Abstract  The purpose of this study was to determine the safety, effectiveness, and feasibility of microwave ablation (MWA) of small renal cell carcinomas (RCCs) in selected patients. Institutional review board and informed consent were obtained. From December 2007 to January 2009, 12 patients (8 male, 4 female) were enrolled in a treatment group, in which percutaneous MWA of small RCCs was performed under contrast-enhanced ultrasound guidance. The tumors were 1.7–2.9 cm in diameter (mean diameter, 2.0 cm). Therapeutic effects were assessed at follow-up with computed tomography. All patients were followed up for 3–14 months (mean, 6 months) to observe the therapeutic effects and complications (according to SIR classification). Assessment was carried out with CT imaging. No severe complications or unexpected side effects were observed after the MWA procedures. In all cases technical success was achieved. Clinical effectiveness was 100%; none of the patients showed recurrence on imaging. In conclusion, our preliminary results support the use of MWA for the treatment of small renal tumors. This technology can be applied in select patients who are not candidates for surgery, as an alternative to other ablative techniques.

Keywords  Renal cell carcinoma · Contrast-enhanced ultrasound guidance · Microwave ablation

Introduction

The incidence of renal cell carcinoma (RCC) is rising worldwide [1–4]. In addition, the increase in cross-sectional imaging—including computed tomography (CT), ultrasound (US), and magnetic resonance imaging (MRI)—as a first-line investigation for a multiplicity of indications has resulted in earlier detection of asymptomatic renal tumors that may have otherwise remained undetected [1]. The standard therapy for RCC has been radical nephrectomy [5]. Given the morbidity and mortality associated with this procedure, alternative treatments have been sought.
with nephrectomy, less invasive treatment techniques are often sought for smaller and more indolent tumors [6]. A percutaneous technique is desirable, particularly in patients for whom surgical procedures pose a high risk [7]. Nephron-sparing approaches have proven to have equivalent oncologic outcomes in select renal tumors [8, 9], so some authors have reported on minimally invasive ablative approaches in the management of renal tumors [10, 11]: these include radiofrequency thermal ablation (RFA) and cryoablation. A relatively new percutaneous approach is microwave ablation (MWA), which allows cellular destruction of localized tumors while preserving the uninvolved renal parenchyma [7, 10].

We report the treatment of a series of 12 patients with RCCs smaller than 3 cm by percutaneous MWA. The aim of this report is to evaluate the feasibility, safety, and preliminary clinical outcome of MWA for small RCCs [7, 10, 12].

Materials and Methods

Patient and Tumor Characteristics

Informed consent was obtained before the start of the study. This was a retrospective observational study. Inclusion criteria are summarized in Table 1. Twelve patients were enrolled in the study (eight male and four female), with a mean age of 79 years (range, 71–83 years). One week before the treatment session all patients underwent percutaneous renal mass biopsy under US guidance. In nine cases neoplasms were located in the right kidney (all at lower pole), and in the other three patients tumors were located in the left kidney (two in the lower pole and the other one in the middle third); all lesions had characteristic exophytic neoplasms. The diameter of the lesions at the widest point ranged from 1.5 to 2.9 cm (mean diameter, 2.0 cm) (Table 2; Fig. 1). Principal indications for enrollment included comorbid disease or advanced age (eight patients), need for nephron-sparing treatment (three patients), and patient preference (one patient). Two patients needed a nephron-sparing procedure because of their renal insufficiency (serum creatinine level, ≥1.5 mg/ml). All patients had normal coagulation parameters. Informed written consent was obtained from all patients.

Baseline Imaging

Pretreatment workup included abdominal imaging with CT before and after i.v. contrast administration and chest imaging with a chest radiograph or CT scan. All multirow CT scans were obtained with a section thickness of 0.5 mm, at 120 kV and 250 mA. Dual-phase enhanced scans were obtained with an injection of 100 ml of a iodinated contrast agent (Visipaque 320; GE Healthcare) at a rate of 3 ml/s, followed by a saline solution flush of 40 ml injected at a rate of 2 ml/s. Patients with renal insufficiency underwent a pretreatment workup that included hydration (100 ml/h for 12 h before CT examinations) and N-acetylcysteine, 600 mg twice a day (Figs. 1A, B).

Treatment Procedures

Patients were given moderate sedation using a combination of midazolam (0.07–0.08 mg/kg), propofol (0.5–2 mg/kg), and fentanyl (1–2 μg/kg) administered i.v. depending on patient weight. Continuous monitoring of heart rate, electrocardiographic tracing, oxygen saturation, and respiratory rate were obtained; blood pressure was determined every 4 min. Local anesthesia at the puncture site was achieved by subcutaneous injection of a solution of 2% carbocaine. All patients were continuously monitored by an anesthesiologist throughout the MWA procedure. Antibiotic prophylaxis against infection was provided with 1 g i.v. cefazolin sodium (Ancef; SmithKline Beecham Pharmaceuticals, Philadelphia, PA, USA) administered every 8 h for 24 h, beginning just prior to the procedure.

Imaging Guidance Equipment and Procedure

US and contrast-enhanced US (CEUS) were used as imaging guidance in all cases; in one patient CEUS was associated with C-arm cone-beam CT as a combined modality (Table 1; Figs. 2A, B). US and CEUS were performed using an iU22 unit (Philips, Bothell, WA, USA). A bolus of 2.5 ml second-generation contrast agent (SonoVue; Bracco, Milan, Italy) was administered i.v. just before needle positioning (Figs. 3A–C). C-arm cone-beam CT was performed using an Allura X-per CT unit (Philips, Best, Netherlands).

Microwave Ablation Equipment and Procedure

A MWA system (Vivant Medical, Mountain View, CA, USA) including a generator capable of producing 45 W of power at a frequency of 915 MHz and a coaxial cable to connect the generator with a straight (14.5-gauge)
microwave antenna with a radiating section length of 3.7 cm. The device does not need to be grounded. A single-application MWA at 45 W for 10 min through one antenna was inserted into the lesion center to obtain an approximate volume of necrosis 3.5 cm in diameter as indicated by the manufacturer’s specification. The microwave probe shaft was cooled by continuous flow of a saline solution according to the manufacturer’s specifications. At the end of the procedure a second CEUS examination was performed (with another bolus of 2.5 ml of sonographic contrast medium).

Follow-Up

Patients were followed up with CT before and after injection of i.v. contrast material 1–3 months after the procedure. At regular intervals thereafter patients were re-evaluated with

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**Table 2** Patient and tumor characteristics

<table>
<thead>
<tr>
<th>Patient no./gender</th>
<th>Tumor size (cm)</th>
<th>Type</th>
<th>Site</th>
<th>MWA time (s)</th>
<th>Power (MHz)</th>
<th>Follow-up method (months)</th>
<th>Imaging</th>
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<tbody>
<tr>
<td>1. F</td>
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<td>Exophytic</td>
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<td>CT (7)</td>
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<td>1.7</td>
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<td>3. M</td>
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<td>Exophytic</td>
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<td>CT (8)</td>
<td>CEUS</td>
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<td>5. M</td>
<td>2.5</td>
<td>Exophytic</td>
<td>Right</td>
<td>10</td>
<td>45</td>
<td>CT (3)</td>
<td>CEUS</td>
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<td>6. F</td>
<td>2.1</td>
<td>Exophytic</td>
<td>Left</td>
<td>10</td>
<td>45</td>
<td>CT (3)</td>
<td>CEUS + CCBCT</td>
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<td>7. M</td>
<td>1.6</td>
<td>Exophytic</td>
<td>Right</td>
<td>10</td>
<td>45</td>
<td>CT (8)</td>
<td>CEUS</td>
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<td>8. M</td>
<td>1.7</td>
<td>Exophytic</td>
<td>Right</td>
<td>10</td>
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<td>CT (7)</td>
<td>CEUS</td>
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<tr>
<td>9. M</td>
<td>2.1</td>
<td>Exophytic</td>
<td>Right</td>
<td>10</td>
<td>45</td>
<td>CT (3)</td>
<td>CEUS</td>
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<td>10. M</td>
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<td>Exophytic</td>
<td>Right</td>
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<td>11. M</td>
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<td>12. M</td>
<td>2.8</td>
<td>Exophytic</td>
<td>Right</td>
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<td>CEUS</td>
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MWA microwave ablation, CT computed tomography, CEUS contrast-enhanced ultrasound, CCBCT C-arm cone-beam CT

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Fig. 1 A Pretreatment contrast-enhanced CT scan shows an enhanced mass (arrow) in the lower pole of the right kidney. This mass resulted in a biopsy-proven renal cell carcinoma (RCC). B Contrast-enhanced CT scan shows a solid enhancing mass (arrow). This tumor was biopsied and proven to be a RCC.
CT before and after injection of i.v. contrast material, in addition to a complete serum metabolic panel and a chest radiograph. For all CT scans obtained for follow-up, a region of interest was used to interrogate each treated tumor on the scans before and after i.v. contrast material injection to assess for evidence of tumor enhancement. When scans obtained after i.v. contrast injection showed a lack of contrast enhancement (<10 HU for CT) in the treated RCC compared with pre-contrast-enhanced scans, this was considered the absence of evidence of disease. The presence of enhancement in the treated tumor on the first, or a subsequent, follow-up scan was interpreted as residual tumor.

The length of time, measured in months, from the procedure to the most recent follow-up scan was recorded. The total volume of the ablated tissue achieved with the single probe was calculated using a volume software package (Vitrea 2, software 3.8; Vital Images Inc., Minnetonka, MN, USA).

Clinical Outcomes

Technical success was defined as correct deployment of the antenna into the tumor. Clinical effectiveness was defined as complete tumor ablation at imaging follow-up. All complications were recorded and classified as major or minor according to SIR classification [13].

All patients were asked about postablation syndrome, which is a common phenomenon after RFA of solid abdominal tumors and consists of transient flu-like symptoms (fever, malaise, pain, myalgia, nausea, and vomiting) [14]. Pain was scheduled according to standardization of terms and reporting criteria for image-guided tumor ablation [15]. In one case a small hematoma occurred; it did not require any specific therapy.

Serum urea nitrogen and creatinine were tested up to 1 week before treatment and 3 days after procedures for all patients to evaluate renal function.

Results

All tumors were small clear cell carcinomas on pathological examination. Technical success rate was 100%; in all cases the antenna was correctly placed in the lesion.

Clinical effectiveness was 100%; no patients showed recurrence on imaging. The ablation zone was well defined on contrast-enhanced CT, and lack of contrast enhancement was observed at CT imaging in all patients, considered to be the absence of evidence of recurrence (Figs. 3B–D).

Serum urea nitrogen and creatinine did not change significantly after MWA; none of the patients showed worsened renal function during follow-up (Table 2).

No major complications occurred during or immediately after MWA. After treatment one patient experienced mild pain at the puncture site, requiring no analgesic medication. The pain was grade 1 according to standardization of terms and reporting criteria for image-guided tumor ablation [15].

The mean volume of ablation was 17.2 cm$^3$ (range, 10.2–25.1 cm$^3$).
All patients underwent CT investigation for an average period of 6 months (range, 3–14 months). Three patients had a follow-up period of 3 months; five patients, of 7 months; three patients, 8 months; and one patient, 11 months.

Discussion

Local ablative techniques have been developed to enable local control of tumors and cytoreduction, above all of primitive liver tumors, without damage to the uninvolved parenchyma [16]. In particular, for kidney, percutaneous ablative therapy allows treatment of renal tumor while preserving renal function; this is an important advantage, especially in patients with impaired renal function or with only a functional kidney [11, 17–19]. Moreover, a minimally invasive approach is recommended in patients at high surgical risk or in patients prone to recurrent renal surgery due to hereditary disorders.

Ablative therapies applied to renal tumors entail RFA [11, 18–23] and cryoablation [17, 18], whereas RFA remains the most widely used ablative technique worldwide. The main problems with RFA have been the high local recurrence rates in the treatment of masses larger than 3.0 cm in diameter and the incomplete tumor ablation near blood vessels because of the heat sink effect of local blood flow [7, 24].
More recently microwave energy has been proposed in different regions such as the liver [25–27], lung [28], adrenal glands [7], pancreas [29], and bone [7]. At this time only a few experiences with treatment of RCC have been reported, including a small number of patients [7, 10, 12]. Microwave radiation lies between infrared and radiowave radiation, with frequencies of from 900 to 2450 MHz. Heating of the tissue is based on agitation of water molecules inducing cellular death via coagulation necrosis; the electrical charge on the water molecule flips back and forth 2 to 5 billion times a second, depending on the frequency of the microwave energy [7].

MWA offers many of the benefits of other ablation techniques, in particular, RFA, and offers several other advantages, including higher intratumoral temperatures, larger tumor ablation volumes, faster ablation times, the ability to use multiple applicators simultaneously, optimal heating of cystic masses and tumors close to the vessels, and less procedural pain [7, 30–33]. With RFA, the zone of active tissue heating is limited to a few millimeters surrounding the active electrode, with the remainder of the ablation zone being heated via thermal conduction [7]. Thanks to its better convection profile, microwave energy produces a larger zone of active heating (up to 2 cm surrounding the antenna), thus allowing more uniform cell kill in the ablation zone [34]. RFA is also limited by the increase in impedance with tissue boiling and charring, because water vapor and char act as electrical insulators [35]. Due to the electromagnetic nature of microwaves, ablations do not seem to be subject to this limitation.

Like other ablation techniques, MWA allows for different approaches, including percutaneous, laparoscopic, and open surgical access. The percutaneous approach can be performed with US or CT guidance, according to lesion site and operator preference. As reported, in our experience when the procedure is performed in the angiographic suite on the angiographic bed, the US-guided positioning of the antenna can be aided using C-arm cone-beam CT, to confirm correct positioning of the needle inside the tumor. In our experience CEUS examination can be useful to identify hypervascular lesions during the procedure and to confirm complete ablation soon after the procedure. In the literature and in our experience, renal MWA is usually performed applying a power of 45 W for 10 min.

Several preclinical studies have been published that assess the safety of microwave energy application, to evaluate the morphology, size, and histologic features of the ablation area in different tissues, and to analyze the effects of different antenna patterns [30, 31, 33, 36–38]. Other phase I clinical trials [7, 26, 27] have been performed to confirm the effectiveness of MWA in patients undergoing tumor resection (ablate and resect intraoperative trials). Regarding the kidney, in particular, Clark et al. [10] reported a phase I study of 10 patients with renal carcinoma scheduled for radical nephrectomy; after 10 min of MWA, a specimen underwent pathologic examination, which showed a mean ablated volume of 27 and 105 cm³ with a single probe and a three-probe array, respectively; uniform cell death in the ablated area was confirmed by histochemical examination. In our cases the ablative volume is apparently less than that reported in other studies. This is probably due to the different methods used to calculate the volume; we did not use an approximate volume calculated using larger diameters of ablated area but, rather, a software program that calculates the real volume.

There are only a few phase II studies in the literature [25, 26, 39, 40], including lung and hepatic tumors. Only a few experiences with MWA of renal tumors are reported [7, 10, 12]. To compare the effect of microwave energy on the kidney versus other tissue, such as the liver, we should consider the difference in hemodynamic and electrical characteristics [9]: blood flow and electrical conductivity is greater in kidney compared to liver.

After any ablative therapies strict follow-up is mandatory to exclude microscopic foci of viable neoplastic cells undetectable with imaging methods [41]. However, in the study by Clark et al. [10], histopathologic examination after MWA showed no viable cells inside the ablation zone. In the same series [10], histochemical examinations revealed no cell death beyond the ablation area: this is particularly important in renal ablation to preserve healthy parenchyma and, above all, vascular and calceal structures.

In a series of 12 patients Liang et al. [12] obtained complete necrosis in four lesions in four patients with neoplasms smaller than 2 cm treated with a single antenna, although they used a needle with a smaller diameter (18 G) coupled with a higher-frequency generator (2450 MHz). But although we used a larger needle we recorded no relevant differences in complication rate.

At our institution patients treated with RFA for small renal carcinoma (unpublished data) experienced more pain than patients treated with MWA, and in addition, MWA procedures were twice as fast as RFAs.

Study Limitations

Limitations of our study were as follows. (1) Inclusion criteria were relatively strict, and tumor size was limited to ≤3 cm. Further studies including larger RCCs are needed. (2) Only twelve patients were included in this study. (3) The follow-up has been relatively short to date, so we are not certain of the long-term results. (4) Further studies are necessary to confirm short- and long-term effectiveness of
the MWA method and to compare it with other ablative techniques, especially RFA.

**Conclusion**

Our preliminary results support the use of MWA for treatment of small renal tumors. This technology can be applied in select patients who are not candidates for surgery, as an alternative to other ablative techniques. MWA seems to be superior for cystic tumors larger than 3 mm; in addition, the low complication rate, minimal side effects, and faster procedure strongly favor MWA as a curative approach for select small RCCs.

**References**
