tumor descriptors of the tumor, node and metastasis (TNM) classification of lung cancer.[2] As the authors explained, before the 7th edition of the TNM classification, there was no specific code to describe lymphangitic carcinomatosis in the lung, which is mainly a situation found at clinical staging. To help register cases in a uniform way, the code cLy was proposed for prospective testing. This code is an optional descriptor that is not integrated in the T or the M components of the classification. Therefore, it has to be registered separately and added to the regular TNM. For example, a right upper lobe tumor invading the chest wall presenting with radiological signs of lymphangitis in the upper and middle lobes, but without nodal disease or distant metastasis, would be classified as cT3N0M0 cLy3.

In the International Association for the Study of Lung Cancer (IASLC) database,[3] data on the cLy descriptor are scarce. This descriptor is available for patients registered prospectively through the electronic data capture system, only, and not for those registered retrospectively. In total, there were 69 patients with non–small-cell lung cancer (NSCLC) with some degree of lymphangitis: cLy1 33 (48%), cLy2 9 (13%), cLy3 14 (20%), and cLy4 13 (19%). Ten additional patients with small-cell lung cancer also presented with lymphangitis. Among patients with NSCLC, lymphangitis was more frequent in larger tumors (29 cT2, 9 cT3, and 27 cT4) than in earlier ones (3 cT1 and 1 cTX). The survival analysis of these patients does not clarify the prognostic impact of this descriptor as the estimated 1-year survival is approximately 41% for patients with cLy1, cLy2, and cLy4, with a paradoxically high 61% estimated 1-year survival for patients with cLy3. So, with these data, solid conclusions cannot be drawn. We certainly need this information on a larger number of patients to fully assess the prognostic relevance of the anatomical extent of lymphangitis. The IASLC database used for the revision of the 7th edition of the TNM classification is predominantly surgical, with 85% of registered patients having been treated surgically, either with surgery alone or in combination with chemotherapy and radiotherapy. This explains why there are so few patients with lung cancer and associated lymphangitis.

We thank Drs. Singh, Baldi, and Behera for their interest in the IASLC Lung Cancer Staging Project and for having pointed out the prognostic implications of lymphangitis. Only with larger and more detailed databases, we will be able to further refine and better understand its prognostic impact.

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REFERENCES

1. Singh N, Baldi M, Behera D. Inclusion of lymphangitis as a descriptor in the new TNM staging of lung cancer: filling up the blank spaces. *J Thorac Oncol* 2015; 10: e119.
2. Rami-Porta R, Bolejack V, Crowley J, et al.; IASLC Staging and Prognostic Factors Committee, Advisory Boards and Participating Institutions. The IASLC Lung Cancer Staging Project: proposals for the revisions of the T descriptors in the forthcoming eighth edition of the TNM classification for lung cancer. *J Thorac Oncol* 2015;10:990–1003.
3. Rami-Porta R, Bolejack V, Giroux DJ, et al.; International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee, Advisory Board Members and Participating Institutions. The IASLC lung cancer staging project: the new database to inform the eighth edition of the TNM classification of lung cancer. *J Thorac Oncol* 2014;9:1618–1624.

Cryotherapy for Lung Metastases

A Justifiable Procedure?

To the Editor:

The report of 1-year results from the nonrandomized study "Evaluating cryoablation of metastatic lung tumors in patients-safety and efficacy: the ECLIPSE trial-interim analysis at 1-year"[1] has shown that this technique is moderately efficacious in terms of local control of disease. But like so many similar reports of techniques for removal or ablation of pulmonary metastases, it is based on the uncertain premise that removing a few asymptomatic "oligometastases" improves patients' survival.

The oligometastatic state is poorly defined and has no demonstrable basis in cancer biology or biostatistics.[2] The term was first coined in 1995 but citations only began to increase in the 2000s. Writing in 2014 an interdisciplinary group of authors, including Weichselbaum, one of the originators of the term, suggested that there might be more wishful thinking than evidence.[3] Although de Baere et al.[1] believe that metastasectomy is "the standard of care," the only evidence they cite is a registry of surgeons' self-reported results from the 1945 to 1995. The recent literature on surgical metastasectomy is considerably more circumspect.[4] There are no known randomized trials or other controlled studies to prove effectiveness. This is the reason for running the Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC) randomized controlled trial now open internationally.

The practice of lung metastasectomy is very highly selective and targets those with one or very few metastases and longer intervals between primary resection and lung metastasectomy. These are inherently the longest living patients at the tail end of the survival distribution of metastatic cancer. Some are alive for 5 years with or without treatment. These patients, destined to survive without metastasectomy, are greatly over represented in the groups selected for surgery creating the illusion of effectiveness.[5] In ECLIPSE, 75% of the patients had had a variety of prior treatments for metastases. By 12 months, 40% had developed new metastases, with a mean time to developing them of 10.7 months, but none had died of cancer. This suggests that these patients had widespread but slow growing subclinical metastatic disease and raises questions about the justification

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DOI: 10.1097/JTO.0000000000000694

ISSN: 1556-0864/15/1012-e120

for trying to ablate a few radiologically detectable pulmonary metastases.

Although there is insufficient evidence that removing lung metastases by any modality improves survival, is it good palliation? Patients selected for surgical metastasectomy have almost always been asymptomatic. It is unusual for lung metastases to contribute to symptoms near the end of life or to contribute to the mode of death. This study shows that cryotherapy is not a harmless treatment. One in five patients had a postprocedural pneumothorax. The information in this small series of patients is insufficient to assess other complications, but it is likely that they will suffer some of the effects of cavitating lung disease including infection and hemoptysis.

On the available evidence, removal or ablation of asymptomatic lung metastases by any modality cannot be justified for survival or palliation. The oncological community should not accept it as "standard" but should collaborate in randomized trials to assess its effectiveness.

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REFERENCES

1 de Baere T, Tselikas L, Woodrum D, et al. Evaluating cryoablation of metastatic lung tumors in patients-Safety and efficacy: the ECLIPSE trial-interim analysis at 1-year. *J Thorac Oncol* 2015;10:1468–1474.
2. Treasure T. Oligometastatic cancer: an entity, a useful concept, or a therapeutic opportunity? *J R Soc Med* 2012;105:242–246.
3. Palma DA, Salama JK, Lo SS, et al. The oligometastatic state—separating truth from wishful thinking. *Nat Rev Clin Oncol* 201411:549–557.
4. Fiorentino F, Vasilakis C, Treasure T. Clinical reports of pulmonary metastasectomy for colorectal cancer: a citation network analysis. *Br J Cancer* 2011;104:1085–1097.
5. Treasure T, Milošević M, Fiorentino F, Macbeth F. Pulmonary metastasectomy: what is the practice and where is the evidence for effectiveness? *Thorax* 2014;69:946–949.

Reply to Dr. Macbeth Letter

In reply:

We thank Dr. Macbeth and his coworkers for the interest they placed in reading our publication in *Journal of Thoracic Oncology*[1] and greatly appreciated their comments. We do agree that there is no level I evidence of benefit of lung metastasectomy for overall survival, although many large series suggest that a benefit might exist. A randomized control trial as Pulmonary Metastasectomy in Colorectal Cancer[2] is an interesting way to try to answer the question of benefit in terms of overall survival, but the randomization between lung metastasectomy and active surveillance in the PULMICC study has limitations such as the following:

- recruitment, because it is difficult for a patient accessible to surgery that the choice in between surgery and no treatment will be made after "flipping a coin," and this is probably one of the reason why PULMICC study is recruiting slowly.
- definition of what is active surveillance and when to treat a patient under active surveillance? Is it possible/ethical to refuse surgery in the active surveillance arm? What about a single lung metastasis that grows from 1.5 to 3.5 cm in 18 months, remains single location of disease and is now abutting the pleura? Will we be really able to measure the benefit of active surveillance when crossover is unavoidable?
- difficulty in measuring possible benefit of resection or ablation to the patient beside overall survival. What is the benefit of being disease free for a mean of 10 months after ablation?
- cancelation of any chance of cure in the active surveillance arm, even if such cure is limited with 13.1 ± 1.7% patients free of disease at 4 years after radiofrequency ablation (RFA) in our series of 566 patients with 1037 lung metastases.[3]

Concerning the "moderate efficacy" of cryoablation describe by Dr. Macbeth, we report 1-year efficacy of 94.2% with cryoablation[1] and 89% at 4 years with RFA,[3] which is in the range to what usually reported after surgical resection.[4] Concerning safety of cryoablation, no major side effects were recorded, and most common side effect was pneumothorax requiring small bore chest tube placement in 18.8% of patients with tube retrieval at day 1 or 2 after treatment.[1] This compares favorably with surgery requiring large bore chest tube insertion in all patients with later retrieval.

Trying to answer the question of Dr. Treasure, "Is cryoablation of lung metastases a justifiable procedure?," the first answer is that we are convinced that minimal-invasive ablation techniques including cryotherapy or RFA are more justifiable than surgery due to their high efficacy and low morbidity, thus avoiding "the inevitable downside of pain of thoracotomy and, with larger resections, loss of lung function" as describe elsewhere by Dr. Treasure.[2] Then, even in a randomized trial as suggested by Dr. Macbeth, it might be difficult to "see the signal from the noise with the inevitable use of combinations of therapies making it impossible to discern the effect of surgery on survival" as explain by Dr. Treasure.[2] Percutaneous ablation might provide the gain of complete control of the disease and avoid the inevitable downside of surgery and replace surgery for small size metastases in a selected population. We do think that cryoablation of lung metastases is a justifiable procedure when trying to approach individual patients care when there is lack of level I evidence.

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DOI: 10.1097/JTO.0000000000000695

ISSN: 1556-0864/15/1012-e121