# Colon and Rectum

## Protocol applies to all invasive carcinomas of the colon and rectum. Carcinoid tumors, lymphomas, sarcomas, and tumors of the vermiform appendix are excluded.

*Protocol revision date: January 2004*
*Based on AJCC/UICC TNM, 6th edition*

### Procedures

- **Incisional Biopsy** (No Accompanying Checklist)
- **Excisional Biopsy, Polypectomy**
- **Local Excision (Transanal Disk Excision)**
- **Segmental Resection**
- **Rectal Resection (Low Anterior Resection; Abdominoperineal Resection)**

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# Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2004*
*Applies to invasive carcinomas only*
*Based on AJCC/UICC TNM, 6th edition*

## COLON AND RECTUM: Polypectomy

Patient name:
Surgical pathology number:

***Note: Check 1 response unless otherwise indicated.***

### MACROSCOPIC

**Tumor Site**
___ Cecum
___ Right (ascending) colon
___ Hepatic flexure
___ Transverse colon
___ Splenic flexure
___ Left (descending) colon
___ Sigmoid colon
___ Rectum
___ Not specified

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

**Polyp Configuration**
___ Pedunculated with stalk
Stalk length: ___ cm
___ Pedunculated, no stalk
___ Sessile
___ Fragmented



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## MICROSCOPIC

**Histologic Type**
___ Adenocarcinoma
___ Mucinous adenocarcinoma (greater than 50% mucinous)
___ Medullary carcinoma
___ Signet-ring cell carcinoma (greater than 50% signet-ring cells)
___ Small cell carcinoma
___ Undifferentiated carcinoma
___ Other (specify): _____
___ Carcinoma, type cannot be determined

**Histologic Grade**
___ Not applicable
___ Cannot be determined
___ Low-grade (well to moderately differentiated)
___ High-grade (poorly differentiated to undifferentiated)

**Extent of Invasion**
___ Cannot be determined
Invasion (deepest):
___ Lamina propria
___ Muscularis mucosae
___ Submucosa
___ Muscularis propria

**Margins (check all that apply)**

Deep Margin (Stalk Margin)
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
Distance of invasive carcinoma from margin: ___ mm
___ Involved by invasive carcinoma

Mucosal/Lateral Margin
___ Not applicable
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma
___ Involved by in situ carcinoma/adenoma

**Lymphatic (Small Vessel) Invasion (L)**
___ Absent
___ Present
___ Indeterminate

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***Venous (Large Vessel) Invasion (V)**
*___ Absent
*___ Present
*___ Indeterminate

***Type of Polyp in Which Invasive Carcinoma Arose**
*___ Tubular
*___ Villous
*___ Tubulovillous
*___ Serrated
*___ Hamartomatous
*___ Indeterminate

***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ Active colitis
*___ Other (specify): _____

***Comment(s)**



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# Surgical Pathology Cancer Case Summary (Checklist)

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## RECTUM: Local Excision (Transanal Disk Excision)

Patient name:
Surgical pathology number:

***Note: Check 1 response unless otherwise indicated.***

### MACROSCOPIC

**Specimen Integrity**
___ Intact
___ Fragmented
*Number of pieces: ___

***Tumor Site**
*Distance from anal verge (per clinical report): ___ cm
*___ Distance from anal verge unknown

***Tumor Configuration**
*___ Exophytic (polypoid)
*___ Infiltrative
*___ Ulcerating
*___ Other (specify): _____

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

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## MICROSCOPIC

### Histologic Type

___ Adenocarcinoma
___ Mucinous adenocarcinoma (greater than 50% mucinous)
___ Medullary carcinoma
___ Signet-ring cell carcinoma (greater than 50% signet-ring cells)
___ Small cell carcinoma
___ Undifferentiated carcinoma
___ Other (specify): _____
___ Carcinoma, type cannot be determined

### Histologic Grade

___ Not applicable
___ Cannot be assessed
___ Low-grade (well to moderately differentiated)
___ High-grade (poorly differentiated to undifferentiated)

### Pathologic Staging (pTNM)

Primary Tumor (pT)

___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ, intraepithelial (no invasion)
___ pTis: Carcinoma in situ, invasion of lamina propria
___ pT1: Tumor invades submucosa
___ pT2: Tumor invades muscularis propria
___ pT3: Tumor invades through the muscularis propria into the subserosa or the nonperitonealized pericolic or perirectal soft tissues
*___ pT3a/b: Tumor invades through the muscularis propria into the subserosa or the nonperitonealized pericolic or perirectal soft tissues, invades 5 mm or less beyond the border of the muscularis propria
*___ pT3c/d: Tumor invades through the muscularis propria into the subserosa or the nonperitonealized pericolic or perirectal soft tissues, invades greater than 5 mm beyond the border of the muscularis propria
___ pT4: Tumor directly invades adjacent structures

Regional Lymph Nodes (pN)

___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in 1 to 3 lymph nodes
___ pN2: Metastasis in 4 or more lymph nodes
Specify: Number examined: ___
Number involved: ___



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**Margins (check all that apply)**

Lateral Margin
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
Distance of invasive carcinoma from closest lateral margin: ___ mm
*Specify location (eg, o'clock position), if possible:
_____
___ Involved by invasive carcinoma
*Specify location (eg, o'clock position), if possible:
_____
*___ Involved by carcinoma in situ/adenoma

Deep Margin
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
Distance of invasive carcinoma from margin: ___ mm
___ Focal involvement by invasive carcinoma
___ Multifocal involvement by invasive carcinoma

**Lymphatic (Small Vessel) Invasion (L) (check all that apply)**
___ Absent
___ Present
*___ Intramural
*___ Extramural
___ Indeterminate

**Venous (Large Vessel) Invasion (V) (check all that apply)**
___ Absent
___ Present
*___ Intramural
*___ Extramural
___ Indeterminate

***Perineural Invasion**
*___ Absent
*___ Present

***Tumor Border Configuration**
*___ Pushing
*___ Infiltrating

***Intratumoral/Peritumoral Lymphocytic Response**
*___ None
*___ Mild to moderate
*___ Marked (including Crohn-like response)

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***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ Adenoma(s)
*___ Chronic ulcerative proctocolitis
*___ Crohn disease
*___ Dysplasia
*___ Other polyps (type[s]): _____
*___ Other (specify): _____

***Comment(s)**



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# Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2004*
*Applies to invasive carcinomas only*
*Based on AJCC/UICC TNM, 6th edition*

## COLON AND RECTUM: Resection

Patient name:
Surgical pathology number:
Other identifiers:

***Note: Check 1 response unless otherwise indicated.***

### MACROSCOPIC

**Specimen Type**
___ Right hemicolectomy
*Length: ___ cm
___ Transverse colectomy
*Length: ___ cm
___ Left hemicolectomy
*Length: ___ cm
___ Sigmoidectomy
*Length: ___ cm
___ Rectal/rectosigmoid colon (low anterior resection)
*Length: ___ cm
___ Total abdominal colectomy
*Length: ___ cm
___ Abdominoperineal resection
*Length: ___ cm
___ Other (specify): _____
*Length: ___ cm
___ Not specified

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**Tumor Site**
___ Cecum
___ Right (ascending) colon
___ Hepatic flexure
___ Transverse colon
___ Splenic flexure
___ Left (descending) colon
___ Sigmoid colon
___ Rectosigmoid
___ Rectum
___ Colon, not otherwise specified
___ Cannot be determined (see Comment)

***Tumor Configuration**
*___ Exophytic (polypoid)
*___ Infiltrative
*___ Ulcerating
*___ Other (specify): _____

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

***Mesorectum**
*___ Not applicable
*___ Complete
*___ Near complete
*___ Incomplete

**MICROSCOPIC**

**Histologic Type**
___ Adenocarcinoma
___ Mucinous adenocarcinoma (greater than 50% mucinous)
___ Medullary carcinoma
___ Signet-ring cell carcinoma (greater than 50% signet-ring cells)
___ Small cell carcinoma
___ Undifferentiated carcinoma
___ Other (specify): _____
___ Carcinoma, type cannot be determined



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**Histologic Grade**
___ Not applicable
___ Cannot be assessed
___ Low-grade (well to moderately differentiated)
___ High-grade (poorly differentiated to undifferentiated)
___ Other (specify): _____

**Pathologic Staging (pTNM)**

Primary Tumor (pT)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ, intraepithelial (no invasion)
___ pTis: Carcinoma in situ, invasion of lamina propria
___ pT1: Tumor invades submucosa
___ pT2: Tumor invades muscularis propria
___ pT3: Tumor invades through the muscularis propria into the subserosa or the nonperitonealized pericolic or perirectal soft tissues
*___ pT3a/b: Tumor invades through the muscularis propria into the subserosa or the nonperitonealized pericolic or perirectal soft tissues, invades 5 mm or less beyond the border of the muscularis propria
*___ pT3c/d: Tumor invades through the muscularis propria into the subserosa or the nonperitonealized pericolic or perirectal soft tissues, invades greater than 5 mm beyond the border of the muscularis propria
___ pT4a: Tumor directly invades other organs or structures
___ pT4b: Tumor penetrates the visceral peritoneum

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in 1 to 3 regional lymph nodes
___ pN2: Metastasis in 4 or more regional lymph nodes
Specify: Number examined: ___
Number involved: ___

Distant Metastasis (pM)
___ pMX: Cannot be assessed
___ pM1: Distant metastasis
*Specify site(s): _____

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**Margins (check all that apply)**

Proximal Margin
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma
___ Carcinoma in situ/adenoma absent at proximal margin
___ Carcinoma in situ/adenoma present at proximal margin

Distal Margin
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma
___ Carcinoma in situ/adenoma absent at distal margin
___ Carcinoma in situ/adenoma present at distal margin

Circumferential (Radial) Margin
___ Not applicable
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma (tumor present 0-1 mm from CRM)

*Mesenteric Margin
*___ Cannot be assessed
*___ Uninvolved by invasive carcinoma
*___ Involved by invasive carcinoma

Distance of invasive carcinoma from closest margin: ___ mm *OR* ___ cm
Specify margin: _____

**Lymphatic (Small Vessel) Invasion (L) (check all that apply)**
___ Absent
___ Present
*___ Intramural
*___ Extramural
___ Indeterminate

**Venous (Large Vessel) Invasion (V) (check all that apply)**
___ Absent
___ Present
*___ Intramural
*___ Extramural
___ Indeterminate

***Perineural Invasion**
*___ Absent
*___ Present


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***Tumor Border Configuration**
*___ Pushing
*___ Infiltrating

***Intratumoral/Peritumoral Lymphocytic Response**
*___ None
*___ Mild to moderate
*___ Marked (including Crohn-like response)

***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ Adenoma(s)
*___ Chronic ulcerative proctocolitis
*___ Crohn disease
*___ Dysplasia
*___ Other polyps (type[s]): _____
*___ Other (specify): _____

***Comment(s)**



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## Background Documentation

*Protocol revision date: January 2004*

# I. Incisional (Endoscopic) Biopsy

### A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous colon adenoma(s)/carcinoma(s)
      (2) familial adenomatous polyposis syndrome
      (3) hereditary non-polyposis colon cancer syndrome
      (4) familial hamartomatous polyposis syndrome
      (5) inflammatory bowel disease
   b. Relevant findings (eg, colonoscopic and/or imaging studies)
5. Clinical diagnosis (eg, Crohn disease)
6. Procedure (eg, colonoscopic biopsy)
7. Operative findings
8. Anatomic site(s) of specimen(s)

### B. Macroscopic Examination

1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Number of pieces
   c. Largest dimension of each piece
   d. Description of other tissues, as appropriate
2. Submit entire specimen for microscopic evaluation
3. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, molecular studies [specify type], cytogenetic analysis)

### C. Microscopic Evaluation

1. Tumor (Note **A**)
   a. Histologic type (Note **B**)
   b. Histologic grade (Note **C**)
   c. Extent of invasion, as appropriate
2. Additional pathologic findings, if present
   a. Colitis
   b. Adenoma
   c. Other(s)
3. Results/status of special studies (specify)
4. Comments
   a. Correlation with other specimens, as appropriate
   b. Correlation with clinical information, as appropriate

## II. Excisional Biopsy, Polypectomy

### A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous colon adenoma(s)/carcinoma(s)
      (2) familial adenomatous polyposis syndrome
      (3) hereditary nonpolyposis colon cancer syndrome
      (4) familial hamartomatous polyposis syndrome
      (5) inflammatory bowel disease
   b. Clinical diagnosis
   c. Procedure (eg, polypectomy)
   d. Operative findings
   e. Anatomic site(s) of specimen(s)

### B. Macroscopic Examination

1. Specimen
   a. Tissue(s) included
   b. Unfixed/fixed (specify fixative)
   c. Number of pieces
   d. Dimensions
   e. Orientation, if indicated by surgeon
   f. Descriptive features (eg, color, consistency)
2. Polyp
   a. Configuration (eg, pedunculated, sessile)
   b. Size (3 dimensions)
   c. If pedunculated, length of stalk (margin of stalk may be inked)
   d. Dimension of carcinoma (diameter), if possible
3. Tissue(s) submitted for microscopic evaluation
   a. Transverse (coronal) section(s) through polyp; include
      (1) polyp apex and stalk or base in same section, if possible
      (2) carcinoma, point of deepest invasion
      (3) longitudinal section of polyp stalk, as appropriate
4. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, molecular studies [specify type], cytogenetic analysis)

### C. Microscopic Evaluation

1. Polyp
   a. Histologic type
2. Tumor (carcinoma within polyp)
   a. Histologic type (Note **B**)
   b. Histologic grade (Notes **C** and **D**)
   c. Extent of invasion (Note **D**)
   d. Venous/lymphatic vessel invasion (Note **D**)
   e. Distance of carcinoma from margin, in millimeters (Note **D**)

3. Results/status of special studies (specify)
4. Comments
    a. Correlation with other specimens, as appropriate
    b. Correlation with clinical information, as appropriate

## III. Local Excision

**(Transanal Disk Excision)**

**A. Clinical Information**

1. Patient identification
    a. Name
    b. Identification number
    c. Age (birth date)
    d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
    a. Relevant history
        (1) previous colon adenoma(s)/carcinoma(s)
        (2) familial adenomatous polyposis syndrome
        (3) hereditary nonpolyposis colon cancer syndrome
        (4) familial hamartomatous polyposis syndrome
        (5) inflammatory bowel disease
    b. Relevant findings (eg, colonoscopic and/or imaging studies)
    c. Clinical diagnosis
    d. Procedure (eg, transanal resection)
    e. Operative findings
    f. Anatomic site(s) of specimen(s)

**B. Macroscopic Examination**

1. Specimen
    a. Unfixed/fixed (specify fixative)
    b. Number of pieces
    c. Dimensions
    d. Orientation of specimen, if indicated by surgeon
    e. Descriptive characteristics (eg, color, consistency)
    f. Layers of colon/rectum present, if grossly discernible
    g. Results of intraoperative consultation
2. Tumor (Note **A**)
    a. Configuration (Note **E**)
    b. Dimensions (3)
    c. Distance of tumor edge from closest margin
    d. Estimated depth of invasion
    e. Lesions in noncancerous colon/rectum (eg, colitis, polyps)
3. Additional pathologic findings, if present
4. Tissue(s) submitted for microscopic evaluation (Note **F**)
    a. Carcinoma, including
        (1) points of deepest penetration (at least 3 sections; optimally 5 sections)
        (2) interface with adjacent colon
        (3) margins closest to tumor edge if less than 5.0 cm
    b. Frozen section tissue fragment(s) (unless saved for special studies)

5. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, molecular studies [specify type], cytogenetic analysis)

**C. Microscopic Evaluation**

1. Tumor
   a. Histologic type (Note **B**)
   b. Histologic grade (Note **C**)
   c. Extent of invasion (Note **G**)
   d. Venous/lymphatic vessel invasion (Note **H**)
   e. Perineural invasion (Note **H**)
   f. Extramural venous invasion (Note **F**)
   g. Intratumoral or peritumoral lymphocytic response (Note **I**)
   h. Pattern of growth at tumor periphery (Note **J**)
      (1) infiltrating border
      (2) pushing border
2. Margins
   a. Distance of carcinoma from closest mucosal margin and/or deep margin
3. Additional pathologic findings, if present
   a. Colitis
   b. Dysplasia
   c. Adenomas
   d. Hyperplastic polyps
   e. Other(s)
4. Results/status of special studies (specify)
5. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

## IV. Segmental Resection of Colon

**A. Clinical Information**

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous colon adenoma(s)/carcinoma(s)
      (2) familial adenomatous polyposis syndrome
      (3) hereditary nonpolyposis colon cancer syndrome
      (4) familial hamartomatous polyposis syndrome
      (5) inflammatory bowel disease
   b. Relevant findings (eg, colonoscopic and/or imaging studies)
   c. Clinical diagnosis
   d. Procedure (eg, right colectomy, transverse colectomy, left colectomy, sigmoidectomy)
   e. Operative findings

f. Anatomic site(s) of specimen(s) (eg, cecum, right, transverse, descending, sigmoid colon)

**B. Macroscopic Examination**

1. Specimen
   a. Organ(s)/tissue(s) included
   b. Unfixed/fixed (specify fixative)
   c. Number of pieces
   d. Dimensions
   e. Orientation of specimen, if indicated by surgeon
   f. Results of intraoperative consultation
2. Tumor
   a. Location (Note **A**)
   b. Configuration (Note **E**)
   c. Dimensions (3 dimensions)
   d. Descriptive characteristics (eg, color, consistency)
   e. Ulceration/perforation
   f. Distance from margins (Note K)
      (1) proximal
      (2) distal
      (3) circumferential (radial soft tissue margin closest to deepest tumor penetration)
   g. Appearance of serosa overlying tumor (Note **G**)
   h. Estimated depth of invasion (Note **G**)
3. Lesions in noncancerous colon/rectum (eg, colitis, other polyps)
4. Regional lymph nodes (Note **G**)
5. Nonregional lymph nodes (Note **G**)
6. Metastasis to other organ(s) or structure(s) (Note **G**)
7. Colon/rectum uninvolved by tumor
8. Other tissue(s)/organ(s)
9. Tissues submitted for microscopic evaluation (Note **F**)
   a. Carcinoma, including:
      (1) points of deepest penetration (at least 3 sections; optimally 5 sections)
      (2) interface with adjacent colon/rectum
      (3) visceral serosa overlying tumor
   b. Margins (Note **K**)
      (1) proximal
      (2) distal
      (3) circumferential (radial soft tissue margin closest to deepest tumor penetration)
   c. All lymph nodes (Note **G**)
   d. Other lesions (eg, polyps/colitis)
   e. Frozen section tissue fragment(s) (unless saved for special studies)
10. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, molecular studies [specify type], cytogenetic analysis)

**C. Microscopic Evaluation**

1. Tumor
   a. Histologic type (Note **B**)
   b. Histologic grade (Note **C**)
   c. Extent of invasion (Note **G**)

   d. Blood/lymphatic vessel invasion (Note **H**)
   e. Perineural invasion (Note **H**)
   f. Extramural venous invasion (Note **F**)
   g. Intratumoral or peritumoral lymphocytic response (Note **I**)
   h. Pattern of growth at tumor periphery (Note **J**)
      (1) infiltrating border
      (2) pushing border
   i. Associated pericolorectal abscess formation, if present
   j. Associated pneumatosis intestinalis, if present
2. Margins (Note **K**)
   a. Proximal
   b. Distal
   c. Radial (specify distance of carcinoma from closest radial margin)
3. Regional lymph nodes (Note **G**)
   a. Number
   b. Number involved by tumor
4. Additional pathologic findings, if present
   a. Inflammatory bowel disease
   b. Dysplasia
   c. Adenomas
   d. Other types of polyps
5. Distant metastasis, specify site (Note **G**)
6. Other tissue(s)/organ(s)
7. Results/status of special studies (specify)
8. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

## V. Rectal Resection

**(Low Anterior Resection; Abdominoperineal Resection)**

### A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous colon adenoma(s)/carcinoma(s)
      (2) familial adenomatous polyposis syndrome
      (3) hereditary nonpolyposis colon cancer syndrome
      (4) familial hamartomatous polyposis syndrome
      (5) inflammatory bowel disease
   b. Relevant findings (eg, colonoscopic endoscopic ultrasound and/or imaging studies)
   c. Clinical diagnosis

d. Procedure (eg, low anterior resection, abdominoperineal resection)
e. Operative findings
f. Anatomic site(s) of specimen(s) (eg, rectosigmoid, rectum, and anal canal)

**B. Macroscopic Examination**

1. Specimen
   a. Organ(s)/tissue(s) included
   b. Unfixed/fixed (specify fixative)
   c. Number of pieces
   d. Dimensions
   e. Appearance of mesorectal envelope (Note **L**)
   f. Results of intraoperative consultation
2. Tumor
   a. Location (Note **A**)
   b. Configuration (Note **E**)
   c. Dimensions
   d. Descriptive characteristics (eg, color, consistency)
   e. Ulceration/perforation
   f. Distance from margins (Note **K**)
      (1) proximal
      (2) distal
      (3) circumferential (radial soft tissue margin closest to deepest tumor penetration)
   g. Appearance of serosa overlying tumor, if applicable (Note **G**)
   h. Estimated depth of invasion (Note **G**)
3. Lesions in noncancerous rectum (eg, proctitis, other polyps)
4. Regional lymph nodes (Note **G**)
5. Metastasis to other organ(s) or structure(s) (Note **G**)
6. Rectum uninvolved by tumor
7. Other tissue(s)/organ(s)
8. Tissues submitted for microscopic evaluation
   a. Carcinoma, including
      (1) points of deepest penetration
      (2) interface with adjacent sigmoid colon/anal canal
      (3) visceral serosa overlying tumor, if applicable
   b. Margins (Note **K**)
      (1) proximal
      (2) distal
      (3) circumferential (radial soft tissue margin closest to deepest tumor penetration)
   c. All lymph nodes (Note **G**)
   d. Other lesions (eg, polyps/colitis)
   e. Frozen section tissue fragment(s) (unless saved for special studies)
9. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, molecular studies [specify type], cytogenetic analysis)

**C. Microscopic Evaluation**

1. Tumor
   a. Histologic type (Note **B**)
   b. Histologic grade (Note **C**)
   c. Extent of invasion (Note **G**)

   d. Blood/lymphatic vessel invasion (Note **H**)
   e. Perineural invasion (Note **H**)
   f. Extramural venous invasion (Note **F**)
   g. Peritumoral lymphocytic response (Note **I**)
   h. Pattern of growth at tumor periphery (Note **J**)
      (1) infiltrating border
      (2) pushing border
   i. Associated pericolorectal abscess formation, if present
   j. Associated pneumatosis intestinalis, if present
2. Margins (Note **K**)
   a. Proximal
   b. Distal
   c. Circumferential (specify distance of carcinoma from closest circumferential margin)
3. Regional lymph nodes (Note **G**)
   a. Number
   b. Number involved by tumor
4. Additional pathologic findings, if present
   a. Inflammatory bowel disease
   b. Dysplasia
   c. Adenomas
   d. Other types of polyps
5. Distant metastasis, specify site (Note **G**)
6. Other tissue(s)/organ(s)
7. Results/status of special studies (specify)
8. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

## Explanatory Notes

### A. Anatomic Sites

The protocol applies to all carcinomas arising in the colon and rectum.[1] It excludes carcinomas of the vermiform appendix.

The colon is divided into 4 parts: the right (ascending), the middle (transverse), the left (descending), and the sigmoid. The right colon is subdivided into the cecum (peritoneally located and measuring about 6 x 9 cm) and the ascending colon (located retroperitoneally and measuring 15 to 20 cm long). The descending colon, also located retroperitoneally, is 10 to 15 cm in length. The posterior surfaces of the ascending and descending colon lack a peritoneal covering and are in direct contact with the retroperitoneum. These posterior, nonperitonealized surfaces are the equivalent of the circumferential resection margins of these segments (see Note **K**). In contrast, the anterior and lateral surfaces of the ascending and descending colon are covered by a visceral peritoneum (serosa). The transverse colon is entirely intraperitoneal and is supported on a long mesentery that is attached to the pancreas. The descending colon becomes the sigmoid colon at the origin of the mesosigmoid, and the sigmoid colon becomes the rectum at the termination of the sigmoid mesentery. The transition from

sigmoid to rectum is marked by the fusion of the tenia coli of the sigmoid to form the circumferential longitudinal muscle of the rectal wall. This occurs approximately 12 to 15 cm from the dentate line. The rectum is about 12 cm in length and extends from the fusion of the tenia to the puborectalis ring. The upper third is covered by peritoneum on the front and both sides. The middle third is covered by peritoneum only on the anterior surface. The lower third (also known as the rectum or rectal ampulla) has no peritoneal covering.[1] The anal canal, which measures 3 to 5 cm in length, extends from the puborectalis sling to the anal verge.

Tumors located at the border between 2 subsites of the colon (eg, cecum and ascending colon) are registered as tumors of the subsite that is more involved. If 2 subsites are involved to the same extent, the tumor is classified as an "overlapping" lesion. The rectum is defined clinically as the distal large intestine commencing opposite the sacral promontory and ending at the upper border of the anal canal. When measuring below with a rigid sigmoidoscope, it extends 16 cm from the anal verge. A tumor is classified as rectal if its inferior margin lies less than 16 cm from the anal verge or if any part of the tumor is located at least partly within the supply of the superior rectal artery.[2] A tumor is classified as rectosigmoid when differentiation between rectum and sigmoid according to the above guidelines is not possible.[3]

**B. Histologic Types**

For consistency in reporting, the histologic classification proposed by the World Health Organization (WHO) is recommended and is shown below.[4] However, this protocol does not preclude the use of other systems of classification or histologic types.

**WHO Classification of Colorectal Carcinoma**

Adenocarcinoma
Medullary carcinoma[#]
Mucinous (colloid) adenocarcinoma (greater than 50% mucinous)[##]
Signet-ring cell carcinoma (greater than 50% signet-ring cells)[###]
Squamous cell carcinoma
Adenosquamous carcinoma
Small cell carcinoma[###]
Undifferentiated carcinoma[###]
Other (specify)^

[#] Medullary carcinoma is a histologic type that is strongly associated with a high degree of microsatellite instability (MSI-H) indicative of loss of normal DNA repair gene function.[5-7] Medullary carcinoma may occur either sporadically[6] or in association with the hereditary nonpolyposis colon cancer syndrome (HNPCC).[7] This tumor type is characterized by uniform polygonal tumor cells that exhibit solid growth in nested, organoid, or trabecular patterns and that only focally produce small amounts of mucin. In addition, medullary carcinomas are typically infiltrated by lymphocytes (tumor infiltrating lymphocytes) and have no immunohistochemical evidence of neuroendocrine differentiation.

[##] The prognostic significance of mucinous carcinoma is controversial.[5,8]

### By convention, signet-ring cell carcinomas, small cell carcinomas and undifferentiated (histologic type) carcinomas are high grade (see below). The only histologic types of colorectal carcinoma that have been shown to have adverse prognostic significance independent of stage are signet-ring cell carcinoma and small cell carcinoma.[8] Nevertheless, signet-ring cell carcinoma may occur in HNPCC in association with MSI-H, and in this setting, the prognostic significance may differ.[9]

^ The term "carcinoma, NOS" (not otherwise specified) is not part of the WHO classification.

**C. Histologic Grade**

A number of grading systems have been suggested in the literature, but a single widely accepted and uniformly employed standard for grading is lacking. Among the suggested grading schemes, the number of grades as well as the criteria for distinguishing among different grades vary markedly. In some systems, grades are defined on the basis of a single microscopic feature, such as the degree of gland formation, and in other systems, a large number of features are included in the evaluation. Irrespective of the complexity of the criteria, however, most systems stratify tumors into 3 or 4 grades as follows:

| | |
|---|---|
| Grade 1 | Well differentiated |
| Grade 2 | Moderately differentiated |
| Grade 3 | Poorly differentiated |
| Grade 4 | Undifferentiated |

The appearance of individual histologic features may vary widely enough to make implementation of even the simplest grading systems problematic and, ultimately, subjective. Thus, a significant degree of interobserver variability in the grading of colorectal cancer has been shown to exist.[8,10] Despite this variability, histologic grade has repeatedly been shown by multivariate analysis to be a stage-independent prognostic factor.[8,11,12] Specifically, it has been demonstrated that high tumor grade is an adverse prognostic factor. It is noteworthy that in the vast majority of studies documenting the prognostic power of tumor grade,[8] the number of grades has been collapsed to produce a 2-tiered stratification for data analysis as follows.

| | |
|---|---|
| Low-grade: | Well differentiated and moderately differentiated |
| High-grade: | Poorly differentiated and undifferentiated |

In general practice, a 2-tiered grading systems would also be expected to greatly reduce interobserver variability, since the widest variations in grading concern the stratification of low-grade tumors into well- or moderately-differentiated categories. Pathologic identification of poorly differentiated or undifferentiated tumors is more consistent, and interobserver variability in diagnosing high-grade carcinoma is relatively small. Therefore, in light of its proven prognostic value, relative simplicity, and reproducibility, a 2-tiered grading system for colorectal carcinoma (ie, low-grade and high-grade) is recommended.[5] The following criteria for grading based on gland formation alone are suggested.[5]

Low-grade = greater than or equal to 50% gland formation

High-grade = less than 50% gland formation

**D. Carcinoma in an Adenomatous Polyp**

Colorectal adenomas containing invasive adenocarcinoma that extends through the muscularis mucosae into the submucosa have been defined as "malignant polyps." These polyps constitute a form of early (ie, curable) colorectal carcinoma. The definition of malignant polyps excludes adenomas with intraepithelial carcinoma or intramucosal carcinoma (invasive carcinoma limited to the lamina propria or invading no deeper than the muscularis mucosae) because these polyps possess no biological potential for metastasis (see Tis in Note **G**).

The term malignant polyp encompasses both polypoid carcinomas in which the entire polyp head is replaced by carcinoma and adenomas with focal malignancy.

Malignant polyps removed by endoscopic polypectomy require evaluation of histologic parameters that have been determined to be significant prognostic factors related to the risk of adverse outcome (ie, lymph node metastasis or local recurrence from residual malignancy) following polypectomy.[8,13-29]

Pathologic features that have been shown to have independent prognostic significance and are crucial for evaluating risk and determining the possible need for further surgical treatment (eg, segmental colectomy) include:
• histologic grade of the carcinoma
• extent (level) of invasion of the carcinoma within the polyp
• status of the resection margin
• lymphatic/venous vessel involvement

Specifically, an increased risk of adverse outcome has been shown to be associated with:
• grade 3 (poorly differentiated) carcinoma
• tumor at or less than 1 mm from the resection margin
• presence of lymphatic/venous vessel involvement

**E. Tumor Configuration**

Configurations include exophytic (fungating), endophytic (ulcerative), and diffusely infiltrative (linitis plastica) or annular, but overlap among these types is common. Exophytic is divided into pedunculated and sessile. Overall, gross tumor configuration has no independent influence on prognosis.[5,8] The uncommon linitis plastica type represents a possible exception. It has an unfavorable prognosis, but its association with adverse outcome is probably related to the underlying histologic type of tumor (signet-ring cell carcinoma) rather than the macroscopic configuration itself.

**F. Venous Invasion**

Extramural venous invasion has been demonstrated by multivariate analysis to be an independent adverse prognostic factor.[12,30-34] Invasion of extramural veins, in particular, has been shown to be an independent indicator of unfavorable outcome and increased risk of occurrence of hepatic metastasis.[33,34] It has been shown that the submission of 5 or more blocks of tumor significantly enhances the likelihood of finding extramural venous invasion when it exists and reduces false negativity due to sampling error.[35]

The significance of intramural venous invasion is less clear, because data specific to this issue are lacking. Nevertheless, it is recommended that the presence or absence of venous invasion and its anatomic location should be reported in all cases.[5]

The V classification as shown below may be used to record venous invasion.

**G. TNM and Stage Groupings**

Surgical resection remains the most effective therapy for colorectal carcinoma, and the best estimation of prognosis is related to the pathologic findings on the resection specimen. The anatomic extent of disease is by far the most important prognostic factor in colorectal cancer.[11]

The protocol recommends the TNM staging system of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC)[1,36] but does not preclude the use of other staging systems.

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.

**Primary Tumor (T)**

TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Tis Carcinoma in situ - intraepithelial or invasion of lamina propria[#]
T1 Tumor invades submucosa
T2 Tumor invades muscularis propria
T3 Tumor invades through the muscularis propria into the subserosa or into the nonperitonealized pericolic or perirectal tissues[##]
*Optional subclassification[3] of T3*
T3a Minimal invasion: less than 1 mm beyond the border of the muscularis propria
T3b Slight invasion: 1 to 5 mm beyond the border of the muscularis propria
T3c Moderate invasion: greater than 5 mm to 15 mm beyond the border of the muscularis propria

T3d Extensive invasion: greater than 15 mm beyond the border of the muscularis propria

T4 Tumor directly invades other organs or structures[###] (T4a) and/or perforates visceral peritoneum^ (T4b)

[#] For colorectal carcinomas, "carcinoma in situ" (Tis) as a staging term includes cancer cells confined within the glandular basement membrane (intraepithelial carcinoma) or invasive into the mucosal lamina propria, up to but not through the muscularis mucosae (intramucosal carcinoma). This may be confusing because, in all other organ systems, the term "carcinoma in situ" is used to refer exclusively to malignancy that does not invade the underlying stroma. Therefore, for colorectal cancer, the terms "intraepithelial carcinoma" and "intramucosal carcinoma" are recommended as descriptive terms to subclassify pTis and to clarify the status of the tumor.[5,37] Tumor extension through the muscularis mucosae into the submucosa is classified as T1. Some pathologists classify intraepithelial carcinoma as *severe or high-grade dysplasia,* especially in cases of inflammatory bowel disease.

[##] The extent of perimuscular invasion has been reported to influence prognosis, regardless of whether regional lymph node metastasis is present. Thus, an optional expansion pT3 has been proposed.[3] Extramural extension greater than 5 mm has been shown to be the critical subdivision associated with adverse outcome in most studies. Thus, a simpler subdivision, based on extension of less than 5mm versus greater than 5mm (ie, pT3a,b vs. pT3c,d), may be justified.[3] Extension of the tumor within lymphatics or veins does not count as local spread of tumor as defined by the T classification.[3]

[###] Direct invasion of other organs or structures includes invasion of other segments of colorectum by way of the serosa or mesocolon, for example, invasion of the sigmoid colon by carcinoma of the cecum. In such a case, both an adjacent organ and the visceral peritoneum are penetrated by tumor. Intramural extension of tumor from 1 subsite (segment) of the large intestine into an adjacent subsite or into the ileum (eg, for a cecal carcinoma) or anal canal (eg, for a rectal carcinoma) does not affect the pT classification.[3]

Tumor that is adherent to other organs or structures macroscopically is classified as T4. However, if no tumor is found within the adhesion microscopically, the tumor should be assigned T3.[1]

Tumor in veins or lymphatics does not affect the pT classification. The L and V classifications can be used to record such spread (see below).
For rectal tumors, invasion of the external sphincter is classified as T3, whereas invasion of the levator ani muscle(s) is classified as T4.

^ Subdivision of T4 into T4a and b is justified because a number of large studies that have evaluated serosal penetration as an independent prognostic variable have demonstrated by multivariate analysis that it has a strong negative impact on prognosis.[3,30,38-40] Specifically, it has been shown that the frequency of distant metastasis is higher in cases with perforation of the visceral peritoneum compared to cases with direct invasion of adjacent organs or structures without perforation of the visceral peritoneum (occurring in about 50% and 30% of cases, respectively).[3]

Furthermore, the median survival time following surgical resection for cure has been shown to be shorter for patients with pT4b tumors compared to those with pT4a tumors (with or without distant metastasis) as follows[3]:

| | **5-Year Survival Rate** | **Median Survival Time (Months)** |
|---|---|---|
| pT4a, M0 | 49% | 58.2 |
| pT4b, M0 | 43% | 46.2 |
| pT4a, M1 | 12% | 22.7 |
| pT4b, M1 | 0% | 15.5 |

A study by Shepherd et al[39] has suggested that the prognostic power of local peritoneal involvement in curative resections may supersede that of either local extent of tumor (T category) or regional lymph node status (N category). However, serosal penetration is often difficult to assess histopathologically and may be underdiagnosed. Documentation of peritoneal involvement by tumor demands meticulous pathologic analysis and may require extensive sampling and/or serial sectioning as it can be missed on routine histopathologic examination. It has been shown that cytologic examination of serosal scrapings reveals malignant cells in as many as 26% of tumor specimens categorized as pT3 by histologic examination alone.[39,41] In addition, the histopathologic findings associated with peritoneal penetration are heterogeneous, and standard guidelines for their diagnostic interpretation are lacking. Therefore, interobserver variability in the diagnosis of peritoneal penetration may be substantial, and since most pathologists tend to err on the side of conservative interpretation, under-diagnosis is likely for this reason as well.

Shepherd et al[39] analyzed the spectrum of microscopic features that may be seen with local peritoneal involvement by tumor, and defined 3 types of local peritoneal involvement as follows: (1) a mesothelial inflammatory and/or hyperplastic reaction with tumor close to, but not at, the serosal surface; (2) tumor present at the serosal surface with inflammatory reaction, mesothelial hyperplasia, and/or erosion/ulceration; and (3) free tumor cells on the serosal surface (in the peritoneum) with underlying ulceration of the visceral peritoneum.

All 3 types of local peritoneal involvement were associated with decreased survival, especially types 2 and 3. In contrast, tumor well clear of the serosa had no independent adverse effect on prognosis. Therefore, it is recommended that in that diagnosis of T4b encompass at least types 2 and 3 of serosal involvement detailed above.[5]

Free perforation of a colorectal carcinoma into the peritoneal cavity is always classified as T4.

**Regional Lymph Nodes (N)**[#]

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in 1 to 3 lymph nodes
N2 Metastasis in 4 or more lymph nodes[##,###]

[#] The regional lymph nodes for the anatomical subsites of the large intestine are as follows.

Cecum: anterior cecal, posterior cecal, ileocolic, right colic
Ascending colon: ileocolic, right colic, middle colic
Hepatic flexure: middle colic, right colic
Transverse colon: middle colic
Splenic flexure: middle colic, left colic, inferior mesenteric
Descending colon: left colic, inferior mesenteric, sigmoid
Sigmoid colon: inferior mesenteric, superior rectal sigmoidal, sigmoid mesenteric
Rectosigmoid: perirectal, left colic, sigmoid mesenteric, sigmoidal, inferior mesenteric, superior rectal, middle rectal
Rectum: perirectal, sigmoid mesenteric, inferior mesenteric, lateral sacral, presacral, internal iliac, sacral promontory, superior rectal, middle rectal, inferior rectal

[##] Nodes along the sigmoid arteries are considered pericolic nodes, and their involvement is classified as N1 or N2 according to the number involved.

[###] Perirectal lymph nodes include the mesorectal (paraproctal), lateral sacral, presacral, sacral promontory (Gerota), middle rectal (hemorrhoidal), and inferior rectal (hemorrhoidal) nodes. Metastasis in the external iliac or common iliac nodes is classified as distant metastasis.[3]

*Important Notes on Lymph Nodes*
Submission of lymph nodes for microscopic examination: All grossly negative or equivocal lymph nodes are to be submitted entirely.[5] Grossly positive lymph nodes may be partially submitted for microscopic confirmation of metastasis.

It has been shown that 12 to 15 negative lymph nodes predict for regional node negativity. Therefore, if fewer than 12 nodes are found, additional techniques (ie, visual enhancement techniques) should be considered.[5] If fewer than 12 nodes are found after the use of visual enhancement techniques, this should be communicated in the pathology report. 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.[5]

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 (see below).

Lymph nodes replaced by tumor: A tumor nodule in the pericolonic/perirectal fat without histologic evidence of residual lymph node tissue is classified in the N category as regional nodal metastasis (lymph node replacement by tumor) if the nodule has the form and smooth contour of a lymph node. If the nodule has an irregular contour, it is recommended that the nodule be classified in the pT category as discontinuous extramural extension.[1,3] Extramural smooth contour tumor nodules are counted individually as replaced lymph nodes when assigning the pN category.

Micrometastasis and Isolated Tumor Cells: Routine assessment of regional lymph node metastasis is limited to the use of conventional pathologic techniques (gross assessment and histologic examination). A micrometastasis is defined as tumor measuring greater than 0.2 mm but less than or equal to 2.0 mm in greatest dimension. Micrometastases are classified as N1(mic) or M1(mic) in lymph nodes or at distant sites, respectively. Isolated tumor cells (ITCs) are defined as single tumor cells or small clusters of tumor cells measuring 0.2 mm or less, usually found by special techniques such as immunohistochemical staining, and are classified as N0 or M0.[3] Since the biologic significance of ITCs (either a single focus in a single node, multiple foci within a single node, or micrometastatic involvement of multiple nodes) is as yet is unproved, N0 is considered justified. The number of lymph nodes involved by micrometastases or ITCs should be clearly stated.[5]

Currently, the data are insufficient to recommend special measures to detect micrometstasis or ITCs. Thus, neither multiple tissue levels of paraffin blocks nor the use of special/ancillary techniques such as immunohistochemistry for epithelial and/or tumor-associated antigens (eg, cytokeratin, carcinoembryonic antigen) or polymerase chain reaction (PCR) techniques to identify tumor RNA/DNA are recommended for routine examination of regional lymph nodes.[5] Guidelines for annotation for ITCs found on pathologic examination are shown below.

**Regional Lymph Nodes (pN0): Isolated Tumor Cells**
Isolated tumor cells (ITCs) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITCs found by either histologic examination, immunohistochemistry, or nonmorphologic techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be classified as N0 or M0, respectively. Specific denotation of the assigned N category is suggested as follows for cases in which ITCs are the only evidence of possible metastatic disease.[3,42]

| | |
|---|---|
| pN0 | No regional lymph node metastasis histologically, no examination for isolated tumor cells (ITCs) |
| pN0(i-) | No regional lymph node metastasis histologically, negative morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs |
| pN0(i+) | No regional lymph node metastasis histologically, positive morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs |
| pN0(mol-) | No regional lymph node metastasis histologically, negative nonmorphologic (molecular) findings for ITCs |
| pN0(mol+) | No regional lymph node metastasis histologically, positive nonmorphologic (molecular) findings for ITCs |

**Sentinel Lymph Nodes**
The sentinel lymph node is the first node to receive drainage from a primary tumor. There may be more than 1 sentinel node for some tumors. If a sentinel node contains metastatic tumor, it indicates that other more distant nodes may also contain metastatic disease. If sentinel nodes are negative, other regional nodes are less likely to contain

metastasis. Sentinel lymph nodes that have been examined for ITCs are denoted as follows.

| | |
|---|---|
| pN0(i-)(sn) | No sentinel lymph node metastasis histologically, negative morphologic findings for ITCs |
| pN0(i+)(sn) | No sentinel lymph node metastasis histologically, positive morphologic findings for ITCs |
| pN0(mol-)(sn) | No sentinel lymph node metastasis histologically, negative nonmorphologic findings for ITCs |
| pN0(mol+)(sn) | No sentinel lymph node metastasis histologically, positive nonmorphologic findings for ITCs |

**Distant Metastasis (M)**

| | |
|---|---|
| MX | Distant metastasis cannot be assessed |
| M0 | No distant metastasis |
| M1 | Distant metastasis[#] |

[#] Seeding of abdominal organs is considered M1.

**Stage Groupings**

| TNM Stage Groupings | | | | Modified Astler-Coller Stage | Dukes |
|---|---|---|---|---|---|
| Stage 0 | Tis | N0 | M0 | N/A | N/A |
| Stage I | T1 | N0 | M0 | Stage A | A |
| | T2 | N0 | M0 | Stage B1 | A |
| Stage IIA | T3 | N0 | M0 | Stage B2 | B |
| Stage IIB | T4 | N0 | M0 | Stage B3 | B |
| Stage IIIA | T1,T2 | N1 | M0 | Stage C1 | C |
| Stage IIIB | T3,T4 | N1 | M0 | Stage C2,C3 | C |
| Stage IIIC | Any T | N2 | M0 | Stage C1,C2,C3 | C |
| Stage IV | Any T | Any N | M1 | Stage D | N/A |

**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.

**Additional Descriptors**

Residual Tumor (R)
Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

RX Presence of residual tumor cannot be assessed
R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

**Vessel Invasion**
By 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. In all other cases, lymphatic and venous invasion by tumor are coded separately as follows.

Lymphatic Vessel Invasion (L)
LX Lymphatic vessel invasion cannot be assessed
L0 No lymphatic vessel invasion
L1 Lymphatic vessel invasion

Venous Invasion (V)
VX Venous invasion cannot be assessed
V0 No venous invasion
V1 Microscopic venous invasion
V2 Macroscopic venous invasion

**H. Lymphatic (Thin-Walled) Vessel and Perineural Invasion**
In several studies, both lymphatic invasion and perineural invasion have been shown by multivariate analysis to be independent indicators of poor prognosis.[12,29-31,43] The prognostic significance, if any, of the anatomic location of these structures is not defined. Furthermore, it is not always possible to distinguish lymphatic vessels from postcapillary venules, since both are small, thin-walled structures. Thus, the presence or absence of tumor invasion of small, thin-walled vessels should be reported in all cases and its anatomic location within the colonic wall noted.[5]

**I. Lymphoctyic Response to Tumor**
A conspicuous lymphoid reaction at the leading edge of invasive tumor or the presence of lymphoid aggregates in the surrounding tissues (muscularis external and pericolonic

or perirectal fat) have both been shown to be independent favorable prognostic factors.[10,34,44-46] Intratumoral lymphocytic infiltrates are closely associated with microsatellite instability and medullary architecture (see above) and should be distinguished from peritumoral infiltrates. Only moderate- and high-density intratumoral lymphocytes (approximately 4 or more per high-power field) should be considered significant.[5] Reporting of host lymphoid response is optional. If reported, distinction should be made between peritumoral and intratumoral lymphoid infiltrates.

### J. Tumor Periphery: Growth Pattern

The growth pattern at the advancing edge of the tumor has been shown to have prognostic significance independent of stage and may predict liver metastasis.[47-53] Specifically, an infiltrating pattern of growth at the tumor border as opposed to a pushing border is an adverse prognostic factor.

Infiltrating borders have been defined as follows.[48]

**Gross Examination of Glass Slide**

Inability to define limits of invasive border of tumor
and/or
Inability to resolve host tissue from malignant tissue

**Microscopic Examination of Slide**

"Streaming dissection" of muscularis propria (dissection of tumor through the full thickness of the muscularis propria without stromal response)
and/or
Dissection of mesenteric adipose tissue by small glands or irregular clusters or cords of cells
and/or
Perineural invasion

Irregular growth at the tumor periphery has also been referred to as "focal dedifferentiation" and "tumor budding" and defined as microscopic clusters of undifferentiated cancer cells just ahead of the invasive front of the tumor.

### K. Margins

It may be helpful to mark the margin(s) closest to the tumor with ink. Margins marked by ink should be designated in the macroscopic description. Margins include the proximal, distal, and radial margins. The radial margin represents the adventitial soft tissue margin closest to the deepest penetration of tumor. For all segments of the large intestine that are either incompletely encased (ascending colon, descending colon, sigmoid colon, upper rectum) or not encased (lower rectum) by peritoneum, the circumferential (radial) margin is created by blunt or sharp dissection of the retroperitoneal or subperitoneal aspect, respectively, at operation.

The circumferential margin has been demonstrated to be of importance in relation to risk of local recurrence after surgical resection of the rectal carcinomas.[54-56] Multivariate analysis has suggested that tumor involvement of the circumferential margin is the most critical factor in predicting local recurrence in rectal cancer.[54-56] For rectal cancer, a positive circumferential margin increases the risk of local recurrence by 3.5-fold and

doubles the risk of death from disease.[57] For this reason, routine assessment of the circumferential margin is suggested in all rectal cancers and all colon cancers in colonic segments with non-peritonealized surfaces, and the measurement of the distance from the tumor to the radial margin, representing the "surgical clearance" around the tumor, is suggested (see also Note **L**).[58] The circumferential margin is scored as positive if tumor is located 1 mm or less from the inked nonperitonealized surface of the specimen, because local recurrence rates are similar with clearances of 0 to 1 mm. This includes tumor within a lymph node as well as direct tumor extension, but if circumferential margin positivity is based solely on intranodal tumor, this should be so stated. Conversely, the circumferential margin is recorded as negative if the tumor is more than 1 mm from the inked nonperitonealized surface of the specimen.

For segments of the colon that are completely encased by a peritonealized (serosal) surface (eg, transverse colon), the only circumferential/radial margin is the mesenteric resection margin, and it is relevant when the point of deepest penetration of the tumor is on the mesenteric aspect of the colon and extends to this margin with or without penetrating the serosal surface.

Because of its association with local recurrence, involvement of the circumferential margin has implications for adjuvant therapy. Whether the primary tumor is T3 (without serosal penetration) or T4b (with serosal penetration), resection is considered complete only if all surgical margins are negative, including the radial margin. That is, whether or not the tumor penetrates a serosal surface, resection is considered complete if the resection margins (proximal, distal and radial) do not contain tumor. If a radial margin is involved by tumor, adjuvant therapy (eg, local radiation) may be appropriate.

Sections to evaluate the proximal and distal resection margins can be obtained in 2 orientations: (1) *en face* sections parallel to the margin or (2) longitudinal sections perpendicular to the margin. Depending on the closeness of the tumor to the margin, select the orientation(s) that best demonstrate(s) the status of the margin. The distance from the tumor edge to the closest resection margin(s) should be measured. Anastomotic recurrences are rare when the distance to the closest transverse margin is 5 cm or greater. For low rectal cancers resected from a low anterior approach, distal resection margins of 2 cm are considered adequate, and for T1 and T2 tumors, 1 cm may be sufficient distal clearance. In cases of carcinoma arising in a background of inflammatory bowel disease, proximal and distal resection margins should be evaluated for dysplasia and active inflammation.

### L. Mesorectal Envelope

The quality of the surgical technique is a key factor in the success of surgical treatment for rectal cancer, both in the prevention of local recurrence and in long-term survival. Numerous studies have demonstrated that total mesorectal excision (TME) improves local recurrence rates and the corresponding survival by as much as 20%. This surgical technique entails precise sharp dissection within the areolar plane outside (lateral to) the visceral mesorectal fascia in order to remove the rectum. This plane encases the rectum, its mesentery, and all regional nodes. High-quality TME surgery reduces local recurrence from 20% to 30%, to 8% to 10% or less, and increases 5-year survival from 48% to 68%.[59-63] Adjuvant therapy in the presence of a high-quality TME may further reduce local recurrence (from 8% to 2.6%).[63]

Pathologic evaluation of the resection specimen has been shown to be a sensitive means of assessing the quality of rectal surgery. It is superior to indirect measures of surgical quality assessment such as perioperative mortality, rates of complication, number of local recurrences and 5-year survival. It has been shown that macroscopic pathologic assessment of the completeness of the mesorectum of the specimen, scored as complete, partially complete, or incomplete, accurately predicts both local recurrence and distant metastasis.[64] Microscopic parameters such as the status of the circumferential resection margin, the distance between the tumor and nearest circumferential margin (ie, "surgical clearance"), and the distance between the tumor and the closest distal margin are all important predictors of local recurrence and may be affected by surgical technique. There is strong evidence that the status of the circumferential resection margin is a powerful predictor of local recurrence but is inconsistently evaluated and under-reported.[57,65]

The nonperitonealized surface of the fresh specimen is examined circumferentially and the completeness of the mesorectum is scored as described below.[64] The entire specimen is scored according to the worst area.

**Incomplete**

Little bulk to the mesorectum
Defects in the mesorectum down to the muscularis propria
After transverse sectioning, the circumferential margin appears very irregular

**Nearly Complete**

Moderate bulk to the mesorectum
Irregularity of the mesorectal surface with defects greater than 5 mm, but none extending to the muscularis propria
No areas of visibility of the muscularis propria except at the insertion site of the levator ani muscles

**Complete**

Intact bulky mesorectum with a smooth surface
Only minor irregularities of the mesorectal surface
No surface defects greater than 5 mm in depth
No coning towards the distal margin of the specimen
After transverse sectioning the circumferential margin appears smooth

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