

HISTOPATHOLOGIC REPORTING OF MELANOCYTTIC SKIN LESIONS

Problems, thoughts, proposals

*Gerardo Ferrara
Anatomic Pathology Unit
Macerata General Hospital
AV3-ASUR Marche
Macerata, I*

Aims and scope

- **STANDARDIZATION: refer to a unique format**
- To improve the histopathologic report of melanocytic skin neoplasms with reference to its:
 - Completeness
 - Clarity
- To support the Clinician (!) in the management of the patient

Structured report

- Self-explaining and self-documenting
- (Ful)fill predefined data fields and values:
 - Clinical information (age, sex, location; size, history, clinico-dermoscopic problems)
 - Gross pathology (description and handling)
 - Microscopic features (optional)
 - Special techniques (if any implemented)
 - Diagnostic conclusions
 - Further studies (if any scheduled)

Structured report

- Self-explaining and self-documenting
- (Ful)fill predefined data fields and values:
 - Clinical information (age, sex, location; size, history, clinico-dermoscopic dagnosis/problems)
 - Gross pathology (description and handling)
 - Microscopic features (optional)
 - Special techniques (if any implemented)
 - Diagnostic conclusions
 - Further studies (if any scheduled)

Mistakes not born at the microscope

- About 30%
- Pre-analytical:
 - **Sample switches**
 - Mix-ups
 - Tissue processing failure
- Post-analytical:
 - Clerical
- Clinical pictures for every biopsied lesion; re-examination of the pictures after histology
- The cheapest and most effective special technique: the **PHONE**

Structured report

- Self-explaining and self-documenting
- (Ful)fill predefined data fields and values:
 - Clinical information (age, sex, location; size, history, clinico-dermoscopic diagnosis/problems)
 - **Gross pathology (description and handling)**
 - Microscopic features (optional)
 - Special techniques (if any implemented)
 - Diagnostic conclusions
 - Further studies (if any scheduled)

The histological reporting of melanoma

Eduardo Calonje

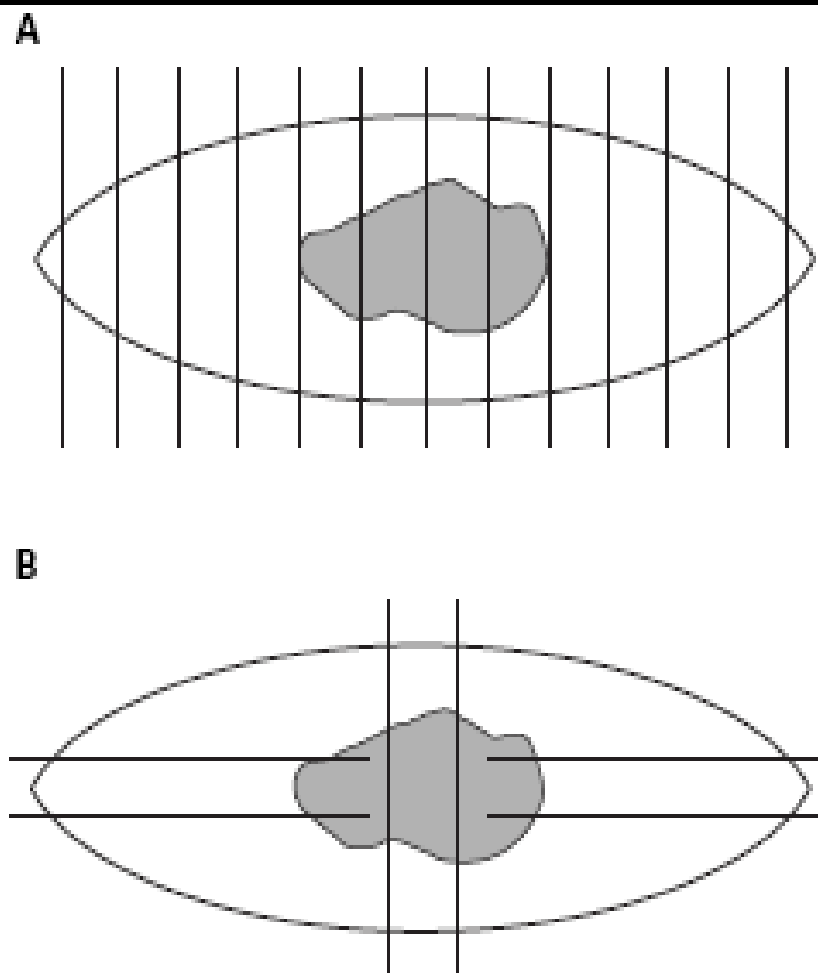
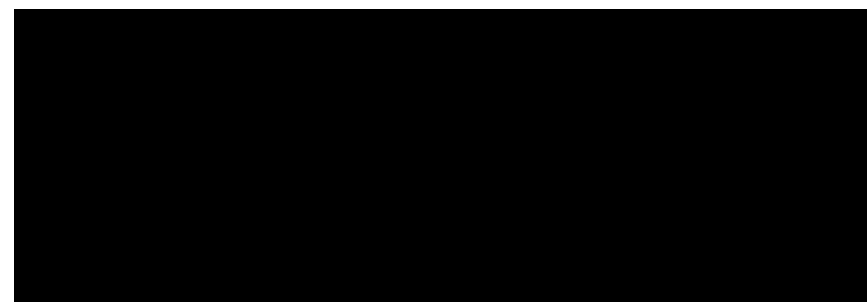
Abstract

The incidence of malignant melanoma has increased steadily over the past 30 years and this type of malignancy is the leading cause of death from cutaneous malignant disease. Cutaneous malignancies, including melanoma, can be detected at a very early stage and a cure is possible with prompt detection and treatment. In recent years, and mainly because of increased awareness of the early detection of melanoma, histopathologists have been exposed more and more to melanocytic lesions. Therefore, it is essential that histopathologists are able to provide a report to the clinician that conveys relevant information in a concise and precise manner. This paper provides a set of guidelines aimed at helping histopathologists with the gross and microscopic description and diagnosis of malignant melanoma.

(*J Clin Pathol* 2000;53:587-590)

Keywords: melanoma; histological reporting; diagnosis

Figure 1 (A) Excisional biopsies of melanocytic lesions should be sectioned transversely, starting from the centre, and all blocks should be processed. (B) Excisional biopsies of melanocytic lesions should not be sectioned by cruciates because this makes interpretation of the architecture of the lesion more difficult.





MAIN PROBLEMS:

- Prognostic assessment
- Distance from the surgical margins



MAIN PROBLEM:

- Diagnosis

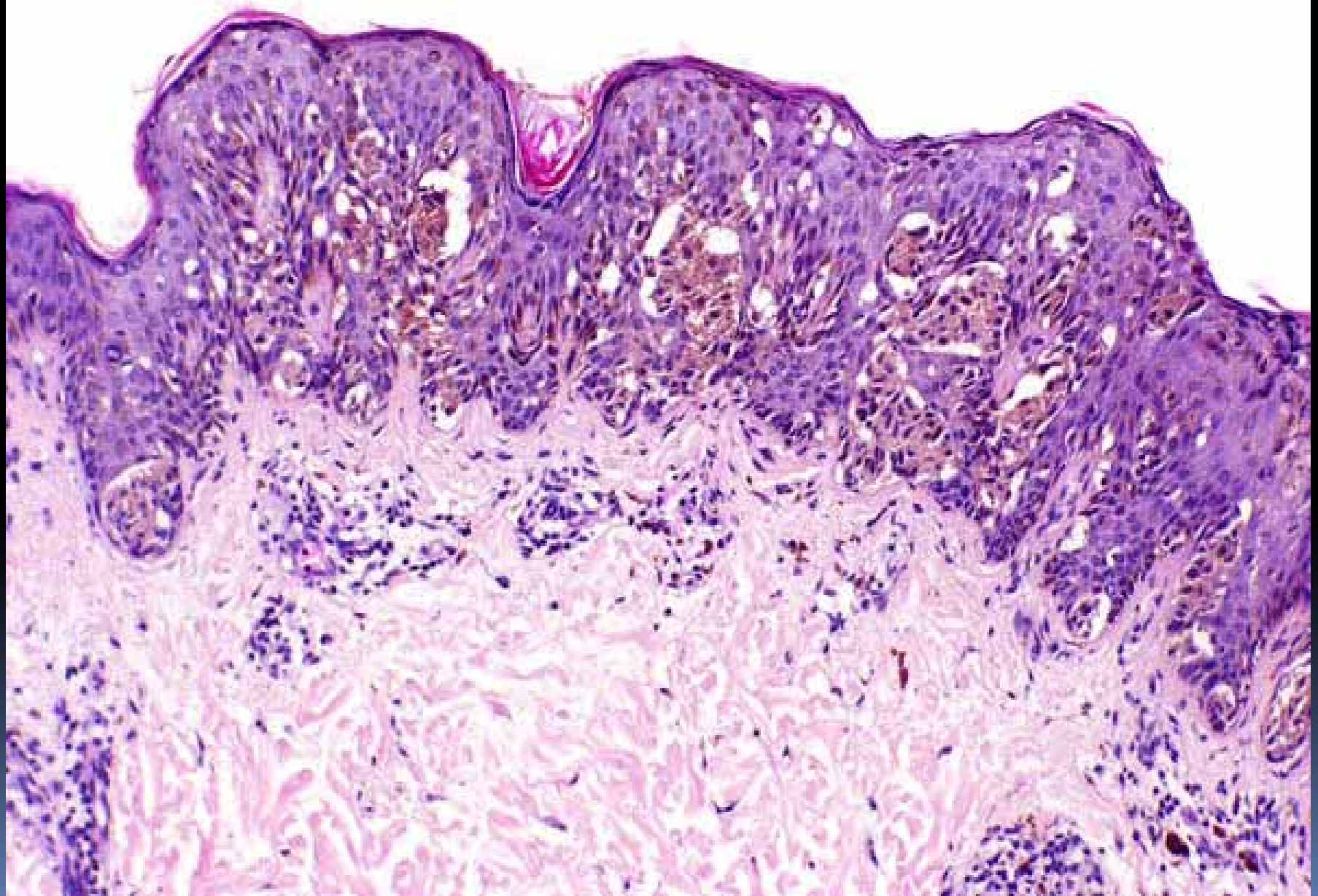
Dr. Harald Kittler, Wien, A











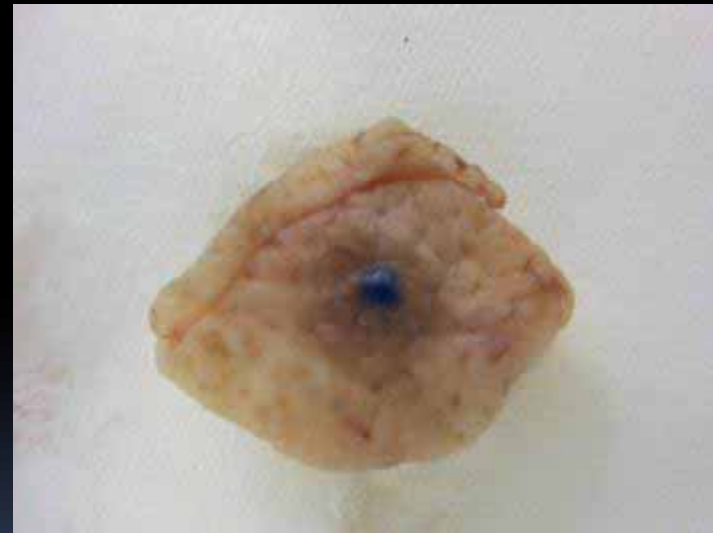
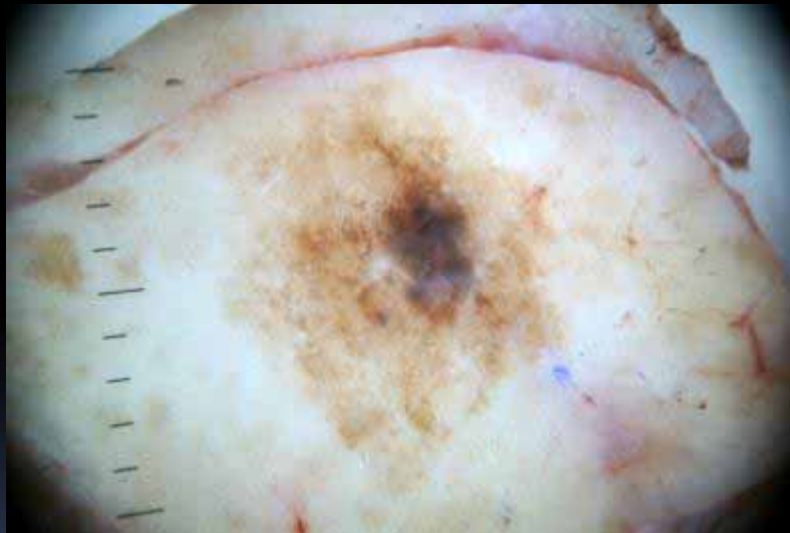
Strategies

- Send the clinicodermoscopic images to the Histopathologist:
 - The level of clinical expertise of the histopathologist can be a limitation or, else, a bias
- Mark the area(s) of interest with liquid eraser or with suture stitches
- Ex vivo dermoscopy with dermdotting

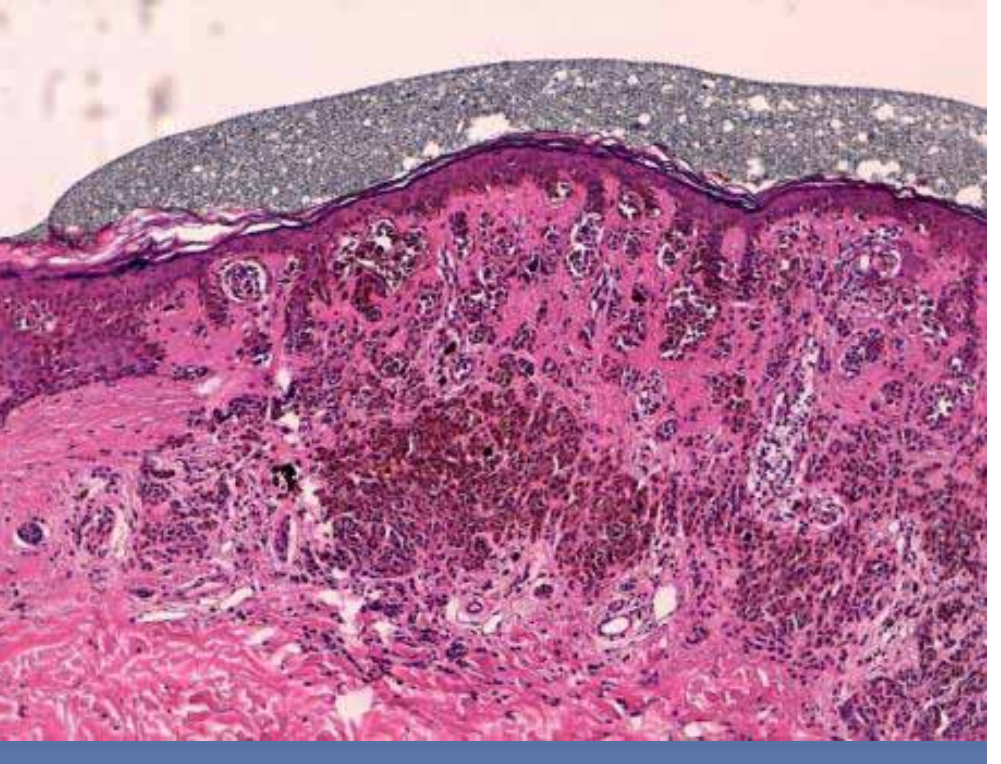
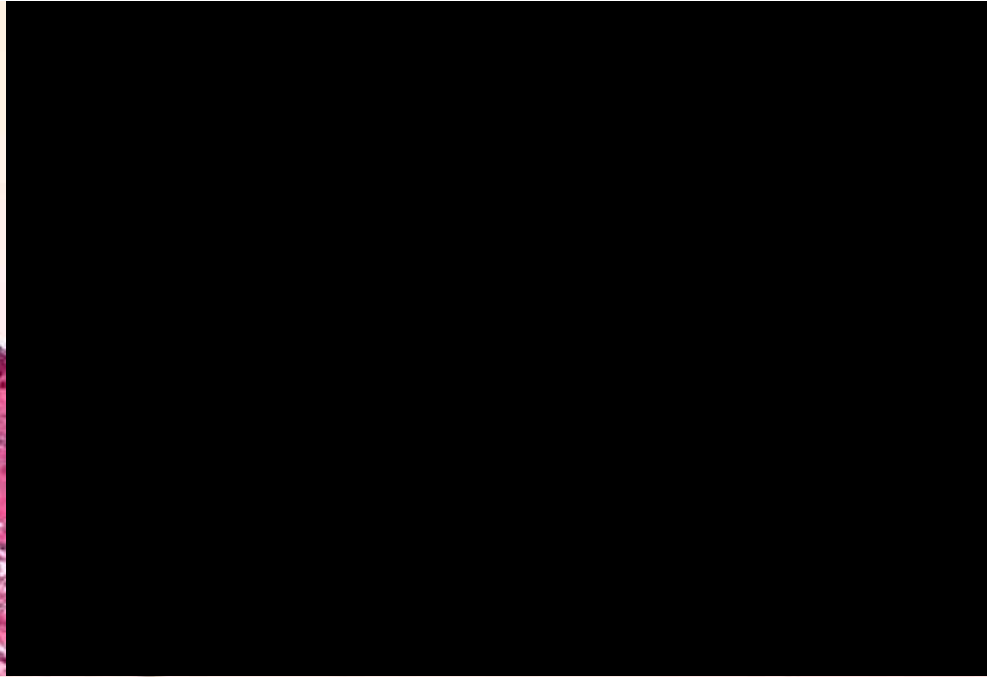
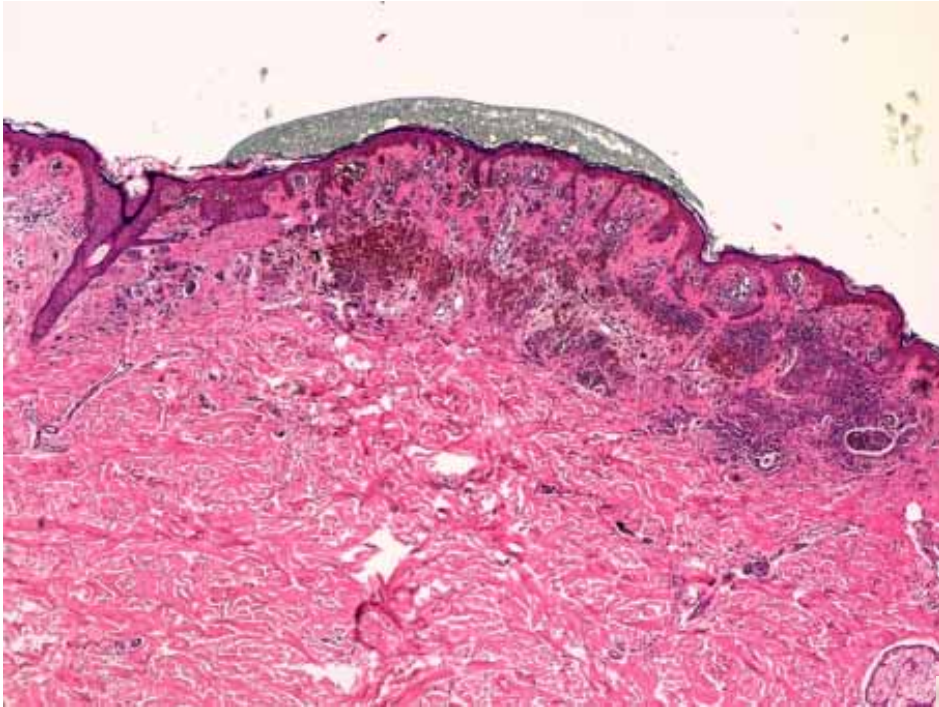
Ex vivo dermoscopy with derm dotting

Slides provided by Dr. Marc Haspeslagh, Gent, B

- Case ID: 1210-50500
- 68 year old male
- Excision nevus with dot on the right shoulder







Structured report

- Self-explaining and self-documenting
- (Ful)fill predefined data fields and values:
 - Clinical information (age, sex, location; size, history, clinico-dermoscopic diagnosis/problems)
 - Gross pathology (description and handling)
 - **Microscopic features (optional)**
 - Special techniques (if any implemented)
 - Diagnostic conclusions
 - Further studies (if any scheduled)

Description of the microscopic features

- Rationale: diagnosis of melanocytic skin neoplasms based on a SUM of morphologic criteria, none of which pathognomonic
 - Assessment of probability
- Bias: the weight given to any single criterion depending on the diagnostic opinion
- The unavowed scope: to highlighten the difficulties of the lesion and the thoroughness of the study performed

Table 1. Morphologic criteria used for the histopathologic diagnosis of melanoma

1. Overall asymmetry
2. Poor lateral circumscription
3. Predominance of single melanocytes over nests
4. Pagetoid spread
5. Poor cohesion of melanocytes within nests
6. Nests showing irregular size, irregular shape, irregular spacing
7. Lack of maturation with the progressive descent into the dermis
8. "Skip areas" and regression
9. Lichenoid lymphocytic infiltrate with irregularly "moth-eaten" dermal nests of melanocytes
10. Cytologic atypia
11. Monocellular necrosis
12. Deep mitoses

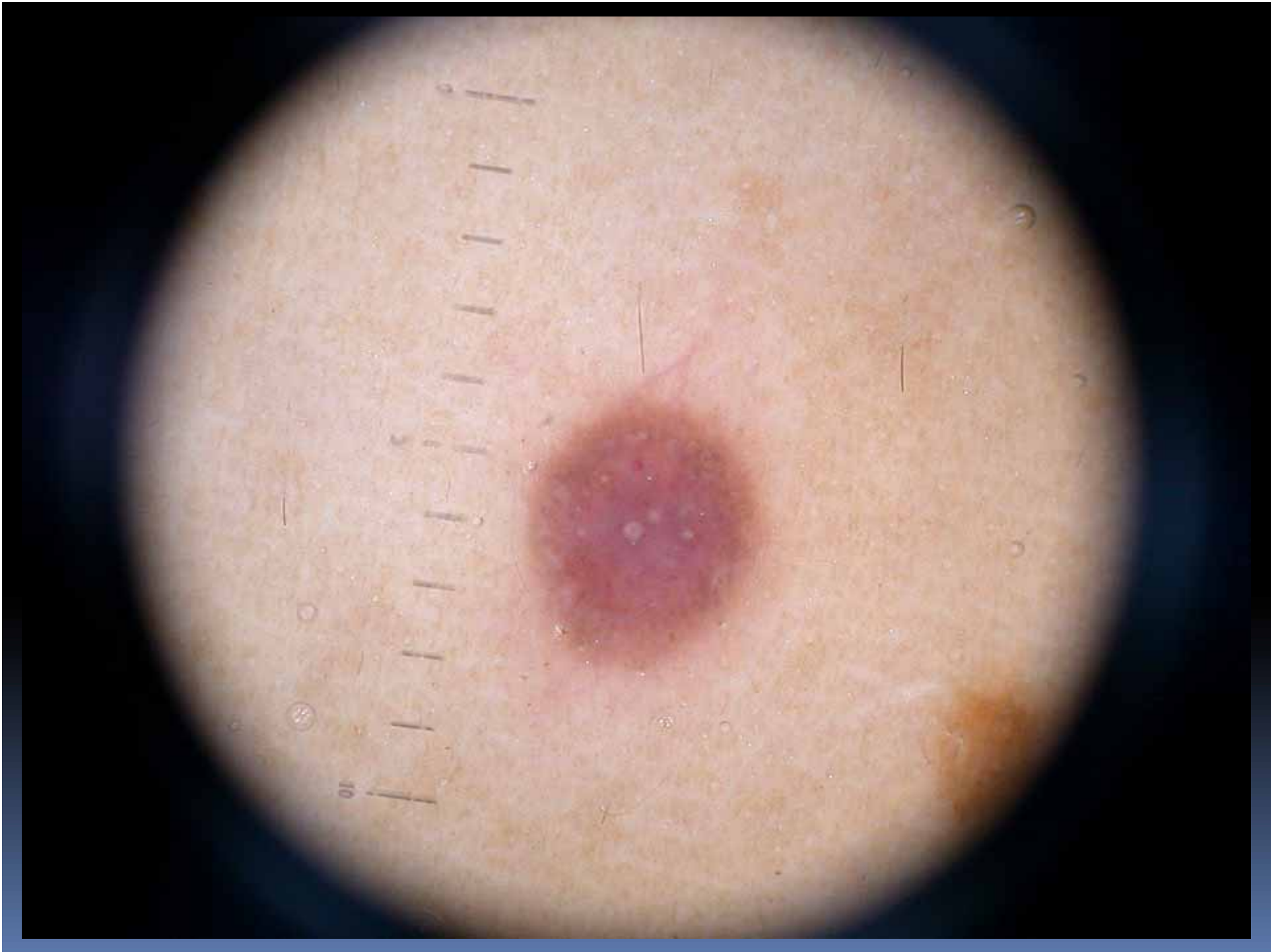
For example, it has been thoughtfully speculated that using the same diagnostic criteria for Spitzoid MSN as for "conventional" (non-Spitzoid) MSN is a conceptual and practical mistake (6). For these reasons, the histopathologic diagnosis of MSN, being based upon the simultaneous evaluation of several criteria, is no more than an *assessment of probability*, and, as such, is often a matter of

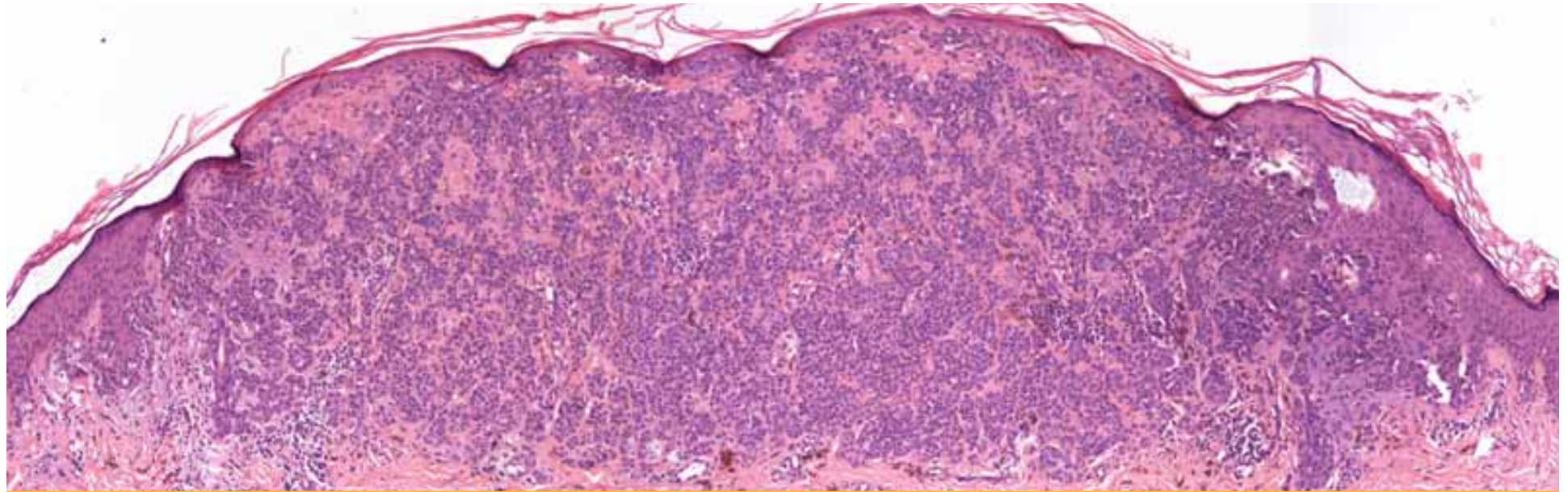
Table 2. Main settings of diagnostic difficulties in melanocytic skin neoplasms

1. Unrecognized melanoma on partial (shave/punch) biopsies
2. Nevoid melanoma versus "common" or "congenital" compound/dermal nevus
3. Desmoplastic melanoma versus desmoplastic nevus versus scar
4. Recurrent/persistent nevus versus (recurrent) melanoma
5. Spindle cell melanoma versus spindle cell nevus
6. Superficial spreading melanoma versus "dysplastic" nevus
7. Superficial spreading melanoma versus haloed nevus
8. Superficial spreading melanoma versus compound nevus with regression-like fibrosis
9. Melanoma with regression versus melanosis
10. Melanoma in situ in chronic sun-damaged skin versus melanocytic hyperplasia
11. Dermal melanoma over congenital nevus versus proliferative nodule in congenital nevus
12. Cellular blue nevus versus dendritic cell (animal-type) melanoma versus blue nevus-like metastatic melanoma
13. Metastatic melanoma versus other high-grade tumors
14. Spindle cell melanoma versus other spindle cell malignancies

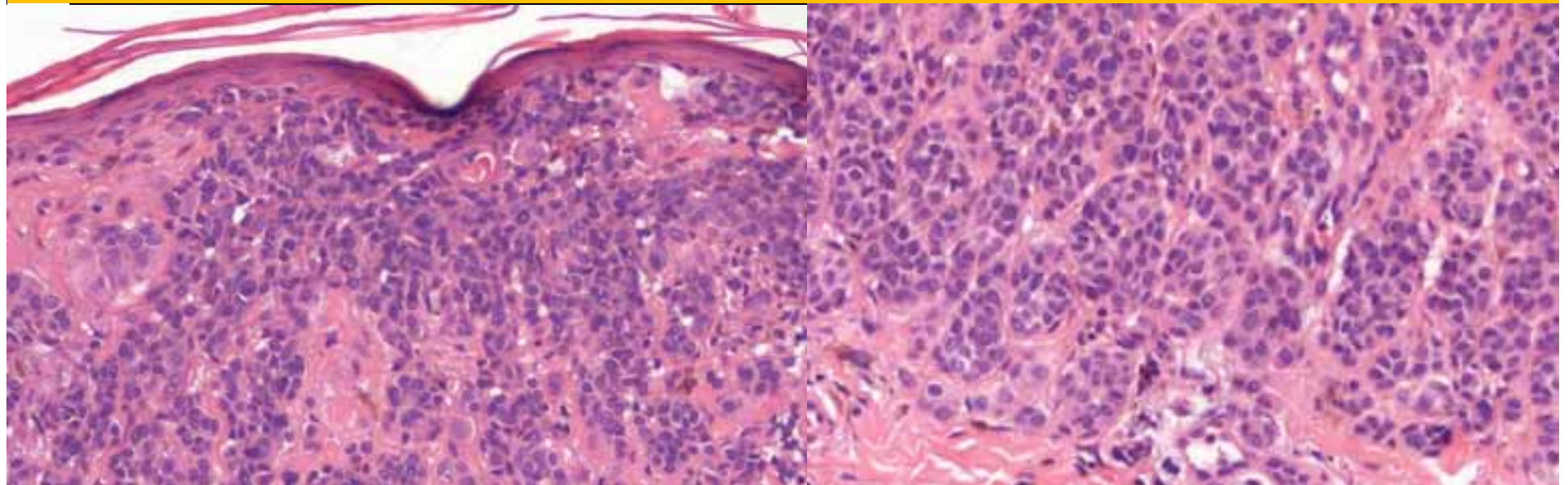
**Courtesy of Drs. Raffaele Gianotti
& Stefano Cavicchini, Milan, I**







**Symmetric or not?
Maturation or pseudo-maturation?**



Description of the microscopic features

- Rationale: diagnosis of melanocytic skin neoplasms based on a SUM of morphologic criteria, none of which pathognomonic
 - Assessment of probability
- Bias: the weight given to any single criterion depending on the diagnostic opinion
- The unavowed scope: to highlight the difficulties of the lesion and the thoroughness of the study performed

Structured report

- Self-explaining and self-documenting
- (Ful)fill predefined data fields and values:
 - Clinical information (age, sex, location; size, history, clinico-dermoscopic diagnosis/problems)
 - Gross pathology (description and handling)
 - Microscopic features (optional)
 - **Special techniques (if any implemented)**
 - Diagnostic conclusions
 - Further studies (if any scheduled)

Fluorescence In Situ Hybridization for Melanoma Diagnosis: A Review and a Reappraisal

Gerardo Ferrara, MD and Anna Chiara De Vanna, PhD

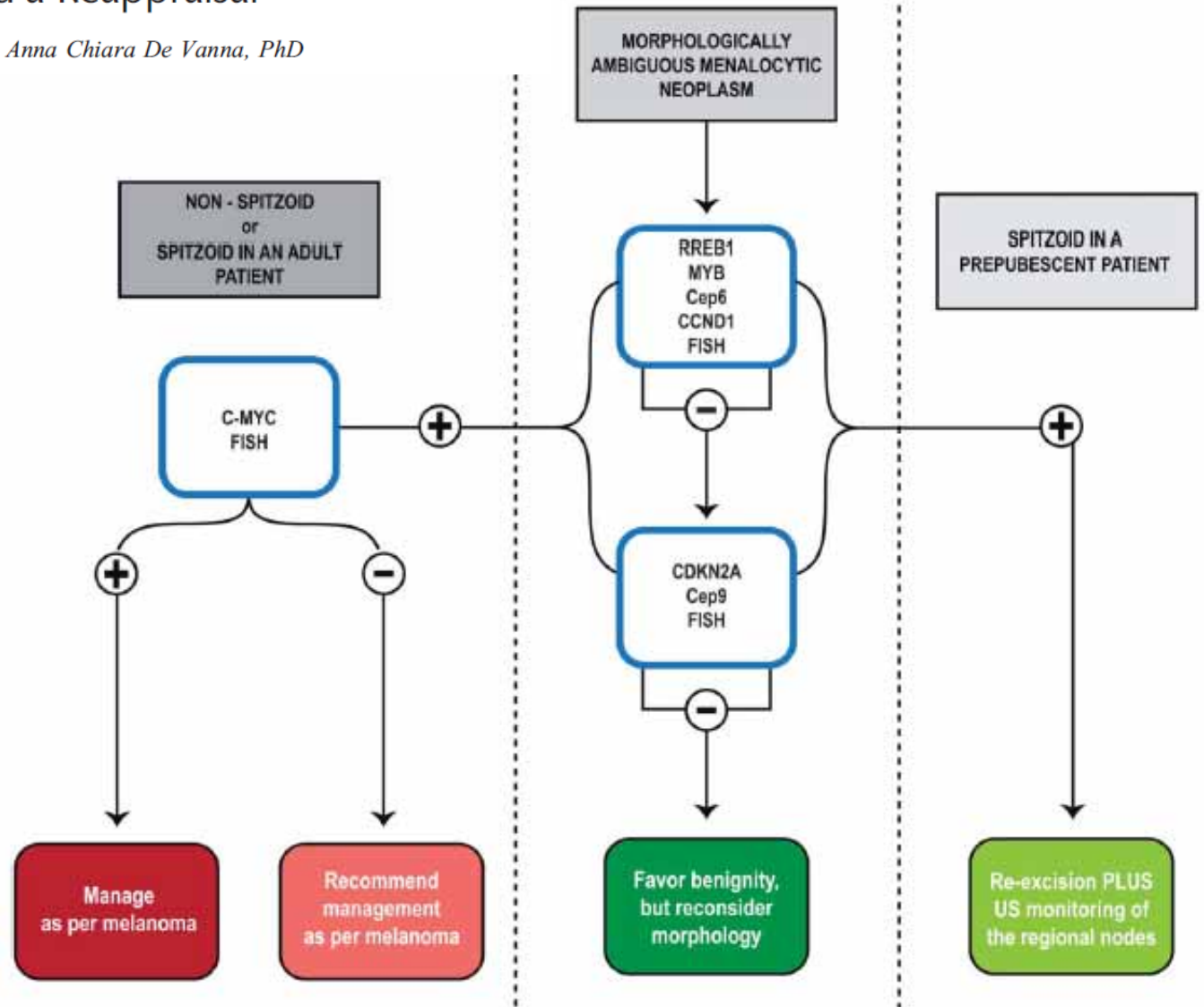
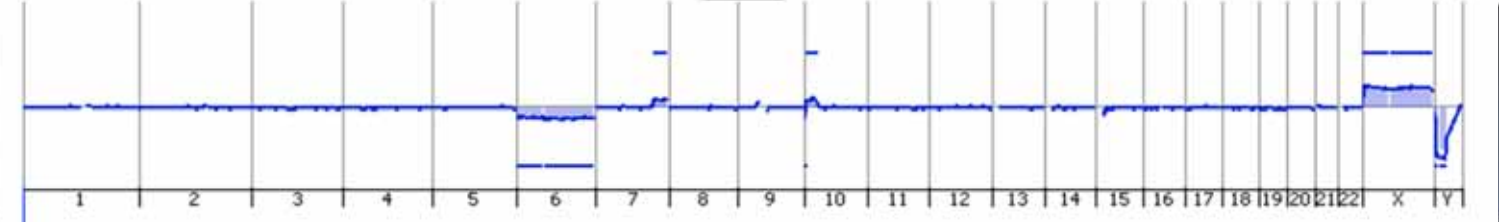
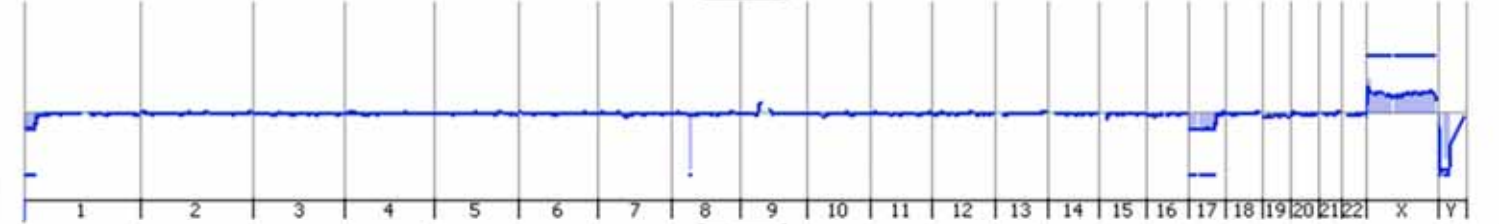
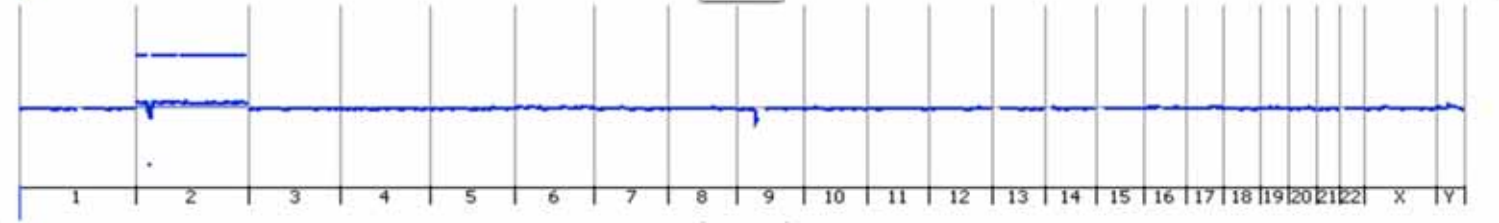
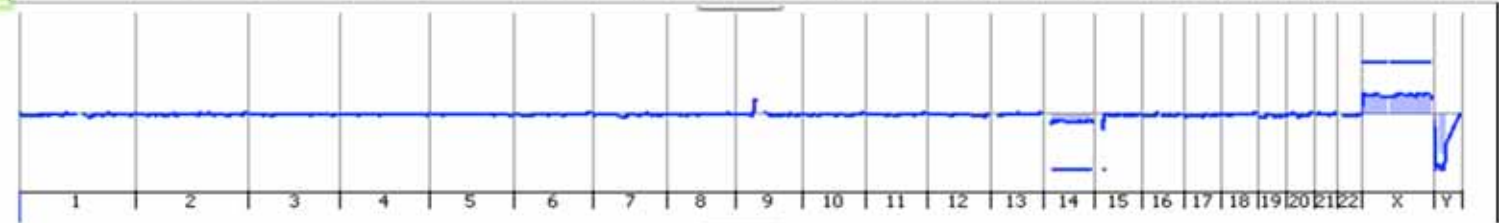
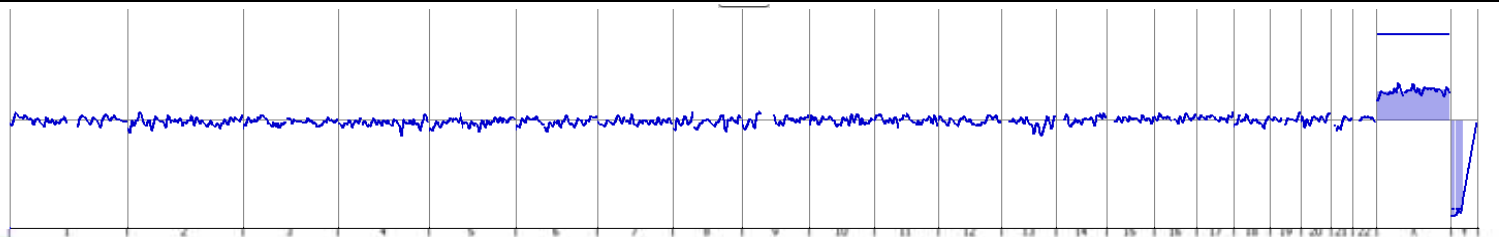
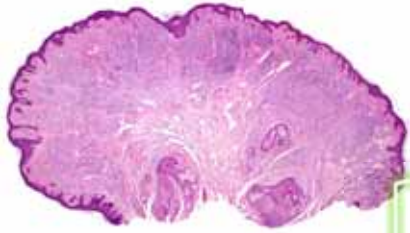
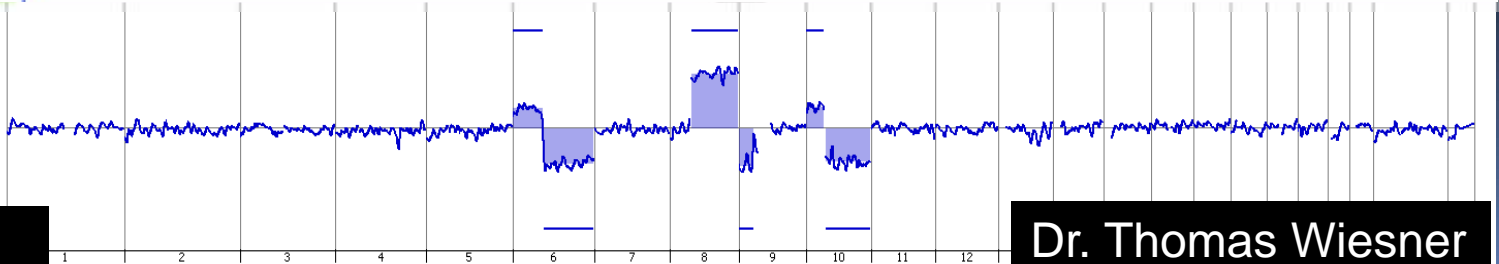
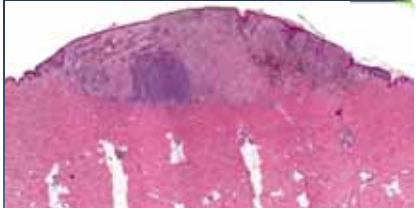


FIGURE 5. Proposal of a FISH algorithm. We underline the need to place the information obtained with FISH examinations in the overall clinicopathological context.

Benign Nevus



Difficult
melanocytic
lesions



Malignant Melanoma

Dr. Thomas Wiesner

Structured report

- Self-explaining and self-documenting
- (Ful)fill predefined data fields and values:
 - Clinical information (age, sex, location; size, history, clinico-dermoscopic diagnosis/problems)
 - Gross pathology (description and handling)
 - Microscopic features (optional)
 - Special techniques (if any implemented)
 - **Diagnostic conclusions**
 - Further studies (if any scheduled)

Kim JC, Murphy GF. Clin Lab Med 2000; 20:691-712.

Reporting of a 'surely benign' lesion

- Always report the KIND of nevus:
 - for clinicopathologic correlation
 - for diagnostic purposes (r.o. melanoma)

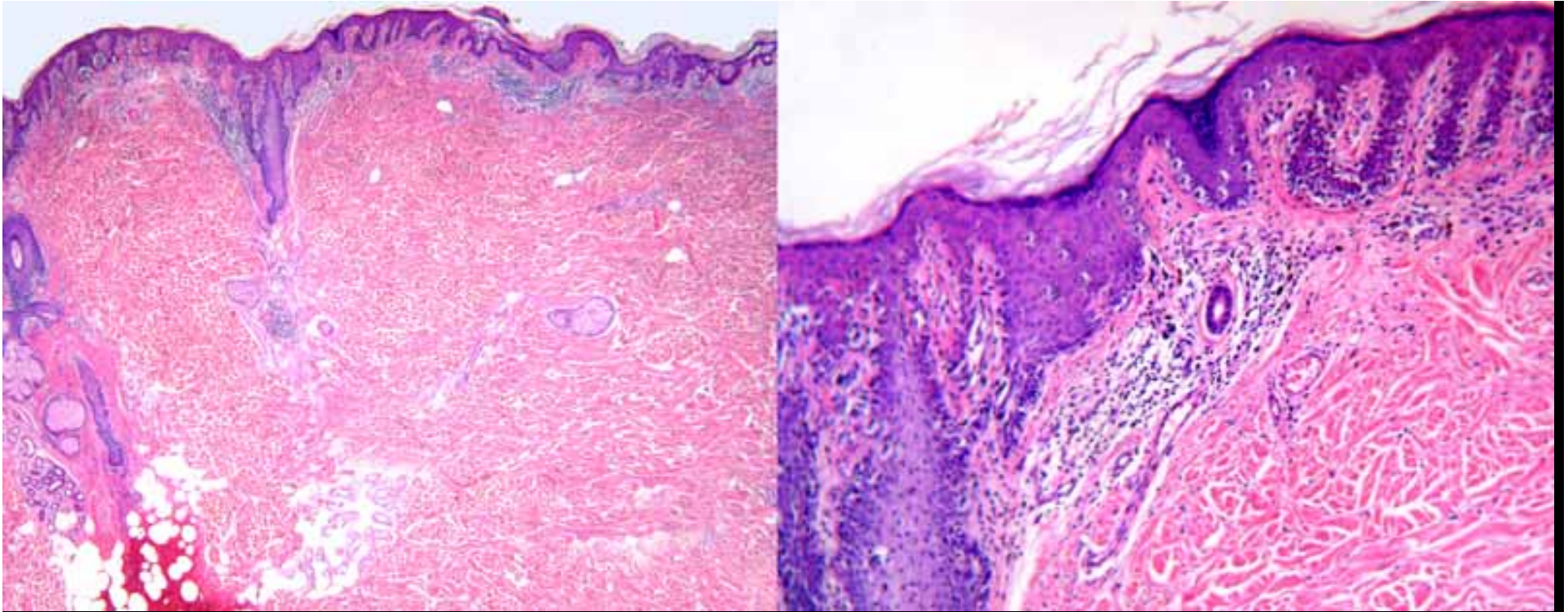
- Always report the status of the surgical margins:
 - Possible exceptions: shave and punch biopsies ("surgical margins not evaluated because of the surgical procedure")

Reporting of a 'probably benign' lesion

- **ATYPICAL NEVUS**: a nevus which 'deviates' from its 'normal' (stereotypical) counterpart
- More or less subjective diagnostic uncertainty and NOT a 'biologically intermediate' lesion between nevus and melanoma
- Always list the atypical features in the 'microscopic features' section of the histopathologic report
- Assessment of the surgical margins mandatory, but distance between the lesion and the surgical margins not required

Reporting of a 'possibly malignant' lesion (derived from: Elder-Xu, 2004)

- **SUPERFICIAL ATYPICAL MELANOCYTIC PROLIFERATION OF UNCERTAIN SIGNIFICANCE (S.A.M.P.U.S.)** = neoplasm in a radial (horizontal) growth phase ~/= no evidence of any focus of prevailing dermal growth
- **MELANOCYTIC TUMOR OF UNCERTAIN MALIGNANT POTENTIAL (MEL.T.U.M.P.)** = prevailing dermal growth (esp. with sheets of cells and/or ulceration and/or brisk mitotic activity)



Ddx: lentiginous 'dysplastic' nevus
vs. lentiginous melanoma

Differential diagnosis

Lentiginous dysplastic nevus

- Young patients
- Small-to-medium size
- Sharp circumpcription
- Junctional nests common
- No pagetoid spread
- Bland dermal component

Lentiginous melanoma

- Middle aged to old patients
- Large size
- Poor circumscription
- Junctional nests inconsistent
- Some pagetoid spread
- No dermal component

S.A.M.P.U.S. is in between!
Can also use 'L.A.M.P.'

Melanocytic Tumors of Uncertain Malignant Potential

Results of a Tutorial Held at the XXIX Symposium of the International Society of Dermatopathology in Graz, October 2008

Lorenzo Cerroni, MD, Raymond Barnhill, MD,† David Elder, MD,‡
Geoffrey Gottlieb, MD,§ Peter Heenan, MD,|| Heinz Kutzner, MD,¶
Philip E. LeBoit, MD,# Martin Mihm, Jr, MD,**
Juan Rosai, MD,†† and Helmut Kerl, MD**

57 cases divided into:

- **Favorable behavior:**
NED, at least after 5 yrs
- **Intermediate (borderline) behavior:** small nodal deposits
- **Unfavorable behavior:** metastasis and/or death

The screenshot shows a web page header for 'FACULTY OF 1000 MEDICINE' with the tagline 'GLOBAL LEADERS. EXPERT KNOWLEDGE'. To the right is a 'MEDICINE REPORTS' logo with the text 'NEW from Faculty of 1000 Fast reports on hot topics'. Below the header is a navigation bar with links: 'My F1000 | Browse | Top 10s | Advanced Search | My Details | About | Faculty Members | Associate FMs | F1000 Reports | Compose Evaluation'. The main content area features a 'Must Read' badge with 'F1000 Factor 6.0' and a dropdown menu set to 'EndNote'. The article title is 'Melanocytic Tumors of Uncertain Malignant Potential: Results of a Tutorial Held at the XXIX Symposium of the International Society of Dermatopathology in Graz, October 2008.' The authors listed are Cerroni L, Barnhill R, Elder D, Gottlieb G, Heenan P, Kutzner H, Leboit PE, Mihm M, Rosai J, Kerl H. The citation is 'Am J Surg Pathol 2010 Jan 20' with links for 'abstract on PubMed', 'citations on Google Scholar', 'related articles', and 'full text'. A blue box at the bottom indicates the article was 'Selected by | Giuliana Crisman and Gerardo Ferrara' and 'Evaluated 4 Feb 2010', with links for 'Browse relevant Sections' and 'View additional Info'.

Main data

Atypical Spitz (n=35)

- Mean age: 26.1
- M:F= 1:1.6
- Mean thickness: 3.98
- Favorable behavior: 10
- Intermediate behavior: 10
- Unfavorable behavior: 15

Atypical blue (n=22)

- Mean age: 33.6 yrs
- M:F=1:1.3
- Mean thickness: 3.66 mm
- Favorable behavior: 7
- Intermediate behavior: 4
- Unfavorable behavior: 11

Interpretation of data

- EXPERTS unable to reach an acceptable diagnostic agreement
- Morphologic features not allowing a reliable distinction between cases with a benign and cases with a malignant behaviour
- As a consequence,
SPITZ/BLUE TUMORS = MELANOMAS
- Relatively favourable outcome when considering the great thickness

LOW-GRADE MALIGNANCIES?

**THE CONCEPT OF LOW-GRADE MELANOMA HAS YET TO BE ACCEPTED;
THUS, SO FAR NO CLINICAL PROTOCOLS ARE SET UP**

Melanoma reporting

- Compulsory parameters -

- Breslow's thickness
- Ulceration Y/N
 - Report 'non-ulcerated' if not found
- **Dermal mitotic figures**
 - **Report 'o' if not found**
- Regression
 - Report if present
- Vascular invasion
 - Report if present
- Microsatellitosis
 - Report if present
- Distance from the closest margin

MICROSTAGING

Breslow's thickness

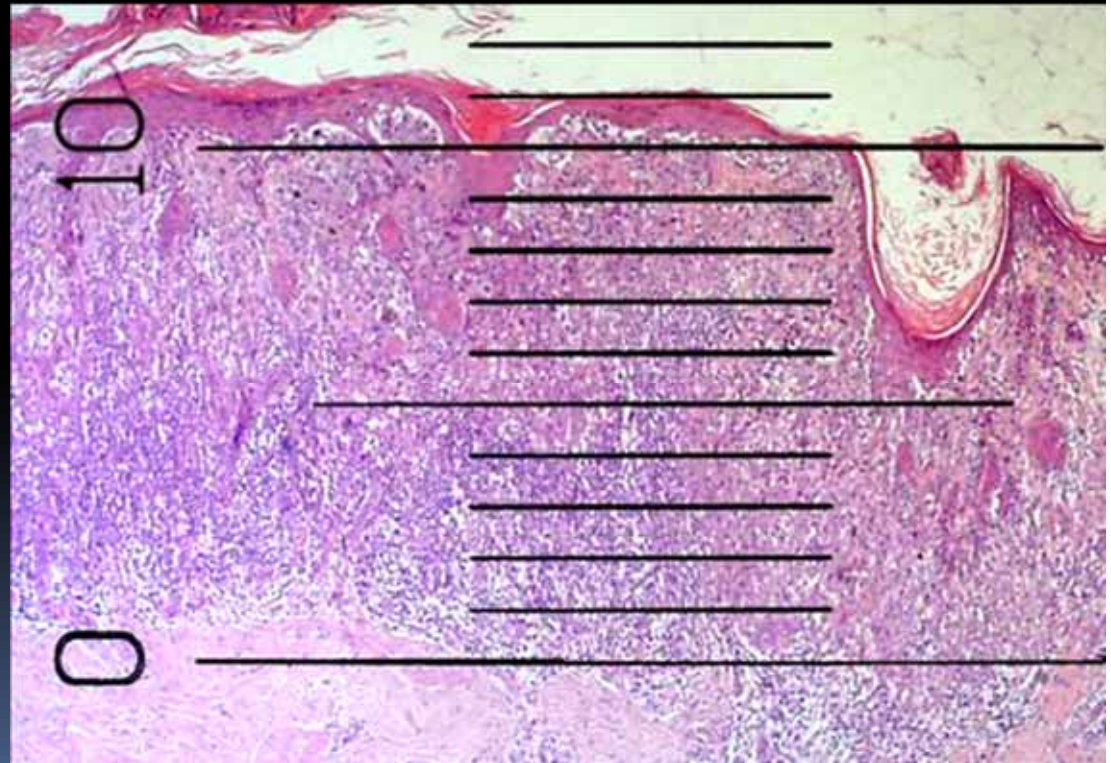
Measured with an ocular micrometer from the granular layer (or from the floor of the ulceration) to the point of deepest invasion

pT1: ≤ 1.0 mm

pT2: 1,01 – 2.0 mm

pT3: 2,01 – 4.0 mm

pT4: > 4.1 mm



Courtesy of Dr. Roberto Ricci, Parma, I



AJCC
American Joint Committee on Cancer

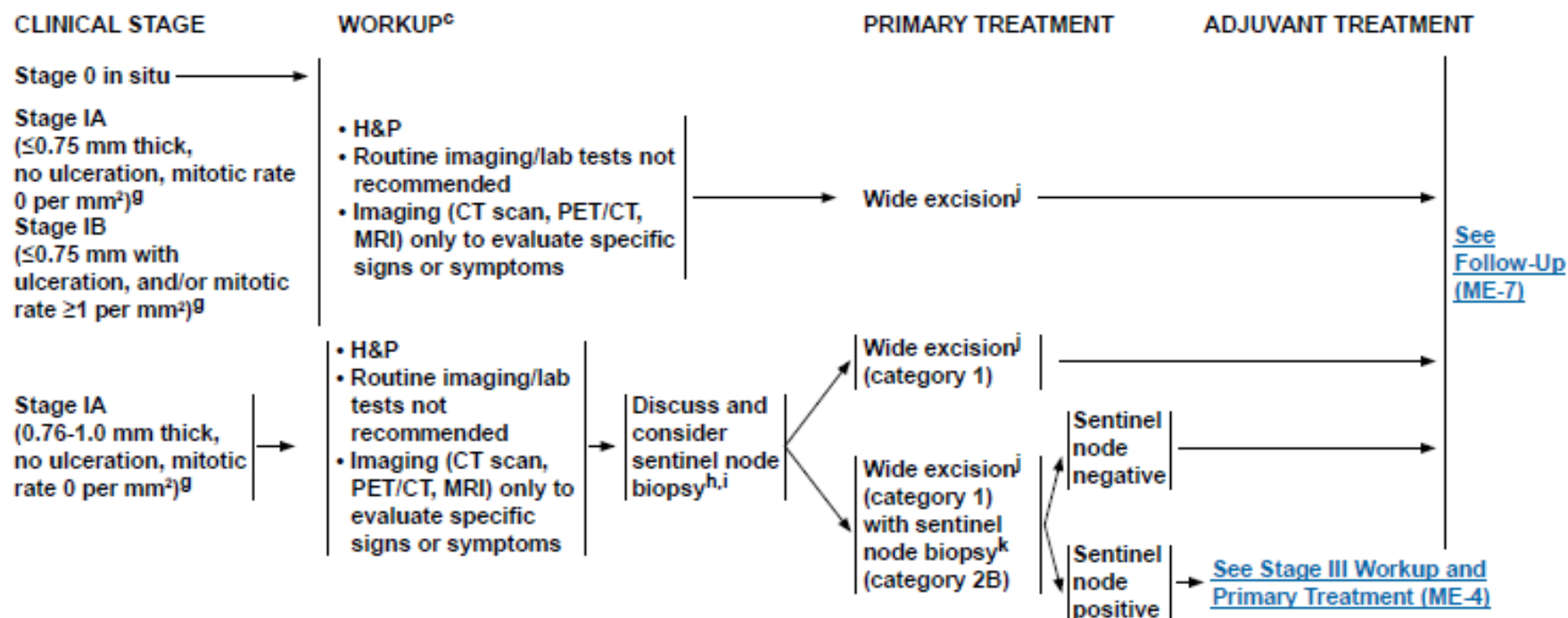
AJCC Cancer Staging Manual

Eighth Edition

 Springer

Breslow's thickness in the AJCC8

- Recorded to the nearest 0.1 mm
 - Lower 0.1 from 0.01 to 0.04
 - Upper 0.01 from 0.05 to 0.09
- T1b defined by ulceration and/or BT ≥ 0.8 mm
 - Comprises melanomas ≥ 0.75 mm



^gIn general, SLNB is not recommended for primary melanomas ≤0.75 mm thick, unless there is significant uncertainty about the adequacy of microstaging. For melanomas 0.76-1.0 mm thick, SLNB may be considered in the appropriate clinical context. In patients with thin melanomas (≤1.0 mm), apart from primary tumor thickness, there is little consensus as to what should be considered “high-risk features” for a positive SLN. Conventional risk factors for a positive SLN, such as ulceration, high mitotic rate, and lymphovascular invasion (LVI), are very uncommon in melanomas ≤0.75 mm thick; when present, SLNB may be considered on an individual basis.

^cWhile there is interest in newer prognostic molecular techniques such as gene expression profiling to differentiate melanomas at low-versus high-risk for metastasis, routine (baseline) genetic testing of primary melanomas (before or following SLNB) is not recommended outside of a clinical trial. Mutational analysis is recommended if patients are being considered for either routine treatment or clinical trials, but not recommended for patients who are otherwise NED.

^dDecision not to perform SLNB may be based on significant patient comorbidities, patient preference, or other factors.

^eSLNB is an important staging tool, but the impact of SLNB on overall survival is unclear.

^fSee [Principles of Surgical Margins for Wide Excision of Primary Melanoma \(ME-B\)](#).

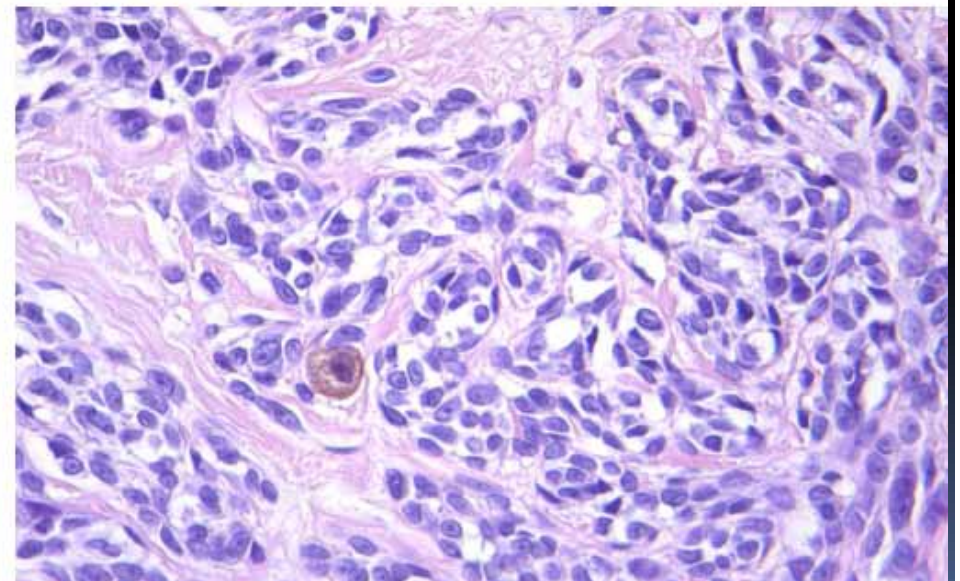
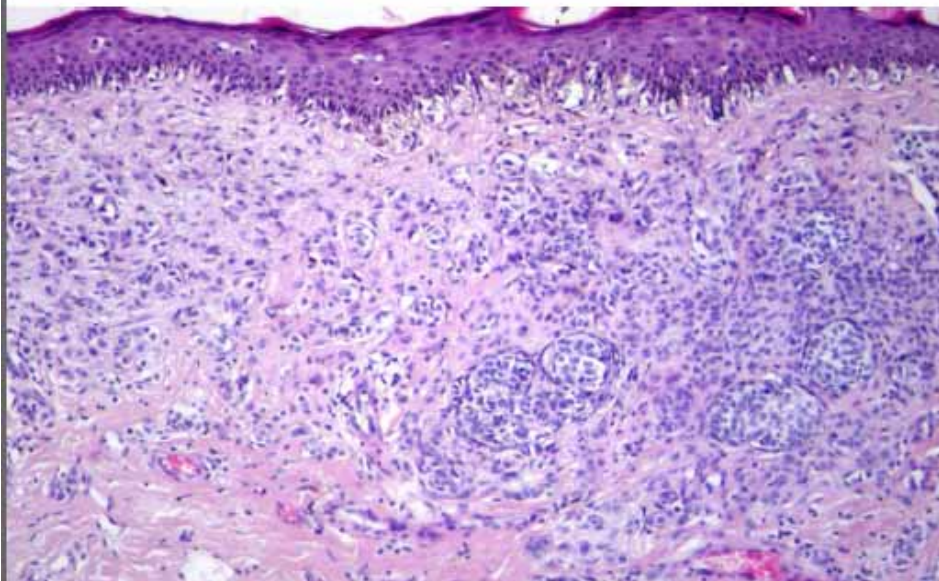
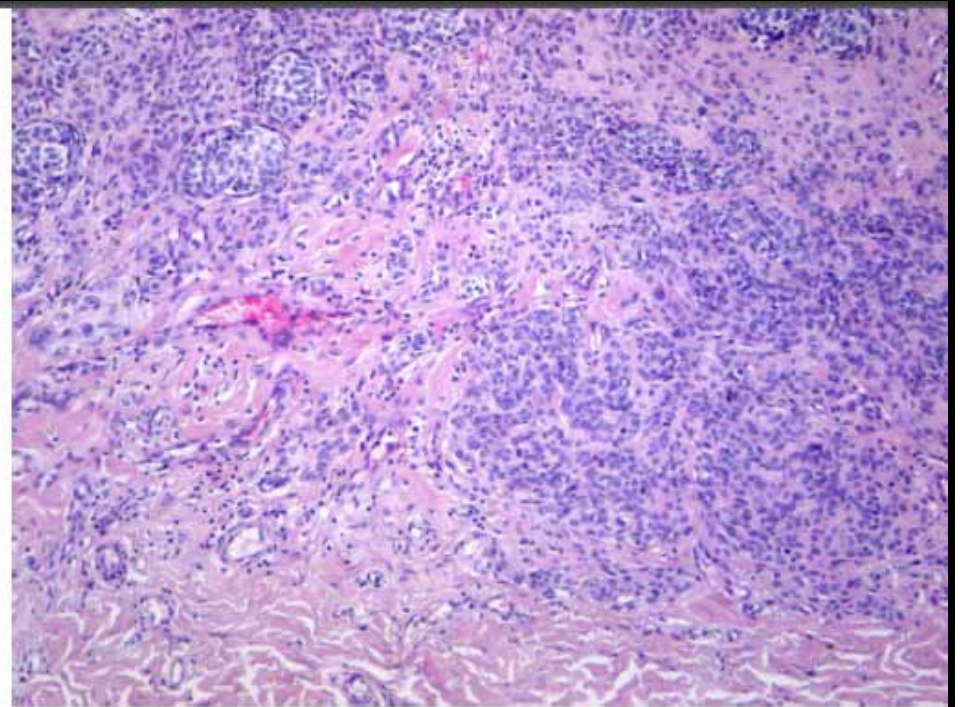
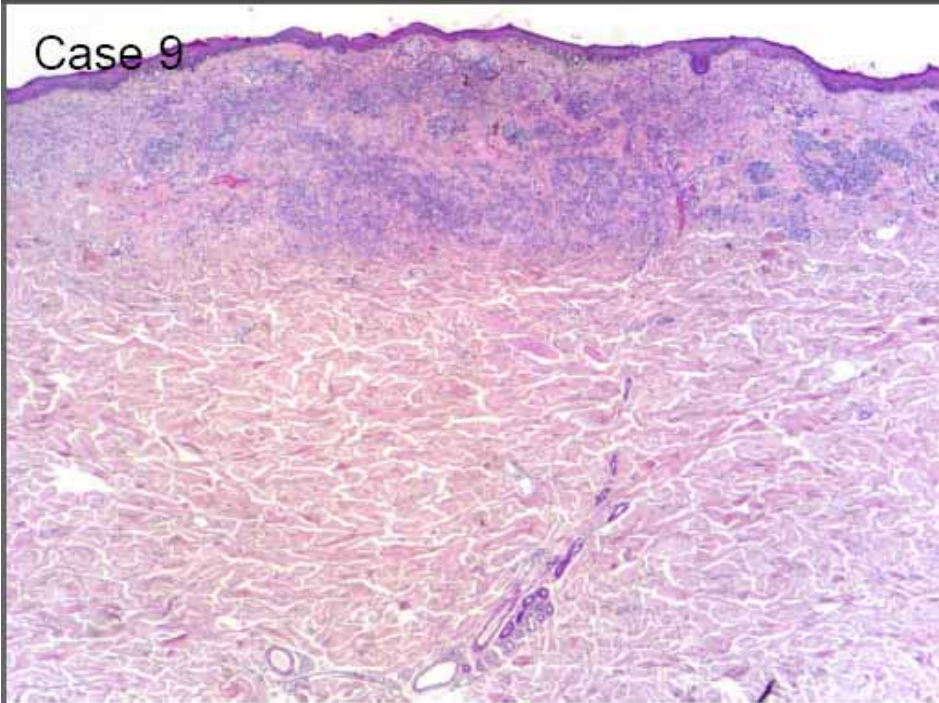
^gSentinel lymph nodes should be evaluated with multiple sectioning and immunohistochemistry.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Troubles with Breslow's

- Regression
 - can underestimate Breslow's
- Pseudomaturation vs nevus-associated melanoma
- Verrucous melanoma
- Adnexotropic melanoma

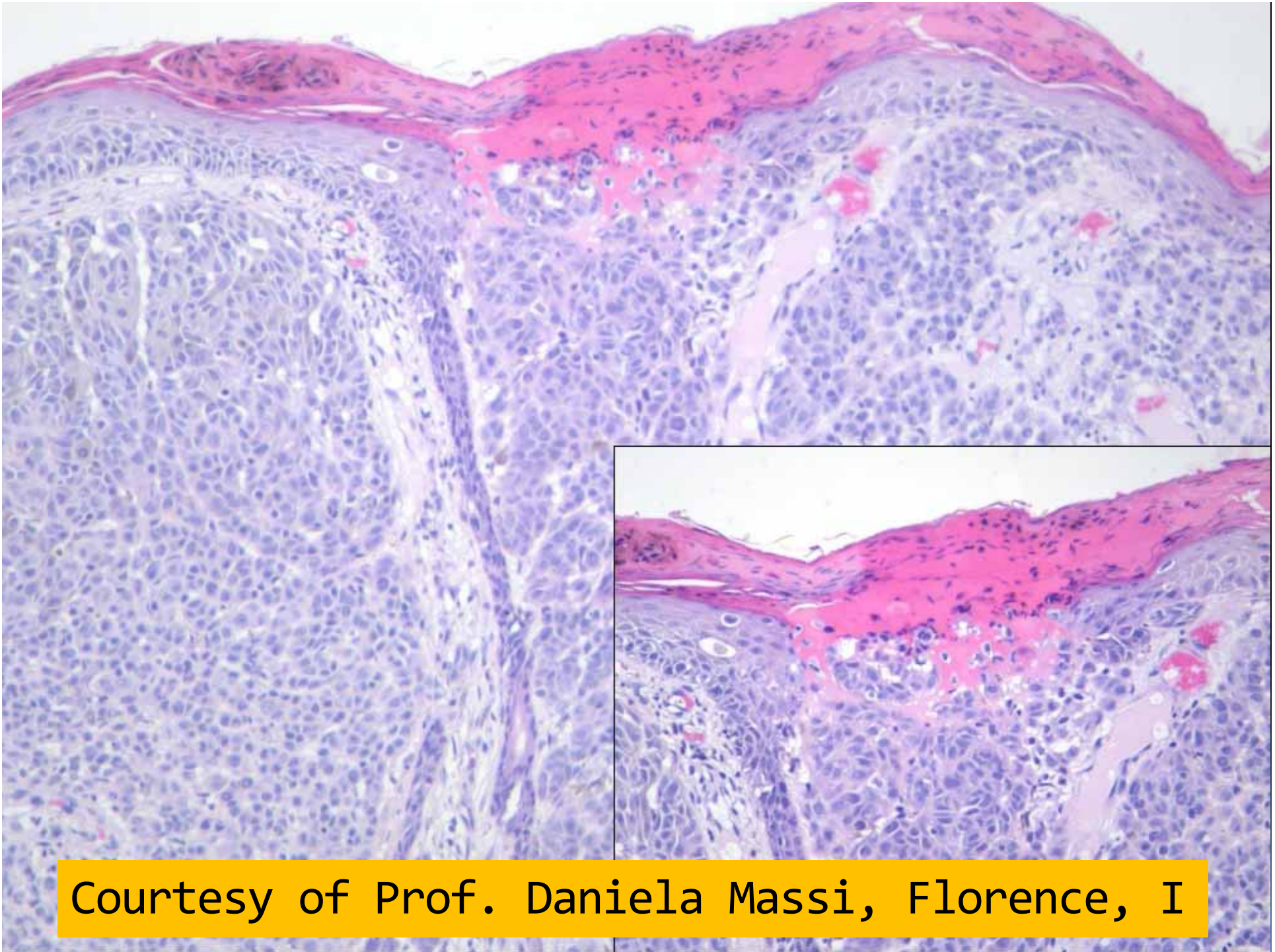
Case 9



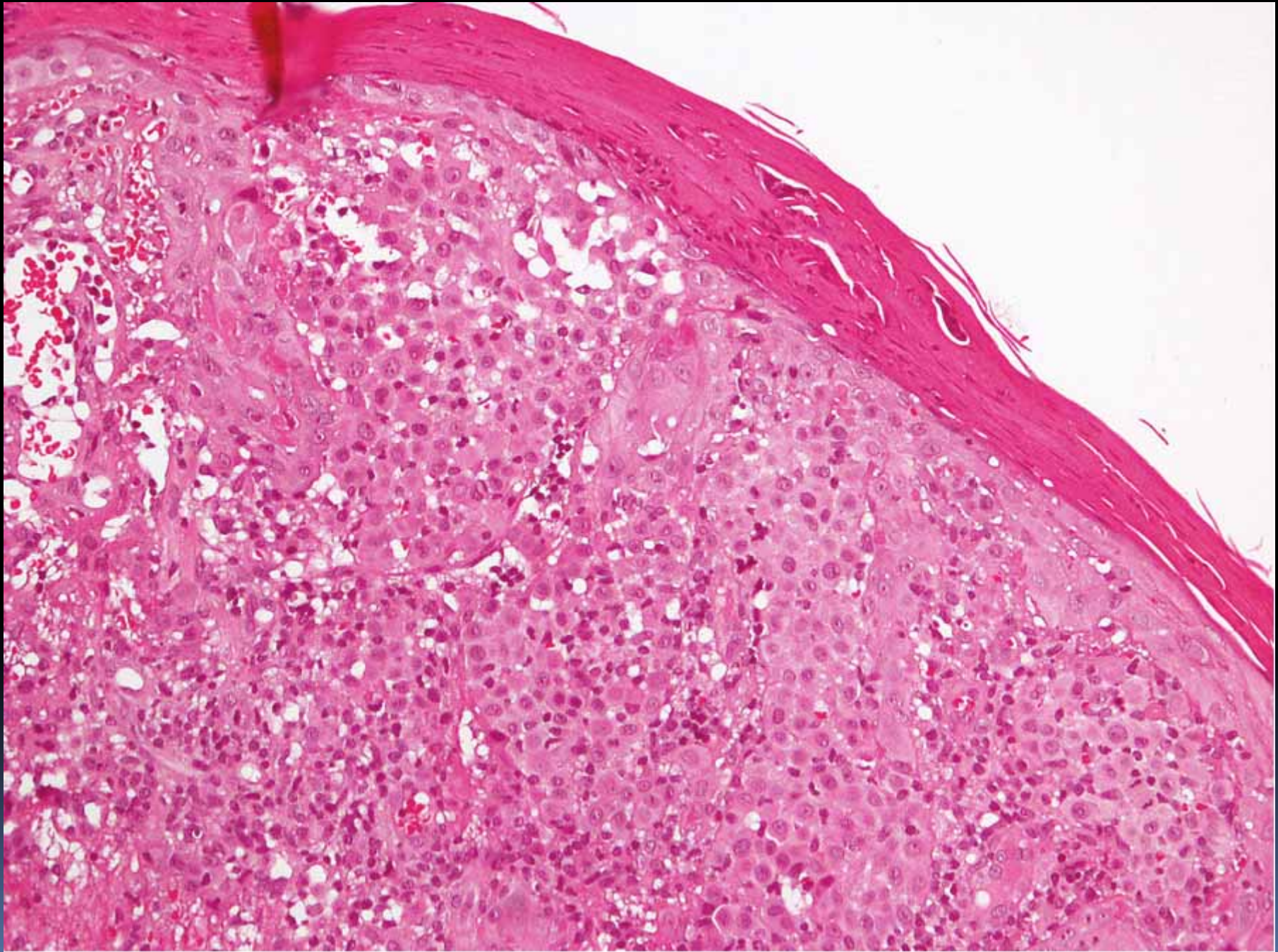
Courtesy of Prof. Daniela Massi, Florence, I

Ulceration

- The strongest prognostic factor after Breslow's
- 'Prognostic impact well established since decades (Day CL Jr, et al. Ann Surg 1982;195: 35)
- Full-thickness epidermal defect with reactive tissue changes (fibrin, neutrophils) and atrophy or hypertrophy of the surrounding epidermis with no history of trauma or surgery
- Report as 'ABSENT' if not found
- In Cochran's survival model (2000): measure of its breadth



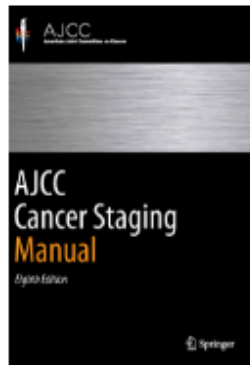
Courtesy of Prof. Daniela Massi, Florence, I



Mitotic figure(s)

- Defined as a SURELY NEOPLASTIC (neither stromal nor inflammatory) nucleus showing: (1) absence of nuclear membrane signifying the end of prophase; (2) presence of condensed chromosomes, either clotted (beginning metaphase), arranged in a plane (metaphase or anaphase) or in separate clots (telophase)
- Strong prognostic parameter
- Also STAGING PARAMETER IN pT₁ (up to Breslow's 1 mm) melanoma

Implementation of AJCC 8th Edition Cancer Staging System



The American Joint Committee on Cancer (AJCC) has been working closely with all of its member organizations throughout the development of the recently published 8th Edition Cancer Staging Manual. The coordination of the implementation for a new staging system is critically important to ensure that all partners in patient care and cancer data collection are working in synchrony.

In order to ensure that the cancer care community has the necessary infrastructure in place for documenting 8th Edition stage, the AJCC Executive Committee, in dialogue with the National Cancer Institute (NCI-SEER), Centers for Disease Control and Prevention (CDC), the College of American Pathologists (CAP), the National Comprehensive Cancer Network (NCCN, the National Cancer Data Base (NCDB), and the Commission on Cancer (CoC), made the decision to delay the implementation of the 8th Edition Cancer Staging System to January 1, 2018.

Clinicians will continue to use the latest information for patient care, including scientific content of the 8th Edition Manual. All newly diagnosed cases through December 31st 2017 should be staged with the 7th edition. The time extension will allow all partners to develop and update protocols and guidelines and for software vendors to develop, test, and deploy their products in time for the data collection and implementation of the 8th edition in 2018.

The AJCC is working together with all of its members as well as software vendors to make this transition as smooth as possible for the oncology community. More communication will follow from the AJCC and the member organizations over the coming weeks.

Regression

- Loss of tumor mass (not necessarily melanoma!) in the absence of any potentially effective therapy
- **TYPICALLY: pale (edematous), with newly formed vessels and with melanophages**
- **But also sclerotic (with untidy collagen bundles)**
- Absent vs present
- Absent vs focal vs extensive
- Absent vs $<75\%$ vs $>75\%$
- Absent vs $\pm 75\%$
- Only if clear-cut
- Underestimation of Breslow's thickness

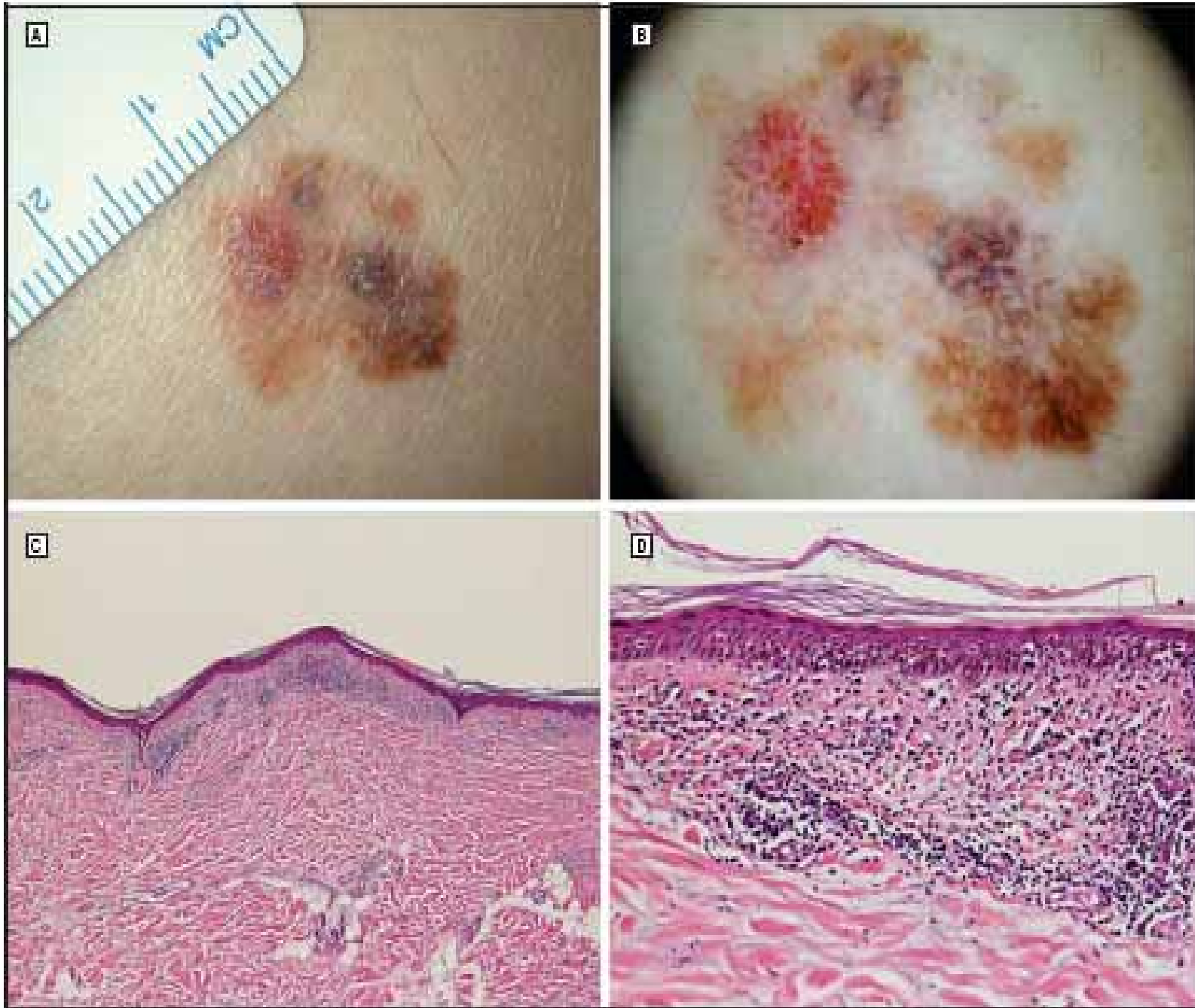
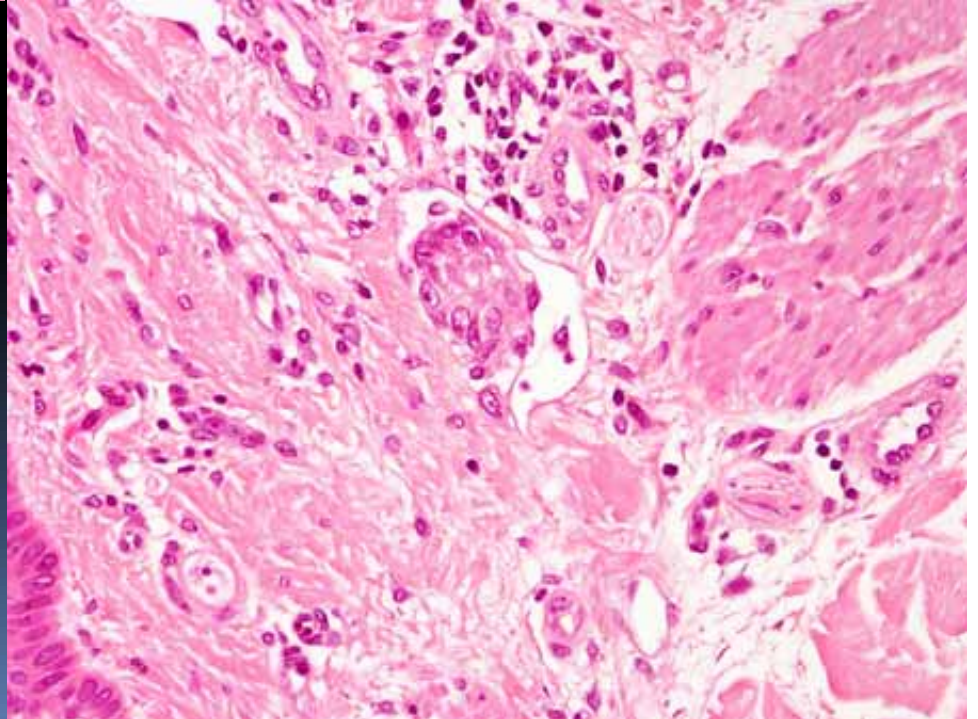
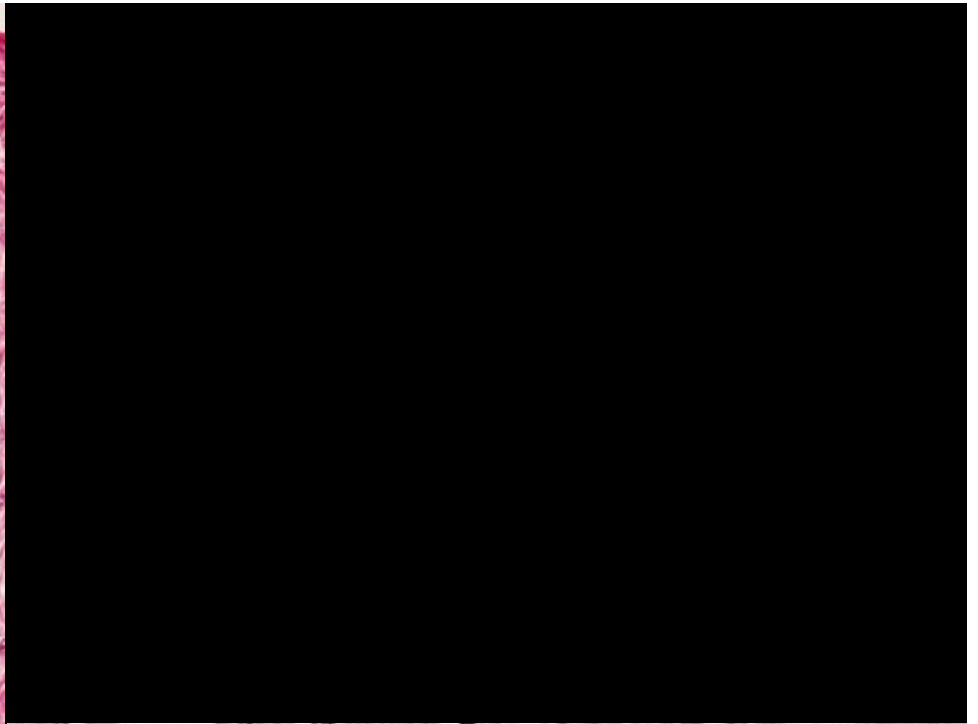
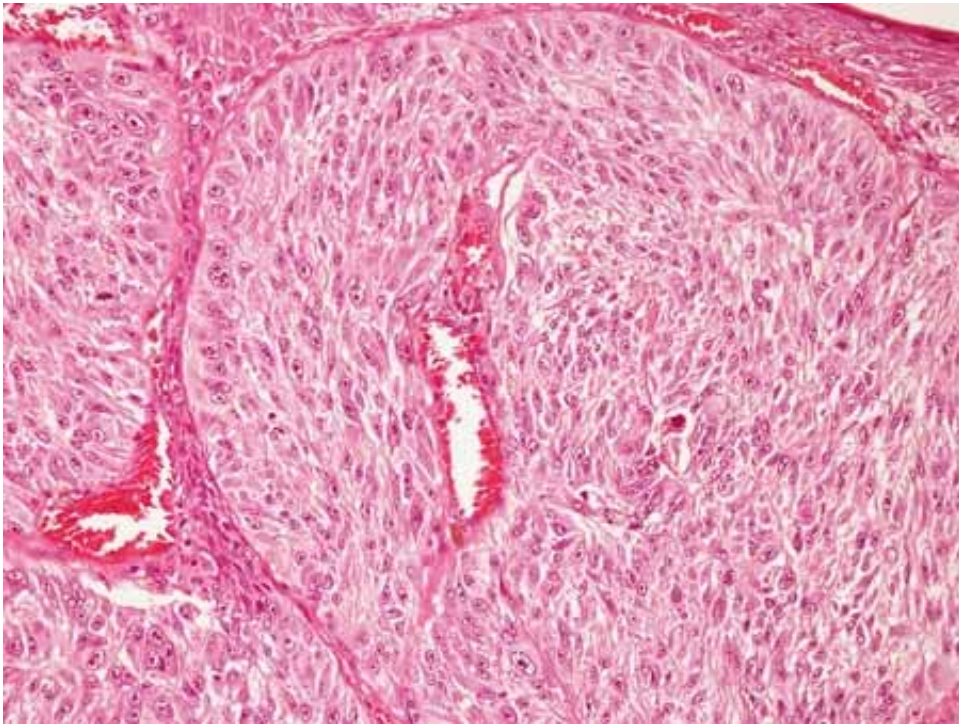


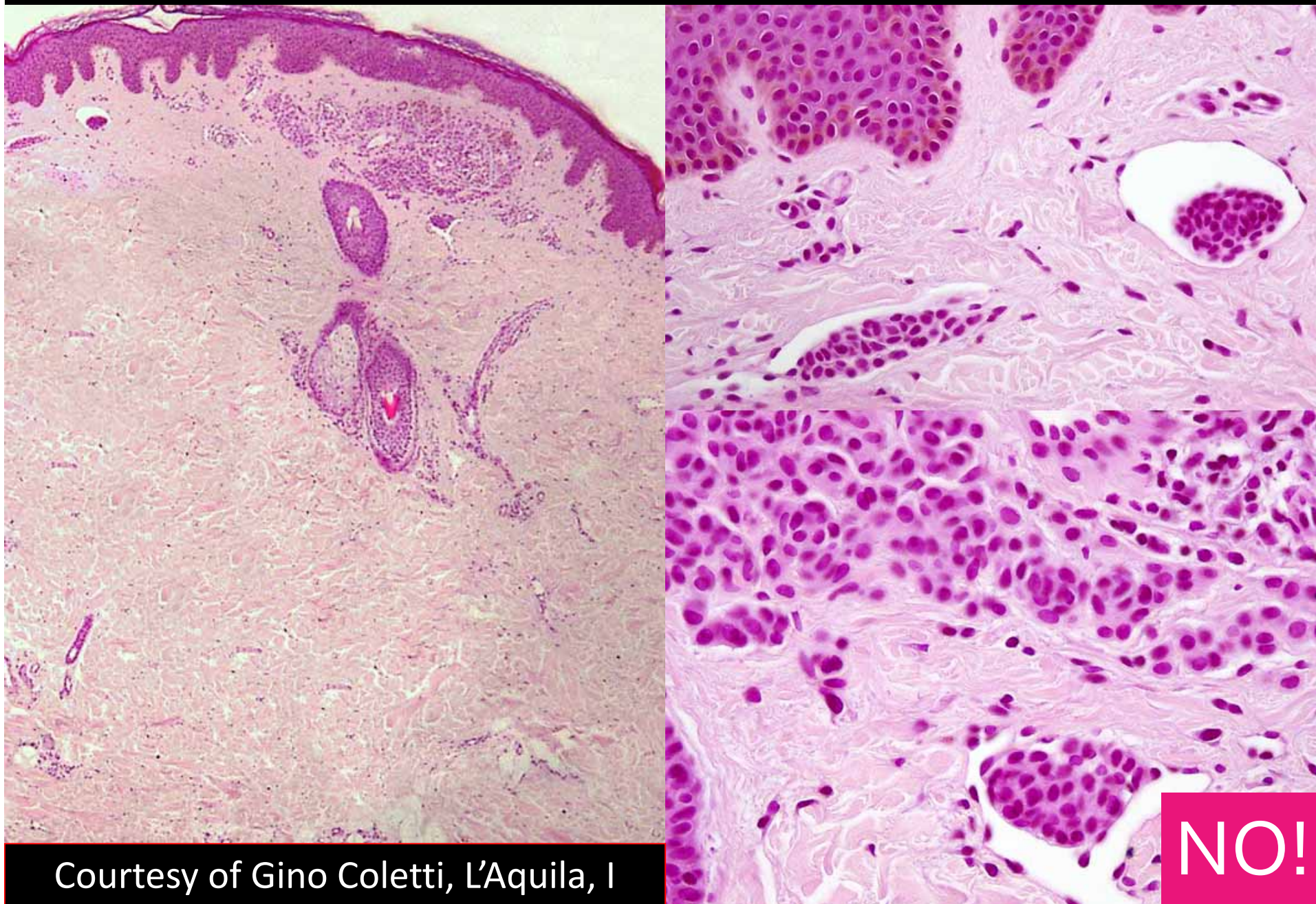
Figure. Pigmented lesion situated on the lower leg of a 49-year-old woman. A, Clinical Image; B, dermoscopic Image; C and D, Histopathologic Images.

Lymphovascular invasion

- No change in the stage
- Strongly related with locoregional relapse
 - Borgestein PG, et al, 1999: in-transist mets in 13/14 patients in stage I with LVI after a median period of 10 months
- Unrelated with the overall survival
 - Careful search IHC probably NOT warranted



Does 'vascular invasion' change the diagnosis?

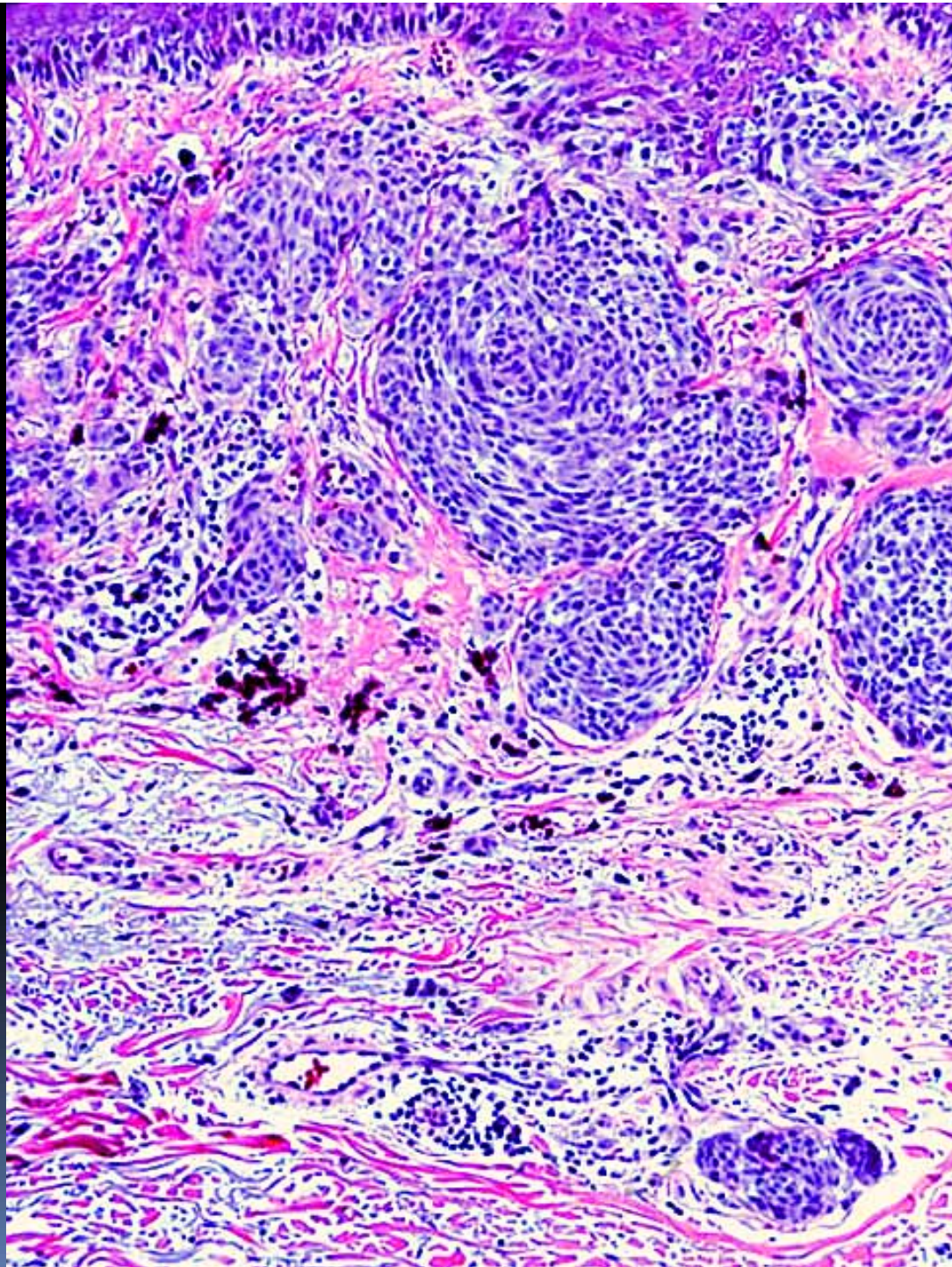


Courtesy of Gino Coletti, L'Aquila, I

NO!

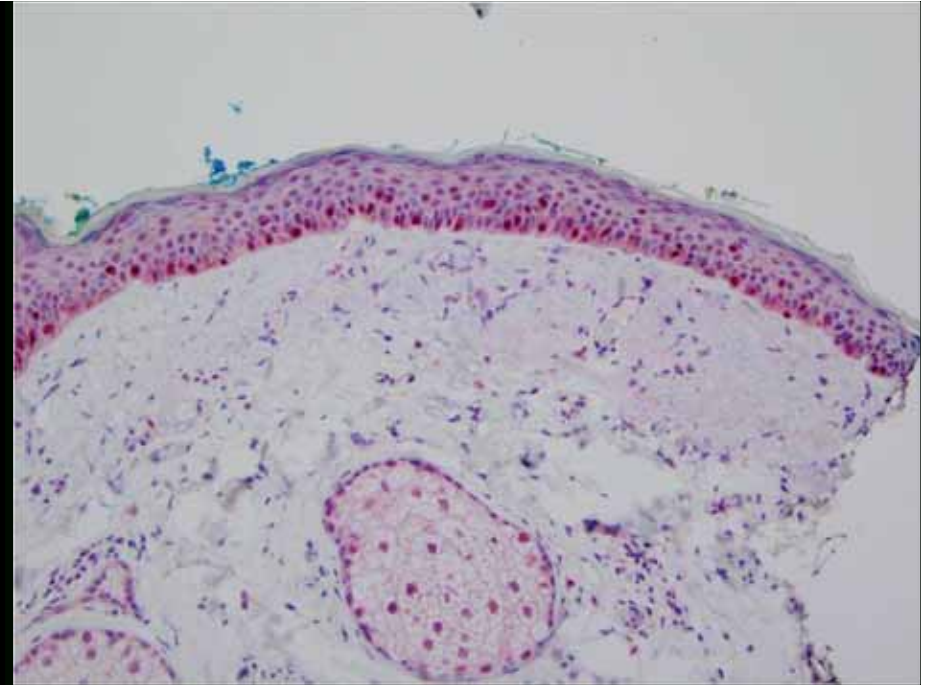
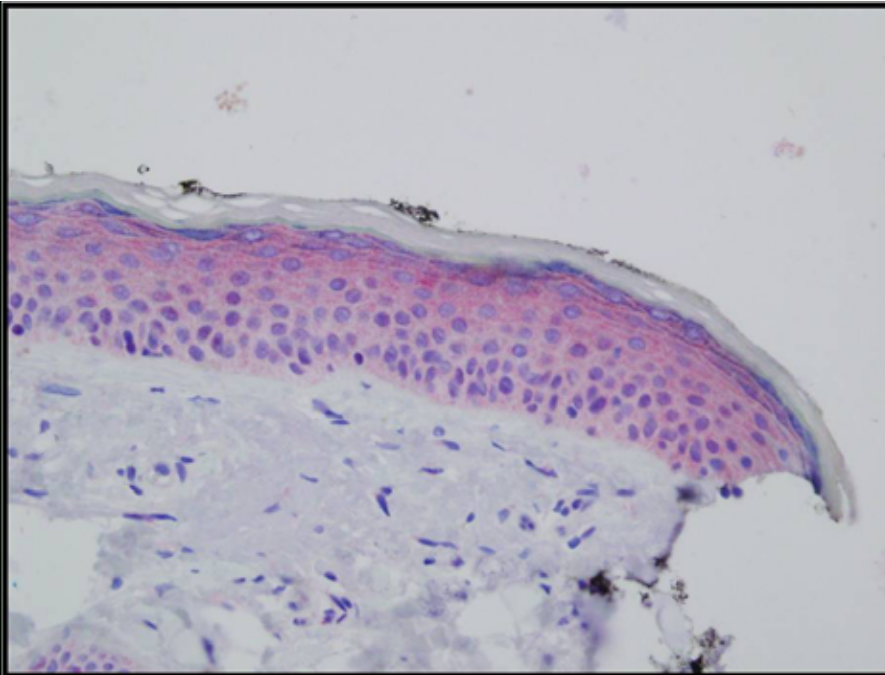
Microsatellites

- Tumor aggregate >0.05 mm separated from the deepest part of the tumor by at least 0.3 mm of normal tissue:
 - Report Y/N only in melanomas involving at least the full thickness of the papillary dermis
 - Malignant cytomorphology
- Gershenwald et al, 2000: the same prognostic significance as macrosatellites (in transit mets)



Distance of the neoplasm from the margins

- Great problems with lentiginous lesions
 - Can prove impossible to solve on a H&E basis alone
 - Immunohistochemical expression of sAC



Utility of sAC in the evaluation of lentigo maligna margins

Negative margin
No obvious highlighting of
Melanocytes by sAC is observed

Lentigo Maligna
An obvious pattern
Of pan nuclear staining
typical of malignant melanoma
In situ is present at the margin

Courtesy of Dr. Cynthia Magro, New York, USA

- **Subtype (WHO, 2007)**
 - Superficial spreading (SSM)
 - Nodular (NM)
 - Lentigo maligna (LMM)
 - Acral lentiginous (ALM)
 - Mucosal lentiginous (MLM)
 - Desmoplastic/neurotropic (DNM)
 - Nevoid (NeM)
 - Melanoma in giant congenital nevus (M-GCN)
 - Melanoma arising in blue nevus (M-BN)
 - Childhood melanoma
 - Persistent melanoma (PM)
 - Melanoma, NOS

- **Cytologic features:**

- Epithelioid
- Spindle cell
- Spitzoid,
- Nevoid
- Neuroid
- Small cell

- **Growth phase:**

- Radial (horizontal)
- Vertical

- **Clark's level**

- **Perivasular/intravascular/perineural invasion**

- **Pigmentation:**

- None
- Mild
- Moderate
- Heavy

- **Entity of the inflammatory infiltrate:**

- None
- Mild
- Moderate
- Heavy

- **Distribution of the inflammatory infiltrate (if applicable):**

- Brisk
- Non-brisk

- **Nevus associated**

- **Distance from all the surgical margins**

- **pTNM**

- **M T/ICD –O-SNOMED code**

OPTIONAL PARAMETERS!!

WHO classification, 2007

WHO histological classification of melanocytic tumours

Malignant melanoma	8720/3	Dermal melanocytic lesions	
Superficial spreading melanoma	8743/3	Mongolian spot	
Nodular melanoma	8721/3	Naevus of Ito and Ota	
Lentigo maligna	8742/2	Blue naevus	8780/0
Acral-lentiginous melanoma	8744/3	Cellular blue naevus	8790/0
Desmoplastic melanoma	8745/3	Combined naevus	
Melanoma arising from blue naevus	8780/3	Melanotic macules, simple lentigo and lentiginous naevus	
Melanoma arising in a giant congenital naevus	8761/3	Dysplastic naevus	8727/0
Melanoma of childhood		Site-specific naevi	
Naevoid melanoma	8720/3	Acral	
Persistent melanoma	8720/3	Genital	
		Meyerson naevus	
Benign melanocytic tumours		Persistent (recurrent) melanocytic naevus	
Congenital melanocytic naevi		Spitz naevus	8770/0
Superficial type	8761/0	Pigmented spindle cell naevus (Reed)	8770/0
Proliferative nodules in congenital melanocytic naevi	8762/1	Halo naevus	8723/0

¹ Morphology code of the International Classification of Diseases for Oncology (ICD-O) [786] and the Systematized Nomenclature of Medicine (<http://snomed.org>). Behaviour is coded /0 for benign tumours, /3 for malignant tumours, /2 for non-invasive tumours, and /1 for borderline or uncertain behaviour.

Unreliability of subtyping!

- WHO 2006 classification largely overlapping with Clark's 1967
- Criteria which are:
 - not purely histopathologic
 - not purely cytopathologic
 - not purely tumor-related (e.g.: 'acral', 'mucosal')
- Different melanomas can have similar features
- A given melanoma can have areas with different features



development of melanoma
709 x 676 - 184 kB - jpg
sccanz.com.au



Amelanotic nodular melanoma
640 x 480 - 82 kB - jpg
dermnetnz.org



may be Nodular Melanoma.
500 x 375 - 140 kB - jpg
molesware.org



skin cancer malignant melanoma
383 x 288 - 20 kB - jpg
skin-cancer-mole-pictu...



Ulcerated nodular melanoma
640 x 480 - 71 kB - jpg
dermnetnz.org



Nodular Melanoma (NM)
546 x 550 - 41 kB - jpg
dermis.net



nodular melanoma
230 x 190 - 10 kB - jpg
chiff.com



Melanoma is the most dangerous
300 x 261 - 20 kB - jpg
jaskin.com



As such, melanoma in situ is
431 x 335 - 81 kB - gif
cancernetwork.com



Nodular melanoma most often
772 x 513 - 45 kB - jpg
courses.washington.edu



nodular melanoma
230 x 190 - 10 kB - jpg
chiff.com



Superficial spreading melanoma
747 x 512 - 64 kB - jpg
courses.washington.edu



Nodular melanoma is an
493 x 335 - 38 kB - jpg
medscape.com



What is Nodular melanoma
338 x 258 - 49 kB - gif
what-is-skin-cancer.bl...



Tumors - Nodular melanoma
640 x 480 - 85 kB - jpg
pathologyoutlines.com



Nodular Melanoma (NM)
550 x 366 - 25 kB - jpg
dermis.net



Malignant melanoma, amelanotic



nevus or nodular melanoma.
400 x 268 - 27 kB - jpg



Nodular malignant melanomas



Amelanotic Melanoma:
504 x 348 - 18 kB - jpg





Nodular melanoma

Cerca immagini

[Torna ai risultati illustrati](#)



[Mostra immagine a dimensione intera](#)

640 × 480 - 85 kB - jpg - www.pathologyoutlines.com/images/skin/nodular...

L'immagine potrebbe essere soggetta a copyright

L'immagine di seguito si trova all'indirizzo pathologyoutlines.com/topic/skintumornodularm...



PathologyOutlines.com

Find Pathology Information Fast



Skin-Melanocytic Tumors

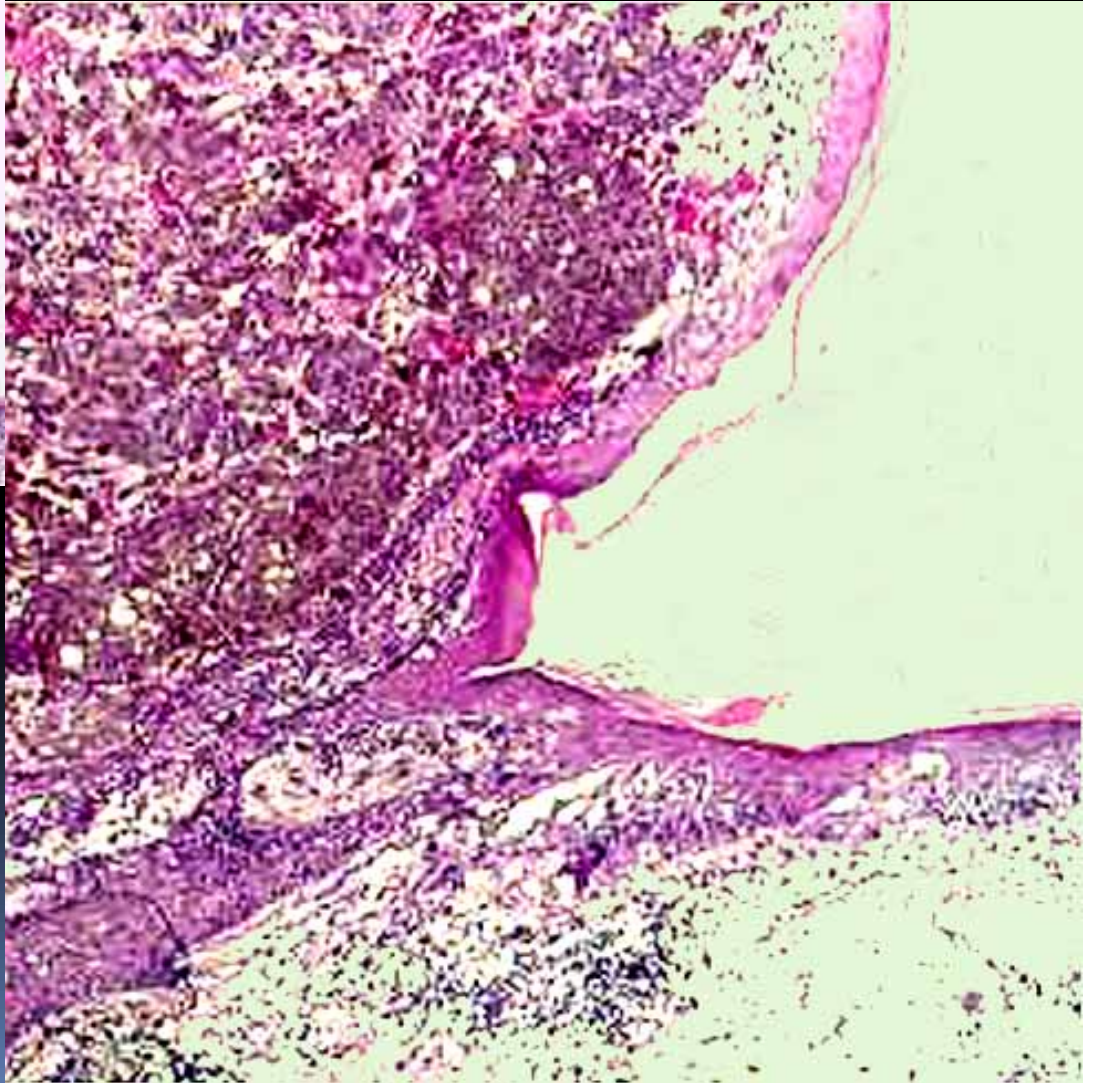
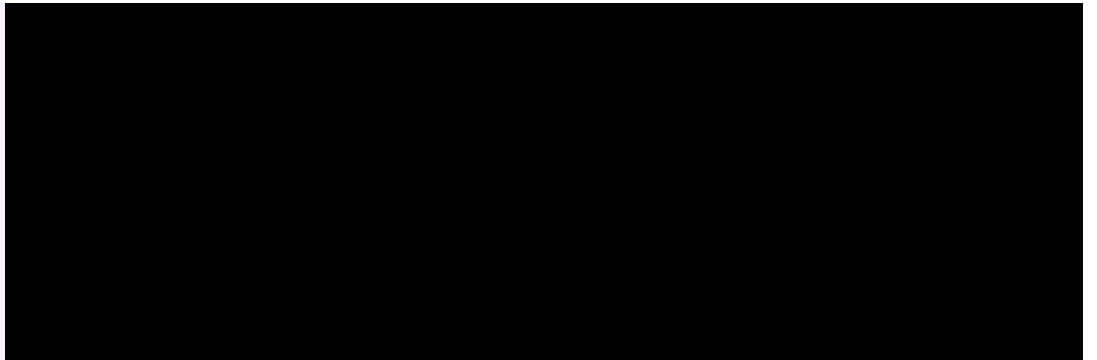
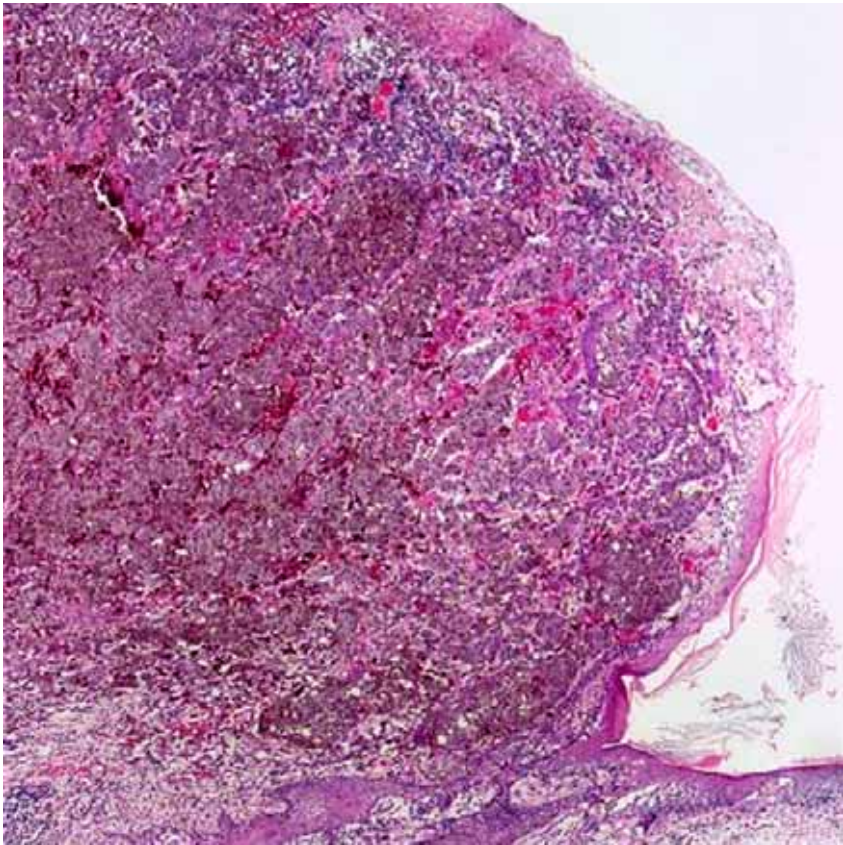
Nodular melanoma

Last major update: November 2008 - next update November 2009

Revised: 22 September 2009

Author: Nat Pernick, M.D., PathologyOutlines.com, Inc.

Copyright: (c) 2002-2009, PathologyOutlines.com, Inc.



Cytologic features

- Poorly reproducible
- Basically no prognostic information
 - Cytologic atypia completely unrelated with prognosis
- Some weak data about a small advantage in survival for thick (>5mm) tumors with Spitzoid and/or spindle cell features

Spatz A, et al. Histopathology 1998;33:406-13.

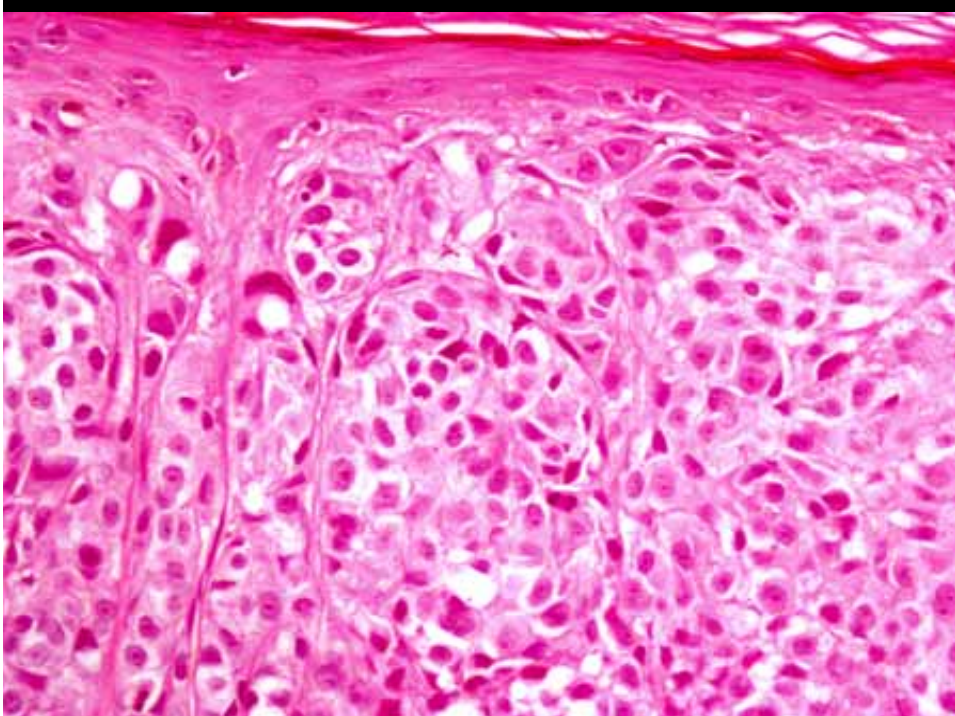
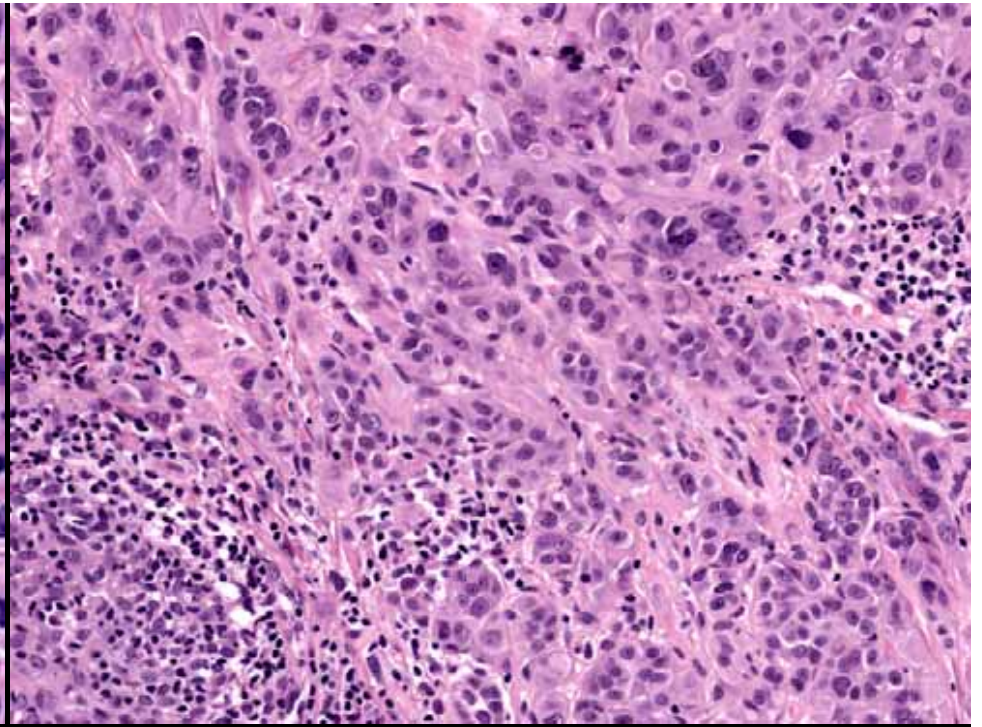
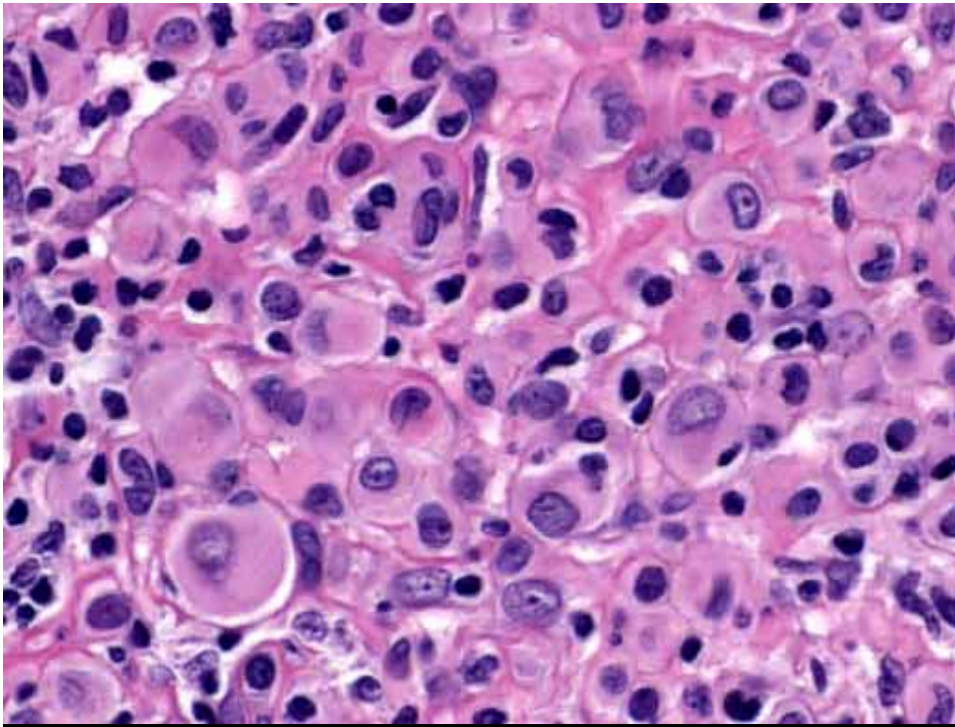


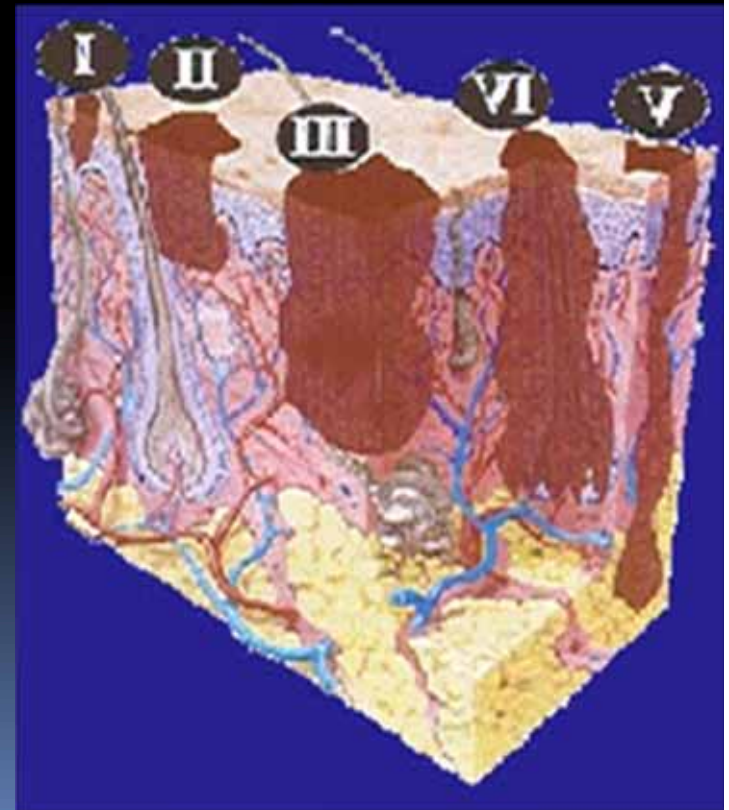
TABLE 31.1. Changes in the melanoma staging system comparing the sixth edition (2002) version with the current version (2009)

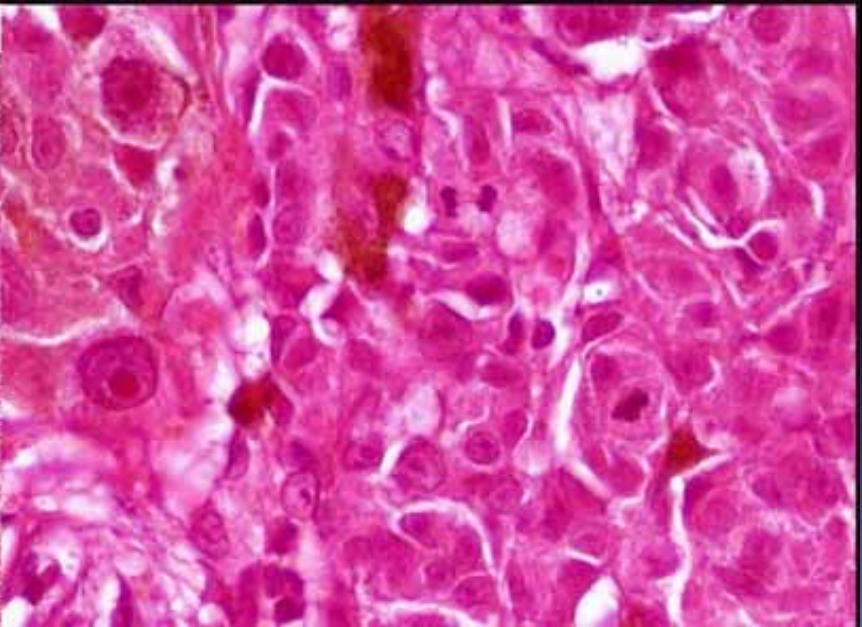
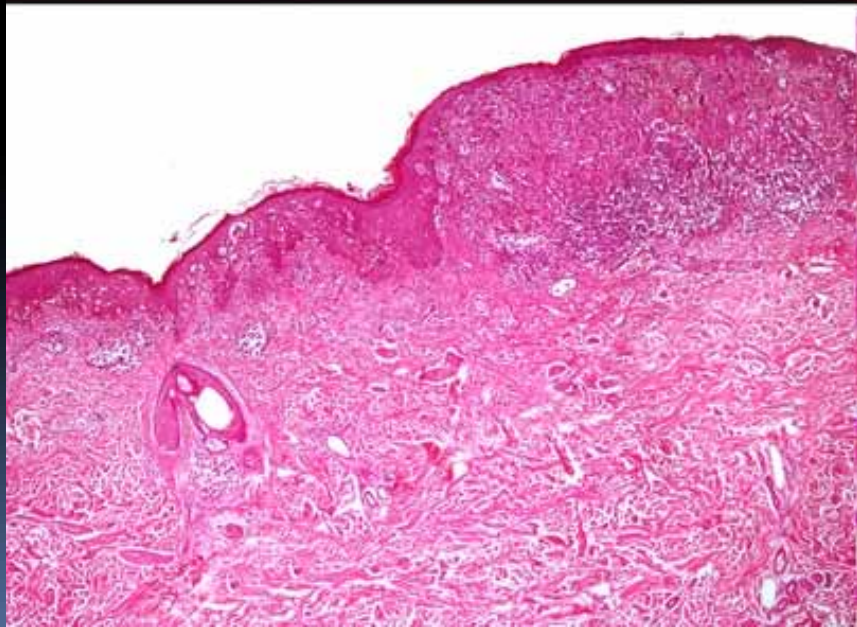
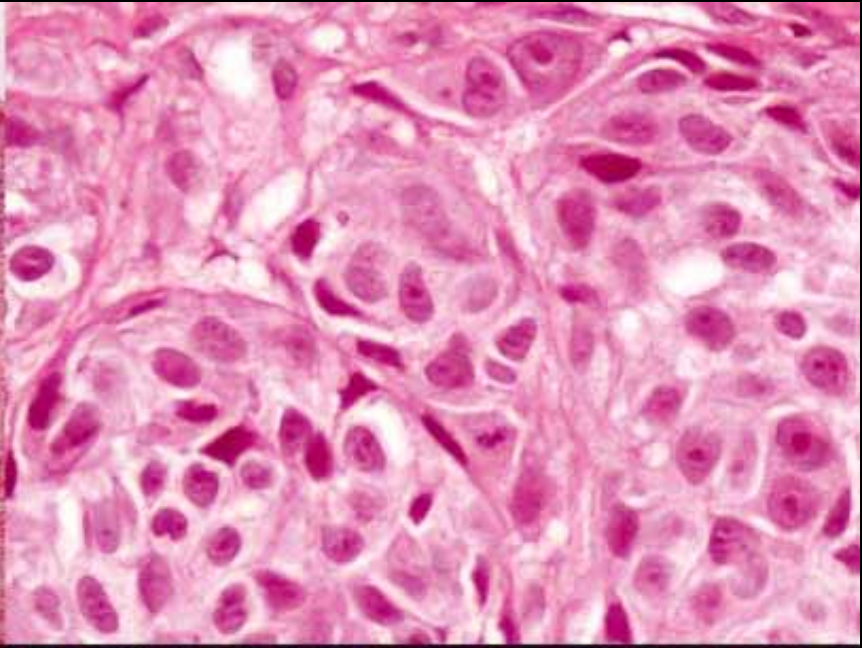
Factor	6th Edition criteria	7th Edition criteria	Comments
Thickness	Primary determinant of T staging; thresholds of 1.0, 2.0, 4.0 mm	Same	Correlation of metastatic risk is a continuous variable
Level of invasion	Used only for defining T1 melanomas	No longer used	Clark's levels \geq IV or V may be used in rare instances as a criterion for defining T1b melanoma <i>only</i> if mitotic rate cannot be determined in a nonulcerated T1 melanoma
Ulceration	Included as a second determinant of T and N staging	Same	Signifies a locally advanced lesion; dominant prognostic factor for grouping Stage I, II, and III
Mitotic rate per mm ²	Not Used	Used for categorizing T1 melanoma	Mitosis \geq 1/mm ² used as a primary determinant for defining T1b melanoma
Satellite metastases	In N category	Same	Merged with in transit lesions
Immunohistochemical detection of nodal metastases	Not allowed	Allowed	Must include at least one melanoma-specific marker (e.g., HMB-45, Melan-A, MART 1)
0.2-mm threshold of defined node-positive	Implied	No lower threshold of staging node-positive disease	
Number of nodal metastases	Dominant determinant of N staging	Same	Thresholds of 1 vs. 2–3 vs. \geq 4 nodes
Metastatic “volume”	Included as a second determinant of N staging	Same	Clinically occult (“microscopic”) vs. clinically apparent (“macroscopic”) nodal volume
Lung metastases	Separate category as M1b	Same	Has a somewhat better prognosis than other visceral metastases
Elevated serum LDH	Included as a second determinant of M staging	Same	Recommend a second confirmatory LDH if elevated
Clinical vs. pathologic staging	Sentinel node results incorporated into definition of pathologic staging		Large variability in outcome between clinical and pathologic staging; Sentinel node staging encouraged for standard patient care and should be required prior to entry into clinical trials

Microstaging

Clark's levels of invasion

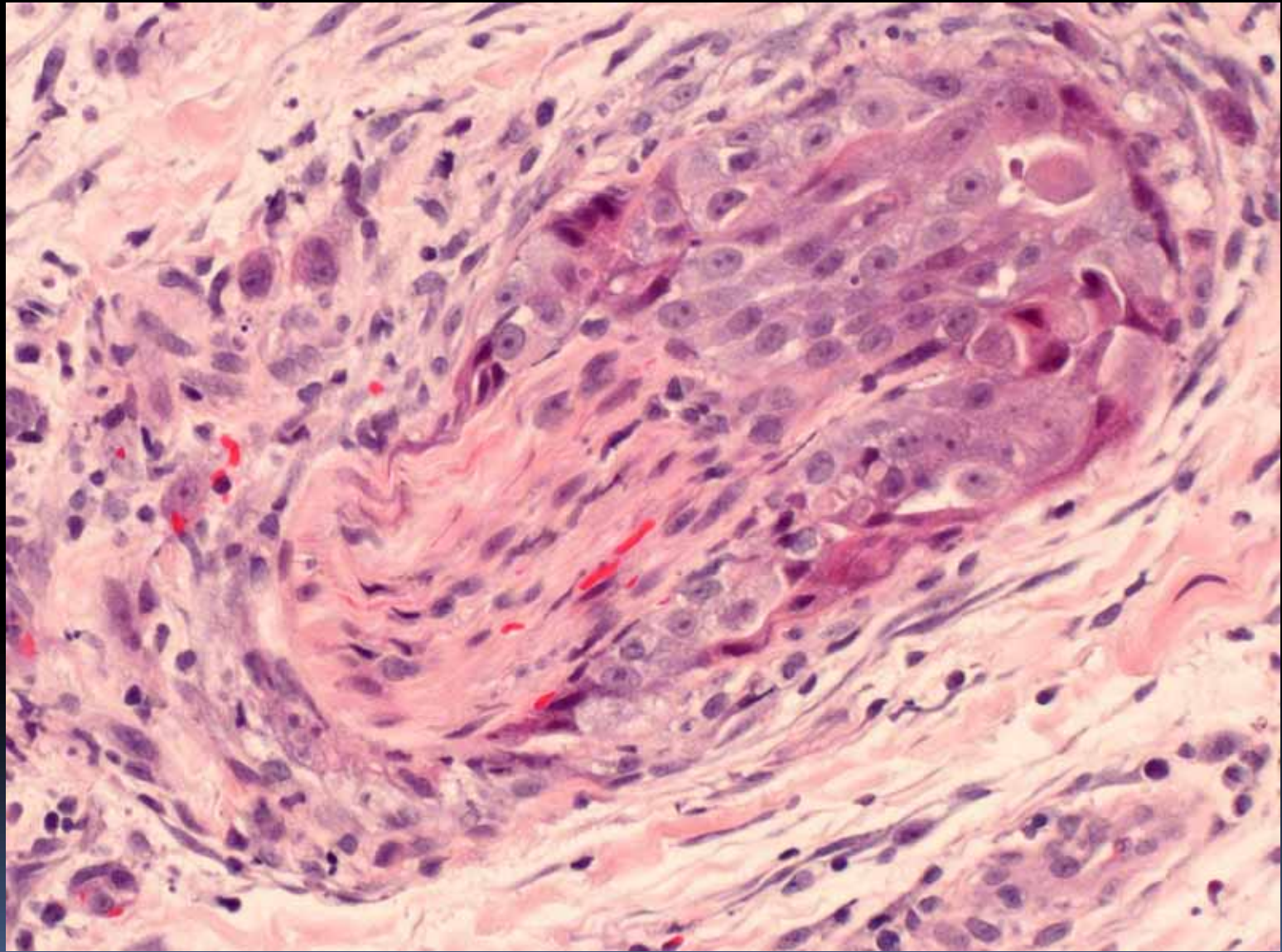
- **I level** Intraepidermal (melanoma in situ)
- **II level** Early invasion of the papillary dermis
 - not full thickness
- **III level** Invasion of the whole papillary dermis
 - compression of the reticular dermis
- **IV level** Invasion of the reticular dermis
- **V level** Invasion of the subcutis or beyond





Perineural invasion

- No change in the stage
- Virtually no study about its prognostic impact
- Typical of desmoplastic/neurotropic melanoma
- Not an unequivocal sign of malignancy:
 - Re-excision perineural invasion (Stern JP, Haupt HM, 1990)
 - Desmoplastic (Spitz) nevus
- Worth to be reported?



Definition of RGP melanoma

- A melanoma in situ or, if invasive, with the largest dermal nest being smaller than the largest intraepidermal nest
- No mitoses within the invasive component
- No ulceration
- No involvement of the reticular dermis

Growth phase

- Problems with reproducibility:
 - Size of the dermal nests also depending on the section plane
- Clark WH, et al., 1989: 501 melanoma patients; no disease-related death after 100 months in 122 cases of RGP
- Guerry D, et al, 1993: 624 melanoma patients; no disease-death after 13.7 yrs in 161 cases of RGP

Entity of pigmentation

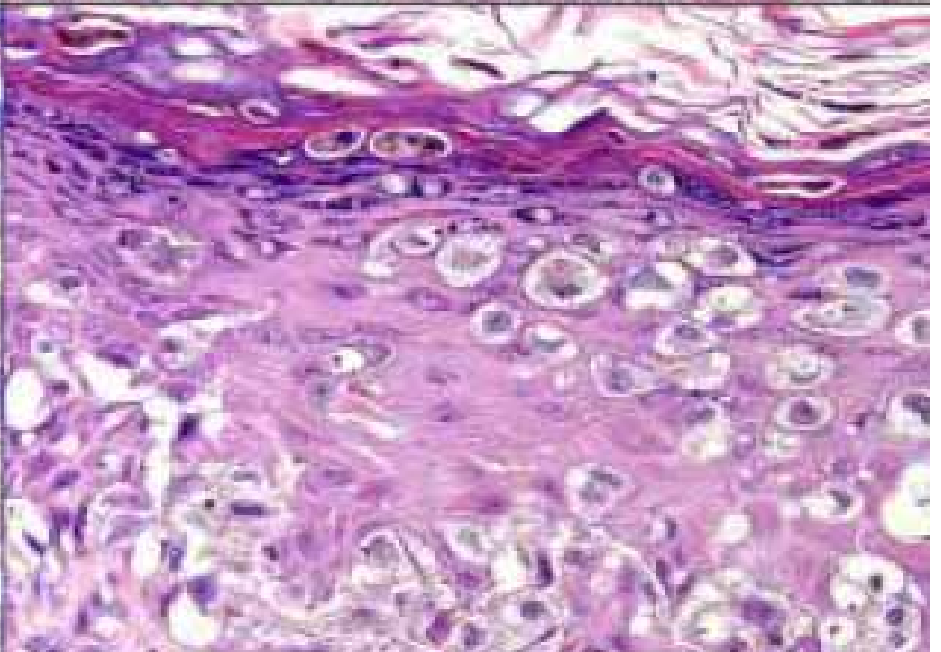
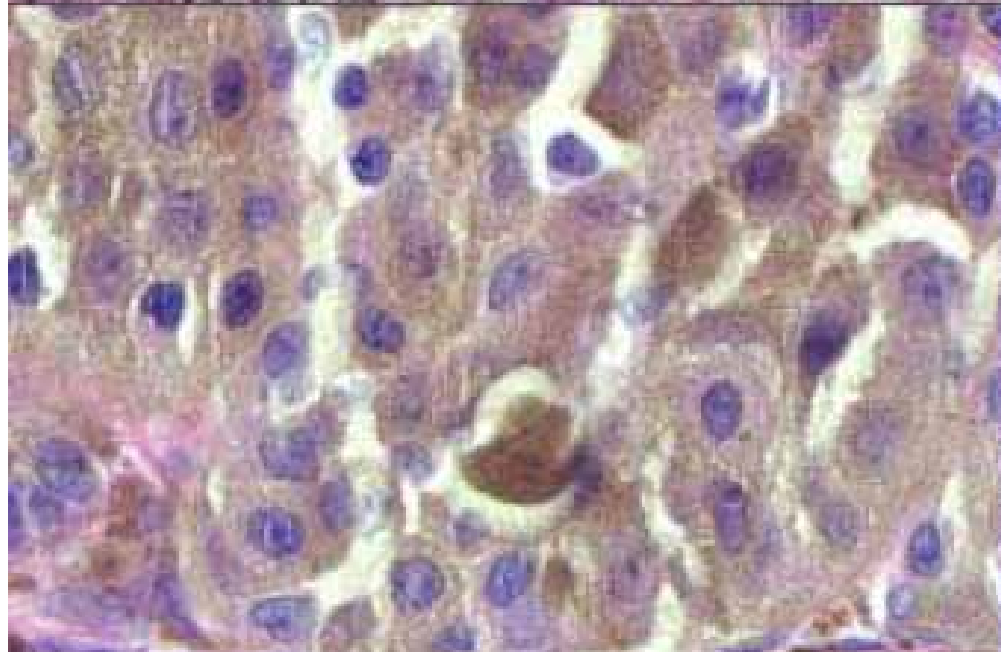
- Highly subjective assessment
- No prognostic significance on UNIVARIATE (!) analysis (Sondergaard K, Schou G. Am J Dermatopathol 1985; 7 suppl.1-4)
- Lack of pigment production associated with ulceration in acral melanoma (Phan A, et al. Br J Dermatol 2007; 157:311)

BRAFomas (Scolyer, 2011)

- Most often SSM
- In sites with intermittent sun-exposure
- Sharply circumscribed
- (Heavily) pigmented
- With prominent pagetoid spread
- With prominent junctional nests
- With large, rounded melanocytes



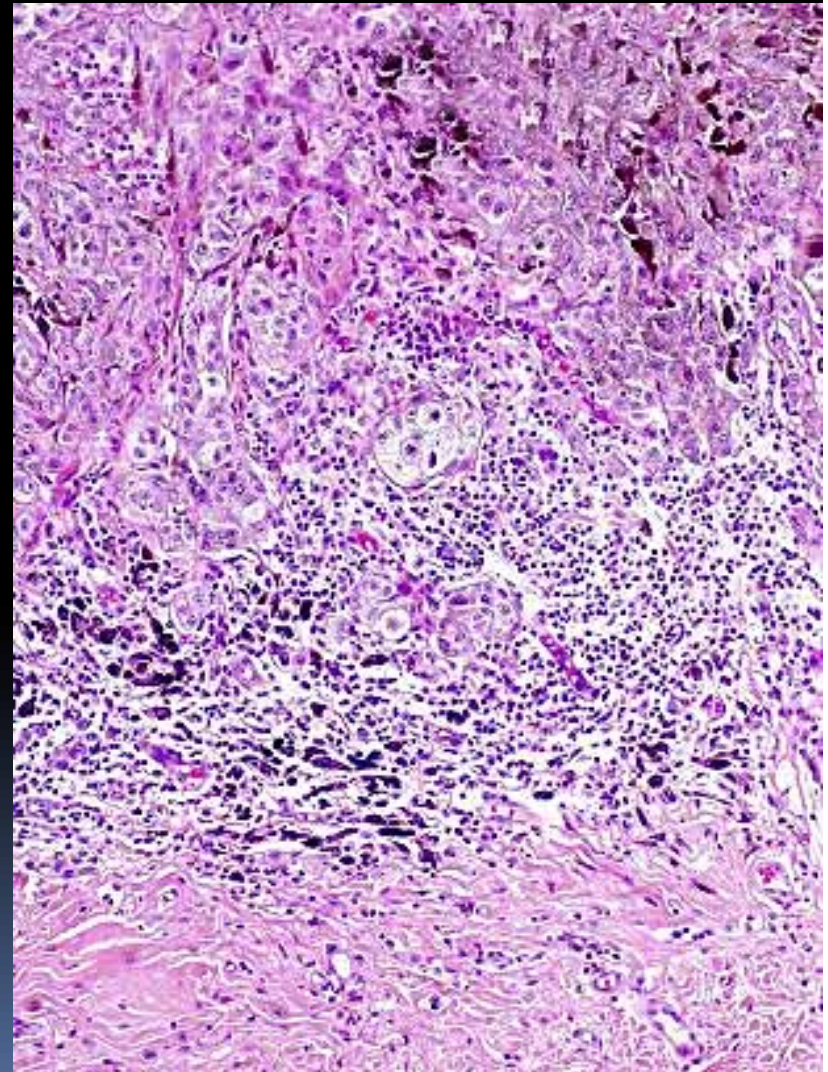
“BRAFOma”

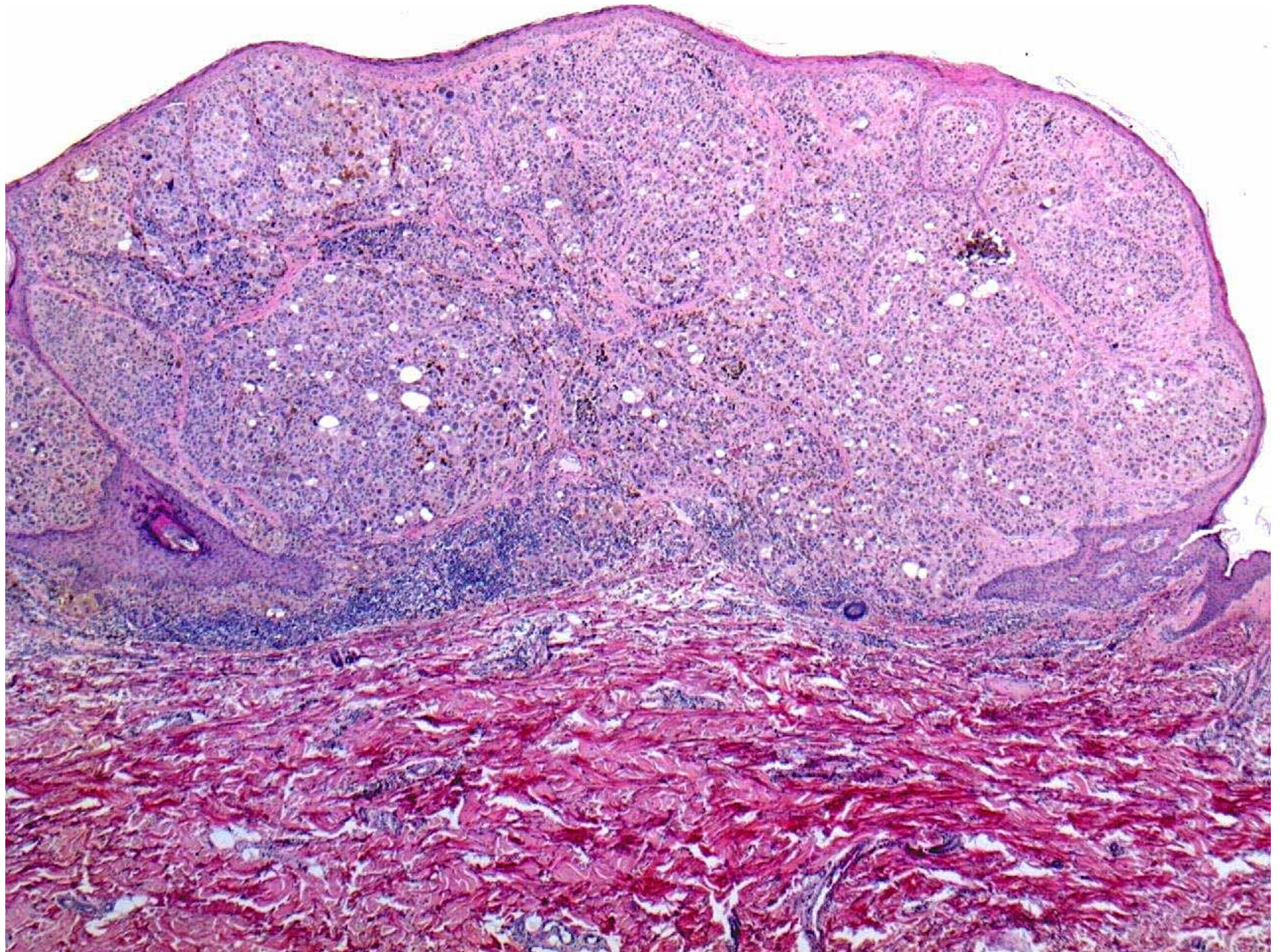


Courtesy of Dr. Richard Scolyer

T.I.L.s in VPGP melanoma

- Clark WH Jr, et al. 1989
- Brisk vs. non-brisk vs. absent
- Evaluation to be carried out along the whole base of the tumor
- 'Brisk' if >90% of the base involved





Prognostic value of tumor infiltrating lymphocytes in the vertical growth phase of primary cutaneous melanoma.

Clemente CG, Mihm MC Jr, Bufalino R, Zurrada S, Collini P, Cascinelli N.

Division of Anatomic Pathology and Cytopathology, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milano, Italy.

Abstract

BACKGROUND: Primary cutaneous melanoma is often infiltrated lymphocytes that provide the opportunity to study what may be the local immunologic reaction to the tumor and to correlate the presence of these lymphocytes with overall survival. In an attempt to delineate the histologic diagnostic criteria, to classify different categories of lymphocytic infiltrates, previously described by Elder et al. as brisk, nonbrisk, and absent, and to verify their prognostic significance, we reviewed 285 consecutive cases of primary cutaneous melanomas (American Joint Committee on Cancer Stage I and II).

METHODS: In addition to clinical variables (age, sex, and location of tumor) and the presence of tumor infiltrating lymphocytes in the vertical growth phase, the histopathologic attributes reviewed included mitotic rate, thickness, and regression. The results were derived from independent histopathologic review by two pathologists (C.G.C., M.C.M., Jr.) on separate occasions. A multivariate analysis of survival was performed with the Cox's regression model.

RESULTS: The 5- and 10-year rates for melanoma with a vertical growth phase and a brisk infiltrate were 77% and 55%, respectively. For tumors with a nonbrisk infiltrate, the 5- and 10-year survival rates were 53% and 45%, respectively, and for tumors with absent tumor infiltrating lymphocytes, the 5- and 10-year survival rates were 37% and 27%, respectively. Mitotic index, thickness, and tumor infiltrating lymphocytes were statistically

(univariate analysis) significant prognostic factors ($P = 0.003$, 0.00001 , 0.0003 , respectively), whereas the presence or absence of regression is not. In the univariate statistical analysis, the sex of patients and site of melanoma also were statistically significant ($P = 0.00001$ and 0.002 respectively), whereas age ($P = 0.98$) was not statistically significant. The multivariate analysis of thickness, mitotic rate, and tumor infiltrating lymphocytes showed that thickness and presence tumor infiltrating lymphocytes were significant and independent histologic prognostic factors. With regard to the clinical factors, sex retained its independent prognostic significance. The histologic characteristics of melanoma with vertical growth phase (brisk, nonbrisk, and absent) are exemplified.

CONCLUSIONS: We demonstrated that when categories of tumor infiltrating lymphocytes are strictly defined, they indeed have very strong predictive value for primary cutaneous melanomas with a vertical growth phase. This work confirms the work of Clark et al. and fully illustrates the brisk, nonbrisk, and absent categories of infiltration. Finally, a multivariate analysis comparing thickness, mitotic rate and presence of tumor infiltrating lymphocytes showed that only thickness and presence of tumor infiltrating lymphocytes are significant and independent positive histologic prognostic factors.

[Hum Pathol](#), 2000 Mar;31(3):327-31.

Individualized prognosis for melanoma patients.

[Cochran AJ](#), [Elashoff D](#), [Morton DL](#), [Elashoff R](#).

Department of Pathology, UCLA School of Medicine, Los Angeles, CA 90095-1732, USA.

Abstract

The clinical course of malignant melanoma is notoriously variable. Current approaches to prognostication allow assignment to risk categories but do not permit accurate assessment of prognosis on an individual patient basis. We analyzed a melanoma histology database that comprises 1,042 sequential melanoma patients evaluated by A.J.C. at UCLA between 1980 and 1990 for 30 separate variables according to a standard protocol. After censoring for absent data, a univariate Cox model analysis was performed that showed 20 individual variables that were significantly linked to clinical outcome. A step-up multivariate analysis was then performed. The combined analysis shows 5 variables: gender, site of primary, age relative to 60 years, Breslow thickness, and presence and width of ulceration to be linked to survival. Probability of survival is calculated using a 2-step approach. The survival-linked variables are multiplied to give an individualized risk score. This is converted into probability of survival by the formula $.987$ (risk score) for 3-year survival, $.975$ (risk score) for 5-year survival, and $.960$ (risk score) for 10-year survival. Thus, a 55-year-old woman with a 1.8-mm nonulcerated melanoma on the leg would have a risk score of $(1 \times 1 \times 1 \times 2 \times 1) = 2$ and a predicted probability of survival at 5 years of $.9752$ (95%) and at 10 years of $.9602$ (92%). We used similar techniques to develop individualized risk scores for likelihood of recurrence. The significant variables in this case are anatomic site of the primary melanoma, melanoma subtype, Breslow thickness, and presence and width of ulceration. The formulae for likelihood of recurrence at different periods after initial surgical removal of the primary melanoma are at 3 years, $.979$ (risk score); at 5 years, $.971$ (risk score); and at 10 years, $.957$ (risk score). This relatively simple approach to prognostication uses readily available demographic information and is likely to be more accurate than single-factor analysis.

PMID: 10746675 [PubMed - indexed for MEDLINE]

Melanoma associated with nevus

- Does not automatically mean that the nevus is the precursor!
- Can be prognostically relevant, but probably only because melanoma is discovered in an earlier growth phase (Kaddu S, et al. Melanoma Res 2002; 12:271)
- Report only when clear-cut

The Transformation Rate of Moles (Melanocytic Nevi) Into Cutaneous Melanoma



A Population-Based Estimate

Hensin Tsao, MD, PhD; Caroline Bevona, MD; William Goggins, ScD; Timothy Quinn, MD

Background: Moles, or melanocytic nevi, are both markers of an increased risk of cutaneous melanoma and direct precursor lesions. Recent strategies to reduce the burden of advanced disease have focused on early detection and ongoing surveillance of moles for malignant degeneration. Inherent in this approach is the notion that moles exhibit a certain risk of transformation into melanoma; however, this risk is unknown.

Objective: To estimate the risk of moles transforming into cutaneous melanoma.

Design: We first constructed a model of transformation based on the assumption that the minimal number of moles turning into cutaneous melanoma per year is roughly equivalent to the number of melanomas diagnosed each year with associated nevic components. The annual risk was then calculated as the number of mole-associated melanomas diagnosed in 1 year (stratified by 10-year age groups) divided by the number of moles in a the same 10-year age group. We also estimated the cumulative risk during the lifetime of an individual mole

by using a modification of the standard life table method.

Results: The annual transformation rate of any single mole into melanoma ranges from 0.0005% or less (ie, ≤ 1 in 200 000) for both men and women younger than 40 years to 0.003% (about 1 in 33 000) for men older than 60 years. The rate is similar between men and women younger than 40 years but becomes substantially higher for men older than 40 years. For a 20-year-old individual, the lifetime risk of any selected mole transforming into melanoma by age 80 years is approximately 0.03% (1 in 3164) for men and 0.009% (1 in 10 800) for women.

Conclusions: The risk of any particular mole becoming melanoma is low, especially in younger individuals. However, since moles can disappear, ones that persist into old age have an increased risk of malignant degeneration. For young people with innumerable moles and no other associated risk factors, systematic excision of benign-appearing lesions would be of limited benefit.

Arch Dermatol. 2003;139:282-288

ANATOMIC STAGE/PROGNOSTIC GROUPS

Clinical Staging*				Pathologic Staging**			
Stage 0	Tis	N0	M0	0	Tis	N0	M0
Stage IA	T1a	N0	M0	IA	T1a	N0	M0
Stage IB	T1b	N0	M0	IB	T1b	N0	M0
	T2a	N0	M0		T2a	N0	M0
Stage IIA	T2b	N0	M0	IIA	T2b	N0	M0
	T3a	N0	M0		T3a	N0	M0
Stage IIB	T3b	N0	M0	IIB	T3b	N0	M0
	T4a	N0	M0		T4a	N0	M0
Stage IIC	T4b	N0	M0	IIC	T4b	N0	M0
Stage III	Any T	≥N1	M0	IIIA	T1 – 4a	N1a	M0
					T1 – 4a	N2a	M0
				IIIB	T1 – 4b	N1a	M0
					T1 – 4b	N2a	M0
					T1 – 4a	N1b	M0
				IIIC	T1 – 4a	N2b	M0
					T1 – 4a	N2c	M0
					T1 – 4b	N1b	M0
					T1 – 4b	N2b	M0
					T1 – 4b	N2c	M0
				Any T	N3	M0	
Stage IV	Any T	Any N	M1	IV	Any T	Any N	M1

<i>T classification</i>	<i>Thickness (mm)</i>	<i>Ulceration Status/Mitoses</i>
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

ICD-O-3 TOPOGRAPHY CODES

C44.0	Skin of lip, NOS
C44.1	Eyelid
C44.2	External ear
C44.3	Skin of other and unspecified parts of face
C44.4	Skin of scalp and neck
C44.5	Skin of trunk
C44.6	Skin of upper limb and shoulder
C44.7	Skin of lower limb and hip
C44.8	Overlapping lesion of skin
C44.9	Skin, NOS
C51.0	Labium majus
C51.1	Labium minus
C51.2	Clitoris
C51.8	Overlapping lesion of vulva
C51.9	Vulva, NOS
C60.0	Prepuce
C60.1	Glans penis
C60.2	Body of penis
C60.8	Overlapping lesion of penis
C60.9	Penis, NOS
C63.2	Scrotum, NOS

ICD-O-3 HISTOLOGY CODE RANGES

8720–8790

Common Melanoma Histology

- Superficial spreading melanoma (8743/3)
 - 70% of melanoma cases
- Nodular melanoma (8721/3)
 - 15% of melanoma cases
- Acral lentiginous melanoma (8744/3)
 - 8% of melanoma cases
- Lentigo maligna melanoma (8742/3)
 - 5% of melanoma cases

Code the invasive component only.

Code the in situ component if the invasive component is NOS (8720/3)

1. Never finalize any report under a **H.A.L.T.** (hungry, angry, late, tired) condition;
2. Make sure that all the pertinent clinical information, comprising the **clinical diagnosis**, will be provided in the final histopathological report;
3. Always achieve **step sections** for controversial cases;
4. Thoroughly report the **microscopic features** of a controversial case along with the differential diagnoses raised; always **discuss the original diagnosis in a 'second opinion' setting**;
5. Submit any controversial case to intradepartmental and interdepartmental **consultation**;
6. Explicitly refer to a **multidisciplinary meeting** for further clinicopathologic evaluations and for any decision about the management;
7. Finalize a **supplementary report** for any diagnostic opinion achieved both in a consultation and in a clinicopathological setting.



SE LA
MONTAGNA
VIENE VERSO
DI TE E TU
NON SEI
MAOMETTO,
CORRI
CRETINO...
E' UNA
FRAVA _