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Tumor size measurements predicted by digital mammography, ultrasonography, and magnetic resonance imaging in primary invasive breast cancer disease

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Abstract

Background and objective: The size of the tumor significantly influences the prognosis and treatment approach for breast cancer patients. The aim of this study was to find the most accurate imaging method for estimating pre-treatment tumor size in women with newly diagnosed primary invasive breast cancer by comparing the predicted tumor size obtained from mammography, ultrasonography, and magnetic resonance imaging with the pathologic size obtained from the surgical specimens.

Methods: This cross-sectional study included 181 primary invasive breast cancer patients from September 2021 to March 2023. The difference in tumor size was evaluated based on imaging and pathological reports. Variables such as age, breast density, and tumor characteristics like histologic type, grade, location, and side were recorded and analyzed. The American College of Radiology Breast Imaging Reporting and Data System was used for reporting. Data analysis, performed using SPSS Statistics software, included descriptive statistics, Spearman's correlation coefficient, and Lin's index. The statistical significance level was set at P <0.05.

Results: The mean tumor size was 29.68, 29.07, 28.37, and 27.7mm by mammography, ultrasonography, magnetic resonance imaging, and pathology, respectively. All diagnostic procedures revealed a statistically significant correlation with pathologic tumor size with the Spearman correlation test, P = 0.000. MRI had the highest Lin's concordance correlation coefficient (0.93).

Conclusion: The study determined that all imaging modalities were accurate in estimating tumor size when compared to the gold standard of pathological specimens and that magnetic resonance imaging outperformed digital mammography and ultrasonography.

Keywords: Tumor size; Breast neoplasms; Pathology; Imaging; Breast density.

Introduction

Breast cancer is a significant health concern. Women worldwide are highly affected by breast cancer, which ranks as the second most common cause of death in women, following lung cancer. Estimates indicate that the probability of a woman having invasive breast cancer during her lifetime is one in eight.[1] Tumor size is an important prognostic determinant in breast cancer, and it has been associated with lymph node involvement, tumor grade, and overall survival rate. Furthermore, it is an additional factor taken into account while making decisions about strategies for treatment such as breast conserving, mastectomy, and neoadjuvant chemotherapy. Therefore, accurately estimating the dimensions of tumors has great significance.[2,3] In terms of clinical practice, the determination of this involves a physical examination and a number of imaging modalities, including mammography (MMG), ultrasonography (USG), and contrast-enhanced magnetic resonance imaging (CE-MRI). Each of these methods has its own advantages and disadvantages in relation to this

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issue.[4-6] According to the World Health Organization, the determination of tumor size in invasive carcinoma relies on measuring the maximum dimension of the tumor. In cases where multiple cancers are detected, the size of the largest invasive cancer is all that is evaluated.

The measurement of tumor size should be conducted with precision to the nearest millimeter, and it does not encompass the presence of adjacent ductal carcinoma in situ (DCIS) that is located outside the invasive carcinoma.[7] Scholarly studies investigated the precision of tumor size measurements obtained using MMG, USG, and MRI and compared them to histopathology specimens obtained from surgical procedures. The results were varied in terms of their level of accuracy.[8,9]

Given the varying results reported in the literature, the aim of this study was to determine the most accurate imaging method for defining pre-therapeutic tumor size in patients with newly diagnosed primary invasive breast cancer, using histological size as the gold standard. The objectives were to determine the average tumor size in the population being studied, how well MMG, USG, and CE-MRI can measure tumor size, and whether there is a relationship between characteristics such as breast density, tumor location, type, and side of the tumor and measurements of tumor size.

Methods

This was a cross-sectional study, and the target population included women over the age of 18 who had MMG, USG, and CE-MRI for breast cancer diagnosis at Erbil Breast Center and Rizgary Teaching Hospital in Erbil, Iraq, between September 2021 and March 2023; all had undergone surgical intervention with a final diagnosis of primary invasive breast cancer and had a known pathological tumor size.

The exclusion criteria were those who had neoadjuvant treatment or surgery, those scheduled for chemotherapy, pregnant or lactating women, those with contraindications for MRI or gadolinium-based contrast agents, and those with incomplete information. Based on these inclusion and exclusion criteria, eligible patients were recruited, and the final study included 184 cases. The ethical considerations were implemented in accordance with the Helsinki Declaration, which provides guidelines for obtaining ethical permission from health authorities, and approval was obtained from the institutional ethics committee. Informed consent was waived. Three devoted board-certified radiologists with 8–10 years of experience in the field read all mammograms and MR images. They also performed all breast USG examinations alone or in consensus, with almost perfect interreader agreement, and were blind to the histopathological diagnosis.

MMG was performed using a digital full-field MMG system in standard craniocaudal and mediolateral oblique views, in addition to supplemental views when needed. USG was performed using the diagnostic Siemens ACUSON S2000 system and the GE Logiq P9, adopting a 7–12 MHz linear transducer probe. The analysis of images was performed using the "breast" default setting, which ensured the repeatability of the examinations. The MRI was performed on 1.5 Tesla with a dedicated breast coil and the patient lying in a prone position. The images included pre-contrast localizer, axial T1-weighted non-fat suppression, axial T2-weighted fat suppression, diffusion weighted imaging (DWI), and dynamic contrast-enhanced T1 fat-suppressed axial and coronal in accordance with the American College of Radiology (ACR) Breast MRI Accreditation Program.[10]

Following image processing, subtraction series were generated, and a maximum intensity projection (MIP) was reconstructed. The index tumor size was measured in the slice showing the largest lesion diameter on 3D dynamic contrast-enhanced T1 or subtracted axial images and the MIP images. The reporting

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of the imaging modalities was based on the ACR Breast Imaging Reporting and Data System (BI-RADS) fifth edition.[11] The histopathology information was obtained from the pathology department reports at the institution. Post-surgical examinations were used to determine the tumor's final histology, size, and grade. Tumor size measurements were obtained from either mastectomy or lumpectomy specimens with negative margins. It is worth noting that all women completed their imaging tests within two weeks and surgical results within two months after the diagnosis.

The study participant's age, ACR breast density, side of the index tumor, location, status of axillary lymph nodes, histopathological invasive tumor type, and grade, as well as the measurements of the index tumor size from written reports of MMG, USG, and CE-MR findings that were available before surgery, were all recorded and analyzed. Breast density was classified into two categories: non-dense breasts and dense breasts. Non-dense breasts include BI-RADS categories A and B, and dense breasts include BI-RADS categories C and D, according to the ACR. The size of the tumor was determined at its greatest dimension at each of the three imaging modalities and was compared to the maximum tumor size recorded on the surgical pathology reports.

Statistical analysis

The data was analyzed using the Statistics software package (SPSS version 25.0) (IBM Corporation, Armonk, NY, USA). The categorical variables were calculated in frequencies, and the numerical variables were described using median, mean, and standard deviation with minimum and maximum values. Spearman's correlation coefficient was calculated for each imaging method, using pathological tumor size as the gold standard. Lin's index was calculated to evaluate the precision and accuracy of different imaging techniques. The Mann-Whitney U-test was used to compare median values for paired parameters, while the Kruskal-Wallis one-way ANOVA test was used for comparisons of other parameters. A *P*-value of less than 0.05 was regarded as statistically significant.

Results

Only 181 cases of invasive breast cancer out of a total of 184 cases had the index tumor identified using the three imaging modalities of MMG, USG, and MRI. The mean age and standard deviation of the studied population were 45.17 and 11.13, respectively, with the majority of participants being between the ages of 40 and 49, followed by those under 40. The majority (79.0%) had invasive ductal carcinoma no special type (IDC-NST) with a high-grade tumor and metastatic lymph nodes. Table 1 presents additional data.

Table 2 presents the overall statistics of the measurements obtained from the three imaging modalities and pathological examinations. According to the results, the smallest tumor size detected using all the diagnostic techniques and histological reports was 10 mm. The largest tumor size was observed in the histopathology report and MRI, measuring 80 mm. However, greater maximum tumor sizes were identified using MMG and USG, with USG reporting the highest. The mean tumor size was 29.68mm by MMG, 29.07mm by USG, 28.37mm by MRI, and 27.7mm by pathology.

When the Spearman's correlation coefficient was calculated, all diagnostic procedures revealed a statistically significant correlation with pathologic tumor size ($P < 0.001$) (Table 3).

Lin's index was 0.78, 0.71, and 0.93 for MMG, USG, and MRI, respectively, indicating that MRI was more precise and accurate than the other techniques (Table 4).

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Table 1 Basic characteristics of the studied population

Variables	N (%)
Age categories:	
< 40	59 (32.6)
40-49	72 (39.8)
50-59	19 (10.5)
≥ 60	31 (17.1)
Pathologic tumor size, n (%):	
≤ 20 mm (%)	34 (18.8)
21-50 mm (%)	134 (74.0)
>50 mm (%)	13 (7.2)
Histological subtype, n (%):	
IDC-NST	143 (79.0)
IDC-other variants	22 (12.2)
Invasive lobular carcinoma	16 (8.8)
Invasive tumor grade, n (%):	
Grade 1 (well differentiated)	12 (6.6)
Grade 2 (moderately differentiated)	80 (44.2)
Grade 3 (poorly differentiated)	89 (49.2)
Axillary lymph node status	
Positive	135 (74.6)
Negative	46 (25.4)
Total	181 (100.0)

Table 2 The overall statistics of the measurements by the three imaging modalities and pathological examinations

Tumor size	N	Minimum (mm)	Maximum (mm)	Median (mm)	Mean (mm)	SD
Histopathology	181	10	80	25.0	27.70	11.15
Mammography	181	10	85	26.0	29.68	12.95
Ultrasonography	181	10	110	25.0	29.07	14.11
MRI	181	10	80	25.0	28.37	11.78

Table 3 Spearman's correlation of the diagnostic techniques versus pathologic tumor size

Diagnostic technique	Spearman rho value	*P*-value
Mammography	0.875	<0.001
Ultrasonography	0.897	<0.001
MRI	0.962	<0.001

Table 4 Lin's concordance correlation coefficient (CCC) of the diagnostic methods

Diagnostic technique	Lin's CCC	95% CI (Confidence interval)
Mammography	0.78	0.72-0.83
Ultrasonography	0.71	0.64-0.77
MRI	0.93	0.91-0.94

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The differences in Lin's indices and the concordance in tumor size measurements determined by all three imaging modalities are illustrated in Figures 1 and 2, respectively.

The pathological mean tumor size was compared with several other characteristics, as presented in Table 5 and Figure 3.

Aside from metastatic axillary lymph nodes and index lesion location, no statistically significant relationships were found between pathologic tumor size and variables such as the ACR breast density category and invasive cancer histologic types and grades. The tumor size was smaller on the right side, with a statistically significant association (P <0.05).

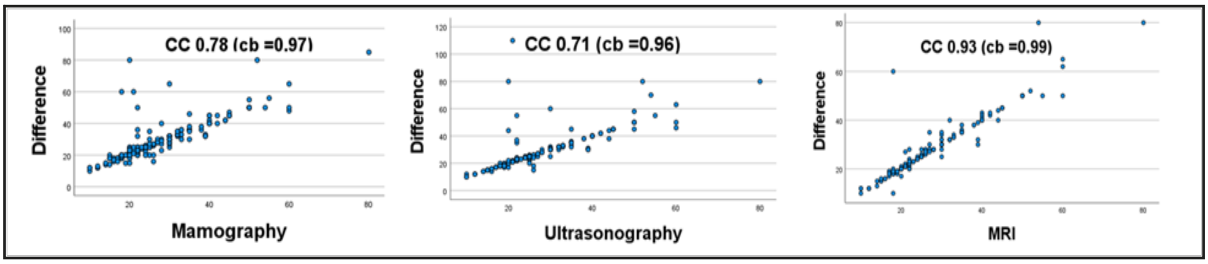

Figure 1 The differences of Lin's values of the three diagnostic methods

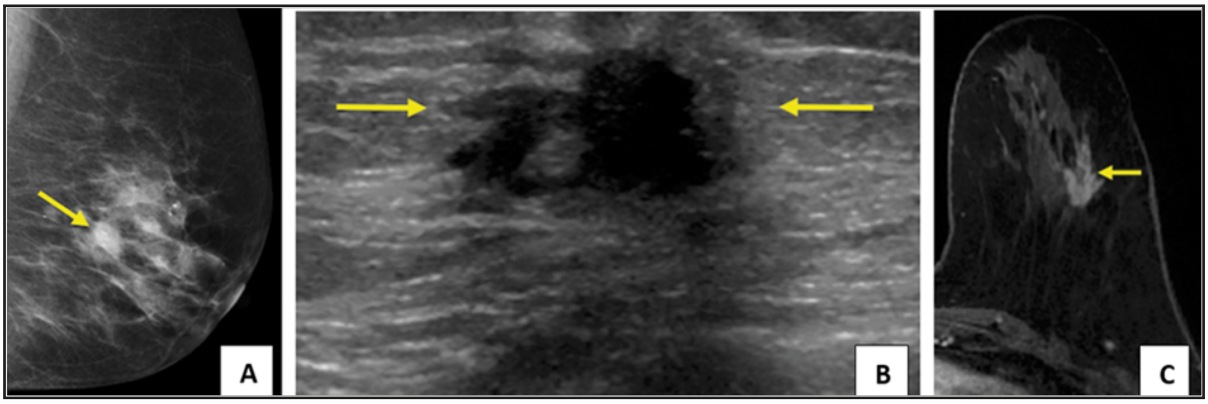

Figure 2 A 51-year-old woman who presented with a mass in the left breast, diagnosed as invasive ductal carcinoma no special type (IDC-NST, grade II) with no associated in situ carcinoma

A: Diagnostic mediolateral oblique mammogram demonstrated an irregular-shaped mass measuring 20 mm (arrow).

B: US depicted an irregular mass with indistinct margins also measuring 20 mm (arrows).

C: MRI depicted the finding as an irregular mass with spiculated margins measuring 20 mm (arrow). The final pathologic size was 20 mm on the mastectomy. The three imaging modalities were accurate in measuring the tumor size.

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Table 5 The associations between the pathological mean tumor size and other variables

Variables	Mean Rank	*P*-value
ACR breast density category		
Dense	93.75	0.322
Non-dense	85.59	
Index lesion location		
Overlapping and Unspecified	173	
Upper Outer Quadrant	89.68	
Upper Inner Quadrant	77.93	
Lower Outer Quadrant	92.42	0.022
Lower Inner Quadrant	70	
Subareolar (Central)	104.15	
Axillary Tail	87.25	
Invasive tumor type		
IDC-NST	91.62	
IDC-other variant	85.05	0.841
ILC	93.66	
Invasive tumor grade		
Grade 1 (well differentiated)	117.88	
Grade 2 (moderately differentiated)	90.91	0.167
Grade 3 (poorly differentiated)	87.46	
Metastatic axillary lymph nodes		
Positive	101.56	<0.001
Negative	60.01	

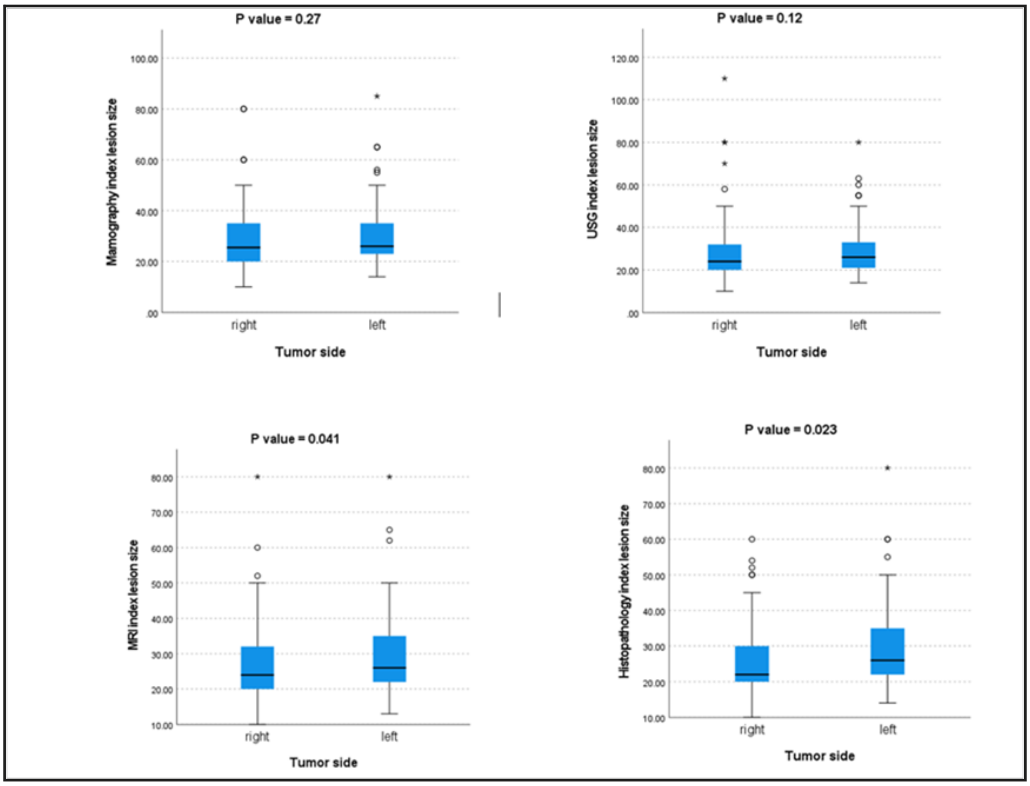

Figure 3 A comparison of various imaging modalities in relation to the tumor side

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Discussion

The importance of precise preoperative tumor size determination is that an overestimation or underestimate of tumor extent may influence treatment decisions. Underestimation might have the potential for a positive resection margin, and overestimation may result in unnecessary mastectomies. Imaging modalities have a significant role in accurately assessing the size of tumors. This study analyzed 181 women who were diagnosed with primary invasive breast cancer and demonstrated that MGM, USG, and MRI exhibit high accuracy in predicting the size of the tumor by comparing their results to the gold standard of pathological measures taken from the surgical specimen.

The effects of various factors on the accuracy of the measurements, including ACR breast density, tumor location, histologic tumor type, tumor grade, and tumor side, were also investigated. The size of invasive tumors can be used to evaluate disease. A review evaluating tumor characteristics in Asia and Africa reveals tumors averaging 3.3 cm in Tunisia and 4.8 cm in Sudan and Nigeria. In Pakistan, 80% of tumors are larger than 2 cm, and the average sizes in Singapore and Malaysia are 2.2 cm and 3.0 cm, respectively.[12] Our study found that the majority of patients had a tumor size between 2 and 5cm with a mean of 2.7cm and median of 2.5cm. The median tumor size by USG and MRI was in concordance with the pathologic size (25 mm), while MMG revealed 26 mm, which means that USG and MRI are more accurate than MMG. The Spearman's correlation coefficients obtained in our study were 0.875, 0.897, and 0.962 for MMG, USG, and MRI, respectively. Therefore, MRI was the most accurate modality for tumor size assessment compatible with Azhdeh et al. and Kim et al. studies.[6,13] The diagnosis is achieved with a higher sensitivity by MRI compared with mammography or ultrasound, as the malignant tissues draw a stronger contrast from the surrounding normal tissues in MRI. Small, invasive early-stage tumors in young women are better detected by MRI.

In the current study, we found higher concordance between size on MRI and histopathology, which is consistent with Taydaş et al.[14] While Cuesta et al.[15] indicated that MRI underestimates size, Gruber et al.[16] and Leddy et al.[17] stated that MRI overestimates tumor size. Guadalupe and Baek's studies found that MRI had the highest error rate for estimating tumor size.[18,19]

The disagreement between the various studies could be attributable to methodologies such as patient selection and characteristics, equipment selection, tumor characteristics (primarily histologic type), and others. The MRI in this study had a high concordance value because it used a multiparametric breast technique that includes DWI and MID. This, along with choosing only invasive breast cancer cases, made the results even more accurate.

This study used Lin's concordance coefficients (CC) to assess the precision of MMG, USG, CE-MRI, and the pathologic size of the index lesion. The highest agreement with pathological size was for the MRI CC 0.93 (95% CI 0.91-0.94), then MMG, and the lowest agreement was for the USG CC 0.71 (95% CI 0.64-0.77). Youn et al.[20] reported a CC for MRI of 0.884 (95% CI 0.791–0.935), indicating less agreement with pathology than in our investigation; however, their lesion sizes were smaller. In contrast, previous studies by Cortadellas et al.[8] and Leddy et al.[17] found that sonographic measurements of tumor size are more accurate than MR imaging. Stein et al.[21] did a larger study with 6,543 patients who had unifocal, unilateral primary breast cancer. They found that MMG gave the most accurate measurements, with a discernible difference in histological sizing. They also reported a slightly higher correlation between MMG and pathological examination than US (r = 0.61 vs. 0.60).

MMG lesion measurements are frequently challenging due to masking and tissue superposition. Furthermore, differences in the distance between the tumor and the detector, poorly defined lesion outlines, inherent zoom from x-ray magnification, and compression of the breast during examination can all affect MMG tumor assessment.

In a very recent study that compared the accuracy of ultrasound and mammography in determining tumor size in 287 breast cancer patients, results showed no significant difference between the two modalities, with ultrasound and mammography underestimating tumor size in 30.6% and 31% of cases, respectively. Ultrasonography was more accurate for smaller tumors.[22] USG is particularly useful in dense breasts; however, numerous researchers [23,24] have reported that it under- or over-estimates tumor size. Explanations include the fact that when vertical lesions are obscured by posterior acoustic shadowing, only the hypoechoic portion of the lesion is evaluated, rather than the hyperechoic speculated border. Furthermore, the in-situ component contributes to the overestimation.

Lee-Felker et al.[25] compared MRI and contrast-enhanced MMG in newly diagnosed breast cancer for the evaluation of the extent of the disease and found that they both have nearly the same sensitivity, but CEM had more PPV.A study by Park JY[26] aimed to evaluate cancer size measurement by computer-aided diagnosis (CAD) and radiologist on breast MRI relative to histopathology, Radiologist-measured size was significantly more accurate than the CAD size.

Regarding the association of tumor size with other variables, this study found that there was a statistically significant correlation between pathologic tumor size and the side of the lesion, with the left-sided breast lesion being larger than those in the right breast. This was true for all of the modalities used to evaluate tumor size. In line with Min et al.,[27]this study found a statistically significant link between tumor location and tumor size. Larger tumors were found in the subareolar (central), overlapping, and unspecified locations, but there was no difference between dense and nondense breast tissue. Tumor size has been associated with positive lymph node status in multiple studies; [27]

In the present study, the tumor size measurement also showed a statistically significant association with metastatic lymph nodes (*P* <0.001).

Limitations should be acknowledged; women who received neoadjuvant chemotherapy were not included; therefore, we cannot conclude that post-neoadjuvant MRI for surgical planning can give a more accurate measurement of residual disease than other types of imaging. The study did not use contrast-enhanced sonography and digital breast tomosynthesis because of their unavailability in our setting.

Conclusion

Mammography, ultrasonography, and MRI can accurately measure the tumor size compared to the gold standard of pathological specimens, and MRI was the most accurate and precise compared to MMG and USG.

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Competing interests

The authors declare that they have no competing interests.

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