In Vivo Efficiency of Multipolar Radiofrequency Ablation with Two Bipolar Electrodes: A Comparative Experimental Study in Pig Kidney

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PURPOSE: To compare in vivo efficacy of multipolar radiofrequency (RF) ablation with two internally cooled electrodes to that of monopolar RF ablation with internally cooled single and cluster needles to induce coagulation in vivo porcine kidneys.

MATERIALS AND METHODS: Twenty-four coagulations were created in the kidneys of 12 pigs by means of laparotomy by using a monopolar or multipolar RF system. In the monopolar mode, RF was applied to a single internally cooled probe (group A) or to a cluster probe (group B) for 12 minutes. In the multipolar mode, RF was applied to two bipolar probes with 2-cm interprobe spacing up to 50 kJ (group C). Technical parameters and the dimensions, shapes, and coefficients of variation of the coagulations were compared among the three groups.

RESULTS: The minimum transverse diameters of the RF-induced coagulations in groups B (3.5 cm ± 0.5) and C (3.8 cm ± 0.6) were significantly larger than that in group A (2.6 cm ± 0.3). The mean coagulation volumes produced in the multipolar group (25.1 cm³ ± 5.2) were greater than those produced in the monopolar groups (11.6 cm³ ± 3.7 and 18.1 cm³ ± 5.8) (P < .05). The mean ratio of transverse diameter to vertical diameter of the coagulations was larger in groups B and C (1.2 ± 0.2 and 1.0 ± 0.1, respectively) than in group A (0.8 ± 0.2) (P < .05). In addition, the coefficients of variation for groups A, B, and C were 0.33, 0.30, and 0.21, respectively. The procedure time was longer with the multipolar technique (27.2 minutes ± 4.9) than with the monopolar technique with a single or cluster probe (12 minutes).

CONCLUSIONS: Multipolar RF ablation showed at least equivalent or better in vivo efficiency for creating a larger coagulation than monopolar RF ablation with single or cluster electrodes, but with a longer procedure time and at slightly greater complexity.


Abbreviation: RF = radiofrequency

RADIOFREQUENCY (RF) ablation is being increasingly used to treat patients with small renal cell carcinoma who are not ideal candidates for surgery (1–6). RF ablation has the potential to preserve renal function while avoiding open surgery. Several preliminary reports regarding renal RF ablation have demonstrated promising results (3–6); however, there have also been reports of RF treatment failures (7–10). Tumor size and location are the two most important factors that govern whether renal cell carcinomas can be successfully treated (1,6). Indeed, RF ablation can be effective for the destruction of small tumors (<3 cm), but success in lesions larger than 3.5 cm in diameter has been less impressive (3,4,7). Because heat decreases exponentially from the RF source, tumors larger than 3.5 cm in diameter pose a substantial challenge for RF ablation, especially because a 0.5–1.0-cm “ablation margin” surrounding the tumor is also preferred.
(11–14). Most RF systems are currently channeled in monopolar fashion, which involves intense heating at an active tip and a large grounding pad on the skin to complete the circuit. The present limitations of monopolar RF ablation for renal tumors include the small dimension of the ablation region generated during a single RF application and questions with regard to the reliability of cell destruction (5,15–17).

Several strategies have been devised to overcome an inadequate volume of tissue coagulation. These include the use of a cluster cooled electrode (Valleylab, Burlington, Mass), a wet electrode (Berchtold, Tuttlingen, Germany), an expandable wet electrode (Starburst Xli; RITA Medical Systems, Mountain View, Calif), and a multitined expandable electrode (LeVeen; Boston Scientific, Natick, Mass) (18–20). Despite the recent development of devices that enable the creation of larger coagulations, the treatment of liver tumors larger than 3.5 cm in diameter often requires multiple overlapping ablations (13,14). However, because this approach is both time-consuming and technically challenging, there is a definite need to increase the coagulation dimensions with a single RF application (12,21).

A few previous studies of the multiple electrode approach in the bipolar (22–24) or multipolar mode (25) have shown that large volumes of coagulation could be produced in the kidney. With the standard monopolar technique, RF power is applied to only a single electrode at a time and uses the dispersive plate as the return electrode. With the bipolar technique, however, RF energy is applied to one electrode, using the other electrode as the return electrode; furthermore, in the multipolar mode (switching bipolar mode), all possible electrode pairs of the multiple electrodes are activated automatically, one after the other, for a defined period of time (25). However, there have been limited data regarding the in vivo efficacy of multipolar RF ablation in the perfused kidney. Herein, we present the results of our systematic evaluation of the in vivo efficacy of multipolar RF ablation with two internally cooled probes compared with standard monopolar RF ablation, which uses a commercially available, internally cooled probe, on the dimensions of the ablation zones in renal tissue.

MATERIALS AND METHODS

Animals, Anesthetics, and Surgical Technique

Approval was obtained from the institutional animal care and use committee before the initiation of this study. Twelve domestic pigs (50 kg), the most widely used animal for in vivo experiments of RF ablation (15,17), were anesthetized with intramuscular injection of 50 mg/kg ketamine hydrochloride (Ketamine; Yuhan, Seoul, Korea) and 5 mg/kg xylazine (Rumpun; Bayer Korea, Ansan, Korea) and prepared for surgery. Booster injections as much as half of the initial dose were administered as needed. Endotracheal intubation was performed and anesthesia maintained with inhaled isoflurane (Isoflo; Abbott Laboratories, North Chicago, Ill). Mechanical ventilation was used throughout the procedure.

The pigs were placed in a supine position and draped. With use of a midline incision, each kidney was exposed by means of dissection. One coagulation was created with monopolar or multipolar RF ablation in each kidney of the 12 pigs by means of laparotomy. Because of the limited access to a computed tomographic (CT) scanner in our institute, we performed the RF ablation procedure by using laparotomy instead of CT guidance. After RF ablation, the incision was closed with nonabsorbable sutures.

RF Ablation Protocol

RF ablation was performed by using one of the two RF systems: a 200-W generator (CC-3; Valleylab) and an internally cooled probe (Cool-tip; Valleylab) (group A); a 200-W generator (CC-3) and a cluster internally cooled probe (Valleylab) (group B); and a 250-W generator (Celon Medical Instruments, Teltow, Germany) and two cooled probes (ProSurge; Celon) (group C). In the three groups, either a single probe or two probes were inserted into the upper or lower pole of the kidney to a depth of 35 mm. The electrodes were placed perpendicular to the cortex so that the needle went from the cortex to the medulla.

In groups A and B, the RF power was manually increased to 200 W and held for 12 minutes. The single internally cooled electrode has a 3-cm-long active distal section, whereas cluster electrodes had an active tip length of 2.5 cm. Needle cooling is ensured by means of peristaltic perfusion of chilled saline by using a peristaltic pump (PE-PM; Valleylab), which enables the probe to maintain tip temperatures of less than 25°C during RF delivery. The impedance control mode allowed maximum power to be delivered until the impedance increased to 10 Ω above the baseline value. At this point, the current was automatically switched off for 15 seconds to avoid further local temperature increase (26).

Grounding for the RF procedure was done by means of two externally (dorsal) attached grounding pads, such that the RF currents were distributed evenly through tissue in the direction of the grounding pads.

In group C, a 250-W generator (Celon) working at 470 kHz and two cooled bipolar probes (ProSurge) were used in multipolar mode. The needle type, cooled bipolar probe has a diameter of 1.8 mm and a shaft length of 15 cm. As appropriate for the anatomy of the porcine kidney, 30-mm conductors were selected. The active (conducting) part of the bipolar RF applicator included 10- and 15-mm electrodes (uninsulated portions) and the insulator (Fig 1). In the multipolar mode, all possible electrode pairs (n = 4) are activated automatically one after the other during a short period of time (2 seconds). Here, a pair of electrodes is not only defined as the two electrodes located on a specific bipolar applicator shaft but also includes all other possible electrode combinations in the various applicators (25). Therefore, the current could pass between one electrode of one applicator shaft and an electrode of the other applicator shaft and thus permitted four possible combinations (pairs of electrodes) between which the current could pass (27,28).

In accordance with the manufacturer’s recommendations, the selected power setting was 1 W per 1 mm of active conductor and, therefore, a power level of 60 W was selected for the two probes with an active conductor of 30 mm each. The target energy was set at 50 kJ. Taking into consideration both the fact that kidney tissue has higher electrical conductivity than liver tissue, as well as the results of a previous ex vivo study involving multipolar RF
ablation (24), we chose 2-cm interelectrode spacing. Lesions were formed by placing the RF probe, as viewed directly, into the pig kidneys. Precise spacing of the electrodes was ensured by using an acrylic puncture aid. The Celon RF system did not require the use of grounding pads. An internal room temperature saline circulation of the applicator was provided by a triple peristaltic pump that was part of the system (Aquaflow III; Celon), and the delivery rate was set at 30 mL per minute.

**Imaging Follow-up**

A multidetector CT unit with 16 detector rows (Sensation 16; Siemens, Forchheim, Germany) was used to monitor ablations 3 days after RF ablation. Axial CT scans were obtained with 1.5 × 16 beam collimation, a reconstruction increment of 3 mm, and a 1.0 pitch and encompassed both lower lobes of the lung and abdomen, including the kidneys, before and after the injection of 120 mL of contrast medium (Ultravist 370; Schering Korea, Seoul, Korea). Contrast medium was injected at a rate of 3 mL/sec through an ear vein. Postcontrast CT scans were obtained 60 seconds after contrast medium administration. CT scans were reconstructed at 3-mm intervals in the axial plane and at 1-mm intervals for multiplanar reconstruction images. The thin-section data set was forwarded to a personal computer containing dedicated three-dimensional software (Rapidia; INFINITT, Seoul, Korea) and reconstructed into 3-mm-thick coronal and sagittal images.

**Assessment of Coagulation Necrosis (Imaging and Pathologic Studies)**

Nonenhancing ablation areas in treated kidneys on contrast medium–enhanced CT scans were measured by using Image J software (http://rsb.info.nih.gov). The area and volume of the nonenhancing region, regarded as the coagulation area (29), were recorded for each section. The volume was computed by integrating the area of each section across the entire lesion.

The pigs were allowed to survive for 72 hours and were then sacrificed after obtaining CT scans. Once harvested, the kidneys were cut along the electrode insertion axis and serially sectioned at 5-mm intervals. The histopathologic study included staining for mitochondrial enzyme activity by incubating thin representative tissue sections for 30 minutes in 2% 2,3,5- triphenyl tetrazolium chloride or TTC (Sigma, St Louis, Mo) at 20°–25°C. This test can be used to determine irreversible cellular injury during the early stages of RF-induced necrosis (30). Because the unstained area of an RF-ablated region has been shown to correspond to the zone of necrosis (29), two observers measured the transverse diameter (Dt) and vertical diameter (Dv) of the unstained area of the RF-ablated region on the coronal plane in consensus. When the coagulation zones had a triangular shape suggestive of an association between necrosis and ischemia, we measured the transverse diameter at the midportion of the coagulation zone along the electrode insertion axis. The number of sections containing the RF-ablated region determined the second transverse diameter (anterioposterior diameter, Dv/2). The volumes of the ablation zones were evaluated by approximating the lesion to a sphere by using the following formula: π(Dv × Dt × Dv/2)/6. RF lesion shape was characterized by the ratio between the transverse diameter and the vertical diameter, as follows: Dv/Dt. Therefore, a ratio close to 1 emphasized the more spherical shape of the RF-induced coagulation. In addition, evaluation of the variation of volume in each group was given by a coefficient of variation calculated by dividing the standard variation by the mean value. The closer the value was to 0, the more reproducible the coagulation. The RF-induced ablated regions of a representative case of each group were fixed in 10% formalin for routine histologic processing and processed by means of paraffin sectioning and hematoxylin-eosin staining for light microscopic study.

**Statistical Analysis**

The dimensions of the thermal ablation area and the technical parameters of the three groups were averaged for each group and compared by using the analysis of variance test. For group-to-group comparison, a Turkey post hoc test was used. Values were expressed as means ± standard deviations. The Spearman correlation test was used to evaluate the correlation between the coagulation volumes measured on the pathologic specimen and the CT scans. For all statistical analyses, a P value of less than .05 was considered statistically significant. Statistical analysis was performed by using the Instat program (GraphPad Software, San Diego, Calif).

**RESULTS**

**Electrical Measurements**

The mean impedance values of groups A (65.9 Ω ± 6.5) and B (51.3 Ω ± 2.6) were significantly lower than those of group C (97.6 Ω ± 28.2) (P < .05). The monopolar RF ablation technique delivered a larger amount of energy per time than did the multipolar RF ablation technique, that is, 5.0 kJ/...
min ± 0.4 in group A, 6.4 kJ/min ± 0.8 in group B, and 1.9 kJ/min ± 0.3 in group C, and the differences among the three groups were statistically significant (P < .05, P < .05) (Table 1).

The procedure time was longer with the multipolar technique (27.2 minutes ± 4.9) than with the standard monopolar technique using a single or cluster probe (12 minutes).

Dimensions and Shape of Ablation Zones

The RF-induced coagulations in all treated kidneys exhibited a character-
istic central white zone surrounded by a red hemorrhagic zone (Fig 2). The margins of the RF lesions were mildly irregular, regardless of which system was used. After staining with 2% 2,3,5-triphenyl tetrazolium chloride, normal renal parenchyma and the peripheral hemorrhagic zone appeared pink, but the central white zone remained unstained (Fig 2).

The minimum transverse diameter of the RF-induced coagulations were 2.5 cm ± 0.3 in group A, 3.1 cm ± 0.6 in group B, and 3.4 cm ± 0.2 in group C (P < .05 between groups A and C). The mean vertical diameter of the coagulations were 3.3 cm ± 0.5 in group A, 3.1 cm ± 0.5 in group B, and 3.7 cm ± 0.3 in group C (P < .05 between groups B and C). The mean volume of the ablation zones obtained in the multipolar RF ablation group was significantly larger than that of the monopolar RF ablation groups: 11.4 cm³ ± 3.7 in group A, 18.1 cm³ ± 5.8 in group B, and 25.1 cm³ ± 5.2 in group C (P < .05). In addition, the coefficients of variation of the ablation volume were very close to those measured on the gross specimen: 12.0 cm³ ± 4.5 in group A, 21.7 cm³ ± 5.0 in group B, and 26.3 cm³ ± 7.0 in group C. There was good correlation between those figures measured on the gross specimen and those measured on CT scans (r = 0.9, P < .05). In addition, the differences in the three diameters measured on CT scans and on the gross specimen were in a range of 1–4 mm.

### Histopathologic Results

Histopathologically, the RF-induced ablation regions of the representative sections of each treated kidney demonstrated a central zone of complete coagulative necrosis surrounded by a peripheral zone of inflammation, interstitial hemorrhage, and partial necrosis. Similar histologic changes were observed in these three groups.

### DISCUSSION

Recently, RF ablation has become the most commonly used thermal ablation technique and is used to treat primary and secondary hepatic malignancies (31). There is a growing body of experience supporting the use of imaging-guided RF ablation for the treatment of primary renal cell carcinoma, and image-guided RF ablation is an option for the treatment of patients who have low-stage renal cell carcinoma but may not be surgical candidates (32). To date, most commonly used RF devices use monopolar electrodes (33). However, one major limitation of monopolar RF ablation is the small ablation region caused by the precipitous drop in current density that occurs with increasing distance from the energy source. Consequently, the therapeutic results of renal RF ablation may depend on tumor size (1–7). Until now, ablation of renal lesions larger than 4–5 cm has been avoided, and even small tumors located in the more vascular central areas of the kidney could not be treated with certainty due to the heat sink effect (10,12).

In previous ex vivo experimental studies of multiple bipolar and multipolar RF ablation for creating large areas of coagulation (24,25), multipolar RF ablation with an internally cooled electrode was able to create a larger ablated zone than bipolar RF ablation with a bipolar probe, in predictable fashion. On the basis of previous studies (24,25), in the present study we tested the in vivo efficiency of multipolar RF ablation by using two internally cooled probes to expand the extent of the RF-induced coagulation.

In our in vivo study, multipolar RF ablation with two internally cooled probes (group C) created a larger coagulation region than RF ablation with an internally cooled probe (group A) (25.1 cm³ ± 5.2 and 11.4 cm³ ± 3.7, respectively) (Fig 2). The larger RF-induced coagulation created with the multipolar RF ablation mode could be attributed to several factors. First, it could be related to the greater amount of heat produced at a given current level in the multipolar mode than in the monopolar mode (23,34,35). In the monopolar mode, heat is diverted from the ablation site in all directions.

### Table 2

Measured Values of RF-induced Coagulation Necrosis in the Monopolar and Multipolar RF Ablation Groups

<table>
<thead>
<tr>
<th>Coagulation Necrosis</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical diameter (cm)</td>
<td>3.3 ± 0.5</td>
<td>3.1 ± 0.5</td>
<td>3.7 ± 0.3</td>
<td>&lt;.05*</td>
</tr>
<tr>
<td>D1 (cm)</td>
<td>2.6 ± 0.3</td>
<td>3.5 ± 0.5</td>
<td>3.8 ± 0.6</td>
<td>&lt;.05‡</td>
</tr>
<tr>
<td>D2 (cm)</td>
<td>2.5 ± 0.3</td>
<td>3.1 ± 0.6</td>
<td>3.4 ± 0.2</td>
<td>&lt;.05†</td>
</tr>
<tr>
<td>Volume (cm³)</td>
<td>11.5 ± 3.7</td>
<td>18.1 ± 5.8</td>
<td>25.1 ± 5.2</td>
<td>&lt;.05§</td>
</tr>
<tr>
<td>Ratio of D1/Dv</td>
<td>0.79 ± 0.2</td>
<td>1.15 ± 0.2</td>
<td>1.02 ± 0.1</td>
<td>&lt;.05‡</td>
</tr>
<tr>
<td>Coefficient of variation of the ablation volume</td>
<td>0.33</td>
<td>0.30</td>
<td>0.21</td>
<td>. . .</td>
</tr>
</tbody>
</table>

Note.—D1 = transverse diameter on the coronal plane, D2 = the second transverse diameter on the perpendicular plane to the probe insertion axis. Group A = monopolar RF ablation with an internally cooled probe, group B = standard monopolar RF ablation with a cluster internally cooled probe, group C = multipolar RF ablation with two bipolar probes.

* There was a statistically significant difference between groups B and C.
‡ There was a statistically significant difference between groups A and B and between groups A and C.
† There was a statistically significant difference between groups A and C.
§ There was a statistically significant difference between each group.
and a precipitous drop in current density occurs with increased distance from the energy source (33). In contrast, in the multipolar mode, one electrode is thermally shielded by the opposing second electrode, which also actively heats tissue in its proximity; therefore, as heat is trapped between the two electrodes, higher temperatures are achieved as less cooling occurs in the direction of the collateral electrode than with monopolar ablation (35). Second, in the multipolar mode, the RF current is passed between the electrodes, thereby crossing the tumor. Therefore, high current density within the tumor could be expected. Third, under microprocessor control, the RF output is divided between the individual electrodes according to the momentary tissue resistance in the multipolar mode. Therefore, RF current delivery in the multipolar mode between the electrode pairs during RF ablation prevents a marked impedance increase and allows continuous current delivery (27).

As demonstrated in this study, an extended volume of coagulation necrosis created by multipolar RF ablation with cooled bipolar probes may increase the clinical utility of RF ablation therapy by enabling the successful treatment of larger renal tumors or reducing the number of sessions needed for the treatment of a given tumor. Multipolar RF ablation, however, has certain drawbacks. First, this technique is more complex to perform under imaging guidance compared with using a single electrode. Although placing two probes into the target tumor can make the RF ablation procedure difficult, it is only minimally more complicated for an experienced clinician to conduct an ultrasonographic-guided procedure compared to insertion of a single probe. Furthermore, insertion of the probes before RF energy instillation may avoid the difficulty of moving the probe from one site to another. Second, there is an increased risk of bleeding and potential tumor seeding related to multiple electrode insertions. However, during our in vivo experiments, we did not observe severe bleeding from the electrode insertion sites. Third, multiple-electrode RF ablation uses more ex-
pensive equipment than a single consecutive RF application. Last, considering that the large volumes of coagulation created may not always be beneficial or desirable and that, in certain circumstances, coagulation extending beyond the tumor boundaries could be detrimental if surrounding structures are damaged or if insufficient tissue is preserved to permit normal organ function, before applying our wet RF ablation technique to humans it will be necessary to evaluate its therapeutic efficacy and safety by using the renal tumor model in large animals.

There are some limitations to the present study. First, all ablations involved the normal renal parenchyma; not tumor tissue. Therefore, this study is limited in the extent to which we can apply these results to the human kidney. Second, the RF ablation procedure was performed as open surgery due to limited access to the CT unit at our institute. Because RF ablation enables us to accurately target the kidney and avoid injury to adjacent bowel, the results of this study might not be representative of that of the percutaneous RF ablation procedure on renal tumors. Third, we performed multipolar RF ablation at 1 fixed interelectrode space. Given that the ideal interelectrode spacing between the two electrodes depends on the local properties of the ablation site, which differ for each ablation, more experimental study will be needed at different interelectrode distances. Fourth, due to the relatively small size of porcine kidneys, we selected probes only up to an active conducting part of 30 mm, which limited the dimensions of the coagulations. Fifth, we calculated the coagulation zone volume by using the assumption of an elliptical lesion. Planimetry and summing up the volume of several sections may improve the accuracy of the measurement of the coagulation zone volume. Last, although expandable electrodes are available, we did not include those electrodes in the present study. Given that the developmental speed of RF technology is currently quite rapid, this study represents a snapshot in time as further refinements and improvements of current techniques will undoubtedly increase the effectiveness and further expand the role of RF ablation.

In summary, multipolar RF ablation showed at least equivalent or better in vivo efficiency for creating a larger coagulation than monopolar RF ablation with single or cluster electrodes, but with a longer procedure time and at slightly greater complexity. An extended volume of coagulation necrosis created by the new multipolar RF system may increase the clinical utility of RF ablation therapy by enabling the successful treatment of larger renal tumors or reducing the number of sessions needed for the treatment of a single tumor.

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