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

Appropriate Use Criteria

Frozen Section of Skin Specimens

- Pallor of the chromatin
- Non-uniform eosinophilia of cell cytoplasm
- Artifically crushed cells
- Enlargement of nuclei
- Melanocytes

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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

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
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

Fig. 3. Lichenoid dermatitis. The pseudonests, indicated by white arrows, were MART-1 positive (A) but S100 negative (B) (original magnification: A, ×400; B, ×600).
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

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.

The American Joint Committee on Cancer (AJCC)

- Melanoma staging system based on the Melanoma Staging Database
- Staging systems
  - 2001 (17,600 patients)
  - 2009 (30,000+ patients)
- Multivariate analysis of different independent prognostic factors
- Seventh Edition for Melanoma

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.
AJCC 7th 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

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

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Melanoma In-Situ, Permanent Section

Superficial Spreading Melanoma (Invasive), Permanent Section
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
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
A retrospective analysis of patients receiving surgical excision (MMS or wide local excision) for National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program.

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% (6,872) were excised by Mohs micrographic surgery.
- Uncertain whether this increased utilization is associated with better outcomes.
Left Preauricular Cheek
Well-differentiated SCC with pigmented SCCIS at the margins
MART-1 Melanocyte Immunostain

Lentigo Maligna Melanoma
Breslow Depth 2.4 mm
Clark Level V
Mitotic Index: Unknown

Misdiagnosis of melanoma

• Misdiagnosis of melanoma
• 13% of all malpractice claims in the period of 1995–2001
• Second most common cause of malpractice litigation in the US
• The missed diagnosis of melanoma was the single most common occurrence for litigation (1995–2001)

Mod Pathol. 2006 Feb;19 Suppl 2:S148-54. 
Medicolegal aspects of neoplastic dermatology.

References

Eyelid repair