

Ellen M. Cosgrove Research Competition

Manuscript Competition

Title of Submission	Let's Cut to the Core Biopsy Enough for Sub Centimeter Breast Cancer			
Role <i>Author, Mentor, Faculty, Other</i>	Full First Name	Full Last Name	Degree	Institution
Author	Brian	Shea	MD	MMC
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Let's Cut to the Core; Is Core Biopsy Enough for Sub Centimeter Breast Cancer?

Let's Cut to the Core.

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G. Lepis was involved in data collection. B. Shea & W. Boyan were involved in creation of project, data collection, writing, editing and overall scope of project. K. Kamrani was involved in data collection. D. Dupree & S. Chang were involved in writing and editing the paper. M. Goldfarb & M. Kohli were involved in creation of project, writing and editing of the paper. WB, BS, KK, DD, SC, MG & MK were all involved in the most recent set of revisions.

Conflict of Interest

The authors have no conflicts of interest to disclose

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Abstract

Background

Breast conservation therapy has become a preferred method of treating early stage breast cancer. As care continues to evolve, certain lesions are allowed less invasive treatment options. A simplified explanation of early breast cancer care is detection, biopsy, surgery and adjuvant therapy. The authors in this article look to challenge that algorithm for a specific type of disease.

Methods

A retrospective review was performed to identify all sub centimeter breast cancer that underwent surgery after core biopsy. These cases (n=115) were analyzed for biopsy technique and outcome of final surgical excision to find when no residual disease was found upon final pathology, potentially rendering the surgical resection an unneeded procedure.

Results

The authors found that seventeen of 115 patients (14.8%) who underwent biopsy for sub cm breast cancer had no residual disease found on final surgical resection. Although the subsets were small, the largest core needle resulted in negative pathology two of three times, while the smallest gauge, never resulted in negative resection at time of surgery.

Discussion

Nearly fifteen percent of patients were found to have no residual disease on final surgical pathology. These results were obtained when the radiologist was simply trying to get tissue diagnosis. The authors postulate that this percentage could be even higher if protocols were initiated to biopsy these small lesions with larger core biopsies, and possibly alleviate the need for formal surgery in these specific, small lesion

Let's Cut to the Core; Is Core Biopsy Enough for Sub Centimeter Breast Cancer?

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Background

Breast conservation has become the mainstay of therapy in patients with tumors surgically amenable to lumpectomy. With advances in technology and screening recommendations for women, smaller breast cancers are being identified with increasing frequency. Identification of these earlier stage breast cancers portends a mortality benefit for patients, as patients with smaller cancers and with negative lymph nodes have been demonstrated to have increased survival when compared to those with larger tumors¹⁻³. Women with mammographic screening abnormalities undergo further diagnostic imaging and subsequent core needle biopsy should the abnormality be suspicious for malignancy. Core needle biopsy has been demonstrated to be an accurate minimally invasive test for the diagnosis of breast cancer as well as for determination of hormone receptor and HER-2 status, and can serve as a guide for surgical and adjuvant management of breast cancer⁴⁻⁵. When a lesion is identified as malignant or premalignant on histologic analysis, optimal management includes surgical resection with appropriate margins followed by adjuvant radiation, hormone therapy and/or chemotherapy as clinically indicated⁶.

Occupying an increasingly significant proportion of women with newly diagnosed breast cancer are women with tumors of one centimeter or less. Patients with sub centimeter breast cancers and negative lymph nodes have an excellent prognosis with high long-term survival rates⁷⁻⁹. With lesions smaller than one centimeter and core needle biopsy being performed for histological confirmation of malignancy, there may be a population of patients with no residual tumor present in surgical specimen, indicating that the entire lesion was removed in the biopsy process. The aim of this study is to identify in a single institution the frequency with which core needle biopsy identified malignancy not present in the subsequent surgical specimen for sub

centimeter breast lesions, indicating the lesion's complete removal in the biopsy process. The tumor's complete removal during the biopsy process may have both prognostic and therapeutic implications, especially in an era when smaller surgical margins are becoming acceptable for oncologic resection¹⁰.

Methods

After obtaining IRB approval, a single institution retrospective review was performed using international classification of diseases codes to identify all patients over the last five years who have undergone breast biopsy for malignant or pre-malignant lesions. Since this was a retrospective chart review of patients already treated, we obtained a waiver for data collection. No alterations were made to patients treatment, therefore no informed consent was required. Of these patients, 126 patients were found to have either invasive ductal carcinoma or ductal carcinoma in situ on biopsy of lesions that were identified as being less than one centimeter on mammography or targeted breast ultrasound. Patients with lesions originally measured to be less than one centimeter on mammogram but were over one centimeter on targeted ultrasound were excluded from the study. Other patients excluded from the study included patients that were BRCA positive, patients that refused further management following diagnosis, and those patients who underwent surgical excisional biopsy rather than core needle biopsy. The pathology, radiology, and operative reports were then analyzed for the remaining 115 patients for demographic data including age and sex, biopsy data including technique for core needle biopsy, type of biopsy needle used, and amount of breast tissue removed during biopsy, histological data including hormone and HER2 status, and surgical data including margin status, concordance with biopsy pathology, and amount of breast tissue removed. The primary endpoint of the study

was the presence or absence of residual tumor on surgical specimen. Fisher exact test was performed to determine correlation between gauge of the biopsy needle used and likelihood of absence of residual tumor on surgical specimen. Fisher exact test was also used to observe if differences in pathology impacted the likelihood of obtaining a specimen with no residual disease. A chi square analysis was used to determine if a particular core biopsy procedure (stereotactic or ultrasound guided) impacted the likelihood of a negative surgical specimen.

Results

The average age of patients in our study population was 59.8 years old. All patients were found to have either a mass less than one centimeter in size or clustered micro calcifications totaling less than one centimeter in size on imaging. Patients underwent either stereotactic (39 patients) or ultrasound guided (76 patients) core needle biopsy. All patients underwent vacuum assisted core biopsy. There was variation in both the gauge of the biopsy needle used and number of passes with the biopsy needle. Of operative reports that included information about the size of the needle used (105 cases), core biopsy was most often performed using a 10-gauge needle (74.3%). Other biopsy needles included 7-gauge (2.9%), 8-gauge (7.6%), 9-gauge (0.9%), 12-gauge (4.8%) and 13-gauge (8.6%). Of the reports that included number of core samples obtained (65 patients), the average number of samples obtained was 5.7 +/- 1.2.

In terms of surgical specimen, there were 24 patients that underwent mastectomy and 93 that underwent breast conserving therapy. Of the mastectomy patients, 4 patients were found to have no residual disease, while 13 patients that underwent breast conserving therapy were demonstrated to have no residual disease on pathology. The average size of the lumpectomy

specimen was 61.5 grams in all patients who underwent breast conserving therapy. This group was further analyzed for differences in size of the lumpectomy specimen between patients with or without residual disease. The average size of the specimen in patients with residual disease was 67.5 grams and without residual disease was 42.2 grams.

Size of core needle was statistically analyzed. The size of needle used and the frequency with which they were used is outlined in Table 1. Given the variation in frequency with which different needles were used, smaller needles (12g and 13g) were grouped together and compared to use of larger needles. Using Fisher's exact test, there was not a statistically higher likelihood of obtaining a negative final surgical pathology through use of a larger needle ($p=0.69$).

The data were also analyzed for biopsy modality as it relates to residual disease. This is demonstrated in Table 2. 39 patients underwent stereotactic biopsy, while 76 patients underwent ultrasound guided biopsy. 21% of patients that underwent stereotactic biopsy had no disease on surgical pathology, while 11.7% of patients that underwent ultrasound guided biopsy were demonstrated to have no residual disease. When comparing the rates of residual disease in these two groups, no significant difference was found using Chi square analysis ($p=0.194$).

Pathology did appear to play a significant role in whether or not there was residual disease on surgical pathology. There were 28 patients that had only DCIS on initial biopsy, and the remaining patients either had mixed pathology invasive cancer. The results of the pathologies are listed in Table 3. When comparing those with DCIS against those with components of invasive cancer, analysis with Fisher's exact test demonstrated that those with only DCIS on initial biopsy were more likely to have a negative surgical specimen ($p=0.03$).

Tumor grade did not appear to be significant as the cases with residual disease came from seven low grade cases (41.2%), seven intermediate cases (41.2%) and three high grade cases (17.6%). Hormonal status was also similar in both groups and is listed in Table 4.

Discussion

Patients with sub centimeter breast lesions overall have improved prognosis when compared to their counterparts with larger cancers. Current standard therapy for these lesions includes surgical resection followed by adjuvant endocrine or chemotherapy and breast radiation. Surgical margins have become an area of recent debate, with recent studies suggesting that smaller margins are adequate for surgical resection of invasive breast cancer. The Society of Surgical Oncology and American Society for Radiation Oncology used a meta-analysis of margin width and ipsilateral breast tumor recurrence to establish the consensus margin guideline of “no ink on tumor” for patients undergoing multidisciplinary breast conserving therapy¹¹.

In the present study, the probability of a sub centimeter breast lesion’s complete removal in the biopsy specimen was investigated. After evaluation of all patients that had sub centimeter lesions biopsied under stereotactic or ultrasound guidance over the last five years, the proportion of patients with no residual disease on surgical specimen was 14.8%. This indicates that nearly fifteen percent of patients had the entirety of their pathology removed during the biopsy process. In this era of small surgical margins, some patients may have achieved the necessary complete resection from the biopsy process, which has important considerations when deciding on appropriate surgical options.

Previous studies have examined association with margins and rates of residual disease. In a retrospective study that examined rates of residual disease in patients that underwent re-

excision for close but negative margins ($<2\text{mm}$), residual disease was found in 40% of patients with positive margins, 38% of patients with margins 0.1-1.0 cm, and 33% of patients with margins of 1.1-1.9cm. Additionally, local recurrence rates at 5 years for patients undergoing re-excision for breast conservation therapy was 3.6%. These data indicate that residual disease rates far exceed local recurrence rates¹². In another meta-analysis analyzing the impact of surgical margins on the rates of local recurrence of breast cancer in women undergoing breast conserving therapy for early stage tumors, margin status had prognostic implications for local recurrence. Increasing margin width was only weakly associated with decreased local recurrence, and this effect was not significant when adjusting for addition of adjuvant therapy, indicating that adoption of wider margins as opposed to narrow margins in patients undergoing breast conservation therapy is unlikely to have an impact of long term local recurrence¹³.

The tenets of breast conservation therapy are to maximize cosmesis while providing adequate oncologic therapy for patients with breast cancer. However, the former is frequently compromised at the expense of the latter. In a recent Dutch retrospective analysis examining all patients who underwent breast conserving surgery for invasive or in situ carcinoma, unsatisfactory margins were reported in 33% of cases. The authors of this study used calculated resection ratio to identify the amount of healthy breast tissue being removed in these specimen, and determined that 2.3 times the optimal resection volume was being removed. These data indicate that in patients undergoing breast conserving surgery, a significant amount of healthy breast tissue was being removed without the added benefit of assurance of adequate oncologic resection and with the added possibility of cosmetic failure¹⁴. Sub centimeter breast cancers represent an excellent example of this principle, as optimal surgical resection volume is invariably much less than the volume of the actual surgical specimen. The average size of the

resected specimen in the present study was 61.5 grams in patients undergoing breast conservation, with 24 patients undergoing mastectomy, indicating the removal of a substantial amount of healthy breast tissue for sub centimeter lesions. It is also important to note that seven patients had positive margins on surgical pathology, demonstrating in some circumstances significant healthy breast tissue being removed without the assurance of negative margins.

The results of these studies taken with the results of the current study would suggest that if negative margins could be demonstrated on core needle biopsy of sub centimeter lesions, biopsy alone would serve as adequate surgical management. However, the feasibility of this approach is questionable, as the goal of ultrasound guided biopsy is to obtain a sample, not achieve resection. Ultrasound is the predominant imaging modality used for this purpose, giving a two dimensional view of a three dimensional lesion. This visualization makes adequate margins difficult to ensure.

In patients that undergo stereotactic biopsy, however, the radiologists target abnormal calcifications for biopsy. A radiograph is then taken of the biopsy specimen and a post procedure mammogram is performed to ensure that the abnormal calcifications targeted with the biopsy are present in the biopsy specimen. This may explain the trend towards higher rates of negative surgical specimen in patients that underwent stereotactic biopsy, though this did not achieve statistical significance.

The only factor in this study that was found to be predictive of having a surgical specimen devoid of pathology was having an initial biopsy with only DCIS. Of note, of these patients, 24 of 28 underwent stereotactic biopsy. Future studies would be able to elucidate the significance of this data, as it relates to the underlying pathology or the biopsy modality used.

In this study, the goal of the radiologist was to obtain a tissue sample for histologic diagnosis to guide further surgical management. This process resulted in the complete removal of the tumor nearly 15% of the time. The information from this study, taken with existing studies regarding appropriate surgical margins, can be used to guide future studies regarding sub centimeter breast cancers. For example, a study can be established in which it is the goal of the radiologist to remove all abnormal calcifications on stereotactic biopsy or the entire visualized abnormality on ultrasound for sub centimeter lesions. The frequency of residual disease in the surgical pathology can then be evaluated to determine if this change in goal in the biopsy process translates to an increased rate of negative surgical specimen.

Conclusion

The margins needed for breast cancer have become increasingly liberal, with many centers adopting “no ink on tumor”. With this standard, adequate surgical resection would simply imply that all pathology has been removed. The authors would recommend further studies to evaluate if attempting to remove the entirety of a sub centimeter abnormality through use of core biopsy would translate into higher rates of negative surgical pathology. Limitations to this study include the retrospective nature and small sample size, and prospective studies would be needed to further evaluate the the impact of core biopsy on obtaining a negative surgical specimen.

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