

RESEARCH ARTICLE

Diagnostic Value of Fine-Needle Aspiration Biopsies and Pathologic Methods for Benign and Malignant Breast Masses and Axillary Node Assessment

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Abstract

Background: The goal of this study was to evaluate the fine needle aspiration (FNA) preoperatively together with Touch Print, Crush Print, frozen section and pathologic methods to reach a diagnosis for patients with breast and axillary masses. **Methods:** This study was conducted on 107 patients, and included 111 samples of breast and 43 of axillary masses taken at surgery. Data on epidemiological and clinical features of the patients were collected using a questionnaire. The results of the methods of FNA, Touch Print, and Crush Print were compared with the results of pathology after operations. **Results:** Comparison between the diagnosis values of FNA with pathology for breast cancer showed sensitivity, sensitivity, positive predictive values, negative predictive values, positive mendacious percentages, and negative mendacious percentages of 80.4%, 98%, 97.3%, 87.6%, 2%, and 19.6% , respectively, and for metastatic axillary lymph nodes, 80%, 95.6%, 94.1%, 84.6%, 4.4%, and 20%. Comparison of diagnosis values of FNA with Touch Print and Crush Print for breast cancer gave values of 82.2%, 89%, 97.3%, 89%, 1.6%, and 17.8%, respectively, and for metastatic axillary lymph nodes 84.2%, 95.8%, 94.1%, 88.4%, 14.2%, and 15.8%. **Conclusion:** Use of these methods, compared with pathology, can decrease cost, time, and a need for a second surgery and related complications.

Keywords: Breast- axillary- mass- fine-needle aspiration- pathology

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Introduction

Palpable breast mass is a common problem among female patients. The diagnostic delays of breast cancer occur due to the generally low index of suspicion. Breast and axillary masses are the most prevalent breast diseases among the women. In case of existence, analyzing them is necessary to reject their malignancy and the accuracy of diagnosis can be increased by a combination of preoperative tests. The valuable diagnostic methods for this case are Fine-Needle Aspiration (FNA), Touch Print, Crush Print, and pathology. Intraoperative evaluation consisted of touch imprint cytology (TIC), frozen section (FS) analysis, scrape cytology or combination of these methods with own advantages and disadvantages (Creager et al., 2004; Van de Vrande et al., 2009).

Fine-needle aspiration (FNAB) has shown to be as a critical component in the investigation of palpable breast masses and is highly accurate method for diagnosing breast lesions (Rubin et al., 1997; Boerner and Sneige, 1998). It is cheaper and is available within a shorter time. FNAB has been demonstrated to have some advantages over core-needle biopsy (CNB) in that it use a smaller needle

and thus has a lower probability of causing hematoma and other rare complications, such as pneumothorax (Dowlatshahi et al., 1987; Evans et al., 1989). It is worth noting that the clinical use of FNAB has been questioned due to variability in performance known as an adjunct to open surgical biopsy that is increasingly being used in the evaluation of breast disease. CNB has been progressively replacing FNAB in this preoperative evaluation role and is a choice in the assessment of micro-calcifications without a correlated mass lesion. CNB may be used as an additional tool when FNAB is not available (Jackson and Reynolds, 1991; Bilous, 2010).

Many studies have 9 CNB to have superior diagnostic accuracy based on solely historical comparisons of CNB and FNA series (Shannon et al., 2001; Pijnappel et al., 2004; El-Sayed et al., 2008). Some studies indicated that CNB yield more conclusive diagnoses as compared to FNA in both malignant and benign lesions (Symmans et al., 1999; Garg et al., 2007; Barra Ade et al., 2008). Both Frozen Section (FS) and touch imprint cytology (TIC) are used to evaluate whether a lesion is malignant or not (Liu et al., 2002; Hentry-Tillman et al., 2002). Intraoperative cytology (IC), including touch imprint (TI) and

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crash preparations (CP), has been applied for diagnosis of breast, thyroid, parathyroid, and salivary gland specimen (Paessler et al., 2001; Shidham et al., 2002).

TIC would allow immediate reporting with no additional intervention or risk to the patient other than the CNB itself. TIC has so far been applied in the diagnosis of screen detected, impalpable breast lesions or in a mixed case load (Sneige et al., 2000; Newman et al., 2001; Green et al., 2001; Kass et al., 2003; Carmichael et al., 2004)

In the present study, FNA preoperatively together with Touch Print, Crush Print, and frozen section intraoperatively are applied to reach a diagnosis for patients with a breast mass and the results of intraoperative Crush Print and Touch Print were compared with permanent pathology.

Materials and Methods

Ethical Committee

The study was carried out according to the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Tehran Heart Center, and informed written consent was obtained from all the patients.

Study population

This cross-sectional study was conducted on 107 patients, who had been referred to Shohada Ashayer Hospital of Khorramabad, between 2012 and 2013. The patients were suffering from breast and axillary masses that included 111 samples of breast masses and 43 samples of axillary masses. All confirmed patients with breast and axillary mass by using clinical examination, mammography, ultrasound and FNA and surgical candidates were included in the study.

Epidemiology and clinical characteristics

After taking the informed consents, the epidemiological and clinical features of the patients were collected by an anonymous questionnaire which completed by a trained assistant through interview. The questionnaire was included: demographic data such as age, sex, marital status, religion, location, age of marriage, as well as questions about a history of heart disease, history of smoking and alcohol consumption, OCP and history of breast and axillary lymph nodes diseases in the family (first and second degree relatives). The anatomical location of the masses was also determined according to the physical examination or mammography and ultrasonography.

FNA and pathology procedures

FNA was done preoperatively, and Touch Print and Crush Print were prepared intraoperatively and then were sent to the Pathology Ward.

In the second part of the questionnaire, Crush Print, Touch Print results were recorded. The results of pathology were also received (an average of 7 to 10 days) and then pathology of breast and axillary lymph nodes were registered in our study. The results of FNA, Touch Print, and Crush Print methods were compared with the results of pathology after operation. The diagnostic values including

sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), positive mendacious percentage, and negative mendacious percentage were estimated for the three methods.

Results

FNA findings of breast masses

The demographic characteristics of the patients with breast masses were showed in Table 1. The mean age of the patients with breast masses was 40.1 ± 13.7 year olds. The highest frequency of breast masses (49%) were seen in the age group of 49-30 years and the lowest frequency were belonged to the group of over 70 years old. (Table 1). The mean age of the patients with malignant tumors of the breast was 49.6 ± 11.7 years and the patients with benign breast lumps 32.8 ± 10.8 years old ($P < 0.001$). Moreover, 77 % of patients with breast masses had married and educational degrees of the majority of them (39%) were high school and 74% of them have been settled in city. Our findings showed that 15.2% of patients had a history of breast disease in their first and second degree relatives. Moreover, 57% of breast lumps were not malignant, while 43% were diagnosed to be malignant, as well as 49% of breast lump was located in right breast. In terms of location of the mass, the most abundant involved quadrant was upper outer quadrant of the right breast (in the case of single mass; 25%) and lowest frequencies was belonged to upper inner quadrant of the right breast (2 %). In cases where the greater number of the masses was observed, the most involved quadrants were the upper outer quadrant of the left breast and central quadrant of the right breast (Table 2 and 3).

Pathological findings of breast masses

Based on the pathological study, the most common benign lumps was fiber adenoma (61.4 %) and the lowest frequency was belonged to papilloma cyst and lipoma and (each one 1.7%), as well as the most common malignant neoplasms was seen to be ductal carcinoma (Table 4).

Our imaging findings of patients with breast masses demonstrated that, among the 69 patients with a sonography, 58% of cases showed the possibility of malignancy and out of 46 patients with mammography, 68.2 % of them had a cancer possibility, (Table 5).

FNA and pathological findings of axillary masses

The mean age of patients with axillary mass was 48.1 ± 13.3 years, the youngest patient with axillary mass was 20 years old and the oldest 77 years old.

The mean age of patients with malignant tumors of the axillary gland was 52.2 ± 12.4 years old while it was 46.3 ± 14.3 in patients with benign axillary masses ($P = 0.32$).

The average age of marriage in patients with axillary mass was 18.3 ± 4.3 years old and the youngest had 10 years old. In these patients, the most frequent axillary mass was observed in the age group of 59-40 years old (57.1%). In addition, 92.9 % of these patients had married and the majority of them (38.1%) were illiterate. It is worth noting that, 78.6 % of patients were living in cities and nine cases of them (21.4%) had family history of breast

Table 1. The Frequency Distribution Characteristics of Patients with Breast Masses by Age, Marital Status, Education Level and Location in Patients

Variable	Frequency	the relative abundance(N)	(Percent) Cumulative Frequency
	25	25	25
Age groups	49	49	74
	23	23	97
	3	3	100
Marital status	Married	77	77
	Single	21	98
	Divorced	2	100
	Illiterate	26	26
Education	Advice and less	23	49
	High school	39	88
	Collegiate	12	100
Address	City	74	74
	Village	26	100

Table 2. Frequency of Smoking and Alcohol and Hormonal Birth Control Pills and History of Breast Disease in First Degree Relatives or II Patients

	Variable	Frequency	The relative abundance(N)	(Percent) Cumulative Frequency
History of breast disease in first degree relatives or second	Yes	15	15.2	(15.2)
	No	84	(84.8)	100
History of smoking and alcohol	Yes	1	1	1
	No	99	99	100
History of ocp	Yes	39	39	39
	No	61	61	100

disease in the first and second degree relatives. one case of these patients (2.4%) had a history of smoking and 21 patients (50%) had a history of oral contraceptive tables (Table 6, 7, 8, 9).

The imaging findings in patients with axillae mass was showed that among 11 patients with ultrasonography evaluation, 81.8 % had probability of malignancy while among 7 patients with mammography, 85.7% of patients showed probability of malignancy (Table 10 and 11).

Comparison of fine needle aspiration and pathology findings

Comparing the diagnosis values of Touch Print and Crush Print with pathology for breast cancer showed sensitivity of 97.8%, specificity of 100%, positive predictive value of 100%, negative predictive value of 98.4%, positive mendacious percentage of 0%, and negative mendacious percentage of 2.2%, and for metastatic axillary lymph nodes, sensitivity of 90%, specificity of 95.6%, positive predictive value of 94.7%, negative predictive value of 91.6%, positive mendacious percentage of 4.4%, and negative mendacious percentage of 10% were obtained. Comparison between the diagnosis values of FNA with pathology for breast cancer showed

sensitivity, sensitivity, positive predictive value, negative predictive value, positive mendacious percentage, and negative mendacious percentage of 80.4%, 98%, 97.3%, 87.6%, 2%, and 19.6% , respectively, and for metastatic axillary lymph nodes, they were 80%, 95.6%, 94.1%, 84.6%, 4.4%, and 20%, respectively. Comparison between the diagnosis values of FNA with Touch Print and Crush Print for breast cancer reported sensitivity, specificity, positive predictive value, negative predictive value, positive mendacious percentage, and negative mendacious percentage to be 82.2%, 89%, 97.3%, 89%, 1.6%, and 17.8%, respectively, and for metastatic axillary lymph nodes they were 84.2%, 95.8%, 94.1%, 88.4%, 14.2%, and 15.8%, respectively (Table11).

Discussion

Breast and axillary masses are the most prevalent breast diseases among the women. In case of existence, analyzing them is necessary to reject their malignancy and the accuracy of diagnosis can be increased by a combination of preoperative tests. In the present study, fine needle aspiration (FNA) preoperatively together with Touch Print, Crush Print, and frozen section intraoperatively was

Table 3. Distribution of the Anatomical Location of the Mass, Quadrant of Breast Masses and Mass Deployment in Patients

Variable		Frequency	The relative abundance(N)	(Percent) Cumulative Frequency
Anatomical location of the mass	Her right breast.	49	49	49
	Left breast	44	44	93
	Both breasts	7	7	100
The nature of mass	Benign	57	57	57
	Malignant	43	43	100
	Foreign upper	25	25	25
Quadrant mass deployment	Right breast.	16	16	41
	Foreign upper left breast	2	2	43
	Internal upper right breast.	12	12	55
	Internal upper left breast	4	4	59
	Foreign bottom right breast.	3	3	64
	External lower left breast	4	4	66
	Lower right internal mammary	6	6	72
	Lower left internal mammary	14	14	86
	Right Breast Center	7	7	93
	Left Breast Center	1	1	94
	Internal lower right breast and the left breast upper outer	2	2	96
Foreign bottom right breast and the left breast center	3	3	99	
Foreign upper right and lower left internal mammary	1	1	100	

Table 4. The Distribution of Mass Pathological Benign and Malignant Breast Lesions in Patients

Variable		Frequency	The relative abundance (N)	(Percent) Cumulative Frequency
Pathological types of benign	Fibroadenomas	35	61.4	(61.4)
	fibrocystic	14	24.5	(85.9)
	papilloma cyst	1	1.7	(87.6)
	Mastitis	6	10.7	(98.3)
	Lipoma	1	1.7	(100)
Pathological types of malignant neoplasms	Ductal carcinoma	41	(93.1)	(93.1)
	Medullary carcinoma	2	(6.9)	(100)

used for diagnosis of patients with a breast mass and the results of intraoperative Crush Print and Touch Print were compared with permanent pathology.

The mean age of the patients with breast masses was 40.1 ± 13.7 year olds. The highest frequency of breast masses (49%) were seen in the age group of 49-30 years and the lowest frequency were belonged to the group of over 70 years old. (Table 4). The mean age of the patients with malignant tumors of the breast was 49.6 ± 11.7 years

and the patients with benign breast lumps 6.10 ± 8.32 years old ($P < 0.001$).

The mean age of patients with axillary mass was 48.1 ± 13.3 years, the youngest patient with axillary mass was 20 years old and the oldest 77 years old.

The mean age of patients with malignant tumors of the axillary gland was 52.2 ± 12.4 years old while it was 46.3 ± 14.3 in patients with benign axillary masses ($P = 0.32$). Hamidian Jahromi et al. was conducted a study

Table 5. Distribution of Breast Masses Imaging Findings in Patients

	Variable	Frequency	The relative abundance(N)	(Percent) Cumulative Frequency
Ultrasound	The possibility of malignancy	40	58	58
	The possibility of benign	29	42	100
Mammography	The possibility of malignancy	30	(68.2)	(68.2)
	The possibility of benign	14	(31.8)	100

Table 6. Comparison of the Diagnostic value of FNA with Pathology in the Diagnosis of Malignant Breast Masses in Patients

Pathology	+Number (%)	-Number (%)	Total.Number (%)
FNA			
+Number (%)	(97.4) 37	(2.6) 1	(100) 38
-Number (%)	(12.3) 9	(87.7) 64	(100) 73
Total.Number (%)	(41.4) 46	(58.6) 65	(100) 111

Type of test, chi-square; X², 74.4; PV < 0.0001

Table 7. Comparison of the Diagnostic Value of Touch Print with Pathology in the Diagnosis of Malignant Breast Tumors in Patients

Pathology	+Number (%)	-Number (%)	Total.Number (%)
Touch Print			
+Number (%)	(100) 45	(0) 0	(100) 45
-Number (%)	(1.5) 1	(98.5) 65	(100) 66
Total.Number (%)	(41.4) 46	(58.5) 65	(100) 111

Statistical analysis, Fisher's exact test; X², 106.9; PV < 0.0001

on 146 sentinel lymph nodes from 74 consecutive patients with invasive breast cancer. They reported that the average age of patients were 49±13.6 (Jahromi et al., 2009). The average age of diagnosis and surgery have been reported in other studies in Iran to be between 46 to 48 years old (Vahdaninia et al., 2003; Akbari et al., 2006; Bakhtiari A, Hah-Ahmadi, 2006). Previous studies had suggested that the age of breast cancer in Iran is lower than the western countries (Less than 10 years), (Mousavi et al., 2007). The mean age of the patients that has been studied by Carlo et al, at Texas was 56.7 years old. Moreover, Yang and colleagues in China, Anyanwa in Nigeria, Sarra et al. in Dakar, have been reported that the mean age of the patients was less than or equal to 45 years (Anyanwu, 2000; Carlo et al., 2005; Yang et al., 2005; Sarra et al., 2006). Although smoking and alcohol are as a risk factor in the occurrence of cancer. Our study show only one patient with breast lumps had a history of alcohol consumption and one patient with axillary mass had history of smoking. It seems that these results have achieved due to gender of patients and also conventional and legal restrictions.

Previous studies have indicated that estrogen levels in the blood of breast cancer patients from are higher as compared to healthy individuals. Although there is no consensus the association of OCP usage of childbearing age with breast cancer, but it seems that it has an estrogen-associated effect on breast cancer risk and consumption of OCP at a younger age, especially before age 20 have a greater effect on the risk of breast cancer (Akbari, 2010). In our study, 39% of patients with breast lumps had a history of OCP and 50 % of those with axillary mass had a history of OCP consumption. In the present study, it seems that this association is stronger as compared to previous studies. Alkuwari et al., (2008) reported that the overall sensitivity of axillary lymph node FNA in all the cases studied was 65% and the specificity was 100%. They stated that FNA of axillary lymph nodes is a sensitive and very specific method with which to detect metastasis in breast cancer patients. Martha et al., (2010) indicated that Of the 224 patients, 51 patients (23%) had a positive ultrasound-guided FNA result, which yields an overall sensitivity of 59% and specificity of 100%.

Table 8. Comparison of the Diagnostic Value of Crush Print with Pathology in the Diagnosis of Malignant Breast Masses in Patients

Pathology	+Number (%)	-Number (%)	Total/Number (%)
Crush Print			
+Number (%)	(100) 45	0(0) 0	(100) 45
-Number (%)	(1.5) 1	(98.5) 65	(100) 66
Total/Number (%)	(41.4) 46	(58.5) 65	(100) 111

Statistical analysis, Fisher's exact test; X², 106.9; PV < 0.0001

Table 9. Comparison of the Diagnostic Value of Touch Print with FNA in the Diagnosis of Malignant Breast Masses in Patients

Touch Print	+Number (%)	-Number (%)	Total/Number (%)
FNA			
+Number (%)	(97.4) 37	(2.6) 1	38(100)
-Number (%)	(11) 8	(89) 65	73(100)
Total/Number (%)	(40.5) 45	(59.5) 66	111(100)

Statistical analysis, chi-square; X²= 106/9; PV < 0.0001

Table 10. Comparison of the Diagnostic Value of Crush Print with FNA in the Diagnosis of Malignant Breast Masses in Patients

Crush Print	+/Number (%)	-/Number (%)	Total/Number (%)
FNA			
	+/Number (%)	(100) 45	(100) 45
	-/Number (%)	(1.5) 1	(100) 66
	Total/Number (%)	(41.4) 46	(100) 111

Statistical analysis, Fisher's exact test; χ^2 , 106.9; $PV < 0.0001$

Table 11. Summary Results of the Diagnostic Value of FNA, Crush Print, and Touch Print with Pathology in the Diagnosis of Malignant Masses in Patients with Breast and Axilla

Accreditation criteria tests		Sensitivity	Property	+	-	% False negative	% False positive	LR+
Breast Masses	FNA	80.4%	98.0%	97.3%	87.6%	19.6%	2.0%	40.2
	Touch Print	97.8%	100.0%	100.0%	98.4%	2.2%	0.0%	-
	Cruch Print	97.8%	100.0%	100.0%	98.4%	2.2%	0.0%	-
Axillary Masses	FNA	80.0%	95.6%	94.1%	84.6%	20.0%	4.4%	18.18
	Touch Print	90.0%	95.6%	94.7%	91.6%	10.0%	4.4%	20.45
	Cruch Print	90.0%	95.6%	94.7%	91.6%	10.0%	4.4%	20.45

Ultrasound-guided FNA of the axillary lymph nodes is most useful in the preoperative assessment of patients with large tumors (> 2 cm) or lymph nodes that appear abnormal. In our study, comparison between the diagnosis values of FNA with pathology for breast cancer showed sensitivity, sensitivity, positive predictive value, negative predictive value, positive mendacious percentage, and negative mendacious percentage of 80.4%, 98%, 97.3%, 87.6%, 2%, and 19.6%, respectively, and for metastatic axillary lymph nodes, they were 80%, 95.6%, 94.1%, 84.6%, 4.4%, and 20%, respectively. In our study, the specificity of FNA was higher than study of Alkuwari et al. but both sensitivity are approximately equal. Furthermore, for metastatic axillary lymph nodes, they were 80%, 95.6%, 94.1%, 84.6%, 4.4%, and 20%, respectively, which compared with previous studies are more sensitive (Mdels et al., 2008; Martha et al., 2010).

Kuenen-Boumeester et al. (Kuenen-Boumeester et al., 2003) recommended that ultrasound-guided FNA be included in the preoperative staging of all primary breast cancer patients. Koelliker et al., (2008) found ultrasound-guided FNA to be beneficial in a selected population of patients with T1 tumors, including one with normal-appearing lymph nodes.

Chen et al., (2010) found that multiple cross-sectional TIC has a sensitivity, specificity, and overall accuracy rate of 92.0, 99.0, and 97.5%, respectively, on a per-patient basis, and it is superior to the standard imprint preparation protocol. It has been found that the sensitivity of TIC has varied widely from 34% to 96%. Nevertheless, these data cannot be compared in terms of sensitivity and accuracy due to patient differences, variation in how the TIC protocol was implemented, final histopathological evaluation, and cytologist experience. Interpretation of imprints is operator dependent, as reflected in the wide range of success in previous studies, with sensitivities ranging from 33.3% to 100% (Chicken et al., 2006).

Chicken et al., (2006) used touch imprint cytology for

the diagnosis of sentinel lymph node metastases in breast cancer. They concluded that TIC detected metastases with a sensitivity of 81.1% and a specificity of 100% and TIC is feasible and enables the rapid diagnosis of SLN metastases with an acceptable accuracy for clinical use in ductal carcinoma of the breast.

In the present study, comparison between the diagnosis values of FNA with Touch Print and Crush Print for breast cancer reported sensitivity, specificity, positive predictive value, negative predictive value, positive mendacious percentage, and negative mendacious percentage to be 82.2%, 89%, 97.3%, 89%, 1.6%, and 17.8%, respectively, and for metastatic axillary lymph nodes they were 84.2%, 95.8%, 94.1%, 88.4%, 14.2%, and 15.8%, respectively. In addition, in terms of Touch Print and Crush Print, our study had high sensitivity, specificity and positive predictive value for the diagnosis of breast cancer. Furthermore, the sensitivity of the Touch Print, Crush Print for evaluation of the axillary mass were higher than previously mentioned studies (Perez-Sanchez et al., 2010; Khanna et al., 2011), indicating the high diagnostic value of Touch Print, and Crush Print.

In conclusion, due to the high sensitivity and specificity and positive predictive value of Touch Print, Crush Print as compared to the frozen section for breast cancer and the high sensitivity of these methods in comparison with the Frozen section for metastatic axillary masses, these methods can be very useful for diagnosis of breast cancer and metastatic axillary lumps.

By using Touch Print and Crush Print, the type of tissue can be detected during the operation in few minutes. Furthermore, due to the high specificity of these methods, are recommended when there is no possibility of using Frozen section. Thus, these methods can save the patient from cost and time, reoperation, and complications.

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