University of Pennsylvania, Ben Franklin in front of "Charles Addams" Building

Melanoma

Classification and Prognosis

Emphasizing Pathology & History

David Elder
University of Pennsylvania

Melanoma Statistics

American Cancer Society

- Cancer of the skin is by far the most common of all cancers.
- Melanoma accounts for less than 5% of skin cancer cases but causes a large majority of skin cancer deaths.
- About 70,000 new melanomas are diagnosed in the United States per year (about 40,000 in men and 30,000 in women).
- About 9,000 people in the US may be expected to die of melanoma per year (about 6,000 men and 3,000 women). (Compare with ~ 2,500 for SCC).
- The death rate has dropped since the 1990s for those younger than 50, but has been stable or rising in older age groups.

Melanoma Statistics - 2

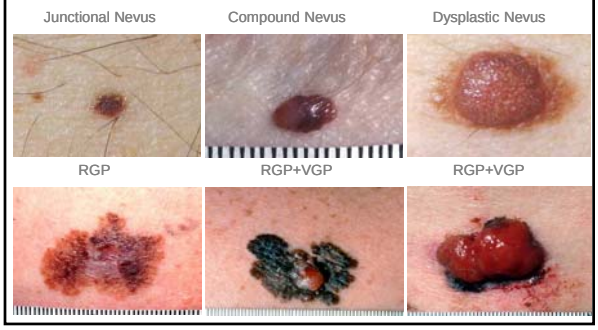
American Cancer Society

- Incidence rates for melanoma have been rising for at least 30 years.
- The lifetime risk of getting melanoma is about 2% (1 in 50) for whites, 0.1% (1 in 1,000) for blacks, and 0.5% (1 in 200) for Hispanics.
- The risk for each person is affected by a number of different factors, including sun susceptibility and exposure, nevi, freckles, family and personal history of melanoma
- Melanoma occurs in younger as well as older people. Rates increase with age, with the highest incidence at age 85, but melanoma is one of the more common cancers in young adults, and occurs in teenagers.

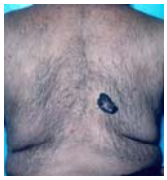
Melanoma and Nevi

- Nevi are important mainly in relation to melanoma, most importantly as simulants but also as risk markers and, occasionally, as precursors.
- Although some melanomas may arise in a pre-existing benign nevus, the general tendency in nevi is to regress over time.
- Nevi and especially dysplastic nevi are among the strongest markers of individuals at increased risk for developing melanoma over time.
- Nevi are also the most important simulants of melanoma, both clinically and histologically.

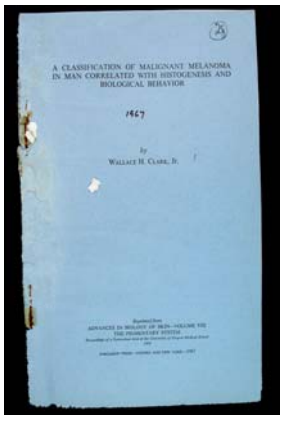
Gross Pathology of Tumor Progression Compartments (SSM) in Melanoma

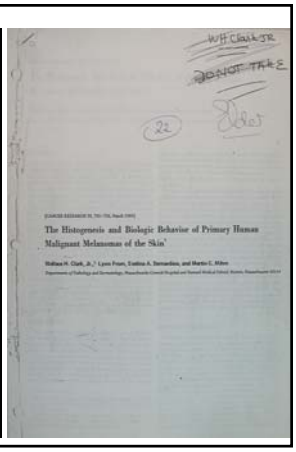


ABCDE's of Melanoma



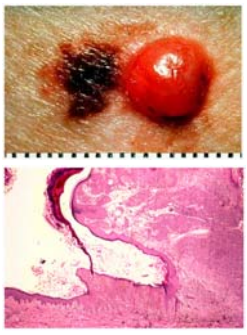
- A = Asymmetry – one half not like the other
- B = Border irregularity – like the map of a small island
- C = Color variegation – shades of tan, brown, black, red, white, blue-gray
- D = Diameter – no lower limit today
- E = Elevation, and Evolution
- Ugly duckling – a mole out of step with the others



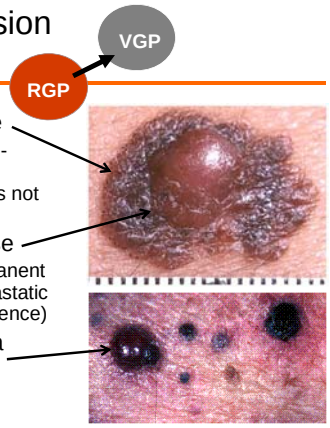


Tumorigenic & Nontumorigenic melanoma (Radial & Vertical Growth Phase)

- ABCD Criteria for RGP
  - Asymmetry
  - Border irregularity
  - Color variegation
  - Diameter > 4-6 mm
- Vertical Growth Phase
  - balloon-like expansion forms nodule
  - often symmetrical, smooth borders
  - color is often quite uniform
  - diameter often less than 6 mm



Tumor Progression in Melanoma



•Radial Growth Phase

In situ or invasive but non-tumorigenic, rarely forms permanent cell lines, does not metastasize

•Vertical Growth Phase

Tumorigenic, forms permanent cell lines. Source of metastatic disease (cytogenetic evidence)

•Metastatic Melanoma

As for VGP, capable of metastasis.

Prognosis of Primary Melanoma

Clark's levels, Breslow thickness, Ulceration, Mitogenicity, TNM Stage

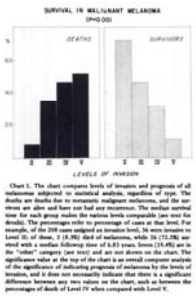
[CANCER RESEARCH 29, 705–726, March 1969]

The Histogenesis and Biologic Behavior of Primary Human Malignant Melanomas of the Skin[1]

Wallace H. Clark, Jr.,[2] Lynn From, Evelina A. Bernardino, and Martin C. Mihm

Departments of Pathology and Dermatology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts 02114

•Evidence is presented suggesting that superficial spreading melanoma and lentigo maligna melanoma … though evolving at different rates, show a long period of superficial growth, followed by the relatively rapid appearance of nodules or deeper invasion within the primary lesion.
•This change in the nature of the primary lesion may be due to the appearance of one or more strains of cells of aggressive biologic potential.
•The subdivision of each of the forms of melanoma into 5 anatomic levels of invasion permits the accurate assignment of prognosis to each case.



Breslow's Thickness

- "One possible reason for the lack of reliability of tumor size in estimating prognosis may be that studies to date have considered size in only two dimensions and have neglected tumor volume".
- "From a retrospective study of 98 invasive melanomas it was found that both tumor thickness and stage of invasion are of value in determining prognosis. By using these two criteria it was possible to identify a group of 45 patients only one of whom developed recurrent or metastatic disease.
- These criteria may be of value in selecting patients for prophylactic lymph node dissection."

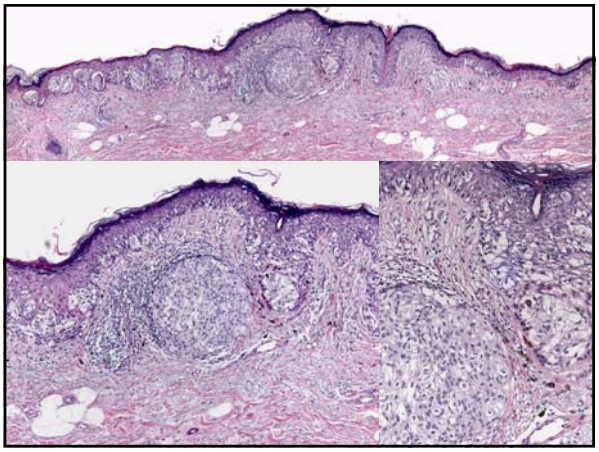
Thickness, Cross-Sectional Areas and Depth of Invasion in the Prognosis of Cutaneous Melanoma

ALEXANDER BRESLOW,* M.D.

From The George Washington University School of Medicine, Washington, D. C.

Annals of Surgery
November 1970

FIG. 7. Maximal thickness of melanomas. None less than 0.76 mm. recurred or metastasized.



7th Edition of Melanoma Staging AJCC/UICC

Balch et al, 2009

- T Stages of primary tumors are based on Breslow's thickness intervals
- Mitogenicity is an independent factor and a rate ≥1 is a modifier of stage T1
- Ulceration is a modifier of all T stages (T1b-T4b).
- Nodal disease may be microscopic, i.e. non-palpable disease detected in sentinel node procedure, or macroscopic, i.e. palpable.
- Cutaneous, nodal and distant metastases have increasingly worse prognosis.

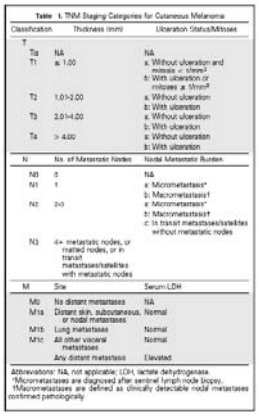


Table 1. TNM Staging Categories for Cutaneous Melanoma

Classification	Thickness (mm)	Ulceration Status/Mitoses
T		
Tis	NA	NA
T1	≤ 1.00	a: Without ulceration and mitosis < 1/mm²
		b: With ulceration or mitoses ≥ 1/mm²
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 with metastatic nodes	
M	Site	Serum LDH
M0	No distant metastases	NA
M1a	Distant skin, subcutaneous, or nodal metastases	Normal
M1b	Lung metastases	Normal
M1c	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.

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JOURNAL OF CLINICAL ONCOLOGY

Final Version of 2009 AJCC Melanoma Staging and Classification

Charles M. Balch, Jeffrey E. Gershenwald, Soo-jong Soong, John F. Thompson, Michael B. Atkins, David R. Byrd, Antonia C. Ruiter, Alistair J. Cochran, Donald G. Coit, Shu-usaan 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

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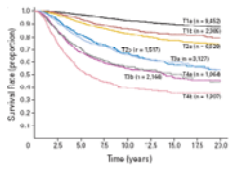


In patients with localized melanoma, tumor thickness, mitogenicity and ulceration are the most dominant prognostic factors

Mitotic rate has replaced Clark Level IV for defining T1b melanomas. [16]

MALIGNANT MELANOMAS AND RELATED LESIONS

- Radial Growth Phase Variants
  - Radial Growth Phase Absent
    - Nodular melanoma (VGP present, RGP absent)
  - Radial Growth Phase Present (with or without VGP)
    - Superficial spreading melanoma
    - Lentigo maligna melanoma
    - Acral-lentiginous melanoma
    - Mucosal-lentiginous melanoma
  - Vertical growth phase variants …

MALIGNANT MELANOMAS AND RELATED LESIONS

- Vertical Growth Phase Variants
  - Nodular Melanoma
  - Desmoplastic melanoma
  - Neurotropic melanoma
  - Malignant blue nevus
  - Melanoma in congenital nevi
  - Minimal deviation melanoma
  - Clear cell sarcoma
  - Malignant melanocytic schwannoma
  - Melanocytic tumor of uncertain malignant potential (MELTUMP)

WHO histological classification of melanocytic tumours

Malignant melanoma

Superficial spreading melanoma	8743/3
Nodular melanoma	8721/3
Lentigo maligna	8742/2
Acral-lentiginous melanoma	8744/3
Desmoplastic melanoma	8745/3
Melanoma arising from blue naevus	8780/3
Melanoma arising from large congenital naevus	
Melanoma of childhood	8770/3
Naevoid melanoma	
Persistent melanoma	

Benign melanocytic tumours

Congenital melanocytic naevi	8761/3
Superficial	
Recurrent persist, superficial	8003/3
Nodular proliferations in deep congenital naevi	8762/1
Blue naevus	8790/0
Patch forms (Ota, Ito and Mongolian spot)	
Cellular blue naevus	8790/0
Deep penetrating naevus	
Combined naevus	
Melanotic macular, simple lentigo and lentiginous naevus	
Dysplastic and recurrent cytoplastic naevus (Clark)	8727/0
Site-specific naevi	
Genital	
Glabrous skin	
Meyerson's with halo eczema	
Spitz naevus	8770/0
Pigmented spindle cell naevus, Reed	8770/0
Halo naevus	8723/0

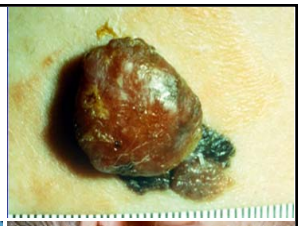
[1] Morphology code of the International Classification of Diseases for Oncology (ICD-O) [820] and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded /0 for benign tumours, /3 for malignant tumours, and /1 for borderline or uncertain behaviour.

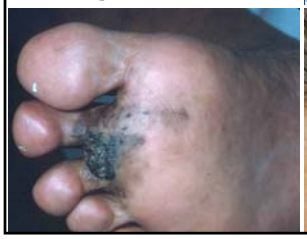
Histogenetic Subtypes

Superficial Spreading (80%)
Intermittent sun exposure

Lentigo maligna (10%)
Chronic continuous exposure

Acral (5%)
No sun exposure



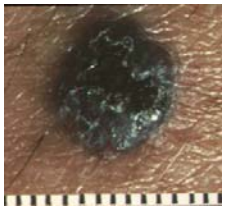


Melanoma Classification

- Reasons to Classify
  - All melanomas are not the same
  - Morphological variation affects diagnostic criteria – nosologic differences
  - Although no differences in prognostic outcome when other variables are controlled, there are differences in local progression and recurrence
  - Different forms of melanoma have different etiologic and genetic basis, and targeted therapy needs to be tailored to these differences.

Nodular Melanoma
Clinical Features

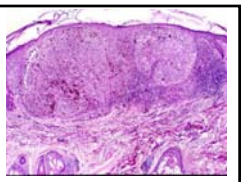
- Detectable RGP is absent by definition
  - Tumorigenic melanoma without an adjacent nontumorigenic component
  - short-lived RGP may be obliterated by the developing tumor.
- ABCD criteria may not apply
  - lesions are often symmetrical nodules/papules with raised discrete borders, fairly uniform color, diameter not always > 6 mm
- prognosis is similar to other melanomas when level and thickness are controlled

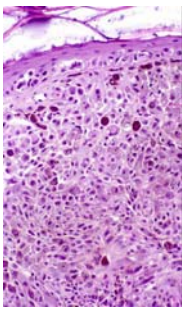


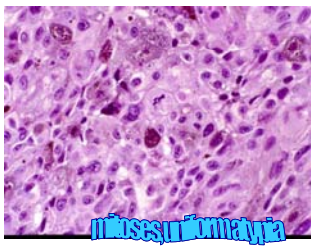
Nodular Melanoma
Histologic Features

- Diagnosis may be tricky especially if there is no high-grade atypia
  - may be quite symmetrical at scanning magnification, but pigmentation and cytology generally vary from side to side.
  - uniform cytologic atypia and mitotic activity in dermis
  - maturation from top to bottom usually absent or imperfect
  - no adjacent radial growth phase by definition
  - epithelial involvement above the tumor may be subtle
    - differential diagnosis includes epidermotropic metastatic melanoma
- Differential diagnosis includes benign lesions such as atypical compound nevi, Spitz nevi, deep penetrating nevi, cellular blue nevi

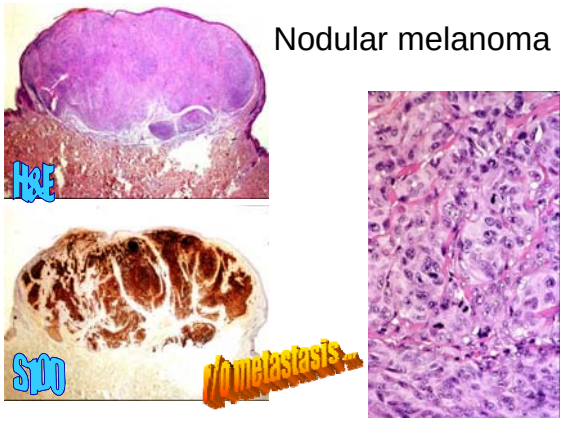
Nodular Melanoma







Nodular melanoma



Nodular Melanoma

• Rate of growth in melanomas: characteristics and associations of rapidly growing melanomas.

Liu W, Dowling JP, Murray WK, McArthur GA, Thompson JF, Wolfe R, Kelly JW. Arch Dermatol 2006.

– Rapidly growing melanomas were more often symmetrical, elevated, amelanotic, regular in border, and symptomatic, occurred more frequently in elderly men and individuals with fewer nevi and fewer freckles

• Early detection of thick melanomas in the United States: beware of the nodular subtype.

Demierre MF, Chung C, Miller DR, Geller AC. Arch Dermatol 2005.

– Nodular melanoma comprised 9% of all recorded cases but 34% of melanomas 2 mm or larger. A substantial number of thick melanomas in the United States are of the nodular subtype, and median thickness of nodular melanoma has not changed during the 12 years of study. New strategies are needed to decrease the incidence of thick melanoma in the United States.

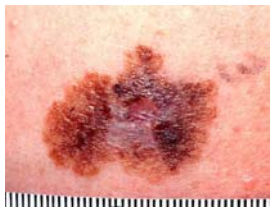
Superficial Spreading Melanoma

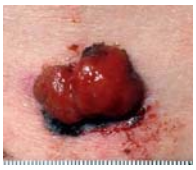
Clinical Features

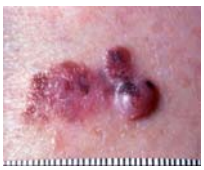
- 70% of all melanoma cases (common melanoma)
- occurs on usually covered, intermittently exposed skin
- relatively young adults – median 50-60 yrs of age
- classic ABCD lesions
  - Asymmetry, Border irregularity, Color variegation, Diameter > 4 mm)
- highly associated with usual risk factors for melanoma:
  - Dysplastic nevi, total nevi, large nevi, sun exposure habits, sun susceptibility, freckles, family or personal history of melanoma
  - More likely than LMM, ALM or MLM to be associated with mutations of the oncogene BRAF

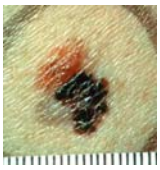
Superficial Spreading Melanoma SSM

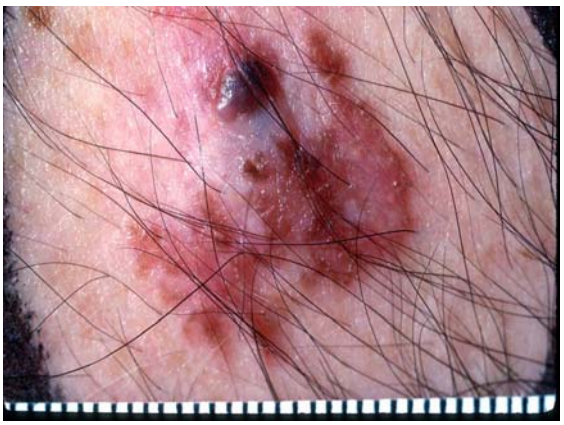
- Asymmetry
- Border irregularity
- Color variegation
- Diameter > 4 mm
- Discrete border







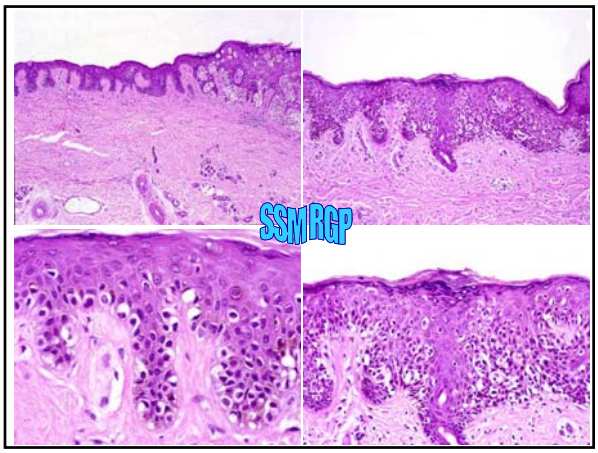


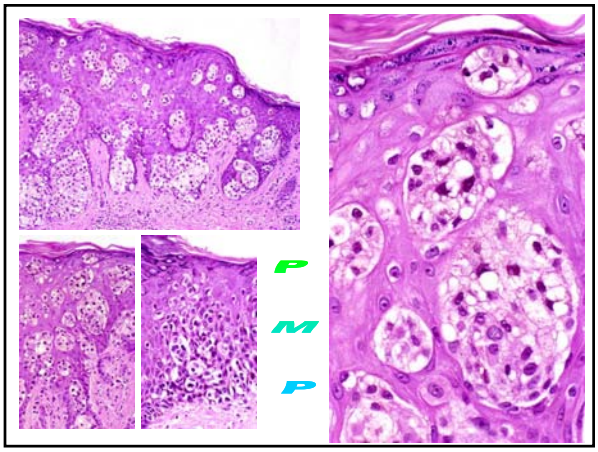


Superficial Spreading Melanoma Histologic Features

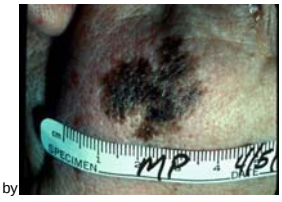
"Pagetoid Melanoma" (McGovern)

- essential features of radial growth phase:
  - pagetoid melanocytic proliferation (PMP), usually high-level and extensive
  - breadth, asymmetry, poor circumscription, irregular epithelial hyperplasia
  - uniform moderate to severe atypia, mitoses in about 1/3
  - invasion without tumor formation ("microinvasive melanoma")
  - may progress to tumorigenic vertical growth phase melanoma
- morphology of VGP is similar to nodular and other melanomas

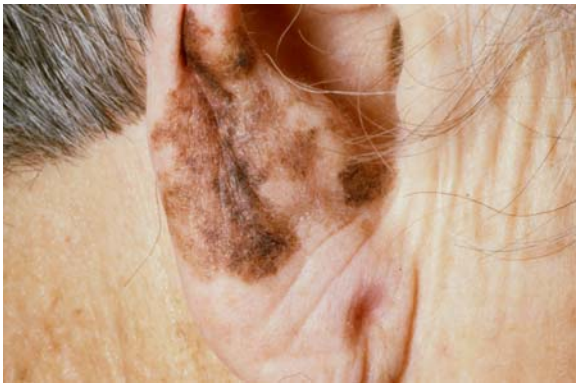




Lentigo Maligna Melanoma Clinical Features



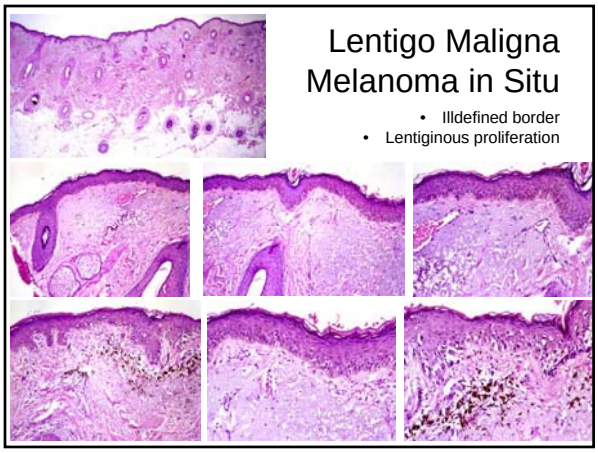
- about 10% of all melanoma
- A “lentiginous melanoma”
- occurs on chronically exposed skin
  - especially head and neck
- elderly population
  - risk for LMM may be increased in outdoor workers
- slow evolution over many years
  - ABCD criteria are ultimately fulfilled by most evolving lesions
- border is illdefined and impalpable
  - shades of tan, brown, black, fine reticulated lines within lesion
- vertical growth phase may develop as exophytic nodule or as endophytic tumor



Lentigo Maligna Melanoma

Histologic Features

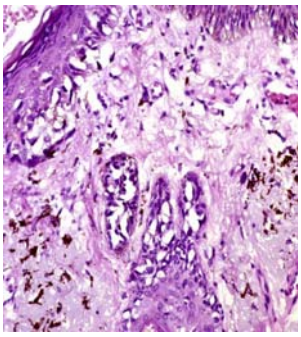
- Lentiginous (basal) melanocytic proliferation pattern
  - mainly near dermal-epidermal junction
  - relatively small cell type – nevoid to small epithelioid cells
  - uniformly atypical melanocytes in contiguity with one another
  - continuous proliferation (extends between rete ridges)
  - nested and pagetoid melanocytic proliferation are less prominent
  - nests hang down from interface in droplet pattern, nests above elastotic dermis
  - changes at periphery may be very subtle – definition of margin issues
- Sun-damaged skin
  - elastosis is usually severe, may be associated actinic lentigines
  - epidermis tends to be atrophic, rete ridges are effaced
- "Final common pathway" in center of advanced lesions:
  - pagetoid proliferation, epithelial hyperplasia, larger cell type
- Desmoplastic and/or neurotropic VGP should be considered
  - especially when predominantly spindle cells

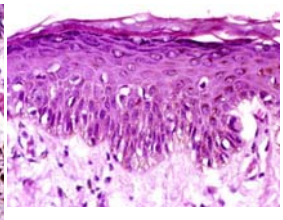


Lentigo Maligna Melanoma in Situ

- Illdefined border
- Lentiginous proliferation

Lentigo Maligna Melanoma in Situ

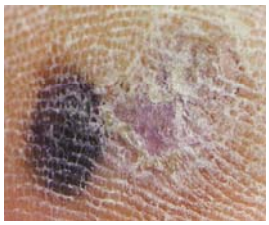


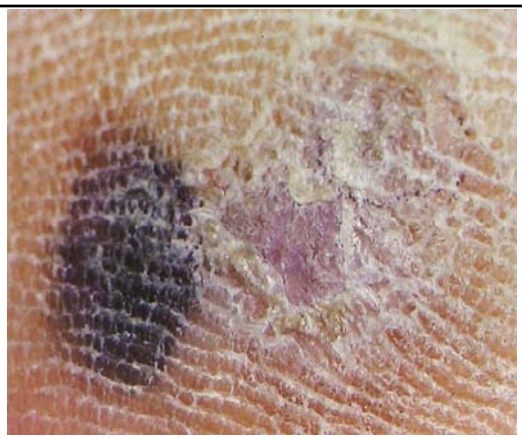


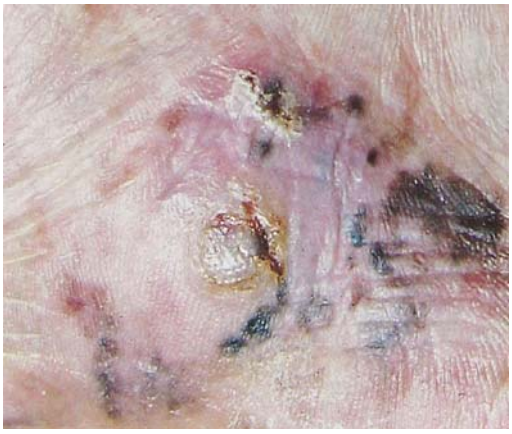
- Epidermal atrophy
- Lentiginous proliferation
  - Usually also slight pagetoid proliferation
- Skin appendage extension
- Actinic elastosis

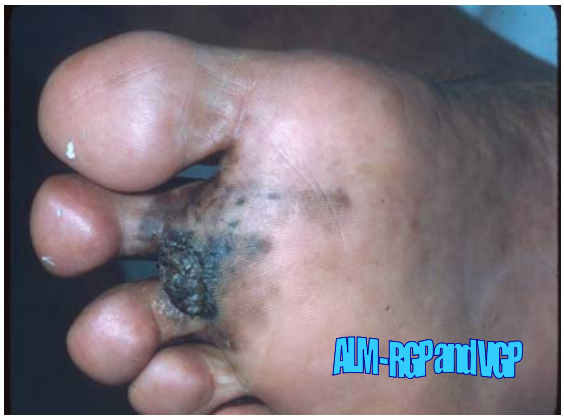
Acral-lentiginous Melanoma

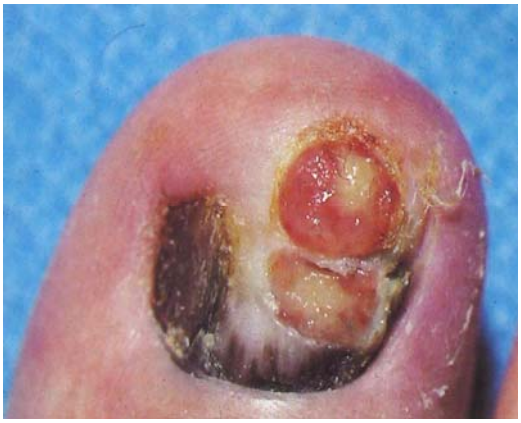
- Palms, soles, subungual
- Great toe region most common
- Incidence similar in all races, thus most common form of melanoma in African, and Asian populations
- May be deceptively thick even in absence of a raised nodule





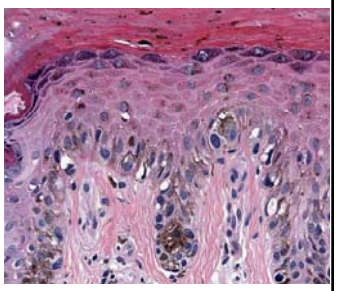


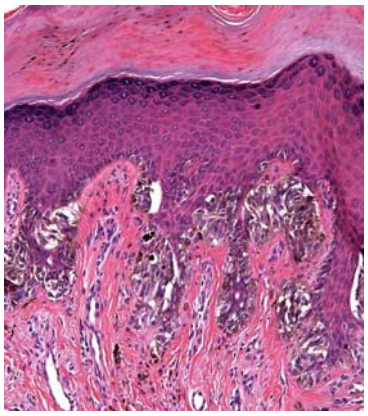

ALM-RGP and VGP

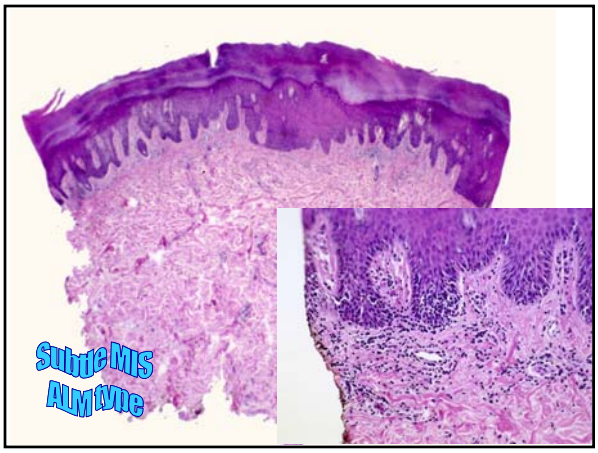


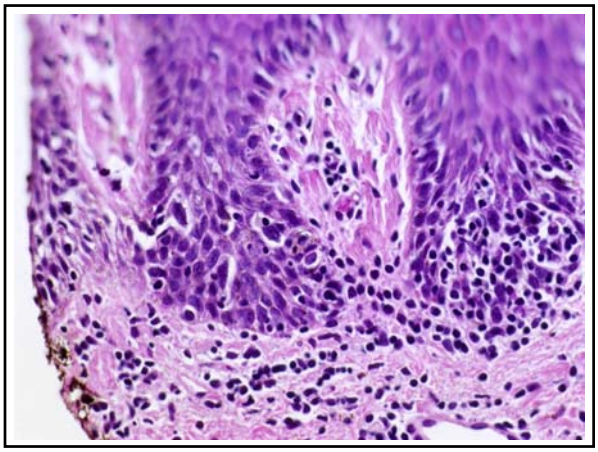
Acral-lentiginous Melanoma

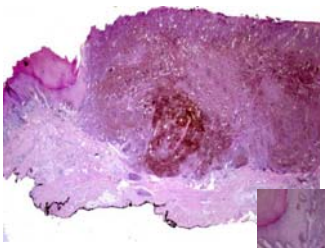
- Lentiginous nontumorigenic compartment (radial growth phase)
- Continuous basal proliferation of uniformly atypical melanocytes
- Often a spindle cell tumorigenic compartment (vertical growth phase)
- May be deceptively thick even in absence of a raised nodule
- Tumorigenic component often desmoplastic and/or neurotropic (local recurrence risk)

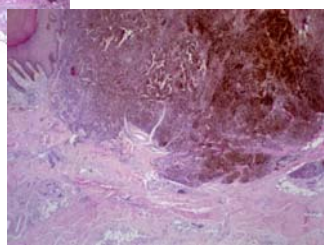




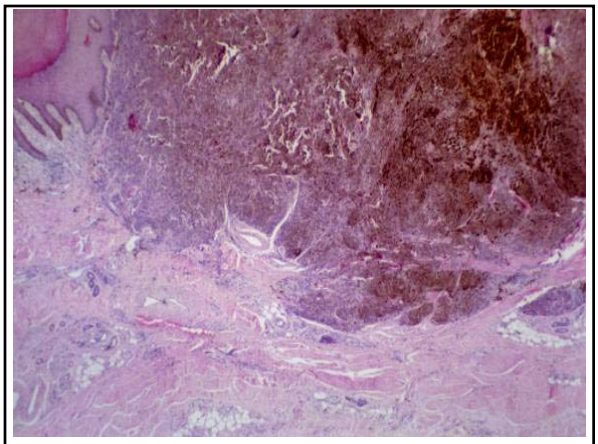


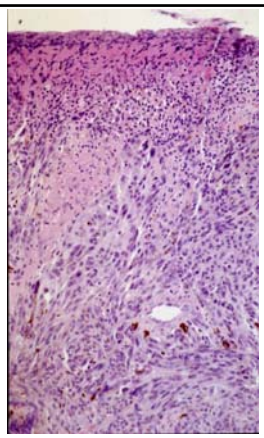
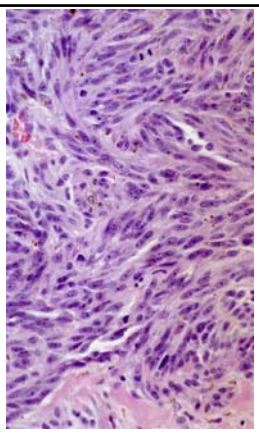






Recurrent melanoma
at site of prior biopsy

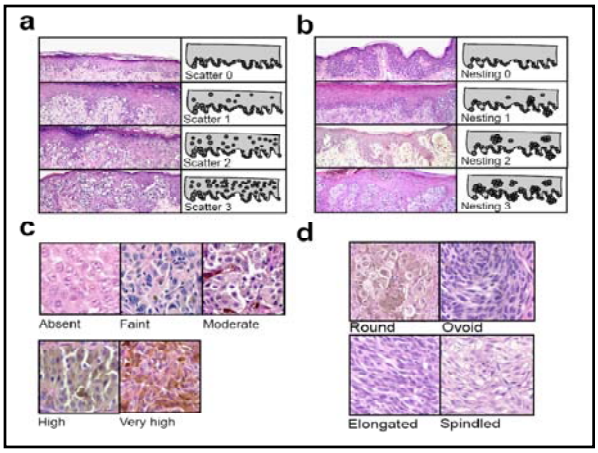


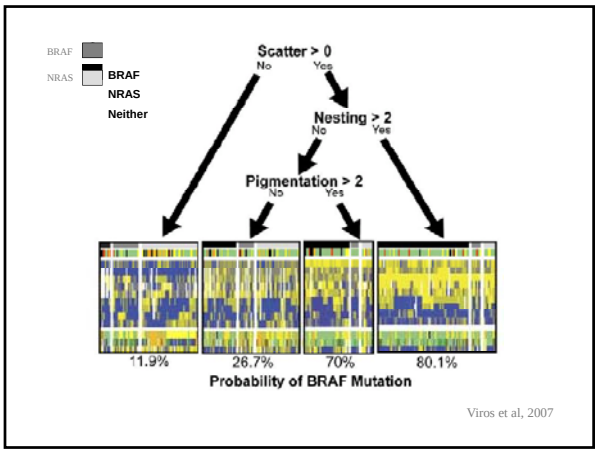



Histomorphological signature of mutation status in melanoma

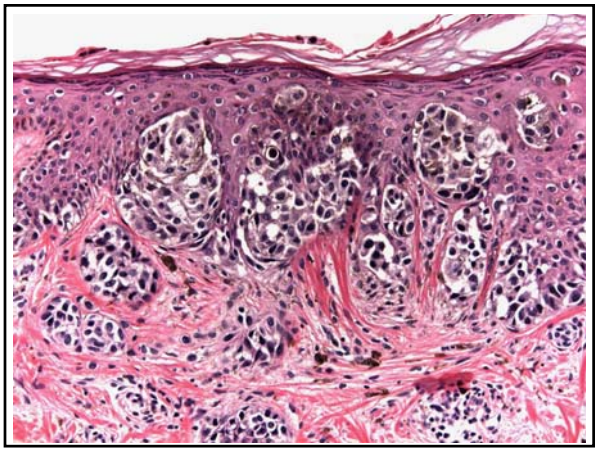
- Simple histomorphological features and patient characteristics were correlated to the mutation status of *BRAF* and *NRAS* in a cohort of 302 primary cutaneous melanomas.
- Univariate analysis showed positive associations with multiple factors
  - *BRAF* mutation associated with nesting, scatter, absent chronic solar damage (CSD), young patient age, sharp circumscription, large cell size, heavy pigmentation, truncal location, round cell and nuclear shape, SSM subtype, large nuclear size, little solar elastosis, and a thickened or hyperplastic epidermal contour.
- Multivariate and prediction analysis showed that a combination of high nesting and scatter, low age, and large cell size predicted *BRAF* mutation with an error estimate of 13%.

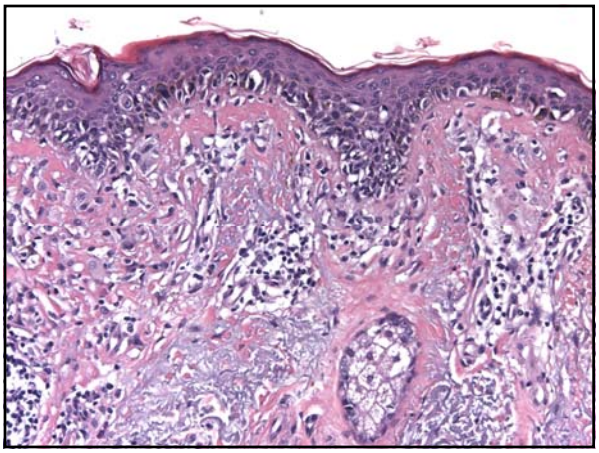
•*Amaya Viros, Jane Fridlyand, Juergen Bauer, John Curtin, Daniel Pinkel, Boris C. Bastian. PLOS Medicine 5:941-951, 2008*





Viros et al, 2007

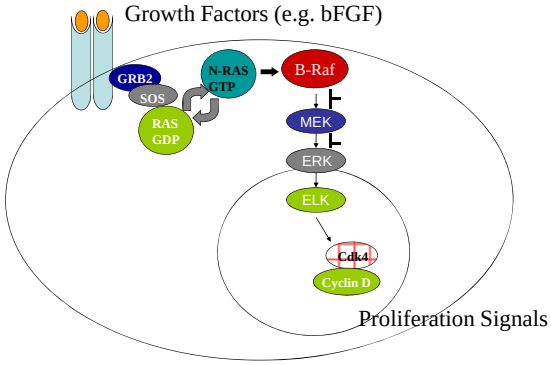




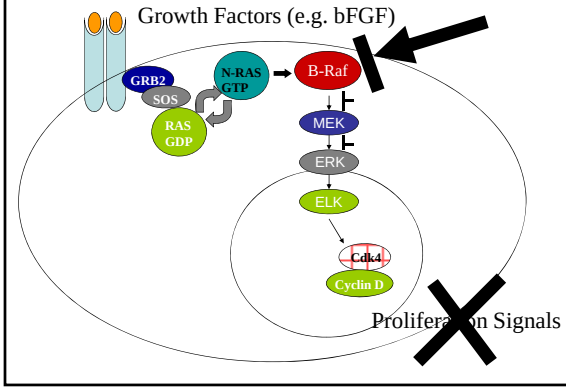
Curing Advanced Disease

- 70% of Melanomas have activated BRAF oncogene which drives progression
  - Davies et al, 2002.
- Plexxikon Company developed a “designer drug” that inhibits common V600E mutation that activates BRAF
- Phase I and II trials of Plexxikon 4032 has been completed.

MAP Kinase Pathway in Melanoma



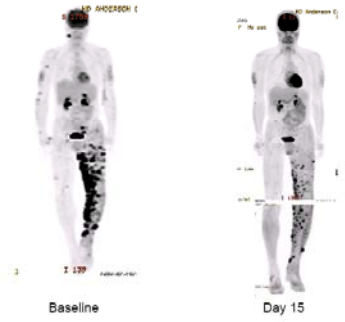
MAP Kinase Pathway in Melanoma



Update on PLX4032 phase I trial

Keith Flaherty et al, U Penn

Patient # 45 PET Scan Glucose Uptake



Similar results with c-Kit inhibiters e.g. Gleevec in patients with c-Kit mutations

A paradigm shift for melanoma therapy

- From HYPERLINK "http://www.medscape.com/news"Medscape Medical News

ASCO 2009: Investigational Targeted Therapy for Metastatic Melanoma Shrinks Tumors, Causes Stir at Meeting

June 4, 2009 (Orlando, Florida) — The targeted-therapy revolution in oncology could be coming to melanoma, especially if the results of a phase 1 trial of an investigational agent are followed by similar results in subsequent trials, according to melanoma experts attending the American Society of Clinical Oncology 45th Annual Meeting.

- In a dose-escalation, proof-of-concept study, more than half of metastatic melanoma patients with this BRAF mutation who received high doses of PLX4032 had tumor shrinkage, said lead study author Keith T. Flaherty, MD, from the Abramson Cancer Center of the University of Pennsylvania in Philadelphia.
- "We are on the verge of a paradigm shift for melanoma therapy," said melanoma expert Boris Bastian, MD, from the University of California at San Francisco, who was not involved in the trial. "This is a decisive step toward personalized medicine," he added.

A Drug Trial Cycle: Recovery, Relapse, Reinvention

The New York Times Feb 2010.

"In the weeks leading up to the annual oncologists' conference here, several of the patients on the trial of the drug known as PLX4032 had relapsed. One had died. Another, Christopher Nelson, who had made what seemed like a miraculous recovery in March, had lost his appetite again. Dr. Flaherty feared what he might see on Mr. Nelson's scan when he returned to his office at the University of Pennsylvania. The drug's ability to stop the melanoma, on average, he told the crowd, "appears to be approximately six months."

Summary

- Early melanoma is curable by simple surgery (complete local excision)
- Advanced melanoma is not yet curable, but for the first time drugs are available that elicit responses in most eligible patients.
- Therapy depends on the presence of mutations appropriate for the targeted therapeutic agents – personalized medicine.

Surgical Pathology Cancer Case Summary (Checklist)

MELANOMA OF THE SKIN:
Biopsy, Excision, Re-Excision
(for reference only)

Grossing

- **Procedure (select all that apply) (Note A)**
- ___ Biopsy, shave
- ___ Biopsy, punch
- ___ Biopsy, incisional
- ___ Excision
- ___ Re-excision
- ___ Lymphadenectomy, sentinel node(s)
- ___ Lymphadenectomy, regional nodes (specify):
  _____
- ___ Other (specify):
  _____
- ___ Not specified

- **Specimen Laterality**
- ___ Right
- ___ Left
- ___ Midline
- ___ Not specified

Tumor Site (Note B)
Specify (if known):
_____
___ Not specified

Tumor Size (required only if tumor is grossly present)
Greatest dimension: __ cm
*Additional dimensions: __ x ___ cm
___ Indeterminate (see "Comment")

Macroscopic Satellite Nodule(s) (required for excision specimens only)
___ Not identified
___ Present
___ Indeterminate

***Macroscopic Pigmentation**
*___ Not identified
*___ Present, diffuse
*___ Present, patchy/focal
*___ Indeterminate

Primary Tumor (pT)

- ___ pTX: Primary tumor cannot be assessed (eg, shave biopsy or regressed melanoma) (see "Comment")
- ___ pT0: No evidence of primary tumor
- ___ pTis: Melanoma in situ (ie, not an invasive tumor: anatomic level I)
- pT1: Melanoma 1.0 mm or less in thickness, with or without ulceration (see Note D)
- ___ pT1a: Melanoma 1.0 mm or less in thickness, no ulceration, <1 mitoses/mm^2
- ___ pT1b: Melanoma 1.0 mm or less in thickness with ulceration and/or 1 or more mitoses/mm^2
- pT2: Melanoma 1.01 to 2 mm in thickness, with or without ulceration
- ___ pT2a: Melanoma 1.01 to 2.0 mm in thickness, no ulceration
- ___ pT2b: Melanoma 1.01 to 2.0 mm in thickness, with ulceration
- pT3: Melanoma 2.01 to 4.0 mm in thickness, with or without ulceration
- ___ pT3a: Melanoma 2.01 to 4.0 mm in thickness, no ulceration
- ___ pT3b: Melanoma 2.01 to 4.0 mm in thickness, with ulceration
- pT4: Melanoma greater than 4.0 mm in thickness, with or without ulceration
- ___ pT4a: Melanoma greater than 4.0 mm in thickness, no ulceration
- ___ pT4b: Melanoma greater than 4.0 mm in thickness, with ulceration

Microscopic Features

- **Histologic Type**
- **Maximum Tumor Thickness**
- **Anatomic Level**
- **Ulceration**
- **Margins (select all that apply)**
- **Mitotic Index**
- **Microsatellitosis**
- **Lymph-Vascular Invasion**
- **Perineural Invasion**
- **Tumor-Infiltrating Lymphocytes**
- **Tumor Regression**
- **Growth Phase**
- **Pathologic Staging (pTNM)**
- **TNM Descriptors**

Metastasis

- **Distant Metastasis (pM)**
- ___ Not applicable
- ___ pM1: Distant metastasis (documented in this specimen)
- *___ pM1a: Metastasis in skin, subcutaneous tissues, or distant lymph nodes
- *___ pM1b: Metastasis to lung
- *___ pM1c: Metastasis to all other visceral sites or distant metastasis at any site associated with an elevated serum lactic dehydrogenase (LDH)
- *Specify site, if known: _____
-
- ***Additional Pathologic Findings (select all that apply)**
- *___ Nevus remnant
- *___ Other (specify): _____
-
- ***Comment(s)**

Regional Lymph Nodes (pN)

- ___ pNX: Regional lymph nodes cannot be assessed
- ___ pN0: No regional lymph node metastasis
- pN1: Metastasis in 1 regional lymph node
- ___ pN1a: Clinically occult (microscopic) metastasis
- ___ pN1b: Clinically apparent (macroscopic) metastasis
- pN2: Metastasis in 2 to 3 regional nodes or intralymphatic regional metastasis without nodal metastasis
- ___ pN2a: Clinically occult (microscopic) metastasis
- ___ pN2b: Clinically apparent (macroscopic) metastasis
- ___ pN2c: Satellite or in-transit metastasis without nodal metastasis
- ___ pN3: Metastasis in 4 or more regional lymph nodes, or matted metastatic nodes, or in-transit metastasis or satellites(s) with metastasis in regional node(s)
-
- ___ No nodes submitted or found
-
- Number of lymph nodes identified: ____
- Number containing metastases identified macroscopically: ____
- Number containing metastases identified microscopically: ____
- Matted nodes:
- ___ Present
- ___ Not identified

Lymph Nodes

- Number of sentinel nodes examined: ____
- Total number of nodes examined (sentinel and nonsentinel): ____
- Number of lymph nodes with metastases: ____
- *Extranodal tumor extension:
- *___ Present
- *___ Not identified
- *___ Indeterminate
- *Size of largest metastatic focus: ___ (mm) (for sentinel node)
- *Location of metastatic tumor (for sentinel node)
- *___ Subcapsular
- *___ Intramedullary
- *___ Subcapsular and intramedullary

Margins

- **Peripheral Margins**
- ___ Cannot be assessed
- ___ Uninvolved by invasive melanoma
- Distance of invasive melanoma from closest peripheral margin: ___ mm (required for excisions only)
- Specify location(s), if possible: _____
- ___ Involved by invasive melanoma
- Specify location(s), if possible: _____
- ___ Uninvolved by melanoma in situ
- Distance of melanoma in situ from closest margin: ___ mm (required for excisions only)
- Specify location(s), if possible: _____
- ___ Involved by melanoma in situ
- Specify location(s), if possible: _____
-
- **Deep Margin**
- ___ Cannot be assessed
- ___ Uninvolved by invasive melanoma
- Distance of invasive melanoma from margin: ___ mm (required for excisions only)
- Specify location(s), if possible: _____
- ___ Involved by invasive melanoma
- Specify location(s), if possible: _____