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# MAMMOGRAPHY-ENHANCED IMMUNOTHERAPY DECISION-MAKING IN NON-SMALL CELL LUNG CANCER (NSCLC): CHARTING A NEW COURSE

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## ABSTRACT

### INTRODUCTION:

Non-small cell lung cancer (NSCLC) is one of the most difficult cancers to treat, but advances in immunotherapy have brought new hope to patients. While traditional imaging tools like CT and PET scans are used to guide treatment, there's growing curiosity about whether mammography - a standard breast cancer screening tool - might also have a role to play. In rare cases, mammography has helped detect breast metastases from NSCLC or changes linked to immune-related side effects. Emerging technologies like AI and radiomics also assist esearchers in spotting mammography imaging patterns that could hint at how a tumour might respond to immunotherapy. Beyond its diagnostic potential, routine mammography could encourage patients to engage more with other screening programs, leading to earlier detection and better treatment outcomes. Although the research is still in its early stages, exploring how mammography might contribute to immunotherapy decision-making could open new doors in the personalised care of NSCLC patients.

### KEYWORDS

Non-small cell lung cancer, immunotherapy, mammography, breast cancer

## INTRODUCTION:

The mortality rate of cancers continues to be a conundrum in the field of medicine, with a death toll of almost 10 million as of recent surveys.[1,2]

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Lung cancer is the leading cause of cancer deaths.[3] It doubles as the second most diagnosed cancer across gender globally, with an estimated incidence rate of 12.4% (2.5 million) and mortality rate of 18.7% (1.8 million).4 Non-Small Cell Lung Cancer (NSCLC) refers to all lung cancers of the epithelial cell layer other than Small Cell Lung Cancer (SCLC) and accounts for 80-85% of all lung cancer cases.[5]

The most common types are squamous cell

carcinoma, large cell carcinoma, and adenocarcinoma, with other less frequently occurring types existing. Various risk factors, especially cigarette smoking, have been identified as predisposing factors for NSCLCs, but adenocarcinomas have also been diagnosed in patients with no smoking history.[6]

Various lung cancer treatment options exist, ranging from radiotherapy to chemotherapy, surgical interventions, and even immunotherapy.[7] Immunotherapy, also known as immuno-oncology, is a biological cancer treatment option that optimises an individual's immune system to equip it to target cancer cells to combat the disease specifically.[8,9] This treatment regimen was identified over two centuries ago by Dr William B. Coley, who used a streptococcal vaccine made of Serratia marcescensas one of its key ingredients, later termed 'Coley's toxin' to treat various malignancies. After which, long-term disease-free survival for more than 5 years was seen in approximately 50% of these patients, specifically those with inoperable sarcomas.[10] Immuno-oncology as a treatment option is altering cancer treatment approaches due to its tolerable safety profile, longer-lasting therapeutic effects enabled by immunological memory, and its effectiveness across a wide range of patients.[11] As earlier stated, the goal of immunotherapy is to improve the tumour-specific immune response, and some of the lung cancer-specific strategies include administration of immune checkpoint inhibitors, cancer vaccine therapy, adoptive transfer of immune cells generated in vitro, immunotherapy with dendritic cells (DCs), and recombinant cytokines.[12]

Mammography screening is a type of breast imaging test that utilises low-dose X-rays to detect cancer even while asymptomatic.[13] It is structured to integrate diverse aspects to represent a measure that allows for early detection of breast cancer, thus leading to reduced mortality rates, better prognosis, and improved treatment options. It also ensures a minimal and acceptable side effect level for clients, is reliable and affordable, and can be applied regularly.[14] Evidence, although sparse, exists of a diagnostic advantage of mammography for improved lung cancer prognosis.[15] At the same time, other studies see mammography as a "teachable moment" to improve the uptake of lung cancer screening (LCS) services.16,17 Regardless of the viewpoint, there appears to be an advantage in utilising mammography.

Consequently, although mammography is not originally a lung cancer screening test, in some cases mammographic findings can provide indirect insights that may influence NSCLC immunotherapy decisions.[18] In cases of NSCLC metastasis to the breast, although rare, mammography can detect such lesions, and if breast metastasis has occurred, it may indicate a more advanced disease stage and thus influence the choice of immunotherapy treatment regimen (combination or monotherapy).[19] Furthermore, some immune-related adverse effects (irAEs) as a result of immunotherapy can cause breast changes. Thus, mammography detecting these changes can prompt a review of the given treatment option.[20] Hence, mammography-informed immunotherapy decision making can revolutionize treatment approaches for NSCLC, the major variant of all lung cancers. Still, a critical examination of the current evidence is necessary.

## CURRENT STATE OF IMMUNOTHERAPY IN NSCLC

### Overview of current immunotherapy approaches

NSCLC accounts for approximately 85% of all cases of lung cancer[21] and has historically been associated with poor survival outcomes, especially in advanced stages.[22] However, the development of novel anticancer agents shows a promising future in improving patients' survival.[23] Over the past decade, immunotherapy, particularly immune checkpoint inhibitors (ICIs), has revolutionized NSCLC treatment by leveraging the body's immune system to eliminate cancer cells.[24] Immune checkpoint inhibitors such as programmed death-1 (PD-1) inhibitors (nivolumab and pembrolizumab), and programmed death-ligand 1 (PD-L1) inhibitors (atezolizumab and durvalumab) are now standard therapies for NSCLC.[25,26] ICIs and chemotherapy combination is also a treatment option for people with NSCLC, especially those with lower PD-L1 expression.[27] Additionally, cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) inhibitors (e.g., ipilimumab) have been combined with ICIs to enhance immune activation.[28] At the same time, adjuvant and neoadjuvant immunotherapy approaches are being explored to improve long-term survival outcomes in early-stage NSCLC.[29]

Most NSCLCs have an immunogenic tumor microenvironment characterised by high infiltration of cytotoxic T lymphocytes and elevated PD-L1 expression, which makes it more responsive to immune checkpoint inhibitors such as anti-PD-1 and anti-PD-L1 therapies.[30,31] Additionally, some NSCLCs exhibit high tumor mutational burden (TMB), which generates neoantigens that can enhance immune system recognition and response.[32] These properties support the clinical efficacy of immunotherapy in NSCLC management.

## Limitations and challenges of current approaches

Although immunotherapy is a promising treatment option for NSCLC, it poses some challenges.[33] Patient selection remains a serious issue in NSCLC immunotherapy, as PD-L1 expression (a core biomarker used in guiding therapy) has inconsistent predictive value due to various factors. These include biopsy-related variability, tumour heterogeneity, and differences in immunohistochemistry (IHC) assay results, which make precise detection challenging.[33] Resistance mechanisms also complicate treatment as both primary and acquired resistance develop due to modifications in the tumour microenvironment (TME) and the increased activation of alternative immune checkpoints, ultimately leading to disease progression.[34] Additionally, immune-related adverse events (irAEs) such as pneumonitis, endocrinopathies, and colitis result in treatment discontinuation, adversely impacting patient outcomes.[35] The tumour response heterogeneity is another challenge, as some tumours show pseudo-progression - initially growing before shrinking, and hyper-progression characterised by rapid tumour growth following immunotherapy.36 Present-day imaging techniques also struggle to distinguish between true tumour progression and immune-related changes, underscoring the urgent need for more refined predictive imaging tools to improve treatment decisions and patient outcomes.[36,37]

### The concept of mammography-informed immunotherapy decision-making

Mammography has been utilised for breast cancer detection over the years. However, in certain contexts, its application in the management of NSCLC has been explored. Reports have shown how mammography was instrumental in identifying breast cancer metastasis from an NSCLC, highlighting its potential beyond primary breast cancer detection.[38] Various studies have also suggested that integrating mammography with other screening methods, such as CT lung cancer screening, can aid the early detection of multiple malignancies, including NSCLC.[39] These findings suggest that mammography may have a wider application in oncology, particularly regarding NSCLC management, by assessing TME characteristics and predicting immunotherapy responses using mammographic imaging features. Mammography shows features such as vascularisation pattern, tumour density, and textural characteristics, which may provide insights into the therapy response or cancer progression.[40,41,42] Advanced imaging methods, including radiomics, have been utilised to extract quantitative data from medical images, enabling the noninvasive assessment of the tumour microenvironment.[43] Combining imaging-derived data with traditional biomarkers, such as PD-L1 expression and tumour mutational burden (TMB), has been explored to improve patient selection and monitor responses to immunotherapy.[44,45,46] Although direct evidence of mammography's application in assessing immune infiltration and guiding immunotherapy in NSCLC is currently limited, the immune system's role in NSCLC progression and treatment response is well-established.[47] If similar imaging principles are applied to NSCLC, mammography could serve as a complementary tool in guiding immunotherapy strategies.

## THE ROLE OF MAMMOGRAPHY IN IMMUNOTHERAPY DECISION-MAKING

### How Mammography Can Inform Immunotherapy Decisions

Mammography, which is a cornerstone of breast cancer screening, may seem out of place in investigative discussions around NSCLC. However, with the current evolutions of cancer treatment, it is worth exploring whether this technology can offer something new. Researchers have hypothesised that certain mammogram features, such as dense breast tissue and calcification patterns (which provide information about the tumour microenvironment), may indicate underlying inflammation and immune system activity, helping identify patients who will benefit from immunotherapy.[48] Cases of NSCLC metastasis to the breast or unusual calcifications seen on mammography may also point to an immune response. These postulations could predict how a patient will respond to immunotherapy, thereby guiding immunotherapy decisions.[49]

There's also a growing interest in whether mammography could help identify new imaging biomarkers, particularly when combined with Artificial Intelligence (AI).[50,51] Various AI algorithms, including deep learning models, have shown great potential in identifying biomarkers such as altered parenchymal tumour texture, atypical vascular patterns, and systemic microcalcifications. Though these markers are not specific to the breast or lung, they help showcase ongoing oncogenic processes.[52] These AI models also detect subtle patterns in mammograms that show an increased risk of lung cancer, suggesting that the breast may be a surrogate site for systemic biomarker discovery. This approach expands the utility of existing screening tools and opens avenues for non-invasive screening for NSCLC.

Another key reason mammography is being discussed in the context of immunotherapy is its role in overall cancer screening. Studies have found that women who get regular mammograms are more likely to follow through with other screenings, including lung cancer screening.[53] Since lung cancer is much easier to treat and immunotherapy works best when it's caught early, using mammography as a gateway to lung cancer screening could improve outcomes.[54,55]

## Examination of the Current Evidence on the Use of Mammography in NSCLC Immunotherapy

Presently, the role of mammography in NSCLC immunotherapy remains more theoretical than an established clinical tool. Imaging techniques like CT scans and PET imaging targeting the lungs are the mainstays for assessing tumor response and progression.[56] Mammography, in contrast, has limited evidence supporting its use in this context.

Some literature has explored how imaging in general may help predict immunotherapy responses, particularly through identifying biomarkers. Other studies have suggested that calcifications (in the breast or other tissues) might correlate with immune activity or tumor stroma characteristics.[51] In theory, mammography could provide a window into how the immune system responds to a tumor, potentially guiding immunotherapy decisions.

Additionally, mammography's ability to detect breast metastasis in NSCLC patients has garnered some interest. Although rare, when NSCLC metastasizes to the breast, mammography could detect these lesions earlier than other methods, offering a head start in treatment planning.[57] However, these findings are limited, and the leap from imaging metastatic spread to making immunotherapy decisions is far from being fully established.

## Critical Analysis of the Strengths and Limitations of the Current Evidence

There are various advantages in utilising mammography in NSCLC immunotherapy decision-making. The primary strength of mammography lies in its widespread availability, its ability to pick up tumour details and changes like microcalcifications that other imaging methods might miss, and its potential to identify novel biomarkers. Mammography could predict immunotherapy outcomes if those changes are linked to tumor-immune interactions. Documented findings also show that women who undergo mammograms tend to be more proactive about other cancer screenings, making it an avenue for earlier diagnosis and prompt commencement of immunotherapy.[53,54] Additionally, since mammograms are already a routine part of healthcare for many women, they provide a valuable opportunity to introduce discussions about lung cancer screening and improve overall participation.

However, mammography has significant limitations when it comes to lung cancer. Firstly, mammograms were not primarily designed for this purpose, making their role in lung cancer and immunotherapy mostly indirect. The lung tissue environment and its cancerous changes differ from what mammography typically captures in breast tissue. Thus, even though calcifications provide valuable information in breast cancer, it is far from clear whether they carry the same significance in NSCLC.

Another challenge is the current lack of extensive evidence. While isolated, some cases hint at mammography's potential role; large-scale clinical trials are needed to draw firm conclusions. Additionally, although some studies suggest that mammograms may provide insights into immune system activity, there is a paucity of solid evidence to establish them as a clinical tool for immunotherapy decisions. Until such research is conducted, the use of mammography in decision-making for NSCLC immunotherapy remains speculative.

Many women still skip breast and lung cancer screening, even when they qualify for it, which limits the impact of using mammography as a gateway for early detection. A mammogram alone will not determine if someone is a good candidate for immunotherapy. It would need to be combined with other tests, such as CT scans, biopsies, and biomarker analysis, to get a full picture.

## POTENTIAL IMPLICATIONS OF MAMMOGRAPHY-INFORMED IMMUNOTHERAPY DECISION MAKING FOR CLINICAL PRACTICE

Integrating mammography-informed decision-making with immunotherapy choices holds significant potential implications for clinical practice. Informed decision-making in mammography involves discussing the benefits, harms, and uncertainties of screening with patients. However, studies show that this process is often limited, with discussions focusing on benefits rather than harms or uncertainties. This imbalance can lead to decisional conflict and dissatisfaction among patients. Nonetheless, when patients are well-informed about their screening results, they may be more likely to participate actively in discussions about subsequent treatment options, including immunotherapy.[58]

The process of weighing the benefits and harms of mammography screening can prepare patients for similar analyses in immunotherapy, where treatments may have significant side effects and varying success rates. This informed approach can facilitate personalised medicine by guiding immunotherapy choices tailored to the patient's specific condition, as revealed by mammography results.[59] For instance, if mammography reveals particular tumour characteristics, this information can be crucial in selecting target immunotherapies. Moreover, the psychological effects of being well-informed about mammography can extend to immunotherapy decisions, potentially reducing anxiety and improving confidence in treatment choices.

In clinical practice, these ideas help improve communication between patients and doctors, making it easier to choose treatments that match patients' preferences and healthcare needs. Decision support tools that integrate information on mammography and immunotherapy can also help patients better understand their treatment options. Furthermore, educating healthcare providers on how to effectively communicate the implications of mammography results for immunotherapy decisions is crucial for optimising patient care.

### Examination of the potential benefits and challenges of implementing this approach

Integrating mammography results with immunotherapy decisions offers significant benefits, particularly in developing personalised treatment plans. By combining detailed tumour characteristics revealed through mammography with immunotherapy options, healthcare providers can tailor treatments to each patient's unique needs. This approach ensures that therapies are better suited to the tumour's specific biology, potentially enhancing treatment effectiveness while minimising unnecessary interventions. As a result, patients may experience more targeted, efficient care, leading to improved outcomes and fewer adverse effects.[60] Another significant benefit is improved resource allocation. By using mammography data to guide treatment choices, healthcare providers can ensure that resources are directed toward the most effective therapies for each patient. This targeted approach helps minimize unnecessary treatments, reduce waste, and improve overall healthcare outcomes. As a result, healthcare systems can operate more efficiently, optimizing patient care and resource utilization.[60]

Enhanced patient engagement is another key advantage of integrating mammography results with immunotherapy decisions. Informed decision-making during mammography can foster greater patient involvement in subsequent treatment choices, including immunotherapy. When patients are well-informed about their screening results, they are more likely to participate in discussions about their treatment options. This leads to better alignment between the treatment plan and the patient's preferences and values, ultimately improving their overall experience and satisfaction with their care.[61]

However, despite these benefits, several challenges need to be addressed. One such challenge is the complexity of overdiagnosis, which can arise from mammography screening. Overdiagnosis occurs when tumours are detected that may never progress to a life-threatening stage, leading to unnecessary treatments. This complicates the decision-making process for immunotherapy, as healthcare providers must carefully evaluate screening results to differentiate between cases requiring intervention and those not. If not managed properly, overdiagnosis can result in overtreatment, which can harm patients and strain healthcare resources.[61]

Another challenge is the need for comprehensive healthcare provider training. Effective integration of mammography-informed decision-making with immunotherapy requires healthcare providers to be well-equipped to communicate complex information to patients. This includes understanding the implications of mammography results for immunotherapy and facilitating clear, informed discussions with patients about their treatment options. Healthcare providers must be skilled in translating technical details into understandable terms and addressing patients' concerns or questions, ensuring patients are empowered to make decisions that align with their values and preferences.[61]

Accessibility and equity represent another significant challenge in implementing this approach. To fully benefit from mammography-informed decision-making in immunotherapy, it is essential to address disparities in access to mammography screening, particularly among vulnerable populations, such as women with disabilities.[62] Barriers such as socioeconomic factors, healthcare worker attitudes, and physical obstacles must be overcome to ensure that all individuals, regardless of background or circumstance, have equitable access to screening and subsequent treatments. Without addressing these inequities, the potential benefits of integrated decision-making may not reach all patients, perpetuating disparities in healthcare outcomes.[62]

Technological and logistical challenges are critical in effectively integrating mammography-informed decision-making with immunotherapy. Specialised expertise and equipment are often required to accurately interpret mammography results, particularly in complex cases, such as those involving breast implants, which can complicate imaging.[63]

Moreover, implementing integrated decision support systems that can seamlessly combine mammography data with immunotherapy decisions demands significant technological and logistical investments. These systems require robust infrastructure, training, and ongoing maintenance to ensure that healthcare providers can rely on them to make accurate, timely decisions, which can be a significant barrier for many healthcare settings.[63]

**Suggestions for future research and directions for clinical implementation**

Future efforts in healthcare should focus on several key areas to enhance the integration of mammography-informed decision-making with immunotherapy, ensuring that patients receive the most effective and personalised care. One of the primary areas for development is improving patient engagement in the decision-making process. This involves creating accessible educational materials and decision aids to help patients better understand the implications of their mammography results for immunotherapy. By empowering patients with knowledge, healthcare providers can ensure that treatment decisions align with patient values and preferences, ultimately improving patient satisfaction and outcomes.

Another critical aspect is providing comprehensive training for healthcare providers to integrate mammography results into immunotherapy decisions effectively. This training should cover the technical skills required to interpret mammography results accurately and essential communication skills to facilitate informed discussions with patients. Programs should emphasise the importance of personalised medicine and the role of mammography-informed decision-making in improving treatment outcomes, ensuring that providers are equipped to deliver the best possible care. Overcoming technological and logistical challenges will also be crucial to the success of this approach. Investments in developing integrated decision-support systems can help streamline the decision-making process by efficiently combining mammographic data with immunotherapy options. Such systems can reduce errors, optimise treatment decisions, and improve patient care by providing healthcare providers with accurate, timely information.

Ensuring equitable access to mammography screening and subsequent treatments is essential for the success of this integrated approach. Addressing systemic barriers, such as socioeconomic disparities and physical accessibility issues, is vital to ensure that underserved populations have the same opportunities to benefit from mammography-informed decision-making. Outreach programs and collaborations with community organisations can help increase access to screening services and treatments for those who might otherwise be excluded. Finally, continued research is necessary to assess the effectiveness of integrating mammography-informed decision-making with immunotherapy. Future studies should evaluate patient satisfaction, treatment efficacy, and cost-effectiveness to understand better how this approach affects overall healthcare outcomes. This research will provide critical insights to guide the further refinement and improvement of the strategy over time, ensuring it becomes an effective and sustainable model for personalised cancer care.

## CONCLUSION

Although mammography has been established as a standard breast cancer screening tool, its potential application in NSCLC management opens up new and intriguing possibilities. Beyond its traditional role, mammography may serve as a valuable adjunct in guiding immunotherapy decisions by detecting metastatic lesions, assessing immune-related changes, and identifying novel imaging biomarkers when enhanced by AI and radiomics. Its widespread use, accessibility, and non-invasive nature make it attractive for integration into wider oncologic strategies. Additionally, mammography may improve patient engagement in screening programs, indirectly contributing to earlier detection and treatment initiation in NSCLC. While current evidence is minimal, these possibilities show the importance of re-evaluating conventional tools in a multidisciplinary, patient-centered medicine framework. As research progresses, mammography could shape future NSCLC treatment and enhance the precision and timeliness of immunotherapy decisions.

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### Author Contributions

PAO, NGU conceived the idea and designed the study's framework. PAO, NGU, HOS and WII conducted the literature review and provided the conceptual framework. TGU and KVK provided essential resources and contributed to the discussion and implications section. RAA and AUJ-I drafted the introduction and background sections, organised the manuscript for better coherence, and ensured logical flow throughout the writing process. PAO formatted and edited the final manuscript. All authors read and approved the final manuscript.

### Competing interest

The authors have no conflicting interests

### List of Abbreviations

- NSCLC: Non-Small Cell Lung Cancer
- SCLC: Small Cell Lung Cancer
- AI: Artificial Intelligence
- CT: Computed Tomography
- PET: Positron Emission Tomography
- TMB: Tumor Mutational Burden
- irAEs: Immune-Related Adverse Events
- ICIs: Immune Checkpoint Inhibitors
- PD-1: Programmed Death-1
- PD-L1: Programmed Death-Ligand 1
- CTLA-4: Cytotoxic T-Lymphocyte-Associated Protein 4
- DCs: Dendritic Cells
- LCS: Lung Cancer Screening
- MRI: Magnetic Resonance Imaging
- IHC: Immunohistochemistry
- LMIC: Low- and Middle-Income Countries

## REFERENCES

1. World Health Organization: WHO. Global cancer burden growing, amidst mounting need for services. who.int. 2024 Feb 1; Available from: https://www.who.int/news/item/01-02-2024-global-cancer-burden-growing--amidst-mounting-need-for-services#:~:text=Lung%20cancer%20was%20the%20most,common%20causes%20of%20cancer%20death.

2. The International Agency for Research on Cancer (IARC). Global Cancer Observatory [Internet]. 2023 [cited 2025 Mar 25]. Available from: https://gco.iarc.fr/en

3. Wolf AMD, Oeffinger KC, Shih TY, Walter LC, Church TR, Fontham ETH, et al. Screening for lung cancer: 2023 guideline update from the American Cancer Society. CA a Cancer Journal for Clinicians [Internet]. 2023 Nov 1;74(1):50–81. Available from: https://doi.org/10.3322/caac.21811

4. World Health Organization: WHO. Cancer [Internet]. 2025. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer#:~:text=Key%20facts,lower%2Dmiddle%2Dincome%20countries.

5. Winston T. Non-Small cell lung Cancer (NSCLC): practice essentials, background, pathophysiology [Internet]. 2024. Available from: https://emedicine.medscape.com/article/279960-overview

6. National Cancer Institute. Non-Small cell lung cancer Treatment (PDQ®) [Internet]. Cancer.gov. 2025 [cited 2025 Mar 22]. Available from: https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq#:~:text=NSCLC%20is%20any%20type%20of,Deaths:%20124%2C730.

7. Miyasaka Y, Sato H, Okano N, Kubo N, Kawamura H, Ohno T. A promising treatment strategy for lung cancer: a combination of radiotherapy and immunotherapy. Cancers [Internet]. 2021 Dec 31;14(1):203. Available from: https://doi.org/10.3390/cancers14010203

8. American Cancer Society. What is immunotherapy? | Immunotherapy for cancer [Internet]. American Cancer Society. 2025 [cited 2025 Mar 24]. Available from: https://www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html

9. National Cancer Institute. Immunotherapy for cancer [Internet]. Cancer.gov. 2019. Available from: https://www.cancer.gov/about-cancer/treatment/types/immunotherapy

10. Steven A, Fisher SA, Robinson BW. Immunotherapy for lung cancer. Respirology [Internet]. 2016 Apr 21;21(5):821–33. Available from: https://doi.org/10.1111/resp.12789

11. Lahiri A, Maji A, Potdar PD, Singh N, Parikh P, Bisht B, et al. Lung cancer immunotherapy: progress, pitfalls, and promises. Molecular Cancer [Internet]. 2023 Feb 21;22(1). Available from: https://doi.org/10.1186/s12943-023-01740-y

12. Yang L, Wang L, Zhang Y. Immunotherapy for lung cancer: advances and prospects [Internet]. 2016. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4858602/#sec7

13. Radiological Society of North America (RSNA) and American College of Radiology (ACR). Mammography [Internet]. Radiologyinfo.org. 2023 [cited 2025 Mar 25]. Available from: https://www.radiologyinfo.org/en/info/mammo

14. Heywang-Köbrunner SH, Hacker A, Sedlacek S. Advantages and Disadvantages of mammography Screening. Breast Care [Internet]. 2011 Jan 1;6(3):2. Available from: https://doi.org/10.1159/000329005

15. Lee B, Harvey S. Incidental lung cancer found on screening breast MRI with eventual lymphatic metastasis to the breast. Breast Disease [Internet]. 2015 Jul 31;35(3):207–10. Available from: https://doi.org/10.3233/bd-150406

16. Sandler KL, Haddad DN, Paulson AB, Osterman TJ, Scott CC, Poulos EA, et al. Women screened for breast cancer are dying from lung cancer: An opportunity to improve lung cancer screening in a mammography population. Journal of Medical Screening [Internet]. 2021 May 4;28(4):488–93. Available from: https://doi.org/10.1177/09691413211013058

17. Wong LY, Yue T, Aghagoli G, Baiu I, Shula L, Lee A, et al. Harnessing Opportunity: Pilot intervention to improve lung cancer screening for women undergoing breast screening mammography. JTO Clinical and Research Reports [Internet]. 2024 Mar 26;5(6):100671. Available from: https://doi.org/10.1016/j.jtocrr.2024.100671

18. Wali A, Leonardo D, MyLungCancerTeam. Can a mammogram detect lung cancer? [Internet]. MyLungCancerTeam. 2024. Available from: https://www.mylungcancerteam.com/resources/can-a-mammogram-detect-lung-cancer

19. Fares NR. Metastases to breast from primary lung cancer. The Egyptian Journal of Radiology and Nuclear Medicine [Internet]. 2023 Mar 21;54(1). Available from: https://doi.org/10.1186/s43055-023-01005-0

20. Gumusay O, Callan J, Rugo HS. Immunotherapy toxicity: identification and management. Breast Cancer Research and Treatment [Internet]. 2022 Jan 11;192(1):1–17. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8841316/

21. Molina J.R., Yang P., Cassivi S.D., Schild S.E. & Adjei A.A. 2008. Non-Small cell lung cancer: Epidemiology, risk factors, treatment, and survivorship. Mayo Clinic Proceedings, 83, 584–594.

22. Lung cancer survival Rates | 5-Year survival rates for lung cancer. n.d. (https://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/survival-rates.html accessed on March 17, 2025).

23. Zhang C., Leighl N.B., Wu Y.-L. & Zhong W.-Z. 2019. Emerging therapies for non-small cell lung cancer. Journal of Hematology & Oncology, 12.

24. Rolfo C., Caglevic C., Santarpia M., Araujo A., Giovannetti E., Gallardo C.D., et al. 2017. Immunotherapy in NSCLC: a promising and revolutionary weapon. Advances in Experimental Medicine and Biology, 97–125.

25. Dantoing E., Piton N., Salaün M., Thiberville L. & Guisier F. 2021. Anti-PD1/PD-L1 Immunotherapy for Non-Small Cell Lung Cancer with Actionable Oncogenic Driver Mutations. International Journal of Molecular Sciences, 22, 6288.

26. Davies M.J. 2019. PD-1/PD-L1 Inhibitors for Non–Small Cell Lung Cancer: Incorporating Care Step Pathways for Effective Side-Effect Management. Journal of the Advanced Practitioner in Oncology, 10.

27. García-González J., Ruiz-Bañobre J., Afonso-Afonso F.J., Amenedo-Gancedo M., Del Carmen Areses-Manrique M., Campos-Balea B., et al. 2020. PD-(L)1 Inhibitors in Combination with Chemotherapy as First-Line Treatment for Non-Small-Cell Lung Cancer: A Pairwise Meta-Analysis. Journal of Clinical Medicine, 9, 2093.

28. Hellmann M.D., Paz-Ares L., Caro R.B., Zurawski B., Kim S.-W., Costa E.C., et al. 2019. Nivolumab plus Ipilimumab in Advanced Non–Small-Cell Lung Cancer. New England Journal of Medicine, 381, 2020–2031.

29. Wakelee H., Liberman M., Kato T., Tsuboi M., Lee S.-H., Gao S., et al. 2023. Perioperative Pembrolizumab for Early-Stage Non–Small-Cell lung cancer. New England Journal of Medicine, 389, 491–503.

30. Wang, Y., Li, C., Wang, Z. et al. Comparison between immunotherapy efficacy in early non-small cell lung cancer and advanced non-small cell lung cancer: a systematic review. BMC Med 20, 426 (2022). https://doi.org/10.1186/s12916-022-02580-1

31. Govindan R, Aggarwal C, Antonia SJ, Davies M, Dubinett SM, Ferris A, Forde PM, Garon EB, Goldberg SB, Hassan R, Hellmann MD, Hirsch FR, Johnson ML, Malik S, Morgensztern D, Neal JW, Patel JD, Rimm DL, Sagorsky S, Schwartz LH, Sepesi B, Herbst RS. Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of lung cancer and mesothelioma. J Immunother Cancer. 2022 May;10(5):e003956. doi: 10.1136/jitc-2021-003956. PMID: 35640927; PMCID: PMC9157337.

32. Cheng J, Kang W, Chen Y, Pan L, Han H, Lv T. Continuous immunotherapy beyond disease progression in patients with advanced non-small cell and small cell lung cancer. Cancer Immunol Immunother. 2025 Feb 25;74(4):124. doi: 10.1007/s00262-025-03958-9. PMID: 39998635; PMCID: PMC11861770.

33. Ma L.-R., Li J.-X., Tang L., Li R.-Z., Yang J.-S., Sun A., et al. 2021. Immune checkpoints and immunotherapy in non-small cell lung cancer: Novel study progression, challenges and solutions (Review). Oncology Letters, 22.

34. Zhou X., Ni Y., Liang X., Lin Y., An B., He X., et al. 2022b. Mechanisms of tumor resistance to immune checkpoint blockade and combination strategies to overcome resistance. Frontiers in Immunology, 13.

35. Fletcher K. & Johnson D.B. 2024. Chronic immune-related adverse events arising from immune checkpoint inhibitors: an update. Journal for ImmunoTherapy of Cancer, 12, e008591.

36. Ma Y., Wang Q., Dong Q., Zhan L. & Zhang J. 2019. How to differentiate pseudoprogression from true progression in cancer patients treated with immunotherapy. (https://pmc.ncbi.nlm.nih.gov/articles/PMC6726978/ accessed on).

37. Lau D, Corrie PG, Gallagher FA. MRI techniques for immunotherapy monitoring. Journal for Immunotherapy of Cancer [Internet]. 2022 Sep 1;10(9):e004708. Available from: https://pubmed.ncbi.nlm.nih.gov/36122963/

38. Guerrouaz M.A., Samba S., BenSghier A., Sbai A. & Mezouar L. 2020. Breast metastasis from a non-small cell lung cancer: a case report. Cureus. , March 29, 2020. , 10.7759/cureus.7460.

39. Mammography and CT Lung Cancer Screening Can Improve Population-Based Health Outcomes [Internet]. UCSF Radiology. 2019 [cited 2025 Mar 23]. Available from: https://radiology.ucsf.edu/blog/mammography-and-ct-lung-cancer-screening-can-improve-population-based-health-outcomes.

40. Huo C.W., Chew G., Hill P., Huang D., Ingman W., Hodson L., et al. 2015b. High mammographic density is associated with an increase in stromal collagen and immune cells within the mammary epithelium. Breast Cancer Research, 17.

41. Chitalia R.D. & Kontos D. 2018. Role of texture analysis in breast MRI as a cancer biomarker: A review. Journal of Magnetic Resonance Imaging, 49, 927–938.

42. Fernández-Nogueira P., Mancino M., Fuster G., Bragado P., De Puig M.P., Gascón P., et al. 2020. Breast mammographic density: Stromal implications on breast cancer detection and therapy. Journal of Clinical Medicine, 9, 776.

43. Xue C, Zhou Q, Xi H, Zhou J. Radiomics: A review of current applications and possibilities in the assessment of tumor microenvironment. Diagnostic and Interventional Imaging [Internet]. 2022 Oct 22;104(3):113–22. Available from: https://www.sciencedirect.com/science/article/pii/S2211568422001966.

44. Yolchuyeva S., Giacomazzi E., Tonneau M., Lamaze F., Orain M., Coulombe F., et al. 2023. Imaging-Based biomarkers predict programmed Death-Ligand 1 and survival outcomes in advanced NSCLC treated with nivolumab and pembrolizumab: a Multi-Institutional study. JTO Clinical and Research Reports, 4, 100602.

45. Kao C., Powers E., Wu Y., Datto M.B., Green M.F., Strickler J.H., et al. 2021. Predictive value of combining biomarkers for clinical outcomes in advanced Non-Small cell lung cancer patients receiving immune checkpoint inhibitors. Clinical Lung Cancer, 22, 500–509.

46. Vanguri R.S., Luo J., Aukerman A.T., Egger J.V., Fong C.J., Horvat N., et al. 2022. Multimodal integration of radiology, pathology and genomics for prediction of response to PD-(L)1 blockade in patients with non-small cell lung cancer. Nature Cancer, 3, 1151–1164.

47. Carbone D.P., Gandara D.R., Antonia S.J., Zielinski C. & Paz-Ares L. 2015. Non–Small-Cell lung cancer: role of the immune system and potential for immunotherapy. Journal of Thoracic Oncology, 10, 974–984.

48. De Mello RA, Veloso AF, Catarina PE, et al. Potential role of immunotherapy in advanced non-small-cell lung cancer. OncoTargets Ther. 2017;10:21-30.

49. Mamdani H, Ahmed S, Sikder RK, et al. Immunotherapy in lung cancer: current landscape and future directions. Front Oncol. 2022;12:8864096.

50. Wali A, Leonardo D, MyLungCancerTeam. Can a Mammogram Detect Lung Cancer? Mylungcancerteam.com. My Lung Cancer Team; 2024. Available from: https://www.mylungcancerteam.com/resources/can-a-mammogram-detect-lung-cancer

51. Ahn JS, Shin S, Yang SA, Park EK, Kim KH, Cho SI, Ock CY, Kim S. Artificial Intelligence in Breast Cancer Diagnosis and Personalized Medicine. J Breast Cancer. 2023 Oct;26(5):405-435. https://doi.org/10.4048/jbc.2023.26.e45

52. Yala A, Mikhael PG, Strand F, Lin G, Smith K, Wan YL, et al. Toward robust mammography-based models for breast cancer risk. Science Translational Medicine. 2021 Jan 27;13(578):eaba4373.

53. Wong L-Y, Yue T, Aghagoli G, et al. Harnessing opportunity: Pilot intervention to improve lung cancer screening for women undergoing breast screening mammography. JTO Clin Res Rep. 2024;5:100671.

54. Novogrodsky E, Liou D, Titan AL, et al. Lung cancer screening among mammography patients: knowledge, eligibility, participation, and interest. JAMA Netw Open. 2023;6:e233789.

55. Becker N, Motsch E, Trotter A, et al. Lung cancer mortality reduction by LDCT screening—Results from the randomized German LUSI trial. Int J Cancer. 2020;146:1503-1513.

56. Hildebrandt MG, Naghavi-Behzad M, Vogsen M. A role of FDG-PET/CT for response evaluation in metastatic breast cancer? Seminars in Nuclear Medicine. 2022 Sep 1 [cited 2022 Nov 1];52(5):520–30. Available from: https://www.sciencedirect.com/science/article/pii/S0001299822000290?via=ihub

57. Sangha Brar J, Lo L, Wong J. Metastases to the breast: great radiological mimicker of primary breast carcinoma and a forgotten entity. A case series of three patients and a review of the literature. BJR|case reports. 2017 Sep;3(3):20160137.

58. Nekhlyudov L, Li R, Fletcher SW. Informed decision making before initiating screening mammography: does it occur and does it make a difference? Health Expect. 2008 Dec;11(4):366-75. doi: 10.1111/j.1369-7625.2008.00514.x. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5060464/.

59. Pérez-Lacasta MJ, Martínez-Alonso M, Garcia M, et al. Effect of information about the benefits and harms of mammography on women's decision making: The InforMa randomised controlled trial. PLoS One. 2019;14(4):e0214057. doi:10.1371/journal.pone.0214057.

60. BMJ Oncology. Benefits and harms of breast cancer screening revisited. BMJ Oncology. 2023;2(1):e000100.

61. ETHICAL ISSUES IN MAMMOGRAPHY SCREENING PROGRAMS. https://air.unimi.it/retrieve/handle/2434/555812/975444/phd_unimi_R10721.pdf. 2025. Available from: air.unimi.it.

62. Alfayez S, Alshammari H, Al-Dosary A, et al. Breaking barriers: improving mammography screening accessibility and quality of care for breast cancer women with disabilities in Saudi Arabia. Front Oncol. 2024;14:1398061. doi:10.3389/fonc.2024.1398061.

63. Moffitt Cancer Center. Mammogram Testing for Breast Cancer. [https://www.moffitt.org/cancers/breast-cancer/diagnosis/screening/mammogram/]. 2025. Available from: moffitt.org.