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Review

Lung ablation: Best practice/results/response assessment/role alongside other ablative therapies

T. de Baere [a,b,*], L. Tselikas [a,b], G. Gravel [a,b], F. Deschamps [a,b]

[a] *Department of Interventional Radiology, Gustave Roussy Cancer Center, 114 rue Edouard Vaillant, 94 805 Villejuif, France*

[b] *Universite Paris-Sud XI, UFR Médecine Le Kremlin-Bicêtre, Le Kremlin Bicêtre, France*

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Today, in addition to surgery, other local therapies are available for patients with small-size non-small-cell lung cancer (NSCLC) and oligometastatic disease from various cancers. Local therapies include stereotactic ablation radiotherapy (SABR) and thermal ablative therapies through percutaneously inserted applicators. Although radiofrequency ablation (RFA) has been explored in series with several hundreds of patients with pulmonary tumours, investigation of the potential of other ablation technologies including microwave ablation, cryoablation, and irreversible electroporation is ongoing. There are no randomised studies available to compare surgery, SABR, and thermal ablation. In small-size lung metastases, RFA seems to produce results very close to surgical series with >90% local control and 5-year overall survival of 50%. In primary lung cancer, the technique is reserved for non-surgical candidates. In future, the low invasiveness of thermal ablative therapies will allow for a combination of ablation and systemic therapies in order to improve the outcomes of ablation alone. Another major advantage of thermal ablation is the possibility to treat several metastases in close proximity to one another and retreatment in the same location in case of failure, which is not possible with SABR.

Introduction

Today, in addition to surgery, other local therapies are available for patients with small-size non-small-cell lung cancer (NSCLC) and oligometastatic disease, including stereotactic ablation radiotherapy (SABR) and thermal ablative therapies through percutaneously inserted applicators. Early reports, including case series and small clinical trials, have demonstrated the potential of various thermal ablation technologies including radiofrequency ablation (RFA), microwave ablation (MWA), cryoablation, and irreversible electroporation for the treatment of pulmonary tumours.[1–7]

In NSCLC, surgical resection is the current standard of care for patients with Stage I or II, mainly due to the benefit of associated lymphadenectomy; however, image-guided ablation and radiation therapy are increasingly offered as alternative therapies in non-surgical candidates.[3,8–12] In lung metastases, local treatments have been accepted since

* Guarantor and correspondent: T. de Baere, Department of Interventional Radiology, Gustave Roussy Cancer Center, 114 rue Edouard Vaillant, 94 805 Villejuif, France. Tel.: +33 (0)1 42 11 54 28; fax: +33 (0)1 42 11 52 78.
E-mail address: thierry.debaere@gustaveroussy.fr (T. de Baere).

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the late 1990s, when an international registry reported actuarial 5-, 10-, and 15-year survival rates of 36%, 26%, and 22%, respectively,[13] despite the fact that the evidence for surgical metastectomy remains controversial because the practice has never been subjected to randomised trials and carries some risk of short-term morbidity, can be responsible for permanent loss of function, and has major cost implications.[14] In oligometastatic lung patients, evidence for the superiority of surgery over other local ablative techniques is weak, as the benefit of lymphadenectomy has not been demonstrated.

Rationale for thermal ablation in the lung

The lung has some organ-specific differences favouring thermal ablation. Indeed, the heat insulation and low electrical conductivity provided by the lung around the tumour is responsible for a larger volume of ablation in the lung than in subcutaneous tissues or in the kidney for a given quantity of radiofrequency current.[15] Indeed, a tumour surrounded by lung parenchyma is highly electrically and thermally insulated by the air-filled lung parenchyma and will require less energy deposition for a given volume of ablation. Because impedance before ablation differs significantly for tumours with >50% of the tumour abutting the pleura (86.5±29.9 Ohms), and those tumours not abutting the pleura (121.3±42.8 Ohms),[3] RFA delivery must be adapted to tumour location.

Several, studies have demonstrated that RFA can completely destroy an area of healthy lung or malignant lung tumours in an animal tumour model.[16,17] A clinical study of RFA before resection demonstrated 100% necrosis at histopathology for nine of nine lung metastases.[18]

Local efficacy of RFA in the lung

A review of 17 of the most recent publications of lung RFA including NSCLC and lung metastases demonstrated a median rate of complete ablation of 90%, with a variability from 38% to 97%.[19] Tumours <2 cm can be ablated in 78–96% of cases according to several reports after a minimum follow-up of 1 year,[3,12] and mean follow-up of 12 months.[20–22] A statistically significant lower success rate of ablation is reported for tumours ranging from 2 to 3 cm.[3,20–22] A ratio >4 in between the area of RFA induced ground-glass opacity (GGO) and total tumour volume has a rate of complete ablation of 96% at 18 months, versus 81% (p=0.02).[3] Margins of GGO induced by RFA of incompletely ablated tumours have been reported to be absent in 85% of patients at post-RFA computed tomography (CT), and the receiver operating characteristic (ROC) analysis confirmed the usefulness of the ablation zone as a predictor of recurrence, with an estimated cut-off of 4.5 mm for a specificity of 100%; i.e., no local recurrence.[23] Histopathological studies demonstrated that a 5 mm margin covers 80% of the microscopic extension for lung adenocarcinoma and 91% for squamous cell carcinoma, and that 8 and 6 mm margins are needed to cover 95% of the microscopic extension, for adenocarcinoma and squamous cell carcinoma, respectively.[24] In metastases, aerogenous dissemination is the most frequent pattern of tumour spread beyond the macroscopic border responsible for local recurrence after surgery.[25] The above-mentioned results clearly emphasise that there is a need for oversizing the ablation zone relative to the tumour volume in order to obtain safety margins that guarantee success.

Recent ablation technologies

New technologies have been developed to overcome the limitations of RFA by extending the volume of ablation or lowering convective cooling close to the bronchi or vessels. RFA provides a volume of ablation with a maximal shortest diameter of 4–5 cm and only one probe that can be activated at a time; consequently, overlapping the ablation zone with subsequent probe replacement is needed to create a larger volume of ablation. Both MWA and cryoablation allows for simultaneous delivery of energy through several probes activated at the same time with a synergistic effect versus subsequent activation of the same probe. In an animal study, a single probe provided a mean ablation diameter of 32.7±12.8 mm perpendicular to the feeding point of the MWA antenna while simultaneous activation of three antenna provided an ablation zone of 54.8±8.5 mm.[26] Such a large ablation volume gives hope for improvement of local control for larger tumours and is under evaluation in clinical practice.

Contact between the targeted tumour and a vessel or bronchi >3 mm in diameter have been reported by several authors as a predictive factor of incomplete local treatment.[20,27] Percutaneous balloon occlusion of the segmental pulmonary artery involved during lung RFA has been reported in five patients with 100% local efficacy at 12 months using combined positron-emission tomography (PET) with CT for follow-up; however, tolerance was poor.[28] MWA, by working at higher temperatures,[29] has been demonstrated to lower convective cooling close to large vessels in animal studies,[30,31] but the benefit in lowering incomplete ablation has not been demonstrated in clinical practice. Early MWA systems seem to suffer from non-reproducibility and non-spherical ablation zones, with disappointing results for tumours >3 cm.[5] More recent technology seems to improve the reproducibility and sphericity of the ablation zone.[32]

Cryoablation allows placement of several probes that can be activated at the same time. Cryoablation of lung metastases has been reported using a mean of 1.7 probes per patient with a promising 94.2% local tumour control at 12 months in a phase 2 multicentre study comprising 40 patients with 60 metastases measuring 1.4±0.7 cm (range 0.3–3.4).[33] Cryoablation enables inserting the probe into the tissue/tumour and providing moderate freezing and moving the probe away from vulnerable neighbouring organs when required. An advantage of having the probe stuck in the tumour is that probe displacement will not occur during treatment as is the case with expandable RFA electrodes, which are very popular in lung ablation.

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