A Primary Care Approach to Skin Cancer

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Disclosures

♦ Speaker for MiMedx
♦ Consultant for MiMedx

NO PERTINENT CONFLICTS OF INTEREST
Objectives

- Identify subtle differences between common non-melanocytic skin cancers
- Differentiate benign from malignant pigmented lesions
- Understand how to manage patients with skin cancer
Agenda

- Non-Melanoma Skin Cancer (NMSC)
- Melanocytic Nevi & Melanoma
Primary Lesions in Dermatology

- Macule
- Patch
- Papule
- Plaque
- Nodule
- Vesicle
- Pustule
- Bulla
- Wheel
- Cyst

Use 1cm as your cutoff
Estimated New Cancer Cases* in the US in 2015

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>26%</td>
<td>29%</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>All other sites</td>
<td>21%</td>
<td>21%</td>
</tr>
</tbody>
</table>

*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.
Estimated Cancer Deaths in the US in 2015

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Men 312,150</th>
<th>Women 277,280</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>28%</td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>9%</td>
<td>15%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>All other sites</td>
<td>24%</td>
<td>23%</td>
</tr>
</tbody>
</table>

% caused by cSCC: <1%
% caused by melanoma: <2%

American Cancer Society
Non-Melanoma Skin Cancer (NMSC)

- Diagnostics
- Staging
- Treatment
Skin CA Risk Factors

- Exposure to UV light
- Chemical / Radiation exposure
  - Arsenic/petroleum and organic
- Immunosuppression
- Chronic wounds
- Inflammatory skin conditions (LSA)
- HPV
- Fair Skin
- Cigarette smoking
  - 2x for SCC
- Genetic syndromes
Physical Examination

- Systematic approach
- Stretch skin/ tangential lighting/ magnify
- Look at peripheral border especially if ulcerated
- History also important
  - Duration
  - Change/behavior
Diagnosis

- Requires histopathologic evaluation
- Proper biopsy technique important
- Experience needed to perform biopsy and interpret the pathology
- Refer to Dermatology for difficult sites/tumors/patients
Biopsy Techniques

- **Shave biopsy**
  - Razor blade or scalpel

- **Punch biopsy**
  - 2 - 4 mm punch for deeper biopsy

- **Incisional biopsy**

- **Excisional biopsy**
Shave Biopsy
Punch Biopsy
CELL CYCLE REGULATION

Proto-oncogenes

Growth factors

Growth factor receptors

Cell membrane

Inhibition
Stimulation
Phosphorylation

Resting

G0

Mitotic signals

Mitosis

G1

Gap 1

Phosphorylated Rb

Unphosphorylated Rb

Rb

E2-F

Cdk

Cyclin-dependent kinase-cyclin complex

Transcription of G1/S cyclins

p21

p16

p15

p27

Cdk inhibitors

Tumor suppressor genes

p53

mdm2

p14 ARF

Cyclin waves drive cell cycle progression

G0

G1

S

G2

M

G2 check point

Gap 2

DNA synthesis

Gap 1

G1 check point

Basal Cell Carcinoma

- Histologic subtypes correlate with biologic behavior and directly impact treatment plan

- Non-Aggressive
  - Nodular
  - Superficial
  - Pigmented

- Aggressive
  - Morpheaform/sclerotic
  - Infiltrative
  - Micronodular
What is the Classic H&E Finding?

- Peripheral Palisading of the Basal Cells
Nodular
Superficial
Micronodular
Infiltrative
AJCC Cancer Staging Manual, 7th ed

- **T** = Size and Extent of Primary Tumor
- **N** = Involvement of Regional Lymph Nodes
- **M** = Presence of Distant Metastases

### ANATOMIC STAGE/PROGNOSTIC GROUPS

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N2</td>
<td>M0</td>
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<tr>
<td></td>
<td>T Any</td>
<td>N3</td>
<td>M0</td>
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<tr>
<td></td>
<td>T4</td>
<td>N Any</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T Any</td>
<td>N Any</td>
<td>M1</td>
</tr>
</tbody>
</table>

**Low Risk** Stage 0-1  
**High Risk** Stage 2-4
### TNM Classification for Skin Cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension with less than two high-risk features**</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor greater than 2 cm in greatest dimension or Tumor any size with two or more high-risk features*</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor with invasion of maxilla, mandible, orbit, or temporal bone</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor with invasion of skeleton (axial or appendicular) or perineural invasion of skull base</td>
</tr>
</tbody>
</table>

**Excludes cSCC of the eyelid (see Chap. 48).**

**High-risk features for the primary tumor (T) staging**

- Depth/invasion:  
  - Thickness >2 mm  
  - Clark level ≥ IV  
  - Perineural invasion

- Anatomic location:  
  - Primary site ear
  - Primary site non-hair-bearing lip

- Differentiation: Poorly differentiated or undifferentiated

### LN Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastases</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2a</td>
<td>Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2b</td>
<td>Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N2c</td>
<td>Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node, more than 6 cm in greatest dimension</td>
</tr>
</tbody>
</table>

### M Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastases</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>
AJCC High-Risk Cutaneous SCC

- Location of tumor on the ear or lip
- Tumor diameter greater than 2cm
- Poor histologic differentiation
- Perineural invasion
- Deep extension – Clarks Level IV
- >2mm thick – Breslow Depth

Immunosuppression is not included in the AJCC criteria
Eyelid tumors have their own section
Clinical Significance of High-Risk Cutaneous SCC

- Causes 20% of skin cancer related deaths
- 4th most common cause of death in renal transplant
- 5-20% increased metastatic disease risk
Solid Organ Transplant Patients

- High-risk due to need for immunosuppression
- Develop SCCs 65x than general population
- Carry a 5.3 times increased risk of recurrence
- cSCCs occur 10-30 years earlier
Immunosuppression shifts the curve to the left.
NMSC Treatment Options

- Electrodessication and curettage
- Cryosurgery
- Radiation
- Topical medications
- Photodynamic therapy
- Standard excision
- Mohs micrographic surgery
<table>
<thead>
<tr>
<th>H&amp;P</th>
<th>Low Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location/size</td>
<td>Area L &lt; 20 mm</td>
<td>Area L ≥ 20 mm</td>
</tr>
<tr>
<td></td>
<td>Area M &lt; 10 mm</td>
<td>Area M ≥ 10 mm</td>
</tr>
<tr>
<td></td>
<td>Area H &lt; 6 mm&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Area H ≥ 6 mm&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Borders</td>
<td>Well defined</td>
<td>Poorly defined</td>
</tr>
<tr>
<td>Primary vs. Recurrent</td>
<td>Primary</td>
<td>Recurrent</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>(&lt;)</td>
<td>(+)</td>
</tr>
<tr>
<td>Site of prior RT</td>
<td>(&lt;)</td>
<td>(+)</td>
</tr>
<tr>
<td>Pathology</td>
<td>Nodular, superficial</td>
<td>Aggressive growth pattern&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Subtype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perineural involvement</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Location independent of size may constitute high risk in certain clinical settings.

<sup>2</sup> Having morpheaform, sclerosing, mixed infiltrative, or micronodular features in any portion of the tumor.

**Note:** All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
## RISK FACTORS FOR RECURRENT

<table>
<thead>
<tr>
<th>H&amp;P</th>
<th>Low Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location/size(^1)</td>
<td>Area L &lt; 20 mm</td>
<td>Area L ≥ 20 mm</td>
</tr>
<tr>
<td></td>
<td>Area M &lt; 10 mm</td>
<td>Area M ≥ 10 mm</td>
</tr>
<tr>
<td></td>
<td>Area H &lt; 6 mm(^3)</td>
<td>Area H ≥ 6 mm(^3)</td>
</tr>
<tr>
<td>Borders</td>
<td>Well-defined</td>
<td>Poorly-defined</td>
</tr>
<tr>
<td>Primary vs recurrent</td>
<td>Primary</td>
<td>Recurrent</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>Site of prior RT or chronic inflammatory process</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>Rapidly growing tumor</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>Neurologic symptoms</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>Pathology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Degree of differentiation</td>
<td>Well differentiated</td>
<td>Moderately or poorly differentiated</td>
</tr>
<tr>
<td>Adenoid (acantholytic), adenosquamous (showing mucin production), or desmoplastic subtypes</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>Depth: Clark level or thickness(^2)</td>
<td>I, II, III, or &lt; 4 mm</td>
<td>IV, V, or ≥ 4 mm</td>
</tr>
<tr>
<td>Perineural or vascular involvement</td>
<td>(-)</td>
<td>(+)</td>
</tr>
</tbody>
</table>

### Notes
- **Area H**: “mask areas” of face (central face, eyelids, eyebrows, peri orbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.
- **Area M**: cheeks, forehead, scalp, and neck.
- **Area L**: trunk and extremities.

\(^1\) Must include peripheral rim of erythema.

\(^2\) A modified Breslow measurement should exclude parakeratosis or scale/crust, and should be made from base of ulcer if present.

\(^3\) Location independent of size may constitute high risk in certain clinical settings.

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**Note:** All recommendations are category 2A unless otherwise indicated.

**Clinical Trials:** NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
PRIMARY TREATMENT

C&E:
- In non-hair-bearing areas
- If fat reached, surgical excision must be performed

or

Excision with POMA:
- If lesion can be excised with 4-6 mm clinical margins and secondary intention, side-to-side repair, or skin graft

or

RT* (category 2B) for non-surgical candidates

ADJUVANT TREATMENT

Mohs or resection with CCPDMA or Re-excision with POMA for area L* regions or RT*

Positive

Margins

Negative

See Follow-up (SCC-7)

Local, Low-Risk Squamous Cell Skin Cancer

C&E = curettage and electrodesiccation
POMA = postoperative margin assessment
CCPDMA = complete circumferential peripheral and deep margin assessment with frozen or permanent section

*See Principles of Treatment for Squamous Cell Skin Cancer (SCC-B).
*See Principles of Radiation Therapy, Squamous Cell Skin Cancer (SCC-C).
*RT generally reserved for patients over 60 y because of concerns about long term sequellae.
*L = trunk and extremities. (See SCC-A)
Squamous Cell Skin Cancer

Primary Treatment

- Excision with POMA
  - Lesion ≥ 20 mm in area L with no other high-risk factors, if can be excised with 10 mm clinical margins + primary repair
  - or
- Mohs or resection with CCPDMA
  - or
- RT (category 2B) for non-surgical candidates

Adjuvant Treatment

- Positive Margins → Mohs or resection with CCPDMA or RT
- Negative
  - Positive → RT
  - Negative → If extensive perineural or large-nerve involvement, recommend adjuvant RT

POMA = postoperative margin assessment
CCPDM = complete circumferential peripheral and deep margin assessment with frozen or permanent section

Any high-risk factor places the patient in the high-risk category.
See Principles of Treatment for Squamous Cell Skin Cancer (SCC-B).
See Principles of Radiation Therapy Squamous Cell Skin Cancer (SCC-C).
RT generally reserved for patients over 60 y because of concerns about long term sequelae.
Area L = trunk and extremities. (See SCC-A)
In certain high-risk lesions consider sentinel lymph node mapping, although the benefit of this technique has yet to be proven.
For complicated cases, consider multidisciplinary tumor board consultation.
If invasion to parotid fascia, superficial parotidectomy.
Negative margins unachievable by MOHS surgery or more extensive surgical procedures.
If large nerve involvement is suspected, consider MRI to evaluate extent and rule out skull involvement.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Electrodessication & Curettage
Standard Excision
Buried vertical mattress suture
Simple interrupted suture
Unna Wraps

- Apply 5-Flourouracil 5% (1/2 tube per leg) with petrolatum
- Wrap with unna boot and Coban or Kerlix
- Repeat weekly for 4 to 6 weeks
- Stop: erosions with normal tissue in between
- May give 1-2 weeks off if have social events
- Biopsy lesions that are not responding to therapy
- Consider test for dihydropyrimidinedehydrogenaseenzyme if develop systemic symptoms

Check for dihydropyrimidine dehydrogenase enzyme deficiency
Follow-Up

Table 1. Guidelines for the Examination and Follow-Up of OTRs

- Review of systems exam (i.e., constitutional, lungs).
- Full-body skin exam including scalp, genitalia, and feet at least annually. Regional sun-exposed skin exam at other visits.
- Reevaluation of previous sites of NMSC, including regional lymph node exam with attention to the primary drainage basin(s).
- Treat actinic keratoses early.
- Low threshold for skin biopsy—full-thickness biopsy is recommended for definitive diagnosis and histologic evaluation.
- Laboratory and radiologic studies are reserved for patients with signs and symptoms of metastatic disease.
- Patient education with regard to sun exposure and self-examination of the skin and lymph nodes should be given.

Abbreviations: NMSC, nonmelanoma skin cancer.

## Follow-Up

### Table 2. Guidelines for Follow-up Intervals for OTRs\(^\text{63}\)

<table>
<thead>
<tr>
<th>Patient Risk Factors</th>
<th>Frequency of Skin Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factors except immunosuppression</td>
<td>Initial exam + exam every 12–24 months</td>
</tr>
<tr>
<td>Risk factors but no history of malignant/premalignant lesions</td>
<td>Initial exam + exam every 6–12 months</td>
</tr>
<tr>
<td>Actinic keratoses or warts</td>
<td>Initial exam + treatment + exam every 3–6 months</td>
</tr>
<tr>
<td>One basal cell carcinoma</td>
<td>Initial exam + treatment + exam every 3–6 months</td>
</tr>
<tr>
<td>One SCC</td>
<td>Initial exam + treatment + exam every 3–6 months</td>
</tr>
<tr>
<td>Multiple NMSC</td>
<td>Initial exam + treatment + exam every 3 months</td>
</tr>
<tr>
<td>High-risk SCC</td>
<td>Initial exam + treatment + exam every 1–3 months</td>
</tr>
<tr>
<td>Metastatic SCC</td>
<td></td>
</tr>
</tbody>
</table>

*Because of the increasingly high risk of skin cancer development from the time of transplantation, periodic skin evaluation is recommended for the life of the patient.*

Abbreviation: NMSC, nonmelanoma skin cancer; SCC, squamous cell carcinoma.

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Patient Education

Examine head and face, using one or both mirrors. Use blow-dryer to inspect scalp.

Check hands, including nails. In full-length mirror, examine elbows, arms, underarms.

Focus on neck, chest, torso. Women: Check under breasts.

With back to the mirror, use hand mirror to inspect back of neck, shoulders, upper arms, back, buttocks, legs.

Sitting down, check legs and feet, including soles, heels, and nails. Use hand mirror to examine genitals.

Patient Education

Three simple steps to follow

Step #1: Daily Sun Protection

1. Use broad spectrum sunscreen daily with SPF of 30 or greater. See Sunscreen Facts for more information.
2. Use protective clothing. This is defined as long sleeve shirts with conservative neckline and long pants with a tight fabric weave. Clothing such as this is usually considered by many as very hot, and thus not worn. However, this does not have to be the case. Loose, light-weight fabrics can be worn that are protective and stylish. Most clothing provides adequate protection as long as it is worn. The one exception to this may be a white cotton T-shirt, worn by many during the warm seasons, which provides a UPF of only ~5.
3. Wear a broad-brimmed hat. Baseball style caps provide no protection for the ears, which is a common area for skin cancer to occur.
4. Avoid sun exposure as much as possible between the hours of 10AM and 4PM. Attempt to concentrate outdoor activities into early morning, late afternoon, and evening. If your shadow is shorter than you are, you’re likely to sunburn.
5. Avoid tanning beds. A tan obtained in a tanning bed does NOT provide protection from harm sunrays.
6. Wear sunglasses.
7. Seek shade.
8. Don’t stay in the sun for prolonged periods of time, even if you are wearing sunscreen.
9. For more detailed information on each of these sun protective behaviors please check the Sun Smart site (link to http://www.sunsmart.com.au/sun_protection)

Step #2: Monthly Self Skin Examination

In a brightly lit room, with two mirrors, look over your entire skin surface. Do this once a month. A family member may assist with examination of the back, but if they are not consistently available, you can use two mirrors for this exam. (link to http://www.skincarephysicians.com/SkinCancerNet/skin_examinations.html)

Step #3: Timely Skin Examination by a Dermatologist

You should receive at least one complete skin examination by a dermatologist closely after the time of your transplant (within 4 months if possible).

Your physician will then recommend how often you should receive subsequent skin examination. This depends on the number of risk factors for skin cancer, and the amount of skin disease and sun damage that you have. It may range from every month to only as needed (provided that your primary care or transplant physicians were examining your skin on routine yearly exams.)

Find an ITSCC Transplant Dermatologist in your Area

http://www.itscc.org/patients/skin_cancer/prevention.php
What is Mohs Surgery?
Frederich E. Mohs, MD

- General Surgeon
- Developed in 1936
- Originally dubbed “chemosurgery”
- Zinc chloride paste fixing method
- Now use frozen section
Mohs Micrographic Surgery

- Used on tumors with contiguous growth
- Precise microscopic margin control of tumor margins
- 100% of peripheral & deep margin examined
  - Traditional vertical sections examine less than 1%
- Highest cure rate (97% - 99%)
- Most tissue conservation
Mohs Micrographic Surgery

**Critical Location**
(Cosmetic and Functional)

- Periorbital
- Perioral
- Periauricular
- Perinasal
- Hands and feet
- Genitalia
Mohs Micrographic Surgery

Aggressive Histology

- Infiltrating BCC
- Micronodular BCC
- Morpheaform BCC
- Metatypical BCC
- Perineural invasion
- Poorly differentiated SCC
- Acantholytic SCC
Recurrent Tumors

- Tumors that have recurred after prior treatment
- Can be more aggressive than original tumor
  - More difficult to cure
  - Have even higher subsequent recurrence
  - More ill-defined
  - Have higher metastatic potential
Mohs Micrographic Surgery

Other Cutaneous Tumors

- Dermatofibrosarcoma protuberans (DFSP)
- Atypical fibroxanthoma (AFX)
- Sebaceous carcinoma
- Merkel cell carcinoma
- Microcystic adnexal carcinoma
- Verrucous carcinoma
- Angiosarcoma
Mohs Surgery Advantages

- Highest Cure Rate
  - 97% - 99% for primary tumors
  - 94% for recurrent tumors
  - Entire margin evaluated microscopically
  - Cure rates of other methods
    - Standard excision: 89.9%
    - Destruction: 81% - 96%
    - Radiation: 91%
Mohs Surgery Advantages

All of peripheral & deep margin examined

- Less than 1% examined in standard vertical sections

Standard “breadloafing” of tissue is only small sample
The Proverbial “Tip of the Iceberg”
Visible lesion on skin

1. First thin layer removed

2. Another thin layer removed

3. Another thin layer removed

4. Final layer of cancer removed
Mohs Surgery: Summary

- Highest cure rate (97-99%)
  - Entire margin evaluated
  - Fewer recurrences

- Leaves the smallest surgical defect possible
  - Preserves maximal amount of tissue
  - Increases the chance of a good aesthetic result

- Most cost effective treatment of select tumors
  - Outpatient setting
Mohs Surgery Advantages

Cost Effective

- Outpatient office setting, not OR
- Pathology reading included
- Local anesthesia rather than general
- Lowest recurrence rate
Mohs Cost Effectiveness

Figure 1. Comparison layout of costs included in calculations.
† - Secondary intention wound healing was calculated as $0 repair.
‡ - Excision costs were added whenever not bundled with repairs.
Radiation Therapy Recurrence $4,558 / 5-9%

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Nose</th>
<th>Ear</th>
<th>Eyelid</th>
<th>Face</th>
<th>Scalp or Neck</th>
<th>Trunk or Extremity</th>
<th>Hands or Feet</th>
<th>Genitalia</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMS</td>
<td>996.50</td>
<td>803.38</td>
<td>1,042.70</td>
<td>876.17</td>
<td>783.02</td>
<td>827.88</td>
<td>651.72</td>
<td>596.22</td>
</tr>
<tr>
<td>Office excision, permanent</td>
<td>1,219.13</td>
<td>1,347.50</td>
<td>1,330.45</td>
<td>1,142.88</td>
<td>921.88</td>
<td>863.31</td>
<td>1,036.38</td>
<td>886.25</td>
</tr>
<tr>
<td>Office excision, frozen</td>
<td>1,322.88</td>
<td>1,451.25</td>
<td>1,434.20</td>
<td>1,246.63</td>
<td>1,025.63</td>
<td>967.06</td>
<td>1,140.13</td>
<td>989.99</td>
</tr>
<tr>
<td>ASC excision, frozen</td>
<td>3,853.19</td>
<td>4,004.12</td>
<td>4,059.90</td>
<td>2,982.65</td>
<td>2,685.58</td>
<td>2,309.81</td>
<td>3,178.54</td>
<td>2,640.81</td>
</tr>
</tbody>
</table>
Radiation Therapy ADRs

Radiation Induced Malignancies

- May occur in chronic radiation sites or may not have had evidence of chronic radiation
- Sun damage is additive
- When do they occur?
  - 20-40 yrs
- MC tumor?
  - 1. BCC 2. SCC
Merkel Cell Carcinoma

CLINICAL PRESENTATION

Suspicious lesion
- H&P
- Complete skin and lymph node examination

Preliminary Workup

Biopsy
- H&E
- Immunopanela

Diagnosis

Merkel cell carcinoma

Clinical N0

- Imaging studies as clinically indicated
- Consider multidisciplinary tumor board consultation

Clinical N+

- See Primary and Adjuvant Treatment (MCC-2)

Clinical M1

- See Treatment (MCC-4)

Clinical N0

- See Primary and Adjuvant Treatment (MCC-3)

An appropriate immunopanel should preferably include CK-20 and thyroid transcription factor-1 (TTF-1).

bImaging (CT, MR, or PET-CT) may be useful to identify and quantify regional and distant metastases. Imaging may also be useful to evaluate for the possibility of a skin metastasis from a noncutaneous primary neuroendocrine carcinoma (eg, small cell lung cancer), especially in cases where CK-20 is negative.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
After wide local excision, sentinel lymph node biopsy may be considered in selected patients, although accuracy of results may be compromised, especially in non-extremity regions.

See Principles of Radiation Therapy (MCC-A).

Consider observation of the tumor bed, in cases where the primary tumor is small, widely excised with no other adverse risk factors.

The preferred treatment sequence is for the sentinel lymph node biopsy to precede the excision.

In the head and neck region, risk of false negative sentinel lymph node biopsy is higher, due to aberrant lymph node drainage and frequent presence of multiple sentinel lymph node basins.

An appropriate immunopanel for SLN examination should preferably include CK-20, and pancytokeratins (AE1/AE3).

See Principles of Excision (MCC-B). In selected cases in which complete surgical excision is not possible, surgery is refused by the patient, or would result in significant morbidity, radiation mono-therapy may be considered (See Principles of Radiation Therapy MCC-A1).

For lymph nodes that are positive only by immunohistochemical methods but not H&E, consider RT as the sole therapy to the draining nodal basin(s).

See Chemotherapy Agents (MCC-C).

Available retrospective studies do not suggest prolonged survival benefit for adjuvant chemotherapy.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
PRINCIPLES OF EXCISION

Goal:
• Clear surgical margins when clinically feasible.

Varied Approaches:
• 1-2 cm margins to investing fascia of muscle or pericranium with clear pathologic margins, when clinically feasible.
• Mohs technique\(^1,2\)
• Modified Mohs = Mohs technique with additional final margin for permanent section assessment.
• CCPDMA= Complete circumferential and peripheral deep-margin assessment.\(^3\)

Reconstruction:
• Immediate reconstruction in most cases.
• It is recommended that any reconstruction involving extensive undermining or tissue movement be delayed until negative histological margins are verified.
• When primary closure is not possible, consider split-thickness skin grafting (STSG) to monitor for recurrence.

\(^1\) Mohs technique is used primarily in MCC to insure complete removal and clear margins, and secondarily for its tissue sparing capabilities.
\(^2\) If Mohs is used for MCC, a debulked specimen of the central portion of the tumor should be sent for permanent section microstaging.
\(^3\) Usually performed as a meticulous, comprehensive en face permanent section examination of all surgical margins.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
# NCCN Guidelines™ Version 1.2012 Staging Merkel Cell Carcinoma

## Staging

### Table 1

**American Joint Committee on Cancer (AJCC)**  
**TNM Staging Classification for Merkel Cell Carcinoma**  
(7th ed., 2010)

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th><em>Clinical detection of nodal disease may be via inspection, palpation, and/or imaging.</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor (e.g., nodal/metastatic presentation without associated primary)</td>
</tr>
<tr>
<td>Tis</td>
<td>In situ primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Less than or equal to 2 cm maximum tumor dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Greater than 2 cm but not more than 5 cm maximum tumor dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Over 5 cm maximum tumor dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Primary tumor invades bone, muscle, fascia, or cartilage</td>
</tr>
</tbody>
</table>

**Regional Lymph Nodes (N)**

| NX                | Regional lymph nodes cannot be assessed                                          |
| N0                | No regional lymph node metastasis                                               |
| cN0               | Nodes negative by clinical exam* (no pathologic node exam performed)            |
| pN0               | Nodes negative by pathologic exam                                               |
| N1                | Metastasis in regional lymph node(s)                                            |
| N1a               | Micrometastasis**                                                                |
| N1b               | Macronodometastasis***                                                           |
| N2                | In transit metastasis****                                                        |

**Distant Metastasis (M)**

| M0                | No distant metastases                                                           |
| M1                | Metastasis beyond regional lymph nodes                                          |
| M1a               | Metastasis to skin, subcutaneous tissues or distant lymph nodes                 |
| M1b               | Metastasis to lung                                                               |
| M1c               | Metastasis to all other visceral sites                                           |

---

*Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original and primary source for this information is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC (SBM). For complete information and data supporting the staging tables, visit [www.springer.com](http://www.springer.com) Any citation or quotation of this material must be credited to the AJCC as its primary source. The inclusion of this information herein does not authorize any reuse or further distribution without the expressed written permission of SBM, on behalf of the AJCC.*
### Staging

**Table 1 (continued)**

<table>
<thead>
<tr>
<th>TNM Staging Classification for Merkel Cell Carcinoma (7th ed., 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 0</strong></td>
</tr>
<tr>
<td><strong>Stage IA</strong></td>
</tr>
<tr>
<td><strong>Stage IB</strong></td>
</tr>
<tr>
<td><strong>Stage IIA</strong></td>
</tr>
<tr>
<td><strong>Stage IIB</strong></td>
</tr>
<tr>
<td><strong>Stage IIC</strong></td>
</tr>
<tr>
<td><strong>Stage IIIA</strong></td>
</tr>
<tr>
<td><strong>Stage IIIB</strong></td>
</tr>
<tr>
<td><strong>Stage IV</strong></td>
</tr>
</tbody>
</table>

**ANATOMIC STAGE/PROGNOSTIC GROUPS**

Patients with primary Merkel cell carcinoma with no evidence of regional or distant metastases (either clinically or pathologically) are divided into two stages: Stage I for primary tumors ≤ 2 cm in size and Stage II for primary tumors >2 cm in size. Stages I and II are further divided into A and B substages based on method of nodal evaluation. Patients who have pathologically proven nodal negative disease (by microscopic evaluation of their draining lymph nodes) have improved survival (substaged as A) compared to those who are only evaluated clinically (substaged as B). Stage II has an additional substage (IIC) for tumors with extracutaneous invasion (T4) and negative node status regardless of whether the negative node status was established microscopically or clinically. Stage III is also divided into A and B categories for patients with microscopically positive and clinically occult nodes (IIIA) and macroscopic nodes (IIIB). There are no subgroups of Stage IV Merkel cell carcinoma.
Muir Torre Syndrome

- Lynch II assoc...what are the Lynch syndromes?
  - Hereditary Non-polyposis Colon CA
  - Lynch 1: Colorectal CA only
  - Lynch 2: Colorectal CA + other CA

- Ophthalmic sebaceous tumor can be the presenting sign

- Needs endoscopy/GI x-ray

- Internal malignancies typically precede cutaneous lesions

- DNA Mismatch repair genes MLH1, MSH2
Melaocytic Nevi and Melanoma

- Your Melanoma Biopsy Threshold
- Melanoma Basics
- Treatment
Melanocytic Nevi

http://www.imperial.ed u/~thomas.morrell/Pict ure2.jpg
Melanoma Incidence

How do we improve diagnosis at an early stage?
How do we predict who will not survive?
What criteria do you use to evaluate risk for melanoma?

How do you know what and when to biopsy?
Focus is on improving your “batting average”

<table>
<thead>
<tr>
<th></th>
<th>Disease (number)</th>
<th>Non Disease (number)</th>
<th>Total (number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (number)</td>
<td>A (True Positive)</td>
<td>B (False Positive)</td>
<td>$T_{Test~Positive}$</td>
</tr>
<tr>
<td>Negative (number)</td>
<td>C (False Negative)</td>
<td>D (True Negative)</td>
<td>$T_{Test~Negative}$</td>
</tr>
</tbody>
</table>

$T_{Disease}$, $T_{Non~Disease}$, Total
Understanding Melanoma Risk

Subjective Risk Factors

Objective Risk Factors

- ABCDEs
- Density of Nevi – atypical vs normal
- Degree of Lentiginosus
- Perceived Similarity Clusters
Melanoma Risk Factors

- Family/personal history of melanoma
- Red or blond hair
- Actinic keratoses/NMSC
- Fair skin types
- >3 blistering sunburns before age 20
- >3 outdoor summer jobs before age 20
Melanoma Risk Factors

- One or two risk factors = 3- to 4-fold increase
- Three or more risk factors = 20-fold increase

Lacking Multivariate Analysis, but...
This sets your initial threshold

Familial Melanoma

- CDKN2A mutations: 20% of tested melanoma families
- CDKN2A mutation
  - 30% risk for melanoma by age 50
  - 67% risk for melanoma by age 80
  - Varies with risk area.

Risk of Melanoma or skin cancer with p16 gene mutation

- Melanoma By Age 50: Up to 76%
- Melanoma By Age 80: Up to 76%
- Pancreatic Cancer By Age 75: Up to 17%

*Based on US data
Molecular Targets in Melanoma from Angiogenesis to Apoptosis
Jeffrey A. Sosman and Igor Puzanov
Clin Cancer Res 2006;12:2376s-2383s
Understanding Melanoma Risk

- Subjective Risk Factors
- Objective Risk Factors
  - ABCDEs
  - Density of Nevi – atypical vs normal
  - Degree of Lentiginosus
  - Perceived Similarity Clusters
Melanocytic Nevi

- Junctional
- Dermal
- Compound
- Congenital vs Acquired
- Atypical
Atypical Nevi

- Atypical vs Dysplastic
- Mild, Moderate, vs Severe Atypia
- Nevi of Special Sites
Melanocytic Nevi Description

ABCDEs?
- A = Asymmetry
- B = Border irregularity
- C = Color variation
- D = Diameter >6 mm
- E = Evolution

Definition of an atypical nevus
- >5mm
- 2 of 3: Symmetry, Border, Color

<table>
<thead>
<tr>
<th>No. of Nevi by Type</th>
<th>No. of Cases</th>
<th>No. of Controls</th>
<th>Adjusted RR</th>
<th>Adjusted† RR</th>
<th>Adjusted‡ RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevi &gt;2 mm and &lt;5 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-24</td>
<td>258</td>
<td>658</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0 . . .</td>
</tr>
<tr>
<td>25-49</td>
<td>163</td>
<td>190</td>
<td>2.4</td>
<td>1.6</td>
<td>1.8 (1.3-2.5)</td>
</tr>
<tr>
<td>50-99</td>
<td>169</td>
<td>107</td>
<td>4.5</td>
<td>2.5</td>
<td>3.0 (2.1-4.4)</td>
</tr>
<tr>
<td>≥100</td>
<td>123</td>
<td>43</td>
<td>8.5</td>
<td>3.1</td>
<td>3.4 (2.0-5.7)</td>
</tr>
<tr>
<td>Nondysplastic nevi &gt;5 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>239</td>
<td>507</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0 . . .</td>
</tr>
<tr>
<td>1</td>
<td>135</td>
<td>224</td>
<td>1.3</td>
<td>1.0</td>
<td>0.9 (0.7-1.3)</td>
</tr>
<tr>
<td>2-4</td>
<td>188</td>
<td>195</td>
<td>2.0</td>
<td>1.4</td>
<td>1.3 (1.0-1.8)</td>
</tr>
<tr>
<td>5-9</td>
<td>86</td>
<td>51</td>
<td>3.7</td>
<td>1.9</td>
<td>1.7 (1.0-2.7)</td>
</tr>
<tr>
<td>≥10</td>
<td>65</td>
<td>21</td>
<td>7.2</td>
<td>2.3</td>
<td>2.3 (1.2-4.3)</td>
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<tr>
<td>Congenital nevi</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>605</td>
<td>881</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0 . . .</td>
</tr>
<tr>
<td>Solitary</td>
<td>74</td>
<td>85</td>
<td>1.3</td>
<td>1.1</td>
<td>1.1 (0.7-1.7)</td>
</tr>
<tr>
<td>Multiple</td>
<td>34</td>
<td>32</td>
<td>1.6</td>
<td>1.1</td>
<td>1.3 (0.7-2.5)</td>
</tr>
<tr>
<td>Dysplastic nevi§</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>301</td>
<td>778</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0 . . .</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>72</td>
<td>127</td>
<td>1.5</td>
<td>1.1</td>
<td>1.0 (0.7-1.6)</td>
</tr>
<tr>
<td>1</td>
<td>64</td>
<td>50</td>
<td>3.8</td>
<td>2.2</td>
<td>2.3 (1.4-3.6)</td>
</tr>
<tr>
<td>2-4</td>
<td>121</td>
<td>33</td>
<td>11</td>
<td>6.9</td>
<td>7.3 (4.6-12)</td>
</tr>
<tr>
<td>5-9</td>
<td>45</td>
<td>15</td>
<td>8.6</td>
<td>4.4</td>
<td>4.9 (2.5-9.8)</td>
</tr>
<tr>
<td>≥10</td>
<td>55</td>
<td>6</td>
<td>32</td>
<td>12</td>
<td>12 (4.4-31)</td>
</tr>
</tbody>
</table>
Dysplastic Nevus Syndrome

- Familial melanoma/dysplastic nevus syndrome
- Families with dysplastic nevi and two or more blood relatives with melanoma,
- Estimated melanoma in affected family members approaches 85% by age 48 years
- Epidemiologic study, not a genetic study

Special Considerations

Special Sites
- Scalp
- Nipple
- Axillary
- Genitalia
- Acral

Other Atypical Nevi
- Recurrent
- Halo
- Large Congenital
Giant Congenital Nevus

- Trunk is most common site
- Growth is proportional with body
- Melanoma incidence is 2-15%
  - 60% within the 1st decade
  - 50% of MM develops in deep structures
  - 40% of MM in childhood occurs in GCMN
- Neurocutaneous melanosis
  - Greatest risk is with axial lesions
  - 50% of NCM will develop leptomenigeal melanoma
  - GCMN need screening MRI
Understanding Melanoma Risk

- Subjective Risk Factors
- Objective Risk Factors
  - ABCDEs
  - Density of Nevi – atypical vs normal
  - Degree of Lentiginosus
  - Perceived Similarity Clusters
Table 6.—Estimated Relative Risk of Melanoma by Number of Dysplastic Nevi and Freckling Index*

<table>
<thead>
<tr>
<th>Freckles</th>
<th>None</th>
<th>Indeterminate</th>
<th>1</th>
<th>2-4</th>
<th>≥5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.0</td>
<td>1.8</td>
<td>2.9</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>95% CI</td>
<td>...</td>
<td>0.5-7.0</td>
<td>0.7-12</td>
<td>3.5-163</td>
<td>2.0-106</td>
</tr>
<tr>
<td>Cases:controls</td>
<td>21:102</td>
<td>3:8</td>
<td>3:5</td>
<td>5:1</td>
<td>3:1</td>
</tr>
<tr>
<td>Few</td>
<td>RR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.4</td>
<td>2.6</td>
<td>4.6</td>
<td>11</td>
<td>27</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.8-2.3</td>
<td>1.4-5.0</td>
<td>2.2-9.8</td>
<td>5.1-21</td>
<td>11-67</td>
</tr>
<tr>
<td>Moderate</td>
<td>RR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.9</td>
<td>5.6</td>
<td>9.4</td>
<td>26</td>
<td>22</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.7-4.9</td>
<td>2.8-11</td>
<td>4.3-20</td>
<td>11-58</td>
<td>9.4-52</td>
</tr>
<tr>
<td>Case:controls</td>
<td>122:202</td>
<td>32:28</td>
<td>29:15</td>
<td>53:10</td>
<td>41:9</td>
</tr>
<tr>
<td>Many</td>
<td>RR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.1</td>
<td>1.4</td>
<td>6.9</td>
<td>36</td>
<td>21</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.7-5.6</td>
<td>0.4-5.4</td>
<td>2.4-20</td>
<td>10-121</td>
<td>6.8-64</td>
</tr>
<tr>
<td>Case:controls</td>
<td>41:65</td>
<td>3:10</td>
<td>10:7</td>
<td>22:3</td>
<td>17:4</td>
</tr>
</tbody>
</table>

*RR indicates relative risk; and CI, confidence interval.
Perceived Similarity Clusters

- 2.8 average per pt
- Look for the “Ugly Duckling”

Dermoscopy

Another Lecture?
<table>
<thead>
<tr>
<th>Melanoma Categories</th>
<th>Frequency</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial Spreading</td>
<td>60-70%</td>
<td>More pagetoid, less solar elastosis</td>
</tr>
<tr>
<td>Nodular</td>
<td>15-30%</td>
<td>Nodule with vertical growth</td>
</tr>
<tr>
<td>Lentigo Maligna</td>
<td>5-15%</td>
<td>Slow growth on sun-damaged skin</td>
</tr>
<tr>
<td>Acral lentiginous</td>
<td>5-10%</td>
<td>Commonest in darker skin types</td>
</tr>
</tbody>
</table>
Pigmented Nail Lesions

Nail-specific “ABCDEF”

A: Age: Range 20-90 y, peak 5th-7th decades; Race: African-American, Native American, Asian

B: Band (nail band): Pigment (Brown-Black) Breadth (≥3 mm) Border (irregular/blurred)

C: Change: Rapid increase in size/growth rate of nail band Lack of Change; Failure of nail dystrophy to improve despite adequate treatment
Pigmented Nail Lesions

Nail-specific “ABCDEF”

- **D:** Digit involved: Thumb > hallux > index finger; Single digit > multiple digits, Dominant hand
- **E:** Extension: Extension of pigment to involve proximal or lateral nail fold (Hutchinson’s sign) or free edge of nail plate
- **F:** Family or personal history: Of previous melanoma or dysplastic nevus syndrome
Melanoma

How do I do the biopsy?
- Punch
- Shave
- Incisional
- Excisional
Melanoma

WHY IS THIS SO IMPORTANT?

Melanoma prognosis depends primarily on the depth of invasion, so the biopsy must afford the pathologist the ability to measure this depth. This then allows you to both properly counsel your patient and provide appropriate definitive treatment and follow-up.
Melanoma

Prognosis and tx dictated by depth of invasion

- How is depth measured?
- What do the numbers mean?

- Clark first defined levels of invasion (1-5)
- Breslow later found that precise measurement of tumor thickness proved a more accurate predictor of survival
Melanoma

Clark Levels

1 - tumor confined to epidermis (in situ)
2 - tumor invades papillary (upper) dermis
3 - tumor fills and expands papillary dermis
4 - tumor invades reticular (lower) dermis
5 - tumor invades subcutaneous tissue
Melanoma

Breslow thickness

- Pathologist uses ocular micrometer to measure distance from the top of the granular layer of the epidermis (just beneath stratum corneum) to the deepest tumor cell
- Reported in millimeters (mm)
Staging and Treatment

- Staging based on TNM system
- Wide local excision for localized disease
- Sentinel lymph node biopsy
- Adjuvant therapy for metastatic disease
<table>
<thead>
<tr>
<th>Classification</th>
<th>Thickness (mm)</th>
<th>Ulceration Status/Mitoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
| T1            | ≤ 1.00        | a: Without ulceration and mitosis < 1/mm²  
                              |                             | b: With ulceration or mitoses ≥ 1/mm²  |
| T2            | 1.01-2.00     | a: Without ulceration  
                              |                             | b: With ulceration            |
| T3            | 2.01-4.00     | a: Without ulceration  
                              |                             | b: With ulceration            |
| T4            | > 4.00        | a: Without ulceration  
                              |                             | b: With ulceration            |

<table>
<thead>
<tr>
<th>N</th>
<th>No. of Metastatic Nodes</th>
<th>Nodal Metastatic Burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>
| N1             | 1                       | a: Micrometastasis*  
                              | b: Macrometastasis†  |
| N2             | 2-3                     | a: Micrometastasis*  
                              | b: Macrometastasis†  |
| N3             | 4+ metastatic nodes, or matted nodes, or in transit metastases/satellites with metastatic nodes | c: In transit metastases/satellites without metastatic nodes |

<table>
<thead>
<tr>
<th>M</th>
<th>Site</th>
<th>Serum LDH</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastases</td>
<td>NA</td>
</tr>
<tr>
<td>M1a</td>
<td>Distant skin, subcutaneous, or nodal metastases</td>
<td>Normal</td>
</tr>
<tr>
<td>M1b</td>
<td>Lung metastases</td>
<td>Normal</td>
</tr>
<tr>
<td>M1c</td>
<td>All other visceral metastases</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Any distant metastasis</td>
<td>Elevated</td>
</tr>
<tr>
<td>Clinical Staging*</td>
<td>Pathologic Staging†</td>
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<td><strong>T</strong></td>
<td><strong>N</strong></td>
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<td>0</td>
<td>Tis</td>
<td>N0</td>
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<tr>
<td>IA</td>
<td>T1a</td>
<td>N0</td>
</tr>
<tr>
<td>IB</td>
<td>T1b</td>
<td>N0</td>
</tr>
<tr>
<td></td>
<td>T2a</td>
<td>N0</td>
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<tr>
<td>IIA</td>
<td>T2b</td>
<td>N0</td>
</tr>
<tr>
<td></td>
<td>T3a</td>
<td>N0</td>
</tr>
<tr>
<td>IIB</td>
<td>T3b</td>
<td>N0</td>
</tr>
<tr>
<td></td>
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<td>N0</td>
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<tr>
<td>IIC</td>
<td>T4b</td>
<td>N0</td>
</tr>
<tr>
<td>III</td>
<td>Any T N &gt; N0</td>
<td>M0</td>
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<tr>
<td>IIIIC</td>
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<td>N1b</td>
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<tr>
<td>IV</td>
<td>Any T Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
Melanoma

Where do metastases occur?

Site of initial mets

- 63 % local LNs
- 22 % local skin
- 5 % lung, distant skin
- 1 % GI, brain, liver, bone
Survival Curves
Sentinel Lymph Node Biopsy

- Recommended for intermediate depth melanomas with no evidence of metastasis
- Best performed at time of excision
- Its role/utility still being defined by ongoing studies
Sentinel Node Biopsy

**Indications:**  ≥1 mm or >0.75 mm if >1 mit or ulceration

**Sentinel Lymph Node Biopsy**

- Lymphoscintigraphy ($^{99}$Tc)
- Blue Dye
- Hand-held gamma probe
- Surgical dissection
- H&E, IHC
- ?RT-PCR (Sn, but ↓Sp)
# PRINCIPLES OF SURGICAL MARGINS FOR WIDE EXCISION OF PRIMARY MELANOMA

<table>
<thead>
<tr>
<th>Tumor Thickness</th>
<th>Recommended Clinical Margins²</th>
</tr>
</thead>
<tbody>
<tr>
<td>In situ¹</td>
<td>0.5-1.0 cm</td>
</tr>
<tr>
<td>≤1.0 mm</td>
<td>1.0 cm (category 1)</td>
</tr>
<tr>
<td>1.01-2 mm</td>
<td>1-2 cm (category 1)</td>
</tr>
<tr>
<td>2.01-4 mm</td>
<td>2.0 cm (category 1)</td>
</tr>
<tr>
<td>&gt;4 mm</td>
<td>2.0 cm (category 1)</td>
</tr>
</tbody>
</table>

- Margins may be modified to accommodate individual anatomic or functional considerations.
Melanoma

Advanced Stage

- Multidisciplinary approach invaluable when disease no longer localized to the skin
- Tumor board important forum
- Utilize medical and surgical oncology, ENT, plastic surgery, dermatology, pathology, radiation oncology...
To Biopsy or Not to Biopsy

- Understand Underlying Risk
- Use Your ABCDEs
- Determine the Density of Nevi
- Measure the Degree of Lentiginosus
- Count the Number of Perceived Similarity Clusters
- Find the Ugly Ducklings
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