Protocol for the Examination of Specimens from Patients with Carcinoma of the Exocrine Pancreas

Protocol applies to all epithelial tumors of the exocrine pancreas. Endocrine tumors and tumors of the ampulla of Vater are not included.

Based on AJCC/UICC TNM, 7th edition
Protocol web posting date: February 1, 2011

Procedures
• Partial Pancreatectomy
• Pancreatecoduodenectomy (Whipple Resection)
• Total Pancreatectomy

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CAP Pancreas (Exocrine) Protocol Revision History

Version Code
The definition of the version code can be found at www.cap.org/cancerprotocols.

Version: PancreasExocrine 3.1.0.0

Summary of Changes
The following changes have been made since the October 2009 release.

Resection Checklist

Regional Lymph Nodes (pN)
Specify: Number examined / Number involved, has been changed to:

___ No nodes submitted or found

Number of Lymph Nodes Examined
Specify: ____
___ Number cannot be determined (explain): ______________________

Number of Lymph Nodes Involved
Specify: ____
___ Number cannot be determined (explain): ______________________
Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: February 1, 2011

PANCREAS (EXOCRINE): Resection (Note A)

Select a single response unless otherwise indicated.

Specimen (select all that apply)
___ Head of pancreas
___ Body of pancreas
___ Tail of pancreas
___ Duodenum
___ Stomach
___ Common bile duct
___ Gallbladder
___ Spleen
___ Adjacent large vessels
   ___ Portal vein
   ___ Superior mesenteric vein
   ___ Other large vessel (specify): ______________________
___ Other (specify): ___________________________
___ Not specified
___ Cannot be determined

Procedure
___ Pancreaticoduodenectomy (Whipple resection), partial pancreatectomy
___ Pancreaticoduodenectomy (Whipple resection), total pancreatectomy
___ Partial pancreatectomy, pancreatic body
___ Partial pancreatectomy, pancreatic tail
___ Other (specify): ___________________________
___ Not specified

Tumor Site (select all that apply) (Note B)
___ Pancreatic head
___ Uncinate process
___ Pancreatic body
___ Pancreatic tail
___ Other (specify): ___________________________
___ Cannot be determined
___ Not specified

Tumor Size
Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm
___ Cannot be determined (see Comment)

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Histologic Type (select all that apply) (Note C)
- ___ Ductal adenocarcinoma
- ___ Mucinous noncystic carcinoma
- ___ Signet-ring cell carcinoma
- ___ Adenosquamous carcinoma
- ___ Undifferentiated (anaplastic) carcinoma
- ___ Undifferentiated carcinoma with osteoclast-like giant cells
- ___ Mixed ductal-endocrine carcinoma
- ___ Serous cystadenocarcinoma
- ___ Mucinous cystic neoplasm
  - ___ Noninvasive
  - ___ Invasive
- ___ Intraductal papillary-mucinous carcinoma
  - ___ Noninvasive
  - ___ Invasive
- ___ Acinar cell carcinoma
- ___ Acinar cell cystadenocarcinoma
- ___ Mixed acinar-endocrine carcinoma
- ___ Other (specify): ____________________________

Histologic Grade (ductal carcinoma only) (Note D)
- ___ Not applicable
- ___ Gx: Cannot be assessed
- ___ G1: Well differentiated
- ___ G2: Moderately differentiated
- ___ G3: Poorly differentiated
- ___ G4: Undifferentiated
- ___ Other (specify): ____________________________

Microscopic Tumor Extension (select all that apply)
- ___ Cannot be assessed
- ___ No evidence of primary tumor
- ___ Carcinoma in situ
- ___ Tumor is confined to pancreas
- ___ Tumor invades ampulla of Vater or sphincter of Oddi
- ___ Tumor invades duodenal wall
- ___ Tumor invades peripancreatic soft tissues
  - ___ Tumor invades retroperitoneal soft tissue
  - ___ Tumor invades mesenteric adipose tissue
  - ___ Tumor invades mesocolon
  - ___ Tumor invades other peripancreatic soft tissue (specify): ____________________________
- ___ Tumor invades extrapancreatic common bile duct
- ___ Tumor invades other adjacent organs or structures (specify): ____________________________

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Margins (select all that apply) (Note E)
___ Cannot be assessed
___ Margins uninvolved by invasive carcinoma
   Distance of invasive carcinoma from closest margin: ___ mm
* Specify margin (if possible): ____________________________
___ Margins uninvolved by carcinoma in situ
___ Margin(s) involved by carcinoma in situ
   ___ Carcinoma in situ present at common bile duct margin
   ___ Carcinoma in situ present at pancreatic parenchymal margin
___ Margin(s) involved by invasive carcinoma
   ___ Uncinate process (retroperitoneal) margin (nonperitonealized surface of the
      uncinate process)
   ___ Distal pancreatic margin
   ___ Common bile duct margin
   ___ Proximal pancreatic margin
   ___ Other (specify): ____________________________
* ___ Invasive carcinoma involves posterior retroperitoneal surface of pancreas

Treatment Effect (applicable to carcinomas treated with neoadjuvant therapy)
(select all that apply) (Note F)
___ No prior treatment
___ Present
   * ___ No residual tumor (complete response, grade 0)
   * ___ Marked response (grade 1, minimal residual cancer)
   * ___ Moderate response (grade 2)
___ No definite response identified (grade 3, poor or no response)
___ Not known

Lymph-Vascular Invasion (Note G)
___ Not identified
___ Present
___ Indeterminate

Perineural Invasion (Note H)
___ Not identified
___ Present
___ Indeterminate

Pathologic Staging (pTNM) (Note I)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple primary tumors)
___ r (recurrent)
___ y (post-treatment)
Primary Tumor (pT)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ
___ pT1: Tumor limited to the pancreas, 2 cm or less in greatest dimension
___ pT2: Tumor limited to the pancreas, more than 2 cm in greatest dimension
___ pT3: Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery
___ pT4: Tumor involves the celiac axis or the superior mesenteric artery

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Regional lymph node metastasis
___ No nodes submitted or found

Number of Lymph Nodes Examined
Specify: _____
___ Number cannot be determined (explain): __________________________

Number of Lymph Nodes Involved
Specify: _____
___ Number cannot be determined (explain): __________________________

Distant Metastasis (pM)
___ Not applicable
___ pM1: Distant metastasis
   * Specify site(s), if known: __________________________

*Additional Pathologic Findings (select all that apply) (Note J)
*___ None identified
*___ Pancreatic intraepithelial neoplasia (highest grade: PanIN ___)
*___ Chronic pancreatitis
*___ Acute pancreatitis
*___ Other (specify): __________________________

*Ancillary Studies (Note K)
*Specify: __________________________

*Clinical History (select all that apply) (Note L)
*___ Neoadjuvant therapy
*___ Familial pancreatitis
*___ Familial pancreatic cancer syndrome
*___ Other (specify): __________________________
*___ Not specified

*Comment(s)

* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.
Explanatory Notes

A. Tumors
This protocol applies to epithelial tumors of the exocrine pancreas. It excludes endocrine tumors and tumors of the ampulla of Vater. More than 90% to 95% of malignant tumors of the pancreas are exocrine carcinomas. For these tumors, surgical resection remains the only potentially curative approach, and the prognosis is primarily dependent on the anatomic extent of disease and performance status.

B. Definition of Location
The anatomic subdivisions defining location of tumors of the pancreas (Figure 1) are as follows:

- Tumors of the head of the pancreas are those arising to the right of the left border of the superior mesenteric vein. The uncinate process is part of the head.
- Tumors of the body of the pancreas are those arising between the left border of the superior mesenteric vein and the left border of the aorta.
- Tumors of the tail of the pancreas are those arising between the left border of the aorta and the hilum of the spleen.

Figure 1. Anatomic subsites of the pancreas. From Greene et al. 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.

C. Histologic Type
A classification of malignant and borderline (uncertain malignant potential) epithelial tumors of the exocrine pancreas recommended by the World Health Organization...
(WHO) is shown below. However, this protocol does not preclude the use of other histologic types or systems of classification.

**WHO Classification of Epithelial Tumors of the Exocrine Pancreas**

**Malignant Tumors**

**Ductal adenocarcinoma**
- Mucinous noncystic carcinoma
- Signet-ring cell carcinoma
- Adenosquamous carcinoma
- Undifferentiated (anaplastic) carcinoma
- Undifferentiated carcinoma with osteoclast-like giant cells
- Mixed ductal-endocrine carcinoma

**Serous cystadenocarcinoma**

**Mucinous cystadenocarcinoma**
- Noninvasive
- Invasive

**Intraductal papillary-mucinous carcinoma**
- Noninvasive
- Invasive (papillary-mucinous carcinoma)

**Acinar cell carcinoma**
- Acinar cell cystadenocarcinoma
- Mixed acinar-endocrine carcinoma

**Pancreatoblastoma**

**Solid pseudopapillary carcinoma**

**Others**

# By convention, signet-ring cell carcinomas are assigned grade 3 (see below).

## By definition, undifferentiated carcinomas are grade 4 (see below).

### These histologic types are not usually graded.

**D. Histopathologic Grade**

For adenocarcinomas, a histologic grade based on the extent of glandular differentiation is suggested, as shown below:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>Cannot be assessed</td>
</tr>
<tr>
<td>1</td>
<td>Well differentiated (greater than 95% of tumor composed of glands)</td>
</tr>
<tr>
<td>2</td>
<td>Moderately differentiated (50% to 95% of tumor composed of glands)</td>
</tr>
<tr>
<td>3</td>
<td>Poorly differentiated (49% or less of tumor composed of glands)</td>
</tr>
</tbody>
</table>

Tumors with no differentiation or minimal differentiation that is discernible only in rare, tiny foci (undifferentiated carcinomas by WHO classification) are categorized as grade 4.

For pancreatic ductal carcinoma, histologic grade has been shown to have prognostic significance, with high grade (grades 3 and 4) being an unfavorable prognostic factor.

In comparisons between the Klöppel grading system and the TNM grading system, no
differences in predictive value have been demonstrated.\textsuperscript{6} Other systems based on patterns of infiltration of predominant and secondary tumor patterns have been proposed\textsuperscript{5} but not widely adopted to date.

E. Margins
The nonperitonealized surface of the uncinate process (uncinate margin) constitutes the retroperitoneal margin for pancreaticoduodenectomy specimens (Figure 2) and should be inked; sections through the tumor at its closest approach to this margin should be submitted.\textsuperscript{3}

![Figure 2. Posterior view of tumor arising in the pancreatic head, with dotted line indicating the location of the confluence of the portal and superior mesenteric veins. The hatched area shows the retroperitoneal (uncinate process) margin. From Greene et al.\textsuperscript{21} 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.]

Because local recurrences of invasive pancreatic adenocarcinoma arise in the pancreatic bed corresponding to the retroperitoneal margin and to the deep retroperitoneal posterior surface of the pancreas, the American Joint Committee on Cancer (AJCC) and this protocol also recommend inking the posterior surface of the pancreas and submission of sections through the tumor at its closest approach to this surface, as well as the retroperitoneal (uncinate) margin.

When dealing with an intraductal tumor, the distal resection margin, the common bile duct margin (Whipple resection), or the proximal resection margin of the pancreas (distal pancreatectomy) are the most critical. Complete en face sections through the pancreatic margin and the common bile duct margin should be taken.

F. Treatment Effect
Response of tumor to previous chemotherapy or radiation therapy should be reported.
Although grading systems for tumor response have not been established, in general, 3-category systems provide good interobserver reproducibility. The following system is suggested:

**Tumor Regression Grade**

<table>
<thead>
<tr>
<th>Description</th>
<th>Tumor Regression Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>No viable cancer cells</td>
<td>0 (Complete response)</td>
</tr>
<tr>
<td>Single cells or small groups of cancer cells</td>
<td>1 (Moderate response)</td>
</tr>
<tr>
<td>Residual cancer outgrown by fibrosis</td>
<td>2 (Minimal response)</td>
</tr>
<tr>
<td>Minimal or no tumor kill; extensive residual cancer</td>
<td>3 (Poor response)</td>
</tr>
</tbody>
</table>

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

This protocol does not preclude the use of other systems for assessment of tumor response, such as the scheme reported by investigators at MD Anderson Cancer Center.

**G. Venous/Lymphatic Vessel Invasion**

Venous/lymphatic (small vessel) invasion has been shown to be an adverse prognostic factor.

**H. Perineural Invasion**

Perineural invasion has been shown to be an adverse prognostic factor.

**I. TNM and Anatomic Stage/Prognostic Groupings**

The TNM staging system for carcinoma of the exocrine pancreas of the AJCC and the International Union Against Cancer (UICC) is recommended and shown below. The post-resection prognosis of a patient with pancreatic carcinoma is primarily determined by the anatomic extent of disease as defined by the TNM stage groupings.

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 (eg, 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.

**Primary Tumor**

<table>
<thead>
<tr>
<th>T category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor limited to the pancreas, 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor limited to the pancreas, more than 2 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor)</td>
</tr>
</tbody>
</table>

If more than 1 tumor is present in the pancreas, the tumor with the highest T category should be classified according to the pT definitions and either the multiplicity (“m”) or the actual number of simultaneous multiple tumors (eg, “3”) should be indicated in parentheses after the T category of the primary tumor (eg, pT3[m] or pT3[2]). This applies only to grossly recognizable, synchronous primary carcinomas and not to a single, grossly detected tumor with multiple separate microscopic foci.

Multiple synchronous carcinomas of the exocrine pancreas may be:
- Multiple noninvasive tumors
- Multiple invasive tumors
- Multiple invasive tumors with associated carcinoma in situ

PanIN-3 (see Note D) is the equivalent of carcinoma in situ and should be assigned pTis.

Tumor size has been shown to have independent prognostic significance.

For T3, extension beyond the pancreas may include invasion of soft tissues adjacent to the pancreas, the extrapancreatic biliary system, and/or duodenum (including the ampulla of Vater). Specifically, peripancreatic tissues include the surrounding retroperitoneal fat (retroperitoneal soft tissue), including mesentery (mesenteric fat), mesocolon, greater and lesser omentum, and peritoneum.

Invasion of the portal vein also has been shown to have independent prognostic significance as an adverse factor.
Figure 3. T1 (left of dotted line) is defined as tumor measuring 2 cm or less in greatest dimension and limited to the pancreas. T2 (right of dotted line) is defined as tumor measuring more than 2 cm in greatest dimension and limited to the pancreas. From Greene et al.21 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.
Figure 4. T3 is defined as tumor that extends beyond the pancreas but without involvement of the celiac axis or superior mesenteric artery. A. To the left of the dotted line, tumor invades the common bile duct without involving the superior mesenteric artery. To the right of the dotted line, tumor invades the peripancreatic tissues without involving the celiac axis. B. Tumor invades duodenum without involvement of superior mesenteric artery. C. Tumor invades spleen without involvement of celiac axis or superior mesenteric artery. From Greene et al.\textsuperscript{21} Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the \textit{AJCC Cancer Staging Atlas} (2006) published by Springer Science and Business Media LLC, www.springerlink.com.
Figure 5. T4 tumor involves the celiac axis (above dotted line) or the superior mesenteric artery (below dotted line). T4 tumors are considered unresectable and are rarely encountered in surgical pathology specimens. From Greene et al.21 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.

Regional Lymph Nodes (N)

NX  Regional lymph nodes cannot be assessed
N0  No regional lymph node metastasis
N1  Regional lymph node metastasis

# The regional nodes may be subdivided as follows (Figures 6 and 7):

Superior  Lymph nodes superior to head and body of pancreas
Inferior  Lymph nodes inferior to head and body of pancreas
Anterior  Anterior pancreaticoduodenal, pyloric, and proximal mesenteric lymph nodes
Posterior  Posterior pancreaticoduodenal, common bile duct or pericholedochal, and proximal mesenteric nodes
Splenic  (For tumors in body and tail only) Nodes of the splenic hilum and tail of pancreas

## The following lymph nodes are also considered regional: hepatic artery nodes, infrapyloric nodes (for tumors in head only), subpyloric nodes (for tumors in head only), celiac nodes (for tumors in head only), superior mesenteric nodes, pancreaticocoliac nodes (for tumors in body and tail only), splenic nodes (for tumors in body and tail only), retroperitoneal nodes, and lateral aortic nodes. Tumor involvement of other nodal groups is considered distant metastasis.

### The presence of lymph node metastases has been shown to have independent prognostic significance as an adverse factor.9,12,14,16-18 A minimum of 15 lymph nodes has been suggested to achieve optimal staging for node-negative pancreatic cancer;19 however, this proposed guideline requires further study before its widespread adoption is recommended.
Figure 6. Regional lymph nodes of the pancreas (anterior view). From Greene et al.\textsuperscript{21} Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the \textit{AJCC Cancer Staging Atlas} (2006) published by Springer Science and Business Media LLC, www.springerlink.com.

Figure 7. Regional lymph nodes of the pancreas (anterior view with pancreatic body removed to reveal retroperitoneal vessels and lymph nodes). From Greene et al.\textsuperscript{21} Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the \textit{AJCC Cancer Staging Atlas} (2006) published by Springer Science and Business Media LLC, www.springerlink.com.

**Distant Metastasis (M)**

- **M0** No distant metastasis
M1    Distant metastasis

Peritoneal seeding or ascitic peritoneal fluid containing cytologic evidence of malignancy is considered M1. Positive peritoneal cytology in patients without ascites is also considered M1 because the data suggest that this finding predicts a short survival.

Stage Groupings

<table>
<thead>
<tr>
<th>Stage</th>
<th>T category</th>
<th>N category</th>
<th>M category</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IB</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T4</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y,” “r,” and “a” 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 (ie, 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 (ie, before initiation of neoadjuvant therapy).

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

The “a” prefix designates the stage determined at autopsy: aTNM.

Vessel Invasion

According to AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category.

J. Additional Pathologic Findings

Pancreatic Intraepithelial Neoplasia (PanIN)

Noninvasive dysplastic lesions of the ductal epithelium often are found in the pancreatic parenchyma surrounding ductal adenocarcinoma. These lesions are collectively known
as pancreatic intraepithelial neoplasia (PanIN). PanINs have been classified at a National Cancer Institute Think Tank as follows:²⁰

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Nonmucinous flattened or cuboidal epithelium without dysplasia</td>
</tr>
<tr>
<td>PanIN-1A</td>
<td>Flat mucinous epithelium without dysplasia</td>
</tr>
<tr>
<td>PanIN-1B</td>
<td>Papillary mucinous epithelium without dysplasia</td>
</tr>
<tr>
<td>PanIN-2</td>
<td>Flat or papillary mucinous epithelium with mild-to-moderate dysplasia</td>
</tr>
<tr>
<td></td>
<td>(mild-to-moderate nuclear irregularity, hyperchromasia, and loss of polarity)</td>
</tr>
<tr>
<td>PanIN-3</td>
<td>Flat or papillary mucinous epithelium with severe dysplasia (marked nuclear irregularity, hyperchromasia, and loss of polarity), often with cribriforming and intraluminal blebbing (budding off of noncohesive cells)</td>
</tr>
</tbody>
</table>

PanINs are thought to progress from flat to papillary lesions with increasing degrees of dysplasia and increasing numbers of alterations in cancer-associated genes. PanINs are believed to be the precursor lesions of ductal adenocarcinoma of the pancreas. Many of the cytological changes included in the PanIN spectrum are seen in cystic tumors of the pancreas, such as mucinous cystic neoplasms and papillary mucinous neoplasms, but PanINs, by definition, occur in nondilated ducts.

PanIN occurring at the resection margins of an otherwise completely resected malignancy should be noted in the pathology report. In this setting, the biologic significance of low-grade PanIN remains unclear, because these ductal changes may be seen in pancreata with benign lesions, but PanIN-3 is the equivalent of carcinoma in situ and should be reported as Tis.

Other Findings
In addition to the examination of other tissues and organs that are part of pancreaticoduodenectomy specimens, pathologic evaluation may also include examination of the gastric antrum for gastritis (eg, Helicobacter pylori gastritis or chemical gastritis) and the duodenum for duodenitis, peptic ulcer disease, and ampullitis.

K. Ancillary Studies
No specific molecular or immunohistochemical studies are recommended at this time for pancreatic cancer.

L. Clinical History
Predisposing conditions for pancreatic cancer include familial pancreatic cancer syndromes, which are relatively rare and account for less than 10% of cases.¹ Germline mutations in BRCA2 and p16 have been linked to increased risk, and patients with hereditary pancreatitis have at least a 4-fold higher risk. Pre-existing chronic pancreatitis probably accounts for a small minority of cases. Diabetes mellitus and smoking have also been associated with increased risk.

References
