

## Curative-Intent Volumetric Modulated Arc Therapy for Locoregional and Oligometastatic HER2-Positive Breast Cancer: A Case Report

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### ABSTRACT

#### Introduction:

Breast cancer is the most common prevalent malignancy in among women worldwide. Although metastatic breast cancer is generally regarded as incurable, the concept of oligometastasis—characterized by the limited spread of cancer to a few metastatic sites—offers the potential for durable remission through aggressive local treatment. Advanced radiotherapy techniques such as Volumetric Modulated Arc Therapy (VMAT) allow for precise delivery of high doses to complex targets with optimal protection of normal organs, making it suitable for curative use in selected cases.

**Case Illustration:**

A 52-year-old woman with a left breast mass was diagnosed with invasive carcinoma type of no special type (NST) grade II, HER2-positive, and hormone receptor-negative. Following a mastectomy and four cycles of chemotherapy, a single encapsulated lung lesion was discovered. The patient underwent external beam radiation on July 15, 2025, using the VMAT technique after CT simulators revealed internal metastases in the contralateral mammary lymph nodes. A curative dose of 50 Gy/25 fractions was administered to PTV50 and the locoregional area. Organ at Risk (OARs) doses: spinal cord 0.876 Gy, thyroid 2.601 Gy, esophagus 2.147 Gy, right lung 2.199 Gy, left lung 2.022 Gy, and heart 2.784 Gy. No post-radiation adverse effects were observed, and the patient was scheduled for further metastatic evaluation and continued chemotherapy.

**Discussion:**

This case highlights the potential role of VMAT in delivering radiotherapy with curative intent in HER2-positive breast cancer with limited metastases. VMAT offers superior dose conformity and protection of OARs compared to conventional 2D or 3D techniques. The literature supports metastasis-directed therapy, which achieves a 4-year overall survival of 59% and local control of 89%. Given the limited radiotherapy facilities in Indonesia, cases with curative intent such as this should be prioritized to minimize disease progression and optimize treatment outcomes.

**Conclusion:**

VMAT radiotherapy with curative intent represents a feasible and precise approach for managing both locoregional and oligometastatic breast cancer, with optimal tumor control and minimal toxicity. Adaptive treatment planning and timely delivery are crucial to maximize clinical outcomes, particularly in resource-limited settings.

**Keywords:** Breast cancer, VMAT, oligometastasis, radiotherapy, HER2-positive, curative therapy.

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## INTRODUCTION

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Breast cancer is the most common malignant tumour among women worldwide, accounting for approximately 36% of all oncology patients. This cancer arises from uncontrolled cell growth within the breast tissue, most commonly originating in the ducts or lobules. The incidence of this malignancy is increasing across all regions of the world, with the highest rates observed in industrialised countries, which account for nearly half of global cases. In Indonesia, breast cancer represents the most prevalent cancer among women, with an incidence rate of 42.1 per 100,000 women and a mortality rate of 16.6 per 100,000 women in 2020.<sup>1</sup> The highest crude mortality rate from this malignancy in Indonesia has been recorded at 17 per 100,000 population.<sup>2</sup> The general classification of breast cancer distinguishes between locally or regionally confined disease, which is potentially curable with local therapy, and metastatic disease. Approximately 50% of breast cancer metastases involve fewer than three metastatic lesions.<sup>3</sup> Bone metastases are the most common sites of dissemination, and patients with solitary bone metastases constitute nearly half of all cases. Bone metastases may occur through direct extension from involved intramammary lymph nodes or as isolated intramammary bone metastases. Several retrospective studies have shown that patients with oligometastatic disease who receive local therapy have a good prognosis, with overall survival rates of 82% at 10 years and 53% at 20 years.<sup>4</sup> Radiotherapy is an essential modality in the management of breast cancer and may be administered with curative, adjuvant, or palliative intent. For many years, metastatic breast cancer was generally regarded as an incurable condition. However, it is now recognised as a heterogeneous disease, ranging from solitary metastases to widespread involvement. Patients with isolated or limited metastatic lesions—referred to as oligometastases—who undergo aggressive multimodality therapy, may remain disease-free for over a decade without developing additional metastatic sites. It remains uncertain whether this outcome reflects the selection of patients with good prognostic factors or the true benefit of treatment.<sup>5</sup>

Three-dimensional conformal radiotherapy (3D-CRT) and more advanced techniques are indicated as adjuvant postoperative treatments for patients undergoing radiotherapy for oligometastatic disease. Moreover, this approach provides significant advantages in the management of metastatic disease, as the target volume encompasses only the metastatic lesions, thereby avoiding unnecessary irradiation of large volumes of normal tissue. Consequently, this leads to a substantial reduction in the radiation dose delivered to surrounding healthy structures.<sup>5</sup> The clinical application of volumetric modulated arc therapy (VMAT) in breast cancer has demonstrated potential as a promising option for both comprehensive and partial breast irradiation, using either conventional or modified fractionation schemes—including sequential or simultaneous integrated boost, hypofractionation, and even single-fraction regimens. From a technological standpoint, several innovative VMAT variants have been proposed and evaluated *in silico* to explore future therapeutic possibilities.<sup>6</sup> Radiotherapy plays a crucial role in breast cancer management by reducing local recurrence rates in patients treated with breast-conserving surgery or mastectomy. However, waiting times for the initiation of radiotherapy have increased markedly worldwide.<sup>7</sup> Timely commencement of cancer treatment remains a cornerstone of effective oncological care, particularly for highly prevalent malignancies such as breast cancer. Even minor delays between diagnosis and treatment can significantly affect survival outcomes. Nevertheless, treatment delays continue to be prevalent in clinical practice, influenced by a combination of patient-related, provider-related, and systemic factors.<sup>8</sup> Therefore, this case discusses a patient with locoregional metastatic breast cancer who received curative-dose radiotherapy.

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### CASE ILLUSTRATION

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Ms S, a 52-year-old woman, presented with a complaint of a progressively enlarging mass in her left breast over the three months prior to diagnosis. An ultrasound examination in August 2024 revealed a mass measuring approximately 7 cm, suspected to be malignant. A fine needle aspiration biopsy (FNAB) of the left breast was performed on 25 September 2024, revealing features suspicious of malignancy — suspicious ductal carcinoma in situ with cystic degeneration, with a

differential diagnosis of fibrocystic changes with atypical cells. Subsequently, a mastectomy with histopathological examination was performed on 2 October 2024, confirming invasive carcinoma of no special type (NST), Grade II, with all surgical margins free of tumour cells. The axillary lymph node showed reactive lymphoid hyperplasia. Immunohistochemistry (IHC) performed in October 2024 demonstrated the following results: ER negative, PR negative, and HER2 overexpressed (strong intensity, complete membranous pattern in more than 30% of tumour cells, scored 3+). Ki-67 was moderately to strongly expressed in 25% of tumour cells, indicating high proliferative activity. The overall conclusion was HER2-positive (non-luminal) breast carcinoma. The patient received four cycles of chemotherapy, which were completed in February 2025. Following chemotherapy, external radiotherapy was recommended. However, as the patient resides in Sampit, Kalimantan, and preferred to undergo treatment in her hometown, external radiotherapy was only initiated on 15 July 2025. A CT simulation revealed metastasis to the contralateral internal mammary lymph node (right IMN). Using the Volumetric Modulated Arc Therapy (VMAT) technique, curative-dose external beam radiotherapy was delivered to the right IMN (PTV50: 50 Gy in 25 fractions) and to the locoregional left breast area (50 Gy in 25 fractions), with plans for post-radiation evaluation. The recorded doses to organs at risk (OARs) were as follows: spinal cord 0.876 Gy, thyroid 2.601 Gy, oesophagus 2.147 Gy, right lung 2.199 Gy, left lung 2.022 Gy, and heart 2.784 Gy. No post-radiation side effects were observed. Upon completion of radiotherapy, the patient was referred back to the oncologic surgery department for evaluation of metastatic lesions, further metastatic work-up, and continuation of chemotherapy.

SPV Displayed

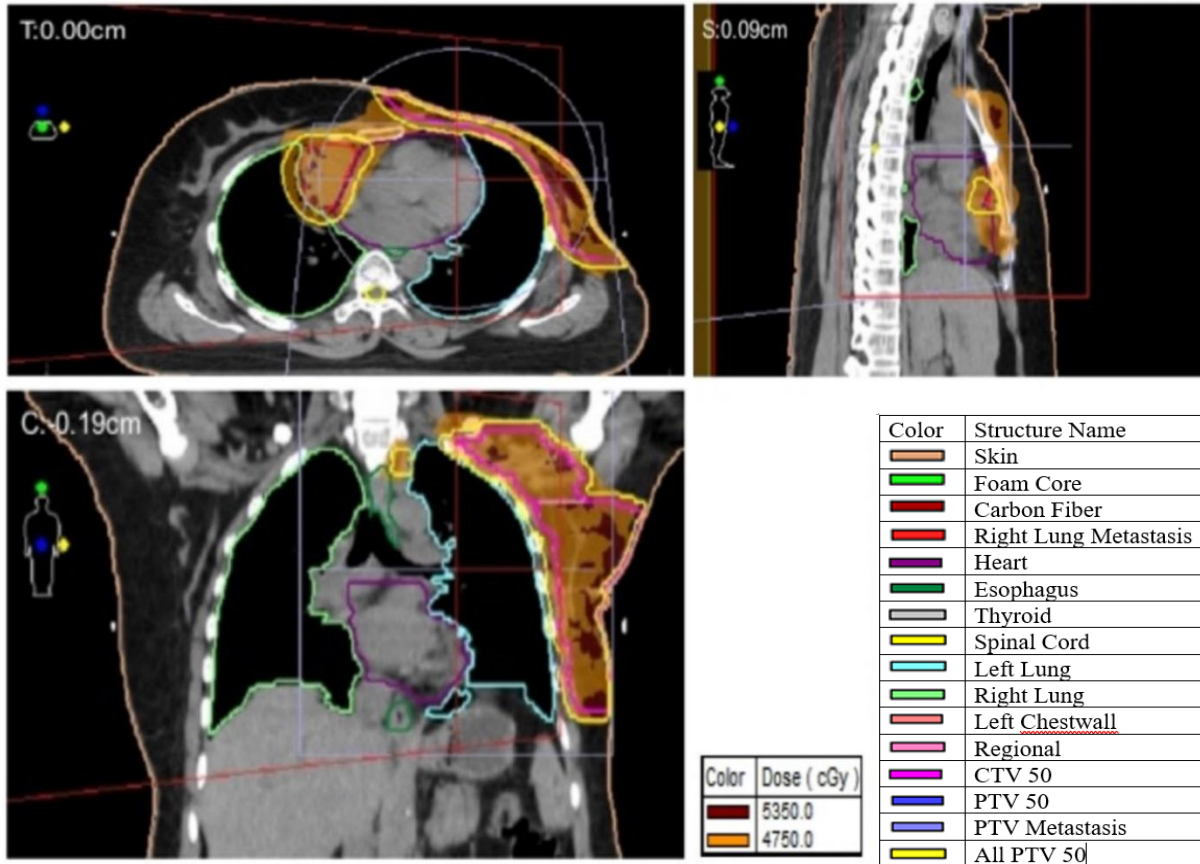


Figure 1. VMAT dose distribution showing optimal conformity and OAR sparing

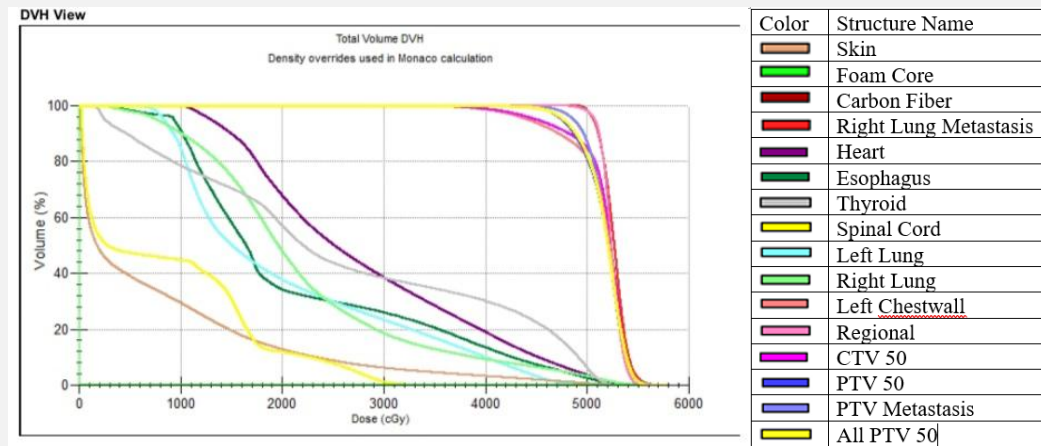


Figure 2. DVH Distribution

### DISCUSSION

This case describes a 52-year-old female patient with invasive breast carcinoma of no special type (NST), Grade II, HER2-positive (non-luminal), who was found to have a solitary contralateral internal mammary lymph node (right IMN) lesion following left mastectomy and chemotherapy, suspected to represent contralateral IMN metastasis. The patient subsequently underwent volumetric modulated arc therapy (VMAT) radiotherapy with a dose of 50 Gy in 25 fractions to both the left locoregional mammary region and the suspected contralateral IMN metastasis simultaneously. Based on these findings, radiotherapy was selected with curative intent to eradicate the single metastatic lesion, taking into consideration the potential delay in treatment that would have occurred had a biopsy been performed on the suspected right IMN metastasis. This approach is supported by increasing evidence regarding oligometastatic disease<sup>9,10</sup>, the feasibility of using VMAT techniques to treat two distinct and anatomically distant target regions (the breast and contralateral IMN) with high precision and accurate dose delivery while sparing surrounding healthy tissue<sup>11,12</sup>, and a growing trend toward individualised treatment strategies that adapt to tumour response.<sup>13</sup> The regular morphology and encapsulated appearance of the lesion suggest classic oligometastasis, which can potentially be controlled with aggressive local therapy. Several studies have reported high local control rates and curative potential in patients presenting with a limited number of metastases (typically 1–5 lesions).<sup>3,14</sup>

Curative radiotherapy for pulmonary oligometastases in breast cancer is increasingly recognised as an evidence-based therapeutic approach. The concept of oligometastasis refers to a state in which only a limited number of metastatic lesions are present (typically 1–5), rather than widespread disease throughout the body, making aggressive local treatment such as radiotherapy or surgery potentially effective for disease control.<sup>9</sup> Patients receiving curative-intent therapy have demonstrated a 4-year overall survival rate of 59% and a local control rate of 89%, with the most favourable outcomes observed in those with a single metastatic lesion, small tumour volume, and bone-only metastasis.<sup>9</sup> In such patients, the presence of a solitary lesion with regular and encapsulated morphology serves as a favourable prognostic indicator for therapy aimed at eradicating all cancer cells within the affected area. Current evidence supports this approach, suggesting that an aggressive, multidisciplinary treatment strategy in cases of oligometastasis can achieve durable disease control, with some patients remaining disease-free for more than a decade without the emergence of new metastatic sites.<sup>10</sup> Although randomised controlled trials (RCTs), such as NRG-BR002, did not demonstrate a significant survival benefit from metastasis-directed therapy, most patients enrolled in that trial had hormone receptor (HR)-positive/HER2-negative tumours — a molecular subtype distinct from the present case, which involves more aggressive HER2-positive tumour biology that typically responds well to HER2-targeted agents.<sup>15</sup>

The selection of the VMAT technique for this case is supported by strong clinical and technical considerations, particularly given the complexity of the target area, which includes the locoregional left mammary glands and mediastinal lesions requiring curative doses. Conventional two-dimensional (2D) radiotherapy techniques for breast cancer employ standardised field boundaries: the medial boundary at the mid-sternal line, the lateral boundary at the mid-axillary line or at least 2 cm beyond the palpable breast, the superior boundary at the clavicular head or the second intercostal space, the inferior boundary 2 cm below the inframammary fold, the inner boundary 2–2.5 cm from the outer rib towards the lung, and the outer boundary 2 cm from the skin marker. The conventional radiotherapy dose for the

entire breast is 25 fractions of 2 Gy each, followed by a tumour bed boost of 5–8 fractions of 2 Gy, delivered to areas with positive or close surgical margins. However, in complex cases such as this, where simultaneous irradiation of the locoregional breast and pulmonary lesions is required, conventional 2D techniques face substantial limitations in achieving optimal dose conformality. VMAT enables highly conformal dose delivery that closely follows the tumour contour, ensuring that the entire target volume receives the prescribed dose while better sparing surrounding healthy tissues compared with conventional radiotherapy techniques.<sup>12</sup> Comparative studies have shown that VMAT outperforms conventional three-dimensional (3D) techniques across several parameters in breast cancer patients requiring comprehensive regional nodal irradiation. The proportion of healthy tissue exposed to radiation with VMAT is nearly half that of 3D techniques (2.7% vs. 5.3%), with lower doses delivered to the shoulder and back regions.<sup>11</sup> In this case, VMAT facilitated simultaneous irradiation of the left locoregional breast and lung lesion with a dose of 50 Gy in 25 fractions, achieving high precision while minimising radiation to organs at risk (OARs). The OAR doses achieved—spinal cord 0.876 Gy, thyroid 2.601 Gy, oesophagus 2.147 Gy, right lung 2.199 Gy, left lung 2.022 Gy, and heart 2.784 Gy—were all well below established tolerance limits, demonstrating the superiority of VMAT in sparing critical organs from excessive radiation. Lung dose constraints were strictly maintained to prevent radiation pneumonitis, considering that the target encompassed the thoracic region and pulmonary lesions, necessitating the preservation of healthy lung parenchyma. The very low spinal cord dose (<1 Gy) effectively eliminated the risk of radiation myelopathy, while minimal thyroid and oesophageal doses supported long-term tolerability without significant toxicity. In addition, VMAT offers a shorter delivery time (average 3 minutes) compared with Helical Tomotherapy (average 17 minutes), thereby reducing the impact of tumour motion due to respiration—an important advantage for thoracic targets.<sup>11</sup> Pneumonitis remains a potential complication of breast cancer radiotherapy, typically developing within three months post-treatment and possibly leading to pulmonary fibrosis several months later. Similar to radiation-induced lung cancer, the risk of pneumonitis increases with higher radiation doses to the lung. Radiological pneumonitis (RP) observed on

chest X-rays and CT scans in irradiated breast cancer patients correlates with common dosimetric parameters, including lung dose-volume constraints such as  $V_{20} < 30\%$  and mean lung dose (MLD)  $\leq 20\text{--}30$  Gy, as well as ipsilateral  $V_{13}$ ,  $V_{20}$ , and  $V_{30}$ .<sup>16,17</sup> In clinical practice, contralateral lung dose can be minimised by limiting the number of beams or by employing partial arcs in rotational therapy to avoid beam entry through the contralateral lung. The inclusion of lymph nodes and the use of IMRT techniques tend to increase lung exposure, whereas breathing-adapted techniques and prone or lateral decubitus positioning can effectively reduce lung dose. However, the implementation of new positioning strategies remains limited by the requirement for specialised equipment and concerns regarding daily reproducibility.<sup>18</sup>

Prioritisation and the impact of treatment delay are critical aspects to be discussed in this case. The patient underwent surgery on 2 October 2024, completed chemotherapy in February 2025, but only commenced radiotherapy on 15 July 2025—an interval of nearly five months after chemotherapy, or nine months after surgery. Several studies have demonstrated that delays in breast cancer treatment exceeding 90 days from diagnosis adversely affect both disease-free and overall survival.<sup>7</sup> Retrospective studies from Indonesia and other developing countries indicate that limitations in radiotherapy infrastructure and prolonged waiting lists frequently result in clinically significant delays that may negatively influence prognosis.<sup>19</sup> In this case, the decision to prioritise (cito) radiotherapy following the discovery of pulmonary lesions was likely based on the awareness that further postponement could compromise local tumour control and facilitate metastatic spread. Evidence suggests that delays in initiating radiotherapy increase the risk of recurrence, even in cases of ductal carcinoma in situ (DCIS), highlighting the importance of timely treatment initiation.<sup>20</sup> Although this patient underwent mastectomy rather than breast-conserving surgery (BCS), the same principle applies: a prolonged interval between surgical local control and radiotherapy increases the likelihood of undetected microscopic cancer cell proliferation. Studies have reported decreased disease-specific survival in patients with locally advanced breast cancer who experienced treatment delays of  $\geq 60$  days.<sup>7</sup> The detection of

pulmonary lesions during this prolonged interval underscores the necessity of re-staging prior to radiotherapy and reinforces the urgency of initiating definitive therapy without further delay—particularly in countries with limited healthcare resources.

Post-radiation evaluation allows sufficient time to observe the treatment response while retaining the option to modify the therapeutic plan if necessary. A reduction in lesion size confirms its malignant nature and radiosensitivity, ensuring the complete eradication of cancer cells within the targeted area. Although literature on mid-treatment evaluation in oligometastatic radiotherapy remains limited, the concept has a clear radiobiological basis: most tumour responses to radiation occur progressively during therapy, and interim assessment can provide insight into tumour radiosensitivity. The description of the pulmonary lesion as “regular with a capsulated appearance” may raise diagnostic uncertainty as to whether it represents true metastasis or a benign/granulomatous lesion. The radiation dose administered in this case aligns with the stereotactic body radiotherapy (SBRT) regimen typically used for pulmonary oligometastases. Evidence suggests that a higher biological effective dose (BED) correlates with improved local control in oligometastatic disease, with an equivalent  $BED_{10}$  exceeding 100 Gy often recommended for extracranial lesions.<sup>21</sup> Conversely, if a lesion demonstrates characteristics inconsistent with a radiotherapeutic response or requires histological verification, surgical resection (pulmonary metastasectomy) serves as an alternative local therapy option. This approach has been shown to achieve favourable local control and survival outcomes in selected patients with pulmonary oligometastases from breast cancer.<sup>22,23</sup> Systematic reviews have reported a pooled 5-year survival rate of approximately 46% following pulmonary metastasectomy, with the most favourable prognostic factors being solitary metastasis, a disease-free interval of more than three years, and hormone receptor (HR)-positive status.<sup>24</sup> This decision exemplifies a multidisciplinary treatment strategy that integrates treatment response, tumour biology, and patient condition to determine the most appropriate therapeutic modality—using observed treatment response as a biomarker to guide subsequent management decisions.

The limitations of this case and their implications for clinical application must be acknowledged. Firstly, this is a single case report without a control group; therefore, conclusions regarding the effectiveness of the curative approach to oligometastasis should be interpreted with caution. In case reports, there is an inherent selection bias, as patients with more favourable conditions are often chosen for aggressive therapies, making it difficult to determine whether positive outcomes (if observed) are attributable to treatment or to the patient's baseline characteristics.<sup>25</sup> Secondly, the lack of long-term follow-up data at the time of writing limits the ability to evaluate whether this approach truly provides a survival benefit or merely delays disease progression. Studies with extended follow-up have shown that approximately 25% of oligometastatic patients achieve disease-free survival beyond 25 years; however, the limited median follow-up duration precludes definitive conclusions regarding curability.<sup>26,27</sup> Thirdly, the HER2-positive tumour biology in this case introduces another confounding factor: the patient received chemotherapy that included anti-HER2 therapy (trastuzumab), which is known to be highly effective in HER2-positive metastatic disease. It remains unclear from the case description whether the patient continued adjuvant anti-HER2 therapy following chemotherapy; if not, this may represent a missed opportunity, given robust evidence that one year of adjuvant trastuzumab significantly improves disease-free survival and reduces recurrence by approximately one-third in HER2-positive breast cancer.<sup>28</sup> In practical terms, implementing mid-treatment assessment at fraction 40 introduces logistical complexity and additional costs, as it requires further imaging and potential replanning. This approach may not be feasible in all clinical environments, particularly in resource-limited settings. Cost-effectiveness analyses have demonstrated that adaptive radiotherapy with replanning incurs substantial expenditure and places additional demands on human resources, especially where staffing is limited.<sup>29,30</sup> Nevertheless, this case underscores the importance of a multidisciplinary approach in managing oligometastatic disease, in which treatment decisions (radiotherapy vs. surgery vs. further systemic therapy) must be made collaboratively, taking into account tumour characteristics, patient factors, and healthcare system constraints.<sup>31</sup> The patient was referred back to the surgical

oncology team for further evaluation of the metastatic lesion, comprehensive metastatic work-up, and consideration of additional chemotherapy. Follow-up recommendations include periodic imaging (chest CT or PET-CT) every three months during the first year to enable early detection of both local and distant disease progression. This is consistent with various guidelines for the management of oligometastatic patients, which emphasise whole-body staging every 3–6 months and regular reassessment of the treatment strategy based on therapeutic response and tolerability.<sup>29,32</sup>

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### **CONCLUSION**

This case illustrates the practical application of the oligometastatic concept in a patient with HER2-positive breast cancer presenting with a solitary pulmonary metastasis, in whom curative radiotherapy using volumetric-modulated arc therapy (VMAT) was selected as the definitive treatment modality. VMAT provides the advantages of enhanced radiation precision and optimal sparing of vital organs surrounding the complex target regions, namely the locoregional mammary area and the pulmonary lesion. The post-radiation evaluation approach reflects an adaptive treatment strategy guided by tumour response, which is a rational and evidence-based concept, although long-term follow-up is required to confirm its clinical effectiveness. The limited radiotherapy resources in Indonesia highlight the need for careful case prioritisation and a multidisciplinary approach to optimise outcomes in potentially curable oligometastatic patients.

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