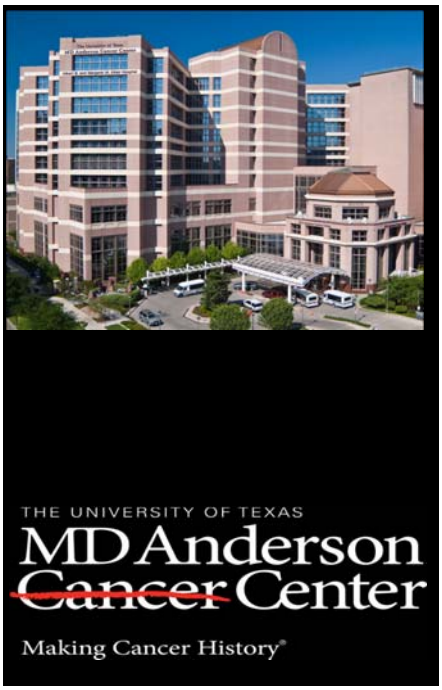


AJCC Physician to Physician

8th Edition AJCC Melanoma Staging System

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

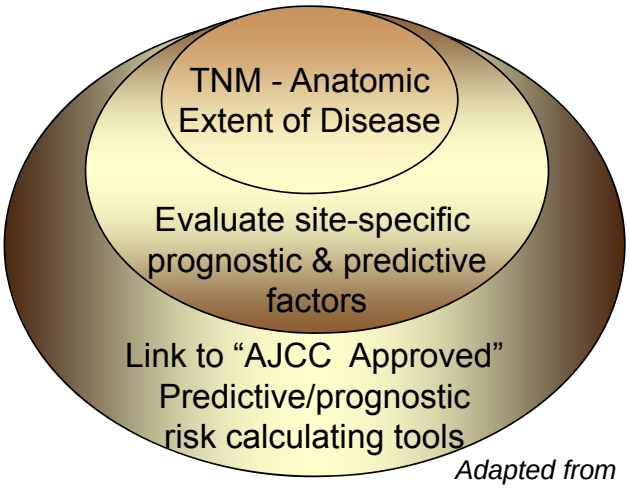
2 February 2018

The New AJCC: 8th Edition and Beyond

AJCC
American Joint Committee on Cancer
Validating science. Improving patient care.

American Joint Committee on Cancer (AJCC) 8th ed. Editorial Board Strategy

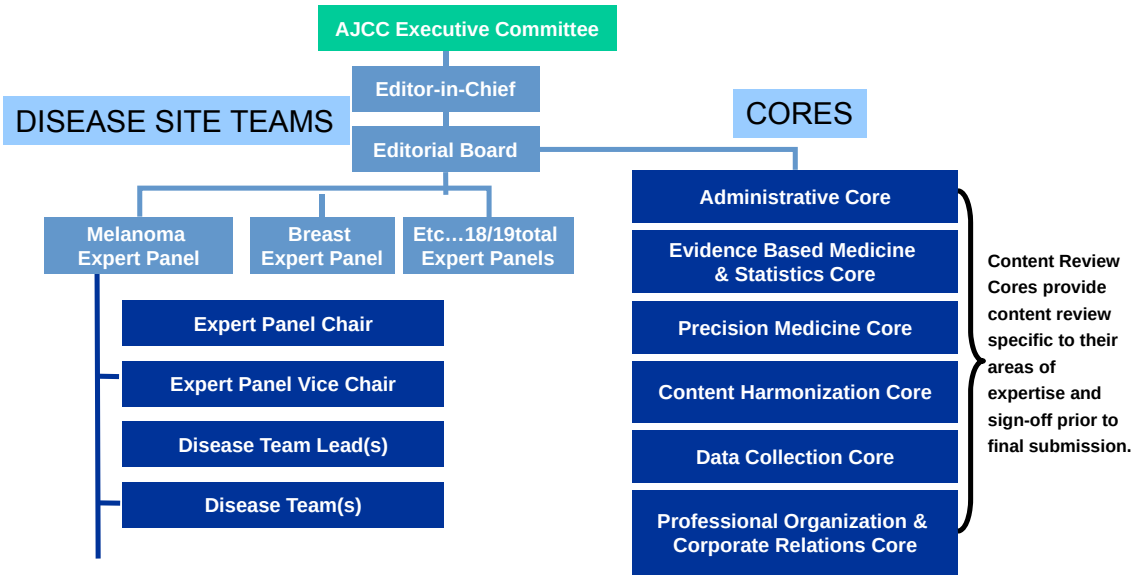
- Maintain anatomic extent of disease - TNM foundation
- Incorporate evidence-based non-anatomic factors, including molecular markers
- Era of precision medicine → evolution from a "population based" to a "more personalized" approach
- "One size fits all" model does not exist



Adapted from Mahul Amin

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

8th Edition Editorial Organization & Structure



AJCC Cancer Staging 8th Edition

Melanoma of the Skin

AJCC

American Joint Committee on Cancer

Validating science. Improving patient care.

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

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AJCC 8th Edition Melanoma Staging System Melanoma Expert Panel

Surgical Oncology
Jeffrey E. Gershenwald – Chair
Charles M. Balch
Karl Bilimoria
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

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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

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., Edge, S.B., Greene, F.L., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. NY: Springer;

CA
A Cancer Journal for Clinicians

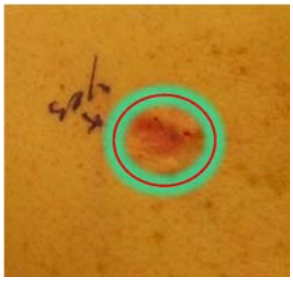
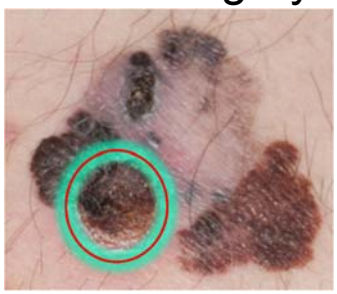
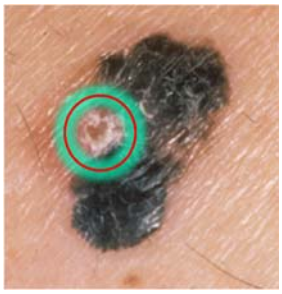
CA CANCER J CLIN 2017;00:00–00

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

Jeffrey E. Gershenwald, MD [1†]; Richard A. Scolyer, MD [2,3†]; Kenneth R. Hess, PhD [4†]; Vernon K. Sondak, MD [5]; Georgina V. Long, MBBS, PhD [6]; Merrick I. Ross, MD [7]; Alexander J. Lazar, MD, PhD [8]; Mark B. Faries, MD [9]; John M. Kirkwood, MD [10]; Grant A. McArthur, MD, BS, PhD [11]; Lauren E. Haydu, PhD [12]; Alexander M. M. Eggermont, MD, PhD [13]; Keith T. Flaherty, MD [14]; Charles M. Balch, MD [15]; John F. Thompson, MD [16]; for members of the American Joint Committee on Cancer Melanoma Expert Panel and the International Melanoma Database and Discovery Platform

Gershenwald, Scolyer, Hess, Sondak et al. CA Cancer J Clin. 2017 Oct 13. doi: 10.3322/caac.21409. [Epub ahead of print]

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

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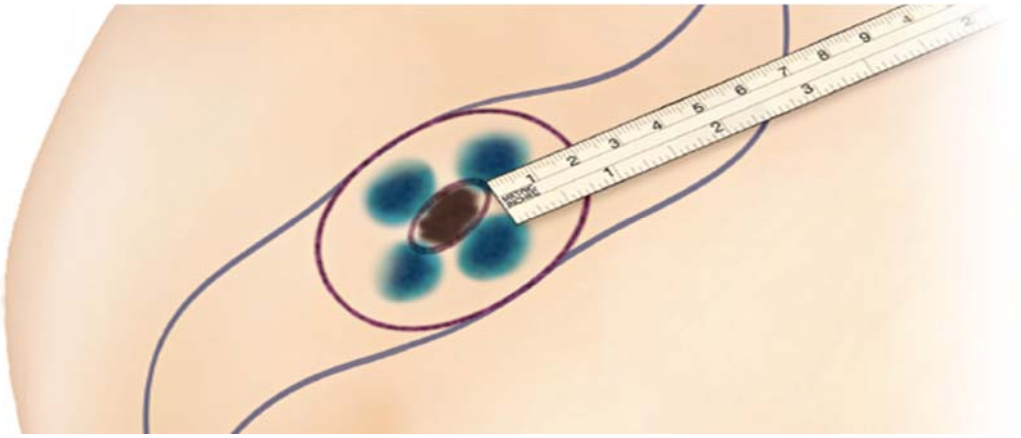
Assessing the Primary (T)

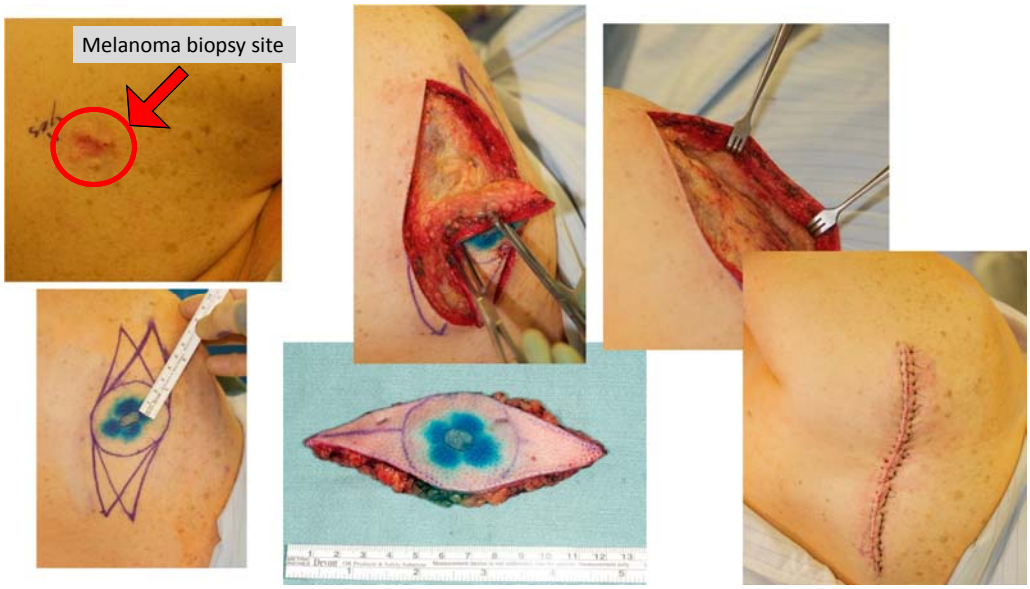
- By convention, clinical staging is performed:
  - after biopsy of the primary melanoma (including primary tumor microstaging) AND
  - clinical or biopsy assessment of regional LNs
- Pathological staging uses information gained from *both:*
  - microstaging of the primary melanoma AND
  - Microstaging 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



2010 AJCC T Classification
7th Edition

Stage	Breslow Thickness (mm)	Definition
T1	≤1.00	a: No ulceration and <1 mitosis/mm^2 b: Ulceration or ≥1 mitosis/mm^2
T2	1.01-2.00	a: No ulceration b: Ulceration
T3	2.01-4.00	a: No ulceration b: Ulceration
T4	> 4.00	a: No ulceration b: Ulceration

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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)

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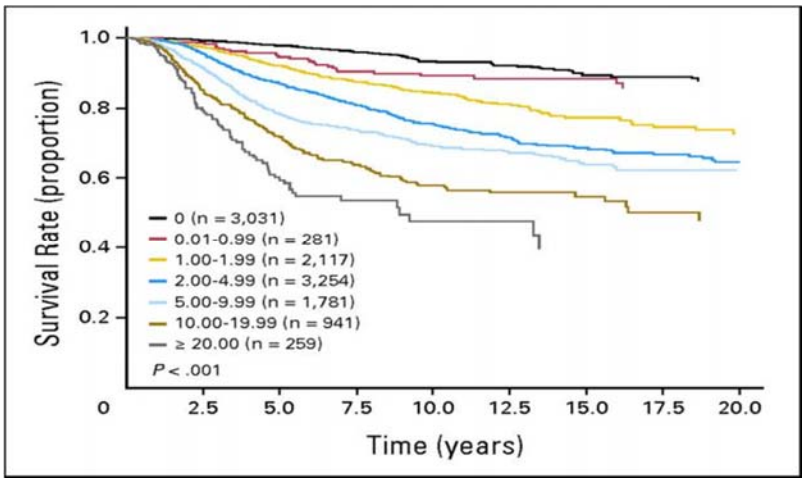
AJCC 8th Edition
Primary Tumor (T)

- 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

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., Edge, S.B., Greene, F.L., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

7th Edition AJCC Stages I/II Survival by # of mitoses (per mm^2)



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

Thompson et al., J Clin Oncol, 1 June 2011

Definition of Primary Tumor (T) - AJCC 8th Edition

T Category	Thickness	Ulceration status
Tis (melanoma *in situ*)	Not applicable	Not applicable
T1	≤1.0 mm	Unknown or unspecified
T1a	<0.8 mm	Without ulceration
T1b	<0.8 mm 0.8–1.0 mm	With ulceration With or without ulceration
T2	>1.0–2.0 mm	Unknown or unspecified
T2a	>1.0–2.0 mm	Without ulceration
T2b	>1.0–2.0 mm	With ulceration
T3	>2.0-4.0 mm	Unknown or unspecified
T3a	>2.0–4.0 mm	Without ulceration
T3b	>2.0–4.0 mm	With ulceration
T4	>4.0 mm	Unknown or unspecified
T4a	>4.0 mm	Without ulceration
T4b	>4.0 mm	With ulceration

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., Edge, S.B., Greene, F.L., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

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Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., Edge, S.B., Greene, F.L., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

Unknown Primary or No Evidence of Primary

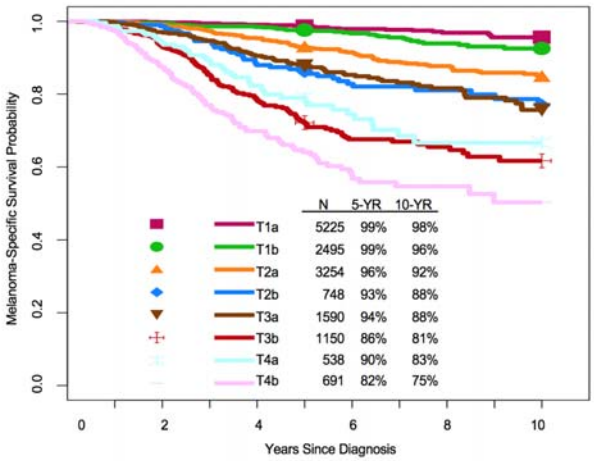
- T0
  - No evidence of primary tumor
  - Primary site of tumor is unknown
  - Staging based on clinical suspicion of primary organ site
  - T0 not available in all sites, cannot suspect primary from nodes/mets

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

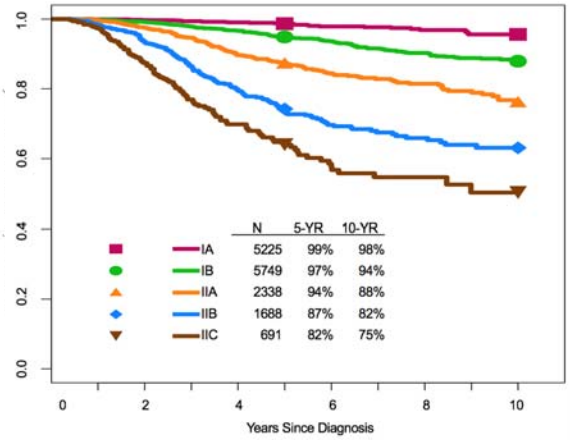
When T is…	And N is…	And M is…	Then the pathological stage group is…
Tis	N0	M0	0
T1a	N0	M0	IA
T1b	N0	M0	IA
T2a	N0	M0	IB
T2b	N0	M0	IIA
T3a	N0	M0	IIA
T3b	N0	M0	IIB
T4a	N0	M0	IIB
T4b	N0	M0	IIC

Stages I/II MSS by T category & T stage group

T category



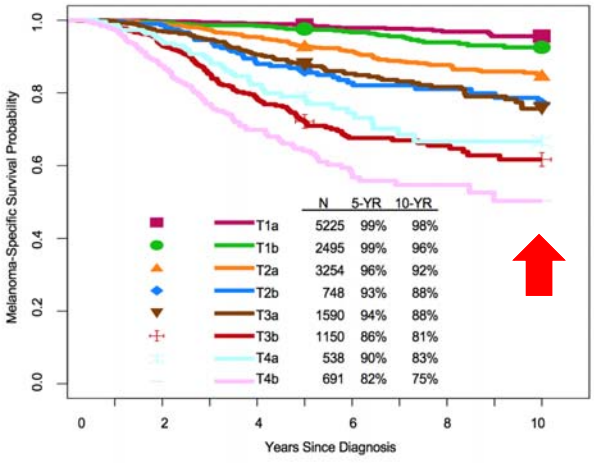
T stage group



Gershenwald, Scolyer, Hess, Sondak et al. CA Cancer J Clin. 2017 Oct 13. doi: 10.3322/caac.21409. [Epub ahead of print]

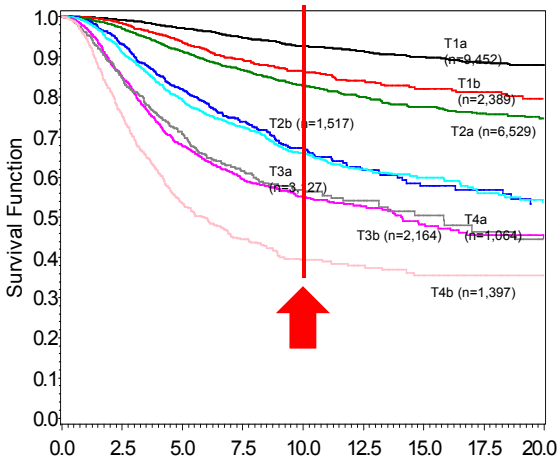
Stages I/II survival curves by T-category

8th edition



CA Cancer J Clin. 2017 Oct 13. [Epub ahead of print]

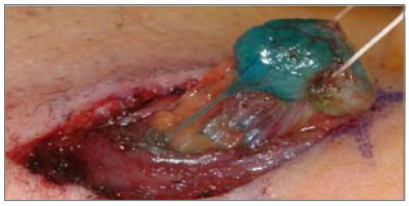
7th edition

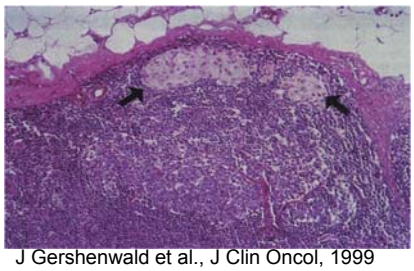


AJCC 7th edition, 2009

AJCC N Category Criteria

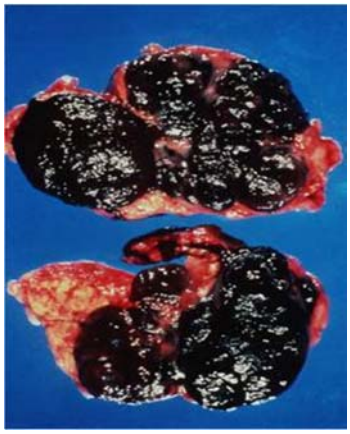
Clinically occult regional lymph nodes (SLN+)



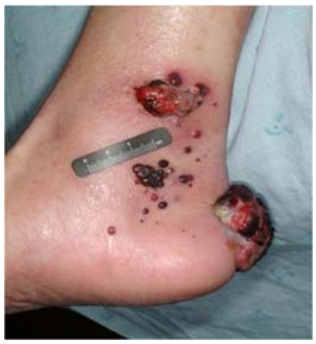


J Gershenwald et al., J Clin Oncol, 1999

Clinically detected regional lymph nodes



In-transits, satellites, & microsatellites



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Satellite & In-transit Disease

- 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

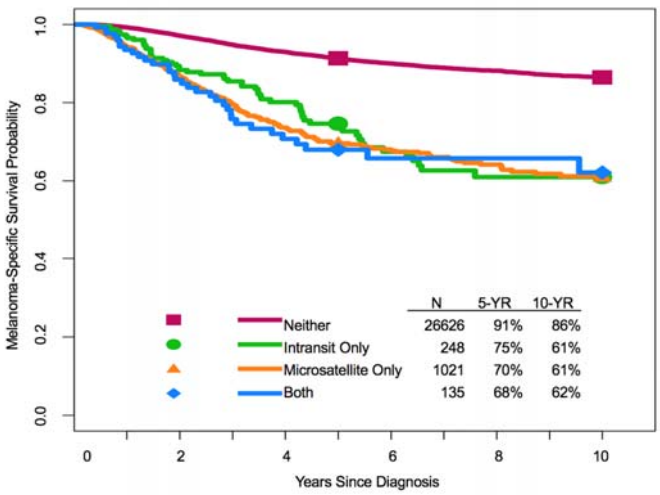
Gershenwald, MDACC

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



Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., Edge, S.B., Greene, F.L., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed.; 2017

AJCC 8th Edition N-category criteria

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

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

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

AJCC 8th Edition N-category criteria

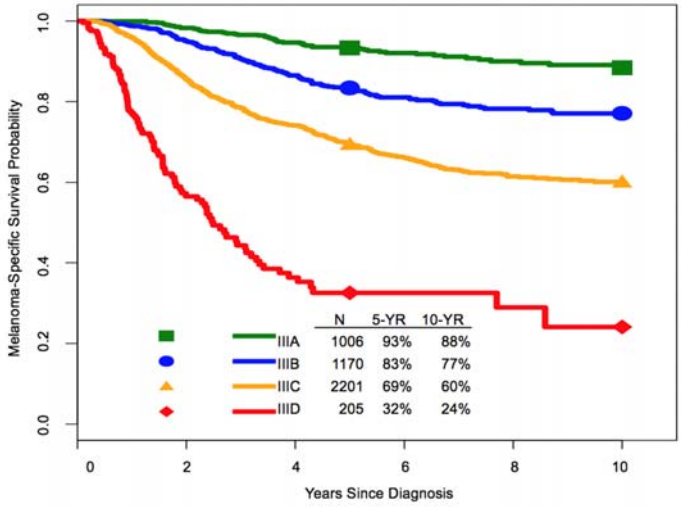
N Category	Number of tumor-involved regional lymph node	Presence of in-transit, satellite, and/or microsatellite metastases
N0	No regional metastases detected	No
N1	One tumor-involved node or in-transit, satellite, and/or microsatellite metastases with no tumor-involved nodes	
N1a	One clinically occult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

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

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

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



Gershenwald, Scolyer, Hess, Sondak et al. CA Cancer J Clin. 2017 Oct 13. doi: 10.3322/caac.21409. [Epub ahead of print]

AJCC Stage III Stage Groups

When T is…	And N is…	And M is…	Then the pathological stage group is…
T1a/b–T2a	N1a or N2a	M0	IIIA
T1a/b–T2a	N1b/c or N2b	M0	IIIB
T2b/T3a	N1a–N2b	M0	IIIB
T1a–T3a	N2c or N3a/b/c	M0	IIIC
T3b/T4a	Any N ≥N1	M0	IIIC
T4b	N1a–N2c	M0	IIIC
T4b	N3a/b/c	M0	IIID
T0	N1b, N1c	M0	IIIB
T0	N2b, N2c, N3b or N3c	M0	IIIC

AJCC Eighth Edition
Melanoma Stage III Subgroups

N Category	T Category								
	T0	T1a	T1b	T2a	T2b	T3a	T3b	T4a	T4b
N1a	N/A	A	A	A	B	B	C	C	C
N1b	B	B	B	B	B	B	C	C	C
N1c	B	B	B	B	B	B	C	C	C
N2a	N/A	A	A	A	B	B	C	C	C
N2b	C	B	B	B	B	B	C	C	C
N2c	C	C	C	C	C	C	C	C	C
N3a	N/A	C	C	C	C	C	C	C	D
N3b	C	C	C	C	C	C	C	C	D
N3c	C	C	C	C	C	C	C	C	D

Instructions
(1) Select patient's N category at left of chart.
(2) Select patient's T category at top of chart.
(3) Note letter at the intersection of T&N on grid.
(4) Determine patient's AJCC stage using legend.

N/A=Not assigned, please see manual for details. REF

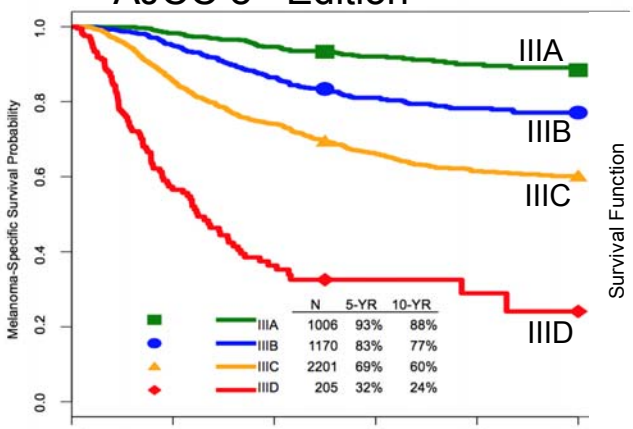
Legend

A	Stage IIIA
B	Stage IIIB
C	Stage IIIC
D	Stage IIID

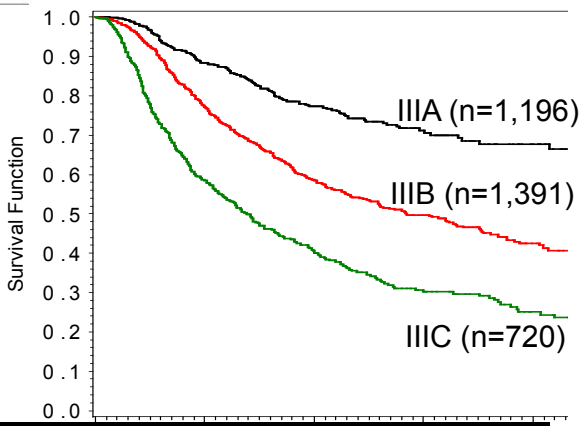
Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., Edge, S.B., Greene, F.L., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed., 2017
Gershenwald, Scolyer, Hess, Sondak et al. CA Cancer J Clin. 2017 Oct 13. doi: 10.3322/caac.21409. [Epub ahead of print]

MSS according to AJCC Stage III Group

AJCC 8th Edition

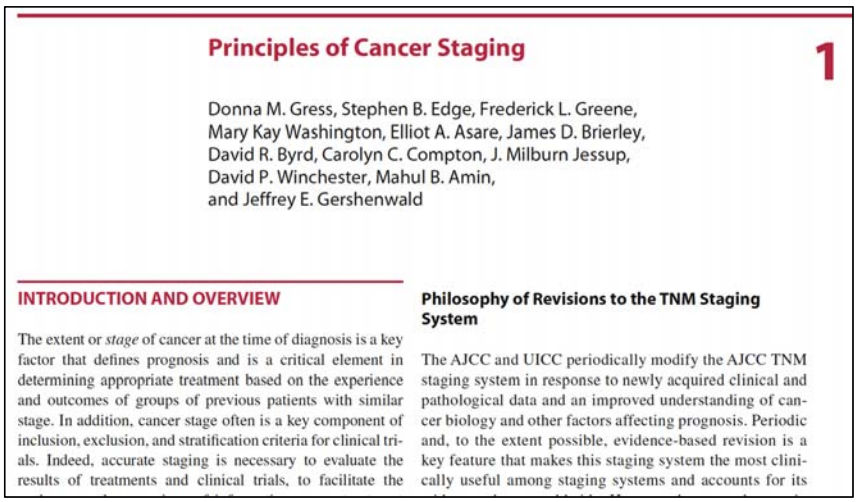


AJCC 7th Edition



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

8th Edition AJCC Cancer Staging Manual



Principles of Cancer Staging 1

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

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

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)

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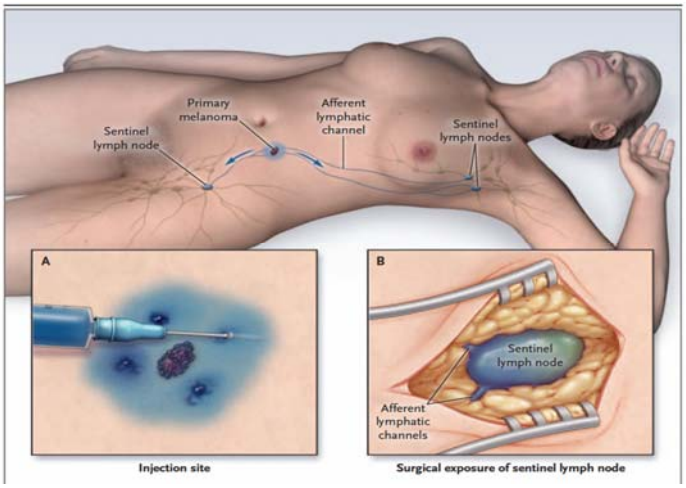
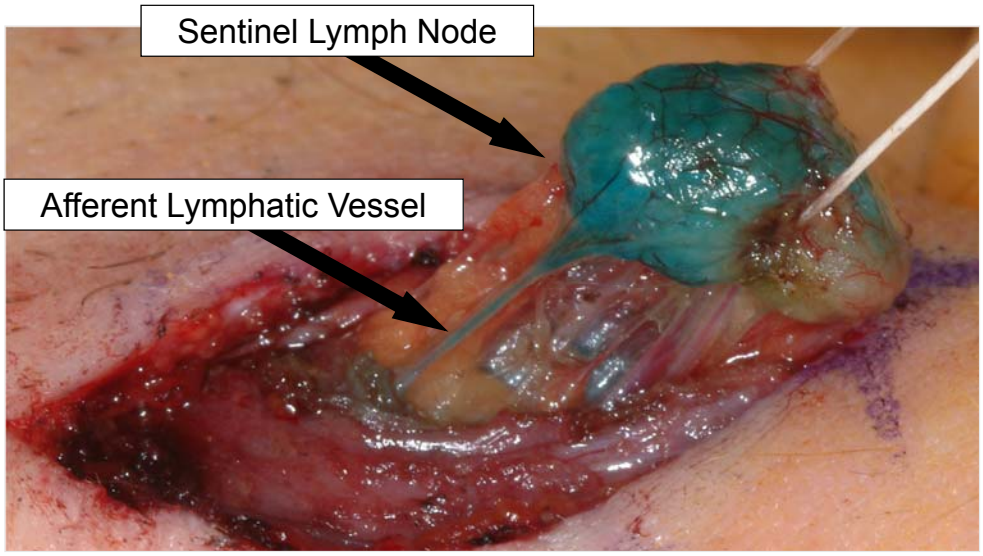
Lymphatic Mapping & Sentinel Node Biopsy

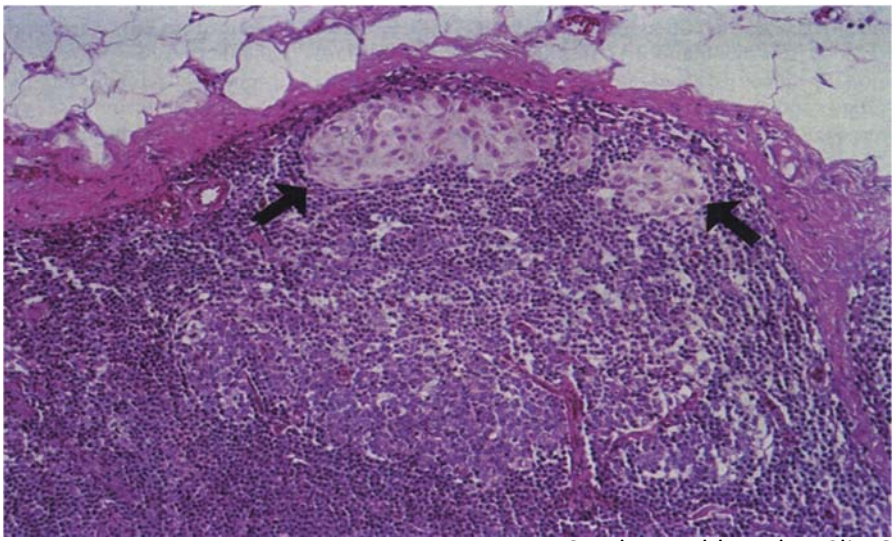
- Lymphatic drainage of finite regions of skin drain specifically to an initial node within a nodal basin - the "SENTINEL NODE"
- Different regions of the skin will drain to different SENTINEL NODES
- Represent most likely node(s) to contain metastatic disease



Gershenwald and Ross, N Engl J Med 2011;364:1738-45.



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)

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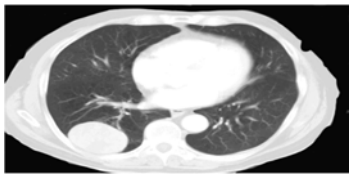
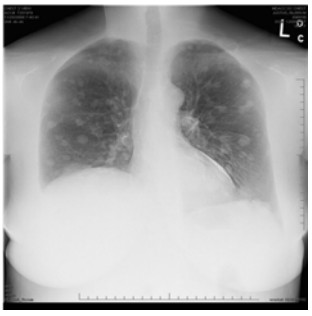
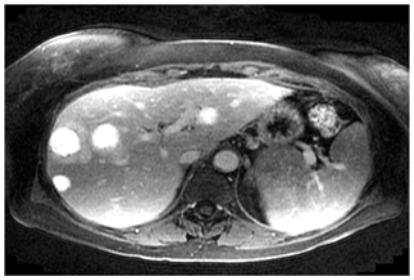
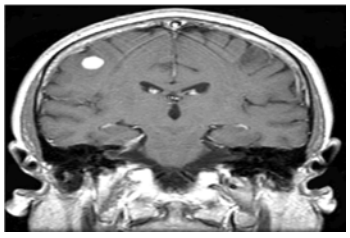
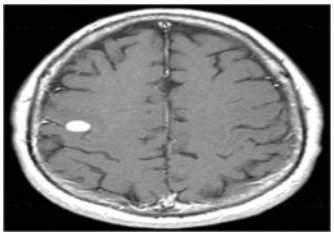
Melanoma Distant Metastases M1











Distant Metastasis (M)

M Category	M Criteria	
	Anatomic site	LDH level
M0	No evidence of distant metastasis	Not applicable
M1	Evidence of distant metastasis	See below
M1a	Distant metastasis to skin, soft tissue including muscle, and/or nonregional lymph node	Not recorded or unspecified
M1a(0)		Not elevated
M1a(1)		Elevated
M1b	Distant metastasis to lung with or without M1a sites of disease	Not recorded or unspecified
M1b(0)		Not elevated
M1b(1)		Elevated

M Category	M Criteria	
	Anatomic site	LDH level
M1c	Distant metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease	Not recorded or unspecified
M1c(0)		Not elevated
M1c(1)		Elevated
M1d	Distant metastasis to CNS with or without M1a, M1b, or M1c sites of disease	Not recorded or unspecified
M1d(0)		Normal
M1d(1)		Elevated

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

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

Distant Metastasis (M)

M Category	M Criteria	
	Anatomic site	LDH level
M0	No evidence of distant metastasis	Not applicable
M1	Evidence of distant metastasis	See below
M1a	Distant metastasis to skin, soft tissue including muscle, and/or nonregional lymph node	Not recorded or unspecified
M1a(0)		Not elevated
M1a(1)		Elevated
M1b	Distant metastasis to lung with or without M1a sites of disease	Not recorded or unspecified
M1b(0)		Not elevated
M1b(1)		Elevated

M Category	M Criteria	
	Anatomic site	LDH level
M1c	Distant metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease	Not recorded or unspecified
M1c(0)		Not elevated
M1c(1)		Elevated
M1d	Distant metastasis to CNS with or without M1a, M1b, or M1c sites of disease	Not recorded or unspecified
M1d(0)		Normal
M1d(1)		Elevated

- 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

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

Distant Metastasis (M)

M Category	M Criteria	
	Anatomic site	LDH level
M0	No evidence of distant metastasis	Not applicable
M1	Evidence of distant metastasis	See below
M1a	Distant metastasis to skin, soft tissue including muscle, and/or nonregional lymph node	Not recorded or unspecified
M1a(0)		Not elevated
M1a(1)		Elevated
M1b	Distant metastasis to lung with or without M1a sites of disease	Not recorded or unspecified
M1b(0)		Not elevated
M1b(1)		Elevated

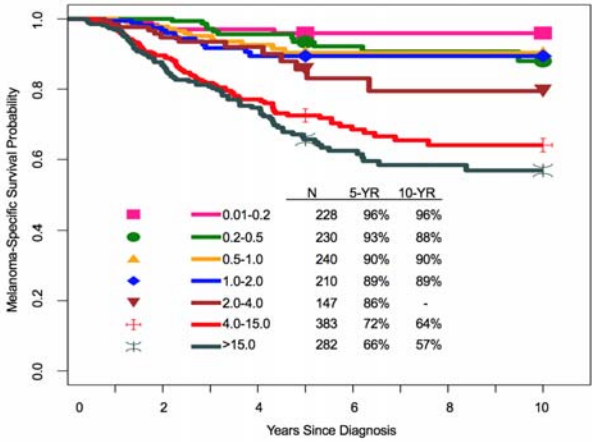
M Category	M Criteria	
	Anatomic site	LDH level
M1c	Distant metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease	Not recorded or unspecified
M1c(0)		Not elevated
M1c(1)		Elevated
M1d	Distant metastasis to CNS with or without M1a, M1b, or M1c sites of disease	Not recorded or unspecified
M1d(0)		Normal
M1d(1)		Elevated

- 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.

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

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



CA Cancer J Clin. 2017 Oct 13. [Epub ahead of print]

Gershenwald, Scolyer, et al. Melanoma. In Amin, M.B., et al. (Eds.) AJCC Cancer Staging Manual. 8th Ed. New York: Springer; 2017

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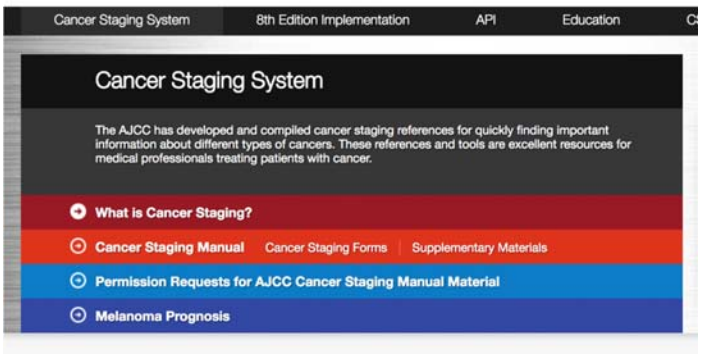
New Features: Precision Medicine Vision

- 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.

AJCC 8th Edition Staging: 1-Page Guide

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

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Critical assessment of clinical prognostic tools in melanoma

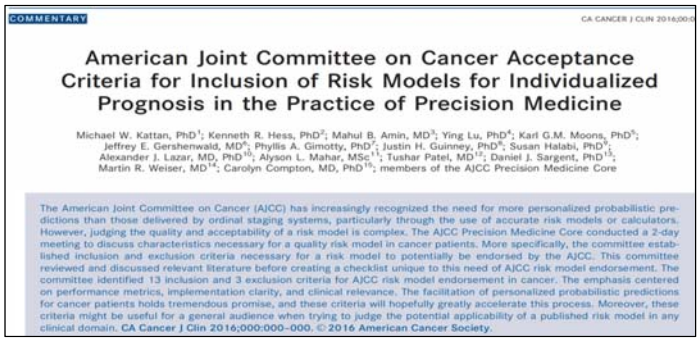
- Systematic search of the published literature web-based resources.
- A priori criteria were used to evaluate quality and clinical relevance
- **Results**: 17 clinical prognostic tools for primary cutaneous melanoma.
  - Patients with stages I-III and T1 or thin melanoma were the most frequently considered 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**



COMMENTARY

CA CANCER J CLIN 2016;00:0

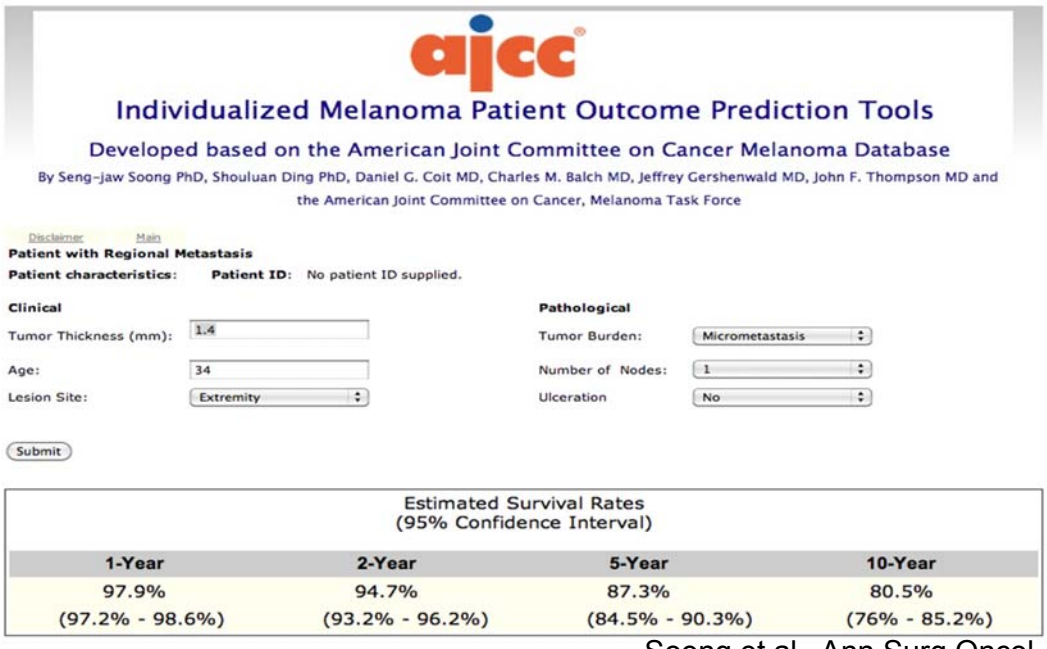
American Joint Committee on Cancer Acceptance Criteria for Inclusion of Risk Models for Individualized Prognosis in the Practice of Precision Medicine

Michael W. Kattan, PhD[1]; Kenneth R. Hess, PhD[2]; Mahul B. Amin, MD[3]; Ying Lu, PhD[4]; Karl G.M. Moons, PhD[5]; Jeffrey E. Gershenwald, MD[6]; Phyllis A. Gimotty, PhD[7]; Justin H. Guinney, PhD[8]; Susan Halabi, PhD[9]; Alexander J. Lazar, MD, PhD[10]; Alyson L. Mahar, MSc[11]; Tushar Patel, MD[12]; Daniel J. Sargent, PhD[13]; Martin R. Weiser, MD[14]; Carolyn Compton, MD, PhD[15]; members of the AJCC Precision Medicine Core

The American Joint Committee on Cancer (AJCC) has increasingly recognized the need for more personalized probabilistic predictions than those delivered by ordinal staging systems, particularly through the use of accurate risk models or calculators. However, judging the quality and acceptability of a risk model is complex. The AJCC Precision Medicine Core conducted a 2-day meeting to discuss characteristics necessary for a quality risk model in cancer patients. More specifically, the committee established inclusion and exclusion criteria necessary for a risk model to potentially be endorsed by the AJCC. This committee reviewed and discussed relevant literature before creating a checklist unique to this need of AJCC risk model endorsement. The committee identified 13 inclusion and 3 exclusion criteria for AJCC risk model endorsement in cancer. The emphasis centered on performance metrics, implementation clarity, and clinical relevance. The facilitation of personalized probabilistic predictions for cancer patients holds tremendous promise, and these criteria will hopefully greatly accelerate this process. Moreover, these criteria might be useful for a general audience when trying to judge the potential applicability of a published risk model in any clinical domain. CA Cancer J Clin 2016;000:000–000.

- 13 inclusion criteria
- 3 exclusion criteria

Kattan MW, CA: A Cancer Journal for Clinicians, (2016)66: 370–374.



ajcc

Individualized Melanoma Patient Outcome Prediction Tools

Developed based on the American Joint Committee on Cancer Melanoma Database

By Seng-jaw Soong PhD, Shouluan Ding PhD, Daniel G. Coit MD, Charles M. Balch MD, Jeffrey Gershenwald MD, John F. Thompson MD and the American Joint Committee on Cancer, Melanoma Task Force

Disclaimer Main

Patient with Regional Metastasis

Patient characteristics: **Patient ID:** No patient ID supplied.

Clinical		Pathological	
Tumor Thickness (mm):	1.4	Tumor Burden:	Micrometastasis
Age:	34	Number of Nodes:	1
Lesion Site:	Extremity	Ulceration	No

Submit

Estimated Survival Rates
(95% Confidence Interval)

1-Year	2-Year	5-Year	10-Year
97.9%	94.7%	87.3%	80.5%
(97.2% - 98.6%)	(93.2% - 96.2%)	(84.5% - 90.3%)	(76% - 85.2%)

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

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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

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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

Thank you

AJCC
American Joint Committee on Cancer
Validating science. Improving patient care.

633 N. Saint Clair, Chicago, IL 60611-3211
cancerstaging.org