

Update on Head & Neck Melanoma



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Disclosures

- I have no disclosures



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Some things don't change . . .

Treatment: Wide Local Excision

<u>Tumor Thickness</u>	<u>Recommended Margins</u>	
In Situ	0.5 cm	
≤ 1.0 mm	1.0 cm	} Category I consensus
1.01 – 2.0 mm	1-2 cm	
2.01 – 4.0 mm	2.0 cm	
> 4.0 mm	2.0 cm	

**** Margins modified to accommodate
anatomic/ cosmetic considerations**



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Therapeutic Neck Dissection

- STAGE III – Standard of Care
 - Neck Dissection (selective vs. modified) preserving:
 - Sternocleidomastoid Muscle
 - Internal Jugular Vein
 - Spinal Accessory Nerve
 - Superficial or **Total** Parotidectomy for areas that drain to the parotid basin:
 - Temple
 - Forehead
 - Cheek
- STAGE IV – Consider for locoregional control

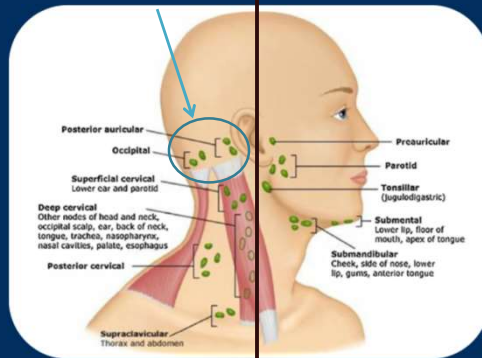


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Extent of Neck Dissection

Postauricular and occipital nodes important for posterior scalp



- MRND preserving
 - SCM
 - IJV
 - CN XI
- Superficial or total parotidectomy
 - Temple
 - Forehead
 - Cheek

Plane defining anterior versus posterior drainage



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Sentinel Lymph Node Biopsy

- Most important prognostic factors for melanoma include:
 - Primary tumor depth of invasion.
 - Ulceration at the primary site.
 - *Regional lymph node involvement*
- Pathologic status of SLN is **the most important prognostic factor** for both recurrence and survival

612 Stage I/II Patients

Tumor Thickness	HR = 1.23
Clark Level > III	HR = 2.32
SLN Status	HR = 6.53

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



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Indications for SLNB

- N0
- T1b or greater
- Other adverse prognostic variables to consider:
 - Tumor extension to deep margin
 - Ulceration
 - Lymphovascular invasion
 - Extensive regression to 1.0 mm
 - Young age
 - High mitotic rate ($\geq 1\text{mm}$)



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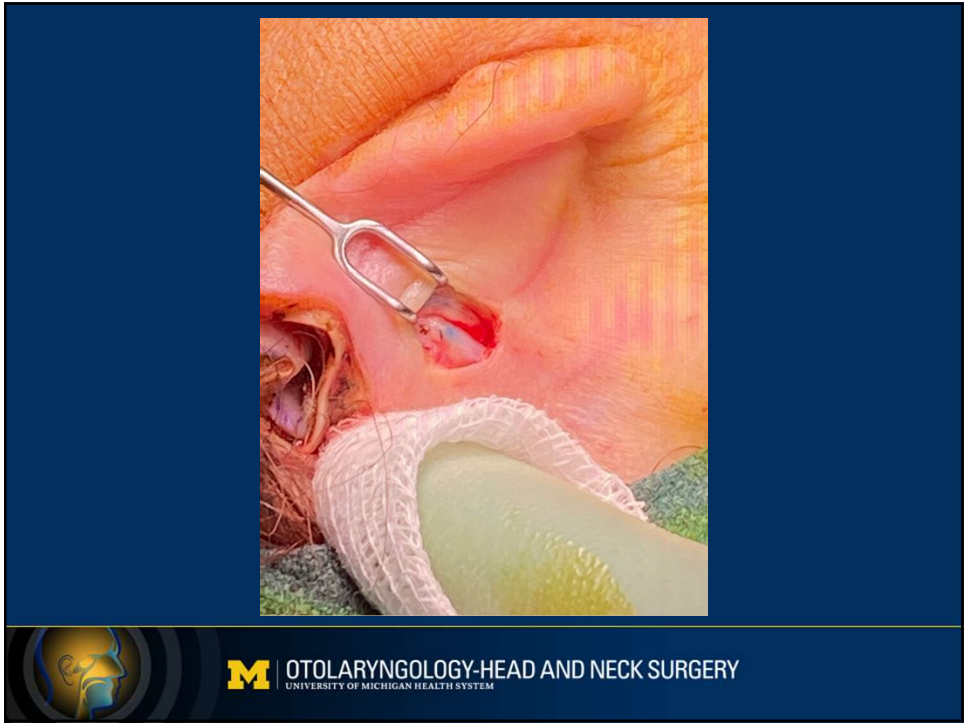
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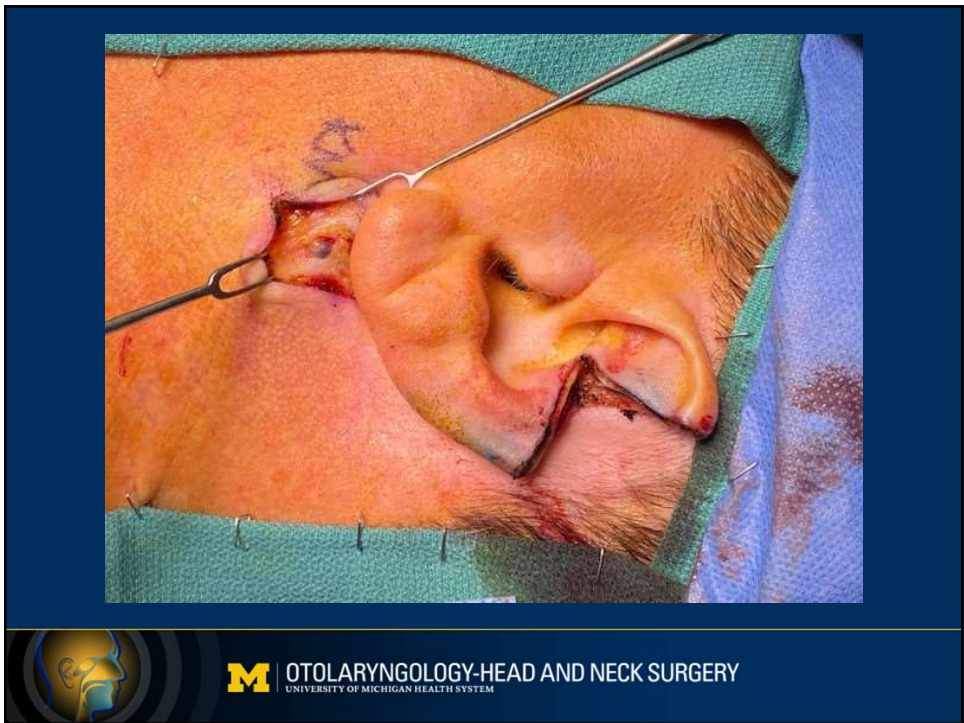
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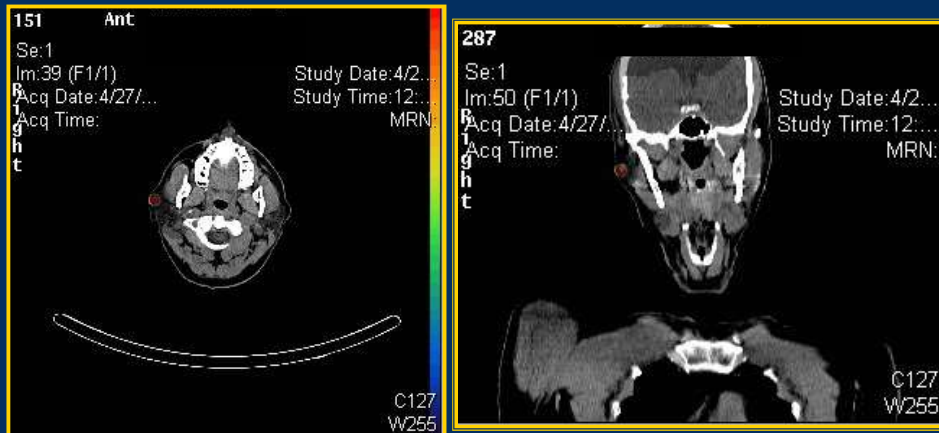


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SPECT/CT for Parotid SLN



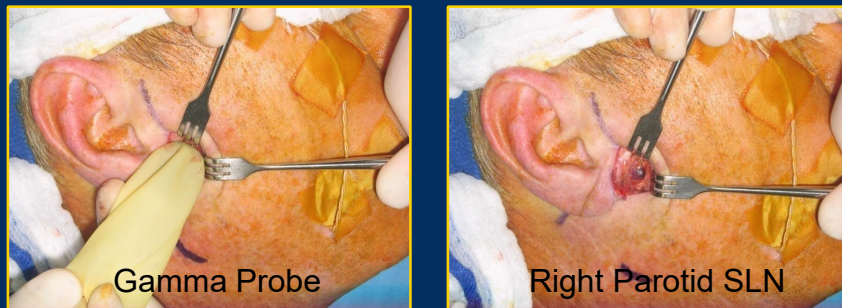
Images courtesy of Cecelia Schmalbach, MD

Right Parotid SLN



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Parotid SLN Mapping



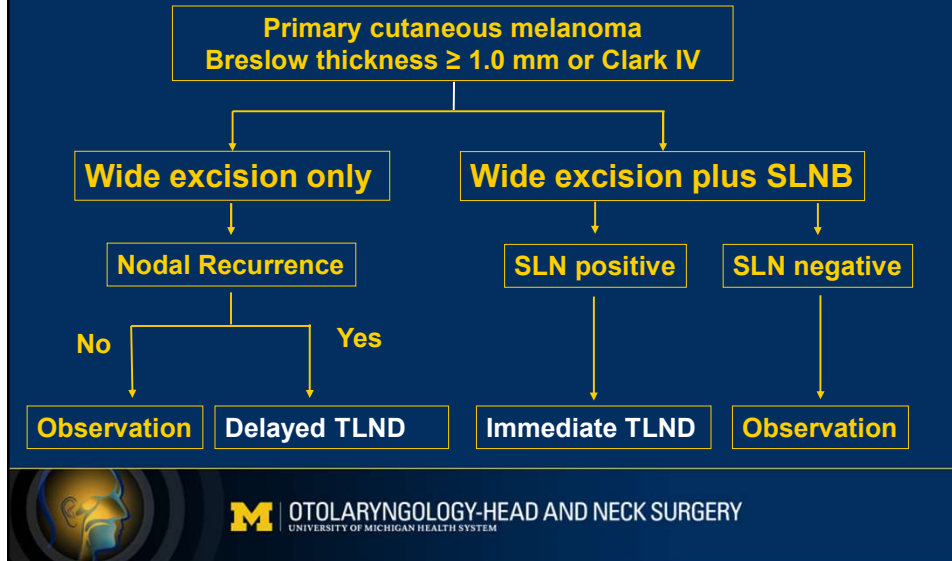
Images courtesy of Cecelia Schmalbach, MD



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? Survival Benefit of SLNB: MSLT-I

Multicenter Selective Lymphadenectomy Trial



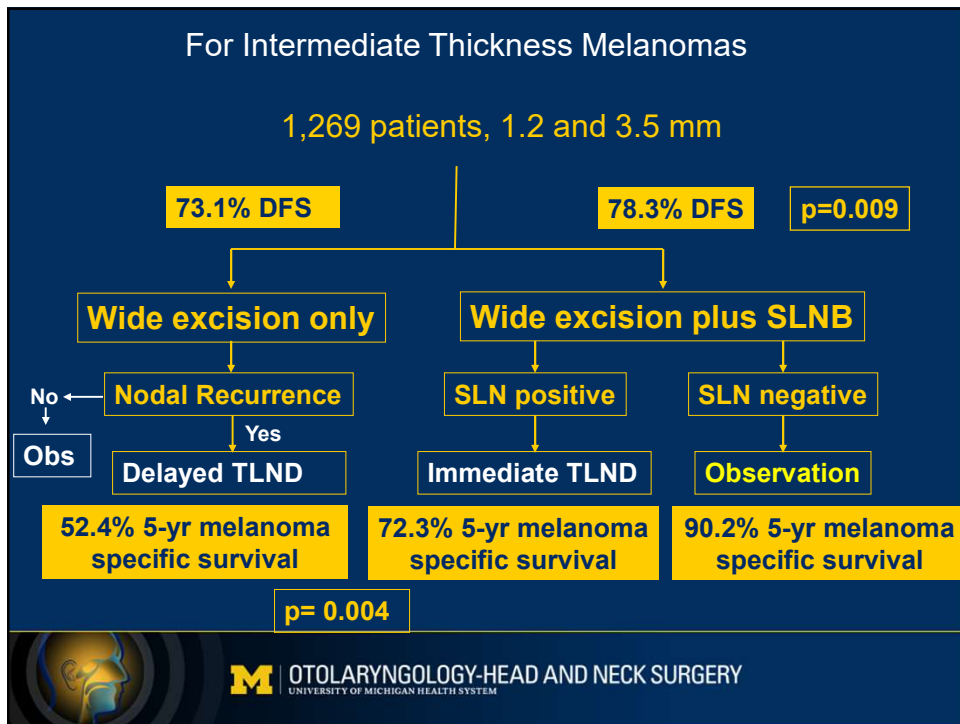
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MSLT-1: Results

- WLE + SLNB: 16.0% ≥ 1 positive SLN
- WLE only: 15.6% regional nodal relapse
- 7.4% (56/755) with a negative SLNB failed in the regional lymph node basin
- SLNB can accurately identify occult nodal dz that will lead to advanced palpable nodal disease if left *in situ*.
- Mean # of tumor-involved nodes was 1.4 in the SLN group vs. 3.3 in the observation group ($p < 0.001$), indicating disease progression during observation

Morton DL, et al. NEJM 355;1307; 2006

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Largest Single Institutional H&N SLN Study

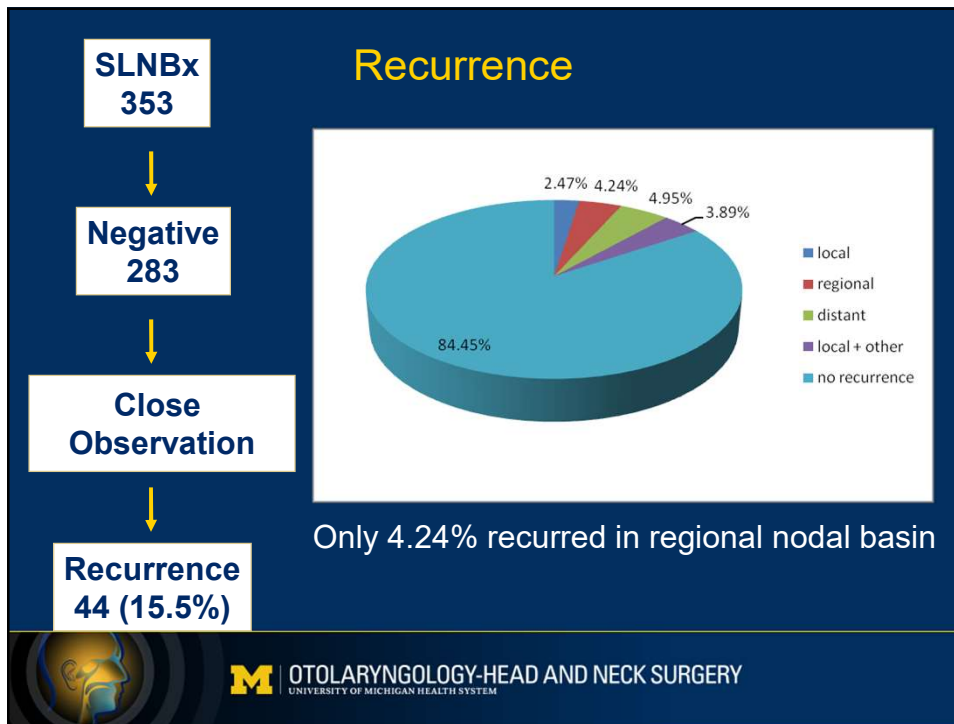
University of Michigan Melanoma Database: April 1997 - December 2007

- 353 Evaluatable patients
 - Median age 54 years (range 2 to 84 years)
 - Mean follow-up 48 months (min. 12 months)
 - *Longest follow-up to date*
- 19.6% positive sentinel node
- No major complications, high degree of accuracy

Erman AB, Collar R, Johnson TM, Bradford CR, et al. Cancer 118(4):1040, 2012.

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Significance

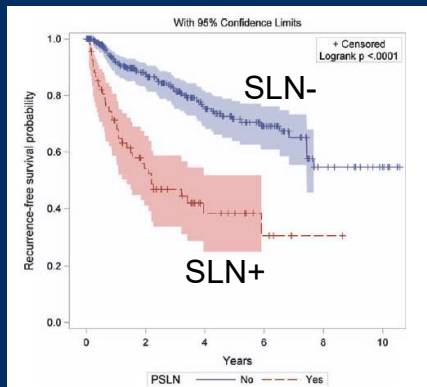
- Negative predictive value of a negative sentinel lymph node: NPV = 95.8%*
 - *this is the important number!
- Patients with local control and a negative SLN failed in the regional basin in 4.2% of cases

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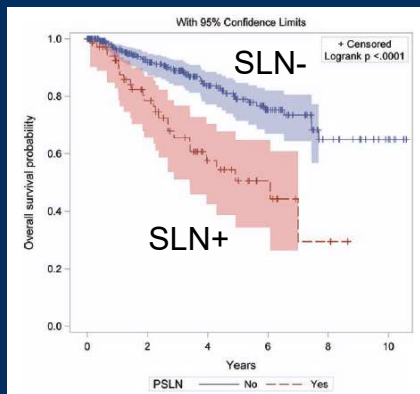
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Importance of SLN Status

Recurrence-Free Survival



Overall Survival



Erman AB, Collar R, Johnson TM, Bradford CR, et al. *Cancer*. 118(4):1040, 2012.



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A Positive SLN is Predictive of Poorer Survival: Best Fit Multivariate Model

Recurrence-Free Survival

Characteristic	Hazard Ratio (95% CI)	P
Breslow depth, 1-mm increase	1.15 (1.04-1.27)	.0049
Age at diagnosis, 1-year increase	1.03 (1.02-1.04)	<.0001
PSLNB	4.23 (2.73-6.54)	<.0001

Abbreviations: CI, confidence interval; PSLNB, positive sentinel lymph node biopsy.

Overall Survival

Characteristic	Hazard Ratio (95% CI)	P
Ulceration, present vs absent	2.05 (1.22-3.45)	.0069
Age at diagnosis, 1-year increase	1.03 (1.02-1.05)	<.0001
PSLNB	3.33 (1.99-5.58)	<.0001

Abbreviations: CI, confidence interval; PSLNB, positive sentinel lymph node biopsy.

Erman AB, Collar R, Johnson TM, Bradford CR, et al. *Cancer*. 118(4):1040, 2012.



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Conclusions

- Sentinel lymph node biopsy is a safe and effective tool to characterize the regional nodal basin in patients with cutaneous melanoma of the head and neck.
- Status of the sentinel lymph node is highly predictive of overall and disease-free survival
- Patients with a negative sentinel lymph node should be followed closely for recurrent disease.



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Prior to MSLT II . . .

- Positive SLN biopsy
 - Distant metastatic work up
 - Therapeutic lymphadenectomy
 - Counseling for adjuvant interferon α -2b & radiation
 - Negative SLN biopsy
 - Followed clinically
- } NCCN Standard of Care



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Completion Dissection or Observation for Sentinel-Node
Metastasis in Melanoma

Multicenter Selective Lymphadenectomy Trial –2 (MSLT-2)

Intermediate Thickness + SLNB

Lymphadenectomy Arm:
824 pts

Observation Arm:
931 pts

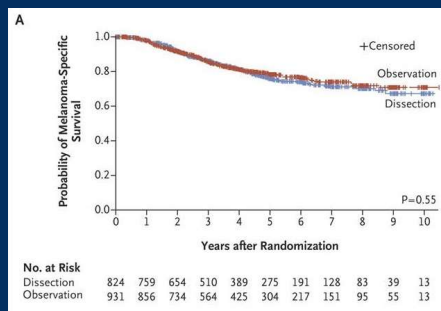


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MSLT-II: Need for Completion
Lymphadenectomy?

- Melanoma-specific survival did not differ significantly between the groups



Faries MB et al. *N Engl J Med* 2017;376:2211-2222

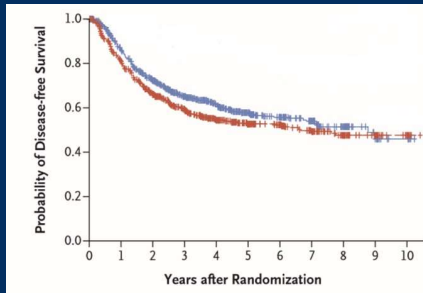


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MSLT-II: Need for Completion Lymphadenectomy?

- DFS slightly higher in the dissection group than the observation group ($p = 0.05$)
- Due to increased disease control in the regional nodal basin



Lymphadenectomy
68% +/- 1.7%

Observation
63% +/- 1.7%

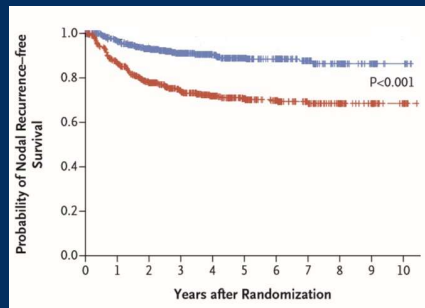


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MSLT-II: Need for Completion Lymphadenectomy?

- Higher probability of nodal recurrence-free survival with CLND
 - Recurrence is less likely in dissected basin



P<0.001

Lymphadenectomy
92 +/- 1.0%

Observation
77 +/- 1.5%



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MSLT-II

- Non-sentinel node metastases were discovered on pathologic assessment of 11.5% of CLND patients
 - Actuarial increase over time
 - 17.9% (3yr)
 - 19.9% (5yr)
- Observational arm showed non-sentinel node metastases located by US or PE in 22.9% (3yr) and 26.1% (5yr)
- CLND more likely to experience an adverse event
 - 24% lymphedema



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MSLT-II Conclusions

- Immediate CLND increases regional disease control and provides additional prognostic information (non-SLN metastasis)
- **No impact on melanoma-specific survival**
- Compliance with US follow up
- Caution with higher nodal burden SLNs
- Now what?



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MSLT-II Implications

- Immediate CLND no longer the default decision
- Patient-centered shared decision making
- Positive non-sentinel nodes portend a poor prognosis
 - CLND opportunities to drive adjuvant RX?
- Unclear if observation protocols can be safely applied to patients with larger nodal metastatic deposits
 - MINITUB trial of the European Organization for Research and Treatment of Cancer (EORTC)
 - Examining small metastases and patterns of nodal burden (i.e. subcapsular vs parenchymal location)
 - Results expected in 2023



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Changes in practice?

- NCCN & ASCO-SSO guidelines modified
- New University of Michigan study of surgical activity during the year before, year after, and two years after MSLT-II
 - 235 consecutive SLNB+ patients
 - 67% CLND year before, 33% year after, 26% 2 years after
- HN melanoma patients more likely to undergo CLND
 - 59% vs 33%, $p = 0.003$ (OR 5.22, $P = 0.002$)
- Higher SLN tumor burden more likely to undergo CLND
 - 43% vs 10% for tumor burden ≥ 0.1 mm, $p < .001$ (OR, 8.64, $P = 0.002$)



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Summary

- We are seeing steady, progressive adoption of regional observation in appropriate SLNB positive patients
- Reticence applying new recommendations to the group that was least represented in the MSLT-II cohort
- Low enrollment of HN patients in large melanoma trials is a common challenge and one that must be addressed in future trials
- In the meantime, as the data evolves and surgeons gain experience with surveillance protocols, we must continue to make decisions with our patients based on the best available evidence



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??? Questions ???

National Comprehensive Cancer Network:

www.nccn.org

AJCC Cancer Staging Manual

7th Edition (2010):

www.cancerstaging.net

National Cancer Institute

Current Melanoma Clinical Trials:

www.cancer.gov

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