

## Computed Tomography-Guided Radiofrequency Ablation of Malignant Lung Lesions: Early Experience

José M. Galbis-Caravajal,<sup>a</sup> Yolanda Pallardó-Calatayud,<sup>b</sup> Antonio Revert-Ventura,<sup>b</sup> Jesús G. Sales-Badía,<sup>a</sup> Rafael Esturi-Navarro,<sup>c</sup> and María Cuenca-Torres<sup>d</sup>

<sup>a</sup>Servicio de Cirugía Torácica, Hospital Universitario de La Ribera, Alcira, Valencia, Spain

<sup>b</sup>Servicio de Radiología, Hospital Universitario de La Ribera, Alcira, Valencia, Spain

<sup>c</sup>Servicio de Anestesia, Hospital Universitario de La Ribera, Alcira, Valencia, Spain

<sup>d</sup>Unidad de Investigación, Hospital Universitario de La Ribera, Alcira, Valencia, Spain

**OBJECTIVE:** To present our early experience in the treatment of primary malignant and metastatic lung lesions by radiofrequency ablation.

**PATIENTS AND METHODS:** From August 2004 through January 2007 we treated 19 patients (in 26 procedures) with curative or palliative intent. None of the lesions was amenable to surgery and some had been treated previously. The procedure was performed in the radiology room under conscious sedation-analgesia administered by an anesthesiologist. Fourteen patients were treated for pulmonary lesions and 5 for metastatic lung disease in a context of controlled primary disease. Treatment was with curative intent in 15 cases and palliative in 4.

**RESULTS:** The radiofrequency technique was applicable in 26 procedures and the mean follow-up was 8.68 months. The principal complications of radiofrequency treatment were pneumothorax in 4 patients, requiring drainage in only 2 cases; pneumonitis in 4; self-limiting pulmonary hemorrhage in 1; and pleural effusion in 5. There were no procedure-related deaths. Six patients died during the follow-up period.

**CONCLUSIONS:** In our experience, radiofrequency offers a safe and minimally invasive option for the treatment of malignant lung lesions in appropriately selected, nonsurgical patients. Morbidity is low, and in combination with other treatments this technique opens up a wide range of possibilities still to be explored.

Ablación mediante radiofrecuencia guiada por tomografía computarizada de las lesiones pulmonares malignas: experiencia inicial

**OBJETIVO:** Presentar la experiencia inicial en el tratamiento de las lesiones pulmonares malignas (primarias y metastásicas) mediante la ablación por radiofrecuencia (RF).

**PACIENTES Y MÉTODOS:** De agosto de 2004 a enero de 2007 tratamos a 19 pacientes (mediante 26 procedimientos) con intención curativa o paliativa. Todos los casos correspondían a lesiones no quirúrgicas, tratadas o no previamente. La técnica se practicó en la sala de radiología, con sedoanalgesia consciente llevada a cabo por el anestesiólogo. Se trató a 14 pacientes con lesión pulmonar y a 5 con enfermedad metastásica pulmonar, con la enfermedad primaria controlada. En 15 casos el tratamiento se realizó con intención curativa y en 4 era paliativo.

**RESULTADOS:** La técnica de RF pudo realizarse en los 26 procedimientos. La media de seguimiento fue de 8,68 meses. Las principales complicaciones derivadas del tratamiento de RF fueron: neumotórax en 4 pacientes, de los que sólo 2 requirieron drenaje; neumonitis en 4; hemorragia pulmonar autolimitada en 1, y derrame pleural en 5. No hubo mortalidad en relación con el procedimiento. Durante el periodo de seguimiento fallecieron 6 pacientes.

**CONCLUSIONES:** Según nuestra experiencia, la RF puede ser una opción segura y mínimamente invasiva para el tratamiento de las lesiones pulmonares malignas en pacientes no quirúrgicos adecuadamente seleccionados, con una baja morbilidad. La combinación con otros tratamientos ofrece un amplio abanico de posibilidades pendientes de discernir.

**Key words:** Radiofrequency ablation. Stage I lung cancer. Lung metastases. CT-guided puncture.

**Palabras clave:** Ablación por radiofrecuencia. Carcinoma pulmonar estadio I. Metástasis pulmonares. Punción dirigida por TC

### Introduction

Radiofrequency ablation of lesions, considered a minimally invasive treatment,<sup>1</sup> has been used successfully in tumors located in the kidney, breast, bone, liver, and

adrenal glands.<sup>2</sup> Radiofrequency was introduced in 1990, the year in which the first primary and metastatic liver tumors were treated.<sup>3</sup> It is based on the use of a high-frequency (460-480 kHz) alternating current to generate a localized electromagnetic field that heats the target tissue to desiccation or coagulative necrosis,<sup>4</sup> leading to death of the cells after exposure to this thermal effect. Its application in the treatment of lung lesions is in an experimental phase and experience is limited both by the number of patients treated and by the length of follow-up.

Correspondence: Dr J.M. Galbis-Caravajal  
Servicio de Cirugía Torácica, Hospital Universitario de La Ribera  
Ctra. Corbera, km 1, 46600 Alcira, Valencia, Spain  
E-mail: josegalbiscar@gmail.com

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TABLE 1  
Characteristics of the Patients Treated Using Pulmonary Radiofrequency Ablation

Case	Age, y	Histology	Intent	Type of Carcinoma	Size, cm <sup>a</sup>	Number of Procedures	Previous Surgery <sup>b</sup>	Stage	Survival <sup>c</sup>	Follow-up, mo
1	82	Squamous cell	Curative	Primary	2	3	No	I	Yes	29
2	69	Renal carcinoma	Curative	Metastatic	2	2	Yes	M	Yes	25
3	71	Giant cell	Curative	Primary	4	1	No	I	Yes	18
4	59	Adenocarcinoma	Palliative	Recurrence	5	3	Yes	II	No	8
5	81	Adenocarcinoma	Palliative	Recurrence	2	1	Yes	III	No	8
6	77	Pancoast	Palliative	Primary	7	1	Yes	III	No	2
7	73	Carcinoma	Curative	Primary	2	1		I	Yes	3
8	54	Squamous cell	Curative	Recurrence	4	1	Yes	I	No	5
9	84	Squamous cell	Curative	Recurrence	3	1	Yes	I	No	13
10	76	Cancer of the colon	Curative	Metastatic	2	1	No	M	Yes	12
11	80	Giant cell	Curative	Recurrence	2	2	No	I	Yes	13
12	80	Carcinoma	Curative	Primary	3	1	No	I	Yes	10
13	43	Pancoast	Palliative	Primary	5	1	No	IV	No	3
14	61	Cancer of the colon	Curative	Metastatic	3	2	Yes	M	Yes	9
15	68	Adenocarcinoma	Curative	Primary	2	1	No	I	Yes	3
16	74	Adenocarcinoma	Curative	Primary	2	1	No	I	Yes	3
17	81	Cancer of the colon	Curative	Metastatic	2	1	No	M	Yes	3
18	75	Squamous cell	Curative	Primary	2	1	No	I	Yes	1
19	63	Cancer of the colon	Curative	Metastatic	2	1	Yes	M	Yes	1

Abbreviation: M, metastatic.

<sup>a</sup>Largest diameter of the tumor.

<sup>b</sup>Oncologic thoracic surgical resection prior to radiofrequency ablation.

<sup>c</sup>At study closure.

TABLE 2  
Indications for Pulmonary Radiofrequency Ablation

1. Malignant lung tumors (primary or metastatic)
2. Tumors of the chest wall
3. Complementary to chemotherapy and/or radiotherapy in the absence of a response
4. In combination with radiotherapy to reduce tumor mass
5. Palliation of pain in bone metastases and Pancoast tumors
6. Palliation of other tumor-derived symptoms
7. In patients with a previous thoracotomy in order to preserve lung parenchyma

Although surgical resection continues to be the treatment of choice,<sup>5</sup> some patients are not candidates for surgery due to poor respiratory reserve or concomitant disease. This group represents a target population for local disease control by radiofrequency ablation. The technique is also indicated for palliation of symptoms (such as pain) and as a complement to standard treatments, including radiotherapy and chemotherapy,<sup>6</sup> an area of great interest for future research. The technique is based on evidence of good local control of the disease with beneficial effects both on quality of life and on survival in the selected population.<sup>7</sup>

The aim of this study is to present the initial experience of an interdisciplinary team responsible in our hospital for the workup, treatment, and follow-up of lung lesions amenable to this therapy.

## Patients and Methods

### Patient Selection

Between August 2004 and January 2007, 19 patients (18 men, 1 woman) with a mean (SD) age of 71.05 (10.07) years (range,

43-84 years) were treated with curative or palliative intent for primary malignant or metastatic lung lesions. The patient characteristics are shown in Table 1.

The mean size of the lesions was 2.86 (1.43) cm (range, 1.2-7 cm). The mean forced expiratory volume in the first second (FEV<sub>1</sub>) was 65.89% (23.79%) (range, 22%-92%). However, this figure varied when the patients were classified according to primary or metastatic disease, with lower figures in the group with primary lung cancer (FEV<sub>1</sub>, 54%).

We selected patients using a specifically designed protocol (Table 2) and surgery had been excluded as a therapeutic option given the stage of the disease in all cases. Before starting radiofrequency therapy, a detailed clinical evaluation, laboratory tests, imaging studies, lung function tests, and bronchoscopy were performed. The patients were adequately informed and filled in and signed the informed consent drawn up for this purpose. The decision to use this therapy was taken by an interdisciplinary team that included members of the Chest Committee of the Hospital Universitario de La Ribera (Alcira, Valencia, Spain), after approval by the hospital ethics committee.

### Radiofrequency Technique

After positioning the patient, 4 rectangular dispersive electrodes were applied, 2 on the anterior aspect of each thigh. Infiltration with local anesthetic was then performed and the needle was inserted into the lesion using a coaxial system. Whenever possible, an anterior approach was used for greater patient comfort and easier management by the anesthesiologist.

The procedure was performed under computed tomography (CT) fluoroscopic guidance (Xpress SX, Toshiba, Japan). The RITA 1500 generator (RITA Medical Inc, Mountain View, California, USA) was used in the first 5 patients, with real-time recording of temperature, power, and impedance. The puncture device was the 10 or 15 cm Starburst XL probe (RITA Medical Inc), with a diameter of 14F and 7 to 9 extensible electrodes (3-5 cm spheres). In the other patients, the procedure was performed with an array type LeVeen electrode (Boston Scientific, Natick, Massachusetts, USA) with sphere diameters that varied between 2 and 4 cm. A coaxial introducer was used in all patients

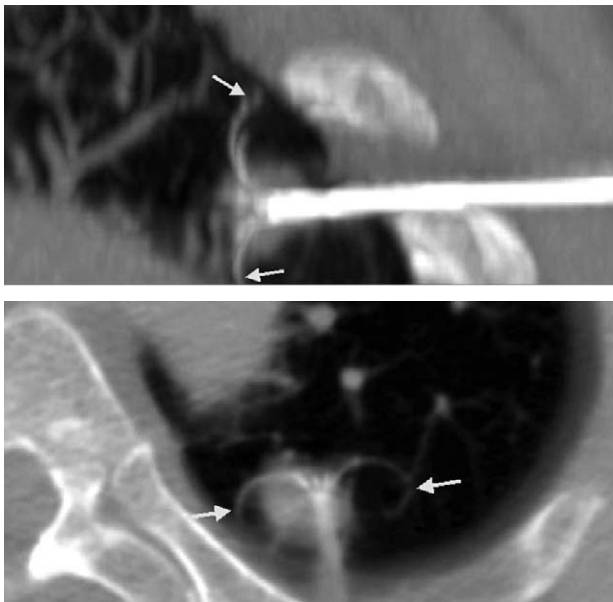


Figure 1. Reconstructions in different spatial planes and with maximum intensity projection enabled the correct coverage of the lesion to be ensured and the exact site of the tips of the electrodes (arrows) and their relationship to adjacent structures to be seen.

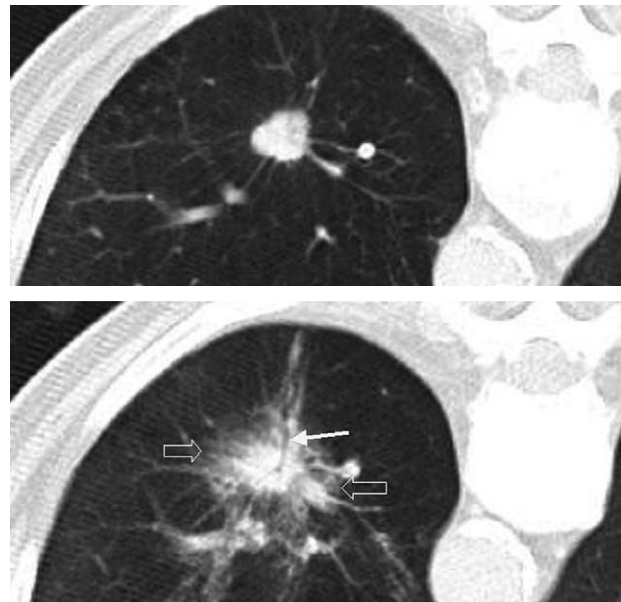


Figure 2. When the whole lesion has been adequately treated, a ground glass halo (hollow arrows) appears in the imaging study immediately after treatment. Note the linear shadow of the trajectory of insertion of the needle (filled arrow). Parenchymal hemorrhage visible on computed tomography performed immediately after the radiofrequency ablation.

in whom the LeVein system was employed; the radiofrequency generator was the RF 3000 (Boston Scientific) and power was administered in a stepwise manner. Final ablation was indicated by a marked increase in impedance (called the roll-off).

Multiplanar reconstructions or maximum intensity projections (Figure 1) were used when there was doubt about adequate coverage of the tumor by the electrodes or when necessary to determine the relationship with neighboring structures. Overlapping spheres were used for lesions greater than 3 cm to ensure adequate coverage.

#### Anesthetic Technique

In all cases a complete preanesthetic evaluation was performed. The patients were informed about the anesthetic technique and of its possible complications, after which they gave their informed consent.

On the day of the procedure, premedication was administered and standard monitoring was maintained continuously. The radiology room had a cardiac arrest trolley, equipment for the insertion of pleural drains, an oxygen supply, and the material that the anesthesiologist brought at the time of the procedure. Conscious sedation-analgesia was used; this is considered to provide a minimal depression of the level of consciousness that allows the patient to remain awake, without the need for respiratory support, and to hear and respond to simple orders.

#### Statistical Analysis

Due to the nonparametric distribution of the quantitative variables, they were described using the median and 25th and 75th percentiles. The Kaplan-Meier method was used to plot survival, and the log rank test for the comparison of functions between groups. A *P* value less than .05 was considered significant in comparisons to test hypotheses.

## Results

### Procedure

The procedure was successful in all the patients in whom radiofrequency treatment was prescribed. In those treated with curative intent, technical success was defined as complete coverage of the tumor with the development of a halo of alveolar pattern around the lesion as a safety margin (Figure 2). In patients treated with palliative intent, the technique was considered successful when complete ablation of the parietal pleura in contact with the tumor was achieved.

### Radiological Follow-up

Imaging studies were performed in all patients at 24 hours, 1 month, and then every 3 months using chest CT with and without contrast, with a dynamic study in the early phase (30 seconds), venous phase (50 seconds), and at equilibrium. Magnetic resonance imaging (MRI) was also performed with and without gadolinium contrast, including a dynamic study of the nodule with contrast.

### Immediate Complications

The complications and their treatment are listed in Table 3. In the patients who developed pneumothorax requiring drainage, a pleural drain was inserted before leaving the radiology room. A drain was inserted if the pneumothorax was greater than 10% or if the oxygen saturation fell by more than 5 points. Pleural drains with a diameter of 16F

TABLE 3  
Early Complications of Radiofrequency  
in our Study

Complication	Number	Treatment
Pneumothorax	4	Chest drain in 2/conservative management in 2
Pneumonitis	4	Oral antibiotics, 7 days
Endotracheal intubation	1	Immediate extubation on completion of the procedure
Bronchospasm	1	Bronchodilators
Intraparenchymal bleeding	1	Oral antibiotics for 7 days + oral corticosteroids
Axonal degeneration of the primary trunk of the brachial plexus	1	—
Pleural effusion	5	—

were used. No postprocedural needle aspiration of a pneumothorax was performed.

There were no anesthetic complications except for conversion to general anesthesia in 1 patient who was uncooperative due to uncontrollable pain.

After the ablation, patients were transferred to the recovery room and from there to the hospital ward; none required admission to the intensive care unit.

The mean length of stay was 1.24 days (range, 1-4 days). The longest stay was for a patient with shoulder pain due to infiltration by a Pancoast tumor. During his hospitalization, intravenous analgesia was increased until the effect of the ablation was noted.

#### Outpatient Follow-up and Survival

All patients attended a first outpatient visit at 3 to 5 days after the ablation. At this first outpatient revision, 3 patients reported bloodstained sputum, 8 nonspecific pleuritic pain in the area treated, and 2 a low-grade fever during the first 48 hours. If a residual image or tumor recurrence (nodular uptake or irregularity of the borders) was detected in medium-term or long-term follow-up, radiofrequency ablation was repeated (n=5). Six patients died during the study period. The 4 patients who were treated with palliative intent died within a few months due to disease progression, although local pain control was achieved. Patients with Pancoast tumors had the poorest prognosis (they died at 2 and 3 months). The other deaths occurred in patients who were treated for local recurrence of the tumor after oncologic surgery; the disease finally progressed to affect other sites and this was the cause of death.

After a mean duration of follow-up of 8.68 (8.08) months (range, 1-29 months) the median overall survival was 10 months (Figure 3), and this varied with the indication for radiofrequency ablation (palliative or curative) and with the type of tumor treated (primary or recurrent). The median survival among patients treated with palliative intent was 4 months, and in those treated with curative intent was 12 months ( $P=.26$ ).

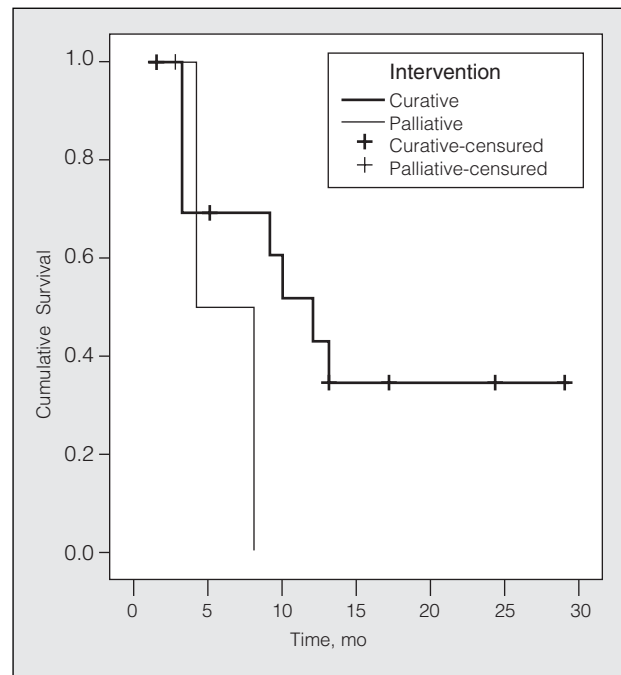


Figure 3. Cumulative proportion surviving plotted against survival time according to treatment intent (palliative vs curative) of the radiofrequency ablation.



Figure 4. Cockade sign: in an imaging study performed at 24 hours, the treated nodule can be seen to be hypodense (secondary to coagulative necrosis), with a halo of low attenuation (hollow arrow) surrounded by another halo of higher density (filled arrows). Minimal secondary pleural effusion (triangle).

#### Radiologic Response

As has been stated, the presence of a characteristic ground glass halo around the tumor was evaluated in the imaging studies immediately after treatment. This finding was compared to the images obtained immediately after puncture, when the ground glass opacities could be secondary to alveolar hemorrhage caused by movement of the needle within the parenchyma. Twenty-four hours after the procedure, the image obtained in response to the treatment is described as the “cockade phenomenon” (Figure 4). In the successive follow-up studies, the size of the nodule, uptake of contrast, and presence of cavitation were evaluated.

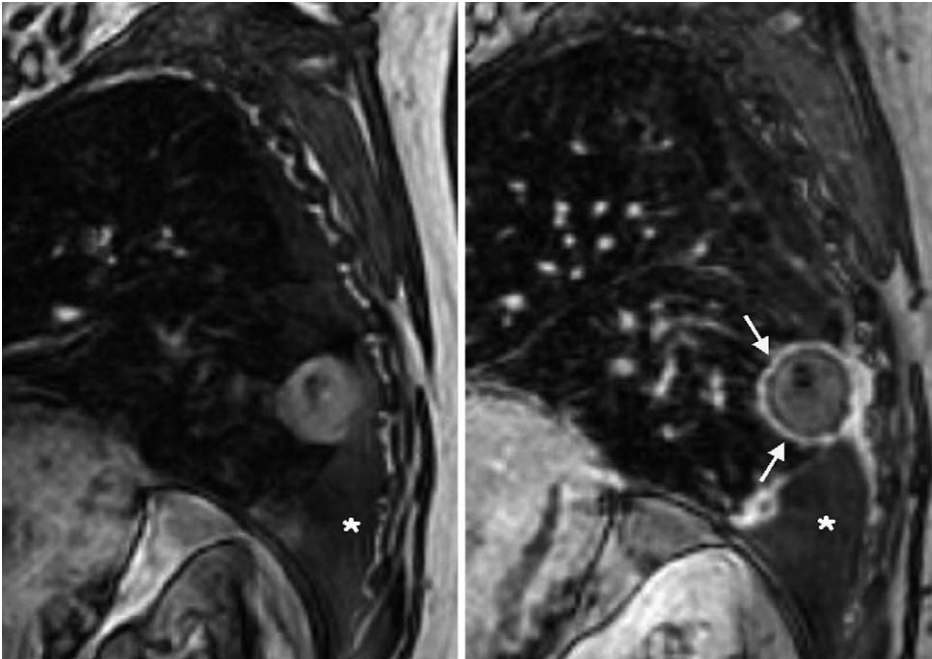


Figure 5. Magnetic resonance image from a patient being followed for stage I lung cancer treated 9 months previously by radiofrequency ablation. The peripheral halo around the lesion is a sign of disease progression.

The uptake of contrast by the lesion was evaluated by both CT and MRI. The presence of a smooth, peripheral halo of uptake was defined as an inflammatory reaction of the lung parenchyma (Figure 5). Irregular and, particularly, nodular uptake in the periphery were usually indicative of disease progression. Absence of the uptake of contrast by the lesion on both CT and MRI was considered to indicate a complete response.

## Discussion

Lung cancer, known to be the most common tumor, is often diagnosed at an advanced stage or when patients present marked morbidity, thus excluding surgery as a therapeutic option. In these cases, the alternative is to use chemotherapy, radiotherapy, or a combination of the two. Radiofrequency ablation is considered to be a new option for local treatment when administered alone or it may be used in combination with either of the above.<sup>8</sup> It is a relatively simple procedure and offers patients an effective therapeutic alternative. In addition, in the case of the lung, the air present in the tissue provides adequate insulation<sup>9</sup> that allows the energy to be concentrated in the relevant area. Careful patient selection by an interdisciplinary team is one of the main pillars underpinning the success of the technique.<sup>10</sup>

In the case of metastases, radiofrequency ablation opens a door to patients with previous lung resections, in whom further thoracotomy has a high associated morbidity and the options for surgical examination of the thorax are limited.<sup>11</sup> In addition, many of these lesions are not radiosensitive and some are resistant to chemotherapy.<sup>12</sup> One of the advantages of radiofrequency ablation is that, in the case of recurrent metastatic lesions, the technique can be repeated,<sup>13</sup> as it saves healthy pulmonary tissue. Two patients with metastases were treated by repetition

of the radiofrequency procedure. This group of patients presented fewer complications and a better response in the follow-up as they were younger and had a better FEV<sub>1</sub> and fewer comorbid conditions. The possibility for the simultaneous radiofrequency treatment of liver and lung lesions must also be highlighted; we performed this in 2 patients, both of whom tolerated the treatment well.

In patients with pain due to involvement of the parietal pleura (which we treated with palliative intent), radiofrequency therapy can aid in its control, with good results due to its cytoreductive effect. All these patients had a poor prognosis and died within a few months.

The results are particularly promising for the control of stage I primary lung disease; there are a few complications,<sup>15</sup> tolerance to the procedure is excellent, and it has a minimal effect on lung function.<sup>16</sup> In our series of patients, this group achieved the longest follow-up and survival, despite being patients in whom surgery was contraindicated due to their functional status or concomitant conditions.

Radiofrequency ablation is also a possibility that should be evaluated in patients with local disease recurrence after oncologic surgery. Survival was much lower in the patients we treated for local recurrence than in those in whom we used radiofrequency ablation as the first therapeutic option for primary carcinoma. These data coincide with those published by Lee and coworkers,<sup>17</sup> who also used radiofrequency ablation as the primary treatment in a group of patients with stage I lung cancer; they found a longer survival in these patients than in the group of patients with previously treated cancer or those treated with purely palliative intent.

One of the indications for which radiofrequency ablation offers greater possibilities is in combination with other treatments such as radiation therapy, where it is seen as an interesting option. In a recent study,<sup>18</sup> the efficacy of external radiation therapy was discussed based on the

results achieved in 60 patients with stage I or II disease, detecting local progression in 53%, with a median disease-free interval of 18.5 months, and postradiation pneumonitis in 8.3%. We used this treatment in a sequential manner in 1 patient with primary cancer, seeking to obtain an additive effect of the two techniques. Thus, radiofrequency ablation was used in the central regions, in which there is greater hypoxia, and radiotherapy was then used for control of the more peripheral areas of the tumor, in which the greater blood flow and oxygen concentration make it more effective.<sup>19</sup>

Radiofrequency ablation should be performed in a sufficiently spacious hospital room with the means to treat possible complications.<sup>20</sup> In our center, we performed the procedure in a radiology room that had been equipped with the material necessary to treat complications, and an anesthesiologist was present.

There is no consensus on which is the best anesthetic technique in these cases.<sup>21</sup> Local anesthesia alone does not provide sufficient pain control, and the majority of hospitals combine this with sedation. We performed appropriate monitoring and optimal sedation-analgesia that offers guarantees to the patient and achieves the immobilization necessary for the radiologist to perform the procedure. In one patient with a large tumor extensively adherent to the parietal pleura, it was necessary to perform orotracheal intubation due to pain secondary to the ablation.

A number of complications have been reported, the most common of which is pneumothorax; this has occurred in 20% to 40% depending on the series,<sup>22</sup> although only half have required drainage.<sup>23</sup> The area of necrotic lung tissue and the degree of emphysema present in the lungs are 2 factors that determine the risk of air leakage. In our series of patients there were 4 cases of pneumothorax (Table 3). The expectoration of dark sputum is relatively common in the hours after the procedure, and is due to necrosis of the lung parenchyma; it is well tolerated with the use of bronchodilators and broad-spectrum antibiotic coverage. At the outpatient follow-up performed a few days after the procedure, we detected the presence of a number of complications: bloodstained sputum, pleural effusion, mild fever, retention of secretions, and pleuritic pain. Such complications are considered to be minor<sup>24</sup> and have been reported by other authors.<sup>25</sup> We attributed the absence of major complications to the peripheral situation of the lesions and an adequate immobilization of the patients (optimal degree of sedation and analgesia), allowing the technique to be performed with safety.

One of the greatest difficulties is to evaluate the response to treatment.<sup>26</sup> Changes in the treated lesion can be detected by CT, with or without a reduction in the volume of the lesion.<sup>27</sup> We believe that positron emission tomography-CT is a very valuable test that helps to determine the future therapeutic strategy by providing information on the activity of the lesion that has been treated and possible disease progression in other areas.<sup>28</sup> We requested this study on 3 occasions due to doubt regarding the presence of tumor tissue in the treated area after an interval of more than 6 months after the ablation. In 1 case, disease progression affecting the homolateral hilar lymph nodes was detected, and in another patient a degree of tumor activity was

observed in the lesion already treated; this latter patient underwent a third radiofrequency ablation of the lesion.

We did not perform percutaneous biopsy during follow-up as this has been described in few studies. Like other authors, we recognize the difficulty of obtaining tissue from the exact site where there may be some tumor remnant<sup>29</sup> and, at present, we rely on imaging techniques for the evaluation and follow-up of lesions that have been treated.

There is an interesting, ongoing debate on the efficacy of radiofrequency ablation for the control of lung cancer compared to surgical techniques with limited resection (videothoracoscopy, segmentectomy, etc). However, the questionable efficacy of palliative surgical techniques for the local control of oncologic disease and its inherent morbidity, which is even greater in high risk patients, could establish the place of radiofrequency ablation as an alternative to these procedures; multicenter studies with a larger number of patients will be necessary to resolve these issues.<sup>30</sup>

In conclusion, radiofrequency ablation of lung lesions is a minimally invasive procedure that is useful in primary and metastatic tumors. The small number of patients treated and the short follow-up period do not enable us to draw conclusions at the present time, although it is clear that, due to its excellent tolerance, it could be an alternative treatment (alone or as a complementary procedure) for patients who are not candidates for surgery. Working groups must be created to define and evaluate the procedures to be performed and to draw up a working guideline that will be useful for all interested centers.

## Addendum

The development of the technique described has been possible thanks to the coordinated work of the Chest Committee of the Hospital Universitario de la Ribera in Valencia, Spain. The members of this committee, who come from different specialties and hospitals, are José Fonet Fayos (Radiology, Hospital de La Ribera), Pedro Cordero Rodríguez (Respiratory Medicine, Hospital de La Ribera), Elsa Naval Sendra (Respiratory Medicine, Hospital de La Ribera), Cristóbal Gaspar Martínez (Oncology, Hospital de La Ribera), Regina Gironés Sarrió (Oncology, Hospital de Luis Alcañiz, Játiva, Valencia, Spain), Enrique Mollá Olmos (Radiology, Hospital de La Ribera), María Jesús Mengual (Internal Medicine, Hospital de La Ribera), Miguel Soler (Servicio de Radiotherapy, Hospital de La Ribera), José Luis Monroy (Radiotherapy, Hospital de La Ribera), and Miquel Forment (Radiology, Hospital de La Ribera).

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GALBIS-CARAVAJAL JM ET AL. COMPUTED TOMOGRAPHY-GUIDED RADIOFREQUENCY ABLATION OF MALIGNANT LUNG LESIONS: EARLY EXPERIENCE

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