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Diagnostic Accuracy of Imprint Cytology in Determining Margin Positivity in Patients Undergoing Breast Conservation

Rizwana, Sadaf Afridi, Warda Ali, Ishrat Alam, M. Furqan Ullah Babar, Mah Muneer Khan

ABSTRACT

Objectives: To determine the diagnostic accuracy of imprint cytology in identifying margin positivity in patients undergoing breast-conserving surgery for breast cancer, using histopathology as the gold standard.

Study Design and Setting: This cross-sectional validation study was conducted in the Department of Surgery at Khyber Teaching Hospital, Peshawar

Methodology: A total of 154 women aged 30–80 years diagnosed with malignant breast lumps and undergoing breast-conserving surgery were enrolled using non-probability convenience sampling. Imprint cytology was performed intraoperatively by pressing clean glass slides against the resected margins of the lumpectomy specimen. Slides were air-dried, stained with hematoxylin and eosin, and examined microscopically. Final margin status was determined by histopathological examination, which served as the reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy of imprint cytology were calculated.

Results: The mean age of participants was 51.15 ± 11.87 years. Imprint cytology demonstrated a sensitivity of 40.8%, specificity of 78.3%, PPV of 61.7%, NPV of 60.7%, and overall diagnostic accuracy of 61.0% in detecting margin positivity. The chi-square test showed a statistically significant association between imprint cytology and histopathology findings ($p = 0.010$).

Conclusions: Imprint cytology provides a rapid and economical method for intraoperative margin assessment during breast-conserving surgery, particularly useful in resource-limited settings. However, its diagnostic reliability is operator-dependent and requires standardization for broader clinical application.

Keywords: Biopsy, Breast Conservation, Breast Neoplasms, Diagnostic Accuracy, Histopathology, Intraoperative Care, Lumpectomy

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Rizwana
Resident, Department of General Surgery
Khyber Teaching Hospital, Peshawar
Email: rizwankhan1795rk@gmail.com

Sadaf Afridi
Resident, Department of General Surgery
Khyber Teaching Hospital, Peshawar
Email: sfpk95@gmail.com

Warda Ali
Resident, Department of General Surgery
Khyber Teaching Hospital, Peshawar
Email: wardali46@gmail.com

Ishrat Alam
Resident, Department of General Surgery
Hayatabad Medical Complex Peshawar
Email: ishratalam94@gmail.com

M. Furqan Ullah Babar
Resident, Department of General Surgery
Khyber Teaching Hospital, Peshawar
Email: drfurqanbabar@gmail.com

Mah Muneer Khan
Professor, Head Department of General Surgery
Khyber Teaching Hospital, Peshawar
Email: mah.muneer@kmc.edu.pk

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INTRODUCTION

The human breast is a complex structure primarily composed of glandular tissue responsible for milk production.1 These milk-producing lobules are connected to the nipple via a branching ductal system. Alongside this secretory network, the breast contains a rich lymphatic system and abundant adipose and connective tissue that collectively support the organ's architecture and physiological functions. The cellular turnover in lobules and ducts is naturally high due to hormonal influences, but this turnover is usually tightly regulated. However, when this regulation is disrupted, uncontrolled cellular proliferation can occur, giving rise to neoplastic changes.[2]

Breast cancer is one of the most common malignancies affecting women globally, although it can also affect men.[3] It typically develops in a stepwise manner, beginning with hyperplasia or dysplasia, progressing to carcinoma in situ, and eventually transforming into invasive carcinoma. The most common presenting symptom is a painless lump in the breast, though patients may also report nipple discharge, changes in breast contour, or retraction of the nipple.[4] Clinical

examination often reveals a palpable mass, sometimes accompanied by skin dimpling or lymphadenopathy. Enlarged axillary lymph nodes may signify regional or distant metastasis.[5]

Early detection significantly improves the prognosis of breast cancer. This can be achieved through awareness campaigns promoting regular breast self-examinations and timely clinical assessments of any suspicious lesions. Imaging techniques such as mammography and ultrasound, alongside biopsy, are essential diagnostic tools.[6] However, the definitive treatment of breast cancer often requires surgical excision of the tumor.

Historically, mastectomy, the complete removal of the breast, was the standard surgical approach. However, in recent decades, the concept of breast-conserving surgery (BCS), including lumpectomy followed by radiotherapy, has gained momentum as an effective alternative for early-stage breast cancer.[7] This shift reflects a growing demand for preserving breast aesthetics and improving quality of life without compromising oncological safety.[8]

One of the critical challenges in breast-conserving surgery is ensuring complete tumor excision with negative surgical margins. The presence of cancer cells at the resected margin significantly increases the risk of local recurrence and may necessitate additional surgery.[9] Thus, intraoperative assessment of margin status is vital to reduce reoperation rates and enhance treatment outcomes. However, determining margin status during surgery can be technically difficult without reliable, rapid, and cost-effective diagnostic tools.

Imprint cytology has emerged as a promising technique for intraoperative margin assessment. The method involves pressing freshly excised tissue onto a glass slide to transfer cells, which are then stained and evaluated microscopically. This approach is less expensive, faster, and more straightforward compared to frozen section analysis, which is currently considered the gold standard. In a study evaluating imprint cytology, sensitivity and specificity were reported as 80.0% and 85.0%, respectively, with a high negative predictive value (NPV) of 97.0%.[10] These results indicate its potential utility in confirming clear margins during surgery, thereby minimizing the need for repeat procedures.

Another study involving 522 patients reported that imprint cytology identified 26.1% of patients as margin-positive and 73.9% as margin-negative.[11] However, imprint cytology was slightly less accurate than frozen section analysis, particularly in terms of false-positive rates, which were reported to be as high as 13.4%. Nevertheless, the false-negative rate was remarkably low at 0%. Moreover, when combined with frozen section analysis, the false-positive rate decreased significantly to 2.5%, suggesting that the integration of both techniques might offer a balanced approach in clinical practice.[12]

Despite its promising profile, imprint cytology is underutilized in many clinical settings, particularly in low-resource regions. One significant limitation in adopting imprint cytology more broadly is the variability in its diagnostic accuracy reported across different international studies. These differences may stem from variations in technique, interpretation, and patient demographics, thus limiting the generalizability of existing findings.

The rationale of this study stems from the observed gap in the literature regarding the diagnostic accuracy of imprint cytology for intraoperative margin assessment in breast-conserving surgeries, especially in local contexts where advanced pathology facilities may not be readily available. Understanding the reliability of imprint cytology in these settings is critical to optimizing surgical decision-making, improving patient outcomes, and reducing the need for secondary procedures. Therefore, this study aimed to determine the diagnostic accuracy of imprint cytology in identifying margin positivity in patients undergoing breast conservation surgery.

METHODOLOGY

This cross-sectional validation study was conducted at the Department of Surgery, Khyber Teaching Hospital, Peshawar, over a period of six months from 1st October 2024 to 31st March 2025. Before initiating the study, ethical clearance was obtained from the Institutional Research and Ethical Review Board (IREB) of Khyber Medical College, Peshawar, under approval number 714/DME/KMC, dated 19th September, 2024.

The sample size was calculated using a sensitivity and specificity-based formula, assuming an anticipated breast cancer prevalence of 40.0%, a sensitivity of imprint cytology at 80.0%, a specificity of 85.0%, a margin of error of 10%, and a 95% confidence level.[11] A total of 154 participants were included in the study.

Patients were recruited from the indoor surgical department using a non-probability convenient sampling technique. The study population included women aged between 30 and 80 years, diagnosed with malignant breast lumps and scheduled for breast-conserving surgery (lumpectomy). Women were excluded from the study if they had received neoadjuvant chemoradiotherapy, underwent intraoperative conversion to non-conservative surgery, had a recurrent breast lump, secondary lesions in the breast, or evidence of distant metastasis. The diagnosis of breast cancer was confirmed preoperatively through fine-needle aspiration cytology (FNAC) or core needle biopsy. Malignancy was identified based on cytological criteria, including increased nucleus-to-cytoplasm ratio, cellular atypia, hyperchromasia, and nuclear irregularities.

During surgery, imprint cytology was performed intraoperatively. Clean glass slides were gently pressed against the anticipated surgical margins of the excised lumpectomy specimen. The number of slides used was

determined by the operating surgeon. The slides were air-dried, stained with hematoxylin and eosin (H&E), and examined immediately by a consultant histopathologist under a light microscope. If malignant cells were seen on imprint cytology, the margin was labeled as positive; if no malignant cells were observed, the margin was considered negative. After margin clearance was confirmed, the lumpectomy specimen was sent to the hospital's pathology lab for histopathological examination, which served as the gold standard for determining margin status.

All participants provided written informed consent before inclusion in the study. Baseline demographic and clinical parameters were documented using a structured proforma. These included patient age (in years), body mass index (BMI in kg/m²), side of the affected breast, involved quadrant, lump size (in centimeters), duration of symptoms (in weeks), menopausal status (pre- or post-menopausal), and history of oral contraceptive pills (OCPs), hormone replacement therapy (HRT), and comorbidities such as diabetes mellitus and hypertension.

After surgery, the results of imprint cytology were compared with the histopathology findings of the surgical specimen to determine the diagnostic accuracy of imprint cytology in detecting margin positivity. The outcomes of interest included sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

All collected data were entered and analyzed using SPSS version 26. Descriptive statistics were applied to compute means and standard deviations for continuous variables and frequencies with percentages for categorical variables. Inferential statistics included the generation of 2×2 contingency tables to compare imprint cytology with histopathological results. Diagnostic accuracy metrics such as sensitivity, specificity, PPV, and NPV were calculated accordingly. In addition, effect modifiers such as age, menopausal status, lump size, and presence of comorbidities were controlled through stratification, and post-stratification analyses were conducted to assess their impact on diagnostic performance.

RESULTS

The study included a total of 154 women with a mean age of 51.15 ± 11.87 years. Most participants were above 50 years of age (51.3%), while 48.7% were aged 50 or below. The mean BMI was 23.83 ± 2.64 kg/m², with 51.9% of participants having a BMI of 24.0 or below. The average duration of symptoms was 6.16 ± 2.84 weeks, and the majority (63.0%) presented within six weeks of symptom onset. Post-menopausal women comprised 63.0% of the cohort, while 37.0% were pre-menopausal. In terms of parity, 53.2% were nulliparous and 46.8% were multiparous. Comorbid conditions were common; 27.9% of participants had diabetes mellitus, and 33.8% had hypertension. A positive family history of breast cancer was reported in 23.4% of the cases. Regarding hormonal factors, 22.1% of participants had a history of oral contraceptive pill (OCP) use, and 13.6% reported hormone replacement therapy (HRT) use. As for the side of involvement, 46.1% had lumps in the right breast, 45.5% in the left, and 8.4% had bilateral breast involvement. Hormone receptor status was positive in 53.9% of participants and negative in 46.1%. (Table 1) Among the 154 patients assessed, imprint cytology was positive for malignant cells in 46.1% of the cases, while 53.9% were negative. Histopathological examination, considered the gold standard, confirmed margin positivity in 30.5% of the specimens, whereas 69.5% were margin-negative. (Table 2)

By comparing imprint cytology with histopathology, the gold standard, revealed a sensitivity of 40.8% and a specificity of 78.3%. The positive predictive value (PPV) was calculated at 61.7%, while the negative predictive value (NPV) was 60.7%. The overall diagnostic accuracy of imprint cytology in detecting margin positivity was found to be 61.0%. The association between imprint cytology results and histopathological findings was statistically significant, as indicated by a chi-square test with a p-value of 0.010.

The stratified analysis revealed notable variability in the diagnostic performance of imprint cytology across different clinical and demographic subgroups. Age-wise, diagnostic accuracy was relatively better in women aged over 50 years compared to those 50 or younger, indicating age-related tissue and cellular changes may influence interpretation. Participants with a BMI =24.0 exhibited higher sensitivity and predictive values, suggesting leaner patients may offer better-quality specimens for cytological evaluation. In terms of menopausal status, pre-menopausal women showed higher specificity and positive predictive values compared to post-menopausal women, which may reflect hormonal influences on tissue morphology. Nulliparous women demonstrated slightly better diagnostic accuracy than multiparous women. Lateralization of the lesion also influenced results, with right-sided tumors yielding higher specificity and PPV compared to left or bilateral lesions, while imprint cytology performed poorest in bilateral cases.

Patients without a history of oral contraceptive or hormone replacement therapy showed notably higher specificity and PPV, suggesting less hormonal influence on cellular features that could mimic atypia. Additionally, better performance was observed in hormone receptor-positive tumors compared to receptor-negative ones, likely due to more distinct cytological features in these cases. Overall, imprint cytology demonstrated variable sensitivity and specificity depending on patient and tumor characteristics, emphasizing the need to consider individual clinical profiles when interpreting intraoperative cytology results. This stratified analysis highlights the importance of tailored clinical application and further supports the need for standardization and expertise in utilizing imprint cytology effectively. (Table 4)

DISCUSSION

In the present study, the mean age of participants was 51.15 ± 11.87 years, with the majority being older than 50 years. This age distribution reflects the global epidemiological trend where breast cancer risk significantly increases after the fourth decade of life, which also serves as a rationale for the initiation of breast cancer screening protocols in most countries. Our findings are comparable to those reported by Yadav et al., who documented a mean age of 48.1 ± 10.6 years, with most participants in their sixth decade.[13] Similarly, Ashraf et al. reported that 63.3% of their patients were above the age of 50 years, and Hashmi et al. observed a mean age of 53.4 ± 12.4 years.[14, 15] These findings reinforce the well-established association between advancing age and the incidence of breast cancer. However, in contrast to our results, a study by Vinod K et al. reported a younger cohort, with most participants between 40 and 50 years of age.[16] This discrepancy could be attributed to differences in selection criteria and regional patient demographics.

Regarding body mass index (BMI), approximately half of the participants in our study had values exceeding the healthy range. Ashraf et al. similarly reported a mean BMI of 25.75 kg/m² among breast cancer patients.[14] In a broader epidemiological study by Lofterod et al., 30.7% of patients with breast cancer were found to be living sedentary lifestyles, and 34.3% were overweight or obese.[17] Obesity is a well-recognized modifiable risk factor for breast cancer, especially in post-menopausal women, and is believed to increase breast cancer risk by approximately 1.33 times.[18] Nonetheless, the relationship between elevated BMI and breast cancer risk is complex and can be influenced by various factors including menopausal status, hormone levels, and genetic predisposition.

The majority of our study population was post-menopausal, consistent with global trends. A study conducted in India found that 52.0% of breast cancer patients were post-menopausal.[19] The higher prevalence of breast cancer in post-menopausal women is thought to be related to hormonal imbalances, prolonged estrogen exposure, and age-related cellular changes.[10]

When evaluating the diagnostic accuracy of imprint cytology for intraoperative margin assessment, we observed a sensitivity of 40.8%, specificity of 78.3%, positive predictive value (PPV) of 61.7%, and negative predictive value (NPV) of 60.7%. The overall accuracy was 61.0%. These values suggest moderate diagnostic utility, with relatively better performance in ruling out margin positivity than confirming it. Comparatively, Vinod et al. reported significantly higher sensitivity and specificity of 91.6% and 100.0%, respectively.[16] Yadav et al., in their study focusing on sentinel lymph node evaluation, also reported high diagnostic values with 87.5% sensitivity and 100.0% specificity.[13] In contrast, our results are more aligned with those reported by Ahuja

Table 1. Descriptive Statistics and Baseline Sociodemographic and Clinical Parameters of the Study Cohort (n = 154)

Parameter	Category	n (%) / Mean ± SD
Age (years)	—	51.15 ± 11.87
	= 50	75 (48.7%)
	> 50	79 (51.3%)
BMI (kg/m²)	—	23.83 ± 2.64
	= 24.0	80 (51.9%)
	> 24.0	74 (48.1%)
Duration of Symptoms (weeks)	—	6.16 ± 2.84
	= 6	97 (63.0%)
	> 6	57 (37.0%)
Menopausal Status	Pre-menopausal	57 (37.0%)
	Post-menopausal	97 (63.0%)
Parity	Nulliparous	82 (53.2%)
	Multiparous	72 (46.8%)
Diabetes Mellitus (DM)	Yes	43 (27.9%)
	No	111 (72.1%)
Hypertension (HTN)	Yes	52 (33.8%)
	No	102 (66.2%)
Family History of Breast Cancer	Positive	36 (23.4%)
	Negative	118 (76.6%)
OCP Use	Yes	34 (22.1%)
	No	120 (77.9%)
HRT Use	Yes	21 (13.6%)
	No	133 (86.4%)
Laterality of Lump	Right	71 (46.1%)
	Left	70 (45.5%)
	Bilateral	13 (8.4%)
Hormone Receptor Status	Positive	83 (53.9%)
	Negative	71 (46.1%)

Table 2. Imprint Cytology and Histopathology Findings of the Study Cohort (n = 154)

Outcome Variable	Category	n (%)
Imprint Cytology	**Positive**	71 (46.1%)
	Negative	83 (53.9%)
Histopathology	**Positive**	47 (30.5%)
	Negative	107 (69.5%)

Table 3. Diagnostic Accuracy of Imprint Cytology Against Histopathology as Gold Standard (n = 154)

Histopathology	Imprint Positive	Imprint Negative	Total
Positive	29 (61.7%)	18 (38.3%)	47
Negative	42 (39.3%)	65 (60.7%)	107
Total	71 (46.1%)	83 (53.9%)	154

Diagnostic Accuracy Measures:
Sensitivity: 40.8%, Specificity: 78.3%
Positive Predictive Value (PPV): 61.7%
Negative Predictive Value (NPV): 60.7%
Overall Accuracy: 61.0%, Chi-square test: p = 0.010

Table 4. Stratified Analysis of Diagnostic Accuracy of Imprint Cytology by Clinical and Demographic Variables Using Histopathology as Gold Standard (n = 154)

				Imprint		Total	
				+ve	-ve		
Age (years)	**=50**	**H/P**	+ve	13 (68.4%)	6 (31.6%)	19 (100%)	Sen = 35.1%, Sp = 84.2%,
			-ve	24 (42.9%)	32 (57.1%)	56 (100%)	PPV= 68.4%, NPV= 57.1%
	>50	**H/P**	+ve	16 (57.1%)	12 (42.9%)	28 (100%)	Sen = 47.0%, Sp = 73.3%,
			-ve	18 (35.3%)	33 (64.7%)	51 (100%)	PPV= 57.1%, NPV= 64.7%
BMI (kg/m^2)	**=24.0**	**H/P**	+ve	20 (69.0%)	9 (31.0%)	29 (100%)	Sen = 48.7%, Sp = 76.9%,
			-ve	21 (41.2%)	30 (58.8%)	51 (100%)	PPV= 68.9%, NPV= 58.8%
	>24.0	**H/P**	+ve	9 (50.0%)	9 (50.0%)	18 (100%)	Sen = 30.0%, Sp = 79.5%,
			-ve	21 (37.5%)	35 (62.5%)	56 (100%)	PPV= 50.0%, NPV= 62.5%
Meno-pause	**Pre**	**H/P**	+ve	10 (76.9%)	3 (23.1%)	13 (100%)	Sen = 40.0%, Sp = 90.6%,
			-ve	15 (34.1%)	29 (65.9%)	44 (100%)	PPV= 76.9%, NPV= 65.9%
	Post	**H/P**	+ve	19 (55.9%)	15 (44.1%)	34 (100%)	Sen = 41.3%, Sp = 70.5%,
			-ve	27 (42.9%)	36 (57.1%)	63 (100%)	PPV= 55.8%, NPV= 57.1%
Parity	**Nulli**	**H/P**	+ve	17 (65.4%)	9 (34.6%)	26 (100%)	Sen = 44.7%, Sp = 79.5%,
			-ve	21 (37.5%)	35 (62.5%)	56 (100%)	PPV= 65.3%, NPV= 62.5%
	Multi	**H/P**	+ve	12 (57.1%)	9 (42.9%)	21 (100%)	Sen = 36.6%, Sp = 76.9%,
			-ve	21 (41.2%)	30 (58.8%)	51 (100%)	PPV= 57.1%, NPV= 58.8%
Laterality	**Right**	**H/P**	+ve	16 (72.7%)	6 (27.3%)	22 (100%)	Sen = 40.0%, Sp = 80.6%,
			-ve	24 (49.0%)	25(51.0%)	49 (100%)	PPV= 72.2%, NPV= 51.0%
	Left	**H/P**	+ve	13 (59.1%)	9 (40.9%)	22 (100%)	Sen = 46.4%, Sp = 78.5%,
			-ve	15 (31.3%)	33 (68.8%)	48 (100%)	PPV= 59.0%, NPV= 68.7%
	Bilateral	**H/P**	+ve	0 (0.0%)	3 (100.0%)	3 (100%)	Sen = 0.0%, Sp = 70.0%,
			-ve	3 (30.0%)	7 (70.0%)	10 (100%)	PPV= 0.0%, NPV= 70.0%
OCPs	**Yes**	**H/P**	+ve	7 (43.8%)	9 (56.35)	16 (100%)	Sen = 53.8%, Sp = 57.1%,
			-ve	6 (33.3%)	12 (66.7%)	18 (100%)	PPV= 43.7% , NPV= 66.7%
	No	**H/P**	+ve	22 (71.0%)	9 (29.0%)	31 (100%)	Sen = 37.9%, Sp = 85.4%,
			-ve	36 (40.0%)	53 (59.6%)	89 (100%)	PPV= 70.9%, NPV= 59.5%
HRT	**Yes**	**H/P**	+ve	3 (25.0%)	9 (75.0%)	12 (100%)	Sen = 50.0%, Sp = 40.0%,
			-ve	3 (33.3%)	6 (66.7%)	9 (100%)	PPV= 25.0%, NPV= 66.7%
	No	**H/P**	+ve	26 (74.3%)	9 (25.7%)	35 (100%)	Sen = 40.0%, Sp = 86.7%,
			-ve	39 (39.8%)	59 (60.2%)	98 (100%)	PPV= 74.2%, NPV= 60.2%
Receptors	**+ve**	**H/P**	+ve	16 (72.7%)	6 (27.3%)	22 (100%)	Sen = 37.2%, Sp = 85.0%,
			-ve	27 (44.3%)	34 (55.7%)	61 (100%)	PPV= 72.7%, NPV= 55.7%
	-ve	**H/P**	+ve	13 (52.0%)	12 (48.0%)	25 (100%)	Sen = 46.4%, Sp = 72.0%,
			-ve	15 (32.6%)	31 (67.4%)	46 (100%)	PPV= 52.0%, NPV= 67.3%

et al., who observed a sensitivity of 45.3% and specificity of 60.0%.[10] Similarly, Nikhat AF also reported findings close to our study, highlighting the variable diagnostic performance of imprint cytology in different settings.[19] Maloney et al. reported higher accuracy metrics, with a sensitivity of 72.0% and specificity of 97.0%, which again underscores the variability depending on technique, operator expertise, and patient characteristics.[20]

One of the key advantages of imprint cytology lies in its rapid turnaround time and ease of use during surgery, making it a practical intraoperative tool. However, its effectiveness is highly operator-dependent, and accurate interpretation requires substantial expertise in differentiating atypical from malignant cells. Errors may arise due to cautery artefacts, poor staining, suboptimal drying, or sampling from necrotic or fibrotic areas. These technical limitations can affect the reliability of results and partially explain the relatively lower diagnostic accuracy observed in our study.

The application of imprint cytology is not restricted to breast cancer surgery. Tambane et al. demonstrated its utility in assessing surgical margins in cancers of the skin, oral cavity, and colon, reporting a combined sensitivity and specificity

of 46.15% and 86.6%, respectively.[21] Furthermore, Hashmi et al. evaluated imprint cytology for axillary lymph node metastases in breast cancer and reported an accuracy of 83.7%, which, although lower than that of frozen section analysis, was still acceptable in resource-limited settings.[15] However, when it came to the detection of micrometastasis and macrometastasis, cytology was found to be less reliable.

In short, while imprint cytology provides a practical and cost-effective option for intraoperative margin assessment in breast-conserving surgery, its diagnostic accuracy can be influenced by several technical and biological factors. It may serve as a useful adjunct in settings where frozen section is not feasible, but caution should be exercised when interpreting borderline or ambiguous findings. Further training of personnel, standardization of procedures, and integration with other diagnostic modalities may help enhance its clinical utility.

The findings of this study hold important clinical relevance, particularly in low-resource settings where access to intraoperative frozen section analysis is limited. Imprint cytology presents as a cost-effective, rapid, and simple method for evaluating surgical margins during breast-conserving surgery. Its real-time applicability allows surgeons to make immediate intraoperative decisions about margin re-excision, potentially reducing the need for second surgeries and minimizing psychological and physical burden on patients. While the sensitivity observed in this study was relatively low, the moderate specificity and acceptable negative predictive value suggest that imprint cytology may be useful in ruling out margin positivity in selected cases. In addition, the procedure does not require specialized cryostat equipment, making it ideal for routine surgical practice in secondary care hospitals and peripheral institutions. When used by trained cytopathologists, and in conjunction with preoperative imaging and clinical assessment, imprint cytology can serve as a valuable adjunct to surgical decision-making and improve oncologic outcomes in breast cancer care.

Despite its potential, this study had several limitations that must be acknowledged. First, the relatively low sensitivity of imprint cytology observed in our results may have been influenced by operator-dependent variability in sample collection, staining technique, and microscopic interpretation. The accuracy of imprint cytology is highly reliant on the cytopathologist's experience and may vary significantly across institutions. Second, artefacts introduced during cauterization and inadequate drying or staining of slides can impair cellular visualization and contribute to false negative or false positive results. Third, the study employed a non-probability sampling technique and was conducted at a single tertiary care center, which may limit the generalizability of the findings to broader populations. Additionally, the relatively small sample size and lack of comparison with frozen section or molecular methods may have impacted the comprehensive evaluation of imprint cytology's diagnostic performance. Finally, the study did not assess interobserver variability, which is an important consideration in cytological interpretation. Future multicenter studies with larger cohorts and standardized protocols are recommended to validate these findings and explore the integration of imprint cytology with other intraoperative diagnostic tools.

CONCLUSION

In conclusion, imprint cytology offers a practical, rapid, and economical intraoperative technique for margin assessment in breast-conserving surgery, especially in settings where frozen section is unavailable. Although the sensitivity observed in this study was modest, its reasonable specificity and negative predictive value highlight its potential role as a supportive diagnostic tool in guiding real-time surgical decisions. Its simplicity, cost-effectiveness, and adaptability to resource-constrained environments make it a valuable adjunct in the surgical management of breast cancer. However, the effectiveness of imprint cytology remains heavily dependent on operator expertise and standardized techniques. Integrating this method with clinical, radiological, and histopathological assessments may enhance its utility in reducing reoperation rates and improving patient outcomes. Further large-scale, multicenter studies are warranted to validate its diagnostic reliability and establish its role alongside existing intraoperative modalities.

Authors Contribution:
Rizwana: Introduction + Discussion, data collection+ conclusion
Sadaf Afridi: Data Collection + review article
Warda Ali: Data Collection + review article
Ishrat Alam: Data Collection + review article
M. Furqan Ullah Babar: Data Collection + data analysis
Mah Muneer Khan: review article and dissociation

REFERENCES

1. Biswas SK, Banerjee S, Baker GW, Kuo CY, Chowdhury I. The Mammary Gland: Basic Structure and Molecular Signaling during Development. Int J Mol Sci. 2022 Mar 31;23(7):3883. doi: 10.3390/ijms23073883. PMID: 35409243; PMCID: PMC8998991.
2. Natale G, Stouthandel MEJ, Van Hoof T, Bocci G. The Lymphatic System in Breast Cancer: Anatomical and Molecular Approaches. Medicina (Kaunas). 2021 Nov 19;57(11):1272. doi: 10.3390/medicina57111272. PMID: 34833492; PMCID: PMC8624129.
3. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. Br J Radiol. 2022 Feb 1;95(1130): 20211033. doi: 10.1259/bjr.20211033. Epub 2021 Dec 14. PMID: 34905391; PMCID: PMC8822551.
4. Shetty MK. Imaging of the Symptomatic Breast. Breast & Gynecological Diseases: Role of Imaging in the Management: Springer; 2021. p. 27-79. https://doi.org/10.1007/978-3-030-69476-0_2
5. Grover S, Avasthi A, Majid A. Clinical Practice Guidelines for mental health and well-being in patients with chronic medical illnesses. Indian J Psychiatry. 2024 Jan;66(Suppl 2):S338-S352. PMID: 38445289; PMCID: PMC10911329.

6. Steyerova P, Burgetova A. Current imaging techniques and impact on diagnosis and survival—a narrative review. Annals of Breast Surgery. 2022 Sep 30;6. doi: 10.21037/abs-21-22
7. Subhy Alsheikhly A, Ahmed Subhy Alsheikhly M. A Comprehensive Review of Breast Cancer and the Latest Advancement in Diagnosis and Treatment [Internet]. Oncology. IntechOpen; 2025. Available from: http://dx.doi.org/10.5772/intechopen.1008946
8. M Rassam, B Davoudi, A Comprehensive Overview of Breast Cancer Surgery Strategies: Advances, Options, and Considerations,EJCMPR. 2024; 3(2):629-643 https://doi.org /EJCMPR/ 20240611
9. Bundred JR, Michael S, Stuart B, Cutress RI, Beckmann K, Holleczek B, Dahlstrom JE, Gath J, Dodwell D, Bundred NJ. Margin status and survival outcomes after breast cancer conservation surgery: prospectively registered systematic review and meta-analysis. BMJ. 2022 Sep 21;378:e070346. doi: 10.1136/bmj-2022-070346. PMID: 36130770; PMCID: PMC9490551.
10. Ahuja S, Yadav P, Fattahi-Darghlou M, Zaheer S. Comparison of Intraoperative Imprint Cytology versus Frozen Section for Sentinel Lymph Node Evaluation in Breast Cancer. A study along with Systematic Review and Meta-analysis of literature. Asian Pac J Cancer Prev. 2024 Apr 1;25(4):1113-1119. doi: 10.31557/APJCP.2024.25.4.1113. PMID: 38679970; PMCID: PMC11162742.
11. Uno Y, Akiyama N, Yuzawa S, Kitada M, Takei H. The value and practical utility of intraoperative touch imprint cytology of sentinel lymph node(s) in patients with breast cancer: A retrospective cytology-histology correlation study. Cytojournal. 2020 May 12;17:11. doi: 10.25259/Cytojournal_80_2019. PMID: 32547631; PMCID: PMC7294180.
12. Tamanuki T, Namura M, Aoyagi T, Shimizu S, Suwa T, Matsuzaki H. Effect of Intraoperative Imprint Cytology Followed by Frozen Section on Margin Assessment in Breast-Conserving Surgery. Ann Surg Oncol. 2021 Mar;28(3):1338-1346. doi: 10.1245/s10434-020-08955-z. Epub 2020 Aug 19. PMID: 32815080.
13. Tamanuki T, Namura M, Aoyagi T, Shimizu S, Suwa T, Matsuzaki H. Effect of Intraoperative Imprint Cytology Followed by Frozen Section on Margin Assessment in Breast-Conserving Surgery. Ann Surg Oncol. 2021 Mar;28(3):1338-1346. doi: 10.1245/s10434-020-08955-z. Epub 2020 Aug 19. PMID: 32815080.
14. Ashraf Aem, Mustafa Ez, Fattouh Mk, Manal Me. Margin Assessment in Breast Conservative Surgery and Concordance between Frozen and Paraffin Section Results: A Retrospective Study. The Medical Journal of Cairo University. 2022;90(12):2481-7. DOI: 10.21608/mjcu. 2022. 295323
15. Hashmi AA, Naz S, Ahmed O, Yaqeen SR, Afzal A, Asghar IA, Irfan M, Faridi N. Diagnostic Accuracy of Intraoperative Touch Imprint Cytology for the Diagnosis of Axillary Sentinel Lymph Node Metastasis of Breast Cancer: Comparison With Intraoperative Frozen Section Evaluation. Cureus. 2021 Jan 28;13(1):e12960. doi: 10.7759/cureus.12960. PMID: 33659115; PMCID: PMC7920232.
16. Vinod K, Aroul T, Vaithi KAR. Diagnostic Utility of Imprint Cytology for Assessment of Breast Lumps. Journal of Datta Meghe Institute of Medical Sciences University. 2022;17(3):709-12. DOI: 10.4103/jdmimsu.jdmimsu_189_20
17. Lofterød T, Frydenberg H, Flote V, Eggen AE, McTiernan A, Mortensen ES, Akslen LA, Reitan JB, Wilsgaard T, Thune I. Exploring the effects of lifestyle on breast cancer risk, age at diagnosis, and survival: the EBBA-Life study. Breast Cancer Res Treat. 2020 Jul;182(1):215-227. doi: 10.1007/s10549-020-05679-2. Epub 2020 May 20. PMID: 32436147; PMCID: PMC7275030.
18. Wei S. Hormone receptors in breast cancer: An update on the uncommon subtypes. Pathol Res Pract. 2023 Oct;250:154791. doi: 10.1016/j.prp.2023.154791. Epub 2023 Sep 3. PMID: 37672851.
19. Devi RS, Kumar A, Singh A, Durgapal P, Kishore S. Ravi Hari Phulware; Department of Pathology and Laboratory Medicine, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India. Journal of Cytology. 2024 Nov 1;41:S39. DOI: 10.4103/joc.joc_145_24
20. Maloney BW, McClatchy DM, Pogue BW, Paulsen KD, Wells WA, Barth RJ. Review of methods for intraoperative margin detection for breast conserving surgery. J Biomed Opt. 2018 Oct;23(10):1-19. doi: 10.1117/1.JBO.23.10.100901. PMID: 30369108; PMCID: PMC6210801.
21. Tamhane AN, Shukla S, Acharya S, Acharya N, Hiwale K, Bhake A. Intraoperative Surgical Margin Clearance - Correlation of Touch Imprint Cytology, Frozen Section Diagnosis, and Histopathological Diagnosis. Int J Appl Basic Med Res. 2020 Jan-Mar;10(1):12-16. doi: 10.4103/ijabmr.IJABMR_325_18. Epub 2020 Jan 3. PMID: 32002379; PMCID: PMC6967348.