Diagnostic and Interventional Imaging (2014) **95**, 677—682

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New tumor ablation techniques for cancer treatment (microwave, electroporation)

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KEYWORDS
Ablation;
Tumor;
Radiofrequency;
Microwave;
Electroporation

Abstract Since the introduction of radiofrequency ablation (RFA) for the treatment of liver tumors at the end of the 1990s, indications for local ablation techniques have been extended to other organs, in particular, the lungs, kidneys and bones. These techniques have also been improved, in particular to try and overcome the limitations of radiofrequency techniques, especially the significant decrease in complete ablation rates for tumors larger than 3 cm and tumors that are contiguous to vessels larger than 3 mm. Microwave ablation is a rapidly developing thermal ablation technique similar to RFA but with numerous differences. Electroporation, a non-thermal ablation technique with other possibilities, is in earlier stages of clinical development.

Microwaves

Principal

Microwave ablation involves the thermal destruction of tissue and is based on three different phenomenon:

- thermal production, which is proportional to the amount of energy delivered to the tissue and the interaction of this energy with the tissue. This interaction rapidly decreases as the distance from the microwave needle applicator increases;
- thermal conduction is the way the heat is obtained via diffuse energy that spreads to neighboring tissue. Different tissues have different conduction properties;

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http://dx.doi.org/10.1016/j.diii.2014.04.001
2211-5684/

- thermal convection is the dissipation of heat when it is transported by a fluid that crosses heated tissues. In the liver, convection is mainly due to vascularization, while in the lungs, it involves vascularization as well as bronchioaveolar structures. More precisely, the effects of convection can be distinguished in relation to the microcirculation or macrocirculation. For the microcirculation, the well-known ''heat sink effect'', which has been reported and identified in numerous publications, is the reason that it is difficult to destroy tumors that are contiguous to vessels that measure more than 2 to 3 mm. The microcirculation is responsible for convection and explains why the volume of thermal ablation obtained ex-vivo, (in non-vascularized tissue) is always larger than that obtained in vivo (in vascularized tissue);

  Overall, these three phenomena are the cause of the thermal equilibrium, which depends on the distance from the electrode, the type and quantity of energy delivered, and the length of treatment and type of tissue as well as its vascularization.

Microwaves cause thermal destruction that is not specific for the tumor. The goal is to heat tissues to temperatures above 60 °C.

Microwave frequencies used for medical applications vary between 915 MHz and 2450 MHz (Table 1). These frequencies are much higher than radiofrequency ablation (400 kHz), resulting in a shorter wavelength of approximately 30 cm, which allows microwave antennas to emit in the body without ground pads. The physical property that controls microwave penetration in tissue is permittivity. Permittivity has been found to be greater and therefore result in better diffusion of microwaves in tumoral tissue than in normal tissue [1]. Organs that seem to respond best to microwave ablation are those with marked differences in permittivity between tumors and the surrounding tissue. For example, this is true for breast tissue with the fat that surrounds the tumors and lungs with the air that surrounds the tumors.

When microwaves are applied, the electric dipole moment of the water molecules in tissue are agitated and seek to realign with the rapidly changing electric field, resulting in heating by friction. With microwave tissues in contact with the needle antenna reach temperatures of 160° to 180 °C, which is higher than that obtained with radiofrequency because they are limited to the boiling temperature of tissue, or slightly above 100 °C [2]. The increase in temperature is also faster with microwave than with radiofrequency, even bipolar [3]. The temperature 5 mm away from the microwave antenna is 100 °C while it is only 70 °C with radiofrequency [2]. Because of this improved thermal profile, much of the microwave energy is obtained by thermal heating and there is less room left for diffusion than during radiofrequency. Thus, in experimental animal models in vivo, thermal convection has less effect on zones of microwave ablation than zones of radiofrequency ablation. However, there is still loss of convection because an experimental study in healthy animal lungs showed a moderate heat sink effect in 30% of the vessels smaller than 6 mm, in 12% of the vessels between 3 and 6 mm and in 10% of the vessels smaller than 3 mm [4].

Because of the rapid heating along the entire length of the antenna, the use of microwave is limited to 60 W to avoid burns along the needle path. For this reason, most existing systems have a cooled shaft antenna with heating of the active distal tip of the needle. In addition, certain systems have a choke between the active distal tip and the proximal parts of the needle to limit reflection of energy from the heated tip. Cooled shaft antennas have been shown to be more effective because non-cooled shaft antennas cannot deliver more than 60 W of power in 10 min, while cooled shafts can deliver 60 W for at least 20 min [2]. Moreover, the ablation zones obtained with cooled shaft antennas seem to be more spherical [5].

All of these improvements have increased the ablation zone volumes than can be obtained with a single microwave session to reach a transverse diameter of approximately 3.5 cm. It has not been determined whether the best frequency for medical microwave use is 915 Mhz or 2450 Mhz. Although existing systems can deliver 100 W for several minutes, there are very few published results evaluating this amount of power.

Whatever the ablation zone volume that can be obtained with a single microwave antenna, one of the interests of this type of energy is the possibility of activating several antennas (Figs. 1 and 2) at the same time (as long as several generators are available), which is not possible with radiofrequency devices. It has been shown that simultaneous activation of 3 microwave antennas results in greater ablation volumes than sequential activation. Indeed, simultaneous activation produces an ablation zone volume of $43.1 \pm 4.3\,cm^3$ while sequential activation results in a volume of $14.6 \pm 5.2\,cm^3$ [6]. Studies are ongoing to determine the ideal distance between probes, but between 1.7 and 2 cm seems to be the most effective distance [6]. It appears that the greater the amount of energy delivered, the more the antennas can be separated without having non-coagulated areas between the antennas.

Clinical results

Hepatocellular carcinoma

In 2002, a series comparing radiofrequency and percutaneous microwave coagulation ablation in the treatment of 99 hepatocellular carcinomas between 1 and 3 cm in diameter (= 2.2) showed complete ablation in 96% of the tumors with radiofrequency and 89% with microwave ablation ($P = 0.26$) [7]. Three years later, a very recent series using a more effective microwave device treated HCC of between 3—5 cm in 89 patients and 5—7 cm in 20 patients using either radiofrequency or microwave ablation. The size of the tumors remained a predictive factor whatever the technique. There was no significant difference between the rate of complete ablation with radiofrequency ablation (89.8 %) and microwave ablation (95.9 %) [8]. In that study, complete tumor ablation, recurrence and alpha-fetoprotein above 1200 ng/mL were independent predictive factors with a hazards ratio of 4.15, 1.56 and 1.59, respectively.

Liver metastases

There are very few results in the literature with the most recent generation microwave cooled shaft antennas. Ten