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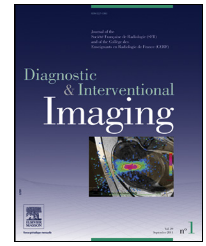

REVIEW / *Interventional imaging*

Percutaneous thermal ablation of lung tumors — Radiofrequency, microwave and cryotherapy: Where are we going?

J. Palussière*, V. Catena, X. Buy

Department of Imaging, institut Bergonié, 229, cours de l'Argonne, 33000 Bordeaux, France

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Abstract Main indications of percutaneous pulmonary thermal ablation are early stage non-small cell lung carcinoma (NSCLC) for patients who are not amenable to surgery and slow-evolving localized metastatic disease, either spontaneous or following a general treatment. Radiofrequency ablation (RFA) is the most evaluated technique. This technique offers a local control rate ranging between 80 and 90% for tumors <3 cm in diameter. Other more recently used ablation techniques such as microwaves and cryotherapy could overcome some limitations of RFA. One common characteristic of these techniques is an excellent tolerance with very few complications. This article reviews the differences between these techniques when applied to lung tumors, indications, results and complications. Future potential associations with immunotherapy will be discussed.

In the last 20 years, different technologies have been developed and used for image-guided percutaneous thermal ablation of tissue including mainly radiofrequency ablation (RFA), microwave ablation (MWA) and cryotherapy [1]. These image-guided ablation techniques have emerged as a safe, cost-effective, minimally invasive treatment alternative for patients who do not require surgery. Since 2000, RFA has been the first-choice technique to be proposed for lung tumors and to date, it has been the most evaluated technique.

Despite apparent drawbacks such as insulating effects intrinsic to lung tissue, these techniques treat lung tumors particularly well. Another positive point to underline with lung is the excellent tumor visualization due to the important differences in density between the tumor and the non

* Corresponding author.
E-mail address: j.palussiere@bordeaux.unicancer.fr (J. Palussière).

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tumoral lung parenchyma. Targeting and device positioning can be optimal and then accurately assessed on multiplanar reconstructions.

In this article, we review the main results obtained using RFA, MWA and cryotherapy in patients with primary and secondary lung tumors and discuss future potential association with immunotherapy.

Basic concepts of RFA, MWA and cryotherapy

RFA is an electric current-based technique that heats tissue due to fractioning electrons at a frequency of 400 KHz. This electronic agitation is mainly present at the interface with the device. The thermal effect is due both to active heating along the device and passive progressive diffusion of the temperature through to the target. The conduction of heat is crucial to be able to treat a sufficient volume. In lungs, the air-filled spaces insulate the heated volume thermally and electrically therefore, thermal inertia is low and electrical impedance is high compared to other tissues. It has been demonstrated that tissue characteristics affect ablation outcomes, for example, ablation volume is larger for a given quantity of energy in the lung than in the kidney or soft tissues [2]. An expandable multitined array with an electrode diameter at least 10 mm larger than the target tumor has been shown to successfully ablate tumors with < 10% local recurrence. Conversely, an array diameter < 10 mm larger than the target tumor resulted in 30% local recurrence [3].

MWA is a field-based technology. The electromagnetic field created around the ablation device varies from 915 MHz to 2450 MHz, which heats tissue through rotating water molecules, resulting in frictional heat. In contrast to RFA, temperature rises higher and more rapidly due to the friction of water molecules, and the active heating zone is wider allowing better thermal build-up. Consequently, this type of thermal ablation relies less on conduction into tissues, and may not be influenced as much by the heat-sink effect that limits RFA thereby yielding a more uniform ablation zone [4].

Cryotherapy damages and kills tumoral cells through a complex combination of different mechanisms during tissue freezing and thawing. At −20 °C, cells are killed by protein denaturation and membrane disruption. The successive repetition of the freeze-thaw cycles increases cellular injury with formation of both intra- and extra-cellular ice crystals. Indirect actions include vasoconstriction and occlusion of blood vessels, secondary osmotic changes and local tissue edema resulting in hypoxic tissue injury and coagulative necrosis. The alveolar structure, mostly composed of air, can interfere with the creation of the ice ball, limiting the freezing. This could be resolved by water; consequently, to increase the water content in the area of treatment, a first short freezing and thawing is carried out. Following that, fluid and hemorrhage replace the air and fill the alveoles resulting in an estimated 20-fold increase of thermal conductivity [5]. This results in a larger ice ball during subsequent freezing phases. Hence, a triple-freeze cycle are recommended by Hinshaw et al. [5]. The authors also noted that a triple-freeze protocol could be exploited not only to create larger zones of ablation but also to shorten the overall procedure time.

Cryoablation preserves collagenous architecture of the area of ablation [6], which may be advantageous in treating lesions adjacent to the bronchi. As a result, cryotherapy could be recommended for treatment of central tumors. Furthermore, cryotherapy may result in less pain in the treatment of tumors along the pleura and chest wall [7].

Patient selection and procedure

Main indications of percutaneous thermal ablation of lung tumors are non-small cell lung cancer at early or advanced stages and metastatic disease from different primaries. To date, there are no guidelines regarding the maximum number of pulmonary metastatic tumors that can be treated. Thermal ablation can also be proposed as a salvage therapy when a local recurrence occurs within a previously radiated site [8]. An impaired pulmonary function is not an absolute contraindication. However, severe lung emphysema with bullae is a contraindication due to the risk of intractable fistula and respiratory failure. Ideally, the procedure is performed under general anesthesia, in particular, for subpleural tumors. Interrupted treatments with severe pain in this indication were reported; consequently, epidural anesthesia was often used [9]. General anesthesia with high-frequency jet ventilation allowing repeated breath-holds immobilize the target and may facilitate positioning of ablation probes. When a general anesthesia is not possible or available, cryotherapy that creates less procedural pain due to local anesthetic effects of freezing, could be an interesting option in this indication.

The work-up is generally the same as for all methods of percutaneous thermal ablation. Procedures are performed under computed tomography (CT) or cone beam CT (CBCT) guidance. CBCT with live three-dimensional (3D) needle guidance is a useful and user-friendly technique for percutaneous pulmonary thermal ablation [10].

Non-small cell lung carcinoma (NSCLC) treatment

Besides surgery, and stereotactic body radiotherapy (SBRT) percutaneous thermal ablation is one of the therapeutic options for early-stage NSCLC [11]. Current American College of Chest Physicians (ACCP) guidelines include percutaneous ablation as a therapeutic option in medically inoperable patients with stage I NSCLC. Thermal ablation techniques do not provide regional control of the disease and hence, do not allow controlling lymph nodes. Surgery that gives access to lymph node resection remains the gold standard for treatment. However, many patients are not candidates for surgery due to co-morbidities and represent indications for non or mini-invasive techniques. SBRT has even been accepted for operable patients. Despite better surveillance and screening, about 30% of NSCLCs are discovered at advanced-stage. With the development of targeted therapies and immunotherapies, improvement in survival have been observed. Consequently, strategies combining an aggressive local treatment to a systemic treatment have become possible for some patients.

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