Protocol for the Examination of Specimens from Patients with Well-Differentiated Neuroendocrine Tumors (Carcinoid Tumors) of the Colon and Rectum

Version: 4.1.0.0
Protocol Posting Date: June 2021
CAP Laboratory Accreditation Program Protocol Required Use Date: March 2022

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:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection</td>
<td>Includes specimens designated as low anterior resection and abdominoperineal resection, total, partial, or segmental resection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-differentiated neuroendocrine tumor</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
</tr>
<tr>
<td>Excision biopsy (transanal disk excision or polypectomy)</td>
</tr>
<tr>
<td>Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy)</td>
</tr>
<tr>
<td>Recurrent tumor</td>
</tr>
<tr>
<td>Cytologic specimens</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poorly-differentiated neuroendocrine carcinoma including small cell and large cell neuroendocrine carcinoma (consider the Colon and Rectum Carcinoma protocol)</td>
</tr>
<tr>
<td>Other epithelial carcinoma of the colon and rectum including mixed neuroendocrine-non-neuroendocrine neoplasm (consider the Colon and Rectum Carcinoma protocol)</td>
</tr>
<tr>
<td>Gastrointestinal stromal tumor (consider the GIST protocol)</td>
</tr>
<tr>
<td>Non-GIST sarcoma (consider the Soft Tissue protocol)</td>
</tr>
</tbody>
</table>

Authors
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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.

* Denotes primary author.
Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- **Core data elements** are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is “not applicable” or “cannot be determined.”
- **Conditional data elements** are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- **Optional data elements** are identified with “+” and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

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 ie, all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

**v 4.1.0.0**
- General Reformatting
- Revised Margins Section
- Revised Lymph Nodes Section
- Added Distant Metastasis Section
- Removed pTX and pNX Staging Classification
Reporting Template

Protocol Posting Date: June 2021
Select a single response unless otherwise indicated.

CASE SUMMARY: (COLON AND RECTUM NEUROENDOCRINE TUMOR)
Standard(s): AJCC-UICC 8
This case summary is recommended for reporting local excision and polypectomy specimens, but is not required for accreditation purposes.

SPECIMEN (Note A)

Procedure
___ Right hemicolectomy
___ Transverse colectomy
___ Left hemicolectomy
___ Sigmoidectomy
___ Low anterior resection
___ Total abdominal colectomy
___ Abdominoperineal resection
___ Transanal disk excision (local excision)
___ Polypectomy
___ Other (specify): _________________
___ Not specified

TUMOR

Tumor Site (Note B) (select all that apply)
___ Cecum: _________________
___ Right (ascending) colon: _________________
___ Hepatic flexure: _________________
___ Transverse colon: _________________
___ Splenic flexure: _________________
___ Left (descending) colon: _________________
___ Sigmoid colon: _________________
___ Rectosigmoid junction: _________________
___ Rectum: _________________
___ Ileocecal valve: _________________
___ Colon, not otherwise specified: _________________
___ Cannot be determined (explain): _________________

Histologic Type and Grade# (Notes C,D)
# For poorly differentiated neuroendocrine carcinomas, the College of American Pathologists (CAP) checklist for carcinoma of the colon and rectum should be used.
___ G1, well-differentiated neuroendocrine tumor
___ G2, well-differentiated neuroendocrine tumor
___ G3, well-differentiated neuroendocrine tumor
___ Other (specify): _________________
___ GX, well-differentiated neuroendocrine tumor, grade cannot be assessed
___ Not applicable
Histologic Grade Determination (select all that apply)

Mitotic rate and/or Ki67 labeling index is required to determine histologic grade.

**Mitotic rate (Note D)**

- Mitotic rate should be reported as number of mitoses per 2 mm², by evaluating at least 10 mm² in the most mitotically active part of the tumor (e.g., if using a microscope with a field diameter of 0.55 mm, count 42 high power fields (10 mm²) and divide the resulting number of mitoses by 5 to determine the number of mitoses per 2 mm² needed to assign tumor grade).
- Specify number of mitoses per 2 mm²: __________ mitoses per 2 mm²
- Less than 2 mitoses per 2 mm²
- 2 to 20 mitoses per 2 mm²
- Greater than 20 mitoses per 2 mm²
- Cannot be determined (explain): __________________
- Not applicable

**Ki-67 labeling index**

- Specify Ki-67 percentage: _________________ %
- Less than 3%
- 3% to 20%
- Greater than 20%
- Cannot be determined (explain): __________________
- Not applicable

**Tumor Size (Note E)**

- Greatest dimension in Centimeters (cm) (specify size of largest tumor if multiple tumors are present): __________ cm
- Additional Dimension in Centimeters (cm): _____ x _____ cm
- Cannot be determined (explain): __________________

**Tumor Focality**

- Unifocal
- Multifocal

**Number of Tumors**

- Specify number: _________________
- Other (specify): _________________
- Cannot be determined: __________________
- Cannot be determined: __________________

**Multiple Primary Sites (e.g., hepatic flexure and transverse colon)**

- Not applicable (no additional primary site(s) present)
- Present: _________________

*Please complete a separate checklist for each primary site*

**Tumor Extent**

- Invades lamina propria
- Invades submucosa
- Invades muscularis propria
- Invades through muscularis propria into subserosal tissue without penetration of overlying serosa
- Invades visceral peritoneum (serosa)
___ Invades other organ(s) or adjacent structure(s) (specify): _________________
___ Cannot be determined: _________________
___ No evidence of primary tumor

**Lymphovascular Invasion**
___ Not identified
___ Present
___ Cannot be determined: _________________

**Perineural Invasion**
___ Not identified
___ Present
___ Cannot be determined: _________________

**Tumor Comment:** _________________

**MARGINS (Note F)**

**Margin Status**
___ All margins negative for tumor

**Closest Margin(s) to Tumor (select all that apply)**
___ Proximal: _________________
___ Distal: _________________
___ Radial or mesenteric: _________________
___ Mucosal: _________________
___ Deep: _________________
___ Other (specify): _________________
___ Cannot be determined: _________________

**Distance from Tumor 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: _________________
___ Tumor present at margin

**Margin(s) Involved by Tumor (select all that apply)**
___ Proximal: _________________
___ Distal: _________________
___ Radial or mesenteric: _________________
___ Mucosal: _________________
___ Deep: _________________
___ Other (specify): _________________
___ Cannot be determined: _________________
___ Other (specify): _________________
___ Cannot be determined (explain): _________________
___ Not applicable
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): _________________

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
___ Liver: _________________
___ Lung: _________________
___ Ovary: _________________
___ Nonregional lymph node(s): _________________
___ Peritoneum: _________________
___ Bone: _________________
___ Other (specify): _________________
___ Cannot be determined: _________________

PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th Edition) (Note G)
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.

TNM Descriptors (select all that apply)
___ Not applicable
___ m (multiple primary tumors)
___ r (recurrent)
___ y (posttreatment)
**pT Category**

*For any T, add “(m)” for multiple tumors [TX(#) or TX(m), where X = 1–4 and # = number of primary tumors identified]; for multiple tumors with different T, use the highest. For example: If there are two primary tumors, only one of which invades through the muscularis propria into the subserosal tissue without penetration of the overlying serosa, we define the primary tumor as either T3(2) or T3(m).*

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
___ pT1: Tumor invades the lamina propria or submucosa and is less than or equal to 2 cm
    ___ pT1a: Tumor less than 1 cm in greatest dimension
    ___ pT1b: Tumor 1-2 cm in greatest dimension
    ___ pT1 (subcategory cannot be determined)
___ pT2: Tumor invades the muscularis propria or is greater than 2 cm with invasion of the lamina propria or submucosa
___ pT3: Tumor invades through the muscularis propria into subserosal tissue without penetration of overlying serosa
___ pT4: Tumor invades the visceral peritoneum (serosa) or other organs or adjacent structures

**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 has occurred
___ pN1: Regional lymph node metastasis

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

___ Not applicable - pM cannot be determined from the submitted specimen(s)
___ pM1: Distant metastasis
    ___ pM1a: Metastasis confined to liver
    ___ pM1b: Metastases in at least one extrahepatic site (e.g., lung, ovary, nonregional lymph node, peritoneum, bone)
    ___ pM1c: Both hepatic and extrahepatic metastases
    ___ pM1 (subcategory cannot be determined)

**ADDITIONAL FINDINGS (Note H)**

+Additional Findings (select all that apply)
    ___ None identified
    ___ Tumor necrosis
    ___ Other (specify): _________________

**COMMENTS**

Comment(s): _________________
Explanatory Notes

A. Application and Tumor Location
This protocol applies to well-differentiated neuroendocrine tumors (carcinoid tumors) of the colon and rectum. Poorly differentiated neuroendocrine carcinomas (including small cell carcinomas and large cell neuroendocrine carcinomas) and tumors with mixed glandular/neuroendocrine differentiation are not included.1

Because of site-specific similarities in histology, immunohistochemistry, and histochemistry, neuroendocrine tumors of the digestive tract have traditionally been subdivided into those of foregut, midgut, and hindgut origin (Table 1). In general, the distribution pattern along the gastrointestinal (GI) tract parallels that of the progenitor cell type, and the anatomic site of origin of GI neuroendocrine tumors is an important predictor of clinical behavior.2

Table 1. Site of Origin of Gastrointestinal Neuroendocrine Tumors

<table>
<thead>
<tr>
<th>Site</th>
<th>Foregut Tumors</th>
<th>Midgut Tumors</th>
<th>Hindgut Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromogranin A</td>
<td>Stomach, Proximal Duodenum</td>
<td>Jejunum, Ileum, Appendix, Proximal Colon</td>
<td>Distal Colon, Rectum</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serotonin</td>
<td>86%-100% +</td>
<td>82%-92% +</td>
<td>40%-58% +</td>
</tr>
<tr>
<td></td>
<td>50% +</td>
<td>95%-100% +</td>
<td>94%-100% +</td>
</tr>
<tr>
<td></td>
<td>33% + 3</td>
<td>86% + 3</td>
<td>45%-83% +</td>
</tr>
</tbody>
</table>

Other Immunohistochemical Markers

| Rarely, + for pancreatic polypeptide, histamine, gastrin, vasoactive intestinal peptide (VIP), or adrenocorticotropin hormone (ACTH) | Prostatic acid phosphatase + in 20%-40% 5,6,7 | Prostatic acid phosphatase + in 20%-82% 3,4,5,6,7,8,9 |

Carcinoid syndrome

| Rare | 5%-39% 10,11 | Rare |

References
9. Nash SV, Said JW. Gastroenteropancreatic neuroendocrine tumors: a histochemical and immunohistochemical study of epithelial (keratin proteins, carcinoembryonic antigen) and


**B. Site-Specific Features**

Rectal neuroendocrine tumors are not uncommon, constitute approximately one-quarter of GI neuroendocrine tumors. They are usually small, solitary, and clinically silent, most commonly occurring 4 cm to 13 cm from the anal verge. Mitotically inactive rectal neuroendocrine tumors or those smaller than 2.0 cm are almost always clinically indolent. Metastases and carcinoid syndrome are very rare. L-cell NETs are usually seen in the rectum. Colonic neuroendocrine tumors outside the ileocecal region and rectum are extremely rare; most are large, bulky, highly invasive tumors that are metastatic at presentation. Two-thirds of them arise within the cecum or right colon. Many well-differentiated neuroendocrine tumors involving the ileocecal valve represent tumors arising in the terminal ileum, rather than in the large bowel.

**References**


**C. Histologic Type**

The World Health Organization (WHO) classifies neuroendocrine neoplasms as well-differentiated neuroendocrine tumors (either the primary tumor or metastasis) and poorly differentiated neuroendocrine carcinomas. Historically, well-differentiated neuroendocrine tumors have been referred to as “carcinoid” tumors, a term which may cause confusion because clinically a carcinoid tumor is a serotonin-producing tumor associated with functional manifestations of carcinoid syndrome. The use of the term “carcinoid” for neuroendocrine tumor reporting is therefore discouraged for these reasons.

Classification of neuroendocrine tumors is based upon size, functionality, site, and invasion. Functioning tumors are those associated with clinical manifestations of hormone production or secretion of measurable amounts of active hormone; immunohistochemical demonstration of hormone production is not equivalent to clinically apparent functionality.

Although specific histologic patterns in well-differentiated neuroendocrine tumors, such as trabecular, insular, and glandular, roughly correlate with tumor location, these patterns have not been clearly shown independently to predict response to therapy or risk of nodal metastasis and are rarely reported in clinical practice. Immunohistochemistry and other ancillary techniques are generally not required to diagnose well-differentiated neuroendocrine tumors. Specific markers that may be used to establish neuroendocrine differentiation include chromogranin A, synaptophysin, and CD56. Because of their relative sensitivity and specificity, chromogranin A and synaptophysin are recommended. It should be noted that hindgut neuroendocrine tumors often do not express appreciable amounts of chromogranin A. Rectal neuroendocrine tumors express prostatic acid phosphatase, a potential diagnostic pitfall for tumors arising in male patients.
References

D. Histologic Grade
Cytologic atypia in well-differentiated neuroendocrine tumors has no impact on clinical behavior of these tumors. The WHO classification\(^1\) and others\(^2\) use mitotic rate and/or Ki-67 index as one of the criteria for potential for aggressive behavior. Mitotic rate should be reported as number of mitoses per 2 mm\(^2\), by evaluating at least 10 mm\(^2\) in the most mitotically active part of the tumor. Only clearly identifiable mitotic figures should be counted; hyperchromatic, karyorrhectic, or apoptotic nuclei are excluded. Because of variations in field size, the number of high-power fields (HPF) (at 40X magnification) for 10 mm\(^2\) (thereby 2 mm\(^2\)) must be determined for each microscope (Table 2). For example, if using a microscope with a field diameter of 0.55 mm, count 42 HPF and divide the resulting number of mitoses by 5 to determine the number of mitoses per 2 mm\(^2\) needed to assign tumor grade.

Table 2. Number of HPF Required for 10 mm\(^2\) Using Microscopes With Different Field Diameter

<table>
<thead>
<tr>
<th>Field Diameter (mm)</th>
<th>Area (mm(^2))</th>
<th>Number of HPF for 10 mm(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.40</td>
<td>0.125</td>
<td>80</td>
</tr>
<tr>
<td>0.41</td>
<td>0.132</td>
<td>75</td>
</tr>
<tr>
<td>0.42</td>
<td>0.139</td>
<td>70</td>
</tr>
<tr>
<td>0.43</td>
<td>0.145</td>
<td>69</td>
</tr>
<tr>
<td>0.44</td>
<td>0.152</td>
<td>65</td>
</tr>
<tr>
<td>0.45</td>
<td>0.159</td>
<td>63</td>
</tr>
<tr>
<td>0.46</td>
<td>0.166</td>
<td>60</td>
</tr>
<tr>
<td>0.47</td>
<td>0.173</td>
<td>58</td>
</tr>
<tr>
<td>0.48</td>
<td>0.181</td>
<td>55</td>
</tr>
<tr>
<td>0.49</td>
<td>0.189</td>
<td>53</td>
</tr>
<tr>
<td>0.50</td>
<td>0.196</td>
<td>50</td>
</tr>
<tr>
<td>0.51</td>
<td>0.204</td>
<td>49</td>
</tr>
<tr>
<td>0.52</td>
<td>0.212</td>
<td>47</td>
</tr>
<tr>
<td>0.53</td>
<td>0.221</td>
<td>45</td>
</tr>
<tr>
<td>0.54</td>
<td>0.229</td>
<td>44</td>
</tr>
<tr>
<td>0.55</td>
<td>0.238</td>
<td>42</td>
</tr>
<tr>
<td>0.56</td>
<td>0.246</td>
<td>41</td>
</tr>
<tr>
<td>0.57</td>
<td>0.255</td>
<td>39</td>
</tr>
<tr>
<td>0.58</td>
<td>0.264</td>
<td>38</td>
</tr>
<tr>
<td>0.59</td>
<td>0.273</td>
<td>37</td>
</tr>
<tr>
<td>0.60</td>
<td>0.283</td>
<td>35</td>
</tr>
<tr>
<td>0.61</td>
<td>0.292</td>
<td>34</td>
</tr>
<tr>
<td>0.62</td>
<td>0.302</td>
<td>33</td>
</tr>
<tr>
<td>0.63</td>
<td>0.312</td>
<td>32</td>
</tr>
<tr>
<td>0.64</td>
<td>0.322</td>
<td>31</td>
</tr>
</tbody>
</table>
Ki-67 index is reported as percent positive tumor cells in area of highest nuclear labeling (“hot spot”), although the precise method of assessment has not been standardized. A number of methods have used to assess Ki-67 index, including automatic counting and “eyeballing”.\(^3\)\(^4\) Automated counting is not widely available and requires careful modification of the software to circumvent the inaccuracies.\(^3\) Eye-balling can be used for most tumors; however, for tumors with Ki-67 index close to grade cut-offs, it is recommended to perform the manual count on the print of camera-captured image of the hot spot. It has been recommended that a minimum of 500 tumor cells be counted to determine the Ki-67 index and a notation is made if less cells are available. Grade assigned based on Ki-67 index is typically higher than that based on mitotic count, and the case is assigned to the higher of the 2 if both methods are performed.\(^1\)

It is important to note that there are a small group of well-differentiated neuroendocrine tumors with a Ki-67 index >20% and a mitotic rate usually <20 per 10 HPF. In WHO-2010, these tumors were considered as G3 poorly differentiated neuroendocrine carcinomas. However, they have typical morphology of well-differentiated tumors. Previous studies (most on pancreatic neuroendocrine tumors) have demonstrated that these tumors have a worse prognosis than grade 2 (Ki-67=3-20 % and mitosis <20/10 HPF) neuroendocrine tumors, but they are not as aggressive as poorly differentiated neuroendocrine carcinomas.\(^6\) In addition, these tumors do not have the genetic abnormalities seen in poorly differentiated neuroendocrine carcinomas.\(^6\) Furthermore, unlike poorly differentiated neuroendocrine carcinomas, they are less responsive to platinum-based chemotherapy.\(^2\) In WHO-2019 blue book of digestive system tumors and AJCC 8th edition, those with typical morphology of well-differentiated tumors are classified as "well differentiated neuroendocrine tumor" but as grade 3 (Table 3).\(^1\)\(^8\)

### Table 3. Recommended Grading System for Well-Differentiated Gastroenteropancreatic Neuroendocrine Tumors

<table>
<thead>
<tr>
<th>Grade</th>
<th>Mitotic Rate (per 2mm²)</th>
<th>Ki-67 index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-differentiated neuroendocrine tumor, G1</td>
<td>2</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Well-differentiated neuroendocrine tumor, G2</td>
<td>2-20</td>
<td>3-20</td>
</tr>
<tr>
<td>Well-differentiated neuroendocrine tumor, G3</td>
<td>&gt;20</td>
<td>&gt;20</td>
</tr>
</tbody>
</table>

References


**E. Tumor Size**
For neuroendocrine tumors in any part of the gastrointestinal tract, size greater than 2.0 cm is associated with a higher risk of lymph node metastasis. Rectal carcinoids smaller than 1.0 cm are almost always clinically indolent, and local excision is generally considered sufficient for tumors 1.0 cm or smaller, as well as many tumors between 1.0 cm and 2.0 cm. More extensive procedures (eg, right hemicolectomy and abdominoperineal resection) are usually reserved for patients with rectal tumors larger than 2.0 cm, rectal tumors with regional metastasis, and most colonic neuroendocrine tumors.

**F. Circumferential (Radial or Mesenteric) Margin**
In addition to addressing the proximal and distal margins, assessment of the circumferential (radial) margin is necessary for any segment of gastrointestinal tract either unencased (Figure, C) or incompletely encased by peritoneum (Figure, B). The circumferential margin represents the adventitial soft-tissue margin closest to the deepest penetration of tumor and is created surgically by blunt or sharp dissection of the retroperitoneal or subperitoneal aspect, respectively. The distance between the tumor and circumferential (radial) margin should be reported, if applicable. The circumferential (radial) margin is considered positive if the tumor is present at the nonperitonealized surface. This assessment includes tumor within a lymph node as well as direct tumor extension, but if circumferential (radial) margin positivity is based solely on intranodal tumor, this should be so stated.

The mesenteric resection margin is the only relevant circumferential margin in segments completely encased by peritoneum (eg, transverse colon) (Figure, A). Involvement of this margin should be reported even if tumor does not penetrate the serosal surface.

![A, Mesenteric margin in viscus completely encased by peritoneum (dotted line). B, Circumferential (radial) margin (dotted line) in viscus incompletely encased by peritoneum. C, Circumferential (radial) margin (dotted line) in viscus completely unencased by peritoneum.](image)

**G. Pathologic Stage Classification**
The TNM staging system for neuroendocrine tumors of the colon and rectum of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended.\(^1\)

By 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 unfeasible) 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,” “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 following 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 prior to 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.

N Category Considerations
The regional lymph nodes of the colon and rectum are as follows:

**Cecum:** Pericolic, anterior cecal, posterior cecal, ileocolic, right colic

**Ascending colon:** Pericolic, ileocolic, right colic, middle colic

**Hepatic flexure:** Pericolic, middle colic, right colic

**Transverse colon:** Pericolic, middle colic

**Splenic flexure:** Pericolic, middle colic, left colic, inferior mesenteric

**Descending colon:** Pericolic, left colic, inferior mesenteric, sigmoid

**Sigmoid colon:** Pericolic, inferior mesenteric, superior rectal (hemorrhoidal), sigmoidal, sigmoid mesenteric

**Rectosigmoid:** Pericolic, perirectal, left colic, sigmoid mesenteric, sigmoidal, inferior mesenteric, superior rectal (hemorrhoidal), middle rectal (hemorrhoidal)
**Rectum:** Perirectal, sigmoid mesenteric, inferior mesenteric, lateral sacral, presacral, internal iliac, sacral promontory (Gerota’s), internal iliac, superior rectal (hemorrhoidal), middle rectal (hemorrhoidal), inferior rectal (hemorrhoidal)

References

**H. Additional Findings**
Coagulative tumor necrosis, usually punctate, may indicate more aggressive behavior and should be reported

References