Protocol for the Examination of Specimens from Patients with Carcinoma of the Anus

Protocol applies to all invasive carcinomas of the anal canal.

Based on AJCC/UICC TNM, 7th edition
Protocol web posting date: October 2009

Procedures
- Excisional Biopsy
- Local Excision (Transanal Disk Incision)
- Abdominoperineal Resection

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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the “Surgical Pathology Cancer Case Summary (Checklist)” portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: October 2009

ANUS: Excisional Biopsy or Local Excision (Transanal Disk Excision)

Select a single response unless otherwise indicated.

Specimen (select all that apply)
___ Anal canal
___ Anorectal junction
___ Rectum
___ Perianal skin
___ Other (specify): _____
___ Not specified

Procedure
___ Excisional biopsy (polypectomy)
___ Local excision (transanal disk excision)
___ Other (specify): _____
___ Not specified

Specimen Integrity (Note A)
___ Intact
___ Fragmented
*Number of pieces in fragmented specimens: ___
___ Other (specify): _____

Tumor Site (Note B)
_____ Anal canal
_____ Anorectal junction
_____ Anal margin
_____ Anus, not otherwise specified
_____ Unknown
_____ Other (specify): _____

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

Histologic Type (Note C)
___ Squamous cell carcinoma
___ Adenocarcinoma
___ Mucinous adenocarcinoma
___ Small cell carcinoma
___ Undifferentiated carcinoma
___ Paget disease
___ Other (specify): _____

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

Histologic Grade (Note D)
___ Not applicable
___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ G4: Undifferentiated
___ Other (specify): _____

Microscopic Tumor Extension
___ Cannot be assessed
___ No evidence of primary tumor
___ Carcinoma in situ
___ Tumor invades lamina propria
___ Tumor invades muscularis mucosae
___ Tumor invades submucosa
___ Tumor invades sphincter muscle
___ Tumor invades perianal skin

Margins (select all that apply)
___ Cannot be assessed
___ Margins uninvolved by invasive carcinoma
    Distance of invasive carcinoma from closest margin: ___ mm
    Specify margin (if possible): _____
    ___ Carcinoma in situ absent at mucosal margin
    ___ Carcinoma in situ present at mucosal margin
___ Margin(s) involved by invasive carcinoma
    Specify margin (if possible): _____
___ Not applicable (specify reason): _____

Treatment Effect (applicable to carcinomas treated with neoadjuvant therapy) (Note E)
___ No prior treatment
___ Present
    *____ Complete response (no viable tumor cells, grade 0)
    *____ Moderate response (single cells or small groups of tumor cells, grade 1)
    *____ Minimal response (residual tumor outgrown by fibrosis, grade 2)
___ No definite response identified (grade 3, poor or no response; extensive residual tumor)
___ Not known

***Lymph-Vascular Invasion**
*___ Not identified
*___ Present
*___ Indeterminate

***Perineural Invasion**
*___ Not identified
*___ Present
*___ Indeterminate

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

Pathologic Staging (pTNM) (Note F)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple primary tumors)
___ r (recurrent)
___ y (post-treatment)

Primary Tumor (pT)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ
___ pT1: Tumor 2 cm or less in greatest dimension
___ pT2: Tumor more than 2 cm but not more than 5 cm in greatest dimension
___ pT3: Tumor more than 5 cm in greatest dimension
___ pT4: Tumor of any size with invasion of adjacent organ(s); eg, vagina, urethra, bladder (involvement of sphincter muscles alone is not classified as T4).

***Additional Pathologic Findings (select all that apply) (Note G)**
*___ None identified
*___ Crohn disease
*___ Condyloma accuminatum
*___ Dysplasia
*___ Associated rectal carcinoma (Paget disease)
*___ Other (specify): _____

***Ancillary Studies (Note H)**
*****Specify: _____
*____ Not performed

***Clinical History (select all that apply) (Note I)**
*___ Solid organ transplantation
*___ HIV/AIDS
*___ Human papilloma virus infection
*___ Crohn disease
*___ Neoadjuvant therapy (specify type, if known: _____)
*___ Other (specify): _____
*___ Not known

***Comment(s)**

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

Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: October 2009

ANUS: Abdominoperineal Resection

Select a single response unless otherwise indicated.

Specimen (select all that apply)
___ Anal canal
___ Anorectal junction
___ Rectum
___ Perianal skin
___ Other (specify): _____
___ Not specified

Procedure
___ Abdominoperineal resection
___ Other (specify): _____
___ Not specified

Tumor Site (select all that apply) (Note B)
_____ Anal canal
_____ Anorectal junction
_____ Anal margin
_____ Anus, not otherwise specified
_____ Unknown
_____ Other (specify): _____

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

Histologic Type (Note C)
___ Squamous cell carcinoma
___ Adenocarcinoma
___ Mucinous adenocarcinoma
___ Small cell carcinoma
___ Undifferentiated carcinoma
___ Paget disease
___ Other (specify): _____
___ Carcinoma, type cannot be determined

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

Histologic Grade (Note D)
___ Not applicable
___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ G4: Undifferentiated
___ Other (specify): _____

Microscopic Tumor Extension
___ Cannot be assessed
___ No evidence of primary tumor
___ Carcinoma in situ
___ Tumor invades lamina propria
___ Tumor invades muscularis mucosae
___ Tumor invades submucosa
___ Tumor invades into but not through sphincter muscle
___ Tumor invades into but not through muscularis propria of rectum
___ Tumor invades through sphincter muscle into perianal or perirectal soft tissue without involvement of adjacent structures
___ Tumor directly invades adjacent structures (specify): _____
___ Tumor invades perianal skin

Margins (select all that apply)

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

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

Circumferential (Radial) Margin
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma

If all margins uninvolved by invasive carcinoma:
Distance of invasive carcinoma from closest margin: ___ mm
    Specify margin: _____

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

Treatment Effect (applicable to carcinomas treated with neoadjuvant therapy) (select all that apply) (Note E)

___ No prior treatment
___ Present
    *____ Complete response (no viable tumor cells, grade 0)
    *____ Moderate response (single cells or small groups of tumor cells, grade 1)
    *____ Minimal response (residual tumor outgrown by fibrosis, grade 2)
___ No definite response identified (grade 3, poor or no response; extensive residual tumor)
___ Not known

***Lymph-Vascular Invasion**

*___ Not identified
*___ Present
*___ Indeterminate

***Perineural Invasion**

*___ Not identified
*___ Present
*___ Indeterminate

Pathologic Staging (pTNM) (Note F)

TNM Descriptors (required only if applicable) (select all that apply)

___ m (multiple primary tumors)
___ r (recurrent)
___ y (post-treatment)

Primary Tumor (pT)

___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ
___ pT1: Tumor 2 cm or less in greatest dimension
___ pT2: Tumor more than 2 cm but not more than 5 cm in greatest dimension
___ pT3: Tumor more than 5 cm in greatest dimension
___ pT4: Tumor of any size with invasion of adjacent organ(s); eg, vagina, urethra, bladder (involvement of sphincter muscles alone is not classified as T4).

Regional Lymph Nodes (pN)

___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in perirectal lymph nodes
___ pN2: Metastasis in unilateral internal iliac and/or inguinal lymph node(s)
___ pN3: Metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or inguinal lymph nodes

Specify: Number examined: ___
Number involved: ___

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

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

***Additional Pathologic Findings (select all that apply) (Note G)**
*___ None identified
*___ Crohn disease
*___ Condyloma accuminatum
*___ Dysplasia
*___ Associated rectal carcinoma (Paget disease)
*___ Other (specify): _____

***Ancillary Studies (Note H)**
*Specify: _____

***Clinical History (select all that apply) (Note I)**
*____ Solid organ transplantation
*____ HIV/AIDS
*____ Human papilloma virus infection
*____ Crohn disease
*____ Neoadjuvant therapy (specify type if known)_____
*____ Other (specify): _____
*____ Not known

***Comment(s)**

Explanatory Notes

A. Specimen Integrity and Handling

For specimens from local excision procedures, all relevant margins, including the deep resection margin, should be inked. Evaluation of margins and invasion is facilitated if the specimen is pinned before fixation in formalin.

B. Location

Documentation of tumor location within the anal canal is important for purposes of stage assignment. Because of possible differences in staging and regional lymph nodes at risk of metastasis among cancers of the anal canal, the rectum, and the perianal skin, it is essential to assure that the anatomic site of the tumor is the anal canal. For the pathologist, however, the documentation of location may be problematic. Currently, most anal canal carcinomas are managed successfully without surgery, using combination chemotherapy and radiation therapy;[1] and resection specimens of anal tumors are seen only infrequently (primarily for small anal margin lesions or after failure of other treatment modalities). Although histological diagnosis is almost always performed on small biopsies, determination of the primary tumor location from biopsy specimens may be difficult or impossible. Therefore, documentation of anatomic site often requires clinical correlation.

A major problem complicating determination of anatomic site clinically or pathologically is the controversy over the anatomic definition of the anal canal itself. The surgical definition of the anal canal is the one most widely accepted for practical reasons and is the preferred definition of the American Joint Committee on Cancer (AJCC).[2] However, it is based on clinically identifiable landmarks that are difficult or impossible for the pathologist to locate. By this definition, the anal canal begins at the point where the rectum enters the puborectalis sling at the apex of the anal sphincter complex, a landmark that is palpable in vivo on digital exam as the anorectal ring. The termination of the anal canal is defined as the squamous mucocutaneous junction (ie, the junction of the distal squamous mucosa of the anal canal with the perianal hair-bearing skin).[2] Thus defined, the anal canal (Figure 1) contains three epithelial zones: a proximal narrow zone (approximately 1 to 2 cm) of rectal-type glandular mucosa, an anal transition zone of variable length interposed between colorectal mucosa and squamous epithelium, and a squamous epithelial zone lacking skin appendages. The squamous zone gradually merges into the perianal skin, which contains hair follicles, sweat glands, and sebaceous glands. The anal transition zone may contain a variety of epithelial types, including multilayered transitional mucosa resembling squamous metaplasia or urothelium, which is often present at the dentate line. Anal glands may be found subjacent to the mucosa extending across the internal sphincter in the region of the dentate line.

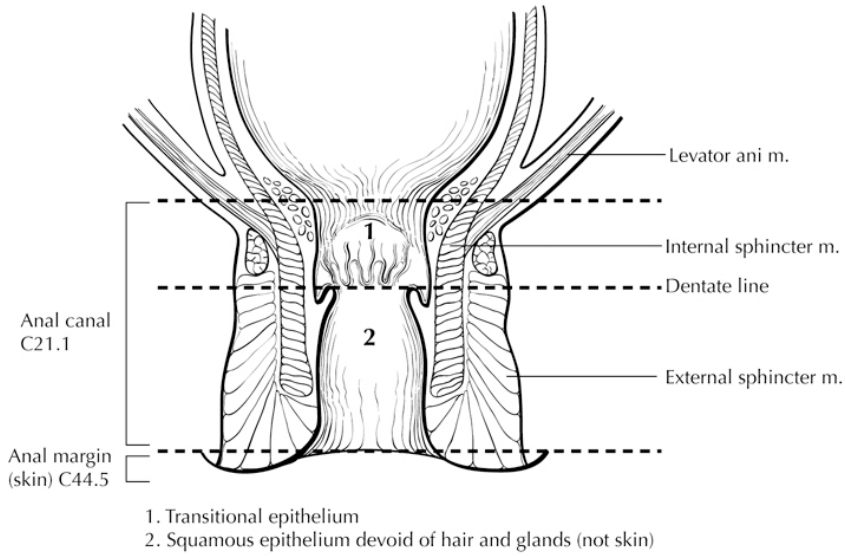

Figure 1. Anatomy of the anal canal. From: Greene FL, Compton, CC, Fritz AG, et al, eds. *AJCC Cancer Staging Atlas.* New York: Springer; 2006. Copyright © American Joint Committee on Cancer. Used with permission.

Tumors involving the anorectal junction should be classified as rectal cancers if the epicenter is more than 2 cm proximal to the dentate line and as anal cancers if the epicenter is 2 cm or less from the dentate line.[2]

Cancers that arise in the perianal skin are termed "perianal cancers" and are biologically similar to other skin tumors. They are staged according to the classification for cancers of the skin[2] (see CAP protocols for skin).

C. Histologic Type

For consistency in reporting, the histologic classification proposed by the World Health Organization (WHO) is recommended.[3] However, this protocol does not preclude the use of other systems of classification or histologic types.

The great majority of carcinomas of the anus are squamous cell carcinomas.[4] The previous edition of the WHO classification included 3 subtypes of squamous cell carcinoma (SCC): large cell keratinizing, large cell nonkeratinizing, and basaloid. However, because most SCCs of the anal canal show more than one subtype, the diagnostic reproducibility of these subtypes has been low. Furthermore, no significant prognostic differences between subtypes have consistently been established, although the basaloid subtype of squamous cell carcinoma may be associated with a higher risk of distant metastasis.[5] Therefore, the WHO now recommends that the generic diagnostic term "squamous cell carcinoma" be used for all squamous malignancies of the anal canal. However, additional descriptive comment regarding specific histologic features, such as predominant cell size, basaloid features, degree of keratinization, or adjacent intraepithelial neoplasia, is encouraged. Prominent basaloid features and small tumor cell size are related to infection with "high-risk" human papilloma virus.[3] SCC with a predominantly basaloid differentiation pattern was formerly known as cloacogenic carcinoma, but this term is now considered obsolete.

Two variants of SCC of the anal canal deserve note because they differ in prognosis from typical squamous tumors. One is verrucous carcinoma (also known as giant condyloma or Buschke-Lowenstein tumor), which resembles a condyloma macroscopically but is larger and fails to respond to conservative therapy. These lesions are regarded as biologic intermediates between condylomas and SCCs, with a better prognosis than SCC. However, nearly half of these lesions undergo malignant transformation. Another important variant is SCC with mucinous microcysts (well-formed cystic spaces containing Alcian blue- or PAS-stainable mucin). This entity has an unfavorable prognosis as compared with that of SCC.[3]

Finally, two rare types of anal canal carcinoma, anaplastic carcinoma and small cell carcinoma (high-grade neuroendocrine carcinoma), are tumors with aggressive biologic behavior and an unfavorable prognosis when compared with typical SCC. Tumors of the more distal anal canal and especially anal margin (mucocutaneous junction) are generally purely squamous in type and show fewer basaloid or glandular features.

WHO Classification of Carcinoma of the Anal Canal [3]

Intraepithelial neoplasia
- Squamous or transitional epithelium
- Glandular
- Paget disease

Carcinoma
- Squamous cell carcinoma
- Adenocarcinoma
- Mucinous adenocarcinoma
- Small cell carcinoma[#]
- Undifferentiated carcinoma[#]
- Others

[#] By convention, these histologic types are assigned grade 4.

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

D. Histologic Grade

Histologic grades for anal canal squamous carcinoma are as follows:

Grade X Grade cannot be assessed
Grade 1 Well differentiated
Grade 2 Moderately differentiated
Grade 3 Poorly differentiated

If there are variations in the differentiation within the tumor, the highest (least favorable) grade is recorded as the overall grade.

Histologic grades for adenocarcinoma of the anal canal based on the proportion of gland formation by the tumor are suggested as follows:

Grade X Grade cannot be assessed
Grade 1 Well differentiated (greater than 95% of tumor composed of glands)

Grade 2 Moderately differentiated (50% to 95% of tumor composed of glands)
Grade 3 Poorly differentiated (less than 50% of tumor composed of glands)

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

E. Treatment Effect

Response of tumor to previous chemotherapy or radiation therapy should be reported. Although grading systems for tumor response have not been established, three-category systems generally provide good interobserver reproducibility.[6] The following system is suggested:

Tumor Regression Grade

Description	Tumor Regression Grade
No viable cancer cells	0 (Complete response)
Single cells or small groups of cancer cells	1 (Moderate response)
Residual cancer outgrown by fibrosis	2 (Minimal response)
Minimal or no tumor kill; extensive residual cancer	3 (Poor response)

F. TNM and Anatomic Stage/Prognostic Groupings

The TNM staging system for anal carcinoma of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended by the protocol and shown below.[2] The primary tumor is staged according to its size and local extension, as determined by clinical or pathologic examination. For most histologic types of anal canal cancer, the diameter of the tumor correlates with the depth of penetration. The staging system applies to all carcinomas arising in the anal canal, including carcinomas that arise within anorectal fistulas and anal glands, but excluding melanomas, low-grade neuroendocrine tumors (carcinoid tumors), and sarcomas.

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 infeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

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

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

The “y” prefix indicates those cases in which classification is performed during or after initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor before multimodality therapy (ie, before initiation of neoadjuvant therapy).

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

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

T Category Considerations
T categories for anal canal cancer are illustrated in Figures 2 through 5.

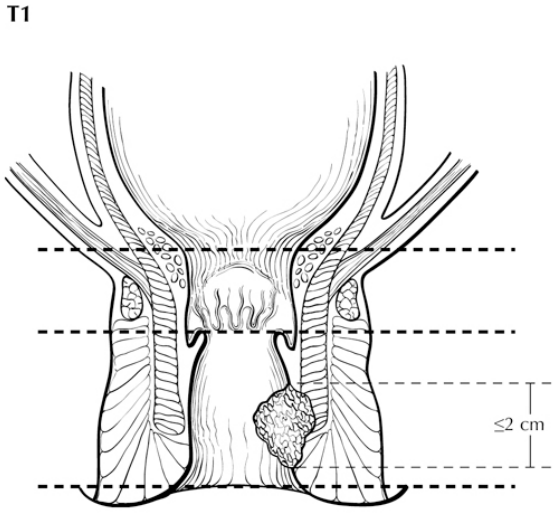

Figure 2. T1 is defined as tumor 2 cm or less in greatest dimension. From: Greene FL, Compton, CC, Fritz AG, et al, eds. *AJCC Cancer Staging Atlas.* New York: Springer; 2006. Copyright © American Joint Committee on Cancer. Used with permission.

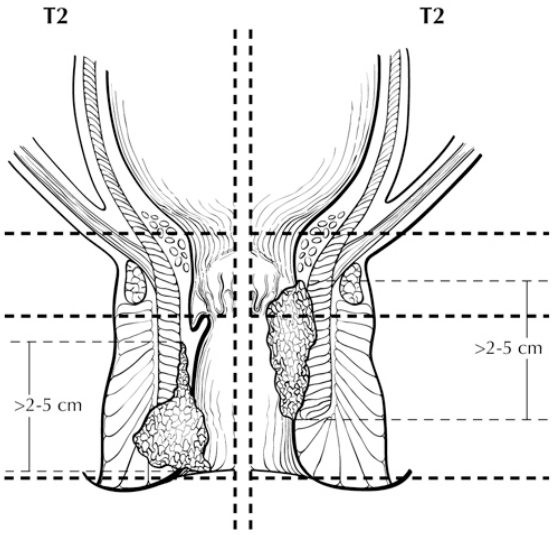

Figure 3. T2 is defined as tumor measuring more than 2 cm but 5 cm or less in greatest dimension. From: Greene FL, Compton, CC, Fritz AG, et al, eds. *AJCC Cancer Staging Atlas.* New York: Springer; 2006. Copyright © American Joint Committee on Cancer. Used with permission.

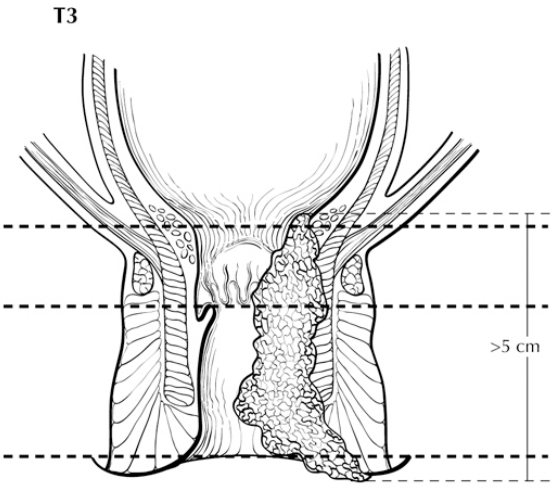

Figure 4. T3 is defined as tumor measuring more than 5 cm in greatest dimension. From: Greene FL, Compton, CC, Fritz AG, et al, eds. *AJCC Cancer Staging Atlas.* New York: Springer; 2006. Copyright © American Joint Committee on Cancer. Used with permission.

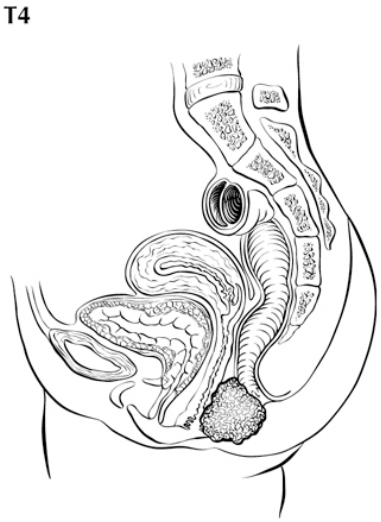

Figure 5. T4 is defined as tumor of any size invading adjacent organs such as vagina (illustrated), urethra, or bladder. From: Greene FL, Compton, CC, Fritz AG, et al, eds. *AJCC Cancer Staging Atlas.* New York: Springer; 2006. Copyright © American Joint Committee on Cancer. Used with permission.

N Category Considerations

Regional lymph nodes (N) (Figure 6) consist of the perirectal (anorectal, perirectal, and lateral sacral), the internal iliac (hypogastric), and the inguinal (superficial and deep femoral).[2] All other nodal groups represent sites of distant metastasis (M). The sites of regional node involvement correspond to the local lymphatic drainage, above to the rectal ampulla and below to the perineum. Tumors that arise in the anal canal usually spread initially to the anorectal and perirectal nodes, and those that arise at the anal margin spread to the superficial inguinal nodes.

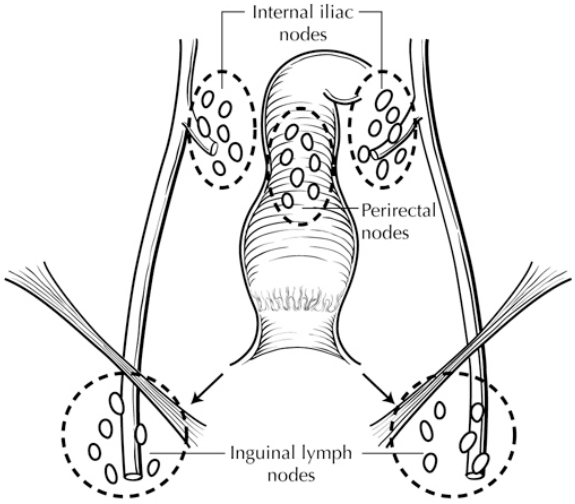

Figure 6. Regional lymph nodes of the anal canal. From: Greene FL, Compton, CC, Fritz AG, et al, eds. *AJCC Cancer Staging Atlas.* New York: Springer; 2006. Copyright © American Joint Committee on Cancer. Used with permission.

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 5 cm in greatest dimension
T3	Tumor more than 5 cm in greatest dimension
T4	Tumor of any size invades adjacent organ(s), eg, vagina, urethra, bladder[#]

[#]Direct invasion of the rectal wall, perianal skin, subcutaneous tissue, or the sphincter muscle is not classified as T4.

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis[#]
N1	Metastasis in perirectal lymph node(s)
N2	Metastasis in unilateral internal iliac and/or inguinal lymph node(s)
N3	Metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or inguinal lymph nodes

Distant Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis

Stage Groupings

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
	T3	N0	M0
Stage IIIA	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
	T4	N0	M0
Stage IIIB	T4	N1	M0
	Any T	N2	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

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.

G. Additional Findings

Predisposing conditions to anal canal carcinoma that may be found in the pathologic specimen include condyloma accuminatum associated with human papilloma virus infection.[7] Squamous intraepithelial neoplasia is recognized as a precursor lesion for squamous cell carcinoma of the anal canal,[8] and its presence should be reported. Both adenocarcinomas and squamous cell carcinomas have been reported in the setting of chronic anorectal fistulae arising in long-standing Crohn disease,[9] although the association of benign inflammatory lesions and anal cancer remains controversial.[10,11]

H. Ancillary Studies

Immunohistochemistry may be helpful in establishing tumor type for poorly differentiated carcinomas; squamous cell carcinomas of the anal canal express cytokeratin (CK) 7, CK5/6, p53,[12] and p63,[13] but are negative for CK20. In contrast, anal gland carcinomas are mucin positive and express CK 20 and CK7, but are negative for CK5/6 and p63.[12,14]

Immunohistochemical studies may also aid in distinguishing primary anal Paget disease from secondary Paget disease of the perianal area, which is associated with colorectal and anal canal carcinoma. CK7 expression is a sensitive method for detection of both primary and secondary Paget cells within involved anal and perianal epithelium. In addition, however, the specific immunophenotype of Paget cells has been shown to correlate with pathogenesis and may be important in patient management. Demonstration of CK20 expression has been shown to identify Paget disease that is likely to be associated with underlying rectal adenocarcinoma (presenting either synchronously or metachronously). In contrast, Paget cells that do not express CK20 but instead are positive for gross cystic disease fluid protein (GCDFP), a marker for apocrine differentiation, are likely to represent primary cutaneous intraepithelial malignancy.[3,8,15]

I. Clinical History

Predisposing conditions for anal canal carcinomas include immunosuppression, most commonly from solid organ transplantation, or HIV/AIDs infection.[16] The association between human papilloma virus infection and anal cancer has been firmly established.[7]

References

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