

# Comparison of Radiofrequency Ablation with Saturated Saline Preinjection and Renal Artery Occlusion: *In Vivo* Study in Canine Kidneys<sup>1</sup>

고주파 소작술에서 포화식염수 주입과 신동맥 폐색술의 비교: 잡견의 신장에서 생체연구<sup>1</sup>

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**Purpose:** To compare the ablation zone after radiofrequency ablation (RFA) with saturated saline preinjection and renal artery occlusion in canine kidneys.

**Materials and Methods:** RFA was induced in the kidneys of six mongrel dogs. A total of 24 ablation zones were induced using a 1-cm tip internally cooled needle electrode in three groups: RFA (Control group), RFA with 0.5 mL saturated saline preinjection (SS group), and RFA with renal artery occlusion by atraumatic vascular clamp (Occlusion group). Ablation zone diameters were measured along transverse and longitudinal sections of the needle axis, and volumes were calculated. Temperature, applied voltage, current, and impedance during RFA were recorded automatically.

**Results:** The RFA zone volume was the largest in the SS group ( $1.33 \pm 0.34 \text{ cm}^3$ ), followed by the Occlusion group ( $1.07 \pm 0.38 \text{ cm}^3$ ) and then the Control group ( $0.62 \pm 0.09 \text{ cm}^3$ ). Volumes for the SS and Occlusion groups were significantly larger than those for the Control group ( $p = 0.001$ ,  $p = 0.012$ ). There was no significant difference in volumes between the SS and Occlusion groups ( $p = 0.178$ ).

**Conclusion:** Saturated saline preinjection is as effective as renal arterial occlusion for expanding the ablation zone. RFA with saturated saline preinjection could help to treat large renal tumors.

## Index terms

Experimental Study  
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## INTRODUCTION

Radiofrequency ablation (RFA) is a minimally invasive treatment used for renal cell carcinomas that preserves renal function (1, 2). Previous clinical studies on renal RFA reported good results for treatment of small renal tumors (1-6). However, large renal tumors (> 3 cm) were not completely eradicated by RFA using a single electrode in one treatment session (2-6).

For complete tumor ablation, RFA should induce an ablation zone large enough to cover the entire tumor with the ideal ablative margin (0.5-1 cm) (7). Monopolar RFA using a single electrode in one treatment session has limitations in regards to its ability to induce an adequately sized ablation zone for large tumor. Sequentially overlapping single electrode ablation can be used for large tumors (8); however, repositioning the electrode into an untreated tumor area is difficult and requires additional

time. Therefore, attempts have been made to expand the ablation zone using a single RFA session (9).

Among the various modified RFA methods, RFA combined with renal artery occlusion is considered effective for expanding the ablation zone in the kidney (10-14). Despite the effectiveness of blood flow occlusion for this purpose, there is the risk of renal infarction, which limits its use in clinical practice. RFA combined with hypertonic saline administration is another strategy (15-23), and has been used clinically to treat large hepatic tumors (17, 18). Renal RFA combined with hypertonic saline administration has also been used for this purpose in animal studies (19-23).

Comparative studies of modified RFA methods have been performed; however, to the best of our knowledge, no studies have simultaneously compared these two RFA methods in the kidney. Here, we present the results of our study, which was designed to compare saturated saline preinjection and renal artery occlusion with respect to ablation zone volumes in renal RFA.

## MATERIALS AND METHODS

The study protocol was approved by the Committee on the Ethics of Animal Experiments. Six mongrel dogs (13-20 kg; mean,  $15.8 \pm 2.4$  kg) were included in this study. Two RFAs were performed in the upper and lower poles of each kidney. A total of 24 ablation zones were induced using a 1-cm tip internally cooled needle electrode in the following 3 groups: RFA only (Control group,  $n = 8$ ), RFA with 0.5 mL saturated saline preinjection (SS group,  $n = 8$ ), and RFA with renal artery clamping (Occlusion group,  $n = 8$ ).

The animals were first administered an intramuscular injection of atropine sulfate, 0.04 mg/kg (Atropine sulfate; Jeil Pharm., Seoul, Korea), and general anesthesia was induced by intravenous administration of 6 mg/kg propofol (Provive injection; Myungmoon Pharm., Seoul, Korea). After endotracheal intubation, anesthesia was maintained with 0.8-1.25% isoflurane (Ifiran®; Hana Pharm., Seoul, Korea) in oxygen using a semi-closed circle-breathing circuit. Cardiac and respiratory parameters were monitored throughout the procedure. Dogs were placed in a supine position. The upper area of the back was shaven and grounding pads were attached. Grounding for RFA was accomplished using two external dorsally attached grounding pads,

and the radiofrequency (RF) currents were distributed evenly through the tissue in the grounding pad's direction. The upper area of the abdomen and epigastrium were shaved and sterilized. A midline incision was made to expose the kidney.

All experiments were conducted using a 200 W RF current (480 kHz) generator (CTRF-220; Valleylab, Boulder, CO, USA) capable of producing currents of up to 2000 mA. An 18-gauge electrode with a 1-cm active tip (Big tip®; RF Medical Co. Ltd., Seoul, Korea) was used in all groups. For all procedures, the needle tip of the electrode was placed approximately 1.5 cm deep relative to the renal capsule. RF was applied to the kidneys in the monopolar mode, and RF energy was delivered to the electrodes for 5 minutes. Energy was delivered at half power (100 W) in the impedance control mode. A peristaltic pump (PE-PM, Radionics, Burlington, MA, USA) simultaneously cooled the electrode internally so that the electrode temperature was maintained below 25°C. Before all experiments, the electrode was internally cooled at least 1 minute before placement. Circuitry incorporated in the generator allows for continuous monitoring of impedance between the active parts of the internally cooled needle electrodes and grounding pads. A thermocouple embedded in the electrode ensures constant monitoring of the temperature at the electrode tip. The applied current, power output, and impedance were automatically recorded (Real Time Graphics Software V 2.0, Radionics, Burlington, MA, USA).

In the SS group, before placement of the internally cooled needle electrode, a total of 0.5 mL 36% saturated saline solution was delivered slowly through the 1-cc syringe along the electrode axis. In the Occlusion group, the renal artery was identified and transiently clamped using an atraumatic vascular clamp without occluding the renal vein, and then the RFA was performed as described above. The clamping time was within 15 minutes to prevent renal parenchyma injury. Renal arterial blood flow was immediately restored to the kidney after ceasing RFA.

Dogs were euthanized with intravenous pentobarbital, and each kidney was removed en block. The kidney blocks were sectioned along the longitudinal plane (electrode insertion axis) and then cut transversely and perpendicularly to the longitudinal plane (transverse plane). RFA zone diameters were assigned as the consensus of measurements made by 2 observers. The RFA zone was considered as an elliptical cone. The



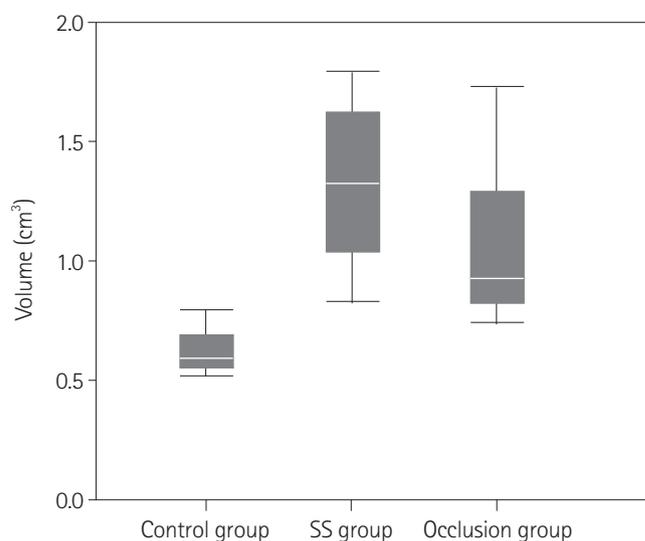
**Fig. 1.** Images of the gross specimen in each group show central white coagulation zone (arrows) with a surrounding dark hemorrhagic rim. The needle electrode tract is clearly observed in the central portion of the ablation zone. Ablation zone volumes are largest in the Saturated Saline group (B), followed by the Occlusion group (C) and then the Control group (A).

central white coagulation zone was measured excluding the surrounding hemorrhagic rim (Fig. 1). The longitudinal diameter was defined as the maximum diameter along the electrode insertion axis (T long), and the transverse diameter was defined as the maximum diameter perpendicular to the electrode insertion axis in the cortex (D cortex). The volume was calculated using the formula that describes the volume of an elliptical cone:  $1/6 \times \pi \times \text{height (T long)} \times \text{base diameter (D cortex)}^2$ . The measured diameters and calculated RFA zone volumes are reported as mean  $\pm$  standard deviation and compared between each group using the Mann-Whitney U test. Statistically significant differences were defined as  $p$  values  $< 0.05$ .

## RESULTS

The mean T long values of the ablation zones were as follows (long to short): SS group (16.7 mm  $\pm$  1.1), Occlusion group (15.8 mm  $\pm$  1.8), and Control group (13.9 mm  $\pm$  1.1). The T long value of the SS group was 20% greater than the value of the Control group ( $p = 0.000$ ). The T long value of the Occlusion group was 14% greater than the value of the Control group ( $p = 0.024$ ). No statistically significant difference was observed between the mean T long values of the SS and Occlusion groups ( $p = 0.258$ ).

The ablation zones' mean D cortex values were as follows (long to short): SS group (12.3 mm  $\pm$  3.3), Occlusion group (12.0 mm  $\pm$  1.7), and Control group (9.4 mm  $\pm$  1.3). The value of the SS group was 31% greater than those of the Control group ( $p = 0.048$ ). The value of the Occlusion group was 28% greater than those of the Control group's ( $p = 0.004$ ). The values of the SS and



**Fig. 2.** Group Volumes. There are significant differences in ablation zone volumes between the Control and Saturated Saline groups ( $p = 0.001$ ), and between the Control and Occlusion groups ( $p = 0.012$ ). No significant difference between Saturated Saline and Occlusion groups was observed ( $p = 0.178$ ). The RFA zone volume of the Saturated Saline group varied more than the volume of the other two groups. Note.—RFA = radiofrequency ablation

Occlusion groups were not significantly different ( $p = 0.860$ ).

Mean ablation zone volumes were as follows (large to small): SS group (1.33 cm<sup>3</sup>  $\pm$  0.34), Occlusion group (1.07 cm<sup>3</sup>  $\pm$  0.38), and Control group (0.62 cm<sup>3</sup>  $\pm$  0.09). The value of the SS group was 114% greater than those of the Control group ( $p = 0.001$ ). The values of the Occlusion group was 72% greater than those of the Control group ( $p = 0.012$ ). The value of the SS group was 24% greater than those of the Occlusion group, but this difference was not statistically significant ( $p = 0.178$ ). The variation in ablation zone volumes for the SS and Occlusion groups was greater than that in the Control group (Fig. 2). The results are

**Table 1. Comparison of Ablation Zones**

	Control (n = 8)	SS (n = 8)	Occlusion (n = 8)	p value C vs. SS/C vs. O/SS vs. O
T long (mm)	13.9 ± 1.1	16.7 ± 1.1	15.8 ± 1.8	0.000/0.024/0.258
D cortex (mm)	9.4 ± 1.3	12.3 ± 3.3	12.0 ± 1.7	0.048/0.004/0.860
Volume (cm <sup>3</sup> )	0.62 ± 0.09	1.33 ± 0.34	1.07 ± 0.38	0.001/0.012/0.178

Values are presented as mean ± standard deviation.

Note.—C = Control group, SS = Saturated Saline group, O = Occlusion group

**Table 2. Radiofrequency Ablation Data**

	Control (n = 8)	SS (n = 8)	Occlusion (n = 8)	p value C vs. SS/C vs. O/SS vs. O
Temperature (°C)	15.6 ± 6.6	14.7 ± 8.3	13.7 ± 5.4	0.813/0.543/0.786
Watts (W)	11.7 ± 1.8	25.7 ± 7.8	8.7 ± 1.6	0.001/0.003/0.000
Impedance (Ω)	101 ± 12	76 ± 8	116 ± 10	0.000/0.017/0.000
Current (mA)	291 ± 26	550 ± 130	237 ± 30	0.001/0.002/0.000

Values are presented as mean ± standard deviation.

Note.—C = Control group, SS = Saturated Saline group, O = Occlusion group

summarized in Table 1.

The SS group showed decreased impedance and increased current values that were significantly greater than those of the Control and Occlusion groups (*p* < 0.001). Administration of the saline solution into the renal tissue affected the parameters of the RF generator. The results are summarized in Table 2.

## DISCUSSION

Various modified RFA methods have been developed to expand the ablation zone. RFA combined with vascular inflow occlusion is one strategy for expanding the ablation zone by reducing the heat sink effect (9), which refers to heat removal by blood flowing in adjacent vessels, thereby limiting the size and altering the shape of the ablation zone (7). Therefore, RFA with vascular inflow occlusion induces a larger ablation zone than that without occlusion. RFA with renal artery occlusion was attempted in previous animal studies by using a vascular clamping, balloon occlusion, or intraarterial embolization (10-13). Chang et al. (13) reported that renal artery occlusion effectively expanded the ablation zone. They suggested that RFA combined with selective intraarterial tumor embolization was useful for treating large renal tumors. Furthermore, Yamakado et al. (14) used RFA combined with arterial embolization for large renal cell carcinomas (> 3.5 cm) in eleven patients. Our results also showed that renal artery occlusion by vascular clamping

effectively expanded the ablation zone, which is consistent with other animal studies (10-13). However, our results showed more variation in ablation zone diameters and volumes, which is in contrast to the results reported in the animal study performed by Chang et al. (13).

RFA with hypertonic saline administration is another strategy that has been used to expand the ablation zone and is considered effective in the liver (9, 15-18), and has been attempted in the kidney (19-23).

Injected hypertonic saline improves the tissue electrical and thermal conductivity during RFA by modulating the biologic environment of treated tissue. This effect can be maximized by using saturated saline (24). Therefore, saturated saline was used in this study. Saturated saline injection without RFA can induce patch necrosis of tissue, but the volume of necrosis is smaller than that induced by RFA only (24). RFA with 14.6% hypertonic saline preinjection was feasible for both the normal parenchyma and VX-2 tumor implanted in the rabbit kidney (20, 21). RFA combined with preinjection and additional continuous infusion of 14.6% hypertonic saline was also feasible for a VX-2 tumor implanted in the rabbit kidney (22). In contrast, Collyer et al. (23) reported that RFA combined with preinjection and additional continuous infusion of 14.6% hypertonic saline applied to a porcine model induced colonic injury and resulted in irregular-shaped ablation lesions when compared to cryotherapy. They suggested that leakage of the hypertonic saline resulted in

current delivery to surrounding structures, which induced adjacent organ injury. In hepatic RFA with saline administration, spilling of uncontrolled saline into tissue was also shown to cause irregular-shaped ablation zones (25).

Additional hypertonic saline continuous infusion during RFA increases the amount of spilled saline into tissues. A relatively large amount of spilled saline causes an irregular-shaped ablation zone, and can lead to adjacent organ injury. Therefore, in the present study, only a bolus hypertonic saline preinjection was used to control and decrease the amount of infused saline. We also used saturated saline to decrease the amount of spilled saline, which effectively expanded the ablation zone. Although this amount was small, more variation in the diameters and volumes of ablation zones were caused by RFA with, than without, saturated saline preinjection. Further studies are therefore needed to optimize saline solution administration.

Our study showed that both saturated saline preinjection and renal artery clamping effectively expanded the ablation zone in canine kidneys. Saturated saline preinjection resulted in larger ablation zones than those induced by renal artery clamping, although the differences were not statistically significant. Because our interpretations were limited by the small sample size, more studies are required.

Our study had other limitations. First, we used an internally cooled needle electrode with a 1 cm active tip, instead of a 2 cm or 3 cm active tip, because of the smaller size of the canine kidney. We used a lower level of RF energy for a shorter time than that employed in standard clinical practice. Second, an animal tumor model was not used due to the lack of a widely available inexpensive and reproducible large animal tumor model. Furthermore, there may be differences in ablation zone sizes and shapes between tumor and normal renal tissues. Third, the RFA zone diameter of the gross specimen was measured, and the volume of the ablation zone was calculated based on diameter measurements. A more comprehensive evaluation of ablation zone shape using an imaging modality such as computed tomography will be required to more accurately determine the volume and shape of the RFA zone.

In conclusion, both RFA with saturated saline preinjection and renal artery clamping effectively expanded the ablation zone, and RFA with saturated saline preinjection resulted in a slightly larger ablation zone when compared to RFA with renal artery

occlusion. Therefore, RFA with saturated saline preinjection may help in the treatment of large renal tumors.

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## 고주파 소작술에서 포화식염수 주입과 신동맥 폐색술의 비교: 잡견의 신장에서 생체연구<sup>1</sup>

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**목적:** 잡견의 신장에서 포화식염수 주입과 신동맥 폐색술 후 고주파 소작술의 소작범위를 비교하고자 하였다.

**대상과 방법:** 6마리 잡견의 신장을 이용하여 고주파 소작술을 시행하였다. 1 cm 길이의 냉각형 전극침을 이용하여 3군으로 나누어 총 24개의 소작술을 시행하였다. 일반 고주파 소작술군(대조군), 0.5 mL 포화식염수를 주입 후 소작술을 시행한 군(SS군), 혈관 클램프를 이용한 신동맥 폐색술 후 소작술을 시행한 군(폐색군)으로 나누었다. 소작범위는 바늘의 장축면과 횡단면의 길이를 측정하여 부피를 구하였다. 소작술 중 온도, 전압, 전류, 임피던스를 기록하였다.

**결과:** 소작부피는 SS군( $1.33 \pm 0.34 \text{ cm}^3$ ), 폐색군( $1.07 \pm 0.38 \text{ cm}^3$ ), 대조군( $0.62 \pm 0.09 \text{ cm}^3$ ) 순으로 컸다. SS군과 폐색군이 대조군보다 통계학적으로 유의하게 컸다( $p = 0.001$ ,  $p = 0.012$ ). SS군과 폐색군 간의 차이는 없었다( $p = 0.178$ ).

**결론:** 포화식염수 주입은 소작범위를 넓히는 데 신동맥 폐색술만큼 효과적이다. 포화식염수를 이용한 고주파 소작술은 큰 신장암의 치료에 도움이 될 수 있다.

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