

Scrape Cytology in Rapid Intraoperative Diagnosis of Tumors

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Abstract:

Background: Intraoperative diagnosis of surgically removed specimens can be achieved by gross examination with the help of frozen sections & or cytologic examinations. Various cytologic techniques including imprint, fine needle aspiration, image guided aspiration cytology; squash smears and scrape cytology may be used for intraoperative evaluation of tumors & surgical margins. Histopathology remains the ultimate gold standard in the tumor diagnosis.

Aims / Objectives: To evaluate the role of scrape cytology for rapid intraoperative diagnosis of tumors. It can be utilized as a learning tool for cytopathologist and postgraduate students.

Material and Method: In this study surgically removed specimens of tumors from various systems were studied. Scrapings were collected from each specimen before formalin fixation and the smears were stained with rapid H&E.

Results: For surgical specimens studied by scrape cytology the diagnostic accuracy rate was 93.49 %. Out of 169 cases studied, 158 were correctly diagnosed as benign or malignant lesions.

Conclusion: Intraoperative scrape cytology is a simple inexpensive, rapid, accurate cytodagnostic technique, where frozen section facilities are not available. . It can also be used to assess the clearance of surgical margins. The material obtained from scrape cytology can be utilized as teaching material for post graduate students. Knowledge and expertise developed can also be used for interpretation of fine needle aspiration cytology.

Keywords: Intraoperative, Scrape cytology, FNAC.

I. Introduction

The diagnostic applications of frozen sections and imprint cytology are well known. This study was conducted to evaluate the role of scrape cytology, which is a modification of imprint cytology, in the rapid intraoperative diagnosis of tumors.^[1] Many studies have been done in the past to evaluate the role of cytology in intraoperative diagnosis of tumor. These studies have concluded that cytology has the advantage of being much less time consuming, easy to adopt, reliable and does not require special instruments or set ups.^[1-3] In the present study, 169 surgical specimens studied by scrape cytology, the diagnostic accuracy was 93.49%. The diagnostic accuracy was better than reported for imprint cytology or frozen sections alone in various studies. Scrape cytology is advocated as a routine intraoperative procedure, especially where frozen section facilities are not available.^[1] Scrape cytology can be employed routinely in the intraoperative diagnosis in conjunction with frozen section.^[1-4] The use of either frozen section or cytological examination alone has an acceptable rate (93–97%) of correct diagnosis, with regard to interpretation of benign versus malignant.^[3,4] Commonly used methods for obtaining and preparing cells for cytological evaluation are touch preparation, fine needle aspiration cytology (FNAC) and scrape smear preparation. Scrape preparations yield cellular smears.^[3]

II. Material And Method

This study was a prospective study. Surgically removed specimens were sent to our department for histopathological examination. Gross examination of these specimens was done. Specimen was then cut with a sharp knife into two halves. The cut surface was wiped off the excess blood with the filter paper gently. The most appropriate and representative area was selected for scraping. The area was scraped with glass slide. Semiliquid drop obtained was spread over a glass slide in the same manner as FNA. 3-4 slides per case were taken from different representative areas. These slides were immediately fixed in 95 % ethyl alcohol and stained with rapid H&E stain (Pathozyme). These slides were examined immediately and reported as benign or malignant. Total time taken for smear preparation, staining & reporting was about 15 minutes. Specimens were fixed in 10 % formalin. Sections were taken from different areas. Tissue processing was done in routine way in automatic tissue processor and paraffin blocks were performed. 3-5µm thick sections were stained with H & E. The diagnosis of scrape cytology was compared with final histopathological diagnosis.

III. Results

The diagnostic accuracy of scrape cytology was satisfactory with 93.49 % of cases correlated with final histopathological diagnosis. This study included surgically removed specimens (Table 1) from various sites of body such as oral cavity, thyroid, parathyroid, lung, GIT, liver, kidney, testis, breast, ovary and soft tissue (Figures 1- 5).

Table 1

Systemwise Distribution of cases diagnosed on cytology and histology

Organs/System No of cases	Cytological diagnosis	Histopathological diagnosis
Oral Cavity 5	Squamous cell carcinoma (5)	Squamous cell carcinoma(5)
Thyroid 17	Multinodular goiter (6) Follicular neoplasm (6) Follicular Carcinoma (1) Poorly differentiated carcinoma (1) Papillary carcinoma (3)	Multinodular goiter (6) Follicular adenoma (5) Follicular Carcinoma (2) Poorly differentiated carcinoma (1) Papillary carcinoma (3)
Parathyroid 1	Parathyroid adenoma (1)	Parathyroid adenoma (1)
Lung 3	Aspergiloma (1) Adenocarcinoma (1) Squamous cell carcinoma (1)	Aspergiloma (1) Adenocarcinoma (1) Squamous cell carcinoma (1)
Oesophagus 7	High grade dysplasia (1) Squamous cell carcinoma (5) Poorly differentiated Carcinoma (1)	Squamous cell carcinoma (6) Adenocarcinoma (1)
Stomach 5	Adenocarcinoma (4) GIST (1)	Adenocarcinoma (4) GIST (1)
Small intestine 2	GIST (1) Carcinoid (1)	GIST (1) Carcinoid (1)
Colon 6	Adenocarcinoma (6)	Adenocarcinoma (6)
Rectum 3	Inflammation with moderate dysplasia (1) Adenocarcinoma (2)	Adenocarcinoma (3)
Liver 2	Hepatoblastoma (1) HCC (1)	Hepatoblastoma (1) HCC (1)
Kidney 4	Hydatid cyst (1) Angiomyolipoma (1) Renal cell carcinoma (2)	Hydatid cyst (1) Angiomyolipoma (1) Renal cell carcinoma 2 {Clear cell carcinoma (1) Papillary variant(1)}
Testis 5	Granulomatous inflammation (1) Xanthogranulomatous inflammation (1) Seminoma (2) Germ cell tumor (1)	Granulomatous inflammation (1) Xanthogranulomatous inflammation (1) Seminoma (2) Embryonal carcinoma (1)
Breast 18	Fibroadenoma (6) Proliferative breast disease (1) Phyllode (1) Benign breast lesion (1) Colloid carcinoma (1) Ductal carcinoma(7) Ductal Carcinoma (1)	Fibroadenoma (6) Adenomyoepithelioma (1) Phyllode (2) Colloid carcinoma (1) Infiltrating Ductal carcinoma(7) Infiltrating Lobular carcinoma (1)

Organs/System No of cases	Cytological diagnosis	Histopathological diagnosis
Ovary 72	Benign serous cystadenoma (18) Serous Cystadenocarcinoma (12) Benign mucinous cystadenoma (17) Mucinous Cystadenocarcinoma (6) Teratoma mature (12) Inconclusive (2) Sertoli cell tumor (1) Granulosa cell tumor (1) Germ cell tumour (2) Metastatic signet ring cell carcinoma (1)	Benign serous cystadenoma (19) Serous Cystadenocarcinoma (11) Benign mucinous cystadenoma(16) Borderline mucinous cystadenoma(1) Mucinous Cystadenocarcinoma (6) Teratoma mature (11) Immature teratoma (1) Twisted ovarian cysts (2) Sertoli cell tumor (1) Granulosa cell tumor (1) Dysgerminoma (1) Mixed germ cell tumour (1) Metastatic signet ring cell carcinoma (1)
Soft tissue 19	Lipoma (7) Benign spindle cell tumour s/o benign PNST(2) No opinion possible (1) No opinion possible (1) Low grade spindle cell sarcoma (1) Malignant fibrous histiocyoma (3) Spindle cell sarcoma (1) Liposarcoma (1) Pleomorphic sarcoma (2)	Lipoma (7) Neurofibroma (1) Neurilemmoma (1) Lymphangioma (1) Hemangioma (1) Proliferating fasciitis (1) Malignant fibrous histiocyoma (3) MPNST (1) Liposarcoma (1) Pleomorphic sarcoma (2)

The systemic distribution of cases, diagnosis and cytohistological correlation are mentioned in Table 1. Accuracy rate, number of concordant and discordant cases, number of false negative and false positive cases were mentioned in Table 2. Diagnosis was inconclusive in 4 cases. Two cases were twisted ovarian tumors; one case was of hemangioma and one of lymphangioma. In these three cases scrape cytology smears were haemorrhagic and in the case of lymphangioma no cells were seen.

Table2-Organ wise distribution of cases correctly diagnosed as benign or malignant.

Organ/system	Total cases	no.of	Correctly diagnosed	Histopathological diagnosis	
				Concordant (diagnostic accuracy)	Discordant
Oral cavity	5		5	100%	
Thyroid	17		16	94.11%	1 False negative
Parathyroid	1		1	100%	
Lung	3		3	100%	
Oesophagus	7		6	85.71%	1 false negative
Stomach	5		5	100%	
Small intestine	2		2	100%	
Colon	6		6	100%	
Rectum	3		2	66.66%	1 false negative
Liver	2		2	100%	
Kidney	4		4	100%	
Testis	5		5	100%	
Breast	18		18	100%	
Ovary	72		67	93.05%	2- Inconclusive

				2 false negative 1- false positive
Soft tissue	19	16	84.21%	2-Inconclusive 1- false positive
Total	169	158	93.49%	11

In seven cases cytological diagnosis was discordant with histopathology. In thyroid, cytologically follicular carcinomas and adenomas were labeled as follicular neoplasms, as we could not comment on capsular invasion in cytology. This is a known limitation of cytology. But in one case in the gross specimen small nodular extension of tumor was seen beyond the capsule. Scrape was taken from that nodule, which showed features of follicular neoplasm.

Fig. 1

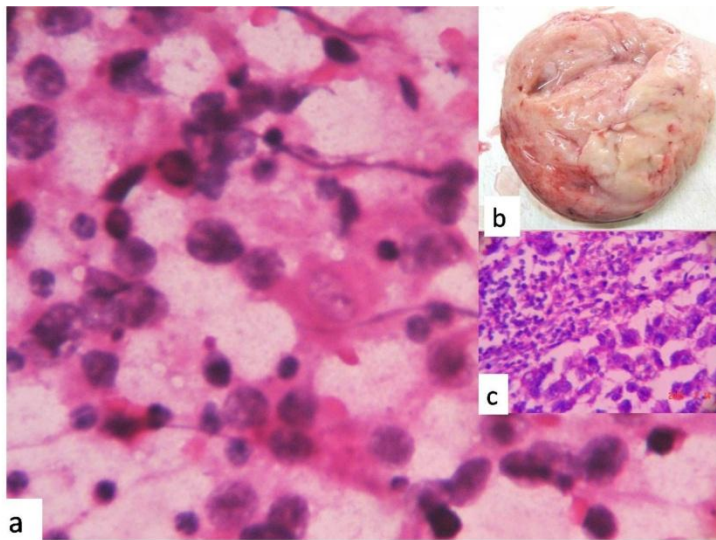


Fig. 2

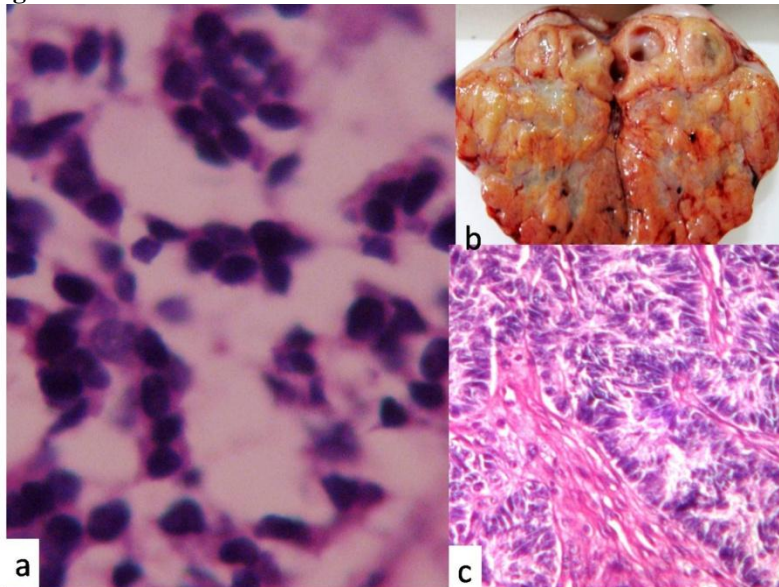


Fig.3

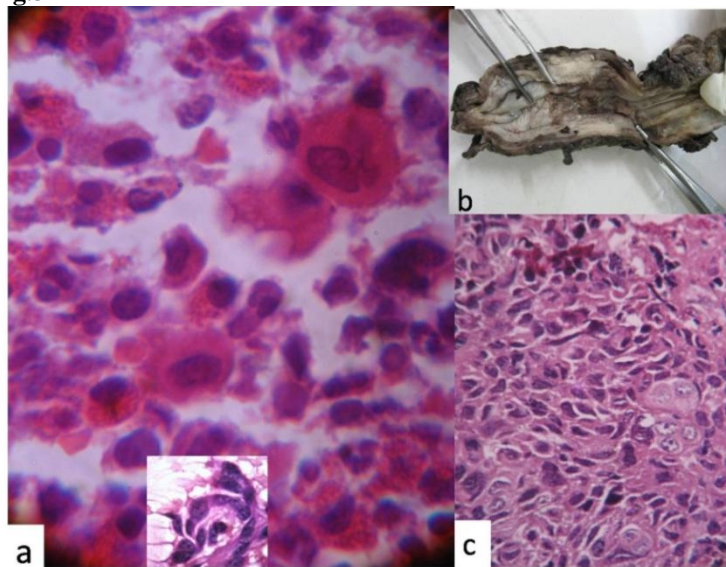


Fig.4

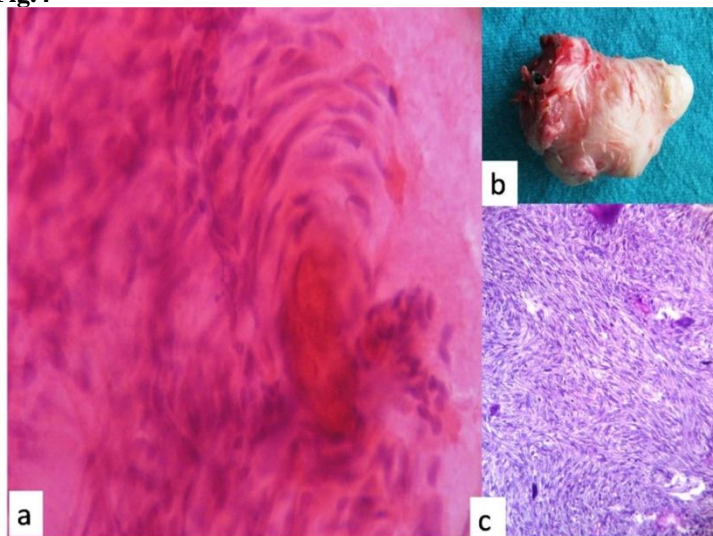


Fig.5

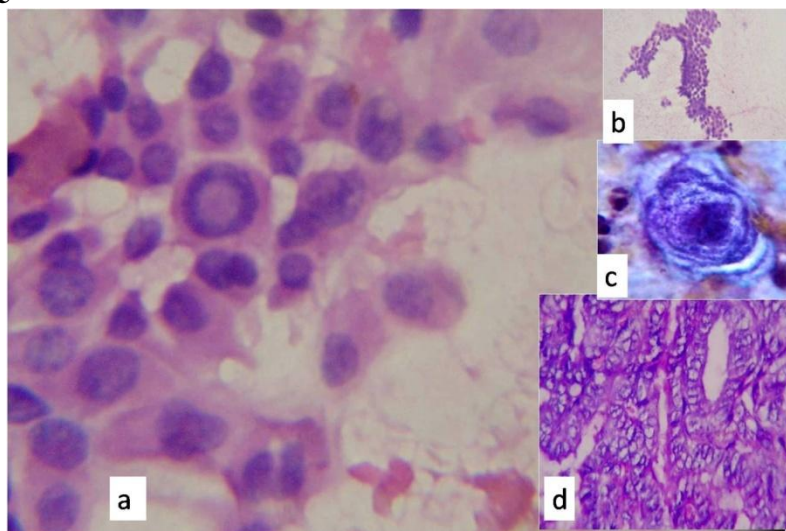


Fig.6

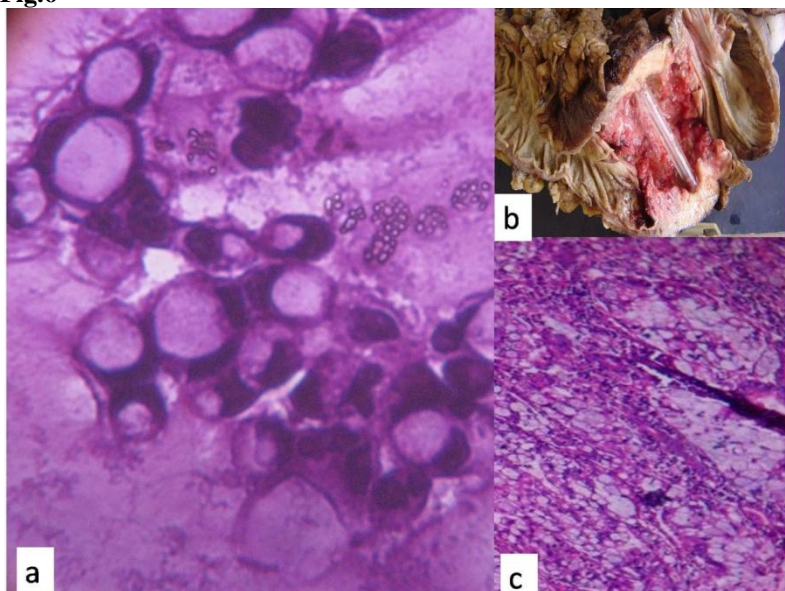
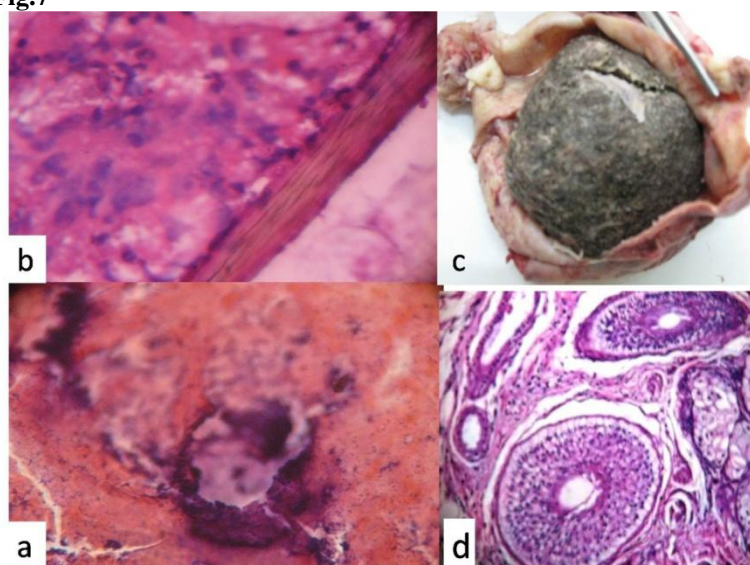


Fig.7



So cytologically this case we could report as follicular carcinoma. In oesophagus, less cellularity with few mature squamous cells was seen in one case. So it was misdiagnosed as high grade dysplasia but histologically that turned out to be well differentiated squamous cell carcinoma. In rectum, also one case was cytologically misinterpreted as inflammation with moderate dysplasia. Histological diagnosis was well differentiated adenocarcinoma. There was extensive desmoplasia and stricture formation which led to less cellular yield in scrape cytology and misdiagnosed as dysplasia. One serous cystadenoma of ovary was overdiagnosed cytologically as serous cystadenocarcinoma due to high cellular yield. One case of borderline mucinous tumor was misdiagnosed as mucinous cystadenoma as cellular atypia was not significant and proliferative changes were seen focally on histology. This is also a known limitation of cytology. One case of immature teratoma was misinterpreted as mature teratoma cytologically due to inadequate sampling. Immature elements were not sampled properly in cytology. In soft tissue, one case of proliferating fasciitis was overdiagnosed as low grade spindle cell sarcoma. Overall diagnostic accuracy was satisfactory.

IV. Discussion

Scrapings of the cut surface prior to fixation facilitates the harvesting of cells, hence scrape cytology could be preferred over touch preparation / imprint cytology as the former technique would yield much more material than the latter. ^[5] In scrape preparations, cut surface of the specimen is scraped with the edge of the

glass slide. Relevant clinical data & gross morphological features are valuable information for evaluating the cytological smears.

Touch preparation yields less cellular smears than scrape smears.^[6] Esteban et al also found that smears prepared after scrapings of tumor yielded uniformly cellular smears.^[7] Intra operative cytology increases diagnostic accuracy of frozen sections for the confirmation of various lesions. Scrape cytology can be an excellent adjunct to frozen section technique.^[1, 8] Dudgeon and Patrick were first to describe the use of imprint smears of fresh tissues in rapid microscopic diagnosis of tumors. Scraping of the cut surface prior to smearing facilitates the harvesting of cells. Hence, scrape cytology could be preferred over touch preparation/imprint cytology as the former technique would yield much more material than the latter.^[9]

Sidham et al conducted a study to evaluate the role of scrape cytology, which is a modification of imprint cytology, in the rapid intra operative diagnosis of tumors. The diagnostic accuracy was 98.4 % & the false positive rate was 0.4 %. The diagnostic accuracy was better than reported for imprint cytology or frozen sections alone. Scrape cytology can be an excellent adjunct to frozen section technique.^[11]

We also found that scrape cytology smears gave very good yield and uniformly cellular smears. Gross examination is very important for interpretation of cytology. Cytology of various neoplasms may be difficult to interpret alone without any accompanying data. Clinical details and gross morphology are always important in arriving at a diagnosis on cytology.

Mair S et al compared the diagnostic accuracy and quality of frozen section and cytological preparation from 206 surgical specimens with the use of both techniques, 99.5 % of cases were interpreted correctly, at least in regard to benign versus malignant diagnoses. Because significant additional time, equipment, stains, laboratory space or personnel are not needed to implement intra operative cytologic studies in a routine anatomic pathology laboratory. The authors advocate the simultaneous use of Frozen Section & cytologic studies in the specified context.^[4]

Gal R studied the cases of breast carcinoma in which only lumpectomy was performed. Here author used scrape cytology as a method for examination of lumpectomy margins. Good cytological and histopathological correlation was found.^[2]

We achieved 100 % accuracy in diagnosing benign or malignant lesions of stomach, small intestine, colon, liver, kidney, testis and breast.

Rao et al^[10] studied the scrape cytology in ovarian neoplasms. Authors came to the conclusion that scrape cytology is a simple rapid, accurate, adjunctive cytodagnostic method and its routine utilization in ovarian lesions could aid in expanding the cytological knowledge of ovarian neoplasms. Characteristic cytological pattern was noted in various types of surface epithelial, sex cord stromal and germ cell tumors. This technique had limited value in mucinous tumors to distinguish borderline cases from invasive carcinoma. Formalin did not interfere or produce any remarkable changes in cytomorphology.^[10]

Khunamornpong S. and Siriaungkul S. evaluated the application of scrape cytology in the diagnosis of ovarian lesions. Accuracy rate of scrape cytology was 95 % in benign, 47 % in the low malignant potential and 98% in the malignant group. So they came to conclusion that there are limitations of scrape cytology in the diagnosis of Low malignant potential and mucinous tumors which require histologic architectural evaluation & adequate histologic sampling. Scrape cytology is simple, rapid and inexpensive adjunctive technique that should be used in intra operative consultation for ovarian lesions. Intraoperative diagnosis of ovarian lesions can be achieved by gross examination with the help of frozen sections and/or cytologic examination. Various cytologic techniques, including imprint, fine-needle aspiration, and scrape, may be used. In this study, authors evaluated the application of scrape cytology in the diagnosis of ovarian lesions. The cytologic diagnosis was primarily based on findings in air-dried, Diff-Quik-stained smears in correlation with clinical and intraoperative findings were cytologically examined. There was no misdiagnosis between the benign and malignant categories. The histologic subtypes were correctly predicted in 78% of cases.^[11]

We also came to the conclusion that whenever the architecture is required along with cellular features for the diagnosis, cytology has few limitations. Due to that we also misdiagnosed one case of borderline mucinous tumor as benign mucinous cystadenoma and a case of serous cystadenoma overdiagnosed as serous cystadenocarcinoma on scrape cytology. In thyroid, cytologically one case of follicular carcinomas was labeled as follicular neoplasms, as we could not comment on capsular invasion. This is a limitation of cytology. But in one case in the gross specimen small nodular extension of tumor was seen beyond the capsule. Scrape was taken from that nodule, which was showing features of follicular neoplasm. So cytologically this case was interpreted as follicular carcinoma.

Rapid intraoperative scrape cytological examination for diagnosing surgical margin involvement of specimens obtained by breast conservation surgery was evaluated. Four surgical margins (nipple side, two lateral sides and distal side) of the removed breast tissue were cytologically examined and histologically compared following segmentectomy in 50 breast cancer patients (200 margins). Intraductal carcinoma had a tendency to spread most extensively to the nipple, compared with other margins. The margin positive rate of

tumors with ductal spread (DS) of over 20 mm was significantly higher than in tumors with a DS under 20 mm (52.2% vs 7.4%) ($P < 0.001$). Of 50 candidates 10 patients underwent total mastectomy due to positive margins on repeat cytologic examination after re-excision. The sensitivity, specificity and accuracy of cytology were 96.4%, 90.7% and 91.5%, respectively. Scrape cytology is useful to determine surgical margin involvement after segmentectomy for breast cancer, although overestimation of involvement will tend to result. To conclude, intraoperative scrape cytology is a simple inexpensive, rapid, accurate cytodiagnostic technique, where frozen section facilities are not available. The material obtained from scrape cytology can also be utilized as teaching material for post graduate students. Knowledge and expertise developed can also be used for interpretation of fine needle aspiration cytology.

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Legends to figures-

- [1]. Figure 1-(a) Photomicrograph of scrape cytology smear of seminoma of testis showing polygonal to round, loosely cohesive cells; round nucleus with prominent nucleolus and scattered lymphocytes in the background (H & E, x400). (b) Gross photograph (c) Histopathology of the same.
- [2]. Figure 2- (a) scrape cytology smear of sertoli cell tumor showing columnar to cuboidal cells in groups and tubular arrangement. (H&E, x400). (b) gross photograph showing circumscribed yellow tumor mass. (c) histopathology of the same.
- [3]. Figure 3-(a) Photomicrograph of scrape cytology showing many keratinized squamous cells with moderate nuclear enlargement, dyskeratosis, hyperchromatism of nuclei & few inflammatory cells (H&E, x400) (b) Gross photograph (c) Histopathology of same.
- [4]. Figure 4 (a) Photomicrograph of scrape smear of GIST of small intestine showing fragment of benign spindle cells in whorling and interlacing pattern. The cells have uniform nuclei. (b) Gross photograph (c) Histopathology of the same GIST.
- [5]. Figure 5-(a) Photomicrograph of scrape cytology of papillary carcinoma of thyroid showing ground glass nuclei and intranuclear inclusion (arrow) (H&E, x1000), (b) scrape smear showing papillary frond (H&E, x100) (c) Histopathology of the same.
- [6]. Figure 6 (a) Photomicrograph of scrape smear of mucin secreting adenocarcinoma showing signet ring cells with large mucin vacuole. Background also shows mucin. (H&E, x 10000). (b) gross photograph (c) Histopathology of the same tumor.