

# Pancreatic frozen section nightmares

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## Abstract

Pancreatic resections have steadily increased over the past few decades and as a consequence so have the number of pancreatic specimens submitted for intraoperative frozen section consultation. Frozen section evaluation of the pancreas is generally performed for tumour confirmation and the assessment of margin status. An accurate and prompt diagnosis is therefore critical in guiding surgical management. However, pancreatic frozen sections are among the most challenging specimens submitted to the pathologist. While the main diagnostic dilemma is between adenocarcinoma and chronic pancreatitis, the spectrum of reactive changes, preinvasive neoplasms, neoadjuvant treatment effect and incidental lesions can further confound this assessment. The purpose of this review is to briefly discuss practical guidelines in specimen handling, common tissue artifacts, non-neoplastic and neoplastic frozen section histology, and challenging scenarios. In addition, it is our hope that this review will serve to facilitate better communication between the surgeon and pathologist to enhance patient care.

**Keywords** adenocarcinoma; chronic pancreatitis; grossing; intraoperative consultation; IPMN; neoadjuvant chemotherapy; pancreas; PanIN

## Introduction

The number of pancreatic resections has progressively increased over the past few decades. This rise is likely multifactorial and can be attributed to advancements in surgical technique, decreasing perioperative mortality, and an increased number of surgeons with pancreatobiliary training.<sup>1,2</sup> Moreover, the frequent use of imaging modalities to detect diseases involving the pancreas and associated structures, growing clinical awareness of these diseases, and expansion in resection criteria may also be responsible. As a consequence of this increase in surgeries, the number of pancreatic specimens submitted for intraoperative frozen section consultation has also risen.

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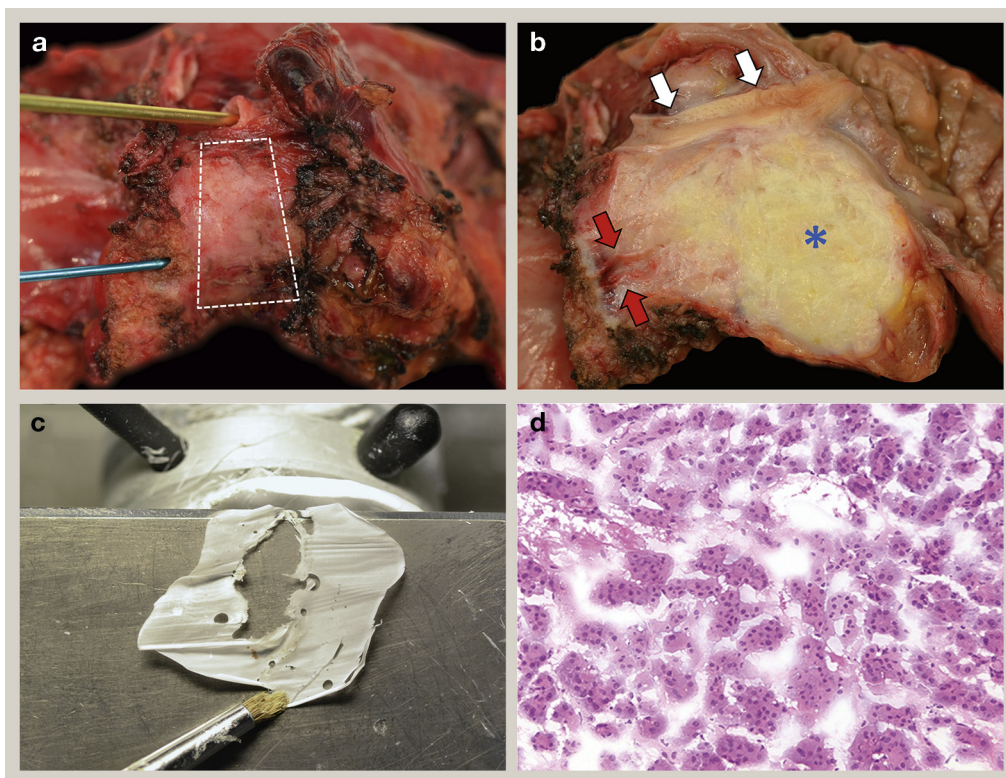
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Intraoperative frozen sections of the pancreas are generally performed for tumour confirmation and the assessment of margin status. Accurate and prompt frozen section diagnoses are therefore critical in guiding surgical management. However, pancreatic frozen sections are some of the most challenging specimens submitted to the surgical pathologist. Diagnostic difficulties are related to technical and morphologic factors with the main problematic differential diagnosis between adenocarcinoma and chronic pancreatitis. The purpose of this review is to briefly discuss practical guidelines in specimen handling, commonly encountered frozen section tissue artifacts, non-neoplastic pancreatic frozen section histology, pathologic features of adenocarcinoma on frozen section, and challenging issues or “grey areas” that may confront the surgical pathologist.

## Gross specimen handling

The first steps in any frozen section evaluation, regardless of whether it pertains to the pancreas, should be careful review of the clinical history and understanding of the specific clinical questions. This information will help guide both initial gross examination and subsequent frozen section evaluation. The next step is to orient the pancreatic specimen and identify the surgical resection margins. With advancements in surgical technique, resections of the pancreas are no longer limited to classic pancreaticoduodenectomy (Whipple procedure) and distal pancreatectomy, but also include pylorus-preserving pancreaticoduodenectomy, modified Appleby procedure, central pancreatectomy, enucleation, and ampullectomy. While the complexity of these specimens may be intimidating to even the most experienced surgical pathologist, familiarity with the gross anatomy can alleviate any associated anxiety.

The classic pancreaticoduodenectomy is an effective treatment for both malignant and benign diseases involving the head of the pancreas, distal common bile duct, ampulla of Vater and duodenum. These specimens consist of the pancreatic head, uncinate and neck, distal segment of the common bile duct, gastric pylorus, and C-shaped loop of the duodenum. The pancreaticoduodenectomy is best oriented on the grossing bench with distal stomach to the left, duodenum to the right and the head of the pancreas facing the prosector. A triangular-to-trapezoid shaped, smooth-surfaced area should be identifiable and corresponds to the vascular groove, where the superior mesenteric/portal vein was once present (Figure 1a).<sup>3,4</sup> An ovoid pancreatic neck margin is to the left of the vascular groove and often cauterized and roughened. To the right of the vascular groove is another variegated area that corresponds to the uncinate margin. The common bile duct margin is located at the superior tip of the vascular groove. In some cases, the gallbladder is received attached to the specimen and as the cystic duct joins the common bile duct distally, may serve as a further aid in identifying the common bile duct margin. Upon identification of these landmarks, both the pancreatic neck and common bile duct margins are shaved at least 2–3 mm in thickness, and submitted enface for frozen section evaluation. Care should be taken when shaving the pancreatic neck margin to include the main pancreatic duct orifice, which is often situated within the upper right periphery of the pancreatic neck. In addition, for cases where the gallbladder is absent, the common bile duct margin



**Figure 1** (a) The appropriate resection margins for frozen section evaluation in a classic pancreaticoduodenectomy can be easily identified by laying the specimen with the stomach to the left, duodenum to the right and the head of the pancreas facing the prosector. A trapezoid shaped, smooth-surfaced area corresponds to the vascular groove, where the superior mesenteric/portal vein was once present. An ovoid pancreatic neck margin is to the left of the vascular groove (blue probe within the pancreatic duct), while to the right of the vascular groove is the uncinata margin. The common bile duct margin is located at the superior tip of the vascular groove (gold probe within the bile duct). (b) Once the margins have been taken for evaluation, probes placed in the pancreatic duct and distal common bile duct can be used as a guide to transect the specimen. If performed successfully, the two ducts (red arrows, pancreatic duct; white arrows, distal common bile duct) will be cut in half, the pancreas fileted open and the duodenum transected. A careful inspection of the pancreas should be performed to locate any lesions (blue asterisk, pancreatic mass) and document their relationship to the margins of resection. (c) Prior to the evaluation of frozen sections, a number of tissue artifacts may be encountered. In this example, a fatty pancreatic specimen proved difficult to section as it had a tendency to curl away from the embedding medium leaving a hole in place of the tissue. (d) Fixation of frozen section slides can also present with specific artifacts. A prolonged amount of time between tissue adherence to a warm slide and fixation can result in drying artifact, which results in cellular enlargement, nuclear smudging and blurring of cytoplasmic borders.

may consist of two lumens, which represent the distal common bile duct and cystic duct. Due to the difficulty in distinguishing between the two, it has been our practice to include both within the common bile duct margin for frozen section evaluation. In cases of pylorus-sparing pancreaticoduodenectomy, frozen section evaluation should also encompass the proximal duodenal resection margin. Although infrequent, our institution has experienced a number of adenocarcinomas involving the proximal duodenal resection margin and, thus, if positive, the surgeon can be alerted to extend their resection to incorporate the distal stomach. The remaining margins, such as the uncinata, vascular groove and distal duodenal are typically submitted for routine processing of formalin-fixed paraffin-embedded tissue.

A distal pancreatectomy is performed for diseases involving the body and/or tail of the pancreas. For locally advanced cancers of the pancreatic body involving the celiac or hepatic artery, an Appleby operation may be indicated. Both specimens are much easier to handle than pancreaticoduodenectomies. The spleen helps identify the distal aspect of the gland, and the cut surface of the pancreas is the pancreatic neck. A shave of the

pancreatic neck is typically the only margin submitted for frozen section evaluation; while the retroperitoneal and, for Appleby specimens, the vascular resection margins are submitted for routine processing.<sup>4</sup>

The remaining surgical procedures are performed for small lesions involving the pancreas and associated structures. Benign diseases and low-grade neoplasms within the pancreatic neck that extend into the main pancreatic duct can be removed by central pancreatectomy. The evaluation of the proximal and distal margins is imperative to ensure completeness of resection; however, if the specimen margins are received undesignated, distinguishing between the two margins can be challenging. In these circumstances, the surgeon should be contacted to designate these margins before frozen section evaluation. Small lesions within the pancreatic neck, body or tail that do not communicate with the main pancreatic duct can be treated by enucleation. Rather than a shave margin, a perpendicular section of the lesion closest to the cauterized margin is taken for frozen section evaluation. An ampullectomy is performed for small lesions involving the ampulla of Vater. These specimens consist of

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