UPDATE IN RADIOLOGY

Pulmonary radiofrequency ablation (Part 1): Current state

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Abstract The risks involved in surgical treatment and conventional radiotherapy in patients with early lung cancer or lung metastases often make these treatments difficult to justify. However, on the other hand, it is also unacceptable to allow these lesions to evolve freely because, left untreated, these neoplasms will usually lead to the death of the patient. In recent years, alternative local therapies have been developed, such as pulmonary radiofrequency ablation, which has proven to increase survival with a minimal risk of complications. There are common recommendations for these treatments, and although the specific indications for using one technique or another have yet to be established, there are clearly defined situations that will determine the outcome of the treatment. It is important to know these situations, because appropriate patient selection is essential for therapeutic success. This article aims to describe the characteristics and constraints of pulmonary radiofrequency ablation and to outline its role in thoracic oncology in light of the current evidence.

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PALABRAS CLAVE
Ablación; Ablación por radiofrecuencia; Tumores pulmonares; Cáncer de pulmón; Metástasis; Tratamiento; Guía de imagen

Radiofrecuencia pulmonar (parte 1): Estado actual

Resumen Frecuentemente, los riesgos quirúrgicos y de la radioterapia convencional en los pacientes con cáncer de pulmón precoz o con metástasis pulmonares son inasumibles, pero dejarlos que evolucionen libremente es inaceptable porque la enfermedad neoplásica será la causa más frecuente de muerte del paciente. En los últimos años se han desarrollado terapias locales alternativas, como la radiofrecuencia pulmonar, que ha demostrado mejorar la supervivencia con un riesgo mínimo de complicaciones graves. Existen recomendaciones comunes para aplicar estas terapias y, aunque el papel concreto diferenciador de cada una está aún por establecer, hay situaciones claramente definidas que condicionarán el resultado.
del tratamiento. Conocer estas es importante, pues seleccionar adecuadamente al paciente será clave para el éxito terapéutico. El objetivo de este artículo es describir las características y condicionantes de la ablación pulmonar con radiofrecuencia y esbozar su papel en el ámbito de la oncología torácica de acuerdo a la evidencia actual.

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Introduction

Lung cancer (LC), with 1.3 million new cases a year, is the second type of cancer in frequency and the third deadliest cancer in both sexes in the USA surpassing colon, breast and prostate cancers combined.1-4 Global survival at 5 years is 15–16% and 47–50% in stage I tumors; 19, 115 people died of LC in Spain in 2005.5 Non-Small Cell Lung Carcinoma (NSCLC) accounts for 85–90% of LC.6 Its treatment in stages I–II is lobectomy with examination of mediastinal ganglia.5,6 Survival at 5 years is 71–77% in stage IA,7 & 35–58% in IB but only 20% are resectable8 and, of these, 15–30% (30% in >75 years)9-11 are inoperable because of comorbidities, particularly a limited pulmonary reserve.6,12,13 In addition the relative risk and annual incidence of LC in COPD is 1.83–2.64 and 4–5 times greater, respectively.14 Interest in patients with high surgical risk is growing, and contrary to the belief that they were dying because of their comorbidities, over 50% will die of complications related to neoplasms left to evolve freely.15,16 Also because of its vascular richness and oxygenation, the lung is the second most affected organ due to extrathoracic tumor metastasis,17 in 25–30% (50% in autopsies) of patients who die from cancer.6 In one-fifth of patients with metastasis only the lung is affected,18 generally in sarcomas, kidney, head and neck cell cancer.19 Metastasectomy in selected patients (few metastases and preserved pulmonary reserve)19 can be the therapy of choice though evidence is weak on this regard.20

External radiotherapy (RT) is the most frequently used alternative in patients with LC11,22 or inoperable pulmonary oligometastasis.19 The results are discreet11–15–25% survival at 5 years for stage I-II NSCLC,6.22,24 much less than with surgery.22 Moreover, it causes radical pneumonitis in over 16%, as well as pulmonary function impairment (10%) reduction of forced expiratory volume [FEV1] in the first, second and potentially fatal consequences.7,9,22 When early NSCLC and potentially resectable lung-limited oligometastasis have high surgical risk, traditional therapies fail or the patient does not want to have surgery; alternative procedures such as the sublobar resection (SLR), the stereotactic radiotherapy (SRT) and from 2000 onwards ablative procedures can increase survival.26 They have less risk of respiratory failure, disability and death than lobectomy.9 Today observation as therapeutic alternative in early NSCLC is acceptable only if the patient has severe comorbidities and the disease appears in an indolent way–slow progression in successive image studies.15

The goal of this article is to describe the characteristics and determinants of pulmonary radiofrequency ablation (RFA) and outline its role in the setting of chest oncology based on present-day evidence. To this end, we retrieved articles published in English or Spanish in PubMed filtered by: (radiofrequency OR ablation [Title]) AND (lung OR pulmonary OR chest OR thoracic [Title]) NOT atrial (Title), “last 5 years”, “reviews” and “humans”. We precluded those about heart ablation and searched manually starting from quotes in the articles retrieved.

Concept and principles of radiofrequency ablation

Ablation is the thermal or chemical therapy applied directly on a focal tumor in order to destroy it.22 Radiofrequency is present the most widely used ablative procedure for the management of malignant lung neoplasms.17,26 Although the FDA approved it for soft-tissue tumors it is more and more used for lung tumors.27 It uses a high-frequency alternating current (400–500 kHz) and 100–250 W of power produced by a generator25 and it is released into the tissue through the tip of a needle that is the active electrode (“active tip”). From there it travels to the pads (dispersing electrodes) located on the patient’s legs or back that dissipate the current in a monopolar circuit or to a second electrode near the first one, in a bipolar circuit.19,25 The needle is introduced in the tumor percutaneously. It has also been applied experimentally through CT-guided optical fibrobroscoopy, but with smaller ablation volumes.28,29 The patient is part of the electrical circuit as the resistance.12 Thanks to the difference in size between the surface of the tip of the needle and that of the pads, the current concentrates around the tip of the needle.12 The ions of the adjacent tissue oscillate trying to follow the change of direction of the current,23 generate resistance and cause a fast ionic agitation and molecular collision. The heat generated destroys the tissue through coagulative necrosis. The greater the current the more vigorous the ionic agitation and the higher the temperature.30 The systems of radiofrequency monitor the temperature of tissues and the changes in impedance.27 Although the threshold can vary the heating up of the tumor will damage the cells irreversibly if the temperature is maintained >45°C for hours, >50°C for at least 5 min and at temperatures of ≥60°C,19,22,21-23 almost instantly. Healthy cells–more resistant–die at temperatures of >60°C and tumor cells at 41°C.34 Beyond 100°C vaporization and carbonization occur,6,19,24,31 which decreases the efficient current conduction into the tissue, increases impedance and
diminishes the volume of necrosis. This is why temperatures between 60 and 100 °C are ideal. The goal is to attain an ablation volume capable of embracing both the tumor and the peritumoral parenchyma thickness (“ablation margin”) of at least 0.5–1 cm conditioned by the characteristics of the lung and the radiofrequency. The aired, healthy lung works as an insulator. That is why the ablation of tumors surrounded by lung vessels less energy than those having pleural contact. Thermal and electrical conductivity is low and the heat concentrates in a small volume of tissue around the electrode. This protects the healthy peritumoral lung from the current but it also makes it difficult to attain optimal ablation volumes. This is why it is important to position the electrode in the center of the tumor.

Both the blood flow and the healthy lung as well as the peritumoral aired bronchi have a cooling effect (heat sink effect) dissipating heat with insufficient temperature peaks that limit the volume of ablation. Attempts to increase it experimentally in animal models occluding vessels and bronchi have not been well tolerated.

### Systems of radiofrequency ablation

The most frequently used radiofrequency monopolar systems accepted by the FDA are:

a. **Cool-tip system (Valleylab)** (Covidien, Boulder, CO, USA),. It consists either of a single electrode or a cluster of three electrodes parallel to 17–20 G, separated 1.5–2.5 cm, hollowed, isolated and cooled internally with cold saline solution except for the active tip (generally 2 or 3 cm long) that releases energy into the tumor. Cooling prevents carbonization and improves the ablation volume. Energy pulses are applied for short periods of time (10–30 min).

b. **Umbrella systems.** They are the most widely used. (1) Bos System with LeVeen electrodes (Boston Scientific, Natick, MA, USA) and (2) RITA Systems (RITA Medical Systems, Fremont, CA, USA). They are made respectively, of 17 or 14–15 G electrodes, and 8–12 or 7–9 expansible active tips with an opening similar to that of an umbrella. Each tip is an electrode. They must be folded before they are withdrawn or repositioned. They generate more spherical and irregular ablation volumes. Each generator has its own ablation algorithms.

To limit tissue damage there are automatic disconnection modes in the event of a concrete increase in impedance (Bos and Valleylab) or temperature (RITA). There are no studies comparing the results of the three systems. The diameter of the ablation area is usually 3–5 cm with the cluster and umbrella electrodes, and 1–3 cm with single electrodes.

For lesions <2 cm only one ablation can be performed with one single electrode whose active tip length, adapted to tumoral size, attains an ablation margin of 0.5–1 cm. In larger lesions it is necessary to increase ablation volume which can be achieved by:

1. Increasing the electrode active surface:
   - With a longer active tip or overlapping ablation areas sequentially (Fig. 1). Although it is a long process, if only this option is available, it is convenient to perform the first ablation distally and centrally and the second one more proximally. Some authors recommend doing it only with <2 cm lesions, with umbrella electrodes, with several electrodes near one another, exchanging the current among them with a switch (Fig. 2). Regardless of the type of needle, only one can be activated at any given moment but due to the synergetic effect among them, ablation volume is attained before and it is exponentially greater to that obtained with the same number of ablations applied sequentially separately. This synergy also diminishes the cooling effect.

2. Increasing temperature with more electrode power or heating time.

3. Increasing energy slowly and progressively (not performed in other organs) so that impedance rises gradually avoiding carbonization.

4. Cooling the needles with cold saline solution (Cool-tip systems).

5. Cooling the tissue with cold saline. Some systems allow us to perfuse the saline solution around the tumor improving electrical conductivity, reducing the risk of carbonization and increasing the volume of ablation. They are not widely used because the distribution of the saline solution and the size of the ablation area cannot be foreseen which can have serious complications.

6. Using bipolar and multipolar systems. The current goes from one electrode to the next instead of going to the pads. They heat the area among the electrodes better than the monopolar ones. They attain elliptical ablation, but with a smaller diameter (14 mm), they require inserting more electrodes and they are less available.

### Results of radiofrequency ablation

**A. Recurrence and progression factors.**

An insufficient ablation volume favors local recurrence and progression and diminishes median survival. In RFA the reasons can be:

- >3 cm tumor (Fig. 3). It predicts incomplete ablation, recurrence and local progression regardless of the procedure used. The volume is <50% in >3 cm tumors, whereas <2 cm tumors can be nectrotized completely in 78–96% of the cases. Although it varies depending on the series (e-table 2a), intrapulmonary recurrence in <3 cm and >3 cm tumors is 22–25% and 50%, respectively; 35% progresses and if they are >3 cm, up to 75%, they are with a median progression time of 45 months in <3 cm tumors, and 12 months in >3 cm tumors. In >3 cm primary tumors and metastasis treated through radiofrequency, survival decreases independently in short (one year) and long terms (5 years). Thus the maximum tumor size to consider RFA is ≤3 cm for LC and metastasis. In <0.5–1 cm ablation margin (Figs. 3–5). It corresponds to the thickness of post-ablation peritumoral ground-glass
Figure 1  Stage IIB LUL pulmonary epidermoid carcinoma treated with chemoradiotherapy because the patient refused surgery. He relapsed locally a year later and was treated through radiofrequency ablation (RFA). The mass (arrowheads) was 3.4 cm before RF. Due to its size, 3 consecutive ablations were applied through a Cool-tip needle.

Figure 2  Simultaneous ablation of 3.5 cm colon adenocarcinoma pulmonary metastatic mass; (a) with two radiofrequency (RF) Cool-tip needles (arrowheads) (b). Lesion growth the following day (c) due to the effect of treatment.
Figure 3  Recurrence risk factors. Radiofrequency ablation of a lesion >3 cm (measurement taken in a). Ground-glass peripheral halo post-3 RF cycles is incomplete (white arrowheads in b). Nodular enhancement 9 months after radiofrequency (asterisks in e) suggesting tumor relapse. In the region where it also enhanced pre-RF (asterisks in c) we can see that it was not surrounded by the ground-glass halo post-RF (b) which did not enhance after treatment (d), stage 1 pulmonary epidermoid carcinoma.

area\(^7\) and defines the ablation volume. Since the maximum ablation diameter attainable through radiofrequency is 4–5 cm, selecting ≤3 cm tumors will allow us to obtain complete ablation volumes, with 1 cm\(^3\)\(^3\)\(^3\)\(^3\) ablation margins; a 4:1 ratio between the ground-glass area and the pretreatment tumor area correlates significantly with a high complete ablation index (96%) at 18 months.\(^10,33\) The adenocarcinoma expands microscopically through the peritumoral tissue up to 8 mm, and the squamous cell carcinoma up to 6 mm.\(^10,33\) If we could attain these margins of ablations would be covering 95% of microscopic disease.\(^6\)

- >3 mm diameter proximal vessel.\(^22,33,41\) It predicts incomplete ablation,\(^31\) with high indexes of local tumoral progression.\(^7\) Treatment must be reconsidered in these cases\(^2\) (Fig. 4).
- >2 mm diameter proximal bronchi\(^22\) (Fig. 4).
- Location near sulci, pleural or central surfaces\(^11\) (Fig. 5), which presumably prevent an adequate ablation margin.\(^18\)
- Cool-tip systems\(^6,18,39\) It is controversial because they were used mainly in large, central tumors.\(^23\)
- High stage of the disease.\(^43,44\)

There are no differences in local recurrence based on whether the tumor is primary or metastatic\(^10,24,37\) (e-tables 1–3).

B. Survival and recurrence indexes (comparison with other local therapies in e-table 1).

It is hard to know the survival and control of pulmonary neoplastic disease through RFA and how it compares to other local therapies due to the modality level of development\(^25,33\) and the heterogeneity of patients studied, the follow-up methods used and the terms used to reflect local survival and control.\(^10,17\) Patients treated through RFA usually have more comorbidities than the rest\(^15\) which falsely increases the mortality attributed to radiofrequency. It translates into a lower overall survival—that does not distinguish among causes of mortality than other therapies but with cancer-specific, disease-free and median survivals apparently similar to that of SLR\(^36\) and SRT (e-table 2) (Fig. 6). Nevertheless these are short-term (2–3 years) controversial scarce results.\(^5\)

Considering that we only have provisional results, in early-stage NSCLC patients with high surgical risk who would nonetheless tolerate general anesthelia and a slight decrease of lung function, the best alternative to lobectomy seems to be the anatomical segmentectomy type-SLR\(^36\) that allows us to resect ganglia with less and less aggressive approaches—video-assisted thoracoscopy. Nevertheless, survival is worse and local recurrence is greater than with lobectomy,\(^2,40\) except in <2 cm tumors (N0M0), where the overall survival indexes at 5 years,\(^19,40\) disease-free survival\(^5\) and local recurrence\(^2,39,40\) are similar and morbimortality is lower and it is being researched as an alternative to lobectomy. Tumors treated through radiofrequency relapse more locally than those treated through SLR,\(^5\) but it is not clear that they worsen the overall survival\(^22\) (e-table 2a). The SRT is an important alternative to the SLR but it does not treat frequent adenopathies (15–20%) even in small, peripheral LC. Their pros and cons are controversial both with not inconsiderable morbimortality (Fig. 6) (e-table 1). Preliminary results of systematic reviews comparing SRT and RFA suggest that SRT controls better local disease—yet for RFA it is acceptable in <3 cm\(^3\) tumors, provides a better overall survival at 5 years (but similar up to 3 years)\(^19,44\)—and more controversial is not only a better early NSCLC survival\(^46\); but also a greater loss of lung function and toxicity, especially in apical, juxtadiaphragmatic tumors\(^15\) and even high risk
of death in central tumors.\textsuperscript{16,27,45} The RFA is technically limited in apical, central and juxtadiaphragmatic tumors\textsuperscript{7,15} and it does not treat adenopathies either. Its advantages are that it can be repeated a limitless number of times (Fig. 7), which increases survival,\textsuperscript{6} reduces morbimortality, cost and length of hospital stay.\textsuperscript{7,12,24,37,47} Today there is not enough evidence to develop differentiating indications between thermal ablation and the SRT.\textsuperscript{17}

Although more controversial that in the NSCLC, in selected patients with single pulmonary metastasis and oligometastasis the SLR (metastasectomy) can be the treatment of choice. Survival has increased according to retrospective studies\textsuperscript{1-4,8} (Fig. 8). The RFA is an alternative in patients that are not fit for metastasectomy (Fig. 8), with good prognostic results\textsuperscript{8} studied mainly on colorectal cancer.\textsuperscript{7} Survival at 2 years is similar to that of metastasectomy,\textsuperscript{10} with good local control (e-table 2b) yet still controversial.\textsuperscript{14,42} The morbidity of RFA is highly variable (15.2\textendash{}55.6\%)\textsuperscript{8,48} but complications are usually mild and self-limited.\textsuperscript{49} There are few studies comparing the RFA to the rest of the therapies. There is more experience with radiofrequency than with SRT but still not much. Since it does not alter lung function, radiofrequency is recommended when there is high surgical risk or recurrent metastasis after resection, even with good lung function. Also the new surgery would have a high risk of metastasis and complication\textendash{}bleeding or prolonged air leaks.\textsuperscript{40} Radiofrequency seems to have a greater role in the oligometastatic disease than in NSCLC.

With the information collected we present a provisional therapeutic algorithm for stage I NSCLC patients and pulmonary oligometastases (Fig. 8).

### Combined therapies

1. RFA and radiotherapy. Although high tissue temperatures are attained with radiofrequency, the thermal, heterogeneous diffusion in a tumor, especially with
proximal vessels, prevents complete uniform ablation; 40–42°C hyperthermias cause reversible cellular damage but also increases cellular susceptibility to RT and CHT (chemotherapy). The synergy between RFA and RT leads to greater tumoral necrosis volumes. The RFA is more effective in the center of the tumor with frequent posterior peripheral relapses, while external RT and SRT post-RFA are more effective in the periphery due to the high oxygenation and the hypothermia ring of RFA-treated tissue though the literature does not specify a specific method of application. Median survival in stage I and II NSCLC patients treated with RFA and RT is greater than that of the two individual modalities with controversial toxicity figures. They have been recommended for >3 cm tumors and metastasis.

2. RFA and antiangiogenic chemotherapy. The necrotized area increases injecting intratumoral doxorubicin percutaneously since it targets vascularized areas such as the hyperthermia ring. It is a therapy still in the pipeline with certain limitations. The arsenic trioxide administered before the RFA decreases the vessels cooling effect.

3. RFA and surgery. Neoadjuvant, pre-surgery RFA can turn advanced, inoperable NSCLC and metastasis into operable ones.

Indications

1. Curative intention, in order to increase survival and local control in high-risk patients or surgical refusal without extrapulmonary disease, in:
   - Stage I peripheral NSCLC, preferably T1 (<3 cm), recommendation level 2C, or T2N0M0. Tumors with response to RT-CHT but with a persistent, solitary peripheral tumoral focus. Post-surgery, post-RT or post-CHT recurrence, with limited retreatment (anatomical distortion, RT risks).

2. Neoadjuvance. In advanced NSCLS, N0, small satellite node ablation occasionally turns inoperable tumors into operable ones:
   - In T3 with nodules in the same lobe it can turn a lobectomy into a segmentectomy and this one into a SLR.
   - In T4 with nodules in another lobe, the additional nodules can be treated through RFA and the primary tumor can be resected.

3. Support treatment in patients who are not eligible or who are refractory to surgery, RT and CHT (recommendation level 4 according to the ACR (Appropriateness Criteria) or to alleviate symptoms–pain due to invasion of chest wall, hemoptysis, and coughing.)

Figure 5  Recurrence risk factors. Node adjacent to a sulcus (white arrow in b) with incomplete ground-glass halo (hollow white arrowheads), present only at a distance from the sulcus, 24 h after RF. Recurrence 4 months after RF; the lesion has grown showing IV contrast uptake areas (white arrowheads in c and d) that did not exist 24 h after RF (a), they are larger in the area adjacent to the sulcus (asterisk in d), where it was not encircled by the ground-glass halo after the procedure. Compare (c) and (d) to images taken 24 h after radiofrequency in the same planes (a) and (b). Mild post-radiofrequency pleural effusion (asterisk in a). Stage I pulmonary epidermoid carcinoma. Same case as in Fig. 3. Figure in detail online (e-fig. 5).
Radiofrequency (RF): Similar Survival (Sv) at 1 year but better after 2 (90%) and 5 (83%) years for the SLR (53 years cancer-specific and cancer free Sv comparable between the RSL and ablative modalities (16).

There are no significant differences in the Sv at 3 years cancer-specific and cancer free Sv between the RF an the SRL, cryoablation and Qx but the experience is limited (1).

There are no significant differences in the overall Sv at 3 years, cancer-specific and cancer free between the RF and the SLR (23).

Greater local recurrence with RF (1) but it is dubious if it is detrimental to the overall survival (4). In selected patients, the RF has a better Sv than the Qx (4).

Lower risk of respiratory failure, disability and death than lobectomy (1). Lower mort-mortality, risk of complications (most minor), hospital stay and cost than that of open Qx (29).

Shorter hospital stay (1-6 days) than the SLR (26).

The pulmonary function post-RF is not affected significantly (31).

Sublobar resection (SLR): Compared to the lobectomy-review/sample of mediastinal ganglia (treatment of choice):

- More local relapses with the SLR (22%) than with the lobectomy (5%) but they improve with the anatomic SLR, the review of ganglia and the use of brachitherapy (17).
- Better local control and greater Sv in lobectomies. In tumors <2cm N0M0 there are no differences between the SLR and the lobectomy in the overall Sv at 5 years (14,31) the disease free Sv (1) or the rates of local relapse (14).
- Better Sv in the presence of anatomic than non-anatomic resection. Lower morbimortality, complications and hospital stay and greater preservation of the pulmonary function in the SLR (1).

Better prognostic outcomes for the SRT (excellent local control and Sv) than for the conventional RT (15) and fewer complications (22). The SRT is preferred over the conventional RT for the Tm <5 cm (1).

Local control, the overall Sv, the cancer-specific Sv (37) and the 5 year Sv (SRT, RF, and external RT 40-47%, 20-27% and 19%, respectively) are worse for the RF than for the SRT (16). Local control is acceptable for the RO in Tm <3cm (41).

1 year (68.2 -95% vs 81-85.7%) and 3 year Sv (66-87.5% vs 42.7-50%) are similar between the RF and the SRT (31). The RF does not worsen the pulmonary function (4,5). It is minimally invasive and has a lower morbimortality (non radical pneumonitis, most of its complications are minor) and cost than the SRT (23,38).

There is no limit in the number of RF sessions which increased Sv in cases of progression (2). It is applicable in one single session.

Fewer experience with RF in NSCLC than with SRT.

Stereotactic RT (SRT): In a study with matched patients based on age, partially based on comorbidities, tumor stage and tumor locations a non-significant >Sv for the SLR (55 vs 37 months for the SLR and the SRT, respectively) influenced by the different comorbidities. More complications occurred in the SLR (3).

It has more risk of lobar and regional relapse than lobectomy (1)

Local control at 3 years similar to lobectomy: 88-98% (8). There is no control and therapy failure similar between the SRT and the SLR (3).

Annual Sv similar between the SRT and the SLR but better at 2 years (90%) and 5 years (83%) for the SLR (5).

Sv comparable to that of the Qx (retrospective studies) (8).

There were no differences in the rates of local recurrence, global Sv or disease free Sv or disease specific Sv between the SRT and the Qx (4).

Therapy volume of the SRT similar to that of the SLR (3).

No risk Qx.

Fewer toxicity, complications and hospital stay than the SLR with similar local control and cancer-specific Sv yet despite they were patients with more comorbidities (3).

Greater cardiopulmonary dysfunction with the SRT than with the SLR (13).

Contraindications

1. Depending on the patient. Those who can tolerate a percutaneous lung biopsy are generally candidates to RFA with the same precautions. Contraindications are relative: uncontrolled coagulopathy with INR >1.5 –1.817; thrombocytopenia <50 x 10³ /µL; FEV1 <1 L15; <0.618 or <35% of the predicted FEV1 value30; serious pulmonary high pressure, mainly in central lesions, due to risk of vascular lesion10; pneumonectomy15 due to risk of post- ablation pneumonitis;
functional state ≥3 and low life expectancy (<1 year (1) ≤3 months); since theoretically it can be exacerbated, cause respiratory failure and death or serious respiratory disease, asymptomatic tumor and life expectancy <1 year; sepsis, respiratory infection, infection in the puncture site, leukemia, multiorganic failure or poor heart function.

The pacemakers must be set on automatic mode and their generators must be protected from the radiofrequency current with a magnet. Implantable automatic defibrillators (IAD) must be turned off and a pacemaker or external defibrillator must be available if required. The pads must be placed in such a way that favors the fact that the radiofrequency current gets away from the cardiac device and if possible, it is recommended to insert the electrodes >5 cm away from the pacemaker or the IAD. The cardiologist/electro-physiologist should check them before and after the procedure.

2. Depending on the tumor: >5 cm tumors, <1 cm from bronchi or great vessels or >3 tumors in the same lung though some consider it is acceptable up to 5. Although there is little experience, it improves the indexes of local relapse and survival since the tumor size of >3 cm does not have an impact on survival at one, 2 or 3 years in NSCLC or metastasis. Some electrodes are thicker (12–17 G). They can spread through the vessels and damage tissue at a distance. There is a greater risk of pneumothorax (39%). They do not require pads, but third-degree skin burns have been reported. Both the size of the ablation area and the clip effect are unpredictable. It can cause thrombosis and interfere with pacemakers and defibrillators.

Other percutaneous ablation modalities

The microwave electromagnetic field causes ionic agitation and fast molecular oscillations of tumoral and peritumoral water. Part of that kinetic energy is transformed into heat by friction causing coagulative necrosis. Cryoablation alternates extremely cold temperatures (−160 °C) with defrosting cycles which cause intra- and extracellular ice crystals, water diffusion toward the inside and outside of the cell and cellular lysis. It forms an ice ball around the applicator.

Unlike radiofrequency, microwaves achieve temperatures of 150 °C. They spread through different kinds of tissues even those with low thermal and electrical conductivity (healthy lungs) and high impedance (bones, healthy carbonized lungs). Its ablation diameter, area and volume are experimentally 25%, 50% and 133% greater than those of RFA, respectively and they are obtained with the same caliber of needle. Since the current does not pass through the intercostal nerves theoretically speaking it is not as painful and is better in peripheral, subpleural tumors, and the chest wall, with controversy in practice. It heats cystic lesions better. It is less susceptible to the cooling effect of the great vessels. Although there is little experience, it improves the indexes of local relapse and survival since the tumor size of >3 cm does not have an impact on survival at one, 2 or 3 years in NSCLC or metastasis. Some electrodes are thicker (12–17 G). They can spread through the vessels and damage tissue at a distance. There is a greater risk of pneumothorax (39%). They do not require pads, but third-degree skin burns have been reported. Both the size of the ablation area and the clip effect are unpredictable. It can cause thrombosis and interfere with pacemakers and defibrillators.
Figure 8 Therapeutic algorithm in stage I NSCLC patients with pulmonary oligometastasis. It includes lobectomy, sublobar resection, radiofrequency and stereotactic radiotherapy. CP, lung cancer; NSCLC, no-small cell lung cancer; CMPD, carbon monoxide pulmonary diffusion; FEV1, forced expiratory volume in the first second; Mtx, metastasis; pV02, mixed vein oxygen pressure; CHT, chemotherapy; Qx, surgery; RF, radiofrequency; RHB, rehabilitation; SLR, sublobar resection; RT, radiotherapy; SRT, stereotactic radiotherapy; Sv, survival; O.T., optimal tumor; Tm, tumor; VATS, video-assisted thoracic surgery.

* It is not possible to identify a FEV1 absolute cut value capable of differentiating patients without risk from high surgical risk patients and the latter from patients with prohibitive surgical risk since other factors are important as well including tumor location and pulmonary functional contribution of the affected segment. Nevertheless, FEV1 values of 40% are useful for the identification of patients with high surgical risk that deserve to be studied with special consideration.

** Prognostic factors in patients to undergo metastasectomy.

- Good prognosis: complete resection—it can be shown by imaging techniques, Qx and pathological anatomy, free interval of the disease ≥ at 36 months and germinal cell tumors. - Bad prognosis: age <65, gender (controversial), free interval of the disease <12 m or <24 m, incomplete resection, single mtx, and extrapulmonary disease—there is an independent association between extrapulmonary mtx and less survival (18), >3–4 resected nodes, synchronic disease, previous metastasectomy, large metastasis—the >3 cm ones are independently associated with a decrease of short term (a year) and long term (5 years) survival, adenopathies, reduced FEV1, location of mtx, anatomopathological nodular type in melanoma (primary of oral cavity or cervix) surgical complications and adjuvant therapy.

*** In LC, observation as an alternative to therapy is acceptable only if the patient’s comorbidities do not let him tolerate any therapies while the tumor-assessed in successive follow-up imaging examinations continues its indolent course. This scheme is protected by the author’s intellectual property rights and is not an adaptation of other publications. Source (for explanatory reasons): Pua et al.,2 Sánchez de Cos Escuin,4 Abtin et al.,11 Schroedel et al.,14 Sharma et al.,18 Chen et al.,41 Abbas et al.,42 Brace,43 De Baere,48 Pua et al.,42 and Lo et al.48

Because cryoablation does not damage tracheobronchial collagen, great vessels or muscles, it is promising for central tumors close to the diaphragm and the mediastinum.40 It is less susceptible to the thermal dissipating effect.26 It looks better in emphysematous patients but in cases of serious emphysema or pulmonary fibrosis, it presents risks of hemorrhage with progression to serious respiratory failure.15 It is better for >3 cm tumors.13 Up to 25 applicators can be
used simultaneously to increase the ablation area.\textsuperscript{22} Its anesthetic effect makes it suitable for tumors close to the pleura or the thoracic wall\textsuperscript{13} yet its 4–5 cm ablation area can damage the skin in peripheral lesions.\textsuperscript{22} It does not interfere with electrical circuits (pacemakers) or require pads.\textsuperscript{2} Based on the little evidence that we have the 3-year cancer-specific survival to SLR, RFA and cryoablation is similar.\textsuperscript{13,22} The needles are thicker (13–17 G),\textsuperscript{22} therapy lasts longer (25 min) and since the trajectory cannot be customized, the risk of bleeding (intrapulmonary 36–62%), tumoral implants\textsuperscript{36} and pneumothorax increases with (12–50%) and without tube.\textsuperscript{11,13} They are both more expensive modalities than the RFA.

Conclusion

Managing patients with NSCLC and pulmonary oligometastasis who are not eligible for surgery with RFA improves survival, provided the patients are adequately selected. We have presented the advantages and limitations of the procedure when it comes to other local therapies and the known factors that will condition the outcomes of this procedure; however integrating RFA in thoracic oncology calls for more research.

Ethical responsibilities

Protection of people and animals. Authors declare that for this investigation no experiments on human beings or animals were performed.

Data confidentiality. The authors declare that in this article there are no data from patients.

Right to privacy and informed consent. The authors declare that in this article there are no data from patients.

Conflict of interests

The author declares no conflict of interests.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.rxeng.2014.12.002.

References