資料 4

JIVROSG-0701(RRFA-I/II)　重篤な有害事象の急送報告書（48 時間以内）

FAX 送付先：　086-235-7313　　(全＿＿＿枚)

JIVROSG-0207 研究代表者：岡山大学医学部放射線科　金澤　右　宛　(TEL:086-235-7313)

研究代表者への報告日　　年　　月　　日

施設名　　**FAX**　　**TEL**

施設研究責任者名　　記入者名

I. 症例に関する情報

JIVROSG 試験番号　　症例登録番号

有害事象発生時年齢　　歳　　性別　　男性、女性

II. 有害事象の転帰

有害事象発生日　　年　　月　　日　　**IVR 治療日**　　年　　月　　日

- ☐ 治療中及び治療完了日から **30** 日以内に発生したすべての死亡
- ☐ 治療に関連して発生した、重篤で、予期していない **grade 4** の有害事象
- ☐ その他　（＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿）

有害事象の概要（有害事象の具体的内容、関連する治療歴や検査データを含む）

III. 有害事象と因果関係が疑われる治療

☐ **IVR 治療**　☐ 薬物療法　☐ 放射線治療　☐ その他の治療

治療の概要

IV. プロトコール治療との因果関係についての報告者の評価

☐ **definite**	明確な	死亡との因果関係があると思われる有害事象 →
☐ **probable**	多分、十中八九は	
☐ **possible**	ありそうな	
☐ **unlikely**	ありそうにない	「腫瘍増悪,急死,事故,自殺,殺人,不明」から死因選択 →
☐ **not related(unrelated)**	関係ない	
☐ **unassessable**	評価不能	

V. 研究代表者の記録欄

1) 報告受領日　＿＿＿年＿＿＿月＿＿＿日　　研究代表者署名＿＿＿＿＿＿＿＿

2) グループ代表者への報告日＿＿＿年＿＿＿月＿＿＿日

3) 本有害事象への研究代表者としての対応

参加施設への通知日　＿＿＿年＿＿＿月＿＿＿日

症例登録一時中止日（データセンターへの連絡日）　＿＿＿年＿＿＿月＿＿＿日

効果・安全性評価委員会への審査依頼日　＿＿＿年＿＿＿月＿＿＿日

資料 5

JIVROSG-0701(RRFA-I/II)　重篤な有害事象の通常報告書（15 日以内）

FAX 送付先：086-235-7313　　(全＿＿＿枚)

JIVROSG-0701 研究代表者：岡山大学医学部放射線科 金澤 右 宛 (TEL:086-235-7313)

研究代表者への報告日　　年　　月　　日

施設名　　**FAX**　　**TEL**

施設研究責任者名　　記入者名

I. 症例に関する情報

JIVROSG 試験番号　　症例登録番号

有害事象発生時年齢　　歳　　性別　　男性、女性

II. 有害事象の分類

有害事象発生日　　年　　月　　日　　**IVR 治療日**　　年　　月　　日

- ☐ 死亡　　(**IVR 治療日より、**☐ **30 日以内** ☐ **31 日以降**)
- ☐ 生命を脅かすもの　　(☐ 予期していないもの　　☐ 予期されるもの)
- ☐ 予期していない **grade 2,3** の有害事象
- ☐ 永続的または顕著な障害/機能不全
- ☐ その他　(＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿)

III. 有害事象の内容とプロトコール治療の因果関係

AE/ARの内容	Grade	因果関係が疑われる治療法・薬物	因果関係の程度*	発生時期（何日目）	転帰

*因果関係の程度：definite(明確な)、probable(多分、十中八九)、possible(ありそうな)、unlikely(ありそうにない)、not related(関係ない)、unassessable(評価不能)のいずれかを記載。死亡の場合、死因が有害事象と「unlikely」、「not related」場合、「AE/AR の内容」に「腫瘍増悪、急死、事故、自殺、殺人、不明」のいずれかを記入。

IV. 症例報告の詳細　(別紙添付＿＿枚)

V. 研究代表者の意見書 (別紙添付＿＿枚)

VI. 研究代表者の記録欄

1) 報告受領日　　年　　月　　日　　研究代表者署名＿＿＿＿＿＿＿＿

2) グループ代表者への報告日　　年　　月　　日

3) 本有害事象への研究代表者としての対応

参加施設への通知日　　年　　月　　日

症例登録一時中止日（データセンターへの連絡日）　　年　　月　　日

効果・安全性評価委員会への審査依頼日　　年　　月　　日

4) 当該企業への「副作用自発報告」の提出確認日　　年　　月　　日

(付表 6)ラジオ波凝固プロトコール参照案 (JIVROSG-0701 RRFA-Ⅰ/Ⅱ)

1. Cool-tip システム

① 電極針の選択

active-tip の長さは腫瘍最大径よりも大きなものが原則。ただし刺入予定方向から見た腫瘍径が最大径と著しく異なる場合、消化管などを避ける上で必要不可欠である場合最大腫瘍径よりも小さな active-tip を選択することが許容される。

② 通電アルゴリズム

インピーダンスコントロールモードで通電する。

1焼灼個所につき12分間通電する(後述する場合は12分以上の通電となる)。

最大出力は140W とする。

通電出力

	2-cm active tip	3-cm active tip
開始出力	30 or 40W	50 or 60W
出力上昇率	10W/分	10W/分

ブレークダウンが生じた場合もそのまま通電を継続する。ただし再開する場合は 10-20W 出力を低下させる。あるいはブレークダウンが生じた出力の半分から再開する。

12 分間の通電終了後先端温度を測定し、60℃以上であった場合その焼灼個所の治療は終了とする。

ブレークダウンが 12 分間で生じなかった場合あるいは先端温度が 60℃未満であった場合は適宜焼灼を追加する。めやすは最大出力で 3-6 分の通電。この場合は 1 焼灼部位の通電時間が 12 分を超えることになる。

強度の疼痛に対しては鎮痛剤の追加で対処する。疼痛のため一旦通電を中断した場合、疼痛対策ののち、はじめから再開する。

③ オーバーラップ

15mm までの腫瘍の場合は中央を穿刺して焼灼する。穿刺が中央をはずれた場合は反対側に追加焼灼することが望ましい。

15mm を超える場合は複数カ所の焼灼を計画することが望まれる。

腎門側は十分に電極針を近接させて焼灼すること。

2. LeVeen システム

① 電極針の選択

展開径は腫瘍最大径よりも大きなものが原則。ただし刺入予定方向から見た腫瘍径が最大径と著しく異なる場合、消化管などを避ける上で必要不可欠である場合最大腫瘍径

よりも小さな展開径を選択することが許容される。

② 通電アルゴリズム

1焼灼個所につき 2 回の通電を基本とし、1 回の通電はそれぞれ最大15 分間通電する。

最大出力は190W とする。

通電出力

	2-cm 展開径	3-cm 展開径
開始出力	40W	60W
出力上昇率	10W/分	10W/分

1 回目の通電でロールオフが生じた場合、ロールオフが生じた最大出力の半分の出力から 30 秒後に 2 回目を開始する。

1 回目の通電でロールオフが生じなかった場合、その最終出力から 30 秒後に 2 回目を開始する。2 回目の通電でロールオフが生じなくても 15 分間の通電で終了する。

以上のごとく 2 回の通電を 1 セットとして 1 焼灼部位の通電を終了する。

強度の疼痛に対しては鎮痛剤の追加で対処する。疼痛のため一旦通電を中断した場合、疼痛対策ののち、はじめから再開する。

③ オーバーラップ

原則として中央を穿刺して焼灼する。穿刺が中央をはずれた場合は反対側に追加焼灼することが望ましい。

腎門側は十分に電極針を近接させて焼灼すること。

別添 4

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
該当なし							

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Arima K et al,	Percutaneous radiofrequency ablation with transarterial embolization is useful for treatment of stage 1 renal cell carcinoma with surgical risk: results at 2-year mean follow up.	Int J Urol.	14 (7)	585-90	2007

International Journal of Urology (2007) 14, 585–590 doi: 10.1111/j.1442-2042.2007.01740.x, 10.1111/j.1442-2042.2007.01849.x

Original Article: Clinical Investigation

Percutaneous radiofrequency ablation with transarterial embolization is useful for treatment of stage 1 renal cell carcinoma with surgical risk: Results at 2-year mean follow up

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Objectives: Despite laparoscopic partial nephrectomy and laparoscopic cryotherapy being performed lately, an even less invasive treatment would be desirable in high-risk patients. Under local anesthesia with i.v. sedation, we were able to perform percutaneous radiofrequency ablation (RFA) combined with renal arterial embolization for unresectable stage 1 (T1NoMo) renal cell carcinoma (RCC). We evaluated the feasibility, safety and therapeutic effects of this technique after a 2-year mean follow up.

Methods: Thirty-one patients who were not candidates for surgery underwent RFA for 36 stage 1 RCC. Twenty-eight tumors were percutaneously ablated 6 days after the tumor vessels were embolized. Dynamic contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) were performed to evaluate treatment at completion.

Results: Tumor enhancement was eliminated after two RFA sessions in all tumors. Thirty tumors remained free of enhancement during a mean follow-up period of 24.3 months. There were no major complications related to the procedures though one instance of pyonephrosis, two of subcapsular hematomas, one of retroperitoneal hemorrhage and one of nausea were seen after RFA. Two patients died of other diseases (i.e. colon cancer and cerebral bleeding) 20 and 26 months after RFA treatment. One patient had a local recurrence of tumor and underwent re-RFA. The recurrence rate of RCC after successful RFA was 2.8%. There was no recurrence in patients who had tumors of less than 4 cm after RFA at a mean follow-up period of 24.3 months. Local control was achieved in 100% of T1NoMo tumors including the recurrence case that underwent re-RFA.

Conclusions: The result of the present study at 2-year mean follow up showed percutaneous RFA was a feasible, safe and promising therapy for the treatment of unresectable stage 1 RCC, especially those smaller than 4 cm.

Key words: embolization, radiofrequency ablation, renal cell carcinoma, stage 1.

Introduction

Despite the development of less invasive surgical procedures such as laparoscopic nephrectomy, there is still demand for further reductions in therapy and general anesthesia related to morbidity. Nephron-sparing surgery has been reported to be an equally effective curative treatment for patients with a single, small renal cell carcinoma (RCC).[1,2] Recently, laparoscopic partial nephrectomy[3] and laparoscopic cryotherapy[4] has been performed in select patients. However, particularly in high-risk patients, an even less invasive treatment would be desirable. Under local anesthesia or i.v. sedation, we were able to perform percutaneous radiofrequency ablation (RFA) combined with renal arterial embolization for unresectable stage 1 (T1NoMo) RCC. We evaluated the feasibility, safety and therapeutic effects of this technique after a 2-year mean follow up.

Materials and methods

From May 2002 to June 2005, 31 patients with 36 T1NoMo RCC underwent RFA. This study was approved by our institutional review board and written informed consent was obtained from each patient and their family members. The mean patient age was 71.8 years (range, 43–87). A total of 17 tumors were found in the right kidney and 19 in the left. Tumor size ranged 1.2–6.5 cm in largest diameter, with a mean diameter (± SD) of 3.1 ± 1.2 cm. Diameter was 4 cm or less for 30 tumors and greater than 4 cm for another six tumors. Tumor location was classified according to the definition of Gervais *et al.*[5] Fourteen tumors were exophytic, 3 central, and 19 mixed. All patients had T1NoMo tumors according to the tumor node metastasis (TNM) staging system. One patient with von Hippel-Lindau disease had five lesions in a single kidney. She had undergone a right nephrectomy for RCC 13 years earlier. Another one had bilateral tumors. These patients were not candidates for surgery due to their receiving treatment for other cancers ($n = 7$), single kidney ($n = 4$), emphysema ($n = 4$), liver cirrhosis ($n = 4$), poor renal function ($n = 3$), lung metastases with pneumonia ($n = 1$), heart failure receiving renal dialysis ($n = 1$) or refusal of surgical treatment ($n = 7$) (Table 1). The diagnosis of RCC was based on the results of needle biopsy.

Selective arterial embolization

The 28 tumor vessels except in the patients with a poorly functioning kidney were selectively embolized 6 days before RFA. Tumor vessels were selectively embolized with a 3-F microcatheter (MicroPheret, William Cook Europe, Bjaevevskov, Denmark). Ethanol mixed with iodized oil or polyvinyl alcohol (PVA Foam, Cook, Bloomington, IN, USA) was used as the embolic material. The needle biopsy was

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Table 1 Eligibility criteria for radiofrequency ablation (RFA)

Under chemotherapy for double cancer	Seven cases (23%)
Single kidney	Four cases (13%)
Emphysema	Four cases (13%)
Liver cirrhosis	Four cases (13%)
Poor renal function	Three case (10%)
Lung metastases with pneumonia	One case (3%)
Heart failure receiving renal dialysis	One case (3%)
Refusal of surgical treatment	Seven cases (23%)

performed just after selective arterial embolization. The results showed that each tumor was clear cell carcinoma.

Percutaneous radiofrequency ablation

Radiofrequency ablation was performed using an RF generator (Cool-tip Radiofrequency Ablation System, Radionics, Burlington, MA, USA) under local anesthesia using conscious sedation with 0.1 mg of i.v. phentanyl citrate (Phentanest, Sankyo, Tokyo, Japan). The RF electrode (single cool-tip or cluster) was placed under real-time computed tomography (CT) fluoroscopic guidance.[6] The electrode was placed in the tumor based on the tumor size and shape to create overlapping volumes of ablated tumor tissue.[6]

Because the deeper central portion of the tumor near the renal pedicle tended to have insufficient ablation, the deep margin of the tumor was initially ablated, followed by a second more superficial treatment. The target probe temperature was set at 100°C. Tumors were heated to a maximum of 50 W to reach tissue temperatures greater than 65°C for a 12-min cycle. The tissue temperature around the electrode tip was measured immediately after RF application. If tissue temperatures failed to be maintained or achieved, a second 12-min RF cycle was applied to each tumor, with the electrodes repositioned to create overlapping volumes. As the treatment probe was withdrawn, RF energy was again applied to cauterize the intra-parenchymal needle track to limit back bleeding and external needle track to limit tumor seeding.[7] One large tumor was located adjacent to the descending colon. Saline solution (100 mL) was injected around the descending colon (anterior perirenal space) via an 18-G percutaneous transhepatic cholangiographic drainage needle. After that, the tumor was separated from the descending colon and ablated. Antibiotics were administered before and for 2 days after each embolization or RFA procedure.

Evaluation

Therapeutic effects were evaluated based on the findings observed in contrast-enhanced dynamic CT and magnetic resonance imaging (MRI) obtained within 1 week after RFA (Fig. 1). CT images were acquired using a multi-detector row CT scanner (HiSpeed Advantage Qx/I, GE Medical Systems, Milwaukee, WI, USA). MRI studies were performed using a 1.5-T MRI scanner (Signa Horizon, GE Medical Systems). Any lesion that showed enhancement of more than 10 HU in CT images acquired after the injection of contrast medium was considered to be an untreated tumor. Tumor enhancement in MRI was evaluated qualitatively. The endpoint of RFA was the presence of an area of non-enhancing tissue fully containing the treated tumor in enhanced CT and MRI. The second RFA treatment was added when an enhancing area of tumor tissue was still present. Follow up was based on contrast-enhanced CT and MRI studies performed every 2–3 months after RFA.

Results

Procedures and therapeutic effects

Radiofrequency ablation were technically successful in all patients and tumor enhancement was eliminated after 1–4 RF sessions in all tumors. A second RFA was performed 1 week later on eight tumors because we suspected that the results of the first RFA were insufficient through careful check-up of the imaging modalities, resulting in the elimination of enhancement. The tissue temperature increased to more than 65°C after the completion of RF ablation at each site. All tumors became smaller after RFA, with a significant reduction from 3.1 ± 1.2 cm to 2.6 ± 1.3 cm ($P < 0.05$) observed at the last follow-up examination. As the image observed for the longest period (Fig. 1c) showed a sequential image at 4-year follow up, it demonstrated the size reduction of the ablated lesion and no enhancement 4 years after RFA. On a patient with a large tumor located adjacent to the descending colon, the saline solution was injected around the colon to separate from the tumor. RFA could be also successful in multiple renal tumors of the patient with von Hippel-Lindau disease (Fig. 2). As the patient was scheduled to have 2-stage RFA, the second RFA was performed 1 week later. In the fourth tumor of Figure 2, near renal pedicle, the deep margin of the tumor was initially ablated, followed by a second superficial session. Figure 2(b) demonstrated no enhancement of the ablated lesions 1 month after RFA. Figure 2(c) demonstrated no growth or enhancement of those at 2-year follow up. The patient subsequently died of cerebral bleeding connected with the resection of cerebral hemangio-blastoma 26 months after RFA.

Complications

There were no major complications during the procedures. As an intraoperative complication, nausea was observed in one patient (3%, 1/31). All patients experienced pain and a burning feeling during RFA, but these were within tolerable limits. As postoperative complications, subcapsular hematoma was observed in two patients (6%, 2/31) and retroperitoneal hemorrhage in one patient (3%, 1/31). As a late complication, pyonephrosis appeared and an abscess developed in the ablated tumor in one patient (3%, 1/31) 2 months after treatment. This patient had suffered from methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia 3 months before RFA treatment. The abscess was percutaneously drained, and the drainage tube was indwelling. MRSA was detected in the discharged pus. The abscess was eliminated 2 weeks after drainage and the tumor became atrophic (Table 2). No significant differences were observed before and after RF ablation in the mean serum creatinine level (1.3 ± 0.8 mg/dL and 1.4 ± 0.9 mg/dL, respectively) or the mean creatinine clearance value (45.7 ± 21.6 mL/min and 50.4 ± 21.0 mL/min, respectively).

Follow-up findings

Two patients died of other disease such as cerebral bleeding and colon cancer 20 and 26 months after RFA treatment, respectively. One patient (3%, 1/31) with a tumor measuring 4 cm had a local recurrence of the tumor and underwent re-RFA 9 months after the first RFA treatment. The other 28 patients had no growth or enhancement of the ablated lesions during a mean follow-up period of 24.3 months. No patients had metastases during the follow-up period. The recurrence rate of

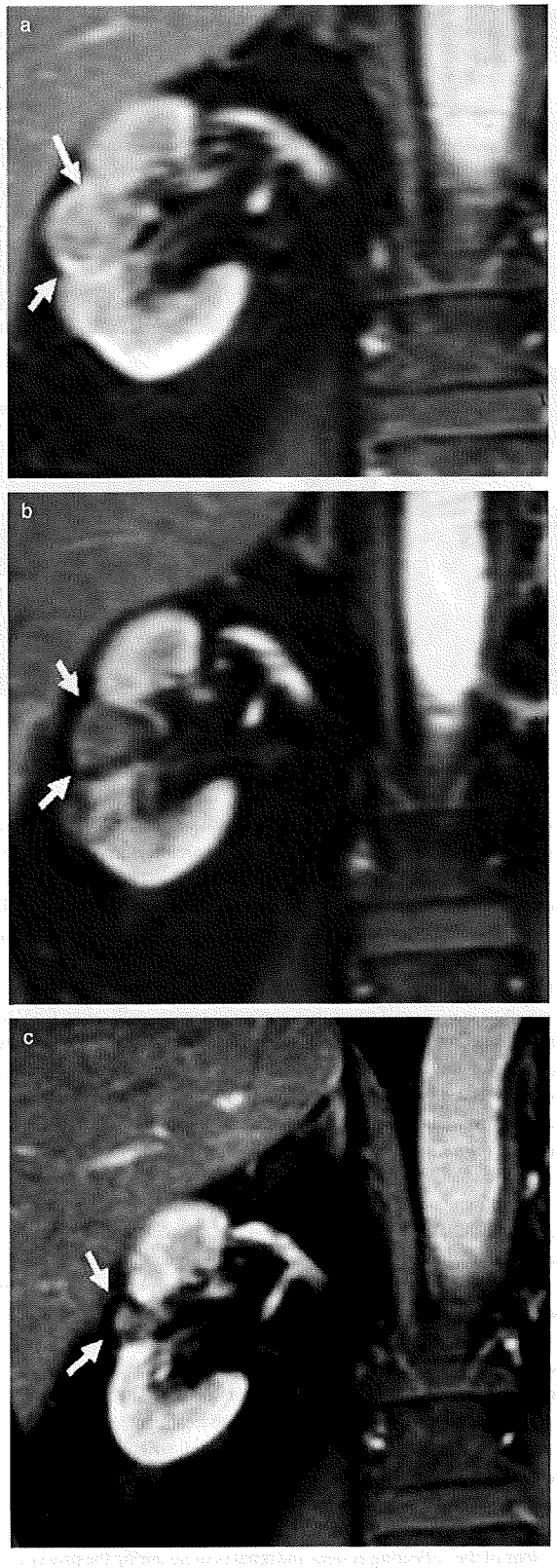

Fig. 1 Sequential images of the ablation area of the mixed type renal cell carcinoma (RCC) measuring 3.5 cm observed for the longest period. (a) Dynamic magnetic resonance imaging (MRI) before radiofrequency ablation (RFA); (b) dynamic MRI 5 days after RFA; (c) dynamic MRI 4 years after RFA.

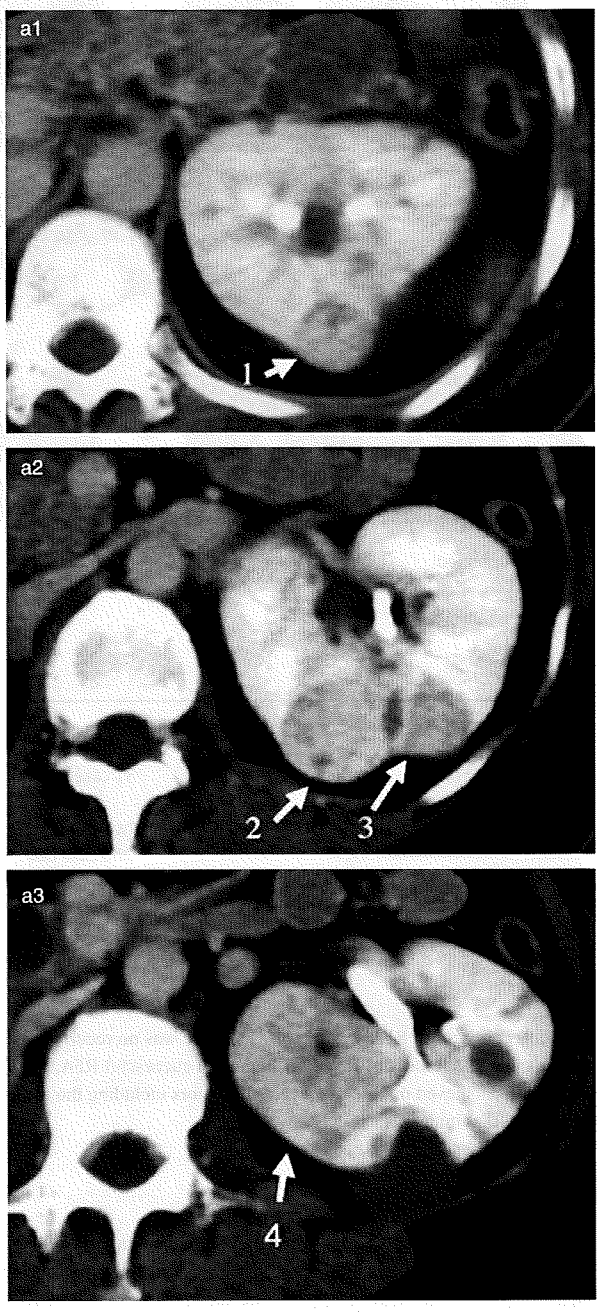

Fig. 2 Sequential images of the ablation area of multiple RCC due to von Hippel-Lindau disease. (a) Contrast-enhanced computed tomography (CT) before RFA; (b) contrast-enhanced CT 1 month after RFA; (c) contrast-enhanced CT 2 years after RFA.

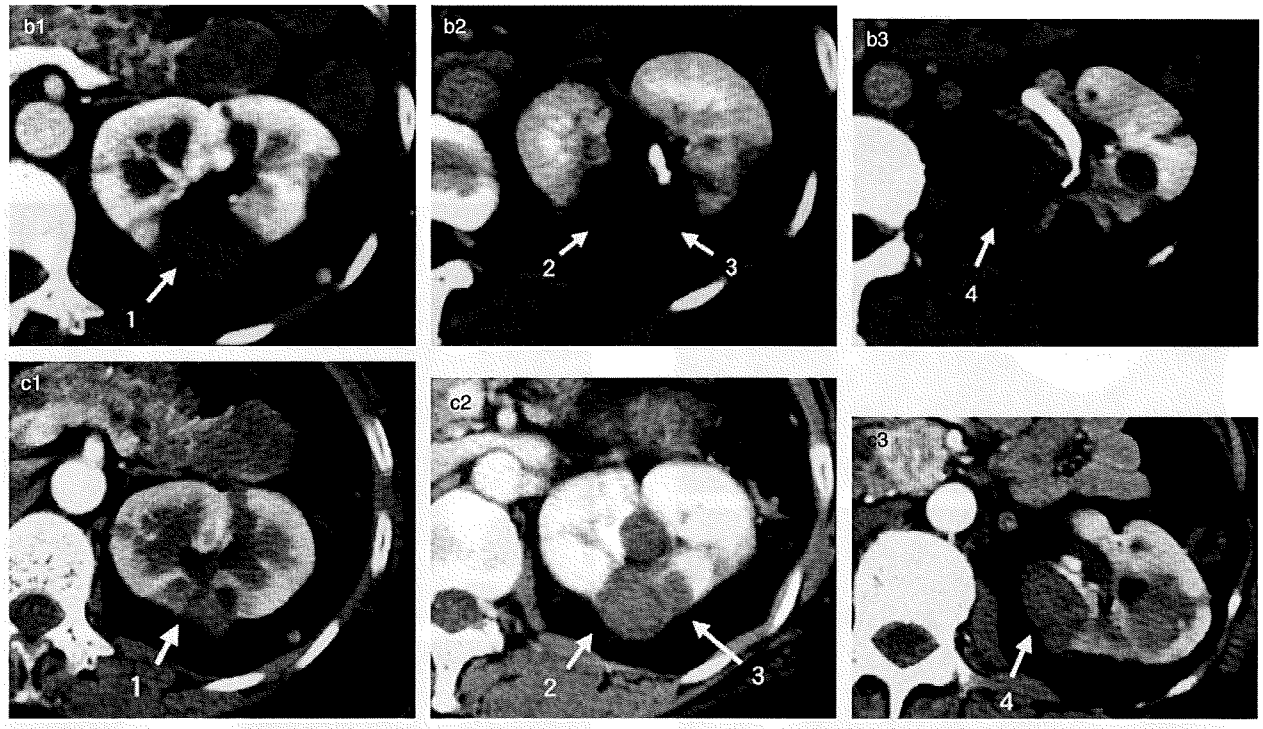

Fig. 2 Continued.

Table 2 Complications of RFA

Intraoperative complications	
Nausea	One case (3%)
Pain and burning feeling during RFA	31 cases (100%)
Postoperative complications	
Subcapsular hematoma	Two cases (6%)
Retroperitoneal hemorrhage	One case (3%)
Late complication	
Pyonephrosis	One case (3%)

RCC after successful RFA was 3% (1/31). There was no recurrence in patients that had tumors of less than 4 cm after successful RFA. Local control was achieved in 100% of T1NoMo tumors including the recurrence case that underwent re-RFA.

Discussion

Zlotta *et al.*[8] referred to the application of RFA in the treatment of RCC first. RFA has lately been used for controlling local bleeding during laparoscopic partial nephrectomy.[9,10] The therapeutic effects of RFA were contradictory in several reports. Matoraga *et al.*[11] revealed that RFA led to inactivity of cancer cells. Gervais *et al.*[5] eliminated tumor enhancement in 100% (3/3) of small tumors measuring 3 cm or less. They recently reported 42 tumors treated with a total of 140 ablations during 54 patient visits.[12] They found that all exophytic tumors (29/29) were treated successfully at 13.2-month mean follow up. On the other hand, Michaels *et al.*[13] reported RFA was not satisfactory from pathological changes of the resected tissue after RFA. It is known that hematoxylin–eosin staining shows the architecture of the ablated tissues is preserved immediately after RFA.[11,13–15] Therefore, immunohistochemical staining such as nicotinamide-adenine dinucleotide (NADH) and terminal deoxynucleotidyl transferase-mediated 2′-deoxyuridine 5′-triphosphate nick end labeling (TUNEL) staining that was used to detect apoptosis are necessary to evaluate cell viability.[11] Itoh *et al.*[14] confirmed that apoptotic cancer cells after RFA had become necrotic over time. We also experienced hematoxylin–eosin staining of the resected tumor specimen 6 weeks after RFA showed well-preserved cancer cells intermingled with hemorrhage and necrosis. However, almost all tumor cells were stained in the TUNEL staining. Therefore, it is suggested that the ablated tumor cells developed apoptotic change.

Radiofrequency ablation is primarily indicated as a treatment for exophytic renal masses of less than 4 cm in greatest dimension. It is useful in treating such lesions in patients with comorbidities that preclude a major surgical procedure such as partial nephrectomy or laparoscopic partial nephrectomy. The use of RFA is primarily considered in contraindicated patients who have intra-parenchymal tumors, as injury to the collecting system might result. Besides, because of potential thermal injury to adjacent organs, tumors that are situated laterally or posteriorly are considered more amenable to treatment via image-guided percutaneous RFA. As a matter of fact, ureteral stricture formation and renal insufficiency associated with RFA have reported.[12,16] Ureteral protection should be considered when RFA is to be performed in a tumor near the pelvis and ureter. We fortunately experienced no major complications of the collecting system and renal pedicle during the procedures. We injected the contrast medium just before RFA to avoid the ureteral and renal pelvic injury. Placement of a ureteral stent with cold saline perfusion before RFA are recommended to ablate tumors near the pelvis

and ureter.[12] Also, the instillation of saline or carbon dioxide into the retroperitoneal cavity is recommended to separate the ureter and tumor.[12] It is also recommended to separate the other organs and anteriorly-situated tumors.[17] In the present study at 2-year mean follow up, we had no instances of renal dysfunctions such as hydronephrosis or an atrophic kidney. Neither were volume reduction of a normal portion in the kidney or injury of the other organ found. Zogoria *et al.*[18] showed tumor location, histology and the presence of renal disease did not correlate with treatment success. We also believe that percutaneous RFA should now be indicated as a treatment for any lesions of small RCC in patients with comorbidities that preclude a major surgical procedure. Patients with von Hippel-Lindau disease are also considered to represent an ideal group for RFA as they typically present with multifocal, low-grade, low-stage clear cell RCC over their lifetime.[7]

The technical success of RFA appears to be related to the size of the tumors.[19] Tumors larger than 4 cm tend to require repeated treatment for effective ablation.[9–13,17] Varkarakis *et al.*[20] reported the imaging failure of renal tumors less than 4 cm after successful RFA was diagnosed in three of 56 patients (5.3%) at 2-year mean follow up. Our recurrence rate (3%) of stage 1 RCC after successful RFA at 24.3 months mean follow up was superior to that. Besides, there was no recurrence in patients who had tumors less than 4 cm.

The temperature of tumor tissue after RFA appears to be related to the success of tumor ablation. Tumors facing large vessels near the renal pedicle are resistant to the ablation due to too much blood flow. Experimental studies in animals have also shown that the thermal lesion volume in the normal kidney is strongly influenced by blood flow. Blockade of renal arterial blood flow minimizes heat loss by convection.[21,22] Because most renal cell carcinomas are hyper-vascular, the selective renal artery embolization reduces blood flow in the tumor and is considered to be useful in achieving consistent coagulation necrosis within the tumor. We therefore selectively embolized the 28 tumor vessels except in the patients with poorly functioning kidneys. The temperature in the center of tumor might be approximately 75°C. The tissue temperature rose to more than 60°C in all tumors, even those facing the renal sinus. Renal arterial embolization appears to enhance the anticancer effects of RFA. In the present study, the therapeutic response rates are comparable or superior to those that have been achieved for small renal tumors by RFA alone.[5,23]

Major complications, such as the hemorrhage requiring transfusion and ureteral stent placement, have been reported.[5] But those could be managed without an operative procedure in most cases.[5] Varkarakis *et al.*[20] reported patient death on post-procedural day 3. This was proved at autopsy to be due to aspiration pneumonia.[20] Uzzo and Novick,[24] in a review of nephron-sparing surgical procedures published during the past decade, established complication rates for these procedures. They found that rates of major complications ranged 4–30% in nine series, with a cumulative total of 155 (13.7%) complications in 1129 procedures.[24] Among these complications were 14 deaths, three splenic injuries, 78 urinary fistulas, 19 infections or abscesses, 27 hemorrhages, and 18 instances in which patients had to undergo postoperative dialysis.[24] Our results of RFA are favorable compared with this standard, especially when one considers that many patients would be at extremely high risk.

Miki *et al.*[25] recently showed that percutaneous cryoablation guided by horizontal open MRI of small renal tumors appeared to be safe and feasible. Like percutaneous cryoablation, our procedure is also minimally invasive and possible to be performed without expensive apparatus. Although the local control of ablated tumor was achieved in 100% of patients, including the recurrence case that underwent re-RFA at 2-year mean follow up, the long-term safety and efficacy in cancer control is still under investigation.

Conclusions

The result of the present study at 2-year mean follow up showed percutaneous RFA is a feasible, safe and promising therapy for the treatment of unresectable stage 1 RCC, especially those smaller than 4 cm. Continued maturation of data will be necessary to determine long-term efficacy.

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Editorial Comment

Nowadays, a majority of small renal tumors are detected serendipitously, partly due to widespread use of cross-sectional imaging techniques. Thus, we are frequently faced with a therapeutic dilemma posed by incidentally detected renal masses smaller than 4 cm in asymptomatic patients. There exist several options in treating these small renal tumors in a minimally invasive fashion, including: laparoscopic partial nephrectomy, minimum-incision endoscopic partial nephrectomy and ablative technologies such as radiofrequency or cryotherapy.[1] Arima *et al.* have presented their initial experience in percutaneous radiofrequency ablation with selective transarterial embolization in the present issue of *International Journal of Urology*.[2] Thirty-six clinical stage T1 renal cell carcinomas in 31 patients unfit for surgery were treated with percutaneous radiofrequency ablation with transarterial embolization, with a local recurrence rate of 2.8% at a mean follow-up period of 2 years. The procedure described here is a combination of transarterial embolization and radiofrequecncy ablation. Although it is uncertain what the contribution of each treatment alone represents, it is possible that embolization of tumor vessels prior to the ablation might increase thermal lesion volume of the ablation by decreasing the cooling effect of blood flow. A prospective trial would be needed to compare the combination of radiofrequency ablation and transarterial embolization, and ablation monotherapy. It should be noted that a combination of ethanol injection and radiofrequency ablation, which has been used in the treatment of hepatocellular carcinoma, has also been applied to small renal tumors recently.[3] Although the initial outcome is encouraging, long-term studies are necessary to confirm lasting efficacy.

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