Jeffrey E. Gershenwald, MD, FACS
Dr. John M. Skibber Professor, Department of Surgical Oncology
Professor, Department of Cancer Biology
Medical Director, Melanoma and Skin Center
Co-Leader Melanoma Moon Shot
Chair, AJCC Melanoma Expert Panel

2 February 2018

AJCC Physician to Physician
8th Edition
AJCC Melanoma Staging System

The New AJCC: 8th Edition and Beyond
American Joint Committee on Cancer (AJCC) 8th ed. Editorial Board Strategy

- Maintain anatomic extent of disease - TNM foundation
- Incorporate evidence-based non-anatomic factors, including molecular markers
- Era of precision medicine → evolution from a “population based” to a “more personalized” approach
- “One size fits all” model does not exist

AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

8th Edition Editorial Organization & Structure

Content Review Cores provide content review specific to their areas of expertise and sign-off prior to final submission.
Common Language

- AJCC  TNM staging is the common language of cancer
- Allows for worldwide consistency
- Essential for accurate communication
Melanoma Staging

- Principle communication tool
  - Clinician – patient
  - Clinician – clinician
  - Registry reporting: e.g., state, national, etc.
- Risk stratification defines groups of patients
- Treatment recommendations → often stage-based
- Clinical trial eligibility, stratification, analysis
- Translational/correlative science

AJCC 8th Edition Melanoma Staging System
Melanoma Expert Panel

**Surgical Oncology**
Jeffrey E. Gershenwald – Chair
Charles M. Balch
Karl Blimoria
David Byrd
Alexander M. Eggermont
Daniel G. Coit
Mark B. Faries
Merrick I. Ross
Vernon K. Sondak
John F. Thompson
Sandra L. Wong

**Dermatology**
Claus Garbe
Allan C. Halpern
Timothy Johnson
Arthur J. Sober

**Pathology**
Richard A. Scolyer – Vice-Chair
Raymond Barnhill
Alistair Cochran
David E. Elder
Alexander J. Lazar
Martin C. Mihm, Jr.
Victor G. Prieto

**Medical Oncology**
Michael B. Atkins
Antonio Buzaid
Paul Chapman
Keith T. Flaherty
John M. Kirkwood
Anne W.M. Lee – UICC representative
Georgina V. Long
Grant A. McArthur

**Biostatistics**
Kenneth Hess – Lead Biostatistician
Phyllis A. Gimotty

**Radiology**
Richard L. Wahl

**Radiation Oncology**
James Brierley – UICC Co-Chair

**MD Anderson International Database and Discovery Platform (IMDDP)**
Lauren E. Haydu
Julie Gardner
AJCC 8th Edition Melanoma Staging System

International Database Contributors – Wave I

- Newly created international database housed at MD Anderson
- 1998+
- Stages I-III
- N>49,000 patients
- US, Australia, Europe (Italy, Greece, Spain)
- Additional sites onboarding for planned tool development


Melanoma Staging: Evidence-Based Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual

Jeffrey E. Gershenwald, MD; Richard A. Scolyer, MD; Kenneth R. Hess, PhD; Vernon K. Sondak, MD; Georgina V. Long, MBBS, PhD; Merrick I. Ross, MD; Alexander J. Lazar, MD, PhD; Mark B. Faries, MD; John M. Kirkwood, MD; Grant A. McArthur, MD, BS, PhD; Lauren E. Haydu, PhD; Alexander M. Eggermont, MD, PhD; Keith T. Flaherty, MD; Charles M. Balch, MD; John F. Thompson, MD; for members of the American Joint Committee on Cancer Melanoma Expert Panel and the International Melanoma Database and Discovery Platform

Melanoma Clinical Classification
T category

By convention, cT is performed after biopsy of the primary melanoma (including primary tumor microstaging) with clinical or biopsy assessment of regional lymph nodes

Assessing the Primary (T)

- By convention, clinical staging is performed:
  - after biopsy of the primary melanoma (including primary tumor microstaging) AND
  - clinical or biopsy assessment of regional LNs

- Pathological staging uses information gained from both:
  - microstaging of the primary melanoma AND
  - Microstaging of the wide excision AND
  - Pathological evaluation of the regional node basin after SLN biopsy (required for >T1 melanomas) and/or complete regional lymphadenectomy
Melanoma Wide Excision:
Assessing margins and extent of surgery

Primary Melanoma – Wide Excision

Melanoma biopsy site
## Primary Tumor (T) - 8th Edition

- **Impracticality/imprecision of tumor thickness measurements to nearest 0.01mm, esp. for tumors >1mm thick**
- **Recorded to nearest 0.1mm (not nearest 0.01mm)**
- **Tumors ≤1mm:**
  - May be measured to nearest 0.01mm
  - Reported rounded to the nearest 0.1mm.
  - **Examples:**
    - 0.75mm to 0.84mm → reported as 0.8mm (T1b)
    - 1.04mm → reported as 1.0mm (T1b)
AJCC 8th Edition
Primary Tumor (T)

- T1 - subcategorized by tumor thickness strata at 0.8-mm threshold.
- Tumor mitotic rate (MR) – removed as a T1 staging criterion
  - MR should be collected for all invasive melanomas and will be employed for clinical tool development


7th Edition AJCC Stages I/II Survival by # of mitoses (per mm²)

- Univariate 5-year survival → 59%-98%
- Multivariate analysis – mitotic rate 2nd most powerful independent predictor of survival after tumor thickness

©2011 by American Society of Clinical Oncology
Thompson et al., J Clin Oncol, 1 June 2011
### Definition of Primary Tumor (T) - AJCC 8th Edition

<table>
<thead>
<tr>
<th>T Category</th>
<th>Thickness</th>
<th>Ulceration status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis (melanoma in situ)</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>T1</td>
<td>≤1.0 mm</td>
<td>Unknown or unspecified</td>
</tr>
<tr>
<td>T1a</td>
<td>&lt;0.8 mm</td>
<td>Without ulceration</td>
</tr>
<tr>
<td>T1b</td>
<td>&lt;0.8 mm</td>
<td>With ulceration</td>
</tr>
<tr>
<td></td>
<td>0.8–1.0 mm</td>
<td>With or without ulceration</td>
</tr>
<tr>
<td>T2</td>
<td>&gt;1.0–2.0 mm</td>
<td>Unknown or unspecified</td>
</tr>
<tr>
<td>T2a</td>
<td>&gt;1.0–2.0 mm</td>
<td>Without ulceration</td>
</tr>
<tr>
<td>T2b</td>
<td>&gt;1.0–2.0 mm</td>
<td>With ulceration</td>
</tr>
<tr>
<td>T3</td>
<td>&gt;2.0–4.0 mm</td>
<td>Unknown or unspecified</td>
</tr>
<tr>
<td>T3a</td>
<td>&gt;2.0–4.0 mm</td>
<td>Without ulceration</td>
</tr>
<tr>
<td>T3b</td>
<td>&gt;2.0–4.0 mm</td>
<td>With ulceration</td>
</tr>
<tr>
<td>T4</td>
<td>&gt;4.0 mm</td>
<td>Unknown or unspecified</td>
</tr>
<tr>
<td>T4a</td>
<td>&gt;4.0 mm</td>
<td>Without ulceration</td>
</tr>
<tr>
<td>T4b</td>
<td>&gt;4.0 mm</td>
<td>With ulceration</td>
</tr>
</tbody>
</table>
Unknown Primary or No Evidence of Primary

- **T0**
  - No evidence of primary tumor
  - Primary site of tumor is unknown
  - Staging based on clinical suspicion of primary organ site
  - T0 not available in all sites, cannot suspect primary from nodes/mets

- **Example**
  - Metastatic melanoma to an axillary lymph node
  - No evidence of primary tumor
  - T0

<table>
<thead>
<tr>
<th>When T is...</th>
<th>And N is...</th>
<th>And M is...</th>
<th>Then the pathological stage group is...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
<td>0</td>
</tr>
<tr>
<td>T1a</td>
<td>N0</td>
<td>M0</td>
<td>IA</td>
</tr>
<tr>
<td>T1b</td>
<td>N0</td>
<td>M0</td>
<td>IA</td>
</tr>
<tr>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
<td>IB</td>
</tr>
<tr>
<td>T2b</td>
<td>N0</td>
<td>M0</td>
<td>IIA</td>
</tr>
<tr>
<td>T3a</td>
<td>N0</td>
<td>M0</td>
<td>IIA</td>
</tr>
<tr>
<td>T3b</td>
<td>N0</td>
<td>M0</td>
<td>IIB</td>
</tr>
<tr>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
<td>IIB</td>
</tr>
<tr>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
<td>IIC</td>
</tr>
</tbody>
</table>
Stages I/II MSS by T category & T stage group


Stages I/II survival curves by T-category

AJCC N Category Criteria

Clinically occult regional lymph nodes (SLN+)

Clinically detected regional lymph nodes

In-transits, satellites, & microsatellites

Regional spread of tumor via lymphatic vessels in the dermis or subcutaneous tissue outside of nodal basins usually between primary and regional nodal basin

Includes the entire biologic spectrum of:
- local metastases
- satellites
- In-transits

Gershenwald, MDACC
Assessing Regional Disease (N)

- By convention, clinical staging is performed:
  - after biopsy of the primary melanoma (including primary tumor microstaging) AND
  - clinical or biopsy assessment of regional LNs

- Pathological staging uses information gained from both:
  - microstaging of the primary melanoma AND
  - Microstaging of the wide excision AND
  - Pathological evaluation of the regional node basin after SLN biopsy (required for >T1 melanomas) and/or complete regional lymphadenectomy

AJCC 8th Edition N-category

- Regional nodes
- Non-nodal regional disease
  - In-transits (ITM)
  - Satellites
  - Microsatellites
- Microsatellites/satellites/ITM grouped together for staging purposes

### AJCC 8th Edition N-category criteria

<table>
<thead>
<tr>
<th>N Category</th>
<th>Number of tumor-involved regional lymph node</th>
<th>Presence of in-transit, satellite, and/or microsatellite metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional metastases detected</td>
<td>No</td>
</tr>
<tr>
<td>N1</td>
<td>One tumor-involved node or in-transit, satellite, and/or microsatellite metastases with no tumor-involved nodes</td>
<td></td>
</tr>
<tr>
<td>N1a</td>
<td>One clinically occult (i.e., detected by SLN biopsy)</td>
<td>No</td>
</tr>
<tr>
<td>N1b</td>
<td>One clinically detected</td>
<td>No</td>
</tr>
<tr>
<td>N1c</td>
<td>No regional lymph node disease</td>
<td>Yes</td>
</tr>
<tr>
<td>N2</td>
<td>Two or three tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with one tumor-involved node</td>
<td></td>
</tr>
<tr>
<td>N2a</td>
<td>Two or three clinically occult (i.e., detected by SLN biopsy)</td>
<td>No</td>
</tr>
<tr>
<td>N2b</td>
<td>Two or three, at least one of which was clinically detected</td>
<td>No</td>
</tr>
<tr>
<td>N2c</td>
<td>One clinically occult or clinically detected</td>
<td>Yes</td>
</tr>
<tr>
<td>N3</td>
<td>Four or more tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with two or more tumor-involved nodes, or any number of mutant nodes without or with in-transit, satellite, and/or microsatellite metastases</td>
<td></td>
</tr>
<tr>
<td>N3a</td>
<td>Four or more clinically occult (i.e., detected by SLN biopsy)</td>
<td>No</td>
</tr>
<tr>
<td>N3b</td>
<td>Four or more, at least one of which was clinically detected, or presence of any number of mutant nodes</td>
<td>No</td>
</tr>
<tr>
<td>N3c</td>
<td>Two or more clinically occult or clinically detected and/or presence of any number of mutant nodes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

- Updated nomenclature – regional LN
- microscopic → clinically occult (“a”)
- macroscopic → clinically detected (“b”)
- N1a/b, N2a/b, N3a/b unchanged


### AJCC 8th Edition N-category criteria

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<td></td>
</tr>
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<td>One clinically occult (i.e., detected by SLN biopsy)</td>
<td>No</td>
</tr>
<tr>
<td>N1b</td>
<td>One clinically detected</td>
<td>No</td>
</tr>
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</tr>
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<tr>
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<td>Four or more, at least one of which was clinically detected, or presence of any number of mutant nodes</td>
<td>No</td>
</tr>
<tr>
<td>N3c</td>
<td>Two or more clinically occult or clinically detected and/or presence of any number of mutant nodes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

- Presence of microsatellites, satellites, or in-transit metastases categorized as N1c, N2c, or N3c based on # of tumor-involved regional lymph nodes

MSS according to Stage III Groups
8th Edition international melanoma database

- Stage group stratification based on both T- and N-category criteria
  - Tumor thickness
  - Ulceration
  - # LNs
  - Microsatellite/ITM/satellites
- Recursive partitioning → final = 4 stage groups
- Significant heterogeneity

MSS according to AJCC Stage III Group

**AJCC 8th Edition**

- IIIA
- IIIB
- IIIC
- IIID

**AJCC 7th Edition**

- IIIA (n=1,196)
- IIIB (n=1,391)
- IIIC (n=720)

Implications for Patient Counseling, Management & Contemporary Adjuvant Clinical Trial Design

---


**Principles of Cancer Staging**

Donna M. Gress, Stephen B. Edge, Frederick L. Greene,
Mary Kay Washington, Elliot A. Asare, James D. Brierley,
David R. Byrd, Carolyn C. Compton, J. Milburn Jessup,
David P. Winchester, Mahul B. Amin,
and Jeffrey E. Gershenwald

**Introduction and Overview**

The extent or stage of cancer at the time of diagnosis is a key factor that defines prognosis and is a critical element in determining appropriate treatment based on the experience and outcomes of groups of previous patients with similar stage. In addition, cancer stage often is a key component of inclusion, exclusion, and stratification criteria for clinical trials. Indeed, accurate staging is necessary to evaluate the results of treatments and clinical trials, to facilitate the

**Philosophy of Revisions to the TNM Staging System**

The AJCC and UICC periodically modify the AJCC TNM staging system in response to newly acquired clinical and pathological data and an improved understanding of cancer biology and other factors affecting prognosis. Periodic and, to the extent possible, evidence-based revision is a key feature that makes this staging system the most clinically useful among staging systems and accounts for its
### Sentinel Node, FNA or Core Biopsy

<table>
<thead>
<tr>
<th>Sentinel node (sn) and FNA or core biopsy (f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>If SLN biopsy is performed in the absence of complete dissection of the nodal basin:</td>
</tr>
<tr>
<td>• the N category should have the sn suffix; for example, pN0(sn).</td>
</tr>
<tr>
<td>If FNA or core biopsy is performed in the absence of a complete dissection of the nodal basin:</td>
</tr>
<tr>
<td>• the N category should have the f suffix; for example, pN0(f).</td>
</tr>
<tr>
<td><strong>Note:</strong> This distinguishes it from a complete nodal dissection, for which the pN is assigned without the (sn) or (f) suffix.</td>
</tr>
</tbody>
</table>

#### N Suffixes: (sn) and (f) Method of Assessment

- **(sn) sentinel node procedure indication**
  - Diagnostic workup & before definitive surgical treatment, cN1–3(sn)
  - Part of initial surgical management, pN1–3(sn)
  - **Note:** suffix NOT used if completion lymph node dissection performed as component of initial surgical management

- **(f) FNA or core needle biopsy of node indication**
  - Diagnostic workup before treatment, cN1–3(f)
  - Part of primary site surgical resection, pN1–3(f)
  - **Note:** suffix NOT used if subsequent completion lymph node dissection as component of initial surgical management
N category-specific Data Collection Variables

- Microsatellites (pathologically detected, not clinically apparent (yes/no)
- In-transit and/or satellite metastasis (in-transit, satellite, both)
- Regional lymph node clinically or radiographically detected (yes/no)
- Microscopic confirmation of tumor metastasis in any regional lymph node clinically or radiologically detected (yes/no)

—

Lymphatic Mapping & Sentinel Node Biopsy

- Lymphatic drainage of finite regions of skin drain specifically to an initial node within a nodal basin - the “SENTINEL NODE”
- Different regions of the skin will drain to different SENTINEL NODES
- Represent most likely node(s) to contain metastatic disease

SLN Micrometastasis

Gershenwald et al., J Clin Oncol, 1999
N category-specific Data Collection Variables

- SLN biopsy performed (yes/no)
- # of nodes examined from sentinel node procedure (whole #)
- # of tumor-involved nodes from sentinel node procedure (whole #)
- Sentinel node tumor burden (largest dimension of largest discrete deposit in xx.x mm)
- ENE in any tumor-involved regional lymph node (LN) (sentinel or clinically detected) (present or absent)
- Completion or therapeutic lymph node dissection performed (yes/no)
- # of LNs examined and # LNs involved from LN dissection
- Matted nodes (yes/no)

Melanoma Distant Metastases M1
Distant Metastasis (M)

- M1 - defined by both anatomic site of distant metastatic disease and serum lactate dehydrogenase (LDH) value for all anatomic site subcategories.


- New M1d designation - includes distant metastasis to the central nervous system (CNS) with or without other distant sites of disease

- M1c – no longer includes CNS metastasis

Distant Metastasis (M)

- Elevated LDH - no longer defines M1c
- Suffixes for M category: (0) LDH not elevated, (1) LDH elevated.
- No suffix is used if LDH is not recorded or is unspecified.


<table>
<thead>
<tr>
<th>M Category</th>
<th>Anatomic site</th>
<th>LDH level</th>
<th>M Category</th>
<th>Anatomic site</th>
<th>LDH level</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No evidence of distant metastasis</td>
<td>Not applicable</td>
<td>M1c</td>
<td>Distinct metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease</td>
<td>Not recorded or unspecified</td>
</tr>
<tr>
<td>M1</td>
<td>Evidence of distant metastasis</td>
<td>See below</td>
<td>M1c(0)</td>
<td>Distinct metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease</td>
<td>Not elevated</td>
</tr>
<tr>
<td>M1a</td>
<td>Distinct metastasis to skin, soft tissue including muscle, and/or nonregional lymph node</td>
<td>Not recorded or unspecified</td>
<td>M1c(1)</td>
<td>Distinct metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease</td>
<td>Elevated</td>
</tr>
<tr>
<td>M1a(0)</td>
<td></td>
<td></td>
<td>M1d</td>
<td>Distinct metastasis to CNS with or without M1a, M1b, or M1c sites of disease</td>
<td>Not recorded or unspecified</td>
</tr>
<tr>
<td>M1a(1)</td>
<td></td>
<td></td>
<td>M1d(0)</td>
<td>Distinct metastasis to CNS with or without M1a, M1b, or M1c sites of disease</td>
<td>Normal</td>
</tr>
<tr>
<td>M1b</td>
<td>Distinct metastasis to lung with or without M1a sites of disease</td>
<td>Not recorded or unspecified</td>
<td>M1d(1)</td>
<td>Distinct metastasis to CNS with or without M1a, M1b, or M1c sites of disease</td>
<td>Elevated</td>
</tr>
<tr>
<td>M1b(0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M1b(1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Additional Factors Recommended for Clinical Care

- Primary tumor mitotic rate
- Level of invasion (Clark level)
- Tumor-infiltrating lymphocytes – absent/nonbrisk/brisk
- Lymphovascular invasion
- Neurotropism
- Melanoma SLN tumor burden
- Extranodal Extension (ENE)
- # of distant metastases

New Features: Precision Medicine Vision

• Prognostic factors
  – Required for prognostic stage grouping
  – Recommended for clinical care
  – Emerging factors (online only)

• Risk Assessment Models for select cancer sites

• Recommendations for Clinical Trial Stratification

Online AJCC Content to Improve Staging Accuracy
“Work in progress”

• Emerging Prognostic Factors for Clinical Care

• Risk Assessment Models

• Recommendations for Clinical Trial Stratification

https://cancerstaging.org/references-tools/deskreferences/Pages/Supplementary-Material.aspx
Classifications

• Stage may be defined at several time points in the care of the cancer patient.

• Time points are termed classifications and are based on the continuum of evaluation
  – Clinical (cTNM)
  – Pathological (pTNM)
  – Post therapy (ycTNM or ypTNM)
  – Recurrence (rTNM)
  – Autopsy (aTNM)

• The staging classifications have a different purpose and therefore can be different. Do not go back and change the clinical staging based on pathologic staging information.

POST NEOADJUVANT THERAPY STAGING CLASSIFICATION RULES

• yc Clinical
  – Includes physical exam and imaging assessment
  – After neoadjuvant systemic/radiation therapy

• yp Pathological
  – Includes all information from yc staging,
  – Surgeon’s operative findings and
  – Pathology report from resected specimen
Clinical Tools and the 8th Edition AJCC Staging System

Critical assessment of clinical prognostic tools in melanoma

- Systematic search of the published literature web-based resources.
- A priori criteria were used to evaluate quality and clinical relevance
- **Results**: 17 clinical prognostic tools for primary cutaneous melanoma.
  - Patients with stages I-III and T1 or thin melanoma were the most frequently considered populations.
  - 75% of tools developed using data collected from patients diagnosed in 2005 or earlier.
  - Well-established factors tumor thickness, ulceration, and age were included in 70% of tools.
  - Internal validity using cross-validation or bootstrapping techniques was performed for two tools only
  - Fewer than half were evaluated for external validity

- **Conclusions**: *Great opportunity to improve these tools* and to foster the development of new, validated tools by the inclusion of contemporary clinicopathological covariates and by using improved statistical and methodological approaches

Mahar A et al., Ann Surg Oncol, 2016
AJCC Precision Medicine Core and Quality Risk Models in the Modern Clinical Arena

- Prediction models (diagnostic or prognostic) are important
- Overwhelming evidence → poor quality of reporting of prediction models
- Recognition of the need for more personalized probabilistic predictions than those delivered by ordinal staging systems
  - **Goal**: accurate risk models/calculators


- 13 inclusion criteria
- 3 exclusion criteria

Soong et al., Ann Surg Oncol, 2010
Towards “Next-Gen” Molecular Classification & Staging in Melanoma

• Significant prognostic/predictive capacity driven principally by *clinicopathological* evidence-based risk-stratification

• Tremendous strides in our understanding of the molecular/immunologic underpinnings and heterogeneity of melanoma

Melanoma Staging/Prognosis in the Era of Precision Medicine Next Steps and Future Directions

• 8th Ed. AJCC melanoma staging system available in print (Springer/Amazon) → implementation January 1, 2018

• Planned:
  • Development and implementation of educational tools
  • Integration with electronic EHRs

• Integration of molecular and additional clinicopathological biomarkers

• Development of validated clinical tools → enhance decision-making
  • Time-dependent – eg, OS, MSS, DFS, DMFS, conditional surv.
  • Time-independent – eg, SLN status, Additional non-SLNs
  • Current era Stage IV

*Additional collaborating centers/registries welcome*
Assigning Stage:
The Role of the Managing Physician

• Staging requires the collaborative effort of many professionals, including the managing physician, pathologist, radiologist, cancer registrar and others

• While the pathologist and the radiologist provide important staging information, and may provide important T-, N-, and/or M-related information, stage is defined ultimately from the synthesis of an array of patient history and physical examination findings supplemented by imaging and pathology data

• Only the managing physician can assign the patient’s stage, since only (s) he routinely has access to all of the pertinent information from the physical exam, imaging studies, biopsies, diagnostic procedures, surgical findings, and pathology reports