Protocol for the Examination of Specimens From Patients With Squamous Cell Carcinoma of the Skin

Protocol applies to invasive squamous cell carcinomas of the skin. Squamous cell carcinomas of the eyelid, vulva, and penis are not included.

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

Procedures
• Biopsy
• Excision
• Re-excision
• Lymph node examination

Authors
Priya Rao, MD*
    Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California
Bonnie L. Balzer, MD, PhD, FCAP
    Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California
Nanette J. Liegeois, MD, PhD
    Department of Dermatology, Johns Hopkins Medicine, Baltimore, Maryland
Jennifer M. McNiff, MD, FASCP
    Departments of Dermatology and Pathology, Yale University School of Medicine, New Haven, Connecticut
Paul Nghiem, MD, PhD
    Division of Dermatology, University of Washington Medical Center, Seattle, Washington
Victor G. Prieto, MD, PhD, FACP
    Departments of Pathology and Dermatology, MD Anderson Cancer Center, University of Texas, Houston, Texas
M. Timothy Smith, MD
    Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, South Carolina
Bruce Robert Smoller, MD, FCAP
    Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, Arkansas
Mark R. Wick, MD, FCAP
    Department of Pathology, University of Virginia Health System, Charlottesville, Virginia
David Frishberg, MD, FCAP†
    Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California
For the Members of the Cancer Committee, College of American Pathologists

*denotes primary author. † denotes senior author. All other contributing authors are listed alphabetically.

Previous contributors (Carcinoma of the skin): Mark R. Wick, MD; Carolyn Compton, MD, PhD; Lyn Duncan, MD; Harley A. Haynes, MD; Gregg M. Menaker, MD; Nicholas E. O’Connor, MD
© 2009 College of American Pathologists (CAP). All rights reserved.

The College does not permit reproduction of any substantial portion of these protocols without its written authorization. The College hereby authorizes use of these protocols by physicians and other health care providers in reporting on surgical specimens, in teaching, and in carrying out medical research for nonprofit purposes. This authorization does not extend to reproduction or other use of any substantial portion of these protocols for commercial purposes without the written consent of the College.

The CAP also authorizes physicians and other health care practitioners to make modified versions of the Protocols solely for their individual use in reporting on surgical specimens for individual patients, teaching, and carrying out medical research for non-profit purposes.

The CAP further authorizes the following uses by physicians and other health care practitioners, in reporting on surgical specimens for individual patients, in teaching, and in carrying out medical research for non-profit purposes: (1) **Dictation** from the original or modified protocols for the purposes of creating a text-based patient record on paper, or in a word processing document; (2) **Copying** from the original or modified protocols into a text-based patient record on paper, or in a word processing document; (3) The use of a **computerized system** for items (1) and (2), provided that the Protocol data is stored intact as a single text-based document, and is not stored as multiple discrete data fields.

Other than uses (1), (2), and (3) above, the CAP does not authorize any use of the Protocols in electronic medical records systems, pathology informatics systems, cancer registry computer systems, computerized databases, mappings between coding works, or any computerized system without a written license from CAP. Applications for such a license should be addressed to the SNOMED Terminology Solutions division of the CAP.

Any public dissemination of the original or modified Protocols is prohibited without a written license from the CAP.

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.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the checklist elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with these documents. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.

The inclusion of a product name or service in a CAP publication should not be construed as an endorsement of such product or service, nor is failure to include the name of a product of service to be construed as disapproval.
Important Note

This protocol supersedes some elements of the previous College of American Pathologists carcinoma of the skin protocol,¹ last revised in 2005, which was optional for squamous cell carcinomas. This new protocol is required only for tumors >2 cm in greatest dimension (which are automatically at least pT2 lesions) and is applicable to squamous cell carcinoma only.

Currently, most cancer registrars do not routinely report cutaneous squamous cell carcinomas. Nevertheless, there is an evolving standard of practice in dermatopathology to report invasive squamous carcinomas in a templated manner (see especially Khanna et al²); this checklist is intended to be helpful in developing such templates.

Important changes include:

Assignment of pT2 has been changed to reflect a combination of size and “high risk factors” (see note F).

pT3 and PT4 categories have been re-defined, and are assigned on the basis of invasion of specific structures (see note F).

Nodal involvement (previous pN1) has been subdivided into N1, N2, and N3, based on number, size, and site (ipsilateral, contralateral, bilateral) of involved nodes (see note F).
Surgical Pathology Cancer Case Summary (Checklist)

Protocol web posting date: October 2009

SQUAMOUS CELL CARCINOMA OF THE SKIN: Biopsy, Excision, Re-excision, Lymphadenectomy

Note: Use of checklist is optional for tumors <2 cm.

Select a single response unless otherwise indicated.

Procedure
____ Biopsy, punch
____ Biopsy, shave
____ Biopsy, other (specify): ____________________________
____ Excision, ellipse
____ Excision, wide
____ Excision, other (specify): ____________________________
____ Re-excision, ellipse
____ Re-excision, wide
____ Re-excision, other (specify): ____________________________
____ Lymphadenectomy, sentinel node(s)
____ Lymphadenectomy, regional nodes (specify): _________________________
____ Other (specify): ____________________________
____ Not specified

Tumor Site (Note A)
Specify, if known: ____________________________
____ Not specified

Tumor Size
Greatest dimension: ___ cm
*Additional dimensions: ___x__ cm
____ Cannot be determined (see “Comment”)

Histologic Type (select all that apply) (Note B)
____ Squamous cell carcinoma (SCC)
    ____ Acantholytic SCC
    ____ Spindle cell (sarcomatoid) SCC
    ____ Verrucous SCC
    ____ Pseudovascular SCC
    ____ Adenosquamous carcinoma
    ____ Squamous cell carcinoma, type not otherwise specified
    ____ 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 C)
___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ G4: Undifferentiated

Maximum Tumor Thickness (Note D)
___ Not applicable
Thickness: ____ mm
Thickness: at least ____ mm (see “Comment”) (Note C)

Anatomic Level (Note D)
___ Not applicable
___ I (carcinoma in situ)
___ II (carcinoma present in but does not fill and expand papillary dermis)
___ III (carcinoma fills and expands papillary dermis)
___ IV (carcinoma invades reticular dermis)
___ V (carcinoma invades subcutaneum)

Margins (select all that apply) (Note E)
Peripheral Margins
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
    *Distance of invasive carcinoma from closest lateral margin: ____ mm
    *Specify location(s), if possible: ____________________________
___ Involved by invasive carcinoma
    Specify location(s), if possible: ____________________________
___ Uninvolved by carcinoma in situ
    *Distance of carcinoma in situ from closest margin: ____ mm
    *Specify location(s), if possible: ____________________________
___ Involved by carcinoma in situ
    Specify location(s), if possible: ____________________________

Deep Margin
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
    *Distance of invasive carcinoma from margin: ____ mm
    *Specify location(s), if possible: ____________________________
___ Involved by invasive carcinoma
    Specify location(s), if possible: ____________________________

Lymph-Vascular Invasion (Note D)
___ 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.
Perineural Invasion (Note D)
___ Not identified
___ Present
___ Indeterminate

Lymph Nodes (Note F)
Number of nodes identified: _____
Number of nodes involved by metastatic carcinoma: _____
   *Size of largest metastatic focus: ___ cm

*Extranodal extension:
*___ Present
*___ Not identified

Pathologic Staging (pTNM) (Note F)

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple)
___ r (recurrent)
___ y (posttreatment)

Primary Tumor (pT)
___ pTX: Primary tumor cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ
___ pT1: Tumor 2 cm or less in greatest dimension with less than two high risk features
___ pT2: Tumor greater than 2 cm in greatest dimension with or without one additional high risk feature, or any size with two or more high risk features
___ pT3: Tumor with invasion of maxilla, mandible, orbit, or temporal bone
___ pT4: Tumor with direct or perineural invasion of skull base or axial skeleton

Regional Lymph Nodes (pN)
___ pNX: Regional lymph nodes cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
___ pN2: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
___ pN2a: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
___ pN2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
___ pN2c: Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
___ pN3: Metastasis in a lymph node, more than 6 cm in greatest dimension

* 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
*Specify: ____________________________

*Comment(s)
Explanatory Notes

A. Anatomic Site
Primary site on ear or glabrous lip is considered a “high-risk factor” in the American Joint Committee on Cancer (AJCC) seventh edition staging system that may be used in upstaging a tumor from pT1 to pT2.3

B. Histologic Subtypes
The World Health Organization (WHO) classification⁴ of squamous cell carcinomas of the skin is shown below:

- Spindle-cell (sarcomatoid) squamous cell carcinoma (SCC)
- Acantholytic SCC
- Verrucous SCC
- SCC with horn formation
- Lymphoepithelial SCC

Variants not included in the WHO classification include:

- Papillary SCC
- Clear cell SCC
- Small cell SCC
- Posttraumatic (eg, Marjolin ulcer)
- Metaplastic (carcinosarcomatous) SCC
- Paget disease
- Mammary Paget disease
- Extramammary Paget disease
- Adnexal carcinomas
- Keratoacanthoma

C. Histologic Grade
Histologic grades are as follows⁵:

Grade 1: Well-differentiated tumors are characterized by squamous epithelium that frequently shows easily recognizable and often abundant keratinization. Intercellular bridges are readily apparent. There is minimal pleomorphism, and mitotic figures are mainly basally located.

Grade 2: Moderately differentiated tumors show more structural disorganization in which squamous epithelial derivation is less obvious. Nuclear and cytoplasmic pleomorphism are more pronounced, and mitotic figures may numerous. Keratin formation is typically limited to keratin pearls, horn cysts, and scattered individually keratinized cells.

Grade 3: In poorly differentiated tumors it may be difficult to establish squamous differentiation, usually by identification of rare intercellular bridges or small foci of keratinization.

Grade 4: Used to denote anaplastic or undifferentiated tumors.
An alternative oft-cited system is Broders' 1932 classification of histologic grading, summarized as follows:

Grade 1: 75% or more of the lesion is well differentiated  
Grade 2: 50% to 75% of the lesion is well differentiated  
Grade 3: 25% to 50% of the lesion is well differentiated  
Grade 4: Less than 25% of the lesion is well differentiated

D. High-Risk Histologic Features
In addition to anatomic site and poor differentiation (high grade), the presence of certain high-risk histologic features may be used in upstaging a tumor from pT1 to pT2 (see note E). These include tumor thickness, anatomic level, presence of perineural invasion, and presence of lymph-vascular invasion.

Maximum tumor thickness (Breslow) is measured with a calibrated ocular micrometer at a right angle to the adjacent normal skin. The upper point of reference is the granular layer of the epidermis of the overlying skin or, if the lesion is ulcerated, the base of the ulcer. The lower reference point is the deepest point of tumor invasion (i.e., the leading edge of a single mass or an isolated group of cells deep to the main mass).

If the tumor is transected by the deep margin of the specimen, the depth may be indicated as “at least ___ mm” with a comment explaining the limitation of thickness assessment.

Anatomic (Clark) levels are defined as follows:

I: Intraepidermal tumor only  
II: Tumor present in but does not fill and expand papillary dermis  
III: Tumor fills and expands papillary dermis  
IV: Tumor invades into reticular dermis  
V: Tumor invades subcutis

In addition to the “high-risk” factors listed above, a number of other prognostic features not specifically employed for the seventh edition AJCC staging system have been reported and include: inflammatory response; association with actinic keratosis; association with human papillomavirus (HPV); association with Bowen’s disease; acantholytic, basaloid, small cell, signet ring, desmoplastic, or spindle cell histological subtypes; and follicular SCC.

E. Margins
If the specimen is oriented, the position of peripheral margins involved by tumor should be indicated. Although a comment on margins is necessary only for excisional biopsies or formal resections, it is commonly employed in many dermatopathology laboratories on all specimens and has been advocated as part of a standard diagnostic template. Measurements of distance from tumor to margins need not be routinely reported but may be done so in special circumstances and/or when requested by the treating physician.

F. TNM and Stage Groupings
The TNM staging system for squamous cell carcinoma of the skin of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended. By AJCC/UICC convention, the designation “T” refers to a primary
Background Documentation  Skin • Squamous Cell Carcinoma of the Skin

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 and depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor cannot be resected for any reason 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.

T Category Considerations

High-Risk Features for Primary (T) Tumor Staging

Clinical: Primary site on ear or glabrous lip
Histologic: ≥4 mm depth
Clark level IV/V
Perineural invasion
Lymph-vascular invasion
Poor differentiation

Stage Groupings

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N0</th>
<th>M0#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0#</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
<td>N0 or N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1 or T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>T1, T2, or T3</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any M</td>
<td>M1</td>
</tr>
</tbody>
</table>

# M0 is defined as no distant metastasis.

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.6

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RX</td>
<td>Presence of residual tumor cannot be assessed</td>
</tr>
<tr>
<td>R0</td>
<td>No residual tumor</td>
</tr>
<tr>
<td>R1</td>
<td>Microscopic residual tumor</td>
</tr>
<tr>
<td>R2</td>
<td>Macroscopic residual tumor</td>
</tr>
</tbody>
</table>

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).

**References**


