Melanoma-Back to Basics... I Thought I Knew Ya!

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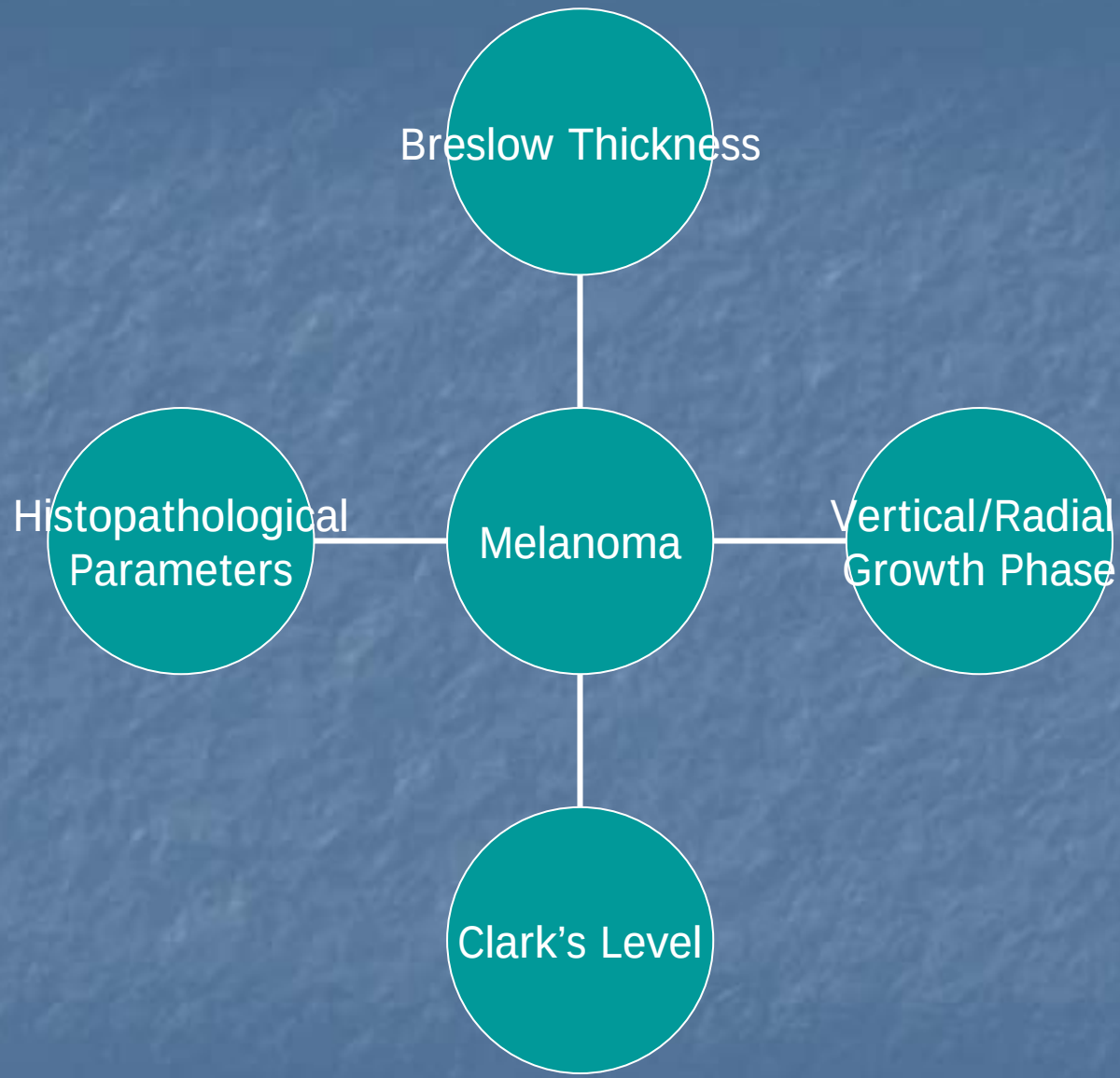
At tumor board, a surgeon insists that all level II melanomas are invasive since they have broken through the basement membrane. Your appropriate reply is...

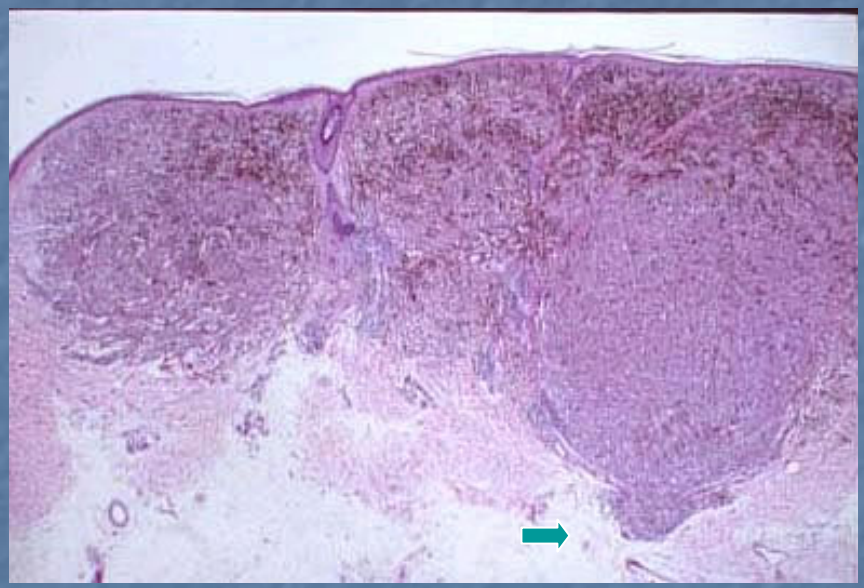
A. I Agree
B. I Disagree
C. It depends upon the body site
D. Level II melanomas do not exist


Breslow Thickness
Histopathological Parameters
Melanoma
Vertical/Radial Growth Phase
Clark's Level

Growth Phase

Vertical growth phase (VGP)	Potential to metastasize
Radial growth phase (RGP)	Believed to lack competence for metastasis

Clark's Levels



I-?

II-Papillary Dermis

III-Filling papillary dermis

IV-Reticular Dermis

V-Subq fat

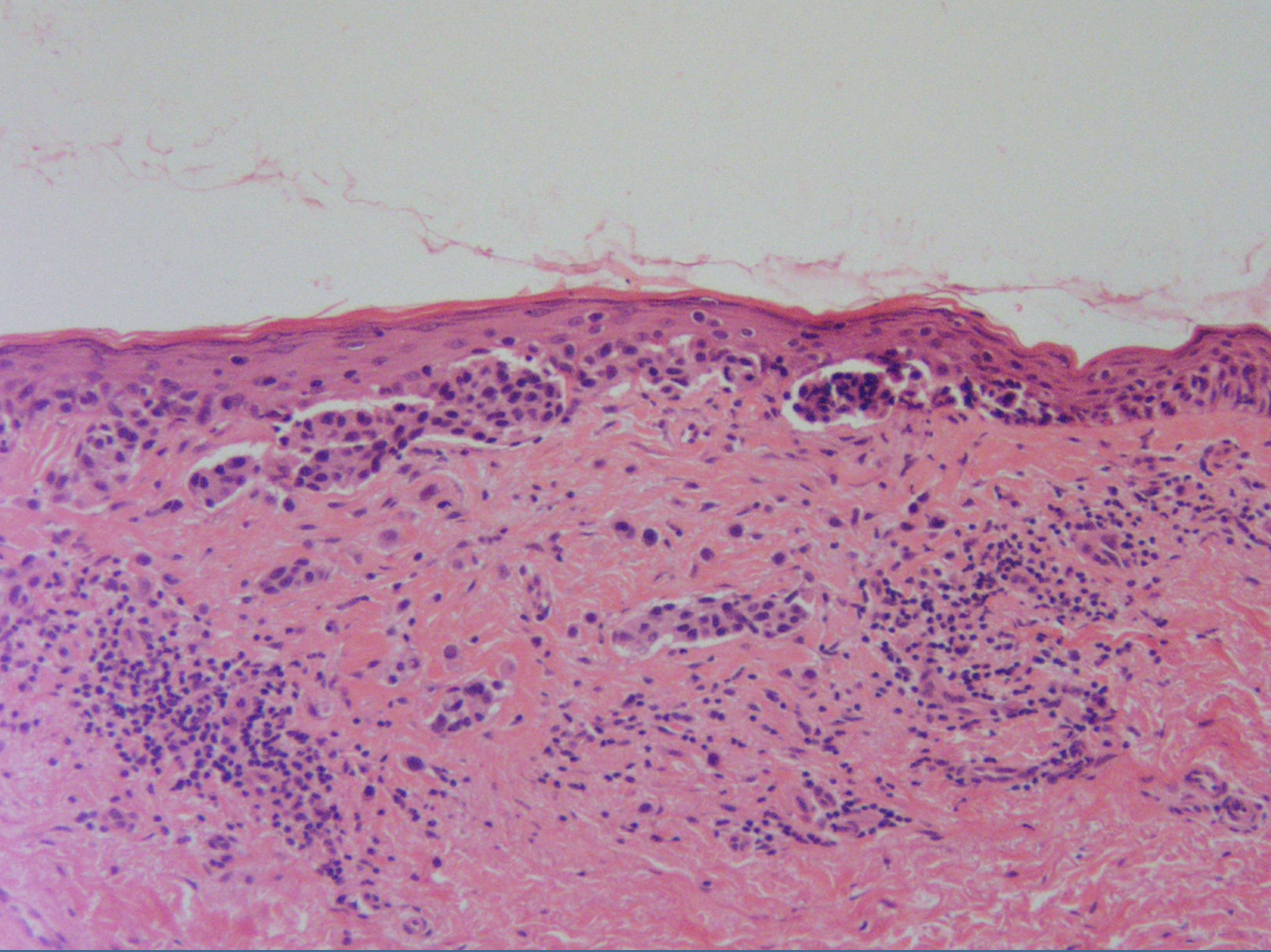
Eliminated in AJCC 2002

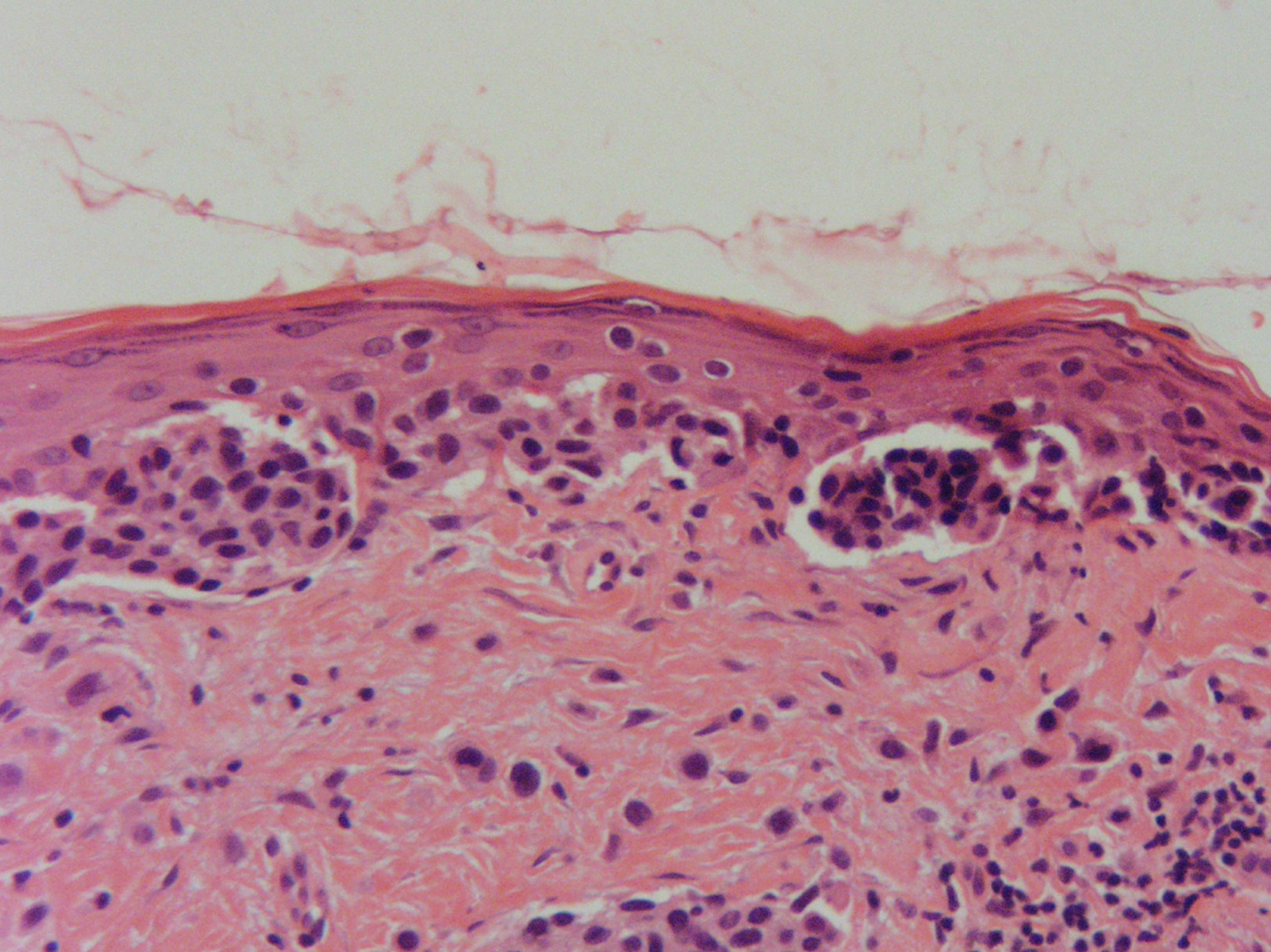
What Invasion IS

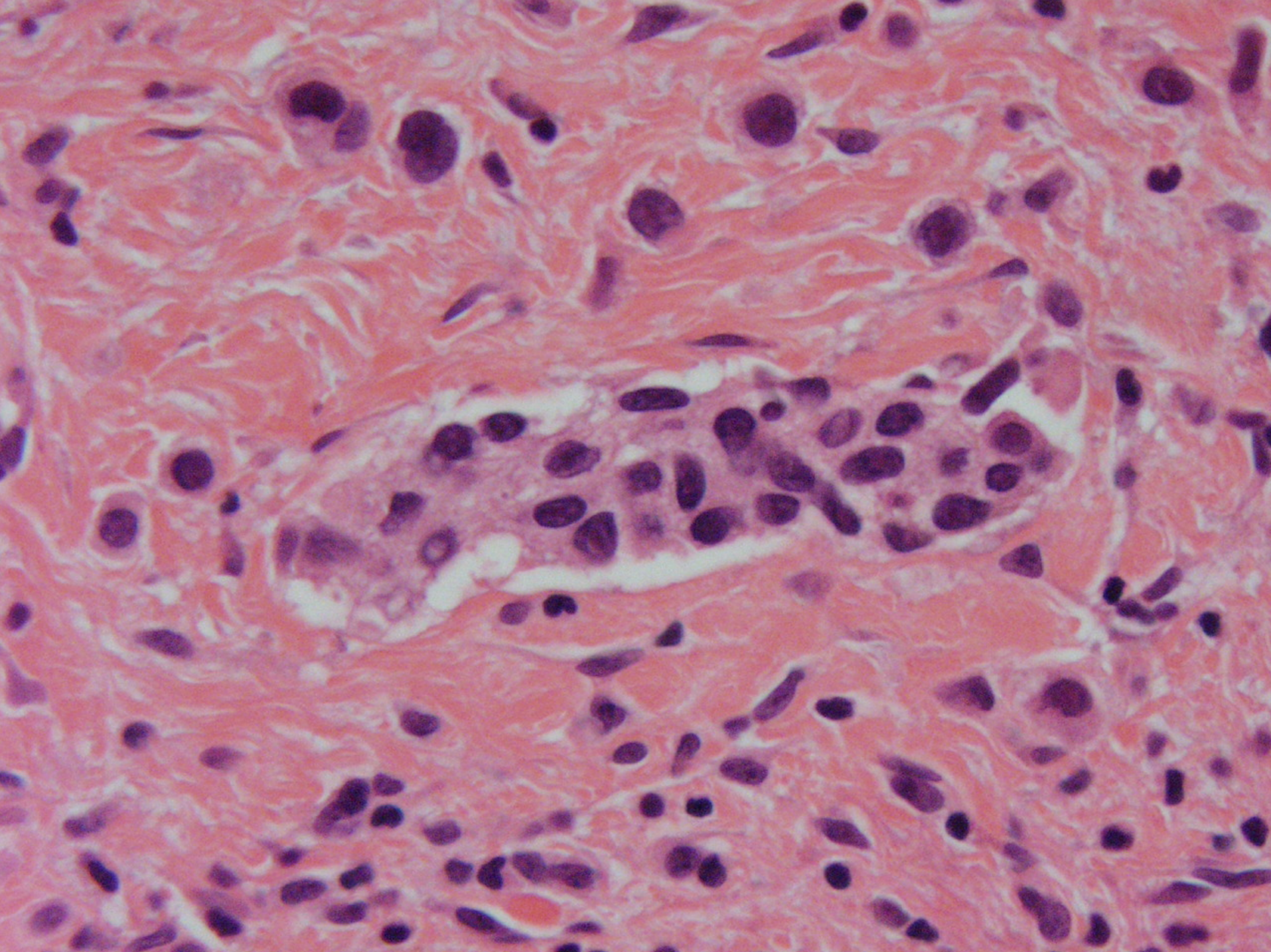
- Expansile nests within the dermis
- Clearly different cytology compared to junctional component
- Mitotic figures

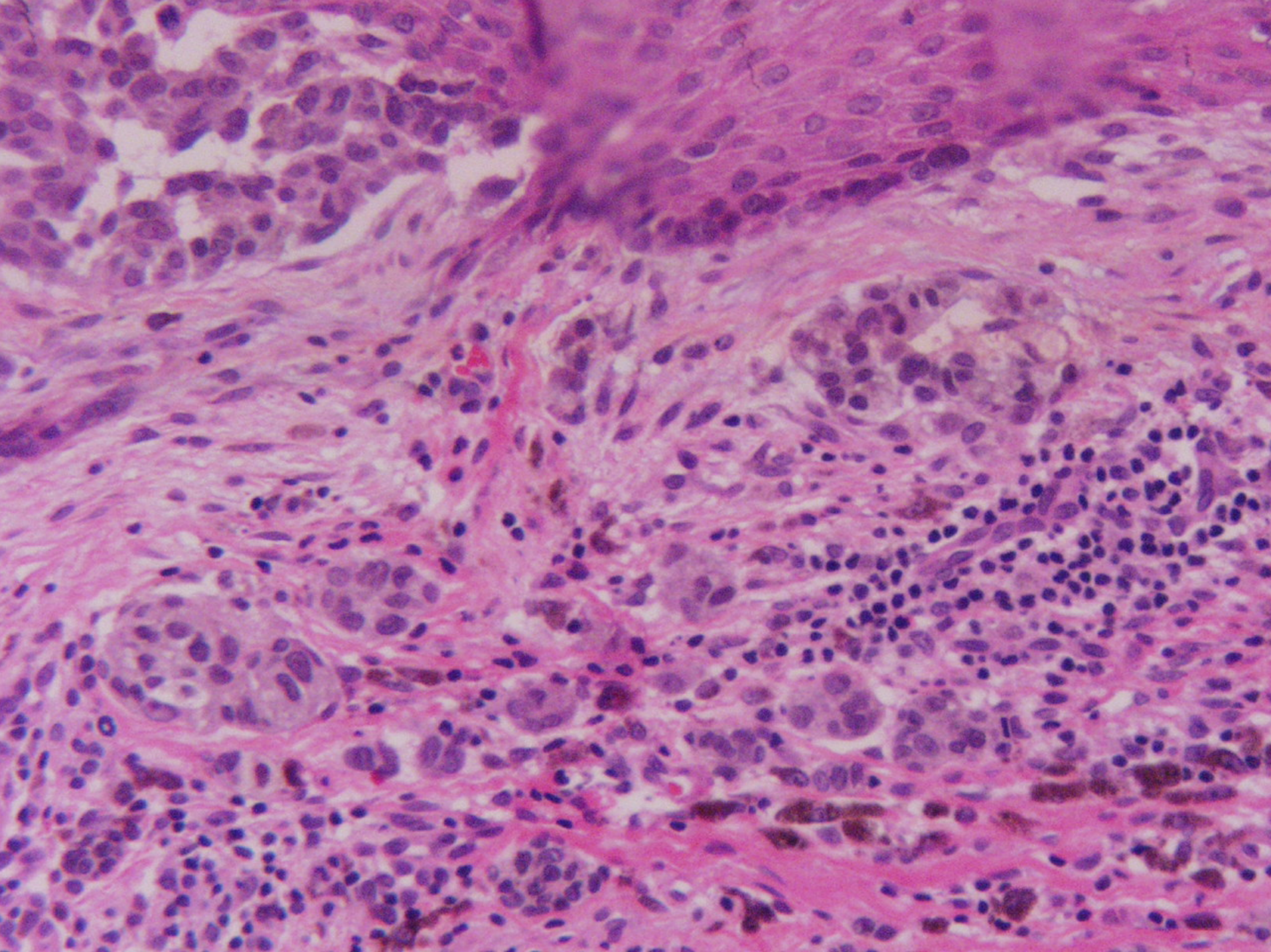
What Invasion ISN'T

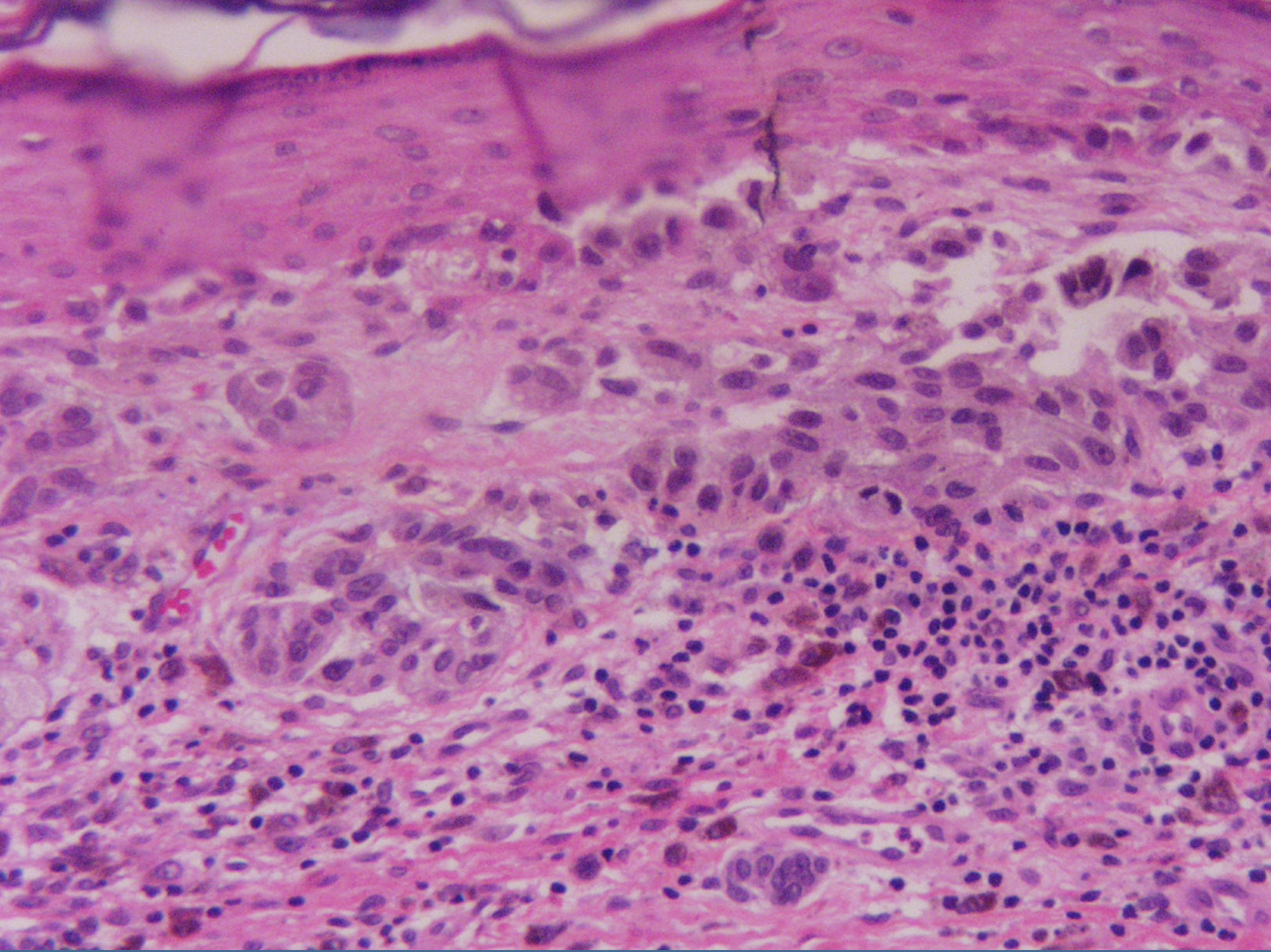
- Melanocytes in the papillary dermis
- Level II

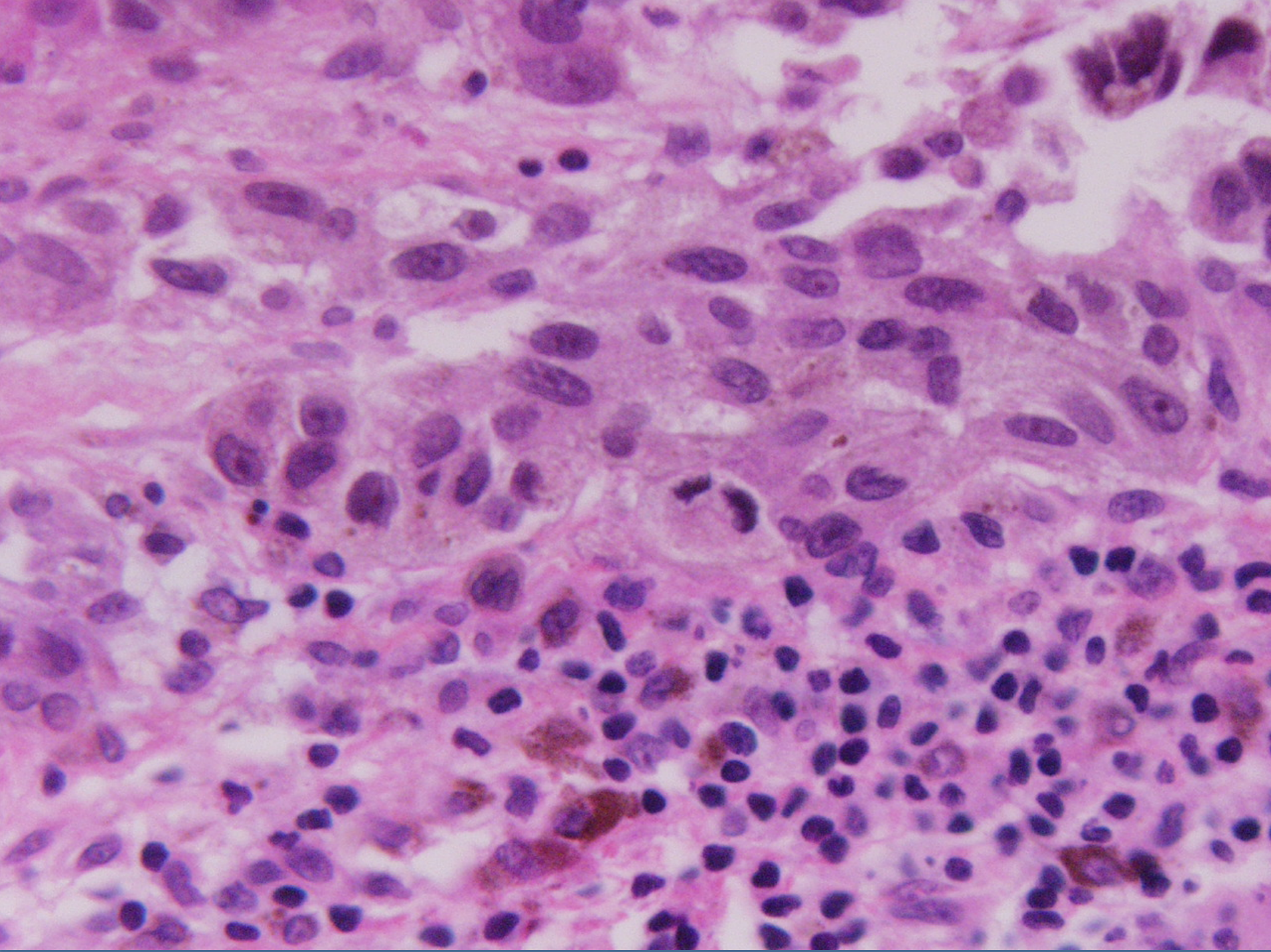


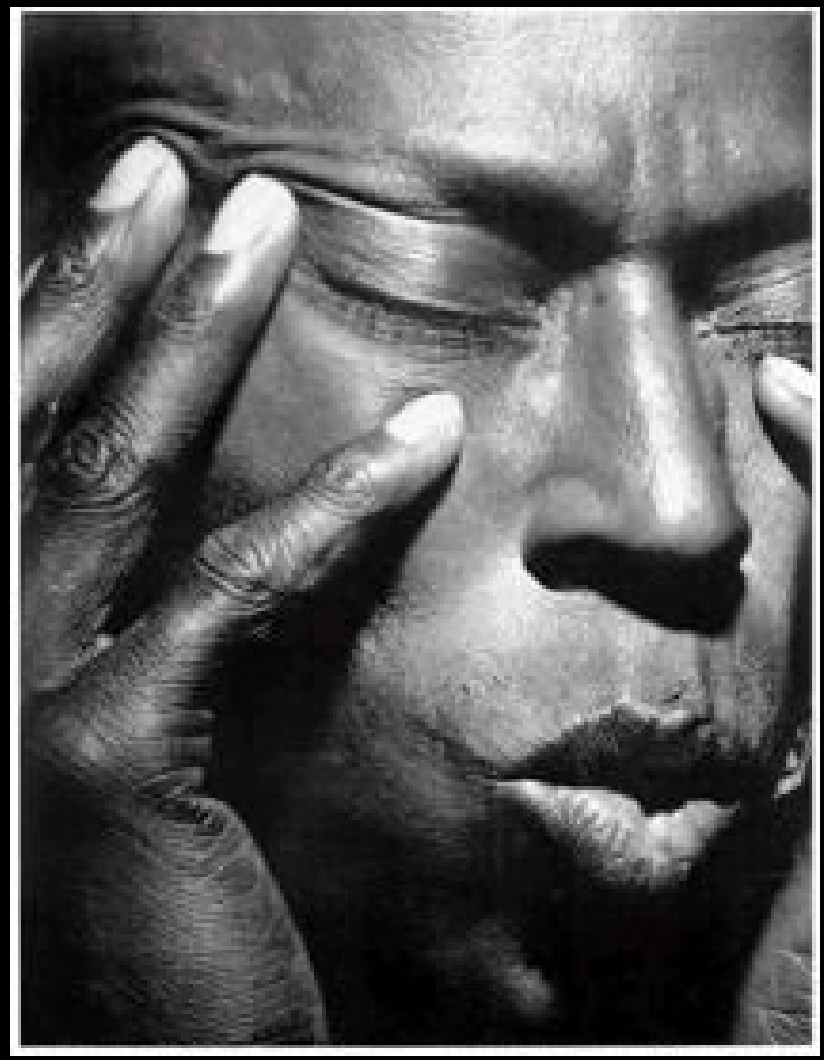












Caveats

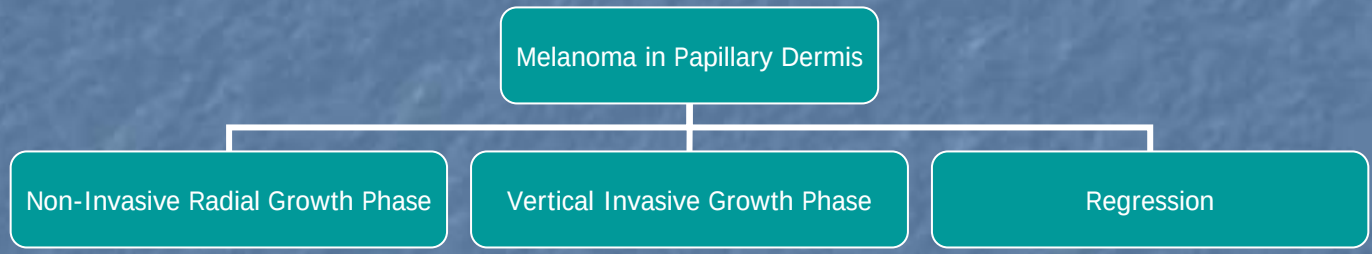
- Re-review of three cases with metastasis of RGP melanomas were re-reviewed
- Deeper sectioning revealed a focus of vertical growth in one case
- In the other two cases, only radial growth was found
  - One case with regressive changes
  - One case with adjacent compound nevus with periadnexal involvement
- CONCLUSIONS
  - True RGP melanomas have an excellent prognosis
  - Possible that strictly defined RGP melanomas may metastasize in very rare cases
  - Caution must be exercised in defining a lesion as having no metastatic potential when:
    - Multiple sections of the primary lesion are unavailable
    - Regressive changes
    - Associated melanocytic nevus

J Cutan Pathol 2002 Aug;29(7):407-14

Caveats

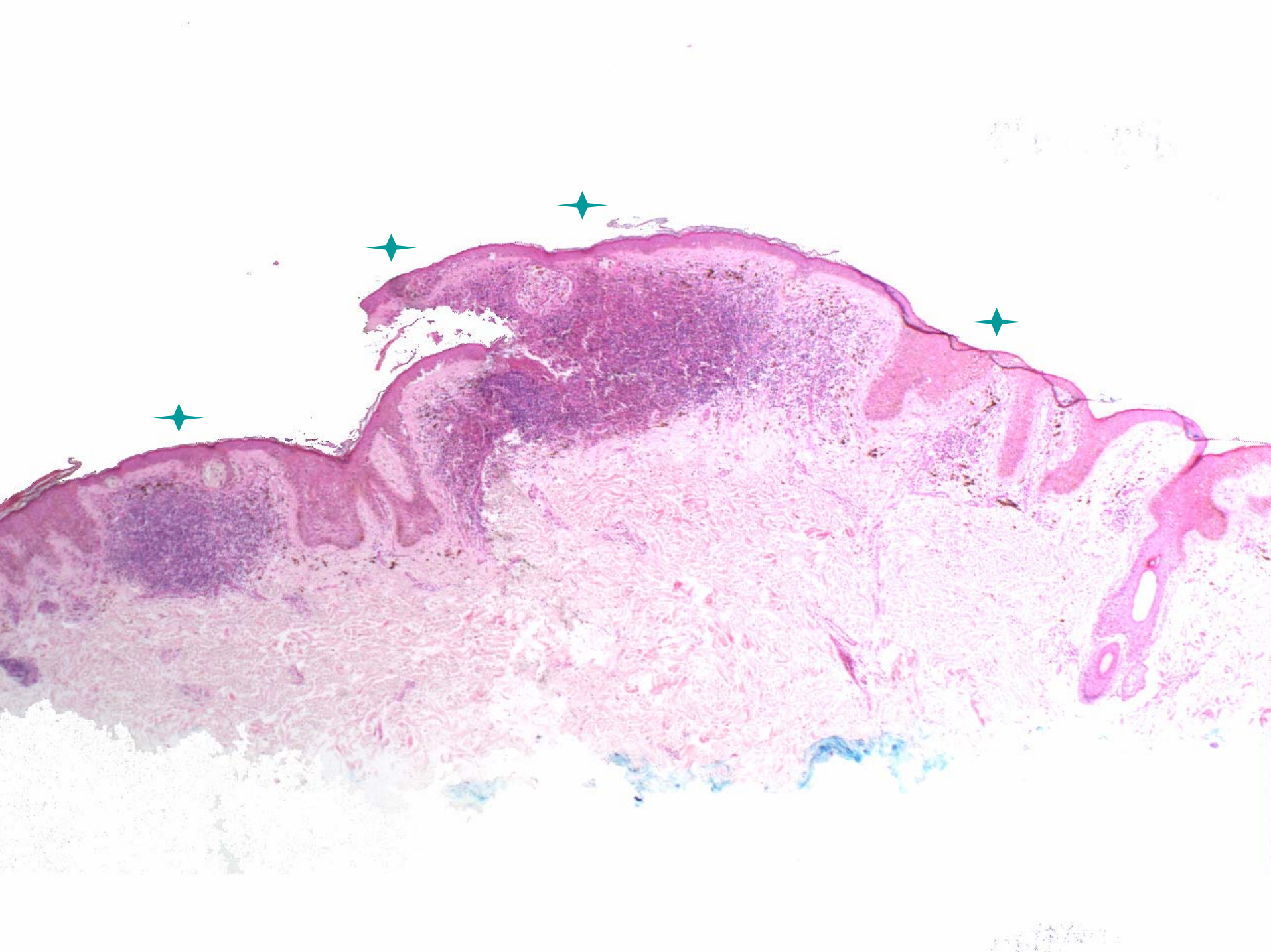
- Retrospective, multicenter, and case-control type study
- Vertical growth phase is the only statistically significant prognostic factor for thin level II cutaneous SSM
- Conclusions
  - Growth phase evaluation should be added to the recommendations for melanoma histologic report, at least for level II SSM
  - Minimum of eight serial sections mandatory not to underdiagnose vertical growth phase

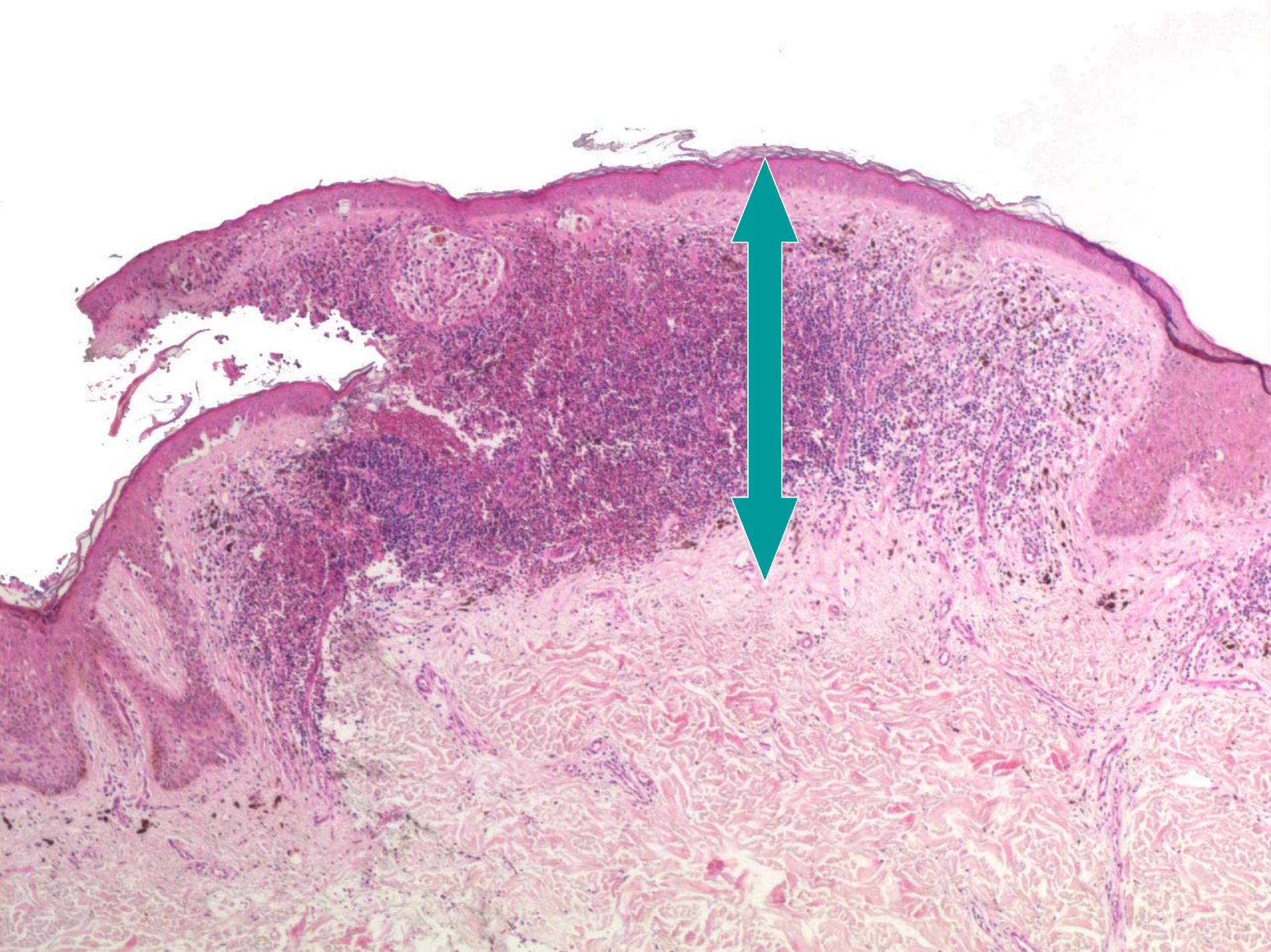
Am J Surg Pathol. 2003 Jun;27(6):717-24.


Melanoma in Papillary Dermis
Non-Invasive Radial Growth Phase
Vertical Invasive Growth Phase
Regression

Measuring the Melanoma

- Measure from granular layer to the deepest extent of the dermal component
- Measure at right angles to surface of skin above tumor, avoid tangential sections
- Avoid hair follicles/adnexal structures
  - Atypical melanocytes in a column perpendicular to the epidermis are probably periappendageal
- Take at least 3 measurements

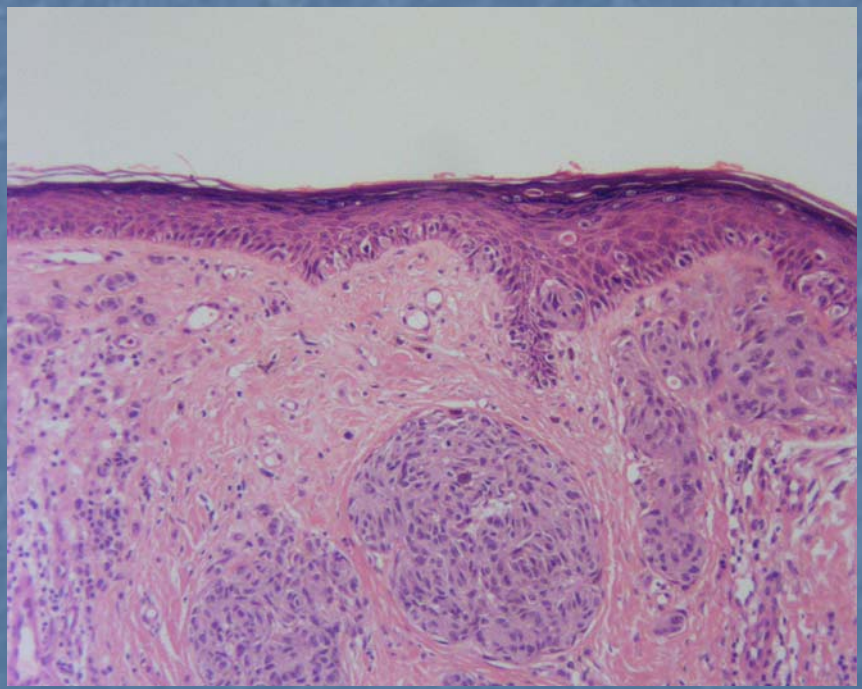




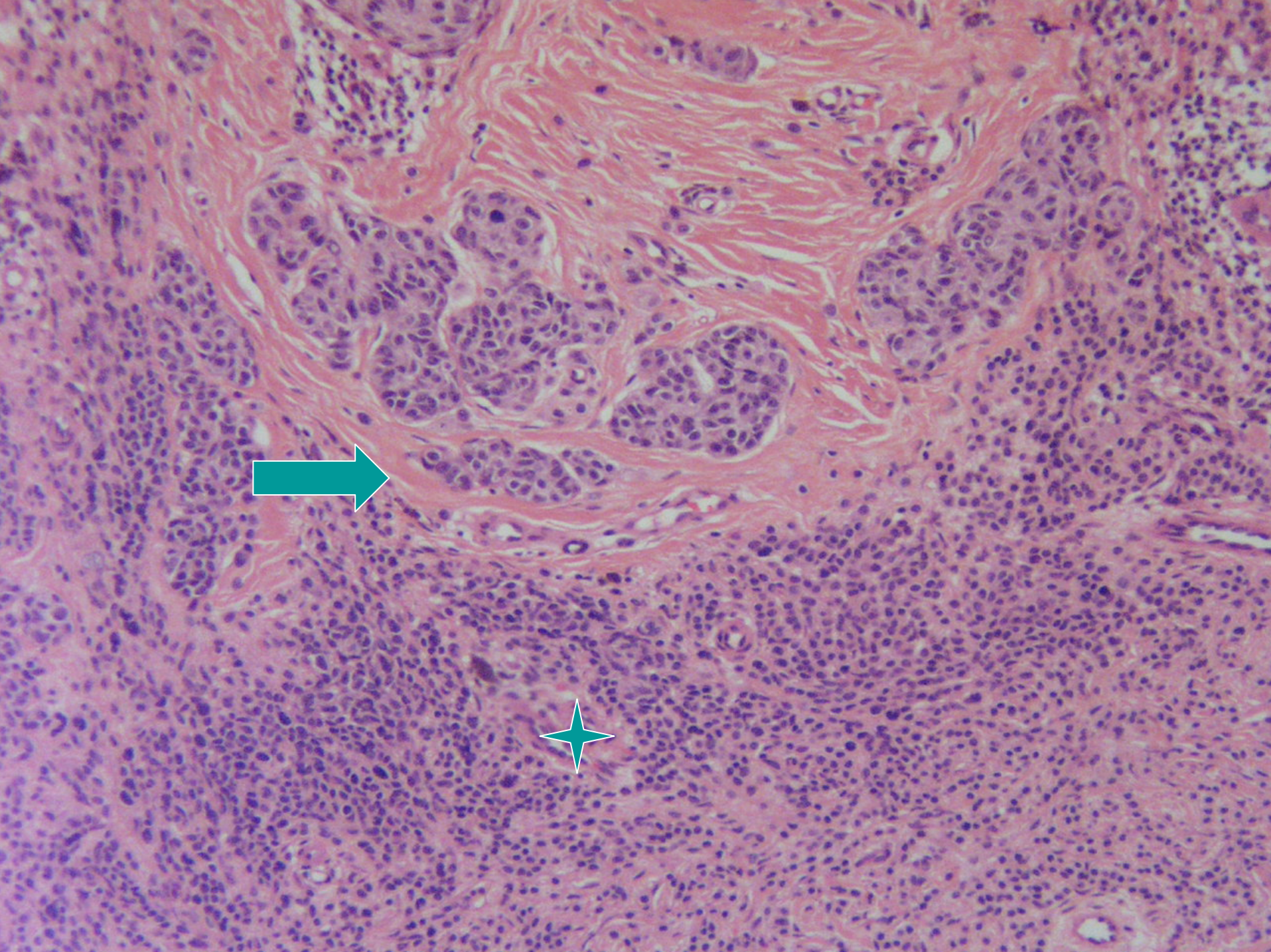
Special Situations

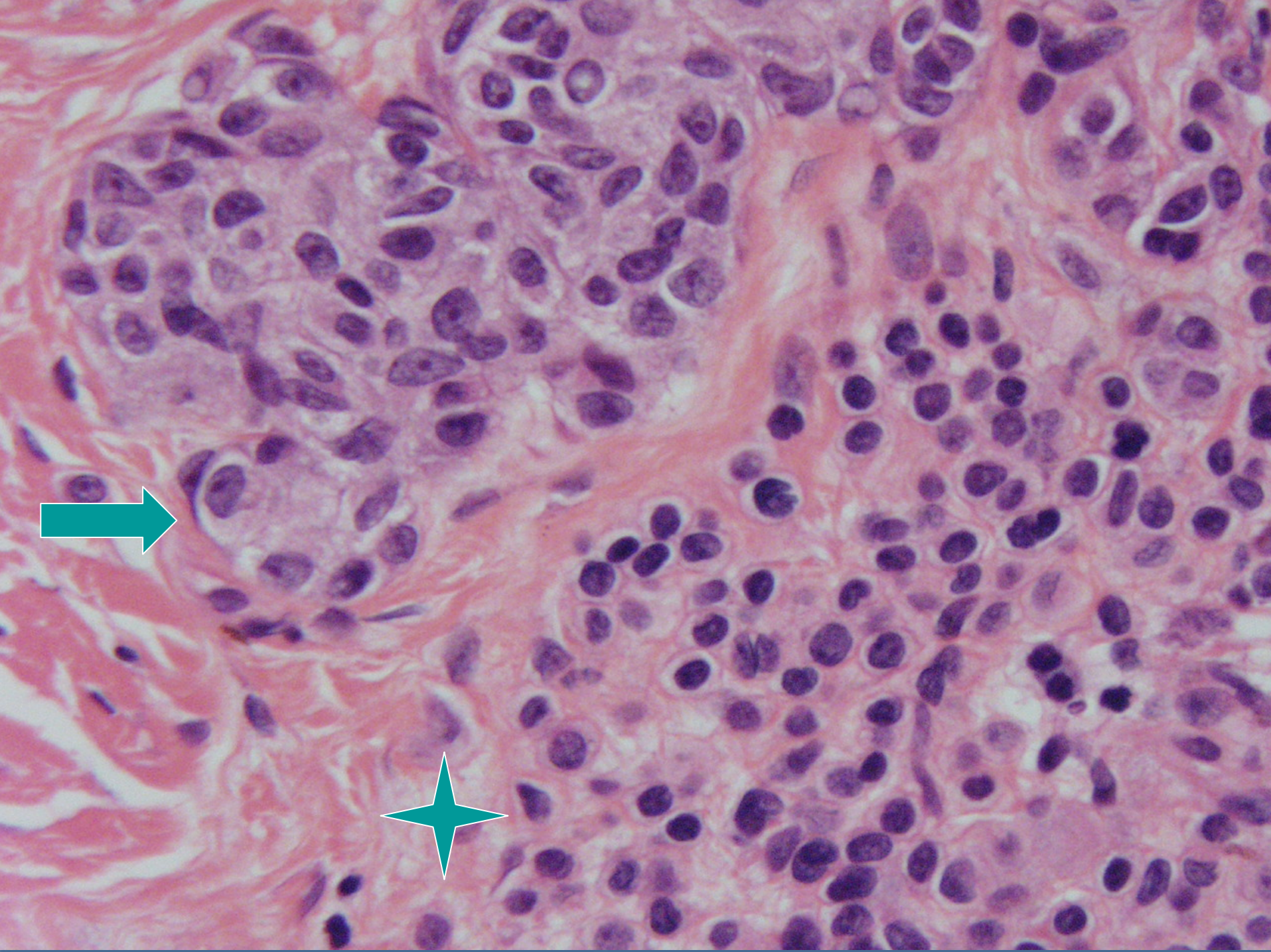
- Arising with pre-existing melanocytic nevus
- Prior biopsy or excision
- Ulceration
- Epidermal thickness
- Polypoid melanomas
- Verrucous melanomas
- Perineural invasion
- Mucosal melanomas
- Melanomas in soft tissue

Melanoma Arising with Nevus

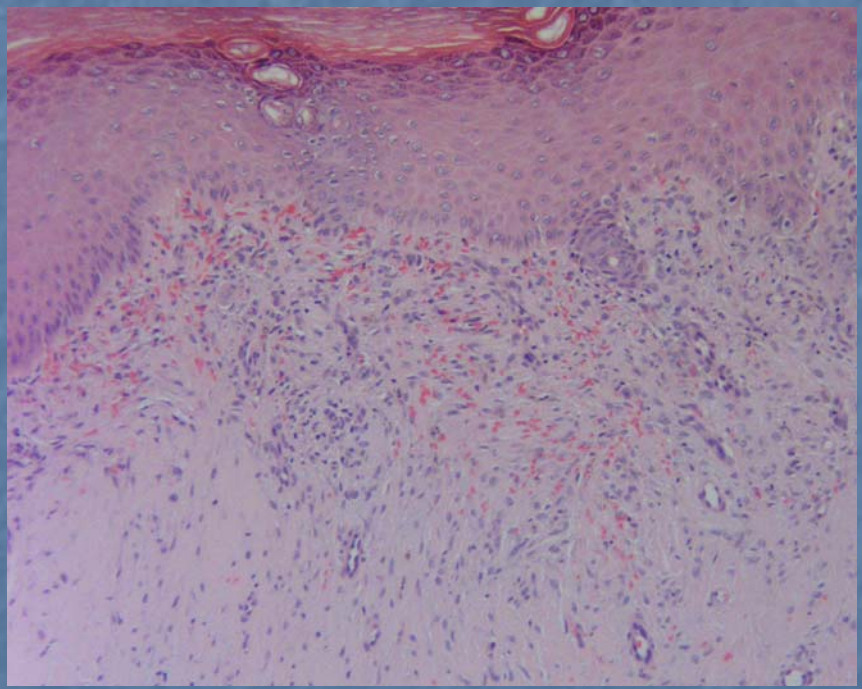


- Morphology
- ?p53, Ki67

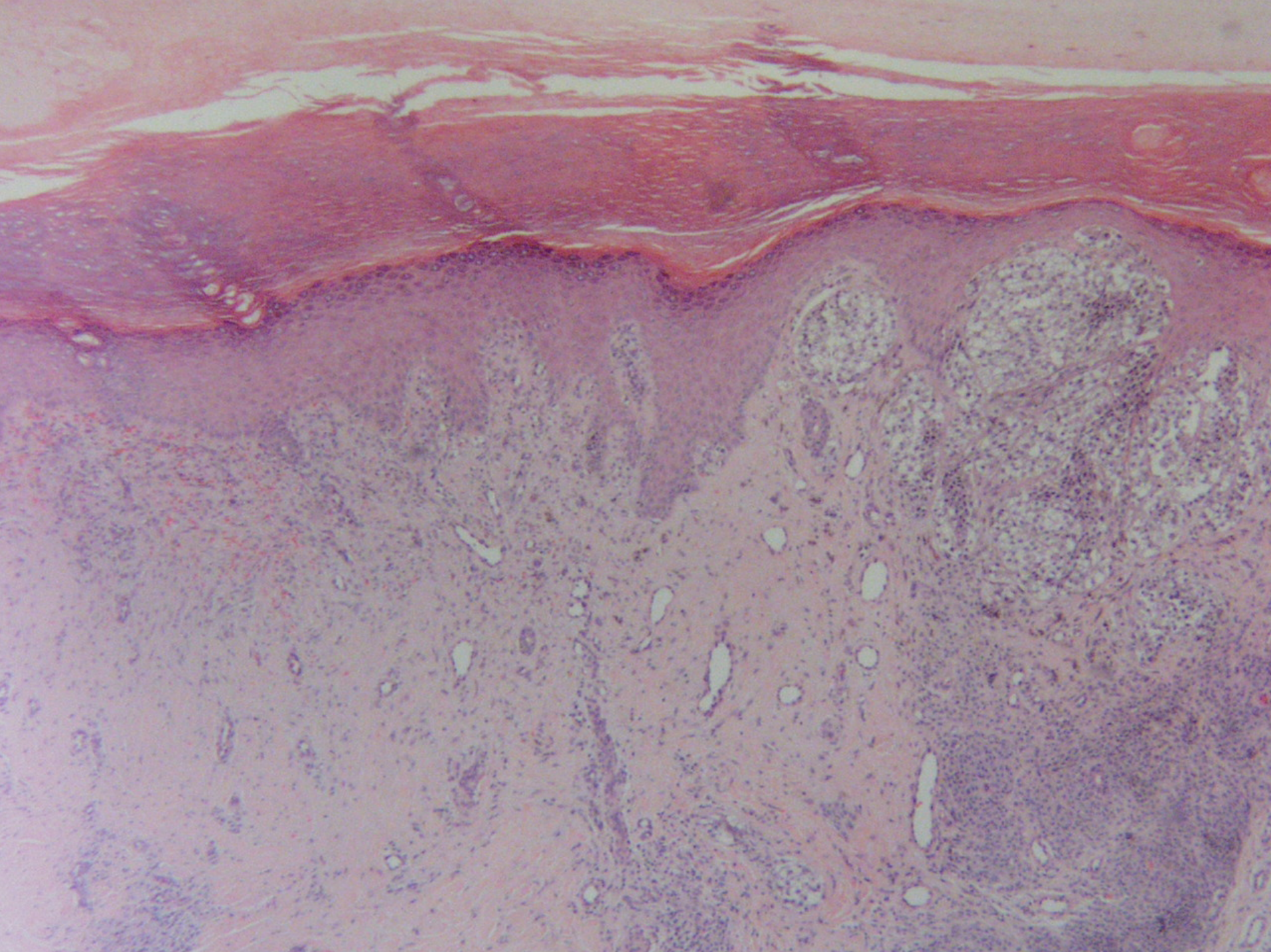


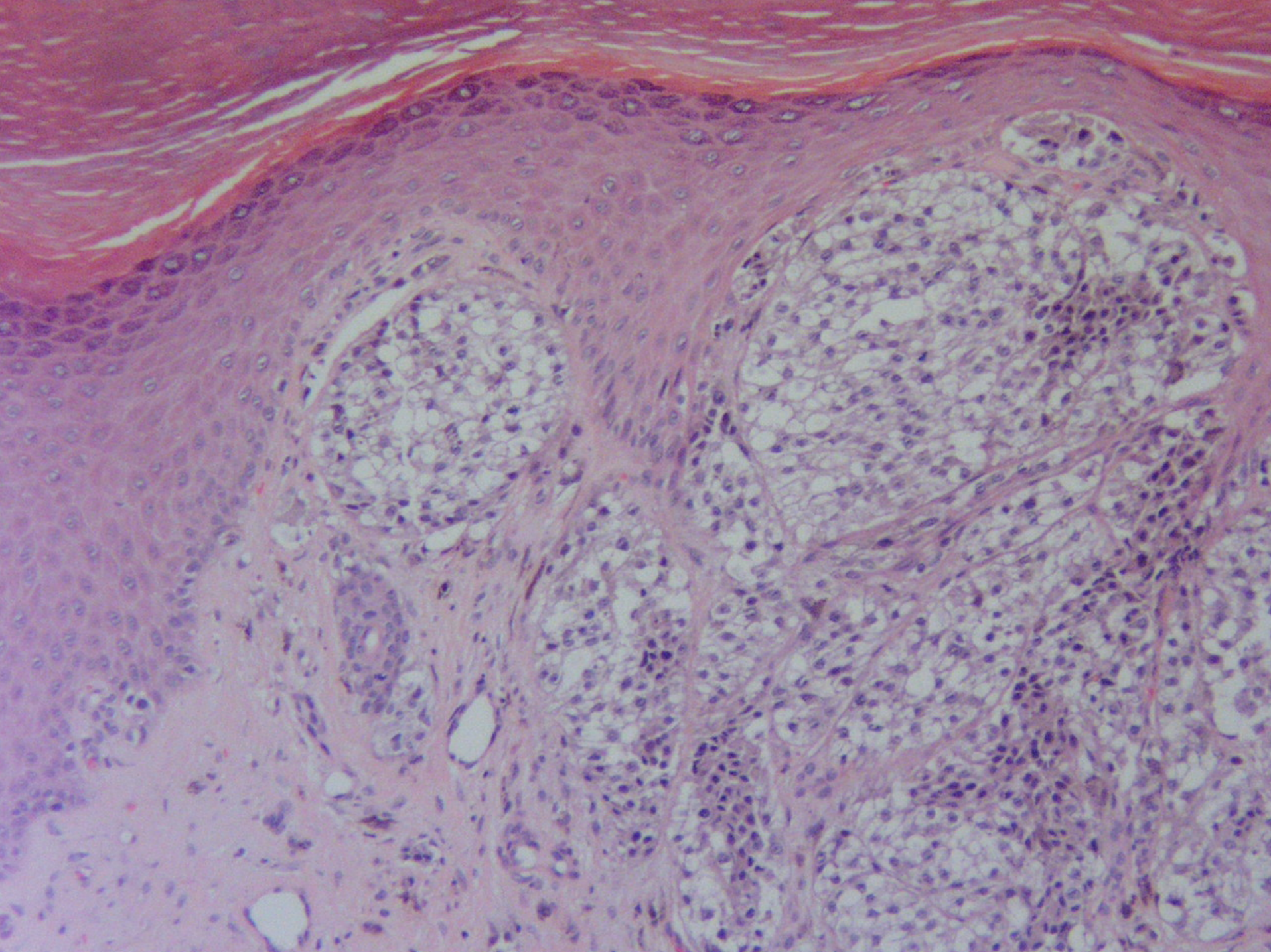


Prior Biopsy or Excision

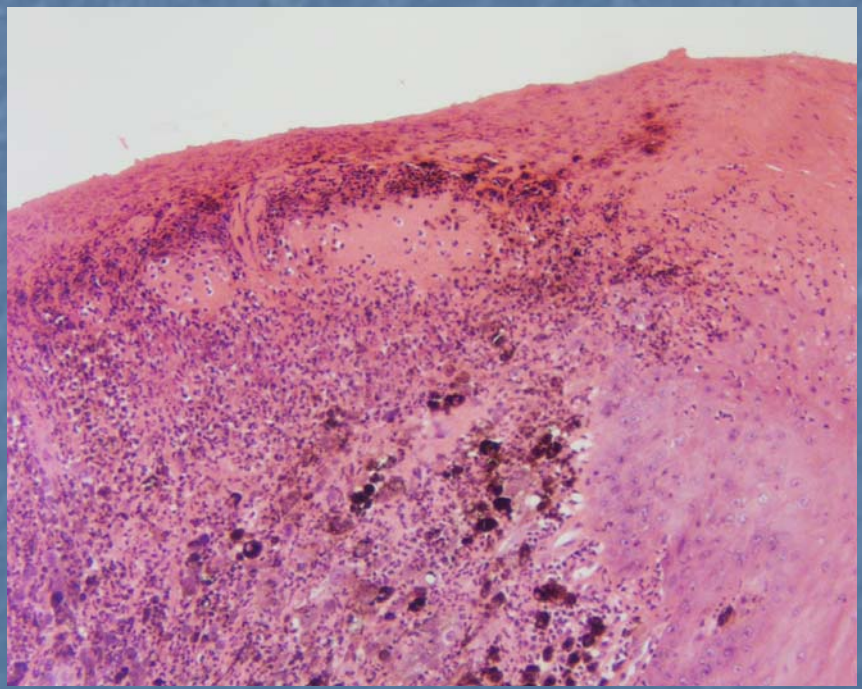


- Depths are not additive
- Measure melanoma away from prior biopsy site



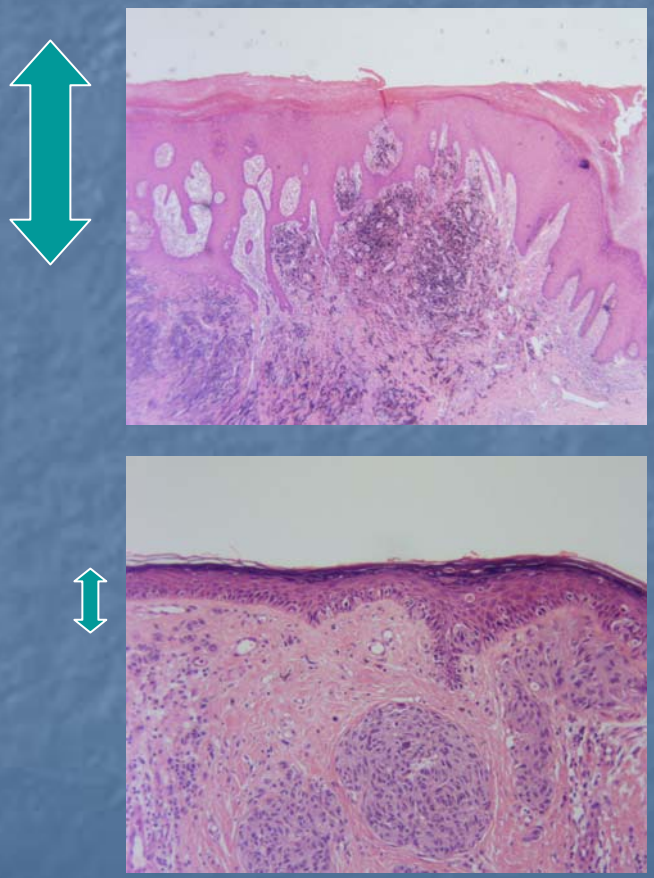


Ulceration



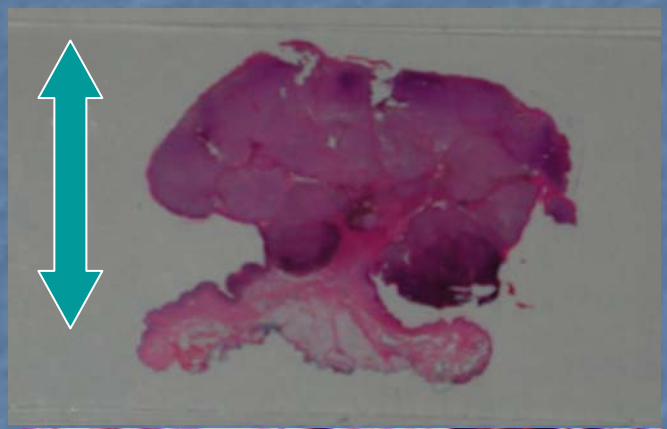
- Measure from base of ulcer to deepest dermal invasion
- Disclaimer that measurement may underestimate true thickness

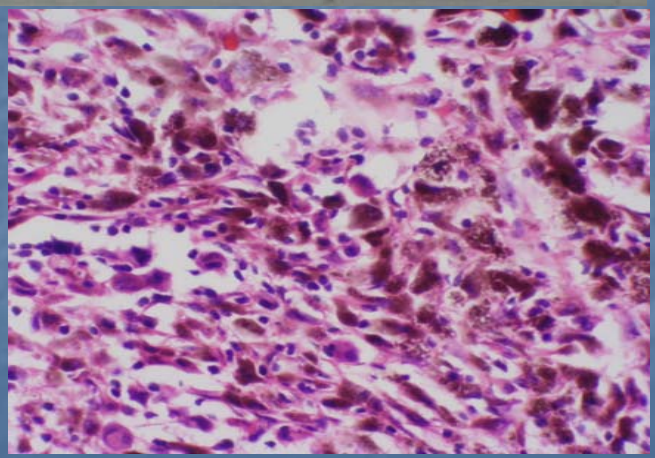
Epidermal Thickness



- Melanomas of acral skin may have epidermal hyperplasia twice as thick as non-acral skin
- If epidermis is thickened, should note that much of measured thickness is due to epidermal hyperplasia

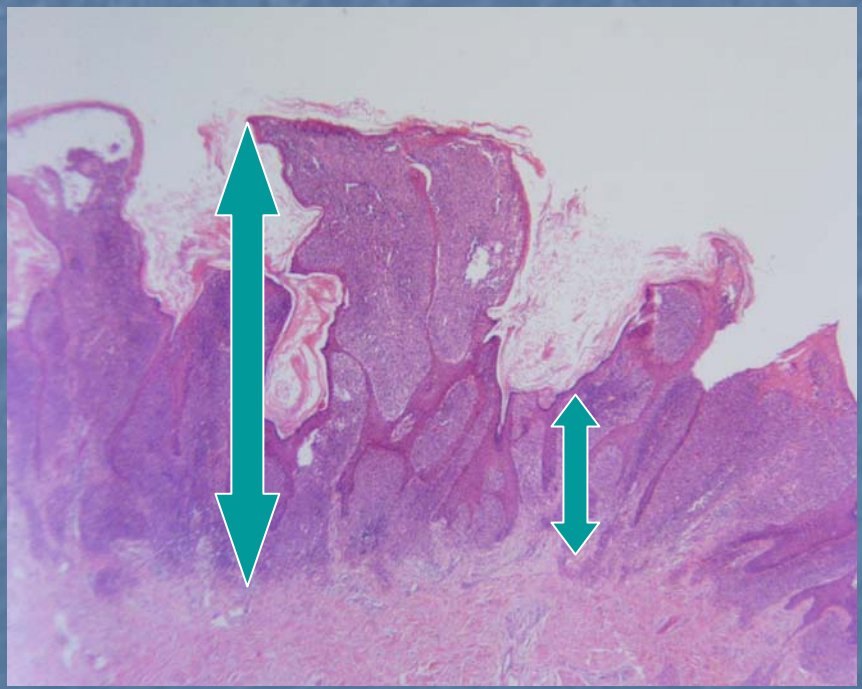
Polypoid Melanomas



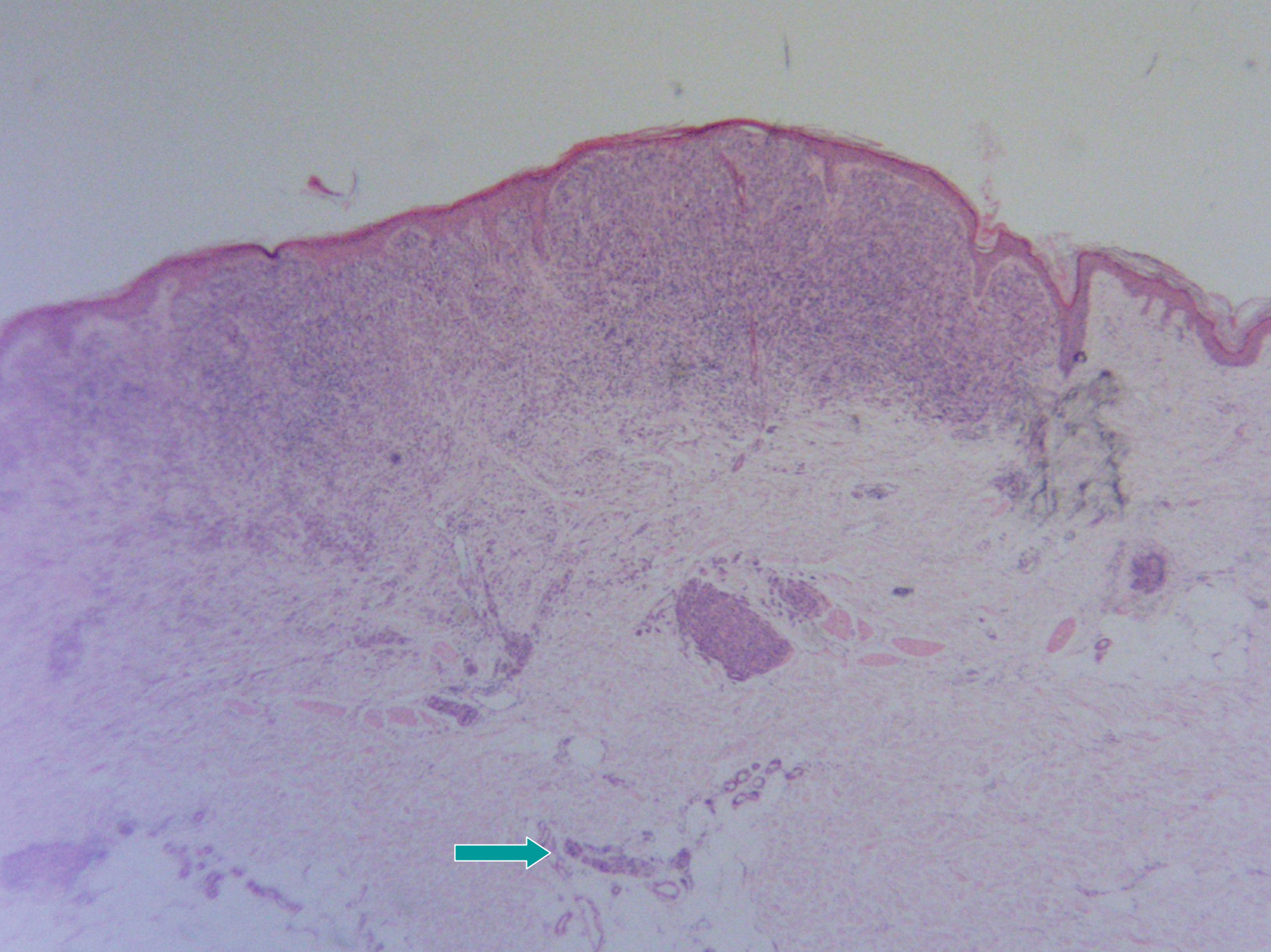


- Clark's levels break down
- Measure thickness
- Consider multiple measurements

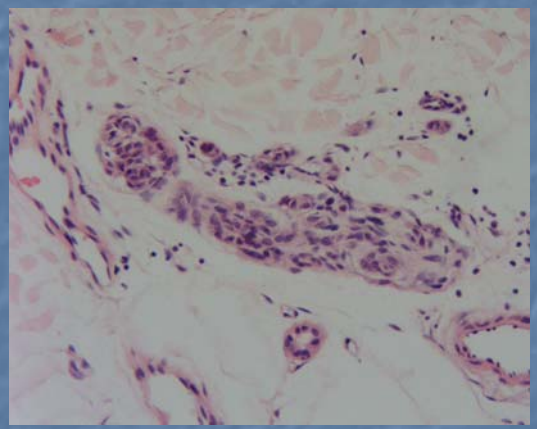
Verrucous Melanomas

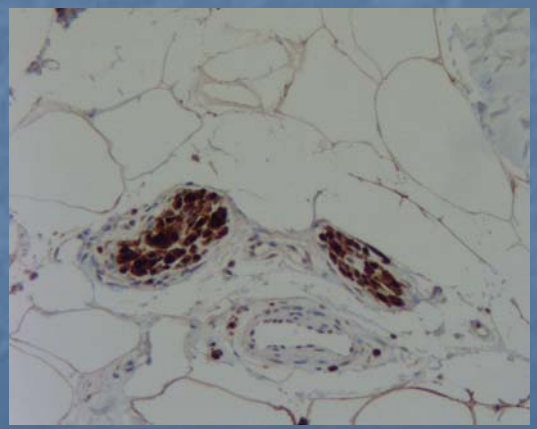


- Take an average of peak to trough
- Report maximal, minimal, and mean

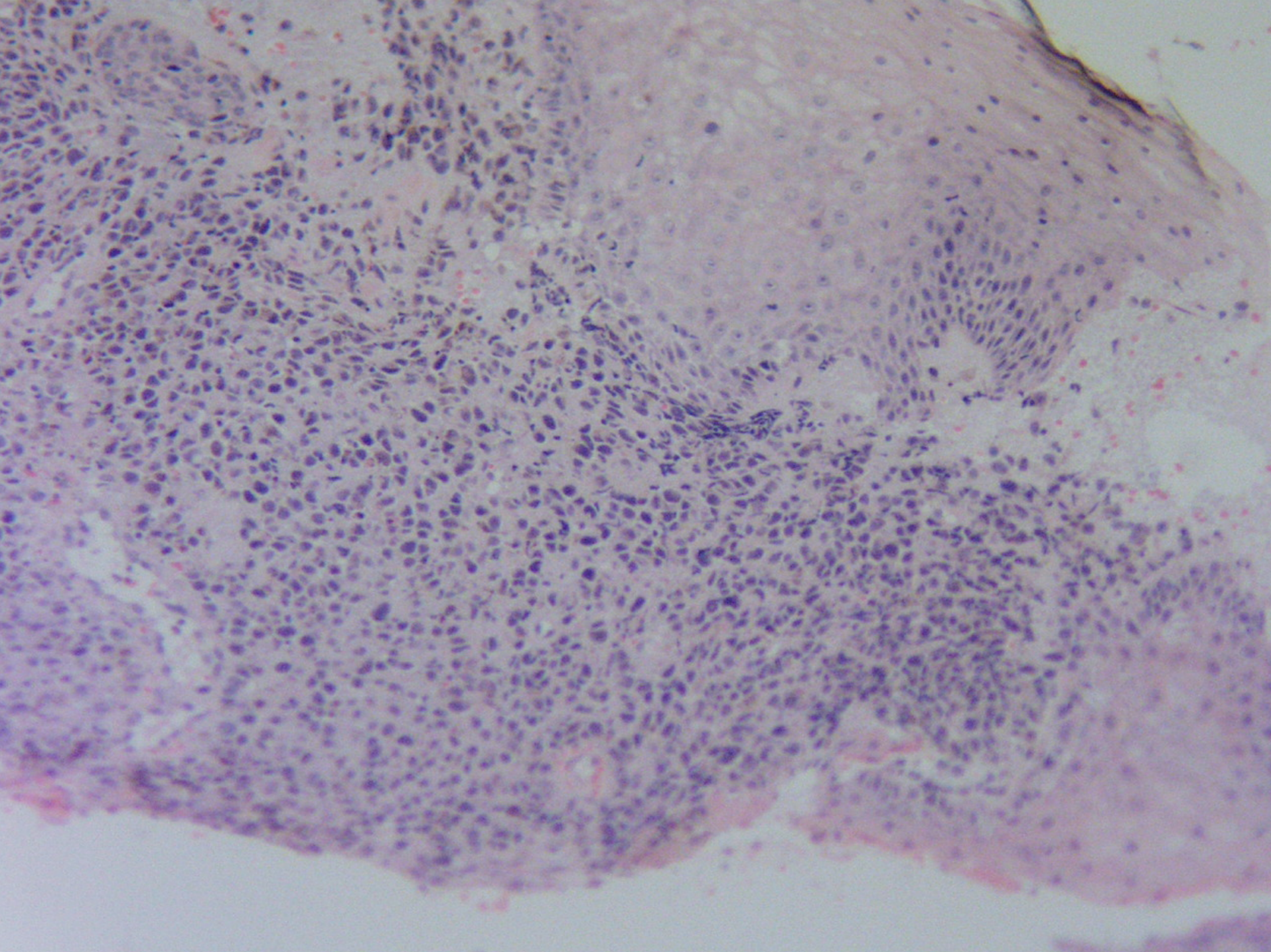


Perineural Invasion

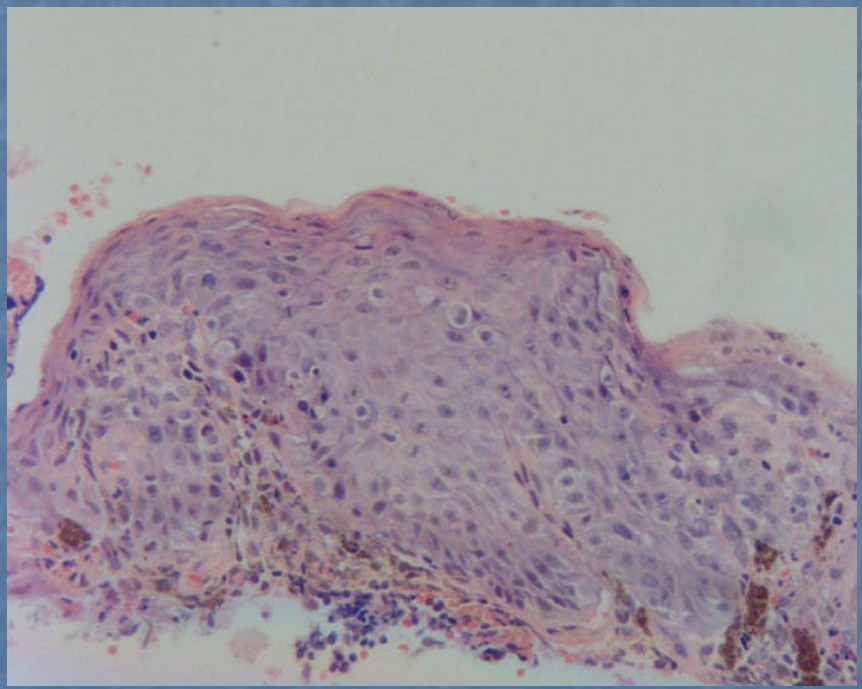




- If melanoma involves the nerve, measurement should include the deepest involved nerve

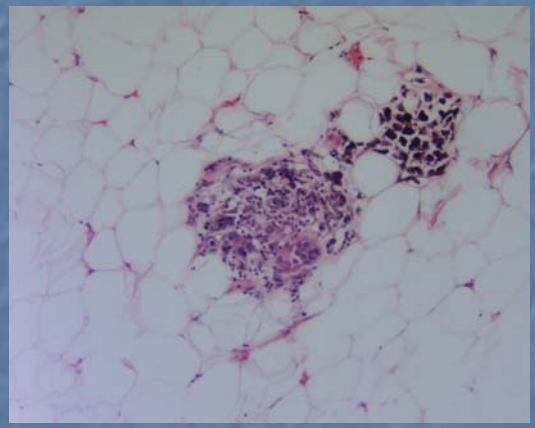


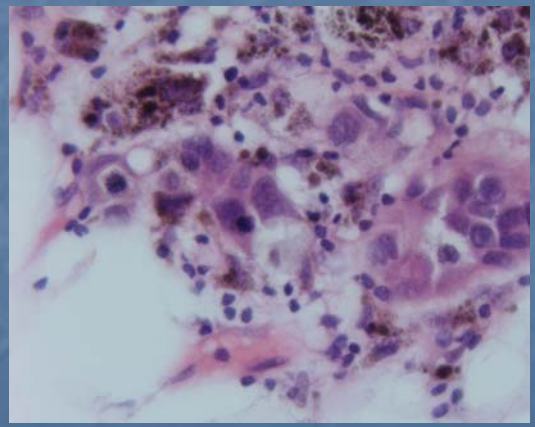
Mucosal Melanomas



- Overall poor prognosis
- Always rule out metastasis
- 37 patients H/N oral mucosa MM
  - 35 surgical resection/2 radiotherapy
  - Twenty-six were dead at follow-up
  - Twenty-one of them died of disease
  - Median survival, 2.4 years
- No prognostic significance was found for tumor thickness, level of invasion, ulceration, mitotic index, or nerve/nerve sheath involvement
- Am J Surg Pathol 2002 Jul;26(7):883-92

Melanomas of Soft Tissue





- Metastasis
- Clear cell sarcoma
- True soft tissue melanoma
  - Current AJCC staging classification, these tumors are considered Stage IV disease (metastatic melanoma with an unknown primary)
  - 11/1800 patients were identified (0.61%) with a single focus of presumed metastatic disease Kaplan-Meier 8 year survival curve was 83%
    Possible these presumed metastatic tumors do not behave like stage IV metastatic disease to the skin but instead behave as primary tumors
  - Arch Dermatol 2000;136:1397-1399

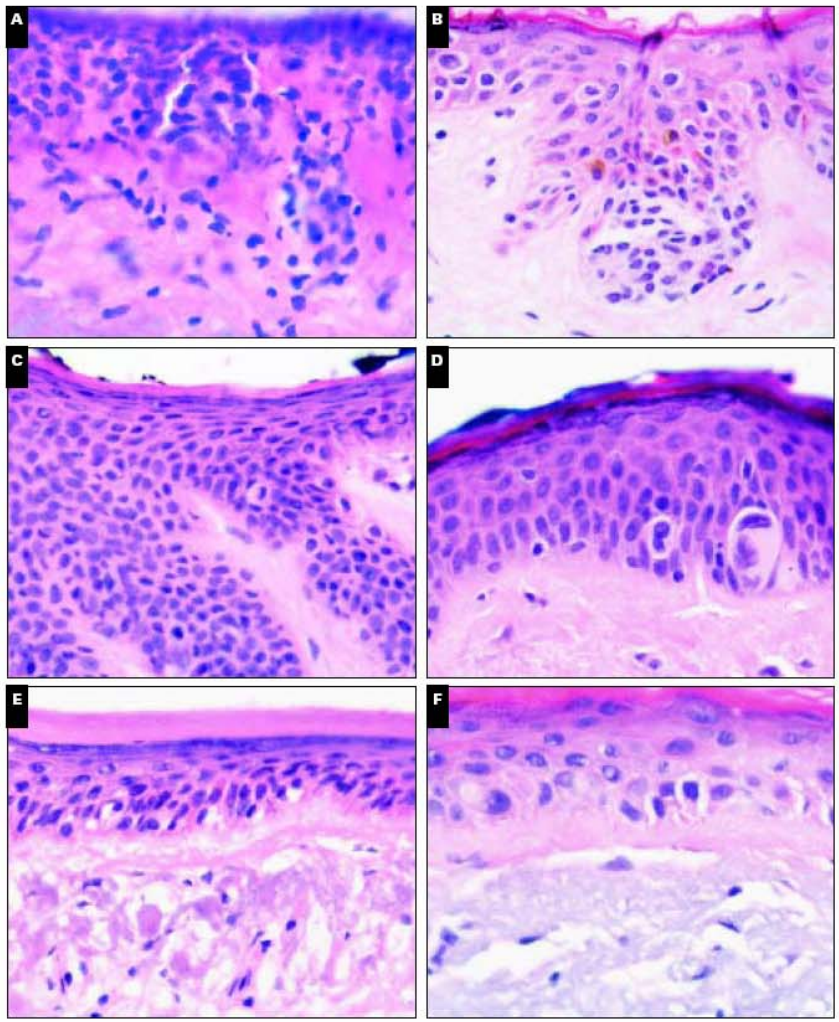
Important Histopathologic Parameters

- Depth of invasion
- Ulceration
- Lymphovascular invasion
- **Margins**
- **Regression**

Melanoma Frozen Section Margins

- Dermatopathologists (15) compared en face frozen sections compared with standard paraffin-embedded sections
- 2 sets of lesions malignant melanomas (MMs) and 10 from nonmelanocytic lesions (NMLs) randomly
- Of 330 evaluations there were 132 diagnostic discrepancies (40.0%)

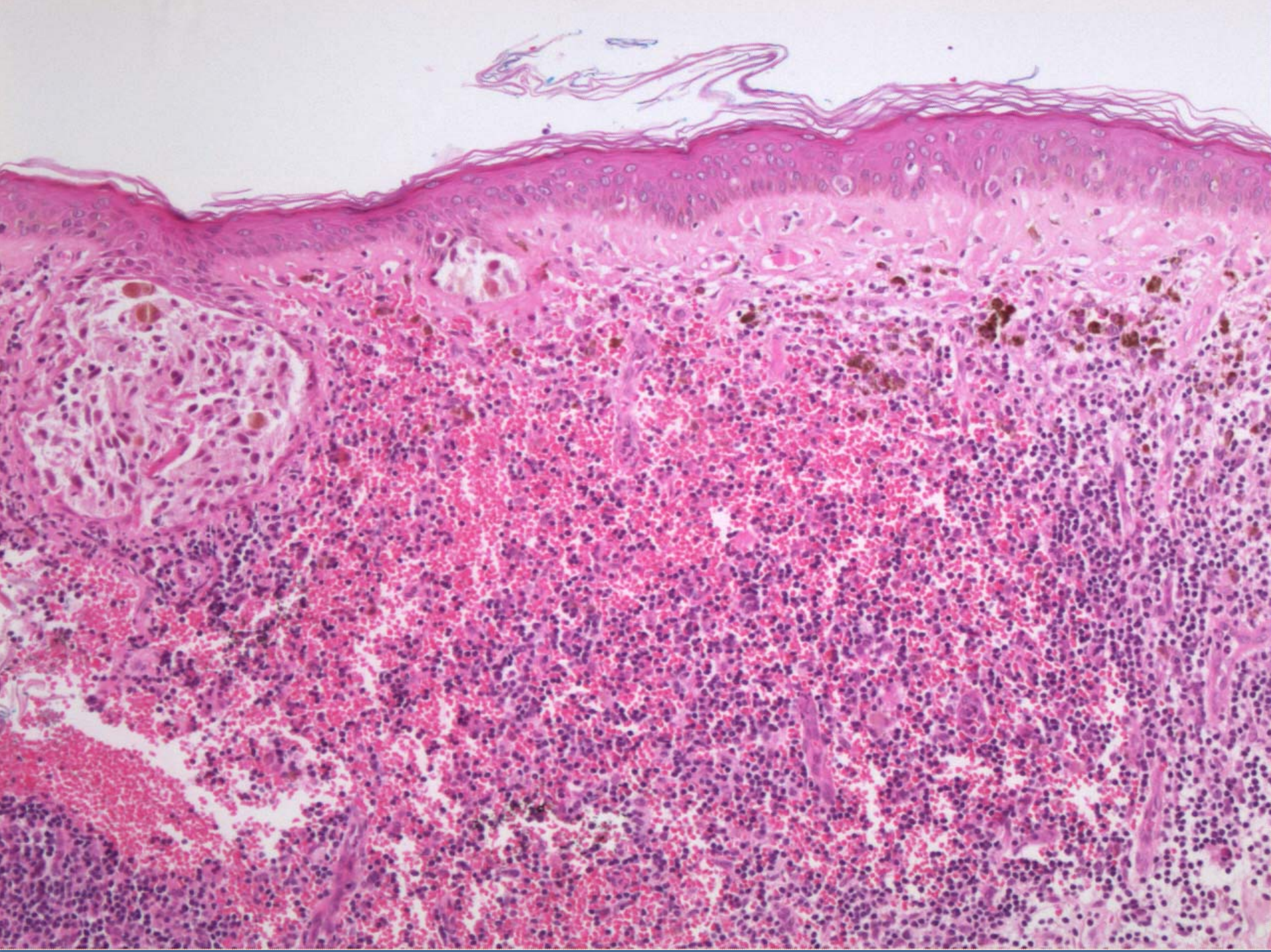
Am J Clin Pathol 2003;120:203-208


A
B
C
D
E
F

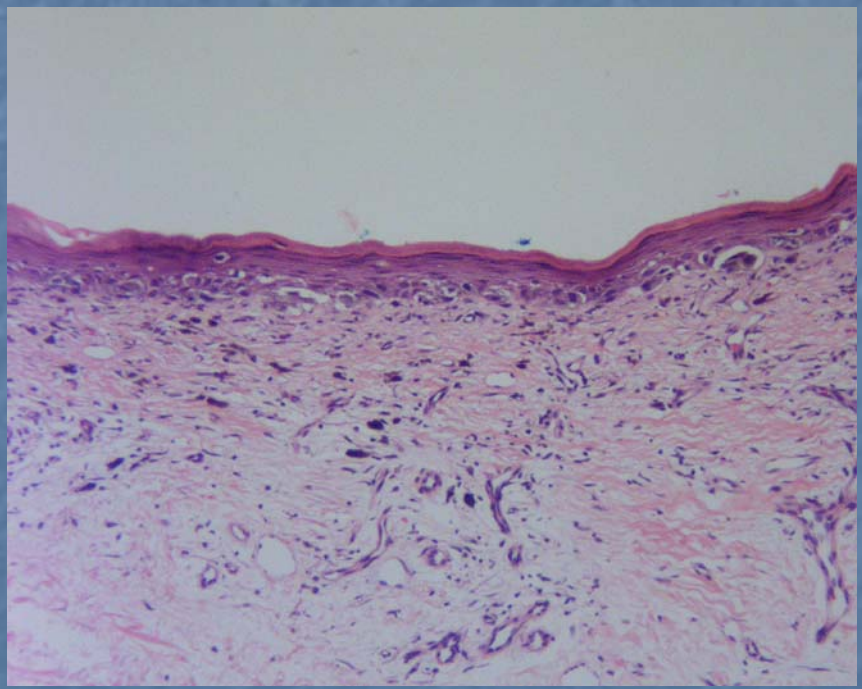
Melanoma Frozen Section Margins

- 66 each for MM and NML (mean per case for both diagnoses, 6)
  - In 9 instances (6.8%), the change was from positive (frozen) to negative (permanent) and in 43 (32.6%), from negative (frozen) to positive (permanent)
  - Poor agreement between frozen and permanent sections

- Conclusions:
  Permanent histology is "gold standard" for histologic evaluation
  En face frozen sections **not** suitable for accurate surgical margin assessment of melanocytic lesions



Regression

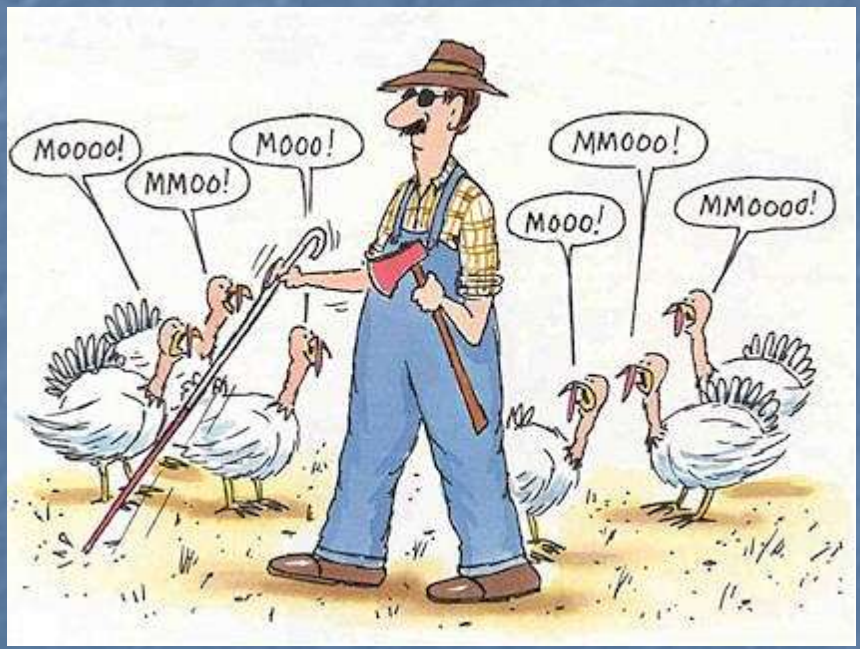


- Measure to deepest extent
- Consider bleach with MART1/S100
- Add disclaimer that it may represent an underestimation of the true biological potential of the melanoma

At tumor board, a surgeon insists that all level II melanomas are invasive since the cells have broken through the basement membrane. Your appropriate reply is...

A. I Agree.
B. I Disagree.
C. It depends upon the body site.
D. Level II melanomas do not exist.

Questions



If confusion is the first step to knowledge, I must be a genius.

Larry Leissner