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Laser pulmonary metastasectomy preserves parenchyma: a single-centre retrospective study from the United Kingdom

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Abstract

Background: Pulmonary metastasectomy (PME) is a modality increasingly employed to control oligometastatic disease from a variety of solid tumours.

We present data from a single UK centre, following the introduction of laser-assisted surgery (LAS) using the Limax[®] 120 Nd:Yag laser (Gebrüder Martin GmbH & Co. KG, Tuttlingen, Germany).

Methods: All patients undergoing PME between September 2015 and August 2018 were included in our study. Those undergoing LAS were compared to a control of conventional stapled wedge metastasectomy (SWM). Data was analysed retrospectively from a prospective kept database. Statistical analysis was performed using JASP (Version 0.14.1).

Results: Fifty-seven procedures in 46 patients, were included in the final analysis. Demographic data was similar at baseline between the LAS and SWM group, with colorectal cancer being the most common primary, 44/57 (77%). LAS was favoured in patients who had previously undergone pulmonary metastasectomy, 9/12 (75%). Patients in the LAS group had a smaller parenchymal volume resected (MD 30.6 cm³, $p = 0.0084$), with a lower incidence of clear histological marginal resection (11/27 vs 29/30, $p < 0.0001$); but no difference in operative time, morbidity, patient-reported outcome measures, or local recurrence between the two groups at 2 years. LAS was associated with a lower procedural cost (MD £452.92, $p < 0.0001$).

Conclusions: Laser-assisted pulmonary metastasectomy presents a safe and acceptable alternative to traditional stapled wedge resection, with notable parenchymal-sparing, no discernible learning curve, and lower direct costs.

Keywords: Laser, Laser-assisted surgery, Lung resection, Lung cancer, Thoracic oncology, Pulmonary metastasectomy

Background

Metastatic disease is the most common cause of cancer deaths worldwide [1]. Pulmonary metastases account for up to 20% of all disseminated disease originating from a variety of solid-organ tumours [2, 3].

The first reported case of pulmonary metastasectomy (PME) dates back to 1882 [4]. Several historical reports

thereafter demonstrate the viability of PME, with good perioperative outcomes [5, 6].

Over recent years, large registry data and other observational series have similarly reported positively on PME for multiple tumour types with varying medium-term survival [7–10]. The Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC) trial was a United Kingdom-based prospective, randomised controlled trial that allocated patients with new pulmonary metastases following resected colorectal cancer to surgical resection or ‘watchful waiting’. As the trial was unable to meet target recruitment, there remains a paucity of adequately

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controlled or randomised evidence on this topic to date [11, 12].

Evidence for percutaneous and non-invasive techniques as alternatives to PME is meanwhile emerging; with increasing experience with thermal ablation using radiofrequency (RFA) or microwaves (MWA) [13], as well as stereotactic ablative radiotherapy (SABR) [14].

Whilst having minimal impact on lung function, and carrying lower periprocedural morbidity, these approaches fail to provide tissue confirmation of the presumed diagnosis, or evidence of complete eradication of treated lesions.

Notwithstanding, PME is ubiquitous in contemporary clinical practice and has become the de facto gold standard for pulmonary metastatic disease. There is much variation in opinion and practice with regard to indications, patient selection, surgical approach and technique [15, 16].

The Nd:Yag laser system has been applied to PME for over 20 years [17], with a well-established safety profile, good medium-term outcomes [18] and a strong contemporary evidence-base for its non-inferiority to traditional surgical resection methods [19]. However, its popularisation and adoption into routine practice outside of select high-volume laser PME centres remains low [15].

Laser-assisted surgery (LAS) was introduced at our centre following approval from the New Interventional Procedures Advisory Group (NIPAG). We report on our early experience and clinical outcomes of LAS, into a well-established conventional PME programme at a large thoracic surgical centre in the UK, and perform a direct cost-analysis and overall hospitalisation expense, together with an evaluation of the associated learning curve.

Methods

All patients undergoing presumed non-anatomical sublobar pulmonary metastasectomy between September 2015 to August 2018 for metachronous lesions, operated on by a single consultant thoracic surgeon at a large thoracic surgical unit in the United Kingdom – from the arrival of a Limax[®] 120 Nd:Yag laser (Gebrüder Martin GmbH & Co. KG, Tuttlingen, Germany) were identified from a prospective database. Additional data was collected retrospectively from patient records, operative software and clinical imaging systems. Patients with no evidence of secondary lung cancer on histology—benign or primary lung cancer—were excluded from the study as were procedures that used laser and stapled resection in the same procedure.

Measurements of total lesion volume and lung parenchyma resected were taken from final histopathological analysis of the intraoperative sample.

Follow-up data for survival, radiological and clinical outcomes was recorded up to 2 years following each patient's final procedure.

Contemporary cost information was obtained from local procurement records at our hospital.

Clinical course

Patients were referred to thoracic surgery through respective specialist multidisciplinary team (MDT) meetings.

In those patients with an indication for PME, the decision for LAS or traditional stapled wedge metastasectomy (SWM) was taken by the consultant surgeon. LAS was preferred in patients who had undergone previous lung metastasectomy and in those with multiple or central lesions anatomically as evidenced on pre-operative computed tomography (CT).

Patients in the LAS group were provided with specific information and a dedicated patient-information-sheet regarding LAS; and consented explicitly to the use of this technology.

Bilateral metastases were tackled as staged procedures, with an interval of 4–8 weeks, depending on postoperative recovery.

All procedures were performed under general anaesthetic, with single-lung ventilation using a double-lumen endotracheal tube. Video-assisted thoracic surgery (VATS) was performed using two- or three-ports. A posterolateral serratus-sparing thoracotomy was adopted for open procedures.

LAS was performed using the Limax[®] 120 Nd:Yag laser (Gebrüder Martin GmbH & Co. KG, Tuttlingen, Germany), and in open procedures the resection cavity sutured to achieve parenchymal approximation. TISSEEL[®] fibrin sealant (Baxter BioSurgery, Deerfield, IL, USA) was used in technically challenging cases.

A single large-bore pleural drain was placed at the end of the operation and set to low-pressure suction.

All patients were nursed postoperatively in dedicated high dependency (level 2) beds on a specialist thoracic surgical ward for 24 h, prior to stepping down to acute ward (level 1) beds on the same ward, until the point of discharge.

Statistical analysis

Data analysis was performed using JASP (Version 0.14.1). All averages are presented as a mean \pm standard deviation. Student's *t* test was used for continuous variables, whilst Pearson's Chi-squared test was used to test for significance in categorical variables. Linear correlation analysis with Pearson's coefficient was additionally applied to test for changes in process and outcome with increasing

familiarity with the technology. P-values of <0.05 were considered significant.

Ethical considerations

This study reports on a clinical evaluation audit governed by the New and Innovative Procedures Approval Group (NIPAG) at our institution, and was deemed not to require additional ethical approval.

Results

Sixty-six non-anatomical resections were performed for presumed secondary pulmonary lesions. Five (8%) of the resected lesions were excluded from the study, as these were found to be primary lung malignancy at histology. Four (6%) additional procedures were excluded from further analysis, due to intraoperative application of a combination of ipsilateral SWM and LAS in the same sitting.

Fifty-seven procedures in 46 patients were included in the comparative analysis: 27 (47%) laser-assisted surgery (LAS), and 30 (53%) stapled wedge metastasectomy (SWM). Thirty-three (58%) procedures were performed by thoracotomy, whilst 24 (42%) were VATS. The distribution of VATS and thoracotomy for LAS and SWM are outlined in Table 1.

Demographic and baseline pre-operative data for the study groups were comparable, and outlined in Table 2. Colorectal cancer was the most common site for primary malignancy, 44/57 (77%), with other extra thoracic metastases from breast, renal, melanoma, testicular, and endometrial origin. LAS was favoured in patients that had previously undergone PME, 9/12 (75%).

Peri-operative results

Operative and resection details are provided in Table 3. The average energy delivered was 26051 ± 466 J over 8 ± 4 min. The average cumulative staple length was 139 ± 87 mm per procedure.

Length of stay was longer in the LAS group, (5.1 vs 2.8 days, $p = 0.0007$). Three patients (11%) in the LAS group suffered a prolonged air leak (defined as > 5 days), which settled spontaneously by day 8. There were no other postoperative complications recorded at Clavien-Dindo grading of II or more. Further information is provided in Table 4.

Table 1 Frequency table for surgical access of LAS and SWM

	Laser-assisted	Stapled	Total
Thoracotomy	23	10	33
VATS	4	20	24
Total	27	30	

Table 2 Patient and baseline clinical characteristics. *Disease-free interval refers to the time between resection of primary malignancy, and detection of metastatic disease

	Laser-assisted (n = 27)	Stapled (n = 30)	P value
Age at metastasectomy, years	62 \pm 12	66 \pm 10	0.1626
Male gender	15 (56%)	19 (63%)	0.5501
Charlson comorbidity index	8.4 \pm 1.3	8.7 \pm 1.3	0.5356
<i>Primary malignancy</i>			
Breast	2 (7%)	2 (7%)	0.3112
Colorectal	23 (85%)	21 (70%)	
Endometrial	0 (0%)	2 (7%)	
Melanoma	1 (4%)	3 (10%)	
Renal	0 (0%)	2 (7%)	
Testicular	1 (4%)	0 (0%)	
Disease-free interval*, months	29 \pm 23	35 \pm 34	0.4372
Bilateral pulmonary lesions	8 (30%)	8 (27%)	0.8037
Extrathoracic metastases	8 (30%)	14 (47%)	0.1871
Previous ipsilateral procedure	9 (33%)	3 (10%)	0.0310*

* $p < 0.05$

Follow-up results

There was no peri-operative or 90-day mortality. Fourteen patients died within the follow-up period, yielding a 2-year survival of 74%.

Patient-centred outcome measures

Routine follow-up letters at 3 months and 1 year were evaluated for the presence of pain, dyspnoea and whether the patient had returned back to their usual activities of daily living. Comparison of the LAS and SWM groups respectively, revealed no difference in dyspnoea (2/27 vs 1/29, $p = 0.5109$ and 0/17 vs 1/22, $p = 0.3590$), pain (7/27 vs 8/29, $p = 0.8885$ and 2/17 vs 1/22, $p = 0.4218$), or failure to return to activities of daily living (5/27 vs 3/29, $p = 0.3824$ and 2/17 vs 4/22, $p = 0.5250$). This data is presented in Table 5.

Thoracotomy vs thoracoscopy

Procedures performed via thoracotomy were associated with a longer chest drain duration (2.6 ± 1.9 days vs 1.5 ± 0.9 days, $p = 0.018$), and subsequently postoperative hospital stay, (4.8 ± 3.2 days vs 2.6 ± 1.0 days, $p = 0.0017$).

There was statistical difference in operative time between procedures performed by thoracotomy and thoracoscopy (88 ± 35 vs 56 ± 26 min, $p = 0.0005$), and

Table 3 Operative characteristics

	Laser-Assisted (n = 27)	Stapled (n = 30)	P value
Right-sided procedure	15 (56%)	14 (47%)	0.5027
Thoracotomy	23 (85%)	10 (33%)	< 0.0001***
Number of lesions resected	1.9 ± 0.9	1.3 ± 0.9	0.0235*
Operative time, min	83 ± 22	67 ± 43	0.1020
Lesion volume, cm ³	4.2 ± 5.4	3.1 ± 4.0	0.3827
Volume of lung resected, cm ³	24.6 ± 36.2	55.2 ± 42.1	0.0084**
Resection: lesion volume ratio	27.4 ± 60.3	91.1 ± 145.4	0.0587
Clear resection margins at histology	11 (41%)	29 (97%)	< 0.0001***

p* < 0.05*p* < 0.005****p* < 0.0005**Table 4** Postoperative recovery

	Laser-assisted (n = 27)	Stapled (n = 30)	P value
Chest tube duration, days	2.7 ± 2.1	1.6 ± 0.7	0.008*
Postoperative length of stay, days	5.1 ± 3.4	2.8 ± 1.1	0.0007**
Recurrence at metastasectomy site	0 (0%)	1 (3%)	0.3385

*Recurrence at metastasectomy site refers to radiological evidence of recurrence during the follow-up period (11 ± 6 months)

p* < 0.05*p* < 0.005****p* < 0.0005**Table 5** Short- and medium-term patient-centred outcomes

	Laser-assisted	Stapled	P value
Dyspnoea at 3 months	2/27 (7%)	1/29 (3%)	0.5109
Dyspnoea at 1 year	0/17 (0%)	1/22 (6%)	0.3590
Surgical-site pain at 3 months	7/27 (26%)	8/29 (28%)	0.8885
Surgical-site pain at 1 year	2/17 (15%)	1/22 (6%)	0.4218
Failure to return to activities of daily living at 3 months	5/27 (19%)	3/29 (10%)	0.3824
Failure to return to activities of daily living at 1 year	2/17 (15%)	4/22 (25%)	0.5250

p* < 0.05*p* < 0.005****p* < 0.0005

the number of lesions resected (1.8 ± 1.1 vs 1.1 ± 0.4 , $p = 0.005$) by either approach.

Peripheral lesions vs central lesions

LAS was preferred to SWM for use in those procedures with central lesions, (20/27 vs 5/30, $p = 0.0027$).

A parenchymal sparing approach for pulmonary metastasectomy?

Patients in the LAS group had a smaller volume of lung parenchyma resected (55.2 ± 42.1 cm³ vs 24.6 ± 36.2 cm³, $p = 0.0084$) and with a lower incidence of

clear histological marginal resection (11/27 vs 29/30, $p < 0.0001$), but no difference in morbidity at 2-year follow-up.

LAS was also the choice of procedure in patients requiring repeated metastasectomy, with 9/27 in the LAS group being a 'redo' procedure, compared to 3/30 in the SWM group, $p = 0.031$.

A learning curve for new technology?

There was no difference in the frequency of metastasectomy performed by LAS between the first and last 4 months of our study, 4/9 (44%) vs 2/7 (29%), p

= 0.5153. Chest drain duration (2.7 ± 2.8 vs 3.0 ± 2.2 days, $p = 0.8369$) and length of postoperative hospital stay (5.7 ± 5.5 vs 6.3 ± 3.7 , $p = 0.8225$) were similar between LAS procedures performed in the first and last 4 months.

There was also no significant demonstrable relationship between increasing surgeon experience with the technology and a reduction in operative time ($r = -0.126$, 95% CI -0.483 to 0.267 , $p = 0.5320$), or in laser energy usage per lesion resected ($r = +0.258$, 95% CI -0.135 to 0.581 , $p = 0.1942$).

Cost analysis

The average procedural cost of consumables was £35.54 \pm 47.71 in the LAS group, versus £488.46 \pm 253.37 for SWM ($p < 0.0001$).

The cost for LAS was significantly higher when approached by VATS (£147.81 vs £16.01, $p = 0.0003$), due to differences in the laser single-use equipment required.

Total hospitalisation cost was calculated per patient using 2018/2019 NHS tariffs, and remained comparable between LAS and SWM groups, (£6408 vs £6220, $p = 0.5700$).

Discussion

Pulmonary metastasis is a frequent manifestation of solid lung tumours. Successful metastatic spread relies on a cascade of sequential steps from a primary site to a distant location. Complex interactions between tumour and host cells in the metastatic niche, make residual micro-metastatic deposits at the time of surgical resection of any overt disease not reliably predictable. Clinically, this means that effective management of metastases focuses on prolonging progression-free survival as opposed to curative intentions [20].

Various clinically measurable factors have predictive validity for medium to long term outcomes following metastasectomy, and may be considered with caution in guiding patient selection for, and informing the prognosis following PME. These include the primary tumour type, disease free interval, lymph node status, and serum tumour marker levels; as well as the completeness of resection [7, 21].

Detailed histological analysis of resected pulmonary metastases from colorectal primaries reveals variable degrees of interstitial growth, inflammatory infiltration and lymphangitic spread from macrometastatic deposits. Ninety-four percent of metastases in the study were also characterised by satellite cells, located up to 6.4 mm (median 0.7 mm) away from the macroscopic lesion's surface [22]. This provides a biological basis to guide acceptable intraoperative margins; which may be

further augmented by other techniques including cytologic analysis of intraoperative lavage of the resection margin that have not widely entered routine practice [23]. Additionally, the fate and significance of any residual satellite tumour cells following resection remains uncertain.

The location of the lesion within the lung, its depth and relation to critical structures has a significant influence on the approach, shape and volume of a traditional wedge resection; and may result in sacrificing excess healthy parenchyma especially for centrally located lesions. The use of thermal dissection allows for better parenchymal preservation, by more-accurately mimicking the contour of any lesion.

The volume of parenchyma spared by this method has not previously been quantified. In our study, stapled wedge parenchymal resections were on average four times larger by volume than laser resections, despite similar lesion sizes across the two groups. There is no evidence of improved residual pulmonary function or lower rates of respiratory symptomatology as a result of parenchymal sparing to this degree.

Diathermy resection, however, leaves residual charred and friable tissue surfaces on the lung, with a variable depth of coagulation to around 0.5 mm [24]. Conversely, the 1318 nm Nd:Yag laser offers more precise cutting, with less thermal spread through adjacent tissues, and a more consistent vaporisation and depth of coagulation of the remaining surface [25]. Tissue vaporisation and coagulation does create some uncertainty in the interpretation of the volume of lung resected and resection margins, by virtue of tissue contraction in response to thermal injury.

This is in fact clinically correlated in our study, and others before it, with a significantly higher rate of histologically 'positive margins' noted with LAS [18, 19]. Our current data shows no evidence of early to mid-term recurrence in those patients in whom complete resection could not be confirmed histologically.

In contrast to other larger series from centres with well-established laser PME programmes, our study demonstrates what we believe to be the first outcome data on this topic in the literature from the United Kingdom; and outlines an excellent safety profile for the introductory period of this technology into clinical practice. This, from both a logistical point of view including operative time, and in terms of morbidity and patient recovery.

We have similarly shown that there is no demonstrable learning curve in terms of operative efficiency and laser energy usage as a proxy for appropriate tissue handling and preservation, in our cohort.

A higher proportion of our LAS metastasectomies were performed via thoracotomy, when compared to the SWM group; although our preliminary experience with VATS laser resection does correspond with that of Meyer and colleagues, who report on the feasibility of VATS Laser Pulmonary Metastasectomy, with a good intraoperative safety profile, and good early oncologic outcomes [26].

We note the ongoing debate with regards to the validity of VATS as an approach to PME of any resection type, due to limitation of systematic palpation of the lung for radiologically undetected lesions [27–30]. This is contextualised by improvements in radiologic and thoracoscopic imaging in recent years, and reiteration of the uncertainty with regards to the fate of residual micrometastases.

Additionally, in our cohort, there was no difference in recovery, symptomatology, or return to activities of daily living at 3 months or 1 year from operation between patients operated by thoracotomy or VATS. This reinforces an acceptability and role for both in clinical practice.

Our study demonstrates that there is a role for both LAS and SWM within pulmonary metastasectomy practice. Further studies are required to determine tailored indications for each approach.

Limitations

Our study is limited by having only a small cohort of patients, operated on at a single centre and with limited follow-up. The choice between LAS and SWM was made by the operating surgeon on an individual-patient basis, whilst we can gauge which factors informed surgeon preference, there was no set criteria. Although there was no significant difference in operative time between the LAS and SWM, there was between thoracotomy and VATS. Due to the retrospective nature of our study, we are unable to separate procedural time from that spent on the surgical approach. Patients undergoing open procedures were offered epidural anaesthesia, resulting in a longer duration of monitoring as per local policy—additional contributing factors for a prolonged hospital stay. In addition, we are unable to objectively comment on post-resection lung function in our patient group.

Our data demonstrates that the per-procedure cost is lower when performing LAS; being around 10% of the consumable costs associated with SWM. This is implicitly more significant where multiple lesions require resection. Capital investment and servicing fees are not included in our financial analysis, particularly as the device has multiple applications other than pulmonary metastasectomy, and such indirect costs would need to be apportioned across services as appropriate. Total

hospitalisation costs are calculated based on NHS tariffs and therefore limited to a UK population.

Conclusions

Laser-assisted pulmonary metastasectomy presents a safe and acceptable alternative to traditional stapled wedge resection, with no impact on process or patient outcome associated with its introduction to a new centre by an experienced surgeon. We additionally demonstrate tangible parenchymal sparing, at a reduced direct procedural cost by adoption of this technique but no difference in overall cost of hospitalisation.

Abbreviations

PME: Pulmonary metastasectomy; LAS: Laser-assisted surgery; SWM: Stapled wedge metastasectomy; MD: Measurement difference; RFA: Radiofrequency ablation; MWA: Microwave ablation; SABR: Stereotactic ablative radiotherapy; PulMiCC: Pulmonary metastasectomy in colorectal cancer; VATS: Video-assisted thoracic surgery; MDT: Multidisciplinary team meeting; CT: Computed tomography; NIPAG: New Interventional Procedures Advisory Group.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s43057-022-00088-1>.

Additional file 1. Video demonstrating left thoracotomy and laser metastasectomy of upper and lower lobe nodules.

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None

Authors' contributions

All authors were involved in planning and methodology of this research. KC and HW curated study data, from which EJC performed statistical analysis. KC and EJC were involved in writing the original draft. SR and AN provided project administration and supervision. All authors reviewed and edited the final draft of this research paper. The author(s) read and approved the final manuscript.

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Availability of data and materials

Available upon request

Declarations

Ethics approval and consent to participate

This study reports on a clinical evaluation audit governed by the New and Innovative Procedures Approval Group (NIPAG) at our institution and was deemed not to require additional ethical approval.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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