

Preoperative Imaging and Underestimation of Breast Tumor Size: Clinical Implications and Strategies

Summary

Accurate assessment of tumor size is crucial for effective surgical planning in cancer patients. Specific to breast cancer, however, preoperative imaging with mammography and ultrasound often underestimates the actual tumor size.¹ This article examines the drivers of underestimation, discusses clinical implications, and reviews methods to minimize the negative impact of underestimation on surgical outcomes.

1. Introduction

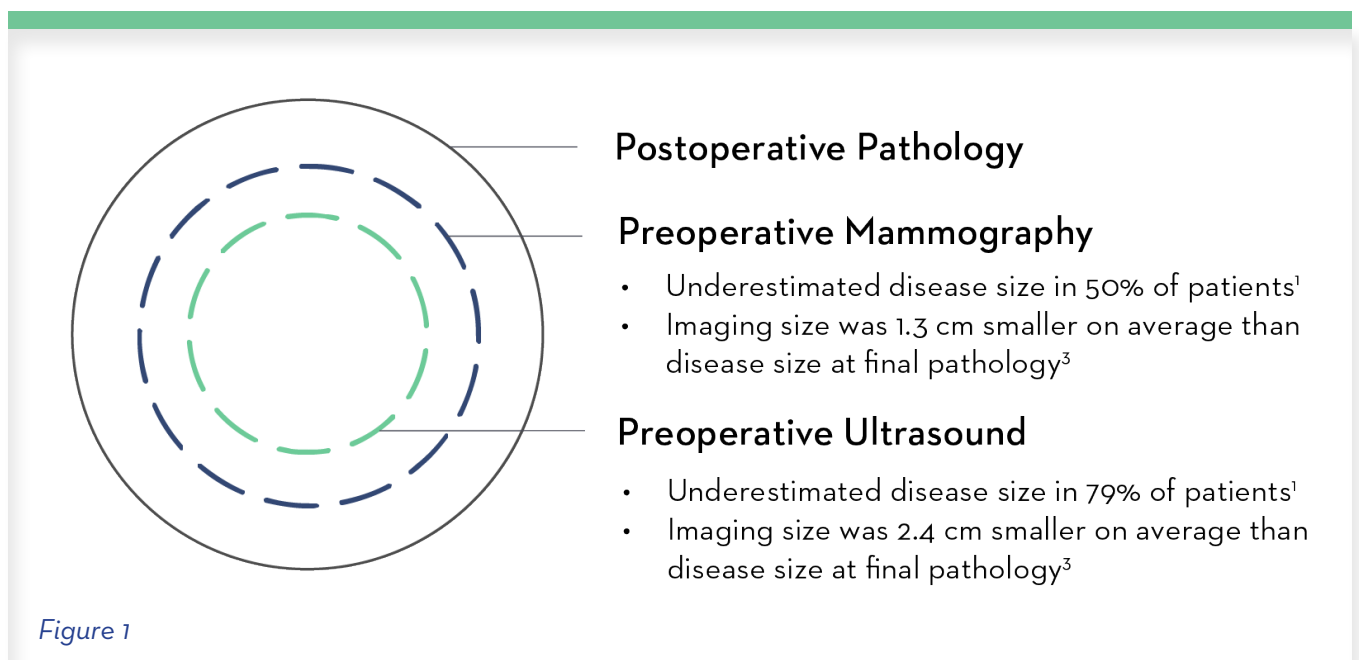
Accurate assessment of tumor size is vital for optimal surgical management of cancer, a significant global health concern. Preoperative imaging techniques play a pivotal role in evaluating tumor extent and planning an appropriate therapeutic strategy.² However, studies have consistently shown that preoperative imaging underestimates true tumor size, which is a key driver of margin clearance and necessitates re-excision surgeries in over 23% of breast lumpectomies.^{1,3,4,5}

1.1 Findings

In breast-conserving surgery, there is a strong correlation between preoperative disease underestimation (via mammography and ultrasound) and patients with residual disease.^{4,6}

Both mammography and ultrasound have demonstrated considerable underestimation of disease extent when compared to final pathology (Figure 1).

Studies have consistently shown that preoperative imaging underestimates true tumor size, which is a key driver of margin clearance and necessitates re-excision surgeries in over 23% of breast lumpectomies.^{1,3,4,5}



2. Reasons for Underestimation

2.1 Radiological Factors

Mammography, the gold standard for breast cancer screening, has limitations in estimating tumor size accurately.⁷ The absence of microcalcifications, compression of the breast during mammography, and dense breast tissue each contribute to tumor size underestimation in 50% of diagnoses.^{1,3}

Ultrasound, while important in determining tumor characteristics, has been shown to underestimate tumor size in over 79% of cases.¹ Particularly in small tumors, acoustic shadowing may hide the posterior edge of the abnormality, while estimating the size of large tumors may be limited if any dimensions exceed the width of the transducer.⁸ Additionally, ultrasound results are strongly influenced by the user's skill and the sophistication of the equipment available.^{1,3}

The inaccuracy of mammography and ultrasound are both directly correlated to increasing tumor size.¹

2.2 Biological Factors

Tumor biology plays a significant role in underestimating tumor size. Ductal carcinoma in situ (DCIS) is typically seen with calcifications, but may present without calcifications in 10-20% of cases.⁹ Mammography relies on the interpretation of microcalcifications, thus studies have shown that non-calcified DCIS presented as a false-negative in 49% of cases.^{10,11}

Mammography relies on the interpretation of microcalcifications, thus studies have shown that non-calcified DCIS presented as a false-negative in 49% of cases.^{10,11}

Some studies have gone as far as excluding patients presenting with DCIS without microcalcifications, likely due to the difficulty of imaging the tumor.⁴ Using ultrasound, non-calcified DCIS may resemble invasive carcinoma due to indistinct or irregular margins.¹¹

For both mammography and ultrasound, visualization of invasive lobular carcinoma (ILC) presented challenges and had the largest difference between preoperative and histological tumor size

measurements.^{8,10} ILC is more difficult to detect than DCIS or invasive ductal carcinoma (IDC) as its growth pattern is less disruptive to the surrounding architecture and tends to spread over a large area in a single-file cellular pattern.^{10,12}

Tumor multifocality and multicentricity can further complicate accurate diagnostic imaging as simultaneous cancers may be missed by mammography and ultrasound.¹³ The rate at which multifocal and multicentric cancers occur varies widely in the literature, likely due to the difficulty with imaging and

3. Clinical Implications

3.1 Surgical Planning

Accurate tumor size assessment is essential for determining the proper therapeutic approach. Tumor size and multifocality may necessitate a more aggressive surgical approach, contributing to the decision to pursue breast-conserving surgery or mastectomy.^{14,15} Tumor size has also been shown to correlate with lymph node involvement, tumor grade, and overall survival rate.² Underestimating tumor size may result in the surgeon not choosing the optimal treatment based on disease extent.

3.2 Re-excisions

Patients with a discrepancy of >50% between pathological and radiological tumor size have a higher chance of residual disease following breast-conserving surgery.⁶ Understanding the limits of available preoperative imaging technologies may help clinicians make informed decisions when deciding on a course of treatment for their patients. While additional breast-conserving surgeries are largely successful, patients whose tumors are more than 50% larger than predicted by preoperative imaging have a higher likelihood of additional surgeries.¹⁶

While additional breast-conserving surgeries are largely successful, patients whose tumors are more than 50% larger than predicted by preoperative imaging have a higher likelihood of additional surgeries.¹⁶

4. Strategies to Optimize Surgical Outcomes

4.1 Multimodal Imaging

Combining different imaging modalities, such as mammography, ultrasound and MRI, can improve tumor size estimation by providing complementary information. This multimodal approach enhances accuracy and reduces the risk of underestimation and may be recommended in the presence of DCIS or ILC. DCIS may be present without calcifications, possibly leading to a false-negative assessment using mammography alone.¹

4.2 Intraoperative Techniques

Conventional intraoperative imaging tools, such as specimen radiography and ultrasound, aid in confirming the location of seeds, clips, and calcifications during surgery. Similar to mammography, they do not have the resolution to visualize margins at the microscopic level. Optical Coherence Tomography (OCT) has 10 times the resolution of X-ray and ultrasound at 2 mm imaging depth, allowing for the detection of microstructures associated with DCIS and other features.¹⁷ This enables real-time assessment of surgical margins, giving surgeons a new tool to potentially help achieve negative margins and minimize the risk of re-excision.¹⁷

“Optical Coherence Tomography (OCT) has 10 times the resolution of X-ray and ultrasound at 2 mm imaging depth, allowing for the detection of microstructures associated with DCIS and other features.”¹⁷

5. Conclusion

Preoperative imaging technologies including mammography and ultrasound commonly underestimate tumor size. Understanding these limitations is crucial for surgeons to optimize surgical planning, minimize re-excision rates, and ensure adequate tumor resection. Incorporating multimodal imaging and intraoperative techniques, such as the use of OCT to visualize margins intraoperatively, may improve accuracy and enhance surgical outcomes.

References

1. Eichler C, Abrar S, Puppe J, Arndt M, Ohlinger R, Hahn M, Warm M. Detection of Ductal Carcinoma In Situ by Ultrasound and Mammography: Size-dependent Inaccuracy. *Anticancer Res.* 2017 Sep;37(9):5065-5070. doi: 10.21873/anticancer.11923. [PMID: 28870935](#).
2. Azhdeh S, Kaviani A, Sadighi N, Rahmani M. Accurate Estimation of Breast Tumor Size: A Comparison Between Ultrasonography, Mammography, Magnetic Resonance Imaging, and Associated Contributing Factors. *Eur J Breast Health.* 2020 Dec 24;17(1):53-61. doi: 10.4274/ejbh.2020.5888. [PMID: 33796831](#); [PMCID: PMC8006785](#).
3. Liu RQ, Que J, Chen L, Dingee CK, Warburton R, McKevitt EC, Kuusk U, Pao JS, Bazzarelli A. Measurements using mammography and ultrasonography underestimate the size of high-volume ductal carcinoma in situ. *Am J Surg.* 2021 Jun;221(6):1167-1171. doi: 10.1016/j.amjsurg.2021.03.043. Epub 2021 Mar 24. [PMID: 33810833](#).
4. Schultek G, Gerber B, Reimer T, Stubert J, Hartmann S, Martin A, Stachs A. Radiological Underestimation of Tumor Size as a Relevant Risk Factor for Positive Margin Rate in Breast-Conserving Therapy of Pure Ductal Carcinoma In Situ (DCIS). *Cancers (Basel).* 2022 May 11;14(10):2367. doi: 10.3390/cancers14102367. [PMID: 35625972](#); [PMCID: PMC9139437](#).
5. Metcalfe LN, Zysk AM, Yemul KS, Jacobs LK, Oker EE, Underwood HR, Thompson AM. Beyond the Margins-Economic Costs and Complications Associated With Repeated Breast-Conserving Surgeries. *JAMA Surg.* 2017 Nov 1;152(11):1084-1086. doi: 10.1001/jamasurg.2017.2661. [PMID: 28768303](#); [PMCID: PMC5831419](#).
6. Mimouni M, Lecuru F, Rouzier R, Lotersztajn N, Heitz D, Cohen J, Fauconnier A, Huchon C. Reexcision for positive margins in breast cancer: A predictive score of residual disease. *Surg Oncol.* 2015 Sep;24(3):129-35. doi: 10.1016/j.suronc.2015.08.003. Epub 2015 Aug 13. [PMID: 26298198](#).
7. Stein, R.G., Wollschläger, D., Kreienberg, R. et al. The impact of breast cancer biological subtyping on tumor size assessment by ultrasound and mammography - a retrospective multicenter cohort study of 6543 primary breast cancer patients. *BMC Cancer* 16, 459 (2016). <https://doi.org/10.1186/s12885-016-2426-7>
8. Sabek EAS, Salem HT. Technical Factors Affecting Ultrasound Breast Tumor Size as Correlated with Pathological Type. *Medicina (Kaunas).* 2019 Oct 25;55(11):713. doi: 10.3390/medicina55110713. [PMID: 31731397](#); [PMCID: PMC6915355](#).
9. Cho KR, Seo BK, Kim CH, Whang KW, Kim YH, Kim BH, Woo OH, Lee YH, Chung KB. Non-calcified ductal carcinoma in situ: ultrasound and mammographic findings correlated with histological findings. *Yonsei Med J.* 2008 Feb 29;49(1):103-10. doi: 10.3349/yymj.2008.49.1.103. [PMID: 18306476](#); [PMCID: PMC2615255](#).
10. Gruber IV, Rueckert M, Kagan KO, Staebler A, Siegmann KC, Hartkopf A, Wallwiener D, Hahn M. Measurement of tumour size with mammography, sonography and magnetic resonance imaging as compared to histological tumour size in primary breast cancer. *BMC Cancer.* 2013 Jul 5;13:328. doi: 10.1186/1471-2407-13-328. [PMID: 23826951](#); [PMCID: PMC3704854](#).
11. Bragg A, Candelaria R, Adrada B, Huang M, Rauch G, Santiago L, Scoggins M, Whitman G. Imaging of Noncalcified Ductal Carcinoma In Situ. *J Clin Imaging Sci.* 2021 Jun 16;11:34. doi: 10.25259/JCIS_48_2021. [PMID: 34221643](#); [PMCID: PMC8247756](#).
12. Pereslucha AM, Wenger DM, Morris MF, Aydi ZB. Invasive Lobular Carcinoma: A Review of Imaging Modalities with Special Focus on Pathology Concordance. *Healthcare (Basel).* 2023 Mar 3;11(5):746. doi: 10.3390/healthcare11050746. [PMID: 36900751](#); [PMCID: PMC10000992](#).
13. Neri A, Marrelli D, Megha T, Bettarini F, Tacchini D, De Franco L, Roviello F. "Clinical significance of multifocal and multicentric breast cancers and choice of surgical treatment: a retrospective study on a series of 1158 cases". *BMC Surg.* 2015 Jan 14;15(1):1. doi: 10.1186/1471-2482-15-1. [PMID: 25586679](#); [PMCID: PMC4324662](#).
14. Steinhof-Radwańska K, Lorek A, Holecki M, Barczyk-Gutkowska A, Grażyńska A, Szczudło-Chraścina J, Bożek O, Habas J, Szyluk K, Niemiec P, Gisterek I. Multifocality and Multicentricity in Breast Cancer: Comparison of the Efficiency of Mammography, Contrast-Enhanced Spectral Mammography, and Magnetic Resonance Imaging in a Group of Patients with Primarily Operable Breast Cancer. *Curr Oncol.* 2021 Oct 8;28(5):4016-4030. doi: 10.3390/currenocol28050341. [PMID: 34677259](#); [PMCID: PMC8534697](#).
15. Masannat YA, Agrawal A, Maraqa L, Fuller M, Down SK, Tang S, Pang D, Kontos M, Romics L, Heys SD. Multifocal and multicentric breast cancer, is it time to think again? *Ann R Coll Surg Engl.* 2020 Jan;102(1):62-66. doi: 10.1308/rcsann.2019.0109. Epub 2019 Sep 6. [PMID: 31891668](#); [PMCID: PMC6937617](#).
16. Simpson D, Allan J, McFall B. Radiological Underestimation of Tumor Size Influences the Success Rate of Re-Excision after Breast-conserving Surgery. *Eur J Breast Health.* 2021 Oct 4;17(4):363-370. doi: 10.4274/ejbh.galenos.2021.2021-4-7. [PMID: 34651116](#); [PMCID: PMC8496123](#).
17. DuPree, B.B., Papez, M.J., Pirruccello, E. et al. Potential Utility of Adjunct Imaging with Wide-Field Optical Coherence Tomography for Gross and Microscopic Evaluation of Breast Specimens in Real-Time in the Operating Suite. *Indian J Surg* 84 (Suppl 3), 751-756 (2022). <https://doi.org/10.1007/s12262-021-03079-4>.