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ORIGINAL ARTICLE

The importance of pre-operative needle core breast biopsy results on resected tissue volume, margin status, and cosmesis

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Summary

Purpose: *This study aimed to evaluate the relationship between pre-operative image-guided large needle core biopsy (LNCB) histopathology results and surgical resection volumes in breast conserving surgery (BCS), with attention to both margin status and cosmetic outcome.*

Methods: *Breast volumes (BV) were calculated using the elliptical cone based formula on mammography images for each patient. Initial resected volume (IRV), final resected volume (FRV), and resected volume ratio (RVR) were calculated and compared according to histopathological diagnosis and cosmetic outcomes. Final pathology results were classified as benign, high risk lesion (HRL), ductal carcinoma in situ (DCIS), or invasive cancer. The cosmetic results were graded based on the Harvard breast cosmesis grading scale.*

Results: *A total of 217 women underwent BCS by the same experienced breast surgeon. The resected volumes (mean, cm^3) were higher among patients who underwent LNCB than those who did not (54.3 vs 26.5 ;p=0.005). The LNCB diagnoses were 16% benign, 19% HRLs, 16% DCIS, and 49% invasive cancers. Reexcision rates were 15.6% and 25.8% for DCIS and invasive cancer, respectively. Cosmesis was excellent in 79.8%. Age, pathological tumor size, IRV and FRV were different among the benign, HRLs and carcinoma groups (p= 0.001).*

Conclusion: *The diagnosis of carcinoma by LNCB leads to the planning of a wider resection, but the need for reexcision is no different than less resection. HRLs are best approached with diagnostic excision, as there is no strong evidence that larger resections reduce the incidence of involved resection margins.*

Key words: *breast, cosmesis, margin, reexcision, volume*

Introduction

Percutaneous image-guided LNCB is used for breast tissue sampling with the intent of establishing preoperative diagnosis, surgical planning, and patient counseling [1]. While LNCB is considered highly reliable when unequivocally positive for malignant or benign lesions, there are circumstances prompting surgical excision to define the final histopathology when LNCB demonstrates HRLs or discordant benign findings.

The volume of excised breast tissue when LNCB reveals malignancy requires a balance between achieving tumor-free margins and a good cosmetic outcome [2]. The resection volume at lumpectomy is a multifactorial decision, taking into consideration tumor size, breast size, and the desired width of tumor-free margin. The correlation between wider excision and negative lumpectomy margins has been previously established, as has an inverse relationship between wider excision and cosmetic outcome [3].

Percutaneous biopsies demonstrating HRLs or discordance with the radiologic findings require surgical follow-up excision and present a new challenge. Should the surgical procedure be considered as a diagnostic approach with the attempt to limit the volume of resection or should it be performed with therapeutic intent leading to wider excision? Considering that up to one fourth of HRLs or discordant cases are upgraded to malignancy, surgeons may have the tendency to per-

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form wide excision, although this approach does not eliminate the positive margin problem [4-7].

In this paper we evaluated the relationship between the diagnosis by LNCB and volume of tissue excised based upon that diagnosis, and the ability to achieve tumor negative margins with a satisfactory cosmetic outcome.

Methods

Data was collected on a total of 217 women who had undergone BCS without oncoplastic surgery by a single dedicated breast surgeon from January to December 2007. Percutaneous image-guided (via stereotactic, magnetic resonance imaging [MRI], or ultrasound [US] guided) LCNB was performed for suspicious lesions in the breast. This took place at one institution by the Breast Surgery Group, which has breast surgeons, breast radiologists and pathology specialists. Of the whole cohort 177 (66%) patients were post-menopausal with mean age 58 years (range 24-87). The radiological abnormalities were identified by mammography, US and/or MRI and defined as microcalcification and/or mass. If an US lesion correlated confidently with a MRI-detected lesion, biopsy was usually performed under US guidance. For MRI-suspected lesions not correlated with US findings, biopsy was usually performed under MRI guidance. Utilized were 9-11 gauge needles for stereotactic or MRI biopsies and 12-16 gauge needles for US-guided biopsies. All patients underwent excision of the index lesion with curative intent and had their definitive therapies at Magee-Womens Hospital. The final pathology results were classified as benign, HRL (atypical ductal hyperplasia [ADH], atypical lobular hyperplasia [ALH], lobular carcinoma *in situ* [LCIS]), DCIS, or invasive cancer and compared with the preoperative diagnosis made by LNCB. A positive margin was defined according to the surgical specimen on pathology and radiology review, established by the National Surgical Adjuvant Breast and Bowel Project (NSABP) as the presence of malignant cells at the immediate edge of the resection of the specimen [8-11]. Close margin was defined as the presence of tumor cells 2 mm or less from the inked margin. Repeat surgery was performed for positive or close margins when the specimen was considered radiologically as close margin either immediately during surgery or soon after the pathological confirmation was obtained.

The measurements of 3D size of the resected breast tissue were obtained from the pathology report and the resection volume of tissue was calculated by using the ellipsoid volume formula (4/3 π * width axis radius * length axis radius * height axis radius) [12]. The IRV and reexcision volume (RXV) were calculated separately. Reexcisions were performed intraoperatively (immediate) for confirmed close margins via specimen radiology, or postoperatively (late) after pathological confirmation. We did not detail the timing of reexcision as immediate or late; we simply combined both of them as reexcision even if it was performed intraoperatively. The total volume of the resected specimen was defined as FRV, and calculated by adding IRV and RXV. Patient breast volume was calculated based on previously published data as an elliptical cone based formula on mammography images for each patient and was defined as BV [13]. The RVR was calculated by dividing FRV by BV [14].

It was reported by Bullstrode et al. that, when more than 20% of the breast was removed, the cosmetic score was poor [14]. We evaluated our RVR as <0.2 and ≥0.2. The resected volumes were classified according to volumes lower than 70 cm^3, from 70 to 125 cm^3 and greater than 125 cm^3, as it was showed that the resection of 70 cm^3 or more of breast tissue was related with poor cosmetic outcome [15]. These calculated breast volumes were compared according to histopathological diagnosis and cosmetic outcomes. The cosmetic results were graded as excellent, good, fair, or poor based on the Harvard breast cosmesis grading scale [16]. Lower category of response was accepted as the final outcome if the surgeon's and patient's responses were discordant.

Statistics

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software (version 17.0). Associations between factors were analyzed with Student's t-test, ANOVA test, and chi-square test. P-values less than 0.05 were considered as statistically significant.

Results

LNCB was performed in 198 (91.25%) patients. Nineteen (8.75%) patients did not undergo LNCB because of patient, physician, or technique related reasons. Lesions were nonpalpable in 58% (126/217) and palpable in 42% (91/217) of the patients. In patients having pathologic diagnosis of malignancy and breast larger than 600 cm^3 in size, the resected volumes were found greater than 70 cm^3 (Table 1). The resected volumes were greater in patients who underwent LNCB compared to those who did not (54.3±42.1 cm^3 vs 26.5±17.5 cm^3; p=0.005; Table 2). Age, pathological tumor size, IRV and FRV were significantly different between the benign, HRLs and carcinoma groups (p<0.001; Table 3).

The diagnosis of LNCB of 198 patients was as follows: 32 (16%) benign, 37 (19%) HRLs (ADH, ALH, LCIS), 32 (16%) DCIS, and 97 (49%) invasive breast carcinomas (Table 3). LNCB and surgical pathology results were concordant in 98.9% of the patients. Two of 37 HRL patients (5.4%) presented showed discordance between LNCB and final pathological diagnosis and were upgraded to in-

Table 1. Factors related with the resected breast volumes

Factors	Resection volume			
	<70 cm^3 (N=150; 75.7%) N (%)	70-125 cm^3 (N=33; 16.7%) N (%)	>125 cm^3 (N=15; 7.6%) N (%)	p-value
Lesion type				
Calcification	45 (30)	4 (12.1)	3 (20)	0.09
Mass	105 (70)	29 (87.9)	12 (80)	
Pathological diagnosis				
Benign	22 (15)	1 (3)	0 (0)	0.002
Invasive carcinoma	62 (41)	25 (76)	12 (80)	
DCIS	29 (19)	5 (15)	2 (13)	
High-risk lesions	37 (25)	2 (6)	1 (7)	
Breast volume (cm^3)				
<600	117 (78)	8 (24)	1 (6.7)	0.0001
600-1000	27 (18)	20 (61)	9 (60)	
>1000	6 (4)	5 (15)	5 (33)	
Margin				
Positive	19 (21)	9 (29)	4 (29)	0.703
Negative	72 (79)	22 (71)	10 (71)	
Cosmetic outcome				
Excellent	125 (83)	25 (76)	8 (53)	0.04
Good	24 (16)	7 (21)	7 (47)	
Fair	1 (0.7)	1 (3)	0 (0)	

Breast volume was measured by elliptical cone based formula on mammography images for each patient [13]. DCIS: ductal carcinoma *in situ*

Table 2. The final resected volume based on initial diagnosis with and without core biopsy

Resected volumes	Core biopsy (N=198)	No core biopsy (N=19)	p-value
Final resected volumes (cm^3), mean±SD	54.3±42.1	26.5±17.5	0.005
Resected volume ratio (cm^3) mean±SD	0.09±0.05	0.07±0.02	0.033
Pathological tumor size (cm) mean±SD	0.99±0.57	0.71±0.27	>0.05

SD: standard deviation.
Tissue volume was calculated by using ellipsoid volume formula (4/3 π × width axis radius × length axis radius × height axis radius) [12].
The resected volume ratio was calculated by dividing the final resected volume by the breast volume.

Table 3. The relation between core biopsy diagnosis and age, tumor size, margin and resected volumes

Core biopsy diagnosis	Benign diagnosis (N=32; 16%)	High risk lesion (N=37; 19%)	Invasive cancer (N=97; 49%)	DCIS (N=32; 16%)	p-value
Age (years), mean±SD	49±11	55±11	62±11	59±13	<0.001
Pathol. tumor size (cm), mean ±SD	1.3±1.5	1.4±1.5	1.4±0.8	0.75±0.7	0.07
Margin (positive), N (%)	-	-	27 (27.2)	5 (15.6)	
Mean resected volume (cm^3), mean±SD					
Initial resected volume	20.6±16.3	34.6±4.9	65.8±42.7	49.6±32.3	<0.001
Reexcision volume	-	13.9±7.4	15.8±18.8	30.2±30.3	0.279
Final resected volume	20.6±16.3	35.2±5.5	72.6±43.5	56.8±34.8	<0.001

DCIS: ductal carcinoma *in situ*, SD: standard deviation.
Volume of tissue was calculated by using ellipsoid volume formula (4/3 π × width axis radius × length axis radius × height axis radius) [12].

vasive cancer and required reexcision for positive margins. Reexcision rate was 24.4% (32/131) in DCIS and invasive cancer lesions. In subgroups, reexcision rates were 15.6% (5/32) and 27.2.8% (27/99) for DCIS and invasive cancer cases, respectively. Cosmetic outcome was excellent in 158 (79.8%) patients. There were no poor cosmetic outcomes.

Patient age, lesion features (mass vs calcification) and BV at diagnosis were not related to cosmetic outcome. Margin positivity, close margin and reexcision were significant for less-than-ex-

Table 4. Cosmetic outcomes of patients regarding age, lesion type, breast volume, resected volume and reexcision

Cosmetic outcome	*Excellent (N=158; 79.8%) N (%)*	*Good (N=38; 19.2%) N (%)*	*Fair (N=2; 1.0%) N (%)*	*p-value*
Age (years), mean±SD	58±12	59.6±10	56.5±10	0.79
Lesion type				
Calcification	45 (28.5)	8 (21.1)	1 (50.0)	0.78
Mass	113 (71.5)	30 (78.9)	1 (50.0)	
Breast volume (cm^3)				
<600	105 (66.5)	21 (55.3)	0 (0.0)	0.127
600-1000	40 (25.3)	14 (36.8)	2 (100.0)	
>1000	13 (8.2)	3 (7.9)	0 (0.0)	
Final resected volume (cm^3), mean±SD	50.7±39.1	73.4±50.1	65.5±11.8	0.01
Final resected volume (cm^3)				
<70	125 (79.1)	24 (63.2)	1 (50.0)	0.04
70-125	25 (15.8)	7 (18.4)	1 (50.0)	
>125	8 (5.1)	7 (18.4)	0 (0.0)	
Resected volume ratio				
<0.2	153 (96.8)	3 (86.8)	2 (100.0)	0.039
≥0.2	5 (3.2)	5 (13.2)	0 (0.0)	
Reexcision				
No	84 (80.8)	19 (65.5)	0 (0.0)	0.009
Yes	20 (19.2)	10 (34.5)	2 (100.0)	
Re-excision volume (cm^3), mean±SD	21.6±18.1	28±24.2	23±24.1	

SD: standard deviation.
Breast volume was measured by elliptical cone based formula on mammography images for each patient [13].
Tissue volume was calculated by using ellipsoid volume formula (4/3 π × width axis radius × length axis radius × height axis radius) [12].
The resected volume ratio was calculated by dividing the final resected volume by the breast volume [14].

cellent cosmetic outcome (p=0.009). The pathological tumor size, FRV< 70 cm^3 and RVR<0.2 were factors related with excellent cosmetic outcome (p=0.01, 0.04, and 0.039, respectively). However, margin positivity and reexcision rate were not related with FRV<70 cm^3, BV or RVR (p= 0.73, 0.273, 0.802, and 0.437, respectively). RXV was not related with the cosmetic outcome either (p= 0.93; Table 4). RV was mostly under 70 cm^3 (78%) when BV was < 600cm^3 (p= 0001; Table 5). There was no relation between performing reexcision and BV and RVR (p= 0.802 and 0.118, respectively).

Discussion

The introduction of LNCB into the management of palpable or radiologically detected breast lesions has dramatically changed the algorithms. The primary goal of characterizing a lesion as benign, thereby avoiding the need for surgical excision, has clearly been accomplished. Demonstration of malignancy with the attendant ability to distinguish *in situ* from invasive cancer and measuring biomarkers allow surgeons to plan resection with curative intent, decide upon whether simultaneous assessment of the axilla is appropriate, or consider the option of primary systemic therapies. The pathologic demonstration of HRLs, such as ADH and lobular neoplasia, represents a "grey zone". Most surgeons will excise these lesions for complete histopathologic assessment with demonstration of upstaging to DCIS or invasive carcinoma. Relevant with this fact, that these cases may constitute 20% of the practice of a dedicated breast surgeon, studies have shown that HRLs will be upstaged to a malignant diagnosis in 5-25% of the cases, depending upon radiological characterization, patient related factors, such as age and family history, biopsy techniques including size and number of cores, and the extent of pathologic investigation [4-6]. According to the results reported in recent studies, there is no uniformity as to the operative approach to all HRLs diagnosed on LNCB, and there is a need for prospective trials with large sample sizes [17,18]. Our study revealed a 5.4% upgrade rate of HRLs to malignancy. The argument can be made that approaching all 37 HRLs in this cohort with therapeutic intent offered benefit to a single patient at

Table 5. The relation of performing reexcision with pathological tumor size and resected volume in carcinoma group

Variables	*Reexcision*		*p-value*
	Yes (N=32)	*No (N=103)*	
Pathologic tumor size (cm^3), mean±SD	1.63±0.95	1.21±0.84	0.028
Breast volume (cm^3)			0.802
<600	18 (22.0)	64 (78.0)	
600-1000	11 (25.6)	32 (74.4)	
>1000	3 (30.0)	7 (70.0)	
Resected volume ratio, mean±SD	0.12±0.05	0.11±0.05	0.188
Resected volume ratio			0.437
<0.2	29 (90.6)	96 (93.2)	
≥0.2	3 (9.4)	7 (6.8)	

Breast volume was measured by elliptical cone based formula on mammography images for each patient [13].
Resected volume ratio was calculated by dividing the final resected volume by breast volume [14].
SD: standard deviation.

most, while subjecting all to decrement in cosmesis as a consequence of larger resection volumes compared to patients with known benign disease.

The current study showed that a LNCB diagnosis of DCIS or invasive cancer leads to significantly larger resection volumes when compared with HRLs or benign lesions. Our patients diagnosed with HRLs on LNCB were approached with therapeutic intent, leaving the excised tissue volume significantly larger than that of patients with benign disease, but still smaller than in patients with malignant diagnosis. A crescendo pattern of excised volume associated with increasing malignancy risk of the lesions has been established in this study. Despite aggressive surgical approach, 24% of the carcinomas were found to have positive or close margins requiring reexcision. The number of studies addressing the relationship between volume of resection and subsequent involvement of surgical resection margins requiring reexcision is small [16,19-24]. Huston et al. [19] reviewed women with FNA/LNCB diagnosis of *in situ* or invasive cancer. They divided their patients into 3 groups based on margin status of the initial surgical attempt. Group 1 underwent lumpectomy with complete resection of 4-6 additional margins, Group 2 had lumpectomy with selective resection of 1-3 additional margins, and Group 3 had lumpectomy alone. They demonstrated that the need for re-operation based on a positive resection margin was substantially lower in group 1, where the volume of resection was 3-fold higher than in group 3 (129.2 vs 37.4 cm^3). The positive margin rate was reduced from 38.7 to 17.7% as the volume of resected tissue increased. The volume excised and reexcision rates are similar to the results in our study. However, the authors did not comment on the relationship between the resection volumes and the cosmetic outcome.

Mook et al. proposed that the mean total volume of tissue was lower when excised with cavity shaving margin (CSM) compared with standard partial mastectomy (SPM) in their study. The mean volume of excision with CSM was 80.66 cm^3 and 165.1 cm^3 in the SPM group (p = 0.0005) [16]. In another study comparing excised breast volumes between BCS and BCS followed by immediate additional margin shaving (BCS+M), patients with positive margins undergoing BCS had 102±105 cm^3 initial and 263±190 cm^3 total resected tissue volume, which is higher when compared with our 106±61 cm^3 initial and 140±76 cm^3 final volumes (according to calculation with formula of [width axis * length axis * height]) [25]. Although these authors had slightly larger tumor size than our malignant group (1.7 vs 1.4 cm) and significantly higher excision volumes in all groups, they reported no better results in regards to attaining negative margins. They presented a total of 19% positive margins (62/320) in the whole BCS cohort compared to our similar positive margin rates for breast carcinoma (24%). In the same study the mean resection volume of margin-negative patients in the BCS group was also significantly higher when compared with the volumes of our patients with initially negative margin (266±29.8 vs 96.7 ±76 cm^3). Although they had significantly higher resection volumes, they did not compare cosmetic outcomes after BCS [25].

The reported rates of positive margin in the literature vary widely from 10-57% [26-30]. Some authors state that there are significantly higher positive margin rates for DCIS compared with invasive breast cancer, while others reject this notion [31,32]. Reexcision rate was 15.6% in DCIS and 27.2 % in invasive cancer in our group. While our reexcision numbers are comparably favorable to the rates reported in the literature, failure to achieve tumor negative margins demonstrates that more criteria besides the volume of tissue removed need to be evaluated. Candidates for BCS will likely benefit from newer imaging modalities that allow more accurate characterization of the extent of disease, and intraoperative techniques permitting more conformal resections. Newer oncoplastic techniques and large tissue block rearrangements may have a role in addressing this issue. Giacalone et al. [26] reported a newer technique of oncoplastic resection and its effects on margin status. In their study, they showed that oncoplastic surgery resulted in fewer secondary operations than standard quadrantectomy (13 vs 18.5%). However the lateral margins were positive or close in 23% and 33% in the oncoplastic and quadrantectomy groups, respectively. In our study, none of a group of 4 women with known malignant core diagnosis (DCIS and invasive cancer) underwent oncoplastic resection, but they were subjected to large tissue block resections with a mean volume of 106±61 cm^3. However, the surgical resection margins were positive in one patient.

Patients with benign disease on LNCB, who underwent subsequent excision because of symptoms or enlargement of the lesion during follow-up, had the greatest benefit of accurate presurgical assessment. The resected tissue volume was lowest and their cosmetic outcome was uniformly graded as excellent. Most of these patients were approached via inframammary or periareolar incision.

We now feel that it is inappropriate to approach HRLs patients with curative resection. A diagnostic excision, which strives to allow complete histopathologic assessment of the HRLs, offers to the vast majority of women assurance of excellent cosmetic outcome. The small sample size of HRLs is a limitation of this study and there is a need for prospective studies with larger number of patients. As radiological-guided LNCB improves, including larger core samplings and molecular pathology techniques, this dilemma may be solved.

Conclusion

Our study reports the use of image-guided LNCB to establish an accurate diagnosis for breast lesions. A concordant benign diagnosis allows limited resection with the expectation of excellent cosmetic outcome. Women undergoing surgical excision for HRL should have limited resection with the intent to reveal malignancy if present and achieve excellent cosmesis. Subjecting all HRL patients to wide excision benefits a limited number of patients at the expense of all the others. Establishing the diagnosis of DCIS or invasive cancer by preoperative image-guided biopsy also allows surgical planning of wider resections, but the need for reexcision for positive margin still remains high, suggesting that positive margin does not seem to be affected by increased volume of tissue resected, but it is likely to be related to other factors. Newer imaging modalities that allow 3D planning (such as tomosynthesis, 3D MRI or automated 3D breast US) of tissue volume resection may improve the success of segmental resection techniques.

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