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Review

From Feasibility to Individualization: Surgery for Breast Cancer Liver and Lung Metastases

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Abstract

Surgical resection of liver and lung metastases in breast cancer is increasingly considered a viable option for select patients with oligometastatic disease. Historically regarded as palliative, surgery is now supported by retrospective data suggesting potential survival benefits, particularly in patients with hormone receptor-positive or HER2-positive tumors, long disease-free intervals, and limited metastatic burden. This narrative review summarizes recent evidence on the surgical management of breast cancer metastases to the liver and lung, with a focus on patient selection, perioperative outcomes, and long-term survival. Liver metastasectomy has shown 5-year overall survival rates of up to 60% in well-selected patients, while pulmonary metastasectomy offers comparable outcomes when resection is complete and nodal involvement is absent. Minimally invasive techniques and non-surgical approaches, such as microwave ablation and stereotactic radiotherapy, expand treatment options for patients unfit for surgery. The review also explores emerging tools influencing surgical decision-making, including circulating tumor DNA for minimal residual disease detection, transcriptomic profiling to predict organotropism, and artificial intelligence (AI)-driven platforms that assist with surgical planning and multidisciplinary case evaluation. While prospective validation remains limited, these technologies may help redefine surgical candidacy through biologically informed algorithms. Ultimately, the integration of surgery within a multimodal, personalized treatment strategy – guided by systemic control, tumor biology, and evolving digital tools – represents a promising direction for selected patients with visceral breast cancer metastases.

Keywords: ablation;: artificial intelligence; breast cancer; ctDNA; liver metastases; lung metastases; metastasectomy

1. Introduction

Breast cancer (BC) remains the most diagnosed malignancy among women and is a leading cause of cancer-related mortality globally [Cardoso 2020]. Despite advancements in early detection and systemic therapies – including endocrine treatment, HER2-targeted agents, and immunotherapy – a significant proportion of patients, estimated at 20–30%, will eventually develop distant metastases [Alghamdi 2023, Ueno 2022].

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The most frequently involved metastatic sites are bone, liver, and lung, with visceral metastases generally portending a poorer prognosis than bone-only disease [Cardoso 2020, Hansson 2025]. Liver and lung metastases represent the most common visceral sites of disease spread in metastatic breast cancer (MBC), observed in approximately 15–25% and 10–20% of cases, respectively [Golse 2017, Shien 2025]. The prognosis of patients with these metastases varies depending on tumor subtype, metastatic burden, response to systemic treatment, and disease-free interval. Reported median overall survival (OS) for patients with liver metastases from BC ranges from 27 to 74 months, with 5-year survival rates up to 53% in selected surgical series [Golse 2017, Paiano 2025, Ueno 2022]. For lung metastases, median OS ranges from 20 to 97 months, with 5-year survival reported between 36% and 46% [Ueno 2022, Hansson 2025].

In recent years, the concept of oligometastatic disease – defined as a state of limited metastatic burden, often involving five or fewer lesions – has reshaped clinical decision-making in MBC [Gion 2022, Ueno 2022]. In this context, surgical management of metastases, once considered purely palliative, is now being investigated as a potentially life-prolonging strategy in carefully selected patients. Surgical resection of liver or lung metastases may offer survival benefit, particularly when performed in combination with effective systemic therapies and in the absence of widespread disease [Golse 2017, Orsi 2023, Ueno 2022].

However, evidence supporting metastasectomy in MBC remains largely retrospective and non-randomized, and thus subject to selection bias. Most data derive from observational cohorts or institutional case series, making it difficult to draw definitive conclusions. Nonetheless, several reports have shown encouraging long-term outcomes after resection of liver or lung metastases, especially in patients with hormone receptor-positive or HER2-positive tumors and long disease-free intervals [Shien 2025, Paiano 2025, Liu 2024]. A recent meta-analysis involving over 1,700 patients confirmed significantly lower mortality at 1, 3, and 5 years in surgically treated patients compared to those receiving systemic therapy alone [Calpin 2023]. A nationwide Swedish case-control study reported a median survival of 77 months after liver resection compared to 28 months in patients treated with systemic therapy alone, reinforcing the potential benefit of surgery in well-selected cases [Sundén 2020].

It is also noteworthy that the biological behavior of metastases may differ by histological subtype. Invasive lobular carcinoma, for instance, is more prone to late and atypical metastatic spread, including to the gastrointestinal tract, which may complicate diagnosis and treatment [Peng 2025, Tasci 2024].

Given the frequency and prognostic relevance of liver and lung metastases in MBC, this review aims to provide a critical evaluation of the surgical management of these two metastatic sites. We will focus on recent evidence, discuss the criteria for patient selection, outline surgical outcomes, and consider emerging minimally invasive and ablative strategies. While metastases to bone or brain are clinically important, our review will center on the liver and lung due to their frequency and the growing clinical interest in their local management [Ueno 2022, Zhang 2025].

2. Methods

This article presents a narrative review focusing on the surgical management of liver and lung metastases in patients with breast cancer. The aim was to synthesize and critically appraise recent literature regarding indications, patient selection criteria, surgical outcomes, and the integration of local therapies with systemic treatment in the context of oligometastatic disease.

The literature search was conducted in December 2025 and focused on studies published in English. Databases consulted included PubMed/MEDLINE and Scopus. Search terms included combinations of “breast cancer,” “metastases,” “liver metastases,” “lung metastases,” “metastasectomy,” “surgical resection,” “oligometastatic,” and “local therapy.” Reference lists of relevant articles were also screened to identify additional studies.

Priority was given to studies published in the past 10 years, with particular emphasis on recent work from 2020 onward. Both retrospective and prospective studies were considered, including

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observational cohorts, registry data, case-control studies, randomized trials where available, as well as expert consensus guidelines and meta-analyses. Studies addressing novel or adjunctive local therapies (e.g., ablation, stereotactic body radiotherapy) were included when relevant to the surgical context. Articles were excluded if they did not provide specific data on surgical outcomes, focused solely on non-visceral metastases, or lacked immediate clinical applicability.

This is not a systematic review, and no formal quality assessment or statistical synthesis of data was performed. Instead, the selected references reflect clinically relevant and methodologically robust contributions to the evolving field of metastasis-directed therapy in breast cancer.

3. Liver Metastases

Epidemiology and Clinical Significance

Liver metastases occur in approximately 5–25% of patients with advanced breast cancer and are the third most common site of distant spread after bone and lung [Sundén 2023; Sen 2024]. While some patients present with liver involvement at diagnosis, others develop metachronous metastases months or years after initial treatment [Rahnemaii-Aza 2025]. The prognosis associated with breast cancer liver metastases (BCLM) remains poor, particularly when extrahepatic disease is present, and median OS is frequently reported in the range of 13–30 months [Sundén 2023; Rahnemaii-Aza 2025; Sen 2024]. Compared to bone or lung metastases, liver involvement is associated with a more aggressive clinical course, often reflecting underlying unfavorable tumor biology such as HER2-negative or triple-negative subtypes [Sen 2024].

Biological and Molecular Characteristics

The receptor profile of liver metastases frequently differs from that of the primary tumor. In a population-based analysis, discordance in estrogen receptor (ER), progesterone receptor (PgR), and HER2 status between primary tumors and liver metastases was observed in 17%, 33%, and 10% of cases, respectively [Sundén 2023]. Subtype conversion occurred in 21% of patients, often resulting in a more aggressive phenotype. Importantly, HER2 amplification in BCLM was associated with improved survival (hazard ratio [HR] 0.28), underscoring the relevance of re-biopsy and molecular reassessment in guiding therapy [Sundén 2023].

Beyond biological subtype, other factors associated with survival in BCLM include patient age, number of liver lesions, and disease-free interval [Rahnemaii-Aza 2025; Sen 2024]. A nomogram based on SEER data for T1–2N0–1 breast cancer patients, with liver metastases identified ER/PR/HER2 status, surgery, and systemic treatment as independent prognostic variables, with a c-index of 0.72 [Wang 2024].

Surgical Resection of Liver Metastases

Surgical resection of BCLM has historically been considered controversial due to the systemic nature of the disease. However, accumulating retrospective evidence suggests that, in selected patients, hepatic resection may confer a significant survival benefit (Table 1). The largest series and meta-analyses to date report median OS ranging from 32 to 60 months following resection, with 5-year survival rates of 25–60%, particularly in hormone receptor-positive or HER2-positive subtypes [Rahnemaii-Aza 2025; Cantalejo-Díaz 2024].

Table 1. Summary of outcomes after liver resection for breast cancer liver metastases.

Study/Series	Design	Patients (n)	Median OS (months)	5-year OS (%)	Key predictors of outcome
LIBREAST [Cantalejo-Díaz 2024]	Multicenter registry	~200	~60	60%	HR+/HER2+, R0 resection, response to systemic therapy

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Masuda et al. [Masuda 2024]	Retrospective	35	49	46%	Disease-free interval >12 months, limited liver disease
Rahnemai et al. [Rahnemai 2025]	SEER-based nomogram	122	38	39%	Single metastasis, ER+/HER2+

The European LIBREAST study, one of the largest multicenter registries of patients undergoing liver resection for BCLM, demonstrated a 5-year OS of 60% and a 5-year disease-free survival (DFS) of 29% [Cantalejo-Díaz 2024]. Similarly, data from Masuda et al. confirm prolonged survival in patients with isolated liver metastases treated surgically, particularly when resection margins were negative (R0) and systemic therapy achieved disease control [Masuda 2024]. In these series, liver resection was often part of a multidisciplinary strategy that included chemotherapy, targeted therapy, and endocrine treatment.

Optimal candidates for surgery typically exhibit a limited number of liver lesions (≤3–5), absence of uncontrolled extrahepatic disease, good performance status, and a long disease-free interval from primary diagnosis [Rahnemaii-Aza 2025; Masuda 2024]. Hormone receptor positivity, HER2 amplification, and response to systemic therapy prior to resection are also associated with improved outcomes.

Despite the absence of randomized trials, these consistent findings across large observational cohorts support the consideration of hepatic surgery in highly selected patients with oligometastatic BCLM. Importantly, surgical decisions must be individualized and made within the context of multidisciplinary team discussions [Cantalejo-Díaz 2024].

Local Ablative Therapies

For patients with unresectable BCLM or those unfit for surgery, image-guided local ablative therapies have emerged as viable alternatives. Techniques, such as microwave ablation (MWA), laser interstitial thermal therapy (LITT) and transarterial chemoembolization (TACE), have been employed either alone or in multimodal regimens. These approaches are particularly relevant in the oligometastatic setting, where local control may contribute to prolonged survival and delay systemic progression [Vogl 2023; Rahnemaii-Aza 2025; Zou 2025].

A large single-center retrospective study evaluated over 1,100 patients treated with various thermal ablation modalities over a 26-year period [Vogl 2023]. MWA yielded the most favorable outcomes, with a median OS of 5.6 years and 5-year survival rate of 89% in a small but highly selected cohort (n=17). LITT, performed in an earlier era, was associated with a median OS of 2.2 years and a 5-year survival rate of 22%, while combination therapy with LITT and TACE yielded comparable survival (median OS 2.1 years, 5-year survival 15%). TACE alone was associated with poor outcomes (median OS 0.8 years; 5-year survival 4%), likely reflecting treatment in more advanced cases (Table 2).

Table 2. Comparative outcomes of locoregional therapies for BCLM.

Treatment modality	Median OS	5-year OS (%)	Patients (n)	Notes
Microwave ablation	5.6 years	89%	17	Highly selected group
LITT	2.2 years	22%	491	Earlier era cohort
LITT + TACE	2.1 years	15%	370	Combined therapy
TACE alone	0.8 years	4%	242	Advanced disease, palliative intent

LITT = laser interstitial thermal therapy; OS = overall survival; TACE = transarterial chemoembolization.
Data source: Vogl 2023.

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MWA has several technical advantages over older methods such as radiofrequency ablation, including faster tissue heating, larger ablation volumes, and less susceptibility to heat-sink effects. LITT, while more time-intensive, offers precise thermal monitoring via MRI guidance and remains suitable for lesions ≤5 cm in diameter [Vogl 2023].

TACE continues to serve as both a palliative modality and a downstaging tool in combination protocols. When used before ablation, it may reduce tumor vascularity and enhance necrosis [Vogl 2023].

Overall, local ablation offers a valuable therapeutic option for well-selected patients and should be considered as part of a multimodal treatment strategy in the absence of surgical indications. SBRT has also emerged as a non-invasive alternative to surgery in selected patients, with favorable local control and toxicity profiles. Breast cancer histology appears to be associated with better outcomes compared to other primaries [Aoki 2020]. Recent data from the OligoCare prospective cohort confirmed a low incidence of acute grade ≥3 toxicities (<1%), reinforcing the safety of SBRT in oligometastatic breast cancer [Alongi 2024]. Recent international consensus recommendations highlight the importance of stratifying future OMBC trials by imaging modality, metastatic site, and biological subtype, and emphasize the integration of modern diagnostics into trial and clinical frameworks [Pasquier 2023].

Minimally Invasive vs. Surgical Approaches

The decision between surgical resection and minimally invasive locoregional therapies for BCLM hinges on tumor burden, anatomic resectability, patient comorbidities, and response to systemic therapy. While hepatic resection remains the standard of care in operable oligometastatic disease, image-guided ablative modalities offer less invasive alternatives for patients who are medically inoperable or have unfavorable lesion locations.

MWA and LITT have demonstrated encouraging long-term outcomes in small cohorts. MWA achieved a 5-year survival rate of 89% in a highly selected population, comparable to surgical outcomes in similar patients [Vogl 2023]. Ablative approaches also carry lower perioperative morbidity, shorter hospital stays, and the potential for repeat treatments, making them attractive in frail or elderly populations [Vogl 2023].

However, surgery may offer superior local control and longer disease-free intervals, especially when complete (R0) resection is feasible and systemic disease is well controlled. For example, the LIBREAST registry reported a 5-year OS of 60% after hepatic resection, highlighting the potential curative intent in select cases [Cantalejo-Díaz 2024]. Conversely, TACE as a monotherapy yields inferior outcomes and is generally reserved for patients with multifocal disease or contraindications to thermal ablation or surgery [Vogl 2023].

In practice, the choice between resection and minimally invasive therapy should be individualized and based on multidisciplinary evaluation. Some centers are adopting combined strategies – using TACE or ablation as neoadjuvant tools to downstage lesions prior to resection or to treat bilobar disease with curative intent [Rahnemai-Azar 2025; Vogl 2023].

The comparative effectiveness of these approaches remains inadequately addressed in prospective studies, underscoring the need for ongoing clinical trials and standardized selection criteria.

Emerging Strategies

The management of BCLM is increasingly guided by individualized, multidisciplinary strategies. A key area of development is conversion therapy, wherein patients with initially unresectable disease are downstaged using systemic therapy or locoregional interventions – such as TACE or thermal ablation – to enable curative-intent surgical resection or combined local therapy [Vogl 2023; Rahnemai-Azar 2025].

Risk-adapted treatment algorithms are also gaining relevance. A recent nomogram, derived from a SEER-based cohort of patients with T1–2N0–1 breast cancer and liver metastases, incorporated

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clinical and molecular features, such as ER, PR and HER2 status, along with brain and bone metastases, to estimate individualized survival probabilities. This model achieved a concordance index of 0.72 and effectively stratified patients into high- and low-risk groups, offering potential guidance for therapeutic decision-making [Wang 2024].

Receptor discordance between the primary tumor and liver metastases, including loss of hormone receptor expression or gain of HER2 amplification, has been documented in up to one-third of cases. This highlights the importance of repeat biopsy and molecular re-evaluation at the time of metastatic progression, particularly when local treatment is being considered [Sundén 2023].

The integration of surgery, systemic therapy, and locoregional techniques remains largely based on retrospective evidence. Prospective studies and randomized trials comparing surgical resection with ablative or non-invasive strategies are urgently needed. In the interim, real-world data and multicenter registries may help refine patient selection and clarify the comparative benefits of available interventions.

As the therapeutic landscape continues to evolve, optimal management of BCLM will depend on the coordinated application of biological, anatomical, and clinical factors within a multidisciplinary framework.

4. Lung Metastases

Epidemiology and Prognostic Impact

Lung metastases are a frequent manifestation of advanced breast cancer, occurring in up to 20–40% of patients with distant recurrence [Soh 2020; Meng 2021]. Isolated pulmonary metastases are less common but represent a distinct clinical scenario that may be amenable to local therapy. The lung is often involved early in metastatic dissemination, particularly in hormone receptor-negative and HER2-positive subtypes [Soh 2020].

The prognosis of patients with lung metastases varies significantly depending on disease burden, molecular subtype, and the feasibility of local control [Xie 2024]. Historical data suggest that median OS for patients with metastatic breast cancer involving the lung ranges from 22 to 36 months [Meng 2021]. In a retrospective study of patients undergoing MWA for breast cancer lung metastases, the reported median OS was 36 months, with 1-, 3- and 5-year OS rates of 96.9%, 53.3% and 17.8%, respectively [Meng 2021].

Compared to liver or bone metastases, lung involvement may carry a slightly more favorable prognosis in selected patients, particularly when the disease is limited in number and confined to the lung. However, it also remains a marker of systemic progression, and long-term disease control is uncommon in the absence of systemic therapy.

Patient Selection for Pulmonary Metastasectomy

The selection of candidates for pulmonary metastasectomy (PM) requires careful clinical judgment and should be guided by multidisciplinary evaluation. Established criteria include the control of the primary tumor, absence of extrapulmonary metastases (or stable extra-thoracic disease), a limited number of lung lesions (typically ≤3), resectability with negative margins, and sufficient cardiopulmonary reserve [Handy 2019].

A disease-free interval greater than 12–24 months has consistently been associated with better outcomes after PM [Handy 2019]. Biological subtype also plays a role, with hormone receptor-positive and HER2-positive tumors more likely to benefit from metastasis-directed interventions.

Surgical Techniques and Outcomes

Surgical resection is considered the standard local approach for isolated or oligometastatic pulmonary metastases from breast cancer in appropriately selected patients (Table 3). The primary objective is to achieve complete resection of all visible disease with negative margins (R0). The most

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employed procedures are non-anatomical wedge resections, which offer effective tumor removal while preserving lung parenchyma. Segmentectomy or lobectomy may be necessary for centrally located lesions or when margin-negative resection is not otherwise feasible [Handy 2019].

Table 3. Summary of outcomes and selection criteria in pulmonary metastases from breast cancer.

Study/Source	Treatment modality	Patients (n)	Median OS	5-year OS (%)	Key selection criteria	Notable findings
Handy 2019 [Handy 2019]	Pulmonary metastasectomy	157	Not specified	38% (LN+) vs. 69% (LN-) at 3 years	≤3 lesions, R0 feasible, no uncontrolled extra-thoracic disease, disease-free interval >12–24 months	LN involvement significantly worsens prognosis; repeat PM feasible in selected cases
Franceschini 2024 [Franceschini 2024]	SBRT (lung and liver OMBC)	24 (lung subgroup)	16.5 months	51.9% at 3 years	Oligometastatic disease, controlled systemic burden	1-, 2-, 3-year local control: 94.9%, 91%, 87.5%; well tolerated
Meng 2021 [Meng 2021]	Microwave ablation	32	36 months	17.8% at 5 years	≤3 lung lesions, no progressive extra-pulmonary disease	96.9% 1-year OS; primary efficacy rate 97.8%; low complication profile

Minimally invasive surgery, particularly video-assisted thoracoscopic surgery (VATS), has become the preferred approach in most centers due to its favorable perioperative profile. Compared with open thoracotomy, VATS is associated with shorter hospital stays, reduced postoperative pain, faster recovery, and comparable oncologic outcomes in terms of recurrence and survival [Handy 2019]. The low morbidity and mortality rates of pulmonary metastasectomy are well established: in a multicenter retrospective study, the 30-day mortality rate was 1.1%, and the overall complication rate was approximately 11% [Handy 2019].

Long-term survival outcomes following metastasectomy are encouraging in selected patients. The 5-year OS rates range from 35% to 60%, depending on factors such as disease-free interval, tumor biology, and extent of disease. Recurrence within the lung occurs in approximately 20–30% of cases, most often after a prolonged disease-free period. However, recurrence does not preclude consideration of repeat surgical intervention, which may offer continued disease control and survival benefit [Handy 2019].

Surgical resection of lung metastases is therefore a viable and generally safe option, provided that patient selection is rigorous and performed within a multidisciplinary context.

Lymph Node Involvement and Prognostic Significance

The presence of mediastinal or hilar LN metastases at the time of PM is an established negative prognostic factor in patients with breast cancer. Nodal involvement reflects a higher systemic disease burden and more aggressive tumor biology, and it is associated with significantly reduced survival outcomes compared to node-negative patients [Handy 2019].

In one of the largest retrospective analyses of PM for breast cancer, patients with positive mediastinal or hilar lymph nodes had markedly worse outcomes, with 3-year OS of 38% compared to 69% in node-negative patients [Handy 2019]. These findings support the recommendation for routine intraoperative lymph node assessment during PM. In the absence of preoperative evidence of nodal disease, systematic sampling or dissection may still be warranted to accurately stage the disease and refine postoperative management.

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The decision to proceed with PM should incorporate the likelihood of nodal involvement, particularly in patients with high-risk subtypes or short disease-free intervals. Preoperative imaging, including PET-CT, may assist in identifying suspicious nodes, although sensitivity remains suboptimal. In cases with confirmed or strongly suspected LN metastasis, the role of surgery must be carefully weighed against the potential benefit of systemic therapy or other non-surgical strategies.

Despite its prognostic impact, nodal positivity does not represent an absolute contraindication to PM, especially in cases of controlled disease and favorable performance status. However, outcomes are clearly superior when nodal involvement is absent, reinforcing the need for thorough staging and multidisciplinary decision-making [Handy 2019].

Repeat Metastasectomy and Long-Term Disease Control

Recurrence following PM is common in breast cancer, occurring in up to 30% of patients within the lungs, often after prolonged disease-free intervals. Importantly, recurrence does not necessarily preclude the possibility of additional surgical intervention. In selected patients, repeat metastasectomy has been shown to be both feasible and beneficial, contributing to extended survival and sustained disease control [Handy 2019].

The decision to perform a second or even third PM depends on multiple factors, including the location and number of recurrent lesions, patient performance status, interval since prior surgery, and response to systemic therapy. Studies have shown that the morbidity of repeat PM is comparable to that of the initial resection, particularly when using minimally invasive techniques, such as VATS [Handy 2019].

Although data are limited, survival outcomes following repeat PM appear similar to those observed after the initial surgery in well-selected patients. This suggests that repeated local treatment may be a reasonable strategy within the broader framework of multidisciplinary care, especially in oligo-recurrent disease with slow progression and good systemic control.

Ultimately, the appropriateness of repeat PM must be assessed case by case, with careful attention to evolving disease biology and treatment goals. When pursued, repeat surgical resection can offer meaningful disease control and contribute to prolonged survival.

Non-Surgical Ablative Therapies

For patients who are not suitable candidates for pulmonary metastasectomy due to comorbidities, multifocal pulmonary involvement, poor functional status, or surgically inaccessible lesions, non-surgical local treatments have become important tools in the management of breast cancer lung metastases. Image-guided ablative therapies and stereotactic body radiotherapy (SBRT) are increasingly used to achieve local control in oligometastatic or oligoprogressive disease settings.

MWA is among the most widely studied thermal ablation techniques. It offers several advantages, including short procedure times, larger and more uniform ablation zones, and reduced heat-sink effects compared to radiofrequency ablation. In a retrospective study by Meng et al. (2021), 32 patients with breast cancer lung metastases underwent CT-guided percutaneous MWA. The technical success rate was 100%, with a primary local control rate of 97.8%. Local progression occurred in 10.9% of lesions, with a median progression time of 10 months. Median OS was 36 months, with 1-, 3- and 5-year OS rates of 96.9%, 53.3%, and 17.8%, respectively. Complications included pneumothorax (23.9%) and pleural effusion (4.3%), but no treatment-related mortality was reported [Meng 2021].

SBRT is another non-invasive option with excellent local control and favorable safety. In a prospective phase II study, SBRT delivered to lung and liver oligometastases from breast cancer resulted in 1-, 2- and 3-year local control rates of 94.9%, 91%, and 87.5%, respectively. The 3-year OS was 51.9%, despite many patients having extra-thoracic but stable disease [Franceschini 2024].

These minimally invasive modalities are particularly valuable in the multidisciplinary management of patients with limited pulmonary disease who are not surgical candidates, offering durable local control with low morbidity. However, the randomized phase II NRG-BR002 trial did

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not show a survival advantage for adding SBRT or surgery to systemic therapy in newly diagnosed oligometastatic breast cancer, highlighting the need for better biological selection criteria [Chmura 2022]. This need is further supported by recent interim data from the EORTC-ESTRO OligoCare study have shown considerable heterogeneity in SBRT dose and fractionation choices, influenced by both primary tumor histology and metastatic site, underscoring the need for harmonized clinical practice [Christ 2024].

Integration with Systemic Therapy and Multidisciplinary Planning

Effective management of pulmonary metastases in breast cancer relies not only on local control strategies but also on the integration of systemic therapy within a multidisciplinary treatment plan. Surgery or ablation alone is rarely sufficient, as breast cancer metastases reflect underlying systemic disease. Thus, local interventions must be timed and selected based on systemic control, tumor biology and patient-specific factors.

Systemic therapy remains the cornerstone of metastatic breast cancer treatment and is typically administered before or after local interventions. Hormone receptor-positive and HER2-positive subtypes particularly benefit from targeted systemic regimens, which can stabilize or reduce disease burden and facilitate subsequent local therapy. In patients with triple-negative disease, systemic therapy plays a more limited role in long-term disease control, further highlighting the importance of patient selection for aggressive local treatments [Handy 2019].

The decision to proceed with pulmonary metastasectomy or non-surgical ablation should be made within the context of a MDT, including thoracic surgeons, medical oncologists, radiation oncologists, and radiologists. The MDT should consider disease distribution, treatment response, patient comorbidities, and preferences. Studies have shown that MDT evaluation improves treatment outcomes and optimizes resource allocation [Handy 2019].

Ultimately, the management of lung metastases in breast cancer must be individualized. Whether through surgery, ablation, or SBRT, local therapies offer a survival advantage only when integrated into a broader therapeutic strategy that accounts for systemic disease dynamics and patient goals.

5. Emerging Technologies and Personalized Strategies

Molecular and Genomic Profiling for Surgical Selection

Recent advances in molecular diagnostics have introduced new opportunities to refine surgical decision-making in metastatic breast cancer, particularly in patients with oligometastatic liver or lung involvement. Molecular profiling – both tissue-based and liquid biopsy – can provide insights into tumor biology, metastatic potential, and minimal residual disease (MRD), thereby informing the appropriateness and timing of surgical interventions.

A key development in this area is the use of circulating tumor DNA (ctDNA) to detect MRD. In a recent study, Garcia-Murillas et al. demonstrated that personalized ctDNA assays can detect relapse in early-stage breast cancer patients with high specificity and sensitivity, often months before radiologic evidence of progression [Garcia-Murillas 2025]. Among 141 patients, ctDNA positivity was associated with significantly shorter distant recurrence-free survival. Importantly, in the subset of patients with isolated distant relapse – many of whom had lung or liver involvement – ctDNA positivity preceded clinical recurrence by a median of 11 months. This aligns with the findings of a systematic review and meta-analysis by Cullinane et al., which confirmed that detectable ctDNA in early-stage and advanced breast cancer is significantly associated with shorter disease-free survival and worse outcomes [Cullinane 2020]. Recent prospective findings from the c-TRAK TN trial indicate that ctDNA-based intervention may have limited benefit if metastases are already established at the time of detection, highlighting the need for earlier and more sensitive molecular surveillance in high-risk settings [Turner 2023].These findings support the use of ctDNA monitoring to identify patients with low-volume, biologically indolent metastases who may benefit from curative-intent local

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therapies, including surgery. Recent translational studies have also emphasized ctDNA's role in real-time treatment adaptation, resistance detection, and guiding metastasis-directed therapies through liquid biopsy-integrated platforms [Borea 2025].

In parallel, transcriptomic profiling is shedding light on the molecular drivers of organ-specific metastasis. Cai et al. applied a deep learning approach to identify gene signatures associated with breast cancer metastases to lung and liver, generating predictive models with improved accuracy over traditional statistical methods [Cai 2024]. These gene sets, once validated in prospective studies, could help stratify patients based on the likelihood of visceral spread and guide surveillance and early intervention strategies, including surgical resection. Recent transcriptomic analyses by Zhang et al. have further delineated subtype-specific metastatic pathways, showing distinct gene expression profiles associated with lung versus liver dissemination in HER2-positive and triple-negative breast cancers [Zhang 2024]. These findings support the integration of subtype-tailored molecular signatures into pre-surgical risk models.

Together, these molecular tools are poised to complement conventional clinical and imaging criteria, enabling a more personalized and biologically informed selection process for surgical candidates with oligometastatic breast cancer.

Artificial Intelligence and Digital Pathology

Artificial intelligence (AI) and computational pathology are rapidly transforming the landscape of oncologic diagnostics and surgical planning. In the context of metastatic breast cancer, these technologies offer tools to improve the precision of preoperative assessments, optimize patient selection for local therapies, and support intraoperative decision-making.

One area of rapid development is digital histopathology. Ivanov et al. demonstrated that AI algorithms applied to histological whole-slide images can accurately classify tumor grade and predict lymph node involvement, surpassing conventional manual assessment in reproducibility and speed [Ivanov 2025]. Such applications may enhance pre-surgical risk stratification, particularly in identifying patients with more indolent tumor biology who could benefit from aggressive local treatments like metastasectomy.

AI is also being applied to intraoperative and perioperative surgical decision support. Li et al. reviewed the expanding role of AI-assisted navigation in breast cancer surgery, highlighting innovations in image recognition, margin assessment, and real-time feedback systems [Li 2025]. hese advances are further supported by the integration of augmented and mixed reality platforms, which enhance anatomical visualization and may improve resection outcomes in hepatic and pulmonary metastasectomy [Chen 2025]. While current tools are largely confined to primary tumor surgery, their adaptation to thoracic and hepatic procedures could enable more accurate resections and reduce rates of incomplete (R1) excision. Moreover, predictive models developed through machine learning may help estimate individual recurrence risk and postoperative outcomes based on multidimensional clinical data. Tan et al. demonstrated the clinical feasibility of using AI-assisted 3D reconstruction of imaging and pathological features to guide resection planning in hepatic metastases [Tan 2024]. This integrative approach improved intraoperative precision and reduced margin positivity in early-phase trials. In parallel, Turner et al. have proposed an AI-based consensus algorithm to support resectability decisions in oligometastatic disease, integrating radiomic, clinical, and biological parameters [Turner 2023]. These platforms offer scalable support for MDTs, particularly in resource-constrained or high-volume settings.

The promise of AI lies not only in its diagnostic utility but also in its integrative potential. AI systems capable of aggregating imaging, pathology, molecular, and clinical data could serve as decision-support platforms in multidisciplinary tumor boards, aiding in the selection of surgical vs. non-surgical interventions for oligometastatic disease.

Although many of these applications are still under clinical validation, the convergence of AI and pathology marks a pivotal shift toward data-driven, personalized surgical oncology.

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As the complexity of metastatic breast cancer management increases, MDT decision-making has become central to optimizing patient outcomes. In this context, AI is emerging as a transformative tool capable of enhancing the consistency, speed, and individualization of clinical decisions, including those regarding surgery for oligometastatic disease.

Mooghal et al. emphasized the growing relevance of AI-supported platforms in the management of oligometastatic breast cancer, particularly in stratifying patients for locoregional interventions such as surgery or stereotactic ablative radiotherapy [Mooghal 2024]. AI-driven tools can assist in evaluating large volumes of multimodal data – including imaging, histopathology, and genomic profiles – enabling more precise estimation of metastatic burden, treatment response, and recurrence risk. These capabilities may improve the timing and appropriateness of metastasectomy or other focal therapies.

Moreover, AI may play a role in standardizing MDT discussions, reducing inter-observer variability in interpretation and facilitating more equitable decision-making across centers. By integrating predictive modeling, AI can simulate treatment outcomes under different scenarios, providing valuable input for complex cases where evidence is limited or conflicting.

However, successful integration of AI into real-world MDT workflows faces several challenges. Mooghal et al. underscore the barriers related to data standardization, digital infrastructure, and the limited adoption of electronic health records in resource-constrained settings. Additionally, regulatory and ethical frameworks for the clinical deployment of AI systems remain in development.

Despite these hurdles, the trajectory of AI in MDT planning is promising. When fully operational, these technologies have the potential to personalize surgical and locoregional treatment strategies, reduce decision-making time, and ultimately improve outcomes for patients with limited metastatic breast cancer.

6. Future Directions and Implementation Challenges

The integration of molecular diagnostics, AI, and digital pathology into surgical oncology presents a transformative opportunity to personalize care for patients with breast cancer metastases (Table 4). However, translating these innovations into clinical practice – particularly in the context of metastasis-directed surgery – requires careful attention to validation, scalability, and equity.

Table 4. Emerging technologies in surgical decision-making for visceral breast cancer metastases.

Innovation	Application	Impact
ctDNA [Garcia-Murillas 2025]	MRD detection, relapse prediction	Identifies candidates for early intervention
Transcriptomic profiling [Cai 2024]	Prediction of organ-specific metastases	Supports personalized surveillance and resection strategies
Subtype-specific signatures [Zhang 2024]	Subtype-based metastatic pattern identification	Refines patient selection by subtype biology
AI Histopathology [Ivanov 2025]	Lymph node status, tumor grading	Enhances surgical risk stratification
AI-assisted surgical navigation [Li 2025]	Margin detection, intraoperative guidance	Improves resection accuracy and reduces margin positivity
3D AI reconstruction for liver resection [Tan 2024]	Pre-surgical planning in hepatic metastases	Enhances intraoperative planning and precision
AI resectability consensus algorithm [Turner 2023]	Multimodal decision-making in oligometastatic disease	Improves selection in complex or low-resource cases
AI-supported MDT platforms [Mooghal 2024]	Scenario modeling and MDT decision support	Standardizes MDT decisions and optimizes timing

One major challenge is the need for prospective validation of AI tools and molecular assays in diverse, real-world settings. Many current models are trained on homogeneous populations or rely

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on retrospective data. Without external validation, their generalizability remains uncertain. As noted by Mooghal et al., the adoption of AI in oncology is particularly limited in low-resource settings due to insufficient digital infrastructure and inconsistent electronic health record (EHR) systems [Mooghal 2024]. This disparity risks widening existing gaps in cancer care unless addressed through coordinated global efforts.

Standardization of data input formats, interoperability across platforms, and the development of regulatory frameworks for AI-driven clinical tools are additional priorities. Initiatives to benchmark performance metrics, such as predictive accuracy or clinical utility in decision-making, will be essential to support integration into multidisciplinary workflows.

Moreover, the convergence of multiple data streams – including imaging, genomic data, and liquid biopsy – poses logistical and analytical challenges. Ensuring that AI platforms can synthesize these data accurately and present actionable insights in real time is critical for their clinical relevance. As Garcia-Murillas et al. demonstrated, early detection of minimal residual disease through ctDNA monitoring could potentially guide the timing of surgical interventions, but such approaches must be operationalized within care pathways that are both timely and scalable [Garcia-Murillas 2025].

Looking ahead, the focus will need to shift from proof-of-concept studies to clinical implementation, with attention to patient-centered outcomes, cost-effectiveness, and health system integration. Bridging these gaps will be key to fully realizing the promise of innovation in the surgical management of metastatic breast cancer.

From Palliative to Precision: Rethinking Surgical Management in Visceral Breast Cancer Metastases

The surgical management of liver and lung metastases in breast cancer is increasingly moving beyond its traditional palliative role. Accumulating evidence suggests that, in selected patients, resection of visceral metastases may contribute to prolonged survival and improved disease control, particularly in the context of oligometastatic disease [Cantalejo-Díaz 2024; Rahnemai-Azar 2025]. This shift is enabled by the refinement of systemic therapies, more nuanced biological profiling, and the availability of minimally invasive surgical and ablative techniques [Handy 2019; Vogl 2023].

Multiple retrospective studies have reported encouraging outcomes, with 5-year OS rates of 30–60% following pulmonary or hepatic metastasectomy in carefully selected patients [Masuda 2024; Handy 2019; Cantalejo-Díaz 2024]. The benefit appears most pronounced in patients with hormone receptor-positive or HER2-positive disease, limited metastatic burden, and long disease-free intervals. However, such data must be interpreted with caution. Most supporting evidence is retrospective, lacking uniform criteria for patient selection or control groups treated with systemic therapy alone [Galiandro 2022; Sen 2024]. In a recent retrospective series, a longer DFI—specifically beyond three years—was significantly associated with better progression-free survival following liver metastasectomy [Sen 2024]. Prospective validation is urgently needed.

Non-surgical alternatives, such as MWA and SBRT, have demonstrated high local control rates and favorable survival outcomes in inoperable patients or those with high surgical risk [Franceschini 2024; Meng 2021]. These modalities offer compelling advantages in terms of morbidity and recovery, but comparative trials are lacking, and the long-term oncologic equivalence to surgery remains uncertain.

The growing integration of molecular diagnostics and AI offers further opportunity to refine decision-making. Circulating tumor DNA (ctDNA) assays have shown promise in detecting minimal residual disease and predicting relapse months before clinical or radiologic evidence emerges, enabling timely identification of patients who might benefit from metastasis-directed interventions [Garcia-Murillas 2025]. Similarly, transcriptomic profiling may identify patients with favorable metastatic biology, while AI-based histopathology and imaging tools are being developed to assist with risk stratification and preoperative planning [Cai 2024; Ivanov 2025; Li 2025]. Tools, such as ctDNA and subtype-specific gene expression signatures, are beginning to move surgical decision-making away from purely anatomical criteria and toward a biologically driven framework.

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The central question is no longer "Can we operate?" but rather "Should we, and when?" Surgical feasibility alone is insufficient justification in an era increasingly guided by precision oncology. Instead, surgery must be offered within a multidisciplinary context, tailored to individual patient biology, disease kinetics, and therapeutic goals (Table 5). AI-enabled tools that integrate radiologic, pathologic, and genomic data are now emerging as adjuncts to MDT decision-making, offering scalable solutions for complex case triage and surgical planning [Tan 2024; Turner 2023; Mooghal 2024].

Table 5. Criteria for patient selection for surgical management of visceral metastases.

Criterion	Liver metastases	Lung metastases
Number of lesions	≤3–5	≤3
Disease-free interval	>12 months preferred	>12–24 months
Extra-visceral disease	Controlled or absent	Controlled or absent
Systemic disease response	Favorable	Favorable
Tumor biology	HR+/HER2+ preferred	HR+/HER2+ preferred
Performance status	ECOG 0–1	ECOG 0–1
Resection feasibility	R0 achievable	R0 achievable
Comorbidities	Acceptable for surgery	Pulmonary reserve adequate

Looking forward, the field must move from anecdotal experience to structured evidence. Prospective trials, real-world registries, and standardized criteria for surgical candidacy are essential. Equally important is the equitable implementation of emerging technologies to ensure access across diverse clinical settings.

Metastasectomy in breast cancer should be seen not as a technical endpoint, but as a strategic component of a personalized, biologically informed treatment paradigm. The next frontier will be prospective validation: defining how, when, and for whom surgical intervention meaningfully alters the natural history of metastatic breast cancer.

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