



## Protocol for the Examination of Specimens from Patients with Carcinoma of the Small Intestine

Version: 4.3.0.0

Protocol Posting Date: June 2025

CAP Laboratory Accreditation Program Protocol Required Use Date: March 2026

The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes specimens designated segmental resection, pancreaticoduodenectomy (Whipple resection), ileocolic resection
Tumor Type	Description
Carcinoma	Including carcinomas arising in the duodenum, jejunum, and ileum

This protocol is NOT required for accreditation purposes for the following:

Procedure
Biopsy
Primary resection specimen with no residual cancer (e.g., following neoadjuvant therapy)
Recurrent tumor
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Carcinoma of the ampulla (consider Ampullary Carcinoma protocol)
Well-differentiated neuroendocrine tumor of the duodenum (consider the Duodenal and Ampullary NET protocol)
Well-differentiated neuroendocrine tumor of the jejunum and ileum (consider the Jejunal and Ileal NET protocol)
Lymphoma (consider the Precursor and Mature Lymphoid Malignancies protocol)
Gastrointestinal stromal tumor (GIST) (consider the GIST protocol)
Non-GIST sarcoma (consider the Soft Tissue protocol)

### Version Contributors

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### Glossary:

**Author:** Expert who is a current member of the Cancer Committee, or an expert designated by the chair of the Cancer Committee.

**Expert Contributors:** Includes members of other CAP committees or external subject matter experts who contribute to the current version of the protocol.

### Accreditation Requirements

Synoptic reporting with core and conditional data elements for designated specimen types\* is required for accreditation.

- Data elements designated as core must be reported.
- Data elements designated as conditional only need to be reported if applicable.
- Data elements designated as optional are identified with "+". Although not required for accreditation, they may be considered for reporting.

This protocol is not required for recurrent or metastatic tumors resected at a different time than the primary tumor. This protocol is also not required for pathology reviews performed at a second institution (i.e., second opinion and referrals to another institution).

Full accreditation requirements can be found on the CAP website under [Accreditation Checklists](#).

A list of core and conditional data elements can be found in the Summary of Required Elements under Resources on the CAP Cancer Protocols [website](#).

*\*Includes definitive primary cancer resection and pediatric biopsy tumor types.*

### Synoptic Reporting

All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
  - Anatomic site or specimen, laterality, and procedure
  - Pathologic Stage Classification (pTNM) elements
  - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location
- Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e., all required elements must be in the synoptic portion of the report in the format defined above.

### **Summary of Changes**

#### **v 4.3.0.0**

- Updates to content and explanatory notes to include modifications to Histologic Type, Tumor Extent, and Margin Status for Non-Invasive Tumor questions and SPECIAL STUDIES section
- Addition of required “Treatment Effect” and “Perineural Invasion” questions
- Lymphovascular Invasion question updated to Lymphatic and / or Vascular Invasion
- Updates to pTNM Classification

## Reporting Template

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**Protocol Posting Date:** June 2025

**Select a single response unless otherwise indicated.**

**CASE SUMMARY: (SMALL INTESTINE)**

**Standard(s):** AJCC 8

### SPECIMEN

#### Procedure

- ☐ Segmental resection
- ☐ Ileocolic resection
- ☐ Pancreaticoduodenectomy (Whipple resection)
- ☐ Other (specify): \_\_\_\_\_
- ☐ Not specified

### TUMOR

#### Tumor Site (Note [A](#))

- ☐ Duodenum: \_\_\_\_\_
- ☐ Jejunum: \_\_\_\_\_
- ☐ Ileum: \_\_\_\_\_
- ☐ Small intestine, NOS: \_\_\_\_\_
- ☐ Other (specify): \_\_\_\_\_

#### Histologic Type (Note [B](#))

- ☐ Adenocarcinoma, NOS
- ☐ Mucinous adenocarcinoma (greater than 50% mucinous)
- ☐ Poorly cohesive carcinoma
- ☐ Signet-ring cell carcinoma
- ☐ Medullary carcinoma
- ☐ Adenosquamous carcinoma
- ☐ Squamous cell carcinoma
- ☐ Large cell neuroendocrine carcinoma
- ☐ Small cell neuroendocrine carcinoma

*# Select this option only if large cell or small cell cannot be determined.*

- ☐ Neuroendocrine carcinoma (poorly differentiated)#
- ☐ Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) (specify components):  
\_\_\_\_\_

- ☐ Undifferentiated carcinoma, NOS
- ☐ Other histologic type not listed (specify): \_\_\_\_\_

**+Histologic Type Comment:** \_\_\_\_\_

#### Histologic Grade (Note [C](#))

- ☐ G1, well-differentiated
- ☐ G2, moderately differentiated
- ☐ G3, poorly differentiated

- ☐ G4, undifferentiated  
☐ Other (specify): \_\_\_\_\_  
☐ GX, cannot be assessed: \_\_\_\_\_  
☐ Not applicable: \_\_\_\_\_

**Tumor Size**

- ☐ Greatest dimension in Centimeters (cm): \_\_\_\_\_ cm  
**+Additional Dimension in Centimeters (cm): \_\_\_\_\_ x \_\_\_\_\_ cm**  
☐ Cannot be determined (explain): \_\_\_\_\_

**Tumor Extent**

- ☐ High-grade dysplasia / carcinoma in situ  
☐ Invades lamina propria  
☐ Invades submucosa  
☐ Invades muscularis propria  
☐ Invades through muscularis propria into subserosa  
☐ Extends into non-peritonealized perimuscular tissue (mesentery or retroperitoneum) without serosal penetration  
☐ Perforates visceral peritoneum  
☐ Directly invades other organ(s) or structure(s)  
*Select all that apply*  
☐ Other loops of small intestine  
☐ Mesentery of adjacent loops of bowel  
☐ Abdominal wall (by way of serosa)  
*For Duodenum Only*  
☐ Pancreas  
☐ Bile duct  
*Other*  
☐ Other (specify): \_\_\_\_\_  
☐ Cannot be determined: \_\_\_\_\_  
☐ Cannot be determined: \_\_\_\_\_  
☐ No evidence of primary tumor

**Macroscopic Tumor Perforation**

- ☐ Not identified  
☐ Present  
☐ Cannot be determined: \_\_\_\_\_

**Lymphatic and / or Vascular Invasion**

- ☐ Not identified  
☐ Present  
☐ Cannot be determined: \_\_\_\_\_

**Perineural Invasion**

- ☐ Not identified  
☐ Present  
☐ Cannot be determined: \_\_\_\_\_

**Treatment Effect (Note [D](#))**

- ☐ No known presurgical therapy
- ☐ Present, with no viable cancer cells (complete response, score 0)
- ☐ Present, with single cells or rare small groups of cancer cells (near complete response, score 1)
- ☐ Present, with residual cancer showing evident tumor regression, but more than single cells or rare small groups of cancer cells (partial response, score 2)
- ☐ Present, NOS
- ☐ Absent, with extensive residual cancer and no evident tumor regression (poor or no response, score 3)
- ☐ Cannot be determined: \_\_\_\_\_

**+Tumor Comment:** \_\_\_\_\_

**MARGINS (Note [E](#))**

**Margin Status for Invasive Carcinoma**

- ☐ All margins negative for invasive carcinoma

**+Closest Margin(s) to Invasive Carcinoma (select all that apply)**

- ☐ Proximal: \_\_\_\_\_
- ☐ Distal: \_\_\_\_\_
- ☐ Radial or mesenteric: \_\_\_\_\_
- ☐ Uncinate (retroperitoneal / superior mesenteric artery): \_\_\_\_\_
- ☐ Bile duct: \_\_\_\_\_
- ☐ Pancreatic: \_\_\_\_\_
- ☐ Other (specify): \_\_\_\_\_
- ☐ Cannot be determined: \_\_\_\_\_

**+Distance from Invasive Carcinoma to Closest Margin**

*Specify in Centimeters (cm)*

- ☐ Exact distance in cm: \_\_\_\_\_ cm
- ☐ Greater than 1 cm

*Specify in Millimeters (mm)*

- ☐ Exact distance in mm: \_\_\_\_\_ mm
- ☐ Greater than 10 mm

*Other*

- ☐ Other (specify): \_\_\_\_\_
- ☐ Cannot be determined: \_\_\_\_\_

- ☐ Invasive carcinoma present at margin

**Margin(s) Involved by Invasive Carcinoma (select all that apply)**

- ☐ Proximal: \_\_\_\_\_
- ☐ Distal: \_\_\_\_\_
- ☐ Radial or mesenteric (tumor present 0-1 mm from margin): \_\_\_\_\_
- ☐ Uncinate (retroperitoneal / superior mesenteric artery) (tumor present 0-1 mm from margin): \_\_\_\_\_
- ☐ Bile duct: \_\_\_\_\_
- ☐ Pancreatic: \_\_\_\_\_
- ☐ Other (specify): \_\_\_\_\_

- ☐ Cannot be determined: \_\_\_\_\_  
☐ Other (specify): \_\_\_\_\_  
☐ Cannot be determined (explain): \_\_\_\_\_  
☐ Not applicable

**Margin Status for Non-Invasive Tumor (select all that apply)**

- ☐ All margins negative for high-grade dysplasia and low-grade dysplasia  
☐ High-grade dysplasia present at margin

**Margin(s) Involved by High-Grade Dysplasia (select all that apply)**

- ☐ Proximal: \_\_\_\_\_  
☐ Distal: \_\_\_\_\_  
☐ Other (specify): \_\_\_\_\_  
☐ Cannot be determined: \_\_\_\_\_  
☐ Low-grade dysplasia present at margin

**Margin(s) Involved by Low-Grade Dysplasia (select all that apply)**

- ☐ Proximal: \_\_\_\_\_  
☐ Distal: \_\_\_\_\_  
☐ Other (specify): \_\_\_\_\_  
☐ Cannot be determined: \_\_\_\_\_  
☐ Other (specify): \_\_\_\_\_  
☐ Cannot be determined (explain): \_\_\_\_\_  
☐ Not applicable

**+Margin Comment:** \_\_\_\_\_

**REGIONAL LYMPH NODES**

**Regional Lymph Node Status**

- ☐ Not applicable (no regional lymph nodes submitted or found)  
☐ Regional lymph nodes present  
☐ All regional lymph nodes negative for tumor  
☐ Tumor present in regional lymph node(s)

**Number of Lymph Nodes with Tumor**

- ☐ Exact number (specify): \_\_\_\_\_  
☐ At least (specify): \_\_\_\_\_  
☐ Other (specify): \_\_\_\_\_  
☐ Cannot be determined (explain): \_\_\_\_\_  
☐ Other (specify): \_\_\_\_\_  
☐ Cannot be determined (explain): \_\_\_\_\_

**Number of Lymph Nodes Examined**

- ☐ Exact number (specify): \_\_\_\_\_  
☐ At least (specify): \_\_\_\_\_  
☐ Other (specify): \_\_\_\_\_  
☐ Cannot be determined (explain): \_\_\_\_\_

**+Regional Lymph Node Comment:** \_\_\_\_\_

## DISTANT METASTASIS

### Distant Site(s) Involved, if applicable (select all that apply)

- ☐ Not applicable
- ☐ Non-regional lymph node(s): \_\_\_\_\_
- ☐ Liver: \_\_\_\_\_
- ☐ Other (specify): \_\_\_\_\_
- ☐ Cannot be determined: \_\_\_\_\_

### pTNM CLASSIFICATION (AJCC 8th Edition) (Note [F](#))

*Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.*

### Modified Classification (required only if applicable) (select all that apply)

- ☐ Not applicable
- ☐ y (post-neoadjuvant therapy)
- ☐ r (recurrence)

### pT Category

- ☐ pT not assigned (cannot be determined based on available pathological information)
- ☐ pT0: No evidence of primary tumor
- ☐ pTis: High-grade dysplasia / carcinoma in situ
- pT1: Tumor invades the lamina propria or submucosa*
- ☐ pT1a: Tumor invades the lamina propria
- ☐ pT1b: Tumor invades the submucosa
- ☐ pT1 (subcategory cannot be determined)
- ☐ pT2: Tumor invades the muscularis propria

*# For T3 tumors, the nonperitonealized perimuscular tissue is, for the jejunum and ileum, part of the mesentery and, for the duodenum in areas where serosa is lacking, part of the interface with the pancreas.*

- ☐ pT3: Tumor invades through the muscularis propria into the subserosa, or extends into nonperitonealized perimuscular tissue (mesentery or retroperitoneum) without serosal penetration#
- ☐ pT4: Tumor perforates the visceral peritoneum or directly invades other organs or structures (e.g., other loops of small intestine, mesentery of adjacent loops of bowel, and abdominal wall by way of serosa; for duodenum only, invasion of pancreas or bile duct)

### T Suffix (required only if applicable)

- ☐ Not applicable
- ☐ (m) multiple primary synchronous tumors in a single organ

### pN Category

- ☐ pN not assigned (no nodes submitted or found)
- ☐ pN not assigned (cannot be determined based on available pathological information)
- ☐ pN0: No regional lymph node metastasis
- ☐ pN1: Metastasis in one or two regional lymph nodes
- ☐ pN2: Metastasis in three or more regional lymph nodes



**pM Category (required only if confirmed pathologically)**

☐ Not applicable - pM cannot be determined from the submitted specimen(s)

☐ pM1: Distant metastasis

**ADDITIONAL FINDINGS (Note [G](#))**

**+Additional Findings (select all that apply)**

☐ None identified

☐ Adenoma(s)

☐ Crohn disease

☐ Celiac disease

☐ Other polyp(s) (specify type[s]): \_\_\_\_\_

☐ Other (specify): \_\_\_\_\_

**SPECIAL STUDIES**

**+Ancillary Studies (Note [H](#))**

☐ Specify: \_\_\_\_\_

☐ Not performed

**COMMENTS**

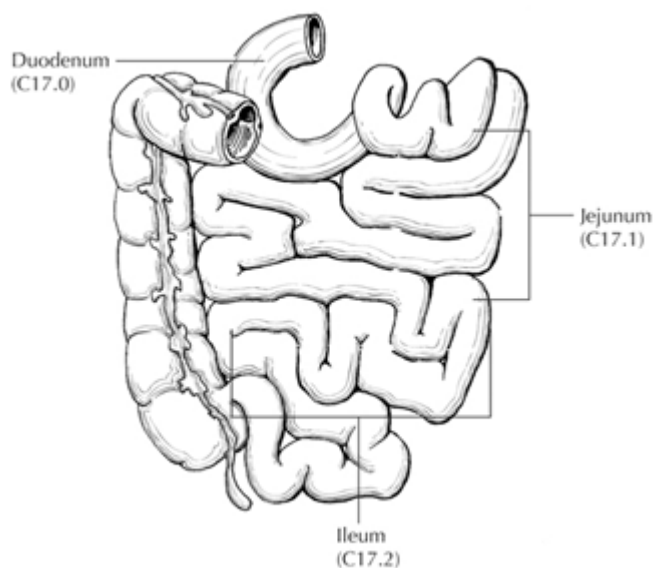
**Comment(s):** \_\_\_\_\_

## Explanatory Notes

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### A. Tumor Site

The majority of small intestinal carcinomas arise in the duodenum (64%),<sup>1</sup> most commonly around the ampulla of Vater (Figure 1). Approximately 20% arise in the jejunum and 15% in the ileum. Duodenal location has been implicated as a risk factor for poorer outcome.<sup>2</sup>



**Figure 1.** Anatomical sites of the small intestine. From: Greene FL et al.<sup>3</sup> Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, [www.springerlink.com](http://www.springerlink.com).

### References

1. Howe JR, Karnell LH, Menck HR, Scott-Conner C. Adenocarcinoma of the small bowel: review of the National Cancer Data Base, 1985-1995. *Cancer*. 1999; 86:2693-2706.
2. Dabaja BS, Suki D, Pro B, Bonnen M, Ajani J. Adenocarcinoma of the small bowel: presentation, prognostic factors, and outcome of 217 patients. *Cancer*. 2004; 101:518-526.
3. Greene FL, Compton CC, Fritz AG, et al, eds. *AJCC Cancer Staging Atlas*. New York: Springer; 2006.

### B. Histologic Type

The most common tumor types arising in the small intestine are adenocarcinomas (24% to 44%), well-differentiated neuroendocrine tumors (20% to 42%), gastrointestinal stromal tumors (7% to 9%), and lymphoma (12% to 27%).<sup>1</sup> Separate CAP cancer protocols apply to well-differentiated neuroendocrine tumors, gastrointestinal stromal tumors, and lymphomas.

For carcinomas of the small intestine, the protocol recommends the histologic classification published by the World Health Organization (WHO).<sup>2</sup>

#### References

1. Zeh HJ. Cancer of the small intestine. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.
2. WHO Classification of Tumours Editorial Board. *Digestive system tumours*. Lyon (France): International Agency for Research on Cancer; 2019. (WHO classification of tumours series, 5th ed.; vol. 1).

#### C. Histologic Grade

A histologic grading system for adenocarcinomas based on the extent of glandular formation in the tumor is recommended, as shown below:

Grade X	Grade cannot be assessed
Grade 1	Well-differentiated (more than 95% of tumor composed of glands)
Grade 2	Moderately differentiated (50% to 95% of tumor composed of glands)
Grade 3	Poorly differentiated (less than 50% of tumor composed of glands)

Grade 4 is reserved for small cell neuroendocrine carcinoma and undifferentiated carcinoma (WHO classification).

Most small bowel carcinomas are moderately differentiated, followed by poorly differentiated; a minority are well differentiated. Grade does not appear to be a strong predictor of outcome.<sup>1,2</sup>

#### References

1. Howe JR, Karnell LH, Menck HR, Scott-Conner C. Adenocarcinoma of the small bowel: review of the National Cancer Data Base, 1985-1995. *Cancer*. 1999; 86:2693-2706.
2. Dabaja BS, Suki D, Pro B, Bonnen M, Ajani J. Adenocarcinoma of the small bowel: presentation, prognostic factors, and outcome of 217 patients. *Cancer*. 2004; 101:518-526.

#### D. Treatment Effect

Response of tumor to previous chemotherapy or radiation therapy should be reported, when applicable. Several scoring systems have been described, and a modified Ryan scheme is recommended, as below:

##### Modified Ryan Scheme for Tumor Regression Score<sup>1</sup>

Description	Tumor Regression Score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near complete response)	1
Residual cancer with evident tumor regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumor regression (poor or no response)	3

Sizable pools of acellular mucin may be present after chemoradiation but should not be interpreted as representing residual tumor.

The size or extent of only the viable tumor should be used to assign the ypT category as appropriate and this requires a combined assessment of both gross and microscopic findings. It is suggested that to estimate the approximate size of the tumor by adding the size of all the viable tumor foci within the tumor mass based in the histologic evaluation.

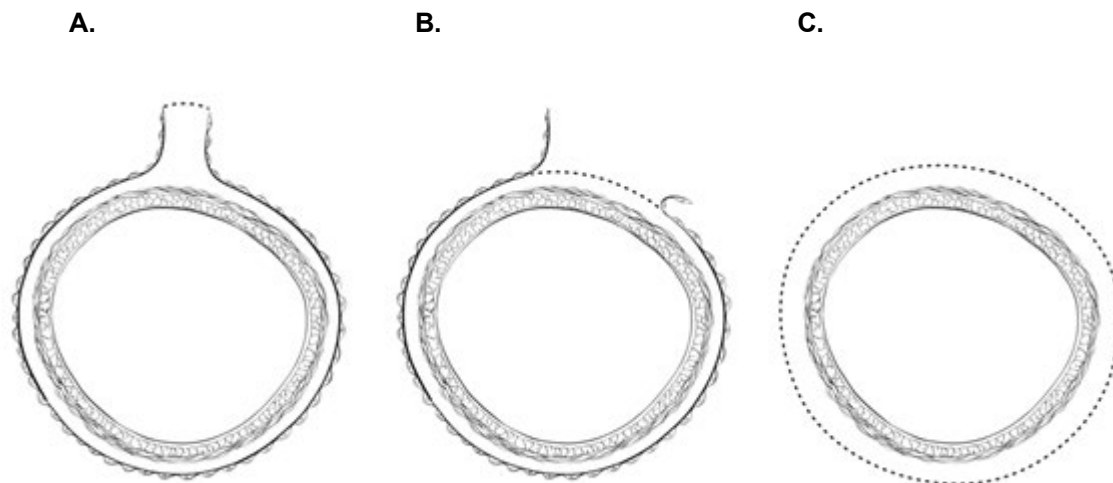
This protocol does not preclude the use of other systems for assessment of tumor response.<sup>2,3</sup> A modification of the above scoring scheme into a 3-tier scheme has been shown to correlate better with outcome: no residual carcinoma (grade 0), minimal residual carcinoma defined as single cells or small groups of cancer cells, <5% residual carcinoma (grade 1), 5% or more residual carcinoma (grade 2).<sup>4,5</sup>

#### References

1. Ryan R, Gibbons D, Hyland JMP, et al. Pathological response following long-course neoadjuvant chemoradiotherapy for locally advanced rectal cancer. *Histopathology*. 2005; 47:141-146.
2. Evans DB, Rich TA, Byrd DR, et al. Preoperative chemoradiation and pancreaticoduodenectomy for adenocarcinoma of the pancreas. *Arch Surg*. 1992; 127:1335-1339.
3. Breslin TM, Hess KR, Harbison DB, et al. Neoadjuvant chemoradiotherapy for adenocarcinoma of the pancreas: treatment variables and survival duration. *Ann Surg Oncol*. 2001;8(2):123-132.
4. Chatterjee D, Katz MH, Rashid A, et al. Histologic grading of the extent of residual carcinoma following neoadjuvant chemoradiation in pancreatic ductal adenocarcinoma: a predictor for patient outcome. *Cancer*. 2012;118(12):3182-3190.
5. Lee SM, Katz MH, Liu L, et al. Validation of a proposed tumor regression grading scheme for pancreatic ductal adenocarcinoma after neoadjuvant therapy as a prognostic indicator for survival. *Am J Surg Pathol*. 2016;40(12):1653-1660.

#### E. Margins

For segmental small bowel and ileocolic resections, margins include the proximal, distal, and mesenteric margins of resection. For all small bowel segments, except the duodenum, the mesenteric resection margin is the only pertinent radial margin (Figure 2). For pancreaticoduodenectomy specimens of carcinomas of the duodenum, the proximal margin of stomach or duodenum (pylorus-sparing Whipple resection) and the distal resection margin of duodenum are more biologically relevant than in pancreaticoduodenectomy procedures performed for pancreatic carcinoma and should always be sampled. The non-peritonealized surface of the uncinate process (uncinate margin) constitutes the inferior-posterior retroperitoneal margin of pancreaticoduodenectomy specimens. A perpendicular section through the closest approach of tumor to the margin should be taken. This margin has also been referred to as *retroperitoneal margin* and *superior mesenteric artery margin*. Complete en face sections through the pancreatic resection margin and the common bile duct margin should also be taken.



**Figure 2.** A. Mesenteric margin in small intestine completely encased by peritoneum (dotted line). B. Circumferential margin (dotted line) in portion of proximal duodenum incompletely encased by peritoneum. C. Circumferential margin (dotted line) in retroperitoneal portion of duodenum completely unencased by peritoneum.

#### F. pTNM Classification

Surgical resection is the most effective therapy for small intestinal carcinoma,<sup>1</sup> and the best estimation of prognosis is related to the anatomic extent (stage) of disease at the time of resection.

The protocol recommends the TNM staging system of the American Joint Committee on Cancer (AJCC)<sup>2</sup> and the International Union Against Cancer (UICC)<sup>3</sup> but does not preclude the use of other staging systems.

According to AJCC/UICC convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary

tumor has been completely removed. If a biopsied tumor is not resected for any reason (e.g., when technically infeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

#### TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y” and “r” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

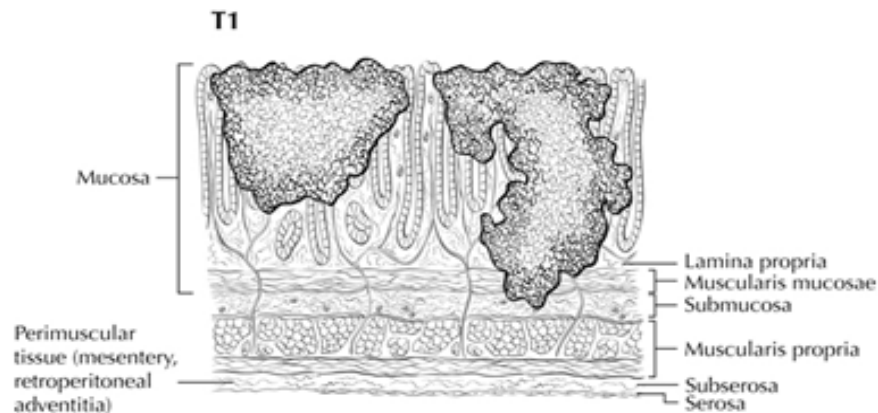
The “m” suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or after initial multimodality therapy (i.e., neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor before multimodality therapy (i.e., before initiation of neoadjuvant therapy). A formal tumor regression grading system has not been specifically developed for this tumor type. If there has been neoadjuvant treatment, at least a semi-quantitative assessment of residual viable tumor should be included in the report.

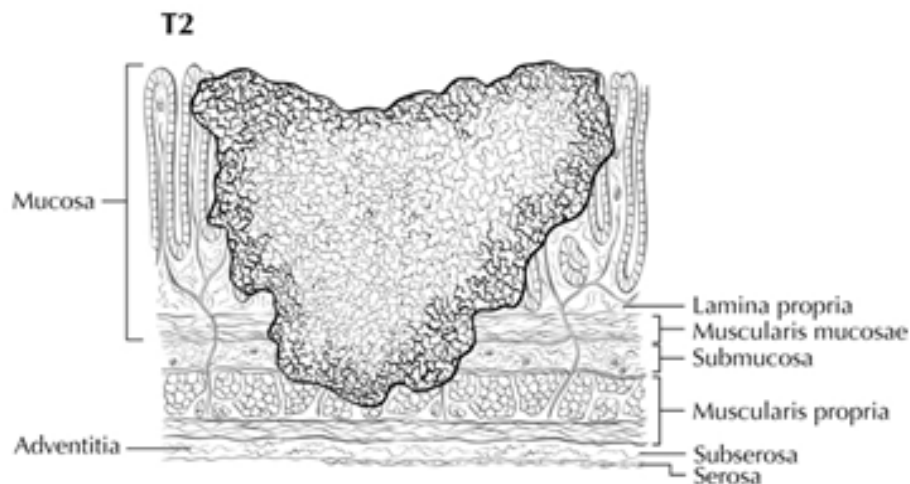
The “r” prefix indicates a recurrent tumor when staged after a documented disease-free interval and is identified by the “r” prefix: rTNM.

#### T Category Considerations

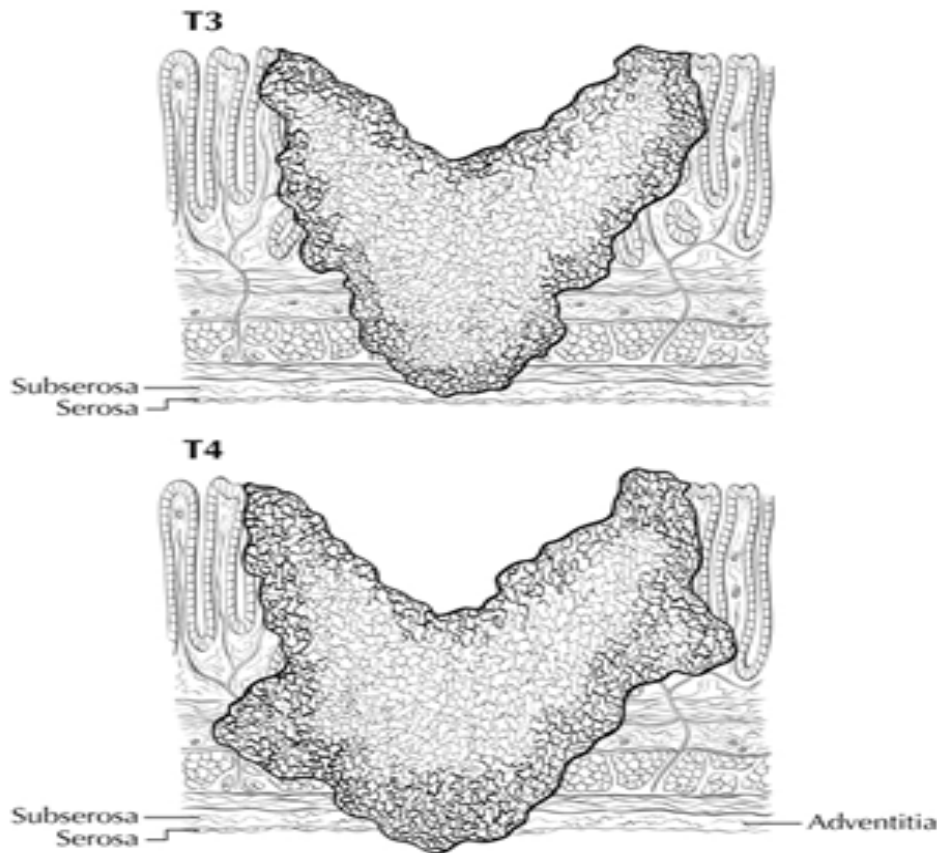
pTis. For small intestinal carcinomas, 'carcinoma in situ' (pTis) as a staging term includes cancer cells confined within the glandular basement membrane (high-grade dysplasia). The term “carcinoma in situ” is not widely applied to glandular neoplastic lesions in the gastrointestinal tract but is retained for tumor registry reporting purposes as specified by law in many states. Tumor invasive into the mucosal lamina propria, up to but not through the muscularis mucosae (intramucosal carcinoma), is classified as pT1a. This designation differs from that for colon, in which tumor extension into the lamina propria is regarded as in situ carcinoma, because of the rich lymphatic network in small intestinal mucosa. Tumor extension through the muscularis mucosae into the submucosa is classified as T1b (Figure 3). T2 tumors invade the muscularis propria (Figure 4), and T3 tumors invade subserosal tissues without extension to the peritoneal (serosal) surface or invasion of adjacent organs (Figure 5).



**Figure 3.** T1a (left side) with tumor invasion of the lamina propria; T1b (right side) with tumor invasion of the submucosa. From: Greene FL et al.<sup>4</sup> Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, [www.springerlink.com](http://www.springerlink.com).



**Figure 4.** T2 is defined as tumor invading the muscularis propria. From: Greene FL et al.<sup>4</sup> Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, [www.springerlink.com](http://www.springerlink.com).

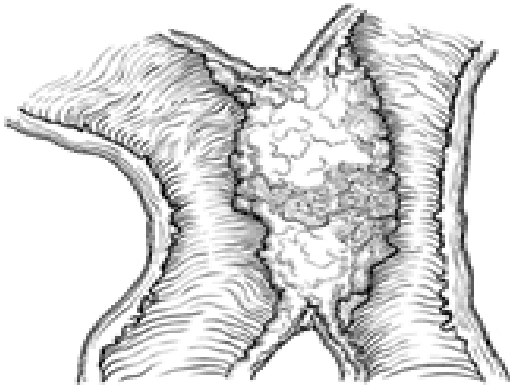


**Figure 5.** T3 tumors invade through the muscularis propria into subserosal adipose tissue; T4 tumor perforates the peritoneal (serosal) surface. From: Greene FL et al.<sup>4</sup> Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, [www.springerlink.com](http://www.springerlink.com).

pT4 includes tumors perforating the visceral peritoneum (Figure 5) or directly invading other organs or structures, including invasion of other segments of small intestine, mesentery of adjacent loops of bowel, and abdominal wall by way of the serosa (Figure 6). In such a case, both an adjacent organ and the visceral peritoneum are penetrated by tumor. Intramural extension of tumor from the terminal ileum into the cecum does not affect the pT classification.<sup>4</sup> For duodenal tumors, invasion of the pancreas and the bile duct is considered as T4 (Figure 7).

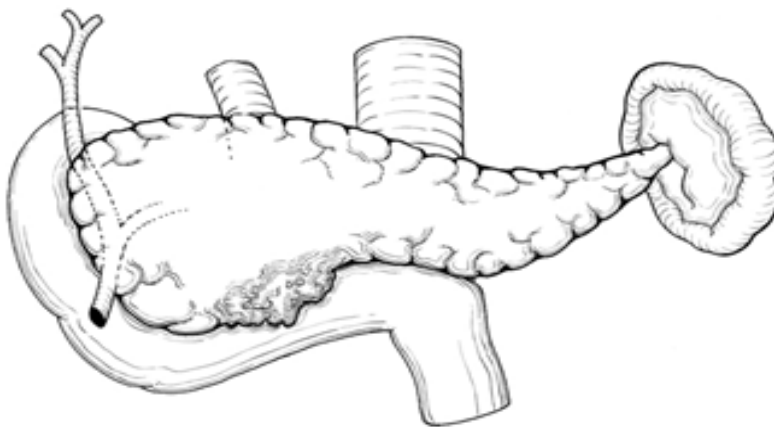


#### T4



**Figure 6.** T4 tumor directly invades other organs or structures, including other loops of small intestine. From: Greene FL et al.<sup>4</sup> Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, [www.springerlink.com](http://www.springerlink.com).

#### T4



**Figure 7.** T4 tumor of the duodenum invades the pancreas. From: Greene FL et al.<sup>4</sup> Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, [www.springerlink.com](http://www.springerlink.com).

Tumor that is adherent to other organs or structures macroscopically is classified as cT4. However, if no tumor is found within the adhesion and no perforation of the visceral peritoneum identified microscopically, the tumor should be assigned pT3.

Tumor in veins or lymphatics does not affect the pT classification.

There are no T4a and T4b subcategories for small intestinal carcinomas in the AJCC 8<sup>th</sup> edition.

### N Category Considerations

The regional lymph nodes for the anatomical subsites of the small intestine are as follows:<sup>2</sup>

Duodenum: retropancreatic, hepatic artery, inferior pancreaticoduodenal, and superior mesenteric

Ileum and jejunum: cecal (terminal ileum only), ileocolic (terminal ileum only), superior mesenteric, mesenteric, NOS

### Submission of lymph nodes for microscopic examination

All grossly negative or equivocal lymph nodes are to be submitted entirely. Grossly positive lymph nodes may be partially submitted for microscopic confirmation of metastasis.

The minimum number of lymph nodes that predicts regional node negativity has not been defined for small intestinal cancers. The pathology report should clearly state the total number of lymph nodes examined and the total number involved by metastases. Data are insufficient to recommend routine use of tissue levels or special/ancillary techniques to detect micrometastases or isolated tumor cells.

### Nonregional lymph nodes

For microscopic examination of lymph nodes in large resection specimens, lymph nodes must be designated as regional versus nonregional, according to the anatomic location of the tumor. Metastasis to nonregional lymph nodes is classified as distant metastasis and designated as M1. Nonregional lymph nodes include celiac and para-aortic nodes.

### Additional Descriptors

#### Lymphatic and/or Vascular Invasion

Lymphovascular invasion (LVI) indicates whether microscopic lymphatic and/or vascular invasion is identified in the pathology report. LVI includes lymphatic invasion, vascular invasion, or lymph-vascular invasion. By AJCC/UICC convention, LVI does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category.

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### **G. Additional Findings**

Conditions that predispose to small bowel malignancy include Crohn disease, celiac disease, inherited polyposis syndromes (including familial adenomatous polyposis and Peutz-Jeghers syndrome), and Lynch syndrome.

Small intestinal adenocarcinomas in Crohn disease arise in the setting of long-standing ileal inflammation; cumulative risk increases after 10 years of Crohn disease, although absolute risk (2.2% at 25 years) remains low.<sup>1</sup> Signet-ring cell carcinomas appear to be more common in Crohn disease than as de novo small intestinal carcinomas.<sup>2</sup>

Small intestinal carcinomas are more frequent in polyposis syndromes, most notably in familial adenomatous polyposis, in which approximately 2.3% of patients developed a duodenal adenocarcinoma;<sup>3</sup> most tumors in these patients develop in the periampullary region, and the duodenum may be carpeted with adenomas. Peutz-Jeghers syndrome<sup>4</sup> is also associated with higher risk of small intestinal carcinoma.

Patients with Lynch syndrome have an approximately 4% lifetime risk of developing a small bowel carcinoma; this risk exceeds that of the normal population by 100-fold. Duodenum and jejunum are the most common primary sites, and the small bowel is the first site of cancer in approximately one-fourth of Lynch syndrome patients who develop small bowel tumors.<sup>5</sup> Histopathologic features of Lynch syndrome-associated small intestinal carcinomas are similar to those of colorectal carcinomas arising in this setting; mucinous carcinomas are overrepresented, and tumors often show a high number of intratumoral lymphocytes and Crohn-like lymphoid reaction.<sup>6</sup>

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#### H. Ancillary Studies

Immunohistochemistry (MMR IHC) and/or microsatellite instability (MSI) testing are now essential not only for identifying Lynch syndrome but also for detecting mismatch repair deficient (dMMR) tumors because FDA approved immune checkpoint inhibitors are now available for any malignancy irrespective of histologic type or location.<sup>1,2</sup> Now NCCN also suggests considering testing it for adenocarcinomas of the small intestine, stomach, pancreas, and biliary tract.<sup>3</sup> Similarly, targeted therapies for HER2 have expanded beyond non-breast and non-gastric gastrointestinal cancers.<sup>4,5</sup> HER2 testing for advanced gastrointestinal cancers (stage IV, recurrent, or unresectable) is becoming more common, although standardized reporting guidelines for non-gastric gastrointestinal cancers are still lacking. While criteria applicable for colorectal cancer have been developed,<sup>6,7</sup> the ASCO/College of American Pathology

guidelines for gastric cancer HER2 scoring have been applied in recent clinical trials for other gastrointestinal cancers.<sup>8</sup> It is suggested that while reporting HER2 it is a good practice to indicate the criteria used. Further details about mismatch repair enzyme immunohistochemistry and PCR for MSI testing, as well as other ancillary molecular testing can be found in the CAP Biomarkers protocol.

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