Laser pulmonary metastasectomy by video-assisted thoracic surgery

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Contributions: (I) Conception and design: A Ojanguren, W Karenovics; (II) Administrative support: All authors; (III) Provision of study material or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: Indications and surgical approach for pulmonary metastasectomy remain controversial as randomized clinical trials are lacking to validate its effectiveness. To this end, non-anatomical lung wedge resection, widely performed by staplers, persists as preferred surgical procedure. With the advent of new technologies, laser assisted surgery evolved and has been advocated mainly for multiple pulmonary metastases in open surgery fashion. However, video-assisted thoracic surgery (VATS) laser pulmonary metastasectomy has been rarely reported. This review is based on a selective search of the PubMed database for articles that were published from 1990 to 2018 and contained the keywords 'laser assisted surgery', 'pulmonary metastasectomy', 'thoracoscopic laser metastasectomy', and 'VATS'. No prospective clinical trial has been performed to provide evidence whether to treat pulmonary metastasis with laser or conventional techniques. According to retrospective cohort studies and descriptive series, open approach laser assisted surgery facilitates the resection of a higher number of metastases, sparing healthy lung parenchyma, while obtaining similar recurrence rates compared to conventional staplers. In central lesions, optimal surgical margins can be achieved around the lesion avoiding injury to deep located structures such as major vessels or bronchus. However, evidence about thoracoscopic laser pulmonary metastasectomy is remarkably poor consisting in only a few small series of patients with one or two resected metastases. Laser assisted pulmonary metastasectomy is safe and effective. Video-assisted laser resection of lung metastases is a marginal technique to date. Postulated benefits of open laser assisted pulmonary metastasectomy could not be assumed by thoracoscopic approach with available data. Further studies are needed to demonstrate whether multiple and centrally lesions could be effectively resected by thoracoscopic laser metastasectomy.

Keywords: Laser assisted surgery; pulmonary metastasectomy; thoracoscopic laser metastasectomy; video-assisted thoracic surgery (VATS)

Received: 28 February 2019; Accepted: 30 March 2019; Published: 12 April 2019.
doi: 10.21037/jovs.2019.03.06
View this article at: http://dx.doi.org/10.21037/jovs.2019.03.06

Introduction

The lung is the second most common site of metastasis after the liver, affecting 30% to 50% of all patients with extra-thoracic tumors (1). Carcinoma of the colon and rectum, breast, kidney and oropharynx are the most common tumors metastasizing to the lung. The International Registry of Lung Metastases retrospectively analyzed 5,206 patients with pulmonary metastasectomy from epithelial tumors, sarcoma, germ cell tumors and melanoma, and demonstrated an increased survival rate in selected patients (2). Up to date, extensive case reports and series support these results (3,4). However, biases are numerous and prospective randomized trials are lacking to validate the effectiveness of pulmonary metastasectomy compared to

no treatment or compared to other treatment alternatives such as chemotherapy or stereotactic radiotherapy (5). Thus, prospective studies with control groups have been demanded by critics arguing patient selection for surgical treatment would influence survival (6,7). In response, the PulMiCC trial for patients with pulmonary metastases from colorectal carcinoma was started, in which patients are randomly assigned to pulmonary metastasectomy or active monitoring. The trial is expected to end in 2021 (8). Hence, since validated data from a prospective randomized study are not yet available, patients should be assessed in a multidisciplinary tumor board on a case-by-case basis.

Besides, criteria for selection of patients suitable for metastasectomy were stablished as early as 1965 by Thomford, and with minor modifications are valid up to this time (9): (I) the patient has adequate functional status to tolerate resection; (II) the metastases are technically resectable, (III) the primary tumor is controlled; and (IV) extrathoracic metastatic disease is absent. Additionally, there must be an absence of alternative therapy with lower morbidity (10). Over the years, parenchyma saving resection techniques and R-0 resection remained uncontroversial (11,12). Pastorino *et al.* (2) demonstrated a significantly more favorable 5-year survival in patients with complete resection (36%), compared to those with incomplete resection (13%). On the other hand, Casiraghi *et al.* (13), in contrast to Pastorino's study, demonstrated that the number of metastastases did not affect survival in a statistically significant way. Hence, there is no consensus among thoracic surgeons whether the disease burden is an overwhelming obstacle. The decisive point would be to achieve complete resection of all sites of disease, not the absolute number of metastases *per se*.

In current practice it is broadly accepted that the objective of the metastasectomy is to achieve complete resection of all pulmonary metastatic tumor and to preserve as much functioning lung parenchyma as possible all the more so as redo-pulmonary metastasectomy may be required. To this end, non-anatomical lung wedge resection, widely performed by staplers, is often the preferred surgical procedure (14,15). However, for central lesions, pulmonary segmentectomy, lobectomy and eventually pulmonectomy may be required. In cases of centrally located metastases and low functional reserve in which wedge resection is not possible, or in presence of multiple metastases, the utility of laser assisted pulmonary resection and electrocautery have become increasingly popular (16,17). Cautery resection was described by Perelman in 1983 (18). This method consists of coring out the metastasis by means of coagulating the surrounding lung tissue and ligating small vessels and bronchi within the resultant cavity. Electrocautery when used in high power setting, not only generates smoke but also the carbonized tissue sticks to the tip of the cautery, which hinders its handling. Additionally, middle size vessels bleed if not properly coagulated and also, air leakage and fistula are a matter of concern because the resection surface is cauterized in an irregular manner (19). Because of above mentioned reasons, this technique has not been applicable by a thoracoscopic approach.

Pulmonary metastasectomy and laser system: background

Laser assisted pulmonary lung resection has—at least theoretically—several significant benefits. Firstly, healthy parenchyma is spared as limited lung resection is feasible in deep-located lesions. Secondly, surrounding tissues are minimally damaged or deformed by laser and thus, anatomy of adjacent structures is fully conserved. Laser also produces lung tissue shrinkage, which brings two additional advantages: mechanical reinforcement of the coagulation effect and air-tightness.

As early as 1967, Minton *et al.* (20) described, within an experimental setting, the use of pulsed laser energy emitted by a 1,064-nm Nd:YAG laser for resection of pulmonary metastasis in rabbit lung. In 1985, even if LoCicero *et al.* (21) established the 1,064-nm Nd:YAG laser for endobronchial interventions, he still favoured the CO_2 laser for lung resections. Later on, CO_2 was proved to be inadequate for lung surgery since CO_2 is a pure cutting laser. In consequence, a number of centers in United States, Europe and Japan focused their investigation on 1,064-nm Nd:YAG laser due to its ability to vaporize and seal lung tissue simultaneously (22-27). Bare fibers and sapphire tips were used for superficial resections but failed with deep located lesions. Further research on laser wave length and lung tissue determinants aimed to develop a laser available for lung parenchyma section. On the basis of lung's high vessel quantity, a laser with effective coagulation capability and excellent cutting property was found to be mandatory to safely resect parenchyma and consequently avoid bleeding and air leaks. Within this context, Rolle *et al.* (17) described that 1,318-nm wavelength provided the intended combination of effects (cutting capability plus coagulation and sealing capability) in a greatly enhanced fashion compared to 1,064-nm wavelength for

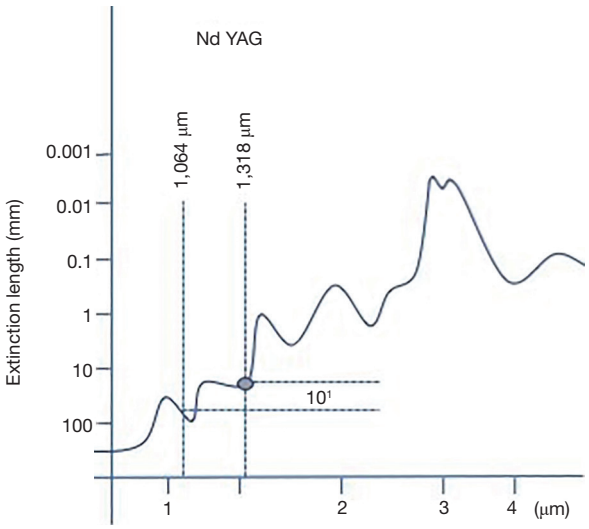

Figure 1 Simplified graphic representing the absorption spectrum of water. The diagram exhibits 1,064- and 1,318-nm wavelengths of Nd:YAG laser and the 10-times higher absorption capacity of the 1,318-nm wavelength laser.

lung parenchyma section. This results were achieved due to the fact that 1,318-nm Nd:YAG had a 10-fold higher absorption coefficient in water compared to the primary 1,064-nm, being capable to accomplish optimal coagulation requirements (*Figure 1*).

Consequently, laser assisted lung metastasectomy has gained popularity as it turned out to be convenient for resection of a high number of lung nodules, as well as for sparing parenchyma in the setting of multiple or centrally located lesions with oncologically safe margins ensuring a low risk of local recurrences.

Pulmonary metastasectomy and surgical approach

The prevailing surgical approach to pulmonary metastasectomy evolved together with surgical technologies across time, ranging from traditional open thoracotomy to VATS. There is no consensus regarding a preference for open thoracotomy over a VATS procedure, as randomized trials comparing outcomes are lacking at the time being. Available retrospective studies and meta-analyses demonstrated that VATS approach is equivalent to open surgery (28,29). However, published retrospective studies have a potential selection bias as patients with multiple nodules were more likely to consent to an open approach, offering VATS for single or few metastases. Thus, depending on surgeons' preference and on the localization and size of the metastases, either approach has been used. Many favoured VATS for minimizing surgical trauma, enhancing postoperative recovery, and decreasing intrathoracic postoperative adhesions, which is particularly important in view of potential future repeated resections for recurrence (30,31). Others promoted an open approach to succeed in the identification of all targeted lesion via bimanual palpation, thus avoiding to overlook deep and centrally located metastases (32).

Laser assisted surgery

The theoretical benefit of laser assisted surgery is the capacity to remove a higher number of metastases due to minimal damage to surrounding tissues, while obtaining similar recurrence rates as conventional techniques. However, only few studies have reported the results for laser assisted lung resection for pulmonary metastases (*Table 1*). The latest studies were consistent in reporting a higher number of metastases removed and similar long-term results, compared to patients treated by other techniques. Most of the available literature is focused on LAS pulmonary metastasectomy by open thoracotomy:

In 2002, Rolle *et al.* (33) described their initial experience with the 1,318-nm Nd:YAG laser for pulmonary metastasectomy in 100 patients. Subsequently, in 2006 (17), the same group published a series of 328 patients, concluding that the laser-system facilitates complete resection of multiple bilateral centrally located metastases, and consequently contributes to spare lung parenchyma.

Osei-Agyemang *et al.* (16) published a retrospective cohort study (n=301) comparing laser-assisted limited resection with conventional wedge or anatomic resections. A significantly higher number of resected lesions was found in the LAS group, however there was no significant correlation between the surgical technique and long-term survival.

In a retrospective study analyzing 237 patients with pulmonary metastases from renal cell carcinoma resected by 1,318-nm laser, Baier *et al.* (34) concluded that completeness of resection was the single most important prognostic factor for survival, even in patients with multiple metastases and unilateral single-station N1/N2 disease. In accordance with this finding, they limited the eligibility criteria for LAS pulmonary metastasectomy to functional and technical

Table 1 Laser assisted pulmonary metastasectomy—summary of main published series

Year	Author	Type of study	Approach, (%)	Device	Nº patients	Nº resected metastases, mean (range)
2002	Rolle	Prospective descriptive	Anterolateral thoracotomy	1,318-nm ND:YAG	100	6.3 [1–124]
2006	Rolle	Retrospective descriptive	Anteroaxillary muscle-sparing thoracotomy	1,318-nm ND:YAG	328	Unilateral: 3 [1–29] Bilateral: 13 [2–124]
2013	Osei-Agyemangt	Retrospective cohort study; LAS *vs.* NLAS	–	1,318-nm ND:YAG; Staplers	301: 62 LAS 239 NLAS	LAS median: 7 NLAS median: 2
2016	Baier	Retrospective descriptive; renal cell PM	Anterolateral muscle sparing thoracotomy	1,318-nm ND:YAG	237	13 [1–110]
2017	Meyer	Prospective descriptive	VATS	1,318-nm ND:YAG	15	2 (1–4)
2017	Franzke	Retrospective cohort study LAS *vs.* NLAS	LAS [56]; thoracotomy NLAS [44]; VATS thoracotomy	1,318-nm ND:YAG; Staplers	178: 99 LAS 79 NLAS	LAS (%), 1 PM: 46; 2 PM: 24; >2 PM: 30; NLAS (%), 1 PM: 69; 2 PM: 25; >2 PM: 6
2018	Mcloughlin	Prospective descriptive	VATS	1,320-nm ND:YAG	7	1 [1–2]
2018	Porrello	Retrospective descriptive	Anteroaxillary muscle-sparing thoracotomy	1,318-nm ND:YAG	106	–
2018	Schmid	Prospective cohort study LAS *vs.* NLAS; Sarcoma PM	Thoracotomy for LAS	1,320-nm ND:YAG	106: LAS 46 NLAS 60	LAS 6.5 [2–11]; NLAS 1 (1–3.5)

PM, pulmonary metastasis; LAS, laser-assisted surgery; NLAS, non-laser assisted surgery; VATS, video-assisted thoracic surgery.

resectability.

Franzke *et al.* (35) reported similar overall survival for patients who underwent LAS and those operated with conventional devices. In this cohort study of 178 patients, a trend for a lower risk of local relapse was found after LAS.

Similarly, Porrello *et al.* (36), in a series of 106 patients, demonstrated that LAS resection of lung metastases obtained as good results as conventional surgical metastasectomy in terms of radicality of the resection and survival.

More recently, Schmid *et al.* (37) performed a cohort study with 106 sarcoma patients, showing that significantly more metastases were resected in the LAS group, with similar recurrence and overall survival in both groups. Limitations of this study included mixing the entities of soft-tissue and osteosarcoma, and the fact that the decision on whether to perform LAS or conventional resection was not standardized and was based on surgeon's preference, localization, number of metastases and logistic reasons.

Laser assisted pulmonary metastasectomy by VATS

It is remarkable to notice the scarcity of studies dealing with VATS approach for laser assisted pulmonary metastasectomy. As early as in the 1990s, some thoracic surgeons published their initial experience with laser as a primary resecting tool or an adjunct to endoscopic stapling techniques to provide optimal tissue preservation by VATS. Such studies were mainly case reports or short series for resection of indeterminate nodules (38-40). At that time, 1,064-nm wavelength Nd:YAG was used, and therefore technical difficulties had yet to be solved (i.e., inefficient energy conversion into heat, higher heat dissipation and scarce penetration into tissues). In fact, it was not until 2017 that Meyer *et al.* (41) published the first series of 15 patients who underwent VATS laser pulmonary metastasectomy. Soon after, in 2018, McLoughlin (42) reported a series of 7 patients.

Meyer *et al.* concluded that VATS for pulmonary

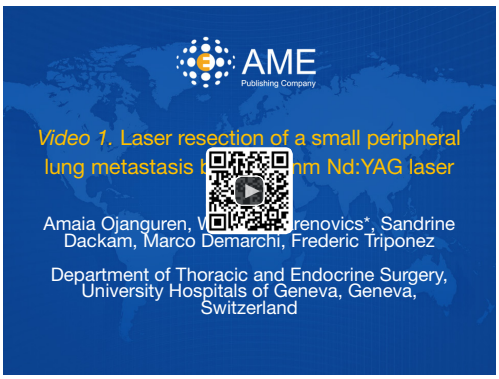

Figure 2 Laser resection of a small peripheral lung metastasis by 1,318-nm Nd:YAG laser. Notice the fully coagulated and sealed surgical site and the high amount of smoke produced during the procedure (43).
Available online: http://www.asvide.com/article/view/31000

metastases is safe and effective. In this pilot study the possibility of palpating the entire lung through a minithoracotomy was highlighted. The authors claimed that systematic palpation of the whole lung could solve the shortcomings of VATS compared to open surgery. According to the authors, the potential risk of missing pulmonary nodules was decreased, even if they agreed with the fact that thanks to the improved quality of CT scans, lung metastases are less frequently overlooked. Likewise, Meyer *et al.* reported that via a utility minithoracotomy the laser hand piece and the smoke evacuator system could be introduced in the same manner as in open surgery. The shortness and the straight design of the laser handpiece (LIMAX 120; KLS Martin GmbH & Co KG) were identified as points to be improved for the development of VATS laser metastasectomy. They suggested to use a small, curved laser fiber holder instead of a laser handpiece as it could be guided to any part of the chest cavity—more convenient for VATS. As it was a pilot study, patients with centrally located lesions were excluded and the number of resected metastases was low (mean 2; range, 1–4).

Lastly, McLoughlin *et al.* reported their preliminary experience with thoracoscopic laser metastasectomy and concluded it is safe and efficient. Similar to Meyer *et al.*, bimanual palpation of lung parenchyma was performed, and an additional smoke evacuator was inserted through the utility port. In the case of too small or deep lesions a hooked wire was placed preoperatively. This measure reduced the likelihood of conversion to open surgery. No technical complications occurred. As a preliminary study, again the number of resected metastases per patient was low (mean 1; range, 1–2).

In summary, there is a weak body of evidence concerning laser pulmonary metastasectomy by VATS. Published data considers VATS laser metastasectomy to be safe and effective. Inherent reduced lung exposure by the thoracoscopic approach seems to be solved by manual palpation through a utility minithoracotomy and/or additional ports. Failure to target small or centrally located lesions could be overcome by preoperative CT guided wire localization.

The most prominent disadvantage of using laser for lung resection is the large amount of smoke generated within the pleural space, therefore, sometimes it has to be evacuated to continue the surgery, this fact being especially tiresome and time consuming. Even if in the latest lasers a smoke evacuator is available, often a high-performance smoke evacuation system would be necessary to keep the pleural cavity clear of smoke. In that sense, advances in technology have facilitated the handling of laser, from initial short rigid laser handpiece to a bare fiber conducted through a guiding tube for endoscopic purposes.

Based on our limited experience comprising only a few patients who underwent laser metastasectomy by VATS, we conclude that for the time being, it is not a safe and recommendable procedure due to already mentioned problems (*Figure 2*).

Limitations for LAS include initial economic investment, staff education in laser safety including the use of protection googles, and the large amount of smoke generated in pleural cavity, hampering visualization and being time consuming.

Summary

LAS is a safe and effective technique for pulmonary metastasectomy. The available literature consists in retrospective studies and case series dealing almost exclusively with open surgery. According to these data, a higher number of metastases are removed and healthy lung parenchyma is spared, while obtaining similar recurrence rates compared to conventional staplers. In central lesions, optimal surgical margins can be achieved around the lesion avoiding injury to deep located structures such as major vessels or bronchi. Over the years, technology evolved obtaining lasers with excellent balance between cutting, hemostasis, and pneumostasis making a good tool for

limited lung resections.

However, the VATS approach for pulmonary metastasectomy with the laser remains poorly spread. In fact, just two series of patients with one or two resected metastases are published. Consequently, there is no evidence to support that the postulated benefits of open laser-assisted lung metastasectomy can be achieved by VATS. At the present time and with the available technology laser lung metastasectomy does not seem to be a technique that can be recommended for general use.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Michel Gonzalez) for the series "Advancement in the Surgical Treatment of Pulmonary Metastasis" published in *Journal of Visualized Surgery*. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jovs.2019.03.06). The series "Advancement in the Surgical Treatment of Pulmonary Metastasis" was commissioned by the editorial office without any funding or sponsorship. FT reports personal fees from Stryker/Novadaq (travel fees), personal fees from Medtronic (travel and consulting fees), outside the submitted work. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/jovs.2019.03.06
Cite this article as: Ojanguren A, Karenovics W, Dackam S, Demarchi M, Triponez F. Laser pulmonary metastasectomy by video-assisted thoracic surgery. J Vis Surg 2019;5:40.

