

## Metastatic Lung Cancers

**In recent years, ECIO has witnessed an increase in the number of speakers and sessions addressing pulmonary cancers, both primary and metastatic. Unsurprisingly: lung cancer accounts for 12% of all cancer cases, and is the leading cause of cancer death. As the pool of case reports grows, so the indications for its use are growing ever clearer.**

This year's congress offered valuable advice on patient selection and optimal delivery, and offered a range of interactive, hands-on and video-learning sessions, alongside traditional lectures.

### Evaluating lung function

Prof. Charles Marquette (Nice/FR) explained the dire outcomes for lung-cancer patients: it has a 5-year survival rate of <15%, and only complete resection of early-stage disease can be curative. Surgery, however, can only be offered to fewer than one in four patients, due to late-stage diagnoses and associated co-morbidities.

85-90% of cases are tobacco-related, and thus associated with other diseases: 50-90% of these patients have underlying chronic obstructive pulmonary disease, and 15-20% underlying coronary heart disease, both of which may be contra-indications for surgery. Pre-operative evaluation is thus crucial, and a delicate balancing act between reducing the cancer burden and preserving lung function is required.



To evaluate pulmonary function, forced expiratory volume (FEV1) and gas exchange capacities (DLCO) should be measured; several low-tech tests can also be used, such as the staircase test (ability to climb 6 floors = low risk; 2-3 = high) or the shuttle-walk test (>400 low risk; <250 high). Post-operative predictions of function should then be calculated using pre-operative FEV1 values  $\times (1-y/z)$  [where Y=number of functional segments to be removed; Z=total number of functional segments].



For those deemed at moderate or high risk, Dr. Marquette's experience indicates SBRT or RFA, although a proper evaluation of possible complications (such as pneumothorax, bleeding or exacerbation of interstitial pneumonia) and contra-indications (coagulation disorders, dyspnea at rest, unstable cardiac condition, performance status III or IV) is mandatory.

### **Surgery in lung metastases**

Thoracic surgeon Prof. Bernward Passlick (Freiburg/DE) gave an excellent overview of the criteria for curative resection of metastases, and the surgical options available.

Currently, uni- or bilateral, sequential or simultaneous thoracotomy are widely employed, with much debate about the value of video-assisted thoracic surgery (VATS), which risks missing additional metastases: a retrospective analysis of pre-operative CT findings at the University of Freiburg showed that for presumed single-lesion patients, additional lesions are found perioperatively in 7%, rising to 27% for patients with multiple lesions. Caution is thus advised for all pursuing minimally invasive treatments in multiple-metastatic patients. For single metastases, there appears to be no difference in long-term survival outcomes between VATS and thoracotomy.

Wedge resection is widely used (70% of cases). It is a straightforward procedure, but some additional lung tissue is always lost if a stapler device is used. Anatomical resection (<10% patients) and dissection of lung tissue is also commonly performed.

Especially exciting are the technical improvements of pulmonary laser surgery: wavelength modifications allow for a quick and very precise resection, entailing minimal blood loss. It can be used for multiple lesions; deep lesions can be sutured in a sequential, multi-layered fashion with resorbable materials. This procedure will result in initial scarring, which may be confused with recurrence on CT, so additional care is required at follow-up.

Lots of variables determine how many metastases can or should be resected, including location, primary tumour type, lung function, co-morbidities and therapeutic alternatives.

Prognostic factors include the primary tumour (germ cell tumours show excellent response, but only account for 4% of primary cancers), disease-free interval and complete resection: the number of metastases does not seem so important. In a systematic review, 5-year survival for single lesions was 54%; for multiple metastases 37%; for normal CEA 43%; and for elevated CEA 22%. Prof. Passlick concluded by restating the tissue preserving benefits of laser-supported metastatectomy, and stressed that therapy decisions are best made in a tumour-board setting.

### **Ablation as a first-line therapy?**

Dr. Alice Gillams (London/UK) gave a brief overview of the indications and protocol for performing pulmonary ablation, before outlining the safety profile and clinical outcomes. Pneumothorax is a common occurrence, with an incidence similar to that associated with lung biopsy (overall 40%; requiring drain insertion 10%; resulting in more than 24-hour hospitalisation <1%).

An important advantage of ablation is its ability to preserve lung function. The preservation of parenchyma is of particular importance to patients who are likely to have multiple metastatic episodes, as it maximises the treatment choices at each stage of the disease.

Dr. Gillams then compared the treatment options for colorectal lung metastases: surgery is unproven, has limited indications and a 5-year survival of 38-60%; chemotherapy can reduce lesion size, but complete eradication is unlikely; SBRT is suitable for 1-2 lesions, but requires fiducial insertion, and is limited in the size and locations it can treat. The data for ablation compares well: three 2015 series on lung metastases demonstrated a 3-year survival rate of 64, 44 and 76%, respectively. These and other studies show that smaller tumours respond better and, in line with the surgical data presented by Prof. Passlick, that the number of lesions is not as important as previously thought.

For sarcoma patients particularly, ablation may have a lot to offer: 40-80% develop intrapulmonary recurrence post-resection, and chemotherapy offers a median survival of just 12-18 months. Not only is RFA a minimally invasive, readily repeatable procedure, but a 2013 study of 22 patients (55 lesions of 0.5-2 cm) achieved primary local tumour control of 95%, an overall mean survival of 51 months, and 2- and 3-year survival of 94% and 85%. Size  $\leq$  1cm, number (solitary or multiple), uni- or bi-lateral, prior surgery or chemotherapy, and trunk vs. extremity primary tumours did not impact survival.

The literature for other tumour types is not so well established. Small series show some benefit – for example, oesophageal and nasopharyngeal ablation achieve outcomes similar to surgery. One study of RFA for RCC metastases (de Baère) demonstrated a five-year survival of 53.8%. Dr. Gillams concluded that ablation represents a safe, effective and repeatable treatment for lung metastases, and should be the first-line option for lesions  $\leq$  3.5 cm.

### **Imaging follow-up**

The optimal imaging schedule to use after surgery, SBRT and ablation was presented by Prof. Robert Suh (Los Angeles, CA/US).

Multiple therapeutic options currently exist for the treatment of both primary and secondary pulmonary malignancies, and reliable and diligent



imaging follow-up is essential. Dr. Suh outlined the expected findings for each modality (resection, metastasectomy, conventional RT, stereotactic RT, radiotherapy and RFA), as well as projected timelines for when follow-up should be performed.

Knowledge of CT and FDG-PET patterns is critical for early identification of tumour recurrence and progression. Operators should be diligent in identifying the pathological completeness of therapy, any confounding inflammatory effects of therapy, and the biological activity of the disease. CECT and PET should be used in conjunction.

### **Evidence from comparative trials**

Dr. Lorenzo Monfardini (Brescia/IT) gave an overview of the existing comparative data for treating pulmonary metastases.

Surgical literature most commonly addresses colorectal metastases (17 studies; 1,684 patients). 5-year survival is 41-56%, and the mortality rate is < 2.5%. The best surgical candidate has a prolonged disease-free interval between the primary and metastatic lesions; normal CEA; no nodal involvement; and a single metastasis. Spirometric changes after pulmonary metastasectomy are affected by the total volume of lung parenchyma resected: the functional loss after 3 or more non-anatomical resections is comparable to that recorded after lobectomy.

The multicentre RAPTURE study (2008) examined RFA in 73 metastatic patients who were unsuitable for surgery, radio- and chemotherapy. Overall survival at two years was 66% for CRM and 64% for other metastases, respectively. In 2013, a 122-cohort study indicated that RFA might be a suitable alternative to surgery for small peripheral tumours. A recent paper (de Baère et al, 2015) demonstrated an overall survival rate of 51% at 5 years, as per major surgical series, and excellent respiratory function outcomes.

Comparing these with SBRT is more difficult – as the “youngest” technique, follow-up data of just two years is available. A 2010 systematic review of SBRT in 175 lesions in 148 patients demonstrated a local control rate of 78.6% at two years. The overall survival at two years was 50.3% (33-73%).

Lack of Phase III trials make it impossible to determine which therapy is best – the real question, to Dr. Monfardini’s mind, is which therapy to use first. Using overall survival, rather than disease-free survival, as a primary marker, and considering the option of reintervention, he would currently recommend ablation as the first choice for treating small pulmonary metastases.

*Presentations are available at [www.esir.org](http://www.esir.org)*