

Touch Imprint Cytology; A reliable and Practical Substitute to Frozen Sections

Saira Bugti^{*}, Altaf Ahmed Shaikh^{**}, Abdul Aziz Shaikh^{***}

ABSTRACT

Objective: To evaluate the accuracy of intra-operative touch imprint cytology (TIC) in the diagnosis of lump in breast.

Methods: Descriptive study, conducted at Department of Pathology, Liaquat University of Medical and Health Sciences Jamshoro, from 1st January 2013 to 31st July 2013. A total of 100 cases of Breast lump surgeries were included, tissue imprints were collected during surgical procedures. Intra-operative TIC results were compared with histo-pathological diagnosis.

Results: TIC has 97% sensitivity, 100% specificity. Out of 100 cases, TIC showed 97 true positive cases (97%) and only 03 false negative cases (03%) and 0 false positives. Positive predictive value was 100%, while negative predictive value was 95.38%.

Conclusion: Intra-operative TIC is a simple, quick and cost effective diagnostic test with better accuracy that can be used as an alternative to frozen section in diagnostic settings and margin assessments.

Key Words: Intra-Operative, Touch Imprint Cytology, Breast Lump

Article Citation: Bugti S, Shaikh AA, Shaikh AA. Touch Imprint Cytology; A reliable and Practical Substitute to Frozen Sections. J Peoples Uni Med Health Sci. 2016;6(4):164-9.

INTRODUCTION:

Cytology is a great success achieved by medical and health sciences in the last century. Because it is a vast field, since then, new and more advanced techniques are being introduced in this field, Pap smear cytology, Fine needle aspiration cytology, fluid cytology, are all very simple, cheap and easy to perform tasks, and a recent addition is Touch imprint cytology (TIC)¹.

TIC like most other cytology tests, is easy, economic and simple to perform. It is used for

evaluating the status of resection margins and sentinel nodes in various surgical procedures².

It can be a better substitute of frozen sectioning because it does not require any specialized equipment, or trained personnel, while the results of TIC are quicker, better and as reliable as of frozen sections. It can also detect micro metastasis more accurately than the routine paraffin sectioning^{1,3}. Due to these qualities, TIC has almost replaced the frozen section technique throughout the world⁴.

TIC can be very helpful in a variety of surgeries, especially during the breast cancer surgeries, where immediate axillary lymph node dissection is advised if the intraoperative sentinel lymph node examination is positive. It is a simple, effective and rapid method for intra-operative evaluation of surgical margins in cancer patients^{3,4}.

In underdeveloped countries, TIC is preferred because it is an economic investigation which can be carried out just beside the O.T. table without any specialized equipment/machinery

- * Associate Professor, Deptt. of Pathology, United Medical & Dental College, Karachi.
- ** Professor, Deptt. of Pathology, Sir Syed College of Medical Sciences, Karachi.
- *** Assistant Professor, Deptt. of Pathology, Liaquat University of Medical & Dental College, Karachi.

Correspondence to:

Dr. Saira Bugti

Associate Professor, Deptt. of Pathology
United Medical & Dental College,
Karachi.
Email: saira.bugti@yahoo.com

unlike frozen sections⁵.

The basic aim of our study is to determine the feasibility and reliability of this technique in our hospital setups. As frozen section services are not available/nonfunctional in most of our tertiary care hospitals.

AIMS AND OBJECTIVES

- ** To evaluate the accuracy of intraoperative TIC in the diagnosis of lump in breast.
- ** To calculate the results and derive conclusions, including sensitivity, specificity, positive and negative predictive values, regarding the diagnostic accuracy of the procedure.

METHODS:

This is an institution based, descriptive study conducted at, Pathology department LUMHS Jamshoro in collaboration with all surgical units of LUMHS Hyderabad/ Jamshoro, from 1st JANUARY 2013 till 31st July 2013. 100 consecutive cases of breast lumps undergoing surgical procedures were included in our study. These cases were selected randomly, detailed history and examination was performed in each case. Later they were followed in the operation theater (O.T) and every specimen was collected in the O.T. and was excised from middle (centre), cut surface was gently pressed against clean glass slide to get imprints of cut surface. The slide was placed in alcohol for fixation, and then stained by H&E.

The results of TIC were compared with excisional biopsy, and were studied prospectively.

A. INCLUSION CRITERIA:

- ** Patients of all age groups
- ** Both male and female patients.
- ** Palpable breast lump of variable duration

B. EXCLUSION CRITERIA:

- ** Patients whose biopsy specimen showed autolytic changes
- ** Improperly processed tissue.

CRITERIA OF INTERPRETATION FOR IMPRINT SMEARS:-

Five groups were defined for diagnosis:^{6,7,8}

Malignant.

Suspicious for malignancy.

Benign.

Inflammatory.

Unsatisfactory.

1. Malignant: The criteria for malignancy were high cellularity, loss of cohesion, pleomorphism, large hyperchromatic nuclei with multiple large nucleoli, high mitotic activity.⁸
2. Suspicious for malignancy: If the smear showed moderately increased cellularity with variable or decreased cohesion, mild to moderate variation in size and shape of cells and nuclei.⁷
3. Benign: When the smears show low cellularity and good cohesion, with uniformity of size and shape of epithelial cells and their nuclei. Many stripped nuclei also appear i.e. nuclei of myoepithelial cells.⁶
4. Inflammatory: These smears revealed sheets of degenerating inflammatory cells, such as neutrophils, lymphocytes, plasma cells, eosinophils and macrophages. The duct cells may show reactive changes e.g.: enlarged nuclei or degenerative changes.⁶
5. Unsatisfactory: When the smears had no epithelial cells or the cells were too few to make a diagnosis.⁶

RESULTS:

This study consisted of 100 cases of imprint cytology and excisional biopsy of breast lumps, over a period of 7 months from January 2013 to July 2013, in this study female patients were 97 while males were 3.

RESULTS OF IMPRINT CYTOLOGY:

During the operative procedure, each specimen was imprinted in O.T. 56 cases were labeled as benign, which were proved to be benign on histopathology.

3 cases were labeled as suspicious of malignancy, and 35 cases were labeled as malignant, all these were confirmed as invasive

ductal cell carcinoma on histopathology reports.

06 cases were labeled as inflammatory, these contained benign epithelial cells along with inflammatory cells and necrotic debris. All these were proved to be inflammatory on histopathological evaluation (Table 1).

HISTOLOGIC DIAGNOSIS:

The results of TIC were compared with histopathologic diagnosis which reveals 38 cases of carcinoma, 37 cases of fibroadenomas, 04 cases of phyllodes tumor, 07 cases of fibrocystic disease, 02 cases each of duct epithelial hyperplasia, chronic mastitis, tuberculosis, chronic suppurative mastitis, fibro-epithelial polyp and normal breast tissue. One of these normal breast tissue was accessory breast tissue and other one was enlarged axillary tail giving the appearance of lump near axilla. 01 case each of intraductal papilloma and gynaecomastia. (TABLE- 2)

From 38 cases of carcinoma, 28 were invasive ductal cell carcinoma, 8 with comedo pattern, 1 was invasive lobular carcinoma, and 1 was invasive papillary carcinoma.

STATISTICAL CALCULATIONS:

In our study of 100 cases, 97 TIC reports matched with the final histopathology report. Out of the 03 cases, TIC gave suspicious cells (but not confirm malignancy).

The histopathology report showed ductal carcinoma in all 03 cases. (TABLE-3) Thus there were 97 true positives, 03 false negatives and no false positive and true negatives in our study.

Diagnostic Accuracy:

Is the percentage of correct diagnosis of all cases studied by the specific tests, i.e.; total of true positives and true negatives divided by the number of total cases.

$$\text{Accuracy} = \frac{\text{True Positive} + \text{True Negative}}{\text{Total Number of Cases}} \times 100$$

$$\text{The accuracy of TIC was: } \frac{97 + 0}{100} \times 100 = 97\%$$

Sensitivity:

The sensitivity of a test is the ability of a test to identify correctly all those who have the disease.

$$\text{Sensitivity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}} \times 100$$

$$\text{The sensitivity of TIC would be: } \frac{97}{97+3} \times 100 = 97\%$$

Specificity:

The specificity of a test is the ability of the study to identify correctly the candidates who do not have the disease.

$$\text{Specificity} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Positive}} \times 100$$

In our study, only cases with a lump in the breast were selected. Therefore in statistical terms, there were no normal individuals i.e. every patient, would reveal some pathology. Hence to give a wider spectrum to our interpretation of the results, we calculated the specificity of TIC for malignant lesions against benign lesions, i.e. "How specific is TIC as a test in the diagnosis of malignancy in a breast lump?"

The specificity of tic for malignancy would be calculated as:

$$\text{Specificity} = \frac{62}{62 + 0} \times 100 = 100\%$$

Positive Predictive Value:

The positive predictive value of a test indicates the probability that the patient with a positive test has in fact the disease in question.

$$\text{Positive Predictive Value} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}} \times 100$$

$$\text{Positive Predictive Value for TIC: } \frac{97}{97+0} \times 100 = 100\%$$

It should be noted that this positive predictive value for FNAC and TIC is a diagnostic test for all patients.

Negative Predictive Value:

The Negative Predictive Value of a test indicates the probability of a patient with a negative test not having the disease in question.

$$\text{Negative Predictive Value} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Negative}} \times 100$$

In the absence of true negatives, we broadened the interpretation of our results by calculating the negative predictive value of the test for malignant against benign lesions.

Negative Predictive Value for TIC:

$$: \frac{62}{62+03} \times 100 = \frac{62}{65} \times 100 = 95.38\%$$

Table-1: Comparison Between Touch Imprint Cytology Results & Histopathological Diagnosis

Impression on Imprint Cytology	No.	Histopathological Diagnosis	No.
Benign	56	Fibrocystic Change	07
		Fibroadenoma	37
		Phyllodes	04
		Miscellaneous	08
Suspicious	03	Carcinoma	03
Malignant	35	Carcinoma	35
Inflammatory	06	Inflammatory	06
Total	100	Total	100

DISCUSSION:

Our study of 100 cases for TIC and histopathology showed 97 true positive, 3 false negative, while no false positive cases were found and true negative cases were not included in this study.

The sensitivity of our TIC when compared with histopathology is 97%. In a similar study performed by Bukhari et al⁹ the sensitivity for imprint cytology of lump in breast was 87.5% and that for margins was 75%. Another study was performed by Bakhshandeh et al¹⁰ for the assessment of surgical margins in lumpectomy specimens, in their study, the intraoperative TIC showed a sensitivity of 97% which is exactly matching our result.

A similar study is performed by Khanna et al¹¹, on the sentinel lymph nodes in breast cancer. They found that the sensitivity of TIC was 88%. While Safai et al¹² also performed TIC for the axillary lymph nodes in breast cancer patients and they calculated that TIC had 90% sensitivity, yet

Table-2: Histo-Pathological Diagnosis in 100 Cases with Breast Lump

INFLAMMATORY LESIONS	Chronic Mastitis	2	6
	Tuberculosis	2	
	Chronic Suppurative Mastitis	2	
BENIGN LESIONS	Fibrocystic Change	7	56
	Fibro Adenoma	37	
	Phyllodes	4	
	Duct Epithelial Hyperplasia	2	
	Fibro Epithelial Polyp	2	
	Intra Ductal Papilloma	1	
	Gyneacomastia	1	
	Accessory Breast Tissue	2	
MALIGNANT LESIONS	Invasive Ductal Carcinoma	28	38
	Comedo Pattern	8	
	Invasive Lobular Carcinoma	1	
	Invasive Papillary Carcinoma	1	
TOTAL		100	100

Table-3: Statistical Values of Imprint Cytology in our Study

Parameters	Imprint Cytology
Sensitivity	97%
Specificity	100%
Diagnostic Accuracy	97%
True Positive	97%
True Negative	---
False Positive	---
Positive Predictive Value	100%
Negative Predictive Value	95.38%

In our study TIC had a diagnostic accuracy 97%. The accuracy of TIC by Bukhari et al⁹ is 92.3%, for margin 95%, the same was 94% by Khanna R et al, 84% by Creager et al¹⁴.

These comparisons reveal that TIC is a quite reliable test and we have already showed that this test requires no special equipment or machinery (as Frozen sections required) neither any special trained or technical staff, so these qualities make TIC a perfect choice in hospital set ups where Frozen section setup is not available.

In our country, where most of the tertiary care hospitals are lacking the facility of frozen section assessment, simply due to shortage of

Table-4: Statistical Comparison of Present Study with National & International

Parameters of TIC	Present Study	Bukhari MG et al ⁹	Maryam Bakhshandeh et al ¹⁰	Khanna R et al ¹¹	Safai A et al ¹²	Tomohiko Aihara et al ¹³	Andrew J Creager et al ¹⁴
Sensitivity	97%	87.5%	97%	88%	90%	86%	53%
Specificity	100%	100%	99%	98%	100%	-	98%
Accuracy	97%	92.3%	-	94%	-	-	84%
PPV	100%	100%	84%	-	-	-	94%
NPV	95.38%	83.3%	99%	-	-	-	82%

another similar study performed by Aihara et al¹³ showed 89% sensitivity.

The specificity of a test shows its ability to correctly identify those who do not have the disease. In our 100 cases of breast lump, we calculated the specificity of TIC for malignancy against non-malignant cases, which was found to be 100% which correlates well with the specificity value by above studies i.e., Bukhari et al⁹ 100%, Bakhshandeh et al¹⁰ 99%, Khanna et al¹¹ 98% and Safai et al¹² 100%. These high specificity value suggest that TIC is a reliable test when compared with the gold standard i.e. histopathology.

The PPV for TIC in our study was 100% and it was 100% by Bukhari et al⁹, 84% by Bakhshandeh et al¹⁰ 94% by Creager et al¹⁴.

The NPV of imprint cytology in our study was calculated 95.38% while Bukhari et al⁹ had NPV 83.3% and 84% (for margin assessments) Maryam Bakhshandeh et al¹⁰ had NPV of 99%, Creager et al¹⁴ calculated a NPV as 82% funds /

financial burdens, the TIC can smoothly fulfill the requirement. This will be available even at small basic laboratories in every small town, wherever a surgeon requires immediate diagnosis / assessment while the patient is on the operation table.

We also believe that intraoperative TIC is advantageous over frozen sectioning for many reasons. TIC is at least as sensitive as frozen sectioning and is as specific. It is less expensive and faster than frozen sectioning. Tissue is not wasted in the cryostat and the pathologist does not have to attempt to cut lymph nodes with the cryostat that have been largely replaced by fat.¹⁵ Also, freezing artifact is not introduced into the tissue when imprints are made. Detection of micrometastatic disease is a significant area for improvement and a cost-benefit analysis is needed to determine the direction of future studies. However, we believe that TIC is the preferred method of intraoperative analysis for sentinel nodes found in breast cancer patients.

CONCLUSION:

TIC is a highly reliable, less expensive, quick and easy method. A high sensitivity and a high PPV indicates that a positive TIC in the breast lumps is highly suggestive of definite diagnosis of the concerned pathology when compared with the final histology report. The high specificity and a high NPV for malignancy illustrated the high accuracy of TIC in the diagnosis of malignancy in the breast.

Recommendations:

TIC should be used for the confirmation of at-hand diagnosis and assessment of surgical margins during the operative procedures in O.T. TIC should be used for the assessment of sentinel lymph nodes (SLNs) during the operative procedures in O.T. TIC should be used as an alternative procedure to frozen section.

REFERENCES:

- Motomura K, Nagumo S, Komoiko Y, Koyama H, Inaji. Accuracy of imprint cytology for intraoperative diagnosis of sentinel node metastasis in breast cancer. *Ann Surg.* 2008;247(5):839-42.
- Lumachi F, Marino F, Zanella S, Chiara GB, Basso SM. Touch imprint cytology and frozen-section analysis for intraoperative evaluation of sentinel nodes in early breast cancer. *Anticancer Res.* 2012;32(8):3523-6.
- Motomura K, Inaji H, Komoike Y, Kasugai T, Nagumo, Noguchi S, et al. Intraoperative sentinel lymph node examination by imprint cytology and frozen sectioning during breast surgery. *Br J Surg.* 2000;87(5):597-601.
- Shaha S, Rahman AN. Comparative study of imprint cytology and frozen section in the intraoperative diagnosis of thyroid lesions. *Bangladesh J Pathol.* [Online]. 2009;24:1.
- Narang V, Jacob S, Mahapatra D, Mathew JE. Intraoperative diagnosis of central nervous system lesions: Comparison of squash smear, touch imprint, and frozen section. *J Cytol.* 2015;32:1538.
- Mulford DK, Dawson AE. Atypia in fine needle aspiration cytology of nonpalpable and palpable mammographically detected breast lesions. *Acta Cytol.* 1994;38:9-17.
- Lamb J, Anderson TJ. Influence of cancer histology on the success of fine needle aspiration of the breast. *J Clin Pathol.* 1989;42:733-5.
- Novotny DB, Maygarden SJ, Shermer RW, Frable WJ. Fine needle aspiration of benign and malignant breast masses associated with pregnancy. *Acta Cytol.* 1991;35(6):676-86.
- Bukhari M H, Akhtar Z M. Comparison of accuracy of diagnostic modalities for evaluation of breast cancers with review of literature. *Diagn Cytopathol.* 2009;37(6):416-24
- akhshandeh M, Tutuncuoglu O, Fischer G, Masood S. Use of imprint cytology for assessment of surgical margins in lumpectomy specimens of breast cancer patients. *Diagn Cytopathol.* 2007;35(10):656-9.
- Khanna, Bhadani S, Khanna S, Pandey M, Kumar M. Touch imprint cytology evaluation of sentinel lymph node in breast cancer. *World J Surg.* 2011;35(6):1254-9. doi: 10.1007/s00268-011-1094-7.
- Safai, Razeghi A, Monabati A, Azarpira N, Talei A. Comparing touch imprint cytology, frozen section analysis, and cytokeratin immunostaining for intraoperative evaluation of axillary sentinel lymph nodes in breast cancer. *Indian J Pathol Microbiol.* 2012 Apr-Jun;55(2):183-6. doi: 10.4103/0377-4929.97859.
- Aihara T, Munakata S, Morino H, Takatsuka Y. Comparison of Frozen Section and Touch Imprint Cytology for Evaluation of Sentinel Lymph Node Metastasis in Breast Cancer. *Ann.* 2004;11(8):747-750.
- Creager AJ, Geisinger KR, Shiver SA, Perrier ND, Shen P, Shaw JA, et al. Intraoperative Evaluation of Sentinel Lymph Nodes for Metastatic Breast Carcinoma by Imprint Cytology. *Mod Pathol.* 2002;15(11):1140-7.
- Mangia A, Chiratti A, Chiarappa P, Incalza MA, Antonaci G, Pilato B, Simone G, et al. Touch imprint cytology in tumor tissue Banks for confirmation of neoplastic cellularity and for DNA Extraction. *Arch pathol lab Med.* 2008;132(6):974-8.