Protocol for the Examination of Biopsy Specimens From Patients With Melanoma of the Skin

Version: Melanoma Biopsy 4.1.0.0  Protocol Posting Date: August 2019

Accreditation Requirements
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

This protocol may be used for the following procedures AND tumor types:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td></td>
</tr>
<tr>
<td>Tumor Type</td>
<td>Description</td>
</tr>
<tr>
<td>Invasive melanoma</td>
<td>Limited to melanoma of cutaneous surfaces only</td>
</tr>
</tbody>
</table>

The following should NOT be reported using this protocol:

<table>
<thead>
<tr>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excision (consider Skin Melanoma Excision protocol)</td>
</tr>
<tr>
<td>Cytologic specimens</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma in situ without invasive melanoma</td>
</tr>
</tbody>
</table>

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

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Summary of Changes

v4.1.0.0
Separated resection, biopsy case summaries into separate documents.
Modified - Histologic Type
Surgical Pathology Cancer Case Summary

Protocol posting date: August 2019

MELANOMA OF THE SKIN: Biopsy

Notes:
This case summary is recommended for reporting biopsy specimens but is NOT REQUIRED for accreditation purposes. Core data elements are bolded to help identify routinely reported elements.

Select a single response unless otherwise indicated.

Procedure (Note A)
___ Biopsy, shave
___ Biopsy, punch
___ Biopsy, incisional
___ Other (specify): ____________________________
___ Not specified

Specimen Laterality
___ Right
___ Left
___ Midline
___ Not specified

Tumor Site (Note B)
Specify (if known): ____________________________
___ Not specified

Macroscopic Satellite Nodule(s) (applicable to invasive tumor only)
___ Not identified
___ Present
___ Cannot be determined

Histologic Type (Note C)
___ No residual melanoma identified

Invasive Melanoma
___ Superficial spreading melanoma (low cumulative sun damage melanoma)
___ Lentigo maligna melanoma
___ Desmoplastic melanoma
    ___ Pure desmoplastic melanoma
    ___ Mixed desmoplastic melanoma
___ Acral melanoma
___ Melanoma arising in a blue nevus (blue nevus-like melanoma)
___ Melanoma arising in a giant congenital nevus
___ Spitz melanoma (malignant Spitz tumor)
___ Nodular melanoma
___ Nevoid melanoma
___ Melanoma, not otherwise classified
___ Other histologic type not listed (specify): ____________________________

The routinely reported core data elements are bolded.
Melanoma In Situ (anatomic level I)#
___ Melanoma in situ, superficial spreading type (low-CSD melanoma in situ)
___ Melanoma in situ, lentigo maligna type
___ Acral melanoma in situ
___ Melanoma in situ arising in a giant congenital nevus
___ Melanoma in situ, not otherwise classified
___ Other histologic type not listed (specify): ________________________

Note: For melanoma in situ, elements that assess the invasive component are not applicable and should not be reported.

Maximum Tumor (Breslow) Thickness (Note D) (applicable to invasive tumor only)
Specify (millimeters): ___ mm

or

At least (millimeters): ___ mm (explain): _____________________________________________
___ Cannot be determined (explain): _________________________________________________

Ulceration (required for invasive tumor only) (Note E)
___ Present
___ Not identified
___ Cannot be determined

Microsatellite(s) (applicable to invasive tumor only) (Note F)
___ Not identified
___ Present
___ Cannot be determined

Margins (select all that apply) (Note G)

Peripheral Margins#
___ Uninvolved by invasive melanoma
   Distance of invasive melanoma from closest peripheral margin (millimeters): ___ mm
   Specify location(s): _____________________________________________
___ Involved by invasive melanoma
   Specify location(s): _____________________________________________
___ Uninvolved by melanoma in situ
   Distance of melanoma in situ from closest peripheral margin (millimeters): ___ mm
   Specify location(s): _____________________________________________
___ Involved by melanoma in situ
   Specify location(s): _____________________________________________
___ Cannot be assessed

Deep Margin#
___ Uninvolved by melanoma in situ
___ Uninvolved by invasive melanoma
   Distance of invasive melanoma from deep margin (millimeters): ___ mm
___ Involved by melanoma in situ
___ Involved by invasive melanoma
___ Cannot be assessed

*Note: Margin involvement by melanoma in situ should be recorded if in situ disease is present in the specimen, and if margins are uninvolved by invasive melanoma.
Mitotic Rate (applicable to invasive tumor only) (Note H)
___ None identified
___ Specify number /mm² (# mitoses/mm²): ______
___ Cannot be determined

Anatomic (Clark) Level (applicable to invasive tumor only) (Note D)
___ At least level ______
 ___ (explain): ______________________________________
___ II (melanoma present in but does not fill and expand papillary dermis)
___ III (melanoma fills and expands papillary dermis)
___ IV (melanoma invades reticular dermis)
___ V (melanoma invades subcutis)
___ Cannot be determined

Lymphovascular Invasion (applicable to invasive tumor only) (Note I)
___ Not identified
___ Present
___ Cannot be determined

Neurotropism (applicable to invasive tumor only) (Note J)
___ Not identified
___ Present
___ Cannot be determined

Tumor-Infiltrating Lymphocytes (applicable to invasive tumor only) (Note K)
___ Not identified
___ Present, nonbrisk
___ Present, brisk
___ Cannot be determined

Tumor Regression (Note L)
___ Not identified
___ Present
___ Cannot be determined

Pathologic Stage Classification (pTNM, AJCC 8th Edition) (Note M)

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

Primary Tumor (pT)
___ pTX: Primary tumor thickness cannot be assessed (eg, diagnosis by curettage)
 ___ (explain):
___ pT0: No evidence of primary tumor (eg, unknown primary or completely regressed melanoma)
___ pTis: Melanoma in situ (ie, not an invasive tumor: anatomic level I)
___ pT1: Melanoma 1.0 mm or less in thickness, ulceration status unknown or unspecified (see Note D)
 ___ pT1a: Melanoma <0.8 mm in thickness, no ulceration
 ___ pT1b: Melanoma <0.8 mm in thickness with ulceration, or melanoma 0.8 to 1.0 mm in thickness with or without ulceration
___ pT2: Melanoma >1.0 to 2.0 mm in thickness, ulceration status unknown or unspecified
___ pT2a: Melanoma >1.0 to 2.0 mm in thickness, no ulceration
___ pT2b: Melanoma >1.0 to 2.0 mm in thickness, with ulceration
___ pT3: Melanoma >2.0 to 4.0 mm in thickness, ulceration status unknown or unspecified
___ pT3a: Melanoma >2.0 to 4.0 mm in thickness, no ulceration
___ pT3b: Melanoma >2.0 to 4.0 mm in thickness, with ulceration
___ pT4: Melanoma >4.0 mm in thickness, ulceration status unknown or unspecified
___ pT4a: Melanoma >4.0 mm in thickness, no ulceration
___ pT4b: Melanoma >4.0 mm in thickness, with ulceration

Additional Pathologic Findings (select all that apply)
___ Associated nevus (specify type)
___ Other (specify): ____________________________

Ancillary Studies

Note: For molecular genetic reporting, the CAP Melanoma Biomarker Template should be used. Pending biomarker studies should be listed in the Comments section of this report.

Comment(s)
Explanatory Notes

A. Procedure
Optimal pathologic evaluation of melanocytic lesions requires complete excision that incorporates the full thickness of the lesion removed intact.1 "Shave" procedures that do not include the intact base of the lesion are suboptimal for pathologic evaluation and should be avoided unless clinically indicated. Similarly, "punch" procedures may not include intact peripheral borders of the lesion thereby limiting assessment of symmetry and lateral circumscription, which can be essential for distinction of melanoma from melanocytic nevus.2,3 Partial biopsies of melanocytic tumors are associated with an increased risk of misdiagnosis with possible consequent adverse clinical outcomes.4 Nevertheless, clinical factors are also important in determining the most appropriate biopsy technique for any lesion. For example, an excision biopsy of a large lesion on a cosmetically or functionally sensitive site may cause cosmetic disfigurement or alter reconstructive options.

The use of frozen sections for evaluation of biopsy or excision of melanocytic lesions is strongly discouraged.5,6 Optimal histologic evaluation of cutaneous melanoma requires well-cut, well-stained hematoxylin-and-eosin (H&E) sections prepared from formalin-fixed paraffin-embedded tissue. Frozen sections of sentinel lymph nodes are similarly discouraged, because the manipulation required for intraoperative handling may decrease the sensitivity of the procedure.7

References

B. Anatomic Site
For cutaneous melanoma, prognosis may be affected by primary anatomic site.1,2

References

C. Melanoma Subtypes
Superficial spreading melanoma (low cumulative sun damage melanoma)
Lentigo maligna melanoma
Desmoplastic melanoma (pure and mixed)
Acral melanoma
Melanoma arising in a blue nevus (blue nevus-like melanoma)
Melanoma arising in a giant congenital nevus
Spitz melanoma (malignant Spitz tumor)
Nodular melanoma
Nevoid melanoma
Melanoma, not otherwise classified

The recent WHO 2018 classification introduced multidimensional pathway classification of melanocytic tumors based on the extent of ultraviolet (UV) radiation damage, the cell of origin, and characteristic genomic findings (Table 1).

Table 1. Classification of melanoma

<table>
<thead>
<tr>
<th>Extent of UV radiation damage</th>
<th>Subtypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanomas found in skin with low cumulative sun damage (low-CSD)</td>
<td>Low-CSD melanoma/superficial spreading melanoma</td>
</tr>
<tr>
<td>Melanomas found in skin with high cumulative sun damage (high-CSD)</td>
<td>Lentigo maligna melanoma</td>
</tr>
<tr>
<td>Melanomas on site with no sun exposure or without known etiological associations with sun exposure</td>
<td>Desmoplastic melanoma</td>
</tr>
<tr>
<td></td>
<td>Malignant Spitz tumor (Spitz melanoma)</td>
</tr>
<tr>
<td></td>
<td>Acral melanoma</td>
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<tr>
<td></td>
<td>Mucosal melanoma</td>
</tr>
<tr>
<td></td>
<td>Melanoma arising in congenital nevus</td>
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<tr>
<td></td>
<td>Melanoma arising in a blue nevus</td>
</tr>
<tr>
<td></td>
<td>Uveal melanoma</td>
</tr>
<tr>
<td>Various sun exposure</td>
<td>Nodular melanoma</td>
</tr>
</tbody>
</table>

References

D. Primary Tumor (Breslow) Thickness and Anatomic (Clark) Levels

Maximum tumor thickness is measured with a calibrated ocular micrometer at a right angle to the adjacent normal skin. The upper point of reference is the upper edge of the granular layer of the epidermis of the overlying skin or, if the lesion is ulcerated overlying the entire dermal component, the base of the ulcer. The lower reference point is the deepest point of tumor invasion (ie, 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. For example, “The maximum tumor thickness cannot be determined in this specimen because the deep plane of the biopsy transects the tumor.” Tumor thickness measurements should not be based on periadnexal extension (either periadnexal adventitial or extra-adventitial extension), except when it is the only focus of invasion. In that circumstance, Breslow thickness may be measured from the inner layer of the outer root sheath epithelium or inner luminal surface of sweat glands, to the furthest extent of infiltration into the periadnexal dermis. Microsatellites or foci of neurotropism or lymphovascular invasion should not be included in tumor thickness measurements.

In the 8th edition of the AJCC melanoma staging system, it is recommended that tumor thickness measurements be recorded to the nearest 0.1 mm, not the nearest 0.01 mm, because of the impracticality and imprecision of measurements, particularly for tumors greater than 1 mm thick. Tumors less than or equal to 1 mm thick may be measured to the nearest 0.01 mm if practical, but should be reported to the nearest 0.1 mm (eg, melanomas measured to be in the range of 0.75 mm to 0.84 mm are reported as 0.8 mm in thickness and hence T1b, and tumors 1.01 to 1.04 mm in thickness are reported as 1.0 mm).

While the principal T category tumor thickness ranges have been maintained in the AJCC 8th edition, T1 is now subcategorized by tumor thickness strata at a 0.8 mm threshold. Tumor mitotic rate as a dichotomous variable is no longer used as a staging category criterion for T1 tumors. T1a melanomas are now defined as non-ulcerated and less than 0.8 mm in thickness. T1b melanomas are defined as 0.8-1.0 mm in thickness or ulcerated melanomas less than 0.8 mm in thickness.
Anatomic (Clark) levels are defined as follows:

I  Intraepidermal tumor only (ie, melanoma in situ)
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

Anatomic (Clark) level of invasion remains an independent predictor of outcome and is recommended by the AJCC to be reported as a primary tumor characteristic. However, assessment of Clark levels is less reproducible among pathologists than is tumor thickness, and Clark levels are not used in the AJCC staging system for pT status. Accordingly, Clark levels are included in this checklist as an optional data item.

References

E. Ulceration

Primary tumor ulceration has been shown to be a dominant independent prognostic factor in invasive cutaneous melanoma, and if present, changes the pT stage from T1a to T1b, T2a to T2b, etc., depending on the thickness of the tumor. The presence or absence of ulceration must be confirmed on microscopic examination. Melanoma ulceration is defined as the combination of the following features: full-thickness epidermal defect (including absence of stratum corneum and basement membrane); evidence of reactive changes (ie, fibrin deposition, neutrophils); and thinning, effacement, or reactive hyperplasia of the surrounding epidermis in the absence of trauma or a recent surgical procedure. Ulcerated melanomas typically show invasion through the epidermis, whereas nonulcerated melanomas tend to lift the overlying epidermis.

Only nontraumatic (“tumorigenic”) ulceration should be recorded as ulceration. If ulceration is present related to a prior biopsy, the tumor should not be recorded as ulcerated for staging purposes. If a lesion has been recently biopsied or there is only focal loss of the epidermis, assessment of ulceration may be difficult or impossible; in this instance it may be difficult to determine whether the epidermal deficiency is due to true ulceration or to sectioning artifact. Absence of fibrin, neutrophils, or granulation tissue from putative areas of ulceration would be clues that the apparent ulceration is actually due to sectioning of only part of the epidermis and this should not be designated as ulceration. If non-traumatic (“tumorigenic”) ulceration is present in either an initial partial biopsy or a re-excision specimen, then for staging purposes, the tumor should be recorded as ulcerated.

Ulceration may be present in an in situ melanoma but does not affect the staging.

A number of studies have demonstrated that the extent of ulceration (measured either as a percentage of the width of the dermal invasive component of the tumor or as a diameter) more accurately predicts outcome than the presence or absence of ulceration alone.

References

F. Microsatellite(s)
A microsatellite(s) is defined as the presence of a microscopic cutaneous metastasis found adjacent or deep to a primary melanoma on pathological examination of the primary tumor site. The metastatic tumor cells must be discontinuous from the primary tumor. If the tissue between the apparently separate nodule and the primary tumor is only fibrous scarring and/or inflammation, this does not indicate a microsatellite, because the aforementioned changes may represent regression of the intervening tumor (but not separated only by fibrosis or inflammation because the features could signify regression of the intervening tumor). There is no minimum size threshold or distance from the primary tumor to define a microsatellite. Before diagnosing the presence of a microsatellite, it is generally recommended that multiple sections from the same tissue block being examined to verify that the microsatellite is indeed discontinuous from the primary tumor. For example, periadnexal extension of tumor or the irregular shape of the peripheral or deep extent of the tumor may result in tumor that is contiguous with the primary tumor appear discontiguous on single sections.

References

G. Margins
Microscopically measured distances between tumor and labeled peripheral (lateral) or deep margins are appropriately recorded for melanoma excision specimens. If a margin is involved by tumor, it should be stated whether the tumor is in situ or invasive.

H. Mitotic Rate
Tumor mitotic rate (of the invasive component of a melanoma) is a strong independent predictor of outcome across its dynamic range in all thickness categories and should be assessed and recorded in all primary melanomas including in both initial and excision biopsies (the highest value in any specimen should be used for prognostic purposes). Although tumor mitotic rate is no longer used as a T1-category criterion in the 8th edition of the AJCC melanoma staging system (due to the more significant prognostic significance of the new tumor thickness strata within T1 melanoma), mitotic rate will likely be an important parameter in prognostic models developed in the future that will provide personalized prediction of prognosis for individual patients. The method recommended for enumerating the tumor mitotic rate in the 8th edition of the AJCC staging system is provided below:

“The recommended approach to enumerating mitoses is to first find the regions in the dermis containing the most mitotic figures, the so-called "hot spot" or "dermal hot spot." After counting the mitoses in the initial high-power field, the count is extended to immediately adjacent nonoverlapping fields until an area of tissue corresponding to 1 mm² is assessed. If no hot spot is found and mitoses are sparse and/or randomly scattered throughout the lesion, then a representative mitosis is chosen and, beginning with that field, the count is then extended to immediately adjacent nonoverlapping fields until an area corresponding to 1 mm² of tissue is assessed. The count then is expressed as the (whole) number of mitoses/mm². If the invasive component of the tumor involves an area less than 1 mm², the number of mitoses should be assessed and recorded as if they were found within square millimeter. For example, if the entire dermal component of a tumor occupies 0.5 mm² and only one mitosis is identified, the mitotic rate should be recorded as 1/mm² (not 2/mm²). The number of mitoses should be listed as a whole number per square millimeter. If no mitoses are identified, the mitotic rate may be recorded as “none identified” or “0/mm².” Only mitotic figures in invasive melanoma cells should be counted. This methodology for determining the mitotic rate of a melanoma has been shown to have excellent interobserver reproducibility, including among pathologists with widely differing experience in the assessment of melanocytic tumors.

To obtain accurate measurement, calibration of individual microscopes is recommended using a stage micrometer to determine the number of high-power fields that equates to a square millimeter.

The data that demonstrated the strong prognostic significance of mitotic rate were obtained from the melanoma pathology reports of routinely assessed H&E stained sections. It therefore is recommended that no additional sections be cut and examined in excess of those that would normally be used to report and diagnose the melanoma to determine the mitotic count (ie, no additional sections should be cut and examined for the sole purpose of determining the mitotic rate, including in situations in which no mitoses are identified on the initial, routinely examined sections). Immunohistochemical stains for identifying mitoses are not used for determining
mitotic rate for staging and/or reporting purposes. A possible exception is the use to dual immunohistochemistry (eg, MART1 and pHH3) to determine if a cell in mitosis is a melanocyte or not (macrophage, endothelial cell, etc).

Although the AJCC recommends reporting "0" rather than "none identified" or "less than 1," for the purposes of cancer registry reporting all of these terms should be considered equivalent.

References

I. Lymphovascular Invasion
Lymphovascular invasion is identified by the demonstration of melanoma cells within the lumina of blood vessels or lymphatics, or both. Immunohistochemistry for vascular endothelial cell markers CD31, CD34 or ERG or the lymphatic marker D2-40 may assist in the identification of the presence of intravascular or intralymphatic tumor by highlighting vascular lumina. Vascular invasion by melanoma correlates independently with worsened overall survival. The detection of LVI is increased in primary melanomas when double labeling of tumor cells and lymphatic endothelium is applied.

References

J. Neurotropism
Neurotropism is defined as the presence of melanoma cells abutting nerve sheaths usually circumferentially (perineural invasion) or within nerves (intraneuronal invasion). Occasionally, the tumor itself may form neur oid structures (termed 'neural transformation' and this is also regarded as neurotropism). Neurotropism is best identified at the periphery of the tumor; the presence of melanoma cells around nerves in the main tumor mass caused by "entrapment" of nerves in the expanding tumor does not represent neurotropism.

Neurotropism is most commonly identified in desmoplastic melanomas (sometimes termed desmoplastic neurotropic melanoma) but may occur in any melanoma subtype. Neurotropism may correlate with an increased risk for local recurrence.

References

K. Tumor-Infiltrating Lymphocytes
A paucity of tumor-infiltrating lymphocytes (TILs) is an adverse prognostic factor for cutaneous melanoma. Tumor-infiltrating lymphocytes may be assessed in a semiquantitative way, as defined below. To qualify as TILs, lymphocytes need to surround and disrupt tumor cells of the invasive component of the tumor.

TILs Not Identified: No lymphocytes present, or lymphocytes present but do not infiltrate tumor at all.
TILs Nonbrisk: Lymphocytes infiltrate melanoma only focally or not along the entire base of the invasive tumor.

TILs Brisk: Lymphocytes diffusely infiltrate the entire base of the invasive tumor (Figure 1, A) or show diffuse permeation of the invasive tumor (Figure 1, B).

References

Figure 1. Brisk tumor-infiltrating lymphocytes. A. Lymphocytes diffusely infiltrate the entire base of the invasive tumor. B. Lymphocytes diffusely infiltrate the entire invasive component of the melanoma.

L. Tumor Regression
Characteristic features of regression include replacement of tumor cells by lymphocytic inflammation, as well as attenuation of the epidermis and nonlaminated dermal fibrosis with inflammatory cells, melanophagocytosis, and telangiectasia.

M. Pathologic Stage Classification
The 8th edition AJCC Cancer Staging Manual includes the following elements of importance to practicing pathologists:

- T1a melanoma now defined as non-ulcerated melanomas less than 0.8mm thick
- T1b melanomas now defined as melanoma between 0.8mm and 1.0mm in thickness OR ulcerated melanomas less than 0.8mm thick
- Tumor mitotic rate no longer used as a T category criterion but remains an important prognostic factor and should be reported in all invasive primary melanomas
- Recommendation to record tumor thickness to the nearest 0.1mm (not the nearest 0.01mm)
- Non-nodal regional metastatic disease (ie, microsatellites, satellites and in transit metastases) now formally stratified by N category according to the number of tumor-involved nodes
- pT1bN0M0 is now pathologic stage IA in contrast to cT1N0M0 which remains clinical stage IB disease

In virtually all studies of cutaneous melanoma, tumor thickness has been shown to be a dominant prognostic factor, and it forms the basis for the stratification of pT. Although anatomic (Clark) levels are also commonly used to indicate depth of invasion of the primary tumor, they are less predictive of clinical outcome than mitotic activity or ulceration.
By AJCC convention, the designation “T” refers to a primary tumor that has not been previously treated. Similarly by convention, clinical staging is performed after biopsy of the primary melanoma (including utilizing pathologic information on microstaging of the primary melanoma) with clinical or biopsy assessment of regional lymph nodes and distant sites.\(^7\) Pathologic staging uses information gained from pathologic evaluation of both the primary melanoma after biopsy \textit{and} wide excision as well as pathological evaluation of the regional node basin after SLN biopsy (required for N categorization of all greater than T1 melanomas) \textit{and/or} complete regional lymphadenectomy.\(^1\) In additional, for pathological staging, if information from any prior biopsy is known and is relevant for staging, this should be documented in the pathology report (in the staging section) and used for assigning T, N and M categories and staging purposes.

### T Category Considerations
Pathologic (microscopic) assessment of the primary tumor is required for accurate staging. Therefore, excision of the primary tumor, rather than incisional biopsy, is advised. The T classification of melanoma is based on the thickness of the primary tumor and presence or absence of ulceration (see also Notes D, and E).

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

Post-therapy or post neoadjuvant therapy classification (yTNM) documents the extent of the disease for patients whose first course of therapy includes systemic or radiation treatment prior to surgical resection or when systemic therapy or radiation is primary treatment with no surgical resection. The extent of disease is classified using the same T, N, and M definitions and identified as post-treatment with a “yc” or “yp” prefix (ycT, ycN, ycTNM; ypT, ypN, ypTNM).

Recurrence or retreatment classification (rTNM) is used because information gleaned from therapeutic procedures and from extent of disease defined clinically may be prognostic for patients with recurrent cancer after a disease-free interval. It is important to understand that the rTNM classification does not change the original clinical or pathologic staging of the case.

Autopsy classification (aTNM) is used to stage cases of cancer not recognized during life and only recognized postmortem.

### Lymphovascular Invasion
Lymphovascular invasion (LVI) indicates whether microscopic lymphatic or vascular invasion is identified and includes lympathic invasion, blood vessel invasion, or invasion of a vessel for which it cannot be determined whether it is a blood or lymphatic vessel (Lymphovascular invasion). By AJCC/UICC convention, LVI does not affect the T category indicating local extent of tumor, ie, foci of Lymphovascular invasion should not be included in the measurement of tumor (Breslow) thickness.\(^8\)

### Pretreatment Serum Lactate Dehydrogenase and Serum Albumin
Data from numerous studies have indicated that an elevated serum level of lactate dehydrogenase (LDH) is an independent predictor of decreased survival in AJCC stage IV melanoma patients.

References
