Original Article

Frozen Section versus Paraffin Section in Diagnosis of Breast Lesions: A Comparative Study

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Abstract

Background: Frozen section (FS) examination has a number of indications such as identification of tissue type, benign versus malignant nature of the tissue, type of malignancy, determination of surgical margins, positivity of lymph nodes, and presence of malignant implants and/or metastasis in other tissues. Contraindications to the use of FS exist such as small lesions that could be destroyed by the freezing and sectioning and leaving no tissue for a definitive diagnosis. Therefore, this prospective study was planned to compare the accuracy of FSs versus paraffin sections in diagnosis of breast lesions. **Subjects and Methods:** The present prospective study was conducted from December 2008 to September 2010 in the Department of Pathology, GSVM. Medical College, Kanpur. A total of 115 cases were studied including benign and malignant breast lesions. Results were compared between FS diagnosis, and gold standard paraffin section diagnosis was evaluated, following Hematoxylin and Eosin staining and analyzed for accuracy in terms of false positivity and false negativity. **Results:** Out of 115 cases in our study, concordance was found in 109 cases. In our study, concordance for malignant breast lesion was 100%, whereas for benign lesions, it was 95.9%. Four cases (3.5%) were deferred to paraffin section diagnosis and two cases (1.8%) were misdiagnosed on FS. **Conclusions:** Diagnosis by FS is accurate to 100% in case of malignancy and confirming up to 96% for benign lesions. Its use, thus during breast surgery, is advocated for better clinical management of patients.

Keywords: *Benign, breast carcinoma, frozen section, malignant, paraffin section*

Introduction

Frozen section (FS) is a rapid diagnostic procedure performed on tissues obtained intraoperatively. FS technique has been used for >100 years.[1] Breast was the earliest organ to be studied by FS in 1891.Since then, FS has become a popular tool for the intraoperative evaluation of various breast lesions and playing a vital role in making appropriate therapeutic decisions. FS has a number of indications including identification of tissue type, to differentiate benign versus malignant nature of tissue, type of malignancy, determination of surgical margins, positivity of lymph nodes, and presence of malignant implants in other tissues.[2,3] FS diagnosis is also extensively used in various branches of pathology such as intraoperative diagnosis has been a useful neurosurgery tool for maximal required resection and minimal morbidity and to differentiate neoplastic from nonneoplastic lesions.[4]

The use of FS consultation in surgery of the head and neck appears an important tool, albeit FS for clearance of surgical margins has a much greater use in head and neck surgery than in any other surgical discipline.[5] Certain special stains for fat and a few immunohistochemical studies, particularly immunofluorescence, can also be performed on FS.

Subjects and Methods

This prospective study was conducted for 2 years during December 2008–September 2010 in Department of Pathology, GSVM Medical College, Kanpur, following the ethical approval from the Ethical Committee of the institute. For the study, fresh breast tissue specimens, operated on the same day, were taken. A total of 115 cases were studied. In this study, fresh specimens from operation theatre were obtained from patients undergoing mastectomy or lumpectomy of breast and sent to the Department of Pathology covered with saline moist gauze. In the department, the tissue was divided into two parts: one for FS and another for permanent paraffin sections.

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- Preparation of FSs: Fresh tissue was kept on special cassette, covered with optical coherence tomography (embedding medium for FS), and allowed to freeze inside cryostat and then sections were cut at 5–7 μ thickness. Sections were stained with Harris hematoxylin for 2 min and then rinsed in tap water for 5 s. After rinsing, the tissue was differentiated in 1% acid alcohol for 1–2 s and again rinsed in water for 5 s and then stained in eosin for 30 s. The tissue was dehydrated, cleared, and mounted in distyrene polystyrene xylene
- Preparation of paraffin section: The tissue was placed in formalin and submitted for permanent paraffin sections which were stained by Hematoxylin and Eosin (H and E), by standardized methods.

The study included only the benign tumors, tumor-like lesions, and malignant lesions of breast of various age groups.

Results were evaluated and grouped into four categories:

1. False positive, when a benign lesion was diagnosed as malignant on FS
2. False negative, malignant lesion was diagnosed as benign on FS
3. Deferred, when a definitive decision was not possible on FS
4. Incorrect histological typing or grade and compared with paraffin block.

Results

In this study of 115 cases, concordance was found in 109 (94.8%) cases, 2 were false negative, and no opinion was possible in 4 (3.5%) cases and deferred on diagnosis by paraffin block. However, none was found as false positive group [Table 1.] The diagnostic accuracy of FS in cases of malignant breast lesions was 100% while 95.9% for benign cases [Figure 1]. Minor modification in grade or typing of lesion was noted in two cases.

Discussion

FS technique for intraoperative pathological diagnosis has been used for >100 years. The development of a cryomicrotome or popularly known as cryostat in 1959 has revolutionized the FS technique.[6] FS provides a rapid microscopic diagnosis that can guide intra- or perioperative management of a patient with various breast lesions.

Table 1: Accuracy of frozen section diagnosis versus paraffin section diagnosis (*n*=115)

Breast lesion	Frozen section diagnosis	Paraffin section diagnosis	False positive	False negative	Accuracy (%)
Benign	46	47	-	2	95.9
Malignant	65	68	-	-	100
Deferral	4	3 malignant 1 benign	-	-	3.5
Total (benign and malignant)	109	115	-	-	94.8

Breast carcinoma is the second most common malignant tumor among rural Indian women after carcinoma cervix, whereas in urban Indian women, breast carcinoma overcomes the incidence of carcinoma cervix. The present prospective study was aimed to evaluate the accuracy of FS diagnosis in comparison and to conventional H and E and to analyze the discrepancies in the diagnosis of various breast lesions if any.

In our study, a total of 115 cases were studied including 47 benign and 68 malignant breast lesions as diagnosed on paraffin embedded, H and E sections.

Out of 115 cases in the present study, 113 cases (98.3%) were females. There were only two cases (1.8%) of male and both were breast carcinoma. According to different studies by Holleb *et al*. and Wainwright, male breast cancer represents only 1% to 2% of all mammary cancer.[7,8]

Analysis of the present study revealed an accuracy rate of 95.9% in case of benign breast lesions, 100% in cases of malignancy, false-positive rate 0%, false-negative rate 1.8%, and rate of deferral as 3.5% well within the range reported in the literature. In the present study, two cases (1.8%) required minor modification on permanent histological section. One case was diagnosed as infiltrating lobular carcinoma on frozen, which on subsequent paraffin section found to be infiltrating ductal carcinoma. This discrepancy was because of the presence of relatively few tumor cells in the tissue examined. The other cases required modification in the grading of the tumor, which was because of poor sectioning and crushing artifacts.

In our study, four cases (3.5%) were deferred to paraffin section analysis. Out of these four cases, one was infiltrating lobular carcinoma, two cases were infiltrating ductal carcinoma, and one case was benign intraductal papilloma. In case of lobular carcinoma due to freezing artifacts, it was quite difficult to ascertain the nature of malignancy. In cases of infiltrating ductal carcinoma, the diagnostic material was insufficient for diagnosis, but patients' history and mammographic findings were in favor of carcinoma, which led to the deferral of these cases. Benign intraductal papilloma was deferred because of its complex ramifications and artifactual nuclear atypia which simulated malignancy on FS.

The lesions most commonly deferred in the past were intraductal carcinoma, intraductal papillomas, epithelial hyperplasia, and lobular carcinoma *in situ*.[9] Agnantis *et al*. recommended that ductal hyperplasia, which appears cytologically atypical but does not reveal either gross or convincing microscopic features of carcinoma, should be deferred.[10]

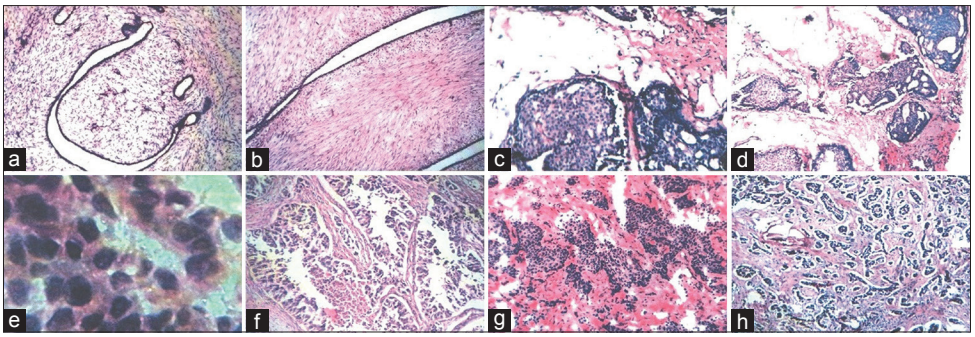

Figure 1: (a) Photomicrograph frozen section showing benign phyllodes tumor (H and E, ×100). (b) Photomicrograph phyllodes tumor breast on paraffin section (H and E, ×100). (c) Photomicrograph of atypical ductal hyperplasia breast on frozen section (H and E, ×100). (d) Photomicrograph atypical ductal hyperplasia breast, paraffin section (H and E, ×100). (e) Photomicrograph infiltrating lobular carcinoma breast on frozen section (H and E, ×400). (f) Photomicrograph infiltrating ductal carcinoma which was misdiagnosed as infiltrating lobular carcinoma on frozen section. (Paraffin section H and E, ×100). (g) Photomicrograph infiltrating ductal carcinoma not otherwise specified on frozen section (H and E, ×100). (h) Photomicrograph infiltrating ductal carcinoma breast grade 2 (H and E, ×100)

In the present prospective study, two cases (1.8%) were misdiagnosed on frozen section. One case was diagnosed as fibroadenoma but found to harbor foci of ductal carcinoma *in situ* on permanent paraffin section. The second case was diagnosed as fibrocystic disease on frozen section, but the case was infiltrating ductal carcinoma with fibrocystic disease changes on paraffin section examination. The discrepancy in diagnosis was due to sampling error. The area harboring the malignancy was not sampled which led to the misdiagnosis.

The malignant lesions which are commonly underdiagnosed as benign are invasive lobular carcinoma and intraductal carcinoma. The incidence of false negativity on frozen tissues increases with diminishing size of the lesion, due to artifactual distortion on freezing and the apprehension about lack of adequate tissue for paraffin section. Hence, the association of directors of anatomic surgical pathology recommends that lesions <1.0 cm should not be frozen.[11] Evidence from literature shows that the benign lesions which were frequently overdiagnosed as malignancy on frozen section included microglandular adenosis, epithelial proliferations, sclerosing adenosis, papillomatosis, and fat necrosis.[12,13]

On analysis of the published data on frozen section of breast lumps between 1976 and 1997, the accuracy rate was found to be between 95.84% and 99.8%, false-positive rate between 0% and 0.79%, false-negative rate between 0.23% and 3.57%, and the rate of deferral was between 0.37% and 20.5%.

Analysis of the present study revealed an accuracy rate of 94.7%, false-positive rate 0%, false-negative rate 1.7%, and the rate of deferral as 3.5%, well within the range reported in literature.

One of the most important elements in maintaining the reliability of breast lesions, and for minimizing the frequency of false positive reports in FS, is the option to defer a diagnosis to permanent paraffin section. In this study, diagnosis was delayed in 3.5% of cases, and nearly half of the lesions proved to be carcinoma and included some of the most difficult breast lesions to interpret, namely those that called for making distinctions between duct and lobular hyperplasia or carcinoma. False-negative cases constituted a smaller percentage than deferred diagnosis. The lesions most likely to be overlooked were noninvasive carcinomas. This well-recognized limitation is the reason to await the final paraffin section report even if the frozen section had been reported to be benign breast lesion.

Conclusion

Our study proved that frozen section procedure for the intraoperative diagnosis of breast lesions is highly accurate in spite of the difficulties facing the pathologist with the frequent borderline or premalignant lesions. In the hands of competent experienced pathologist, the frozen section is one of the most accurate and reliable microscopic diagnostic procedure available. The information obtained from the frozen section could well be used in deciding the available alternatives in the management of various breast lesions.

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Conflicts of interest

There are no conflicts of interest.

References

1. Niu Y, Fu XL, Yu Y, Wang PP, Cao XC. Intra-operative frozen section diagnosis of breast lesions: A retrospective analysis of 13,243 Chinese patients. Chin Med J (Engl) 2007;120:630-5.
2. Ackerman LV, Ramirez GA. The indications for and limitations of frozen section diagnosis; A review of 1269 consecutive frozen section diagnoses. Br J Surg 1959;46:336-50.
3. Jennings ER, Landers JW. The use of frozen section in cancer diagnosis. Surg Gynecol Obstet 1957;104:60-2.
4. Groves R, Hesselvik M. The diagnostic accuracy of the frozen section examination in neurosurgery. Acta Neurol Scand 1966;42:268-74.

5. DiNardo LJ, Lin J, Karageorge LS, Powers CN. Accuracy, utility, and cost of frozen section margins in head and neck cancer surgery. Laryngoscope 2000;110:1773-6.
6. Jaafar H. Intra-operative frozen section consultation: Concepts, applications and limitations. Malays J Med Sci 2006;13:4-12.
7. Holleb AI, Freeman HP, Farrow JH. Cancer of male breast. II. N Y State J Med 1968;68:656-63.
8. Wainwright JM. Carcinoma of the male breast. Arch Surg 1927;14:836-59.
9. Bianchi S, Palli D, Ciatto S, Galli M, Giorgi D, Vezzosi V, *et al.* Accuracy and reliability of frozen section diagnosis in a series of 672 nonpalpable breast lesions. Am J Clin Pathol 1995;103:199-205.
10. Agnantis NJ, Apoatolikas N, Christodoulou I, Petrakis C, Garas J. The reliability of frozen section diagnosis in various breast lesions: A study based on 3451 biopsies. Resent Results Cancer Res 1984;90:205-10.
11. Ferreiro JA, Gisvold JJ, Bostwick DG. Accuracy of frozen-section diagnosis of mammographically directed breast biopsies. Results of 1,490 consecutive cases. Am J Surg Pathol 1995;19:1267-71.
12. Lessells AM, Simpson JG. A retrospective analysis of the accuracy of immediate frozen section diagnosis in surgical pathology. Br J Surg 1976;63:327-9.
13. Tinnemans JG, Wobbes T, Holland R, Hendriks JH, van der Sluis RF, Lubbers EJ, *et al.* Mammographic and histopathologic correlation of nonpalpable lesions of the breast and the reliability of frozen section diagnosis. Surg Gynecol Obstet 1987;165:523-9.