW. The output current can be amplified to 600 A with operation frequencies at about 44 kHz.

A thermocouple device and feedback control component were used to prevent overheating, and was set at 120°C with a variation of ± 2°C. This temperature feedback control system includes a thermocouple (R-type, InterTech Technology Inc., Taipei, Taiwan) and a digital controller that was developed for an electromagnetic thermotherapy system (ETS) to maintain the temperature at the desired setting to treat the target tissue (schematically shown in Fig. 1). While operating the device, the ETS provides a high-frequency current to generate an alternating electromagnetic field to heat the needles as the current passes through the copper coils. The thermocouple, embedded in the needle array, provides a feedback signal to the digital controller. If the monitored temperature is lower than the desired temperature, the temperature feedback control system increases the output power. Conversely, if the monitored temperature is higher than the desired temperature, the temperature feedback control system decreases the output power. With this approach, the temperature can be maintained within a small range. The extension coil weighs only 2 kg and can be easily operated by 1 assistant or placed on an operation table stand. The size and configuration of the coil can be adjusted to suit the surgical procedure and the location on the kidney.

Our laboratory designed and built an array of 20-gauge stainless steel needles with a linear layout and capped with a thermoresponsive material (Thermolite, New Prismatic Enterprise Co., Taipei, Taiwan) that can reversibly change its color at 70°C. Below 70°C, the material is black, and above it, the material turns white. This design allows surgeons to adjust the operating temperature for tissue resection. There are 18 needles, each 3.5-cm long, arranged in 2 parallel rows (9 tines/row) in a 5 cm-long array, with a mean distance of 0.5 cm between the 2 rows. Surgeons can adjust the number of needles simply by cutting the needle array at the desired location using regular surgical scissors. This allows for a variety of spatial configurations when 2 or more arrays with different numbers of needles are required during the same resection.

Animal Experiment and Surgical Procedure

The animal experiments were carried out under humane conditions, with approval from the Laboratory Animal Center at our university and in accordance with the guidelines set forth by the Agriculture Council of Taiwan on animal care. Eighteen male Lanyu pigs (Livestock Research Institute, Taitung, Taiwan) weighing between 20 and 33 kg were randomly divided into 2 groups for comparative study.

Both groups were anesthetized by intramuscular injection of atropine 0.02 mg/kg (Sintong, Taoyuan, Taiwan), xylazine 2 mg/kg (Bayer, Leverkusen, Germany), and Zoletil 10 mg (Virbac, Carros, France). Subsequent to endotracheal intubation, the animals received isoflurane 1%-3% 200 mg/kg/min (Baxter, Guayama, PR) throughout the experiments. Each pig's pulse and oxygen saturation were continuously monitored.

After a left subcostal incision, the left kidney was exposed and mobilized after dissection of the parietal peritoneum. In both groups, using electrocautery, the incision line was plotted circumferentially on the renal capsule, 2 cm from the upper pole. Partial nephrectomy was performed by resecting 2 cm of the upper pole without clamping the renal pedicle.

In the study group, partial nephrectomy was conducted using the electromagnetic thermal surgery system. Stainless steel needle arrays were inserted in the renal parenchyma in 10 pigs according to the planned resection line (2 cm of upper pole) after mobilizing the left kidney. After aligning the needles, all metallic surgical instruments were removed from the abdominal cavity because of the risk of being heated and were replaced by plastic or wooden retractors. The magnetic applicator (a coil) was then activated over the arrays at a distance of 0.5 cm for 6 minutes. The applicator was then withdrawn and the arrays were completely removed. The area treated by the needles showed macroscopic signs of thermal ablation. The kidney was transected along the mid portion of the coagulated zone using a surgical blade. No attempt was made to close the collecting system or do parenchyma reconstruction. Figure 2 shows procedures of the partial nephrectomy using our electromagnetic thermal surgery system.

In the control group, partial nephrectomy was conducted on 8 pigs using an ultrasonic Harmonic Scalpel (Ethicon Endo-Surgery, Cincinnati, OH). No attempt was made to close the collecting system or to do parenchyma reconstruction. Bleeding from the cut surface of the kidney, if observed, was coagulated with monopolar electrocautery or secured with figure-of-Z 4-0 vicryl sutures to achieve complete hemostasis.

After resecting part of the kidney, the remaining kidney was placed into the retroperitoneal space with perirenal fat tissue placed on the surface of the defect and the parietal peritoneum was then closed. The wounds were closed layer by layer. Blood loss was measured by the amount of blood present in the aspirator's bottle and the surgical gauze used during and after resection. Operation time was recorded.

The pigs were observed 14 days after surgery, after which they were euthanized to check for intra-abdominal complications. The remaining kidneys were removed and processed for further histological examinations and the pigs were euthanized according to standard protocol. The ratio of resection was calculated using the formula ratio of resection = (wt of resected

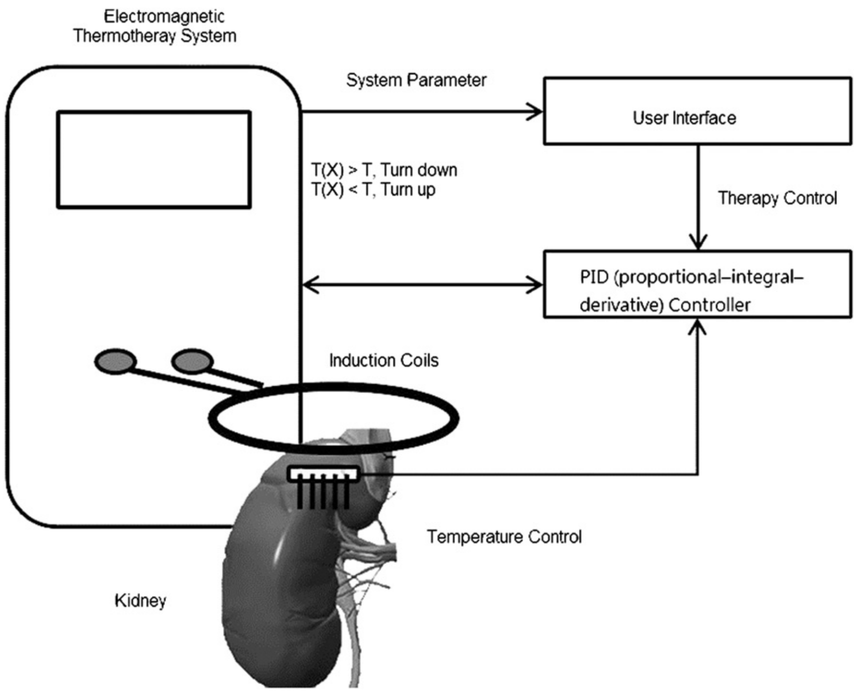

Figure 1. Schematic diagram of the electromagnetic thermal surgery system.

kidney/ [wt of resected kidney + wt of remnant kidney]) × 100%.

Histological Examinations

To examine the immediate effect of electromagnetic thermoablation, one part of the transected kidney was immediately fixed in 10% formalin, sectioned, and stained with hematoxylin and eosin (H&E stain); the other part was frozen at an optimal cutting temperature by using liquid nitrogen. Tissue viability was assessed using nicotinamide-adenine dinucleotide phosphate (NADPH)-diaphorase staining.

The remaining kidney removed on the day of euthanization was fixed in 10% formalin, sectioned, and stained with H&E and Masson's trichrome to examine the repair processes of the kidney.

Biochemistry Parameters

Blood samples were collected on the day of surgery (day 0) and day 14. The samples were checked for the concentration of alanine aminotransferase, aspartate aminotransferase, γ-glutamyl transpeptidase, total bilirubin, blood urea nitrogen, and creatinine.

Statistical Analysis

Data were analyzed using the nonparametric rank sum test or unpaired *t* test; $P < .05$ was considered statistically significant (STAT, Stata Co., College Station, TX).

RESULTS

Average animal weight ranges were 27.3 ± 4.6 kg for the study group (electromagnetic thermal surgery system arm) and 24.2 ± 6.3 kg for the control group (ultrasonic Harmonic Scalpel system arm). There were no significant differences in weight between the 2 groups. The average time to perform the partial nephrectomy with the electromagnetic thermal surgery system from time of kidney exposure to mobilization was 10 minutes. In contrast, it took 12 minutes with the ultrasonic Harmonic Scalpel. Bleeding from the cut surface after partial nephrectomy was controlled with additional monopolar electrocoagulation and sutures in 2 pigs (20%) in the electromagnetic thermal surgery system group, and for all pigs (100%) in the ultrasonic Harmonic Scalpel group. Average estimated blood loss was significantly less in the electromagnetic thermal surgery system group compared to the ultrasonic Harmonic Scalpel group (53.0 ± 73.0 vs 188.8 ± 49.4 mL, respectively, $P = .04$). For both groups, there were no major complications during the operations or during the observation period, including no deaths, no urine leakage, no intra-abdominal abscess, and no damage to surrounding structures from the second (post-euthanasia) laparotomy. No significant changes in serum AST, ALT, GGT, BUN, CRE, or total bilirubin were found between day 0 and day 14 in either group.

The average weight range of the resected kidneys (partial nephrectomy specimens) was 11.7 ± 4.4 g on the day of surgery. After 14 days, the remnant kidneys were removed and the average weight range was 71.0 ± 23.8 g. There was no significant difference between the mean percentage of kidney removed by weight in the study group and the control group (8.1 ± 3.4% vs 12.7 ± 5.5%, respectively; $P > .05$).

Grossly, the thickness of the coagulation zone was 5 mm around the needle array in the study group and 2 mm in the control group (Fig. 3A,B). Microscopically,

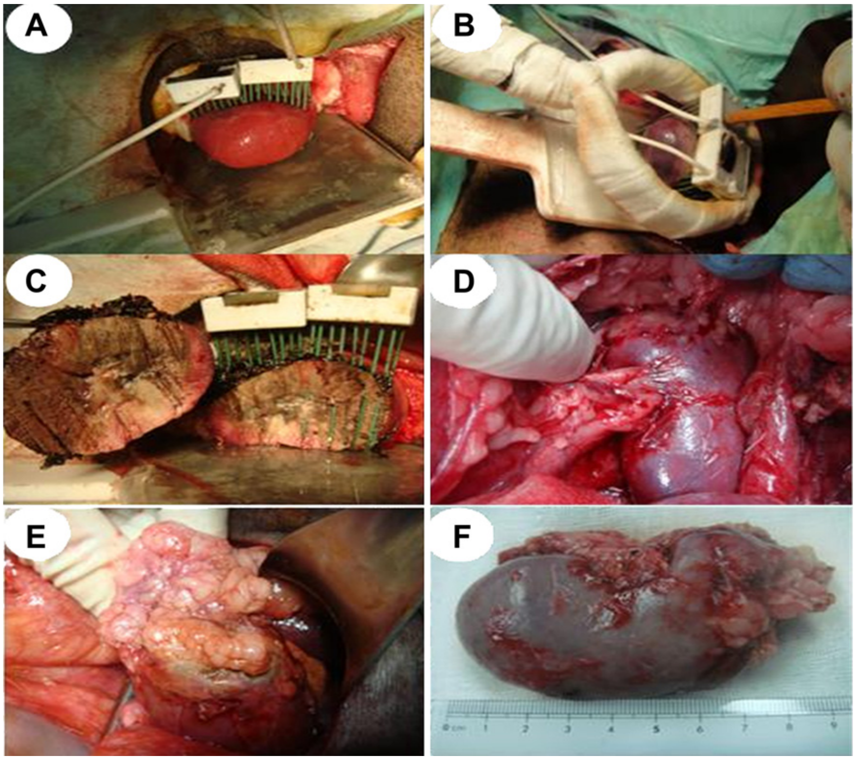

Figure 2. Procedures of the partial nephrectomy using our method of electromagnetic thermotherapy. Subcostal skin incision was made, the needle arrays were inserted into the kidney **(A)**, and heating up needle arrays using induction coil for 6 minutes **(B)**. When the procedure was completed, the coil and the arrays were completely removed. The kidney was transected along the line of ablation using a surgical blade **(C)**.The pigs were observed 2 weeks after the surgery. The remnant kidney is shown immediately after partial resection **(D)** and 14 days later **(E)**. The removed remnant kidneys are shown after the observation period **(F)**. (Color version available online.)

in the immediately resected kidney, the transected arteries were up to 0.5 mm in diameter in both the study and control groups (Fig. 3C,D). Endothelial cell injury and thrombus formation were seen in the arteries. The transected collecting ducts were up to 100 μm in diameter and showed condensed plugs in the lumen in both groups (Fig. 3E,F).

In the study group, the margin of the immediately resected kidney (Fig. 4A,B) showed coagulative necrosis with loss of NADPH-diaphorase activity in the ablated area. After 14 days of recovery, a healing process was observed over the previously resected margin of the remnant kidney with a fibrous band between the viable and necrotic tissues. The viable collecting ducts on the resection margin were sealed by the dense fibrotic tissue (Fig. 4C,D).

COMMENT

The standard technique of partial nephrectomy includes dissecting the renal hilum, clamping the artery, cutting parenchyma, controlling bleeding, sealing off the collecting system, and suturing the parenchyma. This technique requires complex reconstruction, meticulous checking for hemostasis, and usually takes a prolonged operative time.[1-6]

Although renal artery clamping provides better visualization for tumor excision, parenchyma repair, and reduced blood loss, the procedure can cause both acute and chronic renal failure, even if there is a relatively shorter ischemic period. Recent data demonstrate that increasing clamp times of the renal artery exacerbates the likelihood of acute kidney injury, chronic kidney disease, and the sequelae of renal disease.[4-6] In addition, reports indicate that vascular endothelial injury and presumed medial renal injury occurs by using temporary renal artery clamping with commercial atraumatic vascular clamps and silastic rubber vessel loops.[10] Therefore, partial nephrectomy without vascular clamping, yet without much bleeding, is an ideal approach for renal surgeons.

Our study demonstrates that the electromagnetic thermal surgical device can achieve a nearly bloodless incision without renal ischemia using a simple surgical blade. There was no oozing from the resected margins and no need of other measures to maintain hemostasis, with the exception of 2 cases. One involved vessels that could not be occluded because the vascular area was at the junction of 2 needle arrays. The other exception was because of an attempt to resect parenchyma in less than 6 minutes, which was insufficient because the electromagnetic energy needs at least a full 6 minutes to cauterize. In these 2 cases, bleeding was controlled with

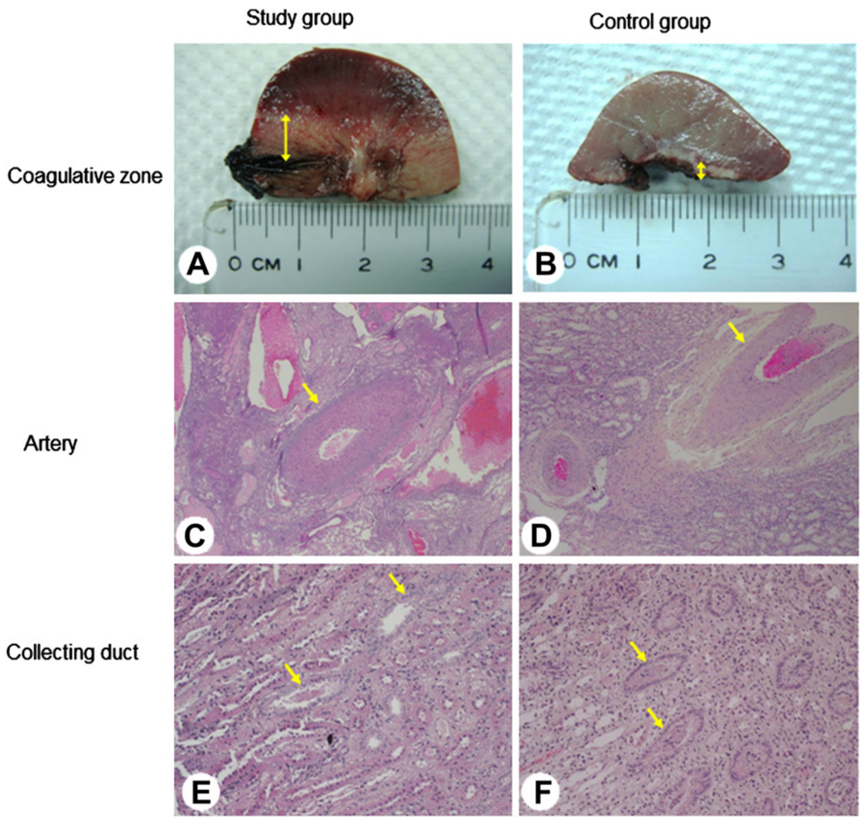

Figure 3. The thickness of the coagulation zone was 5 mm around the needle array in the study group **(A)** and 2 mm in the control group **(B)**. Under histological examination of the kidney immediately after resection, the transected arteries were up to 0.5 mm in diameter in both the study group **(C)** and control group **(D)** original magnification ×40. Endothelial cell injury and thrombus formation were seen in the arteries. The transected collecting ducts were up to 100 μm in diameter and showed condensed plugs in the lumen in both groups **(E and F)** original magnification ×100. (Color version available online.)

monopolar electrocauterization and hemostatic sutures. The amount of blood loss was significantly less than the competing technology, the ultrasonic Harmonic Scalpel technique. When compared with our electromagnetic thermal surgical technique, the ultrasonic Harmonic Scalpel induced obvious oozing over the cut surface of the renal parenchyma, resulting in much more blood loss and necessitating additional hemostatic measures for each pig.

Cold scissors have been the conventional cutting modality for most nephron-sparing surgeries, but this involves clamping with a period of renal ischemia. Energy-based devices, such as the bipolar LigaSure and ultrasonic Harmonic Scalpel, can minimize bleeding during surgical procedures. Nonetheless, adjunctive hemostatic devices should be combined to achieve complete hemostasis. Hemorrhaging from the cut surface of the remaining kidney portion usually requires suture ligatures, parenchyma repair, monopolar electrocautery, argon plasma coagulation, or fibrin glue. Recent advances in technology that can perform bloodless partial nephrectomy without the need for hilar artery clamping are bipolar radiofrequency coagulators and microwave tissue coagulators.[11-13] However, bleeding or oozing during the incision still prompts the requirement for additional hemostatic methods, and the radiofrequency or microwave tissue coagulator is expensive. Moreover, to create an excisional plane for partial nephrectomy, these methods need multiple punctures. These 2 methods are also time consuming.

On the other hand, our system and technology can serve for partial nephrectomy and can complete the procedure in a relatively short time, usually 6 minutes. Our system uses electromagnetic energy instead of radiofrequencies, microwaves, or electric current. The electromagnetic force generates inductive heat uniformly in the needle array, which in turn produces an area of coagulative necrosis that ablates blood vessels and collecting ducts. There is no electric current flowing through the animal body, and therefore no conductive pads are required. Hence, there will be no second-degree skin burns because of inadequate grounding pad placements (3.7%-10%) associated with radiofrequency ablation.[14] The needle arrays are quite easy to apply and the magnetic force is activated simply by turning on the machine. We believe it can be introduced to most surgeons with minimal knowledge of the technicalities of electronics and with limited experience in performing a partial nephrectomy, thereby increasing the availability of partial nephrectomy for most hospitals around the world.

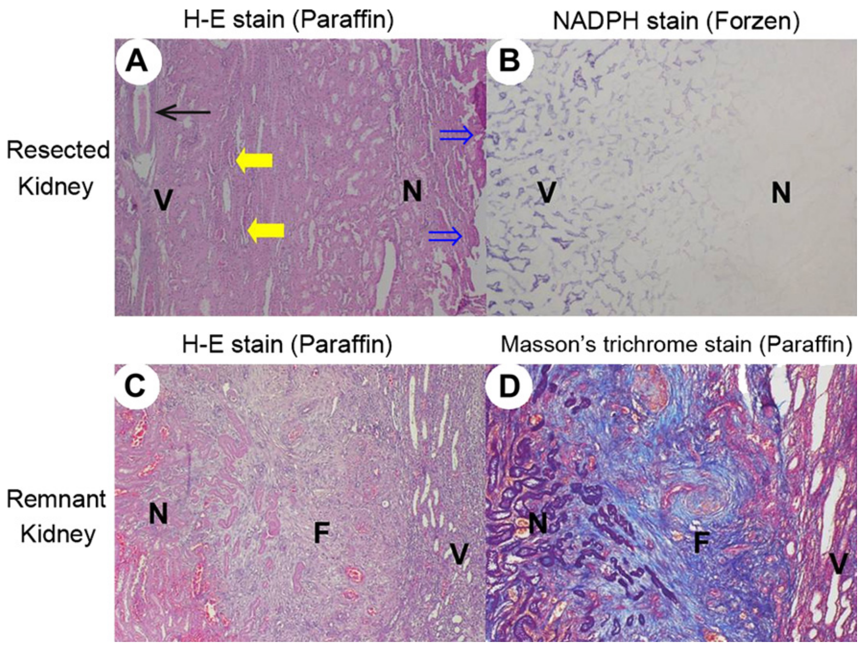

Figure 4. Histological examinations of resected and remnant kidneys in the study group. Histological examination of the resected kidney **(A, B)** showed condensely eosinophilic cauterized tissue near the center of the needle tract (blue double arrows). The blood vessels showed thrombus formation (black thin arrow). Condensed plugs were found in the lumen of some collecting ducts (yellow arrows). Loss of nicotinamide adenine dinucleotide phosphate (NADPH)-diaphorase activity was noted in the necrotic area (N) compared to viable tissue (V) **(B)**. After 14 days, the remnant kidney **(C, D)** showed a fibrous band (F) between viable tissue (V) and necrotic tissue (N). (**A** and **C**: hematoxylin and eosin [H&E] stain; **B**: NADPH stain, for viability from frozen section; **D**: Masson's trichrome stain.) (**A-D** were magnified $\times$40.) (Color version available online.)

Some doctors may raise concerns that coagulative necrosis of the collecting system may cause long-term tissue breakdown and urine leaks. We have checked the pathology after the observation period. Microscopically, condensed plugs are found in the lumen of some collecting ducts. These condensed intraluminal plugs and the condensed cauterized tissue on the resected margin may seal off the collecting ducts. After 14 days of healing, we saw that the viable collecting ducts were sealed by a dense fibrotic band, which provides a long-term barrier to prevent urine leakage.

We acknowledge some limitations of this study. Our study had no routine imaging to look for urine leakage. Recently, we performed intravenous pyelography on 1 additional pig immediately after, and 14 days after, partial nephrectomy using our ETS. No extravasation of contrast medium was observed. Our method was not tested under tumor conditions, because it is impractical to do so in the porcine model. Further, the porcine kidneys are smaller and are not as well vascularized as the human kidney. Our method might destroy a larger mass of healthy renal parenchyma than a standard partial nephrectomy, although no obvious renal impairment was observed. Because of the lack of radiofrequency ablation or microwave ablation equipment for kidney resections in our facility, we did not compare our method directly with those techniques. Also, until recently, this technique could only be applied by open laparotomy, because a way to perform it laparoscopically had not yet been developed. Now, however, we have made longer stainless needles (15-20 cm) that can be inserted into the laparoscopic trocar and pierce the top 5 cm of an ablated kidney, and we look forward to future clinical trials. Also, we have designed a new coil with deep magnetic force penetration. With these modifications, laparoscopic application is now possible. Stainless steel surgical instruments are sensitive to the alternating magnetic force, and if left under the applicator unattended for too long they can generate inductive heat and burn nonsurgical tissue. Therefore, instruments used in the operating room but not intended to produce thermal surgical effects should be made of nonmagnetic-sensitive materials (ie, wood or plastic) for safety.

CONCLUSION

Partial nephrectomy using an electromagnetic thermal surgery system has several advantages, such as eliminating renal ischemia, eliminating additional ligation stitches for hemostasis, and shortening the operation time. Our study demonstrates that the electromagnetic thermal surgery system is a safe, easy, and effective way to perform bloodless partial nephrectomy in a porcine model.

References

1. Novick AC. Nephron-sparing surgery for renal cell carcinoma. *Annu Rev Med.* 2002;53:393-407.

2. Dulabon LM, Lowrance WT, Russo P, et al. Trends in renal tumor surgery delivery within the United States. *Cancer*. 2010;116:2316-2321.
3. Riggs SB, Larochelle JC, Belldegrun AS. Partial nephrectomy: a contemporary review regarding outcomes and different techniques. *Cancer J*. 2008;14:302-307.
4. Thompson RH, Lane BR, Lohse CM, et al. Every minute counts when the renal hilum is clamped during partial nephrectomy. *Eur Urol*. 2010;58:340-345.
5. Funahashi Y, Hattori R, Yamamoto T, et al. Ischemic renal damage after nephron-sparing surgery in patients with normal contralateral kidney. *Eur Urol*. 2009;55:209-215.
6. Thompson RH, Lane BR, Lohse CM, et al. Comparison of warm ischemia versus no ischemia during partial nephrectomy on a solitary kidney. *Eur Urol*. 2010;58:331-336.
7. Shan YS, Zuchini R, Tsai HW, et al. Bloodless liver resection using needle arrays under alternating electromagnetic fields. *Surg Innov*. 2010;17:95-100.
8. Lo CJ, Chen CY, Tsai HW, et al. Partial splenectomy using an electromagnetic thermal surgery system in a porcine model. *Int J Hyperthermia*. 2011;27:108-115.
9. Chen CY, Zuchini R, Tsai WH, et al. Electromagnetic thermal surgery system for liver resection: an animal study. *Int J Hyperthermia*. 2010;26:604-609.
10. Manship LL, Moore WM, Bynoe R, et al. Differential endothelial injury caused by vascular clamps and vessel loops. II. Atherosclerotic vessels. *Am Surg*. 1985;51:401-406.
11. Hirao Y, Fujimoto K, Yoshii M, et al. Non-ischemic nephron-sparing surgery for renal cell carcinoma: complete tumor enucleation using a microwave tissue coagulator. *Jpn J Clin Oncol*. 2002;32:95-102.
12. Zeltser IS, Gupta A, Bensalah K, et al. Focal radiofrequency coagulation-assisted laparoscopic partial nephrectomy: a novel nonischemic technique. *J Endourol*. 2008;22:1269-1273.
13. White WM, Klein FA, Waters WB. Nephron sparing surgery using a bipolar radio frequency resection device. *J Urol*. 2008;180:2343-2347.
14. Goldberg SN, Solbiati L, Hahn PF, et al. Large-volume tissue ablation with radio frequency by using a clustered, internally cooled electrode technique: laboratory and clinical experience in liver metastases. *Radiology*. 1998;209:371-379.