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EDITORIAL

Laser ablation of liver tumors: An ancillary technique, or an alternative to radiofrequency and microwave?

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Abstract

Radiofrequency ablation (RFA) is currently the most popular and used ablation modality for the treatment of non surgical patients with primary and secondary liver tumors, but in the last years microwave ablation (MWA) is being technically improved and widely rediscovered for clinical use. Laser thermal ablation (LTA) is by far less investigated and used than RFA and MWA, but the available data on its effectiveness and safety are quite good and comparable to those of RFA and MWA. All the three hyperthermia-based ablative techniques, when performed by skilled operators, can successfully treat all liver tumors eligible for thermal ablation, and to date in most centers of interventional oncology or interventional radiology the choice of the technique usually depends on the physician's preference and experience, or technical availability. However, RFA, MWA, and LTA have peculiar advantages and limitations that can make each of them more suitable than the other ones to treat patients and tumors with different characteristics. When all the three thermal ablation techniques are available, the choice among RFA, MWA, and LTA should be guided by their advantages and disadvantages, number, size, and location of the liver nodules, and cost-saving considerations, in order to give patients the best treatment option.

Key words: Radiofrequency ablation; Liver neoplasm; Laser ablation; Microwave ablation; Hepatocellular carcinoma; Liver metastases

Core tip: Radiofrequency ablation, microwave ablation, and laser thermal ablation, when performed by skilled operators, can successfully treat all liver tumors eligible for thermal ablation. However, each of them has peculiar advantages and limitations that can make one technique more suitable than the other ones to treat patients and tumors with different characteristics. When all the three techniques are available, the choice should be guided by their advantages and disadvantages, number, size and location of the liver nodules, and cost-saving considerations, in order to give patients the best treatment option.

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INTRODUCTION

Temperatures in excess of 60 ℃ are known to cause relatively instantaneous cell death, and thermal ablation by heating neoplastic tissue to cytotoxic temperatures is becoming increasingly important for treating primary and secondary liver cancer[1]. Radiofrequency ablation (RFA) is currently the most popular and used ablation modality, but in the last years microwave ablation (MWA) is being technically improved and widely rediscovered for clinical use[2-6]. RFA energy is delivered as an alternating current at a frequency of about 400 MHz, resulting in molecular frictional agitation and heat generation known as the joule effect[1,7]. Tissues nearest to the electrode are heated directly, while more peripheral areas are less effectively heated by thermal conduction[8]. MWA is a special case of dielectric heating where the dielectric material is tissue containing water. MWA induces a high-speed (between 900 and 2450 MHz) alternating electric field, causing the rotation of water molecules and generating heat[1,7,9,10]. In contrast to RFA, energy radiates into the tissue with direct heating of the lesion, and charring and vaporization in the proximity of the needle are not obstacles to the delivery of energy[10,11].

The effectiveness and limits of RFA have widely and extensively been reported worldwide. Due to the physical limitations in energy deposition, the effectiveness of RFA in local tumor control decreases with the increase of tumor size[10]. Local control rates over 90% have been reported for nodules up to 3 cm in diameter, and only 6%-10% for tumors greater than 5 cm[12]. Moreover, tumor location close to large vessels can also influence ablation success, because thermal energy is partially shunted away by the cooler blood (the so-called heat-sink effect)[13,14].

The recent technical developments of MWA technology, such as the introduction of a cooling jacket around the MWA antenna and a miniaturized device for MW confinement into the distal portion of the antenna, have minimized the main limits of the earlier MWA systems, allowing for the reduction of back heating effects, increase of the ablation time, and amount of power that can be safely delivered[2,6]. Due to these technical improvements and the characteristics of heat production and energy delivery[9-11], MWA has recently been reported to achieve larger ablation areas than RFA[3,4,15], and appears to be less susceptible to the heat-sink effect[10,11]. Most studies investigating the effectiveness of MWA were conducted before the introduction into clinical practice of the most recent advancements in MWA technology, and at present the best available evidence suggests similar outcomes for RFA and MWA. Reported three- and 5-year survival rates of Child's class A patients with single hepatocellular carcinoma (HCC) less than 5 cm, or up to three HCC less than 3 cm, range from 60% to 78%, and from 50% to 64%, respectively, for RFA[16-18], and from 72% to 73%, and 51%-57%, respectively, for MWA[19,20]. The outcomes of RFA and MWA in patients with up to 6 metastases from colorectal cancer with a maximum diameter of 6 cm are also comparable, with 3-year survival rates of 28%-46% and 46%-51%, respectively, and 5-year survival rates of 25%-46% and 17%-32%, respectively[21-24].

LASER THERMAL ABLATION - WHY CINDERELLA?

However, there is a third hyperthermia-based ablation technique, which uses laser optical fibers to deliver high-energy laser radiation to the tissue. Because of light absorption, temperatures of up to 150 ℃ are reached, leading to coagulative necrosis[7,9,11]. Neodymium:Yttrium Aluminum Garnet (Nd:YAG, wavelength of 1064 nm) and diode (wavelength of 800-980 nm) lasers are most commonly used, as penetration of light is optimal in the near infrared spectrum. Light is delivered *via* flexible quartz fibers with a diameter from 300 to 600 μm. Conventional bare-tip fibers provide an almost spherical thermal lesion of 12-15 mm in diameter, and a beam-splitting device or a multi-source device allow for the use of up to four fibers, simultaneously delivering the light into each single fiber[11,25,26]. Moreover, interstitial quartz fibers with flat or cylindrical diffusing tips have been reported to achieve larger ablation areas[9]. Laser-induced interstitial thermotherapy is a special form of laser technique that uses a unique saline-cooled power laser application system to increase the volume of coagulative necrosis while preventing carbonization at the tip of the laser applicator[10]. The device consists of a 9 French catheter with centimetre markings and a 7 French sheathed catheter with irrigated double lumina. Room temperature saline is used as the irrigation fluid, and a pump is integrated with the laser. This permits reliable cooling of the applicator and expansion of the laser-induced necrosis zone, resulting particularly useful for the treatment of liver metastases that require large safety margins to take care of microscopic disease around the lesions[27].

Laser thermal ablation (LTA) is by far less investigated and used than RFA and MWA, but the available data on its effectiveness and safety are quite good. Most of the studies on LTA are focused on the treatment of HCC. Complete response rates ranging from 82% to 97%, and cumulative 3-year survival rates up to 73% were reported in Child's class A patients with single HCC ≤ 5 cm or up to three nodules ≤ 3 cm treated with multiple bare fibers[28,29]. Moreover, median survival of 3.5 years was achieved in patients with nodules ≤ 5 cm located at high-risk sites by using water-cooled higher power LTA[30]. To date, there are in literature just two randomized trials comparing LTA and RFA in the treatment of HCC, and both of them did not find any significant difference between the two techniques in terms of local tumor control, overall survival, and safety[31,32]. A multicenter study investigating the safety of LTA in five hundred-twenty patients with 647 HCC treated by 1004 LTA sessions reported mortality and major complication rates of 0.8% and 1.5%, respectively[33]. Likewise, also the outcomes of patients with liver metastases from colorectal cancer with diameter up to 5 cm treated with LTA appear comparable to those reported for RFA and MWA, with 3- and 5-year survival rates ranging from 28% to 72.4%, and from 10% to 37%, respectively[9,34-36].

Despite these excellent results, LTA is frequently not considered an effective ablation technique, and the vast majority of reviews, consensus, or position papers dealing with the efficacy or safety of thermal ablation of liver tumors does not even mention LTA among the ablative techniques that are to date available[1,10,37-41].

We do not agree with such an attitude. Although it is true that LTA has been investigated less vigorously than the other ablation techniques, it is also true that the relatively low number of published studies dealing with LTA seems to be due to an unjustified prejudice, rather than to an actual lower efficacy of LTA in comparison with RFA or MWA. All the three hyperthermia-based ablative techniques, when performed by skilled operators, can successfully treat all liver tumors eligible for thermal ablation, and to date in most centers of interventional oncology or interventional radiology the choice of the technique usually depends on the physician's preference and experience, or technical availability. However, in our opinion RFA, MWA and LTA have peculiar advantages and limitations that can make each of them more suitable than the other ones to treat patients and tumors with different characteristics. For instance, RFA is surely the best established thermal technique, and its efficacy has been largely proven, but lesions larger than 2-2.5 cm require multiple overlapping ablations to create an adequate safety margin, and sub-capsular or high-risk location of the tumors is considered a relative contraindication to RFA, even though some reports documented its feasibility[42,43]. Moreover, tumors strictly close to large vessels can be incompletely treated because of the heat-sink effect. MWA has less sensitivity to the heat-sink effect, deeper penetration of energy and better propagation across the poorly conductive tissue than RFA, and can achieve larger ablation volumes. On the other hand, microwave energy is more difficult to distribute than RF energy, is carried in wavelengths which are more cumbersome than the small wires used to feed energy to RF electrodes, and are prone to heating when carrying large amount of power[11]. Consequently, MWA appears less feasible than RFA in the treatment of high-risk located and sub-capsular nodules. Moreover, the latest versions of MWA devices provided with the most recent technical advances are more expensive than RFA.

As regards LTA, the technique proposed by Pacella *et al*[28] and improved by Di Costanzo *et al*[44] uses 300-μm bare optical fibers introduced into the tumor through 21-gauge needles. The diameter of the needles is considerably smaller than RFA electrodes and MWA antennas, making LTA safer and more suitable for ablating lesions in at-risk location or in locations that are difficult to reach[11,45]. Moreover, a multisource device allows to use from one to four fibers at once, enabling to achieve ablation areas from one to 4-5 cm in diameter, and consequently to treat tumors ranging from 5-6 mm to 3 cm in diameter obtaining an acceptable safety margin. Furthermore, in western countries LTA has been reported to be the cheapest ablation technique when up to three fibers are used, and cheaper than MWA when four fibers are used[11]. For these characteristics, LTA has been proposed as a valid alternative to RFA for lesions up to 2 cm[46], and it has been suggested as the technique of choice in presence of multiple small and variably sized liver tumors[45]. On the other hand, the correct placement of the fibers can be challenging, particularly if more than two fibers are needed, and should be performed by very skill operators[11]. Moreover, like RFA, also the efficacy of LTA can be limited by the heat-sink effect.

FINAL CONSIDERATIONS

In the last years, multimodality anti-tumor strategies including surgery, chemotherapy, radiotherapy, ablation techniques, and catheter-based treatments are being more and more advocated, to tailor the best treatment options to patient and tumor characteristics[45,47-49]. Such an approach is often adopted not only to choose the most suitable treatment options, but also to choose the most suitable technique available for each treatment option. For instance, patients candidate to catheter-based treatments can undergo bland embolization, transarterial chemoembolization with lipiodol or with drug-eluting beads, or radioembolization, according to the type of tumor, liver function, and presence or absence of portal venous thrombosis. Likewise, patients candidate to liver surgery can undergo wedge resection, segmentectomy, lobectomy, or transplantation according to the liver function, and number, size, and location of the tumors.

In our opinion, the choice among the thermal ablation techniques should also be based on the same criteria whenever possible. Some authors suggested that the reference centers for thermal ablation should be equipped with all the available techniques so as to be able to use the best and the most suitable one for each type of tumor[26]. Recently, an algorithm has been proposed to tailor thermal ablation on each single patient, according to advantages and disadvantages of RFA, MWA and LTA, number, size, and location of the liver nodules, and cost-saving considerations (Figures 1 and 2)[11]. On the basis of this algorithm, all the three ablation techniques have

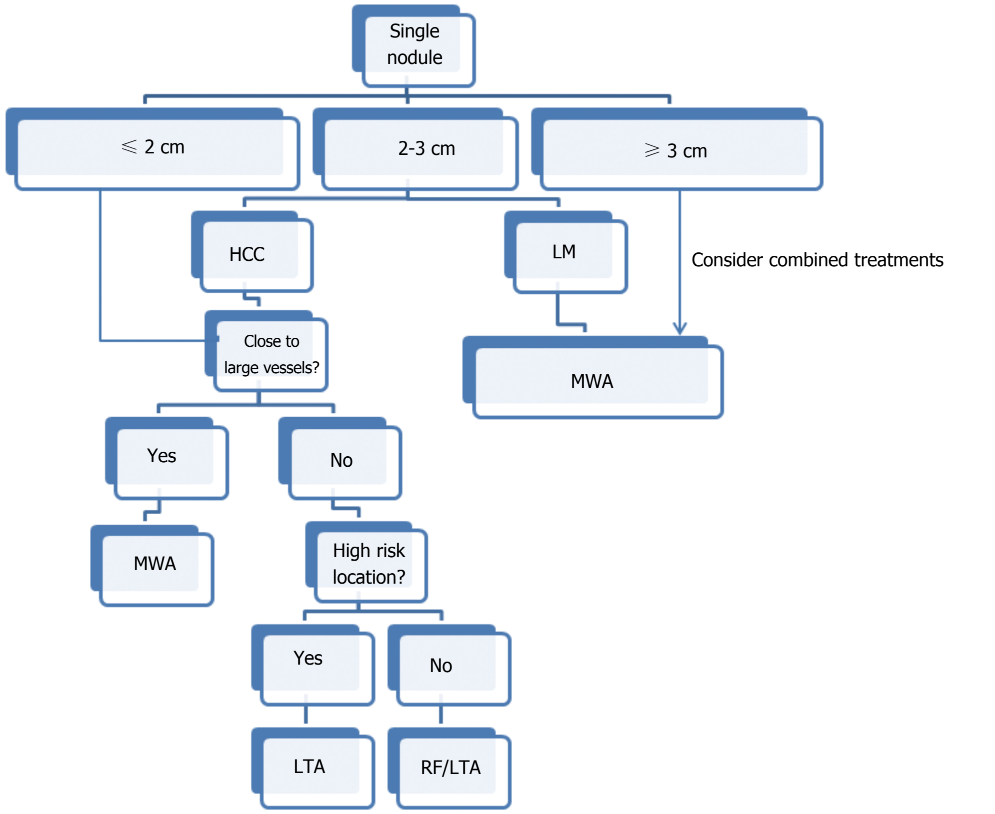

Figure 1 Algorythm proposed by Tombesi *et al*[11] for thermal ablation of single liver tumor. HCC: Hepatocellular carcinoma; MWA: Microwave ablation; LTA: Laser thermal ablation; RF: Radiofrequency.

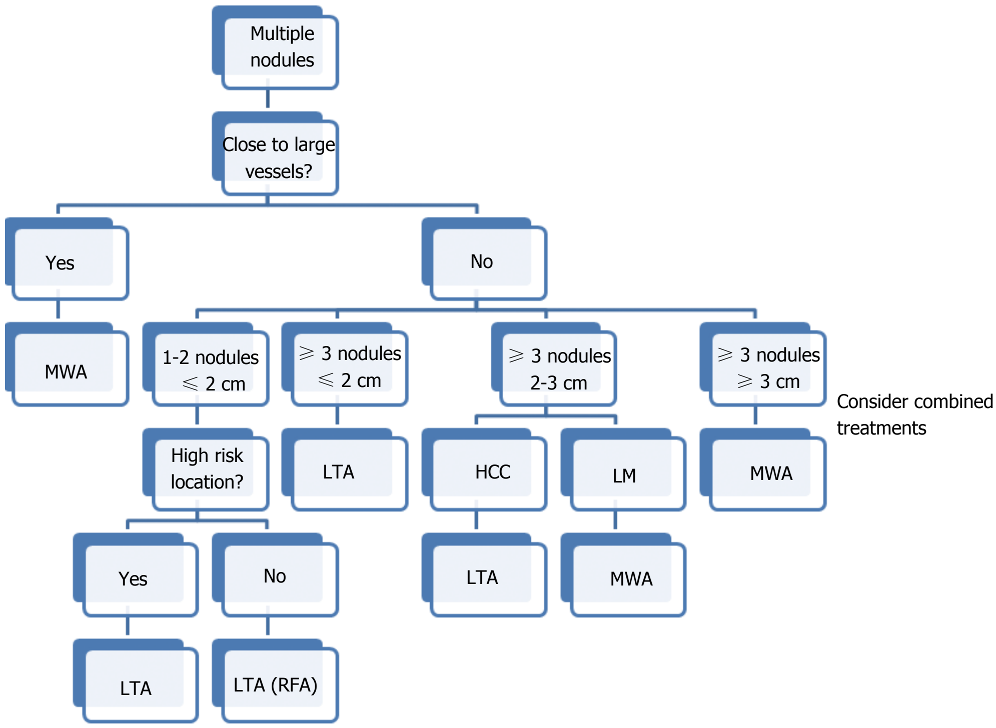

Figure 2 Algorythm proposed by Tombesi *et al*[11] for thermal ablation of multiple liver tumors. HCC: Hepatocellular carcinoma; MWA: Microwave ablation; LTA: Laser thermal ablation; RFA: Radiofrequency ablation.

a preferential role in some specific circumstances. For instance, a single nodule 2 cm or smaller in size can be efficaciously treated using all the thermal modalities, but RFA and LTA are cheaper than MWA and should be preferred. Conversely, MWA should be considered the technique of choice when the tumor is ≥ 3 cm in diameter or is close to large vessels independently of its size, as MWA can achieve larger ablation volumes and is not affected by the heat-sink effect. Multiple small and variably sized lesions should be treated with LTA, and so on (Figures 1 and 2). This algorithm reflects the personal experience and opinion of the authors, and it can surely be modified and improved. However, it is also based on objective considerations that can largely be shared, and in our opinion it could represent the basis for a consensus on the optimal and reasoned use of the thermal ablation modalities.

In conclusion, at present there is no ideal ablation technique that outclasses the other ones. There are ablation techniques that share some main technical aspects and are usually comparable, but each of them has peculiar characteristics that make it the "ideal" technique in some particular settings. We believe we should exploit such peculiarities to give patients the best treatment option.

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