



KDL DermPath Update

Dedicated to Providing Superior Diagnostics

New AJCC System for Melanoma Skin Staging Adopted at KDL

KDL strives to provide clinicians with the most up to date information in patient care and diagnostics. Physicians involved in the care of melanoma patients should be familiar with the new AJCC Melanoma of the Skin Staging.

The final version of the 2009 AJCC Melanoma Staging and Classification was published in December of 2009 and is now being distributed as the 7th Edition of Melanoma of the Skin Staging. This new system was based upon analysis of 30,946 patients with stages I, II and III melanoma and 7,972 patients with stage IV melanoma in an American Joint Committee on Cancer (AJCC) melanoma staging database. The analysis provided recommendations for revision and clarification of TNM classifications and stage grouping criteria. The AJCC Staging and Classification are widely used to estimate prognosis and guide therapy, either inside or outside of melanoma treatment studies.

There are several important findings and new definitions since the 6th edition in 2002. In patients with localized melanoma, tumor thickness, mitotic rate (histologically defined as mitoses/mm²) and ulceration are the most dominant prognostic factors. Mitotic rate replaces level of invasion as a primary criterion for defining T1b melanomas. Among 3307 patients with regional metastases, components that defined the N category were the number of metastatic nodes, tumor burden and ulceration of the primary melanoma. For staging purposes, all patients with microscopic nodal metastases, regardless of tumor burden, are classified as stage III. Micrometastases detected by immunohistochemistry are specifically included. On the basis of multivariate analysis of patients with distant metastases, the two dominant components defining category continue to be site of distant metastases (nonvisceral v lung v all other visceral metastatic sites) and an elevated serum lactate dehydrogenase level.

KDL melanoma diagnostic reports include all information necessary for tumor classification (T). This

microscopic staging for invasive melanoma will document tumor thickness (Breslow), presence or absence of ulceration and mitotic rate (number of mitoses per square millimeter). Other information such as Clark level, regression, microscopic satellites, vascular invasion, perineural invasion, tumor infiltrating lymphocytes, associated nevus, and margins will be noted, as these factors have been shown to be of prognostic significance in many studies over the past thirty years.

KDL pathologists are seldom provided with the patient's status regarding lymph nodes and distant metastases. Therefore, this information will not be included in the KDL pathology report. Lymph node status and distant metastases, however, are requisite elements of clinical and pathologic staging in the AJCC system. These parameters should be documented in the patient's medical record.

In patients with melanomas 1 mm or less in thickness, the presence of ulceration or 1 or more mitoses/mm² will move a patient from Pathologic Stage Ia to Ib. This has significant implications in regards to consideration of sentinel lymph node biopsy. Of note, the presence of any size of lymph node metastasis is considered Pathologic Stage III.

Additional information is provided below and in publications available from AJCC.

References:

1. Balch CM, Gershenwald JE, Soong S, et al. Final version of AJCC melanoma staging and classification. *J Clin Oncol* 27:6199-6206, 2009.
2. Balch CM, Gershenwald JE, Soong S, et al. Multivariate analysis of prognostic factors among 2,313 patients with stage III melanoma: comparison of nodal micrometastases versus macrometastases. *J Clin Oncol* 28:2452-2459, 2010.

(continued)

Melanoma of the Skin Staging

7th EDITION

Definitions

Primary Tumor (T)

- TX** Primary tumor cannot be assessed (for example, curettaged or severely regressed melanoma)
- T0** No evidence of primary tumor
- Tis** Melanoma in situ
- T1** Melanomas 1.0 mm or less in thickness
- T2** Melanomas 1.01–2.0 mm
- T3** Melanomas 2.01–4.0 mm
- T4** Melanomas more than 4.0 mm

NOTE: a and b subcategories of T are assigned based on ulceration and number of mitoses per mm², as shown below:

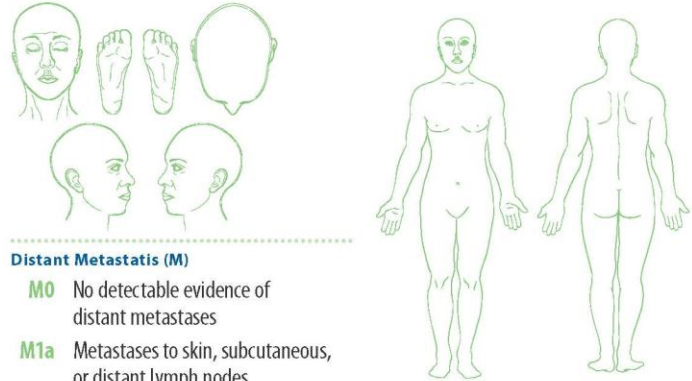
T CLASSIFICATION	THICKNESS (mm)	ULCERATION STATUS/MITOSSES
T1	≤1.0	a: w/o ulceration and mitosis <1/mm ² b: with ulceration or mitoses ≥1/mm ²
T2	1.01–2.0	a: w/o ulceration b: with ulceration
T3	2.01–4.0	a: w/o ulceration b: with ulceration
T4	>4.0	a: w/o ulceration b: with ulceration

Regional Lymph Nodes (N)

- NX** Patients in whom the regional nodes cannot be assessed (for example, previously removed for another reason)
- N0** No regional metastases detected
- N1–3** Regional metastases based upon the number of metastatic nodes and presence or absence of intralymphatic metastases (in transit or satellite metastases)

NOTE: N1–3 and a–c subcategories assigned as shown below:

N CLASSIFICATION	NO. OF METASTATIC NODES	NODAL METASTATIC MASS
N1	1 node	a: micrometastasis ¹ b: macrometastasis ²
N2	2–3 nodes	a: micrometastasis ¹ b: macrometastasis ² c: in transit met(s)/satellite(s) without metastatic nodes
N3	4 or more metastatic nodes, or matted nodes, or in transit met(s)/satellite(s) with metastatic node(s)	



Distant Metastasis (M)

- M0** No detectable evidence of distant metastases
- M1a** Metastases to skin, subcutaneous, or distant lymph nodes
- M1b** Metastases to lung
- M1c** Metastases to all other visceral sites or distant metastases to any site combined with an elevated serum LDH

NOTE: Serum LDH is incorporated into the M category as shown below:

M CLASSIFICATION	SITE	SERUM LDH
M1a	Distant skin, subcutaneous, or nodal mets	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastases Any distant metastasis	Normal Elevated

ANATOMIC STAGE/PROGNOSTIC GROUPS							
Clinical Staging ³				Pathologic Staging ⁴			
Stage	Tis	NO	MO	Stage	Tis	NO	MO
Stage 0	T1a	NO	MO	0	T1a	NO	MO
Stage IA	T1b	NO	MO	IA	T1b	NO	MO
	T2a	NO	MO		T2a	NO	MO
Stage IIA	T2b	NO	MO	IIA	T2b	NO	MO
	T3a	NO	MO		T3a	NO	MO
Stage IIB	T3b	NO	MO	IIB	T3b	NO	MO
	T4a	NO	MO		T4a	NO	MO
Stage IIC	T4b	NO	MO	IIC	T4b	NO	MO
Stage III	Any T	≥ N1	MO	IIIA	T1-4a	N1a	MO
					T1-4a	N2a	MO
				IIIB	T1-4b	N1a	MO
					T1-4b	N2a	MO
				IIIC	T1-4a	N1b	MO
					T1-4a	N2b	MO
				IIIC	T1-4a	N2c	MO
					T1-4b	N1b	MO
				IIIC	T1-4b	N2b	MO
					T1-4b	N2c	MO
IIIC	Any T	N3	MO				
	Any T	N3	MO				
Stage IV	Any T	Any N	M1	IV	Any T	Any N	M1

Notes

- ¹ Micrometastases are diagnosed after sentinel lymph node biopsy and completion lymphadenectomy (if performed).
- ² Macrometastases are defined as clinically detectable nodal metastases confirmed by therapeutic lymphadenectomy or when nodal metastasis exhibits gross extracapsular extension.
- ³ Clinical staging includes microstaging of the primary melanoma and clinical/radiologic evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.
- ⁴ Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial or complete lymphadenectomy. Pathologic Stage 0 or Stage IA patients are the exception; they do not require pathologic evaluation of their lymph nodes.



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AJCC Melanoma Staging

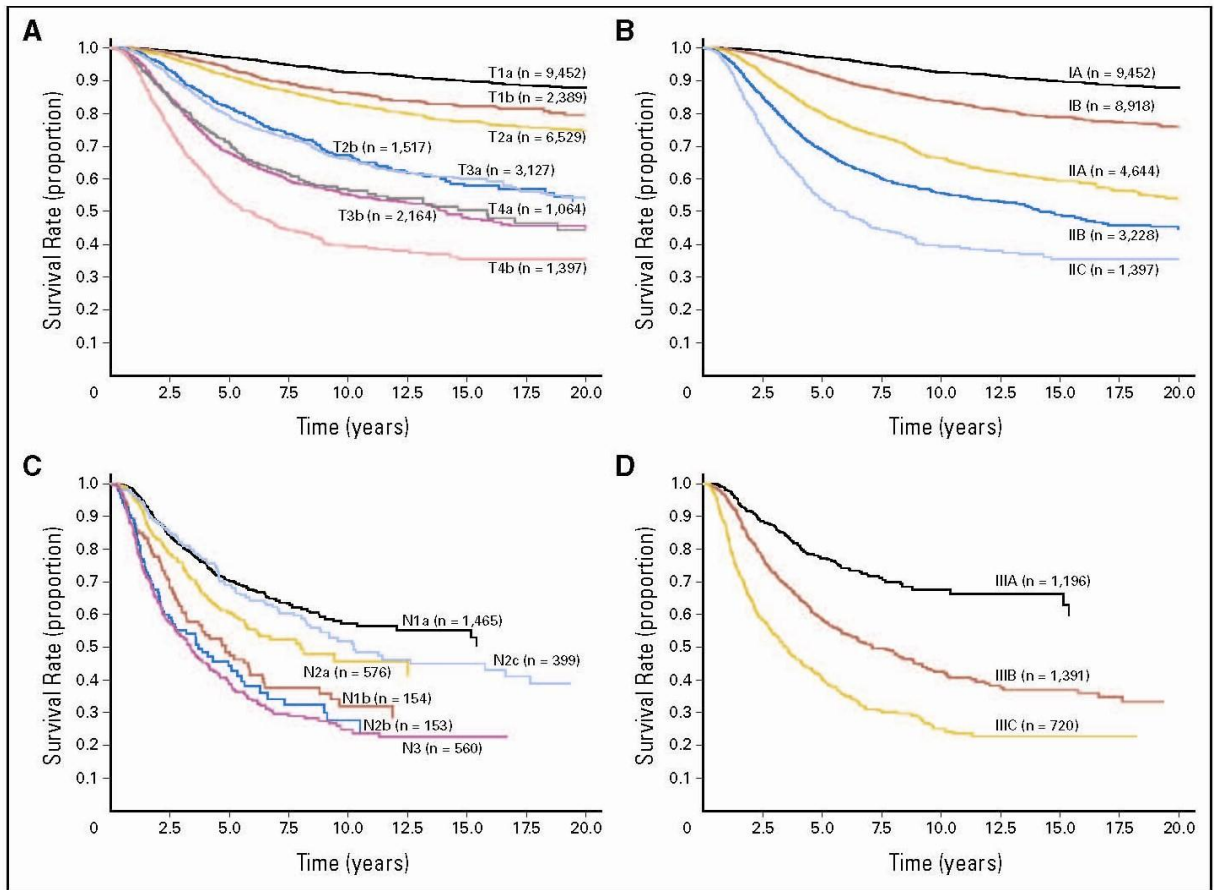


Fig 1. Survival curves from the American Joint Committee on Cancer Melanoma Staging Database comparing (A) the different T categories and (B) the stage groupings for stages I and II melanoma. For patients with stage III disease, survival curves are shown comparing (C) the different N categories and (D) the stage groupings.

Balch et al

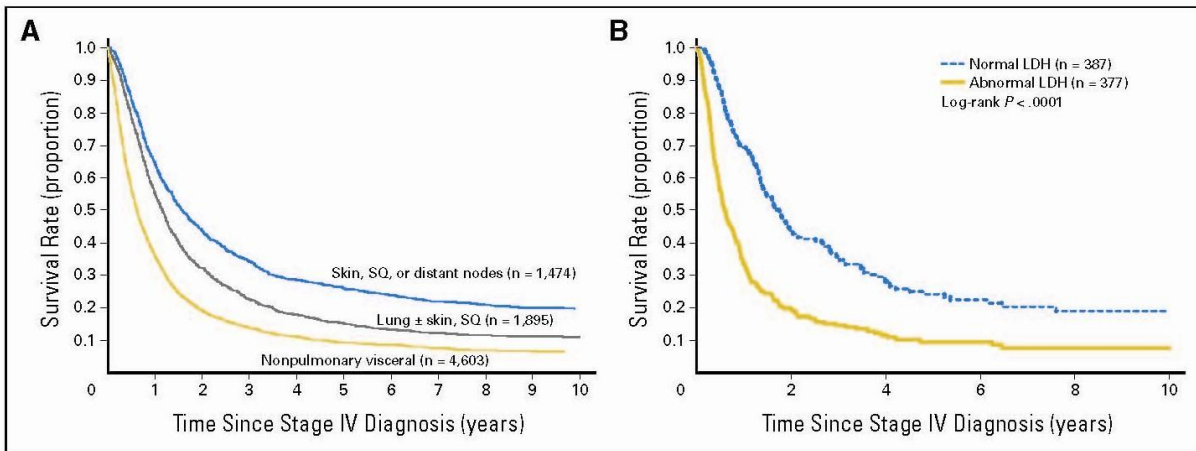


Fig 2. Survival curves of 7,635 patients with metastatic melanomas at distant sites (stage IV) subgrouped by (A) the site of metastatic disease and (B) serum lactose dehydrogenase (LDH) levels. LDH values are not used to stratify patients. Curves in (A) are based only on site of metastasis. The number of patients is shown in parentheses. SQ, subcutaneous.



KDL Pathology

Dedicated to Providing Superior Diagnostics

KDL is dedicated to providing quality surgical pathology services to physicians treating skin diseases.

Diagnostic interpretations are performed by fellowship-trained dermatopathologists, certified by the American Boards of Dermatology and Pathology.

Services:

- Evaluation of skin biopsies/excisions
- Second opinions on biopsies
- Slide preparation available
- Regional couriers
- Immunofluorescence
- Immunohistochemistry
- Expert consultation on problem cases
- Web reporting/available interface with EMR



Paul B. Googe, M.D., Founder and Laboratory Director of KDL, is board certified in dermatopathology and anatomic pathology. A native of Knoxville, TN, he completed his post-graduate training in pathology and dermatopathology at Massachusetts General Hospital in Boston, MA following medical school and an internal medicine internship at The University of Tennessee College of Medicine. Dr. Googe has practiced dermatopathology for over 20 years and holds volunteer faculty appointments as Clinical Professor of Pathology at The University of Tennessee Graduate School of Medicine and Vanderbilt University.



KDL Pathology

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