Abstract. Background: The lung is the most common site for primary cancer worldwide as well as being a common site of metastases for various malignancies. Percutaneous radiofrequency ablation (RFA) is rapidly evolving as a new minimally invasive tool for the treatment of pulmonary tumors. Patients and Methods: A questionnaire was sent by e-mail to 14 centres around the world, which we knew or thought were performing percutaneous pulmonary RFA, to retrospectively survey their experience in this field including the number of ablations done to date, indications, method, peri- and postprocedural complications. Results: Seven centers reported 493 percutaneous procedures in lung tumors. Two deaths have been reported. Complications were subdivided into major and minor complications. Pneumothorax occurred in up to 30% of interventions with less than 10% requiring intercostal drainage. Pleural effusion requiring aspiration occurred in less than 10% of cases. Conclusion: With almost 500 procedures done to date, percutaneous pulmonary RFA appears to be a safe, minimally invasive tool for local pulmonary tumor control with negligible mortality, little morbidity, short hospital stay and gain in quality of life.

Lung cancer is the commonest cause of cancer death in both sexes worldwide with most often advanced and incurable disease at time of diagnosis. Based on current projected smoking patterns it is anticipated that lung cancer will remain the leading cause of cancer death in the world for the coming decades.

Surgery for pulmonary metastases has become an accepted treatment in selected patients with an approximate 25% 10-year survival rate (1) and at least 90% 10-year survivors being free of disease (2). Reliable prognostic factors to help the preoperative selection are scarce, a standardised surgical approach to pulmonary metastatic disease is lacking and published studies utilising randomised prospective methodology are too few (3).

Radiofrequency ablation (RFA), an established minimally invasive treatment method for primary and secondary tumors especially in liver, has gained increasing interest in focal control of unresectable lung primaries and lung metastases. Early attempts to percutaneously radiofrequency-ablate primary and secondary lung tumors in humans have been very promising in our own group.

In this study, we aimed to bring together the data of worldwide experience of pulmonary RFA on both primaries and metastases with regard to the number of tumors, bilateral treatment and the overall morbidity and mortality of this treatment, in order to help our assessment and future utilisation of this technique.

Patients and Methods

Percutaneous pulmonary RFA is mainly being performed with instruments from the three leading companies on the market: RITA Medical Systems (Mountain View, California, USA), Radiotherapeutics (Mountain View, California, USA) and Radionics (Burlington, Massachusetts, USA). While RITA and Radiotherapeutics distribute similar probes with deployable hooks, Radionics distributes straight, internally cooled RF electrodes with uninsulated active tips of variable length.
We mailed a questionnaire to all users of radiofrequency ablation machines in lung who we were aware of, their names either provided by the manufacturer (RITA) – Radiotherapeutics did not answer to our request - or known to us from publications or presentations at radiological or oncological meetings (RSNA, ECR, ASCO). We also included groups we knew had participated in an ablate/resect study with lung RFA done openly after thoracotomy prior to surgical resection without knowing if they had proceeded to a percutaneous approach.

A total of 14 centers were contacted: 7 in the United States, 6 in Europe and 1 in Asia. Including our group in Australia, 15 centers were enrolled in total.

The questionnaire consisted of both closed and open-ended questions; radiologists were asked about the number of procedures completed, whether they ablate lung primaries, metastases or both, the diameter of probe used, the imaging guided modality used to insert the probe, whether ablation was performed in the vicinity of the heart, the aorta, main bronchi or large vessels, what kind of sedation was used, the number of tumors ablated at each procedure, whether one or both lungs were treated at a time, the routine time patients were observed in hospital after the procedure, the rate of minor complications not requiring any further intervention (small pneumothoraces, small haemorrhages, small effusions), the rate of large pneumothoraces requiring a chest tube, the rate of large pleural effusions requiring tapping, the number of deaths related to the procedure and the reason for the death(s), the follow-up CT regime and finally the responders were encouraged to add comments.

After one month a reminder letter was sent to those centers who had not responded, asking whether they needed further time to fill in the form, whether they were the correct persons we had addressed, to notify if they were not willing to participate and to at least confirm they had got the mail. After a total of three months from sending out the questionnaires we analysed the data we had received.

**Results**

Of 14 questionnaires sent out a total of 8 answers were returned within 1 month. Two further answers were returned after the reminder-mail. Six out of the 7 centers in the US answered, 3 had not got the ethics committee approval for pulmonary RFA in humans yet, while the remaining 3 returned completed questionnaires. From the 6 European centers, 3 sent their completed questionnaires back, one was just about to start their first case and the remaining 2 centers did not answer. From all but one group (Asia-South Korea), which we knew were performing percutaneous lung RF, we received filled-in questionnaires.

Ethics committee approval and patients’ informed consent had been obtained in all centers. A total of 493 lung RFAs on primary tumors and metastases have been performed so far in the seven centers included. There is one leading center which has performed more than 300

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**Table Ia. Number of procedures performed, ablated tumor type, probe diameter, imaging guided modality, sedation type, number of tumors ablated per procedure and side of ablations per session.**

<table>
<thead>
<tr>
<th>Center</th>
<th>No. of procedures performed</th>
<th>Tumor type ablated</th>
<th>Diameter of probe used</th>
<th>Imaging guided modality</th>
<th>Sedation per procedure</th>
<th>No of tumors ablated per procedure</th>
<th>Side</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>297</td>
<td>prim/met</td>
<td>15G, 17G</td>
<td>CT</td>
<td>conscious analgosed 20%  analgosed 20% gen. anest 80% analgosedation</td>
<td>&gt; 5 both lungs</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>90</td>
<td>prim/met</td>
<td>17G</td>
<td>CT-fluoro</td>
<td>conscious analgosedation</td>
<td>&lt;3 one lung</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>76</td>
<td>prim/met</td>
<td>15G</td>
<td>CT-fluoro</td>
<td>conscious analgosedation</td>
<td>3-5 both lungs</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>prim/met</td>
<td>15G</td>
<td>CT</td>
<td>conscious analgosedation</td>
<td>&lt; 3 one lung</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>met</td>
<td>15G</td>
<td>CT-fluoro</td>
<td>gen. anesthesia</td>
<td>3-5 one lung</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>prim/met</td>
<td>15G</td>
<td>CT-fluoro</td>
<td>gen. anesthesia</td>
<td>&lt; 3 one lung</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>met</td>
<td>15G</td>
<td>CT-fluoro</td>
<td>conscious analgosedation</td>
<td>&lt; 3 one lung</td>
<td></td>
</tr>
</tbody>
</table>
procedures followed by a middle field with two centers having performed 90 and 76 interventions, respectively: taken together, these three groups have done 463 procedures, equalling 94% of the lung interventions. The death rate was 0.4%, with the first two groups having had one death each.

Except for two European groups, who have only treated metastatic disease so far, the other centers ablate primary lung tumors and metastases equally (Table Ia). Four centers, including the two leading ones, routinely observe their patients for a few hours and treat them on an outpatient base. Two further centers observe their patients overnight, while only one center keeps their patients for more than 24 hours after a lung RFA procedure. The centers who are not following a protocol which only allows inclusion of tumors in the outer two-thirds of the lung, perform ablations close to the heart, main bronchi, aorta and main vessels with only one bleeding complication reported so far related to this.

Conscious sedation is predominantly used; only where there are many lesions to ablate or big lesions that are known to require longer ablation times is general anaesthesia chosen. Two centers do their lung procedures under general anaesthesia only. Two of the three leading centers ablate both lungs at a time, while all other groups only ablate one lung per session (Table Ia).

Except for the three last groups, who have performed ten or fewer pulmonary RFA so far and therefore have not got a population big enough to derive representative rates of complications, the rate of small complications (small pneumothoraces, small pleural effusions, small intraparenchymal haemorrhages) not requiring any further interventions was 10-30% in three of the four leading groups and <10% in the fourth. The rate of large pneumothoraces requiring a chest tube was again 10-30% in the three centres and <10% in the fourth one (Table Ib).

Only the first center reported a pleural effusion rate requiring tapping ranging between 10-30%, but this was apparently related to the fact that multiple lesions are being treated in a population with diminished pulmonary function; the group is aggressive at draining effusions in an effort to restore pulmonary function as completely as possible and thus prevent complications like large atelectatic lung portions, pneumonia, bronchitis, etc. All other groups are below 10% at tapping pleural effusions.

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Table Ib. Structures adjacent to which tumors are being ablated, routine time of observation post procedure, rate of small complications requiring no further intervention, rate of large pneumothoraces requiring chest tube, rate of pleural effusion requiring tapping and deaths.

<table>
<thead>
<tr>
<th>Center</th>
<th>Tumors ablated in proximity to</th>
<th>Routine time of observation post procedure</th>
<th>Rate of small complications requiring no further intervention</th>
<th>Rate of large pneumothoraces requiring chest tube</th>
<th>Rate of pleural effusion requiring tapping</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>heart, main bronchi, aorta</td>
<td>few hours, on outpatient base as well as &gt;24 h</td>
<td>10-30%</td>
<td>10-30%</td>
<td>&gt;30%*</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>heart, main bronchi, aorta</td>
<td>few hours, on outpatient base</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>large vessels</td>
<td>overnight</td>
<td>10-30%</td>
<td>10-30%</td>
<td>&lt;10%</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>none of the structures</td>
<td>overnight</td>
<td>10-30%</td>
<td>10-30%</td>
<td>&lt;10%</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>heart, main bronchi, aorta, large vessels</td>
<td>&gt;24 h</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>large vessels</td>
<td>few hours, on outpatient base</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>none of the structures</td>
<td>few hours, on outpatient base</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>&lt;10%</td>
<td>0</td>
</tr>
</tbody>
</table>

* related to aggressive draining in an attempt to prevent pneumonia, bronchitis, etc. in a patient population with diminished pulmonary function.
Follow-up was usually done as required by protocol, comprising three-monthly follow-up CTs within the first year and then changing to 6-monthly controls.

Discussion

Despite lung RFA being performed for almost five years, the literature on this topic to date is scarce. Dupuy et al. reported on 3 patients successfully treated with CT-guided RFA of both primaries and metastases (4), confirming the successful ablation in another 27 patients (5). Sewell et al. presented short-term results on 10 patients with either unresectable non-small cell lung cancer or refusing surgery who were treated under CT-guidance with RFA, with 100% tumor destruction in all patients confirmed on a short-term follow-up with Positron Emission Tomography (PET) (6). King et al. presented data on 6 patients, all with pulmonary metastases from colorectal carcinoma, with successful percutaneous radio-frequency ablation, few periprocedural complications and good short-term follow-up (7).

It is only recently that new publications have been added to the scarce literature: Dupuy et al. published an overview on clinical applications of RFA in the thorax (8), while Lencioni et al. reported on the successful percutaneous RF-treatment of 5 patients with NSCLC (9), Steinke et al. reported on a successful CT-guided percutaneous RFA of a pulmonary metastasis confirmed by subsequent resection and histological proof of the completeness of tumor destruction (10) and Vaughn et al. reported on a massive haemorrhage during radiofrequency ablation of a pulmonary neoplasm (11).

Although there are no published data on long-term results after pulmonary RFA of primaries and secondaries, an encouraging tendency is observed both in our own and in personally reported experience of other groups with good local disease control.

On autopsy lung metastases have been found in almost one-third of all patients with malignant disease (12). Tumors exhibiting preferential spread to the lungs as the only site of metastasis include sarcoma, renal cell cancer and head and neck tumors, whereas tumors such as breast cancer and melanomas metastasise to multiple organ sites (3). Colorectal carcinoma occupies a position between the two groups with the most common site of metastasis being the liver, but the lung being the most common site of extra abdominal disease spread. A 30-year retrospective review of 287 patients who underwent pulmonary metastatic surgery for metastatic colorectal cancer showed very favorable results with a 5-year survival rate of 40% and a 10-year survival of 32% (13). The effectiveness of pulmonary metastatic surgery has been demonstrated in selected tumors such as osteosarcoma, renal carcinoma, head and neck tumors, colon cancer, germ cell tumors and soft tissue sarcoma (3).

The single significant prognostic factor all studies agreed upon was the completeness of resection, whereas general agreement exists that disease-free interval (DFI) is also prognostically important (3). There is no consensus about tumor doubling-time (TDT), number of metastases to resect, bilaterality of disease, tumor grade, age or sex as factors possibly affecting survival after pulmonary metastasectomy (3). Mineo et al. showed that the type of resection did not significantly affect survival by following 85 patients who underwent pulmonary metastasectomy by either conventional resections with diathermy dissection or stapler suture lines, lobectomy or laser ablation with Nd:YAG laser equipment, with the laser patients even showing shorter periods of air leakage and shorter hospital stay (14).

We believe that, with a compliance of 71% to the e-mail and with 83% completed questionnaires of the groups we knew were performing pulmonary RFA, the descriptive data can be generalised for pulmonary RFA experience and that this is a useful addition to the currently sparse literature.

We are not aware of RFA machines with probes for pulmonary interventions supplied by manufacturers other than the three companies mentioned.

The questionnaires are unanimous in their results. The slightly lower complication rate in the second largest group with fewer pneumothoraces may be on the one hand related to the smaller diameter of probe used and on the other hand to the fact that they treat fewer lesions per procedure compared to the other two big groups and treat only one lung at a time, whereas the other two groups treat both lungs at a time.

The data shows that, with increasing knowledge and experience (the first group with more than 300 ablations having treated almost 3.5 times more patients compared to the second biggest group), the willingness to attempt riskier and more difficult procedures increases as well.

The incidence of pulmonary primary and secondary tumors is similar in the United States, Europe and Australia. We hope that the safety of this minimally invasive treatment modality, the promising short-term results so far, the obvious cost-effectiveness and the gain in quality of life for the patients, documented in recent publications, will turn this modality into an accepted treatment option for a selected patient group.

It must be clearly emphasised that the procedure is only palliative at the moment because we do not know what long-term results will be, and that it is meant for either unresectable tumors, for patients not amenable for surgery due to comorbidities or for those who do not want to undergo thoracic surgery. We would suggest that, if long-term results parallel those of the liver treatment, it might also be a new alternative to surgery or radiation.

RFA offers a means for local tumor control with negligible mortality, very low morbidity, low cost, repeatability and,
above all, gain in quality of life, with routine treatments on
an outpatient base or overnight hospitalisation and the
patients being able to return home or to work within a
minimal period of time.

Conclusion
RFA of both primary and secondary pulmonary tumors is a
safe treatment option in a selected patient group. Future
work is necessary to further investigate the long-term results
and prognostic factors to assess patients who benefit most
from this local tumor control with very low morbidity and
mortality, much shorter hospital stays compared to surgical
procedures, lower costs (an issue not covered in this paper)
and, last but not least, a gain in the patients’ life quality.

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