Review Article

Minimally invasive metastasectomy for skin and soft tissue malignancies: sarcomas, melanoma, and breast cancer: a narrative review

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Background and Objective: Pulmonary metastasectomy (PM) is a thoracic surgery operation in which metastatic disease is surgically resected from the lung. Traditionally, PM has been performed via thoracotomy, to allow surgeons to manually palpate the lung and detect additional disease not detected on preoperative imaging. However, the contemporary widespread use of minimally invasive thoracic surgery raises additional questions about the suitability of a minimally invasive approach. In this narrative review, we cover the relevant considerations of minimally invasive PM for soft tissue sarcoma, breast cancer, and melanoma.

Methods: A literature review was conducted using the PubMed/MEDLINE database including all relevant articles through March 2023. Articles were reviewed for relevance by the authors. There were no restrictions on type of study included.

Key Content and Findings: Preoperative, intraoperative, and postoperative considerations for a minimally invasive approach to PM for soft tissue sarcoma, breast cancer, and melanoma are summarized in this review. Wedge resection was the most common type of resection for all three malignancies. The role of lymph node dissection or sampling remains controversial and underreported in the literature. No studies were identified that demonstrated inferior overall survival or disease-free survival with minimally invasive PM for these malignancies.

Conclusions: For soft tissue sarcoma, breast cancer, and melanoma, a minimally invasive approach to PM is likely appropriate for select patients. Studies focusing on PM in the setting of breast cancer and melanoma are particularly limited and additional reports would be of great benefit to the literature.

Keywords: Sarcoma; breast cancer; melanoma; metastasectomy; minimally invasive thoracic surgery

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Introduction

Background

Pulmonary metastasectomy (PM) is the surgical removal of metastatic disease from the lung. The lungs are a frequent site of metastasis for many different cancers, in part due to their large surface area and blood supply (1). These cancers include, but are not limited to, colorectal cancer, renal cell carcinoma, sarcoma (both soft tissue and osteosarcoma), breast cancer, melanoma, and various head and neck malignancies (2). Patients who are to undergo PM should be carefully selected. There are four generally agreed upon criteria for any patient to undergo PM; these are as follows: (I) the patient is a suitable surgical candidate with appropriate surgical risk. (II) The primary tumor is either controlled or controllable. (III) There are no extrathoracic metastases, and if there are, they should be controllable with either surgery, or another effective treatment such as radiation. (IV) Complete resection of pulmonary metastases is thought to be possible (1,2).

Rationale and knowledge gap

If patients fulfill these criteria and are selected to undergo PM, there are disease-specific factors that should be considered. However, there are few studies that examine the role of PM for these malignancies. Additionally, much of the literature on PM for these malignancies focuses on a traditional approach via thoracotomy. There is limited data regarding a minimally invasive approach, which is particularly relevant in the contemporary era of minimally invasive thoracic surgery.

Objective

In this narrative review, we cover the important preoperative, intraoperative, and postoperative considerations of PM in the setting of soft tissue sarcoma, breast cancer, and melanoma. When possible, we attempt to highlight topics relevant to a minimally invasive approach to PM for these malignancies. We present this article in accordance with the Narrative Review reporting checklist (available at https://vats.amegroups.com/article/view/10.21037/vats-23-46/rc).

Methods

A literature review was conducted using the PubMed/MEDLINE database in March 2023. Various search terms were used, such as "minimally invasive metastasectomy", "pulmonary metastasectomy", or "VATS", along with the Boolean operator AND, followed by "sarcoma", "breast cancer", or "melanoma". Articles were reviewed for relevance by the authors (BAP and MWM). All relevant articles published either in English or articles with a full English translation available were included. There were no date restrictions, nor were there restrictions on type of study included (*Table 1*).

Soft tissue sarcomas

Background

Sarcomas are tumors derived from embryonic mesoderm and are known to frequently metastasize to the lungs (3). PM for soft tissue sarcoma is common, accounting for 751 out of 5,206 cases (14.4%) in the International Registry of Lung Metastasis (2,4). When considering soft-tissue sarcomas, rates of pulmonary metastasis may be as high as 40% (5). A systematic review including 1,004 patients who underwent PM for soft tissue sarcoma identified leiomyosarcoma, malignant fibrous histiocytoma and synovial sarcoma as the most commonly resected subtypes (6). Multiple studies have demonstrated improved survival in patients who undergo PM for soft tissue sarcoma compared to nonsurgical management (7-9). According to the National Comprehensive Cancer Network (NCCN) clinical practice guidelines for soft tissue sarcoma, resection for metastatic disease should be considered if the primary tumor is able to be controlled (10).

Preoperative considerations

It is important to identify patients who will benefit from PM for soft tissue sarcoma. In addition to the four main criteria generally agreed upon for metastasectomy (2), there have been several prognostic factors identified specific to soft tissue sarcomas. A longer disease-free interval (DFI) prior to surgery has been associated with prolonged survival with many studies reporting increased survival with a DFI of at least 1 year (11-15). Several studies exist that demonstrate a larger number of resected nodules portends a worse prognosis, with Casson *et al.* observing improved survival in patients with fewer than 3 nodules resected and Putnam *et al.* observing improved survival in patients with fewer than 4 nodules resected (14,16,17). However, even in patients with a large number of nodules resected, the ability

Table 1 Review methodology

Items	Specification
Date of search	March 1st 2023
Databases and other sources searched	PubMed/MEDLINE
Search terms used	Combinations of relevant search terms such including: "minimally invasive metastasectomy", "pulmonary metastasectomy", "VATS", "sarcoma", "breast cancer", "melanoma". Reference lists of articles were manually reviewed for articles not identified in initial search
Timeframe	No date restriction
Inclusion and exclusion criteria	Inclusion criteria: English. Studies reporting on minimally invasive approaches to pulmonary metastasectomy
	Exclusion criteria: No full English translation available
Selection process	Articles reviewed and selected by B.A.P. and M.W.M.

VATS, video-assisted thoracic surgery.

to completely resect the nodules is still a better predictor of survival (18). The presence of bilateral metastases has not been demonstrated to have any effect on survival (14). Patients with leiomyosarcoma may benefit more from PM compared with other subtypes of soft tissue sarcoma (14).

Intraoperative considerations

Open versus minimally invasive approach

Regarding operative approach, patients may be good candidates for minimally invasive resection if they have few metastases, smaller lesions (<30 mm), peripheral lesions, and a longer DFI (19-21). Studies directly comparing minimally invasive and open approaches for PM in soft tissue sarcoma patients are limited. In a nearly 23-year retrospective review of 539 patients who underwent PM for soft tissue sarcoma, 156 (29%) underwent minimally invasive resection (11). Unsurprisingly, the percentage of minimally invasive resections drastically increased over the course of the study period. There were no differences observed in rate of R0 resection or risk of recurrence between minimally invasive and open approaches. Interestingly, in a multivariable analysis of overall survival, minimally invasive resection was associated with a decreased risk of death compared to an open approach (11). Lin *et al.* also observed increased overall survival with a minimally invasive approach (22). However, in both studies, the observed increase in overall survival was partially attributed to patient selection bias (11,22).

There are other retrospective studies that have not observed any survival benefit of minimally invasive PM for soft tissue sarcoma. Reza *et al.* detailed 118 patients over 13 years who underwent complete R0 resection (23). Of these 118 patients, 44 (37.3%) underwent PM via a video-assisted thoracic surgery (VATS) approach with no observed difference in overall survival compared with an open approach (23). In a similar retrospective review of 48 patients by Predina and colleagues, 13 (27.1%) underwent a VATS procedure. Again, there were no differences observed in overall survival or disease-free survival (24). Notably, none of the aforementioned studies were designed to specifically compare VATS and minimally invasive approaches and this is a topic that warrants further investigation. However, from the body of evidence available, it does seem that a minimally invasive approach is appropriate when complete resection is feasible as no studies demonstrated inferior outcomes with a minimally invasive approach.

Metastatic lung lesions for soft tissue sarcoma are often small. Though computed tomography (CT) imaging has improved significantly with cuts as small as 1 mm used regularly, up to 37% of patients still have lesions discovered during surgery that were not noted on imaging (25). Therefore, manual lung palpation with an open approach has been historically preferred to assist in detection and resection of unknown metastatic disease (21,26,27). Given the concern regarding the inability to palpate the lung with minimally invasive approaches, there have been techniques described to help discover occult metastatic disease. Reza *et al.* in their 13-year series of PM for sarcoma developed a modified VATS technique where nearly all lung parenchyma could be brought into contact with the surgeon's finger through one of the VATS port incisions, allowing for detection of lesions as small as 1 mm. Using this technique,

they did not observe any difference in mean number of lesions detected or mean number of lesions <1 cm that were resected when comparing VATS and open approaches (23).

More recently, intraoperative molecular imaging has been demonstrated to be a promising approach for detection of occult pulmonary lesions from sarcoma. In this technique, near infrared tracers are injected into the patient which then target occult pulmonary metastases. The occult metastatic lesions can then be visualized intraoperatively using near infrared cameras, with a high rate of success (28). Though further investigation is needed, the use of near infrared technology for detection of occult pulmonary malignancy is a natural fit with minimally invasive surgery, during which near infrared imaging is already routinely used.

Extent of pulmonary resection

The extent of pulmonary resection should be a balance between chance of achieving R0 resection while at the same time preserving as much lung function as possible. Many studies report high prevalence of wedge resection for pulmonary sarcoma metastases, which makes sense given that many sarcoma metastases occur in the lung periphery (3,11,19,29-31). For large or centrally located metastases, more extensive lung resection (segmentectomy, lobectomy, or pneumonectomy) may be required (30,32). A consensus has not been agreed upon regarding adequate margins for sarcoma-related PM (30). However, a surgical margin to nodule size ratio of greater than or equal to 1 has been shown to be associated with increased disease-free and overall survival (33). Therefore, similar to primary lung malignancy, if possible, a margin of at least 10–20 mm should be taken (34).

Role of lymph node sampling and dissection

Lymph node metastasis of sarcomas are rare. In a 10-year review of a prospective sarcoma database only 2.6% of sarcomas were found to have lymph node metastases (35). This is consistent with findings from the International Registry of Lung Metastases, which also reported a 2% rate of mediastinal or hilar lymph node involvement (4). Gafencu *et al.* recently published a 20-year single-center retrospective study of 327 patients who underwent PM for sarcoma. In this cohort, 122 patients underwent lymphadenectomy, of which only 6 had positive lymph nodes (4.9%). Lymph node involvement did not impact survival (29). In a smaller study of 139 patients who underwent PM, only one out of 17 metastasectomies for sarcoma (5.9%) had positive lymph node involvement (32). Given the low occurrence of lymph node involvement with sarcomas, and that even with lymph node involvement clinical management is unlikely to be altered, the value of lymphadenectomy for sarcomas is limited and not routinely recommended (3,21).

Postoperative considerations

According to the NCNN guidelines, patients should undergo follow-up imaging every 3–6 months for 2–3 years, every 6 months for the subsequent 2 years, and then annually (10). Many patients with sarcoma metastases to the lungs will require repeat operation, which may be facilitated by a minimally invasive approach (21). In a Kim *et al.* study, 33% of patients who underwent metastasectomy for sarcoma required reoperation (19). Notably, there is still a survival benefit for patients who undergo repeat metastasectomy for sarcoma, as 30–40% of patients who require reoperation will survive an additional 5 years (3,36).

Summary

A minimally invasive approach to PM for soft tissue sarcoma is reasonable for patients with small tumors that are peripherally located. There does not appear to be a significant difference in overall survival or disease-free survival rates between minimally invasive and open PM for soft tissue sarcoma. Though minimally invasive approaches historically have not allowed for manual palpation of the lung to detect small metastases not visualized on preoperative imaging, techniques have been described that may alleviate this limitation. Additionally, a minimally invasive approach may allow for easier future reoperation, which is frequently required for sarcoma metastases. When considering extent of resection, wedge resection is reasonable for most patients, given that R0 resection is feasible. For patients with larger or centrally located disease, more extensive lung resection may be required. Patients who undergo PM for sarcoma require close radiologic follow-up to quickly detect subsequent metastatic disease.

Breast cancer

Background

Breast cancer is the most commonly diagnosed cancer in the United States and accounts for almost one third of all cancer diagnoses in women (37). Approximately 5–10% of cases involve distant metastases at time of diagnosis and

30% of patients experience recurrence (38). In a large, retrospective study of over 1,000 patients with metastatic breast cancer, 17.7% of cases involved the lung (39). In the International Registry of Lung Metastasis, breast cancer accounted for 396 out of 5,206 (7.6%) of cases (2,4). Prior to the advent of endobronchial ultrasound (EBUS) guided biopsy and CT guided biopsy, PM for breast cancer had a dual purpose of being both diagnostic and therapeutic (40). However, with the current widespread availability of these techniques for diagnosis, the purpose of PM for breast cancer has shifted towards a therapeutic intent (40).

Preoperative considerations

The standard of care for treatment of metastatic breast cancer is systemic therapy (38,41). However, in select patients with a limited number of metastatic lung lesions, there may be a role for metastasectomy (38,42). One of the most important preoperative considerations in patients with a lung nodule in the setting of prior breast cancer is to determine whether the nodule represents a metastasis or a primary lung tumor. In patients with breast cancer and a newly discovered lung nodule, it can be difficult to distinguish between the two based on imaging characteristics alone, and therefore tissue diagnosis via biopsy should be obtained prior to surgery (42).

Several prognostic factors have been identified for patient survival following PM for breast cancer. Most patients included in studies examining PM for breast cancer had fewer than 4 pulmonary metastases. Consistently, there was better overall survival observed in patients with fewer than 4 metastases, compared with 4 or more (43). A meta-analysis including 1,937 patients identified several positive prognostic factors for patients with breast cancer undergoing PM that included a DFI greater than 3 years, complete resection of metastases, presence of a single pulmonary metastasis, and hormone receptor positive disease (44). In this study, the 5-year overall survival rate was 46% (44). In comparison, a case series of patients with breast cancer metastases limited to the lung managed with chemotherapy alone observed a survival rate of 16% (45). However, this large difference in survival rates may be confounded by criteria for surgical eligibility, such as a high functional status. In a large, multi-institution retrospective analysis of 253 patients who underwent PM for breast cancer, again, DFI greater than 3 years and complete resection were also identified as positive prognostic factors. Larger tumor size was found to correspond with worse survival (46). However, this may reflect increased difficulty of complete resection with larger tumor size.

Intraoperative considerations

Open versus minimally invasive approach

Very few studies exist that report specifically on minimally invasive PM for breast cancer and no studies exist that directly compare an open versus minimally invasive approach. In studies that compare minimally invasive and open approaches for PM with mixed tumor types, representation of breast cancer patients is too small to draw any meaningful conclusions. This is a significant gap in the literature.

In a Chen *et al.* study of 41 patients who underwent PM for breast cancer, 14 patients underwent resection via a VATS approach. There was no significant difference in a univariate analysis of 5-year overall survival compared with the patients in their study who underwent resection via thoracotomy (47). In an analysis of breast cancer patients from the International Registry of Lung Metastasis, only 4% (n=17) patients underwent resection via a thoracoscopic approach, and they did not observe any difference in survival with respect to operative approach (48). Of note, the data set used in this study included patients who underwent resection from 1960–1994, and since then, minimally invasive thoracic surgery has become much more widespread. In a 13-year case series of patients with a solitary lung nodule in the setting of breast cancer, Rena *et al.* performed VATS lung resection in 33/79 (41%) of cases (49). They suggested that VATS is an acceptable approach for tumors that are peripherally located. Outcomes and survival with respect to operative approach were not compared in this study. Similarly, in a Meimarakis *et al.* study examining PM in 81 breast cancer patients, the authors shared that for peripherally located nodules, thoracoscopy was used. However, specific outcomes from this group were not reported (50).

Extent of pulmonary resection

In an analysis of metastasectomy for breast cancer in the International Registry of Lung Metastases, wedge or segmental resections were performed for 73% of resections. Patients who underwent wedge resection had a 5-year survival rate of 40% and median survival rate of 42 months. Notably, there was no significant difference in 5-year survival rates or median survival observed between type of resection (48). Similar to PM for other malignancy,

lobectomy or more extensive resection may be required if the tumor is not amenable to complete resection via wedge resection (38,51). There are no specific margin guidelines for breast cancer metastases. However, for other pulmonary metastases, a margin of 10–20 mm has been recommended with wedge resection (52).

Role of lymph node sampling and dissection

Thoracic lymph node involvement is common in patients with thoracic metastases of breast cancer, with rates as high as 39% (38,53). However, the role of mediastinal lymph node dissection and/or sampling during PM for breast cancer remains underreported in the literature. According to the Society of Thoracic Surgeons (STS) Expert Consensus Document on Pulmonary Metastasectomy, mediastinal lymph node metastases in the setting of pulmonary metastases from breast cancer may be associated with decreased survival (51). Importantly, these lymph node metastases are frequently overlooked with preoperative imaging. In a Seebacher *et al.* study, unexpected lymph node involvement was found in 35.5% of breast cancer patients who underwent PM (54). Notably, however, in a retrospective of 81 patients where lymph node involvement was associated on univariate analysis with worsened survival (median survival with lymph node involvement 32.1 months, no lymph node involvement 103.4 months, P=0.095), the performance of lymph node dissection itself was not associated with survival (50). Therefore, though mediastinal lymph node dissection and/or sampling likely does not alter survival, it may be worthwhile to perform in order to further define patient prognosis.

Postoperative considerations

Re-examination of tumor receptor status should be performed after resection via immunohistochemistry, since metastases may exhibit different tumor characteristics than the primary breast tumor (55). Patients require close imaging follow-up with CT scans with a suggested interval of every 6 months for the first 2 years, and then every year for at least 5 years (42,56). In the International Registry of Lung Metastasis, there were 19 patients (4.8%) who underwent initial complete resection of pulmonary breast cancer metastases and subsequently underwent a second resection for additional metastatic disease. In these patients, there was a 53% 5-year survival rate, suggesting that repeat PM may be effective in select patients (48).

Summary

Though the mainstay of treatment for stage IV breast cancer is systemic therapy, there may be a benefit to PM for patients with a small number of pulmonary metastases (<4) that are completely resectable in the setting of a longer DFI. Patients with hormone receptor positive tumors may experience more of a survival benefit following PM for breast cancer. The data surrounding minimally invasive PM for breast cancer is much less robust than other malignancies, but outcomes and survival appear to be similar. Wedge resection is appropriate, given that R0 resection is feasible. Lymph node dissection and/or sampling may not provide a survival benefit but can potentially offer additional data regarding prognosis and therefore should be considered for these patients. Postoperatively, patients require close radiologic follow-up and should continue to follow with a medical oncologist.

Melanoma

Background

Melanomas are tumors derived from melanocytes, the melanin-producing cells in the skin. Though melanomas account for only 4% of skin cancers, they are responsible for 75% of skin-cancer related deaths (57). Approximately 4% of melanomas are stage IV with distant metastases at the time of diagnosis, and as high as 40% of metastatic melanoma cases involve the lung parenchyma (58,59). In selected patients, there is a demonstrated survival benefit with PM (60). In the International Registry of Lung Metastasis, PM for melanoma comprised 282 of 5,206 cases (5.4%) (2,4). The role of surgical intervention for pulmonary metastases from melanoma is still evolving as treatments for metastatic melanoma continue to improve (59).

Preoperative considerations

Unfortunately, prognosis for patients with metastatic melanoma is quite poor, with 5-year survival rates of 3–6% and an estimated median survival of 7.5 months in the absence of surgical intervention (59,61,62). However, in selected patients who undergo successful PM, 5-year survival rates have been reported as high as 35.1% with a median survival of 18.3 months (59,63). Several prognostic factors have been associated with worse

survival after PM including a shorter DFI, evidence of extrathoracic metastases, and larger number of pulmonary nodules (4,61,64,65). Patients who have not responded well to systemic therapy are also less likely to benefit from metastasectomy (66). There has been a significant survival benefit associated with utilizing positron emission tomography (PET) scan prior to metastasectomy to exclude additional metastatic disease compared with CT imaging, thus preoperative PET scan should be performed in these patients (67-69).

Pathologic findings may help in determining prognosis, as Petersen *et al.* observed worse survival in patients with a nodular histologic subtype of melanoma (61). Tumor doubling time has also been associated with survival rates. In a study by Ollila *et al.*, melanomas with a tumor doubling time of greater than 60 days were associated with a 5-year survival of 20.7% and median survival of 29.2 months. However, in patients with a tumor doubling time of less than 60 days, the median survival was 16.0 months with a 5-year survival of 0%. Thus, they recommended that PM not be performed if the tumor doubling time cannot be increased to over 60 days with systemic therapy (70). Notably, this study was performed in the late 1990s, prior to the emergence of newer therapies such a cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and programmed cell death-1 (PD-1) checkpoint inhibitors. Therefore, reexamination of this association in the current treatment era may be of benefit.

In summary, patients with melanoma should be considered for PM if they have a longer DFI (>1 year), fewer than 3 completely resectable pulmonary nodules, no evidence of extra-thoracic metastases or lymph node involvement, a tumor doubling time of greater than 60 days, and favorable response to systemic therapy (60). Surgeons should work in close collaboration with medical oncologists to determine the role of neoadjuvant or adjuvant therapy.

Intraoperative considerations

Open versus minimally invasive approach

Similar to other pulmonary metastatic disease, the debate regarding efficacy of minimally invasive PM for melanoma is centered around the inability to detect occult malignancy via manual lung palpation. Andrews *et al.* suggested that thoracoscopic PM for melanoma may be acceptable given that the patients underwent high-resolution chest CT prior to surgery and that the patient had fewer than 3 small peripheral nodules (71). Unfortunately, with pulmonary metastatic melanoma, there are no studies directly comparing a minimally invasive and open approach for resection, and much of the conclusions regarding the results of a minimally invasive approach must be drawn from subsets of larger studies.

In a review of patients included in a large cancer database, Hanna *et al.* reported a high utilization of VATS for PM in melanoma patients. They did not observe any significant differences in rates of positive margins or need for repeat operation when comparing VATS and thoracotomy. Overall and disease-free survival between the two approaches was not reported (72). Leo *et al.* did not observe any impact of surgical approach on survival. However, this study only included 7 patients (2.1%) who underwent thoracoscopic resection, likely limiting the ability to detect any differences between the two approaches (65). Though specific outcomes were not reported between the two approaches, Petersen and colleagues no longer prefer an open approach in melanoma patients and utilize a VATS approach. In their approach, they first inspect the visceral and parietal pleura for any evidence of dissemination, and use either the surgeons' finger through the anterior access port or a thoracoscopic Foerster clamp to palpate the lung (61). Studies do exist that directly compare outcomes of minimally invasive and open metastasectomy of various cancer types, but representation of melanoma patients is low and conclusions are difficult to make that are specific to this subset of patients (31,73-75). A study specifically examining outcomes of minimally invasive PM for melanoma in the current era of high-resolution imaging would be of great benefit to the literature.

Extent of pulmonary resection

Similar to PM for other malignancies, the extent of pulmonary resection should be decided by the ability to achieve R0 resection while preserving as much functional lung parenchyma as possible. For peripheral nodules, wedge resection is likely sufficient, while for larger or centrally located nodules, more extensive resection such as lobectomy may be necessary. In several large studies of PM for melanoma, wedge resection was the most commonly performed procedure. Petersen *et al.* reported a 66% rate of wedge resection and Hanna *et al.* reported a similar rate of 64.6%. Lobectomy was the next most commonly performed operation performed in both studies with 30% (Petersen *et al.*) and 23.2% (Hanna *et al.*) of patients undergoing

lobectomy (61,72).

Role of lymph node sampling and dissection

Patients that are selected to undergo PM for melanoma usually do not have any preoperative evidence of thoracic lymph node involvement (68). Therefore, the role of thoracic lymph node sampling or dissection for patients with metastatic melanoma is not well documented in the literature. Harpole *et al.* analyzed 945 patients with pulmonary metastatic melanoma and observed worse survival in patients with positive lymph nodes. However, in their analysis, they compared all patients with positive lymph node involvement to all patients without, regardless of whether the patients underwent PM (64). Thus, it does not address the question of whether or nodal involvement is a useful prognostic factor for surgical patients. Studies that directly address this question are limited and contradictory.

In a subset analysis of patients with surgically resected pulmonary melanoma metastases in the International Registry of Lung Metastases, nodal involvement did not impact overall survival (65). However, in a separate study of melanoma patients undergoing PM, Chua *et al.* observed a trend-level difference in survival, with patients who had no nodal involvement surviving a median of 27 months after surgical resection versus 16 months in those who did have positive nodes (P=0.074) (68). From their experience, the approach followed by Chua *et al.* is to perform lymph node sampling with intraoperative frozen section analysis on patients with noted bulky lymph nodes (either intraoperatively or preoperative imaging), and if positive, perform a complete lymph node dissection (68). Other surgeons prefer to be more aggressive with lymph node sampling, with an approach similar to lung resections for primary lung cancer; the rationale being that incidental discovery of lymph node involvement has been shown to portend worse survival in colorectal cancer and renal cell cancer (67). No approach has been demonstrated to be superior in terms of survival, and future studies should work to better describe their experience with lymph node sampling and dissection in patients undergoing PM for metastatic melanoma.

Postoperative considerations

Disease recurrence rates have been observed to be as high as 63.8% and therefore patients should receive a new baseline CT immediately following surgery (65,67). Petersen *et al.* observed a 5% rate of repeat metastasectomy, but no significant difference in survival between patients who underwent single versus repeat metastasectomy (61). Leo *et al.* observed a 19% 5-year survival rate in patients who underwent repeat metastasectomy for intra-thoracic disease recurrence alone (65). Thus, repeat metastasectomy is not absolutely contraindicated, given that the subsequent metastases are limited to the thorax and amenable to resection. Patients should continue close follow-up with a medical oncologist to determine the role for any adjuvant therapy.

Summary

PM for melanoma patients should be considered in patients with a small number (fewer than 3) of completely resectable pulmonary nodules, no evidence of extrathoracic disease or lymph node metastases, a DFI of greater than 1 year, and a demonstrated response to systemic therapy. Tumor doubling time of greater than 60 days is also a favorable prognostic indicator. Minimally invasive resection is reasonable in patients who underwent preoperative high-resolution and PET-CT scans, with peripherally located nodules. Wedge resection is acceptable for patients given that complete resection with negative margins is possible. Lymph node sampling and/or dissection is reasonable in order to further define patient prognosis.

Conclusions

For soft tissue sarcoma, breast cancer, and melanoma, a minimally invasive approach to PM is likely appropriate for select patients. Several studies for all three groups of malignancy suggest that minimally invasive PM is acceptable for small, peripherally located tumors. No studies were identified that demonstrated inferior overall survival or disease-free survival with a minimally invasive approach. The most common type of resection for all three malignancies was wedge resection, which is appropriate given that R0 resection is achievable. Larger tumors or those that are centrally located may require more extensive resection, such as segmentectomy or lobectomy. Historically, the common rationale for performing metastasectomy via thoracotomy was that this approach allowed for manual palpation of lung parenchyma by the surgeon. However, techniques have been described with a minimally invasive approach that allow for manual palpation of nearly the entire lung. Additionally, modern improvements in imaging may allow for detection of occult

pulmonary disease that was not previously possible. For all three groups of malignancy, the role of thoracic lymph node dissection and/or sampling remains controversial. When it is performed, it is likely more useful for further defining patient prognosis rather than having any therapeutic effect. Importantly, for soft tissue sarcoma, breast cancer, and melanoma, studies directly comparing the outcomes and efficacy of minimally invasive PM to PM via thoracotomy are limited and often have very small sample sizes. This is a topic worthwhile of future study and any additional reports would be of benefit to the literature.

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Footnote

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