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Utility and Accuracy of Frozen Section Examination for Uterine Tumors- A Cross Sectional Study

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A B S T R A C T

Introduction*:** Intraoperative frozen sections (IFS) play a vital role in guiding surgical procedures, especially in gynaecological oncology. The rapid diagnosis provided by frozen sections allows surgeons to make real time decisions during surgery, which can significantly impact patient outcomes. It is a demanding task for pathologists, requiring keen observation skills and the ability to make quick yet accurate assessments. The information gleaned from frozen sections helps surgeons determine the extent of the surgery needed and whether further interventions such as lymph node dissection, are necessary. This approach enables a more precise and tailored treatment plan for each patient, improving overall care and potentially reducing the need for additional surgeries. ***Objectives: To compare the results of intraoperative frozen section examination with the final histopathology report and assess its accuracy in diagnosing uterine tumors. ***Methods*:** After Institutional Ethics Committee approval, a cross sectional study was carried out on 10 frozen section specimens of uterine origin. Later histopathological evaluation was done. Both frozen section diagnosis and histopathological diagnosis were compared to find out the accuracy of frozen section examination. ***Results*:** Fromthe10 cases studied on frozen section, 5 cases were diagnosed as Endometrial adenocarcinoma. Others included 1 of Low grade endometrial stromal sarcoma, 1 of Smooth muscle tumour of uncertain malignant potential (STUMP) and 3 cases of Cellular leiomyoma. The diagnosis given on frozen section matched the final histopathological diagnosis in all the cases. ***Conclusion*:** We found that frozen section diagnosis in uterine tumors were accurate in all the cases we studied, because it matched the diagnosis given on subsequent histopathology. Hence frozen section can be a useful tool for intraoperative diagnosis of uterine tumors.
Keywords: Frozen section, utility, accuracy, uterine tumors.

INTRODUCTION

Intraoperative frozen section (IFS) examination can prove to be an important diagnostic tool in gynaecological pathology as it's role has not been emphasized earlier as compared to other surgical fields. In gynaecological oncology, IFS serves as a rapid diagnostic tool during surgery, providing real-time information to guide surgical decision-making. It plays an important role in guiding and categorising surgical procedures as benign and malignant. It is also one of the crucial steps in taking intraoperative decision for management of any suspicious adnexal masses. In cases where there is a suspicion of malignancy based on preoperative imaging or clinical evaluation, IFS provides rapid histological confirmation during surgery. This allows surgeons to proceed with appropriate surgical staging procedures, such as hysterectomy, oophorectomy, or lymph node dissection, as indicated by the presence of malignancy. Determining the grade of the endometrial tumour is essential for prognostication and guiding further treatment decisions. IFS allows rapid assessment of tumour grade based on the architectural and cytological features observed microscopically. The depth of myometrial invasion is an important factor in determining the stage and prognosis of Endometrial carcinoma (EC). IFS provides real-time information about the extent of tumour invasion into the myometrium. It is the only way to identify

during surgery, the subgroup of patients who are at a higher risk of extrauterine disease and to provide it's guidance toward optimal surgical staging [1-3]. In our study we studied 10 uterine tumours where frozen section was followed by histopathological examination.

OBJECTIVE: To assess the accuracy of intraoperative frozen section examination in diagnosing uterine tumours.

METHODOLOGY

This study was undertaken after the Institutional Ethics committee approval. It was a cross sectional study in which we included all patients who underwent intraoperative frozen section examination for clinical diagnosis of uterine tumours. Subsequently histopathological examination was also done and the results were compared. The data was documented in Microsoft Excel sheet and tabulated later.

RESULTS

Table 1: Age wise distribution of the uterine tumours

DISEASE	41-50 Yrs	51-60 Yrs	61-70 Yrs	Total
(1) Endometrioid adenocarcinoma	1	1	3	5
(2) Low grade endometrial stromal sarcoma	1	-	-	1
(3) Smooth muscle tumour of uncertain malignant potential (STUMP)	-	1	-	1
(4) Cellular leiomyoma	2	1	-	3
TOTAL	4	3	3	10

All the 10 cases which came for intraoperative frozen section examination were followed by histopathological evaluation. The results were as shown below in Table 2.

Table 2:

Sr. No	Clinical diagnosis and gross examination	Frozen section (FZ) diagnosis	Final histopathological (HP) diagnosis	FZ diagnosis correlated with HP diagnosis
A.	**Clinical diagnosis- Carcinoma endometrium**			
	Case 1) Post menopausal bleeding with cystocele Gross: Received a specimen of uterus with cervix. On cutting a friable mass was seen in the endometrial cavitymeasuring 5.5 x 3.2 x 1 cm.	Endometrioid adenocarcinoma infiltrating into less than ½ of the myometrium	Endometrioid adenocarcinoma infiltrating into less than ½ of the myometrium	Yes
	Case 2) Carcinoma Endometrium Gross: Received an already cut open specimen of uterus with cervix with bilateral fallopian tubes. Endometrial cavity showed a polypoidal growth occupying the entire endometrial cavity measuring 5x3x1cm and grossly seen invading superficial myometrium.	Endometrioid adenocarcinoma invading inner 1/3 of the myometrium	Endometrioid carcinoma with squamous differentiation invading inner 1/3 of the myometrium	Yes
	Case 3) Carcinoma Endometrium Gross: Received a partially cut open specimen of uterus with cervix and bilateral fallopian tubes and ovaries. Cut section of uterus showed a solid white tumour mass in the endometrial cavity measuring 2.5 x2x1cm.	Endometrioid adenocarcinoma (Low Grade), invading the myometrium.	Endometrioid carcinoma involving more than ½ of the myometrium	Yes
	Case 4) Post menopausal bleeding Gross: Received a partially cut open specimen of uterus with cervix with bilateral adnexa.	Endometrioid adenocarcinoma infiltrating less than ½ of the	Endometrioid adenocarcinoma infiltrating less than inner ½ of the	Yes

	Cut surface showed a polypoidal mass in endometrial cavity measuring 3x2.5x2cm Case 5) Diagnosed case of Endometrioid adenocarcinoma Gross: Received an intact specimen of uterus with cervix with bilateral adnexa. On cutting open a polypoidal growth was identified in the endometrial cavitymeasuring 5.5x4.5x3 cm.	myometrium, Endometrioid carcinoma invading less than inner ½ of myometrium (Figure 1a.)	myometrium. Endometrioid adenocarcinoma invading inner ½ ofthe myometrium (Figure 1b.)	 Yes
B.	**Clinical diagnosis-** **? Submucosal fibroid** **? Carcinoma Endometrium** Gross: Received an already cut open specimen of uterus with cervix and bilateral fallopian tubes and ovaries. A firm polypoidal mass measuring 6 x 6 cm wasseen in the endometrial cavity.	Smooth muscle tumour of uncertain malignant potential. (STUMP) (Figure 3a.)	Low grade sarcoma probably leiomyosarcoma invading less than ½ of the myometrium. (Figure 3b.)	STUMP is a differential diagnosis in leiomyosarcoma
C.	**Clinical diagnosis- Carcinoma Endometrium** Gross: Received an intact specimen of uterus with cervix with bilateral fallopian tubes and ovaries. On cutting open an irregular diffuse greyish white tumour mass measuring 4.5 x 4.5 x 3.7cm was seen.	Low grade endometrial stromal sarcoma (Figure 2a.)	Low grade endometrial stromal sarcoma involving more than ½ of the myometrium (Figure 2b.)	Yes
D.	**Clinical diagnosis- Leiomyoma** Case 1) Gross: Uterine fibroid measuring 8x7x3.5 cm Case 2) Gross: Uterine fibroid measuring 10.5x7.5x3.5 cm. Case 3) Gross: Uterine fibroid27x25 x 12 cm	Cellular leiomyoma Cellular leiomyoma Cellular leiomyoma (Figure 4a.)	Cellular leiomyoma Cellular leiomyoma Cellular leiomyoma (Figure 4b.)	Yes Yes Yes

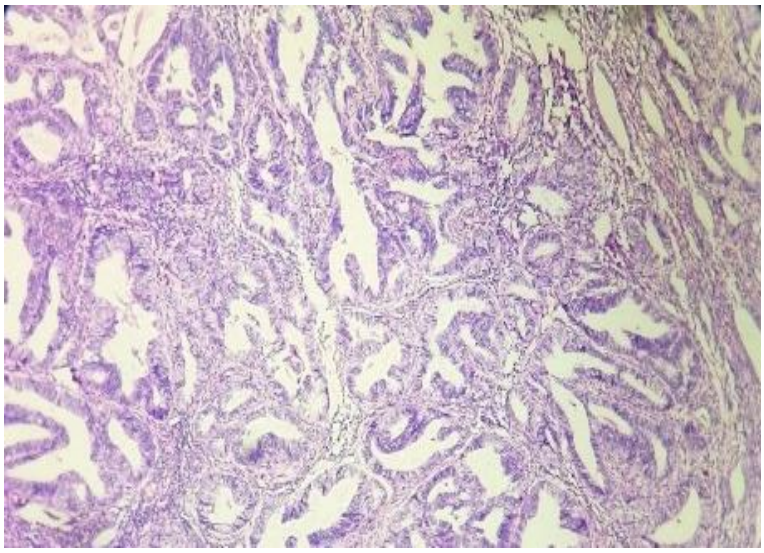

Fig 1a: Endometrioid adenocarcinoma on frozen section: Villoglandular pattern showing glands lined by stratified tall columnar cells showing hyperchromatic nuclei with moderate to scanty cytoplasm. (10x magnification; hematoxylin and eosin stain)

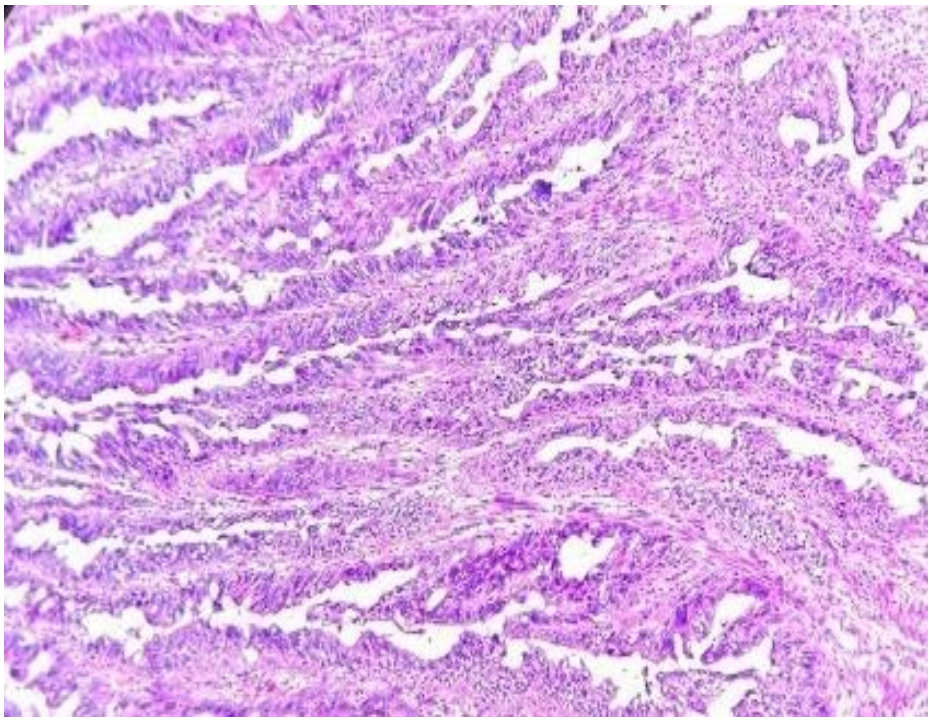

Fig 1b: Endometrioid adenocarcinoma on histopathology: Glandular papillary structures are present. (10x magnification; hematoxylin and eosin stain)

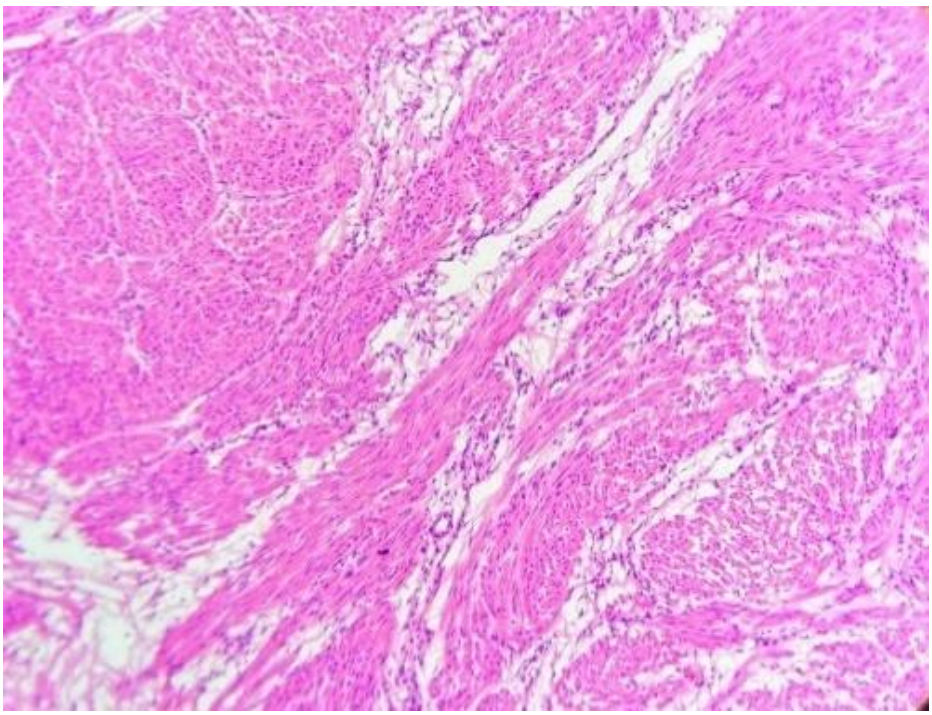

Fig 2a: Low grade endometrial stromal sarcoma on frozen section: Tumour cells arranged in densely packed islands. The tumour cells are round with uniform oval nuclei and scanty cytoplasm. There is mild anisonucleosis. (10x magnification; hematoxylin and eosin stain)

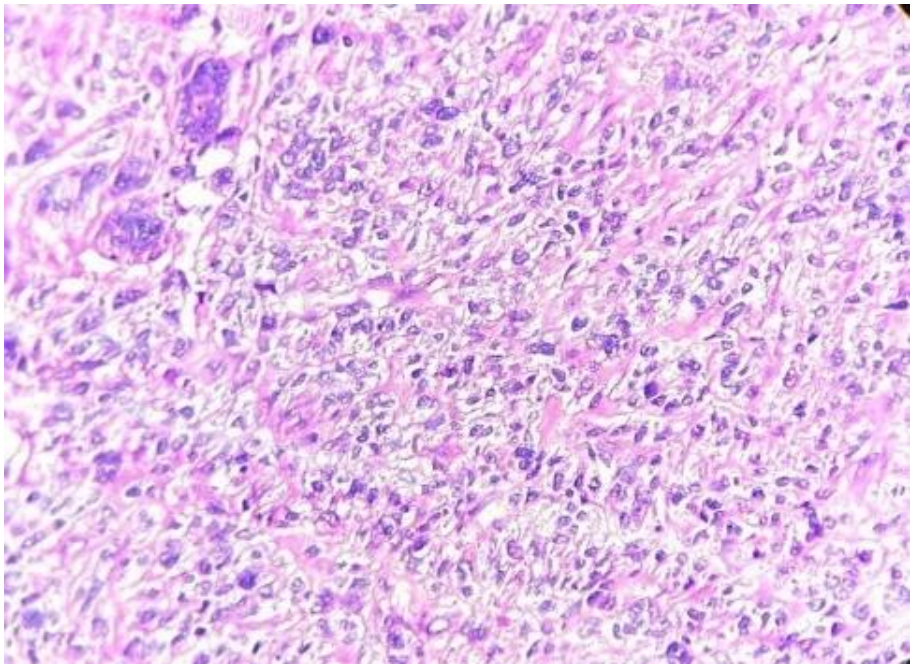

Fig 2b: Low grade endometrial stromal sarcoma on histopathology: Tumour cells arranged in irregular, densely packed islands growing into the myometrium. Cells are round to oval with uniform oval nuclei and scanty cytoplasm. (10x magnification; hematoxylin and eosin stain)

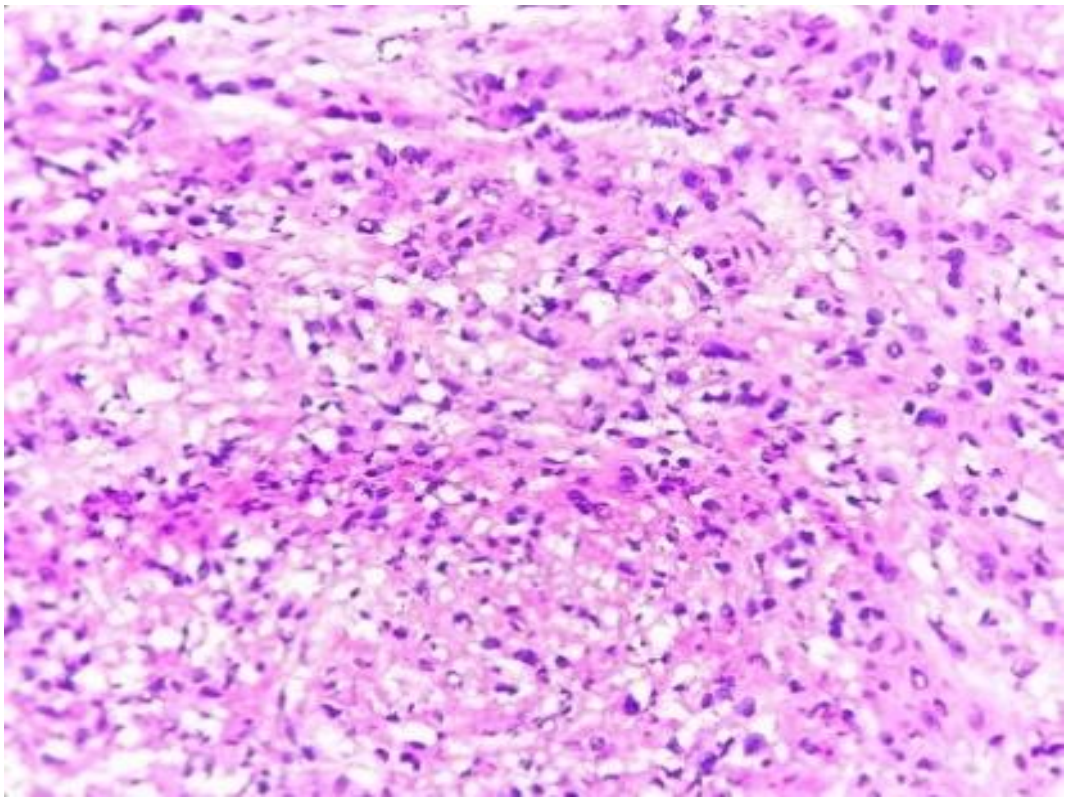

Fig 3a: Smooth muscle tumour of uncertain malignant potential (STUMP)on frozen section showing sheet like proliferation of smooth muscle cells with mild anisonucleosis. (10x magnification; hematoxylin and eosin stain)

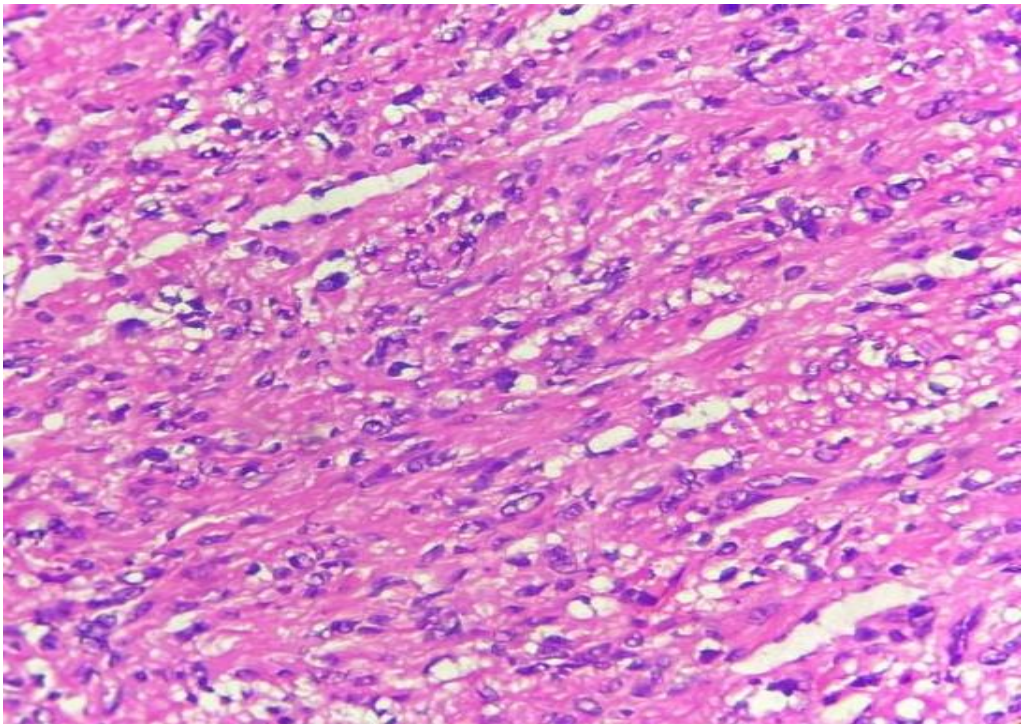

Fig 3b: Smooth muscle tumour of uncertain malignant potential on histopathology: Fasciculate arrangement of tumour cells is seen. Areas showing bizarre cells with large irregular nuclei are present. (10x magnification; hematoxylin and eosin stain)

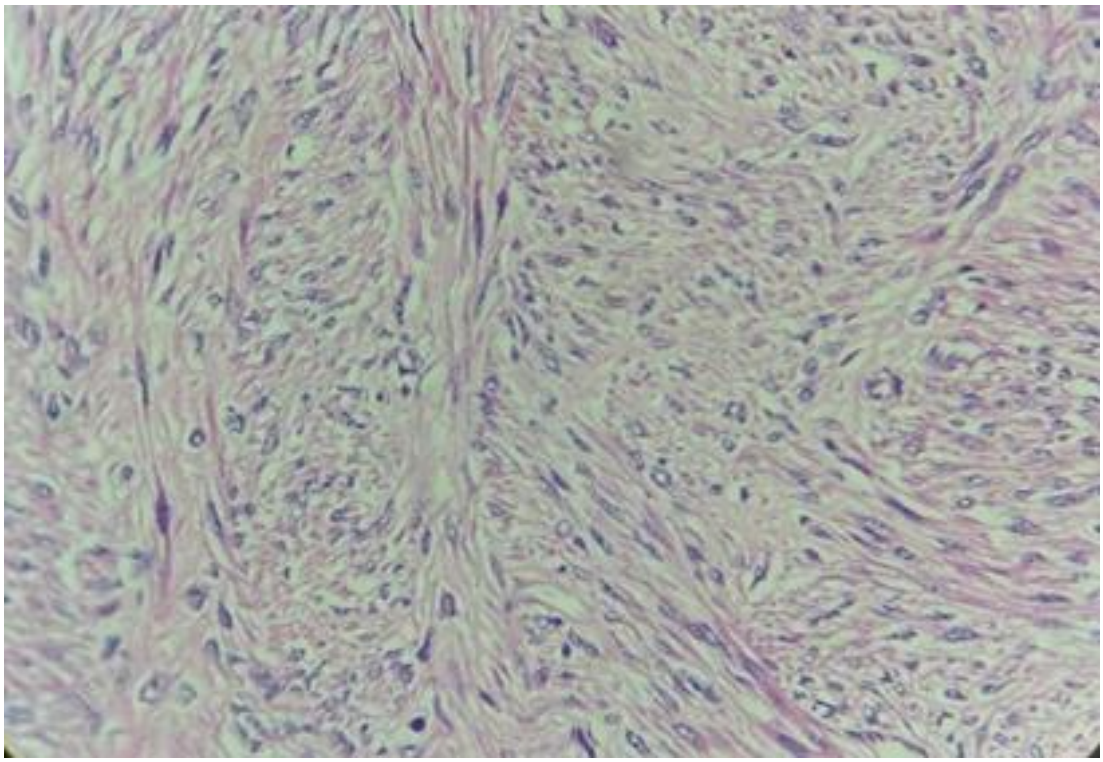

Fig 4a: Cellular leiomyoma on frozen section: Fascicles of smooth muscles arranged in interlacing and intersecting pattern. (10x magnification; hematoxylin and eosin stain)

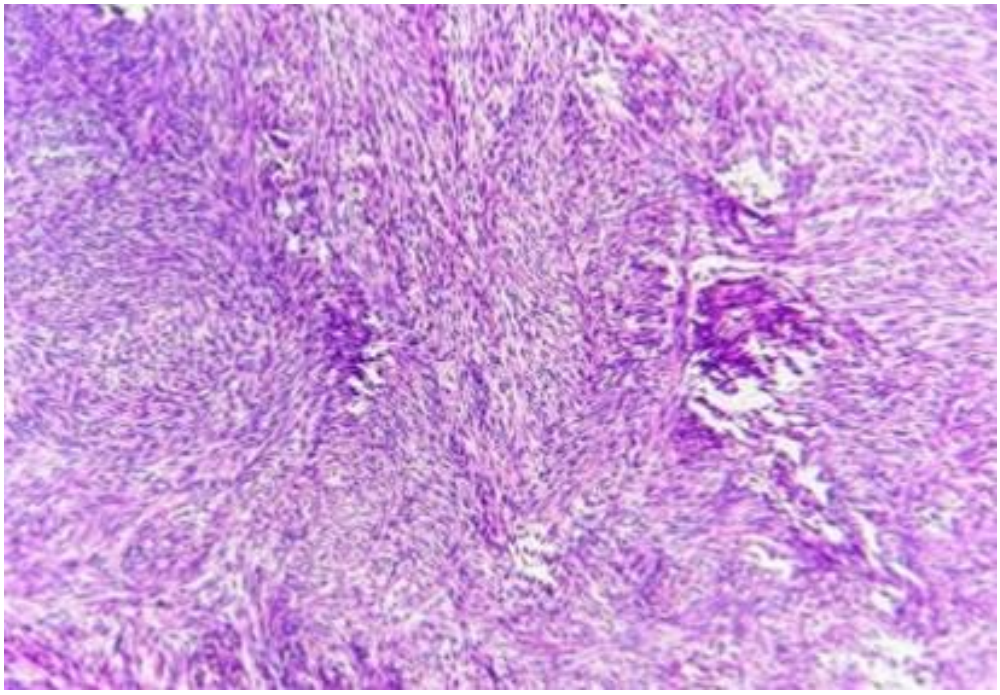

Fig 4b: Cellular leiomyoma on histopathology: Fascicles of smooth muscles arranged in interlacing and intersecting pattern. (10x magnification; hematoxylin and eosin stain

DISCUSSION

Intraoperative Frozen Section Examination involves rapid processing of tissue samples obtained during surgery to provide immediate pathological assessment. It is particularly valuable in large hospitals where timely diagnosis is critical for guiding surgical decisions. The cryostat is an essential instrument used in the process of intraoperative frozen section examination. It is equipped with mechanisms for rapidly freezing tissue samples to a temperature suitable for sectioning. The cryostat also features a microtome that allows thin sections of frozen tissue to be cut for microscopic examination. During surgery, a small portion of the excised tissue is selected for frozen section analysis. When tissue samples are rapidly frozen using the cryostat, the water within the tissue undergoes a phase transition and forms ice crystals. This rapid freezing process effectively preserves the tissue's cellular structure and molecular composition at the moment of freezing. The ice crystals that form within the tissue during rapid freezing serve as a temporary embedding medium. As the tissue is sectioned using the microtome within the cryostat, the ice provides support and stability to the tissue, allowing thin sections to be cut without damaging the cellular architecture. Lowering the temperature makes the tissue firm.Sections are cut,mounted onto slides and then stained for microscopic evaluation by a pathologist. The pathologist examines the tissue under a microscope and provides a preliminary diagnosis to the surgeon within minutes [4].

Endometrial cancer is the most common malignancy of female genital tract. It presents at an early stage, with the tumour confined to the endometrium or the inner lining of the uterus (corpus uteri). This early detection often results in a favourable prognosis compared to cancers diagnosed at later stages. Surgery remains the cornerstone of treatment for early-stage endometrial cancer, and in many cases, it is curative. The primary surgical procedure typically involves hysterectomy, with or without bilateral salpingooophorectomy. During surgery for endometrial cancer, intraoperative assessment of specific factors such as the depth of myometrial invasion, presence of endocervical extension, and tumour size is crucial. Determining depth of invasion into the myometrium helps classify the tumour stage and influences the decision regarding lymphadenectomy. The presence of tumour involvement in the endocervix (cervical canal) may necessitate additional surgical procedures, such as cervical resection. Larger tumors may indicate a higher risk of lymph node involvement and guide the need for more aggressive surgical management. This is important in elderly and patients with endometrial cancers in which the extent of lymphadenectomy might increase the risk of morbidity [5, 6]. The invasion occurs by direct infiltration through the myometrium into the cervix and it mostly metastasize to the pelvic nodes and paraaortic nodes [7].

Most women with Endometrial Adenocarcinoma have favourable prognoses.Patients who have deep myometrial invasion i.e. $\geq$ 50% of myometrial thickness, high-grade, substantial lymph vascular space invasion, and cervical stromal involvement have higher lymphatic involvement. Therefore, to evaluate high-risk factors, intraoperative frozen section examination is urgent for surgical decisions [8, 9]. This is where the intraoperative frozen section plays an important role.

In our study we got 5 cases which were diagnosed as Endometrial adenocarcinoma on frozen section and subsequently confirmed on histopathology.

Endometrial stromal tumors (ESTs) are rare neoplasms arising from the stromal cells of the uterus. These tumors encompass a spectrum of entities, including endometrial stromal nodule, low-grade endometrial stromal sarcoma, and high-grade endometrial stromal sarcoma. Despite their rarity, ESTs can pose diagnostic challenges for pathologists due to their variable histological features and overlapping morphological characteristics with other uterine neoplasms. Although despite frozen section examination's crucial role in finding intraoperative diagnosis, it may lead to over or underestimation of tumour when there is a small sampling area. Distinguishing between cellular leiomyoma and low-grade endometrial stromal sarcoma can indeed be challenging, particularly on intraoperative frozen sections. Bothtumors can exhibit increased cellularity, leading to morphological overlap and diagnostic difficulty [10, 11]. In our case, the clinical diagnosis provided was of Carcinoma endometrium, which on frozen was diagnosed as Low grade endometrial stromal sarcoma. Later on histopathology it was alsoconfirmed as Low grade endometrial stromal sarcoma.

Smooth muscle tumors of uncertain malignant potential (STUMPs) represent a category of uterine smooth muscle tumors that exhibit features intermediate between benign leiomyomas (fibroids) and malignant leiomyosarcomas (LMS). These tumors pose diagnostic challenges because they cannot be definitively distinguished as either benign or malignant based on histological criteria alone. The clinical presentation of STUMPs is mostly similar to that of uterine leiomyomas which includes a combination of symptoms related to the presence of uterine masses and potential complications like abnormal vaginal bleeding, anemia, rapidly growing pelvic mass, pressure symptoms and pelvic pain [12]. In our case, clinical differential diagnosis was of submucosal fibroid or carcinoma endometrium, which on frozen section was diagnosed as Smooth muscle tumour of uncertain malignant potential (STUMP). Microscopically, it showed sheet like proliferation of smooth muscle cells showing mild to moderate anisonucleosis. At places fasciculate arrangement of tumour cells were seen. Some areas showed bizarre cells with large irregular nuclei. Later on histopathological examination it was diagnosed as Low grade sarcoma probably leiomyosarcoma invading less than half of myometrium. Low grade sarcoma comes in the differential diagnosis of STUMP. Other differential diagnosis includes conventional (spindle cell) leiomyoma, cellular leiomyoma, epithelial leiomyoma, myxoid leiomyoma, leiomyoma with bizarre nuclei, mitotically active leiomyoma, conventional leiomyosarcoma, epithelioidleiomyosarcoma and myxoidleiomyosarcoma.

Cellular leiomyoma is a benign smooth muscle tumour originating from the myometrium of the uterus. According to World Health Organization cellular leiomyoma is defined as a leiomyoma with significantly increased cellularity compared to the surrounding myometrium. This increased cellularity can lead to histological features that include predominantly round cells or a mixture of round and spindle cells. These histological characteristics can sometimes mimic other round cell tumors of the female genital tract, posing diagnostic challenges for pathologists. The microscopic features of leiomyomas include spindle-shaped smooth muscle cells, lack of nuclear atypia, well-defined borders, and the presence of hyalinized blood vessels. These features, along with clinical and radiological findings, help distinguish leiomyomas from other uterine tumors. The documentation of thick muscular or hyalinized vessels on microscopic examination is a valuable feature that helps distinguish highly cellular leiomyomas from other tumors of the female genital tract [13]. We had three cases of clinically diagnosed leiomyomas which were sent for frozen section because of their large sizes which were 19 x 17 x 6cms, 10.5 x 7.5 x 3.5 cm and 8 x 7 x 3.5 cm respectively. All 3 cases were Cellular leiomyoma on frozen section and subsequently on histopathology also.

The accumulated data highlights the critical role of intraoperative frozen section analysis in guiding clinicians to perform appropriate surgical interventions, thereby contributing to optimal patient survival outcomes. However, it is also important to acknowledge the limitations and potential pitfalls associated with frozen sections, which can impact patient management and outcome [14-16].

Frozen section examination is a valuable tool in the investigation of women with masses suspected to be early-stage malignancies in the uterus. The decision to use intraoperative frozen section analysis in the management of uterine tumors is influenced by clinical suspicion of cancer, surgical expertise, and the availability of pathology resources. Effective communication and collaboration among healthcare providers are crucial for ensuring appropriate utilization and interpretation of frozen section results and optimizing patient outcomes [17-20].

CONCLUSION

Intraoperative frozen section diagnosis plays a crucial role in guiding surgeons during procedures by providing real-time pathological information that helps determine the appropriate course of action. It empowers surgeons to make timely and informed decisions during surgery, ultimately leading to better outcomes for patients by ensuring appropriate treatment and minimizing the need for additional procedures. Hence a good clinical history from the surgeons is very important for correlation. Careful gross examination of the surgical specimen, proper tissue sampling from representative

areas, and effective communication between the pathologist and surgeon are essential strategies to mitigate the limitations associated with intraoperative frozen section diagnosis. By integrating these strategies into the intraoperative workflow, healthcare teams can enhance the accuracy and reliability of frozen section diagnosis, minimize the risk of diagnostic errors or incomplete surgical resections, and ultimately improve patient outcomes.

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