Greetings from the University of Pennsylvania, founded by Ben Franklin

Disclosures

Consultant to

Myriad Genetics

SciBase

Treatment recommendations for melanocytic lesions (for pathologists)

Paris, January, 2020

David E Elder, University of Pennsylvania

20 min

Treatment recommendations for melanocytic lesions (for pathologists)

Management is Typically Conducted According to National Guidelines

Melanoma Management National Guidelines

- Scolyer RA, Balamurgan T, Busam K, Elder D, Evans A, Gershenwald J, Frishberg DP, McMenamin M, Prieto VG, Shiau C, Swetter S, van den Oord J. (2019) *Invasive Melanoma, Histopathology Reporting Guide, 2nd Edition. International Collaboration on Cancer Reporting; Sydney, Australia.* ISBN: 978-1-925687-32-3.
- Swetter SM, Tsao H, Bichakjian CK, Curiel-Lewandrowski C, Elder DE, Gershenwald JE, Guild V, Grant-Kels JM, Halpern AC, Johnson TM, Sober AJ, Thompson JA, Wisco OJ, Wyatt S, Hu S, Lamina T. Guidelines of care for the management of primary cutaneous melanoma. J Am Acad Dermatol. 2019 Jan;80(1):208-250
- National Comprehensive Cancer Network I. NCCN Clinical Practice Guidelines in Oncology: Melanoma (2019).
- Gershenwald JE, Scolyer RA, Hess KR, Thompson JF, Long GV, Ross MI et al. Melanoma of the Skin. In: M. B. Amin, S. B. Edge, F. L. Greene, D. R. Byrd, R. K. Brookland, M. K. Washington, et al. editors. AJCC Cancer Staging Manual, 8th Edition: Springer International Publishing; 2016.
- Garbe C, Peris K, Hauschild A, Saiag P, Middleton M, Spatz A et al. Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline--Update 2012. Eur J Cancer 2012;48:2375-90.
- Dummer R, Hauschild A, Guggenheim M, Keilholz U, Pentheroudakis G , Group EGW. Cutaneous melanoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of oncology : official journal of the European Society for Medical Oncology / ESMO 2012;23 Suppl 7:vii86-91.
- Bichakjian CK, Halpern AC, Johnson TM, Foote Hood A, Grichnik JM, Swetter SM et al. Guidelines of care for the management of primary cutaneous melanoma. American Academy of Dermatology. Journal of the American Academy of Dermatology 2011;65:1032-47.
- Dummer R, Guggenheim M, Arnold AW, Braun R, von Moos R , Project Group Melanoma of the Swiss Group for Clinical Cancer R. Updated Swiss guidelines for the treatment and follow-up of cutaneous melanoma. Swiss medical weekly 2011;141:w13320.
- Marsden JR, Newton-Bishop JA, Burrows L, Cook M, Corrie PG, Cox NH et al. Revised U.K. guidelines for the management of cutaneous melanoma 2010. The British journal of dermatology 2010;163:238-56.

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AJCC 8th Edition

CA CANCER J CLIN 2017;00:00–00

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

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

Breslow thickness, ulceration and sentinel node status are key elements of staging system

AJCC/UICC Staging Guides Therapy

- Breslow thickness is now measured to one decimal place – improved ease of measurement and reproducibility
- Cutoff of "< 0.8" (i.e. 0.7 or less) corresponds to original "Breslow number" of 0.76)
- Ulceration is a stage modifier in all T stages
- Mitogenicity is no longer a stage modifier, however reporting of mitotic rate continues to be recommended
- Staging of the primary is mostly dependent on Breslow thickness (and ulceration)
- Accurate staging requires SLNB

T Classification	
T1 ≤1.0mm	a. <0.8 mm without ulceration (i.e. 0.7 or less)
	b. <0.8 mm w/ulceration or 0.8-1.0 mm +/- ulceration
T2 >1.0-2.0mm (1.1-20.)	a. Without ulceration
	b. With ulceration
T3 >2.0-4.0mm (2.1-4.0)	a. Without ulceration
	b. With ulceration
T4 >4.0mm (4.1 or greater)	a. Without ulceration
	b. With ulceration
N and M Classification	
N1 1 node or in-transit, satellite, and/or microsatellite metastases with no tumor-involved nodes	a. Clinically occult*
	b. Clinically detected[†]
	c. Intralymphatic metastases[§] without regional lymph node disease
N2 2-3 nodes or in-transit, satellite, and/or microsatellite metastases with one tumor-involved node	a. Clinically occult*
	b. Clinically detected (at least 1)[†]
	c. Intralymphatic metastases[§] with 1 occult or clinically detected regional LN
N3 4 or more tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with two or more tumor-involved nodes, or any number of matted nodes without or with in-transit, satellite, and/or microsatellite metastases	a. ≥4 metastatic clinically occult nodes with no intralymphatic metastases
	b. ≥4 metastatic nodes (at least one clinically detected), or matted nodes (any number) with no intralymphatic metastases
	c. ≥2 clinically occult or clinically detected nodes and/or presence of matted nodes (any number) with intralymphatic metastases
M1a Distant skin, soft tissue (including muscle), and/or non-regional lymph nodes	+/- ↑LDH[&]
M1b Lung metastasis +/- M1a	+/- ↑LDH[&]
M1c Distant non-CNS visceral +/- M1a or M1b	+/- ↑LDH[&]
M1d Distant metastasis to CNS +/- M1a or M1b or M1c	+/- ↑LDH[&]
*Clinically occult tumor-involved regional lymph nodes are microscopically diagnosed after sentinel lymph node biopsy.	
[†]Clinically detected tumor-involved regional lymph nodes are defined as clinically evident nodal metastases confirmed on fine needle aspiration, biopsy, and/or therapeutic lymphadenectomy.	
[§]Intralymphatic metastases are defined by the presence of clinically apparent in-transit/satellite metastasis and/or histologically evident microsatellite metastases in the primary tumor specimen.	
[&]Suffix: (0) LDH not elevated, (1) LDH elevated.	
**CNS = central nervous system	

Guidelines of care for the management of primary cutaneous melanoma

Work Group: Susan M. Swetter, MD (Chair),[a,b] Hensin Tsao, MD, PhD (Co-Chair),[c,d] Christopher K. Bichakjian, MD,[e,f] Clara Curiel-Lewandrowski, MD,[g,h] David E. Elder, MBChB,[i,j] Jeffrey E. Gershenwald, MD,[k,l] Valerie Guild, MS, MBA,[m] Jane M. Grant-Kels, MD,[n,o,p] Allan C. Halpern, MD,[q] Timothy M. Johnson, MD,[e,f] Arthur J. Sober, MD,[c] John A. Thompson, MD,[r,s] Oliver J. Wisco, DO,[t] Samantha Wyatt, MD,[u] Shasa Hu, MD,[v] and Toyin Lamina, PhD[w]

Table I. Clinical questions used to structure the evidence review

Biopsy	• What biopsy techniques are effective in establishing accurate histopathologic diagnosis of CM?
Pathology	• What clinical information should be provided to the pathologist to improve or facilitate diagnosis? • What histopathologic information should be included in the pathology report to improve or facilitate clinical treatment? • Is there a benefit to using new molecular techniques, including GEP, to provide more accurate prognosis beyond currently known clinicopathologic factors?

etc. …

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Surgery	• What are the recommended surgical margins and appropriate depth for invasive CM based on Breslow thickness? • What are the most appropriate clinical margins for MIS (including LM type)? • What is the role of staged excision or MMS for MIS, LM type?
SLNB	• What is the role of SLNB for staging, regional nodal control, and survival in patients with CM? • In what settings should SLNB be considered and/or recommended in patients with CM?
Alternative/adjunctive therapies for MIS (LM type)	• For patients with MIS, LM type, does the evidence support the use of topical imiquimod cream as primary therapy over surgical excision or other therapies? • Among patients with MIS, LM type, that has been "optimally" surgically resected, does the use of adjuvant imiquimod help to prevent local recurrence?

etc. …

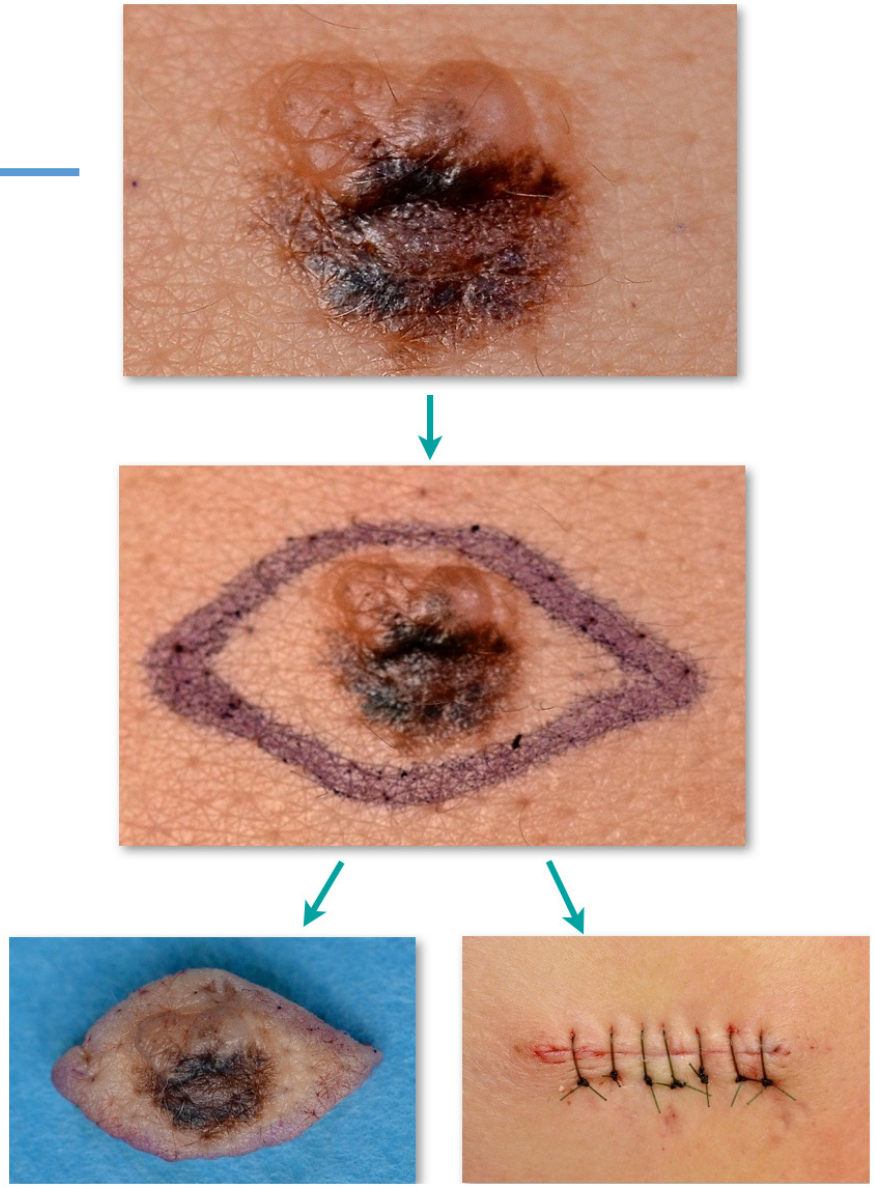
Guidelines of care for the management of primary cutaneous melanoma

Table V. Level of evidence and strength of recommendations for biopsy of suspected cutaneous melanoma, clinical information, and pathology report

Recommendation	Strength of recommendation	Level of evidence	References
Biopsy • Excisional biopsy with 1- to 3-mm clinically negative margins • Partial biopsy in select circumstances • Follow-up excisional biopsy to partial biopsy	B	II	13-30
Clinical information provided to the pathologist	C	III	Expert opinion
Pathology report			
Clinical information	C	III	31
Tumor (Breslow) thickness	A	I/II	9,32-42
Ulceration	A	I/II	9,32-43
Mitotic rate	A	I/II	9,32-42,44,45
Level of invasion (Clark level)	B	II	36,38,39,46
Microsatellitosis	B	II	45,49-51
Angiolymphatic invasion	B	II	45,48,52-54
Histologic subtype	B	II	36,48,54,56
Neurotropism/perineural invasion	C	III	57,58
Regression	B	I/II	42,59-63
Tumor-infiltrating lymphocytes	B	II	42,64,65
Use of ancillary molecular diagnostic techniques for equivocal melanocytic neoplasms	C	III	66-73
Against testing for oncogenic mutations in the absence of metastatic melanoma or outside of a clinical study	C	III	2 Expert opinion

Biopsy Techniques

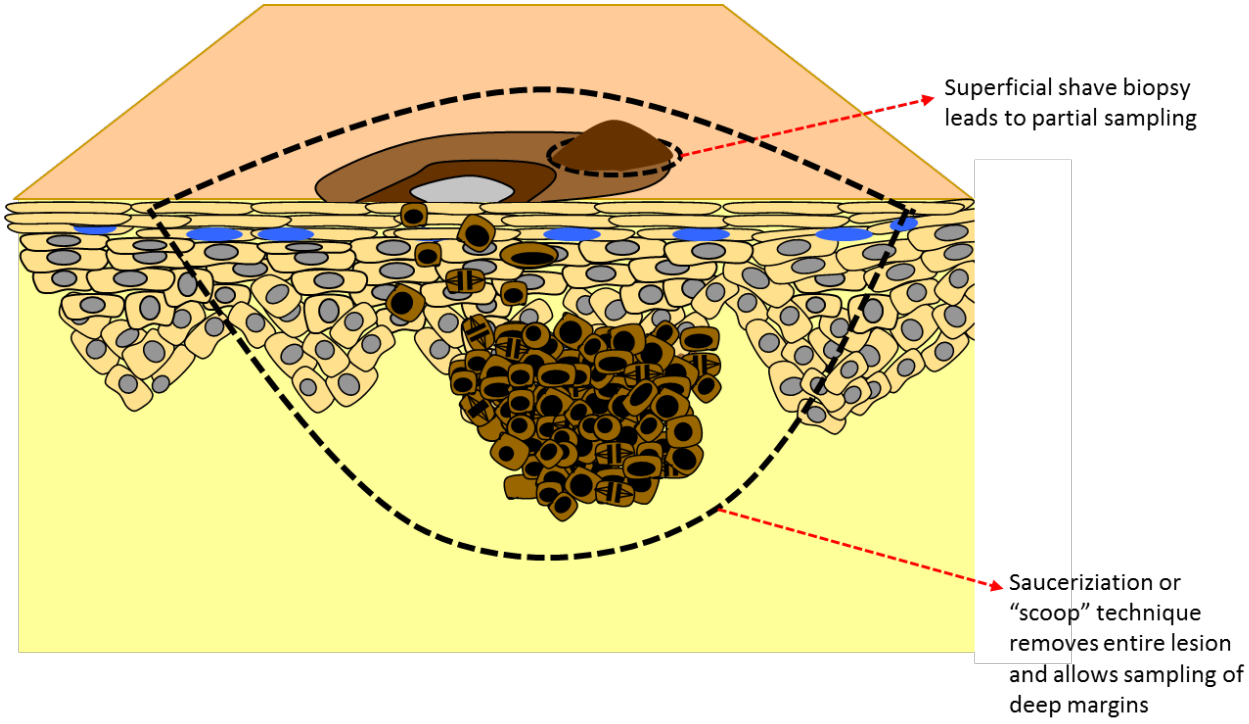
- Preferred biopsy technique is a narrow excisional/ complete biopsy with 1-3 mm clinical margins that encompass the entire breadth of lesion, and of sufficient depth to prevent transection at the base.
- This may be accomplished by fusiform/elliptical or punch excision, or deep shave/ saucerization removal to depth below anticipated plane of lesion.



C Curiel, PharmaDura, MIA

Saucerization versus Shave Biopsy

- A superficial shave biopsy will often lead to incomplete sampling at the specimen base
- Deep scoop shave biopsy allows for full visualization in most cases



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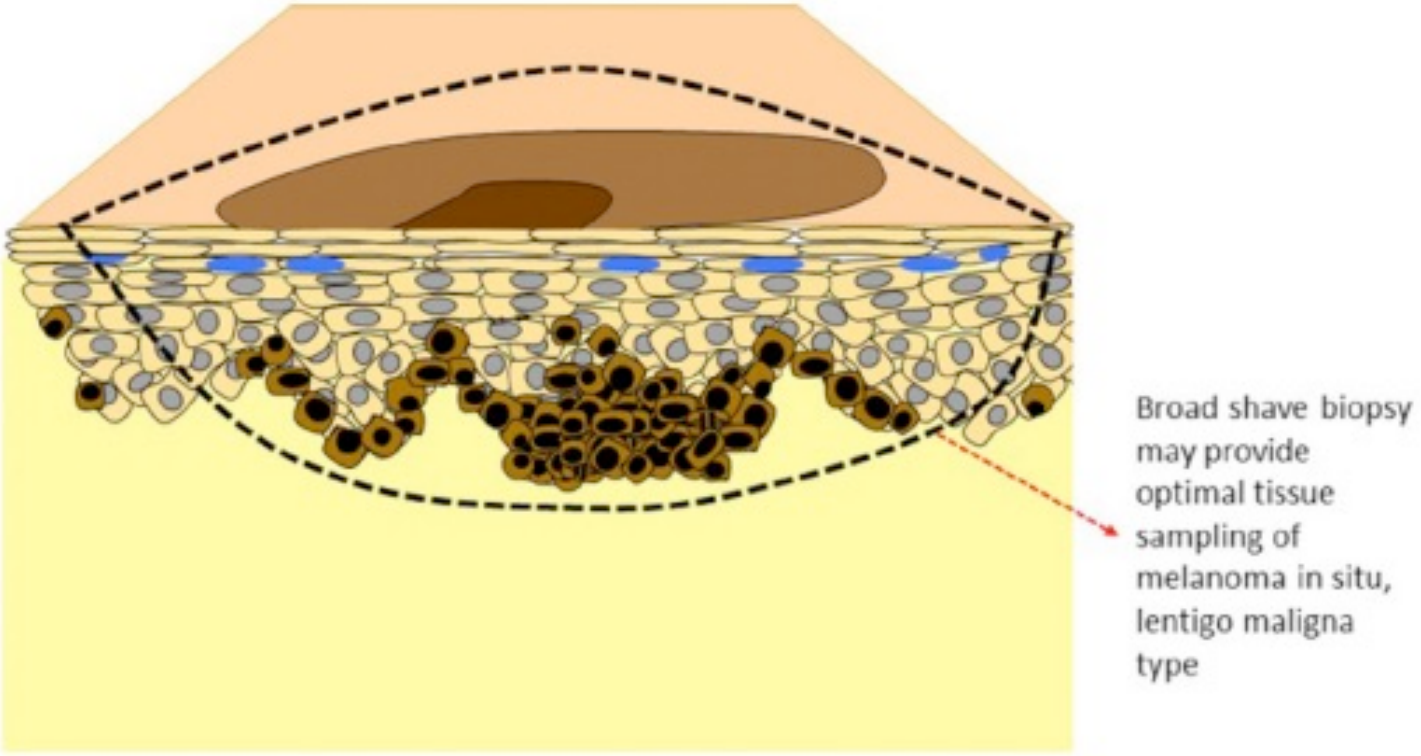
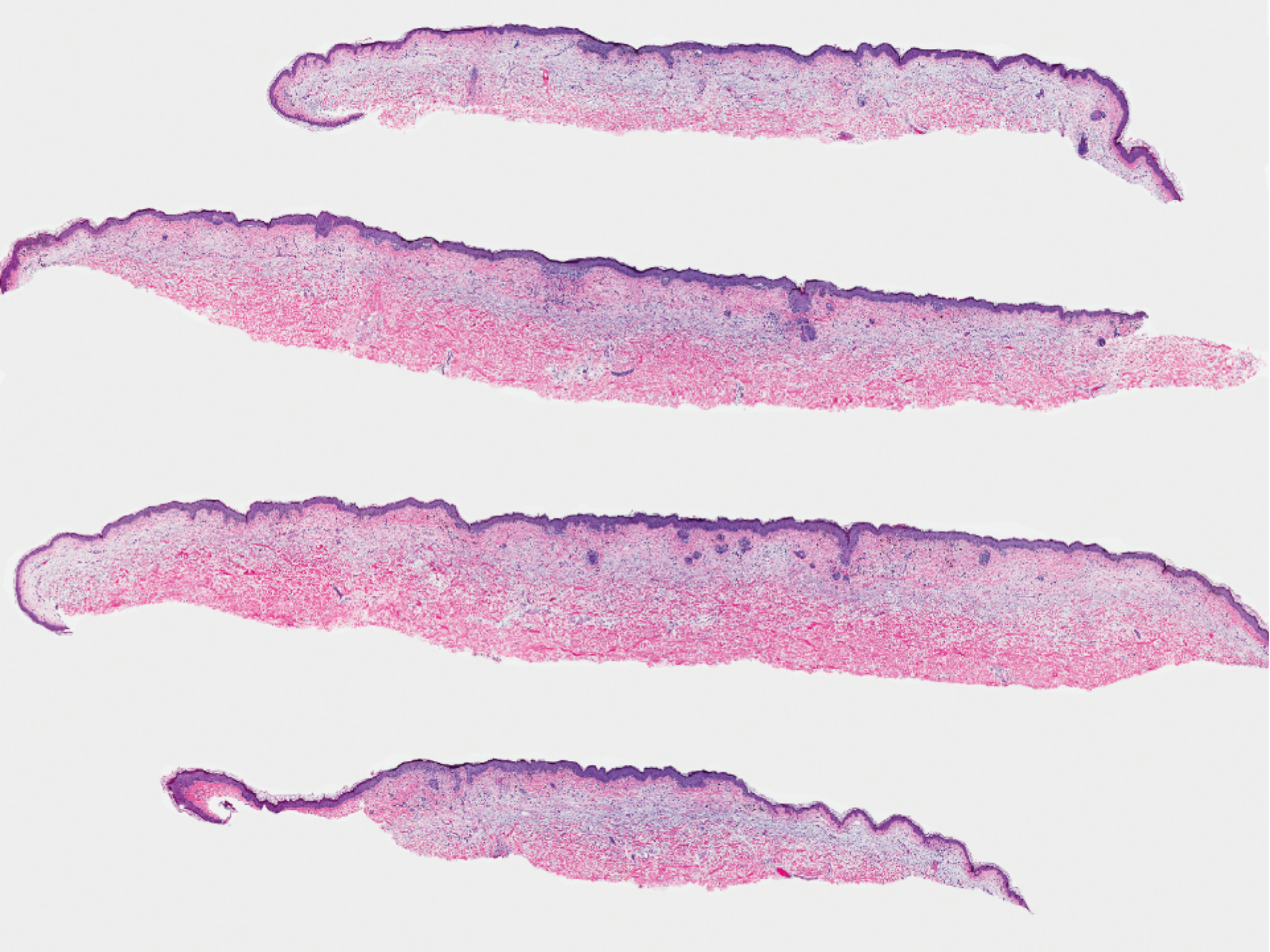
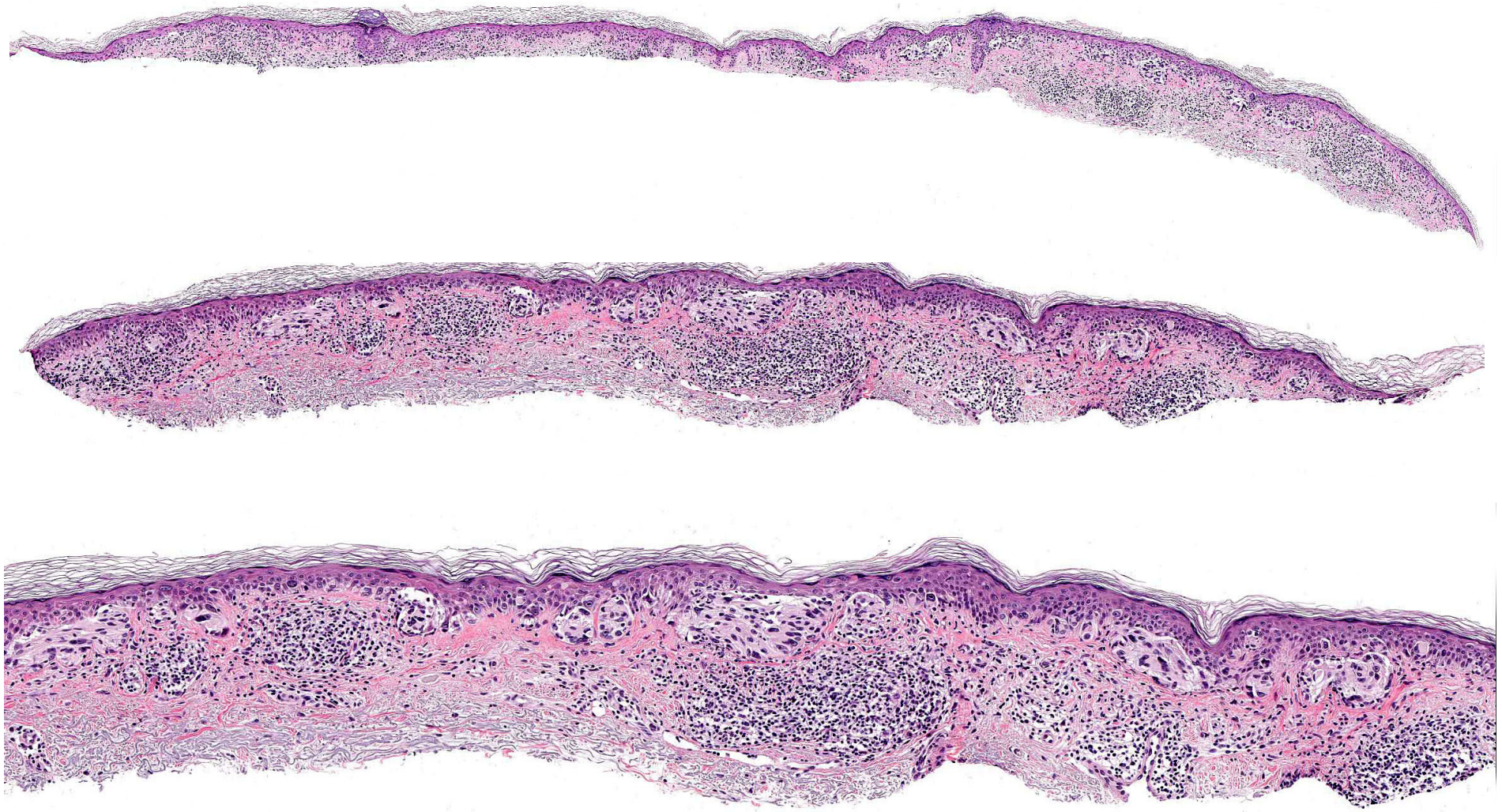


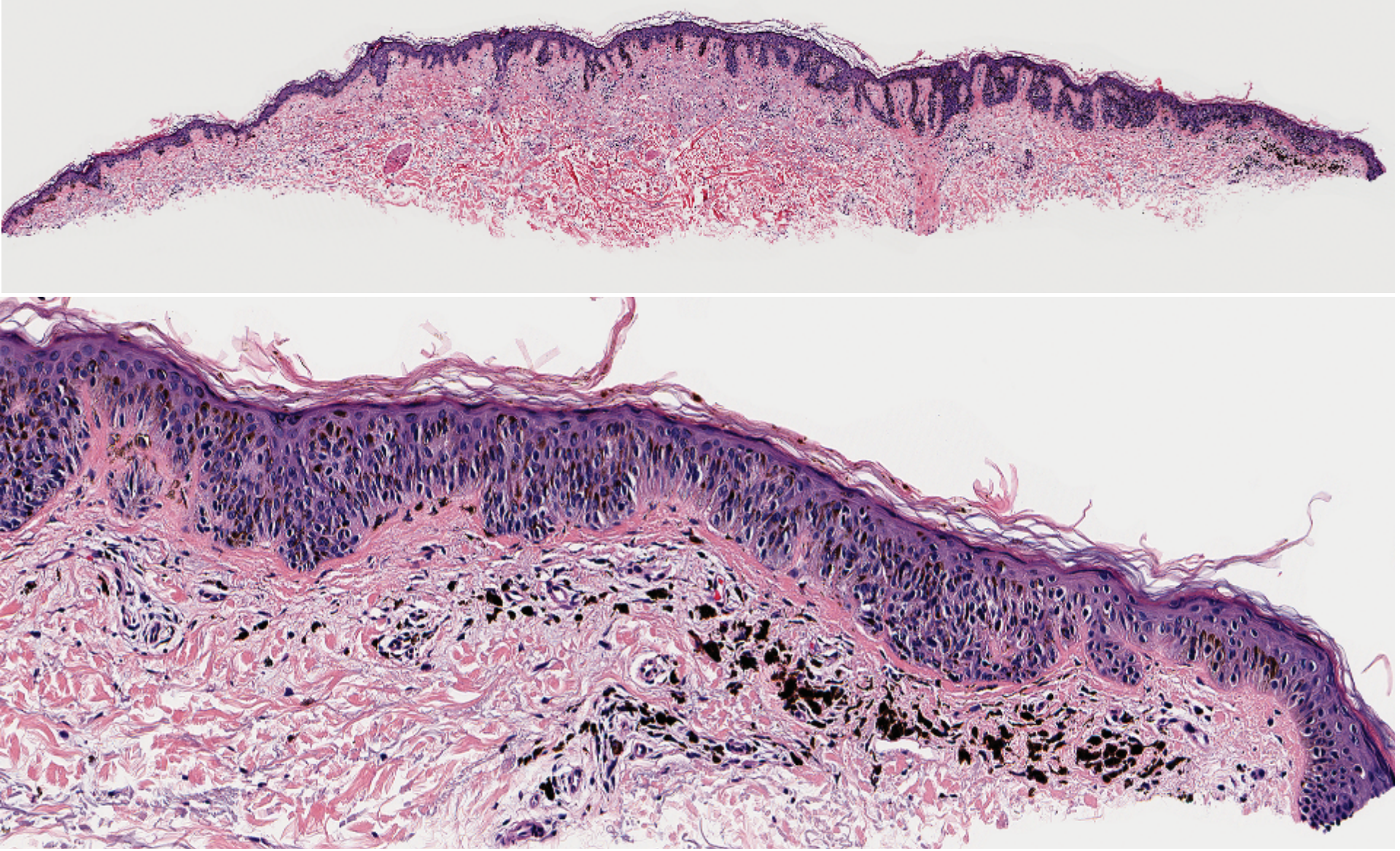
Fig 2. Diagnostic broad shave biopsy for suspected melanoma in situ, lentigo maligna type.

Partial/incomplete sampling (incisional biopsy) is acceptable in select clinical circumstances such as facial or acral location, very large lesion, or low clinical suspicion or uncertainty of diagnosis.

Narrow-margin excisional biopsy may be performed if an initial partial biopsy is inadequate for diagnosis or microstaging, but it should not generally be performed if the initial specimen meets the criteria for consideration of sentinel lymph node biopsy.





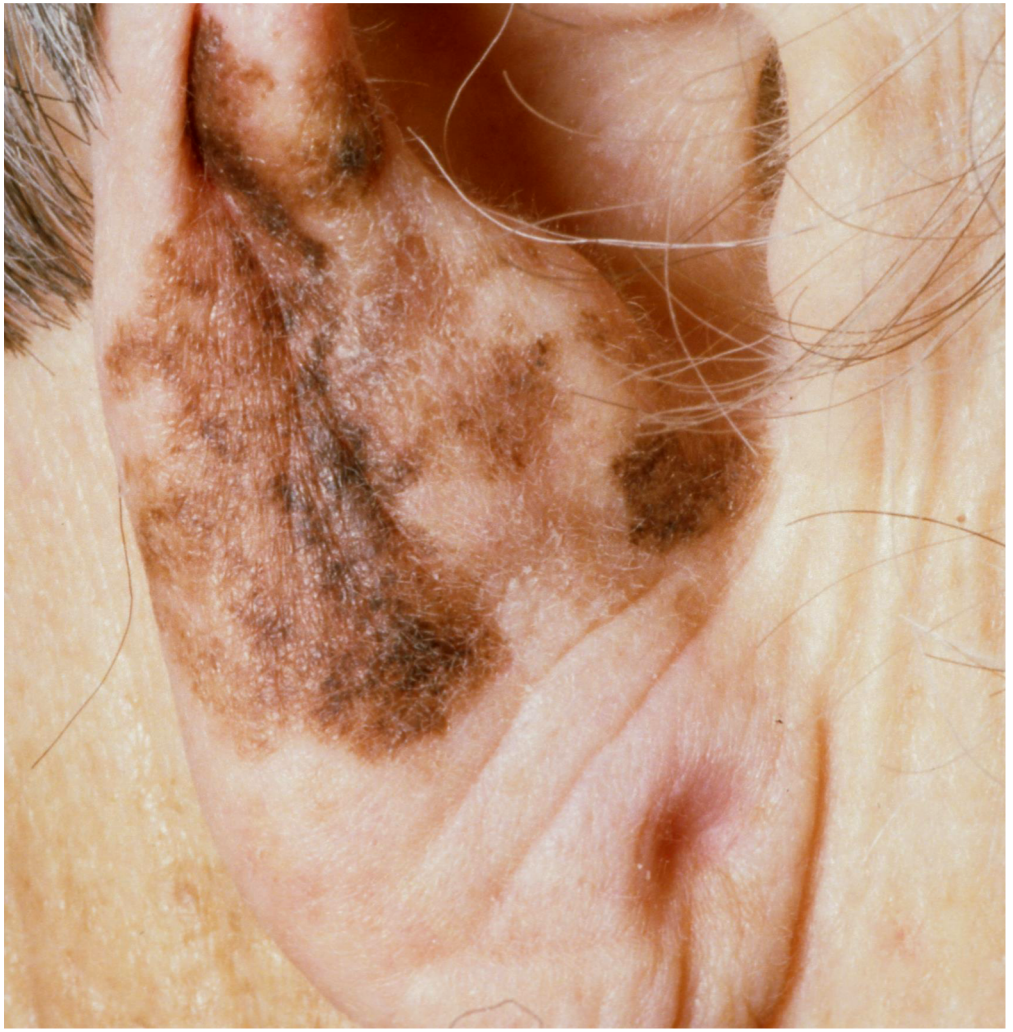


Specimen should include periphery of lesion as well as the base

Biopsy Techniques

Partial/incomplete sampling (incisional biopsy) is acceptable in select circumstances such as :

- facial or acral location,
- very large lesion
- low clinical suspicion or uncertainty of diagnosis



The Impact of Partial Biopsy on Histopathologic Diagnosis of Cutaneous Melanoma

Experience of an Australian Tertiary Referral Service

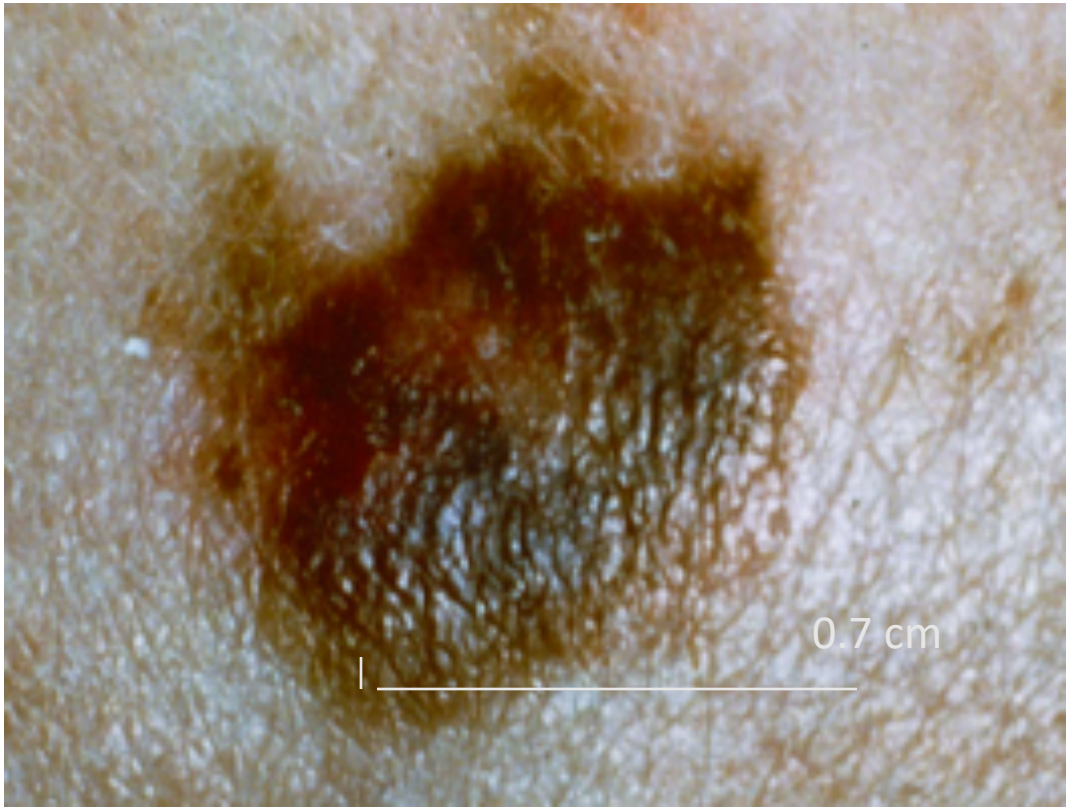
Jonathan C. Ng, MBBS, MBiomedSc; Sarah Swain, MBBS, FRCPA; John P. Dowling, FRCPA; Rory Wolfe, BSc, PhD; Pamela Simpson, BSc; John W. Kelly, MD, BS, FACD Arch Dermatol 146:234-9, 2010

- Compared partial and excisional biopsy techniques in the accuracy of histopathologic diagnosis and microstaging of cutaneous melanoma in a prospective case series (1995-2006.

- Increased odds of histopathologic misdiagnosis were associated with punch biopsy (OR, 16.6) and shave biopsy (OR, 2.6) compared with excisional biopsy.
- Punch biopsy (OR, 5.1) and shave biopsy (OR, 2.3) had increased odds of microstaging inaccuracy over excisional biopsy.
- Punch biopsy was associated with increased odds of misdiagnosis with an adverse outcome (OR, 20).

Case (Clara Curiel)

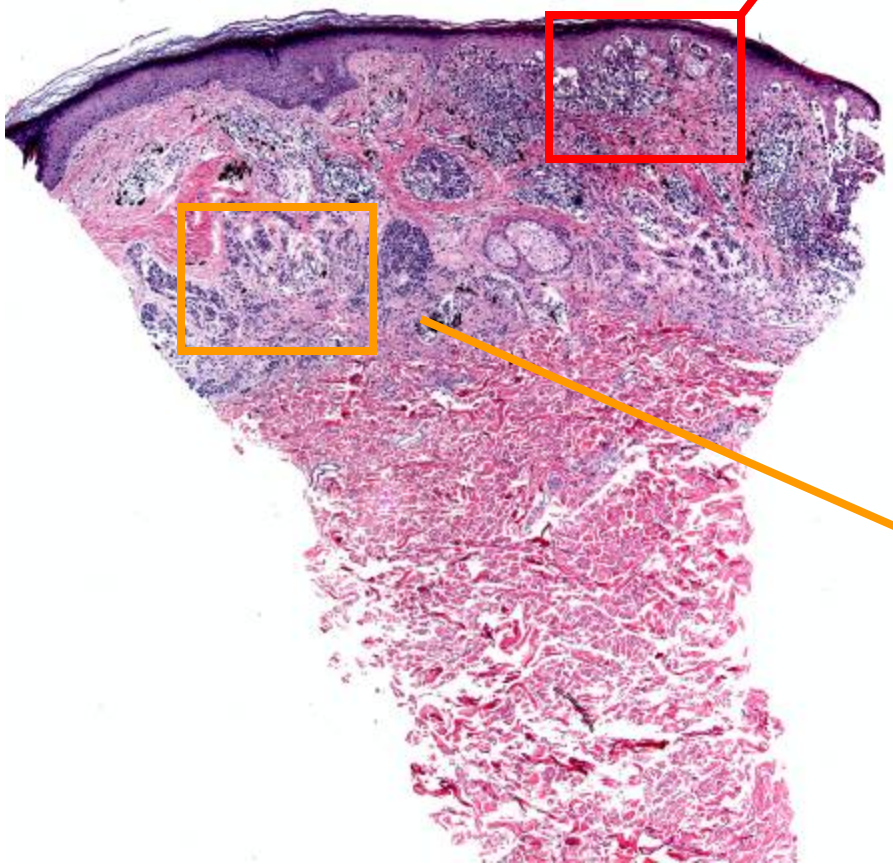
A 42-year-old man presents for evaluation of a pigmented papule on his right shoulder. The “mole” had been present since teenage years, but over the past 8 months the patient’s wife noted that it had increased in size and pigmentation.

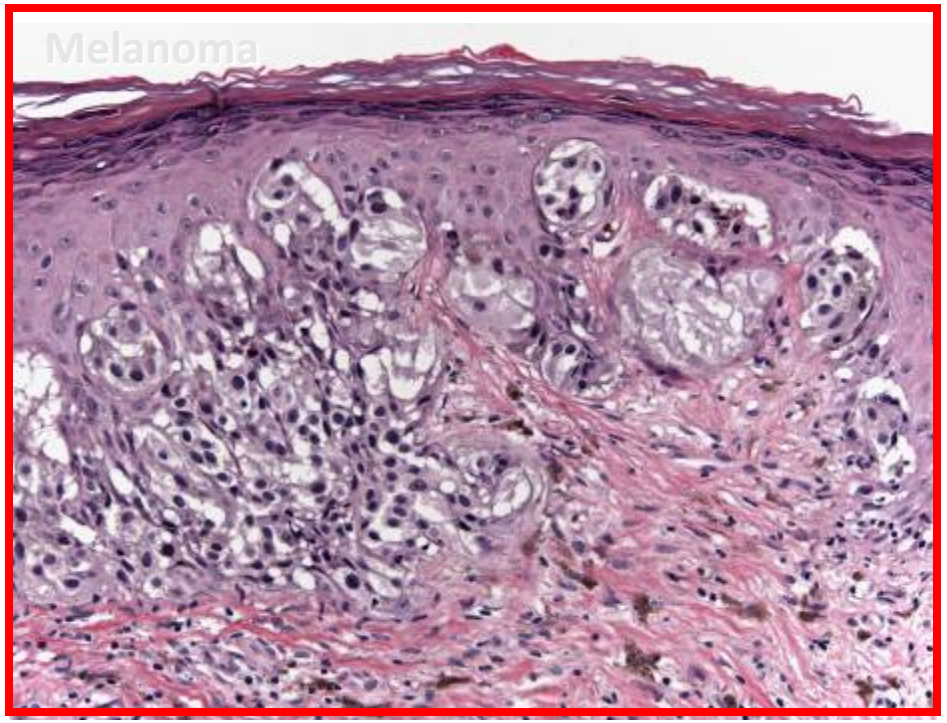


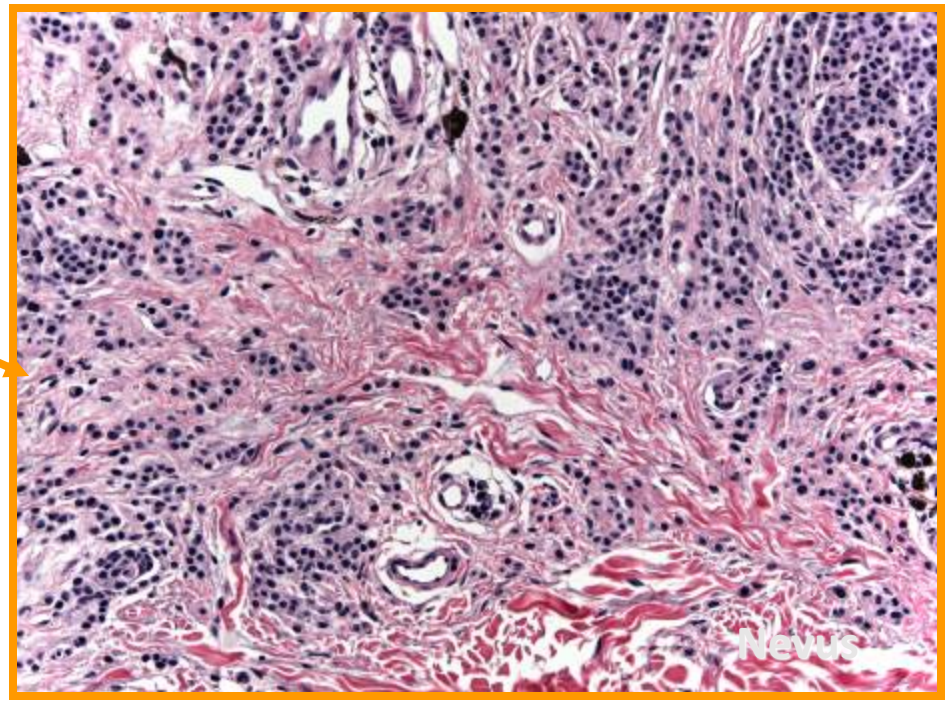
C. Curiel

Melanoma in a nevus

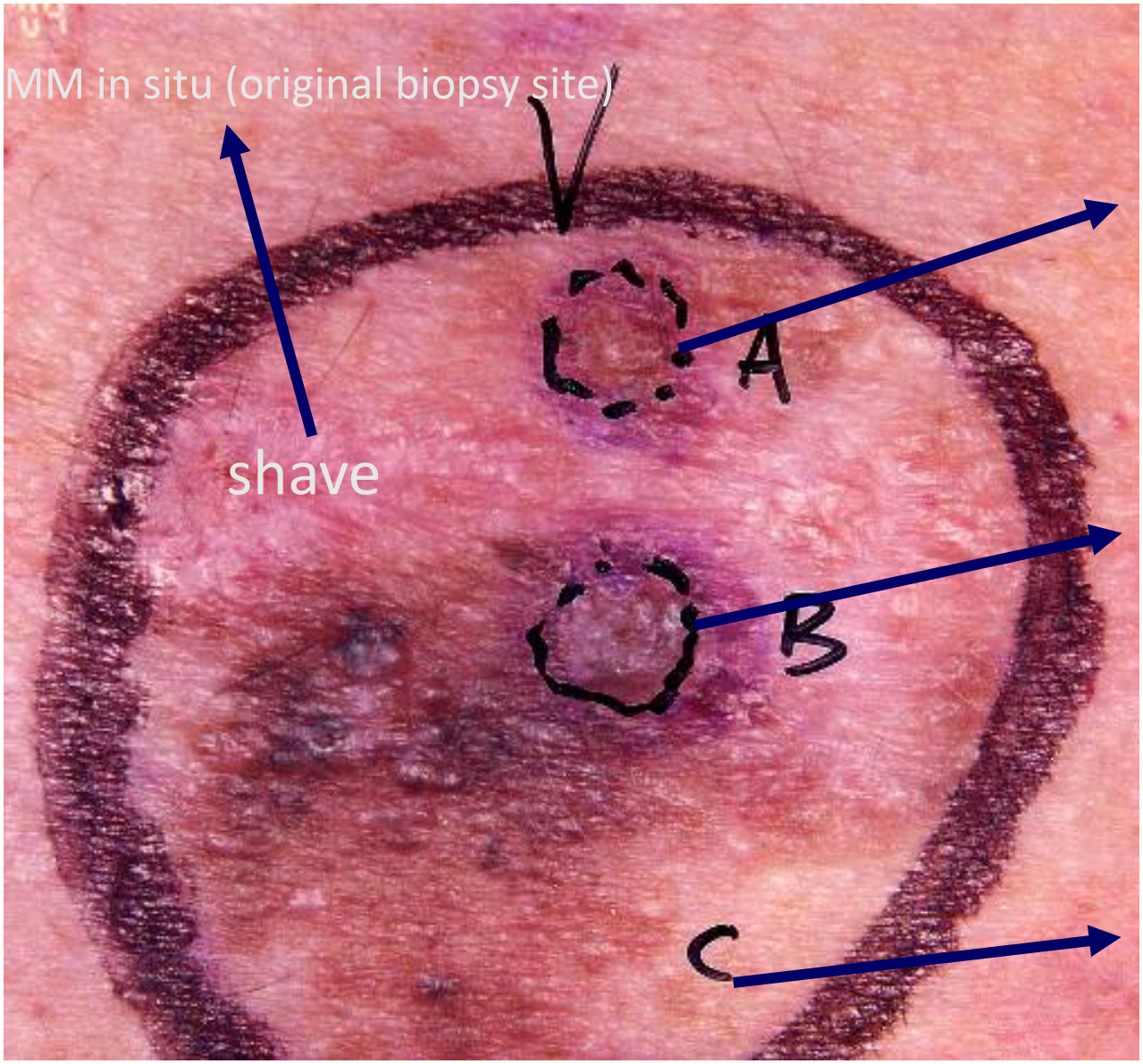
- punch biopsy could easily miss melanoma (right of field below) and lead to erroneous diagnosis of a benign nevus (left)

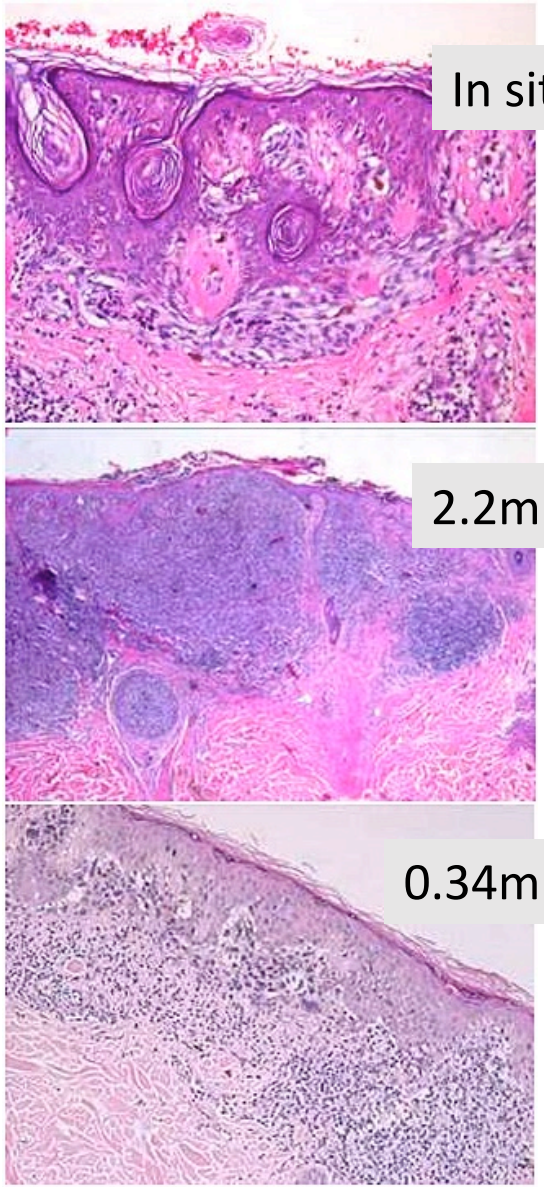






Punch Biopsy (C Curiel, A Marghoob)





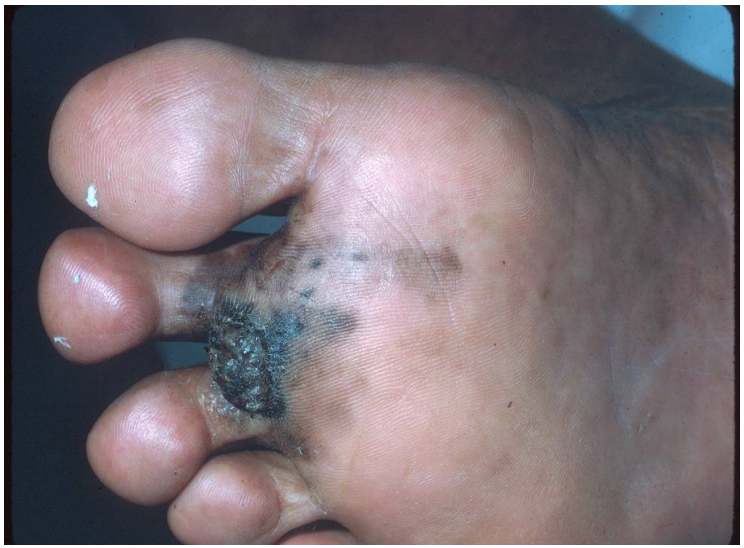
Punch Biopsies

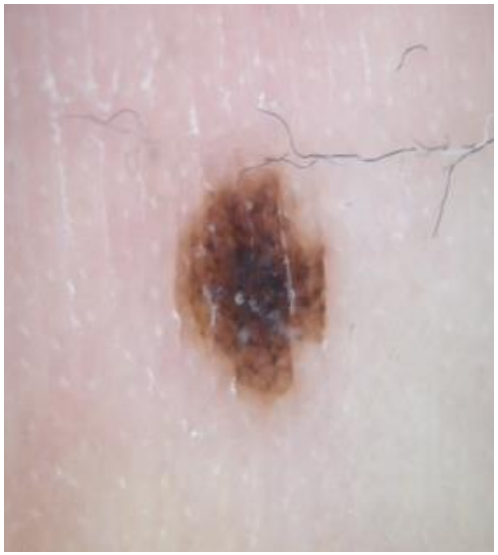
- BE VERY WARY OF PUNCH BIOPSIES
  - And also superficial or partial shave biopsies
  - Incisional biopsies in general

Clinical Information to be Provided with Biopsy

- Age, sex anatomic location are essential
- Intent – sampling or excision?
- Size of lesion is important diagnostic consideration
- Punch, shave, incisional or excisional biopsy?
- Photograph! (or description)

Essential	Strongly Recommended	Optional
Age of patient	- Biopsy intent (excisional or incisional) - Biopsy technique (superficial or deep shave biopsy, punch biopsy, elliptical biopsy)	- Clinical description and history (e.g. changes in size, shape color, bleeding, etc) - Level of suspicion for melanoma - Prior biopsy (if applicable)
Sex	Size of lesion	- Dermoscopic features (with or without photograph)
Anatomic location (including laterality)	Clinical impression/differential diagnosis	
	Macroscopic satellites	
	Clinical photograph (if possible)	





Items for Inclusion in Pathology Report

Essential	Optional
Size of specimen	Gross description of lesion
Tumor thickness (Breslow); mm (nearest 0.1)	Angiolymphatic invasion/lymphovascular invasion
Ulceration	Histologic subtype
Dermal mitotic rate; "hotspot" method; # mitoses per square mm	Neurotropism/perineural invasion
Peripheral and deep margin status (positive (broad or focal)/negative)	Regression
Microsatellitosis	Tumor (T) category for staging
	Tumor infiltrating lymphocytes
	Anatomic level of invasion (Clark level)
	Vertical growth phase

Essential

- Diagnosis of primary melanoma (consider met MM)
- Dimensions of specimen are important to correlate with clinical size
- Tumor thickness and ulceration are essential for AJCC/UICC Staging
- Mitotic rate as a continuous variable is considered essential for prognosis
- Margin status is essential –
  - Positive or negative ("excision complete")
  - Positive margin should be characterized e.g. as "broadly transected" or "focally transected"
  - When margins are "close" (define with surgeon), a measurement may be appropriate

Measurement of Margin Width is Discouraged

- Reporting measurement of distance between tumor and peripheral/deep margins (on both Bx and WLE) is generally discouraged by the WG.
- Treatment measurements are based on the clinical measurement of surgical margins …
- When a margin is narrow it may be appropriate to … provide a measured margin width … practice should be individualized

Although the College of American Pathologists and various international pathology groups[74,81] have recommended reporting measurement (in mm) of distance between the tumor and peripheral and deep margins on both biopsy and WE specimens, this practice is generally discouraged by the WG. It should be emphasized that for primary CM, treatment recommendations are based on the clinical measurement of surgical margins around the tumor and not on histologically measured peripheral or deep margins.[1,2] Routine reporting of histologic margin status (in mm) may result in unnecessary additional WE if the clinician is unaware of this. However, when a clear margin is narrow, it may be appropriate to alert the clinician and provide a measured margin width, recognizing that this is a practice that should be individualized between the dermatologist and pathologist.

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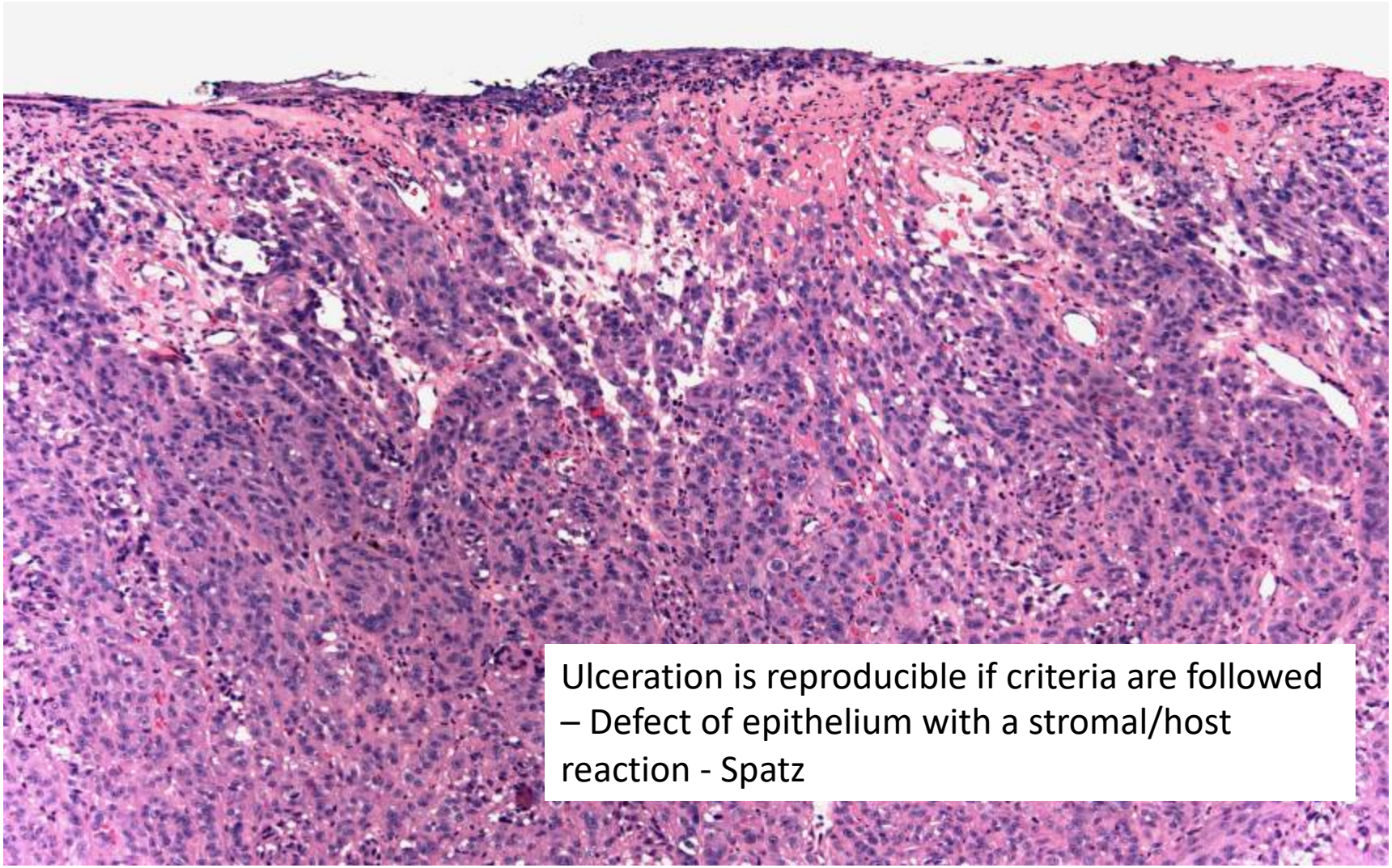
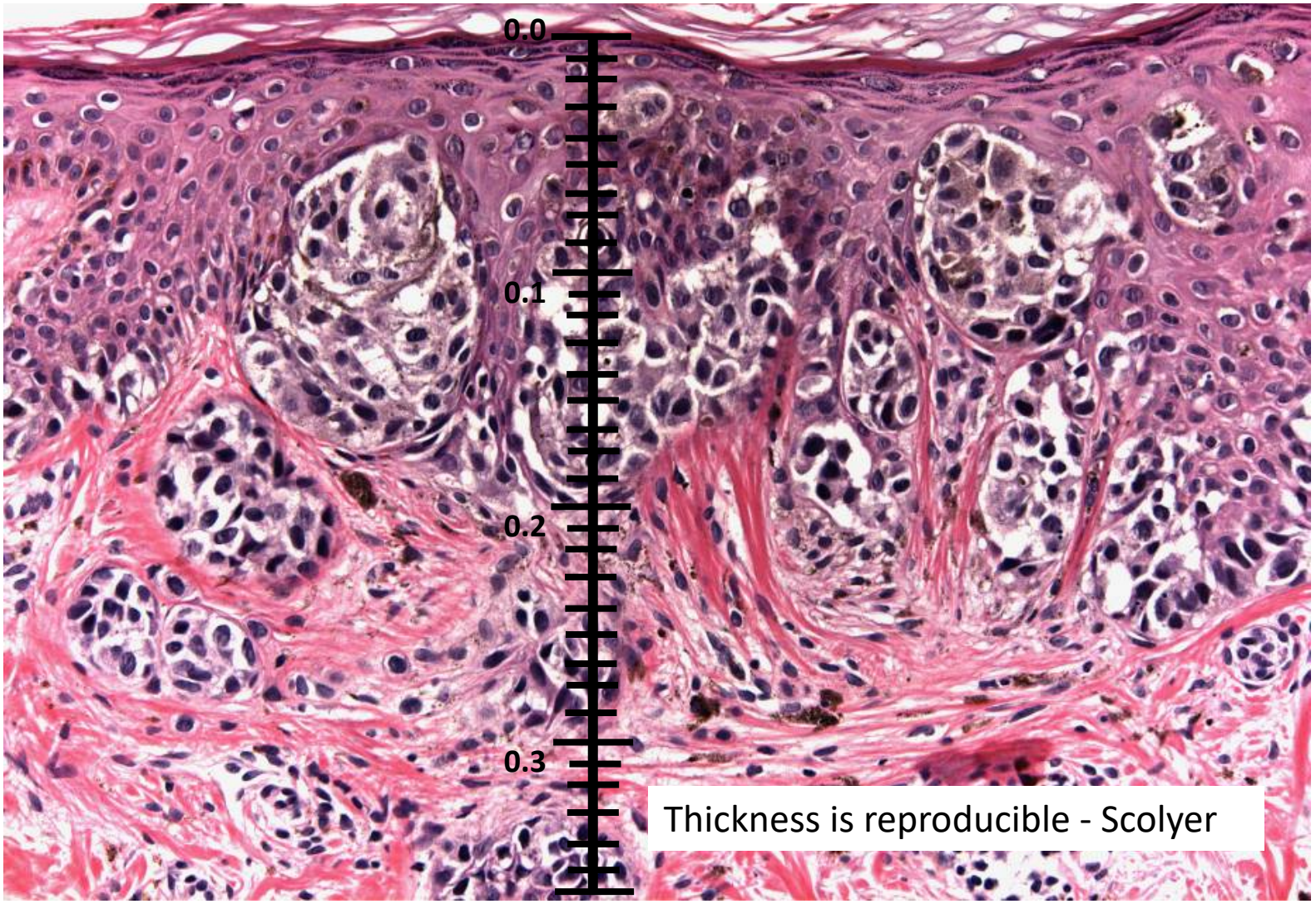
Ulceration of a Melanoma

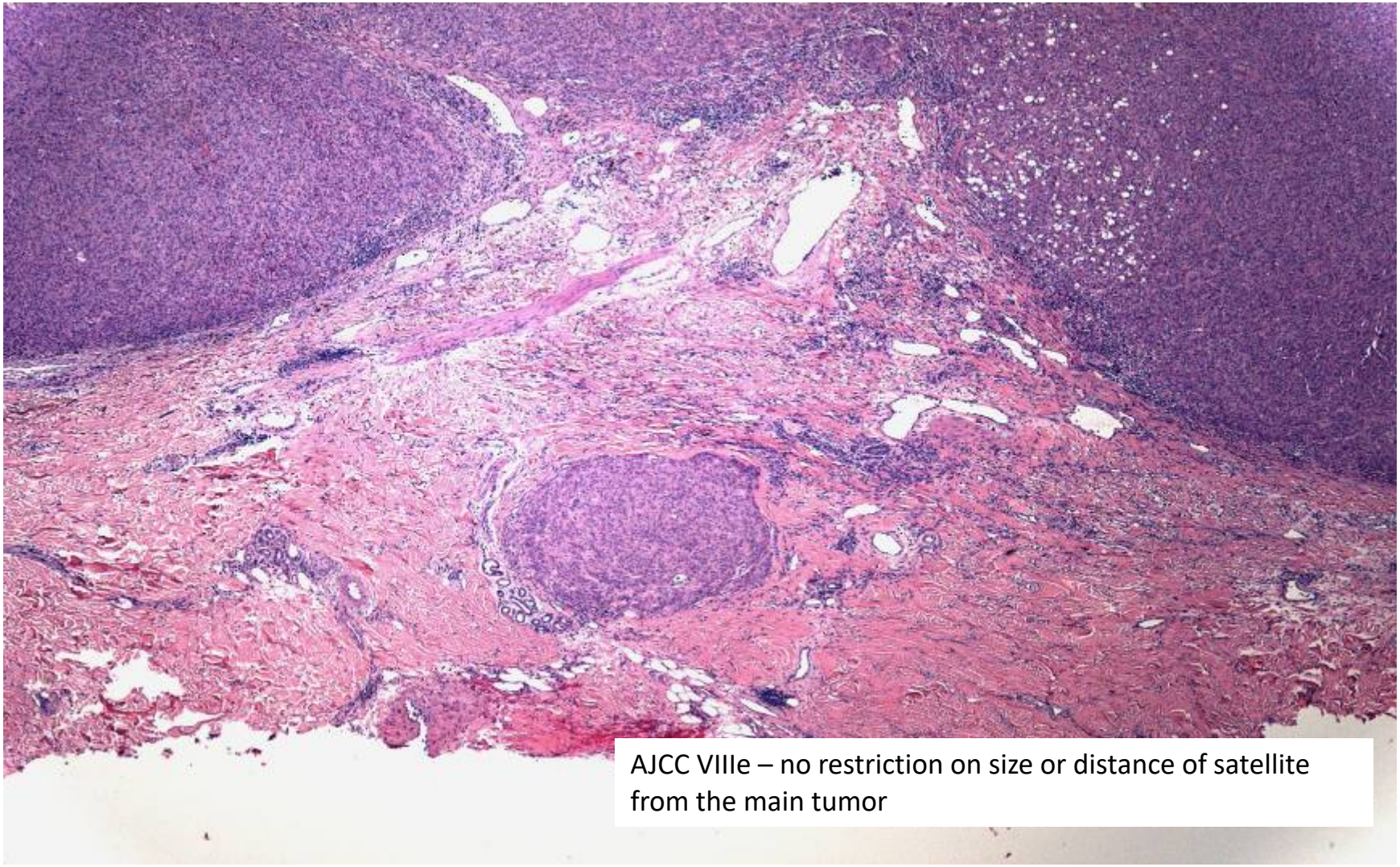


Ulceration is reproducible if criteria are followed
– Defect of epithelium with a stromal/host reaction - Spatz

Thickness measure to 1 decimal place – use 1/100ths or “eyeball”



Satellite Beneath a Melanoma



AJCC VIIIe – no restriction on size or distance of satellite from the main tumor

Desirable Microscopic Information

(Information that has prognostic significance in some databases)

- Dermal mitotic rate:
  - Measured per square millimeter in the “hot spot”
  - If only one mitosis, that is the “hot spot”
  - If area is < 1 sq. mm, use the whole available area and do not extrapolate
- Clark’s Level of Invasion
- Tumor-infiltrating lymphocytes:
  - Absent, Nonbrisk, Brisk
- Solar elastosis
- Vascular/lymphatic invasion (LVI)
- Regression
- Phase of progression:
  - Tumorigenic (vertical growth phase, VGP)
    or Nontumorigenic (radial growth phase only, RGP)
  - Desmoplastic and/or neurotropic?

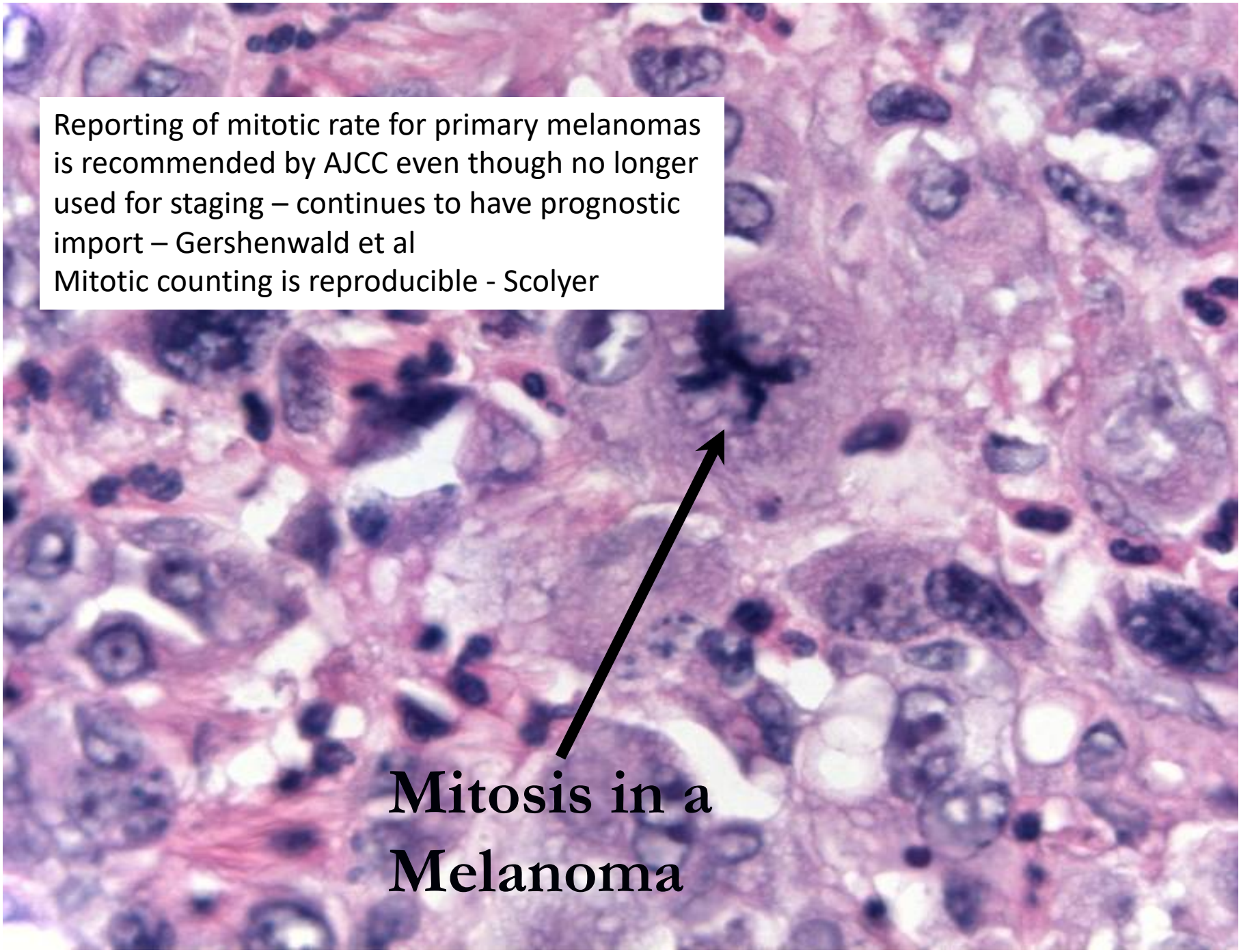
Crowson AN, et al. *Mod Pathol.* 2006;19(suppl 2):S71-S87; Elder DE, et al. *Dermatol Ther.* 2005;18:369-385; Elder DE, et al. *Am J Dermatopathol.* 1984;6(suppl):55-61; Barnhill RL, et al. *J Cutan Pathol.* 2005;32:268-273; Clemente CG, et al. *Cancer.* 1996;77:1303-1310; Mraz-Gernhard S, et al. *Arch Dermatol.* 1998;134:983-987; Lee EY, et al. *Int J Cancer.* 2006; 119:636-642.

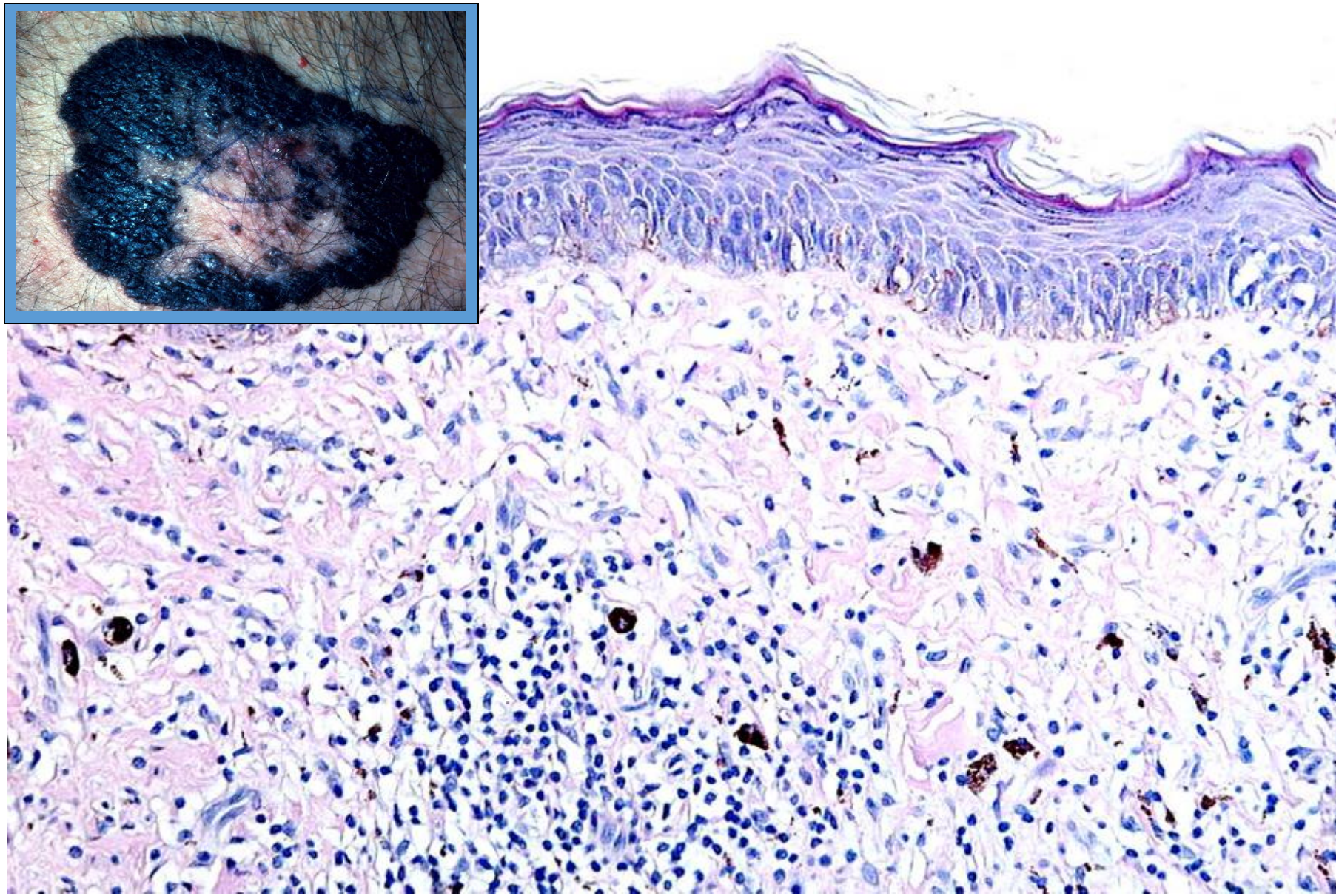
Desirable Microscopic Information

(Information that may have epidemiologic significance)

- Histogenetic type:
  - NM, SSM, LMM, acral, mucosal
  - New genetic information suggests these may be distinct entities – significant for targeted therapy
  - Surgical techniques my differ e.g. SSM v. LMM
- Associated nevus/precursor:
  - Compound, dysplastic, congenital pattern nevus, lentigo, etc.
  - Can indicate patient/family may be at increased risk of future melanoma development

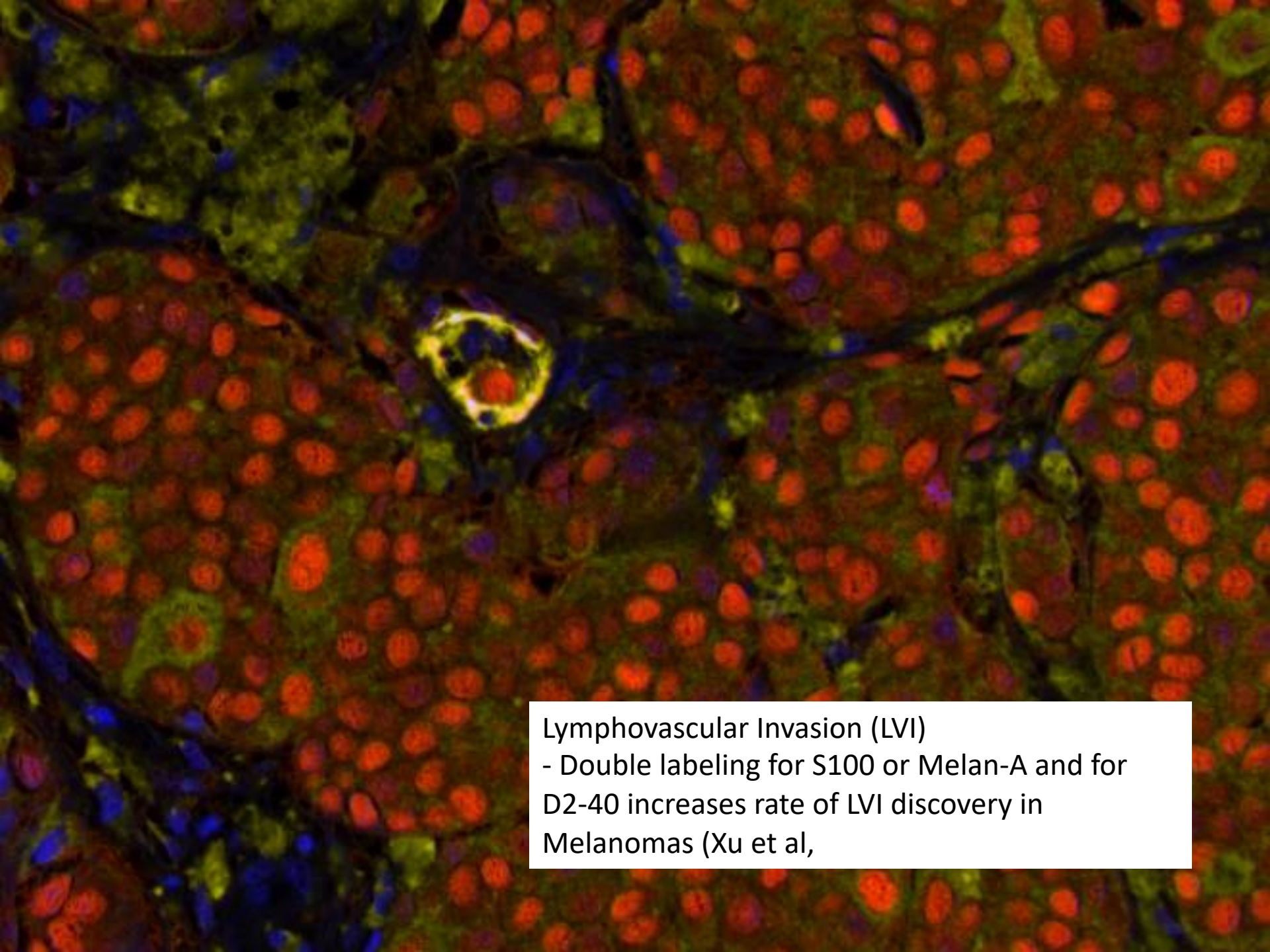
Crowson AN, et al. *Mod Pathol.* 2006;19 (suppl 2):S71-S87.


Reporting of mitotic rate for primary melanomas is recommended by AJCC even though no longer used for staging – continues to have prognostic import – Gershenwald et al
Mitotic counting is reproducible - Scolyer
Mitosis in a Melanoma

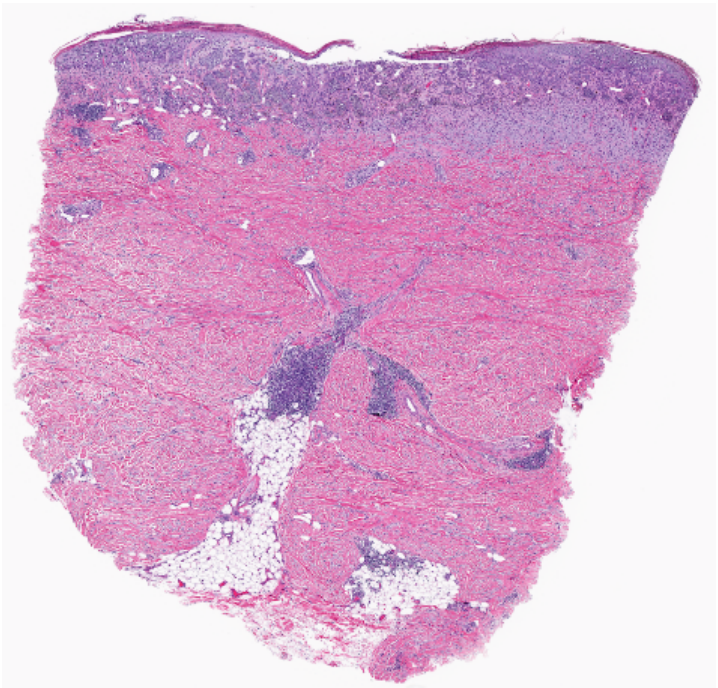


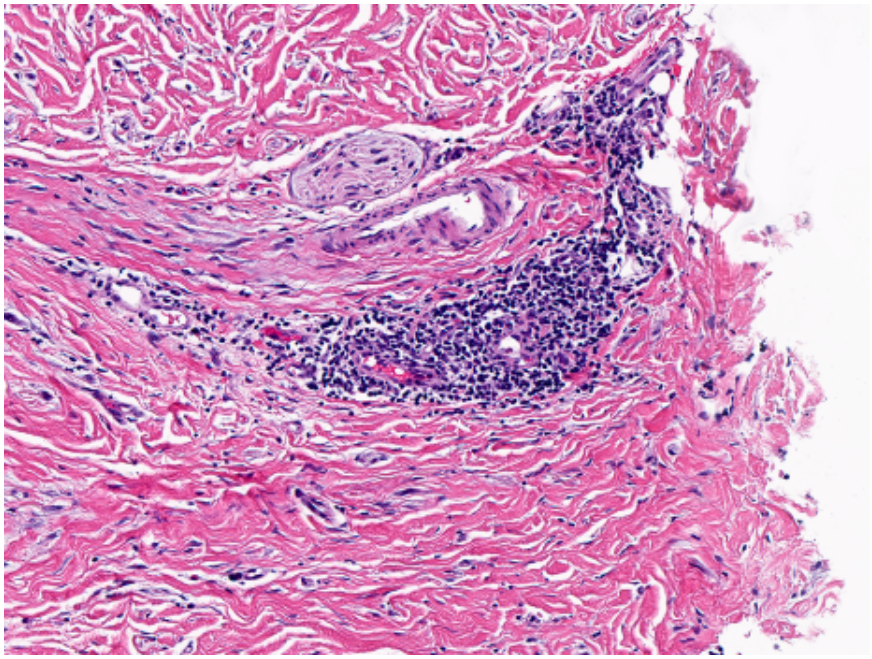
Partial regression of melanoma

Absence of melanoma - fibroplasia, lymphocytes melanophages in papillary dermis usually



Lymphovascular Invasion (LVI)
- Double labeling for S100 or Melan-A and for D2-40 increases rate of LVI discovery in Melanomas (Xu et al,





WHO Pathway Classification of Melanoma (2018)

Pathway I. Low CSD Melanoma/Superficial Spreading Melanoma (SSM)

Pathway II. High CSD Melanoma/Lentigo Maligna Melanoma (LMM)

Pathway III. Desmoplastic Melanoma

Pathway IV. Malignant Spitz Tumor

Pathway V. Acral Melanoma

Pathway VI. Mucosal Melanoma

Pathway VII. Melanoma in Congenital Nevus (MCN)

Pathway VIII. Melanoma in Blue Nevus (MBN)

Pathway IX. Uveal Melanoma

Variable Pathways: Nodular Melanoma

Pathology Reporting

"The pathology of melanocytic tumors should be read by a physician experienced in the interpretation of pigmented lesions" - AAD.

" While therapeutic recommendations may be offered in a pathology report, the surgical and medical management of melanoma is the responsibility of the patients' treating physicians, and the provision of therapeutic recommendations is not a standard of care for pathologists" - DEE.

Ancillary diagnostic molecular techniques

- Ancillary diagnostic molecular techniques (e.g., CGH, FISH, GEP) may be obtained for equivocal melanocytic neoplasms.
- Prognostic molecular testing, including GEP, is not recommended outside of a clinical study or trial.
- Testing of the primary CM for oncogenic mutations (e.g., BRAF, NRAS) is not recommended in the absence of metastatic disease.

Recommendations for surgical management of primary cutaneous melanoma

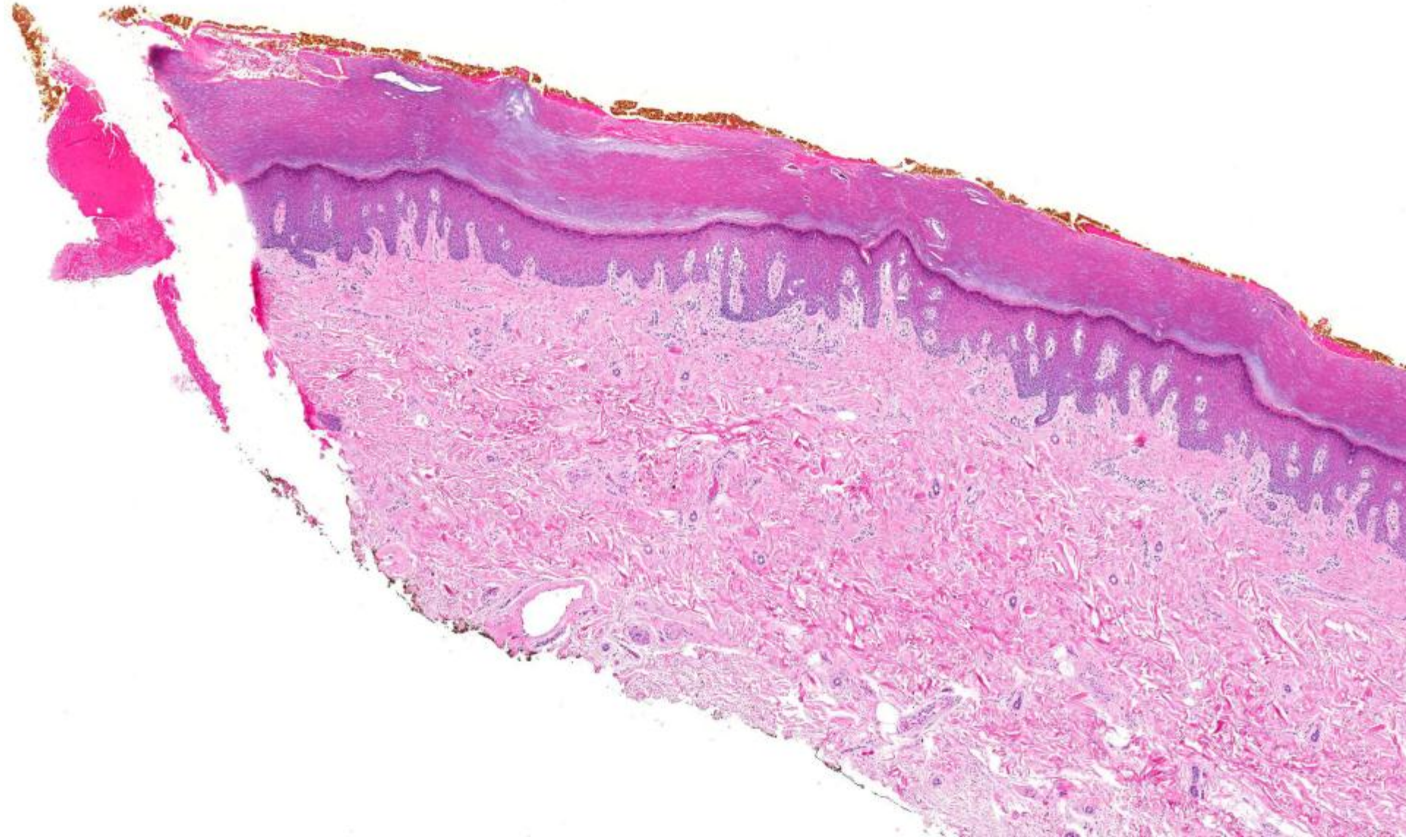
- Surgical margins for invasive CM should be at least 1 cm and no more than 2 cm clinically measured around the primary tumor, although margins may be less to accommodate function and/or anatomic location.
- Margins are based on tumor thickness and
- Margins are NOT histologically determined by the pathologist
- Depth of excision typically to (but not through) the fascia

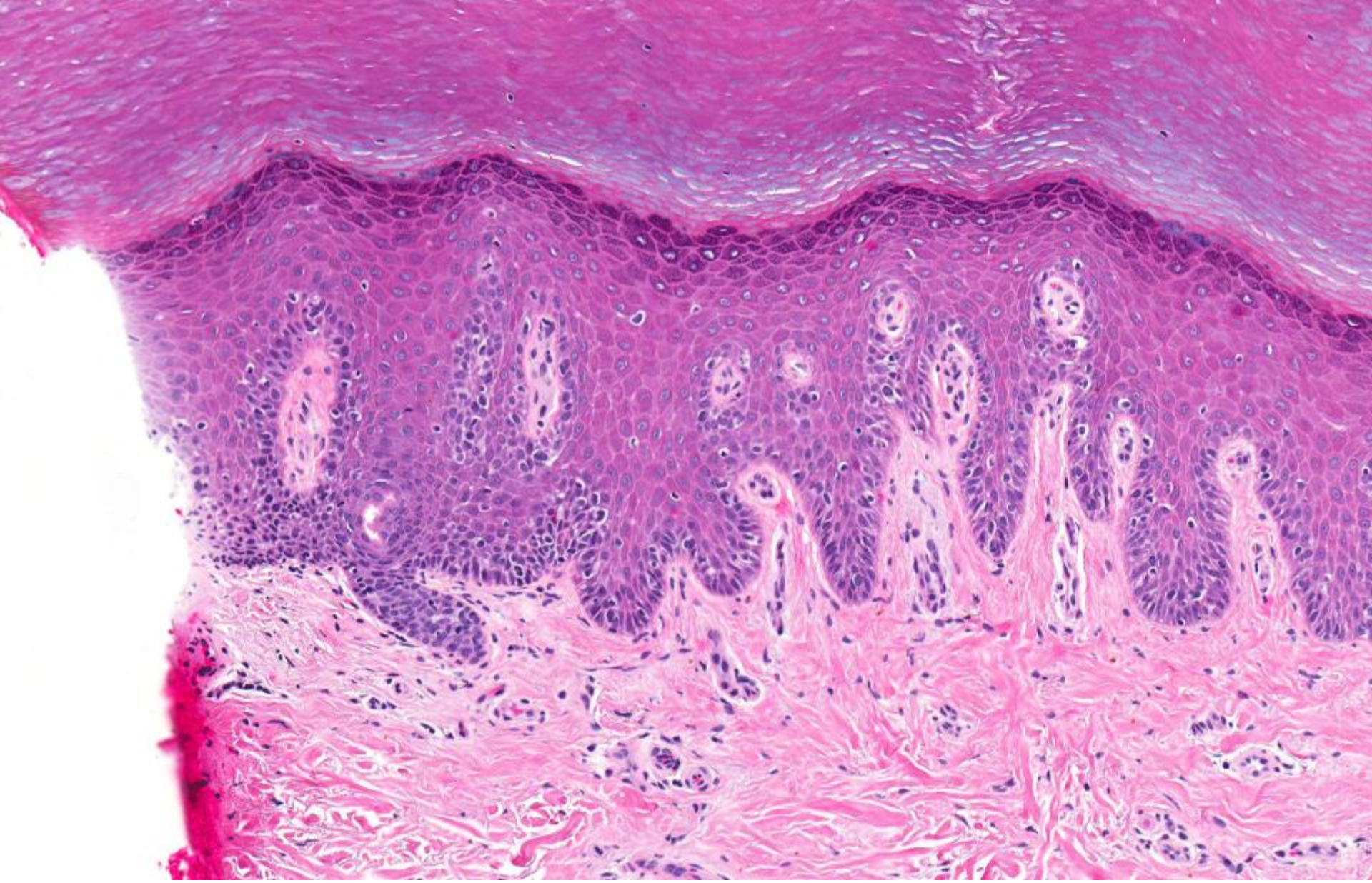
Tumor thickness	Surgical margin*
In situ	0.5-1.0 cm**
≤1.0 mm	1 cm
>1.0 – 2.0 mm	1 – 2 cm
>2.0 mm	2 cm

Excision for MIS

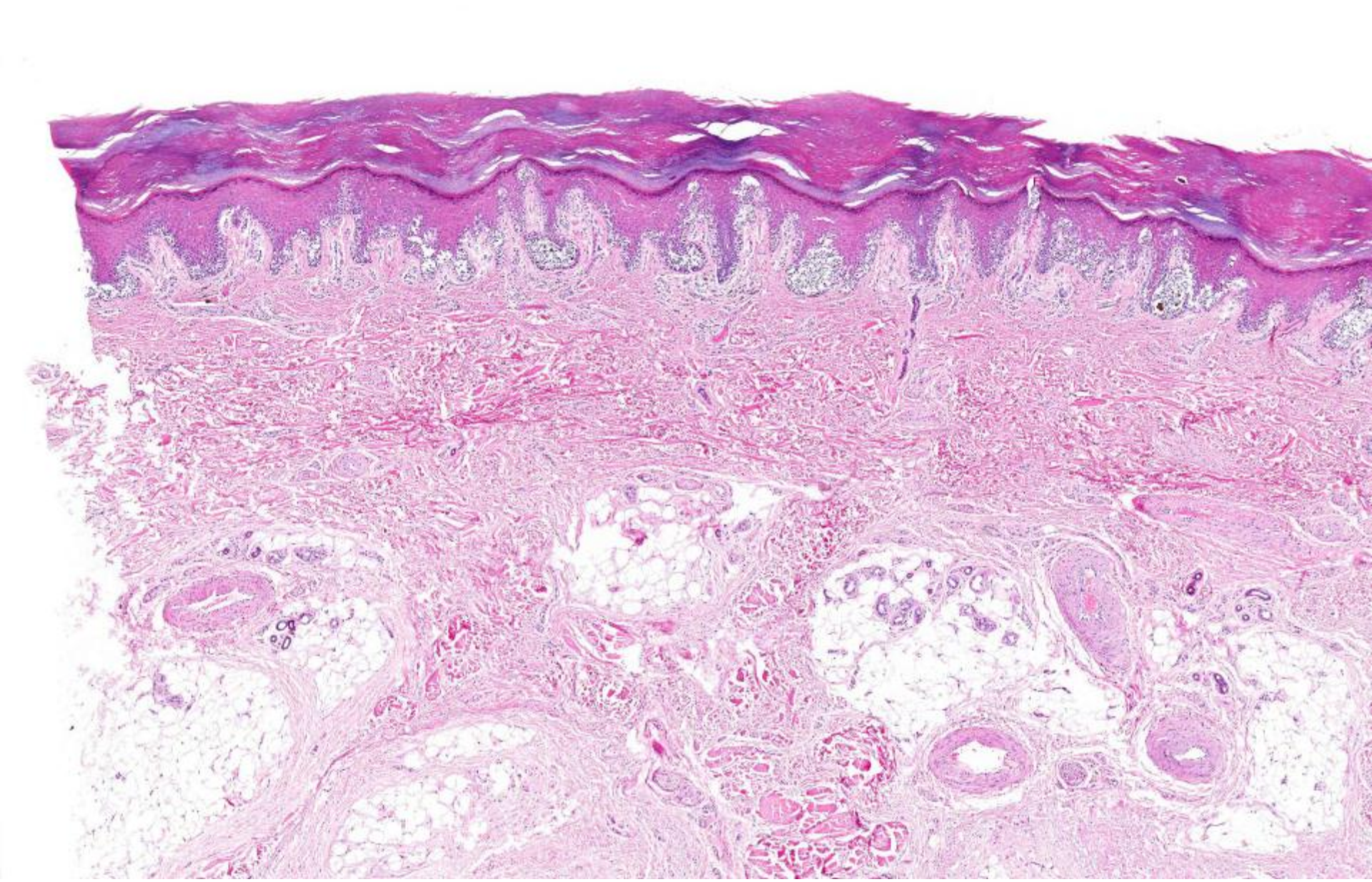
- For MIS, wide excision with 0.5- to 1.0-cm margins is recommended
- LM subtype may require >0.5-cm margins to achieve histologically negative margins because of subclinical extension
- MMS or staged excision with paraffin-embedded permanent sections may be utilized for MIS, LM type on the face, ears, or scalp for tissue sparing excision and exhaustive peripheral margin histologic assessment.
- For MIS, LM type, permanent section analysis of the central MMS debulking specimen is recommended to identify and appropriately stage potential invasive CM. If invasive CM is identified on a MMS section intra-operatively, the tissue should be submitted for formal pathology review.

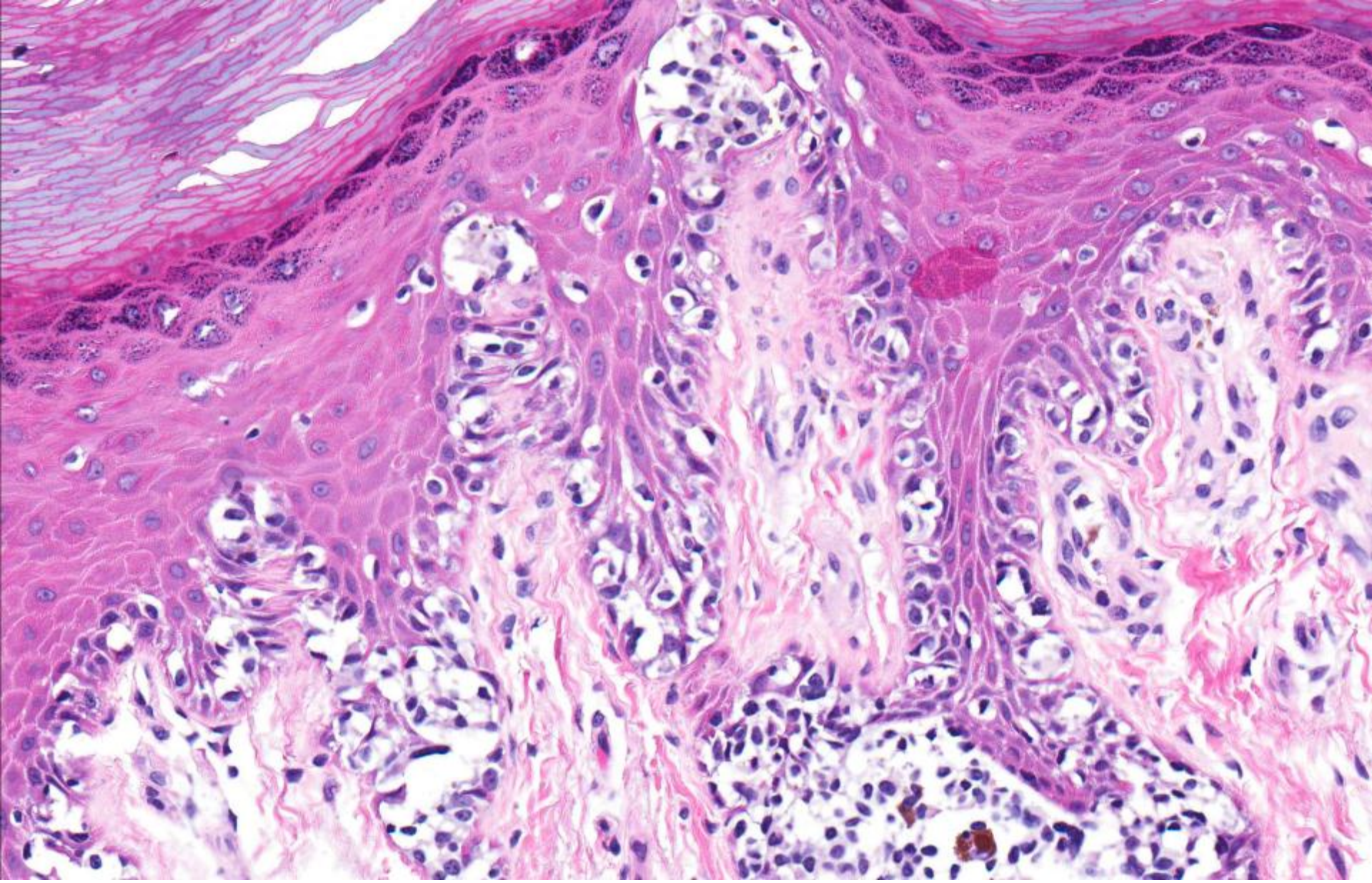
Next Case





2 years Later





Acral Melanoma

Positive margin

Not recognized, no additional treatment

Recurrence at about 2 years – still in situ

Margin assessment is critical

- Positive or negative is sufficient
- May provide a measurement if excision is “close” – e.g. < 1 mm for an invasive melanoma

Structured Reporting Systems

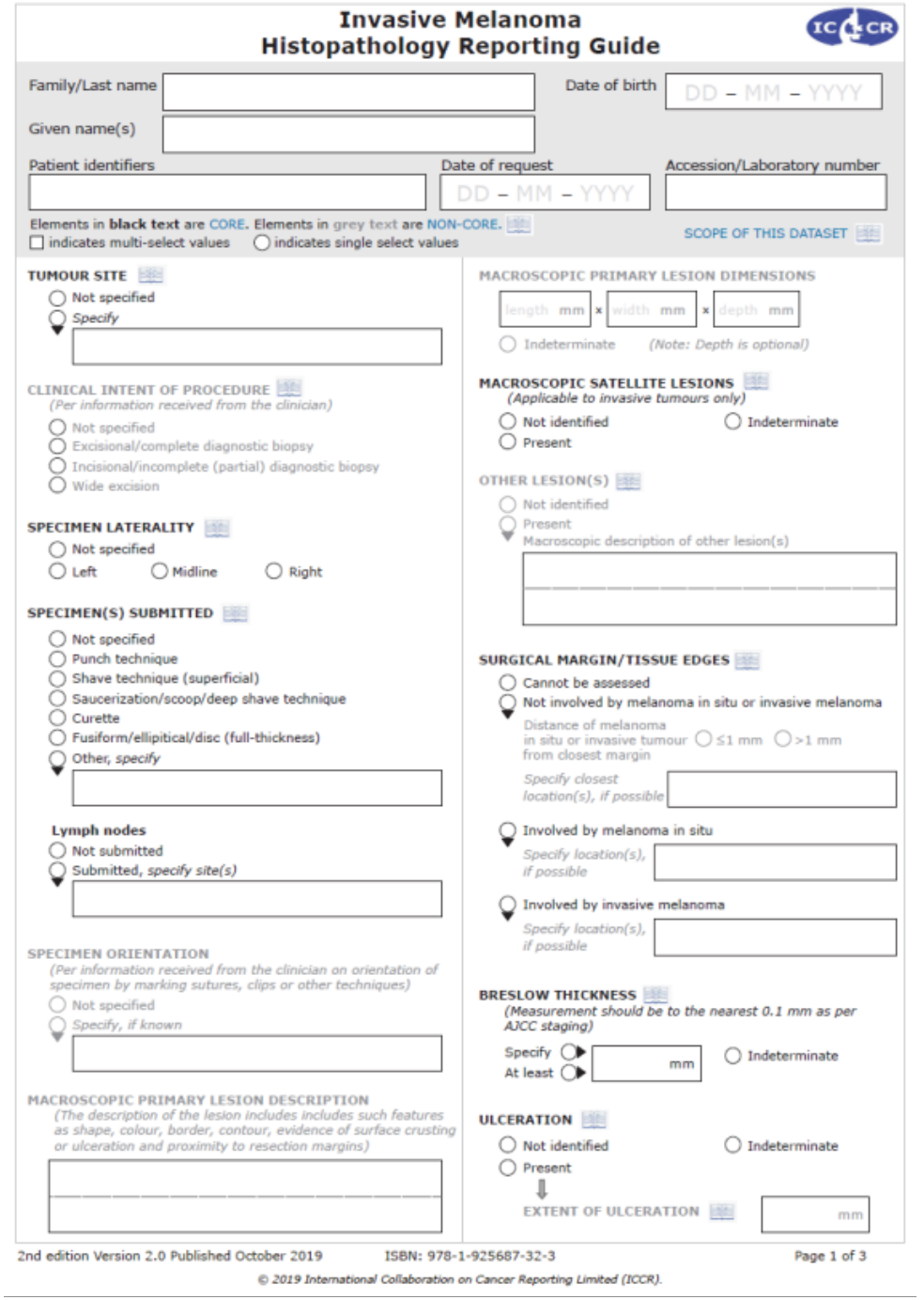
- USCAP
- AAD
- ICCR
- UK – NICE Pathways
- Swiss
- German
- ESMO, others …
- Guidelines placed into structured template to ensure complete reporting
- Required in US for hospital accreditation by Society of Surgical Oncology

Maximum Tumor (Breslow) Thickness (invasive tumor only)
Specify (millimeters): ___ mm or At least (millimeters): ___ mm (explain):
Cannot be determined (explain): _____
Ulceration (required for invasive tumor only) ___ Present ___ Not identified ___ Cannot be determined
Microsatellite(s) (applicable to invasive tumor only) ___ Not identified ___ Present ___ Cannot be determined
Margins (select all that apply)
Peripheral Margins# ___ Uninvolved by invasive melanoma
+ Distance of invasive melanoma from closest peripheral margin (millimeters): ___ mm + Specify location(s): _____
Involved by invasive melanoma + Specify location(s): _____
Uninvolved by melanoma in situ + Distance of melanoma in situ from closest peripheral margin (millimeters): ___ mm
+ Specify location(s): ____
Involved by melanoma in situ + Specify location(s): _____
Cannot be assessed
Deep Margin# ___ Uninvolved by melanoma in situ ___ Uninvolved by invasive melanoma
+ Distance of invasive melanoma from deep margin (millimeters): ____ mm ___ Involved by melanoma in situ ___ Involved by invasive melanoma ___ Cannot be assessed
Mitotic Rate (applicable to invasive tumor only) ___ None identified ___ Specify number /mm2 (# mitoses/mm2): _____ ___ Cannot be determined

ICCR Structured Report

Scolyer RA, Balamurgan T, Busam K, Elder D, Evans A, Gershenwald J, Frishberg DP, McMenamin M, Prieto VG, Shiau C, Swetter S, van den Oord J, 2019.

- CORE 1
- Tumour site
- Specimen laterality
- Specimens submitted
- Lymph nodes
- Macroscopic satellites
- Surgical margin/edges
- Breslow thickness
- Ulceration



Invasive Melanoma
Histopathology Reporting Guide

Family/Last name | Date of birth DD – MM – YYYY
Given name(s)
Patient identifiers | Date of request DD – MM – YYYY | Accession/Laboratory number

Elements in **black text** are CORE. Elements in grey text are NON-CORE.
☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

TUMOUR SITE
◯ Not specified
◯ *Specify*

CLINICAL INTENT OF PROCEDURE
(Per information received from the clinician)
◯ Not specified
◯ Excisional/complete diagnostic biopsy
◯ Incisional/incomplete (partial) diagnostic biopsy
◯ Wide excision

SPECIMEN LATERALITY
◯ Not specified
◯ Left ◯ Midline ◯ Right

SPECIMEN(S) SUBMITTED
◯ Not specified
◯ Punch technique
◯ Shave technique (superficial)
◯ Saucerization/scoop/deep shave technique
◯ Curette
◯ Fusiform/elliptical/disc (full-thickness)
◯ Other, *specify*

Lymph nodes
◯ Not submitted
◯ Submitted, *specify site(s)*

SPECIMEN ORIENTATION
(Per information received from the clinician on orientation of specimen by marking sutures, clips or other techniques)
◯ Not specified
◯ *Specify, if known*

MACROSCOPIC PRIMARY LESION DESCRIPTION
(The description of the lesion includes includes such features as shape, colour, border, contour, evidence of surface crusting or ulceration and proximity to resection margins)

MACROSCOPIC PRIMARY LESION DIMENSIONS
length mm × width mm × depth mm
◯ Indeterminate *(Note: Depth is optional)*

MACROSCOPIC SATELLITE LESIONS
(Applicable to invasive tumours only)
◯ Not identified ◯ Indeterminate
◯ Present

OTHER LESION(S)
◯ Not identified
◯ Present
Macroscopic description of other lesion(s)

SURGICAL MARGIN/TISSUE EDGES
◯ Cannot be assessed
◯ Not involved by melanoma in situ or invasive melanoma
Distance of melanoma in situ or invasive tumour ◯ ≤1 mm ◯ >1 mm from closest margin
Specify closest location(s), if possible
◯ Involved by melanoma in situ
Specify location(s), if possible
◯ Involved by invasive melanoma
Specify location(s), if possible

BRESLOW THICKNESS
(Measurement should be to the nearest 0.1 mm as per AJCC staging)
Specify ◯ / At least ◯ mm ◯ Indeterminate

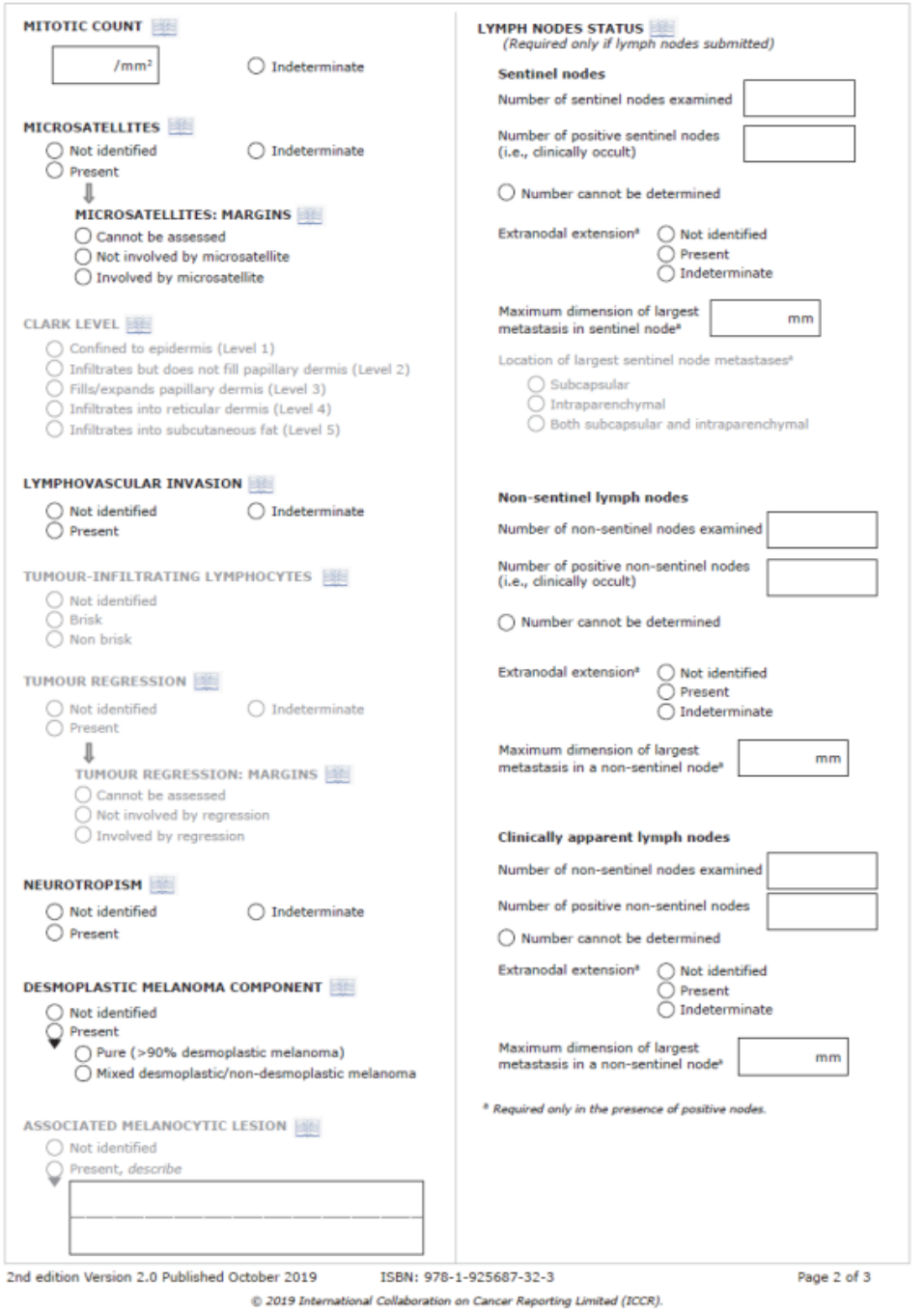
ULCERATION
◯ Not identified ◯ Indeterminate
◯ Present
⇓
EXTENT OF ULCERATION mm

2nd edition Version 2.0 Published October 2019 ISBN: 978-1-925687-32-3

ICCR Structured Report

Scolyer RA, Balamurgan T, Busam K, Elder D, Evans A, Gershenwald J, Frishberg DP, McMenamin M, Prieto VG, Shiau C, Swetter S, van den Oord J, 2019.

- CORE 2
- Mitotic count
- Microsatellites
  - Satellite margins
- LVI
- Neurotropism
- Desmoplastic MM
- LN Status



MITOTIC COUNT
/mm²
Indeterminate

MICROSATELLITES
Not identified
Indeterminate
Present
MICROSATELLITES: MARGINS
Cannot be assessed
Not involved by microsatellite
Involved by microsatellite

CLARK LEVEL
Confined to epidermis (Level 1)
Infiltrates but does not fill papillary dermis (Level 2)
Fills/expands papillary dermis (Level 3)
Infiltrates into reticular dermis (Level 4)
Infiltrates into subcutaneous fat (Level 5)

LYMPHOVASCULAR INVASION
Not identified
Indeterminate
Present

TUMOUR-INFILTRATING LYMPHOCYTES
Not identified
Brisk
Non brisk

TUMOUR REGRESSION
Not identified
Indeterminate
Present
TUMOUR REGRESSION: MARGINS
Cannot be assessed
Not involved by regression
Involved by regression

NEUROTROPISM
Not identified
Indeterminate
Present

DESMOPLASTIC MELANOMA COMPONENT
Not identified
Present
Pure (>90% desmoplastic melanoma)
Mixed desmoplastic/non-desmoplastic melanoma

ASSOCIATED MELANOCYTIC LESION
Not identified
Present, *describe*

LYMPH NODES STATUS
(Required only if lymph nodes submitted)

Sentinel nodes
Number of sentinel nodes examined
Number of positive sentinel nodes (i.e., clinically occult)
Number cannot be determined
Extranodal extension* Not identified / Present / Indeterminate
Maximum dimension of largest metastasis in sentinel node* mm
Location of largest sentinel node metastases*
Subcapsular
Intraparenchymal
Both subcapsular and intraparenchymal

Non-sentinel lymph nodes
Number of non-sentinel nodes examined
Number of positive non-sentinel nodes (i.e., clinically occult)
Number cannot be determined
Extranodal extension* Not identified / Present / Indeterminate
Maximum dimension of largest metastasis in a non-sentinel node* mm

Clinically apparent lymph nodes
Number of non-sentinel nodes examined
Number of positive non-sentinel nodes
Number cannot be determined
Extranodal extension* Not identified / Present / Indeterminate
Maximum dimension of largest metastasis in a non-sentinel node* mm

** Required only in the presence of positive nodes.*

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Sentinel Node Biopsy Recommendations

- Careful discussion of the risks and benefits of the procedure involving surgical oncology input is recommended for all SLNB-eligible patients.
- SLNB is not recommended for patients with MIS or for most T1a melanoma (AJCC 8e).
- SLNB should be discussed and offered in appropriate patients with CM ≥1 mm thickness (T2a and higher), including T4 CM.

Sentinel Node Biopsy Recommendations

- In patients with T1b CM (0.8-1.0 mm or <0.8 mm with ulceration), SLNB should be discussed and considered, though rates of SLN positivity are still relatively low.
- SLNB may be considered for T1a CM (<0.8 mm) if other adverse features are present, including
  - young age, presence of lymphovascular invasion, positive deep biopsy margin (if close to 0.8 mm), or high mitotic rate (not yet defined) – or a combination of these factors.

Completion Dissection or Observation for Sentinel-Node Metastasis in Melanoma

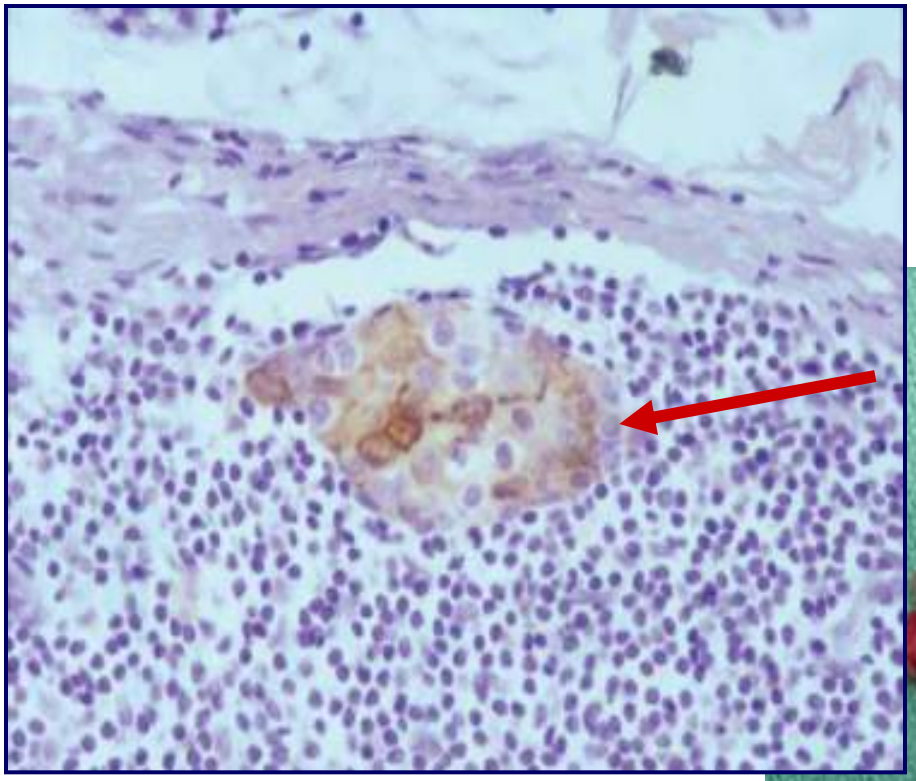
- Faries et al, N Engl J Med, 2017

- BACKGROUND—The value of completion lymph-node dissection for patients with sentinel-node metastases is not clear.
- METHODS—In an international trial, we randomly assigned patients with sentinel-node metastases to immediate completion lymph-node dissection (dissection group) or nodal observation with ultrasonography (observation group).
- CONCLUSIONS—Immediate completion lymph-node dissection increased the rate of regional disease control and provided prognostic information but did not increase melanoma-specific survival among patients with melanoma and sentinel-node metastases.

Completion Dissection

- Completion node dissection is no longer standard of care - interdisciplinary collaboration involving surgical and medical oncologists is recommended for discussion of possible completion lymph node dissection vs regional nodal ultrasound surveillance in the event of a positive SLNB.
- Rational for Completion Dissection
  - Staging
  - Incidence of non-SLN involvement underestimated based on routine pathologic techniques
  - Effectively avoids the appearance of palpable nodes

Microscopic Metastases Will (Likely) Become Macroscopic!



Reasons *Against* Routine Use of Completion Dissections: Cost and *Morbidity*

- Unnecessary costs – incidence of non-SLN is low in most subsets
- Clinical relevance of non-SLN disease?
- Unnecessary surgical morbidity
  - Wound infection/dehiscence
  - Nerve injury
  - Pain
  - Joint dysfunction
  - *Lymphedema*
- Neck dissection: well tolerated
- Axillary dissection: lymphedema rate lower than predicted by breast cancer
- Inguinal dissection: high rate of wound infection, dehiscence, lymphedema, nerve paraesthesia

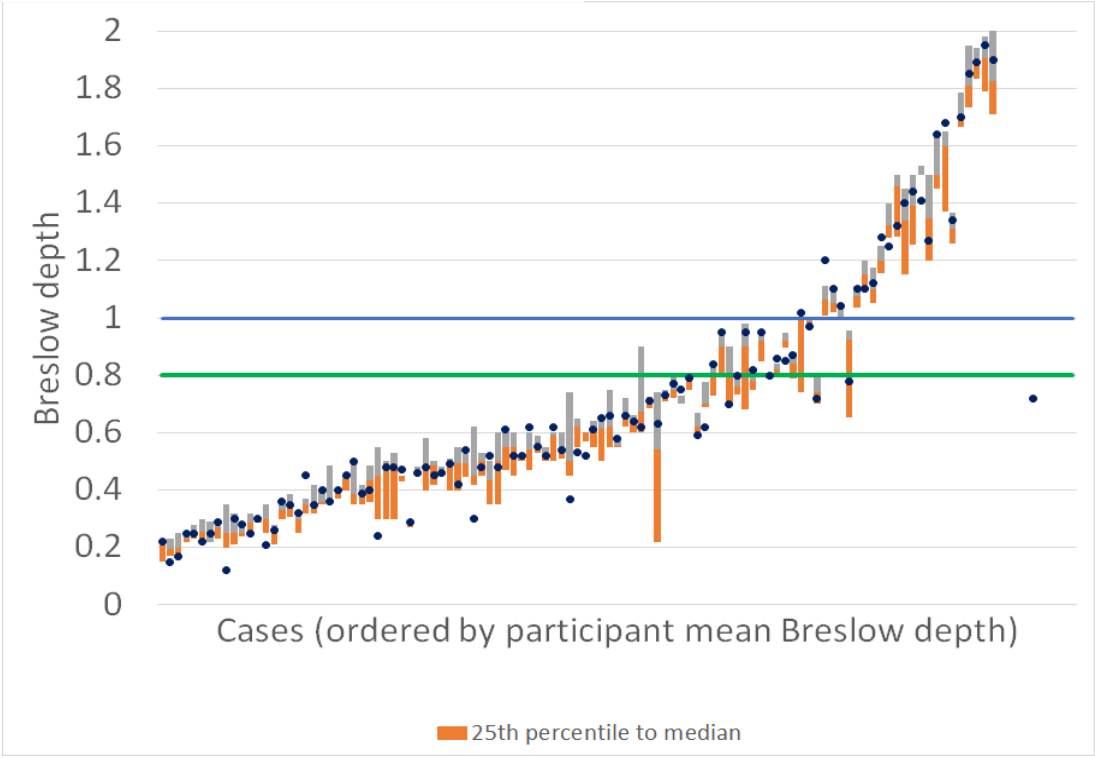
Suggested surveillance intervals and follow-up tests for CM

CM Stage	Follow-up interval and duration	Exam	Radiologic Tests
Stage 0 MIS	at least every 6-12 months for 1-2 years; annually thereafter	• Physical exam with emphasis on assessment for local recurrence, particularly for LM and ALM and mucosal subtypes • Full skin check to ascertain for new primary CM	None
Stage IA-IIA	every 6 to 12 months for 2-5 years; at least annually thereafter	• As for Stage 0 • Comprehensive history (review of systems) • Physical exam with specific emphasis on the skin and regional LNs	None
Stage IIB and higher	Every 3-6 months for the for 2 years; at least every 6 months for years 3-5; at least annually thereafter	• As for Stage 0 • Comprehensive history (review of systems) • Physical exam with specific emphasis on the skin and regional LNs	May be performed for up to 3-5 years

Influence of variability in assessment of Breslow thickness, mitotic rate and ulceration among US pathologists interpreting invasive melanoma, for the purpose of AJCC staging

Laura Taylor[1] | Kyle Hood[2] | Lisa Reisch[3] | Joann Elmore[4] | Michael Piepkorn[5,6] | Raymond Barnhill[7] | Stevan Knezevich[8] | Andrea Radick[3] | David Elder[9]

- J Cutan Pathol, 2017
- M-Path study demonstrated variation in Breslow depth among pathologists
- Agreement was improved using AJCC VIIIe criteria for measurement (i.e. rounding)
- Variability of assignment of stage was increased (more cases have ranges crossing the 0.8 than the 1.0 mm threshold)



The orange bar extends from the 25th percentile to the median, while the gray bar extends from the median up to the 75th percentile. The blue dots represent the medians of the Breslow depths reported by the members of the expert panel for each case. The blue line represents the AJCC 7th Edition T1/T2 cutoff at 1.00. The green line represents the AJCC 8th Edition T1/T2 cutoff at 0.8 mm For ease of interpretation, the figure is truncated at a Breslow depth of 2.00.

Pubmed Search: “MELANOMA” “MANAGEMENT” “GUIDELINES” selected from 120 OF 480 2017-2019

1: Fayne RA, Macedo FI, Rodgers SE, Möller MG. Evolving management of positive regional lymph nodes in melanoma: Past, present and future directions. Oncol Rev. 2019 Nov 28;13(2):433.

2: Grossman D, Kim CC, Hartman RI, Berry E, Nelson KC, Okwundu N, Curiel-Lewandrowski C, Leachman SA, Swetter SM. Prognostic gene expression profiling in melanoma: necessary steps to incorporate into clinical practice. Melanoma Manag. 2019 Dec 17;6(4).

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4: Robinson M, Primiero C, Guitera P, Hong A, Scolyer RA, Stretch JR, Strutton G, Thompson JF, Soyer HP. Evidence-Based Clinical Practice Guidelines for the Management of Patients with Lentigo Maligna. Dermatology. 2019 Oct 22:1-6. PMID: 31639788.

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6: Guillot B, Dupuy A, Pracht M, Jeudy G, Hindie E, Desmedt E, Jouary T, Leccia MT. [Reprint of: New guidelines for stage III melanoma (the French Cutaneous Oncology Group)]. Bull Cancer. 2019 Jun;106(6):560-573. PMID: 31122657.

7: Guillot B, Dupuy A, Pracht M, Jeudy G, Hindie E, Desmedt E, Jouary T, Leccia MT. [New guidelines for stage III melanoma (the French Cutaneous Oncology Group)]. Ann Dermatol Venereol. 2019 Mar;146(3):204-214. French. PMID: 30833037.

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9: Keohane SG, Proby CM, Newlands C, Motley RJ, Nasr I, Mohd Mustapa MF; British Association of Dermatologists (Squamous and Basal Cell Carcinoma Guideline Development Groups), Slater DN; Royal College of Pathologists (Skin Cancer Lead). The new 8th edition of TNM staging and its implications for skin cancer: a review by the British Association of Dermatologists and the Royal College of Pathologists, U.K. Br J Dermatol. 2018 Oct;179(4):824-828. PMID: 29923189.

10: Ow TJ, Grethlein SJ, Schmalbach CE; Education Committee of the American Head and Neck Society (AHNS). Do you know your guidelines? Diagnosis and management of cutaneous head and neck melanoma. Head Neck. 2018 May;40(5):875-885. PMID: 29485688.

11: Sladden MJ, Nieweg OE, Howle J, Coventry BJ, Thompson JF. Updated evidence-based clinical practice guidelines for the diagnosis and management of melanoma: definitive excision margins for primary cutaneous melanoma. Med J Aust. 2018 Feb 19;208(3):137-142. PMID: 29438650.

12: Wong SL, Faries MB, Kennedy EB, Agarwala SS, Akhurst TJ, Ariyan C, Balch CM, Berman BS, Cochran A, Delman KA, Gorman M, Kirkwood JM, Moncrieff MD, Zager JS, Lyman GH. Sentinel Lymph Node Biopsy and Management of Regional Lymph Nodes in Melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Clinical Practice Guideline Update. Ann Surg Oncol. 2018 Feb;25(2):356-377. PubMed PMID: 29236202.

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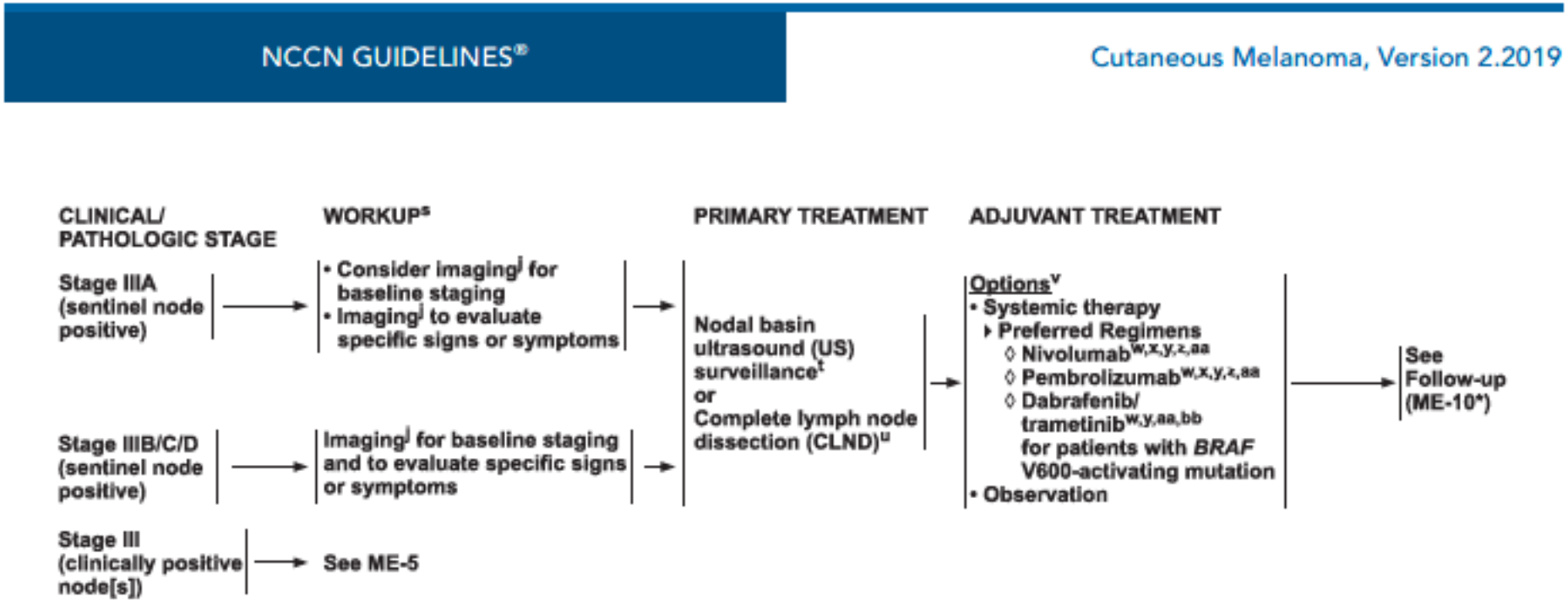
NCCN Guidelines



Mostly for Advanced Disease

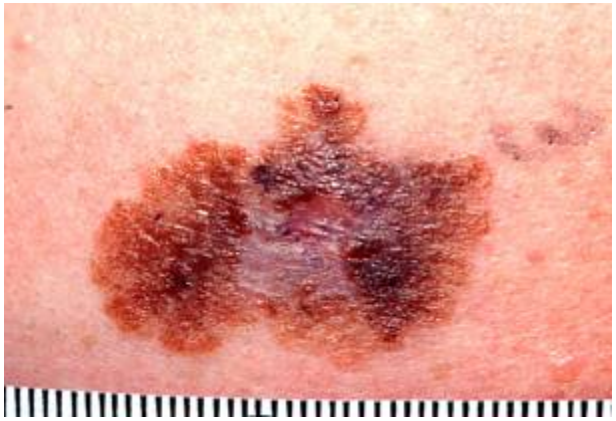
Gross Pathology of Tumor Progression Compartments in Melanoma

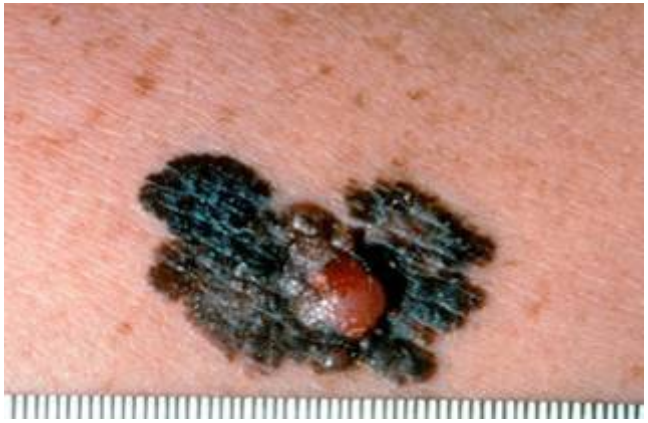
Radial Growth Phase (RGP)

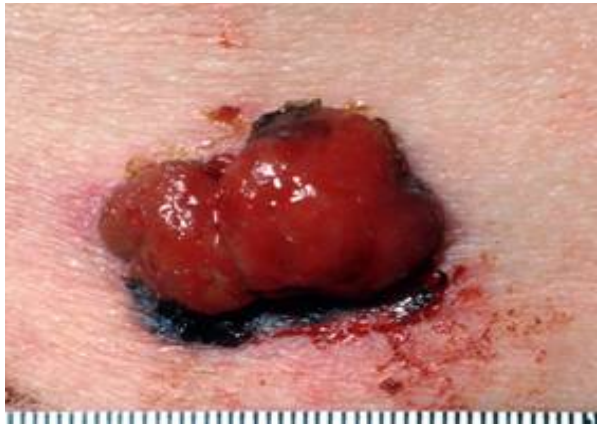
- Flat, thin, clinically indolent
- Nontumorigenic, nonmitogenic
- Capacity for local recurrence, continued progression

Vertical Growth Phase (VGP)

- With or without prior RGP
- Raised, progressively thicker
- Tumorigenic and/or mitogenic
- Capacity for metastasis







Essential Patient and Gross Pathology Information

- Specimen identification and date of procedure
  - Name, age (birth date), MRN, etc
- Anatomic site of tumor
  - Typically provided by surgeon – note that descriptions can be confusing e.g. “back”, “shoulder”, “scapula” all could be the same site
- Specimen Type
  - Incisional/excisional. Punch, Shave (superficial or deep)
- Description of Lesion
  - Size, shape, color, blood/exudate

Essential Microscopic Information

- Diagnosis of primary melanoma
- Size of specimen
- Breslow thickness
- Ulceration: presence or absence
- Dermal mitotic rate, “hotspot” method
- Pathology margin:
  - Negative or positive?
  - Margin width <1 mm (some other number?)
  - Not standard of care to measure margin widths in definitive excisions
- Satellites: present or absent

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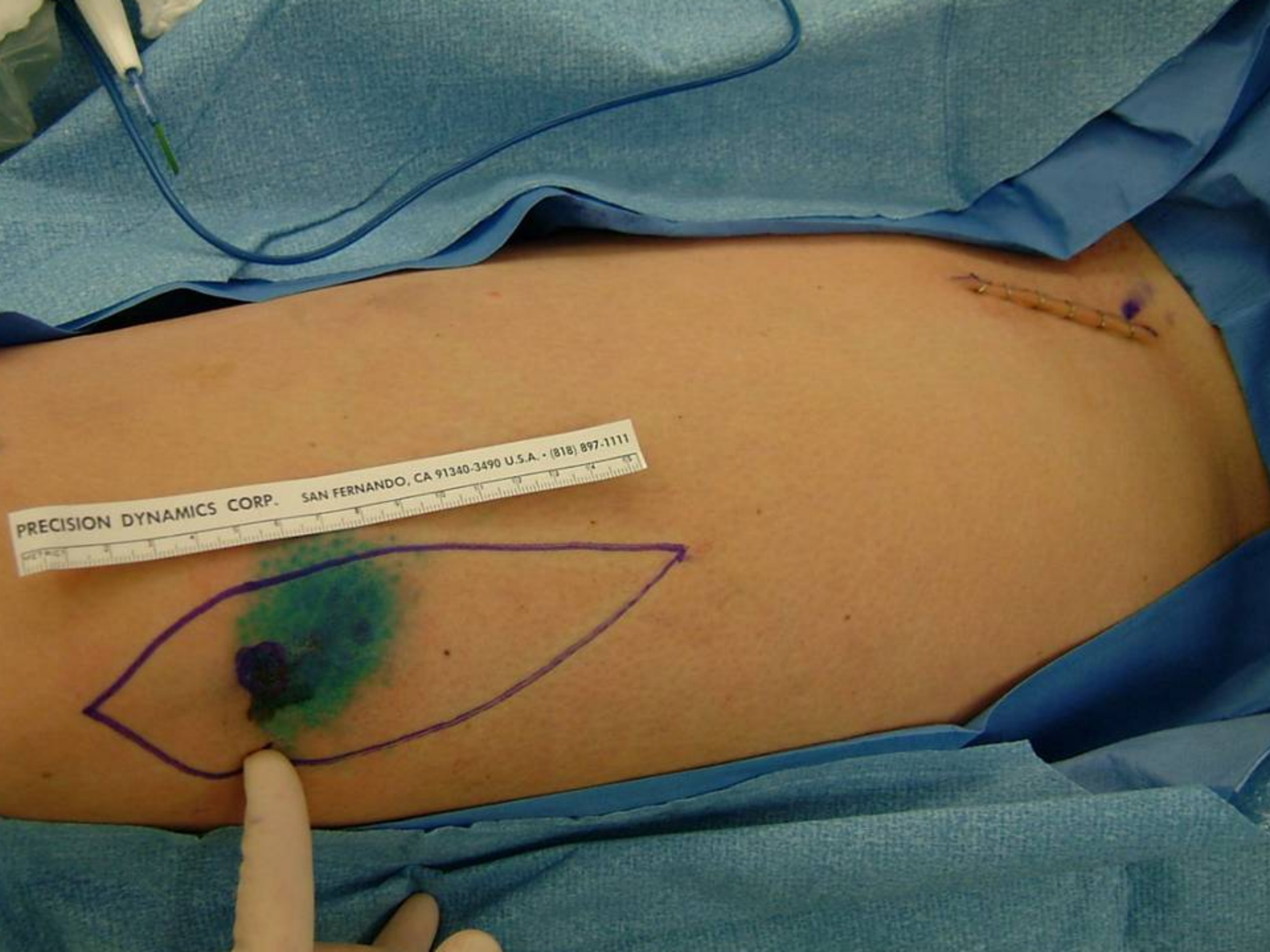
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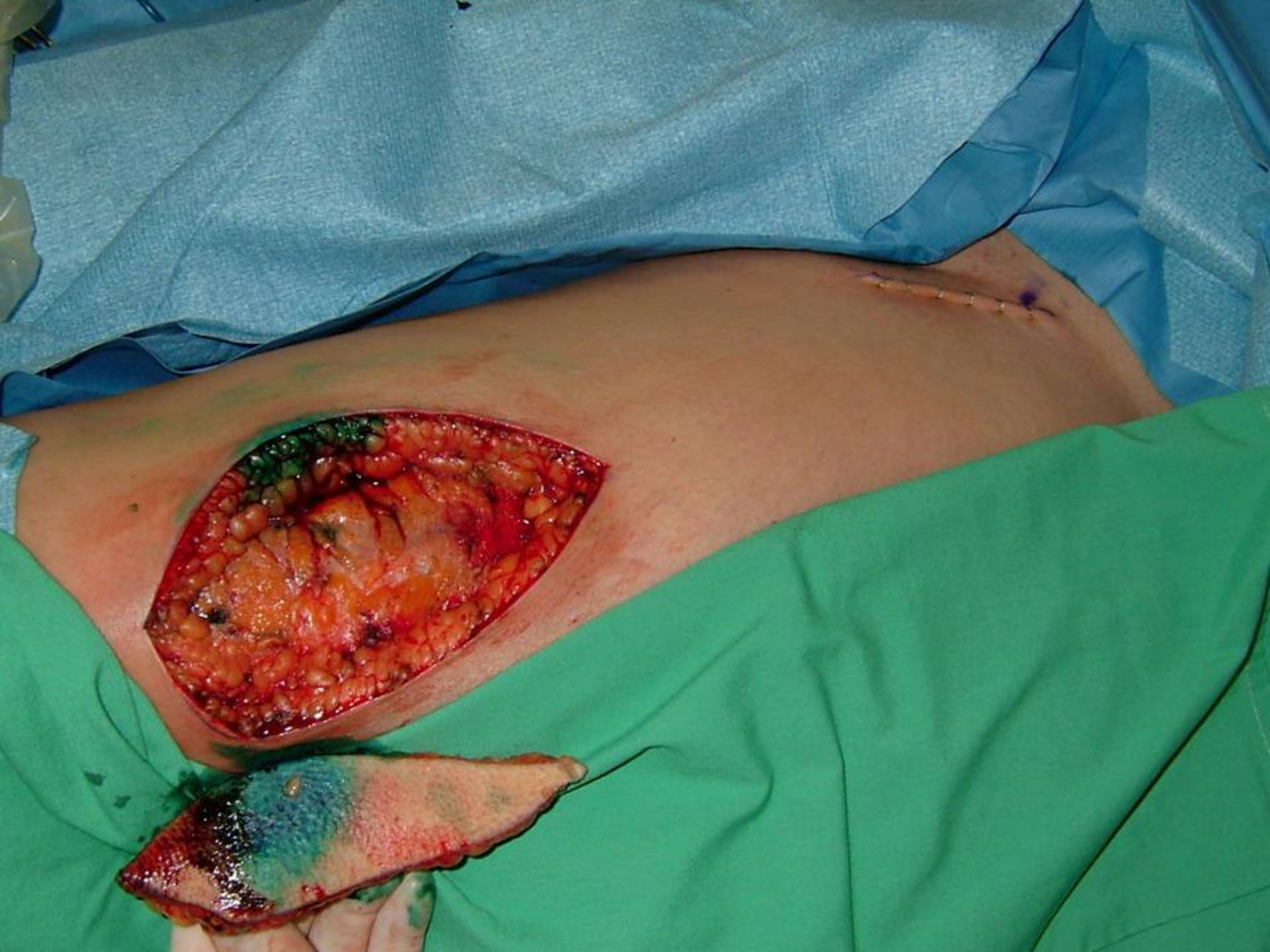
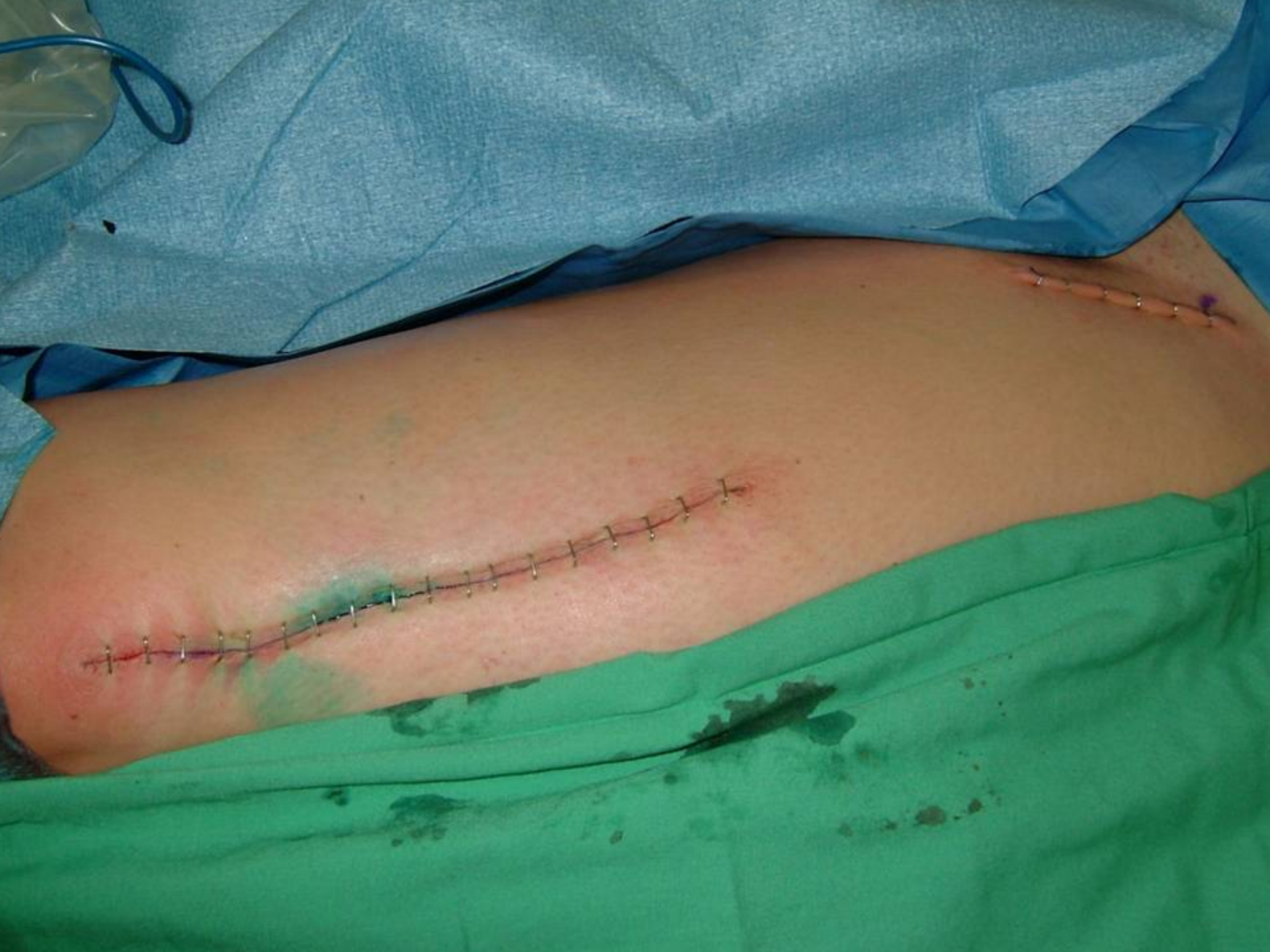
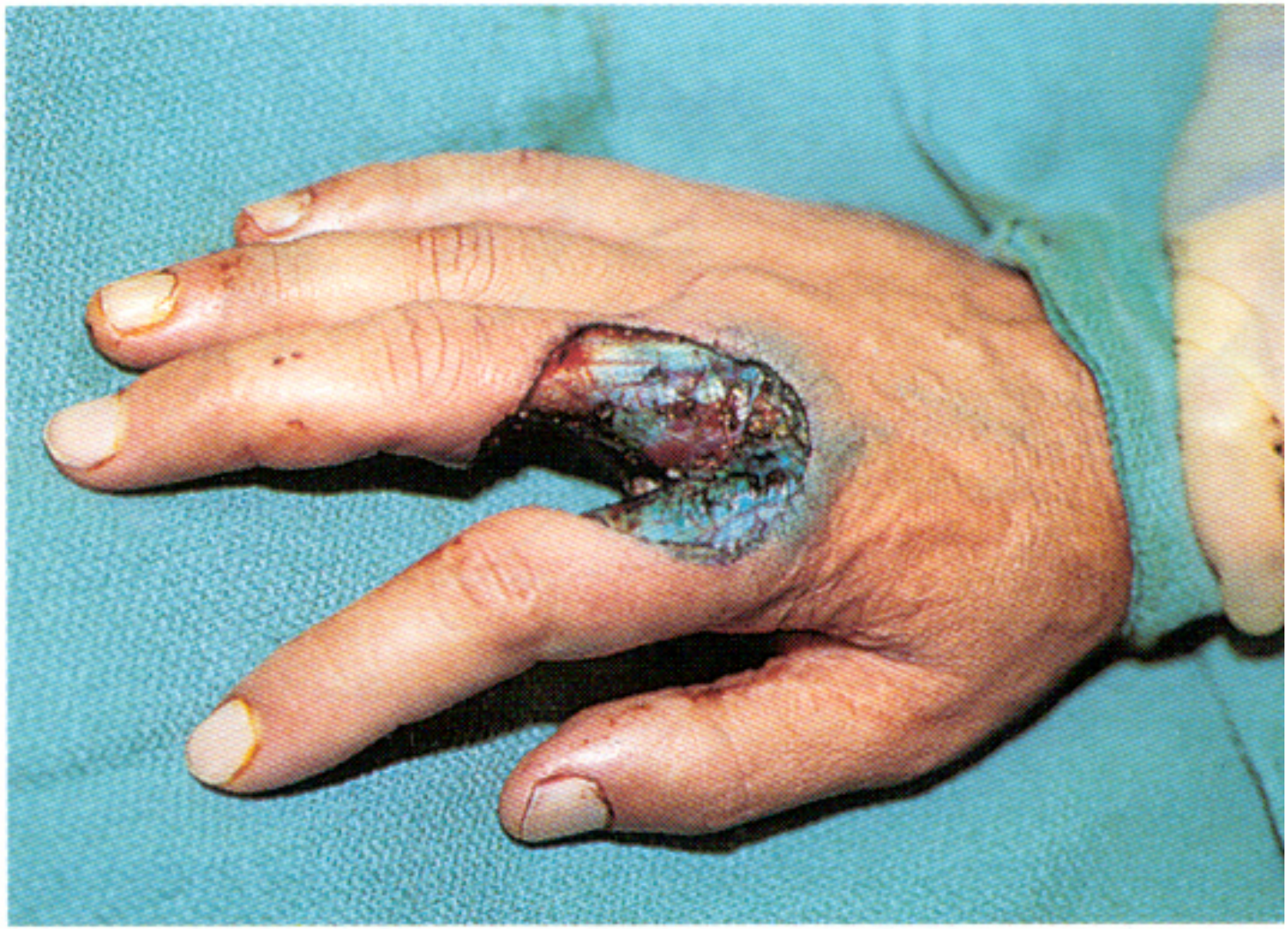
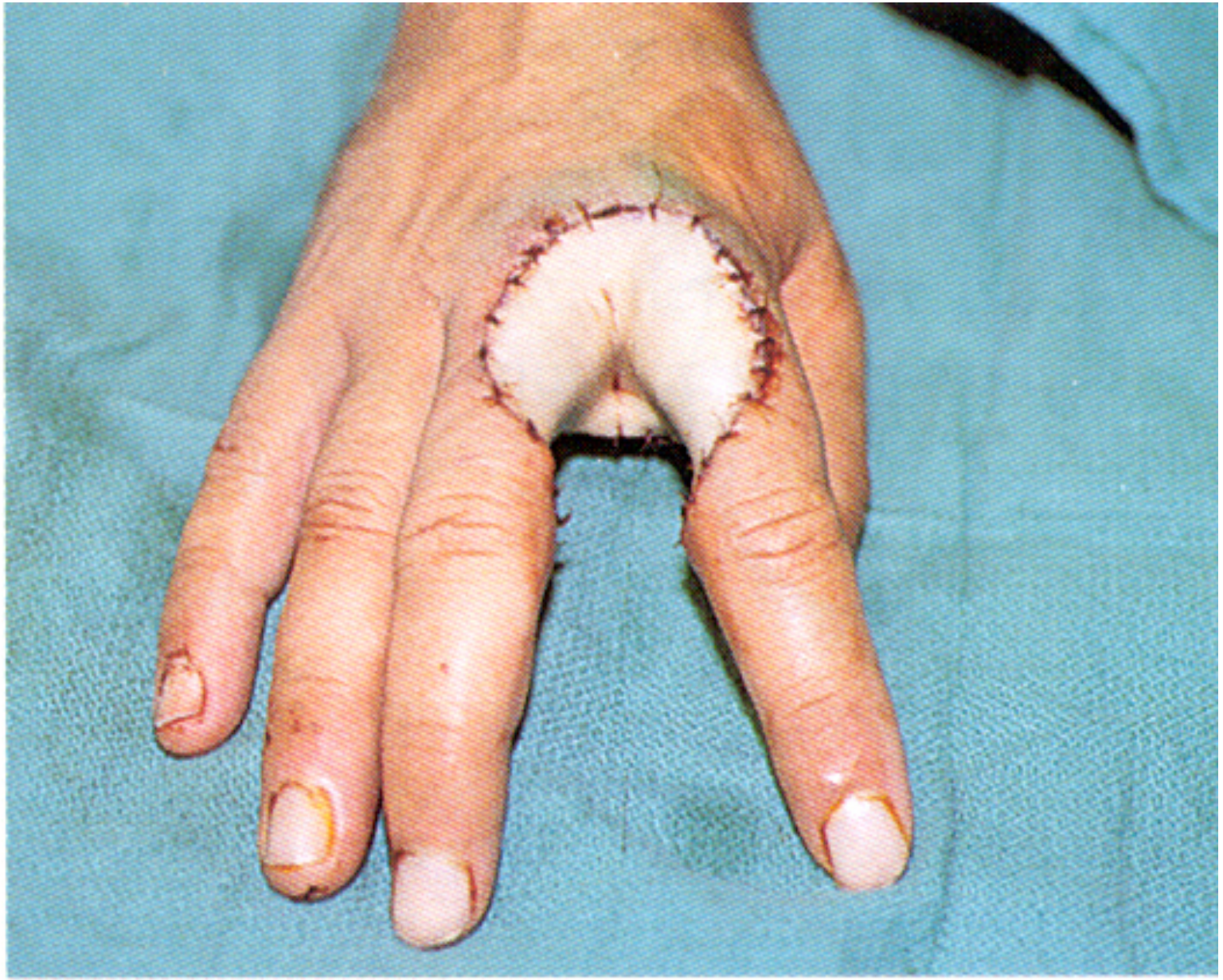
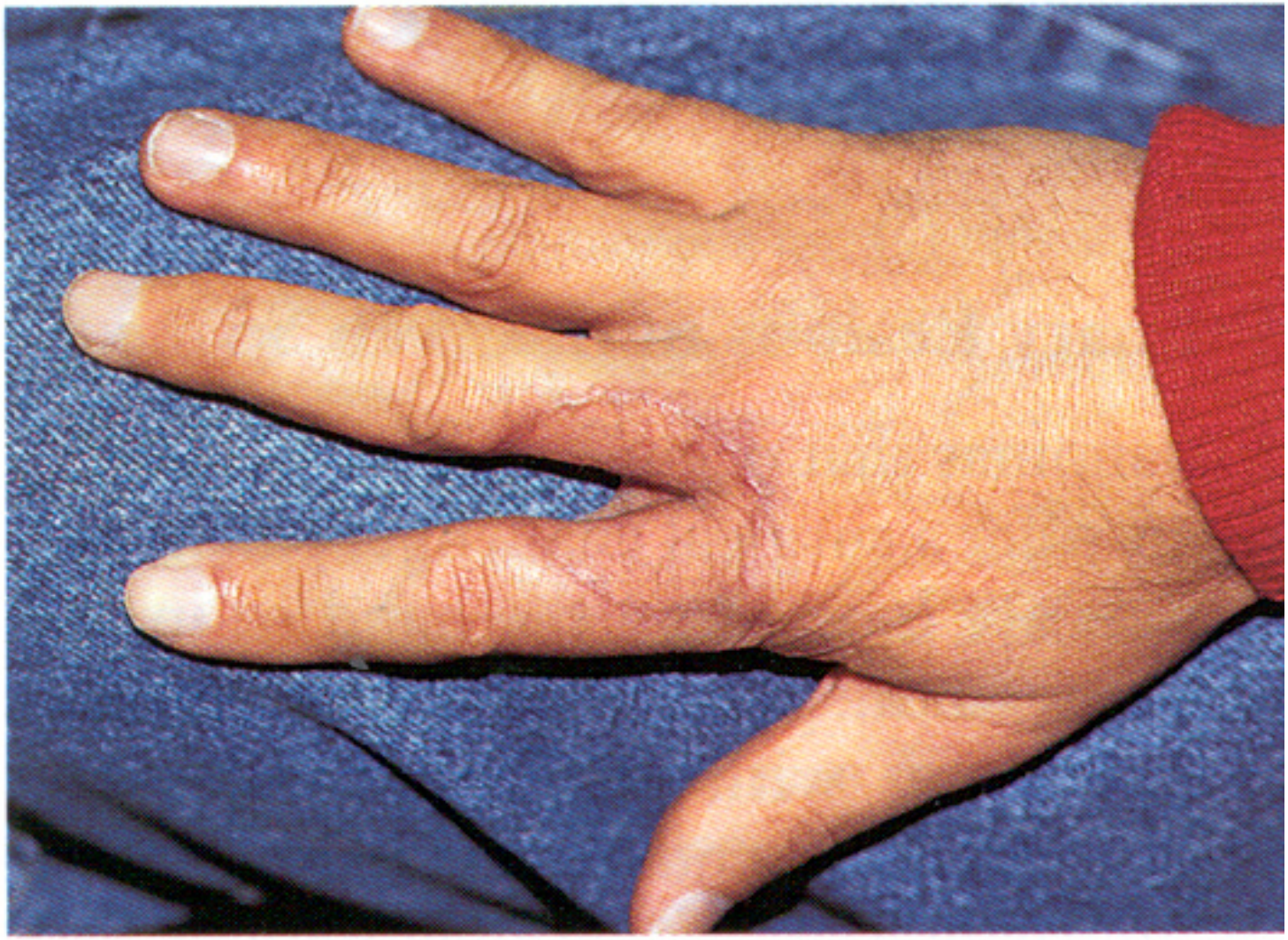






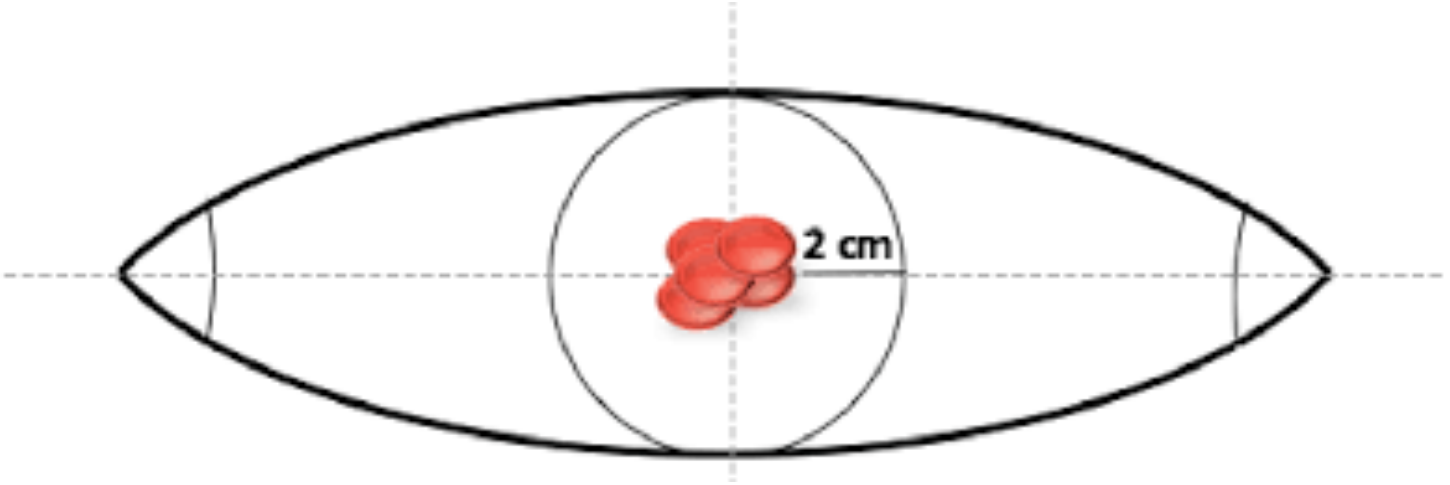


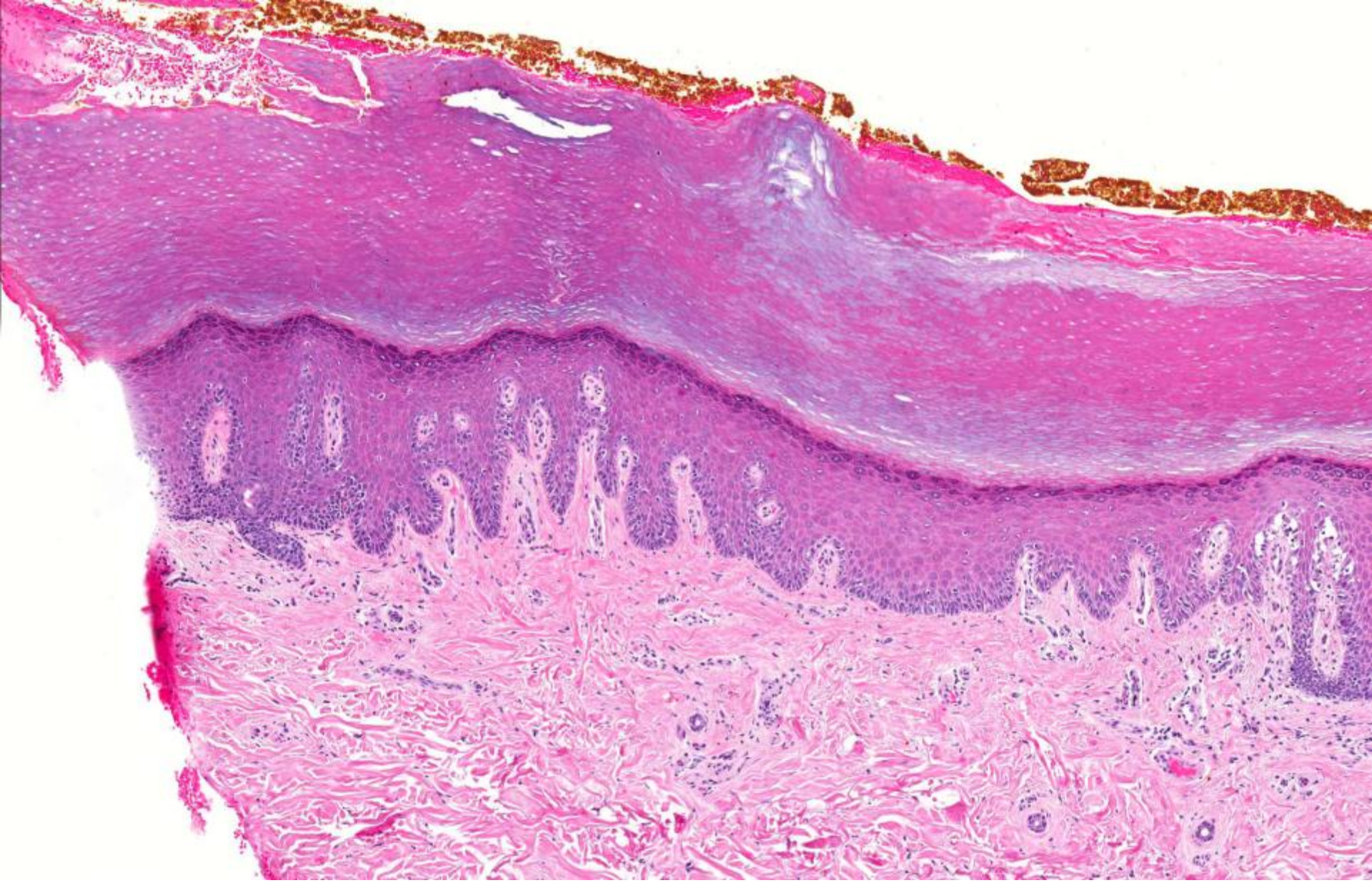


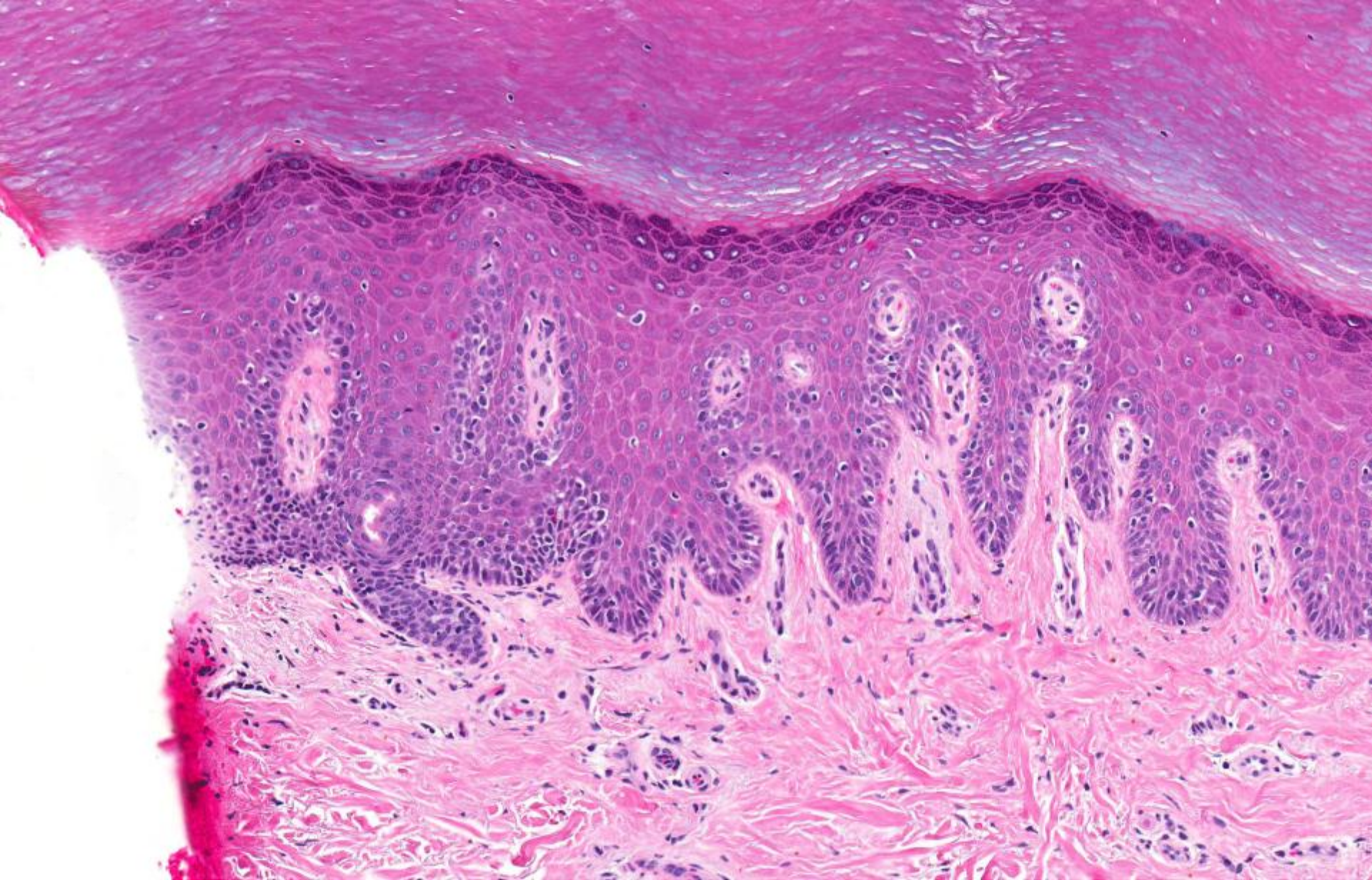
Wide local excision

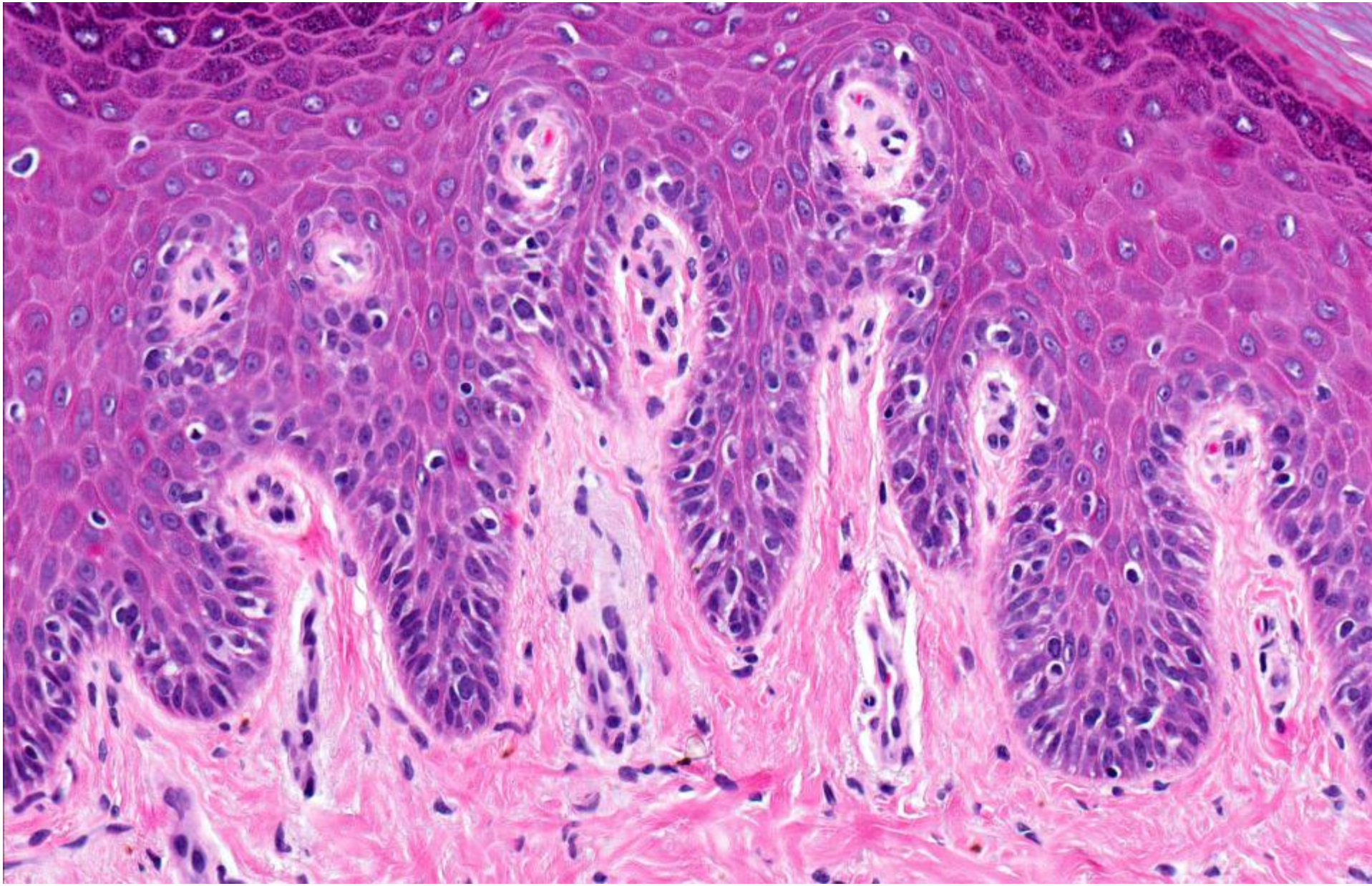
- Final scar may be 3x the width of the re-excision
- Cassileth BR: “Patients’ perceptions of the cosmetic impact of melanoma resection”
  - Patients were more accepting of the impact of a long scar than of a skin graft

Cassileth BR, Lusk EJ, Tenaglia AN. Patients' perceptions of the cosmetic impact of melanoma resection. Plast Reconstr Surg. 1983 Jan;71(1):73-5









Your diagnosis

Nevus?

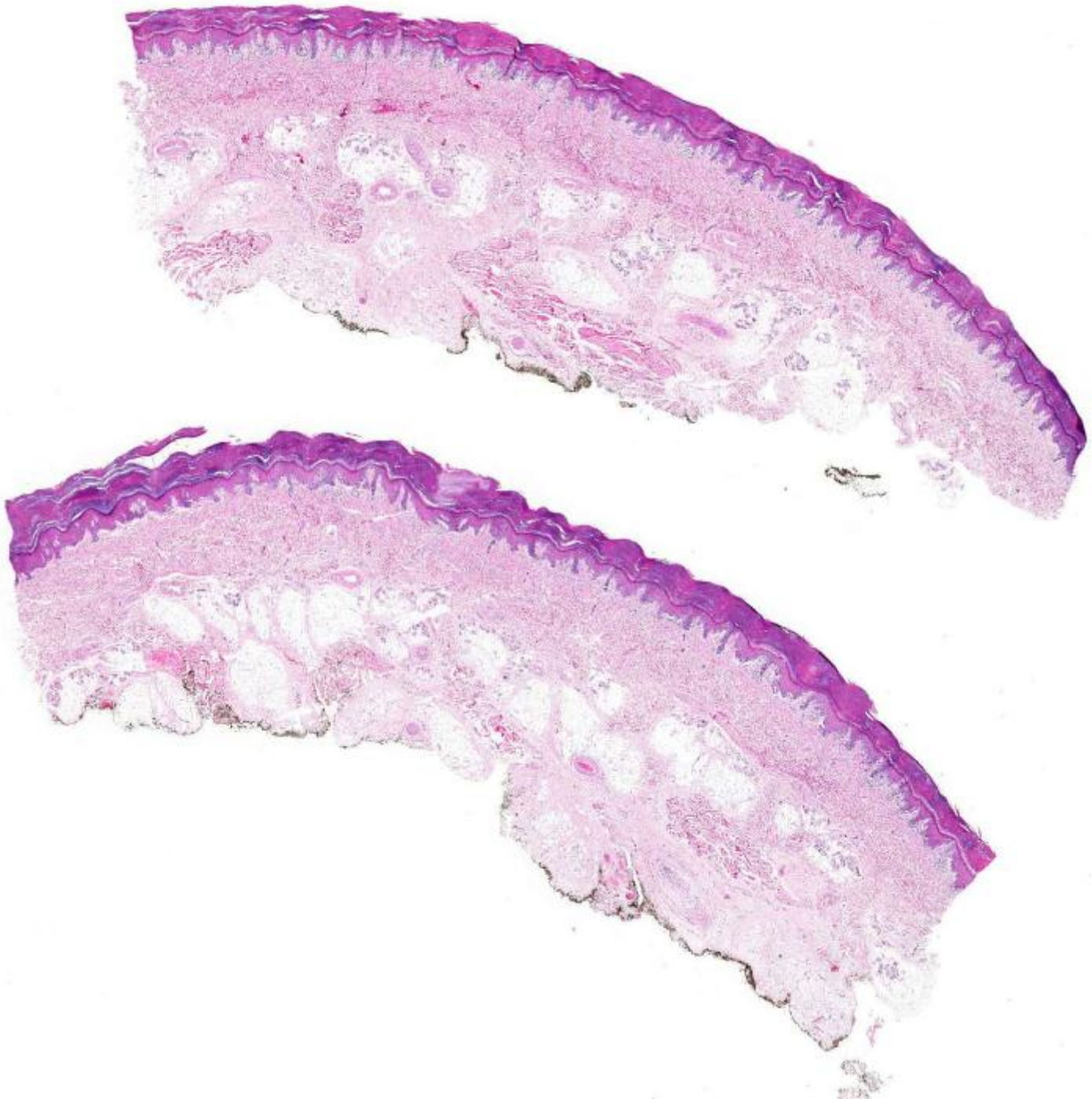
Melanoma?

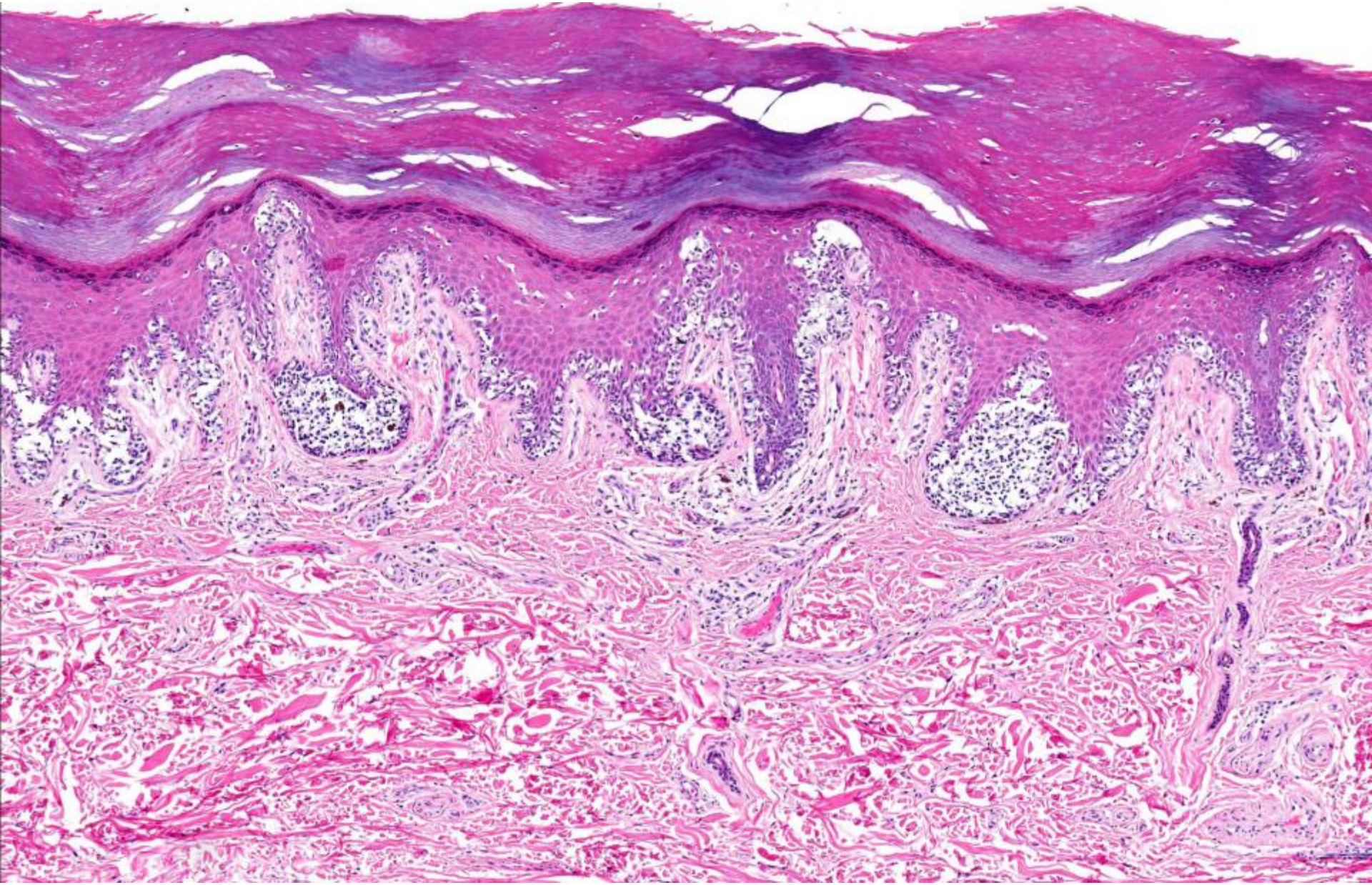
Your diagnosis

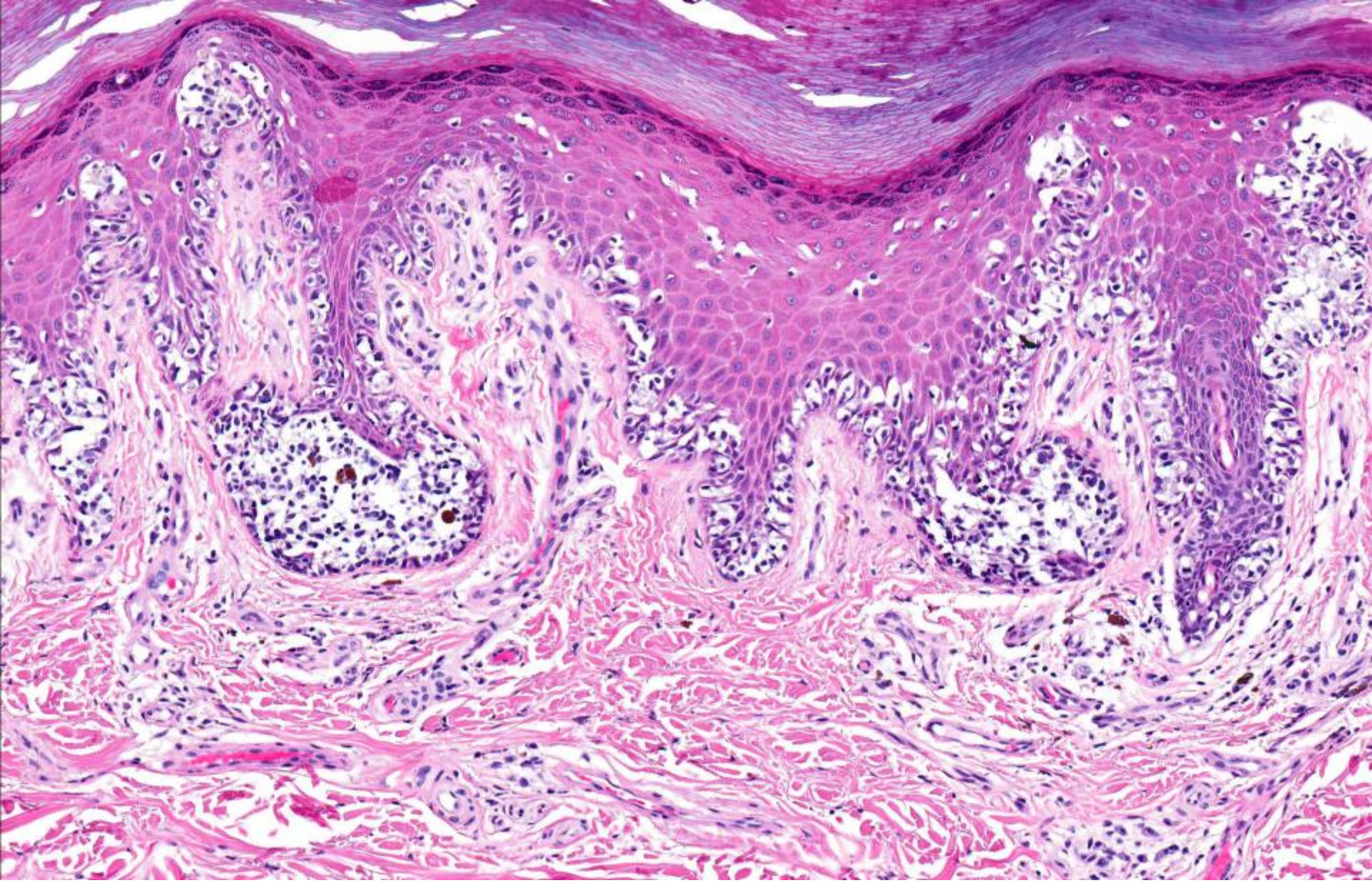
Margin negative?

Margin Positive?

Next Case







Your diagnosis

Nevus?

Melanoma?

Our Diagnosis

Malignant melanoma, acral-lentiginous type

(same as Previous Case, 2 years later)

January Talks

- Jan 16, Paris, France
  - 1000. Treatment recommendations for melanocytic lesions, 20 min
  - 1530. Four case presentations, 12 min each
- Jan 17, Paris, France
  - 0810: Acquired melanocytic nevi, 30 min
  - 1350 M-Path (Melanoma Pathology) classification: New observations 20min