

Nondiagnostic Core Needle Biopsy of the Breast under Imaging Guidance: Result of Rebiopsy

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Objective: To determine the rate and the clinical application of recommendation for repeat biopsy after core needle biopsy (CNB) under imaging guidance and to determine the result of rebiopsy

Material and Method: A retrospective review was performed in 1,306 consecutive women who underwent core needle biopsy under imaging guidance at the breast diagnostic center, the Faculty of Medicine, Ramathibodi Hospital from October 1997 to March 2004.

Results: Among 1,306 patients, there were 44 patients (3.37%) who had undergone rebiopsy. The three most common reasons for recommendation of rebiopsy were discordant imaging and pathology, atypical ductal hyperplasia and inadequate specimen. The authors found 12 malignancies subsequently found in rebiopsy (27.3%). The most common reason for rebiopsy in this group was inadequate specimen.

Conclusion: Core needle biopsy under imaging guidance is a minimally invasive diagnostic tool and promises high accuracy and reliability. However, some patients need rebiopsy to exclude hidden malignancy. The cooperation between the radiologists, surgeons and pathologists are prudent for giving the best care to the patients.

Keywords: Core needle biopsy of the breast, Stereotactic core needle biopsy, Discordant imaging and pathology

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Mammography can reduce breast carcinoma mortality⁽¹⁾. Its wide use results in an increasing number of the discovery of small lesions as well as microcalcifications. These cases are not palpable on the physical examination and histopathologic diagnosis cannot be yielded by routine incisional or excisional biopsies. Thus, the percutaneous core needle biopsy (CNB) under imaging guidance is introduced as a minimally invasive diagnostic tool. It can be done using ultrasound guidance in cases in which the abnormalities are clearly visible by ultrasound such as solid mass or using stereotactic guidance in cases of microcalcifications⁽²⁾. This method promises high accuracy and reliability⁽²⁻⁸⁾. Compared to open biopsy,

CNB decreases physical and psychological stress for the patient, decreases operative and perioperative risks, reduces cost and minimizes postoperative scarring which may lead to impaired diagnostic assessment of future mammograms^(2-5,8-11). The accuracy of CNB depends on the characteristics of the lesion, experience of the radiologist, the radiographers and quality of the machines^(2,3). In addition, certain histopathologic findings particularly atypical ductal hyperplasia (ADH) have a high association with carcinoma, which may have been missed at CNB, and require a wider surgical excision^(2-4,12-16). For these reasons, a high correlation between imaging and histologic findings is mandatory. Discordance between mammographic and histologic findings requires repeat CNB or open biopsy^(2,3,5,17). The CNB is the procedure for sampling tissue. Sometimes, the receiving specimen is inadequate for pathologists to give the histopathologic diagnosis, resulting in

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recommendation for rebiopsy for more tissue. Some certain diagnoses particularly phyllodes tumor frequently cannot be distinguished from fibroadenoma based on CNB alone. Thus, excisional biopsy is required^(3,18-22).

The present study was performed to determine the rate and the clinical application of recommendation for repeat biopsy after CNB under imaging guidance and to determine the result of rebiopsy.

Material and Method

A retrospective review was performed in women for whom the pathologic results from CNB under imaging guidance were nondiagnostic i.e., could not exclude malignancy that might coexist and had undergone repeated biopsy of any type. The cases in which the pathologic results from CNB were proved to be benign, but the patients preferred to undergo excisional biopsy were not included in the present study. Medical records, mammographic, sonographic and histologic findings were reviewed.

The study included 1,306 consecutive CNB cases, attending the Breast Diagnostic Center, Department of Radiology, Ramathibodi Hospital from October 1997 to March 2004. In this period, 841 patients (64.39%) underwent core needle biopsy under ultrasound (US) guidance and 465 patients of which (35.60%) were under stereotactic guidance.

Percutaneous biopsy was offered at this center during the period as an alternative to surgical biopsy for both palpable and nonpalpable lesions that were suspicious or highly suggestive of malignancy. The authors provided two types of imaging-guidance; ultrasound and stereotactic guidance. The choice of guidance modality for percutaneous biopsy was mainly based on the type of lesions. The lesion which was clearly visible on ultrasound, would be biopsied under ultrasound guidance because of it was easier to perform, took less time and lower cost compared to stereotactic guidance⁽²³⁻²⁵⁾. The latter was reserved for the lesion which was invisible or inadequately visible on the ultrasound such as microcalcifications or small architectural distortion.

Sonographically guided biopsy was performed freehand with high-resolution (Linear array L12-5 50 mm) sonographic equipment (HDI 5000; Philips ultrasound, Bothell, WA, USA) and a 13-gauge Co-axial Introducer needle, a 14-gauge cutting needle (MDTECH; Gainesville, FL, USA) with a long-throw, spring-loaded automated gun (Magnum; Bard Peripheral Technolo-

gies, Covington, GA, USA). The patients were in the supine or decubitus position. Six core samples were routinely obtained in noncalcified masses. Stereotactic biopsy was performed with an add-on stereotactic device with digital imaging (Lorad stereoLoc II, Danbury, CT, USA) and 14- or 11-gauge directional vacuum assisted biopsy (VAB) instrument (Mammotome; Biopsy Ethicon Endo-Surgery, Cincinnati, OH, USA). Twelve core samples were routinely obtained for the cluster of microcalcifications. If the post biopsy film revealed inadequate removal of suspicious microcalcifications, the extended stereotactic CNB was attempted until the specimens were adequately retrieved. The authors didn't aim to totally remove all of the suspicious microcalcifications, the aim was only to obtain an adequate specimen for pathologic diagnosis. Specimen radiography was performed for all lesions evident as calcifications^(2,3,26). Three radiologists with expertise in stereotactic and sonographically guided breast biopsy performed the procedures.

After biopsy, histologic results were correlated with imaging findings, and specific recommendation were made to the referring physician. If the CNB yielded benign findings concordant with the imaging characteristics, the patient was referred for 6-month-interval or annual mammography⁽²⁷⁾. If the CNB yielded carcinoma, the patient was referred for definitive surgery. Repeat biopsy with excisional biopsy or less frequently, CNB was suggested if there was "nondiagnostic result" i.e., discordance between histologic findings and imaging characteristics, or the pathologists requested more tissue specimen or certain histologic findings including atypical ductal hyperplasia, radial scar, or possible phyllodes tumor. If more than one reason for rebiopsy existed, the major reason was chosen. For example, if there was a spiculated mass associated with pleomorphic microcalcifications and the pathologic report was atypical ductal hyperplasia, the reason for rebiopsy in this case was discordance of the imaging finding and histologic result.

In the authors' practice, not all the patients with CNB who revealed atypical ductal hyperplasia were referred for excisional biopsy. If the post-biopsy film showed the suspicious microcalcifications were totally removed and the revealed histologic specimen disclosed minimal foci of atypia with adequate margin, the 6-month-interval follow-up mammogram and sonogram were required for these patients⁽²⁸⁾. The other reason was the decision of the surgeons, which

preferred to closely follow-up their patients rather than perform excisional biopsy.

After the rebiopsy, comparison was made between the histologic diagnosis based on CNB specimens and that based on surgically excised specimens for each lesion. A lesion was considered to be upstaging if the surgical results yielded a discordant, higher grade lesion—that is, upstaging was a lesion diagnosed using CNB results as atypical ductal hyperplasia or other benign nature but found at surgical excision to be ductal carcinoma in situ or invasive ductal carcinoma.

Data were entered into a computerized spreadsheet for analysis. Statistical analyses were performed with statistical software (Statistical Package for Social Sciences; SPSS version 11.5). Frequency and percentage were presented to describe the results.

Results

In 44 (3.37%) of the 1,306 women in the present series, performance of a second biopsy was required to make an accurate or definitive diagnosis.

The age of the patients in whom rebiopsy was performed ranged from 30 to 72 years. (Median 48 years) There were 29 married women (65.9%) and 15 single women (34.1%)

Of 841 women who underwent CNB under ultrasound guidance, 24 (2.85%) were referred to rebiopsy; 19 women underwent open surgical excision, the other 5 underwent repeat CNB; 4 cases of which were under US guidance and the other one was under stereotactic guidance.

Of 465 women who underwent stereotactic CNB, 20 (4.3%) were referred to rebiopsy; 15 women underwent open surgical excision, the other 5 underwent repeat CNB; 4 cases of which were under stereotactic guidance and the other one was under US guidance.

For the 44 cases who had undergone repeat biopsy, diagnostic mammograms were performed before the procedure in 42 patients. The other two patients were under 35 years old, so US was used as the diagnostic tool. The most common mammographic finding was a mass (22 cases, 50%). The second rank was microcalcifications (13 cases, 29.5%), followed by a mass containing microcalcifications (5 cases, 11.4%). One patient (2.3%) had architectural distortion. In the remaining one patient, the abnormality was invisible on the mammogram.

US was performed in all cases. Thirteen of 44 patients (29.5%), had microcalcifications seen on the

mammogram and US could not depict the abnormality. The most common sonographic finding was a mass (27 cases, 61.4%), followed by a mass containing microcalcifications (3 cases, 6.8%). In one patient (2.3%), the microcalcifications were numerous enough to be visible on US.

Acquisition of 6 cores were routinely attempted. However, the number of cores depended on a variety of factors, for example, the characteristics as well as the size of the lesions, the volume of calcified specimen obtained (as seen by immediate postbiopsy mammogram, if the calcified target had not been retrieved, more core specimens were attempted), patients' cooperation and the skill of the radiologists. The characteristic of the lesion was the most important determinant. More specimens were required for microcalcifications because it was notorious for sampling error^(2,3,29). After the introduction of mamotome, 12 cores were routinely accomplished for microcalcifications. Combined CNB under US and stereotactic guidance, the range of the number of cores was 4-20 (mean 7.59, median 6.0). The patient in whom the core taken was only 4 cores was a 69-year-old female with a 1.5-cm mass. Unfortunately, active bleeding occurred during CNB under US guidance, resulting in cessation of the procedure. The pathological report disclosed intraductal papilloma with atypical epithelial hyperplasia in which intraductal carcinoma could not be totally excluded due to inadequate specimen. Repeat biopsy was recommended by the pathologist. The surgeon and patient preferred to treat it by modified radical mastectomy. The final pathologic diagnosis was ductal carcinoma in situ (DCIS).

The reasons for recommending rebiopsy after CNB are listed in Table 1. Discordant imaging and histopathologic findings, ADH and inadequate specimen had the same frequency (13 cases; 29.5%). The most common reason in the group of US guidance was discordant imaging and histopathologic findings (8 from 24 cases; 33.3%). While the most common reason in the group of stereotactic guidance was inadequate specimen. (7 from 20 cases; 35%)

The time interval between the first CNB to rebiopsy ranged from 7 to 1122 days (median 36 days). The patient who delayed rebiopsy for 1122 days had pathologic diagnosis of fibroadenoma versus phyllodes tumor from CNB under stereotactic guidance. She was lost to follow-up for almost 3 years. Finally, she returned to her physician because of a persistent palpable mass. Then, excisional biopsy was done and revealed a benign phyllodes tumor.

Table 1. Reasons for rebiopsy

Reasons for rebiopsy	US guidance n = 841	Stereotaxis n = 465	Overall n = 1306	Malignancy found in rebiopsy (cases)
Discordant imaging and pathology	8 (33.3%)	5 (25%)	13 (29.5%)	4
Atypical ductal hyperplasia	7 (29.2%)	6 (30%)	13 (29.5%)	2
Inadequate specimen	6 (25%)	7 (35%)	13 (29.5%)	5
Suspicious for phyllodes tumor	3 (12.5%)	2 (10%)	5 (11.4%)	1
Total	24 (100%)	20 (100%)	44 (100%)	12 (27.3%)
Overall rebiopsy rate	2.85% (24/841)	4.30% (20/465)	3.37% (44/1306)	

Among the 44 cases in which rebiopsy was performed, there were 12 malignancies (27.3%) subsequently diagnosed. The age of the patients in this group ranged from 45 to 72 years (Median 57 years).

The number of core specimens ranged from 5 to 14 (Median 6 cores) in the benign group and from 4 to 20 (Median 6 cores) in the malignant group.

The upstaging rate in the present series was 0.92% (12 from 1306 patients). The details of the pathological upstaging results are listed in Table 2. Three of 6 cases of ductal carcinoma in situ (DCIS) underwent CNB under US guidance and the other 3 cases were under stereotactic guidance. Four cases of invasive ductal carcinoma (IDC) were found, half of them underwent CNB under US guidance and the remainder were under stereotactic guidance. One case had the pathologic result of DCIS with focal microinvasion from open biopsy after CNB under US guidance. One patient had borderline phyllodes tumor from open biopsy after CNB under US guidance.

Inadequate specimen was encountered as the most common reason for rebiopsy which finally revealed malignancies (5 from 12 malignancies; 41.7%) (Table 1). The second rank was discordant imaging and histopathologic findings (4 from 12 malignancies; 33.3%).

Discussion

Core needle biopsy (CNB) under imaging guidance is increasingly an alternative to surgical biopsy for the histologic assessment of breast lesions. Early work with CNB primarily involved fine-needle aspiration, but large-core biopsy is now preferred because of its better characterization of benign and malignant lesions and lower frequency of insufficient samples⁽²⁻¹¹⁾.

In the present series, the overall rebiopsy rate was 3.37% (44 from 1,306 patients). The rebiopsy rate in the group of US guidance was 2.85% (24 from 841 patients) and 4.30% (20 from 465 patients) in the

Table 2. Pathological upstaging results

Image guidance modality	DCIS	IDC	DCIS+IDC	Borderline Phyllodes
US guidance	3	2	1	1
Stereotactic guidance	3	2	0	0
Overall	6	4	1	1

Abbreviations: DCIS = Ductal carcinoma in situ,
IDC = Invasive ductal carcinoma

group of stereotactic guidance. The rebiopsy rate in the stereotactic group in the presented data was comparable to prior studies, which ranged from 2.5-18%^(3,30-32). However, the presented rebiopsy rate might be lower than usual because not all of the presented patients diagnosed with ADH had a second biopsy. Of 45 cases diagnosed with ADH, only 13 patients underwent repeated biopsy (28.89%). The remaining cases had close follow-up, depending on the extent of abnormality removal by initial CNB or the surgeon/patient preference.

In a series of 56 patients who underwent CNB under stereotactic guidance reported by Dershaw et al⁽³⁾, the most frequent reason for repeat biopsy was atypical ductal hyperplasia (ADH), 54%, followed by discordant imaging and pathology. Reasons for repeat biopsy in our study also included atypical ductal hyperplasia was also the most common encountered reason for rebiopsy in the present series, along with, discordant imaging and pathology and inadequate specimen (Table 1).

In the present series, if guided imaging modalities were separately considered, the reason for rebiopsy in the US group was discordant imaging and histology, while in the stereotactic group it was inadequate specimen. Selection bias existed at the time of selection for guidance modality. Almost all the lesions performed CNB under US guidance were masses or masses containing calcifications. To reduce the possibility for sampling error, direct sonographic

visualization of the needle within the mass at the time of the biopsy was used to confirm targeting accuracy. Meanwhile, lesions which required stereotactic guidance were mainly microcalcifications. Thus, they were more difficult to target compared to the mass which was clearly visible on US. The position of the patient and time-consumed are also important factors for target accuracy in stereotactic guidance. Our institution uses add-on stereotactic device in the upright position, that means it is necessary for the patient to remain in a fixed position during the procedure, which required 20 to 45 minutes. Only a subtle movement during the procedure can make a missed target, resulting in sampling error. Unlike US, the patient lies on the bed in supine or lateral decubitus position and the procedure takes only 5-20 minutes, which is much more convenient compared to the stereotactic guidance. These reasons may explain why an inadequate specimen is more frequently encountered in patients who undergo stereotactic CNB.

The present study found 12 from 44 patients had malignancy from the second biopsy (27.3%). This data is less frequent than that seen in the study of Dershaw et al, who reported carcinoma in 44% of the patients who underwent rebiopsy after initial stereotactic CNB⁽³⁾. For the cases in which rebiopsy showed malignancy, the reasons for rebiopsy are also displayed in Table 1.

The principle of CNB is to sampling adequate tissue for histopathologic diagnosis. Sometimes, sampling error exists. This occurs when biopsies only the region of benign tissue or atypical ductal hyperplasia (ADH) in a lesion containing both benign and malignant parts⁽²⁾. Pathologists play important role in this circumstance. The recommendation to obtain more tissue inform the surgeon and radiologist to repeat biopsy.

Concerning the upstaging group, i.e., the histopathologic findings of the repeat-biopsy sample showed malignancy, the presented data found that the most common reason for rebiopsy was inadequate specimen (5 from 12 patients, 41.67%), as mentioned in the pathologic report by the pathologists. This data suggests that multidisciplinary cooperation is important for taking care of the patients.

The authors found the discordance of imaging and pathologic finding to be the second most common reason for rebiopsy in the patient with subsequently disclosed malignancy (4 in 12 patients, 33.33%). A comparable result was also found in the series of Dershaw⁽³⁾. The presented data and Dershaw's

data reinforce the principle that Discordant between imaging findings and histopathologic findings are also the important reason for recommendation rebiopsy. CNB should not be performed without the ability to correlate histopathologic results with imaging findings. In some patients, comparison of the histopathologic and imaging findings strongly suggested that the lesion in question had not been sampled and that rebiopsy was necessary.

Atypical ductal hyperplasia (ADH) is a histologically borderline lesion that has some but not all the features of ductal carcinoma in situ (DCIS). Involvement of a single duct or an aggregate diameter of involvement of less than 2 mm, constitutes a diagnosis of ADH^(2,14). Given the extent of disease in differential diagnosis between ADH and DCIS, the underestimation of a lesion retrieved on a large-core needle biopsy is likely explained by sampling error^(2,14). The development of the directional vacuum-assisted biopsy device as well as using the 11-G needle have allowed improved accuracy in sampling clusters of calcifications and masses^(2,17). Of lesions yielding ADH by these techniques, approximately 0-38% have carcinoma at surgery^(12-16,28).

In the presented series, among 13 patients diagnosed ADH, two patients had carcinoma from rebiopsy (15.4%) (DCIS and invasive ductal carcinoma). One patient had the biopsy performed under US guidance and the other one with stereotactic guidance. Fourteen-G needles were used in both cases, which might be one of the contributing factors for underestimation^(2,14,32). However, limitation existed because in the authors' practice, not all patients diagnosed of ADH subsequently had excisional biopsy. The authors recommended close follow-up in cases where the abnormality required near total removal. Jackman et al⁽²⁸⁾ concluded that ADH was more reliably diagnosed when the patient did not have a personal history of breast carcinoma, the lesion measured less than 10 mm, and/or 100% of the lesion was removed at stereotactic biopsy. The other main reason is not all the presented ADH patients had undergone rebiopsy, because the surgeons preferred to follow-up regardless of the recommendation of the radiologists. There may be carcinoma coexisting in the latter group but it was beyond the scope of the authors' objectives. Further assessment of this topic is planned to be the authors' subsequent investigation.

The authors reported one case of borderline malignant phyllodes tumor from rebiopsy. The patient was a 56-year-old female, who presented with a mass.

The CNB under US guidance was initially performed and the pathology reported fibroepithelial tumor-Fibroadenoma versus phyllodes tumor. The excisional biopsy was performed. The final diagnosis was borderline malignant phyllodes tumor. Both phyllodes tumor and fibroadenoma consist of epithelial and stromal elements which originate from the terminal ductal lobular unit⁽³³⁾. Histologically, phyllodes tumor can be distinguished from fibroadenoma by hypercellular stromal with cytologic atypia and increased mitoses. Therefore, the differentiation between these two conditions may be difficult without adequate tissue. Most investigators recommend excisional biopsy rather than fine-needle aspiration or CNB if the lesion was suggestive of phyllodes tumor, in order to make certain diagnosis and assess its benign or malignant nature^(3,18-22). Anyway, core needle histologic examination of phyllodes tumor allows the surgeon to preoperatively plan definitive management at one surgical procedure, reducing the need for reoperations⁽³⁴⁾.

The potential weakness of the present study concerns the difficult task of estimating the percentage of lesion removal and interobserver or intraobserver accuracy of the pathological interpretation.

Conclusion

In conclusion, Core needle biopsy under imaging guidance is useful as a diagnostic tool and decreases the number of patients requiring open biopsy. However, the clinicians and patients need to realize that additional biopsy procedures may be necessary in certain circumstances, which include discordant imaging and pathology, atypical ductal hyperplasia, inadequate specimen and suspicious phyllodes tumor. The cooperation between the radiologists, the surgeons and the pathologists are prudent for giving the best care to the patients.

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ผลการตรวจชิ้นเนื้อซ้ำหลังการเจาะตรวจชิ้นเนื้อของเต้านม ภายใต้การนำด้วยอัลตราซาวด์ หรือ แมมโมแกรมที่ไม่สามารถให้การวินิจฉัยได้

ชลทิพย์ วิรัตน์พันธ์, บุษณี วิบูลผลประเสริฐ, ศันสนีย์ วงศ์ไวยวรรณ, กมลธรรม พูลภิญโญ

วัตถุประสงค์: เพื่อศึกษาอัตราการตรวจชิ้นเนื้อซ้ำหลังการเจาะตรวจชิ้นเนื้อของเต้านม ภายใต้การนำด้วยอัลตราซาวด์ หรือ แมมโมแกรมที่ไม่สามารถให้การวินิจฉัยได้, เหตุผลในการตรวจชิ้นเนื้อซ้ำ และผลการตรวจชิ้นเนื้อซ้ำ

วัสดุและวิธีการ: รวบรวมข้อมูลจากเวชระเบียน, แมมโมแกรมและอัลตราซาวด์ของผู้ป่วยที่ได้รับการเจาะตรวจชิ้นเนื้อของเต้านมที่ศูนย์ตรวจวินิจฉัยเต้านม ภาคศิริราชศิริวิทยา คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี ตั้งแต่ตุลาคม 2540 ถึง มีนาคม 2547 จำนวน 1,306 ราย

ผลการศึกษา: จากผู้ป่วยจำนวน 1,306 ราย พบผู้ป่วยที่ได้รับการตรวจชิ้นเนื้อซ้ำ 44 ราย (3.37%) เหตุผลสำคัญในการตรวจชิ้นเนื้อซ้ำ 3 ประการ คือ ความไม่เข้ากันระหว่างลักษณะทางแมมโมแกรม และอัลตราซาวด์กับผลทางพยาธิวิทยา, Atypical ductal hyperplasia และ ชิ้นเนื้อไม่เพียงพอสำหรับการวินิจฉัยทางพยาธิวิทยา ในจำนวนผู้ป่วย 44 ราย ที่ได้รับการตรวจชิ้นเนื้อซ้ำ พบมะเร็ง 12 ราย (27.3%) ซึ่งสาเหตุของการตรวจชิ้นเนื้อซ้ำที่พบบ่อยที่สุดในผู้ป่วยกลุ่มนี้ คือ ชิ้นเนื้อไม่เพียงพอสำหรับการวินิจฉัยทางพยาธิวิทยา

สรุป: การเจาะตรวจชิ้นเนื้อภายใต้การนำด้วยอัลตราซาวด์ หรือ แมมโมแกรม ถึงแม้จะเป็นวิธีที่ให้การวินิจฉัยที่แม่นยำ แต่ยังมีผู้ป่วยบางส่วนที่จำเป็นต้องทำการตรวจชิ้นเนื้อซ้ำเพื่อแยกจากมะเร็ง ด้วยเหตุผลหลัก 3 ประการดังที่ได้กล่าวมา ซึ่งต้องอาศัยความร่วมมือระหว่างรังสีแพทย์, ศัลยแพทย์และพยาธิแพทย์
