

# Analysis of stereotactic biopsies for nonpalpable BIRADS 4 breast lesions: Evaluation of predictors for malignancy

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## Abstract

**Aim:** This study aims to determine the malignancy rates of nonpalpable BIRADS 4 breast lesions excised by stereotactic biopsy, the re-excision rates of malignant lesions detected by stereotactic biopsy and to evaluate the factors affecting malignancy rates in these lesions.

**Materials and Methods:** Medical records of female patients admitted to the surgical oncology outpatient clinic between 2012 and 2017 with nonpalpable (<1 cm) BIRADS 4 breast lesions (either detected by USG or mammography) and underwent stereotactic breast biopsy were assessed.

**Results:** The mean age of a total of 208 patients with 235 lesions underwent image-guided breast biopsy was  $49.0 \pm 0.6$ . In 54% of lesions, localization was superior outer quadrant and 51.1% of lesions were at left breast. In 46% of cases, radiological abnormality causing suspicion of malignancy was nodular lesion and the most encountered pathological result was proliferative breast lesion without atypia (62.1%).

The mean age of the malignancy detected group after stereotactic biopsy was higher than benign group ( $p=0.048$ ).

In 16.2% (38/235) of the lesions, malignancy was detected and none of malignant lesions had lymph node metastasis. ER, PR and HER-2 positivity were 88.2% (30/34), 86.7% (26/30), and 30% (6/20), respectively. The re-excision rates of the malignant lesions to ensure oncologically acceptable surgical margins were 23.7% (9/38).

**Conclusion:** Although malignancy, re-excision, and lymph node metastasis rates of non-palpable breast lesions underwent stereotactic biopsy with malignancy suspicion are not too high, careful evaluation of these lesions with malignancy suspicion is suggested in order not to miss malignant cases.

**Keywords:** Breast cancer; core biopsy; mammography; screening; stereotactic breast biopsy; surgical margin

## INTRODUCTION

Increasing awareness of breast cancer among women improved the attendance to screening programs and enabled the detection of breast cancer lesions at earlier stages. Therefore survival and breast-conserving surgery rates have been increased (1-4). The preferred and recommended diagnostic tool for the suspicious breast lesions for malignancy is core or needle biopsy (5). But as the screening programs and technology improve, more and more non-palpable lesions are detected. Unfortunately image-guided percutaneous biopsies sometimes may be ineffective for non-palpable, small lesions. Also, because of technical or economical inabilities this technique may not be easily accessible. In these circumstances, the simplest and safest way to reach an accurate diagnosis may be the surgical excision of the lesion by image-guided wire localization (stereotactic biopsy) which is still frequently performed in our country (6-8).

This study aims to determine the malignancy rates of BIRADS 4 nonpalpable breast lesions detected by either USG or mammography, the relevant factors affecting malignancy rates in these lesions and to evaluate re-excision rates of malignant lesions detected by stereotactic biopsy.

## MATERIALS and METHODS

### Study Design

Female patients admitted to surgical oncology outpatient clinic between 2012 and 2017 with nonpalpable (<1 cm) BIRADS 4 lesions detected by either USG or mammography and underwent stereotactic breast biopsy were identified. These suspicious lesions were marked by image-guided wire localization and surgeries ended after the confirmation of complete removal by radiology.

Demographical and clinical data were evaluated retrospectively. Preoperative age, localization of the

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lesions (central, superior outer quadrant (SOQ), inferior outer quadrant (IOQ), superior inner quadrant (SIQ), inferior inner quadrant (IIQ)), detected radiological pathology (microcalcification, nodule, architectural distortion, mammary dysplasia, ductal widening), radiological methods used for hookwire insertion (USG or mammography), pathology reports of the image-guided excisional biopsy specimens (non-proliferative breast lesion, proliferative breast lesion without atypia, atypical hyperplasia (ductal or lobular), ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), malignancy), estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER-2) positivity, lymph node metastasis status and the need of re-excision in patients with malignancy were assessed. Classification of benign breast disorders were done as previously described by Godfrey SE et al (9).

The study was approved by the ethical committee of Ankara University (decision number: İ6-313-19).

### Statistical Analysis

Demographical and clinical data were expressed using descriptive statistics. Continuous data were presented as mean  $\pm$  standard error of the mean (SEM). Statistical analysis was performed by SPSS version 22 (IBM Corp., Armonk, NY, USA). Student's t test and chi-square tests were used for continuous and categorical factors, respectively. For analysis of categorical factors, if appropriate Fischer's exact test was performed.  $p < 0.05$  were accepted significant.

## RESULTS

Table 1 demonstrates the demographical and clinical details of the study group. There were a total of 208 patients with 235 lesions underwent image-guided breast biopsy. The mean age of the patients was  $49.0 \pm 0.6$ . In 54% of lesions localization was superior outer quadrant and 51.1% of lesions were at left breast. In 46% (108/235) of cases, radiological abnormality causing suspicion of malignancy was nodular lesion and the most encountered pathological result was proliferative breast lesion without atypia constituting 62.1% (146/235) of the lesions. Pathological evaluation of the remaining lesions was 28 (11.9%) atypical hyperplasia (ductal or lobular), 23 (9.8%) nonproliferative breast lesion, 14 (6%) invasive carcinoma, 18(7.7%) DCIS, 6(2.5%) LCIS. Invasive carcinoma group included invasive ductal carcinoma (n=10), tubular carcinoma (n=2), invasive micropapillary carcinoma (n=1), invasive cribriform carcinoma (n=1).

The mean age of the malignancy detected group after stereotactic biopsy was higher than the benign group ( $p=0.048$ ). In 114 lesions USG was the tool for the detection and wire localization of the lesion and in 121 lesions mammography was used. Malignancy rate was higher in mammographically detected and wire-guided excised lesions (25/121 vs 13/114) ( $p=0.054$ ). There was no statistically significant difference in malignancy detection rates according to radiological abnormality.

**Table 1. Demographical and clinical data of study patients**

| Parameter  | All Patients (n=235) | Benign Lesions (n=197) | Malignant Lesions (n=38) | P value |
|--|----------------------|------------------------|--------------------------|---------|
| <b>Age, years, mean (SEM) Side</b>                                       | 49.0 (0.6)           | 48.5 (0.7)             | 51.7 (1.4)               | 0.048   |
| Right/Left   | 115/120              | 95/102                 | 20/18                    | 0.619   |
| <b>Lesion localization N (%)</b>   |                      |                        |                          | 0.543   |
| Superior outer quadrant  | 127 (54)             | 102                    | 25                       |         |
| Central portion  | 40 (17)              | 34                     | 6                        |         |
| Inferior outer quadrant  | 27 (11.5)            | 25                     | 2                        |         |
| Superior inner quadrant  | 22 (9.4)             | 20                     | 2                        |         |
| Inferior inner quadrant  | 19 (8.1)             | 16                     | 3                        |         |
| <b>Radiological abnormality N (%)</b>                                    |                      |                        |                          | 0.386   |
| Nodular lesion   | 108 (46)             | 95                     | 13                       |         |
| Microcalcification   | 102 (43.4)           | 80                     | 22                       |         |
| Mammary dysplasia  | 11 (4.7)             | 10                     | 1                        |         |
| Ductal widening  | 5 (2.1)              | 4                      | 1                        |         |
| Architectural distortion   | 5 (2.1)              | 4                      | 1                        |         |
| Nodular lesion + microcalcification                                      | 4 (1.7)              | 4                      | 0                        |         |
| <b>Radiological method for wire localization (USG/ Mamography) N (%)</b> | 114 / 121            | 101/96                 | 13/25                    | 0.054   |

SEM: Standart error of the mean

In 16.2% (38/235) of the lesions, malignancy was detected and lymph node metastasis was not determined in any of malignant lesions. In 13 of 108 nodular lesions (12%), in 22 of 102 microcalcifications (21.6%), in 1 mammary dysplasia, in 1 ductal widening, and in 1 architectural distortion malignancy was diagnosed after stereotactic excision. The re-excision rate of the malignant lesions to ensure oncologically acceptable surgical margins was 23.7% (9/38) (Table 2). In 6 of 22 microcalcifications, 2 of 13 nodular lesions, and 1 architectural distortion, re-excision needed ( $p=0.241$ ). In 7 of 121 lesions managed by mammography, 2 of 114 lesions managed by USG, reexcision was needed ( $p=0.101$ ).

ER, PR and HER-2 positivity were 88.2% (30/34), 86.7% (26/30), and 30% (6/20) respectively.

All the suspicious lesions described radiologically were completely excised.

**Table 2. Surgical margin positivities after stereotactic biopsies according to tumor types**

| Pathology Result                  | n (%)     | Surgical margin positivity (n=9) |
|-----------------------------------|-----------|----------------------------------|
| Invasive ductal carcinoma         | 10 (26.3) | 2                                |
| DCIS                              | 18 (47.5) | 5                                |
| LCIS                              | 6 (15.9)  | 0                                |
| Tubular carcinoma                 | 2 (5.3)   | 1                                |
| Invasive micropapillary carcinoma | 1 (2.6)   | 1                                |
| Invasive cribriform carcinoma     | 1 (2.6)   | 0                                |
| Total                             | 38        | 9                                |

DCIS: Ductal carcinoma in situ, LCIS: Lobular carcinoma in situ

## DISCUSSION

In this study, the malignancy rate of biopsy recommended non-palpable BIRADS 4 breast lesions with suspicion of malignancy according to radiology reports was 16.2%. The mean age of malignancy group was higher than benign group ( $51.7\pm 1.4$  vs  $48.5\pm 0.7$ ,  $p=0.048$ ). Malignancy detection rate was higher in mammographically managed lesions when compared to ultrasonographically managed group (25/121 vs 13/114,  $p=0.054$ ). The re-excision rate after the diagnosis of malignancy by stereotactic biopsy was 23.7% (9/38) and there was no lymph node metastasis in any of the malignant lesions.

Previous studies about image-guided excisional breast biopsy, malignancy rates were reported to range between 10% and 50% (7,10). Also in the current study malignancy rates of nonpalpables lesions were not low, should alert the physicians about careful evaluation of nonpalpable suspicious lesions.

Up to date being 70 years and over is reported as a risk factor for malignancy in non-palpable suspicious various breast lesions (10,11). In our study the mean age of malignancy group was higher.

The most common localization of breast cancer is superior outer quadrant (12,13), also in the current study, suspicious lesions were mostly localized at SOQ. On the other hand the difference among the localizations of benign and malignant non-palpable suspicious lesions was statistically insignificant.

One of the most serious complication of image-guided excisional biopsy is the failure of complete removal of the suspicious lesion which is reported up to 12% (7,14), in our study, we did not encounter such a problem, because the same breast radiologists always checked the completeness of excision by comparing the excised specimen's radiological images with prior images taken during wire localization (with USG or mammography, but before and after excision images by the same tool).

In our study, there was no statistically significant difference for radiological abnormalities between malignant and benign groups. When it was possible USG was the preferred choice for wire localization because of its convenience and safer application without radiation. But malignancy rates were higher in mammographically detected lesions and this difference was statistically significant.

Recent studies about stereotactic vacuum-assisted biopsy (SVAB) of non-palpable lesions with suspicion of malignancy have reported that SVAB decreases the operation rates for both benign and malignant lesions (15) but underestimation rates of SVAB for DCIS and atypical ductal hyperplasia are not low (15-17). Also it is not always easy to find a center with enough experience and equipment for SVAB even in high volume tertiary centers in developing countries. And in addition to these factors, some patients prefer surgery instead of the follow up of suspicious lesions.

As seen in our results, 84.6% of these lesions are benign and a surgery for a benign disorder should not cause a bad aesthetic outcome. In malignant lesions our re-excision rates were high (23.7%), this may be because of only aiming the insurance of complete removal of the lesion for accurate diagnosis without deterioration the shape and appearance of the tissue. All the malignant lesions detected in the current study were T1, and there was no lymph node metastasis but careful evaluation of axillary region is mandatory even in small sized tumors.

In fifth BIRADS lexicon (18) and high-volume studies microcalcifications are categorized as linear-linear branching, pleomorphic, coarse heterogeneous, or amorphous calcifications with accompanying malignancy rates ranging between 70% to 100%, 29 to 63.2%, 13 to 17.8%, 7.9 to 21%, respectively (10,19). Since our study was retrospective in nature, we were not able to apply that much detailed microcalcification classification as per BIRADS classification (BIRADS 4 a-b-c). Though the current study represents a single institution experience it should be kept in mind that the malignancy rates of nonpalpable suspicious lesions are not low.

## CONCLUSION

In conclusion, malignancy, re-excision, and lymph node metastasis rates of non-palpable breast lesions those underwent stereotactic biopsy with malignancy suspicion are not too high. However, careful evaluation of these lesions with malignancy suspicion is suggested in order not to miss malignant cases.

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