Management of Atypical Nevi & Melanoma.

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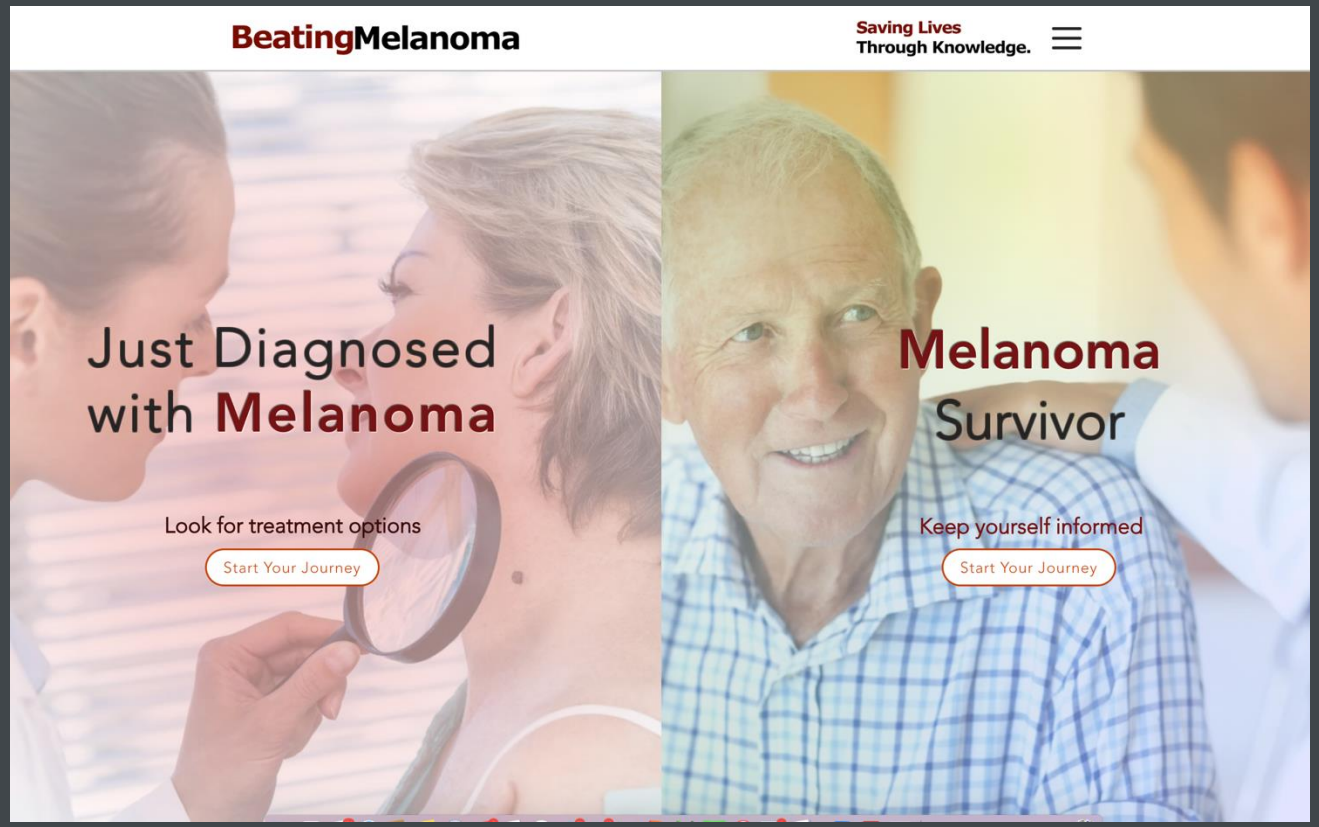
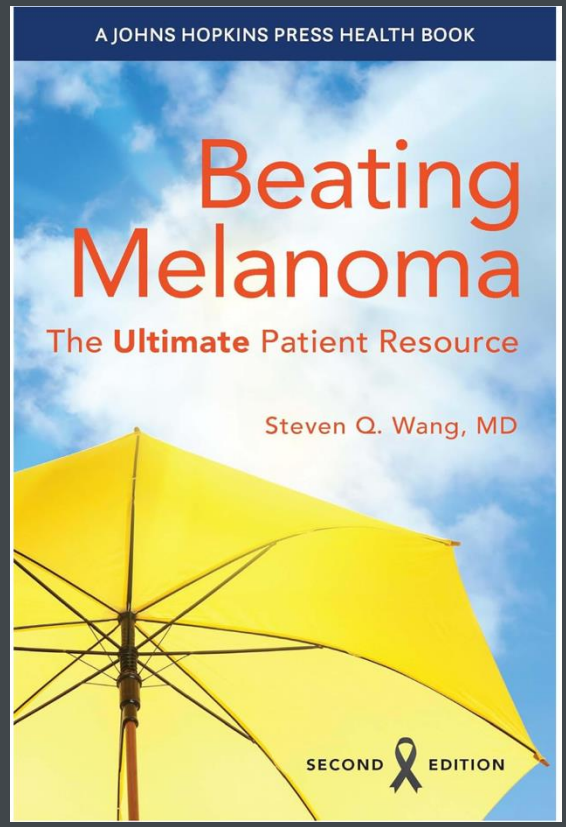
Disclosure.

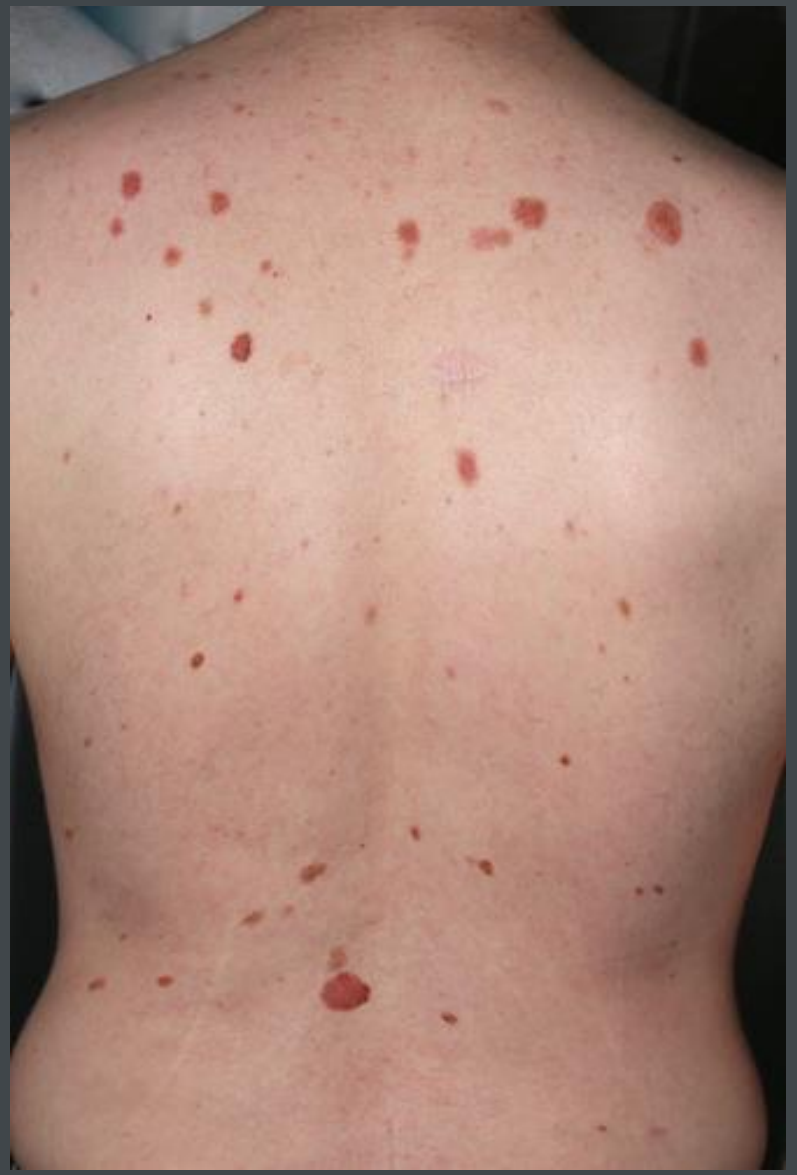
BeatingMelanoma.com





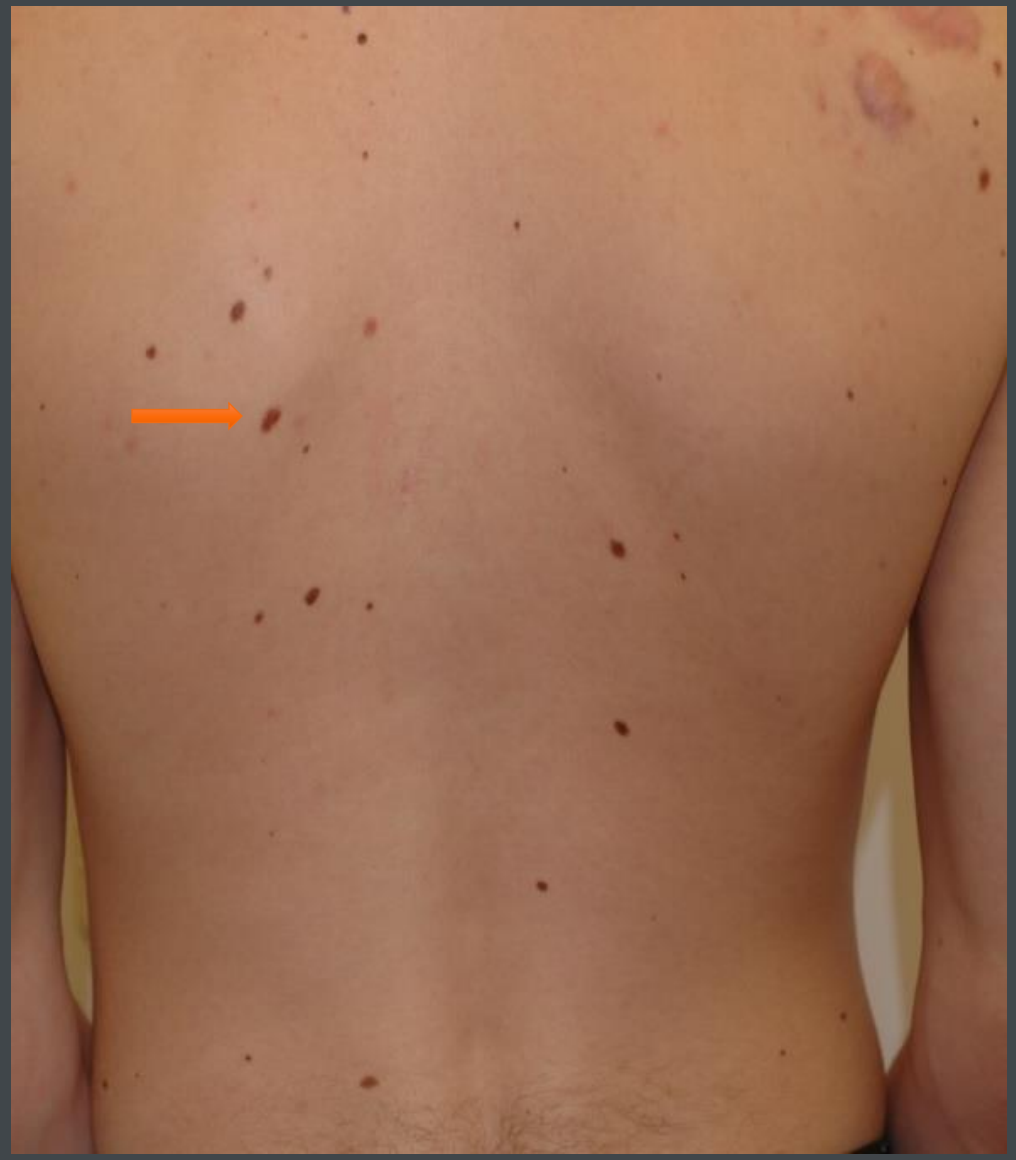
Canfield Scientific Inc.

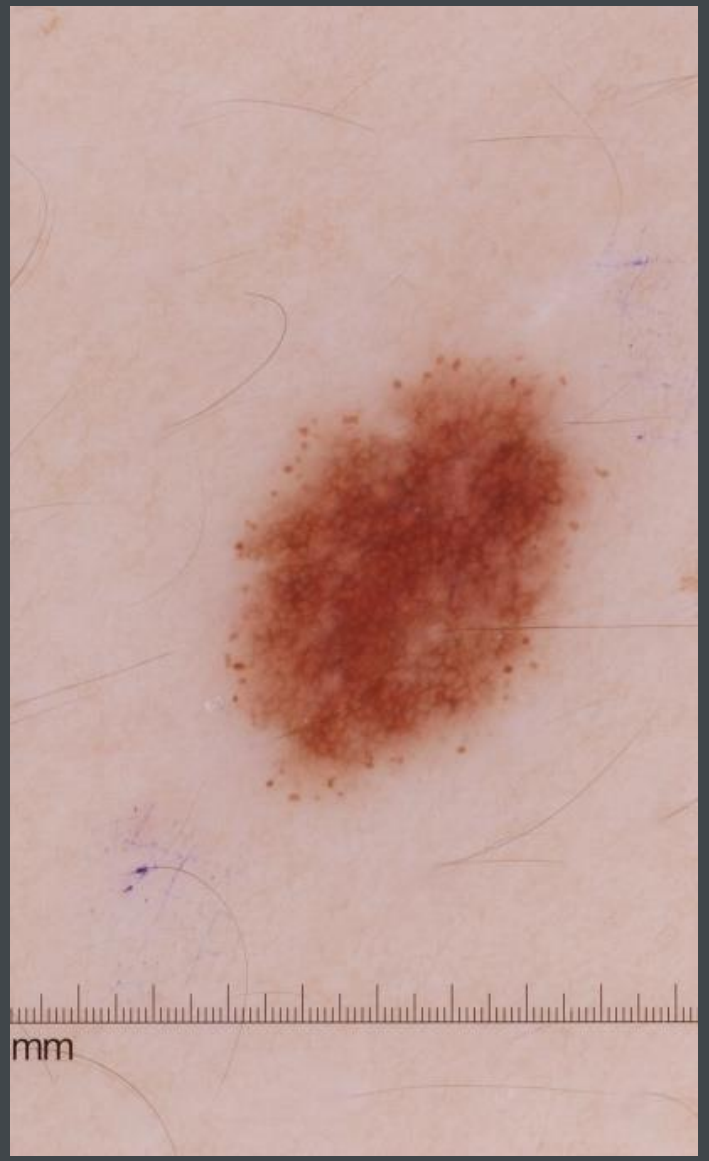
Atypical Nevi.



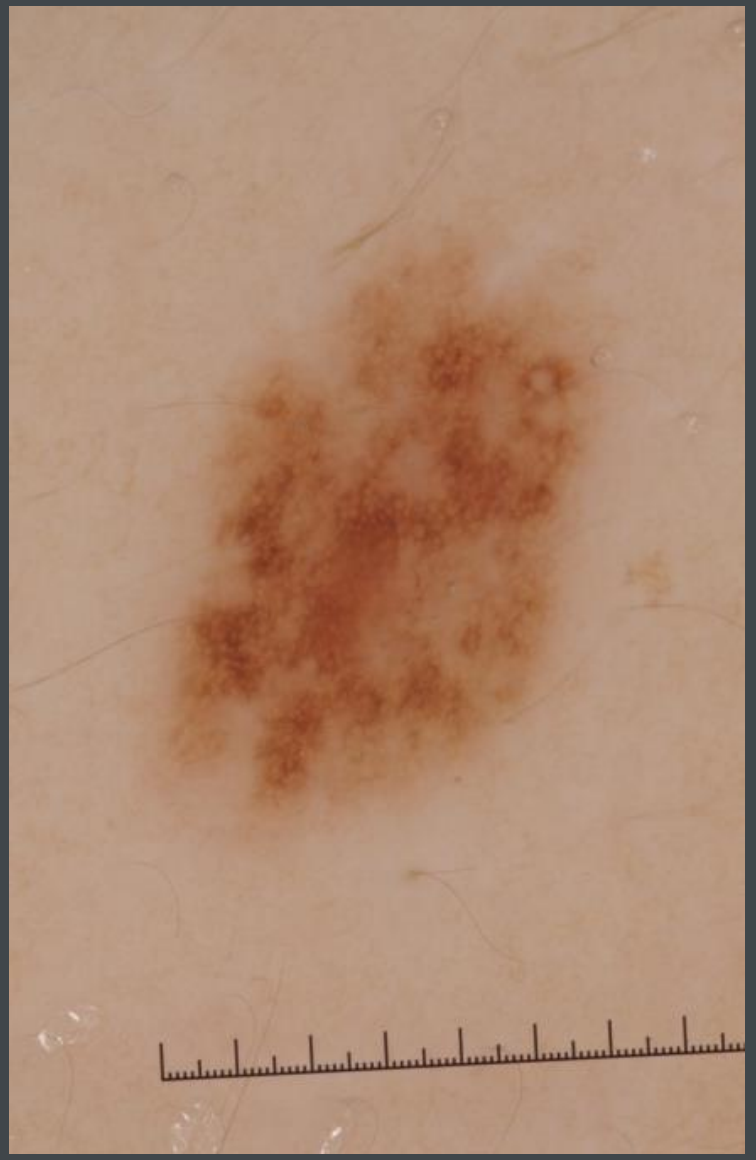
Clinical definition

- Nevus at least 5 mm in size with a flat component
- Two of 3 criteria:
    - Variable pigmentation
    - Irregular asymmetric outline
    - Indistinct borders
- Sun exposure increases number of nevi, especially in kids
- Change in size, shape and dermoscopic pattern



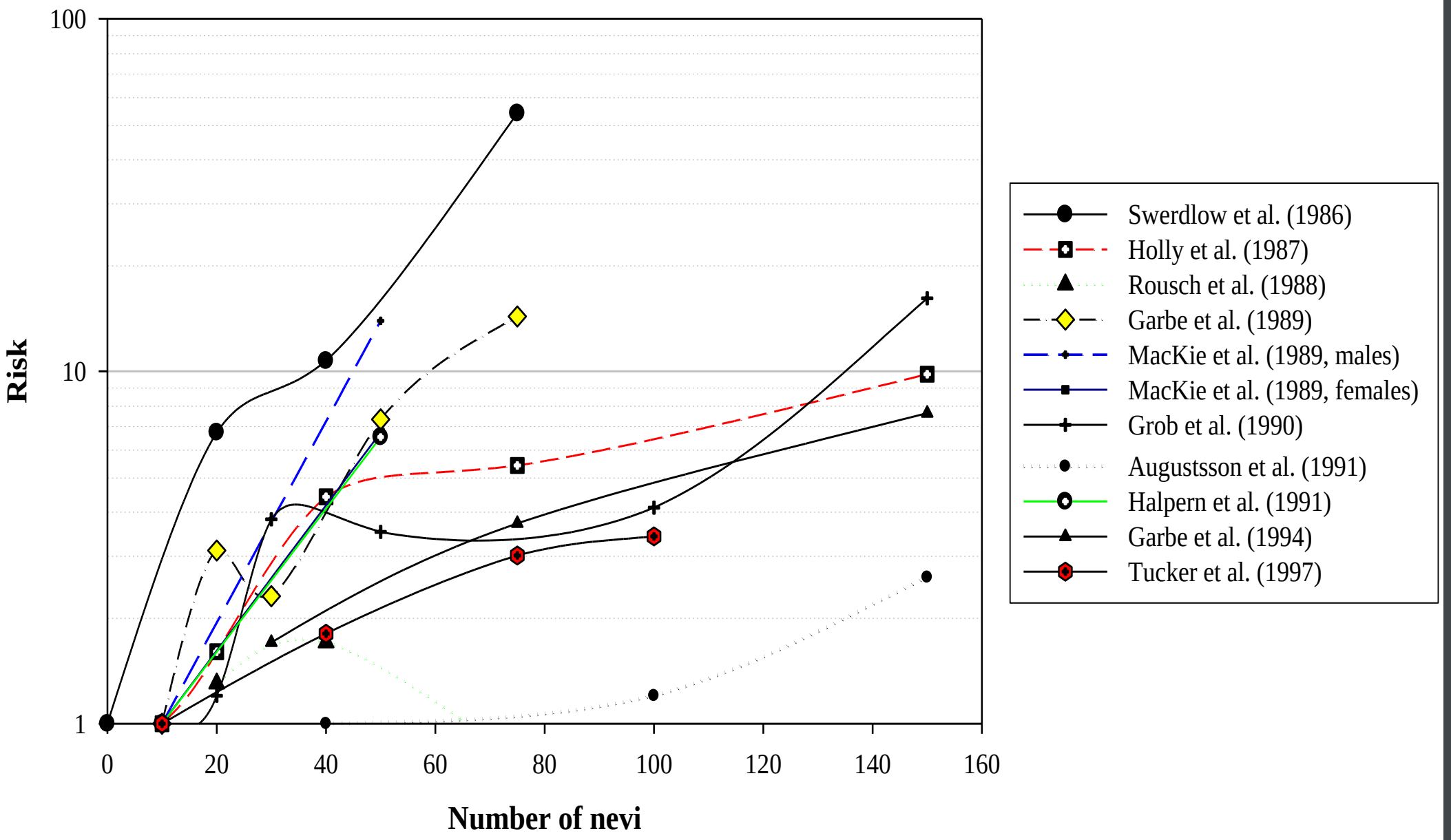


2006

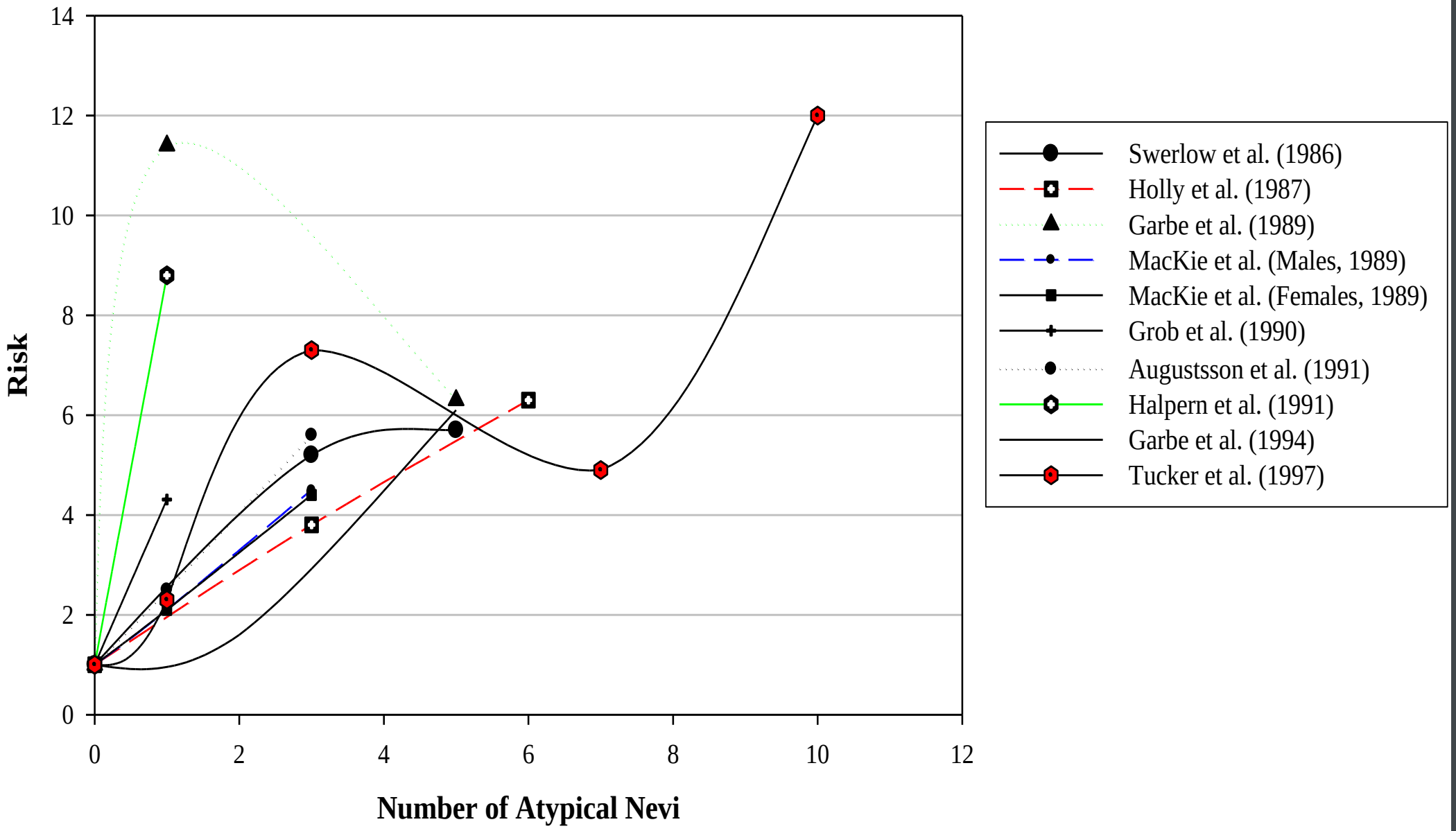


2013

Risk for developing melanoma with increasing number of nevi



Risk for developing melanoma with increasing number of atypical nevi



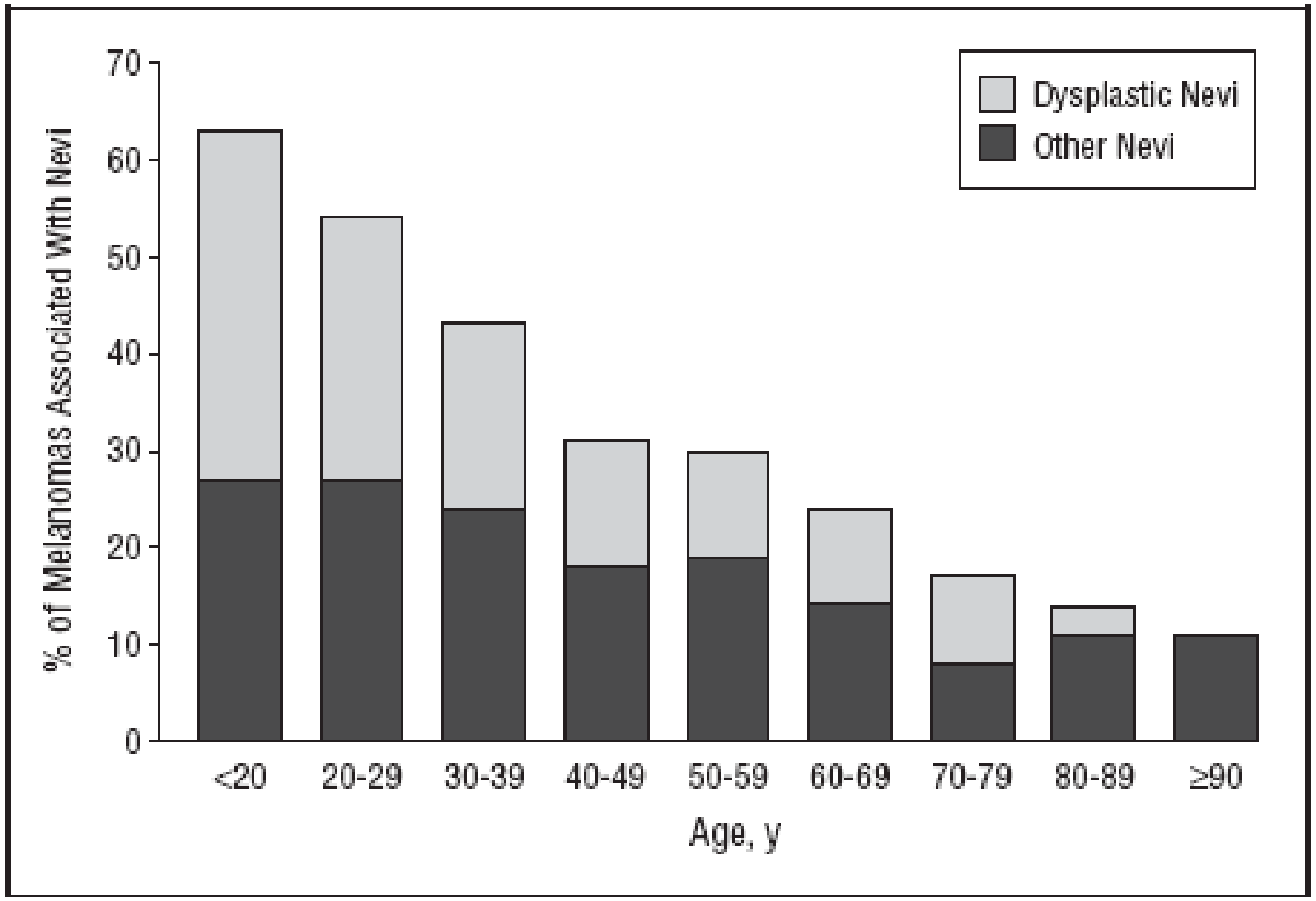


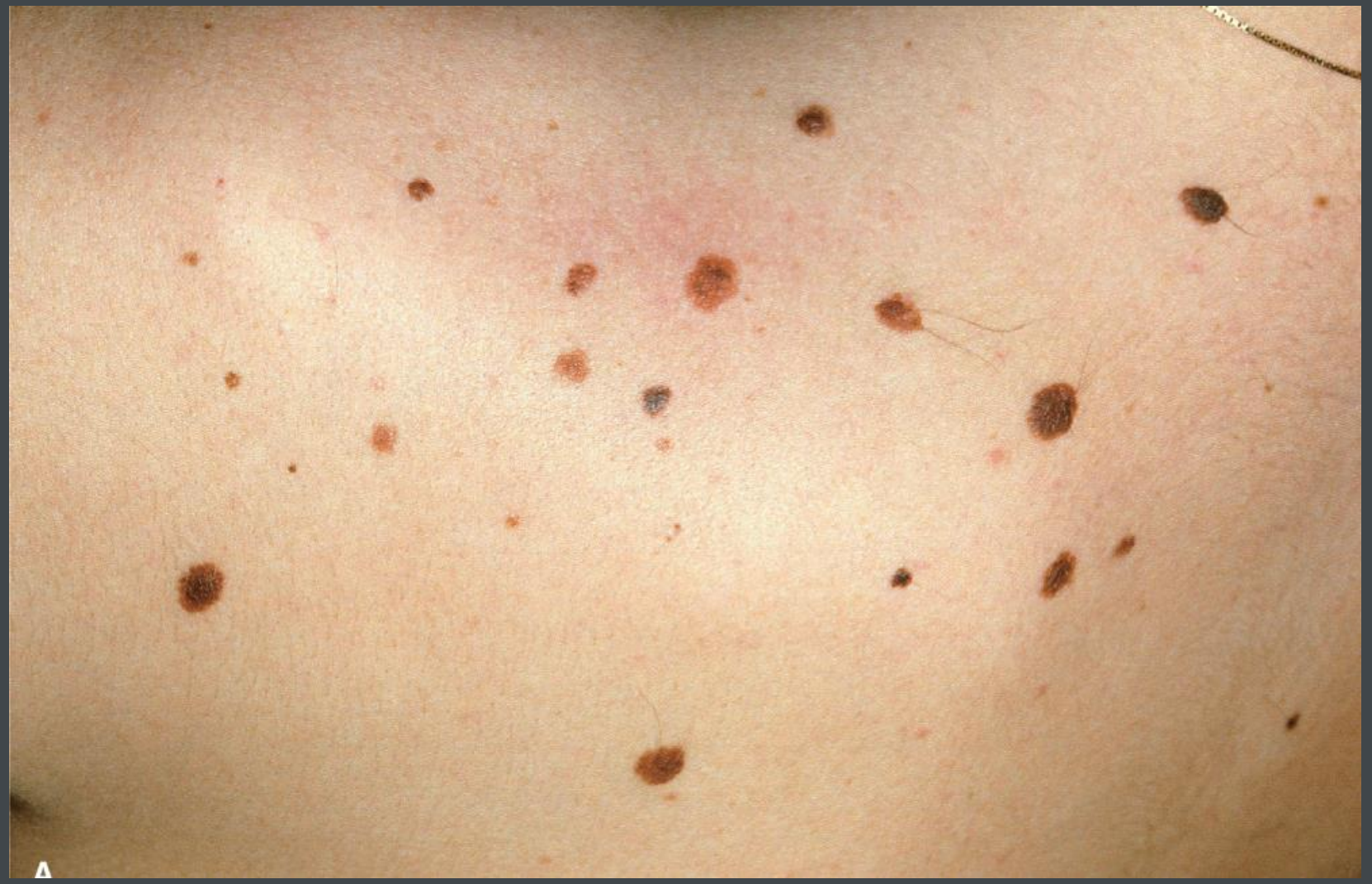
Figure 2. Percentage of melanomas associated with nevi by age group.

Approximately 25% melanomas were histologically associated with nevi

Melanoma-Nevi association decreases with increasing age

Tsao H et al, Arch Dermatol 2003

Atypical Nevi & Melanoma Mimickers:

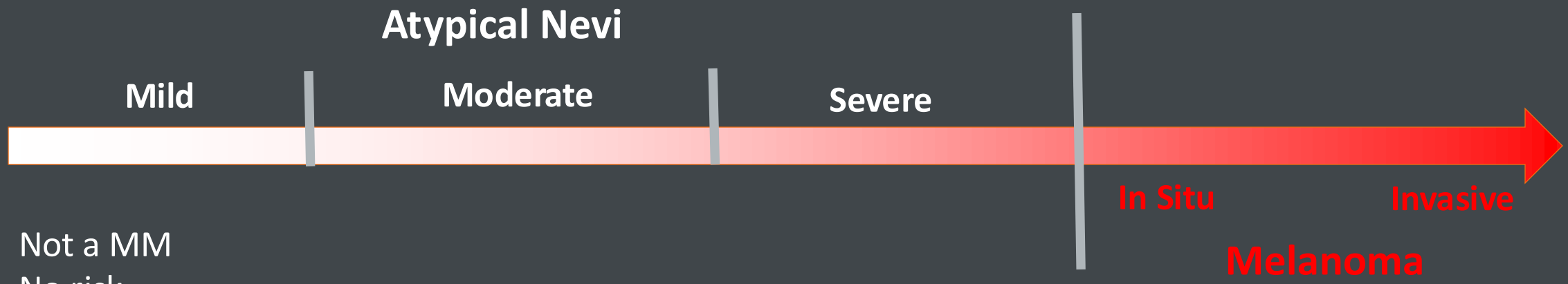


Case #1

- 36. y.o. woman with multiple atypical nevi.
- Biopsy proven atypical nevi with moderate atypia on the right thigh.
- She is very distressed because she was told this was a pre-melanoma.

Pathology Report.

Pathology Report.

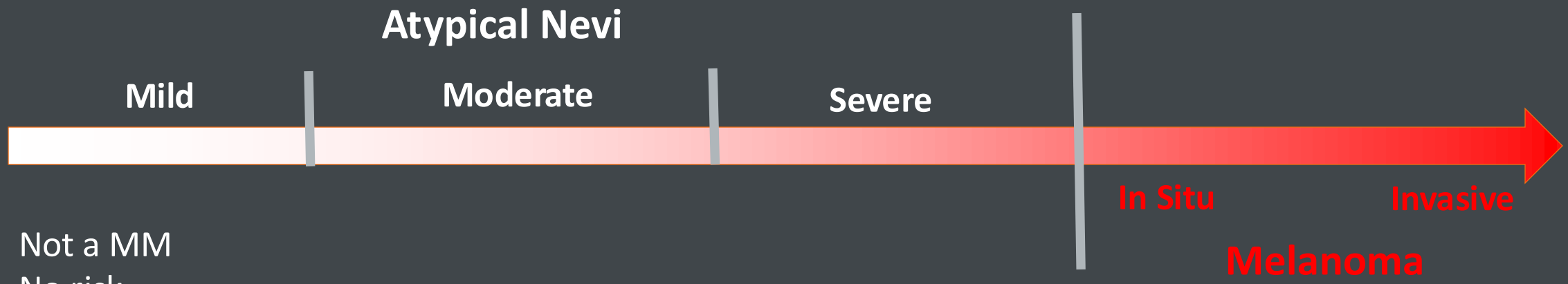


Not a MM
No risk
Watch or excise

Not a MM
No risk
Excise 2-3mm

Not a MM
Risk -> MM if not Rx
Excise 3-5mm

Pathology Report.



Not a MM
No risk
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Not a MM
Risk -> MM if not Rx
Excise 3-5mm

Consultation Highlights:

- Minimize the risk; alleviate fear
- Avoid the phrase “pre-melanoma”
  - connote a sense of inevitability; biological uncertain

Pathology Report.

Path reading:

- “early evolving melanoma in situ cannot be ruled out

Pearls:

- Who is your pathologist? Dermpath or path?
- His/her threshold level
- Over call or under call
- Do not blindly trust the reading

Diagnostic Goals.

1. Detect melanoma at the earliest stage

2. Avoid unnecessary biopsy of mild/mod atypical nevi

Ugly Duckling Sign

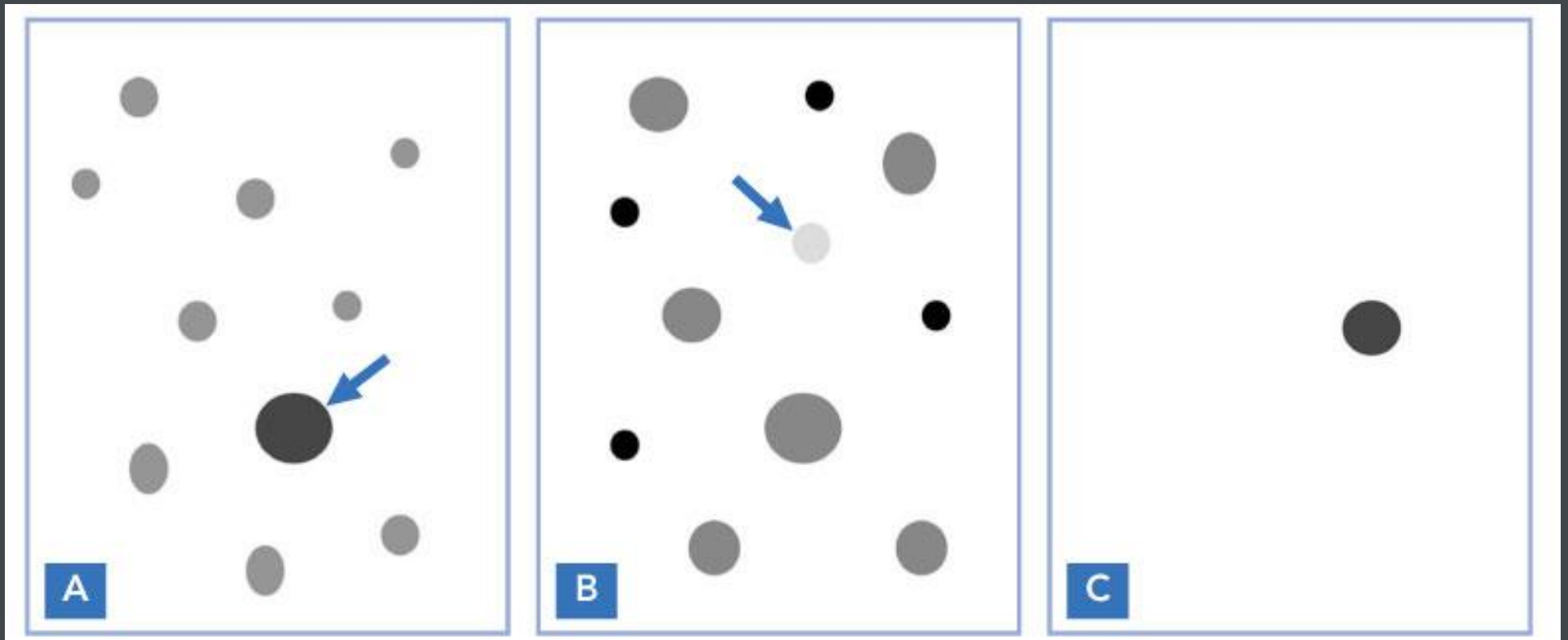
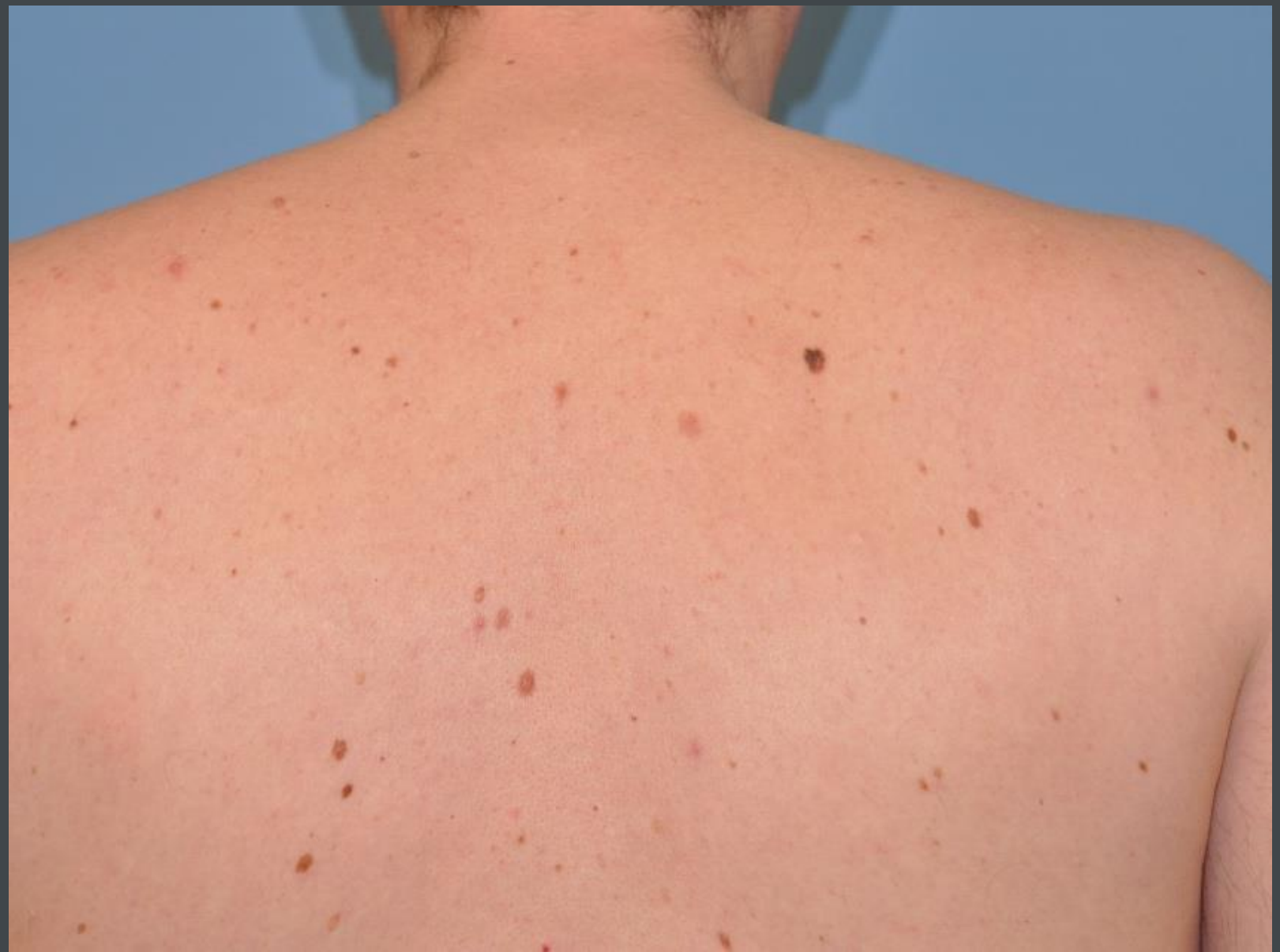
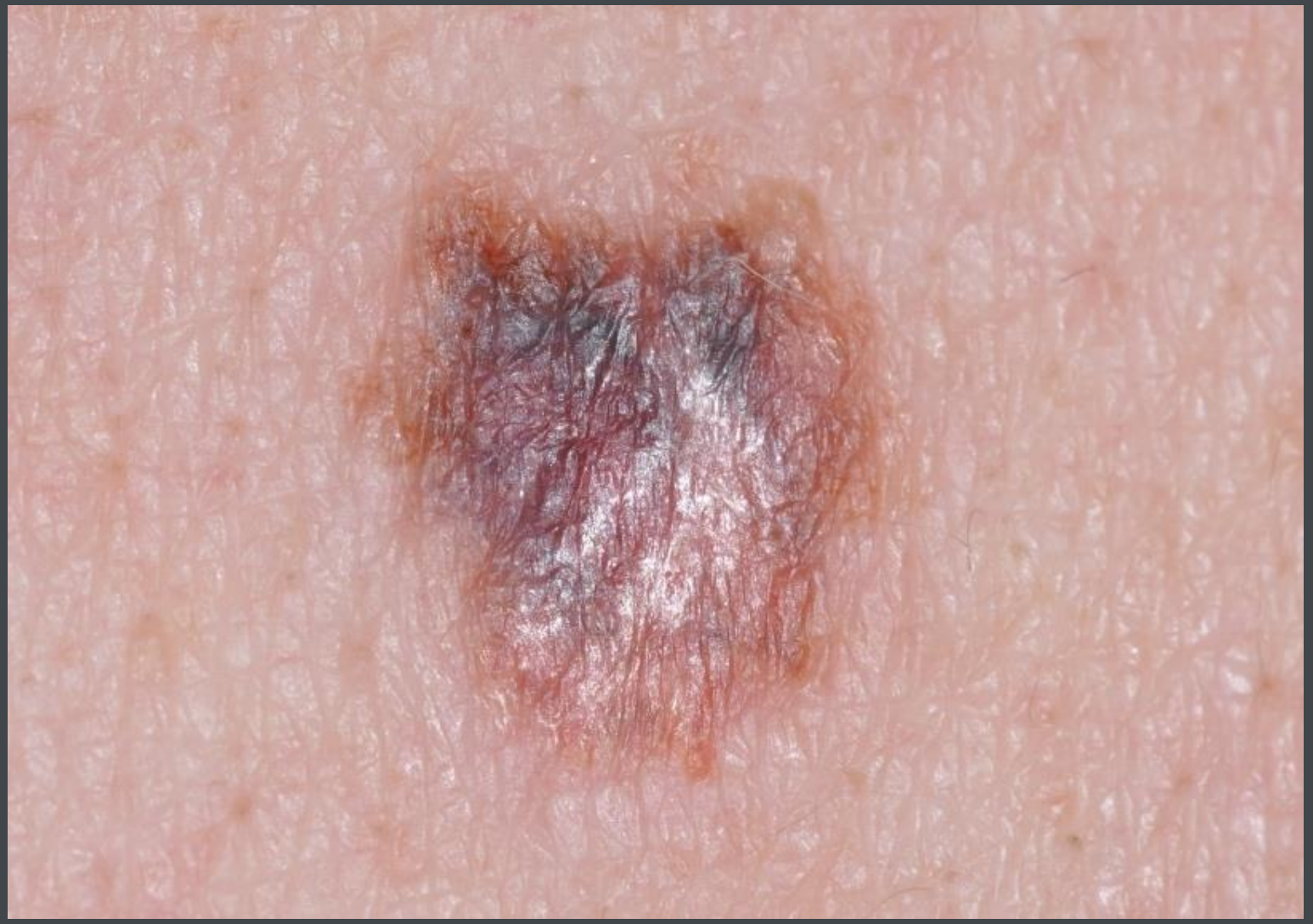


Figure 1. Three Examples of an Ugly Duckling

Ugly Duckling Sign



Ugly Duckling Sign



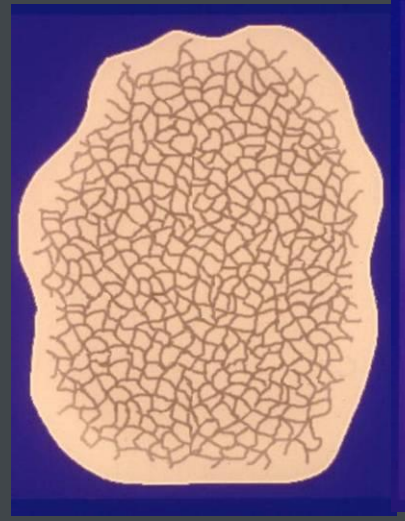
Dermoscopy.

- Increases diagnostic accuracy of clinical exam[2]
  - Sensitivity increases ~ 20% with no loss of specificity[3]
- Rapid; increases total skin exam by only 72 seconds[4]

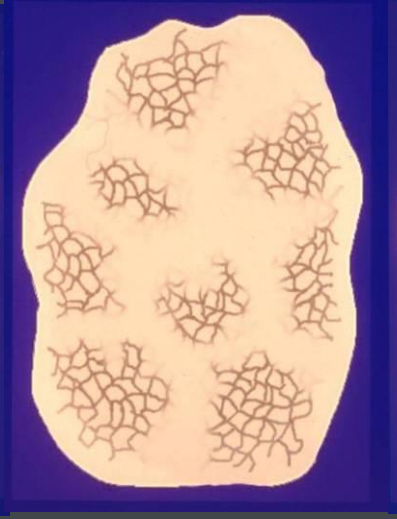
2. H. Kittler, H. Pehamberger, K. Wolff, *et al.* Diagnostic accuracy of dermoscopy Lancet Oncol, 3 (2002), pp. 159–165
3. Vestergaard ME, Macaskill P, Holt PE, Menzies SW. Dermoscopy compared with naked eye examination for the diagnosis of primary melanoma: a meta analysis of studies performed in a clinical setting. The British journal of dermatology 2008;159:669-76.
4. Zalaudek I, Kittler H, Marghoob AA, Balato A, et al. Time required for a complete skin examination with and without dermoscopy: a prospective, randomized multicenter study. Archives of dermatology 2008;144:509-13.

Atypical Nevi

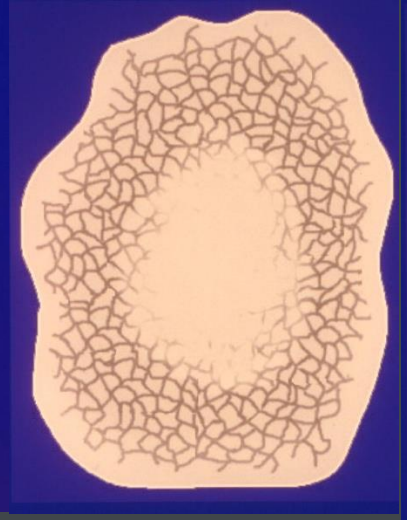
Mild — Moderate



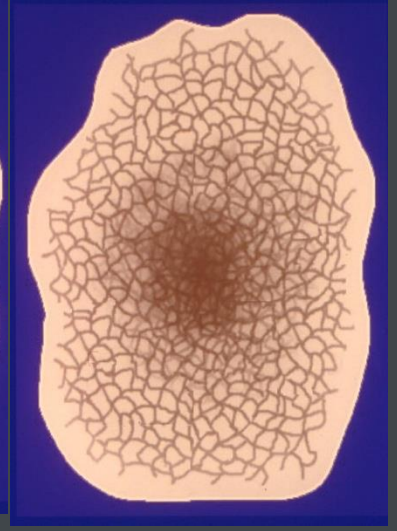
Diffuse Reticular



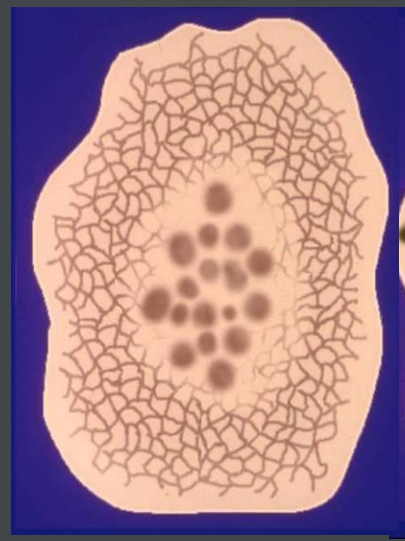
Patchy Reticular



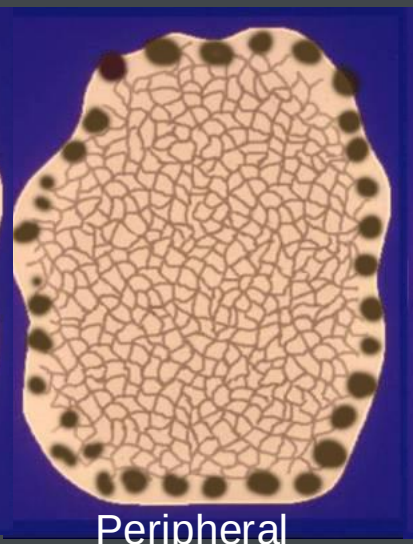
Peripheral Reticular & central hypopigmentation



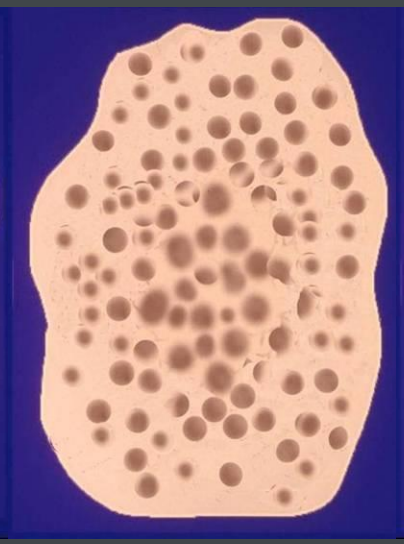
Peripheral Reticular & central hyperpigmentation (blotch)



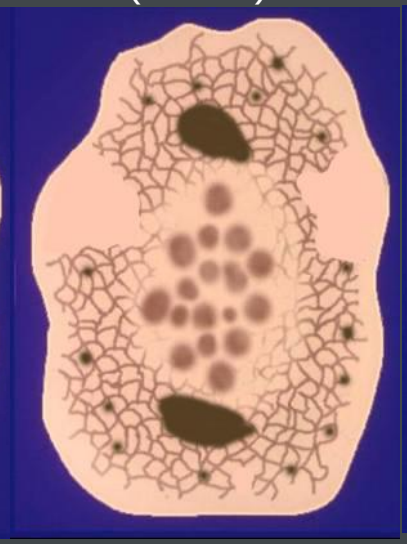
Peripheral Reticular & central globules



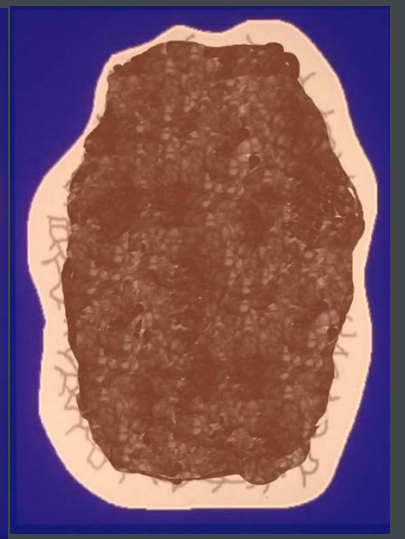
Peripheral globules & central reticular (includes starburst)



Globular (includes cobblestone)



Multi-component (symmetric!)

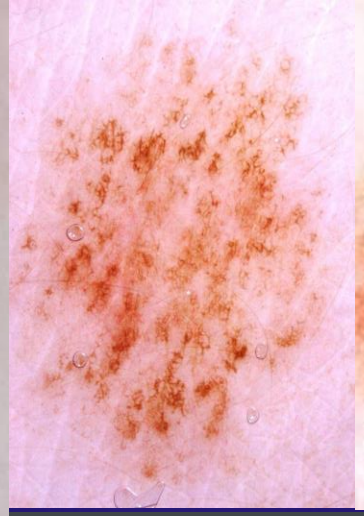


Structureless (homogeneous)

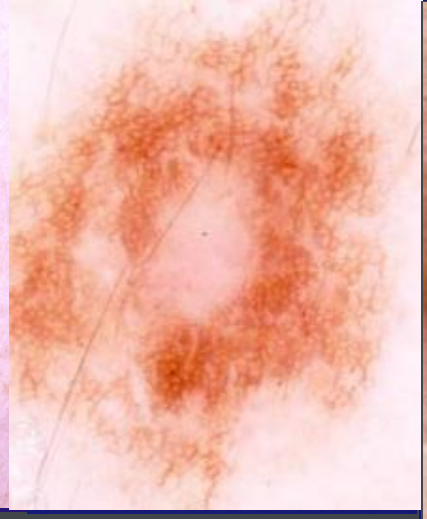
Atypical Nevi

Mild Moderate

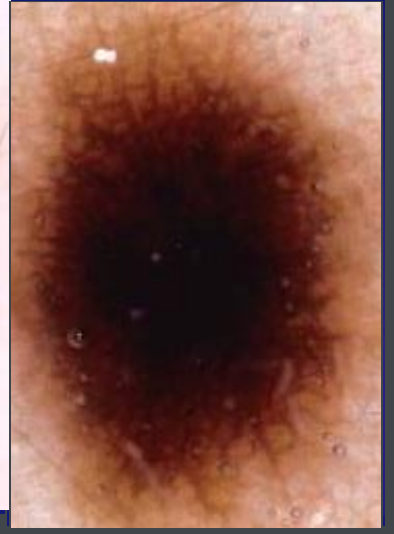
Diffuse Reticular



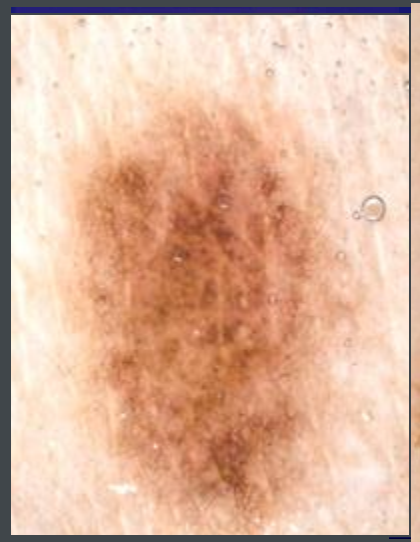
Patchy Reticular



Peripheral Reticular & central hypopigmentation

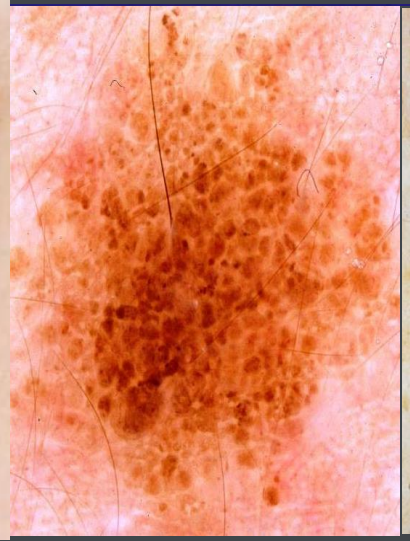


Peripheral Reticular & central hyperpigmentation (blotch)

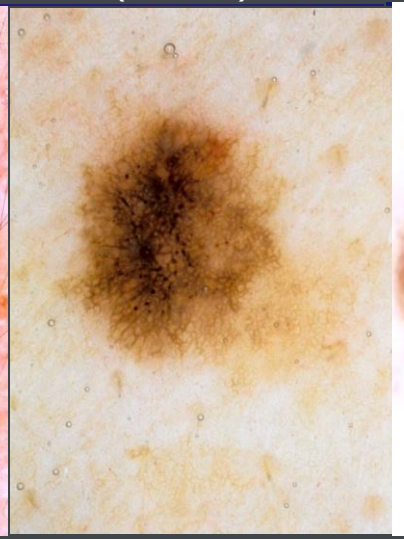


Peripheral Reticular & central globules

globules & central reticular (includes starburst)

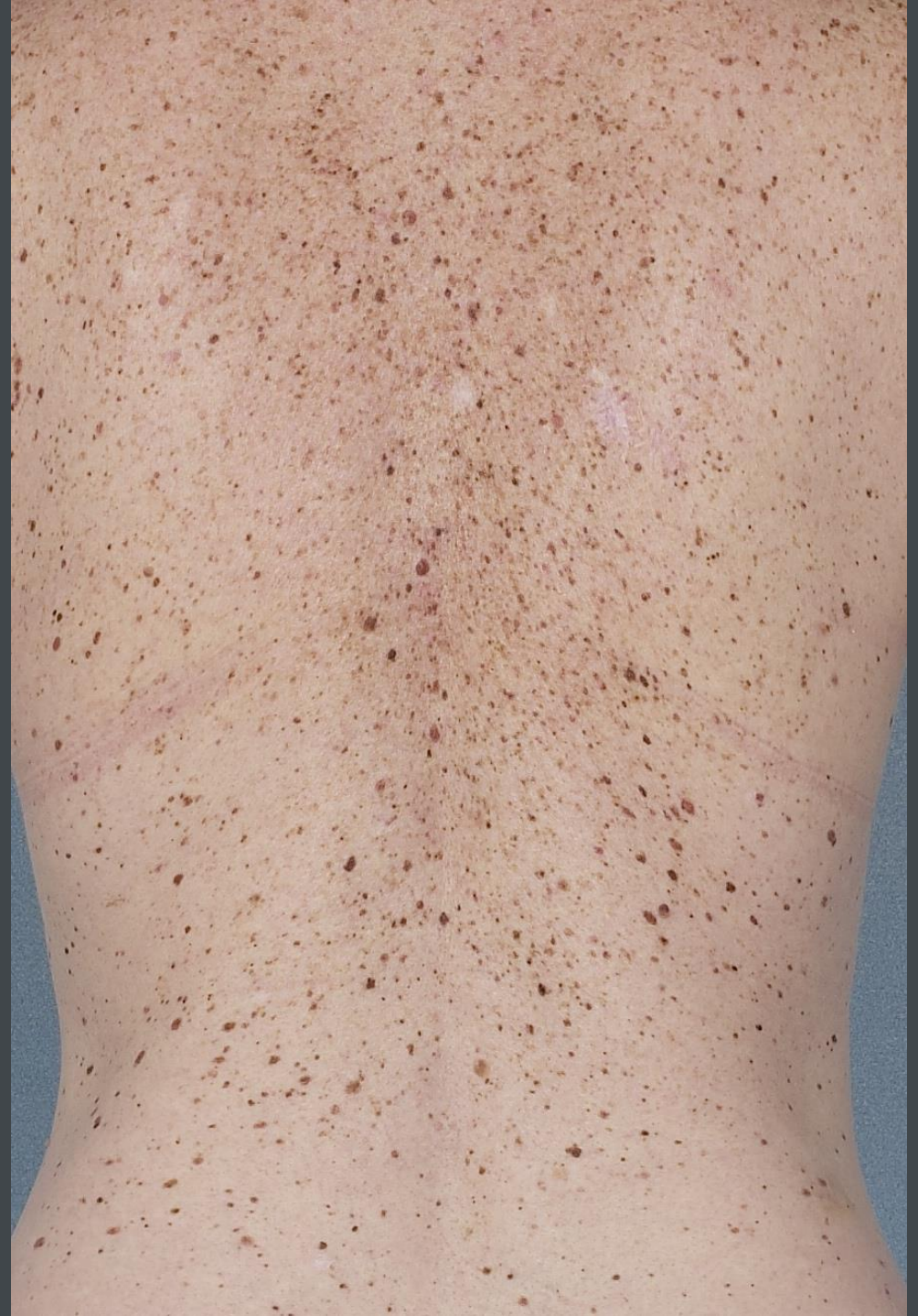


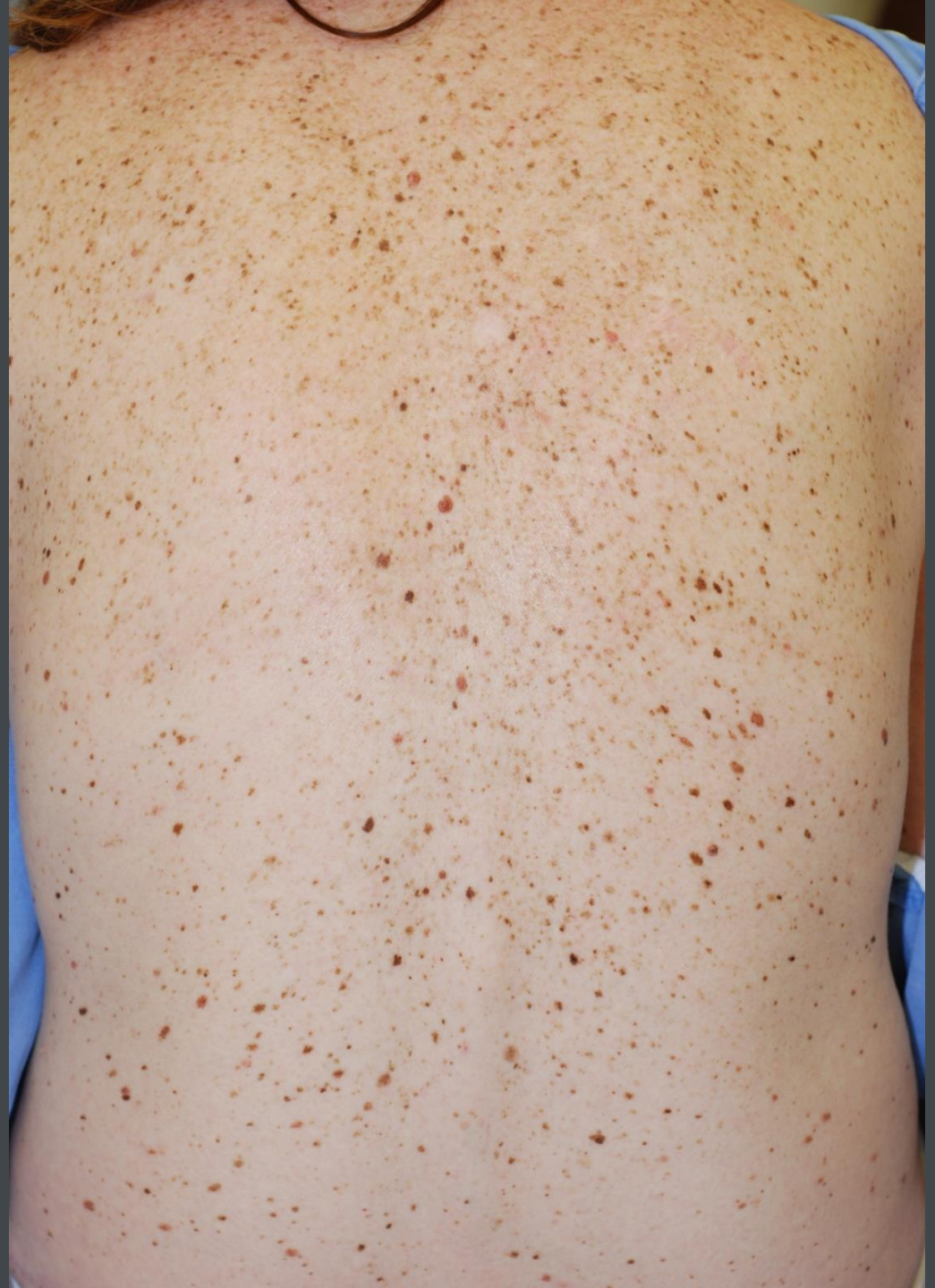
Globular (includes cobblestone)

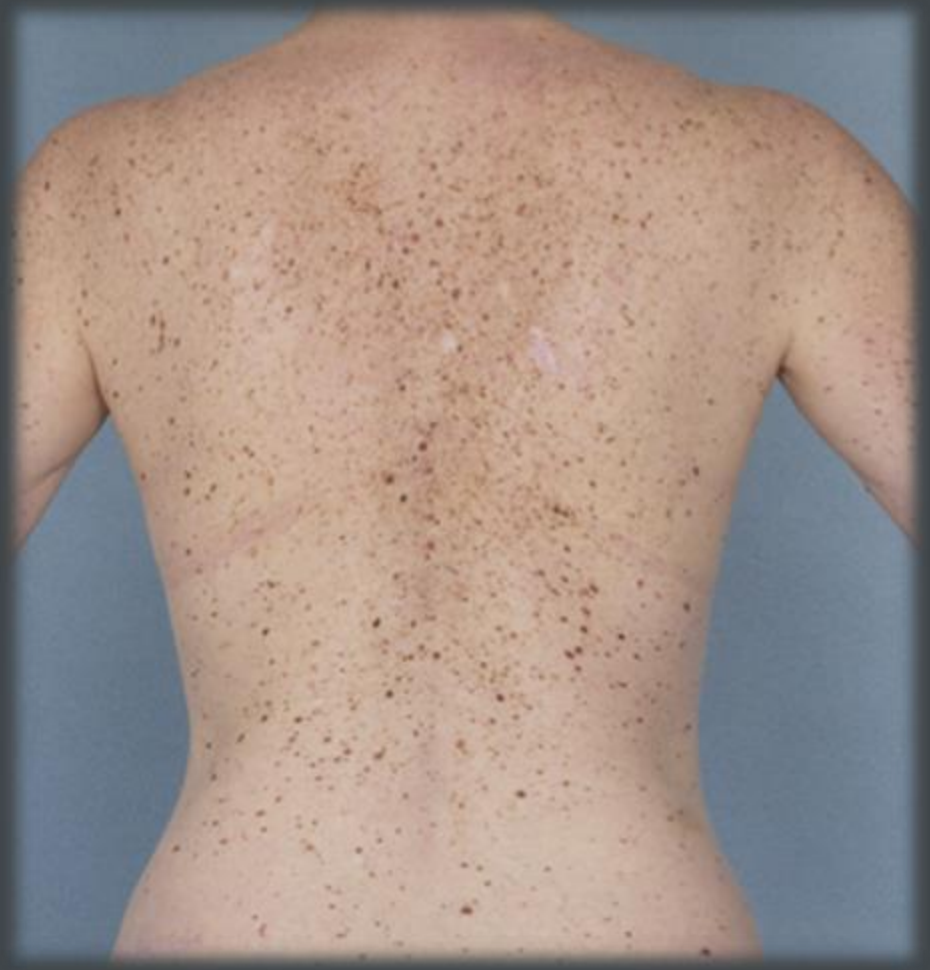


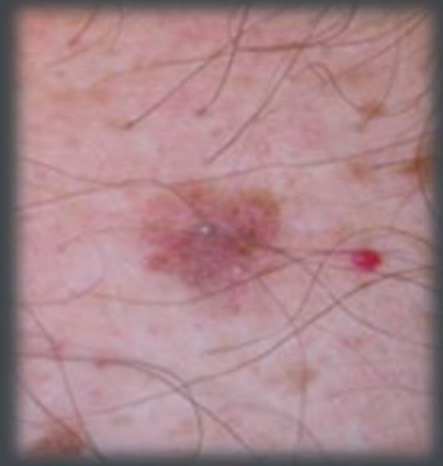
Multi-component (symmetric!)

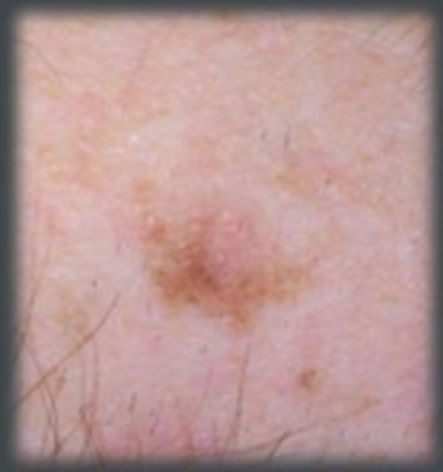
Structureless (homogeneous)











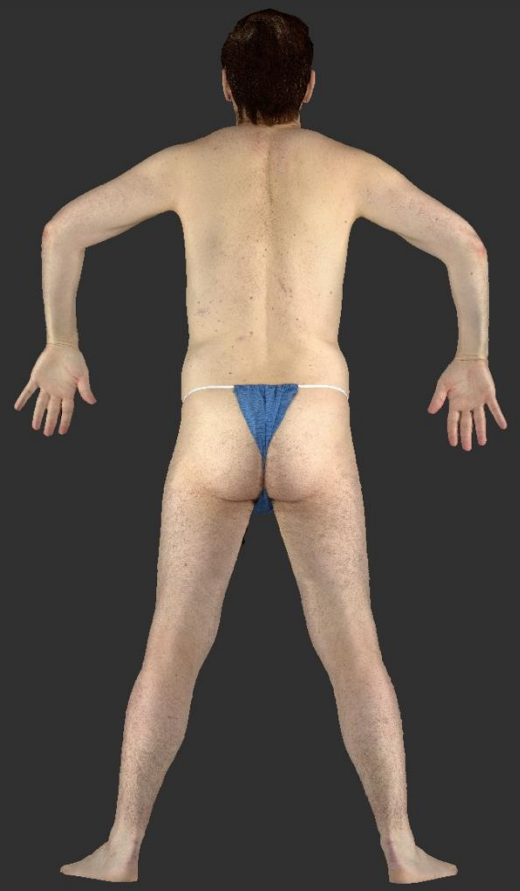
Challenge.

High Risk Melanoma Patients

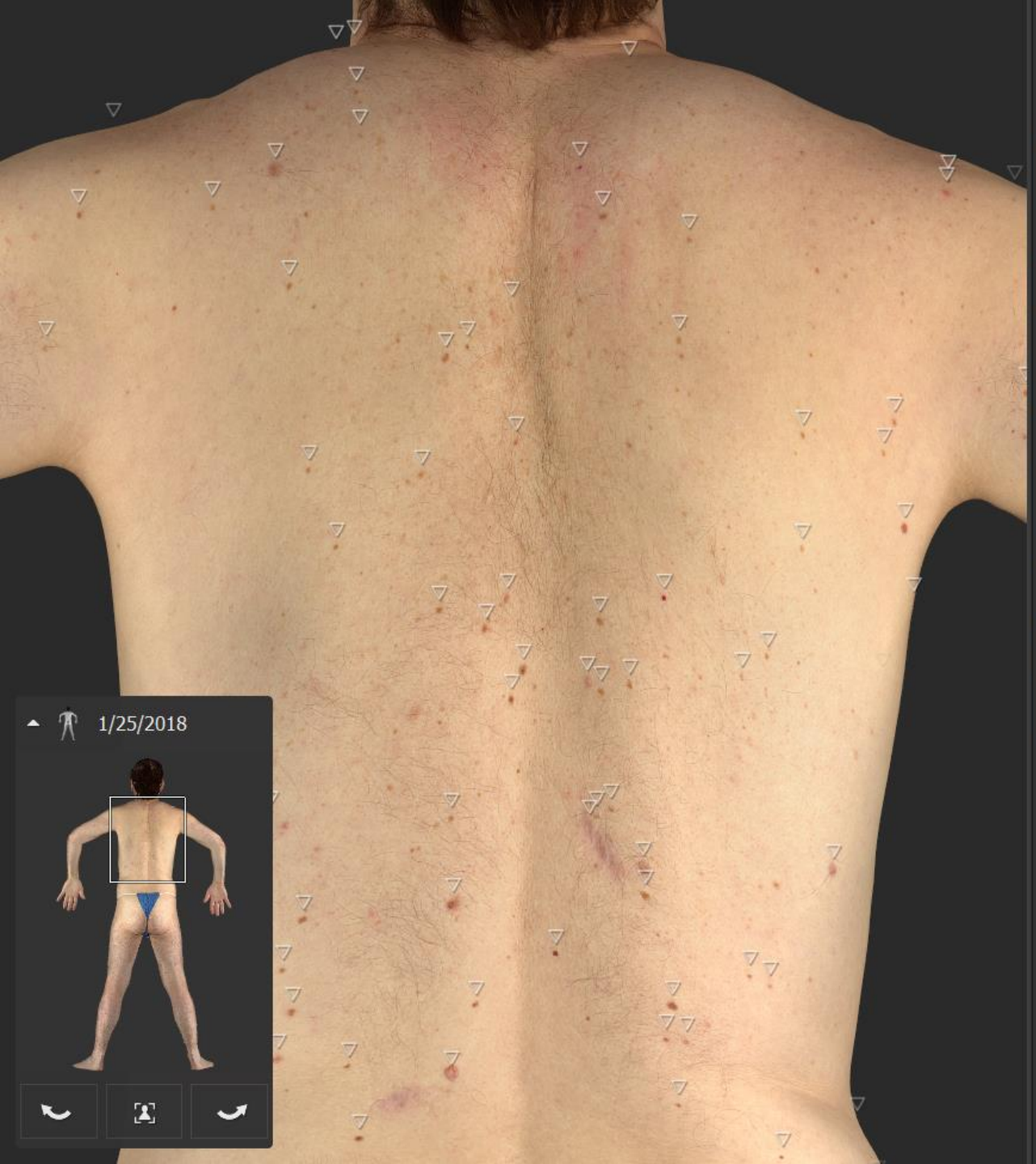
Solution.

VECTRA 3D
Whole Body
Imaging System

3D Full Avatar.



Criteria-Based Lesion Selection.



sort by: Longest Dia

single timepoint

Longest Diameter [mm]

2 4.7 7.4

Contrast

4.5 10.1 15.6

Border Irregularity

1 4.9 8.8

Color Variation

0 5 10

Hue

39 53.9 68.7

Nevus Confidence

0 50 100

Anatomic Site All

filter templates:

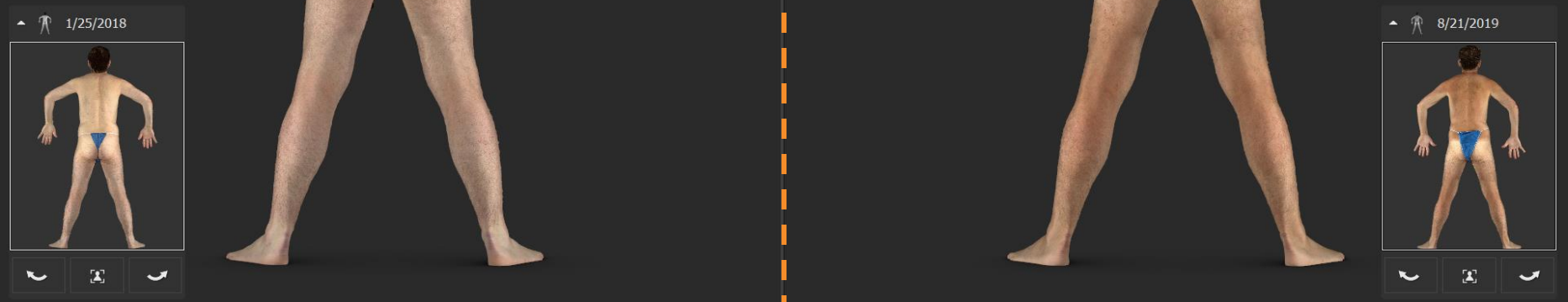
Show All

309
LESIONS

Sequential Imaging & Lesion Tracking.

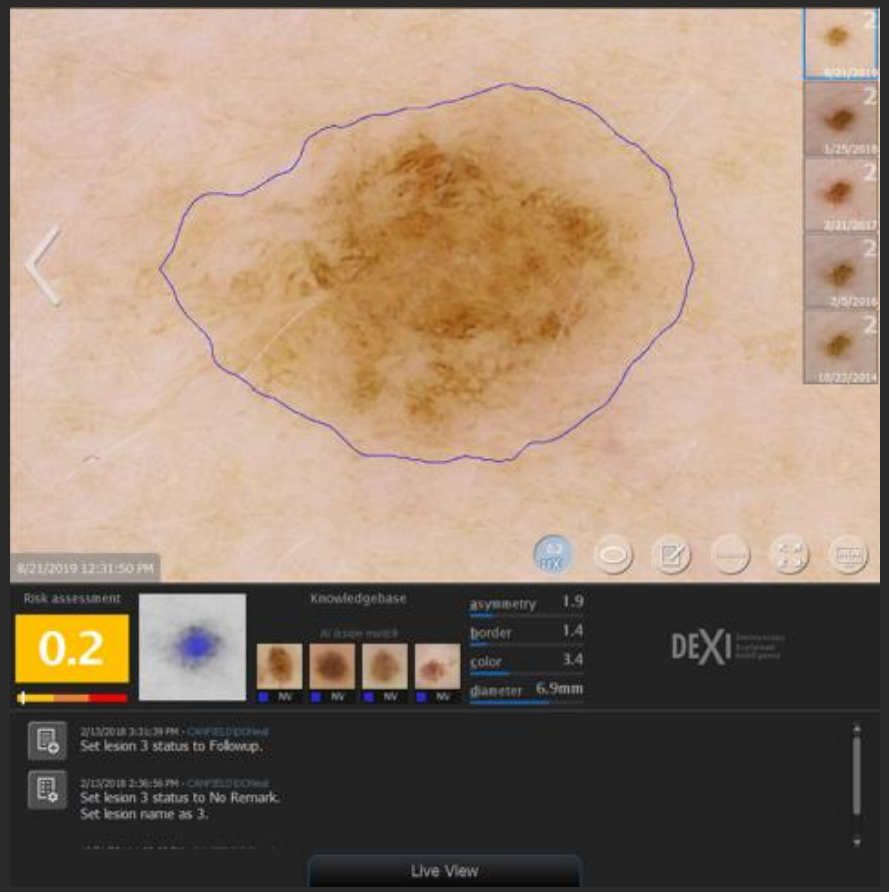
First Encounter

Second Encounter



Compare two encounters side-by-side

AI-Assisted Diagnosis*



*Research Phase

*Research Phase

3D Whole-body skin imaging for automated melanoma detection

Abstract

Background: Existing artificial intelligence for melanoma detection has relied on analysing images of lesions of clinical interest, which may lead to missed melanomas. Tools analysing the entire skin surface are lacking.

Objectives: To determine if melanoma can be distinguished from other skin lesions using data from automated analysis of 3D-images.

Methods: Single-centre, retrospective, observational convenience sample of patients diagnosed with melanoma at a tertiary care cancer hospital. Eligible participants were those with a whole-body 3D-image captured within 90 days prior to the diagnostic skin biopsy. 3D-images were obtained as standard of care using VECTRA WB360 Whole Body 3-dimensional Imaging System (Canfield Scientific). Automated data from image processing (i.e. lesion size, colour, border) for all eligible participants were exported from VECTRA DermaGraphix research software for analysis. The main outcome was the area under the receiver operating characteristic curve (AUC).

Results: A total of 35 patients contributed 23,538 automatically identified skin lesions >2 mm in largest diameter (102–3021 lesions per participant). All were White patients and 23 (66%) were males. The median (range) age was 64 years (26–89). There were 49 lesions of melanoma and 22,489 lesions that were not melanoma. The AUC for the prediction model was 0.94 (95% CI: 0.92–0.96). Considering all lesions in a patient-level analysis, 14 (28%) melanoma lesions had the highest predicted score or were in the 99th percentile among all lesions for an individual patient.

Conclusions: In this proof-of-concept pilot study, we demonstrated that automated analysis of whole-body 3D-images using simple image processing techniques can discriminate melanoma from other skin lesions with high accuracy. Further studies with larger, higher quality, and more representative 3D-imaging datasets would be needed to improve and validate these results.

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TABLE 1 Prediction model variables and their individual ability to discriminate melanoma from non-melanoma lesions.

Variable internal software name	Morphological category	Variable description	ROC area	SE	95% CI	
					Lower	Upper
areaMM2	Size	Area of the lesion	0.8600	0.0361	0.78933	0.93076
minorAxisMM	Size	Smallest diameter of the lesion	0.8712	0.0322	0.80811	0.93425
norm_colour	Colour	Colour variation in the lesion	0.8349	0.0349	0.76653	0.90324
radial_colour_std_max	Colour	Measure of colour asymmetry in the lesion	0.8242	0.0354	0.75486	0.8936
deltaA	Colour	Average contrast in the CIELAB a* channel between the lesion and surrounding skin	0.5239	0.0487	0.42832	0.61942
deltaB	Colour	Average contrast in the CIELAB b* channel between the lesion and surrounding skin	0.7762	0.0308	0.71585	0.83656
deltaL	Colour	Average contrast in the CIELAB L* channel (lightness) between the lesion and surrounding skin	0.7626	0.0372	0.68965	0.83547
deltaLB	Colour	Average contrast in the CIELAB L* and b* channels between the lesion and surrounding skin	0.7617	0.0371	0.68912	0.83437
stdLExt	Colour	Variation in lightness of the surrounding skin	0.7245	0.0365	0.65304	0.79605
area_perim_ratio	Border	Jaggedness of the lesion border	0.6804	0.0391	0.60368	0.75702
symm_2axis_angle	Border	Border asymmetry angle	0.5465	0.0434	0.46146	0.63147
locs1	Anatomic site	Head/neck anatomic site	0.5764	0.028	0.52166	0.63123
locs2	Anatomic site	Anterior torso anatomic site	0.5272	0.0326	0.46327	0.59119
locs3	Anatomic site	Posterior torso anatomic site	0.5531	0.028	0.49823	0.60793
locs4	Anatomic site	Upper extremity anatomic site	0.5216	0.0237	0.47513	0.56799
locs5	Anatomic site	Lower extremity anatomic site	0.5222	0.0301	0.46307	0.58125
Prediction model	NA	NA	0.9399	0.0117	0.9169	0.9629

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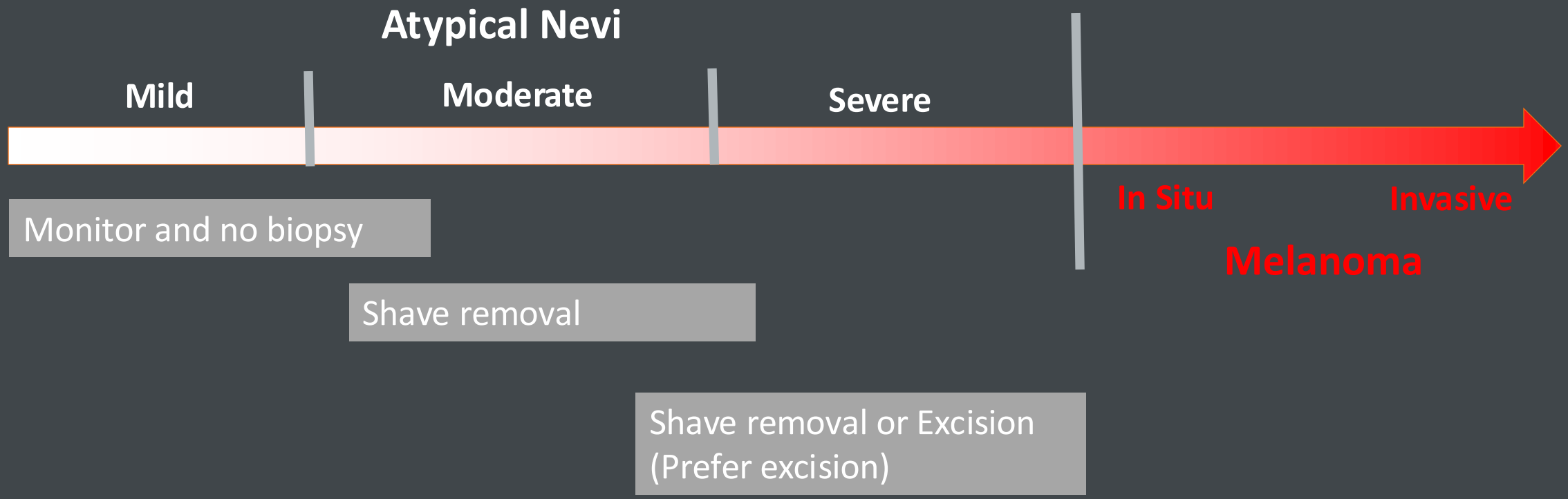
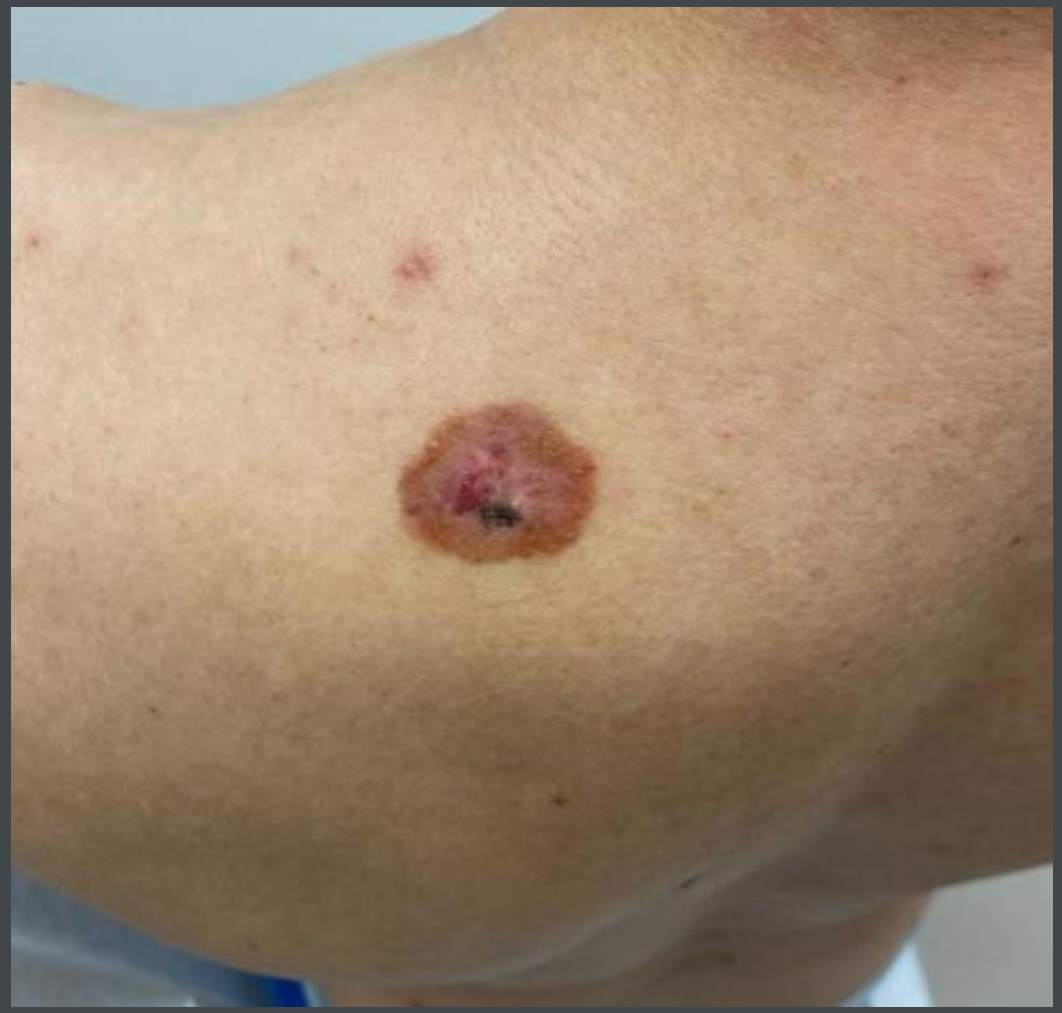
What & How To Biopsy

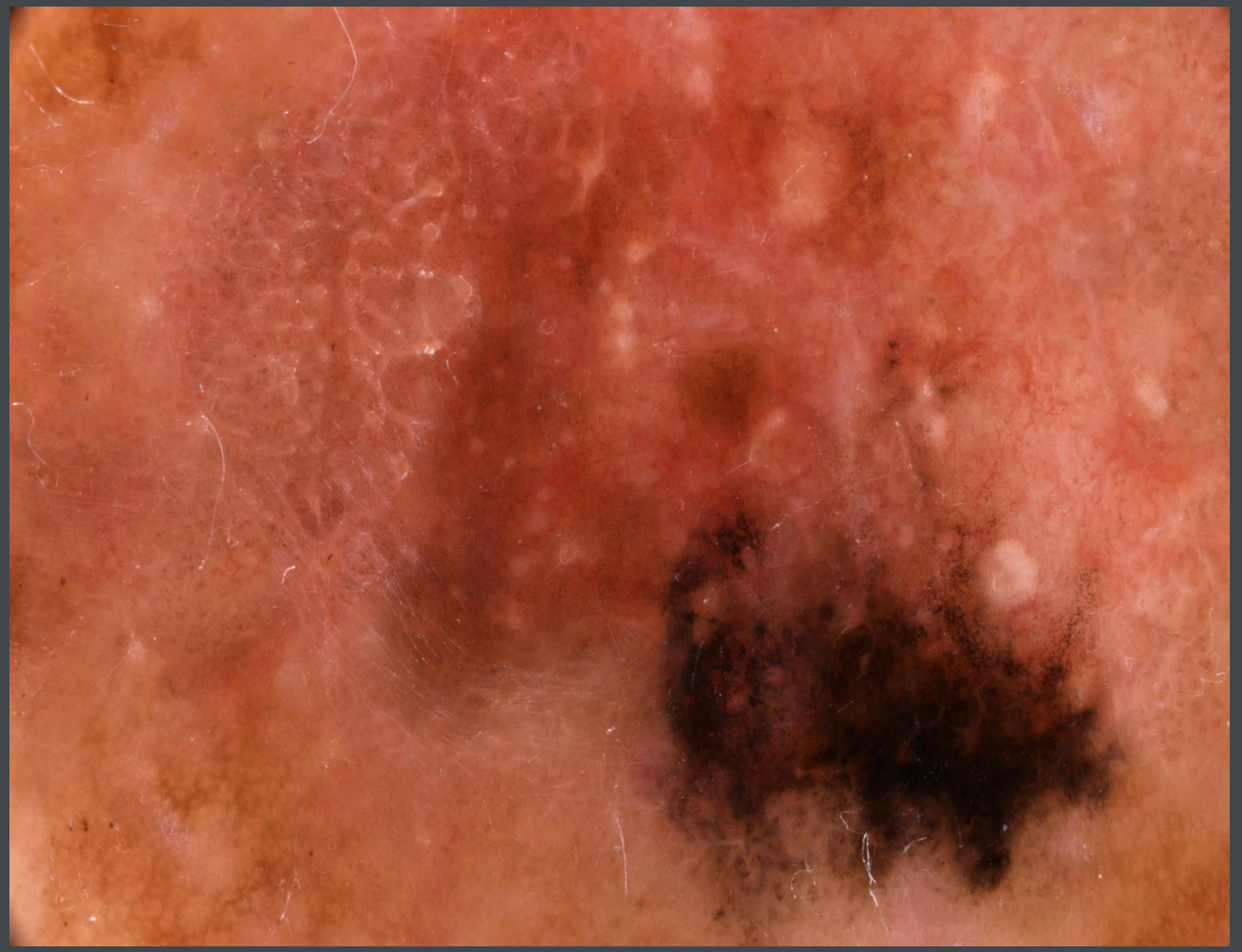


Clinical Pearls:

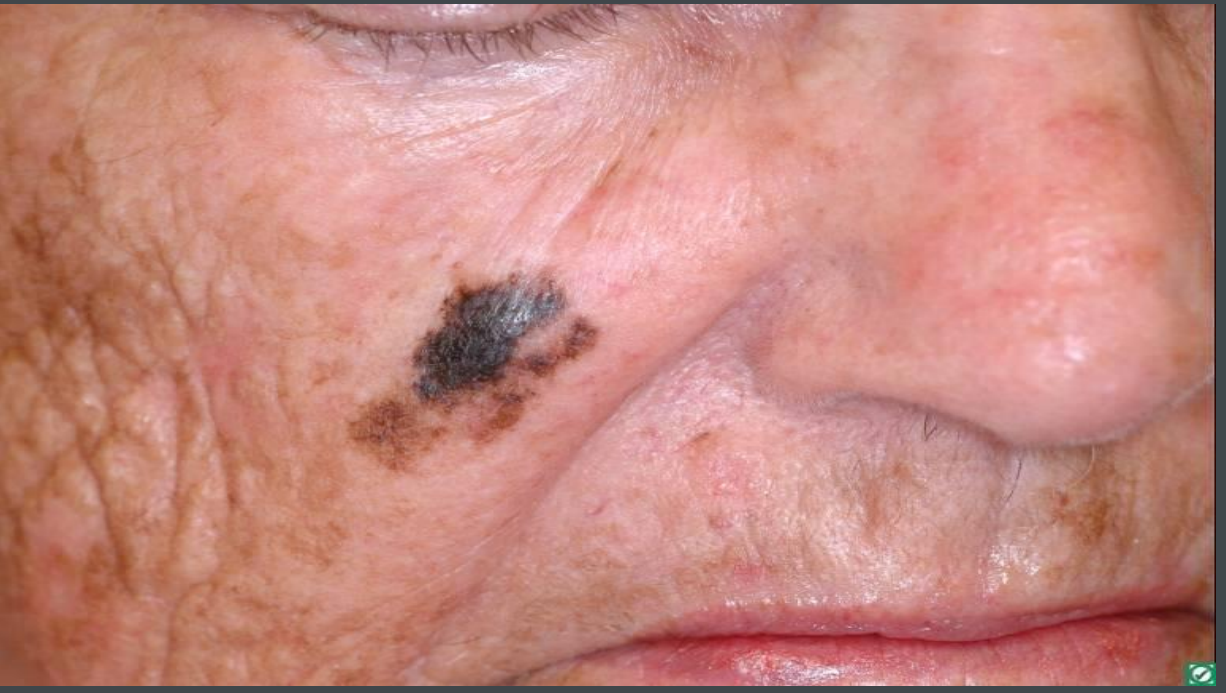
- Avoid partial biopsy
- Shave >> punch
- For large lesions, sample the most concerning area under dermoscopy exam
- Choice of procedure depends in part of the patients (e.g., compliance, age, location)

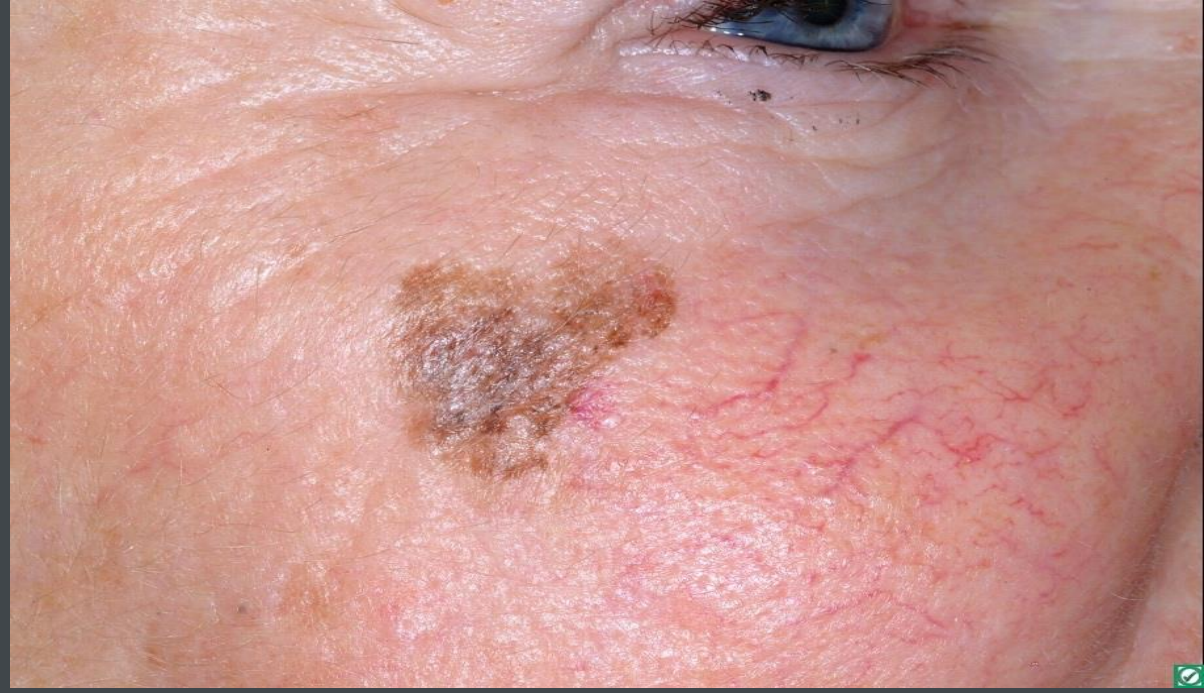


Clinical
(>3cm)

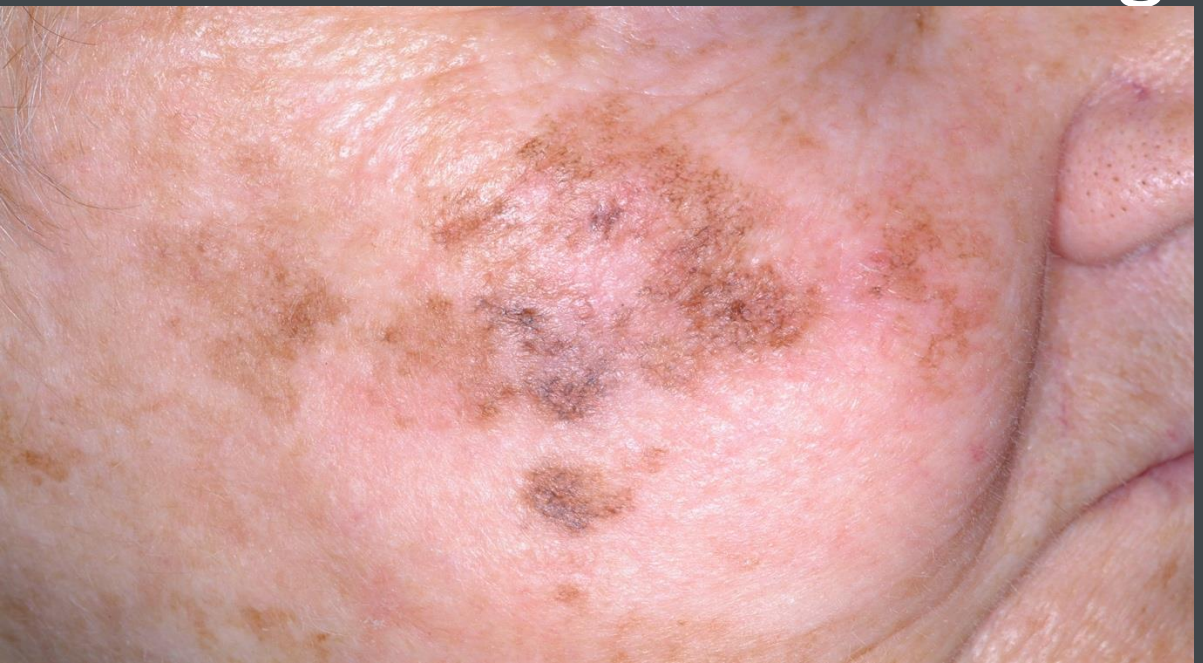


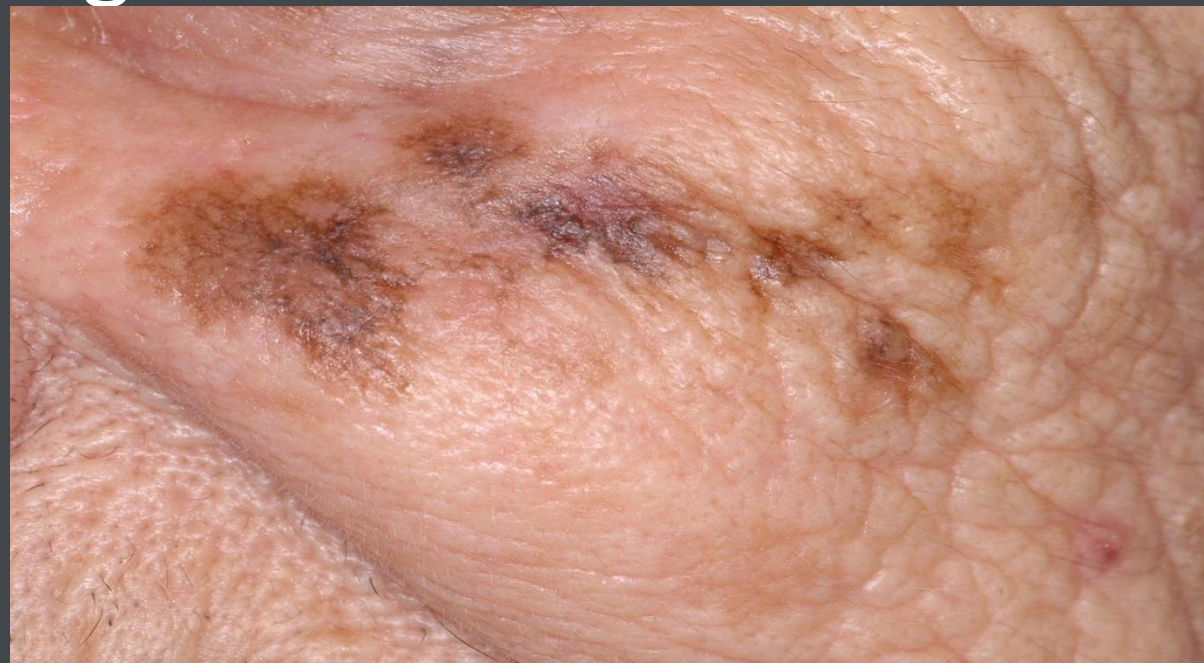
Dermoscopy



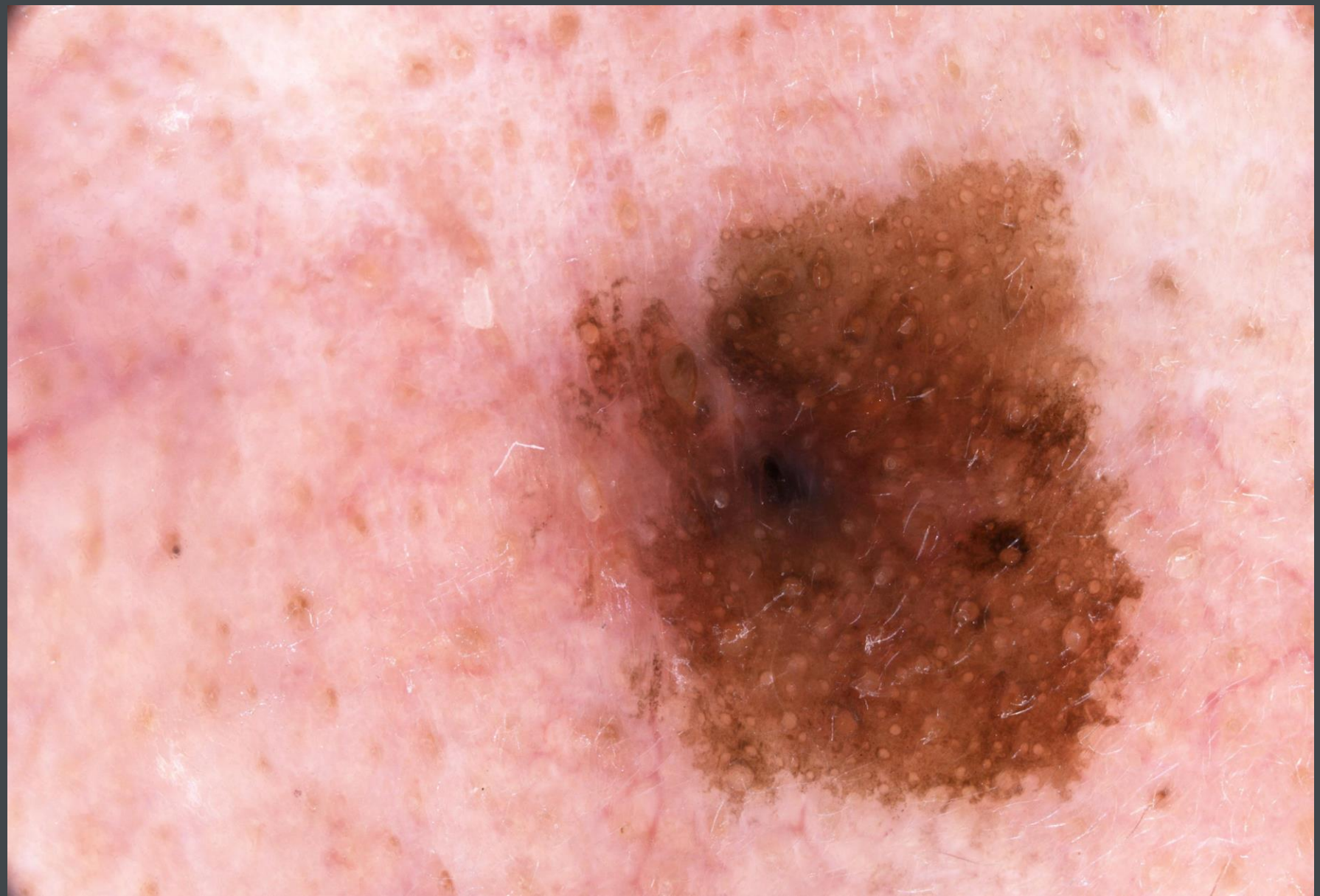


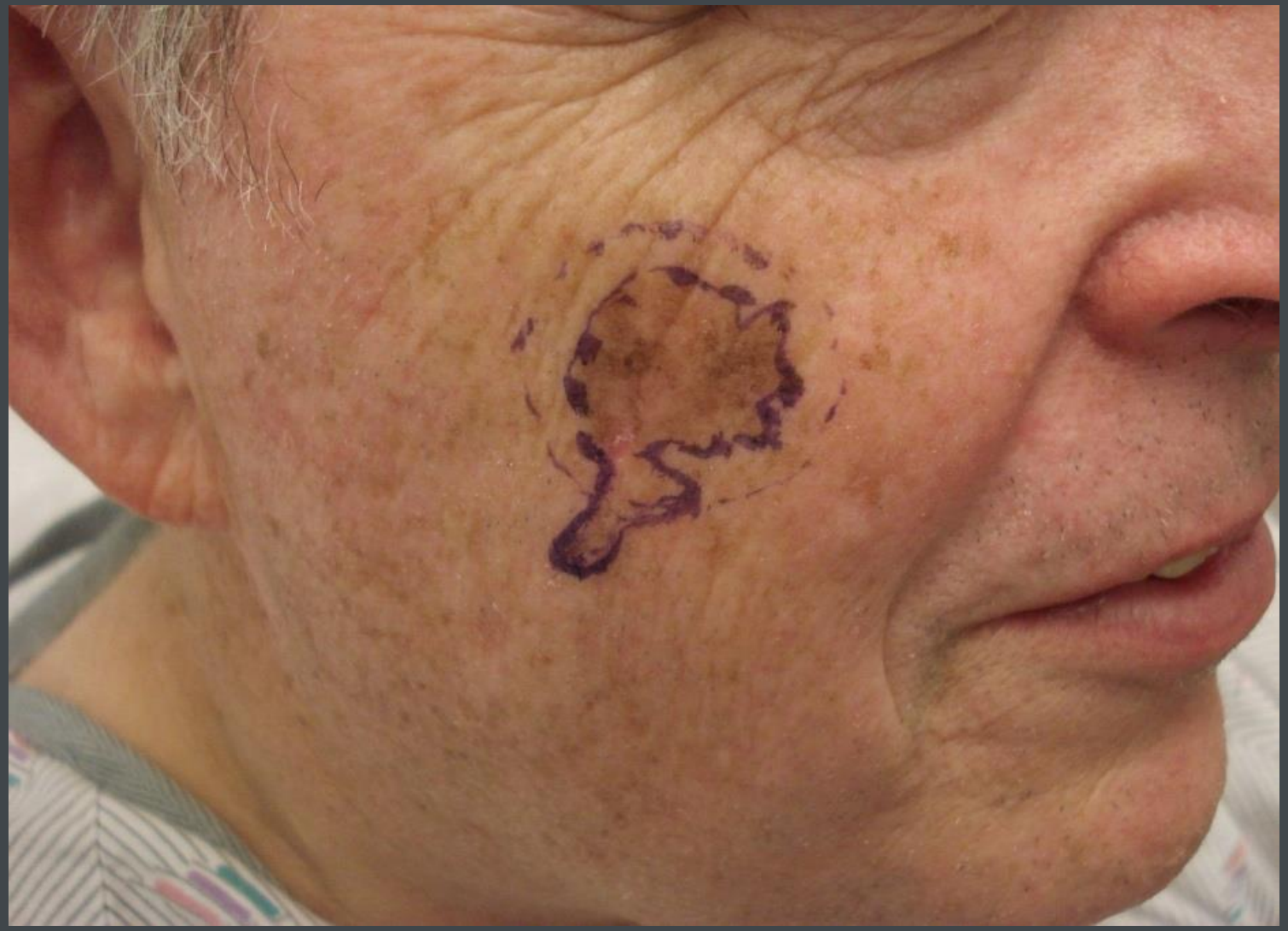
Lentigo Maligna





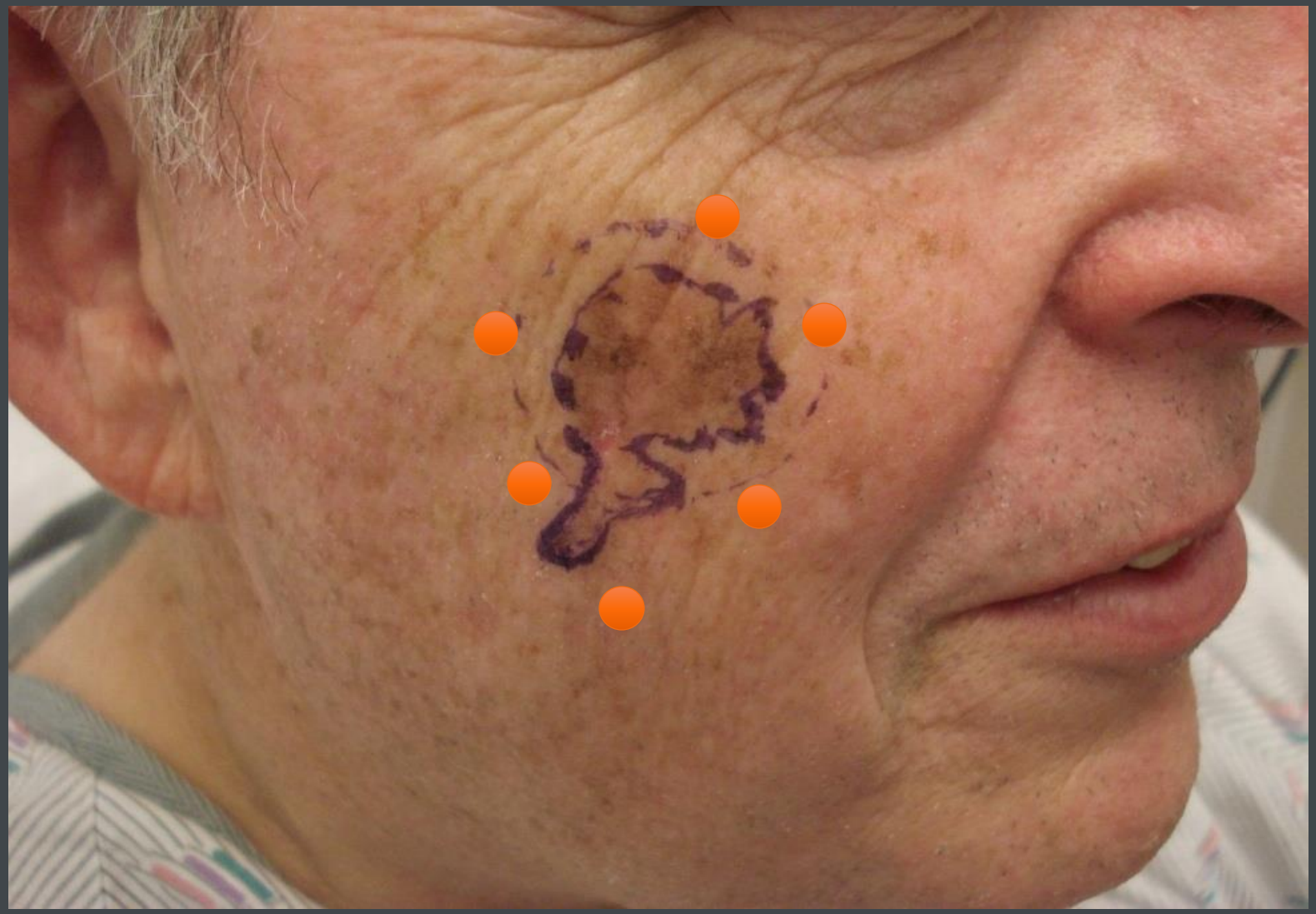
Partial Biopsy of a Nose Lesion





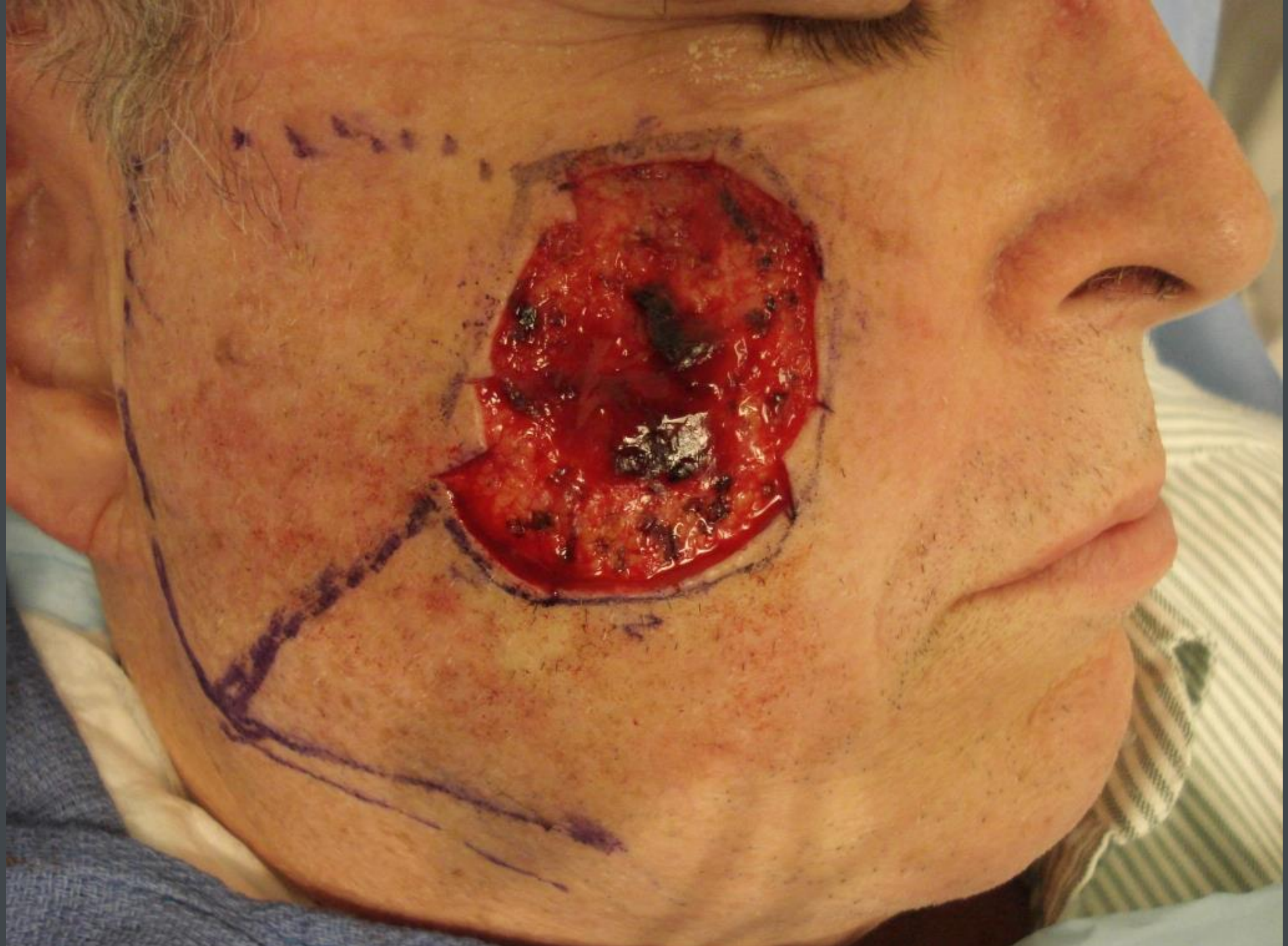
Pre-surgery Preparation:

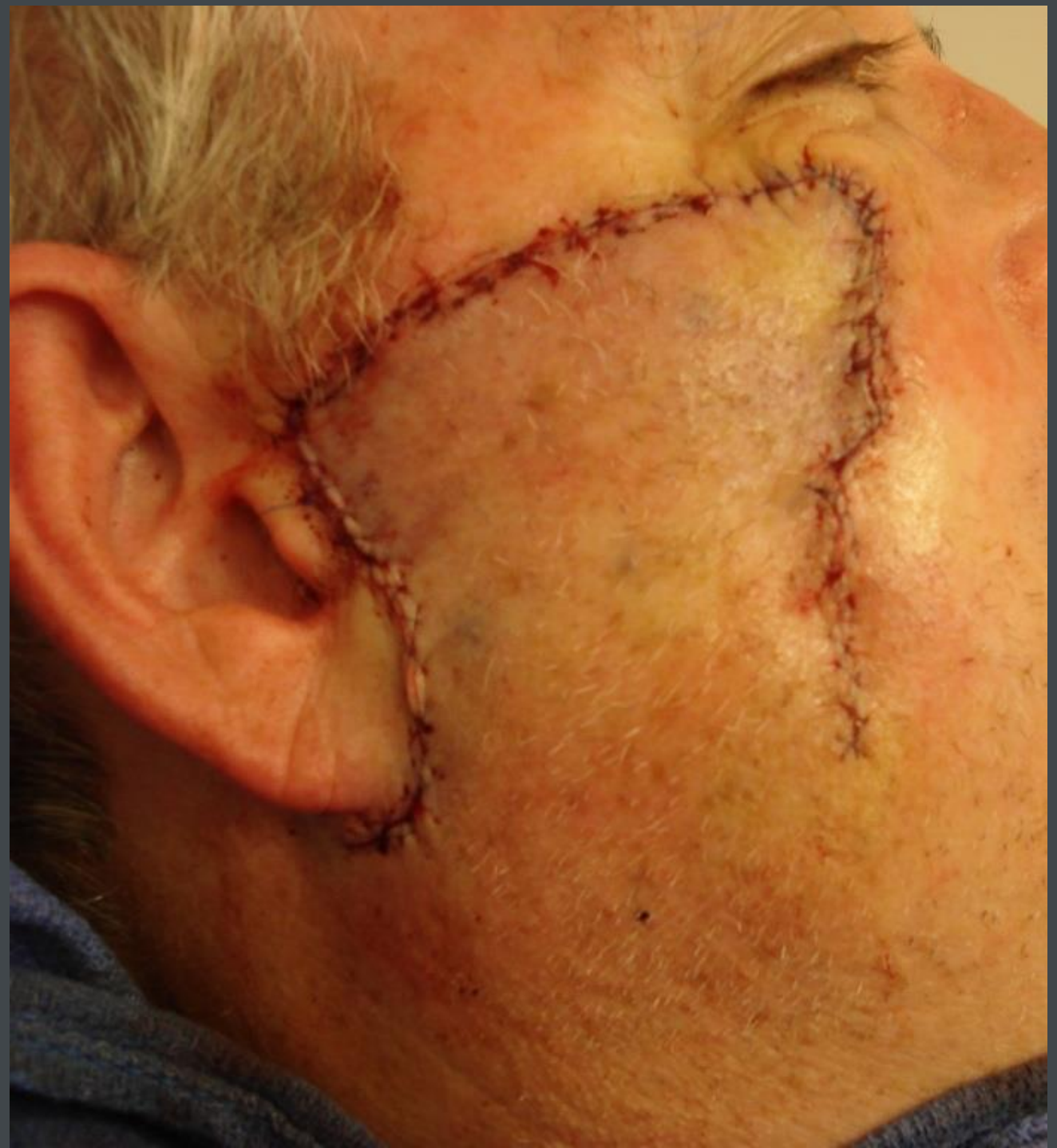
1. Wood’s light
2. Palpation
3. Dermoscopy



Pre-surgery Preparation:

1. Wood’s light
2. Palpation
3. Dermoscopy
4. Scouting Biopsies





Lentigo Maligna: Imiquimod treatment

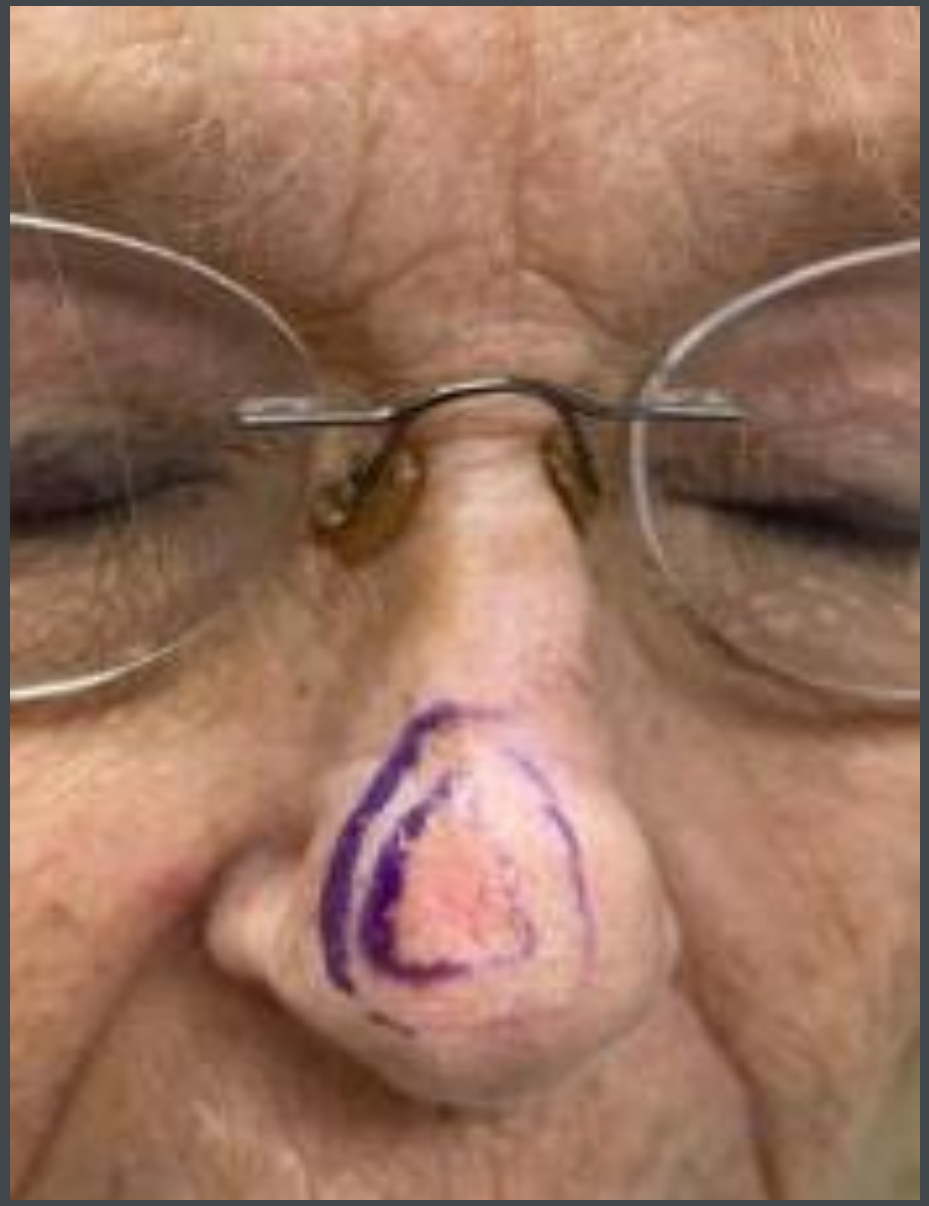
Patient Selections

- Patient refuses surgery
- Poor surgical candidate
- Poor health and multiple medical problem
- Advanced age
- Lesion too large
- difficult anatomic location

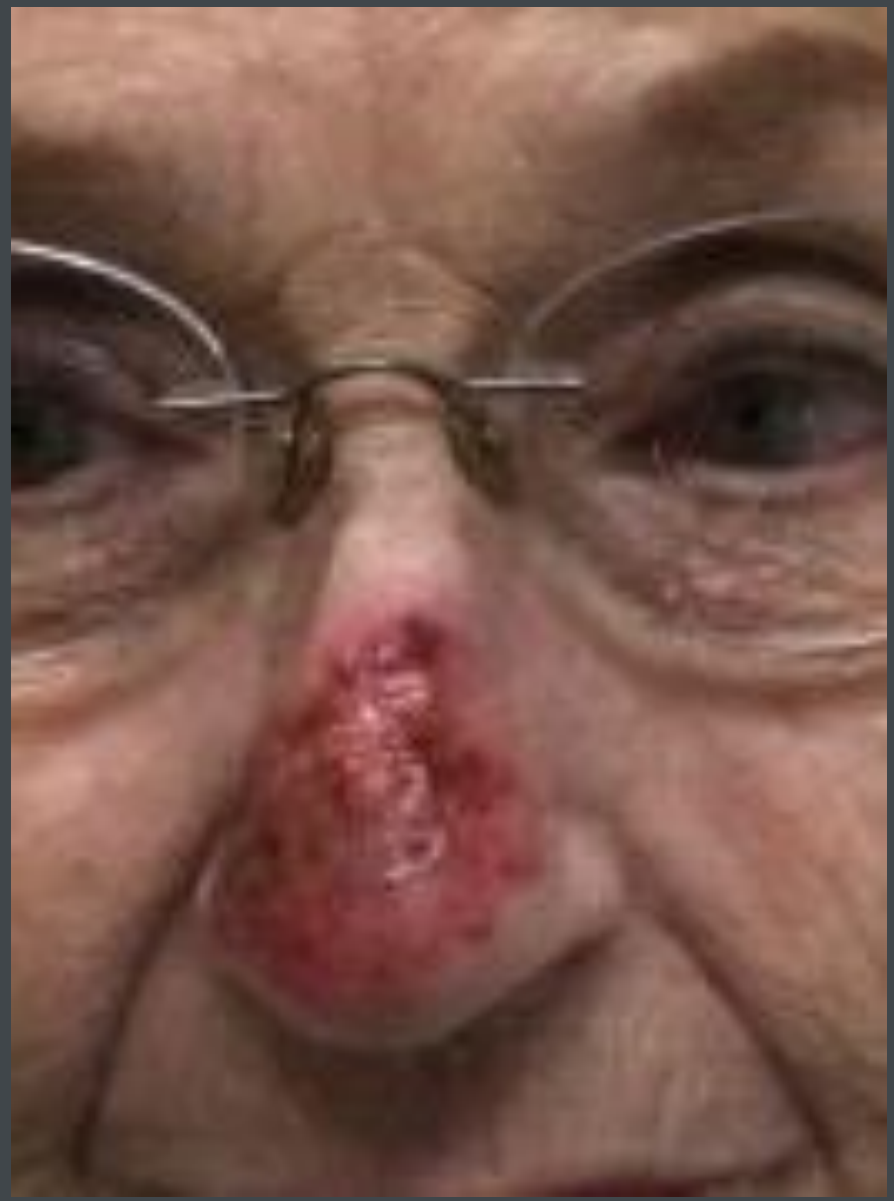
Lentigo Maligna: Imiquimod treatment

Dosing & Follow-up

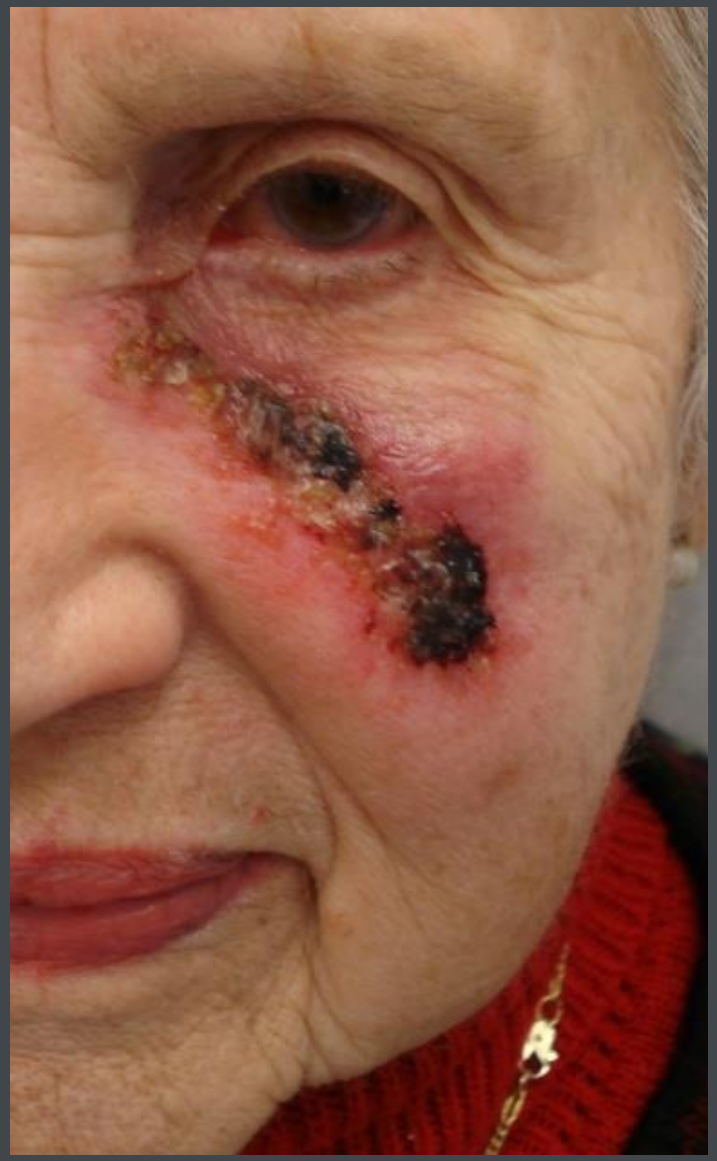
- Not FDA approved
- 5x/wk x12 wks course
- Add Mupiriocin ointment starting at 5th week
- “Messaging” to achieve compliance
- “Hand-holding” visit Q3-4 wks
- 8-12 wk visit after the last dose; then q4-6mo for recurrence
- Beware of flu-like symptoms. Stop or decrease dosing frequency/duration. Vigilant for seniors.

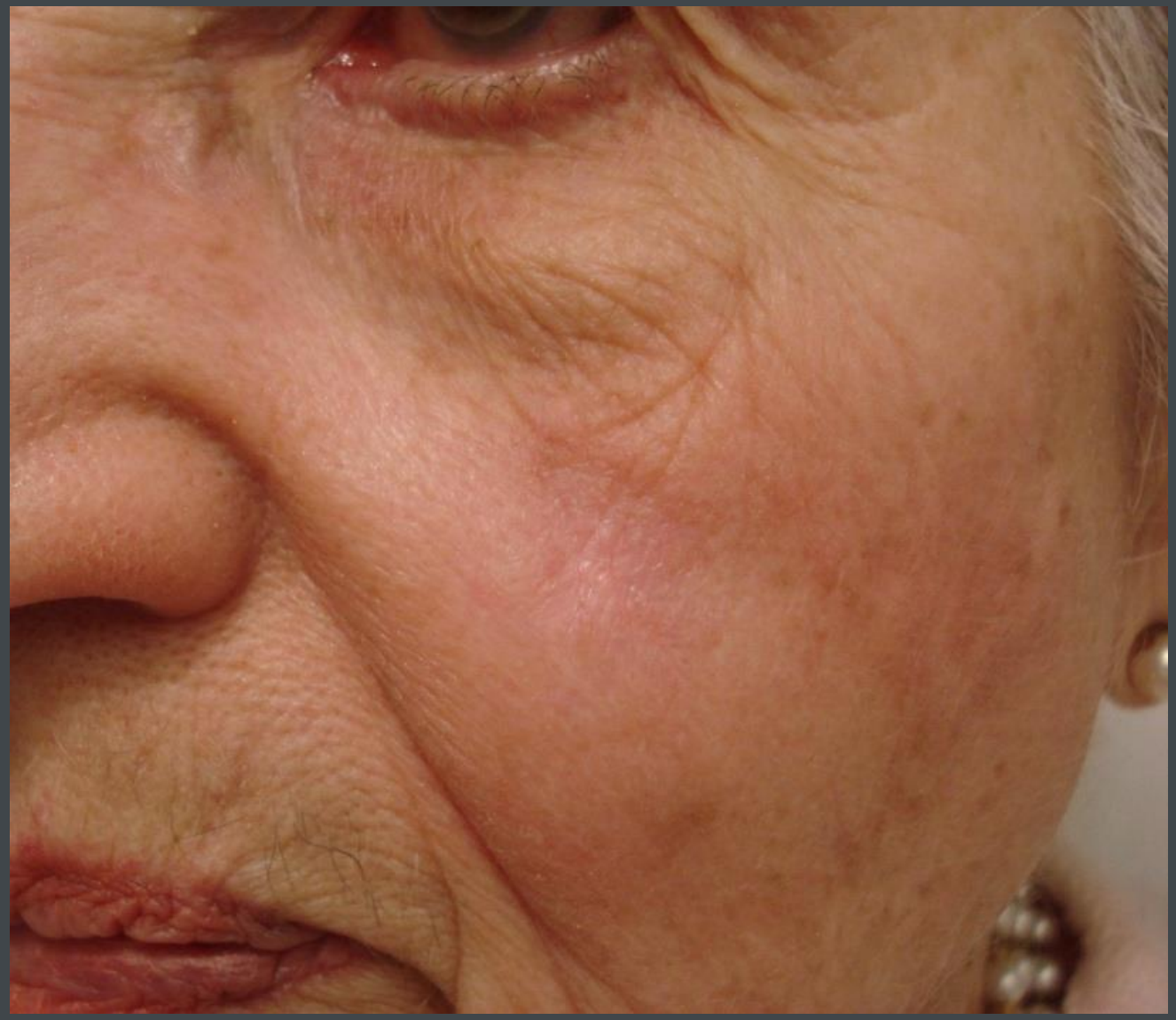


Baseline



4 weeks





Melanoma

Table 1. **American Joint Committee on Cancer (AJCC) Definitions for T, N, M**

T Category	Thickness	Ulceration Status
TX: Primary tumor thickness cannot be assessed (eg, diagnosis by curettage)	Not applicable	Not applicable
T0: No evidence of primary tumor (eg, unknown primary or completely regressed melanoma)	Not applicable	Not applicable
Tis (melanoma *in situ*)	Not applicable	Not applicable
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T1a	<0.8 mm	Without ulceration
T1b	<0.8 mm	With ulceration
	0.8–1.0 mm	With or without ulceration
T2	>1.0–2.0 mm	Unknown or unspecified
T2a	>1.0–2.0 mm	Without ulceration
T2b	>1.0–2.0 mm	With ulceration
T3	>2.0–4.0 mm	Unknown or unspecified
T3a	>2.0–4.0 mm	Without ulceration
T3b	>2.0–4.0 mm	With ulceration
T4	>4.0 mm	Unknown or unspecified
T4a	>4.0 mm	Without ulceration
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*NCCN 2022 Guideline

Melanoma

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Sentinel Lymph Node Biopsy*

Not Needed (<5% risk)

“Discussed & considered” (5-10%risk)

Should be offered (>10% risk)

*AJCC 8th Edition

Pathological Staging (pTNM)**

	T	N	M
Stage 0†	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T3a	N0	M0
Stage IIB	T3b	N0	M0
	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage IIIA	T1a/b, T2a	N1a, N2a	M0
Stage IIIB	T0	N1b, N1c	M0
	T1a/b, T2a	N1b/c, N2b	M0
	T2b, T3a	N1a/b/c, N2a/b	M0
Stage IIIC	T0	N2b/c, N3b/c	M0
	T1a/b, T2a/b, T3a	N2c, N3a/b/c	M0
	T3b, T4a	Any N ≥ N1	M0
	T4b	N1a/b/c, N2a/b/c	M0
Stage IIID	T4b	N3a/b/c	M0
Stage IV	Any T, Tis	Any N	M1

*AJCC 8th Edition

Melanoma-specific survival probability (5- and 10-year)

100%

99% and 98%

97% and 94%

94% and 88%

87% and 82%

82% and 75%

93% and 88%

83% and 77%

69% and 60%

32% and 24%

22% 5y only (44%)

*AJCC 8th Edition

Pathological Staging (pTNM)**

	T	N	M
Stage 0†	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T3a	N0	M0
Stage IIB	T3b	N0	M0
	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage IIIA	T1a/b, T2a	N1a, N2a	M0
Stage IIIB	T0	N1b, N1c	M0
	T1a/b, T2a	N1b/c, N2b	M0
	T2b, T3a	N1a/b/c, N2a/b	M0
Stage IIIC	T0	N2b/c, N3b/c	M0
	T1a/b, T2a/b, T3a	N2c, N3a/b/c	M0
	T3b, T4a	Any N ≥ N1	M0
	T4b	N1a/b/c, N2a/b/c	M0
Stage IIID	T4b	N3a/b/c	M0
Stage IV	Any T, Tis	Any N	M1

Melanoma

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Surgical Margin

- 0.5 -1 cm
- 1cm
- 1-2cm
- 2cm

*NCCN 2022 Guideline

Melanoma

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Surgical Margin

0.5 -1 cm — **Dermatologic Surgeon**

1cm

Derm or Surgical Onc

1-2cm — **Surgical Oncologist**

2cm

*NCCN 2022 Guideline

Melanoma

Stage IV:

4 Classes of Immunotherapy Drugs:

1. **Anti-PD1 Inhibitor:**
   - **Pembrolimzumab (Keytruda)**
   - **Nivolumab (Opdivo)**
2. **Anti-CTLA-4 Inhibitor:**
   - **Ipilimumab (Yervoy)**
3. **Anti-PD-L1 Inhibitor:**
   - **Atezolizumab (Tecentriq)**
4. **Lag-3 Inhibitor**
   - **Opdualag (Relatlimab + Nivolumab)**

BRAF | MEK inhibitors approved by the FDA:

1) Dabrafenib/trametinib
2) Vemurafenib/cobimetinib
3) Encorafenib/binimetinib

Clinical Consideration

- Single vs. dual agent
- which Class of immunotherapy
- Immunotherapy vs. BRAF/MEK
- Side effect profile

Melanoma

Stage III:

Immunotherapy Drugs (adjuvant):

1. **Anti-PD1 Inhibitor:**
2. **Pembrolimzumab (Keytruda)- Nivolumab (Opdivo)**

BRAF | MEK inhibitors approved by the FDA (adjuvant):

1) Dabrafenib/trametinib

Complete Lymph Node Dissection (less popular)

Clinical monitoring + imaging

Stage IIB/C:

Immunotherapy Drugs (adjuvant):

1. **Anti-PD1 Inhibitor: - Pembrolimzumab (Keytruda)**

Clinical monitoring + imaging

BeatingMelanoma

Select the Stage of Your Melanoma.

Stage 0	Stage I	Stage II	Stage III	Stage IV
Stage 0 >	Stage IA >	Stage IIA >	Stage III >	Stage IV >
	Stage IB >	Stage IIB >		
		Stage IIC >		

INTERVIEW WITH THE EXPERTS

01 Dr. Paul Chapman discussing his approach to manage patients with stage IV disease

02 Dr. Paul Chapman discusses the challenges in knowing when to stop treatment. Also defines Progression Free Survival, Overall Survival, Complete response, metabolic Complete response, and Pathologic Complete Response

03 Dr. Paul Chapman discusses immune mediated side effects. How to treat and manage those side effects

04 Dr. Paul Chapman discusses BRAF mutation

05 Dr. Paul Chapman discusses BRAF targeted therapy

06 Dr. Richard Carvajal discusses the consultation process for patients with stage IV disease

Q&A

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