

# Concordance of Core Needle Biopsy and Post-operative Histo-pathological Grading in Breast Cancer Patient

Harme Jalal Mohammed<sup>1\*</sup>, Faruk Hassan Faraj<sup>2</sup>

<sup>1</sup>Department of General Surgery, School of Medicine, Slemani Teaching Hospital, Slemani, Iraq.

<sup>2</sup>Head of Iraqi Board of General Surgery, Sulaimani Center, College of Medicine, Unisersity of Sulaimani, Sulaymaniyah, Kurdistan Region, Iraq.

\*Correspondence to: Harme Jalal Mohammed (E-mail: Jalalharme@gmail.com)

(Submitted: 10 February 2022 – Revised version received: 04 March 2022 – Accepted: 13 April 2022 – Published online: 26 June 2022)

## Abstract:

**Objectives:** This study aimed to evaluate the concordance of histological types, grade and components of grading, between CNB and open surgical specimens.

**Methods:** In this study patients with paired CNB and open surgical biopsy diagnosed with invasive breast cancer are involved, from January 2012 to October 2015 were recreated. Revision of (579) patients were done, but only (116) patients were included in our study according to inclusion criteria, in the breast center department of Slemani Teaching Hospital in Slemani Governorate.

**Results:** There were 116 patients with invasive breast cancer analyzed for concordance rate between CNB and open surgical specimen for tumor type, grade, tubule formation, nuclear pleomorphism, and mitotic count were 93.1%, 73.3%, 77.6%, 73.3%, 62.9% respectively, mitotic count was under estimated in CNB samples (kappa 0.4 P value 0.001).

**Conclusion:** These results indicate that pre-operative CNB can reliably provide useful preoperative prognostic and predictive information in breast cancer patients which can play a major role in planning treatment strategies. Core needle biopsy has significant accuracy in determining invasive breast cancer and histological type and grading.

**Keywords:** Breast neoplasms, biopsy, large-core needle, Nottingham grading, concordance rate

## Introduction

Breast cancer is the most commonly diagnosed cancer among women, accounting for approximately 26% of all incident cancers.<sup>1</sup> It is the second-leading cause of cancer deaths among American women after lung cancer.<sup>1</sup> The lifetime risk of dying of breast cancer is approximately 3.4%.<sup>1</sup>

Triple assessment is a standard method for assessment of breast diseases, they includes (clinical evaluation, radiographic assessment and pathological assessment).<sup>2</sup> Biopsy for breast disease is the gold standard for pathological assessment, including fine needle aspiration cytology (FNAC), core needle biopsy (CNB), and open excisional biopsy (OEB).<sup>2</sup>

Core needle biopsy CNB method is a precise as an (OEB) in the diagnosis of breast diseases, and is now generally taken as the standard procedure for a breast cancer diagnosis.<sup>3</sup> It can also provide prognostic and predictive informations.<sup>4</sup>

There are various factors which may affect CNB accuracy. (1) The gauge of the needle, (2) The number of the cores which are taken, (3) Experience of the operator may be another factors.<sup>5</sup>

Invasive carcinomas are morphologically subdivided according to their growth patterns and degree of differentiation. This subdivision is achieved by assessing histological type and histological grade, respectively.<sup>6</sup> This assessment can be achieved by CNB.<sup>6</sup>

The Nottingham (Elston-Ellis) modification of the Scarff-Bloom-Richardson grading system, also known as the Nottingham Grading System (NGS).<sup>7</sup> Is the grading system recommended by various professional bodies internationally.<sup>7</sup> (World Health Organization) [WHO], American Joint Committee on Cancer [AJCC], European Union [EU], and the Royal College of Pathologists (UK RCPATH).<sup>8,9</sup>

NGS is based on the evaluation of three morphological features:

(a) Degree of tubule or gland formation, (b) Nuclear pleomorphism, and (c) mitotic count.<sup>8,9</sup>

The three separate parameters are scored independently as follows:

**Tubule formation**, tubule score (1): >75% of the neoplasm is composed of tubular structure, tubule scores (2): 10–75% of the tumor has tubular pattern, tubule score (3): <10% tubule formation.<sup>7</sup>

**Nuclear grade**, nuclear score (1): nuclei are small to medium sized, relatively uniform in size and shape, lacking clumped chromatin or prominent nucleoli, nuclear score (2): nuclei are medium to large size, nuclear score (3): nuclear are large and vesicular and or contains coarse clumps of chromatin.<sup>7</sup>

**Mitotic score** is assessed in the peripheral areas of the neoplasm and not the sclerotic central zone, NGS uses a scoring system based on the number of mitosis per 10 HPF (High Power Field):<sup>7</sup> Score 1: 0–5 mitosis. Score 2: 6–10 mitosis. Score 3: >10 mitosis.<sup>7</sup>

## Aim of Study

The aim of this study is to demonstrate the concordance rate between pre-operative CNB and post-operative Histo-pathological grading in invasive breast cancer patients. To assess the accuracy of CNB in forecasting tumor grade which is a powerful prognostic factor for survival and predictive factor for response to treatment.

## Patients and Methods

This is a retrospective cross-sectional study done to identify those patients who had undergone CNB for a suspicious breast lesion and open excisional biopsy (OEB). In the breast center department of Slemani Teaching Hospital in Slemani Governorate. Data were collected from January 2012 to October 2015. Revision of (579) patients was done but only (116) patients were included in our study, as only these

patients are with our study aims. Tumor size was not used as a factor in selection of cases. CNB were performed under ultrasound guidance, the tissue samples were obtained using a semi-automated and full automated biopsy gun with a 14-gauge needle.

Inclusion criteria: (1) Received both CNB and OEB in our center; (2) Found invasive carcinoma in CNB and/or OEB samples; (3) None of the patients had received chemotherapy, radiotherapy, or hormone therapy between CNB and surgical excision, (4) Nottingham grading done in pre-operative CNB and OEB.

Histological grading of invasive carcinoma was based on the Elston's modification of the Bloom and Richardson system, Based on assessment of tubule formation, nuclear pleomorphism, and mitotic count.<sup>7</sup>

## Bio Statistical Methods

The concordance or discordance between core biopsy and surgical biopsy specimens was analyzed by kappa test statistic (SPSS version 21).

Concordances of (<0.2 is poor agreement, 0.4–0.6 is moderate agreement, >0.6 is good agreement, *P* value ≤0.05 regards as significant).

## Results

Concordance between the CNB and the open surgical biopsy specimen for (type, grade, mitoses, tubules, and pleomorphism) in 116 patients with breast cancer was assessed. All the patients were female with a mean age 48.9 (ranging from 29 to 80 years), 67(57.8%) of cases were pre-menopausal and 49(42.2%) were post-menopausal, also 10(8.6%) of cases with positive family history for breast cancer 8(6.6%) of them are first degree relative, 2(1.7%) second degree relatives, ultra sound and mammography was done for all the 116 before CNB which classify them according to the BIRAD classification.

Specimens were obtained under ultra sound guided method, an average of 5 cores per lesion (range: 3–8) cores per lesions by (gauge 14) semi automated and full automatic CNB, associated carcinoma in situ (CIS) was positive in 55 (47.4%) patients, no CIS in 49(42.2%) patients, no information in 22(10.3%) patients, as shown in Figure 1.

The Histo-pathological diagnosis for the Type by CNB was: 92.2% invasive ductal carcinoma which was most

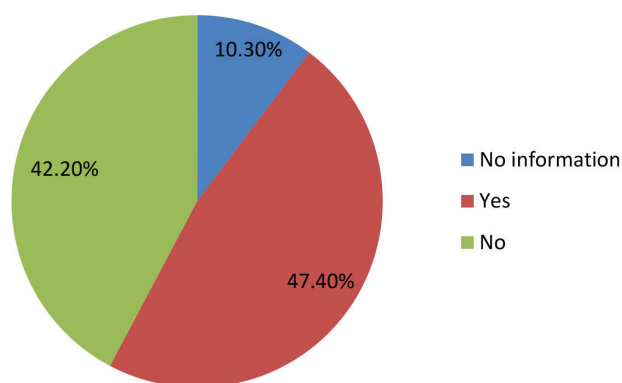


Fig. 1 Frequency and percentage of carcinoma in situ by CNB.

common type, 1.7% other malignancy [mucinous carcinoma: 1(0.9%), Invasive lobular carcinoma: 1(0.9%).], and 6% no malignancy, as shown in Table 1.

Tumor Grade in CNB was: Grade one 6.0%. Grade two 59.9% and Grade three was 36.2%, as shown in Table 2.

Tubule formation was: Score one 1.7%, Score two 25%, Score three 64.7%, as shown in Table 3.

Nuclear pleomorphism was: Score one 4.3%, Score two 47.4%, Score three 39.7%, as shown in Table 4.

Mitotic count was: Score one 27.6%, Score two 48.3%, Score three 15.5%, as shown in Table 5.

The Histo-pathological diagnosis in open surgical specimen for Tumor type 99.1% invasive ductal carcinoma, 0.9% other malignancy (mucinous carcinoma), as shown in Table 6.

Associated CIS was positive in 70(60.30%) patients no CIS in 44(37.9%), no information in 2(1.7%), as shown in Figure 2.

Table 1. Frequency and percentage of tumor type in (116) patients by CNB

Tumor type	Frequency (no.)	%
Invasive ductal carcinoma	107	92.2
No malignancy	7	6.0
Other malignancy	2	1.7
Total	116	100%

Table 2. Frequency and percentage of tumor grade by CNB

Nottingham grading	Frequency (no.)	%
Grade I	7	6.0%
Grade II	59	50.9%
Grade III	42	36.2%
No information	8	6.9%
Total	116	100%

Table 3. Frequency and percentage of tubule formation by CNB

Tubule formation	Frequency (no.)	%
Score 1	2	1.7%
Score 2	29	25.0%
Score 3	75	64.7%
No information	10	8.6%
Total	116	100%

Table 4. Frequency and percentage of nuclear pleomorphism by CNB

Nuclear pleomorphism	Frequency (no.)	%
Score 1	5	4.3%
Score 2	55	47.4%
Score 3	46	39.7%
No information	10	8.6%
Total	116	100%

Table 5. Frequency and percentage of mitotic count by CNB

Mitotic count	Frequency (no.)	%
Score 1	32	27.6%
Score 2	56	48.3%
Score 3	18	15.5%
No information	10	8.6%
Total	116	100%

Table 6. Frequency and percentage of tumor type by post-operative HPE

Post-operative HPE	Frequency (no.)	%
Invasive ductal carcinoma	115	99.1%
Other malignancy	1	0.9%
Total	116	100%

### Postoperative carcinoma in situ

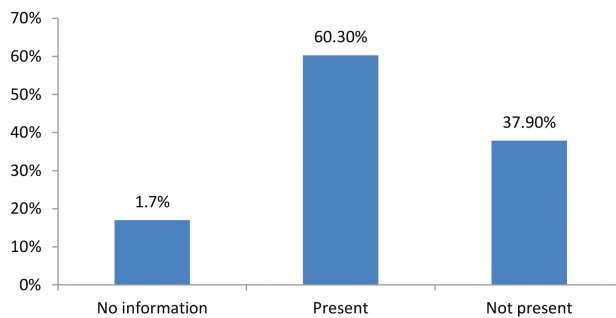


Fig. 2 Frequency and percentage of carcinoma in situ in post-operative HPE.

Table 7. Frequency and percentage of tumor grade in post-operative HPE

Post Nottingham grading	Frequency (no.)	%
Grade I	9	7.8%
Grade II	49	42.2%
Grade III	58	50.0%
Total	116	100%

Tumor grade was: Grade one 7.8%, Grade two 42.2%, Grade three 50%, as shown in Table 7.

Tubule formation was: Score one 1.7%, Score two 25%, Score three 72.4%, as shown in Table 8.

Nuclear pleomorphism was: Score one 3.4%, Score two 52.6%, Score three 43.1%, as shown in Table 9.

Mitotic count was: Score one 24.1%, Score two 48.3%, Score three 26.7%, as shown in Table 10.

The histological type determined on CNB was concordant with types determined on open surgical biopsy in 93.1%, kappa of (0.192), ( $P$  value <0.001) highly significant. Nottingham grading concordance was 73.3%, kappa of (0.554), ( $P$  value <0.001) highly significant. The tubule formation score concordance was 77.6%, kappa of (0.516), ( $P$  value <0.001) highly significant.

Table 8. Frequency and percentage of tubule formation in post-operative HPE

Tubule formation	Frequency (no.)	%
Score 1	2	1.7%
Score 2	29	25.0%
Score 3	84	72.4%
No information	1	0.9%
Total	116	100%

Table 9. Frequency and percentage of nuclear pleomorphism in post-operative HPE

Post pleomorphism	Frequency (no.)	%
Score 1	4	3.4%
Score 2	61	52.6%
Score 3	50	43.1%
No information	1	0.9%
Total	116	100%

Table 10. Frequency and percentage of mitotic count in post-operative HPE

Post mitotic count	Frequency (no.)	%
Score 1	28	24.1%
Score 2	56	48.3%
Score 3	31	26.7%
No information	1	0.9%
Total	116	100%

Table 11. The Concordance between CNB and post-operative for certain diagnostic characteristics

Histopathology	Concordance rate (%)	Kappa	$P$ value
Tumor type	93.1%	0.192	<0.001
Nottingham grade	73.3%	0.554	<0.001
Tubule formation score	77.6%	0.516	<0.001
Pleomorphism score	73.3%	0.535	<0.001
Mitotic count score	62.9%	0.434	<0.001

Pleomorphism score concordance was 73.3%, kappa of (0.535), ( $P$  value <0.001) highly significant, mitotic count score concordance was 62.9%, kappa of (0.434), ( $P$  value <0.001), as shown in Table 11.

## Discussion

In this study for tumor type in CNB there was 7(6%) patients with no malignancy.

Also by CNB there was other types of carcinoma 2(1.7%) patients, mucinous carcinoma 1(0.9%) patient, invasive lobular carcinoma 1(0.9%) patient.

Our study was consistent for type of tumor with Shannon et al. (2001)<sup>10</sup> study analysis of 734 patients was

done for type was (94%), and nearly consistent for grade which was (75%).

Consistent for grading of tumor with Badoual et al. (2005)<sup>11</sup> study analysis of 110 patients done for tumor grade was (73.1%), but not consistency with tumor type which was (74%).

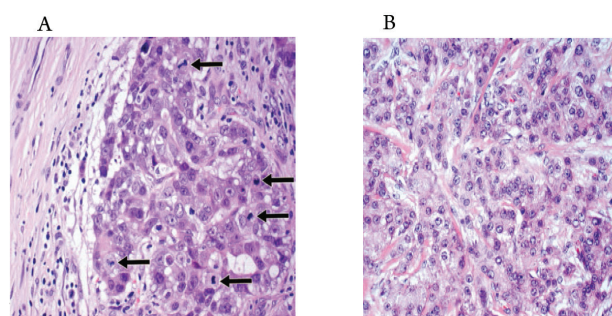
This result is not consistent with O'Leary et al. (2004)<sup>12</sup> study in which analysis of 113 patients was done the concordance rate for type was (65.41%) in our study was (93.1%), grade was (61.65%) in our study was (73.3%), tubule formation was (55.64%) but in our study was (77.6%), nuclear pleomorphism was (57.40%), in our study (73.3%), mitotic count was (59.40%) in our study was (62.9%).

Andrade and Gobbi et al. (2004)<sup>13</sup> study analysis of 120 patients done this study is not consistent with our study, the concordance rates for type was (67%) in our study was (93.1%), grade was (59%) in our study was (73.3%), tubule formation was (55%) in our study was (77.6%), nuclear pleomorphism was (58.9%) in our study was (73.3%), mitotic count was (62%) in our study was (62.9%).

Harris et al. (2003)<sup>14</sup> study analysis of 500 patients this study not consistent with our study, the concordance rate for type was (74%) in our study was (93.1%), grade was (67%) in our study was (73.3%), tubule formation was (82%) in our study was (77.6%), nuclear pleomorphism was (73%) in our study was (73.3%), mitotic count was (58%) in our study was (62.9%).

In all these study's the type grade and components of grade was low figure.

This underestimation may be because of under sampling of the CNB procedure, tissue fixation (fixation is usually rapid and uniform in CNB but may not be so in OEB)<sup>15</sup> and significant heterogeneity of breast cancers with respect to mitosis within a single tumor (mitosis is most energetic on the growing edge of the tumor, at the periphery, which can be appreciated on surgical pathology when the entire tumor is excised) (Figure 2).<sup>16</sup>



**Fig. 3 Female patient with grade 3 invasive ductal carcinoma. A, Photomicrograph (H and E,  $\times 400$ ) of growing edge of tumor shows multiple mitotic figures (arrows). B, Photomicrograph (H and E,  $\times 400$ ) of central area of tumor shows no mitosis. Sampling of area of tumor where mitosis is less active leads to underestimation of overall tumor grade.**

Our results showed that pre-operative CNB and post-operative surgical histopathology has significant concordance rate in determining the type of tumor. Moderately concurs in determining grade, and component of grading, the most component which under estimated is mitotic count. The mitotic component of tumor grading is most often underestimated on the Core biopsy Studies have shown that there is a reduction in visibility of mitoses with increasing length of fixation delay. Thus, it is unlikely that the difference in mitotic counts between OEB and CNB is related to fixation time or time between surgery and fixation.<sup>17</sup>

## Conclusion

These results indicate that pre-operative CNB can reliably provide useful preoperative prognostic and predictive information in breast cancer patients which can play a major role in planning treatment strategies. ■

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