



# Misdiagnosis of Acral Melanoma and Melanoma Diagnosis and Surgery

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# Melanoma Factory



Defect or absence of tumor suppressor Genes

Race

Geography

Childhood exposure

# Cancer Epidemiology, Biomarkers & Prevention

May 1, 2005

Vol. 14 no. 5 1241-1244 Cho, et al.

**Table 1. Number of invasive melanoma cases by site in the Nurses' Health Study (1986-2000), Nurses' Health Study II (1989-1999), and Health Professionals Follow-up Study (1992-2000) 178,000 cancer free people followed for 14 years:**

	Head or neck	Trunk, shoulder, hip, back, or abdomen	Upper extremity	Lower extremity	Total
NHS (women)	17	76	51	93	237
NHS II (women)	12	69	37	70	188
HPFS (men)	20	43	10	13	86
Total	49 (10%)	188 (37%)	98 (19%)	176 (34%)	511

## Why is the diagnosis of melanoma so critical?

- ❑ Incidence increasing faster than any other cancer
- ❑ In 1930's, rate was 1 in 1500
- ❑ In 1988 – rate was estimated to be 1 in 150 in year 2000
- ❑ In 1993 – rate was estimated to be 1 in 105
- ❑ Today – estimate is 1 in 50!

# Why is the diagnosis of melanoma so critical?

## Melanoma 2009

Invasive ---	68,720 new cases
In-situ ---	53,120 new cases
Total ---	121,840

When both invasive and in-situ cases are considered, melanoma incidence is

**1 in 32!**

American Cancer Society, 2009 Cancer Facts and Figures

# Melanoma 2012

- New invasive cases: 76,250 2009 – 68,720
- Males: 44,250 Females: 32,000
- Deaths: 6,060 males /3,120 females
  - Total: 9,180
- Fifth most common cancer in men
- Sixth most common cancer in women
- But melanoma is not among the 10 most fatal cancers for either sex.

Data from the National Cancer Institute, the Centers for Disease Control and Prevention, and the North American Association of Central Cancer Registries and mortality data from the National Center for Health Statistics.

# Melanoma 2015

**American Cancer Society's estimates:**

**73,870 new melanomas:**

**42,670 in men**

**31,200 in women**

**9,940 deaths: about 6,640 men and 3,300 women.**

**The rates of melanoma have been rising for at least 30 years.**

**Melanoma is more than 20 times more common in whites**

**The lifetime risk of getting melanoma is about 2.4% (1 in 40) for**

**whites, 0.1% for African Americans (1 in 1000) and 0.5% in**

**Hispanics (1 in 200)**

**The risk of melanoma increases as people age. The average age at the time it is found is 62. But melanoma is not uncommon even among those younger than 30. In fact, it is one of the most common cancers in young adults (especially young women).**

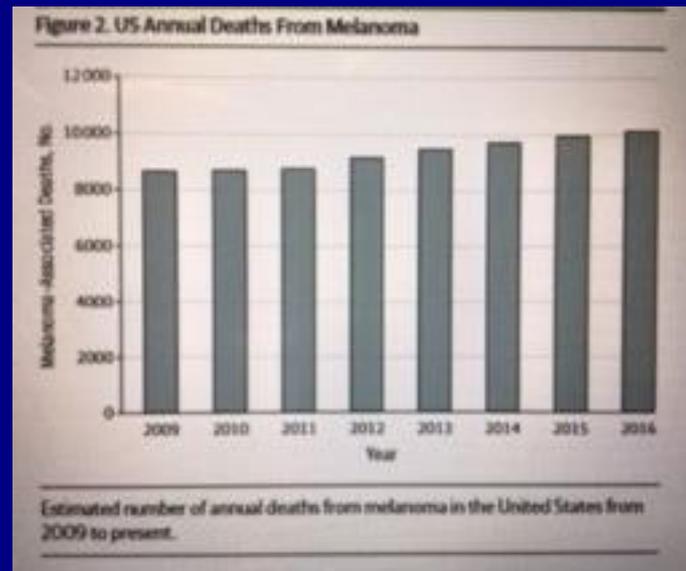
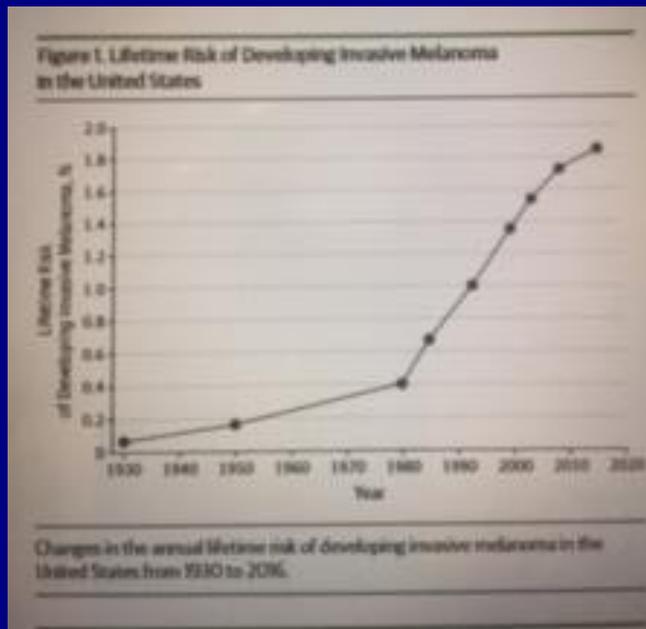
# Melanoma 2017

## 200% increase since 1973

- New invasive cases: 87,110 2012 – 76250
- Males: 52,170 Females: 34,940
- Deaths: 6,380 males /3,350 females  
– Total: 9,730
- 25% of cases under age 45
- **Increase in incidence 15x in 40 years**
- Caucasian Americans 26 x more likely than African Americans

# Melanoma 2009 - 2017

- 2009 New 68720
- 2012 New 76250 Deaths 9180
- 2015 New 73870 Deaths 9940
- 2017 New 87110 Deaths 9730



# Why is the diagnosis of melanoma so critical?

Ann Surg Oncol. 2013 Oct;20(11):3618-25.  
Bello DM, Chou JF, Panageas KS, Brady MS, Coit DG,  
Carvajal RD, Ariyan CE.

## **Prognosis of acral melanoma: a series of 281 patients**

*Acral sites include tip of nose, ears, hands,  
and feet but when referring to melanoma, it is  
palms, soles and nail beds*

**AM had a WORSE DSS compared with  
NACM**

Why is the diagnosis of  
melanoma so critical?

**NO ONE NEED DIE OF MELANOMA!**

# Who is at risk for melanoma?

Ten melanoma risk factors

**Rhodes, et al. JAMA 1987; 258:3146-3154**

- Changed or changing mole
- Adulthood
- One or more large or irregularly pigmented lesions
- Congenital mole
- Caucasian
- Prior cutaneous melanoma
- Immunodeficiency
- Sun sensitivity
- Excessive sun exposure
- Melanoma in parents, children or siblings

# Other delineated melanoma risk factors:

- **Nevi on buttocks**
- **Raised nevi on arms**
- **> 120 nevi between 1 and 5 mm**
- **> 5 nevi between 5 and 10 mm**
- **One atypical nevus**
- **Tendency towards freckling**
- **History of non-melanoma skin cancer**
- **Time spent outdoors between ages 10 and 24**
- **Light skin**
- **Fair complexion**
- **Blue, green, or grey eyes**
- **Blond or red hair**
- **Inability to tan**

# Other delineated melanoma risk factors:

- **Marked freckling of upper back**
- **Three or more blistering sunburns before age 20**
- **Three or more years of outdoor summer work as a teenager**
- **Presence of actinic keratoses**
- **All seem to increase the risk that one will develop melanoma in their lifetime.**

# Key Points



- 1) Is it melanoma?
- 2) Does the lesion meet the established diagnostic criteria for a high index of suspicion?

# Established Criteria



## ABCDE Mnemonic

Asymmetry

Border irregularity

Color variegation

Diameter

Elevation or enlargement

These Are Early Changes!

# Warning signs for melanoma in later stages

## CHANGE IN:

Color (shades of red, white, blue, black)

Size

Shape

Elevation

Surface (roughened, bleeding, ulceration)

Surrounding skin (erythema)

Consistency

# Misdiagnosis of ALM –Review of 90 cases 1983-2004

## National Cancer Institute Surveillance Epidemiology and End Results Program (SEER)

69 cases involved lower extremity  
15 initially misdiagnosed

48% of the cases were at least Clark level IV or V  
(no difference between upper and lower extremity)

Albreski, D, Sloan SB. Melanoma of the feet: Misdiagnosed and misunderstood. *Clin Dermatol.* 2009;27(6):556-563

# Misdiagnosis of Acral Melanoma by Location

## Subungual Lesions

- Onychomycosis
- Onychocryptosis
- Subungual hematoma
- Paronychia

## Plantar

- Verruca plantaris
- Eccrine poroma
- Keratoacanthoma
- Mal perforans
- Callous/corn
- Tinea pedis
- Non-healing ulcer!!!!!!

## Variable location

Trauma, Pyogenic granuloma, Blister, Nevus, Tumor, Foreign body, Gangrene

# Melanocytic Lesions



SSM

# Nodular Melanoma

Little or no  
radial growth



Compact tumor mass

# Acral Lentiginous Melanoma



Upward migration  
of melanocytes



Atypical  
melanocytes

# Melanocytic Lesions



# Melanocytic Lesions



# Pigmented Streaks in Nails

Urgent?



Non-urgent?

# Important Pearl



A pigment change in the nail plate alone continuous with proximal fold must be matrix derived.

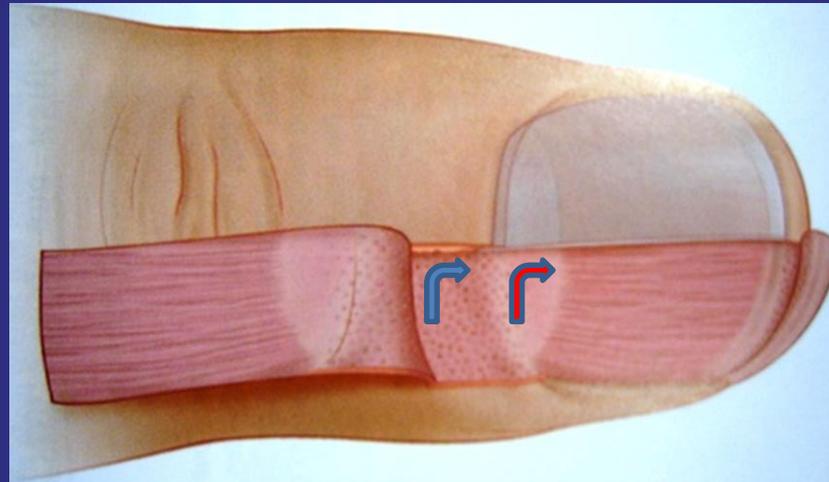
Therefore, biopsy of the nail plate is of limited value!!

# Physiology\*

- Melanocyte density in different parts of the nail unit is definitely varied and will impact on the clinical presentation of lesions
- The quantity of melanocytes in nail units is much less than that in normal skin

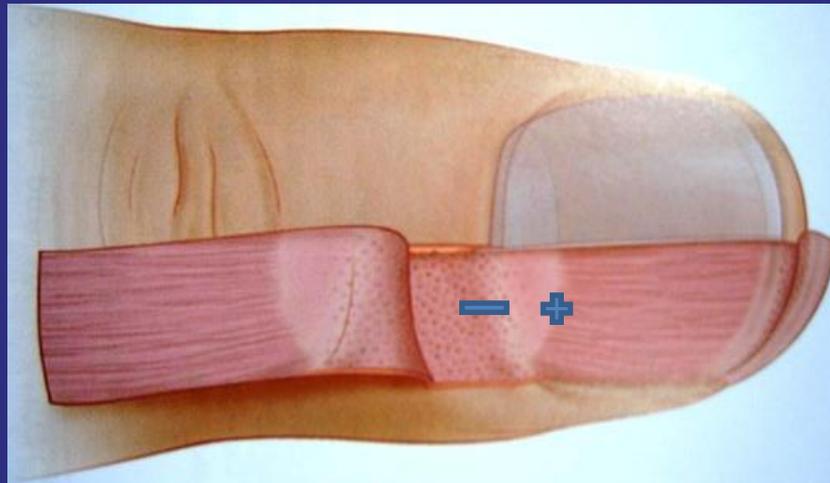
# Physiology\*

- In the proximal nail matrix, melanocytes are mostly located in the lower second to fourth cell layers, as opposed to the distal matrix, where they are more superficial in the first and second cell layers.



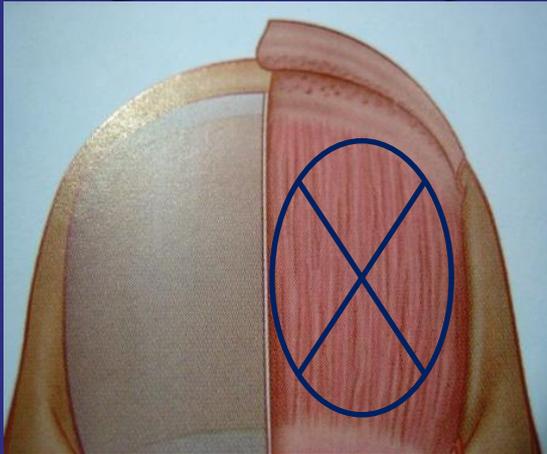
# Physiology\*

- Many proximal matrix melanocytes do not produce melanin, but approximately 50% of distal matrix melanocytes do produce melanin.

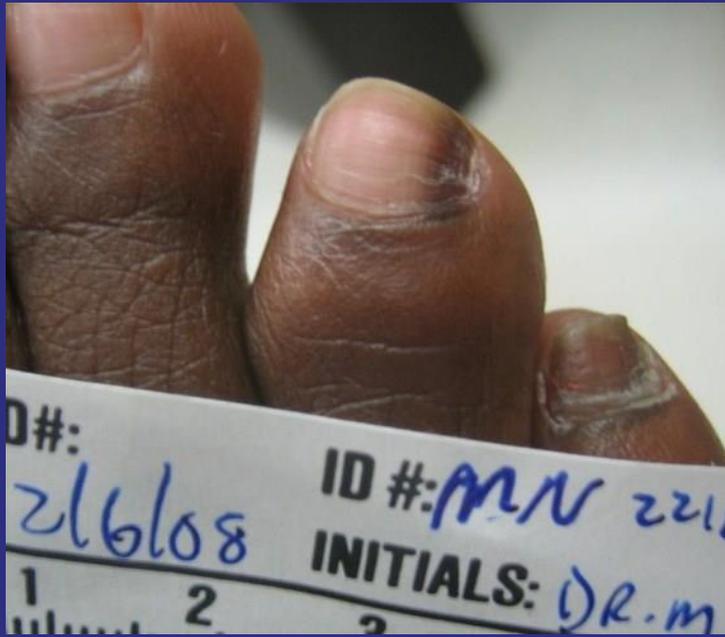


# Physiology\*

- Melanocytes in the nail bed (distal to lunula) are *least* numerous and do not synthesize melanin, which explains why nail bed melanomas are often *amelanotic* and present a *more difficult challenge for timely diagnosis*



\*Ruben, B; Pigmented Lesions of the Nail Unit: Clinical and Histopathologic Features; Seminars in Cutaneous Medicine and Surgery; Elsevier, 2010, pp148-158



# More nail streaks

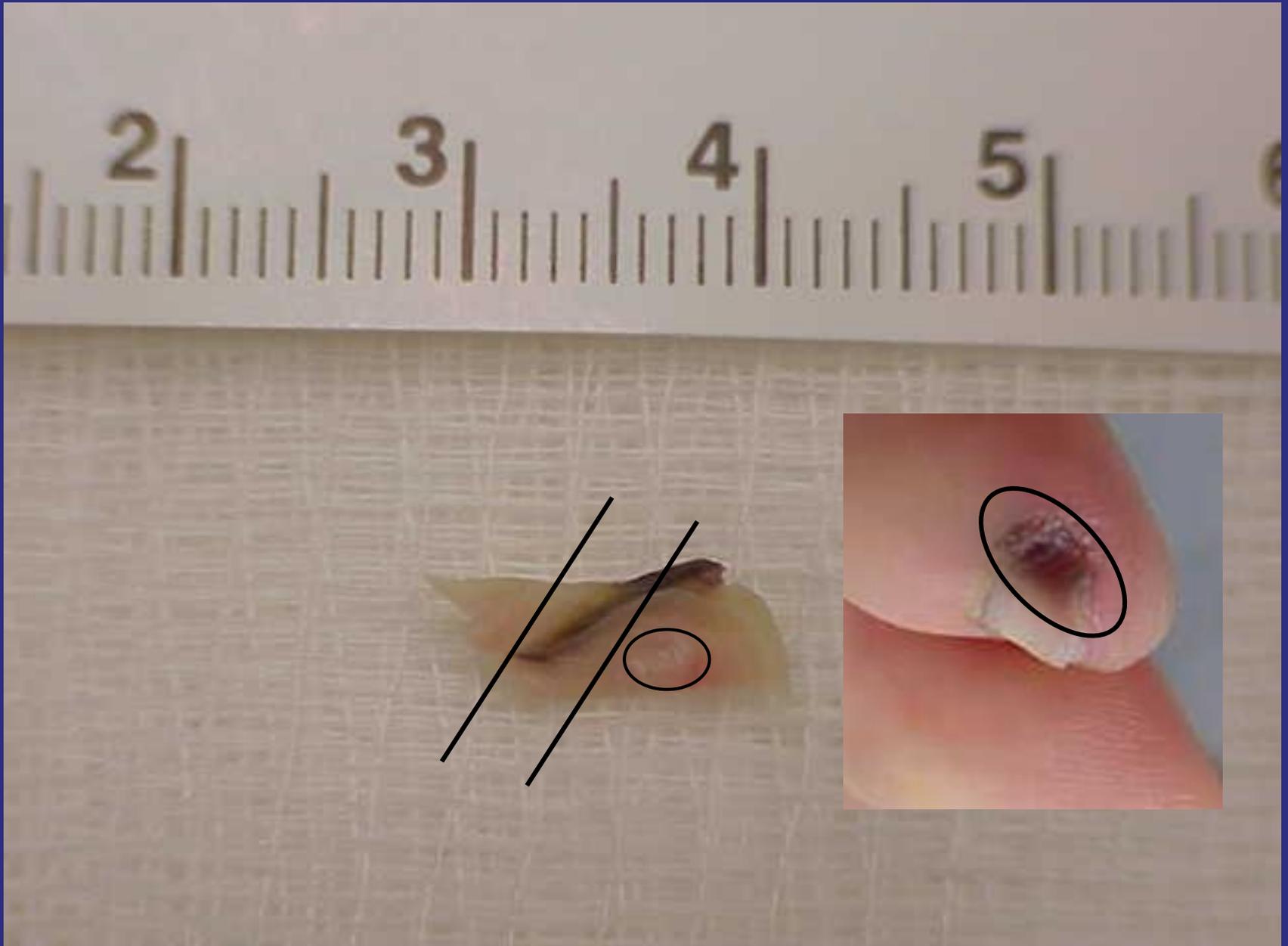


# Recurrent pigmented nail streak post biopsy





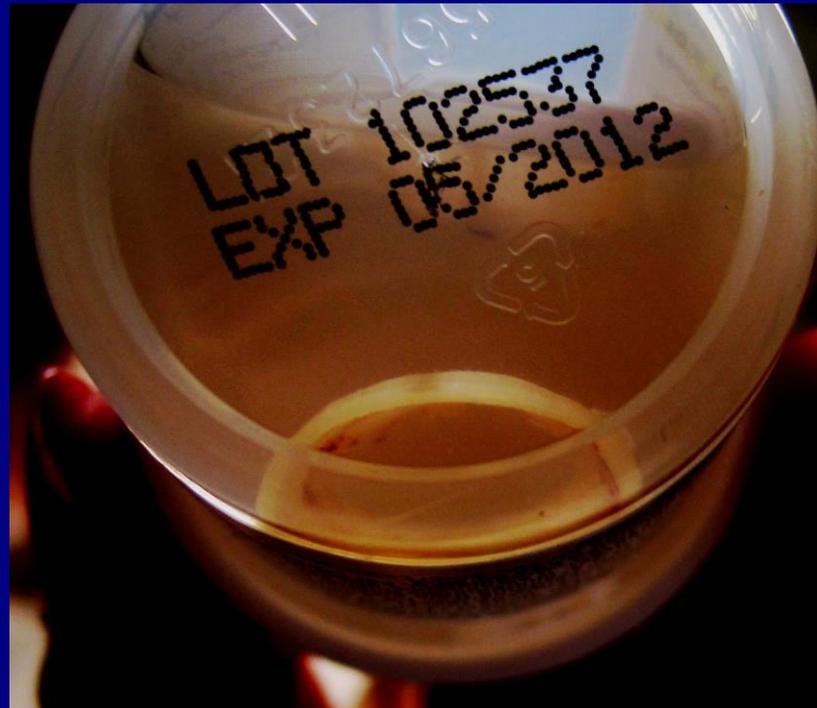




# Longitudinal Melanonychia



# Specimen showing dorsal concentration of pigment



# Immediate Post-Op Matrix Shave Technique



11 Days Post-Op



# 19 Days Post-Op



# 29 Days Post-Op



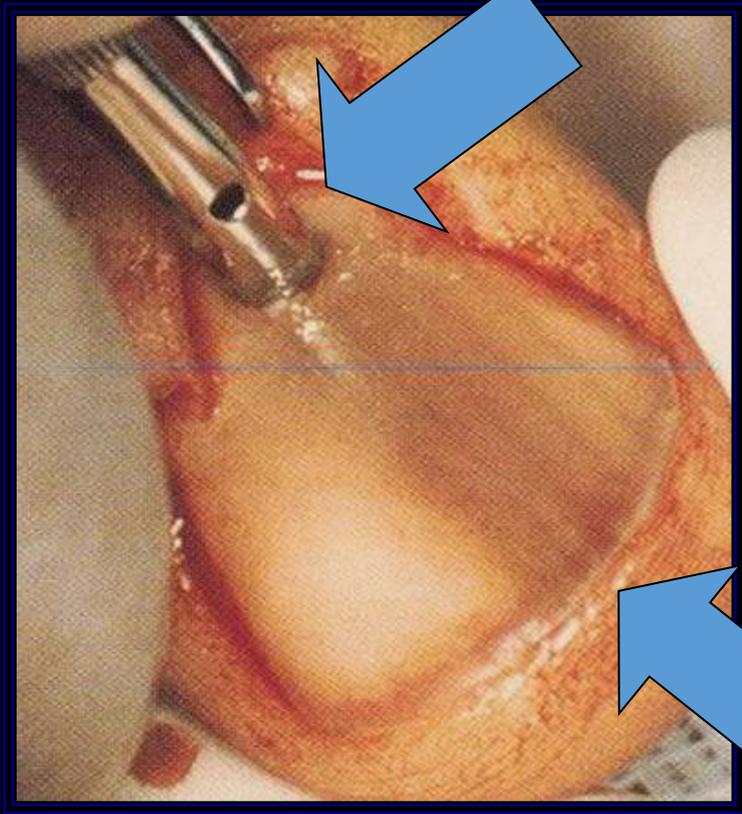
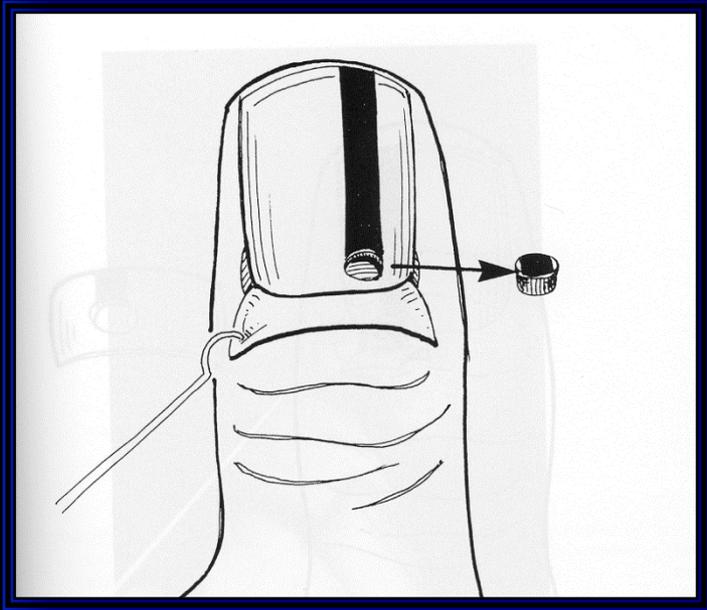
# 78 Days Post-Op Streak resolved



One year post-op



# PUNCH BIOPSY THROUGH INTACT NAIL



# Biopsy of LM and Growth Disturbance



# Criteria over History



# Think Twice



# Think Twice





WOUND #: MELANOMA ID #: Dem  
DATE: 3/31/08 INITIALS: AR

CM 1 2 3 4 5

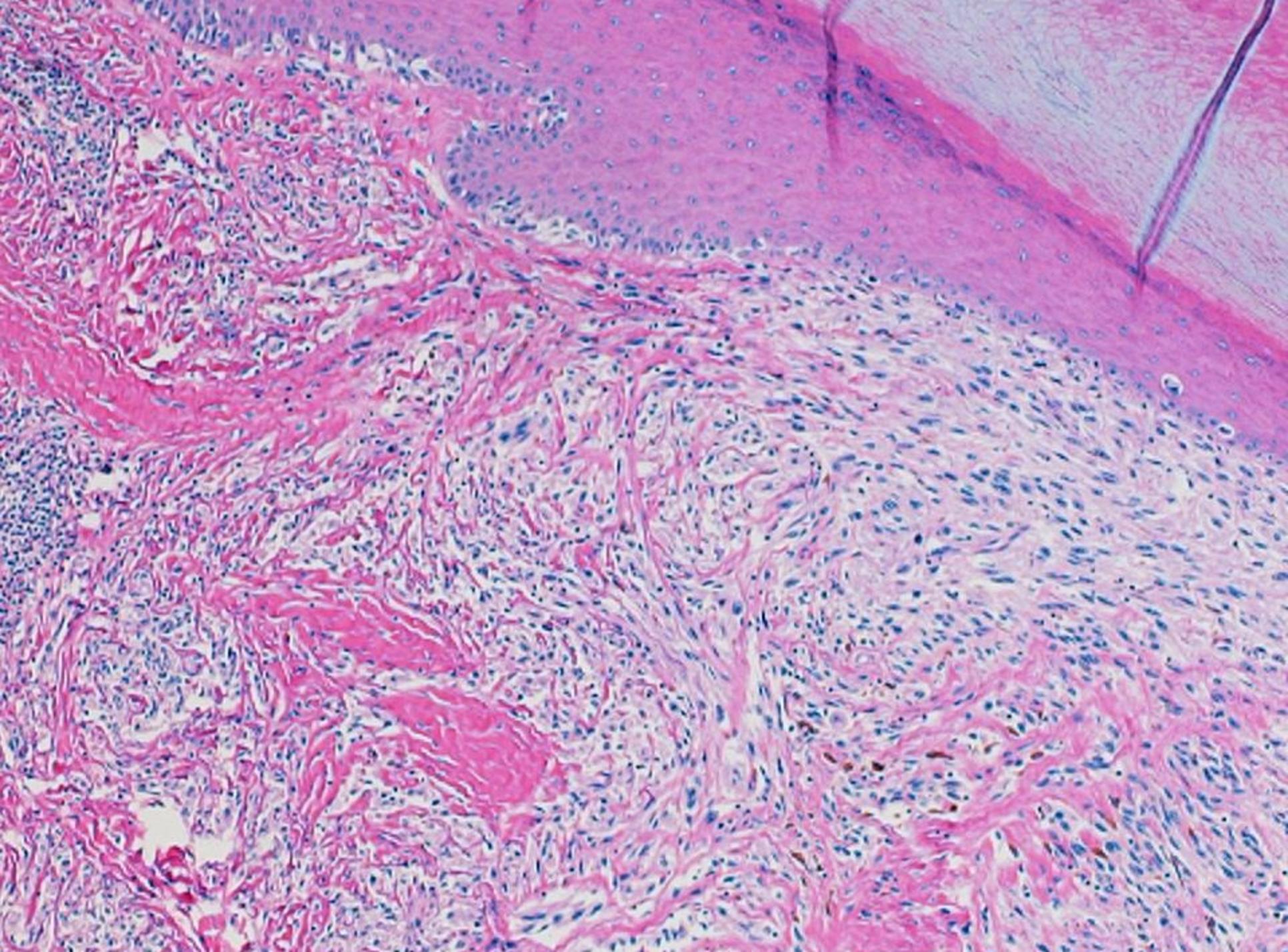
# Think Twice

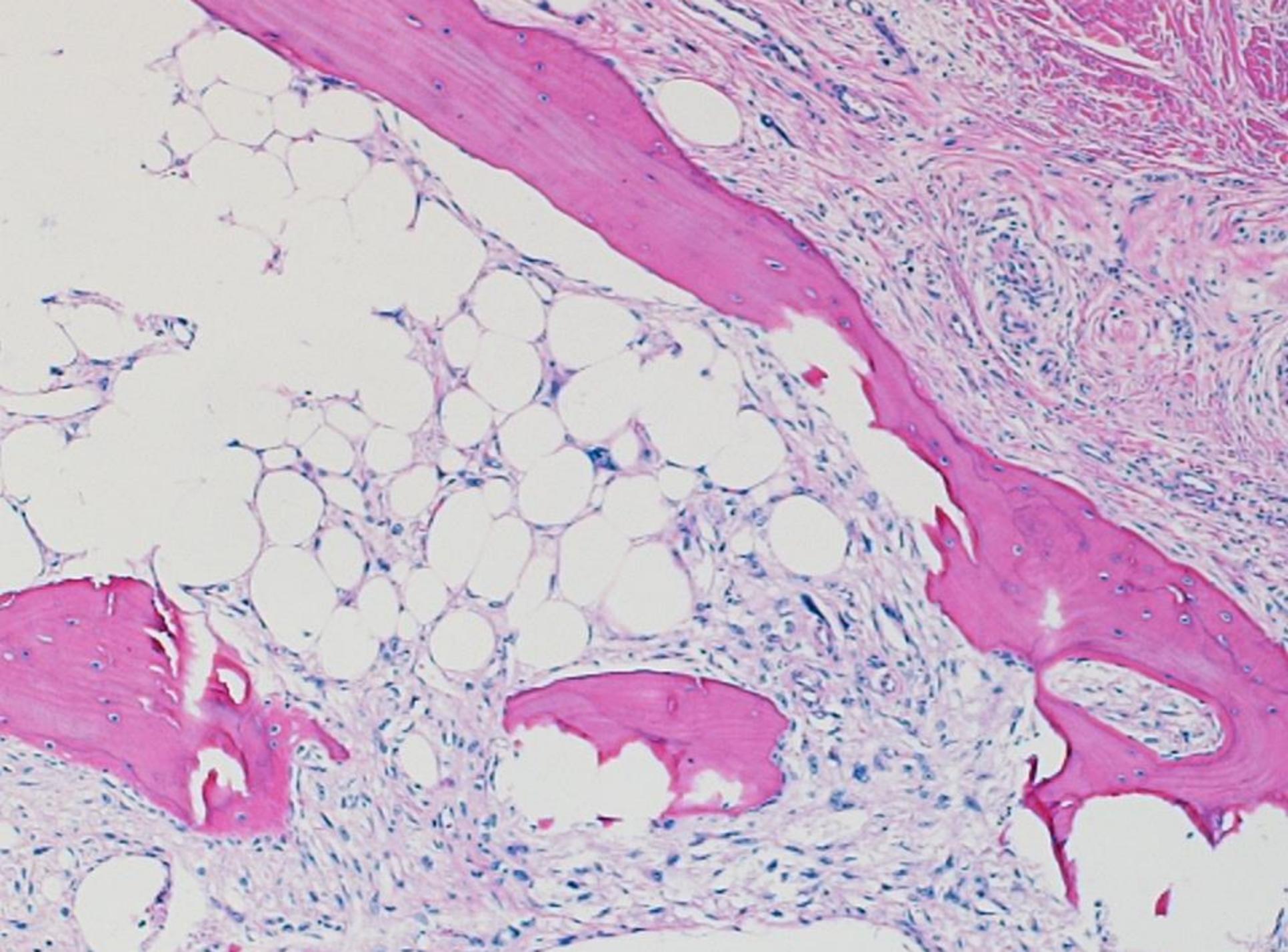


# Section through middle of tumor



11mm





# Pedicure complication?



This patient went for her regular pedicure in 8/09 and states she felt a sharp pain when some instrument was used. She did not bleed. She developed toenail lysis centrally two weeks later and saw a DPM for treatment who assumed infection based on history. Tx continued until she sought another opinion in late January 2010. Patient referred to me and biopsy was performed on 2/15/2010 revealing nodular amelanotic melanoma at least 2.7 mm in depth with many evident mitoses.

# Criteria versus History

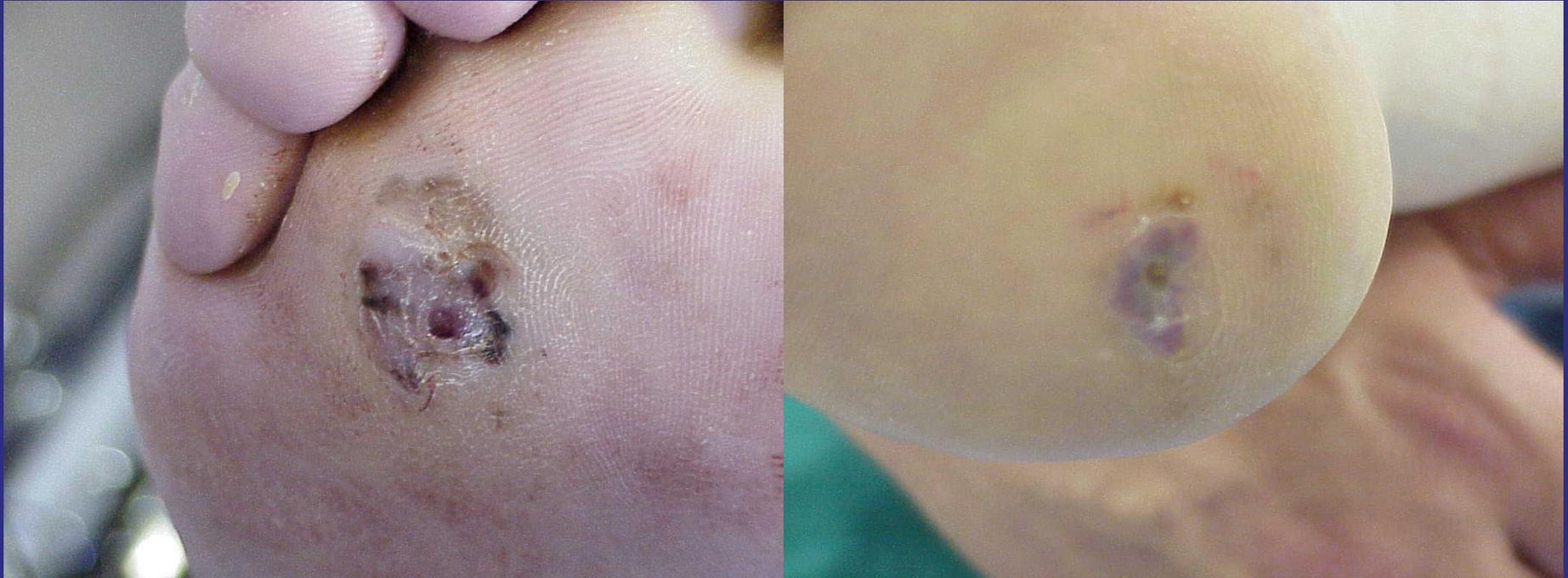


# Normal Things That Recur or Do Not Heal



This “paronychia” recurred over a period of two months when DPM performed a biopsy and referred for consultation.

# Other Lesions That Did Not Go Away



Fungal infection in nursing home for four years that eventually ulcerated

Verruca treated with acid for eight months

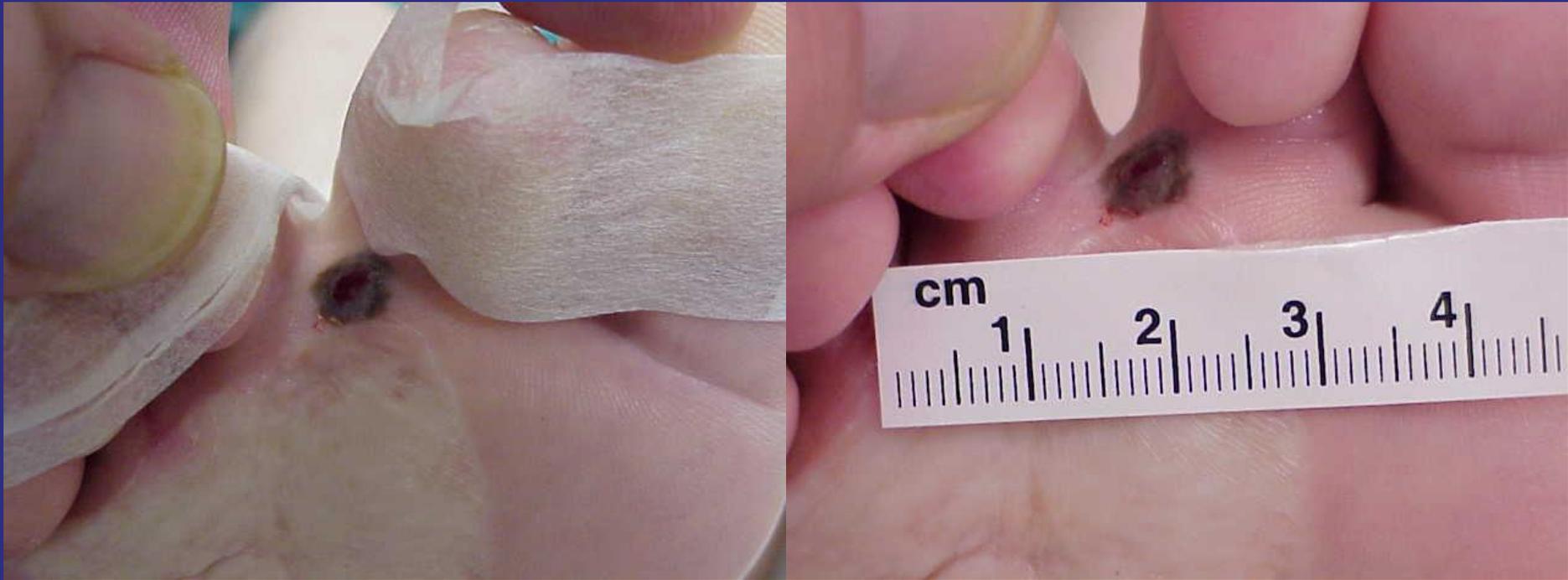
# Level 4 Invasive



# 3 Years s/p STSG



# New Primary Level 4



**Pearl – Treatment and follow up for these problems should be hospital centered and not office based**



**Iso-sulphane Blue Dye Injection**

# Melanocytic Lesions

## Junctional Melanocytic Nevus



Symmetry



Melanocytes in nests  
predominantly at the D-E  
junction



# Melanocytic Lesions

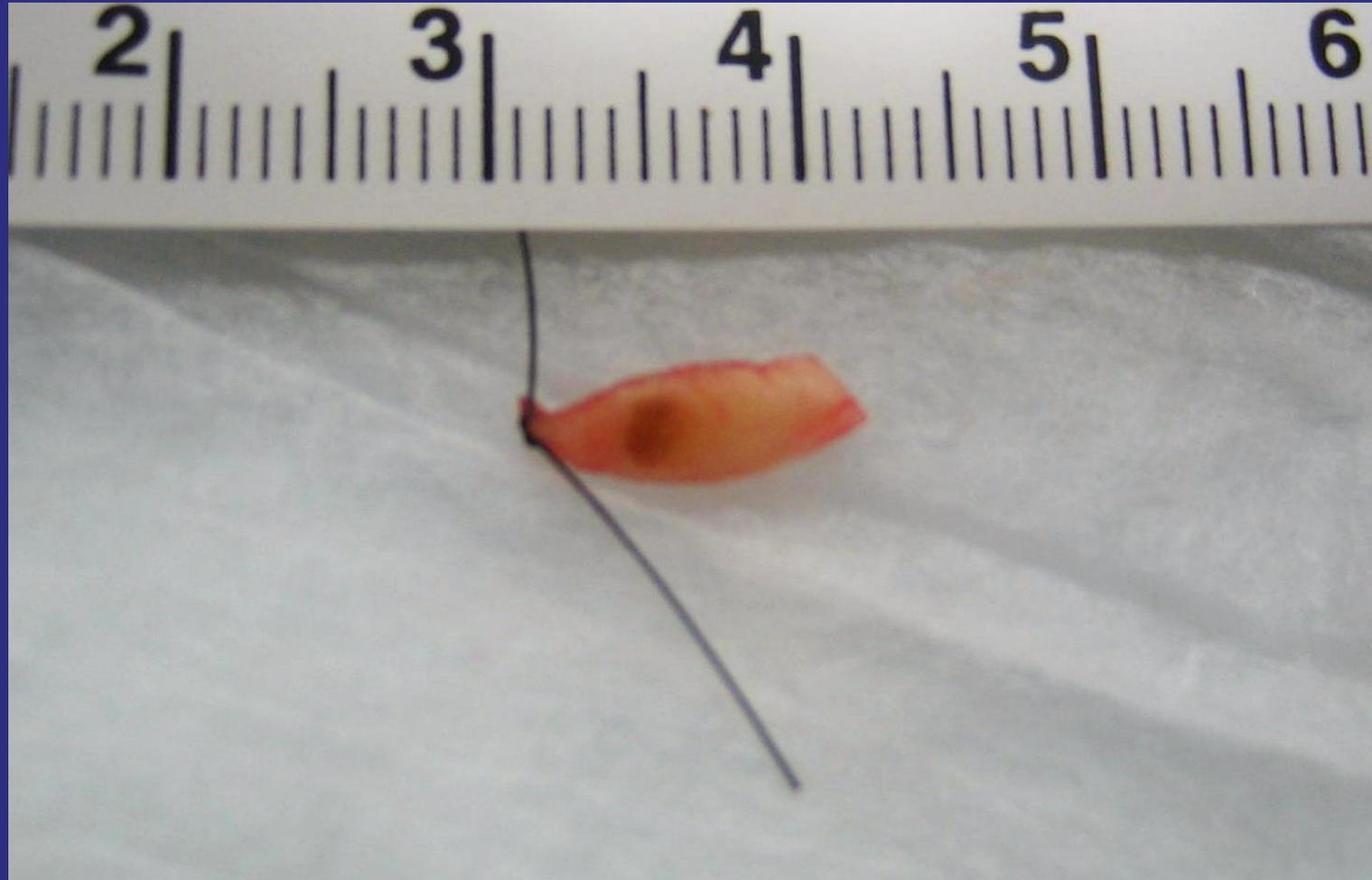


**Junctional nevus**

Surprise!



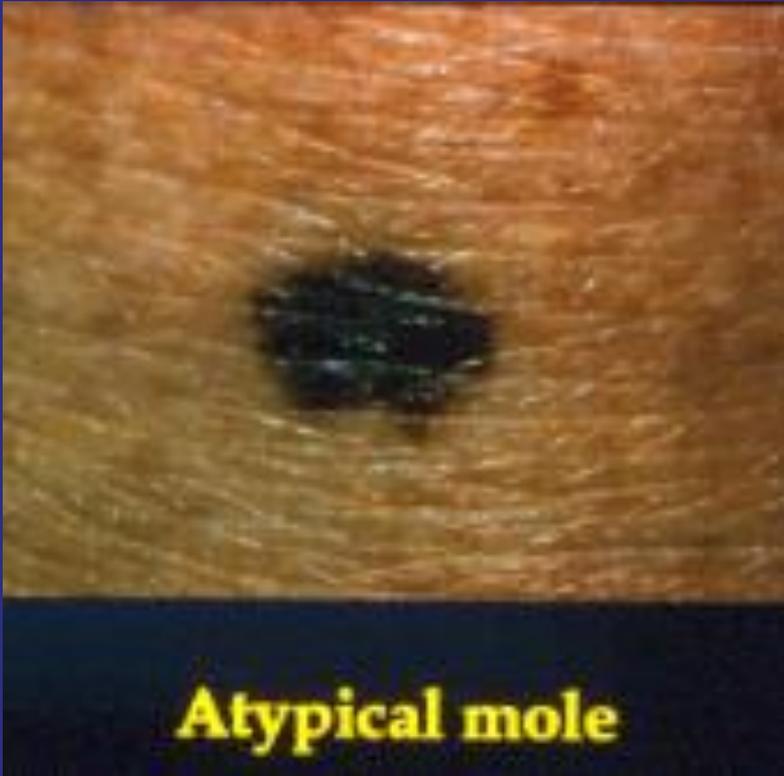
# Lesion Excision



# Melanocytic Lesions



# Melanocytic Lesions

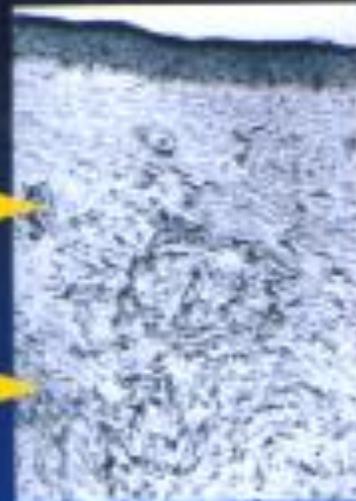


# Melanocytic Lesions

## Blue Nevus



Melanocytes in mid  
and deep dermis



Heavily  
melanized,  
elongated  
cells



# Melanocytic Lesions



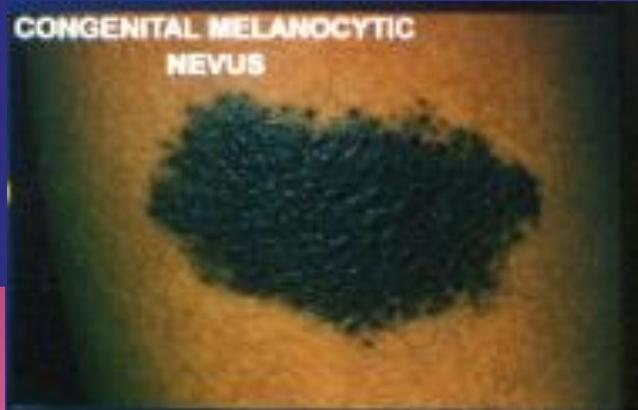
# Melanocytic Lesions



# Melanocytic Lesions



# Melanocytic Lesions



# Melanocytic Lesions



# Excised verrucae must be sent for histologic diagnosis



# Other pigmented lesions



**Kaposi's sarcoma**



# Other pigmented lesions



Perforating collagenosis

# Other pigmented lesions



**Seborrheic  
keratosis**

# Amelanotic Melanoma

- ✓ May be a misnomer as Melanoma by definition means pigment producing cells
- ✓ It is more a case of *deficient* pigment
- ✓ Most commonly seen as ulcerated nodular form
- ✓ These lack a granular layer which accounts for inability to see melanin that was there in the early lesion

# Amelanotic Melanoma

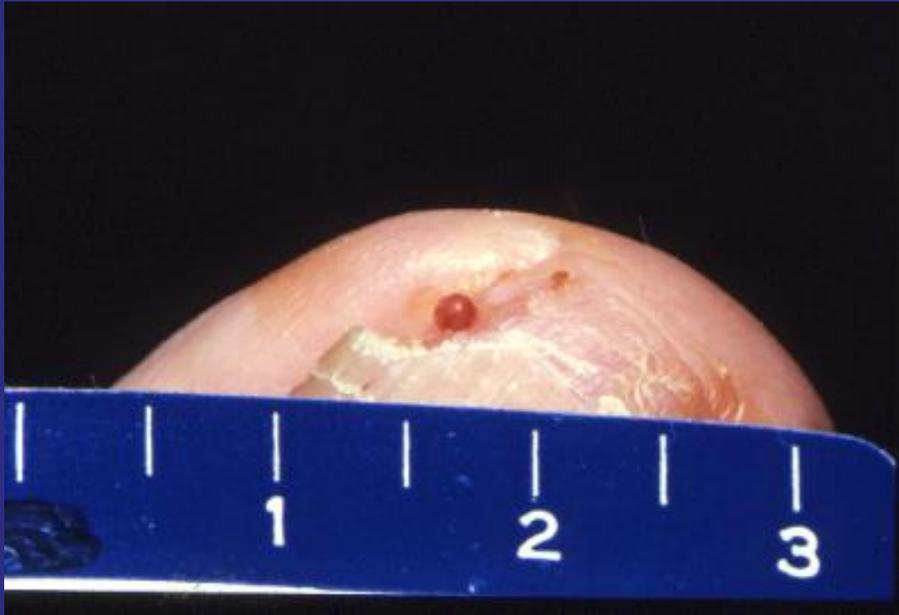


**Amelanotic melanoma**



**Amelanotic melanoma**

# Amelanotic Melanoma ?



# Amelanotic Melanoma ?



April 2007, Courtesy Adam Landsman, DPM Harvard Medical School

# Atypical melanocytic proliferation



# Transplant recipient



# Making the diagnosis

- Suspicious lesion :
  - meets ABCD criteria for high index of suspicion
  - meets dermoscopic pattern and color criteria
  - Patient reports change in character of the lesion
  - You notice a change from visit to visit
  - New pigmented streak in Caucasian patient
  - New lesion in patient with prior melanoma or family history
  - Patient history of risk factors
  - PHOTOGRAPH LESION
  - PHOTOGRAPH LESION

# Perform Biopsy

- Excision – if lesion small enough – elliptical excision to level of fat in shape of a boat, not a pie wedge.
- Punch – 3-4mm to level of fat
- Shave – must include dermis – take deeper portion if pigment still visible

# Histologic Analysis

- Fix specimen in formalin
- Send to Dermatopathologist.
- If using insurance required multi-service lab, ask for reading by dermatopathologist!
- If diagnosis unexpected either way – speak to pathologist about a second look or new cut from paraffin block.

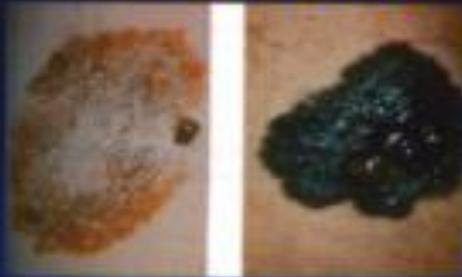
# Risk Management

- Keep a log of all biopsies done that lists:
  - Name of patient
  - Date
  - Type of biopsy
  - Lab sent to
  - Method of sending
  - Date picked up
  - Date report received and put in chart
  - When and how results communicated to patient

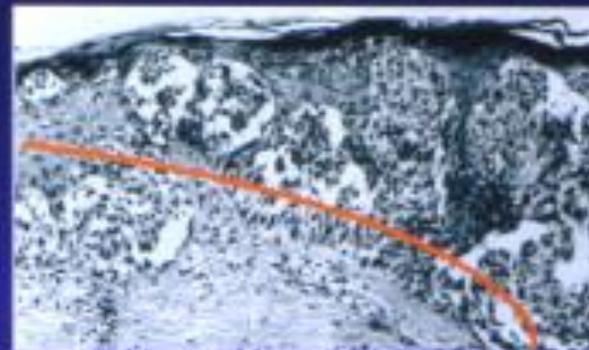
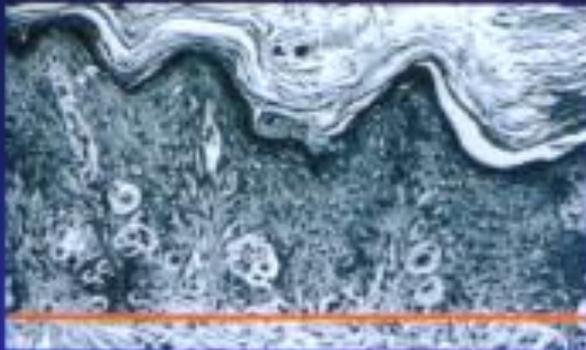
# In-situ versus Invasive

## Melanoma

SSM (In-situ)



SSM (Vertical)



# Diagnosis: Melanoma

In-situ



If lesion totally excised in biopsy procedure – no further local care required



Refer patient for total body skin exam

In-situ



If pathology extends to margins



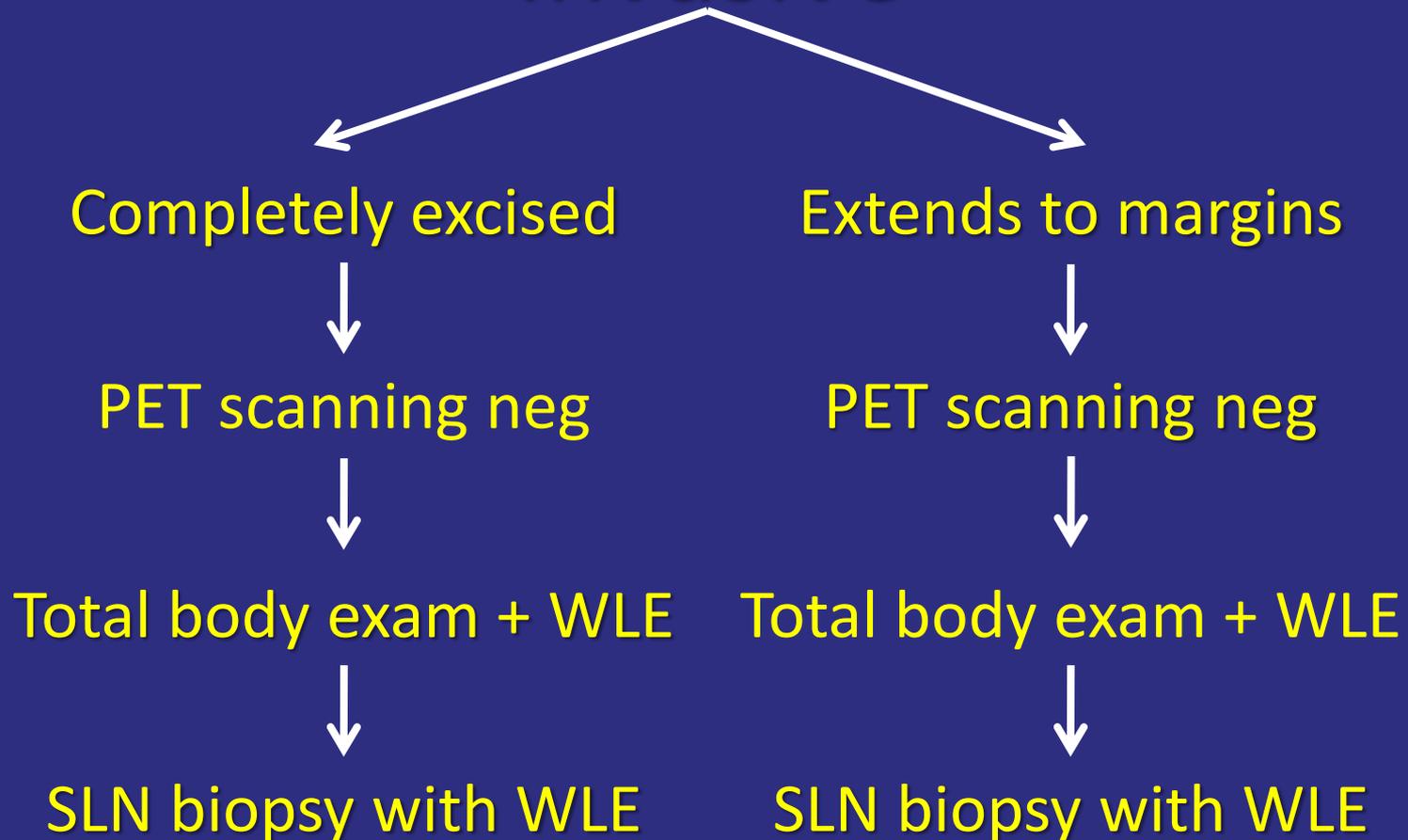
Lesion must be completely excised to make sure all is in-situ and completely excised

# What is a total body skin exam?

- A total body skin examination is a “no modesty protected” completely disrobed examination, including examination of the scalp, genital, breast and anal region regardless of location of primary melanoma
- When patient returns after such an exam, you must frankly ask, “were you disrobed, and were the scalp, genital, and anal regions, and breasts examined?”
- Any hesitation on the part of the patient usually means the exam was lacking
- It is disturbing how many dermatologists fall short on this!
- Also inform patients to let their ophthalmologist and gynecologist know about a skin diagnosis of melanoma

# Diagnosis: Melanoma

## Invasive



# Positron Emission Tomography PET Scanning



Basically a radioactive tracer attached to a sugar molecule which is taken up in tissues used to diagnose, stage and monitor course of disease

# PET Scanning and SLN Biopsy

- If PET Scan positive: may indicate need for further surgery if met(s) are resectable
- If widespread mets are found, further local surgery (WLE) with amputation and/or skin grafting may be moot and therefore not done
- Definitely indicates need for medical oncology referral/possible chemotherapy/clinical trial (molecular targeted therapy or vaccines)
- Significance of negative sentinel node is hopeful but uncertain: tumor may pass through a node without staying there
- Positive sentinel node means same as metastatic but may be hopeful that lesion has been contained, but again uncertain – medical oncology follow up required

# Blood Examination

There are currently no known blood markers for melanoma

# Extent of WLE

- The extent of WLE is dependent on depth in millimeters and has been controversial
- Optimal WLE may only limit local recurrence but not affect long term survival
- In general, 1 cm of resection margin required for each 1 mm of depth, not to exceed 2cm. Depending on anatomical location, this may not be possible or force digital amputation.

# WLE – Mohs Micrographic Surgery

- Acceptable technique for excision of primary and recurrent melanoma in situ and lentigo maligna on **head, neck, hands, FEET, Pretibial surface, Nails, Ankles**
- 99% removal of in situ melanoma with **9mm** margins
- 86% removal of in situ melanoma with **6mm** margins
- Composite of recommendations from AAD, National Comprehensive Cancer Network (NCCN), American College of Mohs Surgery (ACMS), American Society of Dermatologic Surgery Association (ASDSA), American Society for Mohs Surgery (ASMS)

# WLE – Surgical Margins

- Melanoma in situ – Margin size 0.5 – 1.0 cm.
- Invasive smaller than 1mm – Margin size 1.0 cm.
- Invasive 1-2 mm – Margin size 1-2 cm.
- Invasive 2-4 mm – Margin size 2cm.
- Invasive greater than 4 mm – Margin size at least 2 cm

NCCN (2015) and AAD (2011) guidelines

<http://emedicine.medscspe.com/article/2260915>

# Sentinel Lymph Node Biopsy Procedure

- Based on the principle that all spots on the skin have a unique drainage path to a regional node. Foot melanoma usually drains to the inguinal node basin.
- Eliminates the need for initial elective node dissection which has morbidity of infection and permanent swelling

# Sentinel Lymph Node Biopsy and Complete Lymph Node Dissection

- NCCN – 2015 – not recommended for in situ melanoma
- Breslow thickness < 1mm, recommendations are controversial
- NCCN – Not recommended for lesions 0.75mm or thinner
- AAD – 2011 - SLNB recommended in any lesion, including those less than 0.76 mm that demonstrate **Ulceration, Mitosis, Angiolymphatic invasion, Positive deep margin, and Young patient age**

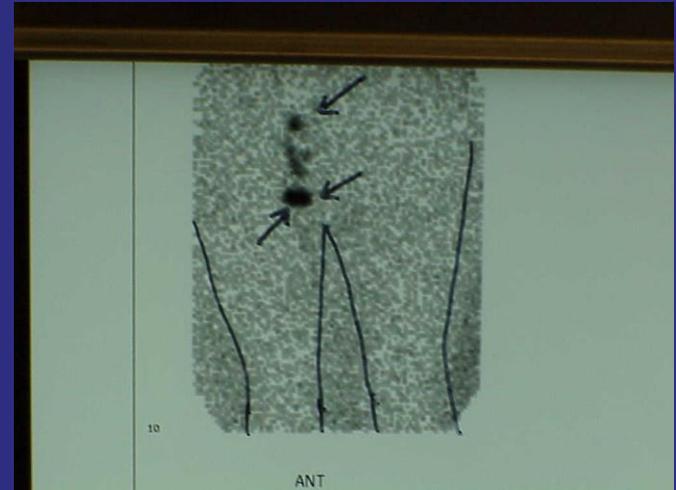
# Sentinel Lymph Node Biopsy and Complete Lymph Node Dissection

- 2012 – Joint Guidelines American Society of Clinical Oncology (ASCO), Society of Surgical Oncology (SSO), and 2009 American Joint Commission for Cancer (AJCC) Melanoma Staging and Classification Committee: **Recommend SLNB for melanomas 1-4 mm in thickness at any anatomic site.**
- CLND recommended for all patients with a positive SLNB. **CLND achieves good regional disease control, but impact on disease free survival is uncertain**

# Pearl – Things That Recur or Do Not Heal Are Suspicious



Sentinel Lymph Node  
Biopsy of Level IV  
Melanoma of Nail Bed

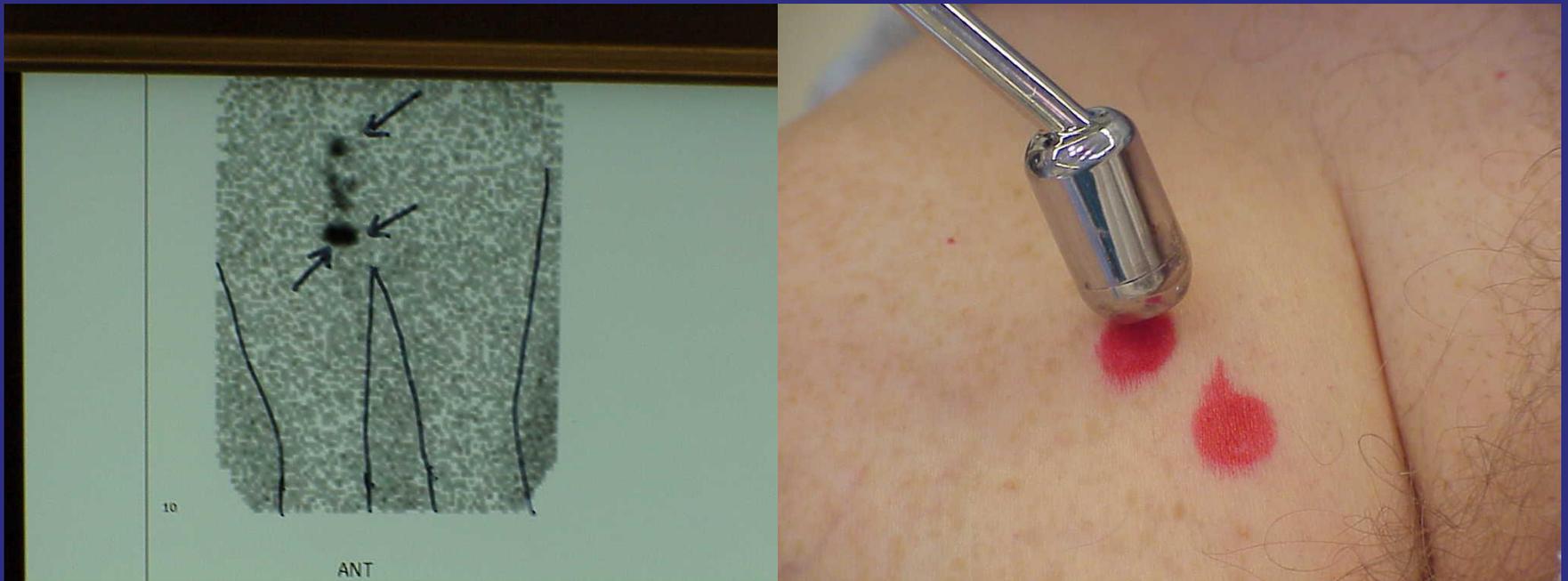


# Sentinel Lymph Node Biopsy



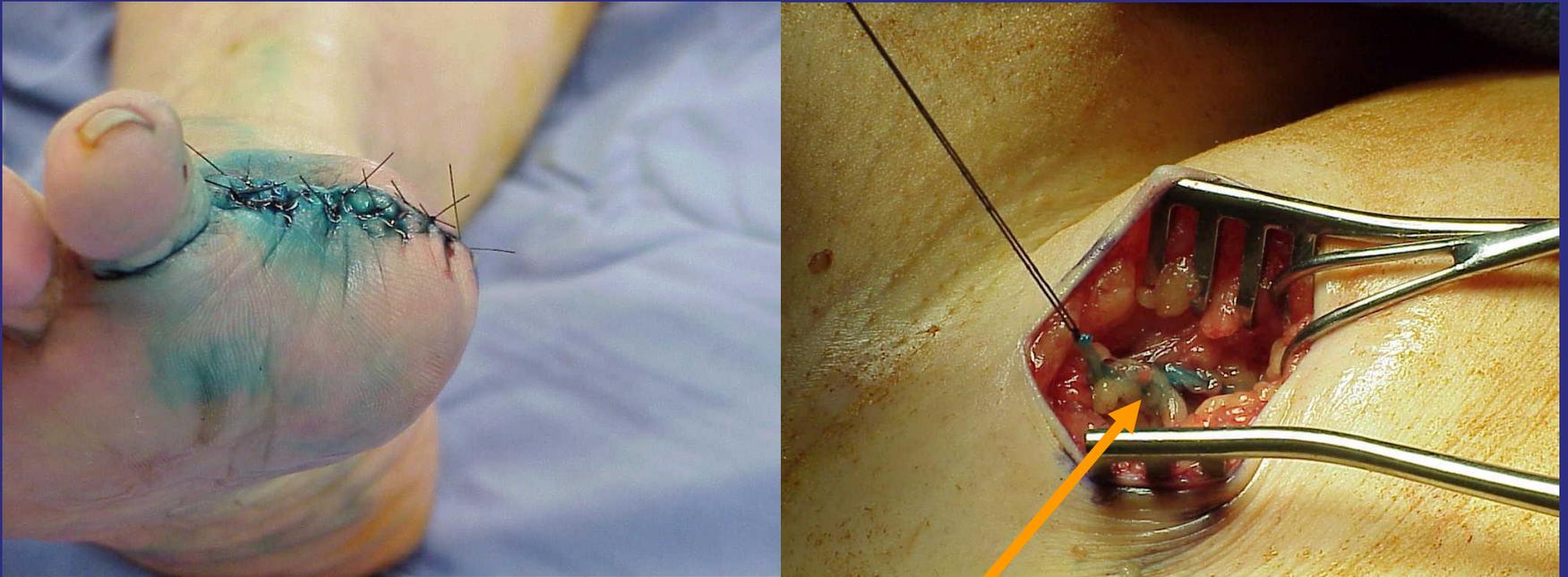
Geiger Counter

# Sentinel Lymph Node Biopsy



Lymphoscintigraphy: 1 Hour prior to surgery – injection of radioactive sulfur colloid at site of lesion. Patient comes to OR with skin markings approximating location of node(s) taking up the tracer.

# Level IV Melanoma of Nail Bed



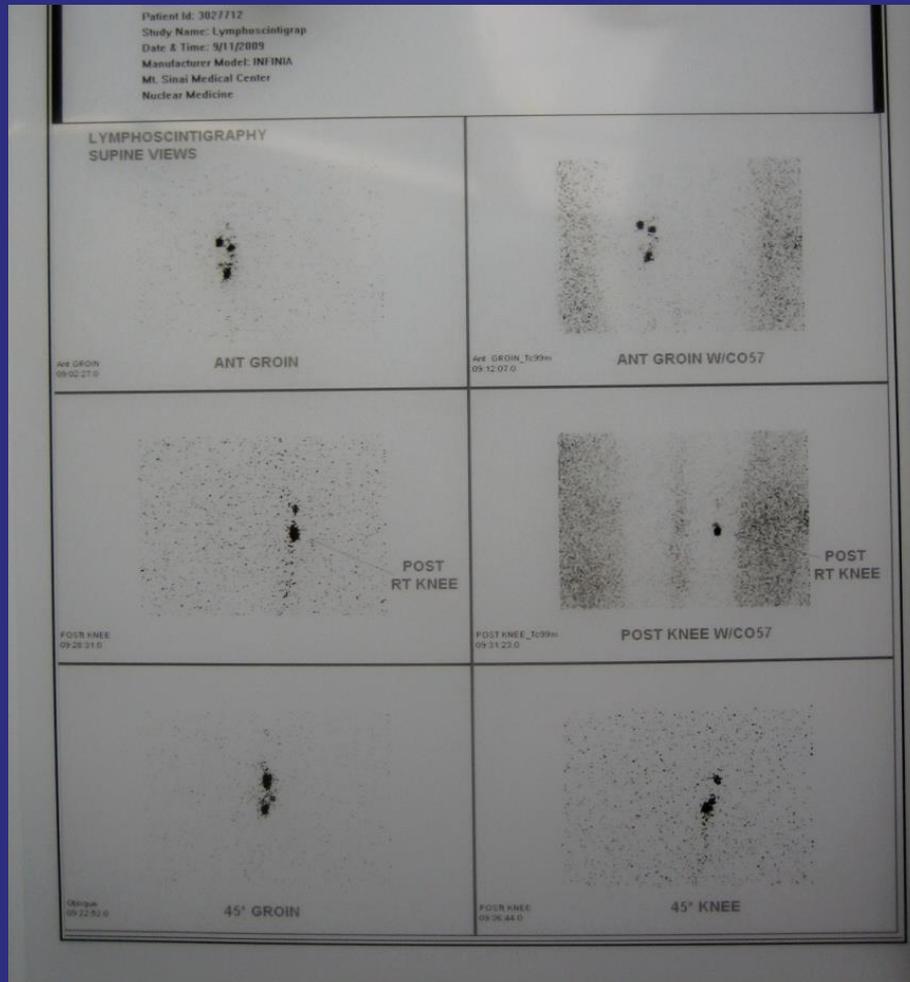
Sentinel “blue” node

**Pearl – Treatment and follow up for these problems should be hospital centered and not office based**

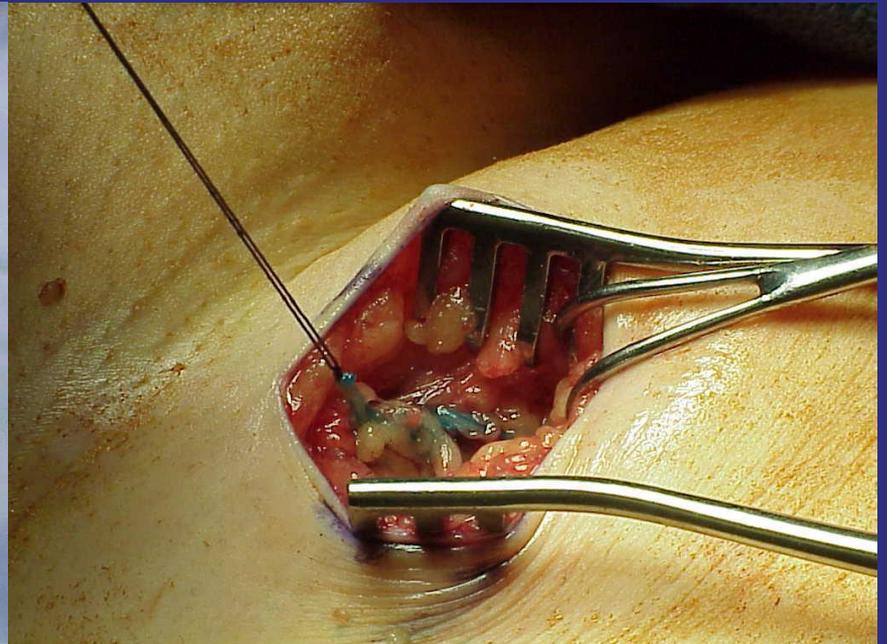


**Iso-sulphane Blue Dye Injection**

# Sentinel Lymph Node Biopsy Blue Dye Injection



# Blue Dye Injection



# Summary

- Excisional biopsy if possible, punch biopsy, and shave for subtle lesions suspicious of melanoma in that order are the best options for pigmented lesion diagnosis
- Specimens should be reviewed by a dermatopathologist
- The management of melanoma, when in-situ, can be an office based situation, but dermatology consultation must be made for total body examination.
- Treatment of invasive melanoma should be hospital centered, as in addition to local podiatric surgery, surgical oncology, medical oncology, nuclear medicine, and other services may be required



American Society  
of Foot and Ankle  
Dermatology



# Melanoma Diagnosis and Surgery



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