

Un granito de arena

María J. Beato

Departamento de Anatomía Patológica
Hospital Universitario “La Paz”
Madrid



Introducción

- Pubmed: “Nuevas entidades y nuevos conceptos en dermatopatología”
- Un artículo distinto, original, y lógico:

CRITICAL REVIEW

The Magic of Numbers: Malignant Melanoma Between Science and Pseudoscience

Wolfgang Weyers, MD

Abstract: In 2009, a new system for staging and classification of

traumatic experiences of a barking dog on the sidewalk and nothing about the immunological state and general condition

From the Center for Dermatopathology, Freiburg, Germany.
Reprints: Wolfgang Weyers, MD, Center for Dermatopathology, Engelbergerstr. 19, 79106 Freiburg, Germany (e-mail: ww@zdpf.de).
Copyright © 2011 by Lippincott Williams & Wilkins

authors,³ whereas other groups found it to be relevant only for melanomas of different thickness,^{4,5} or not at all.⁶⁻⁸ The last major study about the BANS concept was published in 1994.⁹ Thereafter, the concept has vanished.

Am J Dermatopathol • Volume 0, Number 0, Month 2011

www.amjdermatopathology.com | 1

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

Un granito de arena (en sensatez)

Resumen de un artículo de **Wolfgang Weyers**

María J. Beato
Departamento de Anatomía Patológica
Hospital Universitario “La Paz”
Madrid



The Magic of Numbers: Malignant Melanoma Between Science and Pseudoscience

Wolfgang Weyers, MD

Abstract: In 2009, a new system for staging and classification of malignant melanoma has been proposed by the American Joint

traumatic experiences of a barking dog on the sidewalk and nothing about the immunological state and general condition of a patient whose tumor comes across our microscope.

Crítica a los factores pronósticos de la última versión (2009) del estadiaje del melanoma

-Estos factores pronósticos los determina el patólogo

Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Seng-jaw Soong, John F. Thompson, Michael B. Atkins, David R. Byrd, Antonio C. Busaid, Alistair J. Cochran, Daniel G. Coit, Shouluan Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gimotty, John M. Kirkwood, Kelly M. McMasters, Martin C. Mihm Jr, Donald L. Morton, Merrick I. Ross, Arthur J. Sober, and Vernon K. Sondak

Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Seng-jaw Soong, John F. Thompson, Michael David R. Byrd, Antonio C. Buzaid, Alistair J. Cochran, Daniel G. Coit, Shouhuan Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gomoty, John M. Kirkwood, Kel Martin C. Mihm Jr, Donald L. Morton, Merrick L. Ross, Arthur J. Sober, and Vernon K.

Factores pronósticos: son determinados por el patólogo

1. Grosor (Breslow)
2. Ulceración
3. Índice mitótico ~~Clark~~

Table 1. TNM Staging Categories for Cutaneous Melanoma

Classification	Thickness (mm)	Ulceration Status/Mitoses
T		
Tis	NA	NA
T1	≤ 1.00	a: Without ulceration and mitosis < 1/mm ² b: With ulceration or mitoses ≥ 1/mm ²
T2	1.01-2.00	a: Without ulceration b: With ulceration
T3	2.01-4.00	a: Without ulceration b: With ulceration
T4	> 4.00	a: Without ulceration b: With ulceration
N	No. of Metastatic Nodes	Nodal Metastatic Burden
N0	0	NA
N1	1	a: 1 b: 2 c: 3
N2	2-3	a: 1 b: 2 c: 3
N3	4+ metastatic nodes, or matted nodes, or in transit metastases/satellites with metastatic nodes	sd li ta
M	Site	Stage
M0	No distant metastases	NA ^b
M1a	Distant skin, subcutaneous, bone, or nodal metastases	No ^a
M1b	Lung metastases	No ^c
M1c	All other visceral metastases	No ^a
	Any distant metastasis	E ^d

Abbreviations: NA, not applicable; LDH, lactate dehydrogenase.

^aMicrometastases are diagnosed after sentinel lymph node biopsy.

^bMacrometastases are defined as clinically confirmed pathologically.

Table 2. Anatomic Stage Groupings for Cutaneous Melanoma

	Clinical Staging*			Pathologic Staging†					
	T	N	M	T	N	M			
0	Tis	N0	M0	0	Tis	N0	M0		
IA	T1a	N0	M0	IA	T1a	N0	M0		
IB	T1b	N0	M0	IB	T1b	N0	M0		
	T2a	N0	M0		T2a	N0	M0		
IIA	T2b	N0	M0	IIA	T2b	N0	M0		
	T3a	N0	M0		T3a	N0	M0		
IIB	T3b	N0	M0	IIB	T3b	N0	M0		
	T4a	N0	M0		T4a	N0	M0		
IIC	T4b	N0	M0	IIC	T4b	N0	M0		
III	Any T	N > N0	M0	III	T1-4a	N1a	M0		
					T1-4a	N2a	M0		
					III	T1-4b	N1a	M0	
						T1-4b	N2a	M0	
						T1-4a	N1b	M0	
						T1-4a	N2b	M0	
						T1-4a	N2c	M0	
						III	T1-4b	N1b	M0
						T1-4b	N2b	M0	
						T1-4b	N2c	M0	
						III	T1-4b	N3	M0
IV	Any T	Any N	M1	IV	Any T	Any N	M1		

*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.

†Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial (ie, sentinel node biopsy) or complete lymphadenectomy. Pathologic stage 0 or stage IA patients are the exception; they do not require pathologic evaluation of their lymph nodes.

Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Seng-jirw Soong, John F. Thompson, Michael B. Atkins, David R. Byrd, Antonio C. Buzaid, Alistair J. Cochran, Daniel G. Coit, Shouluan Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gimotty, John M. Kirkwood, Kelly M. McMasters, Martin C. Mihm Jr, Donald L. Morton, Merrick I. Ross, Arthur J. Sober, and Vernon K. Sondak

Clasificación y estadaje del melanoma primario:

1. Grosor (Breslow)
2. Ulceración
3. Índice mitótico

Mediante el grosor se mide el tamaño del melanoma, lo cual es lo único que tiene una relación indiscutible con la supervivencia, y que es objetivo y lógico

Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Seng-jirw Soong, John F. Thompson, Michael B. Atkins, David R. Byrd, Antonio C. Buzaid, Alistair J. Cochran, Daniel G. Coit, Shouluan Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gimotty, John M. Kirkwood, Kelly M. McMasters, Martin C. Mihm Jr, Donald L. Morton, Merrick I. Ross, Arthur J. Sober, and Vernon K. Sonneveld

Clasificación y estadaje del melanoma primario:

1. Grosor (Breslow)
2. Ulceración
3. Índice mitótico



grande



pequeño

(T1≤1mm, T2≤2mm, T3≤4mm, T4>4mm)

Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Seng-jirw Soong, John F. Thompson, Michael B. Atkins, David R. Byrd, Antonio C. Buzaid, Alistair J. Cochran, Daniel G. Coit, Shouhuan Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gimotty, John M. Kirkwood, Kelly M. McMasters, Martin C. Mihm Jr, Donald L. Morton, Merrick I. Ross, Arthur J. Sober, and Vernon K. Sondak

1. Grosor (Breslow)
2. Ulceración
3. Índice mitótico

- **Ulceración:** “ausencia de una epidermis intacta en buena parte de la lesión”, excluyendo la úlcera por cirugía y la úlcera traumática (hemorragia, fibrina eosinófila y brillante, y defecto arquitectural)

Table 1. Tumor Staging Categories for Cutaneous Melanoma

Classification	Thickness (mm)	Ulceration Status/Mitoses
T		
Tis	NA	NA
T1	≤ 1.00	a: Without ulceration and mitoses $< 1/\text{mm}^2$ b: With ulceration or mitoses $\geq 1/\text{mm}^2$
T2	1.01-2.00	a: Without ulceration b: With ulceration
T3	2.01-4.00	a: Without ulceration b: With ulceration
T4	> 4.00	a: Without ulceration b: With ulceration
N	No. of Metastatic Nodes	Nodal Metastatic Burden
N0	0	NA
N1	1	a: Micrometastasis* b: Macrometastasis†
N2	2-3	a: Micrometastasis* b: Macrometastasis† c: In transit metastases/satellites without metastatic nodes
N3	4+ metastatic nodes, or matted nodes, or in transit metastases/satellites	



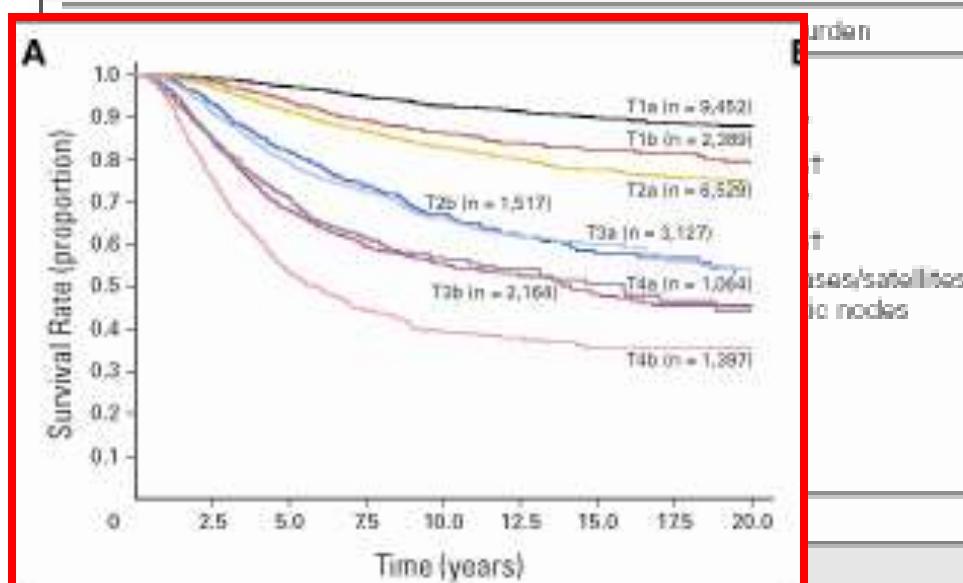
Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Seng-jirw Soong, John F. Thompson, Michael B. A. David R. Byrd, Antonio C. Buzaid, Alistair J. Cochran, Daniel G. Coit, Shouluan Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gimotty, John M. Kirkwood, Kelly M. Martin C. Mihm Jr, Donald L. Morton, Merrick I. Ross, Arthur J. Sober, and Vernon K. Son

- Ulceración:
 - ganglio centinela
 - en general, supervivencia a los 10 años T1 y T2 78% si no ulcerado, 50% si no ulcerado

Table 1. TNM Staging Categories for Cutaneous Melanoma

Classification	Thickness (mm)	Ulceration Status/Mitoses
T		
Tis	NA	NA
T1	≤ 1.00	a: Without ulceration and mitosis $< 1/\text{mm}^2$ b: With ulceration or mitoses $\geq 1/\text{mm}^2$
T2	1.01-2.00	a: Without ulceration b: With ulceration
T3	2.01-4.00	a: Without ulceration b: With ulceration
T4	> 4.00	a: Without ulceration b: With ulceration



Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Seng-jirw Soong, John F. Thompson, Michael B. Atkins, David R. Byrd, Antonio C. Buzaid, Alistair J. Cochran, Daniel G. Coit, Shouluan Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gimotty, John M. Kirkwood, Kelly M. McMasters, Martin C. Mihm Jr, Donald L. Morton, Merrick I. Ross, Arthur J. Sober, and Vernon K. Sondak

1. Grosor (Breslow)
2. Ulceración
3. Índice mitótico (mitogenicidad)

- **Índice mitótico:** Mitosis / mm³
 - El número de mitosis es un parámetro lógico. AJCC: Solo en melanomas <1mm, para ≠ T1a de T1b (1 mitosis)

Table 1. TNM Staging Categories for Cutaneous Melanoma

Classification	Thickness (mm)	Ulceration Status/Mitoses
T		
T ₀	NA	NA
T ₁	≤ 1.00	a: Without ulceration and mitosis < 1/mm ³ b: With ulceration or mitoses ≥ 1/mm ³
T ₂	1.01-2.00	a: Without ulceration b: With ulceration
T ₃	2.01-4.00	a: Without ulceration b: With ulceration
T ₄	> 4.00	a: Without ulceration b: With ulceration
N	No. of Metastatic Nodes	Nodal Metastatic Burden
N ₀	0	NA
N ₁	1	a: Micrometastasis* b: Macrometastasis†
N ₂	2-3	a: Micrometastasis* b: Macrometastasis† c: In transit metastases/satellites without metastatic nodes
N ₃	4+ metastatic nodes, or matted nodes, or in transit metastases/satellites with metastatic nodes	
M	Site	Serum LDH
M ₀	No distant metastases	NA
M _{1a}	Distant skin, subcutaneous, Normal or nodal metastases	
M _{1b}	Lung metastases	Normal
M _{1c}	All other visceral metastases	Normal
	Any distant metastasis	Elevated

Abbreviations: NA, not applicable; LDH, lactate dehydrogenase.

*Micrometastases are diagnosed after sentinel lymph node biopsy.

†Macrometastases are defined as clinically detectable nodal metastases confirmed pathologically.

Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Sung-jaw Soong, John F. Thompson, Michael B. Atkins, David R. Byrd, Antonio C. Busaid, Alistair J. Cochran, Daniel G. Coit, Shoulian Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gimotty, John M. Kirkwood, Kelly M. McMasters, Martin C. Mihm Jr, Donald L. Morton, Merrick L. Ross, Arthur J. Sober, and Vernon K. Sonneveld

Table 1. TNM Staging Categories for Cutaneous Melanoma

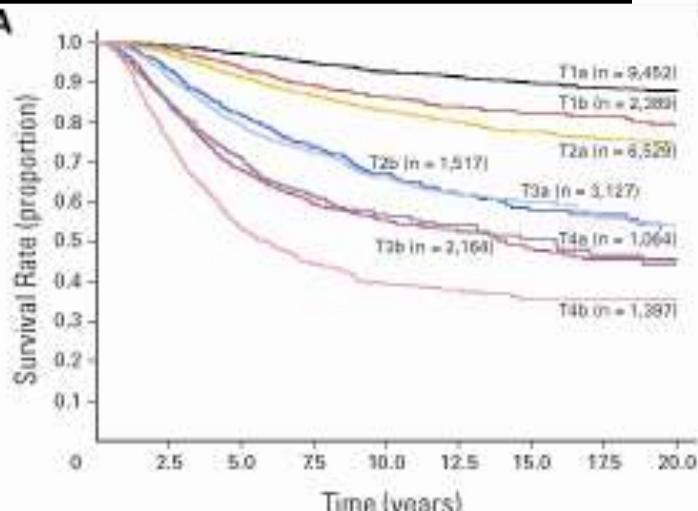
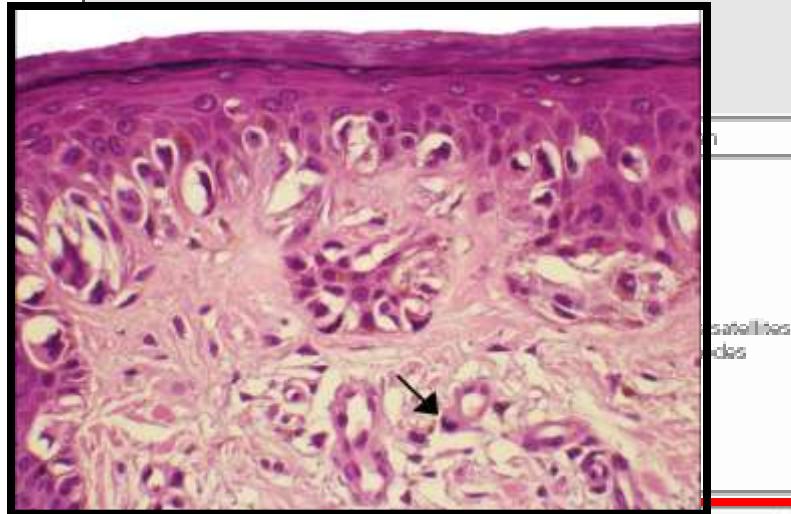
Classification	Thickness (mm)	Ulceration Status/Mitoses
T0	NA	NA
T1	≤ 1.00	a: Without ulceration and mitoses $< 1/\text{mm}^2$ b: With ulceration or mitoses $\geq 1/\text{mm}^2$
T2	1.01-2.00	a: Without ulceration b: With ulceration

Índice mitótico, problemas

.no se encuentran mitosis:

- no dicen si entra el componente epitelial
- picnosis, queratinocitos/cél endoteliales
- ¿cuánto se seria? ¿10, 50, 100 cortes? ¿Cómo sabe uno que la mitosis no está en el siguiente corte?
- sin duda cambia con el patólogo, entre patólogos, entre hoy y mañana

El índice mitótico que se le asigna a cada paciente es un cuestión de azar, pero una sola mitosis conlleva un ganglio centinela y un peor pronóstico





Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Seng-jaw Soong, John F. Thompson, Michael B. Atkins, David R. Byrd, Antonio C. Busaidi, Alistair J. Cochran, Daniel G. Coit, Shoukuan Ding, Alexander M. Eggermont, Keith T. Flaherty, Phyllis A. Gimotty, John M. Kirkwood, Kelly M. McMasters, Martin C. Mihm Jr, Donald L. Morton, Merrick L. Ross, Arthur J. Sober, and Vernon K. Sondak

Análisis estadístico:

1. Grosor (Breslow)
2. Ulceración
3. Índice mitótico

Factores pronósticos melanoma:

- ¿ulceración? ¿una mitosis?
- Clark

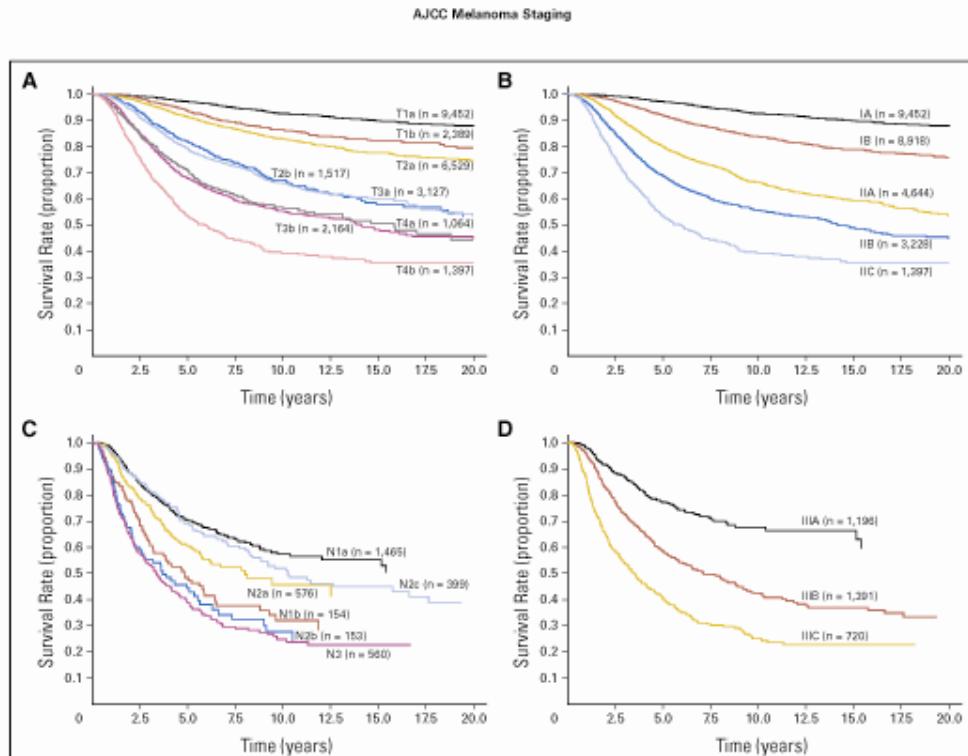
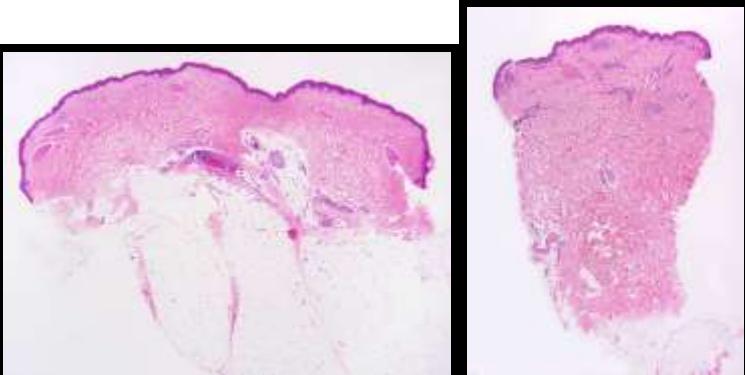


Fig 1. Survival curves from the American Joint Committee on Cancer Melanoma Staging Database comparing (A) the different T categories and (B) the stage groupings for stages I and II melanoma. For patients with stage III disease, survival curves are shown comparing (C) the different N categories and (D)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

30.946 pacientes estadio I, II y III
7.972 pacientes estadio IV

The Magic of Numbers: Malignant Melanoma Between
Science and Pseudoscience

Wolfgang Weyers, MD

Fascinación por los números (datos analizados, resultados), en manos de los estadísticos

- **Numerología:** seudociencia (\approx astrología)
fecha de nacimiento: 25-12-1980
 $2+5+1+2+1+9+8+0=28 \quad 2+8=10 \quad 1$
- Supervivencia 10 años 95% T1a y 88% T1b
(¡por una mitosis!)
.Sin tener en cuenta el estado inmunológico, psíquico,...
.Siempre correcto



Conclusiones

- Hoy por hoy, la función del patólogo es diagnosticar. Y si pronostica, que sea sobre factores pronósticos bien definidos, fáciles de determinar, objetivos y con un verdadero impacto en la supervivencia. En el melanoma, el único factor pronóstico indiscutible es el tamaño. Otros factores lógicos serían la presencia de células tumorales en los vasos, o una gran cantidad de mitosis. Pero no la ulceración o la presencia de una mitosis.
- No obstante, hay grandes avances en biología molecular, que pronto van a permitir clasificar los melanomas en tipos biológicos y grupos pronósticos, en incluso ofrecer tratamientos (BRAF)
- ¿Qué hacer?