FROZEN SECTION UTILIZATION AND ACCURACY, KING ABDULAZIZ UNIVERSITY HOSPITAL EXPERIENCE

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ABSTRACT

OBJECTIVE : The aim of this study is to evaluate the utilization of frozen section service and its cost effectiveness, and to assess accuracy and discrepancy of frozen section service at King AbdulAziz University hospital. Material and methods: This study group consisted of 480 frozen sections specimens, which were examined in the department of Histopathology at King AbdulAziz University Hospital, Jeddah; over five and a half years from January 1997 to May 2002. The Histopathology records of all these frozen sections were retrieved and analysed by matching the frozen section diagnosis with the permanent diagnosis to evaluate the actual need of frozen section based on international standard. The permanent diagnosis is compared with the frozen section diagnosis to find out the discripant cases which were studied in detail. Results: The accuracy of major organs examined is 97-100%, with a mean of 99.1%. There are eight cases with discrepancy between frozen section diagnosis and permanent diagnosis. No false positive case is detected. CONCLUSION: Our frozen section experience showed high utilization of this service with high accuracy rate and proved that it is a very useful diagnostic tool for rapid decision making.

Key words : Frozen section, accuracy. Frozen section utilization, discrepancy.

INTRODUCTION

Historically in the 1800's, hardening of tissue to obtain thin sections for

histological examination was accomplished by freezing, according to McCarty(1) and Bauermeister(2). Since freezing was a temporary method, alternative methods, such as paraffing embedding, were discovered in the late 1800's. Because such permanent embedding required a significant time interval, frozen sections were rediscovered in the early 1900's to provide rapid histological diagnosis at the time of operation. Now, thin sections of good quality can be prepared by using the present day method. Because of this frozen section diagnosis of surgical specimens has found wide acceptance in the medical community, particularly among the surgeons, to make intra-operative decisions. The role and limitations of frozen section diagnosis have been well recognized, as shown by Jennings and Landers(3), Horn(4) and Nakazawa and co-workers(5) .

When defining frozen section technique, it is a rapid decision-making procedure that is required by a surgeon and performed by a qualified pathologist. It has a wide range of therapeutic implication. Its indication is variable from obtaining therapeutic decision at one side and to provide tissue for ancillary study on another side. Other important indications such as tissue identification, check margins of resection, and to determine the extent of the disease and the type of operation. The only contraindication of this procedure is a very small size biopsy, that will not allow enough tissue to be processed for permanent section. The arbitrary minimum size used by M.D. Anderson Group(6) is 3 mm tissue in its largest diameter, a sample size that is difficult to bisect without creating crushed artifacts, and most of the time there isn't enough residual tissue to make a final diagnosis on the basis of the permanent section. There are some other relative contraindications for frozen section variable between different laboratories, such as bony tissue, and potential, infectious specimen(6) . In such case the objective of frozen section is to obtain a diagnosis that may change therapy plan. The role of the pathologist in frozen section in general is to give the diagnosis which enable the surgeon to take a decision and not to make specific disease categories.

The objective of our study is to look at all frozen section performed at King Abdulaziz University Hospital, Department of Pathology, from Janu-

ary 1997 until May 2002 in order to obtain the utilization, accuracy rate and limitations of our intra-operative service. We hope that this study will be used as a quality control measure for our service and will help in further improvement of this service.

Table I – Annual distribution of frozen sections and comparison with total number of operations.

MATERIALS & METHODS

King Abdulaziz University Hospital is a 250-beded hospital located at the Western Part of the Kingdom, carrying out number of operations variable between 2231-5590 per year. Retrospective study is designed to look at all the frozen sections performed during the period of January 1997 until mid of May 2002. The total number of surgical specimens received by Pathology Department during this period were 18973 with total of 480 frozen sections (2.55%) (see table I). Surgical Pathology Department regulation is to book the frozen section on the day prior to the surgery through informing the Pathology lab on the possibility of the frozen section. Therefore. the pathologist on the rotation in that service will be informed. The clinical details and the previous histopathology diagnosis on that case will be reviewed. Large number of frozen sections are performed without previous booking (32%) (See table II Booking Regulation Assessment). Once the tissue is out from the patient in the operating room, the pathologist is called to the frozen section suite where he/she will look at the request, gross evaluate the specimen by cutting it into thin slices, a representative tissue is taken. The sample is put in a cryostat mould containing OCT (optimal cutting temperature solution) and snap freezing by a cryostat –30oC. The time required for freezing is 40-50oseconds. The tissue is sectioned, stained with hematoxylin and eosin stain or methyl blue for cytology smears. A few specimens are grossly reported after careful examination of real thin slices of the tissue. If the frozen section diagnosis suspects a neoplastic process, and the tumor size is large, a sample of fresh tumor tissue is kept at -70C for tumor bank, after removing the fat, normal tissue and necrotic tissue. A representative specimen may be submitted for glutaraldehyde for electron-microscopic examination, if required. The pathologist informs the surgeon directly or by the phone on the frozen section diagnosis. The diagnosis will be written in

ink on the back of the request and submitted with the specimen to the operating room nurse. The permanent resected specimen and the frozen section specimen will be submitted to the Pathology laboratory receiving area. In the Anatomical Pathology laboratory further examination and sectioning of the resected specimen and the frozen section specimen are done. More tissue is submitted for permanent section, and also the frozen section for comparison by the same pathologist(6). The tissue will be processed routinely then, embedding and cutting it and finally stained by hematoxylin, eosin and released to the same pathologist for their final assessment and diagnosis.

The following formula is used to analyze the accuracy rate of frozen section diagnosis, which was defined as the proportion of true results among all test results(7): %Accuracy = Number of True Positive cases / Total number of cases x 100.

All false negative cases at frozen section and all discrepant cases are evaluated by the author by examaning the frozen section slides and the permanent slides of frozen section and other sections individually.

Table III – Analysis of deffered cases with discripency and accuracy rates of major organs examined.

RESULTS

A retrospective study was designed to analyze 491 frozen section cases in time frame of 5.5 years, from january 1997 to May 2002 to compare and match the frozen section diagnosis with the permanent diagnosis. The highest frequency of frozen section requests were obtained from the breast (38%), followed by thyroid (17.5%) followed by ovaries (9.79%) and then lymph nodes (8.33%). The benign cases are 58.5% of these cases (281/480), the malignant cases are 41.9% (199/480). Table IV describes the percentage of benign and malignant lesions with the frequency for each individual organ examined in frozen section in detail. The cases are analyzed to categorise them into accurate diagnosis when the frozen section diagnosis exactly matches the permanent diagnosis; false positive when the lesion was diagnosed positive or malignant on frozen sections but it is different on permanent sections; false negative when the lesion is missed or diagnosed as benign on frozen sections and turned out to be malignant on permanent sections;

completely deferred cases when the final diagnosis on frozen is deferred until permanent sections is obtained, and partially deferred cases when a preliminary diagnosis is given at frozen section and the final diagnosis is awaited till the permanent sections is evaluated. The discrepant cases are classified as those having false positive or false negative cases. We found 8 false negative cases (1.04%) and no false positive case. (See table V). The discrepant cases which is considered as false negative are reclassified by the author based on the analysis into sampling errors, interpretational errors and wording errors. Cases which were deferred during the frozen sections were either completely defered (2 cases = 0.42%) or partially defered. In partially defered cases a preliminary diagnosis was given but final assessment was awaited till the permanent sections were examined. There were 34 cases (7%) which were partially defered. Table III discribes the distribition of thses defered cases for each organ examined-

Table 1. ANNUAL PERCENTAGE OF FROZEN SECTIONS AND COMPARISON WITH TOTAL NUMBER OF OPERATIONS

YEAR	NO. OF FROZEN SECTIONS	NO. OF TOTAL OPERATIONS	TOTAL HISTOPATH SP.	% OF FROZENS
1997	35	2231	2689	1.30%
1998	89	3231	3318	2.68%
1999	119	5586	3592	3.31%
2000	112	3433	3625	3.37%
2001	96	3871	4132	2.74%
2002 (5th Month)	29	1537	1617	2.10%
TOTAL	**480**	**19889**	**18973**	**2.55%**

Table II. BOOKING REGULATION ASSESSMENT
OCTOBER 2002 - MARCH 2002

Specimen	Total	Booked	Unbooked	Change in Management	
				YES	NO
Breast	77	63	14	59	18
Thyroid	51	24	7	21	10
Stomach	1	0	1	1	0
L. node	7	2	5	7	0
Colon	9	4	5	7	2
Ovarian cyst	21	17	7	18	3
Mass	14	4	10	13	1
Others	20	11	9	20	0

Table III. ANALYSIS OF DEFERRED CASES WITH DISCREPANCY AND ACCURACY RATES OF MAJOR ORGANS EXAMINED
(1997 - MAY 2002)

Organs examined	No. of cases	No. of cases partially deffered	No. of cases completely	Discrepancy	Accuracy rate
Thyroid	106	15	1	3	97.2
Breast	262	12	0	2	99.3
Ovary	55	1	0	0	100
Lymph node	43	6	1	0	100
Mean					99.125

Table IV.SUMMARY OF MAIN ORGANS AND BEHAVIOUR OF DISEASE DIAGNOSED ON FROZEN SECTIONS				
ORGANS EXAMINED	BENIGN/MALIGNANT		TOTAL	%
	BENIGN	MALIGNANT		
Breast	80 (44.2%)	101 (55.8)	181	38%
Thyroid	72 (85.7%)	12 (14.3%)	84	17.50%
Ovary	32 (68.1%)	15 (31.9%)	47	9.79%
Lymph Node	18 (45%)	22 (55%)	40	8.33%
Colon	23 (88.5%)	3 (11.5%)	26	5.42%
Abdomen	3 (33.3%)	6 (66.7%)	9	1.88%
Skin	5 (55.5%)	4 (44.5)	9	1.88%
Gastric	2 (25%)	6 (75%)	8	1.67%
Brain	3 (37.5%)	5 (62.5%)	8	1.67%
Gall Bladder	3 (50%)	3 (50%)	6	1.25%
Liver	2 (33.3%)	4 (66.7%)	6	1.25%
Uterine	4 (66.7%)	2 (33.3%)	6	1.25%
Cervix	2 (40%)	3 (60%)	5	1.04%
Spine	2 (50%)	2 (50%)	4	0.83%
Parathyroid	4 (100%)		4	0.83%
Pancreas	3 (75%)	1 (25%)	4	0.83%
Omentum	4 (100%)		4	0.83%
Lung	2 (66.7%)	1 (33.3%)	3	0.63%
Small Bowel	2 (66.7%)	1 (33.3)	3	0.63%
Parotid	2 (100%)		2	0.42%
Placenta	2 (100%)		2	0.42%
Bone	1 (50%)	1 (50%)	2	0.42%
Ear	2 (100%)		2	0.42%
Muscle		1 (100%)	1	0.21%
Vagina	1 (100%)		1	0.21%
Bile duct		1 (100%)	1	0.21%
Tongue		1 (100%)	1	0.21%
Pelvic mass		1 (100%)	1	0.21%
Duodenum		1 (100%)	1	0.21%
Nasopharynx		1 (100%)	1	0.21%
Kidney	1 (100%)		1	0.21%
Adrenal mass	1 (100%)		1	0.21%
Esophagus	1 (100%)		1	0.21%
Groin mass	1 (100%)		1	0.21%
Maxillary	1 (100%)		1	0.21%
Mesentery		1 (100%)	1	0.21%
Testis	1 (100%)		1	0.21%
Peritoneal mass	1 (100%)		1	0.21%
TOTAL	**281 (58.5%)**	**199 (41.9%)**	**480**	**100%**

Table V. DISCREPANT CASES

Tissue	No. of cases	Frozen Section Diagnosis	Final Diagnosis	Type of Errors
Thyroid	3	1. Multinodular goiter	Papillary CA	Sampling error
		2. Adenoma of parathyroid	Clear cell CA	Interpretation error
		3. Multinodular goiter	Papillary CA	Sampling error
Breast	2	1. No tumor deposits	Positive for malignant cells	Interpretation error
		2. Fibrosis, no malignancy	Secondary adenoCA	Interpretation error
Soft tissue	1	Benign nerve sheath tumor	Leiomyosarcoma	Wording error
Skin	1	Papillomatosis with wart	In situ squamous cell carcinoma	Interpretation error
Stomach	1	Lymphocytic infiltrate	Signet cell carcinoma	Interpretation error

DISCUSSION

Frozen section is a critical procedure, that plays a major role in therapeutic design, therefore it requires highly qualified pathologist, to give the right consultation on a critical time. We found from this study that the total number of frozen sections performed during each year is very little compared to the larger medical centers performing frozen section, such as M.D Anderson with average number of 70 cases/day(8). This difference is based on the number of beds, turn around time of each patient and health insurance regulations. However there was a steady increase of frozen section demand in our hospital by surgeons, as described in table I which shows a progressive increase in frozen section percentage from 1.3% to 2.1%. Inspite of increase demand for frozen section the accuracy rate of our results were similar to other larger studies published in literature. For exmaple a large study reproted by Hola-

dy(9) of ten thousand consecutive frozen section retrospectiver analysis focusing on accuracy and quality control reported similar high accuracy rates as ours (99%).

Sampling errors are seen in 2 cases from thyroid. The thyroid cases show papillary carcinoma on top with multinodular goiter. The frozen section sampling overlooked the malignant foci, therefore resulted in benign diagnosis at frozen section (multinodular goiter).

Interpretational errors are seen in 5 cases, one of them from sentinal lymph node to diagnose metastasis. however frozen section missed the cohesisve tumor cell deposits that is present in the cortex and sinus and interpreted them as sinus histiocytosis. the size of lymph node was small. In such cases scraping cytology of the cut section of the lymph node will be helpful to demonstrate tumor cell deposits.

The second case of the breast missed the tumor cells seen in the sclerotic stroma and interpreted it at the time of frozen section as fibrosis, negative for malignancy but permanent section show invasive sclerotic carcinoma. The third case misinterpreted squamous cell carcinoma of skin as verucca vulgaris and the permanant section of the frozen section show invasion of the dermis by well-differentiated squamous cell carcinoma. Absence of deeper sections at frozen section results in such errors.

The fourth case was misinterpretation of signet ring adenocarcinoma of stomach as macrophages. and the diagnosis was discovered on permanent section. Presence of rapid alcian blue staining technique will be very helpful to avoid such error in the future(10) .

The fifth case was diagnosed as adenoma of the thyroid and the permanent section diagnosis was clear cell carcinoma most likely metastatic from the kidney. Lack of adequate clinical data prior to the operation and frozen section create this type of error.

In the wording error we found one case that was diagnosed as spindle cell tumor, benign, nerve sheath origin and it turns out as leiomyosarcoma on permanent. In such case the pathologist could write spindle cell tumor, await permanent, instead of

giving a specific unnecessary disease category.

As we can see all of the interpretational errors could be avoided if the frozensection is partially defered and final assessment awaited permanent. Although this action will not accelerate patient management, yet it will give accurate Pathology Department assessment and better patient care and planning.

If we look at the accuracy rate of the frozen section done in large number of cases as shown in table III, we found that the accuracy rate is variable from 97% - 100% with mean on 99.1%. These high accuracy rates in our experience King Abdulaziz University Hospital demonstrate the value of frozen section as an accurate and useful diagnostic tool. There was no false positive case and the false negative cases (8 cases 1.04%) were within acceptable range.

When we evaluate the deferred cases, majority of them were found in thyroid and lymph node, i.e. 19%(16/84) and 17.5%(7/40). These percentages seems to be acceptable compared to that of the literature(6,8) . All of the defered cases of thyroid were follicular lesions, limiting the pathologist to give an accurate diagnosis of follicualr lesion and to confirm the final diangosis on permanent sections and this is acceptable at frozen section. The deferred cases of the lymph nodes were also having a high suspicion of lymphoma, which is a justifiable reason for deferring the diagnosis until the permanent sections.

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