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Histopathological Correlation with Intraoperative Frozen Section Diagnoses- A Three-Year Study at A Tertiary Care Centre

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Abstract

Introduction: Frozen section is diagnostic procedure used to provide rapid diagnosis and guide intra-operative patient management. The interpretation of frozen section is difficult as compared to paraffin section and hence an experienced competent pathologist is required along with skilled technician and optimum clinical details. Correlation between frozen section and paraffin-embedded sections should be integral part of quality analysis.

Aims and objectives: Aims of the study were to know common indications for frozen section diagnosis, correlate frozen section with histopathology diagnosis, assess diagnostic accuracy of frozen section, evaluate common reasons for misdiagnosis on frozen section

Materials and methods: A retrospective study of frozen sections in a tertiary care center over period of 3 years was carried out. 80 patients underwent intra-operative pathology consultation. Comparison of frozen section and histopathology diagnosis was made. The possible causes of errors were recorded and classified into interpretation error and sampling error. The accuracy, sensitivity, specificity, positive and negative predictive values were calculated.

Results: Intraoperative frozen section was performed for 80 patients in three years. The common indications for frozen section consultation were: primary diagnosis-benign versus malignant and margin status. The most common tissue sent for frozen section was breast. The diagnosis of none of the cases was deferred on frozen section. Out of the 80 cases, the intraoperative frozen section and permanent paraffin section diagnoses were concordant in 75 cases (93.75%). There was no false positive diagnosis. The sensitivity, specificity, accuracy, positive predictive value and negative predictive value of frozen section as a diagnostic tool were 91.89%, 100%, 96.25%, 100% and 93.48%, respectively.

Conclusion: Continuous monitoring should be performed in every pathology department, to recognize the reasons of errors and, if possible, to reduce them.

Keywords: Frozen section diagnosis, comparison of frozen with histopathology

Introduction

Frozen section is a diagnostic procedure used to provide rapid diagnosis and guide intra-operative and peri-operative patient management [1]. The other modalities used for intra-operative consultation include squash cytology, fluid cytology and imprint cytology [2].

Dr. William H. Welch was the first to introduce the frozen section technique in 1891 [3]. The common indications for frozen section include primary diagnosis, status of margins and lymph nodes and to know whether the biopsy is representative of and sufficient for diagnosis and ancillary testing. Mere satisfaction of surgeons' or patients' curiosity does not warrant an intra-operative consultation, as the frozen section cannot be a replacement for the gold standard "histopathological diagnosis" [1-5].

The interpretation of a frozen section is challenging as compared to paraffin embedded section due to artifacts and time constraints and hence an experienced and competent pathologist is required in addition to a skilled technician and optimum clinical details [1, 5]. The pathological should be an authority to decide whether or not a frozen section is worth pursuing [5].

Correlation between frozen section and paraffin-embedded sections should be an integral part of quality analysis [1]. The causes of discordance should be looked into; they include sampling errors and interpretation errors. Identifying the causes of error and means to improve them helps to increase accuracy of diagnosis and build pathologist's and surgeon's confidence [1].

This study aims to know common indications for frozen section diagnosis, to correlate frozen section diagnosis with histopathology diagnosis, to assess diagnostic accuracy of frozen section and calculate sensitivity and specificity and to evaluate the common reasons for misdiagnosis on frozen section.

Materials and methods

A retrospective study of frozen sections performed and reported in a tertiary care center over a period of 3 years(July 2017 to June 2019) was carried out. During this study period, a total of 80 patients underwent intra-operative pathology consultation.The records of frozen sections were retrieved from the register maintained in the Department of Pathology.

The frozen sections were mounted on embedding medium and frozen in a Cryostat and stained with rapid Hematoxylin and Eosin (H&E) stain. And reported by two pathologists. The permanent histopathology sections were made from remnant of frozen tissue and wherever available, the remaining non-frozen tissue. The paraffin sections were stained using conventional H&E along with special stains and immunohistochemistry, wherever required.Comparison of frozen section and histopathology diagnosis was made.

All the interesting and discordant case slides were retrieved and reviewed by two pathologists. The possible causes of errors were recorded. The types of errors were classifiedaccording to Association of Directors of Anatomic and Surgical Pathology: (a) change in category leading to false-positive or false-negative diagnosis, (b) change within the same category (histological subtyping), (c) change in status of resection margin and (d) change in lymph node status.[6]

The accuracy, sensitivity, specificity, positive and negative predictive values were calculated.

Results

During a period of three years, intraoperative frozen section was performed for 80 patients. The common indications for frozen section consultation were: (i) Primary diagnosis- benign versus malignant (ii) Margin status (iii) Primary diagnosis- Tuberculosis versus malignant. The most common tissue sent for frozen

section in our institute was breast, followed by thyroid and ovary (Figure 1).

The diagnosis of none of the cases was deferred on frozen section. Out of the 80 cases, the intraoperative frozen section and permanent paraffin section diagnoses were concordant in 75 cases (93.75%) and discordant in 5 cases (6.25%). The discordant cases are tabulated (Table 1).

There was no false positive diagnosis. Three cases had false negative diagnoses.

The sensitivity and specificity of frozen section as a diagnostic tool were 91.89% and 100%, respectively. The accuracy was 96.25%. The positive and negative predictive values were 100% and 93.48%, respectively.

The details of cases diagnosed on frozen section are enlisted organ-wise:

Breast: The commonest indication for frozen section was primary diagnosis- benign versus malignant (13 out of 17 cases), especially where lesions were small (sub-centimeter) in size or where cytology was inconclusive. The frozen and paraffin diagnoses of all these 13 cases were concordant, seven were fibroadenomas and six carcinomas. Margin status was assessed in three cases, all were concordant.In one case, lymph node status of axillary sampling was revised from negative to positive after more sampling (Figures 2a, 2b).

Female genital tract: The most common tissue sent for intraoperative frozen section was ovary for primary diagnosis- benign versus malignant (9 out of 19 cases).Eight cases had concordant diagnoses; one was discordant (false negative diagnosis). Krukenberg tumour of the ovary was misdiagnosed as fibroma on frozen section (Figures 3a, 3b).Three samples were sent to comment whether it was abdominal (peritoneal/ omental) tuberculosis or metastatic deposits; diagnosis in all three were concordant. Details are tabulated (Table 2).

Thyroid:Eight out of nine thyroid specimens sent for frozen section had a solitary nodule on USG and were sent for intraoperative pathological consultation for primary diagnosis- benign versus malignant. Out of these eight cases, six nodules were reported as benign on frozen as well as paraffin sections and two were malignant. One of the malignant thyroid tumours was misdiagnosed as follicular carcinoma on frozen section; however, it was modified to medullary carcinoma on histopathology (Figures 4a, 4b). The ninth case was diagnosed as MNG with Hashimoto's thyroiditis on both frozen and paraffin sections.

Gastrointestinal tract: A variety of tissues were sent for intraoperative frozen section as mentioned in the table (Table 3). 17 out of 19 cases were concordant. The discordance cases included a pancreatic biopsy that was misdiagnosed as chronic pancreatitis instead of invasive carcinoma (Figures 5a, 5b). Another esophageal biopsy, although correctly diagnosed as malignant on frozen section, was erroneously subtyped as gastrointestinal stromal tumour. It was finally diagnosed as spindle cell squamous carcinoma on histopathology and immunohistochemistry.

Other tissues: The remaining frozen section tissues included oral cavity, musculoskeletal tissue, kidney, ureters, brain and mediastinal tissues (Table 4). All the 17 cases had a concordant diagnoses on frozen and paraffin-sections.

Amongst these, the frozen section done for renal tumour was very crucial. It was a known/ proven case of carcinoma breast with unifocal right renal mass at upper pole. Frozen section and imprint cytology revealed a papillary renal cell carcinoma (i.e. second primary) and hence, a radical nephrectomy was performed along with modified radical mastectomy in the same setting. On histopathology, the breast revealed a Grade 3 invasive

carcinoma of no special type and kidney revealed a papillary renal cell carcinoma, Fuhrman Grade 2.

Discussion

In the present study, the commonest indication of intra-operative frozen section was to determine whether the lesion is benign or malignant followed by margin status. The sensitivity and specificity of frozen section as a diagnostic tool were 91.89% and 100%, respectively. The accuracy was 96.25%. The positive and negative predictive values were 100% and 93.48%, respectively.

Out of the 80 cases, the intraoperative frozen section and permanent paraffin section diagnoses were concordant in 75 cases (93.75%) and discordant in 5 cases (6.25%). Out of these five cases, four were interpretation errors (errors were avoidable in all four cases) and one was sampling error (unavoidable error).

Indications for frozen section include: (a) To establish nature of lesion -benign or malignant (b) To evaluate status of margins (c) To identify lymph node metastasis (d) To identify tissue and unknown pathological processes (e) To confirm presence of representative sample for paraffin section/ ancillary testing (f) To determine nature of lesion that requires ancillary testing so as to preserve the sample in specific preservative. Frozen section facility should not be misused and is not indicated: (a) To satisfy a surgeon's curiosity (b) To compensate for inadequate preoperative evaluation (c) As a mechanism to communicate information more quickly to patient/ patients' family [1-5].

The sensitivity, specificity and accuracy of frozen section as a diagnostic tool varies from 92.7% to 99.4%,96.3% to 99.5% and 94.2% to 98.2% respectively in the various studied conducted worldwide [1,2,4,7-12].

The quality indicators of present study are comparable to these values (Table 5). The diagnostic accuracy of frozen section varies system-wise. The accuracy of diagnosing breast pathology varies from 72.7 to 98.7 % [6]; it was 94.12% in the present study. For thyroid and gynaecological lesions, the average accuracy reported in literature is 90% and 97.5%, respectively [5]; the values were 100% and 94.7%, respectively, in the present study.

Out of the 80 cases, the intraoperative frozen section and permanent paraffin section diagnoses were concordant in 75 cases (93.75%) and discordant in 5 cases (6.25%). A college of American Pathologist (CAP) sponsored review of over 90,000 frozen sections showed a discordance rate of 1.42%; the common causes for the discrepancies being misinterpretation of the original frozen section (31.8%), absence of diagnostic tissue in the frozen material but present in remnant of frozen tissue or in the remaining unsampled tissue [13].In our study, the discordant cases included four interpretative errors (80%), wherein the frozen sections were wrongly interpreted due to causes discussed subsequently. One case had sampling error (20%), wherein there was absence of diagnostic tissue in frozen but present in the remaining unsampled tissue.

A case of invasive adenocarcinoma of pancreas was misdiagnosed as chronic pancreatitis and hence revision surgery was done later after final histopathology report. In this case, the pre-operative serum CA19.9 levels were within reference range and an incidental hard nodule was found intraoperatively in the patient undergoing ERCP for chronic calculus pancreatitis.The frozen section revealed small compressed glands lined by uniform cuboidal cells having round bland nuclei surrounded by fibrosis. Histopathological sections from remnant tissue revealed adenocarcinoma surrounded by desmoplastic reaction. This was an interpretation error. Chronic pancreatitis and pancreatic carcinoma can cause destruction of the normal pancreatic tissue and elicit marked fibroblastic reaction of the stroma and lead to misdiagnosis [5].

In another case, Krukenberg tumour of the ovary was misdiagnosed as fibroma. In this case, patient had presented with lower abdominal pain. Only single ovary was bulky (10 cm). There were no pelvic or peritoneal deposits or omental caking intra-operatively. The ovarian mass had an intact capsule with smooth surface. The mass was entirely solid, homogenous, firm, trabeculated and yellowish white. Frozen sections revealed small tubules lined by cuboidal cells with fairly uniform nuclei within dense fibrous stroma. Considering intra-operative, gross and microscopy findings, a diagnosis of sex cord stromal tumour with predominant fibroma component was offered. However, histopathology sections from remnant tissue and fresh sections from the remaining ovarian tumour revealed adenocarcinoma exhibiting glandular pattern as well as foci of signet ring cellsand a diagnosis of Krukenberg tumour was made and proven on immunohistochemistry. The tumour cells expressed PanCK, CK7 and CK20 and immunonegative for Calretinin, Inhibin and Pax8. Post-operative esophagogastroduodenoscopy revealed an ulcer over greater curvature of stomach that was proven to be adenocarcinoma on biopsy. The paucity of signet ring cells in some cases may lead to misdiagnosis of Krukenberg tumour as fibroma (particularly on frozen section), sclerosing stromal tumour or signet ring stromal tumour [14, 15].In this case, total hysterectomy and bilateral salphingo-oophorectomy was done after frozen section diagnosis. Also, there were no symptoms attributable to gastrointestinal primary in this patient and hence Krukenberg tumour was not clinically suspected. A focus of adenocarcinoma was also found in the other ovary as well. In this case, the surgical management would not have changed as the bulky ovary was already removed.

In the remaining two discordant cases, althoughthe lesions were correctly diagnosed as malignant on frozen section, they were wrongly subtyped due to interpretation error.

An esophageal biopsy was diagnosed as gastrointestinal stroma tumour. The esophagogastroduodenoscopy of this patient revealed a 2 cm well circumscribed submucosal mass in the mid-esophagus with erythematous overlying mucosa. Frozen section revealed a malignant tumour having epithelioid as well as spindle cell morphology. There was significant nuclear atypia and brisk mitoses. In view of submucosal location of tumour, a diagnosis of GIST was favored. Multiple sections studied from excisionspecimen revealed a dysplastic squamous mucosa with tiny mucosal ulcer as well as large invasive tumour in the submucosa. The muscularis propria was uninvolved. The tumour predominantly exhibited spindle cell morphology along with areas of epithelioid morphology. Few keratin pearls were also seen at the surface. Hence, a final diagnosis of poorly differentiated squamous carcinoma with spindle cell morphology was offered and proven on immunohistochemistry (PanCK, p40 positive; c-kit, DOG1, SMA negative). Misinterpretation of diagnosis could be due to histological similarities between different tumours and inappropriate information about tumor location and imaging findings [17].Spindle cell neoplasms of the esophagus include GIST, leiomyosarcoma, schwannoma, inflammatory fibroid polyp and spindle cell squamous carcinoma/ sarcomatoid carcinoma. The mesenchymal tumours are usually located within the submucosa/ muscularis propria as compared to carcinoma, which will arise from mucosa.In the other case, hemithyroidectomy was done for solitary thyroid nodule reported as follicular neoplasm on FNAC, the frozen section was reported as follicular carcinoma. The frozen section revealed a tumour was composed of microfollicles without any intraluminal colloid. Tumour

invasion into and beyond the fibrous capsule was identified and hence reported as follicular carcinoma. On histopathological examination from remnant and fresh sections, the diagnosis of medullary carcinoma was offered. On retrospective analysis, the tumour was misdiagnosed as follicular because of misinterpretation of small nests of tumour cells as microfollicles and due to lack of characteristic nuclear features on frozen sections. The cytological and stromal characteristics may get altered on frozen section due to artifacts [1, 16]. Completion thyroidectomy with ipsilateral neck node dissection was already done in this case after frozen section report. The management would not have changed due to subtyping. A general diagnosis rather than a specific one helps the surgeon to choose the optimal therapeutic option [4].

In the fifth case, axillary sampling was sent for status of lymph nodes in a case of carcinoma breast. Only two nodes were palpable in the fresh tissue, both were free of metastasis on frozen as well as paraffin section. However, 12 more nodes were dissected after fixation. Out of these a tiny (0.2 cm) lymph node revealed metastatic focus. This 0.2 cm axillary lymph node was not identified in fresh specimen, which was easily palpable after fixation. This wasa sampling error. It is a well-known fact that small lymph nodes are always better palpable after fixation.

There were two cases of mucinous neoplasms of the ovary. In both the cases, the frozen sections revealed a lower grade than paraffin section. However, since a note saying “Possibility of higher grade cannot be ruled out” was recorded on paper in both the cases, these cases were considered concordant. In mucinous neoplasms of the ovary, there is great heterogeneity in different areas and generous sampling from solid areas is required for optimum reporting [18, 19].

Conclusion

High diagnostic accuracy of frozen section was demonstrated and hence, the intra-operative consultationis extremely useful aid. The surgeon and pathologist, however, need to be aware of the indications and limitations of the procedure. Continuous monitoring should be performed in every pathology department, to recognize the reasons of errors and, if possible, to reduce them.Frozen sections are used to evaluate a variety of pathologic processes and anatomic sites.

Table 1: Cases having discordance between frozen section and histopathology diagnoses:

Specimen (Organ/ System)	Frozen Section Diagnosis	Histopathology/ Final Diagnosis	Type of Error [6]	Reason for Error	Impact on pathology report
Pancreatic tissue	Chronic pancreatitis	Invasive Adenocarcinoma	Change in category	Interpretation error	False negative
Ovarian mass	Benign neoplasm s/o sex cord stromal tumor (fibroma)	Krukenberg tumor	Change in category	Interpretation error	False negative
Thyroid	Follicular carcinoma	Medullary carcinoma	Change within same category	Interpretation error	Category change
Esophagus	Epithelioid GIST	Poorly	Change within	Interpretation	Category change

		differentiated squamous carcinoma	same category	error	
Breast	Axillary LN- Two reactive nodes; no metastasis	One (0.2 cm node) out of 12 nodes reveals metastasis	Change in lymph node status	Sampling error	False negative

s/o: suggestive of, GIST: Gastrointestinal stromal tumour, N: Lymph node

Table 2: Comparison of frozen section and paraffin section diagnoses of tissues of FGT:

Organ/ Tissue	Indication for FS	FS impression	PS diagnosis	No. of cases	Comparison (C/D)
Ovarian cyst/ mass	Benign versus malignant	Serous cystadenoma	Serous cystadenoma/ cystadenofibroma/ Seromucinous cystadenoma	4	C
		Benign stromal tumour, favour fibroma	Fibrothecoma	1	C
		Mucinous cystadenoma, p/o borderline tumour cannot be ruled out	Borderline mucinous tumour	1	C
		Borderline serous neoplasm, p/o cystadenocarcinoma cannot be ruled out	Serous cystadenocarcinoma	1	C
		Papillary serous adenocarcinoma	Papillary serous adenocarcinoma	1	C
		Benign neoplasm, s/o sex cord stromal tumour	Krukenberg tumour	1	D
Endometrial bits	Benign versus malignant	Squamous carcinoma	Squamous carcinoma	1	C
		No atypia/ malignancy	Disordered proliferation	1	C
Cervix tissue	Benign vs. malignant	Squamous carcinoma	Squamous carcinoma	1	C
Uterine mass	Benign vs. malignant	Adenomyoma	Adenomyoma	1	C
		Invasive mole	Invasive mole	1	C
Labia	Benign vs.	Squamous carcinoma	Squamous carcinoma	1	C

majora	malignant				
Peritoneal / omental biopsy	TB vs. malignancy	Atypical cells, suspicious for malignancy	Metastatic adenocarcinoma	1	C
		Inflammatory lesion, favour TB	TB	2	C
Cervix tissue	Margins	Positive	Positive	1	C

FGT: Female Genital Tract, FS: Frozen Section, PS: Paraffin section, No.: Number, C: Concordant, D: Discordant, vs.: Versus, p/o: possibility of, s/o: suggestive of, TB: Tuberculosis

Table 3: Comparison of frozen section and paraffin section diagnoses of tissues of GIT:

Organ/ Tissue	Indication for FS	FS impression	PS diagnosis	No. of cases	Comparison (C/D)
Gall bladder	Benign vs. malignant	Cholecystitis	Cholecystitis	3	C
		Atypical glands, s/o malignancy	Well differentiated adenocarcinoma	1	C
		Necrosis; no viable tissue	Necrosis; no viable tissue	1	C
Liver tissue	Benign vs. malignant	Negative for malignancy	Negative for malignancy	2	C
		Deposits of adenocarcinoma	Deposits of adenocarcinoma	1	C
		No e/o malignancy	Only fibrosis	1	C
Pancreatic tissue	Benign vs. malignant	Chronic pancreatitis	Chronic pancreatitis	1	C
		Chronic pancreatitis	Invasive adenocarcinoma	1	D
		Invasive adenocarcinoma	Invasive adenocarcinoma	1	C
Distal CBD tissue	Benign vs. malignant	No e/o malignancy	No e/o malignancy	1	C
CBD excision	Benign vs. malignant	Papillary adenocarcinoma	Papillary adenocarcinoma	1	C
Duodenal mucosa	Benign vs. malignant	Brunner gland hyperplasia with chronic non-specific duodenitis	Brunner gland hyperplasia with chronic non-specific duodenitis	1	C
Hepatoga	Benign vs.	Negative for malignancy	Negative for malignancy	1	C

stric ligament	malignant				
Oesophagus	Primary diagnosis	S/o epithelioid GIST	Squamous carcinoma	1	D
Fistula tract	Benign vs. malignant	Atypical cells, suspicious for malignancy	Low grade mucinous adenocarcinoma	1	C
CBD	Lymph nodes	Reactive	Reactive	1	C

FS: Frozen Section, PS: Paraffin section, No.: Number, C: Concordant, D: Discordant, vs.: Versus, p/o: possibility of, s/o: suggestive of, e/o: evidence of

Table 4: Comparison of frozen section and paraffin section diagnoses of tissues of oral cavity, musculoskeletal tissue, kidney, ureters, brain & mediastinal tissues:

Organ/ Tissue	Indication for FS	FS impression	PS diagnosis	No. of cases	Comparison (C/D)
Lateral canthus of eye	Primary diagnosis	Basal cell carcinoma	Basal cell carcinoma	1	C
Lower lip, Buccal mucosa	Margins	Negative for malignancy	Negative for malignancy	3	C
Thigh tumour	Benign vs. malignant	Malignant spindle cell neoplasm	MPNST	1	C
Vertebral mass	Primary diagnosis	Plasma cell dyscrasia	Plasma cell dyscrasia	1	C
Femoral tissue	TB vs non-TB inflammation	No e/o TB	No e/o TB	1	C
Synovial tissue	Infective vs non-infective	Acute inflammation present (>6 PMN/hpf)	Acute inflammation present (>6 PMN/hpf)	1	C
Lymph node	Benign vs. malignant	Metastasis of adenocarcinoma	Metastasis of adenocarcinoma	2	C
		No e/o malignancy	No e/o malignancy	1	C
		Atypical cells	Lymphoproliferative disorder (NHL on IHC)	1	C
Ureter	Margin	Free	Free	2	C
Kidney mass	Primary vs. metastatic	RCC	RCC	1	C

Brain tumour	Primary diagnosis	Pineal parenchymal tumour of intermediate differentiation	Pineal parenchymal tumour of intermediate differentiation	1	C
Mediastinal mass	Benign vs. malignant	Benign spindle cell neoplasm, favour GIST	Benign spindle cell GIST	1	C

FS: Frozen Section, PS: Paraffin section, No.: Number, C: Concordant, D: Discordant, vs.: versus, MPNST: Malignant peripheral nerve sheath tumour, TB: Tuberculous, PMN/hpf: Polymorphonuclear leucocytes/ high power field, NHL: Non-Hodgkin lymphoma, IHC: Immunohistochemistry, RCC: Renal cell carcinoma, GIST: Gastrointestinal stromal tumour.

Table 5: Comparison of quality indicators of present study with literature:

S.N.	Author	No. of cases	Period of study	Con-cordant	Dis-cordant	Deferred cases	Sensitivity	Specificity	Accuracy	PPV (%)	NPV (%)
1	Golam et al [6]	1379	6.5	1354	9	14 (1%)	99.4%	99.3%	98.2%	99.2	99.5
2	Mahe et al [7]	1208	0.5	1156	24	28 (3%)					
3	Jerome et al [8]	404	4			3.90%			94.6%		
4	Hatami et al [9]	306	6	289	6	11 (3.56%)	92.95%	99.55%		98.5	97.8
5	Agarwal et al [2]	224	2				75% for neoplastic	97.54% for neoplastic	94.2%	90.9	94
6	Khoo et al [10]	215	3				97.98%	97.16%	97.56%		
7	Abbasi et al [11]	200	7				93.1%	97.7%	96.5%	96	95
8	Patil et al [4]	100	2	96	3	1%	97.22%	96.3%	96.96%	98.59	92.86
9	Baruah et al [1]	84	3	77	7		92.7%	98.8%	95.81%	98.7	93.2

10	Chandra moulees wari et al [12]	51	1	47	0	3 (6%)					
11	Present study	80	3	75	5	none	91.89%	100%	96.25%	100	93.48

Figure 1: Distribution of cases sent for frozen section:

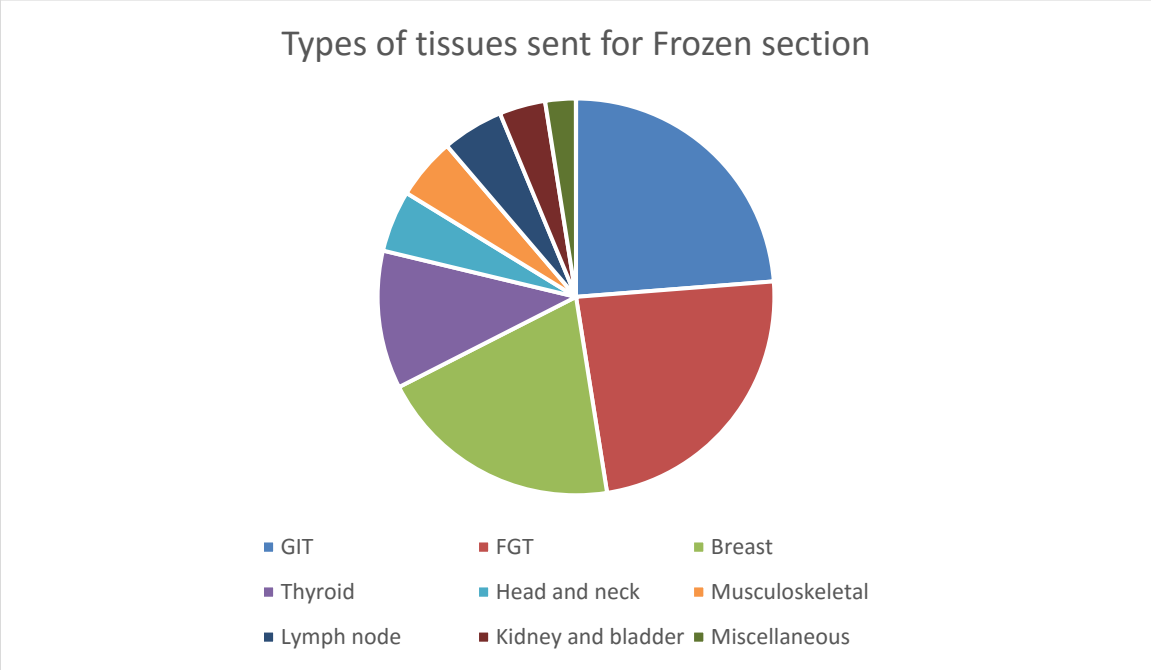


Figure 2a: Frozen section (H&Ex40): Reactive lymph node

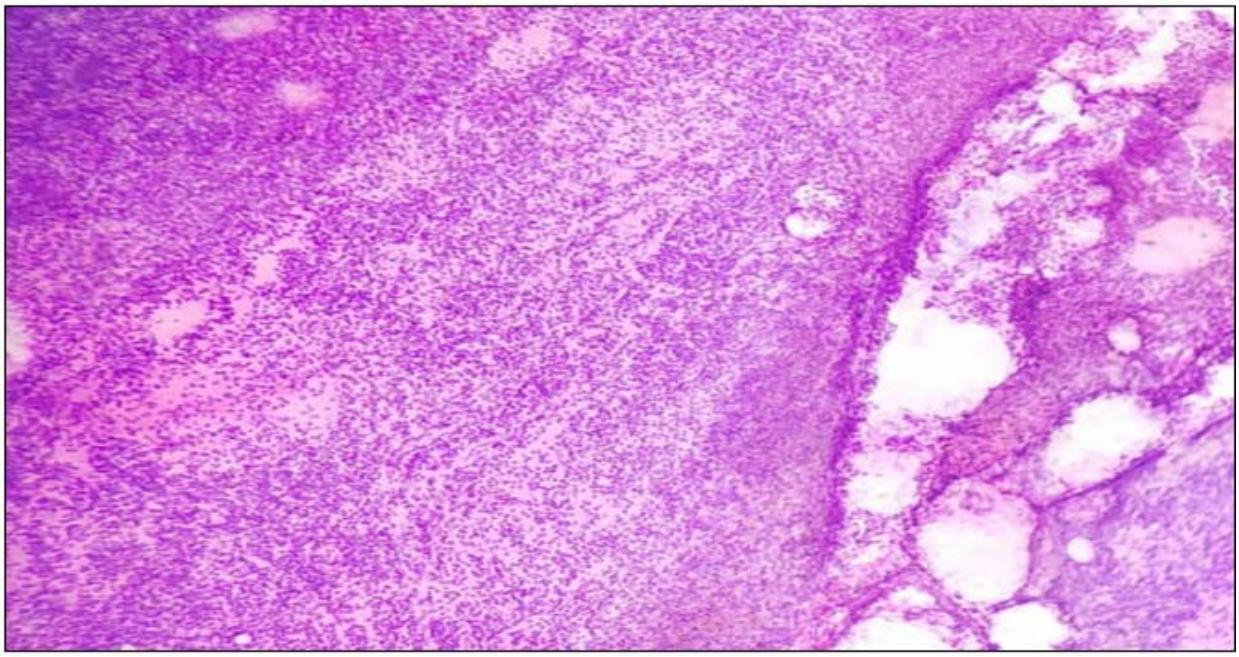


Figure 2b: Paraffin section (H&Ex400): Metastatic deposits of adenocarcinoma in lymph node

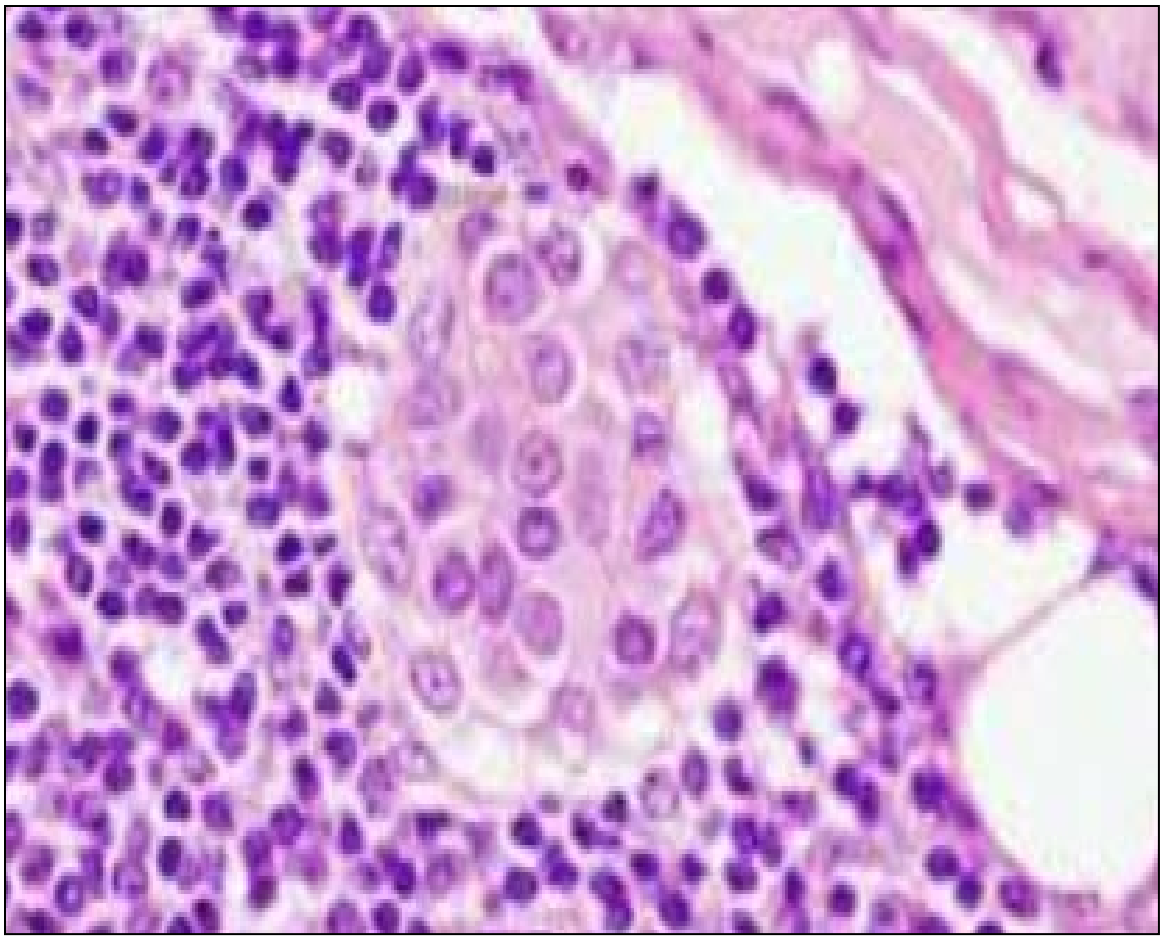


Figure 3a: Frozen section (H&Ex40): Ovarian tumour composed of spindle cells

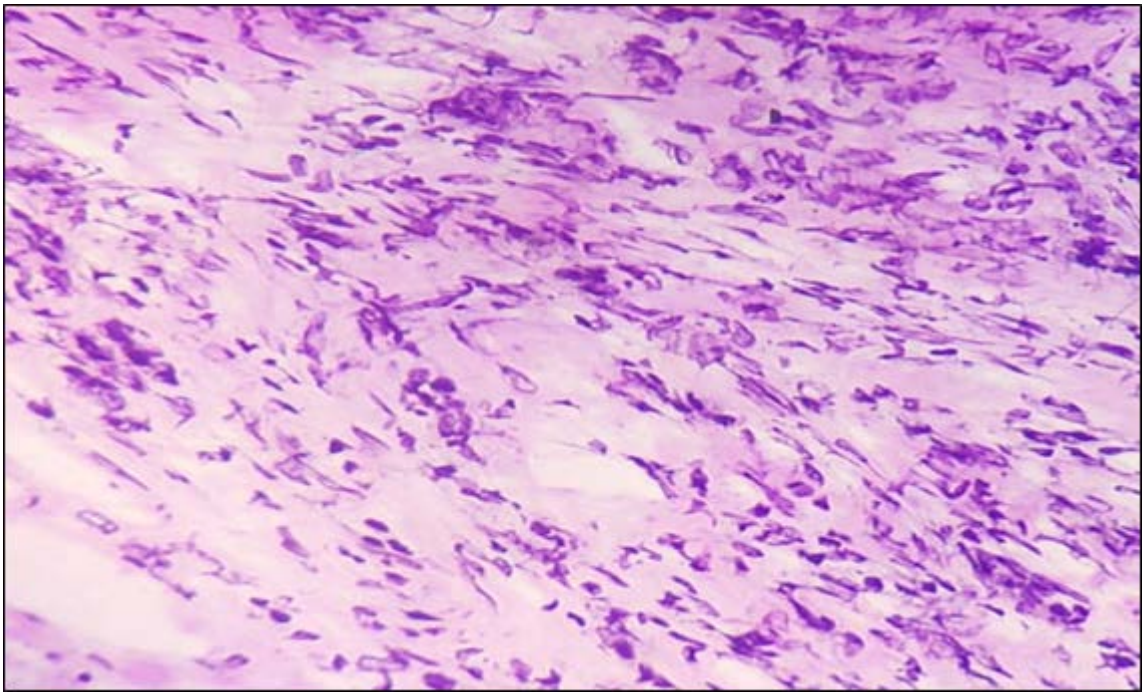


Figure 3b: Paraffin section (H&Ex100): Ovarian tumour composed of signet ring cells

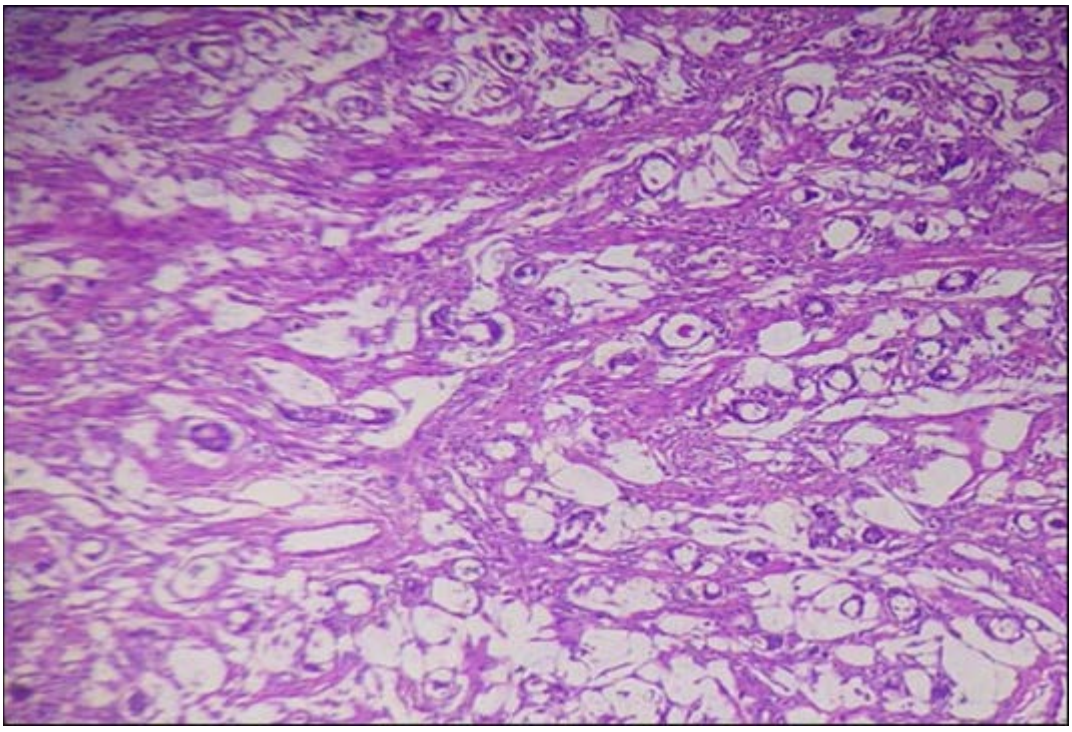


Figure 4a: Frozen section (H&Ex40): Thyroid tumour composed of sheets and microfollicles

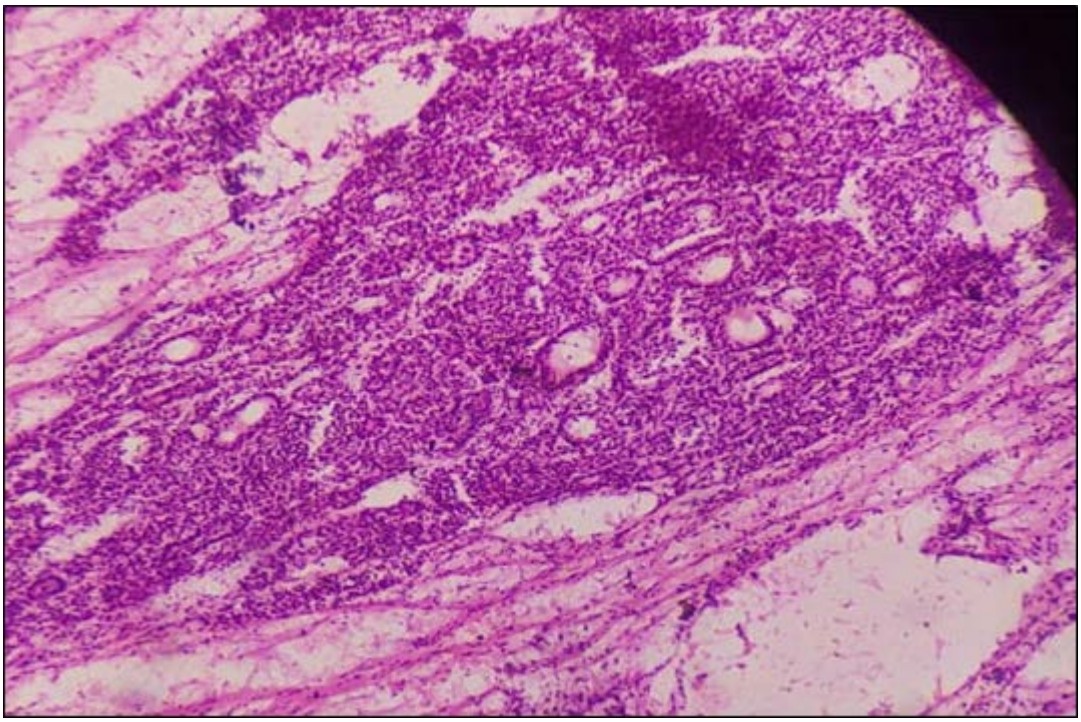


Figure 4b: Paraffin section (H&Ex40): Thyroid tumour composed of nests and trabeculae

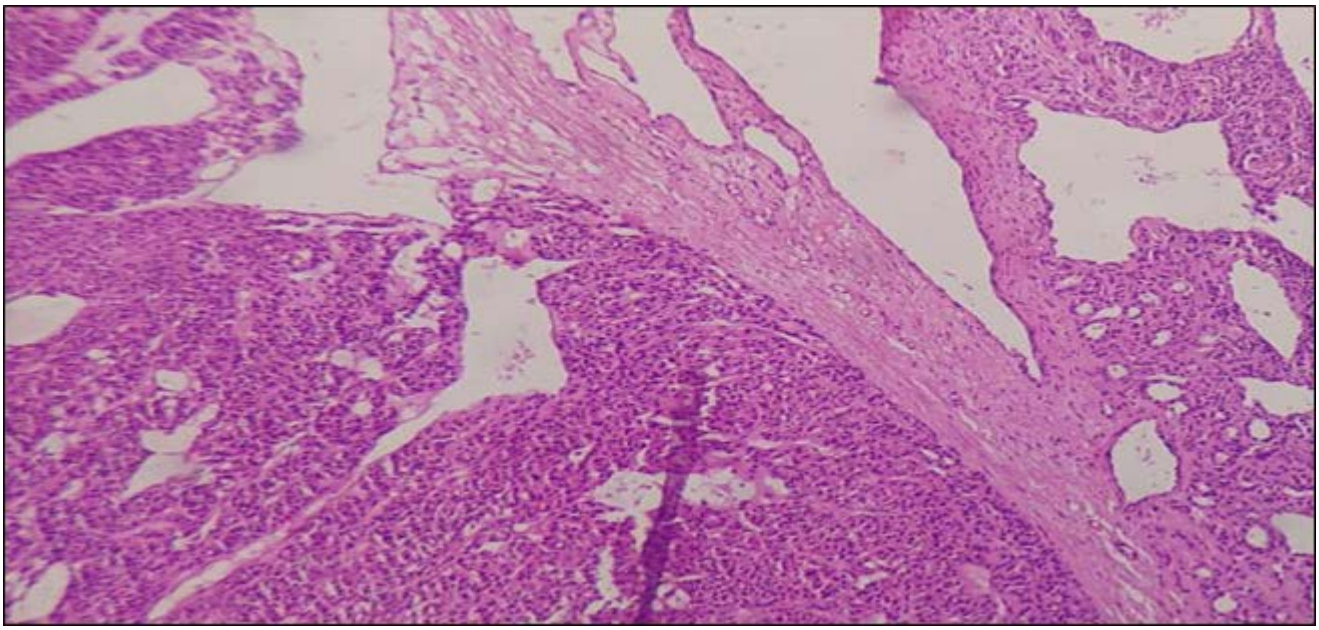


Figure 5a: Frozen section (H&Ex400): Pancreatic tissue showing destroyed acinus with fairly uniform cells

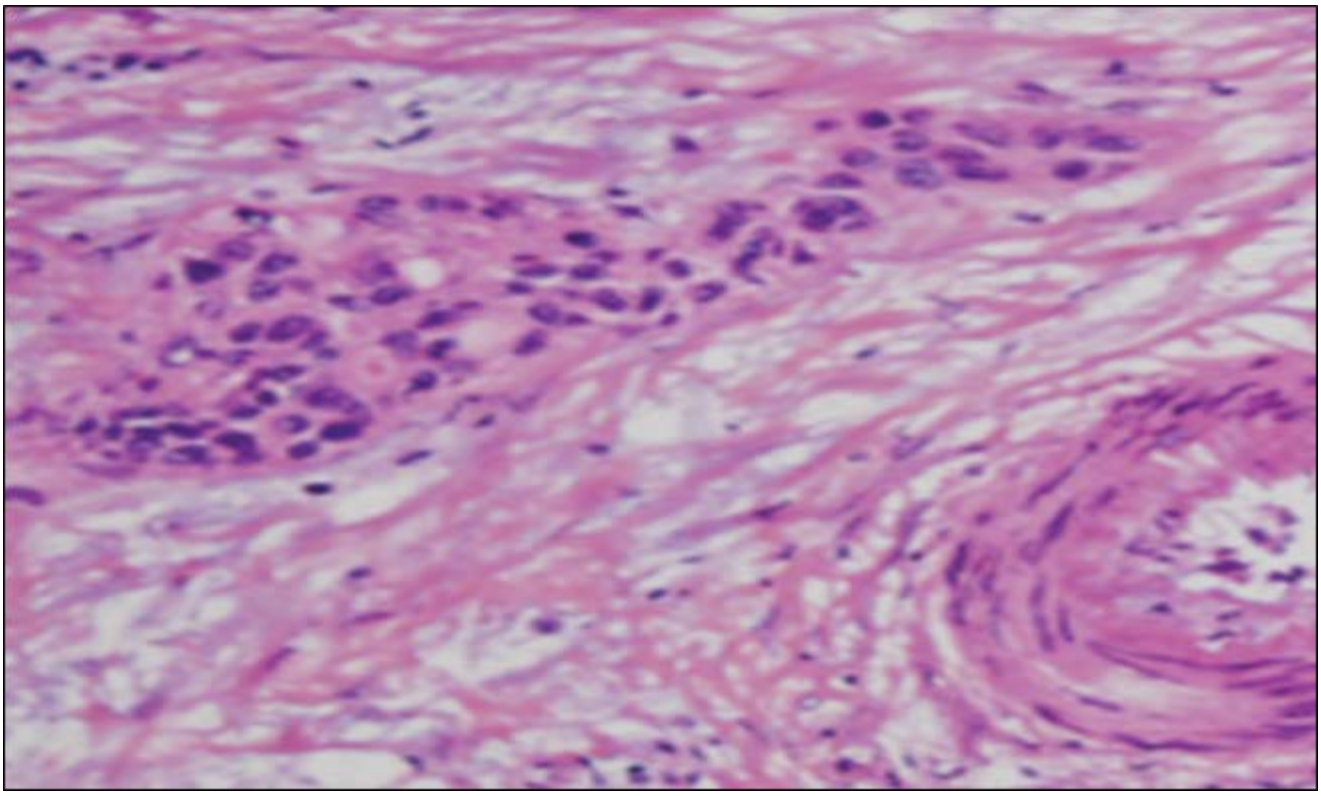
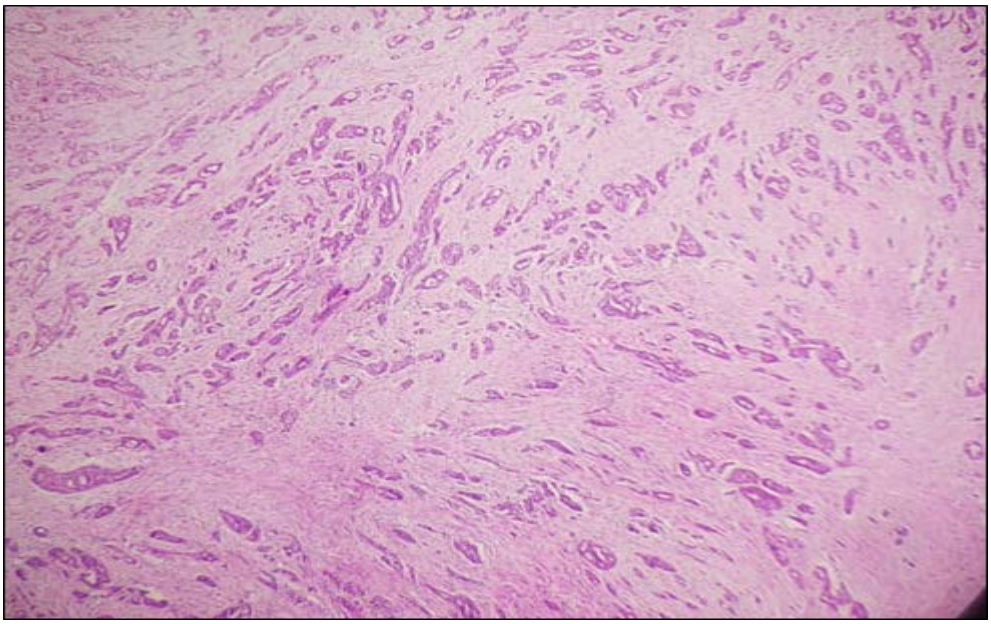


Figure 5b: Paraffin section (H&Ex40): Pancreatic tissue showing adenocarcinoma



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