Mohs Surgery for Melanoma

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Mohs-micrographic surgery (MMS) is appropriate for the treatment of primary and locally recurrent melanoma in-situ and lentigo maligna on the head, neck, genitalia, acral sites, and pretibial leg.

The American Academy of Dermatology
American College of Mohs Surgery
American Society for Mohs Surgery
American Society for Dermatologic Surgery Association

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Protocol for the Examination of Specimens From Patients With Squamous Cell Carcinoma of the Skin

SquamousCell 3.1.0.2
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Surgical Pathology Cancer Case Summary
SQUAMOUS CELL CARCINOMA OF THE SKIN: Biopsy, Excision, Re-excision, Lymphadenectomy

Procedure
Tumor Site
Tumor Size
Histologic Type
Histologic Grade
Maximum Tumor Thickness
Anatomic Level
Margins  (select all that apply)
Peripheral Margins
Deep Margin
Lymph-Vascular Invasion
Perineural Invasion
Lymph Nodes
Number of Lymph Nodes Examined
Number of Lymph Nodes Involved By Metastatic Carcinoma
Pathologic Staging (pTNM)
TNM Descriptors  (required only if applicable)
Primary Tumor (pT)
Regional Lymph Nodes (pN)
Distant Metastasis (pM)
Pallor of the chromatin
Non-uniform eosinophilia of cell cytoplasm
Artifactually crushed cells
Enlargement of nuclei
Melanocytes?????

AJCC 7th/8th edition Recommended Excision margins

- MMIS
  - Lateral margins
    - 0.5 cm
  - Deep margin
    - deep to the adnexal structures

- Invasive melanoma
  - Lateral margins
    - 1 cm for tumors less than 1 mm
    - 2 cm for tumors 1 – 2 cm
  - Deep margin
    - fascia

Mohs for Melanoma How To...

Patient Selection

- Melanoma in-situ
  - Poorly defined tumors
  - Tumors without invasion

- Invasive melanoma
  - Tumors that do not require a sentinel node biopsy
    - less than 1mm Breslow depth
    - Mitotic index <1
  - Determine high-risk features on a per-case basis
General Steps

- Identify tumor
- Send a debulk specimen
  - Allows for assessment of invasion in cases where there is significant residual disease
  - Margins on the debulk specimen vary (3mm, 5mm...)
- Begin the Mohs-assisted excision
- Strongly consider the use of intraoperative immunostains
- Strongly consider a CONTROL BIOPSY (contralateral/ipsilateral location)
• Local recurrence was identified in 0.34% (2/597) lesions with a mean follow-up time of 1026 days (2.8 years).
• Upstaging occurred in 34 of 614 lesions (5.5%), of which 97% (33/34) were detected by the Mohs surgeon before reconstruction.

Conclusion
• Treating melanoma with MMS that combines breadloaf sectioning of the central debulking excision with complete peripheral and deep microscopic margin evaluation
  • Permits identification of upstaging (identification of invasive disease)
  • Allows consideration of sentinel lymph node biopsy before definitive reconstruction
  • Achieves low local recurrence rates compared with conventional excision.
Utilization patterns for Mohs and Melanoma

- A total of 195,768 melanomas
- Mohs micrographic surgery
  - Increased by 60% between the years of 2003 and 2008
  - 3.5% (6872) were excised by Mohs micrographic surgery.
- Uncertain whether this increased utilization is associated with better outcomes

Assessment of melanocytes on frozen sections

- MART-1 frozen section immunostains have proven to be as accurate as formalin-fixed paraffin-embedded immunohistochemical sections
- MART-1 will not stain a purely desmoplastic melanoma
**Immunostains**

- Increase the accuracy of standard stains
- Chosen according to the tumor being evaluated
- May be used on fresh, frozen tissue or paraffin-embedded tissue

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**Immunostain Protocol**

1. Cut frozen sections (4 to 6 microns)
2. Mount onto positively charged slides
3. Air dry
4. Fix
5. Rehydrate
6. Apply blocking diluent
7. Apply primary antibody
8. Rinse
9. Apply the secondary antibody conjugated to an enzyme (peroxidase)
10. Rinse
11. Apply chromogen
12. Rinse
13. Dip in counterstain
14 - 16. Rinse, dehydrate, and clear

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**MART-1 (Melan-A)**

- Melanocytic Antigen Recognized by cytotoxic T lymphocytes from melanoma patients
- Cytoplasmic protein
- Sensitive and specific for melanoma and nevomelanocytes
- Stains pigmented actinic keratoses
- Lack of specificity has led some investigators to determine that it falsely extends surgical margins into normal tissue
Example: MART-1 positive pseudonests in lichenoid dermatitis

Immunostains

- **MART1 (MELAN-A, cytoplasmic)**
  - Stains pigmented keratinocytes (pigmented actinic keratoses, etc.)
  - Risk for over-staining
  - Macrophages may aberrantly label
  - Staining is weak and granular

- **MITF (nuclear)**
  - Present in most melanomas, including some rare cases that do not express S100
  - Does not stain desmoplastic and spindle-cell melanomas
  - Half of S100-negative metastases are MITF positive

- ** Sox-10 (nuclear)**
  - Much more specific than S100 for melanocytic lesions and has shown equal or better sensitivity
Sox 10

- Highly specific for desmoplastic melanoma (80% - 100%)
- Useful in the differentiation between scar and DM

SOX10 showed 100% sensitivity for DM and SOX10 was negative in all histologic mimics of the dermis/subcutis, including spindle cell carcinoma, AFX and sarcomas.

In-Situ Melanoma, Lentigo Maligna type
In-situ Malignant Melanocytes: Histologic Clarification

- Lentigo Maligna
  - Lentiginous proliferation of atypical melanocytes at the dermal-epidermal margin in the background of sun-damaged skin
  - Precursor to desmoplastic melanoma (5% risk of invasion)
- Melanoma in-situ
  - Pagetoid proliferation of atypical melanocytes in the absence of sun damage
  - Precursor to superficial spreading melanoma

In-Situ Melanoma: Histology

- Lentigo Maligna
  - Proliferation of atypical melanocytes at the dermal-epidermal margin in the background of sun-damaged skin
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Melanoma In-Situ, Permanent Section

In-Situ Melanoma: Histology

- Melanoma in-situ
  - Pagetoid proliferation of atypical melanocytes in the absence of sun damage
  - Precursor to superficial spreading melanoma

Melanoma In-Situ, In-Situ
**Desmoplastic Melanomas**

- Spindle cell, “sarcomaoid” subset of melanomas
- May have nerve involvement
- Distribution:
  - Head and neck (51%)
  - Extremities (30%)
  - Trunk (17%)
- Tend to arise on chronically sun-damaged skin

**Desmoplastic Melanoma (DM)**

- Histologically difficult to diagnose
- Resemble fibroblastic or myofibroblastic neoplasms
- Lentigo maligna melanoma in situ precursor
- May present with pure (>90%) desmoplastic feature or with mixed features of DM and nondesmoplastic melanoma
- Lower incidence of lymph node metastasis and,
- In many practices, sentinel lymph node biopsy is not recommended
Desmoplastic Melanomas

- Male predominance 2:1
- Median age at diagnosis is 60 years.
- Often amelanotic, presenting as an erythematous macule or an indurated plaque
- Recurrence is common (22-77%)
- 5-year survival ranges from between 67 and 89%

Tumor Thickness

- Tend to be thicker at the time of diagnosis
- Clark levels IV and V
- Mean Breslow depth ranging between 2.0 to 6.5 mm
- (nondesmoplastic melanomas 2.1 mm)
- Carlson et al found higher 5-year survival for DM tumors greater than 4 mm in thickness compared with other types of cutaneous melanoma greater than 4 mm (72% vs 37%-48%)
- Survival may be the same or slightly improved

Nodal Metastases

- Observed less frequently than in other subtypes of melanoma
- Within desmoplastic melanomas
  - Higher likelihood of nodal positivity in mixed desmoplastic melanoma subtypes (25%)
  - Pure desmoplastic subtype (14%)

Breslow Depth

The Breslow thickness is measured from the top of the epidermal granular layer to the deepest melanocyte of the invasive component of melanoma.

**Least amount of interobserver variability

Breslow Depth Notes

- In-situ involvement of follicular or adnexal structures
- Do not measure follicular/adnexal extension
- Deep perineural invasion
- Some measure to this point
- Controversy
- Ulceration (tumor-induced)
- Measurement from the base of the ulceration to the deepest aspect of the invasive melanoma
- When invasion is peri-follicular/periadnexal
  - Measure from the central portion of the follicular/adnexal structure to the furthest adjacent invasive melanoma cell

AJCC 7th Edition

- Primary tumor mitotic rate (histologically defined as mitoses/mm²) is an important independent adverse predictor of survival. For T1 melanomas, a mitotic rate of at least 1 mitosis/mm² replaces level of invasion as a primary criterion for defining the subcategory of T1b.
Left Preauricular Cheek
Well-differentiated SCC with pigmented SCCIS at the margins
The majority of medical malpractice claims filed between 1985 and 2001 involving the misdiagnosis of melanoma were because of a false negative diagnosis of melanoma.

Medical Malpractice Claims: 1985 - 2001
- Nodular melanoma being misdiagnosed by a clinician or pathologist
- A partial biopsy not capturing the most diagnostically relevant part of the lesion
- Malignant melanoma being misdiagnosed as a dysplastic or spitz nevus
- Unrecognized desmoplastic malignant melanoma
- Metastatic malignant melanoma with an unknown primary or recurrence of melanoma

By the way...

Protocol for the Examination of Specimens From Patients With Squamous Cell Carcinoma of the Skin

Tumor Site | Tumor Size | Histologic Type | Histologic Grade | Maximum Tumor Thickness | Anatomic Level | Margins (select all that apply) | Lymph-Vascular Invasion | Perineural Invasion | Lymph Nodes
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http://www.internalmedicineon.com/index.php?id=2019&type=98&tx_ttnews%5Btt_news%5D=5239&cHash=da03e20e36

**CAP Protocols: Required for Accreditation**

- Commission on Cancer (CoC)
- Joint Commission
- Recent addition of the Cancer Protocols as a part of their Laboratory Accreditation Program

**CAP Protocol: Required Use**

- Definitive resection specimen
- Invasive malignancy
- Breast ductal carcinoma in situ (DCIS)
- The primary operative procedure for patients undergoing multiple operative procedures
- Cutaneous SCC greater than 2 cm

**The Cancer Protocols Not Required:**

- Biopsy specimens
- Resection after neoadjuvant therapy in which no tumor is present
- Resection for recurrent disease
- Resection for in situ disease, dysplasia without malignancy, or non-invasive tumors
  - exception of DCIS

**Potential Issues**

- Margins

**Melanoma in-situ excision with 5 mm margins**

- "Melanoma in-situ, Margins clear"
- "Melanoma in-situ, extending to within 1 mm of the peripheral margins"
“Measurements of distance from tumor to margins need not be routinely reported but may be done so in special circumstances and/or when requested by the treating physician.”

Excision recommendations are based on measured clinical margins taken at the time of surgery and not gross or histologic margins as measured by the pathologist.

Take-home message

As long as your pathologist reports a clear margin and appropriate clinical excision standards have been met

NO FURTHER EXCISION IS RECOMMENDED

Histologic margins can be ambiguous- speak with your dermatopathologist

References