

Comparison of Radiofrequency Ablation Lesion Size with Occlusion of Renal Vessels in Rabbit Kidneys:

Occlusion of Renal Artery, Vein, and Both Vessels¹

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Purpose: The purpose of this study was to compare the in-vivo efficiency of vascular occlusion on radiofrequency ablation (RFA) lesion size in a rabbit kidney model.

Materials and Methods: RFA lesions were created in a single kidney in 20 rabbits using an internally cooled electrode. Twenty ablation zones (1 per kidney) were created using 4 different regimens: RFA without vascular occlusion ($n = 5$), RFA with renal artery occlusion ($n = 5$), RFA with renal vein occlusion ($n = 5$), RFA with renal artery and vein occlusion ($n = 5$). Seven days later, the rabbits were sacrificed and the lesions were excised. These groups were then compared with respect to the dimensions of the ablation zones and the changes in impedance and current during RFA.

Results: The maximum ablation zone width was the greatest in the renal artery and vein occlusion group (21.0 ± 1.4 mm), followed by the renal artery occlusion group (17.8 ± 1.0 mm), the renal vein occlusion group (17.4 ± 1.1 mm), and the nonocclusion group (7.8 ± 2.4 mm) ($p < 0.05$). No significant differences were observed for impedances and currents between the 4 groups.

Conclusion: Vascular occlusion combined with RFA effectively increased ablation zone dimensions compared with RFA alone, and the best effect was accomplished by combined renal artery and vein occlusion.

Index words : Kidney, interventional procedures
Radiofrequency (RF), ablation
Experimental study

Renal cell carcinoma (RCC) is a common renal parenchymal malignancy, and although complete or partial nephrectomy remains the gold standard of management, many minimally invasive treatment tech-

niques, including laparoscopic or open partial nephrectomy, cryotherapy, and radiofrequency ablation (RFA) are emerging.

RFA involves the conversion of an alternating current into heat, which destroys soft tissues by desiccation and coagulative necrosis (1). The sizes of the lesion and lesion configurations created are primarily related to the amount of energy delivered, ablation time, tissue impedance, tissue electrolyte content, and the surface area of the electrode used (2).

However, the inability of RFA to consistently produce a large enough zone of coagulation necrosis to treat

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RCCs exceeding 3 cm in diameter represents a serious limitation (3 - 6). This is attributable partly to the "heat sink" effect, i.e., the relatively cool blood flow acts as a "heat sink," thus limiting the size of radiofrequency-induced lesions and contributing to an unpredictable lesion shape in the immediate vicinity of the vessels. Therefore, an obstruction to the blood flow may increase thermal lesion dimensions, and thus might be useful for the treatment of tumors larger than 3 cm. Moreover, by adopting a blood flow occlusion approach, it might also be possible to reduce hemorrhagic complications after RFA.

Studies conducted on the effect of perfusion on RFA lesion size in the kidney (7 - 10) have reported that RFA lesions created with renal arterial occlusion in animals are larger than those created with normal blood flow. However, there have been no comparative investigations concerning the effects of occluding renal veins and/or renal arteries. Therefore, we decided to undertake this study to compare the in-vivo effects of renal artery, renal vein, renal artery and vein occlusion, and nonocclusion on the efficacy of RFA in a rabbit kidney

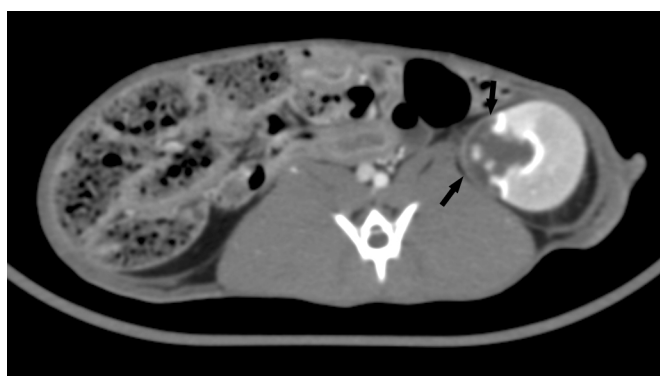
model.

The purpose of our study was to compare the in-vivo efficiency of RFA with renal artery, renal vein, renal artery and vein occlusion, or nonocclusion in a rabbit kidney model.

Materials and Methods

Animals and Surgery

Twenty New Zealand White rabbits (male; weight, 2.5 - 3 kg) were used in this study, and one lesion was created per rabbit. All animals were anesthetized using an intramuscular injection of 50 mg/kg ketamine hydrochloride (Ketamine; Yuhan, Seoul) and 5 mg/kg of xylazine (Rumpun;[Editor1] Bayer Korea, Ansan, Korea). A 10% povidone-iodine solution was then applied topically, and the left kidney was exposed by a paramidline incision. The renal artery and vein were isolated and clamped using atraumatic vascular clamps just before RFA. The renal vessels were declamped immediately after RFA to minimize vascular compromise due to renal infarction. Booster injections of up to one-

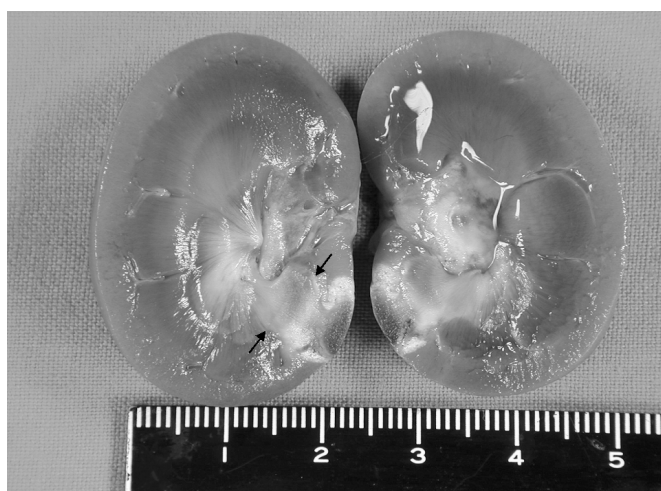


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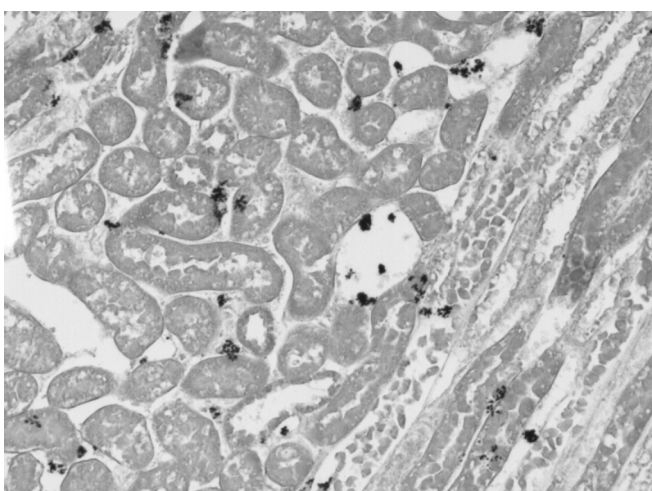
Fig. 1. RFA lesion created without occlusion of renal vessel.

A. Contrast-enhanced CT scan shows lobulating contoured unenhanced region in the lower pole of the left kidney (arrows).

B. The photograph of the gross specimen shows the RFA lesion (arrows).



B



C

half of the initial dose of xylazine were administered as required. *Memo: Please check the change in the trade name.

RFA Protocol

An internally cooled, 17-G electrode (CC-3; Radionics, Burlington, Mass., U.S.A.) with a 1-cm active tip was placed in the lower pole of the left kidney.

Lesions were created using a 500-kHz RF generator (CC-3; Radionics) capable of producing 200 W. During the procedure, tissue impedance and current were monitored every 30 sec using circuitry incorporated within the generator. A peristaltic pump (Watson-Marlow, Medford, Mass., U.S.A.) was used to infuse normal saline solution at 0 into the lumen of the electrode at a rate of 10 - 25 mL/min, which was sufficient to maintain

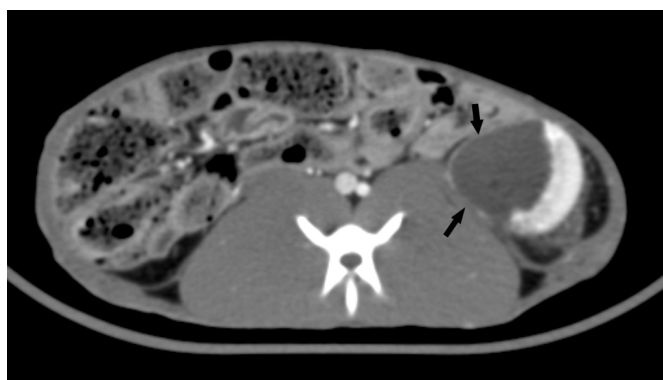
a tip temperature of 20 - 25 . The power output was set at 20 W, and RF energy was applied for 2 min.

CT Protocol

Spiral CT (Somatom Plus 4; Siemens, Erlangen, Germany) was performed 1 week after RFA to monitor its effects. Axial CT scans of both the lungs and the upper abdomen including the kidneys were obtained 60 sec after contrast administration (Ultravist 300; Schering, Berlin, Germany) using a 2-mm slice thickness and a pitch of 1.5. Thirteen milliliters of contrast media was injected at 1 mL/sec through an ear vein.

Lesion Size Measurements

Rabbits were sacrificed by pentobarbital sodium overdose (Somlethal; Anpro Pharmaceutical, Arcadia, Calif.,



A

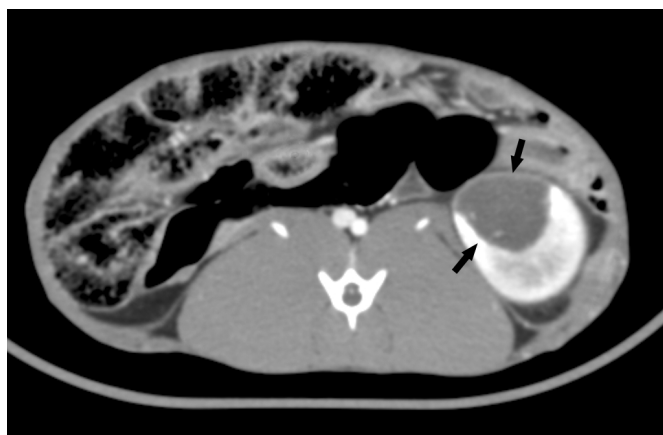


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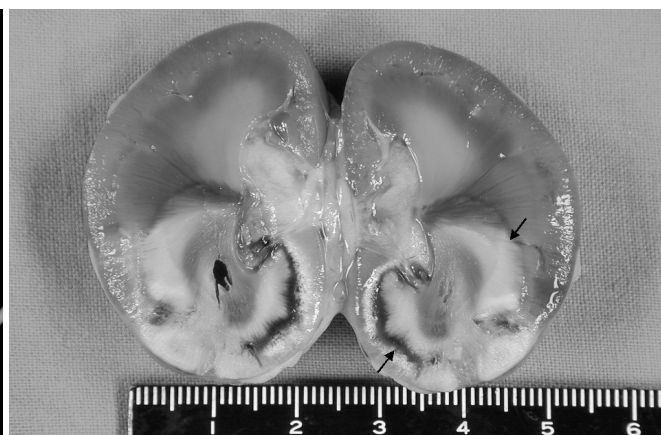
Fig. 2. RFA lesion created with renal artery occlusion.

A. Contrast-enhanced CT scan shows well-defined nonenhancing region in the lower pole of the left kidney (arrows).

B. The photograph of the gross specimen shows the RFA lesion with a smooth well-defined margin (arrows).



A



B

Fig. 3. RFA lesion created with renal vein occlusion.

A. Contrast-enhanced CT scan shows well-defined nonenhancing region in left kidney lower pole (arrows).

B. The photograph of the gross specimen shows the RFA lesion (arrows).

U.S.A.) 7 days after RFA, and the kidneys were excised. Since the white central area of the RF-induced ablation zone has been previously shown to correspond to the zone of coagulation necrosis [11, 12], the maximum widths (perpendicular to the long axis of the RFA electrode) of the RFA lesions were measured by the author (C.H.J.) after all the specimens had been bisected in a plane parallel to the RFA electrode.

Statistical Analysis

Group lesion dimensions, impedances, and RFA currents were compared using factorial analysis of variance. Values are expressed as means \pm SD. P values were calculated by comparing lesion ranks, and the Mann-Whitney test was used for intergroup comparisons. For all statistical analyses, *p* values of < 0.05 were considered significant.

Results

Dimensions of Ablation Zones

Vascular occlusion increased the RFA-ablated tissue volume. The largest RFA lesion widths were observed in the renal artery and vein occlusion group (21.0 ± 1.4 mm) followed by the renal artery occlusion group (17.8 ± 1.0 mm), the renal vein occlusion group (17.4 ± 1.1 mm), and the nonocclusion group (7.8 ± 2.4 mm) (Figs. 1-4). A significant difference in lesion volume was found between the nonocclusion group and all the vascular occlusion groups ($p = 0.01$). Moreover, the mean lesion width in the renal artery and vein occlusion group

was greater than that in the other occlusion groups (vs. the renal artery occlusion group; $p = 0.029$, vs. the renal vein occlusion group; $p = 0.016$).

RFA Parameters

Kidney blood flow conditions did not affect RF impedance and current during this study (Table 1).

RFA related complications

No RFA related complications were detected in the follow-up CT images.

Discussion

Early small renal tumors are now being discovered thanks to the development of imaging modalities, and it has become acceptable to utilize a nephron-sparing approach for treating these lesions. However, partial nephrectomy is associated with significant morbidity, a protracted operating time, increased blood loss, and pro-

Table 1. Values of RFA Parameters after 90 sec of Ablation

Vessel occluded	Number	Impedance (Ω)	Current (mA)
Renal artery and vein	5	128.0 ± 15.3	435 ± 39
Renal artery	5	134.5 ± 16.3	382 ± 28
Renal vein	5	133.6 ± 26.3	392 ± 37
None	5	129.3 ± 10.5	427 ± 36

Note. Values are averages \pm standard deviation

No significant differences between groups were observed with respect to any of the listed parameters ($p > 0.05$)

longed hospital stay as compared with radical nephrec-

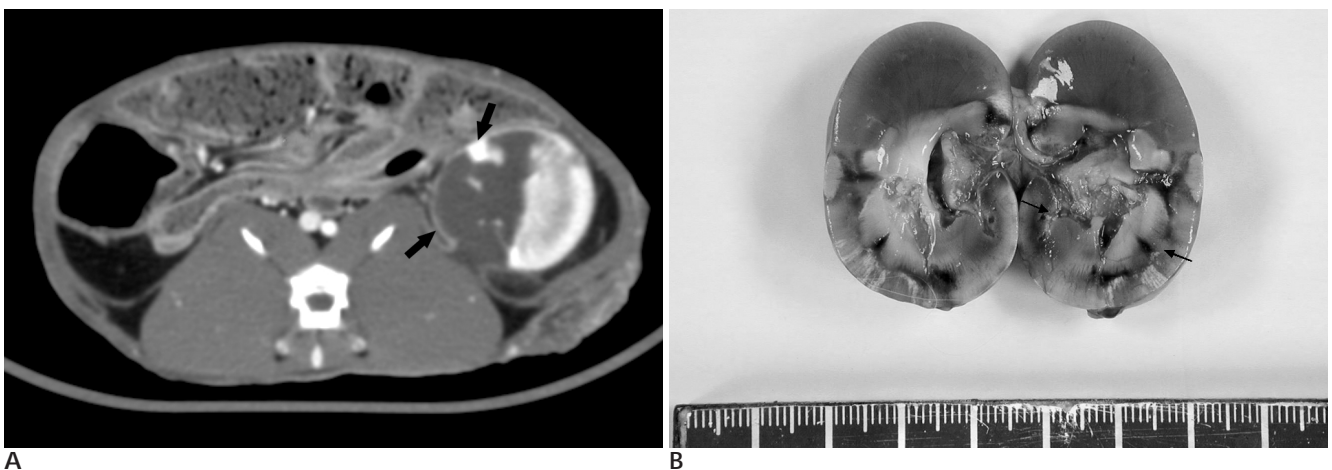


Fig. 4. RFA lesion created with both renal artery and vein occlusion.

A. Contrast-enhanced CT scan shows nonenhanced region in the lower pole of the left kidney (arrows). Note the larger nonenhanced region compared with that observed in other groups.

B. The photograph of the gross specimen shows the RFA lesion (arrows).

tomy (13, 14). Although the efficacy of RFA in the management of small RCC is debated, RFA has gradually been accepted as a good alternative to partial nephrectomy (3 - 6). However, tissue perfusion and blood flow through vessels near target sites may affect the size and shape of RFA lesions. In the liver, lesion volume has been observed to increase on reducing blood flow (15 - 18). Another study reported that the Pringle maneuver (hepatic artery and portal vein occlusion) produced larger RFA lesions than portal vein or hepatic vein occlusion (15). Other studies have also been undertaken to investigate the effect of renal arterial occlusion during RFA (7 - 10), but no comparative study has yet evaluated the effects of renal vein and/or renal artery occlusion during RFA.

In the present study, the occlusion of renal blood flow increased RFA lesion diameter; further, no overlap between lesion diameters obtained using these procedures was observed. Moreover, RFA lesions in the more restrictive renal artery and vein occlusion group were larger than those in the other 2 occlusion groups; these differences were statistically significant (vs. renal artery occlusion; $p = 0.029$, and vs. renal vein occlusion; $p = 0.016$).

Although venous infarcts are known to cause more severe renal parenchymal damage than arterial infarcts, no differences were observed in the nonablated renal parenchyma between the 4 study groups. However, because the vessel clamping time (2 - 3 min) was shorter than that in humans (10 - 12 min) and because histopathological specimens were acquired 1 week after RFA, there is a possibility that normal renal function had recovered to some extent after RFA in our rabbit model. Thus, further investigation should be undertaken to confirm the safety of renal venous clamping during renal RFA in humans.

Our study had several limitations. First, we did not use a tumor model. However, available evidence indicates that tumors are more susceptible to heat damage than normal tissue (19). Nevertheless, further study is needed to apply the vessel occlusion concept to renal tumors. Second, the number of animals used was relatively small. In fact, the study was terminated because a clear statistically significant difference was observed between the renal artery and vein occlusion group and the other occlusion groups in terms of lesion size. A substantially larger cohort would be needed to definitively evaluate RFA lesion differences between the renal artery and renal vein occlusion groups. Finally, in the present

study, RFA and vessel occlusion was performed using an open method, and thus, it diverged from the clinical situation. A percutaneous RFA trial in an animal model is necessary.

In the present study, the RFA time was 2 min, which is shorter than that required for renal parenchymal coagulation. RFA times used to treat rabbit kidneys in previous studies range from 80 sec to 8 min (20 - 23). However, in the present study RFA was performed on normal renal parenchyma; therefore, we shortened the RFA time to 2 min in order to avoid injury to the chief renal vessels.

The present study was undertaken to determine a more efficient means of enlarging RFA lesion dimensions. It was observed that combined renal artery and vein occlusion does effectively enlarge RFA zones. In practice, the occlusion of both the vessels during RFA can be achieved by vascular clamping, intraarterial embolization, or by ballooning. By occluding both the vessels, we consider it likely that large hypervascular tumors and their margins can be effectively treated and that local recurrence rates can be reduced.

In conclusion, vascular occlusion combined with RFA was observed to effectively increase RFA lesion dimensions compared with RFA alone, and this method was found to be most effective when both the renal artery and vein were occluded.

References

1. Polascik TJ, Hamper U, Lee BR, Dai Y, Hilton J, Magee CA, et al. Ablation of renal tumors in a rabbit model with interstitial saline-augmented radiofrequency energy: Preliminary report of a new technology. *Urology* 1999;53:465-472
2. Zlotta AR, Schulman CC. Ablation of renal tumors in a rabbit model with interstitial saline-augmented radiofrequency energy. *Urology* 1999;54:382-383
3. Gervais DA, McGovern FJ, Wood BJ, Goldberg SN, McDougall WS, Mueller PR. Radio-frequency ablation of renal cell carcinoma: Early clinical experience. *Radiology* 2000;217:665-672
4. Hall WH, McGahan JP, Link DP, deVere White RW. Combined embolization and percutaneous radiofrequency ablation of a solid renal tumor. *AJR Am J Roentgenol* 2000;174:1592-1594
5. Zlotta AR, Wildschutz T, Raviv G, Peny MO, van Gansbeke D, Noel JC, et al. Radiofrequency interstitial tumor ablation (RITA) is a possible new modality for treatment of renal cancer: ex vivo and in vivo experience. *J Endourol* 1997;11:251-258
6. McGovern FJ, Wood BJ, Goldberg SN, Mueller PR. Radio frequency ablation of renal cell carcinoma via image guided needle electrodes. *J Urol* 1999;161:599-600
7. Chang I, Mikityansky I, Wray-Cahen D, Pritchard WF, Karanian JW, Wood BJ. Effects of perfusion on radiofrequency ablation in swine kidneys. *Radiology* 2004;231:500-505
8. Aschoff AJ, Sulman A, Martinez M, Duerk JL, Resnick MI,

- MacLennan GT, et al. Perfusion-modulated MR imaging-guided radiofrequency ablation of the kidney in a porcine model. *AJR Am J Roentgenol* 2001;177:151-158
9. Corwin TS, Lindberg G, Traxer O, Gettman MT, Smith TG, Pearle MS, et al. Laparoscopic radiofrequency thermal ablation of renal tissue with and without hilar occlusion. *J Urol* 2001;166:281-284
10. Kariya Z, Yamakado K, Nakatuka A, Onoda M, Kobayasi S, Takeda K. Radiofrequency ablation with and without balloon occlusion of the renal artery: an experimental study in porcine kidneys. *J Vasc Interv Radiol* 2003;14:241-245
11. Lee JD, Lee JM, Kim SW, Kim CS, Mum WS. MR imaging-histopathologic correlation of radiofrequency thermal ablation lesion in a rabbit liver model: observation during acute and chronic stages. *Korean J Radiol* 2001;2:151-158
12. Morimoto M, Sugimori K, Shirato K, Kokawa A, Tomita N, Saito T, et al. Treatment of hepatocellular carcinoma with radiofrequency ablation: radiologic-histologic correlation during follow-up periods. *Hepatology* 2002;35:1467-1475
13. Herr HW. Partial nephrectomy for unilateral renal carcinoma and normal contralateral kidney: 10-year follow-up. *J Urol* 1999;161:33-34
14. Duque JL, Loughlin KR, O'Leary MP, Kumar S, Richie JP. Partial nephrectomy: alternative treatment for selected patients with renal cell carcinoma. *Urology* 1998;52:584-590
15. Chinn SB, Lee FT Jr, Kennedy GD, Chinn C, Johnson CD, Winter TC 3rd, et al. Effect of vascular occlusion on radiofrequency ablation of the liver: results in a porcine model. *AJR Am J Roentgenol* 2001;176:789-795
16. Lu DS, Raman SS, Vodopich DJ, Wang M, Sayre J, Lassman C. Effect of vessel size on creation of hepatic radiofrequency lesions in pigs: assessment of the "heat sink" effect. *AJR Am J Roentgenol* 2002;178:47-51
17. Rossi S, Garbagnati F, Lencioni R, Allgaier HP, Marchiano A, Fornari F, et al. Percutaneous radio-frequency thermal ablation of nonresectable hepatocellular carcinoma after occlusion of tumor blood supply. *Radiology* 2000;217:119-126
18. de Baere T, Bessoud B, Dromain C, Ducreux M, Boige V, Lassau N, et al. Percutaneous radiofrequency ablation of hepatic tumors during temporary venous occlusion. *AJR Am J Roentgenol* 2002;178:53-59
19. Maehara Y, Kusumoto T, Kusumoto H, Anai H, Akazawa K, Sugimachi K. Excised human neoplastic tissues are more sensitive to heat than the adjacent normal tissues. *Eur Surg Res* 1988;20:254-259
20. Ahmed M, Liu Z, Lukyanov AN, Signoretti S, Horkan C, Monsky WL, et al. Combination radiofrequency ablation with intratumoral liposomal doxorubicin: effect on drug accumulation and coagulation in multiple tissues and tumor types in animals. *Radiology* 2005;235:469-477
21. Nakada SY, Jerde TJ, Warner TF, Lee FT Jr. Comparison of radiofrequency ablation, cryoablation, and nephrectomy in the treating implanted VX-2 carcinoma in rabbit kidneys. *J Endourol* 2004;18:501-506
22. Horkan C, Ahmed M, Liu Z, Gazelle GS, Solazzo SA, Kruskal JB, et al. Radiofrequency ablation: effect of pharmacologic modulation of hepatic and renal blood flow on coagulation diameter in a VX2 tumor model. *J Vasc Interv Radiol* 2004;15:269-274
23. Miao Y, Ni Y, Bosmans H, Yu J, Vaninbroux J, Dymarkowski S, et al. Radiofrequency ablation for eradication of renal tumor in a rabbit model by using a cooled-tip electrode technique. *Ann Surg Oncol* 2001;8:651-657

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