Acta Med. Okayama, 2006
Vol. 60, No. 2, pp. 85–91

Acta Medica Okayama
http://www.lib.okayama-u.ac.jp/www/acta/

Original Article

Effects of Radiofrequency Ablation on Individual Renal Function: Assessment by Technetium-99m Mercaptoacetyltriglycine Renal Scintigraphy

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We quantitatively evaluated total and individual renal function by technetium-99m mercaptoacetyltriglycine (Tc-99m MAG3) renal scintigraphy before and after radiofrequency ablation (RFA) of renal tumors. Eleven patients who underwent Tc-99m MAG3 renal scintigraphy 1 week before and after RFA were evaluated (7 men and 4 women; age range: 23–83 years; mean age: 60.6 years). Five patients had solitary kidneys, and five had normally or minimally functioning contralateral kidneys. One patient had a renal cell carcinoma in the contralateral kidney. One patient with a solitary kidney underwent RFA a second time for a residual tumor. In patients with a solitary kidney, MAG3 clearance decreased after 5 of 6 RFAs, and in patients with a normally functioning contralateral kidney, MAG3 clearance decreased after 4 of 5 RFAs, but no significant differences were observed between before and after treatments. In addition to the total MAG3 clearance, the split MAG3 clearance was evaluated in patients with a normally functioning contralateral kidney. MAG3 clearance decreased in 4 of 5 treated kidneys, while it adversely increased in the contralateral kidneys after 4 of 5 RFAs. No significant differences, however, were observed between before and after treatments. The results of our study revealed no significant differences in sCr, BUN, CCr, or MAG3 clearance between pre- and post-RFA values. These results support data regarding the functional impact and safety of renal RFA in published reports. We evaluated total and individual renal function quantitatively using Tc-99m MAG3 renal scintigraphy before and after treatment. This scintigraphy was very useful in assessing the effects of RFA on renal function.

Key words: kidney, renal tumor, radiofrequency ablation, Tc-99m MAG3 renal scintigraphy, individual renal function

Radiofrequency ablation (RFA) has been investigated as an alternative, minimally invasive treatment for various tumors, including liver, bone, and lung tumors [1–3]. Recently, a number of experimental studies have demonstrated the feasibility and safety of renal RFA [4–7].

In contrast to partial nephrectomy, the gold standard of nephron-sparing treatment, RFA, destroys the tumor and a reduced margin of local healthy tissue; it is therefore expected to be less invasive than

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partial nephrectomy. Although there have been a few reports of the effects of RFA on renal function, to our knowledge [4–8], no studies have been performed as yet to evaluate the effects of RFA on individual renal function by scintigraphy. Consequently, we quantitated total and individual renal function by technetium-99m mercaptoacetyltriglycine (Tc-99m MAG3) renal scintigraphy before and after RFA. In addition, we measured serum creatinine (sCr), blood urea nitrogen (BUN), and 24 h urinary creatinine clearance (CCr) compared with the Tc-99m MAG3 clearance.

Materials and Methods

Patient characteristics. This prospective study was undertaken between May 2002 and September 2003 with the approval of our institutional ethics committee. A written informed consent was obtained from all patients before the initiation of treatment. A total of 17 patients with renal cell carcinoma underwent RFA. Among them, we evaluated renal function after 12 RFAs in 11 patients subjected to Tc-99m MAG3 renal scintigraphy 1 week before and after RFA (7 men and 4 women; age range: 23–83 years; mean age: 60.6 years) (Table 1). The tumors size ranged from 7–37 mm in diameter. Diagnosis of renal cell carcinoma was confirmed by needle biopsy in 5 cases. In the remaining 6 patients, diagnosis was established based on CT or MRI showing a renal mass that became significantly enhanced in the arterial phase.

Five patients had solitary kidneys, and 5 had normally or minimally functioning contralateral kidneys. One patient had a renal cell carcinoma in the contralateral kidney. Two had multiple tumors that were treated simultaneously. One patient with a solitary kidney underwent RFA a second time for a residual tumor.

Radiofrequency ablation technique. RFA was performed under CT guidance. The patients' vital signs were continuously monitored throughout the procedure. RFA was performed under local anesthesia, and conscious sedation was induced by intravenously infused fentanyl chloride. The procedure was performed using a single internally cooled electrode the size of a 17-gauge needle (Cool-tip, Radionics, Burlington, MA, USA). Once proper electrode positioning was confirmed, we attached the electrode to a 500-kHz monopolar radiofrequency generator (Cosman Coagulator-1, Radionics). Tissue impedance was continuously monitored using the circuitry incorporated in the generator.

At the end of each treatment, perfusion was stopped and the maximal temperature was recorded. If the temperature exceeded 60℃, the electrode was withdrawn. If the temperature did not exceed 60℃, RFA was repeated at the same site.

On the basis of the size and geometry of the lesion, overlapping ablations were performed by

Table 1 Patient characteristics

Treatment no.	Sex	Age (y)	Side of treated Kidney	Contralateral kidney	Treated tumor (number)	Tumor size (mm)
1	female	76	left	post nephrectomy	1	35
2	male	71	right	post nephrectomy	1	28
3	female	23	left	post nephrectomy	3	20,19,16
4	male	42	right	intact	1	27
5	male	71	right	intact	1	28
6	male	60	right	post nephrectomy	1	32
7	female	77	left	post nephrectomy	1	37
8	male	63	left	post nephrectomy	1	20
9	male	83	left	intact	1	29
10	female	64	bilateral	(bilateral RCC)	3	23,21,7
11	female	26	left	intact	1	15
12	male	71	right	intact	1	34

* Treatment no. 1 and no.7 are done in the same patient.
7 months after first RFA (no.1), second RFA (no.7) was performed for a residual tumor.

repositioning the needle to ablate the entire tumor. If possible, patients were subjected to unenhanced and contrast-enhanced CT immediately after RFA.

Tc-99m MAG3 renal scintigraphy. All the patients underwent Tc-99m MAG3 renal scintigraphy within 1 week before and after RFA. To ensure adequate hydration, the patients were asked to drink 200 ml of water 30 min before the test.

Thereafter, a single-head gamma camera with a general purpose, low-energy collimator (GCA 901A/HG, Toshiba, Tokyo, Japan) was set behind the patient, who was lying in the supine position. Each patient was administered 370 MBq of Tc-99m MAG3 by intravenous bolus injection. Sequential timed-image data stored in a 128×128 matrix were recorded by computer: 60 frames, 2-sec images for the initial 2 min and 168 frames, 10-sec images for 28 min.

Regions of interests (ROIs) were assigned for each kidney and a perirenal background region. Computerized time-activity curves were generated from the sequential image data.

The renal clearance of MAG3 was calculated based on the absolute renal uptake in each kidney according to an equation reported by Itoh *et al.* [9]. This absolute renal clearance was normalized to a body surface area of 1.73 m^2, and we used this value as the MAG3 clearance in this study.

sCr, BUN, and CCr were also measured before and 1 week after RFA.

Statistical analysis. A paired t-test was used to compare sCr, BUN, CCr, and MAG3 clearance before and after treatment. Differences were considered statistically significant at $p < 0.05$.

Results

Although most patients showed no complications, 2 had postoperative perirenal hematomas that resolved spontaneously. There was no evidence of clinically significant injury to the urinary collecting system. Immediately after RFA, 9 patients underwent unenhanced and contrast-enhanced CT. Only 1 of the 13 ablated tumors showed contrast enhancement after administration of the contrast agent. The levels of sCr, BUN, CCr, and MAG3 clearance before and after treatments are shown in Fig. 1–3. The mean sCr was 1.10 mg/dl before treatment and 1.13 mg/dl after the procedure.

In patients with a solitary kidney, sCr increased after 4 of 6 RFAs. CCr decreased after 3 of 5 RFAs, although 1 patient accidentally failed to examine CCr. MAG3 clearance decreased after 5 of 6 RFAs, but no significant differences were observed between pre- and post-RFA values (Fig. 1).

In patients with a normally functioning contralateral kidney, sCr increased after 3 of 5 RFAs, CCr decreased after 3 of 5 RFAs, and MAG3 clearance decreased after 4 of 5 RFAs, but no significant differences were observed between the pre- and post-RFA values (Fig. 2). In 1 patient who underwent RFA for bilateral renal cell carcinoma, changes in sCr, BUN, CCr, and MAG3 clearance after RFA were minimal.

In addition to the total MAG3 clearance, the split MAG3 clearance was evaluated in patients with a normally functioning contralateral kidney (Fig. 3). In the treated kidneys, MAG3 clearance decreased after 4 of 5 RFAs. In contrast, in the contralateral

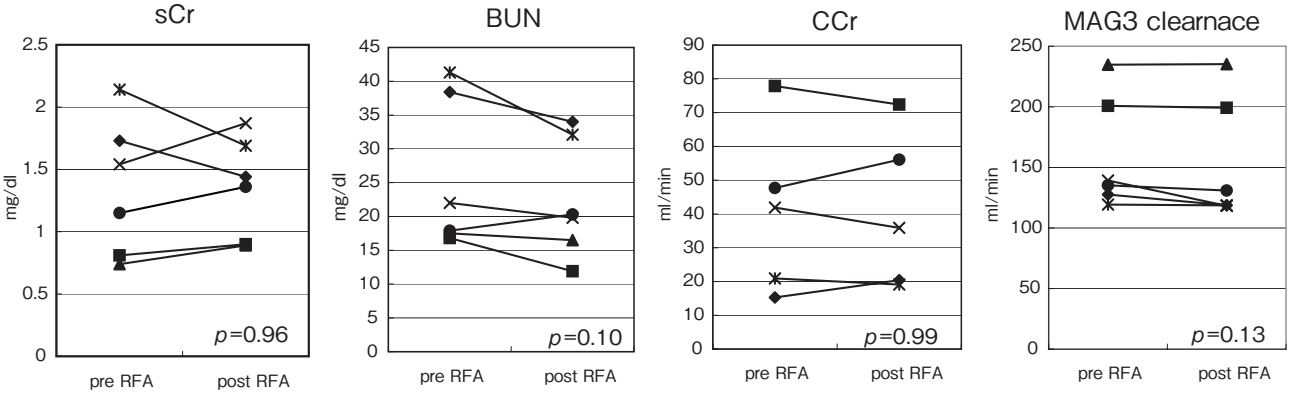


Fig. 1 Plot of sCr,CCr,BUN,MAG3 clearance before and after RFA in patients with a solitary kidney.

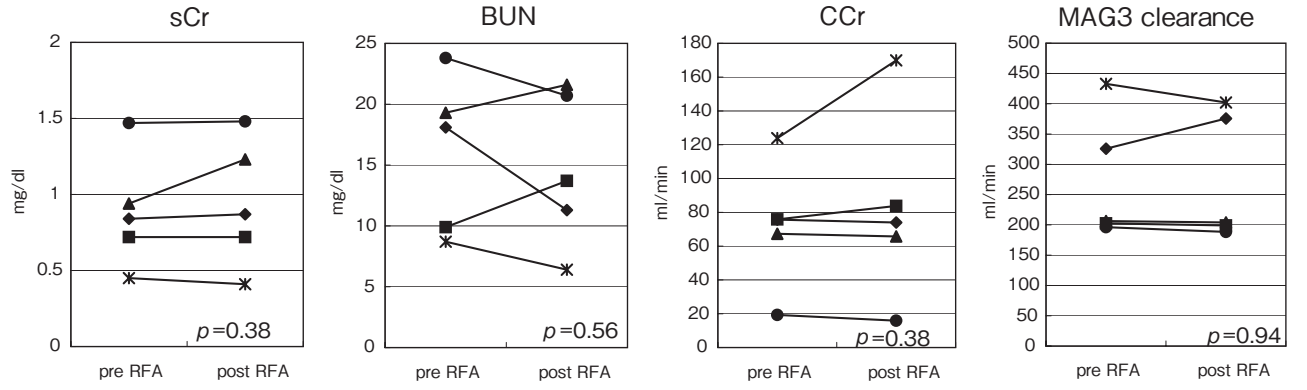


Fig. 2 Plot of sCr,CCr,BUN,MAG3 clearance before and after RFA in patients with a normally functioning contralateral kidney.

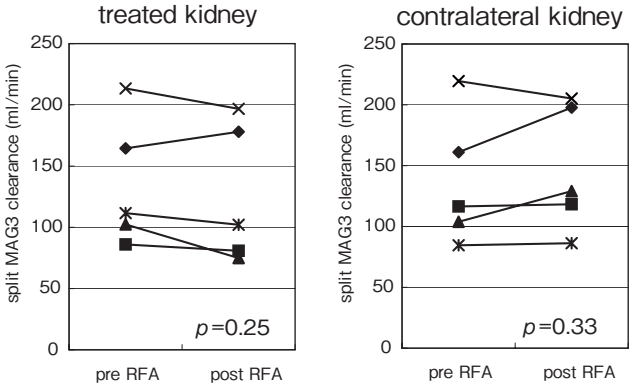


Fig. 3 Plot of split MAG3 clearance in treated and contralateral kidneys before and after RFA.

kidneys, MAG3 clearance adversely increased after 4 of 5 RFAs.

Description of a case. An 83-year-old man with a history of chronic hepatitis was found to have a mass in the left kidney during a periodical ultrasound examination (Fig. 4). Contrast-enhanced CT scan revealed a mass 29 mm in diameter in the left kidney. He refused surgical excision of the renal tumor, and the decision was made to treat the tumor with RFA.

Pretreatment MAG3 clearance of the left and right kidneys were 102.4 ml/min and 103.9 ml/min, respectively. After obtaining informed consent, CT-guided RFA was performed under conscious sedation. For this procedure, a single internally cooled electrode the size of a 17-gauge needle was used. The patient presented no RFA-related complications. There was no evidence of impairment of the urinary collecting system.

Three days after RFA, Tc-99m MAG3 renal scintigraphy was performed. Posttreatment MAG3 clearance of the left kidney decreased to 74.9 ml/min, and MAG3 clearance of the right kidney adversely increased to 129.1 ml/min.

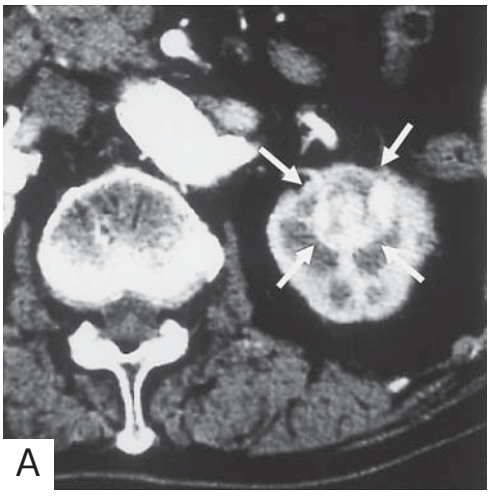
The contrast-enhanced CT scan obtained 3 months after RFA showed no evidence of tumor enhancement. The zone of ablation extending beyond the tumor was minimal.

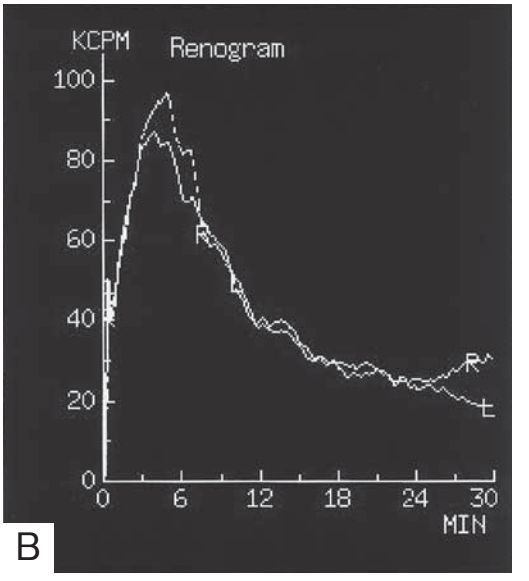
Discussion

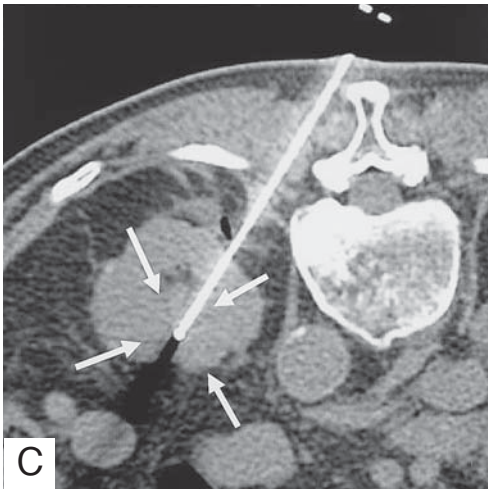
RFA for renal tumors is minimally invasive, and good results have been reported [4–7]. As for complications, hematoma, hematuria, and renal function impairment have been reported [4–7]. RFA for renal tumors that abut calyces increase the risk of injury to the collecting system. The most frequent complication involving the collecting system is hematuia [5]. In our series, most patients followed an uneventful course; however, 2 patients experienced postoperative perirenal hematomas that resolved spontaneously. No patient experienced gross hematuria.

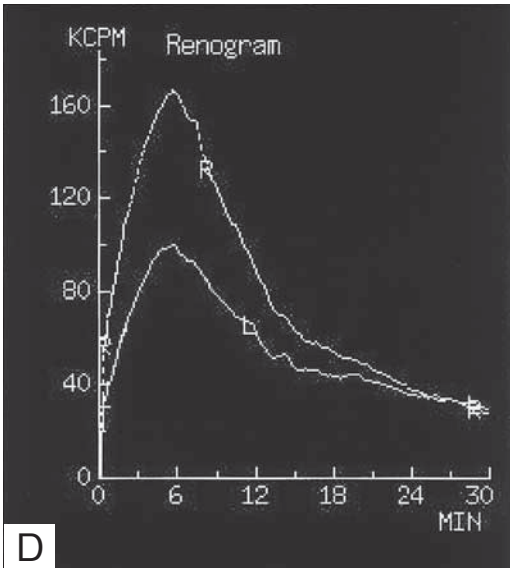
As for the impact of RFA on renal function, Pavlovich *et al.*, in a series of 21 patients subjected to a total of 24 percutaneous RFAs for small renal tumors, found that the mean serum creatinine of the group had not changed 2 months after the procedure, and that no patient had had an increase in serum creatinine greater than 0.1 mg/dl [4].

Gervais *et al.* evaluated 34 patients who underwent RFA for 42 renal tumors [5]. Four complications occurred during or after 54 patient visits to the radiology department for ablation. One patient experienced gross hematuria, and his creatinine levels









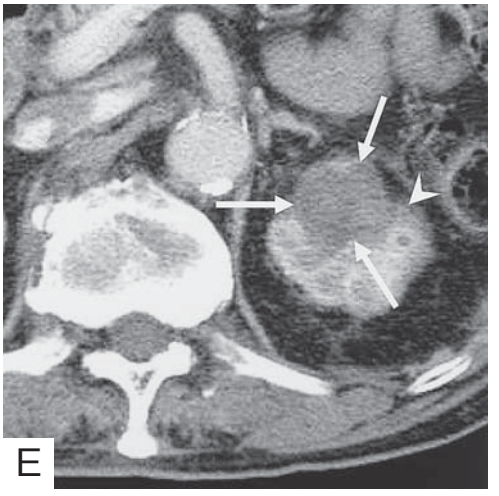


Fig. 4 83-year-old man with a tumor in the left kidney.
A, Contrast-enhanced CT scan before RFA showing an enhanced mass (arrows) 29 mm in diameter in the left kidney; **B**, Pre-RFA MAG3 clearance of the left kidney was 102.4 ml/min, MAG3 clearance of the right kidney was 103.9 ml/min; **C**, CT scan obtained during ablation showing the electrode tip positioned within the tumor (arrows); **D**, Post-RFA MAG3 clearance of the left kidney decreased to 74.9 ml/min and MAG3 clearance of the right kidney adversely increased to 129.1 ml/min; **E**, Contrast-enhanced CT scan obtained 3 months after RFA showing no evidence of tumor enhancement (arrows). Although the area of low attenuation beside the tumor (arrowhead) is suggestive of a small cortical infarction, the zone of ablation extending beyond the tumor was minimal.

did not return to baseline. Another patient with a solitary kidney experienced gross hematuria obstructing the ureter and required hospital admission and treatment consisting of ureteral stenting. This patient's creatinine level returned to a baseline of 1.8 ml/dl after an increase to 2.8 mg/dl. A 3rd patient developed a perirenal hematoma after RFA. This patient's creatinine levels returned to a baseline of 2.5 mg/dl after an increase to 3.5 mg/dl. In another patient with a solitary kidney, a proximal ureteral stricture occurred after RFA. The patient's creatinine levels returned to a baseline of 2.1 mg/dl after an increase to 3.9 mg/dl.

Roy-Choudhury *et al.* performed 14 RFAs for 11 lesions in 8 patients [6]. The mean serum creatinine level was 1 mg/dl before RFA and 1.1 mg/dl after the procedure. Only in 1 patient did the creatinine levels increase steadily from 1.4 to 2.9 mg/dl. This patient had bilateral multiple aggressive renal tumors and left nephrectomy and had undergone multiple RFAs on the contralateral kidney.

Baere *et al.* treated 5 patients with a histologically proven renal cell carcinoma with RFA [7]. Creatinine was 1.07 to 1.41 mg/dl before treatment and remained unchanged after treatment in 3 patients. In the remaining 2 patients, one of whom had a solitary kidney, creatinine increased from 1.39 and 1.4 mg/dl before to 1.64 and 2.02 mg/dl after RFA, respectively. Creatinine returned to baseline in all patients within 2 months of RFA.

Johnson *et al.* evaluated pre- and post-RFA serum creatinine and blood pressure in 25 patients followed up for at least 6 months [8]. Changes in mean serum creatinine were not statistically significant. No patient experienced new-onset hypertension or a worsening of existing hypertension.

In our series, no significant differences were observed between pre- and post-RFA sCr, BUN, CCr, or MAG3 clearance.

We used MAG3 scintigraphy to evaluate the effects of RFA on renal function in patients with renal tumors. Compared to I-131 ortho-iodohippuric acid (I-131 OIH), the biological properties of Tc-99m MAG3 seem to be inferior, but its physiological properties are superior for external imaging. In addition, Tc-99m MAG3 is available as a kit, which facilitates its use in a clinical setting. Image quality is higher with Tc-99m MAG3 than that with I-131 OIH because Tc-99m is a suitable agent for nuclear medicine imaging. Therefore, MAG3 clearance is an excellent index of renal function.

There are 2 methods of quantifying renal function: the plasma-sampling method and the external-counting method. The plasma-sampling method is an accurate method for determining renal clearance. However, this method is technically complicated and requires frequent plasma sampling. The external-counting method using a gamma camera is very simple and enables simultaneous evaluation of renal function. Itoh's method is especially useful for evaluating individual renal function in Japanese. The MAG3 clearance calculated according to Itoh's method is proportional to the OIH clearance [9].

Shirasaki *et al.* evaluated the function of the remaining kidney after nephrectomy for renal cell cancer by Tc-99m MAG3 renal scintigraphy [10]. However, to our knowledge, there have been no reports of the effects of RFA on renal function, as evaluated by Tc-99m MAG3 renal scintigraphy. Shirasaki *et al.* evaluated 30 patients who underwent unilateral radical nephrectomy by Tc-99m MAG3 renal scintigraphy. All patients underwent 3 Tc-99m MAG3 scintigraphy studies. The first study was performed before nephrectomy, the second 1 month after surgery, and the third 1 year after surgery. The mean MAG3 clearance of the remaining kidney increased, with the average percentage increase being 39.5% 1 month after nephrectomy and 40.5% 1 year after. They concluded that adaptive hyperfunction occurs soon after nephrectomy.

Anderson *et al.* have reported that the effective renal plasma flow of the remaining kidney increases by approximately 30% as early as 1 week after unilateral nephrectomy and remains at levels higher than prenephrectomy levels for more than 10 years [11].

In our study of patients with functioning contralateral kidneys, MAG3 clearance of the treated kidneys decreased after 4 of 5 RFAs. In contrast, in the contralateral kidneys, MAG3 clearance increased after 4 of 5 RFAs. A compensatory reaction similar to that reported by Shirasaki *et al.* [10] and Anderson *et al.* [11] may have occurred in the contralateral kidney. However, the contribution of functional impairment in the treated kidney may not be enough to cause a compensatory reaction in the contralateral kidney.

Surgery remains the standard treatment for renal carcinoma. Nephron-sparing surgery was initially used to preserve renal function in patients with a single functioning kidney, and its high success rate in this subset of patients indicates that it could be used to treat small unilateral tumors [12, 13]. For patients who are considered high-risk candidates for surgery, percutaneous RFA represents another treatment option.

Comparisons between nephron-sparing surgery and RFA are important to defining their role in the treatment of renal tumors. Duque *et al.* reviewed 64 patients who underwent 66 partial nephrectomies [13]. The most common complication was an increased creatinine level (twice the baseline value), occurring in 10 (15.1%) procedures. 3 (4.5%) patients required either temporary (n=1) or permanent (n=2) dialysis. Our results are favorable compared with this standard, especially when one considers that most of the patients in our series were ineligible for nephrectomy or at an extremely high risk if subjected to anesthesia and surgery.

Regarding the functional impact of RFA, a potential advantage compared with most cases of partial nephrectomy is that, during RFA, clamping of the renal pedicle is not necessary. Theoretically, this could reduce the risk of renal ischemia and permanent functional loss.

There are some limitations to this study. We used the external counting method to calculate MAG3 clearance, though this method is less reliable than the plasma sampling method. Besides, the number of patients with a normally functioning contralateral kidney was too small to draw a definite conclusion.

We evaluated total and individual renal function quantitatively using Tc-99m MAG3 renal scintigraphy before and after treatment. And this scintigraphy was very useful to assess the effects of RFA on renal function.

Conclusion. The results of our study revealed no significant differences in sCr, BUN, CCr, or MAG3 clearance between pre- and post-RFA values. These results support data regarding the functional impact and safety of renal RFA in published reports. Excellent outcomes in preservation of renal function support the validity of RFA for renal tumors.

Although our findings support the safety of RFA regarding its functional impact, only long-term clinical follow-up will define its role as a minimally invasive, nephron-sparing modality for the treatment of selected renal tumors. Periodic long-term monitoring of renal function is still recommended, especially in patients with a solitary kidney.

Acknowledgments. We gratefully acknowledge the assistance of Toshihide Tsuda M. D. of the Department of Human Ecology, Okayama University Graduate School of Environmental Science, and Isao Nagaya and the other members of the nuclear medicine staff in the Central Division of Radiology, Okayama University Hospital.

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