The Sentinel Node in Head and Neck Melanoma

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Cutaneous Melanoma: Epidemiology (USA)

- 6th leading cause of cancer among men and women
- 68,720 new cases of invasive melanoma in 2009
- 8,650 deaths from melanoma in 2009

*American Cancer Society

Cutaneous Melanoma: Epidemiology (USA)

- Incidence is on the rise (600% increase over past 50 years)*
  - Increasing faster than any other cancer
  - Lifetime risk:
    - 1/1500 for individual born in 1935
    - 1/250 for individual born in 1980
    - 1/74 for individual born in 2000

*SEER Data

Head and Neck Cutaneous Melanoma: Epidemiology (USA)

- 25-30% of melanomas
- Second most common site overall
- More biologically aggressive
- Common anatomic locations
  - Face (40-60%)
  - Scalp (14-49%)
  - Neck (20-29%)
  - Ear (8-11%)

Harris TJ et al. Head Neck Surg 1983;5:197.

Risk Factors

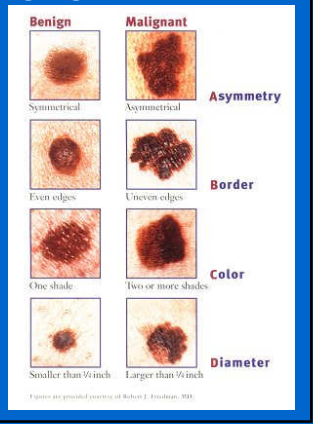
- Sun exposure: frequency, age of exposure
- History of blistering sunburns
- Number of nevi
  - > 20 increases relative risk by 3
  - > 100 increases relative risk by 7
  - 50% of melanomas arise in pre-existing nevi
- Other risk factors: fair skin, red hair, freckling
- Family history

Prevention

- Melanocytic nevi develop mainly during childhood/adolescence
  - – Preventive measures critical during early life
- Public Education
  - – Sun avoidance, protective clothing
  - – Sun screen? Not shown to be preventive
- Screening of high-risk populations

Work-up

- American Cancer Society's ABCD's
  - – A-Asymmetry
  - – B-Border irregularity
  - – C-Color variation
  - – D-Diameter > 6mm
  - – (E-Evolution of change)
- History
  - – Signs: recent change in size, color, shape
  - – Symptoms: Pruritis, crusting, bleeding, tenderness



Work-up

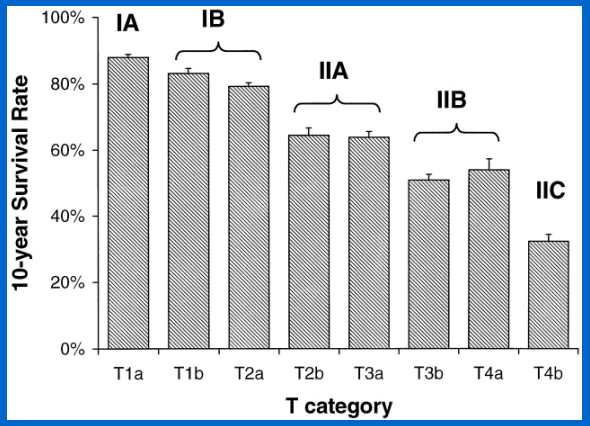
- Biopsy suspicious lesions
  - – Excisional biopsy with 1-2 mm margins
  - – Full-thickness incisional or punch biopsy of thickest portion for larger lesions
  - – NEVER shave biopsy

Staging (AJCC 2002)

T classification	Thickness	Ulceration Status
T1	≤ 1.0 mm	a: without ulceration and level II/III
		b: with ulceration or level IV/V
T2	1.01-2.0 mm	a: without ulceration
		b: with ulceration
T3	2.01-4.0 mm	a: without ulceration
		b: with ulceration
T4	> 4.0 mm	a: without ulceration
		b: with ulceration

Balch CM et al. Final Version of the American Joint Committee on Cancer Staging System for Cutaneous Melanoma J Clin Oncol 2001;19:3635-3648.

Fig 2. Ten-year survival rates comparing the different T categories and the stage groupings for stages I and II melanoma



Balch, C. M. et al. J Clin Oncol; 19:3635-3648 2001

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Staging (AJCC 2002)

N classification	No. of Metastatic Nodes	Nodal Metastatic Mass
N1	1 node	a: micrometastasis*
		b: macrometastasis†
N2	2-3 nodes	a: micrometastasis*
		b: macrometastasis†
		c: in transit met(s)/satellite(s) without metastatic nodes
N3	4 or more metastatic nodes, or matted nodes, or in transit met(s)/ satellite(s) with metastatic node (s)	

Balch CM et al. Final Version of the American Joint Committee on Cancer Staging System for Cutaneous Melanoma J Clin Oncol 2001;19:3635-3648.

In-transit satellite metastasis

Staging (AJCC 2002)

M classification	Site	Serum Lactate Dehydrogenase
M1a	Distant skin, subcutaneous, or nodal mets	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastases	Normal
	Any distant metastasis	Elevated

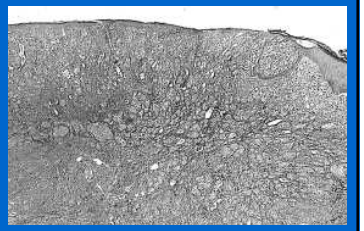
*Micrometastases are diagnosed after sentinel or elective lymphadenectomy.

†Macrometastases are defined as clinically detectable nodal metastases confirmed by therapeutic lymphadenectomy or when nodal metastasis exhibits gross extracapsular extension.

Balch CM et al. Final Version of the American Joint Committee on Cancer Staging System for Cutaneous Melanoma J Clin Oncol 2001;19:3635-3648.

Staging

- Localized (Stage I, II)
  - T_{any} N0 M0
  - Prognostic features
    - Tumor thickness
      - Clark's Level of invasion for (T1)
    - Ulceration



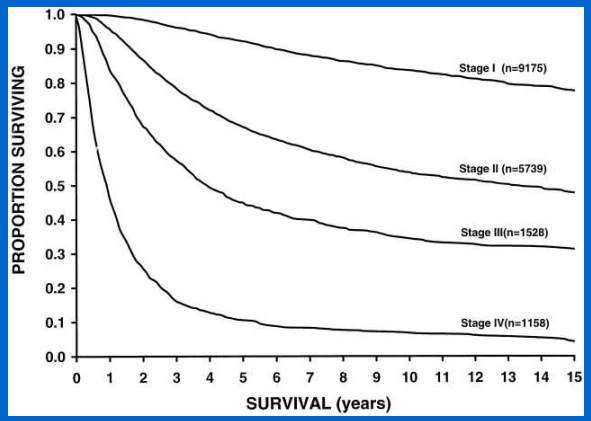
Staging

- Regional metastasis (Stage III)
  - T_{any} N+ M0
  - Prognostic Features
    - Number of metastatic nodes
    - Micro vs. macroscopic disease
    - Intralymphatic metastasis (in-transit satellites)

Staging

- Distant metastasis (Stage IV)
- T_{any} N_{any} M+
  - Prognostic features
    - Anatomic site: distant nodal basin, lung, other visceral organs
    - LDH

Fig 1. Fifteen-year survival curves comparing localized melanoma (stages II and I), regional metastases (stage III), and distant metastases (stage IV)



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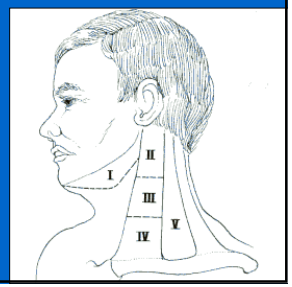
Treatment

- Primary site: margins determined by tumor thickness
  - Melanoma in situ: 5 mm
  - < 1 mm: 1 cm
  - 1 – 2 mm: 1 – 2 cm
  - > 2 mm: 2 cm
  - Margins modified to accommodate anatomic and cosmetic considerations

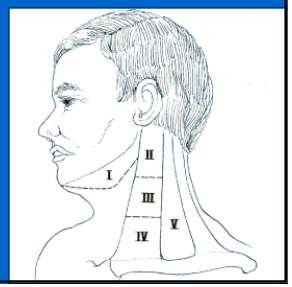
Clinically node-positive melanoma

- Stage III Disease
  - Therapeutic lymph node dissection
    - Preserve when possible the SCM, IJ, spinal accessory nerve

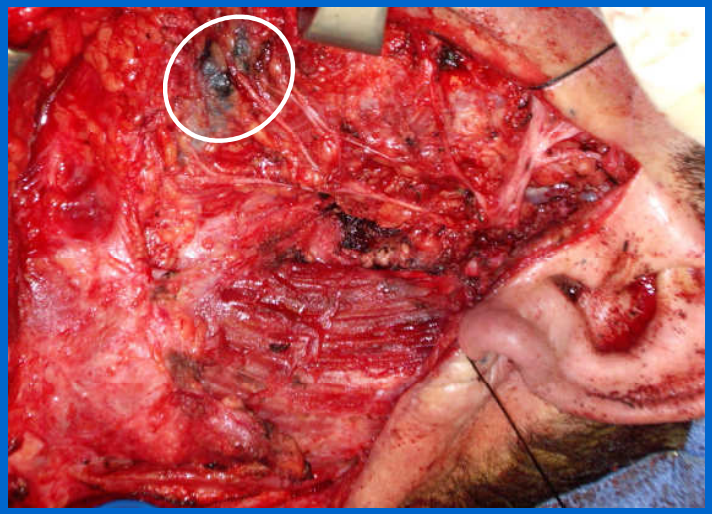


Clinically node-positive melanoma

- Stage III Disease
  - Consider primary site, location of positive node(s)
    - Levels I-III (lower face, lip), II-V (auricle), V + occipital and post-auricular nodes (scalp)
    - Superficial parotidectomy (temple, forehead, cheek)



Multiple melanotic periparotid nodes



- 26 year old female presented with regional node recurrence 6 months following wide excision of 0.45 mm thick right neck melanoma
- Imaging showed multiple level II-IV nodes, invasive of SCM

Completed modified radical neck dissection

Clinically node-negative melanoma

- Risk of occult nodal disease: tumor thickness
  - < 1.0 mm: 5%
  - 1 – 2 mm: 15-20%
  - 2 – 4 mm: 25%
  - > 4 mm: 35%
- Higher in young patients, high tumor mitotic rate
- Lower in desmoplastic, lentigo maligna melanoma

Clinically node-negative melanoma

- Role of elective neck dissection
  - 2 prospective studies (WHO Melanoma Group and Mayo Clinic) failed to demonstrate survival benefit for ELND
  - ELND not routinely performed today

Sentinel lymph node biopsy

- Minimally invasive procedure to identify patients harboring occult nodal disease
  - Identifies patients who warrant therapeutic neck dissection and adjuvant therapy
  - Spares ~80% of patients without regional disease the morbidity of a neck dissection and/or parotidectomy

Sentinel lymph node biopsy

- Directs to nodes at risk
  - Cutaneous lymphatic drainage less predictable than mucosal
- Allows more thorough pathologic assessment than typically performed for complete neck dissection specimen

Sentinel lymph node biopsy

- Most sensitive and specific modality for regional staging
- Most important prognostic factor for recurrence and survival*
- AJCC incorporated SLNB into current staging system

*Gershenwald et al. J Clin Oncol 1999;17;976-983.

Sentinel lymph node biopsy

- Indications for SLNB
  - Thickness: > 1 mm
  - Clark's Level IV or V
  - Ulceration
  - Extensive regression to 1.0 mm
- Relative indications for SLNB
  - Young age
  - High mitotic rate

Sentinel lymph node biopsy

- Contraindications for SLNB
  - Evidence of regional or distant metastasis
  - Flap reconstruction performed for primary tumor resection/closure
    - Native lymphatic drainage channels disrupted

Technique of SLNB

- Intradermal injection of technetium-99 sulfur colloid at the primary site
- Serial images taken with gamma camera
- Sentinel nodes marked on skin
  - Typically 2 to 4

Technique of SLNB

- Pre-incision intradermal injection of blue dye
  - Methylene blue

Technique of SLNB

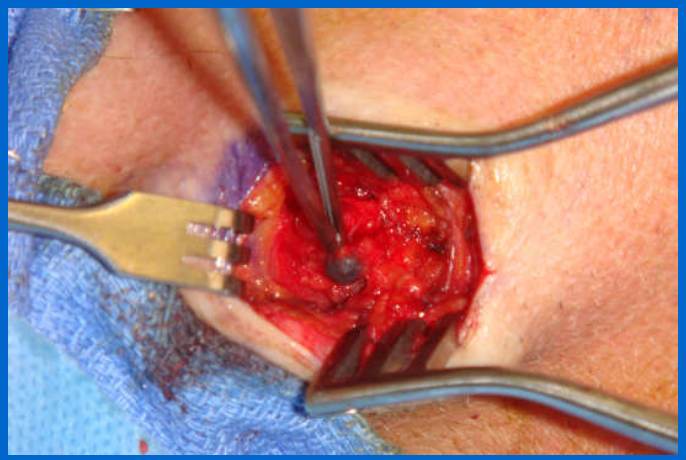
- Use gamma probe for SLN identification

Neo Probe

Node Seeker

Technique of SLNB

- Facial nerve monitor useful



Radio-guided surgery, exploring for blue-colored nodes

- "Ex-vivo" count obtained
- Remaining nodal basin explored, radioactive nodes removed until background count <10% of "hottest" detected node
- Any additional blue or suspicious nodes removed

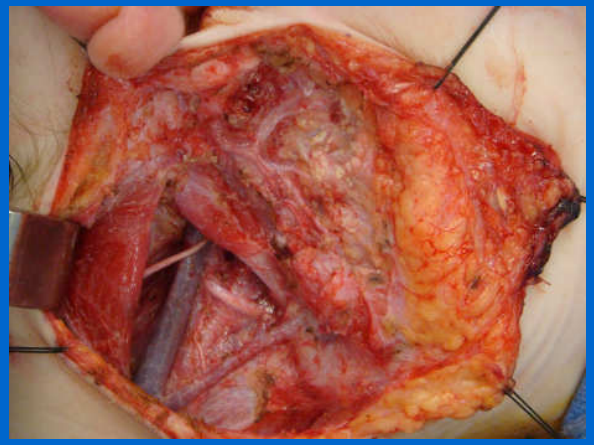
Technique of SLNB

- Frozen section inadequate
- Permanent histologic evaluation
  - Serial sectioning (5 microns)
  - H&E staining
  - Immunohistochemistry higher sensitivity
    - S-100 (97%), HMB-45 (75%), Melan-A (96%)

Sentinel lymph node biopsy

- Positive SLNB
  - – Therapeutic neck dissection +/- parotidectomy
  - – Counseling for adjuvant therapy
    - Interferon alpha-2b
    - Radiation therapy
- Negative SLNB
  - – Follow clinically

2 year old male: Superficial parotidectomy and selective neck dissection levels II/III performed 2 weeks following sentinel lymph node biopsy (2/4 positive intra-parotid sentinel lymph nodes)



Outcome data for SLNB

- Efficacy
  - Successful SLN identification in 96%*
  - Mean # nodes removed=2.8, range 1-7
  - Regional failure in setting of negative SLN-4.5%*
  - No cranial nerve injuries

*Schmalbach CE et al. Arch Otolaryngol Head Neck Surg 2003;129:61-65.

Outcome data for SLNB

- Challenges of H&N SLNB
  - Higher false negative rate in H&N compared to other anatomic nodal basins
    - Complexity of cervical lymphatics
    - Problem of "shine-through"
- Safety of H&N SLNB
  - Damage to vital structures, cranial nerves
  - Intraparotid SLNB
  - There is a learning curve for surgeon
    - ~30 cases to be proficient

Outcome data for SLNB

- MSLT-1 trial: Stage III patients identified through SLNB had improved survival compared to patients who developed palpable metastasis under a watchful waiting policy

Balch CM et al. J Clin Oncol 2001;19:3635.

H&N SLNB

- SLN Working Group
  - 614 H&N melanoma pts underwent SLNB
  - 10.1% positive
  - SLN status most important predictor of disease-free survival
    - Other predictors—tumor thickness, ulceration
  - Scalp site independent predictor of +SLN, recurrence, increased mortality

Leong SPL et al Arch Otolaryngol Head Neck Surg 2006;132:370-373

Adjuvant therapy

- Indications for radiation therapy
  - Close or positive margins
  - Bulky nodes, multiple nodes, ECS
  - No comprehensive neck dissection performed
  - Typical dose: 30 Gy given in 5 large fractions (6 Gy per treatment) over 2 ½ weeks

Adjuvant therapy

- Indications for interferon
  - Completely treated Stage III disease
  - No medical contraindication for Interferon
  - Typical regimen: 4 weeks of high-dose IV IFN, followed by 11 months of self-administered SC IFN

Take-home points

- Cutaneous melanoma incidence rising faster than any other cancer
- 25 - 30% of melanomas occur in the head and neck

Take-home points

- Surgery is primary treatment modality for melanoma
- SLNB: minimally invasive technique for assessment of regional nodes in cutaneous melanoma
- Head and neck surgeon should play a key role in the management of this disease