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Radiological-Pathological Correlation

Tumor size and focality in breast carcinoma: Analysis of concordance between radiological imaging modalities and pathological examination at a cancer center

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ABSTRACT

Context: Accurate assessment of clinical and pathological tumor stage is crucial for patient treatment and prognosis.
Objective: The aim of this study was to assess the concordance between the tumor size and focality between radiological studies and pathology and to evaluate the impact of discrepancies on staging.
Design: Patients who underwent surgery for invasive breast carcinoma from January 1, 2014, to December 31, 2015, were identified.
Results: Three imaging modalities (mammogram, ultrasound and MRI) were compared with gross examination and final pathology. 1152 preoperative radiological studies were evaluated for focality and 1019 were evaluated for tumor size. For all 3 radiographic modalities, there was a statistically significant difference between the mean tumor size on radiology and the final pathology report (mammogram, $P < .001$; ultrasound, $P = .004$; MRI, $P < .001$). In 29% of radiology studies, there was a discrepancy in stage. The error rate for determining focality was 28% for mammograms, 27% for ultrasounds, and 29% for MRIs. Tumor size from gross examination correlated with microscopic tumor size in 57% of cases, but gross examination had 88% concordance with the final pathology report in determining focality.
Conclusion: Our study revealed statistically significant differences in mean tumor size reported across all 3 imaging modalities when compared to the final pathology report. MRI had the highest error rate, with a tendency to overestimate tumor size and number of foci. Among all diagnoses, cases of invasive carcinoma with an extensive intraductal component were most prone to discrepancies with imaging.

1. Introduction

Efforts to utilize radiographic imaging in the assessment of breast cancers date back to 1930, when radiologist Dr. Stafford Warren used the traditional fluoroscopic equipment of the time to obtain roentgenograms of the breast for 119 patients [1]. This study was the first to report the utility of preoperative imaging to discern between benign and malignant lesions. Today, technological advances have provided us with a variety of imaging modalities, often used in conjunction with one other, to assess a tumor's size and focality.

This multimodal approach, which includes mammography, ultrasound, and magnetic resonance imaging (MRI) among other modalities [2-5], is essential for preoperative clinical staging (cT), determining the type of surgery offered to a patient, and assessing the need for neoadjuvant and adjuvant therapies [2-4]. Underestimation of tumor size may lead to close or positive surgical margins, whereas overestimation may preclude patients from receiving breast-conserving therapy (BCT) [6,7]. The estimation of tumor size and focality upon macroscopic gross examination is also important, especially when intraoperative gross examination is used to assess margin status [8].

This study was designed to assess the concordance of tumor size and focality as identified by radiological imaging, gross examination, and the final pathology report as well as to evaluate how discrepancies may potentially impact final tumor staging.

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2. Materials and methods

After receiving institutional review board approval, we retrospectively reviewed the pathology information system (PathNet) to identify all patients who underwent surgical breast excision between January 1, 2014, and December 31, 2015, at our institution.

Inclusion criteria included having invasive breast carcinoma diagnosed via core needle biopsy, surgical excision (lumpectomy or mastectomy), no history of recent excision in the same breast, and preoperative imaging performed at our institution. Exclusion criteria included having benign lesions or only carcinoma in situ, receiving post-neoadjuvant chemotherapy, and having no preoperative imaging performed at our institution.

For data collection, the imaging reports were reviewed, and the tumor size, focality, and cT as recorded in the electronic medical record were documented. At the time of the study, mammograms were performed using a 2D modality. Not all patients underwent all 3 imaging modalities (mammogram, ultrasound, and MRI) preoperatively. In addition, the radiology reports did not uniformly describe the tumor size or focality. Therefore, the number of available imaging studies for analysis varied between the size and focality groups, and as a result tumor focality and size were independently assessed for statistical analysis.

The pathology reports were reviewed, and the tumor size, focality, and pathological stage (pT) were recorded. These variables from the final pathology report were compared with the various preoperative imaging studies and gross description to identify whether discrepancies affected the tumor's staging. A concordance numeric value between the pathology and radiology results was not used in this study because even seemingly insignificant millimeter variations can affect the final pathologic tumor stage and potentially change treatment.

2.1. Tumor size measurement

Imaging studies were interpreted by radiologists subspecialized in breast imaging. For each imaging modality, the largest tumor dimension from the preoperative report was recorded. When discrete masses were identified in areas of non-mass enhancement, the discrete mass's size was chosen for analysis.

The gross tumor size was determined by experienced pathologists' assistants by measuring all tumors in 3 dimensions using a standard ruler. All specimens were examined while fresh during the intraoperative consultation for margin assessment and x-rayed using Faxitron equipment (Tucson, AZ, USA). During intraoperative gross evaluation, specimens were oriented and inked according to the surgeon's designation and sliced at 5 to 10 mm intervals to examine the tumor(s)' dimensions, the presence of a biopsy site/clip and localization device, and the gross margin status. When discrete areas of induration were identified within ill-defined fibrotic areas, the discrete area's size was chosen for analysis. During final grossing, all tumors were re-measured in 3 dimensions, extensively sampled, and mapped (Fig. 1). The thickness of tissue slices were also provided in the gross description. During sign out, the tumor size on the final pathology report was determined by correlating the largest contiguous area of invasion with the grossing maps provided by pathologists' assistants. The size and number of foci on the final pathology report were used as the gold standard.

2.2. Statistical analyses

Paired Student *t*-tests and Mann-Whitney tests were performed, and the differences in tumor size and focality as identified between all imaging modalities, the gross description, and the final pathology report were examined. Mean, median, and range for all methods were obtained. $P \leq .05$ was considered statistically significant.

All imaging studies had a numerical value for focality, but not all imaging studies had a numerical value for size. Imaging studies that lacked numerical values for size were excluded from the statistical analyses for tumor size and staging.

3. Results

A total of 1378 primary breast tumor excisions, including lumpectomies, partial mastectomies, and mastectomies, were performed in-house during the study period. Four hundred ninety (35.5%) of these cases met the inclusion criteria and were included in the study. The 888 excluded cases included 483 cases from patients without imaging studies performed at our institution, 251 cases from patients who received neoadjuvant chemotherapy, and 154 cases from patients with only carcinoma in situ on final excision. Histologic diagnoses of the cases fulfilling the inclusion criteria are shown in Table 1. The average age of the patients in the study was 62 years (range, 24–91 years).

3.1. Tumor size data

For the 490 cases included, a total of 1152 imaging studies across all 3 modalities were reviewed (428 mammograms, 444 ultrasounds, and 280 MRIs). Of these, 1019 studies were included (335 mammograms, 412, ultrasounds, and 272 MRIs) because 133 studies did not mention a numerical value for tumor size and were therefore excluded.

3.1.1. Mammography findings

Three hundred thirty-five mammograms were included (260 mammograms of invasive ductal carcinoma [IDC] cases, 4 of IDCs + invasive lobular carcinomas [ILCs], 36 of ILCs, 22 of invasive carcinomas with extensive intraductal component [ICs + EIC], and 13 of special-type carcinomas). For all tumor types, there was a statistically significant difference ($P < .001$) between the mean (2.14 cm) and median (1.7 cm) tumor size measured by mammogram (range, 0.3–10.7 cm) and the mean (1.73 cm) and median (1.5 cm) tumor size recorded on the final pathology report (range, 0.1–10 cm) (Fig. 2A).

By histologic tumor type, statistical significance between the tumor on the mammogram and the final pathology report was reached for cases of IDC ($P < .001$) and IC + EIC ($P < .001$) (Table 2). Mammography overestimated the tumor size in 145 IDC cases (56%), with 51 of the 145 overestimated cases (35%) having a difference of 1 cm or more. Mammography also overestimated tumor size in 21 IC + EIC cases (95%), with 11 of the 21 overestimated cases (52%) having a difference of 1 cm or more.

3.1.2. Ultrasound findings

Four hundred twelve ultrasounds were included (323 ultrasounds of IDC cases, 10 of IDC + ILCs, 43 of ILCs, 19 of ICs + EIC, and 17 of special-type carcinomas). For all tumor types, a statistically significant difference was reached ($P = .004$) between the mean (1.64 cm) and median (1.4 cm) of tumor sizes measured by ultrasound (range, 0.2–7.8 cm) and the mean (1.82 cm) and median (1.5 cm) on the final pathologic report (range, 0.1–10 cm) (Fig. 2B).

By tumor type, a statistically significant difference between the tumor size on the ultrasound and on the final pathology report was reached for cases of IDC ($P = .02$), ILC ($P = .001$), and IC + EIC ($P = .01$) (Table 3). Ultrasound underestimated tumor size in 165 IDC cases (51%), with 47 of the 165 underestimated cases (28%) having a difference of 1 cm or more. Ultrasound also underestimated tumor size in 42 ILC cases (98%), with 14 of the 42 underestimated cases (33%) having a difference of 1 cm or more. Ultrasound overestimated tumor size in 13 (68%) of the IC + EIC cases, with 7 of the 13 cases (54%) having a difference of 1 cm or more.

3.1.3. MRI findings

Two hundred seventy-two MRI studies were included (196 MRIs of IDC cases, 8 of IDC + ILCs, 42 of ILCs, 19 of ICs + EIC, and 7 of special-

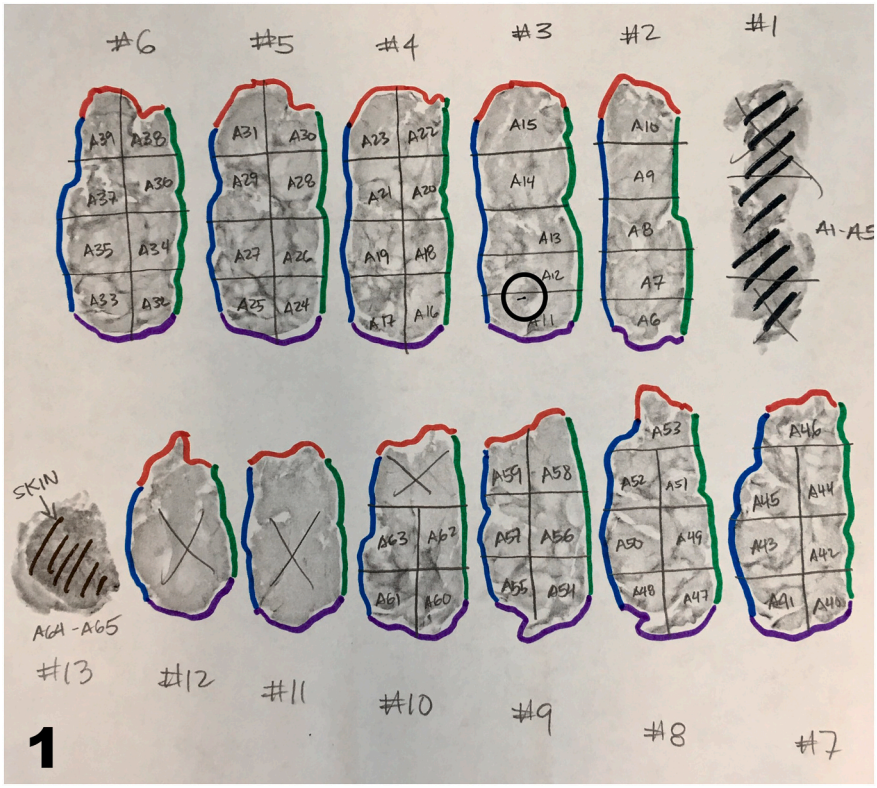


Fig. 1. Example of a gross diagram of a lumpectomy case provided by pathologist assistants after slicing the specimen and taking a Faxitron image. The specimen slices are numbered and the tissue block designation is added to the diagram. The black circle shows the core needle biopsy clip. The colors depict the inks using during intraoperative gross examination to mark the specimen's margins.
(Image courtesy of Warren Gloria, PA.)

Table 1
Microscopic diagnoses of the cases included in the study (n = 490).

Type of carcinoma	Cases, no. (%)
IDC	375 (76.5)
ILC	56 (11.4)
IC + EIC	27 (5.5)
Mixed IDC and ILC	12 (2.4)
Invasive mucinous carcinoma	10 (2.0)
High-grade metaplastic carcinoma	4 (0.8)
Invasive papillary carcinoma	2 (0.4)
Invasive secretory carcinoma	1 (0.2)
Invasive tubular carcinoma	1 (0.2)
Invasive tubulolobular carcinoma	1 (0.2)
Low grade adenosquamous carcinoma	1(0.2)

Abbreviations: IC + EIC: invasive carcinoma with extensive intraductal component; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

type carcinomas). For all tumor types, there was a statistically significant difference ($P < .001$) between the mean (2.87 cm) and median (2.1 cm) of the tumor size measured by MRI (range, 0.4–13 cm) and the mean (1.90 cm) and median (1.5 cm) of the tumor size recorded on the final pathology report (range, 0.1–10 cm), with the MRI overestimating preoperative tumor size by 3 cm or more in 36 cases (13%) (Fig. 2C).

By tumor type, the difference between the tumor size on the MRI and the final pathology report was statistically significant for cases of IDC ($P < .001$), ILC ($P < .002$) and IC + EIC ($P < .001$) (Table 4). MRI overestimated tumor size in 136 (69%) IDC cases (with 50 of the 136 overestimated cases [37%] having a difference of 1 cm or more), 32 (76%) ILC cases (with 17 of the 32 overestimated cases [53%] having a difference of 1 cm or more), and 18 (95%) IC + EIC cases (with all overestimated cases having a difference of 1 cm or more and 12 of the 18 overestimated cases [67%] having a difference of 3 cm or more).

3.1.4. Gross exam findings

There was a statistically significant difference ($P = .003$) between the mean tumor size in the gross description (2 cm) and in the final pathology report (1.8 cm). The difference was statistically significant for cases of IDC ($P < .03$) and IC + EIC ($P = .004$) (Table 5).

Gross examination results correlated with microscopic tumor size in 57.4% of cases. Gross examination overestimated tumor size in 116 cases (24%), including 81 IDC cases (22%), 10 ILC cases (18%), 20 IC + EIC cases (74%), 2 mixed IDC + ILC cases (17%), and 3 special-type carcinoma cases (15%). Furthermore, 39 of the 116 cases (33.6%) were overestimated by 1 cm or more. Gross examination underestimated tumor size in 91 cases (18.6%), including 68 IDC cases (6%), 14 ILC cases (25%), 2 IC + EIC cases (7%), 3 mixed IDC + ILC cases (25%), and 4 special-type carcinoma cases (20%). Additionally, 17 of the 91 (18.7%) cases were overestimated by 1 cm or more.

3.2. Impact of tumor size discrepancy on final staging

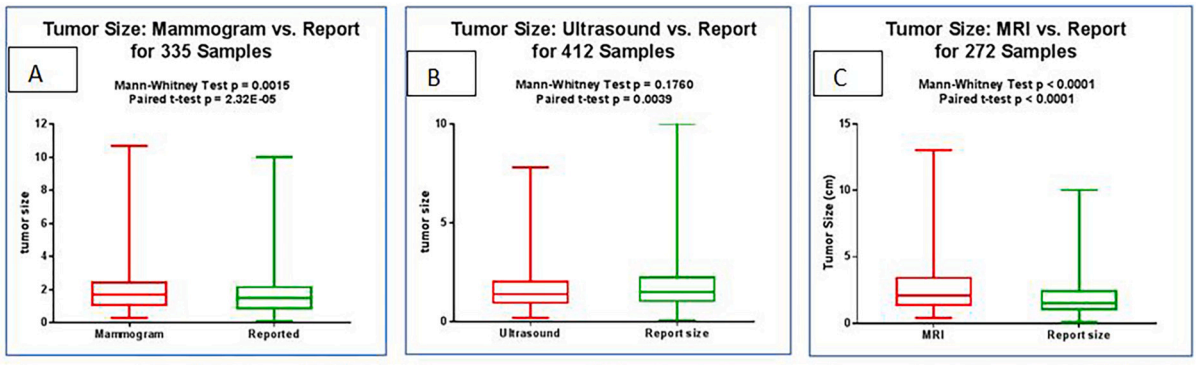
3.2.1. Mammography findings

Three hundred thirty-five mammogram studies were included, and 228 (68%) cases had concordance between the tumor stage on the mammography and the final pathology report. Thirty-one cases (9.2%) were understaged and 76 cases (21.6%) were overstaged using the imaging study. A total of 107 cases had discrepancies in staging, resulting in an error rate of 31.9%.

Per tumor subtype, the group with the highest discrepancy rate was IC + EIC. Of the 27 IC + EIC cases included in the study, 22 had mammograms. In 8 cases (36.4%), concordance in tumor size between the imaging study and the final pathology report was reached, whereas the additional 14 cases (63.6%) were overstaged on the mammogram (Table 6).

3.2.2. Ultrasound findings

Four hundred twelve ultrasound studies were included, and 311 (75.5%) cases had concordance between the tumor stage on ultrasound and the final pathology report. A total of 101 cases had discrepancies in staging, resulting in an error rate of 24.5%. Of the discordant cases, 63 (62.3%) were understaged and 38 (37.6%) were overstaged on the



	Mammo (cm)	Report (cm)
median	1.7	1.5
mean	2.14	1.73
range	0.3 -- 10.7	0.1 -- 10

	US (cm)	Report (cm)
median	1.4	1.5
mean	1.64	1.82
range	0.2 – 7.8	0.1 -- 10

	MRI (cm)	Report (cm)
median	2.1	1.5
mean	2.87	1.90
range	0.4 -- 13	0.1 -- 10

2

Fig. 2. Box-and-whisker plots showing median and interquartile ranges for tumor size for mammogram (A), ultrasound (B), and MRI (C) vs the final pathology report.

Table 2
Tumor size mean based on MG results vs final pathology report (n = 335).

Diagnosis	Samples, no	Mean size based on MG results	Mean size on pathology report	*P* value
IDC	260	2.0165	1.6848	**0.0003**
IDC + ILC	4	1.6250	2.8000	0.3424
ILC	36	1.9139	2.2673	0.8806
IC + EIC	22	3.9909	0.9432	< **0.0001**
Special-type carcinoma	13	2.2538	2.9523	0.2811

Abbreviations: IC + EIC: invasive carcinoma with extensive intraductal component; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; MG, mammogram.

Table 3
Tumor size mean based on US results vs. final pathology report (n = 412).

Diagnosis	Samples, no.	Mean size based on US results	Mean size on pathology report	*P* value
IDC	323	1.6065	1.7522	**0.0191**
IDC + ILC	10	2.1700	2.8900	0.2918
ILC	43	1.4977	1.8471	**0.0011**
IC + EIC	19	1.9579	1.0868	**0.0109**
Special-type carcinoma	17	1.9941	2.3235	2.1222

Abbreviations: IC + EIC: invasive carcinoma with extensive intraductal component; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; US, ultrasound.

Table 4
Tumor size mean based on MRI results vs final pathology report (n = 272).

Diagnosis	Samples, no.	Mean size based on MRI results	Mean size on pathology report	*P* value
IDC	196	2.6133	1.7913	< **0.0001**
IDC + ILC	8	3.5875	3.0375	0.6586
ILC	42	2.9762	2.3250	0.0022
IC + EIC	19	4.9947	1.1053	**0.0002**
Special-type carcinomas	7	2.7857	3.3143	0.4035

Abbreviations: IC + EIC: invasive carcinoma with extensive intraductal component; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; MRI, magnetic resonance imaging.

Table 5
Tumor size mean on gross description vs final pathology report (n = 490).

Diagnosis	Samples, no.	Mean size on gross description	Mean size on pathology report	*P* value
IDC	375	1.8	1.7	**0.02678**
ILC	56	2.1	2.2	0.60165
IDC + ILC	12	2.3	3.0	0.19399
IC with EIC	27	2.7	0.9	**0.00043**
Special-type carcinoma	20	2.7	2.6	0.83448

Abbreviations: IC + EIC: invasive carcinoma with extensive intraductal component; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

imaging.

Per tumor subtype, the group with the highest discrepancy rate was IC + EIC. Of the 27 IC + EIC cases included in the study, 19 had ultrasound reports. In 11 cases (57.9%), concordance between the imaging study and the final pathology report was reached, whereas 6 cases were overstaged and 2 cases were understaged by the ultrasound (Table 6).

3.2.3. MRI findings

Two hundred seventy-two MRI studies were included, and 183 (67.3%) cases had concordance between the tumor stage on the MRI and the final pathology report. A total of 89 cases had discrepancies in staging, resulting in an error rate of 32.7%. Twelve cases (13.5%) were understaged and 77 cases (86.5%) were overstaged on imaging.

Per tumor subtype, the group with the highest discrepancy rate was again IC + EIC. Of the 27 IC + EIC cases included in the study, 19 had preoperative MRI. Six cases (31.6%) were concordant, and the additional 13 cases (68.4%) were overstaged on MRI (Table 6).

3.2.4. Gross exam findings

For the total 490 cases, 453 (92.4%) had concordance in the tumor stage between the gross description and the final pathology report. A total of 37 cases had discrepancies in staging, resulting in an error rate of 7.5%. Twenty cases (54.1%) had an underestimated tumor stage and 17 cases (45.9%) had an overestimated stage based on the gross description.

Per tumor subtype, the IDC + ILC group had the highest discrepancy, with an error rate of 16.7%. Two out of 12 cases (16.6%) had tumor size underestimation based on the gross description (Table 6).

Table 6
Comparison by stage between radiographic methods and final pathology report.

Stage	IDC samples, no. (%)	ILC samples, no. (%)	IDC + ILC samples, no. (%)	IC with EIC samples, no. (%)	Special-type carcinoma samples, no. (%)
Changes in stage based on MG vs path report					
Concordant with path report	182 (70)	27 (75)	3 (75)	8 (36.36)	8 (61.53)
Underestimated	25 (9.62)	5 (13.88)	1 (25)	0 (0)	0 (0)
Overestimated	53 (20.38)	4 (11.11)	0 (0)	14 (63.63)	5 (38.46)
Total	260	36	4	22	13
Changes in stage based on US vs path report					
Concordant with path report	247 (76.47)	35 (81.4)	8 (80)	11 (57.89)	10 (58.82)
Underestimated	46 (14.24)	8 (18.6)	2 (20)	2 (10.53)	5 (29.41)
Overestimated	30 (9.29)	0 (0)	0 (0)	6 (31.58)	2 (11.76)
Total	323	43	10	19	17
Changes in stage based on MRI vs path report					
Concordant with path report	136 (69.38)	28 (66.66)	6 (75)	6 (31.57)	7 (100)
Underestimated	9 (4.59)	3 (7.14)	0 (0)	0 (0)	0 (0)
Overestimated	51 (26.02)	11 (26.19)	2 (25)	13 (68.42)	0 (0)
Total	196 (100)	42 (100)	8	19	7
Changes in stage on gross description vs path report					
Concordant with path report	348 (92.8)	54 (96.42)	10 (83.33)	24 (88.89)	17 (85)
Underestimated	15 (4)	2 (3.57)	2 (16.67)	0 (0)	1 (5)
Overestimated	12 (3.2)	0 (0)	0 (0)	3 (11.11)	2 (10)
Total	375	56	12	27	20

Abbreviations: IC + EIC: invasive carcinoma with extensive intraductal component; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; MG, mammogram; MRI, magnetic resonance imaging; path, pathology; US, ultrasound.

3.3. Tumor focality data

For the included 490 cases, all 1152 imaging studies included a numerical value for focality and were included (428 mammograms, 444 ultrasounds, and 280 MRIs).

3.3.1. Mammography findings

Four hundred twenty-eight mammograms were included, and 307 (71.7%) cases had the same number of foci reported on the mammogram and the final pathology report. Seventy (16.3%) mammograms showed fewer foci and 51 (11.9%) mammograms showed more foci than the final pathology report. In our study, assessment of focality on mammogram had an error rate of 28.3%.

3.3.2. Ultrasound findings

Four hundred forty-four ultrasounds were included, and 323 (72.7%) cases had the same number of foci reported on the ultrasound and the final pathology report. Sixty-four (14.4%) cases showed fewer foci and 57 (12.8%) cases showed more foci on the ultrasound than on the final pathology report. Assessment of focality based on ultrasound results had an error rate of 27.3%.

3.3.3. MRI findings

Two hundred eighty MRIs were included, and 199 (71%) cases had the same number of foci reported on the MRI and the final pathology report. Thirty-three (11.8%) cases showed fewer foci and 48 (17.1%) cases showed more foci on the MRI than on the final pathology report. Assessment of focality based on MRI had an error rate of 28.9%.

3.3.4. Gross examination findings

Four hundred ninety gross descriptions were included, and 432 (88.2%) had the same number of foci reported on the gross description and the final pathology report. Forty-five (9.2%) cases showed fewer foci and 13 (2.6%) cases showed more foci on the gross examination than on the final pathology report. Assessment of tumor focality on gross examination had an error rate of 11.8%.

4. Discussion

Tumor size, defined as the largest diameter of the primary breast tumor, is second only to lymph node status as an independent prognostic factor for patients with invasive breast cancer [1]. In addition, tumor size correlates with the presence of nodal metastasis and is one of the most important factors to consider when deciding treatment options, such as patient eligibility for BCT. Along with size, tumor focality and the presence of an EIC play a significant role in determining the surgical therapy of choice and in the ability to obtain negative margins with surgery [9-13].

Over the years, multiple studies assessing the correlation in pathologic tumor size between various radiographic modalities have been published [6,14-26]. Few studies have also emphasized the importance of the correlation between the macroscopic (gross) and the microscopically confirmed tumor size for accurate final tumor staging [11,12]. To our knowledge, this is the first study to also include tumor focality as a parameter for the assessment of radiologic and pathological correlation.

We found statistically significant differences between the mean tumor size in the final pathology report and the results of all 3 radiographic modalities for all studied tumor types. Discrepancies affecting tumor staging were seen in 29% of the radiographic studies analyzed, with MRI having the highest error rate (32.7%), followed by mammogram (31.9%) and ultrasound (24.5%). This is clinically significant as it has been reported that overestimation of tumor size could lead to decreased chances of qualifying for or being offered BCT among some patients [18,27,28].

In our study, the presence of an EIC was the variable most commonly linked to discrepancies in tumor size and staging between the radiographic and pathologic findings. For tumors with an EIC, the tumor size was overestimated in 95% of cases on mammogram and MRI results and in 54% of cases on ultrasound results. Additionally, 63.6% of tumors with an EIC were overstaged on mammogram, 68.4% were overstaged on MRI, and 32% were overstaged on ultrasound. In concordance with previously published studies [21,25,29,30], preoperative imaging in our study overestimated tumor size for cases of IC + EIC by more than 1 cm on mammogram and ultrasound and by more than 3 cm on MRI. Gross examination also overestimated the tumor size in 74% of

IC + EIC cases, impacting tumor stage in 11.1% of cases.

An extensive intraductal component is defined as a ductal carcinoma in situ (DCIS) that is a major component of the area of invasive carcinoma (approximately 25%) and is also present in the surrounding breast tissue. An EIC can also be defined as an extensive DCIS associated with an invasive carcinoma that is too small for the DCIS to comprise 25% of the area [31]. Detection of an EIC preoperatively by radiographic methods is clinically important because the presence of an EIC is considered an independent risk factor for local recurrence after surgery [13]. An EIC is most commonly identified on imaging by the presence of microcalcifications on mammography [33] or as a non-mass enhancement or nodules adjacent to a mass on MRI [32,33].

In our study, the error rate for focality was close to 30% for all modalities: 28% for mammogram, 27% for ultrasound, and 29% for MRI. There was a tendency to underestimate foci on mammogram and ultrasound and to overestimate foci on MRI. MRI has been found to be superior to other imaging modalities for identifying if a disease is multifocal or multicentric, factors that influence a surgeon's decision of whether to pursue BCT [20,21].

The benefit of using a breast MRI in the preoperative work-up has been the subject of controversy, as some studies have shown that MRI has the highest false positive rate for identifying tumor size and focality [17,18,23,24]. Behjatnia et al. reported that tumor size on MRI matched histological size in only 3% of cases, underestimated it in 27%, and overestimated it in 70%. In their study, MRI underestimated tumor size in 60% of ILC cases, overestimated it in 40%, and matched exact histologic size in none [12]. The latter findings are in line with our study results showing that MRI was the least accurate methodology for the estimation of tumor size in cases of ILC (Table 6).

Carin et al. compared MRI and histological analysis for mastectomy specimens and found a sensitivity of 84.7% for the detection of all invasive foci, 69% for single foci, and 65.7% for multiple foci. The authors concluded that MRI had an excellent positive and negative predictive value for detection of invasive lesions but cautioned that interpretation may be affected by the presence of enhancing high-grade DCIS and fibrocystic background changes [19]. Haraldsdottir et al. studied the use of MRI, mammograms, and ultrasounds in the preoperative assessment of breast cancer patients and reported that MRI under- and overestimated the tumor size by more than 10 mm in 4.6% and 7.5% of cases, respectively, and overestimated focality in 8% of cases. Although MRI was found to be useful in the diagnosis of contralateral and multifocal disease, it showed the highest rate of overestimation. This led to the authors' conclusion that the routine use of MRI in this setting may increase mastectomy rates in a proportion of patients [18]. Similarly, Franca et al. found overestimation of the tumor's size by MRI in 24% of IC + EIC cases [21]. In another study, Grimsby et al. reported that, in addition to an EIC, other factors, such as proliferative lesions or lymphovascular invasion, may result in overestimation of tumor size by MRI [25].

Hamza et al. found concordance in tumor size between gross examination and the reported pathologic size in only 56% of cases, with a higher proportion of mastectomy specimens being concordant than lumpectomy specimens [34]. Behjatnia et al. reported that tumor size identified by gross examination matched histological size in 22% of cases, underestimated it in 57%, and overestimated it in 22%, and the authors advised that random sectioning of lumpectomy specimens in invasive breast carcinoma may result in inaccurate tumor staging [12]. Similar to Hamza et al., gross examination in our study correlated with microscopic tumor size in only 57% of cases. However, the discrepancy resulted in changes in tumor stage in just 7.5% of cases. In determining focality, we found an 88% rate of concordance between the final pathology report and gross examination.

Some limitations of our study include that conventional 2D mammography was used at the time the data were collected. 3D mammography, which is currently used at our institution, has been proven superior for breast cancer detection and characterization [35]. In addition, we did not analyze all 3 modalities for each case and could not compare their utility for each individual case. Finally, we did not investigate if preoperative overestimation of tumor size resulted in higher rates of mastectomy among our patient population.

5. Conclusion

In our study, all imaging modalities, as well as gross examination, misestimated the tumor size of breast carcinomas. Mammogram and MRI tended to overestimate size for all tumor types. Ultrasound tended to underestimate tumor size, except for cases of IC + EIC, which it tended to overestimate. Gross examination also tended to overestimate tumor size; however, a significant impact on final staging was not observed. For tumor focality, all 3 imaging modalities had an error rate close to 30%, whereas gross examination was concordant with the final pathology report in 88% of cases. Similar to previous reports, our study underscores the limitations of preoperative radiological evaluation and reiterates the importance of careful gross and microscopic tumor examination to determine final tumor stage.

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References

[1] Warren SL. A roentgenologic study of the breast. Am J Roentgenol Radium Ther 1930;24:113–24.
[2] National Comprehensive Cancer Network (NCCN). Practice guidelines in oncology: breast cancer. Version 2.2017 Accessed at www.nccn.org, Accessed date: 10 October 2018.
[3] The AJCC cancer staging manual. 8th ed. Springer; 2018.
[4] Gianni L, Pienkowski T, Im YH, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomized multicenter, open-label, phase 2 trial. Lancet Oncol 2012;13:25–32.
[5] Joe BN, Sickles EA. The evolution of breast imaging: past to present. Radiology 2014;273:S23–44.
[6] Yi-Zhou J, Chen X, Wen-Ting P, et al. Preoperative measurement of breast cancer overestimates tumor size compared to pathological measurement. PLoS One 2014;9(1):e86676.
[7] Blair S, McElroy M, Middleton MS, et al. The efficacy of breast MRI in predicting breast conservation therapy. J Surg Oncol Sep 1 2006;94(3):220–5.
[8] Reyna C, DeSnyder SM. Intraoperative margin assessment in breast cancer management. Surg Oncol Clin N Am Jan 2018;27(1):155–65.
[9] Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. Cancer 1989;63:181–7.
[10] Cianfroca M, Goldstein LJ. Prognostic and predictive factors in early-stage breast cancer. Oncologist 2004;9:606–16.
[11] Abner AL, Collins L, Peiro G, Recht A, Come S, Shulman LN, et al. Correlation of tumor size and axillary lymph node involvement with prognosis in patients with T1 breast carcinoma. Cancer Dec 15 1998;83(12):2502–8.
[12] Behjatnia B, Sim J, Bassett LW, Moatamed NA, Apple SK. Does size matter? Comparison study between MRI, gross, and microscopic tumor sizes in breast cancer in lumpectomy specimens. Int J Clin Exp Pathol Feb 22 2010;3(3):303–9.
[13] Ha SM, Cha JH, Shin HJ, Chae EY, Choi WJ, Kim HH. Mammography, US, and MRI to assess outcomes of invasive breast cancer with extensive intraductal component: a matched cohort study. Radiology Aug 2019;292(2):299–308.
[14] Ramirez SI, Scholle M, Buckmaster J, et al. Breast cancer tumor size assessment with mammography, ultrasonography, and magnetic resonance imaging at a community based multidisciplinary breast center. Am Surg 2012;78:440–6.
[15] Chang JM, Han W, Moon HG, et al. Evaluation of tumor extent in breast cancer patients using real-time MR navigated ultrasound: preliminary study. Eur J Radiol 2012;81:3208.
[16] Tadwalkar RV, Rapelyea JA, Torrente J, et al. Breast-specific gamma imaging as an adjunct modality for the diagnosis of invasive breast cancer with correlation to tumour size and grade. Br J Radiol 2012;85:e212–6.
[17] Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology 2004;233(3):830–49.
[18] Haraldsdottir KH, Jonsson P, Halldorsdottir AB, et al. Tumor size of invasive breast cancer on magnetic resonance imaging and conventional imaging (mammogram/ultrasound): comparison with pathological size and clinical implications. SJS 2017;106(1):68–73.
[19] Carin AJ, Moliere S, Gabriele V, et al. Relevance of breast MRI in determining the

size and focality of invasive breast cancer treated by mastectomy: a prospective study. World J Surg Oncol 2017;15:128.
[20] Kuhl C, Kuhn W, Braun M, et al. Pre-operative staging of breast cancer with breast MRI: one step forward, two steps back? The Breast 2007:S34–44.
[21] Lira Franca LK, Vieira Bitencourt AG, Bueno de Toledo Osorio, et al. Tumor size assessment of invasive breast cancers: which pathological features affect MRI-pathology agreement? Appl Cancer Res 2018;38:2.
[22] Hata T, et al. Magnetic resonance imaging for preoperative evaluation of breast cancer: a comparative study with mammography and ultrasonography. JAmCollSurg 2003;198(2):190–7.
[23] Malur S, et al. Comparison of written reports of mammography, sonography and magnetic resonance mammography for preoperative evaluation of breast lesions, with special emphasis on magnetic resonance mammography. Breast Cancer Res 2001;3:55–60.
[24] Boetes C, et al. Breast tumors: comparative accuracy of MR imaging relative to mammography and US for demonstrating extent. Radiology 1995;197:743–7.
[25] Grimsby GM, et al. Is there concordance of invasive breast cancer pathologic tumor size with magnetic resonance imaging? Am J Surg 2009;198:500–4.
[26] Skaane P, Skjorten F. Ultrasonographic evaluation of invasive lobular carcinoma. Acta Radiol 1999;40:369–75.
[27] Jiang YZ, Xia C, Peng WT, Yu KD, Zhuang ZG, Shao ZM. Preoperative measurement of breast cancer overestimates tumor size compared to pathological measurement. PLoS One Jan 29 2014;9(1):e86676.
[28] Pediconi F, Miglio E, Telesca M. Effect of preoperative breast magnetic resonance imaging on surgical decision making and cancer recurrence rates. Invest Radiol 2012;47:128–35.
[29] Jethava A, Ali S, Wakefield D, Crowell R, Sporn J, Vrendenburgh J. Diagnostic accuracy of MRI in predicting breast tumor size: comparative analysis of MRI vs histopathological assessed breast tumor size. Conn Med 2015;79(5):261–7.
[30] Mennella S, Garlaschi A, Paparo F, Perillo M, Celenza M, Massa T, et al. Magnetic resonance imaging of breast cancer: factors affecting the accuracy of preoperative lesion sizing. Acta Radiol 2015;56(3):260–8.
[31] Fitzgibbons PL. Protocol for the examination of resection specimens from patients with invasive carcinoma of the breast. CAP. 2019. [V 4.2.0.0].
[32] Chadashvili T, et al. Nonmass enhancement on breast MRI: review of patterns with radiologic-pathologic correlation and discussion of management. AJR 2015;204:219–27.
[33] Dershaw DD, et al. Ductal carcinoma in situ: mammographic findings and clinical implications. Radiology 1989;170:411–5.
[34] Hamza A, et al. Tumor size in breast carcinoma: gross measurement is important!. Int J Surg Pathol 2018:1–6.
[35] Zackrisson S, et al. One-view breast tomosynthesis versus two-view mammography in the Malmö Breast Tomosynthesis Screening Trial (MBTST): a prospective, population-based, diagnostic accuracy study. LancetOncol 2018. https://doi.org/10.1016/S1470-2045(18)30521-7.