ROLE OF INTRAOPERATIVE IMPRINT CYTOLOGY AND FROZEN SECTION IN THE DIAGNOSIS OF BREAST LUMPS

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Summary

The present cross-sectional study was conducted in the Department of Pathology, Dhaka Medical College Hospital, Dhaka over a period 12 months to evaluate the usefulness of intra-operative imprint cytology in diagnosing various breast lesions and to compare its diagnostic accuracy with those of frozen and paraffin sections. A total of 101 cases of breast tumours, diagnosed clinically or mamographically, who underwent elective surgery were consecutively included in the study. The mean age of the patients was 37.7 ± 14.5 years.

The sensitivity and specificity of imprint cytology in differentiating breast carcinoma from those who did not have breast carcinoma were 91% and 94.1% respectively. The positive and negative predictive values (PPVs and NPVs) of the test were 96.8% and 84.2% respectively. The percentages of false positive and false negative were 3.2% and 15.8% respectively. The overall diagnostic accuracy of imprint cytology was 92%. The sensitivity of frozen sections in correctly diagnosing carcinoma of breast was 95.5%, while the specificity of the test in ruling out those who did not have carcinoma was 97.1%. The positive and negative predictive values of the test were 98.5% and 91.7% respectively. The percentages of false positive and false negative were 1.5% and 8.3% respectively. The overall diagnostic accuracy of the test was 96%.

The overall diagnostic accuracy of the two procedures is almost comparable. However, the imprint cytology has merit over frozen section in that it can be done quickly and thus helps operating surgeons to decide about margin clearance.

Key words

Imprint cytology; frozen section; breast lump.

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Introduction

Breast cancer is one of the most common malignant tumor and a leading cause of carcinoma death in women [1]. Keeping pace with developed world, breast cancer is increasing in the developing countries as well.

To have a good plan in mastectomy or to achieve good prognosis, it is very useful to diagnose a lesion intra-operatively. The need for intra-operative consultation of the nature of the breast tumor has paved the way for the utilization of imprint smears and scrape smears popularly known as touch preparation cytologies [2,3]. Imprint smears recently have gained more popularity for the evaluation of margins in breast conservation surgeries [4]. The diagnostic accuracy has been good with demonstration of better cytologic details compared to frozen section. Imprint cytology can be particularly helpful in several situations such as the examination of small specimens or of small pathologic foci of large specimens. As cryostat facility for frozen section is not available in many hospitals of Bangladesh, intra-operative imprint cytology of breast lesions can be very helpful in the management of patients.

Intra-operative cytology material is almost always of superior quality to that of frozen sections. This is attributed to the fact that slide preparation is controlled and performed under vision. In addition, large portions of any lesion were easily evaluated by intra-operative cytology in contrast to frozen sections where small areas were examined only [5]. Imprint cytology in recent years has been proved to be a simple, inexpensive, rapid and reliable diagnostic tool for the diagnosis of breast lesions [6]. This study was undertaken to evaluate which of the two diagnostic modalities were superior in terms of sensitivity, specificity, positive and negative predictive values and overall accuracy.

Patients and methods

The present cross-sectional study was conducted in the Department of Pathology, Dhaka Medical College Hospital, Dhaka over a period 12 months between July 2009 to June 2010 to evaluate the usefulness of intra-operative imprint cytology in diagnosing various breast lesions and to compare its

diagnostic accuracy with those of frozen and paraffin sections. A total of 101 cases of breast tumours (diagnosed clinically or mamographically) who underwent elective surgery were consecutively included in the study. Patients who have already been treated for malignancy or who had a history of receiving radiotherapy were excluded.

Technique of imprint cytology

After collection of the fresh specimen, an imprint smear of the excised tissue was made immediately. Suspicious area(s) of the tissue were trimmed to approximately half an inch in diameter and was held between the index finger and thumb so that it protruded slightly beyond the finger tips. The tissue was pressed firmly on a clean glass-slide held in the other hand. It was then withdrawn without a sliding movement and pressed once or twice further down the slides, to obtain a series of imprints. The smears immediately fixed in 95% ethyl alcohol and then stained with rapid Papanicolaou stains.

Technique of frozen section

After taking imprint, the fresh biopsy specimen was thoroughly examined about size, shape, colour, consistency and appearances of the cut surface and recorded properly. The specimen was then serially sectioned at 4–5 micron intervals and a single section of tissue was selected and frozen at -18^0 to -25^0C using optimum cutting temperature (OCT) tissue-tek. In most cases, several 5 micron sections were cut in a microtome cryostat (Shandon Cryotome E) and stained using a rapid Haematoxylin and Eosin. A part of tissue and the block used for frozen section were fixed in 10% formal saline and processed for routine paraffin impregnation and stained with Haematoxylin and Eosin. The final diagnosis was made and the results of imprint cytodiagnosis were compared with that of frozen section and histological findings.

Results

The mean age of the patients was 37.7 ± 14.5 years. About half (49.5%) of patients had lump in the right breast and half (50.5%) in the left breast. All of the tumors were palpable on physical examination. Detailed clinical characteristics of the tumor are illustrated in table I. Over 60% of the cases were positive for malignant cells by imprint cytology and 64.4% by frozen sections. Two-thirds (66.3%) of the cases were histologically proved to be malignant. Histological typing identified 62.3% of cases as invasive ductal carcinoma, 27.8% as fibroadenoma, 5.9% fibrocystic changes, 2% invasive lobular carcinoma and 2% as malignant Phyllodes tumour.

About 57% of tumors had well-differentiated cell type, 35.8% moderately differentiated and 7.5% poorly differentiated. About 45% of patients had lymphovascular invasion, 4.4% microcalcification, 29.4% necrosis and only 1(1.5%) patient had perineural invasion.

The sensitivity and specificity of imprint cytology in differentiating breast carcinoma from those who did not have breast carcinoma were 91% and 94.1% respectively. The positive and negative predictive values (PPVs) of the test were 96.8% and 84.2% respectively. The percentages of false positive and false negative were 3.2% and 15.8% respectively. The overall diagnostic accuracy of imprint cytology was 92%. The sensitivity of frozen sections in correctly diagnosing carcinoma of breast was 95.5%, while the specificity of the test in ruling out those who did not have carcinoma was 97.1%. The positive and negative predictive values (PPV) of the test were 98.5% and 91.7% respectively. The percentages of false positive and false negative were 1.5% and 8.3% respectively. The overall diagnostic accuracy of the test was 96%. The strength of agreement between imprint cytology and frozen sections in diagnosis of breast lump was calculated using kappa statistics (k-value). The overall agreement between the two procedures was excellent (k = 0.872).

Table I : Distribution of patients by their clinical characteristics (n = 101)

Clinical characteristics	Frequency	Percentage
Breast involved		
Right	51	50.5
Left	50	49.5
Palpable by physical examination	101	100.0
Location of tumour		
UOQ	27	26.7
UIQ	23	22.8
LIQ	12	11.9
LOQ	22	21.8
Central	16	15.8
Whole breast involvement	01	1.0
Consistency of swelling		
Soft	05	5.0
Firm	74	73.3
Hard	22	21.8
Axillary lymph node (palpable)	33	32.7

Table II : Different techniques to evaluate breast lump.

Tumors diagnosed by different methods	Frequency	Percentage
Imprint cytology		
Positive for malignant cells	61	60.4
Negative for malignant cells	40	39.6
Frozen sections		
Positive for malignancy	65	64.4
Negative for malignancy	36	35.6
Histological diagnosis		
Malignant	67	66.3
Invasive ductal carcinoma, NST	63	62.3
Invasive lobular carcinoma	02	2.0
Malignant Phyllodes	02	2.0
Benign	34	33.7
Fibroadenoma	28	27.8
Fibrocystic changes	06	5.9

Table III : Distribution of patients by findings of histopathology (n = 67).

Results of histopathology	Frequency	Percentage
Differentiation		
Well	38	56.7
Moderate	24	35.8
Poor	05	7.5
Perineural invasion	01	1.5
Lymphovascular invasion	30	44.1
Microcalcification	03	4.4
Necrosis	20	29.4

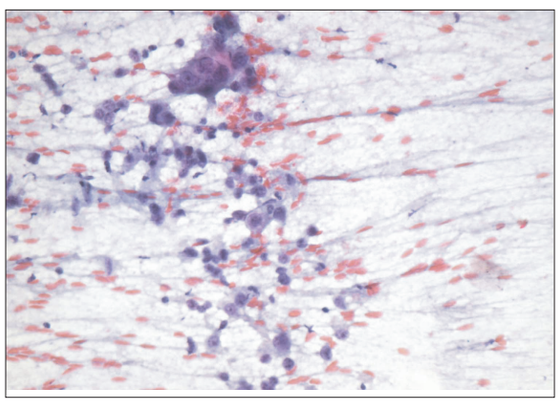

Fig 1 : Photomicrograph of Imprint Cytologic Smear showing positive for malignant cell. Stained by PAP Method (Case 40x40).

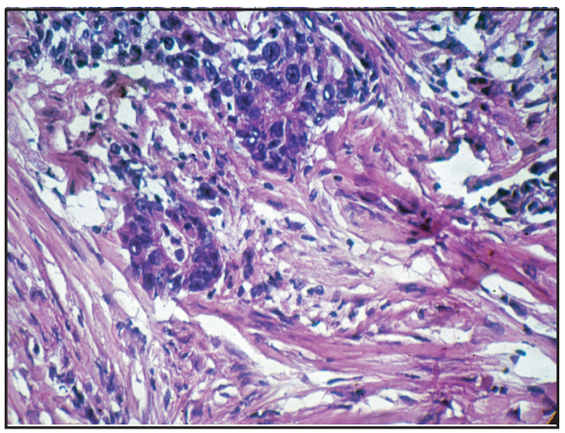

Fig 2 : Photomicrograph of Frozen section showing positive for malignancy (Case 43, H & E x 40).

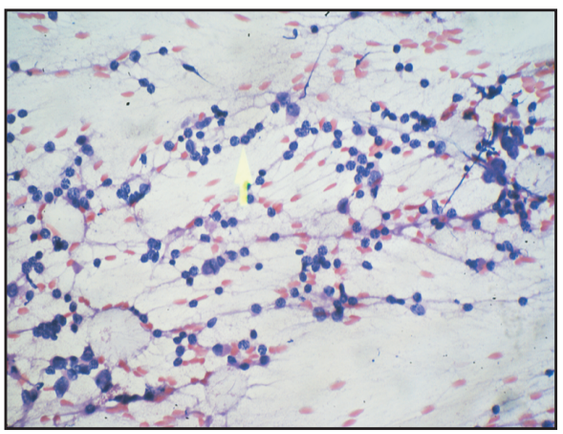

Fig 3 : Photomicrograph of Imprint Cytologic Smear showing positive for malignant cell, Stained by PAP Method, single files are shown. (Case 22x10).

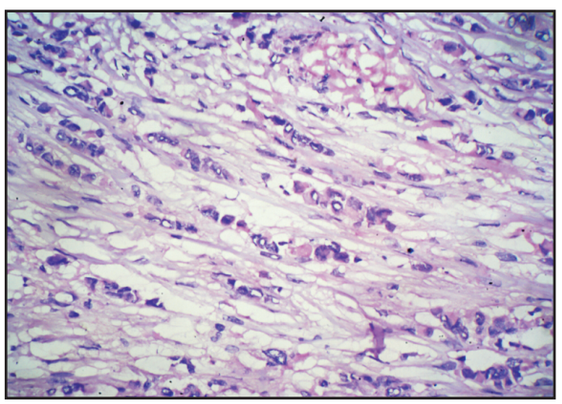

Fig 4 : Photomicrograph of Frozen section showing positive for malignancy, single files are shown (Case 22, H & E x 40).

Discussion

Many studies have so far been conducted regarding the accuracy of imprint cytology and frozen section in the diagnosis of breast lump. Most of these studies demonstrated comparable accuracy. But there is still dispute over the issue. Results of the present study showed that overall diagnostic accuracy of imprint cytology was 92%, sensitivity 91% and specificity 94.1%. The positive and negative predictive values (PPVs) were 96.8% and 84.2% respectively.

Khanna reported a higher sensitivity and specificity for imprint cytology (98.4% and 100% respectively) [7]. In another study Ku evaluated the use of touch preparation cytology to assess lumpectomy margin [8]. The sensitivity (100%), specificity (97.1%) and a diagnostic accuracy (97.7%) for imprint cytology was almost consistent with findings of the present study. Veneti also reported a sensitivity of 97.1%, a specificity of 99.4% and an accuracy of 98.3% for imprint cytology which are nearly consistent with findings of the present study [6]. These results demonstrate that the touch preparation cytology to be a reliable methods to evaluate lumpectomy margin overcoming sampling error and artifact.

Sultana and colleagues demonstrated accuracy rate of frozen section 99%, sensitivity 99.3% and specificity 93% [9]. Positive and negative predictive values were 96.6% and 99.3% respectively which correlates well with the findings of the present study. Van Diest evaluating the data of each patient for frozen section procedure found a sensitivity of 91% and specificity 100%. Issam and Dillip demonstrated sensitivity of imprint cytology 95.8%, specificity 100%, diagnostic accuracy 96.8%, false positive 4.1% false negative 0%, while sensitivity of frozen section 91.7%, specificity 100%, diagnostic accuracy 90.3%, false positive 8.3%, false negative 0% which well-correlated with the findings of the resents study [10,11]. Haeri reported the sensitivity, specificity and accuracy for cytological method to be 87.5%, 95%, 90.5% and for the frozen section 92.4%, 100% and 95.4% respectively which are in close proximity to the findings of the present study [12]. Karve examined the accuracy of frozen section as an intra-operative tool for evaluation of breast lumps [13]. The overall accuracy was 99.5%, false negative 0.42% and false positive 0%. Cserni in his series of 2110 cases by frozen section diagnosis of breast lump found 22 cases of false negative (1%) and 1 false positive [14]. The author described higher yield of false negative in frozen section might be due to misinterpretation, poor quality of frozen section, sampling error during sectioning, ignorance of macroscopic features, lesions difficult to interpret, ductal carcinoma in situ and sections not deep enough. In the present study the positive predictive values of the two diagnostic modalities were fairly high, yielding low false positive. But as the negative predictive value of the imprint cytology was lower (84.2%) than that obtained by frozen section, it yielded a higher false negative (15.8%) compared to the frozen section (8.3%). So if only imprint cytology is done a higher number of carcinoma of breast might be falsely interpreted as not having malignancy.

Intraoperative consultation with a pathologist is one of the most important need to guide surgeon's decision in excising the breast tissue [15]. The frozen section is accepted as a reliable method in intraoperative consultation for many years, although Kim reported the efficacy of intra-operative imprint cytology to be superior to frozen-section analysis [6,16]. However, frozen section examination is costly and time consuming technique. On the contrary intraoperative imprint cytology is a simple, cost-effective and less time consuming method. Therefore, the institutions where the frozen section facilities are not available, imprint cytology can be employed as an alternative technique. Although, the overall diagnostic accuracy of the two procedures is almost comparable, the imprint cytology has merit over frozen section in that it can be performed quickly so that it can help operating surgeons to decide about margin clearance thus minimizing the need for further operation to a certain extent.

Conclusion

The present study revealed that the sensitivity and negative predictive value of Frozen section were a little higher than those of imprint cytology, although the specificity and positive predictive value of the two diagnostic modalities are fairly comparable.

However, the imprint cytology had an added advantage over Frozen section in that it can be performed readily within 2-3 minutes to make a quick decision. So, imprint cytology is very helpful where the cryostat facility is not available.

Disclosure

All the authors declared no competing interest.

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