Protocol for the Examination of Specimens from Patients with Cutaneous Squamous Cell Carcinoma of the Head and Neck

Version: 1.0.0.0

Protocol Posting Date: June 2022

CAP Laboratory Accreditation Program Protocol Required Use Date: March 2023

The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection</td>
<td>Includes wide local excisions and craniofacial resections</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma</td>
<td>Includes ONLY N+, and pT3 and pT4 cutaneous squamous cell carcinoma including squamous cell carcinomas of dry vermillion lip and commissure</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
</tr>
<tr>
<td>Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy)</td>
</tr>
<tr>
<td>Cytologic specimens</td>
</tr>
<tr>
<td>Early-stage cutaneous squamous cell carcinomas (N-, and pT1 and pT2 cutaneous squamous cell carcinomas)</td>
</tr>
<tr>
<td>Non-squamous cell carcinomas of the skin</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell carcinomas of the eyelid (consider the Eyelid protocol)</td>
</tr>
<tr>
<td>Squamous cell carcinomas of the vulva (consider the Vulva protocol)</td>
</tr>
<tr>
<td>Squamous cell carcinomas of the penis (consider the Penis protocol)</td>
</tr>
<tr>
<td>Squamous cell carcinomas of other cutaneous sites (no current protocol)</td>
</tr>
</tbody>
</table>

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

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

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

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

Synoptic Reporting
All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including “Cannot be determined” if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
  - Anatomic site or specimen, laterality, and procedure
  - Pathologic Stage Classification (pTNM) elements
  - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location.

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report ie, all required elements must be in the synoptic portion of the report in the format defined above.
Summary of Changes
v 1.0.0.0

- New protocol
Reporting Template

Protocol Posting Date: June 2022
Select a single response unless otherwise indicated.

CASE SUMMARY: (CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK)
Standard(s): AJCC-UICC 8

SPECIMEN (Note A)

Procedure (select all that apply)
___ 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

Tumor Focality
___ Unifocal
___ Multifocal: ____________________
___ Cannot be determined: ____________________

Multiple Primary Sites
___ Not applicable (no additional primary site(s) present)
___ Present: ____________________

Please complete a separate checklist for each primary site if required as above.

Tumor Site
___ Specify, if known: ____________________
___ Not specified

Tumor Laterality (select all that apply)
___ Right
___ Left
___ Midline
___ Not specified

Tumor Size
___ Greatest dimension in Centimeters (cm): ____________________ cm
   +Additional Dimensions in Centimeters: ___ x ___ cm
___ Cannot be determined (explain): _________________

**Histologic Type (Note B)**

___ Squamous cell carcinoma, not otherwise specified
___ Keratoacanthoma
___ Acantholytic squamous cell carcinoma
___ Spindle cell squamous cell carcinoma
___ Verrucous squamous cell carcinoma
___ Adenosquamous carcinoma
___ Clear cell squamous cell carcinoma
___ Squamous cell carcinoma with sarcomatoid differentiation
___ Squamous cell carcinoma with osteoclast-like giant cells
___ Pseudovascular squamous cell carcinoma
___ Lymphoepithelioma-like carcinoma
___ Other (specify): _________________

**Histologic Grade (Note C)**

___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ G4: Undifferentiated
___ Other (specify): _________________
___ Not applicable

**Tumor Depth of Invasion (DOI) (Note D)**

___ Not applicable
___ Specify depth in Millimeters (mm): _________________ mm
___ At least (mm): _________________ mm
___ Cannot be determined (explain): _________________

**Anatomic Level**

___ 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 subcutaneous)

**Tumor Extent (specify other structures involved): _________________**

**Lymphovascular Invasion**

___ Not identified
___ Present
___ Cannot be determined: _________________
Perineural Invasion (Note E)

___ Not identified
___ Present
    ___ Less than 0.1 mm in caliber
# Location of the involved nerve deep to the dermis serves as a surrogate for this size cut-off and qualifies as greater than or equal to 0.1 mm.
    ___ Greater than or equal to 0.1 mm in caliber#
    ___ Specify: ____________________
    ___ Cannot be determined: _________________

MARGINS (Note F)

Margin Status for Invasive Tumor

___ All margins negative for invasive tumor

+Distance from Invasive Tumor to Closest Margin

Specify in Millimeters (mm)

___ Exact distance: ________________ mm
___ Greater than: ________________ mm
___ Less than 1 mm
___ Other (specify): ________________
___ Cannot be determined: ________________

+Closest Margin(s) to Invasive Tumor

___ Specify location(s) of closest margin(s): ________________
___ Cannot be determined

+Other Close Margin(s) to Invasive Tumor

___ Specify location(s) and distance(s) of other close margin(s): ________________
___ Cannot be determined

___ Invasive tumor present at margin

Margin(s) Involved by Invasive Tumor (select all that apply)

___ Peripheral: ________________
___ Deep: ________________
___ Other (specify): ________________
___ Cannot be determined (explain): ________________
___ Other (specify): ________________
___ Cannot be determined (explain): ________________
___ Not applicable

Margin Status for Noninvasive Tumor

___ Not applicable

___ All margins negative for in situ disease

+Distance from Noninvasive Tumor to Closest Margin

Specify in Millimeters (mm)

___ Exact distance: ________________ mm
___ Greater than: ________________ mm
___ Less than 1 mm
____ Other (specify): ____________________  
____ Cannot be determined: ____________________

+Closest Margin(s) to Noninvasive Tumor  
____ Specify closest margin(s): ____________________  
____ Cannot be determined  
____ In situ disease present at margin  
Margin(s) Involved by Noninvasive Tumor (select all that apply)  
____ Peripheral: ____________________  
____ Deep: ____________________  
____ Other (specify): ____________________  
____ Cannot be determined (explain): ____________________  
____ Other (specify): ____________________  
____ Cannot be determined (explain): ____________________

REGIONAL LYMPH NODES (Note G)

Regional Lymph Node Status  
____ Not applicable (no regional lymph nodes submitted or found)  
____ Regional lymph nodes present  
____ All regional lymph nodes negative for tumor  
____ Tumor present in regional lymph node(s)  
  Number of Lymph Nodes with Tumor  
____ Exact number (specify): ____________________  
____ At least (specify): ____________________  
____ Other (specify): ____________________  
____ Cannot be determined  
Laterality of Lymph Node(s) with Tumor  
____ Ipsilateral (including midline): ____________________  
____ Contralateral: ____________________  
____ Bilateral: ____________________  
____ Cannot be determined: ____________________

Size of Largest Nodal Metastatic Deposit  
Specify in Centimeters (cm)  
____ Exact size (specify): ____________________ cm  
____ At least (specify): ____________________ cm  
____ Greater than: ____________________ cm  
____ Less than: ____________________ cm  
____ Other (specify): ____________________  
____ Cannot be determined: ____________________

Extranodal Extension (ENE) (Note G)  
____ Not identified  
____ Present  
____ Cannot be determined: ____________________  
____ Other (specify): ____________________  
____ Cannot be determined (explain): ____________________
Number of Lymph Nodes Examined
___ Exact number (specify): _________________
___ At least (specify): _________________
___ Other (specify): _________________
___ Cannot be determined

+Regional Lymph Node Comment: _________________

DISTANT METASTASIS

Distant Site(s) Involved, if applicable (select all that apply)
___ Not applicable
___ Lung: _________________
___ Bone: _________________
___ Brain: _________________
___ Liver: _________________
___ Other (specify): _________________
___ Cannot be determined: _________________

PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th Edition) (Note H)
Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician’s responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.

TNM Descriptors (select all that apply)
___ Not applicable
___ m (multiple primary tumors)
___ r (recurrent)
___ y (post-treatment)

pT Category
___ pT not assigned (cannot be determined based on available pathological information)
___ pTis: Carcinoma in situ
___ pT1: Tumor smaller than or equal to 2 cm in greatest dimension
___ pT2: Tumor larger than 2 cm, but smaller than or equal to 4 cm in greatest dimension
___ pT3: Tumor larger than 4 cm in maximum dimension or minor bone erosion or perineural invasion or deep invasion#
___ pT4: Tumor with gross cortical bone / marrow, skull base invasion and / or skull base foramen invasion
___ pT4a: Tumor with gross cortical bone / marrow invasion
___ pT4b: Tumor with skull base invasion and / or skull base foramen involvement
pT4 (subcategory cannot be determined)
pN Category#
# A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(−) or ENE(+).

___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(−)
___ pN2: Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+); or larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−); or in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, ENE(−)
___ pN2a: Metastasis in single ipsilateral node 3 cm or smaller in greatest dimension and ENE(+); or a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−)
___ pN2b: Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(−)
___ pN2c: Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(−)
___ pN2 (subcategory cannot be determined)
___ pN3: Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); or in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); or a single contralateral node of any size and ENE(+)
___ pN3a: Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
___ pN3b: Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); or a single contralateral node of any size and ENE(+)
___ pN3 (subcategory cannot be determined)

pM Category (required only if confirmed pathologically)
___ Not applicable - pM cannot be determined from the submitted specimen(s)
___ pM1: Distant metastasis

Brigham and Women’s (BWH) Tumor Classification System (Note H)
+High-risk Factors (select all that apply)
___ Tumor diameter greater than or equal to 2 cm
___ Poorly differentiated histology
___ Perineural invasion greater than or equal to 0.1 mm in caliber
___ Tumor invasion beyond subcutaneous fat (excluding bone invasion, which upgrades tumor to BWH stage T3)
+BWH Tumor Classification
___ T1: 0 high-risk factor
___ T2a: 1 high-risk factor
___ T2b: 2-3 high-risk factors
___ T3: Greater than or equal to 4 risk factors or bone invasion

ADDITIONAL FINDINGS
+Additional Findings (select all that apply)
___ None identified
___ Immunosuppressed status (specify cause, if known): _________________
___ Other (specify): _________________

SPECIAL STUDIES
Biomarkers tested may be included in the section below. Pending biomarker studies may be listed in the Comments section of this report.

Biomarkers Tested (may repeat for up to 10 biomarkers)
+Specify Test and Result: _________________

COMMENTS

Comment(s): _________________
Explanatory Notes

A. Scope of Guidelines
The reporting of cutaneous squamous cell carcinoma of head and neck is facilitated by the provision of a case summary illustrating the features required for comprehensive patient care. However, there are many cases in which the individual practicalities of applying such a case summary may not be straightforward. Common examples include finding the prescribed number of lymph nodes, trying to determine the levels of the radical neck dissection, and determining if isolated tumor cells in a lymph node represent metastatic disease. Case summaries have evolved to include clinical, radiographic, morphologic, immunohistochemical, and molecular results in an effort to guide clinical management. Adjuvant and neoadjuvant therapy can significantly alter histologic findings, making accurate classification an increasingly complex and demanding task. This protocol tries to remain simple while still incorporating important pathologic features as proposed by the American Joint Committee on Cancer (AJCC) cancer staging manual, the World Health Organization (WHO) classification of tumors, the TNM classification\(^1\), the American College of Surgeons Commission on Cancer, and the International Union on Cancer (UICC). This protocol is to be used as a guide and resource, an adjunct to diagnosing and managing cancers of the oral cavity in a standardized manner. It should not be used as a substitute for dissection or grossing techniques and does not give histologic parameters to reach the diagnosis. Subjectivity is always a factor, and elements listed are not meant to be arbitrary but are meant to provide uniformity of reporting across all the disciplines that use the information. It is a foundation of practical information that will help to meet the requirements of daily practice to benefit both clinicians and patients alike.

References

B. Histologic Subtypes
The World Health Organization (WHO) classification\(^1\) of squamous cell carcinomas of the skin is shown below:

Squamous cell carcinoma, not otherwise specified
Keratoacanthoma
Acantholytic squamous cell carcinoma
Spindle cell squamous cell carcinoma
Verrucous squamous cell carcinoma
Adenosquamous carcinoma
Clear cell squamous cell carcinoma

Other (uncommon) variants
Squamous cell carcinoma with sarcomatoid differentiation
Squamous cell carcinoma with osteoclast-like giant cells
Pseudovascular squamous cell carcinoma
Lymphoepithelioma-like carcinoma

References

C. Histologic Grade
Grading of cutaneous squamous cell carcinoma is not standardized. Classically, tumors graded qualitatively using 4 tiers as follows:

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 be 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.

Broders classification of histologic grading is a popular alternative single parameter quantitative grading system often utilized as well and is summarized as follows:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Less than 25% is undifferentiated</td>
</tr>
<tr>
<td>2</td>
<td>Greater than or equal to 25% but less than 50% is undifferentiated</td>
</tr>
<tr>
<td>3</td>
<td>Greater than or equal to 50% but less than 75% is undifferentiated</td>
</tr>
<tr>
<td>4</td>
<td>Greater than or equal to 75% is undifferentiated</td>
</tr>
</tbody>
</table>

Grade has remained a key independent prognosticator in cutaneous squamous cell carcinoma despite limited data showing weak to moderate interobserver concordance.

From a management perspective, grade is typically reduced to two tiers with poorly differentiated tumors (Grades 3 and 4) constituting the high risk category. However, limited evidence suggests that even moderately differentiated tumors (Grade 2) may show a higher risk for subclinical spread requiring more layers of clearance by Mohs micrographic surgery. Of note, it is this grade of tumors that appears to show the highest interobserver variability.

The application of grading to variant morphologies in cutaneous squamous cell carcinoma is not well studied, though some variants (i.e. keratoacanthoma, verrucous squamous cell carcinoma) have a well-established intrinsic biologic behavior. It is thus reasonable to use the “not applicable” category when a variant morphology comprises the bulk of the tumor.

References

D. Tumor Thickness / Depth of Invasion
While tumor thickness (Breslow)/depth of invasion (DOI) are key risk factors for nodal disease on univariate and multivariate analysis. Both terms are often interchangeable, but as per AJCC 8th edition, whenever possible, DOI, as measured from the granular layer of the adjacent normal epidermis to the base of the tumor is recommended for determining T status. This DOI is measured at a right angle to the adjacent normal skin. The upper point of reference is the granular layer of the epidermis of the adjacent uninvolved epidermis. 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 thickness 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

References

E. Perineural Invasion
While perineural invasion in cutaneous squamous cell carcinoma is an independent poor prognosticator,1 evidence suggests that a more nuanced approach to this parameter allows for improved stratification of patients. Size, location with respect to tumor, anatomic depth, number and even microscopic
extent (circumferential vs focal) are key features to consider. Of these, the diameter of involved nerve is more studied and a diameter of greater than or equal to 0.1 mm is included in the definition of “deep invasion” in pT status. Location of the involved nerve deep to the dermis serves as a surrogate for this size cut-off and can be used even in the absence of a reticle or ocular micrometer to help assign a pT category. In other words, the size of involved nerves deep to the dermis can be classified as greater than or equal to 0.1 mm.

References

F. Margins
Margin status emerges as a key adverse prognosticator on meta-analysis and is a critical factor to consider for consideration of adjuvant radiotherapy and is thus a required reporting element. If the specimen is oriented or can be oriented based on anatomic landmarks, the position of margins involved by tumor should be indicated. Although a comment on margins is necessary only for wide local excisions or formal resections, it is commonly employed in many (dermato)pathology laboratories on all specimens and has been advocated as part of a standard diagnostic template.

Distance of tumor to margins is not well studied in cutaneous squamous cell carcinomas and is thus currently not required. Nonetheless reporting of this parameter is highly recommended to maintain equivalence of reporting standards with mucosal counterparts. Current NCCN guidelines recommend gross clearance of 4-6 mm for tumors less than 2.0 cm, and wider (without specifying) on larger advanced stage tumors under the purview of this protocol. However, only a single prospective study using Mohs technique was the basis for these guidelines. Equivalence to margin distances for wide local excision/resection let alone microscopic margin distances is not established in these guidelines. However, for head and neck sites limited evidence does suggest some prognostic value at a cutoff of 5 mm on univariate analysis.

References

### G. Lymph Nodes

Lymph node status, specifically size, number and extranodal extension have been noted to represent adverse prognosticators. As such they have been incorporated into AJCC N categorization in a fashion similar to that of human papillomavirus (HPV) unrelated mucosal HNSCC. But while these parameters are impactful, the actual performance of this adaptation of mucosal HNSCC N classification system cutaneous HNSCC has been shown to be suboptimal.

### References


### H. TNM and Stage Groupings

The TNM staging system for cutaneous squamous cell carcinoma of the head and neck of the American Joint Committee on Cancer (AJCC) is recommended. By AJCC 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 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**

Deep invasion: Invasion beyond the subcutaneous fat or >6 mm in depth.

Perineural invasion for T3 classification: Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring 0.1 mm or larger in caliber, or presenting with clinical or radiographic involvement of named nerves without skull base invasion or transgression.

**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 (i.e., 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 (i.e., 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.

**Brigham and Women’s Hospital (BWH) Tumor Staging**

The Brigham and Women’s Hospital (BWH) system is an alternative tumor classification system. Prior analysis from a single institution cohort demonstrated that the BWH staging system offers improved distinctiveness, homogeneity, and monotonicity over AJCC 7. Compared to AJCC 8, BWH had higher specificity and positive predictive value for identifying cases at risk for metastasis or death. A systematic review of sentinel node biopsy in CSCC demonstrated that BWH T2b/T3 tumors have a high risk of sentinel node positivity (29.4%).

**T0** In situ SCC
T1  0 high-risk factors*
T2a  1 high-risk factor*
T2b  2-3 high-risk factors*
T3  Greater than or equal 4 risk factors* or bone invasion

* BWH staging high-risk features:
  • Clinical tumor diameter greater than or equal 2 cm
  • Tumor invasion beyond subcutaneous fat, excluding bone invasion, which upgrades tumor to stage T3
  • Poorly differentiated histology
  • Perineural invasion of nerve(s) greater than or equal 0.1 mm in caliber

References