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Original Contribution

The impact of reporting tumor size in breast core needle biopsies on tumor stage: A retrospective review of five years of experience at a single institution

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1. Introduction

Tumor size is a major determinant for staging breast cancer, second only to lymph node status as the strongest prognostic factor. In some cases, the size may be difficult to determine. Contributing factors include multicentricity, multifocality and the fact that not all invasive carcinomas of the breast present as a mass. However, even when they do present as a measurable mass, a proportion may be associated with extensive ductal carcinoma in situ or significant desmoplastic reaction. Histopathologic review is the accepted method to measure the tumor size in breast carcinoma, and the single greatest dimension of the largest focus of invasive carcinoma is used to establish T classification [1].

The tumor size on the excision specimen determines the stage of breast carcinoma. It is not uncommon, however, to have an excision specimen showing biopsy site changes and no residual tumor, or residual tumor that is smaller than the tumor present on the biopsy. It has been previously shown that in cases of invasive carcinoma of the breast, needle core biopsy material contains the greatest extent of carcinoma in 12% of cases. In such cases, the recommendation is to use the size reported on the biopsy as the final size for staging purposes [2].

While there are several studies examining the relationship between radiologic tumor size and the subsequent size on the excisional specimen, there is a paucity of literature comparing the tumor size on breast core biopsy specimens to the size measured on corresponding excision specimens.

The primary objective of this study is to compare the tumor size of invasive breast carcinoma using three measuring techniques: the greatest linear dimension on core biopsies by microscopic measurement, and the greatest dimension on subsequent surgical excisions, measured both grossly and microscopically. For tumors measuring ≤ 2.5 cm on gross assessment, the correlation between gross and microscopic measurements on excision was analyzed based on the following factors: the presence or absence of ductal carcinoma in situ, the histologic type of invasive carcinoma and the gross description of the lesion. We compared the gross size of invasive breast carcinoma to the microscopic size measured on both the core biopsy and the subsequent surgical excision. The aim is to determine the best method to accurately report tumor size in breast carcinoma and assess the impact of size difference on the final pathologic staging of breast carcinoma. This may affect treatment options and patient outcomes as a whole.

2. Materials and methods

This is a retrospective study, performed at the Mount Sinai Medical Center Department of Pathology. The search was limited to cases with core needle biopsies that then had subsequent surgical excision. The cases were obtained using CoPath, the pathology computerized database. The collected data was from 2012 to 2016 and the search was limited to files containing the word “invasive” or “infiltrating” carcinoma. For tumor size in the biopsy specimens the linear extent of the carcinoma was determined microscopically on the glass slide, while the gross measurement in the excision specimens was obtained from the final pathology report.

The inclusion criteria were: cases reported to contain infiltrating (invasive) breast carcinoma, cases where the tumor's greatest linear measurement was either reported or the slides were available for review and cases with subsequent excision specimen with available pathology report and glass slides. The exclusion criteria were: cases of patients who received neoadjuvant therapy, cases of multifocal infiltrating breast carcinoma and cases with no subsequent excision specimen available either on file or glass slides.

The following parameters were collected for the cases that met the criteria: tumor histologic type, final pathologic T stage, the greatest tumor dimension on core biopsy and the greatest tumor dimension on subsequent surgical excision, measured both grossly and microscopically. To compare the tumor size between breast core needle biopsy and surgical excision, XLSTAT (Excel) and GraphPad Prism v7.0 were used to perform Pearson correlation analysis, linear regression

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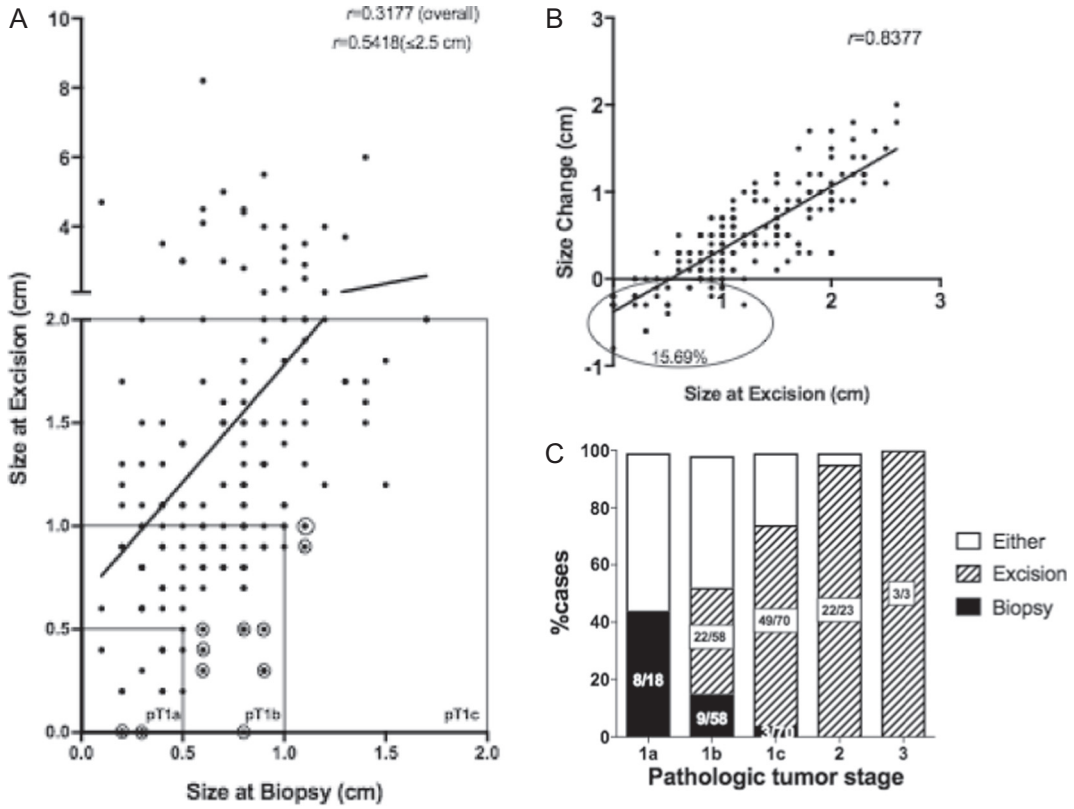

Fig. 1. A. Pair correlation of maximum linear tumor dimension at biopsy versus microscopic maximum linear tumor dimension at excision. There is a significant overall moderate agreement ($r = 0.3177$, $P < 0.0001$, continuous line: linear regression), which increases for cases with a maximum size ≤ 2.5 cm ($r = 0.5418$, $P < 0.0001$, circled dots: cases where size at biopsy determined the T stage). For tumors larger than 2.0 cm, top y axis, the stage was solely determined by size at excision. Note that overlapping plotted data will appear as one. B. Relationship between the size change (microscopic size on excision minus size on biopsy) and the microscopic size at excision. Cases with biopsy size greater than the excision (size change < 0) had a final pathologic stage of T1 (≤ 2.0 cm) representing 15.69% of the cases (27/172). C. Case distribution according to the pathologic stage. Size at biopsy (black) was the critical measurement for determining the final pathologic stage in twenty cases, mainly pT1 stage, with decreasing proportion with increasing stage ($P < 0.0001$). Size at excision (diagonal lines) was more important to determine the pathologic T stage in higher stages. Of note, tumor was identified only at biopsy in eight cases, all T1a stage.

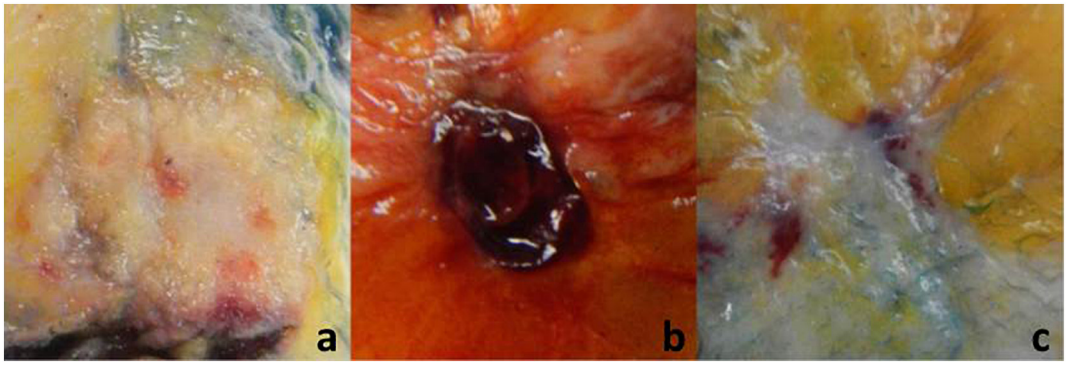

Fig. 2. Gross description of the lesion on excision: a. mass, b. hemorrhagic biopsy site, c. ill-defined firm area.

analysis, and paired and single-tail *t*-tests to determine *P*-values.

3. Results

Patient age ranged from 31 to 97 years, with a mean of 64 years. Among the 172 cases, 146 (84.9%) were invasive ductal carcinoma (no special type), 15 (8.7%) were invasive lobular carcinoma, and 11 (6.4%) were carcinomas of other special types. Ninety-five cases (55%) had associated ductal carcinoma in situ. The tumor size on biopsies ranged from 0.1 to 1.7 cm, while the size range on excision varied from 0 (no residual tumor on excision) to 8.2 cm. There was moderate correlation between the size on biopsy with that on excision, which was statistically significant ($r = 0.3177$, $P < 0.00001$) (Fig. 1A). When comparing the microscopic size at excision with the size change (size at excision minus size at biopsy), there were 27 cases (15.69%) with biopsy size greater than the excision (size change < 0) (Fig. 1B). These cases had a final pathologic stage of T1.

For tumors measuring ≤ 2.5 cm on gross assessment, the correlation between gross and microscopic sizes on excision increases and was statistically significant ($r = 0.5418$, $P < 0.00001$) (Fig. 1A). For these tumors, the correlation between gross and microscopic measurements on excision was analyzed based on the following factors: 1) the presence or absence of ductal carcinoma in situ ($r = 0.5303$ vs $r = 0.5738$, $P = 0.004$ vs $P < 0.00001$, respectively); 2) the type of invasive

carcinoma: ductal carcinoma ($r = 0.5663$, $P < 0.00001$), lobular carcinoma ($r = 0.3711$, $P = 0.5$), and other special types ($r = 0.7074$, $P = 0.1$); 3) the gross description of the lesion which included mass ($r = 0.7139$, $P < 0.00001$), ill-defined firm area ($r = 3782$, $P = 0.002$) and hemorrhagic biopsy site ($r = 0.0704$, $P = 0.03$) (Fig. 2).

Based on the largest linear dimension, the final size was determined (Fig. 1C). The pathologic T stages of the cases were as follows: pT1a in 18 (9.9%), pT1b in 58 (33.7%), pT1c in 70 (40.7%), pT2 in 23 (13.4%) and pT3 in 3 (1.7%). When comparing the size of carcinoma on biopsy to that on subsequent excision, there were 130 (75.6%) cases in which the size on biopsy was smaller, 15 (8.7%) cases where the sizes were equal, and 27 (15.69%) cases in which the size of tumor on biopsy was larger than that on excision, of which 8 (4.7%) had no tumor left on excision. Of significance, there were 20 (11.62%) cases in which the larger size on biopsy determined a higher final pT stage than would otherwise have been the stage based on tumor size on excision alone.

4. Discussion

Concordance between gross and microscopic tumor size and the accurate determination of the pathologic staging is important due to its clinical implication on prognosis and treatment.

When comparing the size of carcinoma on biopsy with that on excision for the same tumor, there were 27 cases (15.69%) in which the size on biopsy was larger. Of these 27 cases, 20 cases (11.62%) had a larger size on biopsy, which determined a higher final pT stage. Of the 27 cases with larger tumor size on biopsy, 8 cases (4.7%) had no residual tumor left on excision.

Rakha et al. in their study of over 40,000 cases of malignant breast core needle biopsies, showed 0.43% of the cases to have no residual tumor left on subsequent excision samples as a result of the complete removal of the lesion in the core. Our rate of complete removal of tumor by the core biopsy is 4.7%, which is higher than what is reported in the aforementioned study [3]. Edwards et al. in their study of 222 cases of core biopsies of breast carcinoma and subsequent excisions, found 12% of the cases (n = 24) in which the size on biopsy was greater than that on excision, including 3% of the cases (n = 6) with no residual tumor on excision and 7.5% (n = 15) where tumor size on biopsy was the sole determinant of a higher final pT stage [2]. Podoll et al. in their study of 223 cases, found 8% of the cases to have a larger tumor size reported on the core needle biopsy than that on subsequent excision [4]. Our results are in agreement with their results.

Size cutoff for pT staging are at 2 and 5 cm. Tumors measuring > 2.5 cm cannot be accurately measured under the microscope because the tumor submitted is limited by the size of the tissue block. The gross measurement on excision is more accurate and should be used instead of microscopic size.

For tumors measuring within ± 5 mm of 2 cm, smaller increments in the size of the tumor can alter the stage, pT1 when ≤ 2 cm or pT2 when > 2 cm. Therefore, investigating the concordance between gross and microscopic size measurements of tumors within ± 5 mm of 2 cm is critically important. We investigated factors that can cause discrepancy between the two measurements including the histologic type of invasive carcinoma, the gross description of the lesion and the presence of ductal carcinoma in situ.

A total of 15 of 172 cases of invasive carcinoma were found to be of lobular type, comprising 8.7% of our study. For tumors measuring within 5 mm of 2 cm, the concordance between gross and microscopic sizes was similar for both invasive ductal carcinoma and invasive lobular carcinoma ($r = 0.53$ vs $r = 0.52$). While lobular carcinoma is notorious for discrepancy in size measurements, in our study we found lobular carcinoma to be concordant in 40% of the cases. Gross measurement overestimated the pathologic stage in 26% of the cases and underestimated the stage in 33%. Our results agree with previous studies where gross measurement of lobular carcinomas was found to have the tendency to underestimate the stage of the tumor. Moatamed et al. concluded that gross measurements underestimate T stage in 40–50% of invasive lobular carcinoma [5]. Hamza et al. found that gross measurement overestimated stage for invasive lobular carcinoma in 7.1% of the cases and underestimated the stage in 12.9% while being concordant with microscopic measurement in 64.8% of invasive lobular carcinoma [6].

Regarding gross and microscopic measurements on tumor of ≤ 2.5 cm, our results showed similar correlation when ductal carcinoma in situ was present or absent. While the presence of ductal carcinoma in situ is accepted as a factor that can cause discrepancy of measurements between gross and microscopic sizes, this effect was not demonstrated in our results given the close correlation of both sizes in the presence and absence of ductal carcinoma in situ.

Another important factor that we analyzed in our study that has an effect on the concordance between gross and microscopic measurements of tumor ≤ 2.5 cm is the gross description of the lesion: mass forming, ill-defined firm area or a hemorrhagic biopsy site (Fig. 2). The correlation was significantly lower when the lesion was non-mass forming, with the correlation dropping from $r = 0.7139$ for mass forming cases to $r = 0.0704$ for hemorrhagic biopsy site cases ($P < 0.00001$, $P = 0.03$ respectively). Hence, microscopic measurement, rather than gross measurement, is more accurate in carcinoma cases where gross lesions are non-mass forming.

5. Conclusion

Our results show that in our institution, the size of carcinoma on the core needle biopsy is larger in 15.69% of the cases when compared to the size of carcinoma on the subsequent excision specimens. Of these cases, 11.62% would have had a higher final T category if the size of carcinoma on the core needle biopsy was used to determine the pathologic staging. These results highlight the importance of reporting the maximum linear dimension on core needle biopsies of breast carcinoma. For tumors that are classified as non-mass forming, the correlation between gross and microscopic measurements is less than optimal and microscopic measurement should be the preferred method to render an accurate tumor size.

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