

ORIGINAL ARTICLE

A novel approach to the intraoperative assessment of the uncinate margin of the pancreaticoduodenectomy specimenMAHMOUD A. KHALIFA¹, VLAD MAKSYMOW¹, CORWYN H. ROWSELL¹ & SHERIF HANNA²*Departments of ¹Pathology and ²Surgical Oncology, Sunnybrook Health Sciences Center, Toronto, Canada***Abstract**

Background. Currently, there is no consensus regarding the pancreaticoduodenectomy (PD) margins examined intraoperatively or the technical protocol for frozen section examination. The aim of this work was to summarize our experience regarding the intraoperative examination of the uncinate margin and to compare it with the published literature. **Materials and methods.** Our local protocol for the intraoperative assessment of the uncinate margin of the PD specimen is described in this article. A PubMed® search limited to English language publications using terms along the theme of *pancreaticoduodenectomy* and *margin* was performed. Retrieved articles were categorized according to whether they discussed frozen section margin examination. **Results.** Ten articles published between 1981 and 2005 were retrieved which discussed the intraoperative examination of PD specimens. Of the 10 articles, 5 discussed the intraoperative consultation for diagnostic purposes only, 2 discussed the consultation for both diagnostic purposes and assessment of margins, and 3 discussed intraoperative assessment of margins only. Of the total of five articles that discussed the intraoperative assessment of margins, none detailed the technical protocol for examining the uncinate margin. **Discussion.** Our proposed protocol for the intraoperative assessment of the uncinate margin of PD specimens allows for its accurate evaluation and has not been described previously in the English literature.

Key Words: *uncinate margin, pancreaticoduodenectomy, Whipple, frozen section***Introduction**

There is increasing evidence to emphasize the importance of the proper handling of the pancreaticoduodenectomy (PD) specimen, also known as Whipple specimen, to improve patient survival and prediction of prognosis [1–4]. This is true both intraoperatively, as the surgeon tries to make critical technical decisions, and postoperatively as the oncologists optimize their categorization of patients for adjuvant therapy and follow-up. Intraoperatively, surgeons may request a pathology consultation for a variety of reasons. In this context, the intraoperative consultation (IOC) represents the first encounter of the pathologist with the resected specimen, which is also the optimal opportunity to start its proper handling. Assessment of the surgical margins is one of the most common indications for IOC during the PD procedure. As critical as this step is, there is no

consensus regarding the margins examined intraoperatively or a standard technical protocol for frozen section examination of the selected margins.

We find that the intraoperative assessment of the uncinate margin is extremely important in cases of adenocarcinoma involving the head or the uncinate process of the pancreas. Achieving a negative resection margin in the uncinate process is complicated by its proximity to the superior mesenteric artery (SMA) and the need to preserve it as well as the nerve plexus around it. This margin is technically difficult to assess by frozen section, since in the resected specimen the uncinate process is covered by a rim of adipose tissue that is a few millimeters thick. Preparing an adequate frozen section from adipose tissue is technically challenging. As a result, over the past year we have changed our local protocol for the intraoperative processing of the uncinate margin. The aim of this work was to summarize our experience in this area

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and to compare it with the published literature. We also hope that through discussing our protocol we can raise awareness of the issues surrounding assessment of the uncinate margin.

Materials and methods

In 2005, our local surgical pathology protocol for intraoperative assessment of the PD specimen with carcinomas in the head or the uncinate process of the pancreas was modified to require inking of the posterior surface of the pancreas including the uncinate process. The tip of the uncinate process, including its distal 1 cm, is then cut off the rest of the specimen (Figure 1) and is serially sectioned at 3 mm intervals perpendicular to its longitudinal axis. This produces five to eight pieces of tissue that are submitted for frozen section examination (Figure 2). All pieces are submitted for frozen section examination, ensuring that the entire length of tissue where the uncinate process comes in proximity with the SMA is examined. The produced frozen section will show the inked margin with an underlying zone of adipose tissue overlying the native pancreatic tissue of the uncinate process. Figure 3 depicts an example of a case with a negative uncinate margin where malignant glands involved the uncinate process. One can see how if this margin was shaved off, submitted *en face* and sections trimmed of fat the produced frozen section would have probably been assessed as 'positive'. This new protocol was also followed for assessment of the uncinate margin on permanent sections in cases where no IOC was requested. The institutional Research Ethics Board approved our request to carry out a retrospectively study, audit, and publish our IOC experience for the PD procedure.

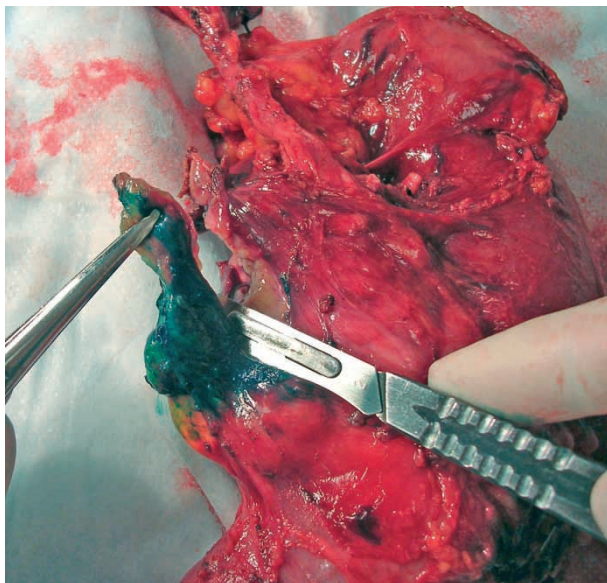


Figure 1. The tip of the uncinate process, including its distal 1 cm is being cut off the rest of the specimen after it has been inked.

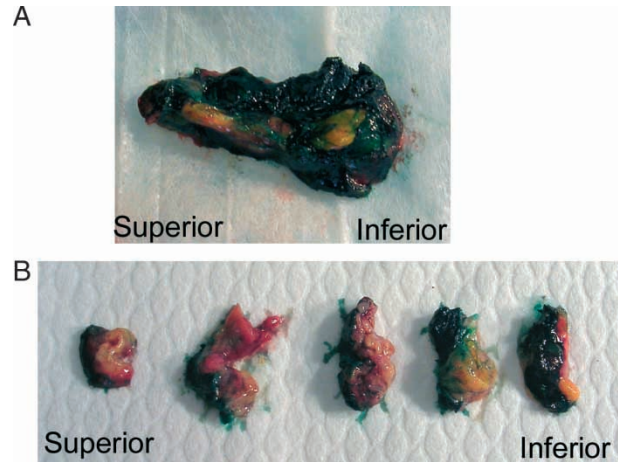


Figure 2. Further processing of the uncinate margin. (A) The tip of the uncinate process including its margin is laid down, inked, and well oriented. (B) It is then serially sectioned at 3 mm intervals perpendicular to its longitudinal axis producing 6–10 pieces of tissue that are submitted for frozen section examination.

The National Library of Medicine and the National Institutes of Health databases were searched for related English language publications. This was conducted through the PubMed® search engine using a combination of two groups of terms. The first group included the terms *pancreas*, *pancreaticoduodenectomy*, *pancreatoduodenectomy* and *Whipple*. The second group included the terms *margin*, *frozen section* and *uncinate*. All possible combinations including one term selected from each group were used. Retrieved articles were categorized according to whether they discussed the IOC of pancreatic margins. Unrelated articles, which appeared in the search but did not address the topic of IOC, were excluded.

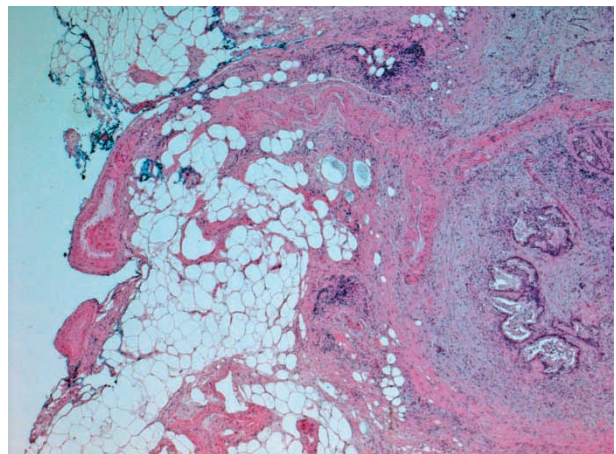


Figure 3. A frozen section of the uncinate margin showing the inked true margin, an underlying rim of adipose tissue, and a portion of native pancreatic parenchyma invaded by adenocarcinoma. Note that the solid tissue on the right side of the section provided support and helped prevent curling of the adipose tissue on the left side.

Results

Since the implementation of our new protocol, the uncinata margin has been assessed 23 times, providing us with the opportunity to master the technique. In 11 cases, the uncinata process was involved by adenocarcinoma but the new protocol allowed us to provide an accurate and confident IOC of the uncinata margin. Figure 3 depicts one of these cases, illustrating how it probably could have been over-called as 'positive', had it been submitted by the traditional *en face* method. To date, the uncinata margin has confidently been deemed positive in three cases.

Ten articles published between 1981 and 2005 were retrieved which discussed the intraoperative examination of PD specimens [5–14]. Of the 10 articles, 5 discussed the IOC for diagnostic purposes only [5–8,12], 2 discussed the consultation for both diagnostic purposes and assessment of margins [11,14], and 3 discussed intraoperative assessment of margins only [9,10,13]. Of the total of five articles that discussed the intraoperative assessment of margins, none went into detail to describe the technique or procedure for submitting and examining the uncinata margin.

Discussion

The standard Whipple procedure involves resecting the antrum of the stomach, the entire four parts of the duodenum, and a small segment of proximal jejunum, as well as the distal common bile duct and head of the pancreas. The neck of the pancreas is transected, thus exposing the portal vein (PV). The final step in removing the Whipple specimen from the patient is transecting the uncinata process. The uncinata process of the head of the pancreas extends posterior to the PV and has a tongue-like projection that touches the right lateral aspect of the SMA. In order to deliver the specimen, the uncinata process needs to be divided as close to the SMA as possible, yet without damaging the SMA or the autonomic nerve plexus surrounding it; since in our experience denuding this peri-arterial nerve plexus often results in a prolonged postoperative gastric ileus. Technically, this is a very challenging step in the Whipple procedure since the uncinata process is very well vascularized and tends to bleed. Also, the SMA is very closely adherent to the most distal aspect of the uncinata process. In view of this, there is a natural tendency on the part of the surgeon to leave behind, in the patient, the bit of uncinata tissue closest to the SMA. This can sometimes lead to a positive uncinata margin of resection.

We define the uncinata margin as the cut surface produced by the surgeon's knife while dissecting the uncinata process from the SMA, which tends to be

granular and irregular. This is different from the smooth and regular retroperitoneal surface to the right of the proximal 3–4 cm of the SMA, which some surgeons may refer to as the 'uncinata margin' [15]. In cases of carcinoma involving the head or the uncinata process of the pancreas, dissecting away from the SMA and closer to the pancreatic tissue may run the risk of producing a positive margin, leaving behind extra-pancreatic malignant cells in the adipose tissue around the SMA or even intra-pancreatic malignancy if a portion of the uncinata process was left adherent to the SMA. Therefore, it is important to enable the pathologist to provide an accurate IOC on the uncinata margin. In cases where excision of additional tissue from the immediate vicinity of the SMA is still technically feasible, the intraoperative reporting of a positive uncinata margin may signal its revision to ensure complete excision of all cancerous tissue by completely stripping the SMA off any adjacent adipose tissue.

A microscopically negative (R0) uncinata margin is not only an important determinant of a good prognosis but is also a prerequisite for enrollment in many, if not all, adjuvant postoperative clinical trials of chemotherapy or radiation. On the other hand, a microscopically positive (R1) resection denotes a poorer prognosis and unfortunately condemns the patient to almost certain local recurrence. A macroscopically positive (R2) resection is an even worse prognostic marker.

Traditionally, examining the uncinata margin in our institute was done by shaving a 3–5 mm thick rim of tissue from the uncinata margin and submitting it *en face* for frozen sectioning. The true margin with the tissue that was closest to the SMA will be facing the knife to be cut first. Although still followed in many other medical centers, this procedure suffers several technical problems. According to this procedure, the first layer of tissue to be cut is almost entirely lipomatous, which is very difficult to cut. This tissue tends to curl, fold, and fragment, leading the operator to continue trimming. As trimming of tissue continues, the true margin gets lost, an inherent problem with any frozen section where the submitted tissue is embedded *en face*. By the time the operator is able to get an intact section adequate for staining and histologic examination, the cryostat blade will most likely be cutting through native pancreatic tissue. The pathologist examining the produced section may run the risk of over-calling the margin as 'positive', since they will typically be looking at deeper pancreatic tissue rather than the true margin. Our proposed protocol technically allows for the production of better sections, as the solid pancreatic tissue on one side of the frozen section acts as a scaffold supporting the softer adipose tissue and decreasing its folding (Figure 3). When malignant cells are present on the

section, this protocol enables the pathologist to measure the distance between the deepest point of invasion and the inked margin (Figure 3). These advantages are lost when the uncinata margin is shaved and submitted *en face*.

To overcome the difficulties with the *en face* submission, some pathologists would rather cut a portion of the uncinata portion and then serially section the produced tissue. Although somewhat similar to our procedure, this latter protocol does not call for assessment of the entire length of the uncinata margin since only a portion of it is examined. In addition, our proposed protocol allows the operator to keep track of whether produced sections were obtained from the superior, middle, or inferior portions of the uncinata margin, which can provide the surgeon with a more precise localization of a positive margin. We have also noticed in most cases that submitting the entire length of the uncinata margin captures the additional superior mesenteric lymph nodes, boosting the number of lymph nodes examined in the specimen.

Our literature search shows that the significance of an accurate intraoperative assessment of the uncinata margin and a detailed description of the technique needed to provide this assessment were not documented in the English literature. One particular article provided a thorough description of the IOC for pancreatic surgery, without detailing the technical procedure [14].

Our proposed protocol for the intraoperative assessment of the uncinata margin of PD specimens allows for its accurate evaluation and has not been previously described in the English literature.

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