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Microwave tumors ablation: Principles, clinical applications and review of preliminary experiences

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ABSTRACT

Local ablative techniques have been developed to enable local control of unresectable tumors. Ablation has been performed with several modalities including ethanol ablation, laser ablation, cryoablation, and radiofrequency ablation. Microwave technology is a new thermal ablation technique for different types of tumors, providing all the benefits of radiofrequency and substantial advantages. Microwave ablation has been applied to liver, lung, kidney and more rarely to bone, pancreas and adrenal glands.
Preliminary works show that microwave ablation may be a viable alternative to other ablation techniques in selected patients. However further studies are necessary to confirm short- and long-term effectiveness of the methods and to compare it with other ablative techniques, especially RF.

1. Introduction

In recent years there has been a growing interest in ablative therapies for the treatment of unresectable tumors in various organs.

Local ablative techniques have been developed to enable local control of tumors and cytoreduction, above all for primitive liver tumors, without damage of the healthy parenchyma.[1] Tumor ablation is defined as the direct application of chemical or thermal energy to a tumor to obtain cellular necrosis.[2] Ablation has been performed with several modalities including ethanol ablation, laser ablation, cryoablation, and radiofrequency ablation.

Radiofrequency ablation remains the most widely used ablative technique worldwide.[3]

Microwave technology is a new thermal ablation technique for different types of tumors, providing all the benefits of radiofrequency and substantial advantages.[2] Preliminary works show that microwave ablation may be a viable alternative to other ablation techniques in selected patients.

2. Principles of microwave ablation

Microwave radiation lies between infrared radiation and radiowaves with frequencies from 900 to 2450 MHz. Heating of the tissue is based on agitation of water molecules inducing cellular death via coagulation necrosis; electrical charge on the water molecule flips back and forth 2–5 billion times a second depending on the frequency of the microwave energy.[2]

Microwave ablation offers many of the benefits of others ablation techniques, in particular RF, and has several other advantages including: higher intratumoral temperatures, larger tumor ablation volumes, faster ablation times, ability to use simultaneously multiple applicators,[4] optimal heating of cystic masses and tumors close to the vessels, and less procedural pain.[2,4–7] Due to this last reason microwave ablation can be proposed also in outsetting patients.

Radiofrequency ablation causes cellular death via thermocoagulation necrosis; heat is generated by ions oscillation and collision proportionally to intensity of radiofrequency current. Alternatively, microwave produces an electromagnetic wave around insulated, electrically independent antenna; electromagnetic wave produces the agitation of polar water molecules within surrounding tissue[8]; heat is generated by molecules friction.

With RF ablation, the zone of active tissue heating is limited to a few millimetres surrounding the active electrode, with the remainder of the ablation zone being heated via thermal conduction.[2] Thanks to a better convection profile, microwave energy produces a larger zone of active heating (up to 2 cm surrounding the antenna) thus allowing more uniform cells kill in the target area.[9]

RF ablation is also limited by the increase in impedance with tissue boiling and charring, because water vaporization and char

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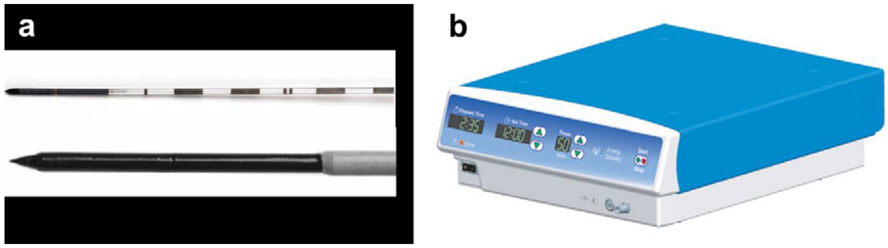

Fig. 1. Microwave ablation system (Evident TM Microwave ablation System/Covidien Ltd): antenna (a); microwave generator (b).

act as electrical insulators.[3] Due to the electromagnetic nature of microwaves, ablations do not seem to be subject to this limitation.

As other ablation techniques, microwave ablation allows for different approaches, including percutaneous, laparoscopic, and open surgical access. Percutaneous approach can be performed with Ultrasound (US) or Computerized Tomography (CT) guide, according to the site of the lesion and the preference of operator. In our experience, when the procedure is performed in angiographic suite on the angiographic bed, the US-guide positioning of the antenna can be aided using C-arm cone-beam CT, a new tool of angiographic systems, to confirm correct position of the needle inside the tumor.

Contrast enhanced US (CUES) can be useful to identify hypervascular lesions and to confirm complete ablation after the procedure.

Laparoscopic and open surgical approaches are used only to ablate lesions not reachable percutaneously or in patients eligible for other abdominal interventions in the same time.

Anyway ablation is performed using a thin (14.5-gauge) antenna that is attached, with a coaxial cable, to the microwave

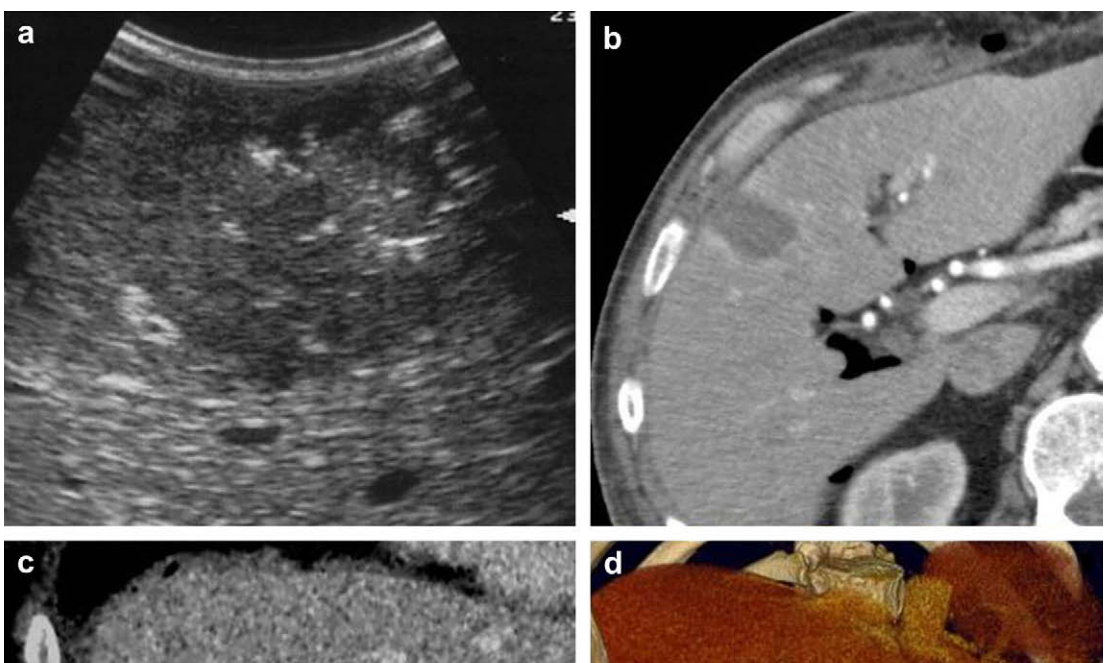

Fig. 2. Microwave ablation of a colorectal metastasis. Pre-procedural US (a). The procedure was performed with laroscopic approach during colon resection (b-c) and C-arm cone-beam CT (d); antenna inside the lesions is well visible (arrows). CT performed 1 months after the procedure with calculation of ablation volume.

generator able to producing 60 W of power at a frequency of 915 MHz.

In literature different protocols of time and power of ablation have been proposed according to the tissue and antenna type. Recently, Hope et al. published an experimental study about renal microwave ablation recommending the application of 45 W for 10 min.[10]

Electromagnetic microwave is emitted from the exposed, non-insulated portion of the antenna.

Due to the properties of microwave ablation does not require the placement of grounding pads.[2]

After clinical introduction, several years ago, microwave energy has not been widely applied because ablated areas produced by the original technology were too small.

Then, advances in the engineering of microwave, in term of material and structure, have overcome size and time limitations, thanks to optimized electromagnetic power deposition into a tissue.

To our knowledge, there is currently only one microwave ablation system (Evident TM Microwave ablation System/Covidien Ltd) (Fig. 1) globally available.

Different shape of antenna (straight or loop) has been proposed.[7,11] At the moment straight morphology is the only available.

The ablation of large tumors can be time consuming to ensure total overlapping coverage of ablation zones; thus the use of multiple electrodes to achieve large coagulation volumes has been proposed.[8] Microwave should be more amenable than radiowave to synchronous ablations using multiple probes to obtain larger coagulation volumes in shorter time.[8]

The procedure may be performed with sedation and local anesthesia in outsetting patients. Pain is lesser than for radiofrequency ablation probably because microwave ablation do not involve the flow of current within the body of the patient.

3. Clinical applications

Microwave ablation has been applied to liver,[2,11,8,12] kidney,[13,14] lung,[15] adrenal glands,[2] pancreas[16] and bone.[2]

In our preliminary experience we treated 4 liver nodules (Fig. 2) (3 metastases from colon carcinoma and 1 recurrence of HCC after radiofrequency ablation), 2 renal carcinomas (Fig. 3), 1 coeliac lymphnode from pancreatic carcinoma, 1 bone metastasis from uterine carcinoma, 1 primitive tumor of the lung (Fig. 4) and 1 pelvic recurrence from rectal cancer (unpublished data). Complete ablation was obtained in 8/10 lesions: in 2/10 patients partial ablation of bone metastasis and pelvic recurrence obtained considerable pain reduction. Mean volume ablated, calculated using a dedicated software (Vitrea 2/software 3.8/Vital Images) was 10.5 cm^3 (unpublished data).

Clinical indications are the same as those reported for other ablation therapies, above all patients not candidates to surgery. In particular percutaneous ablative therapy allow to destroy neoplastic tissue while preserving healthy parenchyma; this is an important advantage above all in patients with impaired hepatic, renal or pulmonary function.[17–21] Therapeutic purpose can be curative or palliative; in this last case microwave ablation is aimed to reduce symptoms, above all pain or recurrent bleeding.[22]

From a technical point of view microwave ablation is preferable in the treatment of lesion larger than 4 cm, with a cystic component or localized close to vessels larger than 3 mm; moreover it can be the first choice in case of recurrence after other ablation techniques.

About primitive or metastatic liver tumors the most frequent limitation of radiofrequency ablation is the difficulty

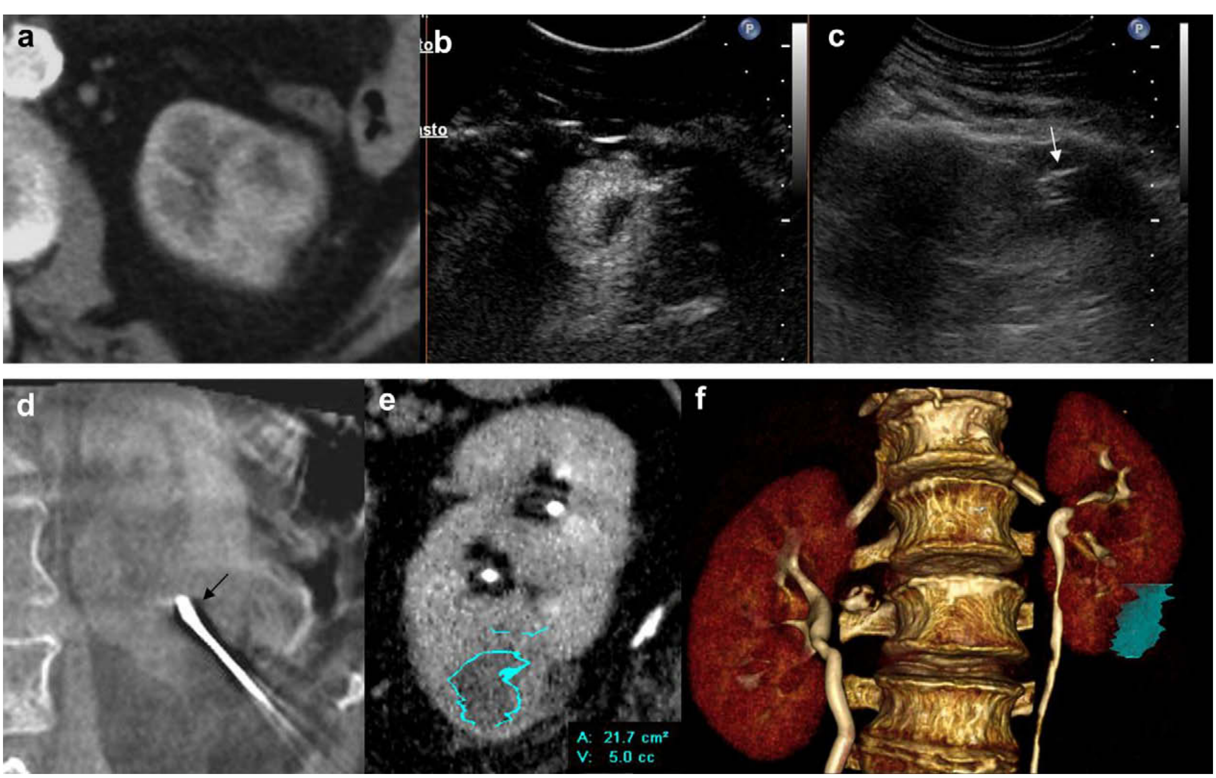

Fig. 3. Microwave ablation of a primitive renal tumor. Pre-procedural CT (a). The procedure was performed with contrast-enhanced US (b-c) and C-arm cone-beam CT (d); antenna inside the lesions is well visible (arrows). CT performed 1 months after the procedure with calculation of ablation volume (e-f).

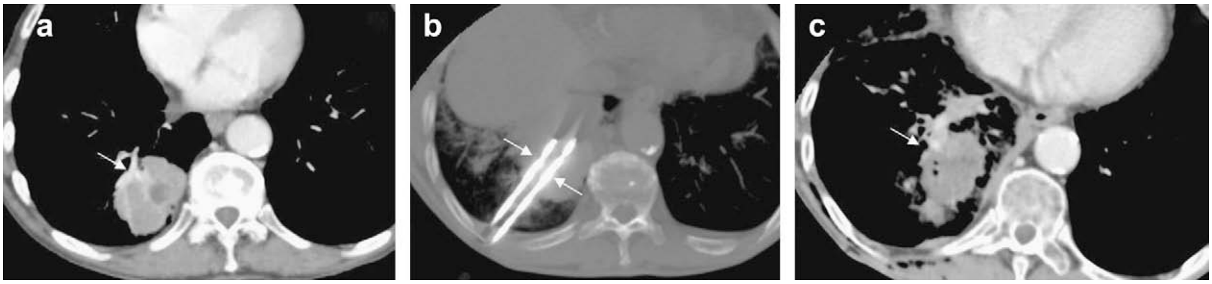

Fig. 4. Microwave ablation of a primitive lung tumor. Pre-procedural TC (a); pulmonary artery branches close to the lesion are well visible (arrow). The procedure was performed under CT-fluoroscopy guide (b) using 2 antennas (arrows); performed after the procedure (c) shows ablated area with air inclusions and integrity of vessels inside the tumor (arrow).

to obtain complete cellular death near blood vessels (especially portal branches and hepatic veins). An ''ablate and resect'' study published by Simon et al.[8] shows a uniform tumor kill extending close to the vessels; moreover large blood vessels (>3 mm) in the resection specimens did not create typical ablation zone distortion because of the minimal heat sink effect observed.[2]

In another study about renal tumors,[14] 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 caliceal structures.

4. Evaluation of the results

After many ablative therapies a strict follow-up is mandatory due to exclude microscopic foci of viable neoplastic cells undetectable with imaging methods.[23] However, in the study by Clark et al.[14] histopathologic examination, after microwave ablation, showed no viable cell inside the ablation zone.

As reported in literature, to evaluate cellular death after thermal ablation, tissue must be analyzed with the vital histochemical NADH stain for the mitochondrial enzyme nicotinamide adenine dinucleotide (NADH) diaphorase.[23]

Hematoxylin–eosin (H–E) staining shows a marked thermal-like effect with maximal intensity close to the antenna site and a surrounding area of hyperemia; nevertheless some areas displayed only a subtle loss of nuclear chromatin detail with minimal cell membrane destruction. NADH staining is able to discern areas with cellular viability and those with uniform cellular death.[8,14]

As reported for RF ablation, at imaging follow-up, lack of contrast enhancement on CT, MR or CEUS, indicates the absence of viable tumor.[21,24–27,13] Evaluation of contrast enhancement is easier in hypervascular tumor such as hepatocarcinoma or renal carcinoma. The detection of residual viable tissue in hypovascular lesions can be aid by MR or PET. MR Imaging may have an edge over CT in the detection of local regrowths due to the high sensitivity of T2-weighted sequence; the role of diffusion-weighted images is under investigation.[28,29]

5. Literature review

Several pre-clinical studies have been published to assess safety of microwave energy application, to evaluate morphology, size and histologic features of ablation area in different tissues and to analyze effects of different antenna patterns.[7,4,5,30–32] Other phase I clinical trials[14,8,11] have been performed to confirm effectiveness of microwave ablation in patients undergoing tumor resection (ablate and resect intraoperative trials). Clark et al.[14] in a trial including 10 renal tumors, ablated with laparoscopic approach using 60 W for 10 min and then resected, reported a mean size of the ablated tissue with a single probe of $4.1 \times 2.7 \times 2.2$ cm (total rectilinear volume, 27 cm^3; prolate spheroid volume, 15 cm^3); with a three-probe array, the mean size of the ablative lesion was $5.7 \times 4.7 \times 3.8$ cm (total rectilinear volume, 105 cm^3; prolate spheroid volume, 56 cm^3). Regarding hepatic ablation, Simon et al.[8] reported a series

Table 1

Author Year	Organ	No of patients Volume of nodules	Approach	Ablation	Results	Follow-up
Iannitti DA 2007[12]	Liver (primitive and metastases)	87 mean 3.6 cm (range 0.5–9 cm)	45%: open, 7%: laparoscopy, 45%: percutaneous (US/CT-fluoroscopy)	clustered or single antenna, 45 W, 10 min	- single antenna ablation volumes: 10.0 ml (range 7.8–14.0 ml) - clustered antennae ablation volumes: 50.5 ml (range 21.1–146.5 ml) - mortality: 0% - local complications rate: 9.1%	19 months, local recurrence rate: 2.7%
Wolf FJ 2008[15]	Lung (primitive and metastases)	50 3.5 ± 1.6	percutaneous (CT-guided)	straight or multitine deployable ring, 1–4 antennae, 45–60 W, 5–10 min	- Initial technical success: 95% - Pneumothorax: 39% - Hemoptysis: 6.6% - Skin burns: 36%	10 months, residual disease: 26%, local recurrence rate: 22%, 1-year local control rate: 67%
Martin RC 2007[33]	Liver (primitive and metastases)	20 pt mean 3 cm (range 1.5–4.5)	open or laparoscopic	straight	- Initial technical success: 100% - related complications: 0%	19 months, local recurrence: 1.5%
Liang P 2008[13]	Kidney (primitive)	12 mean 2.5 (range 1.3–3.8)	percutaneous (US-guided)	Cooled shaft antenna, 50 W, 500 s	- Initial technical success: 100% - related complications: 0%	11 months, local recurrence: 0%

of 10 patients (4 HCC and 6 colo-rectal metastases) treated with intra-operative US-guide with a triple antenna; they obtained an average ablation zone volume of 50.8 cm3 (range, 30.3–65.5 cm3); gross and microscopic examinations of areas after microwave ablation showed clear coagulation necrosis, even surrounding large hepatic vessels (>3 mm in diameter); a marked thermal-like effect was observed with maximal intensity close to the antenna sites; NADH staining confirmed the uniform absence of viable tumor in the ablation zone.

In literature only few phase II studies appeared,[12,13,15,33] including renal, lung and hepatic tumors (Table 1).

6. Conclusion

Our preliminary results and those reported in literature support the use of microwave ablation for the treatment of different type of tumors. This technology can be applied in selected patient not candidate to surgery, as an alternative to other ablative techniques. Its results seem to be similar to RF ablation for lesions smaller than 3 cm; for tumors larger than 3 cm microwave ablation can be conducted using multiple probe simultaneously. Microwave ablation seems to be better for cystic tumors and for lesions close to vessel larger than 3 mm. Further studies are necessary to confirm short- and long-term effectiveness of the methods and to compare it with other ablative techniques, especially RF.

Conflict of interest
None declared.

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Ethical approval
None.

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