JOURNAL OF ENDOUROLOGY
Volume 17, Number 10, December 2003

Bipolar Radiofrequency Ablation of the Kidney: Comparison with Monopolar Radiofrequency Ablation

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ABSTRACT

***Purpose*: We report initial *ex vivo* and *in vivo* studies using bipolar radiofrequency (RF) ablation of porcine kidneys. An internal ground electrode is positioned in the kidney opposite the RF electrode, resulting in ablation of all the intervening renal tissue.**

***Materials and Methods*: *Ex vivo* preparations of 10 porcine kidneys were perfused continuously with Ringer's solution and treated with either standard external grounded RF (N = 3) or bipolar RF ablation with 1 (N = 2), 2 (N = 3), or 3 (N = 2) cm of separation between the ground probe and the RF probe using a Model 30 RITA generator (RITA, Mountain View, CA). Target temperatures were 90°C for 8 minutes. Gross and histologic assessments were made acutely. Four domestic pigs were treated with monopolar RF ablation of the lower pole of one kidney and bipolar RF with a 12-mm separation between the probes of the contralateral lower pole. Animals were harvested 48 hours later to maximize tissue damage for gross measurements and histologic evaluation.**

***Results*: *Ex vivo* studies revealed grossly monopolar lesions 1.5 cm in maximum diameter and 1.75 cm^3 in volume. In comparison, bipolar lesions were 2.8 cm in maximum diameter and 10.3 cm^3 in volume using 3 cm of electrode separation. There was histologic evidence of cell death in all specimens. *In vivo* studies showed two distinct gross lesions with RF: one blanched and one hemorrhagic. Using bipolar RF, larger blanched lesions were achievable than with monopolar RF (2.80 cm^3 *v* 1.63 cm^3). Overall, the combinations of blanched and hemorrhagic lesions were similar with monopolar and bipolar RF (5.01 *v* 5.31 cm^3). Histologic evaluation verified cell death in the blanched lesions and rare areas of normal tissue in the hemorrhagic lesions.**

***Conclusions*: As shown by *ex vivo* data, bipolar RF can create larger lesions than does monopolar RF. *In vivo*, at 48 hours, both blanched and hemorrhagic gross lesions were seen using RF. In this model, blanched lesions predominated when performing bipolar RF.**

INTRODUCTION

TO DATE, THE USE OF "NEEDLE ABLATIVE" TECHNIQUES for smaller renal tumors remains a frontier in urology. The availability of effective ablative energies, including radiofrequency (RF) energy, has led to clinical reports using monopolar RF to treat small renal lesions.[1,2]

Radiofrequency ablation is attractive because it is only needle invasive while being hemostatic and of relatively low cost for most urologists.[3] Present limitations to monopolar RF include the small lesion size, difficulties in targeting, and questions about the reliability of cell kill. With regard to lesion size, Patel and associates[4] reported on the "wet" electrode, which enabled production of significantly larger lesions by RF ablation. Regarding lesion targeting, reports using MRI to monitor tissue destruction exist, similar to those using ultrasound during cryotherapy.[5,6] Regarding cell death, Collyer and associates[7] reported histologic "skip lesions" using both wet and dry RF ablation in the porcine model.

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FIG. 1. Prototype of novel biopolar RF electrode with tines deployed. Electrode (tines on left side) and ground (tines on right) were deployed in tissue. The RF current flows from electrode to ground in concentrated manner. Distance between ground and electrode can be varied to suit desired area of ablation.

Bipolar RF ablation addresses lesion size, targeting, and, possibly, concerns about cell killing. Bipolar RF utilizes an internal ground electrode positioned in the kidney opposite the RF electrode, resulting in ablation of all the intervening tissue. Bipolar RF allows higher current density and more uniform tissue heating than does monopolar RF.[8] Higher current density permits creation of larger lesions and more uniform cell kill. In addition, better control of the energy deposition is enabled because all the current is between the electrodes. Initial work at our institution demonstrated that the bipolar electrode created larger, more predictable, and more extensive ablative lesions in the liver than had been described using monopolar RF.[8] We here present our initial *ex vivo* and *in vivo* studies using bipolar RF in the porcine kidney.

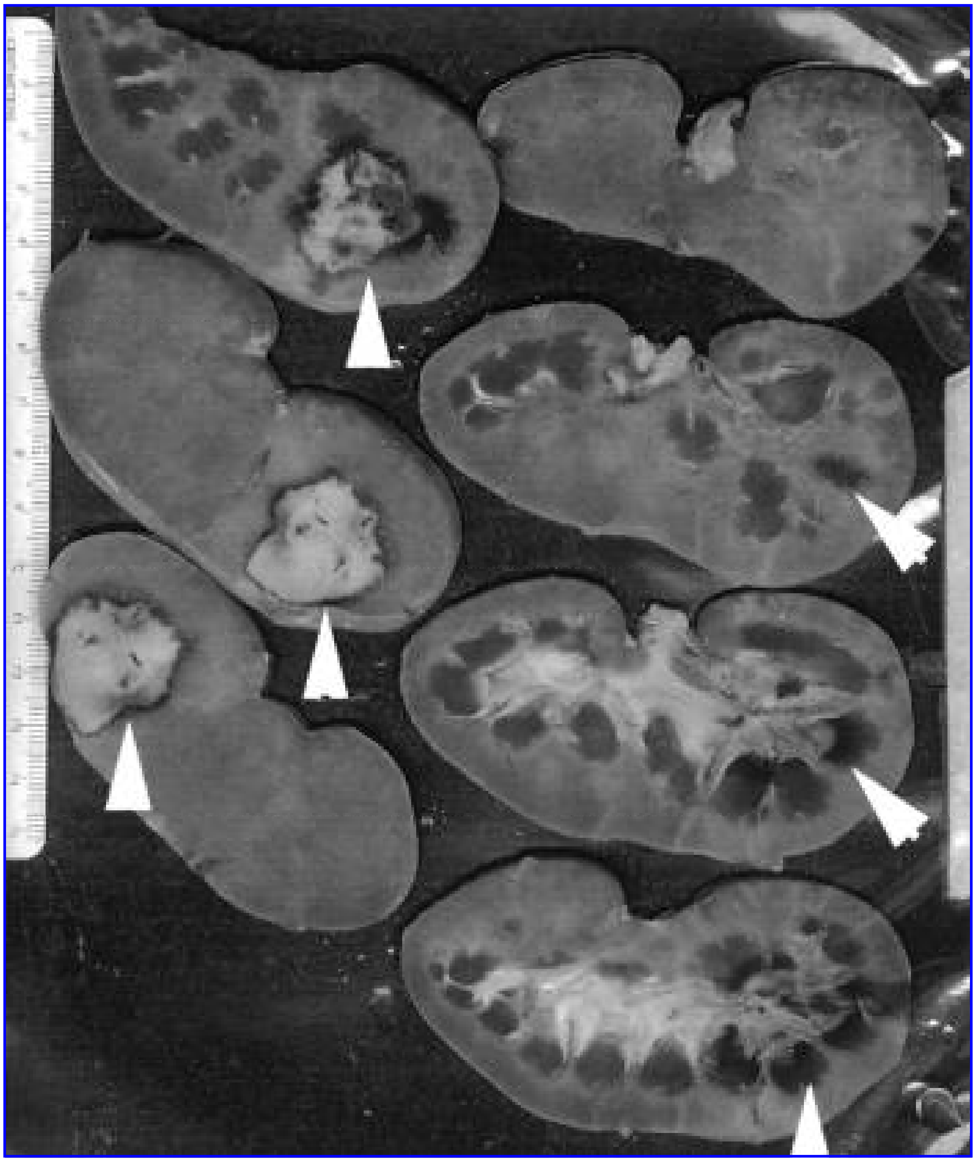

FIG. 2. Slices (2 mm) of kidney treated with bipolar RF ablation for 8 minutes at 90°C. Area of hemorrhagic and blanched lesions were calculated for each slice and added to determine volume.

MATERIALS AND METHODS

Ex vivo *studies*

Kidneys from 10 farm pigs were harvested acutely and perfused continuously with Ringer's solution at 37°C using a standard intravenous infusion pump and a 16-gauge catheter in the renal artery. They were treated with either external grounded RF (three kidneys) or strategically placed internal grounded bipolar RF ablation (seven kidneys) using a RITA Model 30 generator (RITA, Mountain View, CA). Of the kidneys undergoing bipolar RF, two were treated at 1 cm between the ground electrode and the treatment electrode, three kidneys were treated at 2 cm, and two kidneys were treated at 3 cm.

Target temperatures were 90°C for 8 minutes. Gross lesions were measured by a single investigator (TJJ), who determined the maximum diameter and volume using the formula $4/3\pi R^3$. Kidneys were then fixed in Formalin, sectioned, and studied by a single pathologist (TFW).

In vivo *studies*

Following strict animal research committee protocol at our institution, four domestic pigs (20 kg) were anesthetized (tiletamine/zolazepam [Telazol] 7 mg/kg intramuscularly [IM], xylazine 2.0 mg/kg IM for initial tranquilization, followed by halothane [1.0%–2.0% in oxygen] inhaled to effect) and prepared for surgery. The pigs were placed in the supine position and prepared in the midline and draped. Through a midline incision, one kidney was dissected free, and the lower pole was exposed. A 15-gauge conventional (monopolar) RF electrode was inserted into the lower pole of the kidney to a depth of 10 mm, and the tines were deployed at 7 mm. Radiofrequency ablation was performed for 8 minutes with an electrode target temperature of 90°C. These parameters were chosen on the basis of data acquired using bipolar RF in the liver.[8] Grounding for the RF procedure was done via an externally (dorsal) attached grounding pad, such that RF waves distributed evenly throughout the tissue in the direction of the grounding pad. Energy delivery was performed using a temperature-dependent algorithm with dynamic amperage at the probe tip. The kidney was allowed to cool to body temperature, the visible lesion was measured as noted in the *ex vivo* section, and the kidney was replaced *in situ.*

Next, the contralateral kidney was dissected free of connective tissue, and the lower pole was exposed. The prototype bipolar electrode, consisting of two Rita Model 30 15-gauge probes

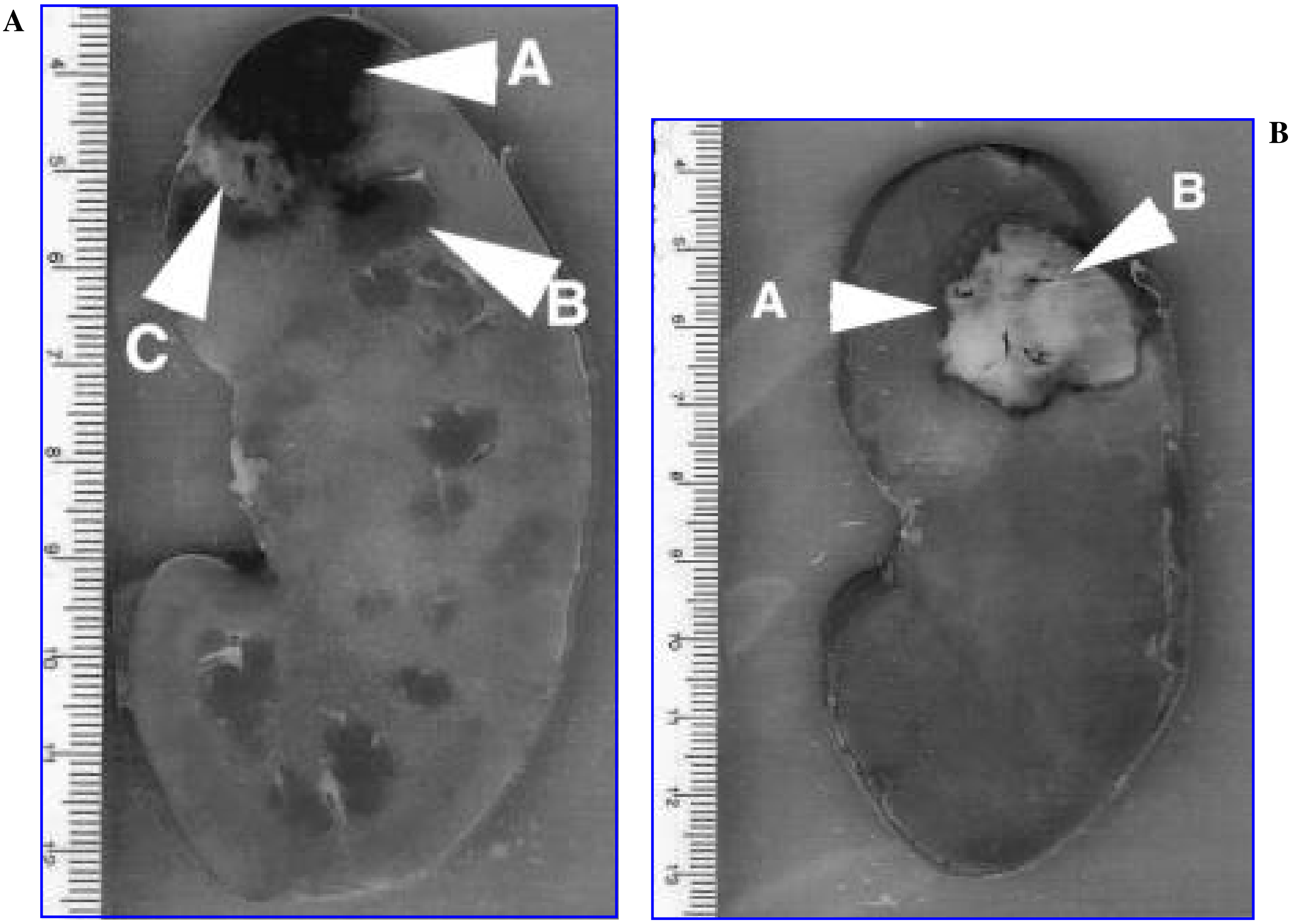

FIG. 3. Typical lesions. **(A)** Monopolar RF ablation. Arrow A denotes large hemorrhagic region, while arrow C denotes modest blanched zone. Arrow B shows area of damage outside confined lesion, illustrating inconsistency of traditional monopolar technique. **(B).** Bipolar RF ablation. Note small hemorrhagic zone (arrow A) surrounding substantial blanched lesion (arrow B). In contrast to monopolar lesions, this lesion is spherical with defined margins.

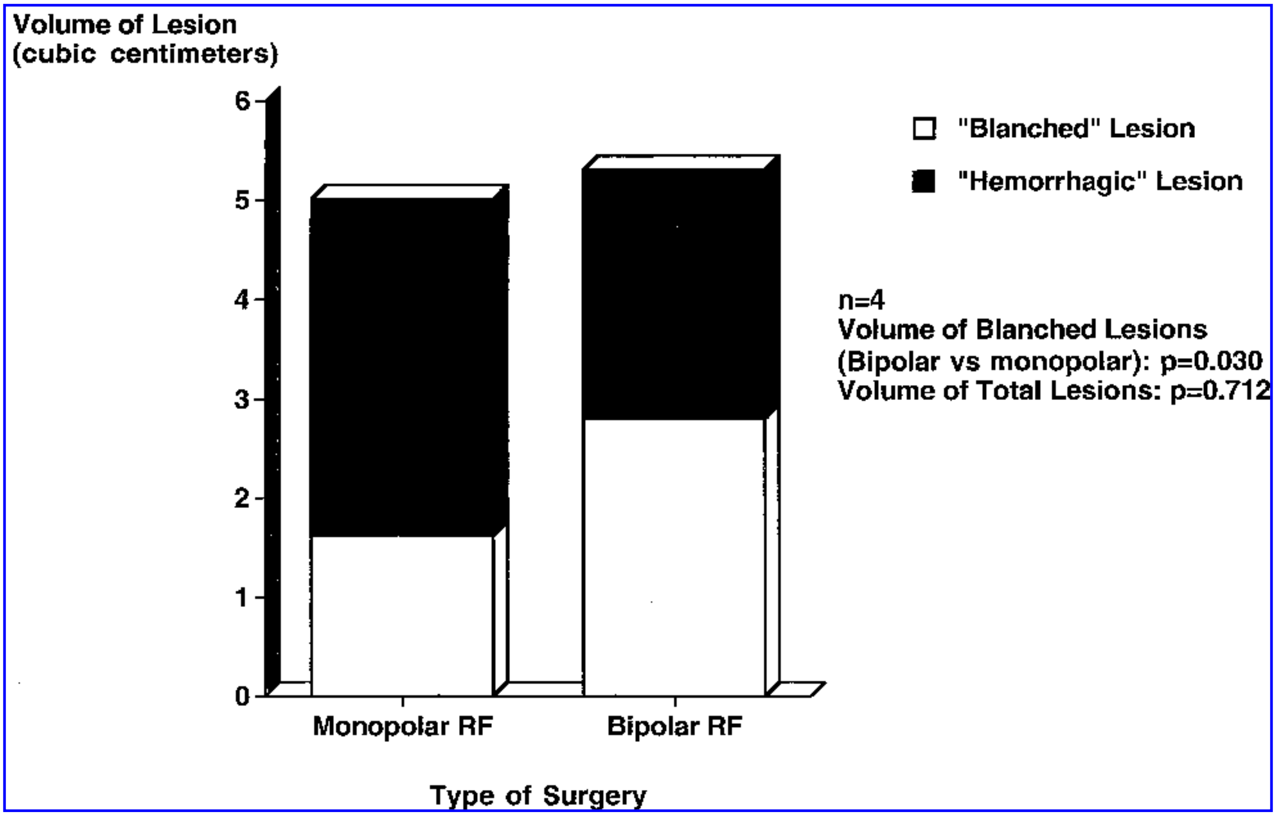

FIG. 4. Differences between bipolar and monopolar RF-induced lesions. No significant difference was seen in overall lesion size ($P = 0.712$), but bipolar RF induced significantly larger blanched lesion than monopolar RF. This, combined with more reliable lesion margins and spherical shape of lesions, may make bipolar technique a more reliable ablative tool.

(one electrode and one ground), was inserted. The electrode probe was inserted 10 mm into the kidney and the ground probe 12 mm further. The bipolar design is sliding, such that the distance between the electrode and the ground is variable (Fig. 1). In this experiment, a 12-mm distance was used on the basis of the *ex vivo* data. It was evident that larger lesions could be created with wider separation of the electrodes, yet because the domestic pig kidney is smaller than that of the farm pigs used in our *ex vivo* experiments, we chose a smaller lesion size. The tines were deployed at 7 mm from the electrode (consistent with the monopolar procedure and reflecting kidney size) and the ground. The RF ablation was performed for 8 minutes with an electrode target temperature of 90°C. Grounding in these procedures was done via the ground probe, such that RF waves were concentrated between the two probes, creating a more targeted ablation. The kidney was allowed to cool to body temperature, the visible lesion was measured as noted in the *ex vivo* section, the kidney was replaced *in situ*, and the incision was closed using nonabsorbable sutures.

*Tissue harvesting and lesion analysis (*in vivo *studies only)*

The pigs were allowed to survive for 48 hours to better evaluate cell death and then sacrificed. Forty-eight hours would allow coagulative necrosis to be identified; however, even longer periods may be more definitive. No postoperative complications were noted. Once harvested, the kidneys were completely perfused with 10% buffered Formalin for immediate fixing, then removed and stored in Formalin for 24 hours to ensure complete fixation. The kidneys were cut into exactly 2-mm thick slices on a commercial meat slicer. Slices were placed on an optical scanner (HP 4C/T; Hewlitt-Packard, Palo Alto, CA) and images saved in an image management program (Photo-

TABLE 1. *EX VIVO* KIDNEY RF STUDIES

Technique	*No.*	*Lesion diameter (cm)*	*Lesion volume (cm^3)*
Monopolar RF	3	1.5	1.8
Bipolar RF 1 cm apart	2	1.0	0.7
Bipolar RF 2 cm apart	3	1.5	1.8
Bipolar RF 3 cm apart	2	2.8	10.3

Shop, Adobe, Inc., San Jose, CA) as JPEG images. Analysis was performed on a Macintosh G3 computer (Apple Computer, Cupertino, CA). The areas of both zones within each slice were calculated using the public domain program NIH Image (U.S. National Institutes of Health: http://rsb.info.nih.gov/nih.image/).

Grossly, all RF lesions exhibited two distinct regions: a blanched or "white" necrotic zone and a surrounding hemorrhagic zone or "red" zone of injury (Fig. 2 and 3). An estimation of lesion volume was calculated by multiplying the area (in square centimeters) by 0.2 (the thickness of each slice) and summing these values for each slice of the kidney (Fig. 4).

Samples of lesions were embedded in paraffin, stained with hematoxylin and eosin (H&E), and reviewed by a pathologist blinded to the treatment (TFW) for determination of cell death, inflammatory changes, and vascular thrombosis. While a good technique, nicotinamide adenine dinucleotide (NADH) staining was not utilized for this study. The calculated volumes for all monopolar and bipolar blanched and hemorrhagic lesions, as well as total lesion volumes, were averaged within each group (Fig. 4). The standard error of the mean (SEM) was determined for each group, and statistical significance was compared with an unpaired Student's *T*-test. *P* values of 0.05 were indicative of statistical significance.

RESULTS

Ex vivo *studies*

Grossly, monopolar lesions were highly irregular and conical. Centrally, the lesions were blanched, with intervening regions of hemorrhage. Margins appeared more easily defined in bipolar RF-treated kidneys. All lesions produced by bipolar RF energy were confined between the electrodes. Gross assessment revealed monopolar lesions 1.5 cm in maximum diameter and 1.75 cm^3 in volume (Table 1). In comparison, bipolar lesions were as large as 2.8 cm in maximum diameter and 10.3 cm^3 in volume using 3-cm electrode separation and more closely approximated monopolar lesion size at between 1- and 2-cm electrode separation (Table 1). The major microscopic change observed was destruction of erythrocytes in the vasculature and glomeruli of the lesions.

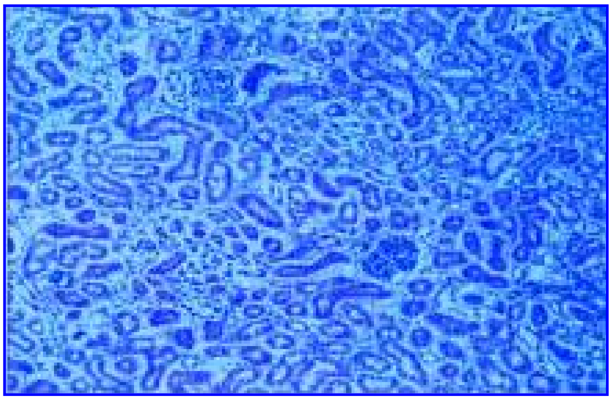

FIG. 5. Histologic view of central (blanched) area of lesion created with bipolar RF energy exhibiting swollen eosinophilic tubular epithelium and glomeruli without erythrocytes. Tubules are ill defined and separated from basal lamina. (H&E; original magnification, ×100.)

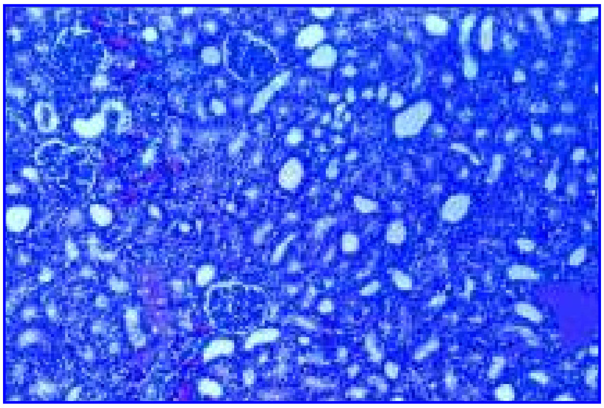

FIG. 6. Normal kidney tissue showing overall basophilic staining and red blood cells in glomerular capillaries (H&E; original magnification ×100).

In vivo *studies*

The RF lesions in all kidney slices exhibited the characteristic blanched necrotic zone surrounded by a red hemorrhagic zone (Figs. 1–3). However, volume analysis determined that the blanched zone in bipolar lesions averaged 2.80 ± 0.35 cm^3 (range 2.0–3.6 cm^3), while blanched lesions produced with monopolar RF ablation averaged 1.63 ± 0.05 cm^3 (range 1.5–1.7 cm^3) ($P = 0.030$; N = 4 (Fig. 4). Hemorrhagic zones in bipolar lesions averaged 2.51 ± 0.27 cm^3 (range 2.4–5.2 cm^3) while in monopolar lesions, this zone was 3.38 ± 0.62 cm^3 (range 2.1–5.2 cm^3) ($P = 0.309$). Total lesion volume analysis showed no significant difference between the two groups, as bipolar lesions were 5.31 ± 0.61 cm^3 and monopolar lesions

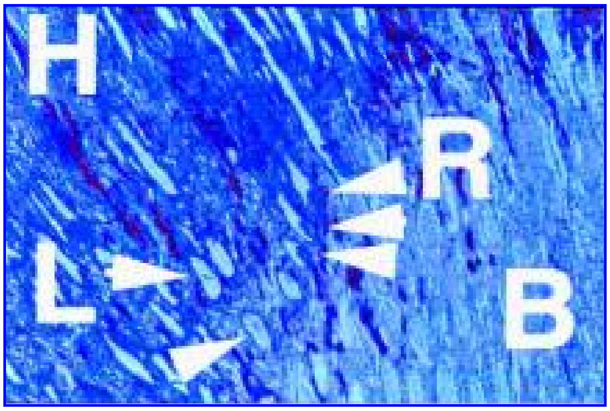

FIG. 7. Histologic view of hemorrhagic/blanched border of lesion created with bipolar RF energy in renal medulla with congested vasa recta. "H" indicates hemorrhagic zone, and "B" indicates blanched zone. "L" marks presence of living tubules in hemorrhagic zone, while "R" denotes tubules undergoing regeneration. (H&E; original magnification, ×100.)

were 5.01 ± 0.28 cm^3 ($P = 0.712$; $N = 4$). No evidence of urine leak or urinoma was seen.

Pathology

The RF lesions demonstrated a central necrotic zone (Fig. 5) surrounded by a peripheral zone consisting of necrotic renal tubules and glomeruli, interstitial hemorrhage, and fragmented polymorphonuclear (PMN) leukocyte infiltrate. Inside the central zone, the outlines of tubules were distinct but swollen; cell borders were frayed and indistinct and were focally separated from the basal lamina. Nuclei were not altered (Fig. 5) but there was focal cytoplasmic vacuolization. In addition, there were no erythrocytes in the glomerular capillaries, and, in most of the veins and arteries, the erythrocytes were degenerating or converted into granular masses. The eosinophilia of this central zone contrasted with the more basophilic normal renal parenchyma surrounding the lesions (Fig. 6). Within hemorrhagic lesions, areas of vascular congestion and hemorrhage were accompanied by advanced necrotic changes, but also focal regenerative changes of the renal tubules and rare patches of living cells were seen (Fig. 7). Similar histologic changes were seen in the bipolar and monopolar lesions. Therefore, only in the hemorrhagic areas were focal regenerative changes of the renal tubules seen. No such areas were identified in blanched regions in either group.

DISCUSSION

Radiofrequency energy is transmitted by direct contact and is tissue destructive via thermal injury, producing tissue necrosis in 3 to 5 minutes.[9] By grounding the subject, the electrical circuit is completed, and the RF energy is released at the uninsulated tip and results in cellular death by coagulative necrosis.[10] While conventional RF ablation is performed by inserting "dry" electrodes into the tissues to be ablated, the use of "wet" electrodes has been advocated to create larger lesions by cooling the electrode and minimizing charring.[4] Bipolar RF represents an advancement in RF ablation. In the presence of a ground electrode, energy moves only from the active electrode to the ground electrode, thus controlling the region of tissue injury. In addition, a higher current density can be achieved using bipolar RF, perhaps enhancing the ablative effect.[8]

The use of RF ablation in renal tumors includes both animal studies and clinical reports.[1,2,4,7,11–13] Animal studies have generally demonstrated feasibility, and the advancement of wet RF has enabled urologists to create larger, more reproducible lesions and thus contemplate its use in renal lesions.[4] Two groups have reported the efficacy of RF in a tumor model in rabbit kidneys, providing preclinical evidence of RF efficacy in treating tumors.[12,13] However, rabbit kidneys are small, thus validating RF only in treating very small lesions. Of great interest is the report of Collyer and associates[7] demonstrating regions of viable tissue within porcine kidneys treated with both dry and wet monopolar RF. In contrast, Hsu and associates[14] recently published acute and chronic observations of dry RF in the porcine model and found adequate cell death using RF and described gross observations similar to those in this study. One clinical report included cases with persistent rims of enhancing tissue following RF ablation.[1]

Our data indicate that two types of gross lesions are created by RF, namely, a blanched, necrotic lesion and a hemorrhagic, predominantly necrotic lesion. The lesions remained smaller than the probe distance, probably because of desiccation near the probes. Perhaps higher target temperatures or longer treatment would eliminate this variable. The lack of current dispersion favors bipolar RF. This finding may explain the feasibility of identifying "skip lesions" in one study[7] and reproducible cell death in others.[12–14] Hsu and colleagues described an "autoamputation" phenomenon in RF lesions in their 90-day survival animals, which may in fact be the end product of the blanched and hemorrhagic lesions described in this study.[14] Of note, our protocol sacrificed the animals after 48 hours rather than 90 days, as in the study by Hsu et al. Over time, we presume that a majority of hemorrhagic lesions would become necrotic, as the blanched lesions would, secondary to inflammatory infiltrate and lack of blood flow. However, our findings of rare living and regenerating cells in the hemorrhagic lesions is a concern. From our data, we deduce that the blanched lesion is more uniform in size, shape, and cell death and can be created more effectively with bipolar RF than with monopolar dry RF. The descriptive nature of the histopathology portion of the study limits any unequivocal statement of cell death, and while NADH staining may provide some additional insight, it is only one of several approaches to assess cell death.

As in other ablative technologies, the targeting and treatment of renal lesions with monopolar RF remains problematic. Because monopolar RF cannot easily be monitored during treatment, using the bipolar electrode to "frame" the lesion is advantageous. In addition, the higher current density in bipolar RF promotes more uniform, larger blanched lesions. Whether there is a limit to the distance and shape of the lesion created using a bipolar probe remains to be seen, and certainly, increasing the temperature and treatment times will be necessary. Using monopolar RF, the energy dispersion could lead to damage to the remaining parenchyma. However, it is certain that our preliminary assessments support a clear advantage of bipolar RF in terms of lesion size, consistency, and targeting.

CONCLUSION

Our *ex vivo* and *in vivo* studies demonstrate that bipolar RF creates larger lesions (*ex vivo* data) with more consistent cellular injury (blanched lesions) than does conventional monopolar RF in this model. While the clinical application of bipolar RF remains conceptual at this time, bipolar RF addresses three key concerns with RF, namely lesion size, lesion targeting, and lesion homogeneity.

ACKNOWLEDGMENTS

We would like to thank Lisa A. Sampson, Department of Surgery, for surgical assistance and Angela M. Baker, Department of Surgical Pathology, for specimen preparation.

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