The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2017

www.ifhorns.net
Skin Cancer /Melanoma: Surgery

Dr. Patrick Gullane
No Disclosures
Presentation

• Be aware of the increasing Incidence of Melanoma

• Understand the changes in the Staging System

• Understand the Evaluation and importance of Prognostic Factors

• Be familiar with Treatment Management-
  • Margins: How Wide - Is there a consensus?
  • Value of Sentinel Node: When, How and Why
  • Management of the Neck

• Be aware of the Role of Adjunctive Treatments
  • Radiation and Systemic therapy
Rising Incidence and Mortality of Melanoma in the US

Figure 1. Age adjusted incidence of malignant melanoma per 100,000 according to age and sex 1992–2004. Note: Y axis is logarithmic scale.

Figure 2. Age adjusted mortality rates from melanoma per 100,000 according to age and sex 1990–2004.

Linos, P et al 2009 J I Derm
Increasing Incidence

- 2009: 68,000/year
- 2014: 76,100/year
  - lifetime risk of melanoma approximately 2.0% (1 in 50) for Caucasians

<table>
<thead>
<tr>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>241,740</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>116,470</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>73,420</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>55,600</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>44,250</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>40,250</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>38,160</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>28,540</td>
</tr>
<tr>
<td>Leukemia</td>
<td>26,830</td>
</tr>
<tr>
<td>Pancreas</td>
<td>22,090</td>
</tr>
<tr>
<td>All Sites</td>
<td>848,170</td>
</tr>
</tbody>
</table>
The Melanoma Epidemic

Lifetime risk of developing melanoma

<table>
<thead>
<tr>
<th>Year</th>
<th>Risk, 1:n</th>
</tr>
</thead>
<tbody>
<tr>
<td>1935</td>
<td>1/1500</td>
</tr>
<tr>
<td>1960</td>
<td>1/800</td>
</tr>
<tr>
<td>1980</td>
<td>1/250</td>
</tr>
<tr>
<td>1991</td>
<td>1/105</td>
</tr>
<tr>
<td>2000</td>
<td>1/74</td>
</tr>
<tr>
<td>2002</td>
<td>1/65</td>
</tr>
</tbody>
</table>

Country | Lifetime risk, 2002
--------|---------------------
UK      | 1:147 (M), 1:117 (F)  
USA     | 1:65                 
Australia | 1:25 (M), 1:34 (F)  

Case Scenario 1 in 2017

- M55
- SSM, 1.8mm
- Not ulcerated
- Clark IV
- Mitotic Rate 1/mm²
Case Scenario 2 in 2017

- F72
- NM, 7.5mm
- Ulcerated
- Clark V
- Mitotic Rate 7/mm²
Case Scenario 3 in 2017

- F17
- SSM, 0.75mm
- Not ulcerated
- Clark III
- Mitotic Rate 1/mm²
Introduction

- 15-20% of melanomas present in head and neck
  - 6-10% are mucosal melanomas
- Behaviour is more aggressive than at other sites
- Risk factors:
  - UV light exposure
  - childhood sunburns
  - fair skin
  - Immunosuppression
  - large congenital nevi
  - sporadic or inherited dysplastic nevi
  - genetic disposition
  - previous melanomas
Cutaneous Head & Neck Melanoma

• Associated with Poorer Prognosis
  – ?influence of scalp primaries

• Risk of nodal metastases - thickness
  – <0.75mm Rare
  – 0.75 – 1mm ~5%
  – 1 – 4 mm 8 – 30%
  – >4mm ~40%
Head & Neck Melanoma

- Most succumb from systemic disease despite regional control
  - Relative Absence of effective systemic agents

- Loss of disease control
  - Anatomical
  - Aesthetic
  - Functional
Staging-7th now 8th edition

### Staging

<table>
<thead>
<tr>
<th>T Classification</th>
<th>Thickness</th>
<th>Ulceration Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
| T1               | ≤1.00 mm  | a: without ulceration and mitosis <1/mm²  
b: with ulceration or mitoses ≥1/mm² |
| 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 |
<table>
<thead>
<tr>
<th>N Classification</th>
<th># 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<sup>a</sup>  
|                  |                      | b: macrometastasis<sup>b</sup>  |
| N2               | 2–3                  | a: micrometastasis<sup>a</sup>  
|                  |                      | b: macrometastasis<sup>b</sup>  
|                  |                      | c: in transit met(s)/satellite(s) without metastatic nodes |
| N3               | 4+ metastatic nodes,  
|                  | or matted nodes, or in  
|                  | transit metastases/satellites  
|                  | with metastatic nodes        |

<table>
<thead>
<tr>
<th>M Classification</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,</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>or nodal metastases</td>
<td></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>
</tbody>
</table>
# AJCC Staging And Survival

## Table 3. Survival Rates for Melanoma TNM and Staging Categories

<table>
<thead>
<tr>
<th>Pathologic Stage</th>
<th>TNM</th>
<th>Thickness (mm)</th>
<th>Ulceration</th>
<th>No. + Nodes</th>
<th>Nodal Size</th>
<th>Distant Metastasis</th>
<th>No. of Patients</th>
<th>Survival ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1a</td>
<td>1</td>
<td>No</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>4,510</td>
<td>99.7 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>IB</td>
<td>1</td>
<td>Yes or level IV, V</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>1,380</td>
<td>99.8 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>T2a</td>
<td>1.01-2.0</td>
<td>No</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>3,285</td>
<td>99.5 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>T2b</td>
<td>1.01-2.0</td>
<td>Yes</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>958</td>
<td>98.2 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>T3a</td>
<td>2.01-4.0</td>
<td>No</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>1,717</td>
<td>98.7 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>T3b</td>
<td>2.01-4.0</td>
<td>Yes</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>1,523</td>
<td>95.1 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>&gt; 4.0</td>
<td>No</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>563</td>
<td>94.8 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>&gt; 4.0</td>
<td>Yes</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>978</td>
<td>89.9 ± 1.0</td>
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<tr>
<td></td>
<td>N1a</td>
<td>Any</td>
<td>No</td>
<td>1</td>
<td>Micro</td>
<td>-</td>
<td>252</td>
<td>95.9 ± 1.3</td>
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<tr>
<td></td>
<td>N2a</td>
<td>Any</td>
<td>No</td>
<td>2-3</td>
<td>Micro</td>
<td>-</td>
<td>130</td>
<td>93.0 ± 2.4</td>
</tr>
<tr>
<td></td>
<td>N1a</td>
<td>Any</td>
<td>Yes</td>
<td>1</td>
<td>Micro</td>
<td>-</td>
<td>217</td>
<td>93.3 ± 1.8</td>
</tr>
<tr>
<td></td>
<td>N2a</td>
<td>Any</td>
<td>Yes</td>
<td>2-3</td>
<td>Micro</td>
<td>-</td>
<td>111</td>
<td>92.0 ± 2.7</td>
</tr>
<tr>
<td></td>
<td>N1b</td>
<td>Any</td>
<td>No</td>
<td>1</td>
<td>Macro</td>
<td>-</td>
<td>122</td>
<td>88.5 ± 2.9</td>
</tr>
<tr>
<td></td>
<td>N2b</td>
<td>Any</td>
<td>No</td>
<td>2-3</td>
<td>Macro</td>
<td>-</td>
<td>93</td>
<td>76.8 ± 4.4</td>
</tr>
<tr>
<td></td>
<td>N1b</td>
<td>Any</td>
<td>Yes</td>
<td>1</td>
<td>Macro</td>
<td>-</td>
<td>98</td>
<td>77.9 ± 4.3</td>
</tr>
<tr>
<td></td>
<td>N2b</td>
<td>Any</td>
<td>Yes</td>
<td>2-3</td>
<td>Macro</td>
<td>-</td>
<td>109</td>
<td>74.3 ± 4.3</td>
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<tr>
<td></td>
<td>N3</td>
<td>Any</td>
<td>Any</td>
<td>4</td>
<td>Micro/macro</td>
<td>-</td>
<td>396</td>
<td>71.0 ± 2.4</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Skin, SQ</td>
<td>179</td>
<td>59.3 ± 3.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Lung</td>
<td>186</td>
<td>57.0 ± 3.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Other Visceral</td>
<td>793</td>
<td>40.6 ± 1.8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17,600</td>
<td></td>
</tr>
</tbody>
</table>
AJCC 7th edition
Staging Changes - Reasons

- Importance of Breslow thickness (Clark’s level only has a role in tumours < 1mm deep)
- Importance of ulceration and mitotic rate
- Importance of in-transit and satellite lesions
- Based on a belief that micrometastatic disease better than clinically enlarged nodes
- Number of nodes not size important
Cutaneous Melanoma

- pT1a and pT1b categories introduced
  - pT1a \( \leq 0.8\text{mm} \)
  - pT1b \( > 0.8\text{mm} - 1\text{mm} \)

- M category
  - M1a Skin, subcutaneous tissue or non regional lymph nodes
  - M1b Lung
  - M1c Other non-central nervous system sites
  - M1d Central nervous system

- M Category modified by elevated or non-elevated LDH
- Stage Revised
Workup prior to definitive treatment?
Investigations for Melanoma

• Primary
  – Routine investigations are not required for asymptomatic patients

• Locoregional
  – +ve SNB – routine investigations are not indicated in the absence of systemic symptoms
  – Macroscopic nodes – CT +/- PET for symptoms, or in cases where change of management may result
  – FNA to confirm stage III disease

• Systemic
  – CT, MRI, PET, serum LDH for symptoms suggestive of systemic disease
  – Further investigations as indicated by treatment
Diagnosis

- **ABCD(E)’s Of Melanoma:**
  - Asymmetry, border, colour variegation, diameter >6mm, evolution
  - Bleeding, ulceration, tingling

- **Full-thickness, excisional biopsy of suspicious lesions**

- **Tumour markers:** HMB-45, S-100
<table>
<thead>
<tr>
<th>Level</th>
<th>Anatomical Invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>Melanoma confined to the epidermis (melanoma in situ)</td>
</tr>
<tr>
<td>Level 2</td>
<td>Invasion into the papillary dermis</td>
</tr>
<tr>
<td>Level 3</td>
<td>Invasion to the junction of the papillary and reticular dermis</td>
</tr>
<tr>
<td>Level 4</td>
<td>Invasion into the reticular dermis</td>
</tr>
<tr>
<td>Level 5</td>
<td>Invasion into the subcutaneous fat</td>
</tr>
</tbody>
</table>
10 Year survival Rates
Prognostic Factors

- **Clinical** prognostic Factors
  - Older age
  - Male
  - Head and neck site

- **Histologic** prognostic factors
  - Nodal metastases
  - Tumor thickness/depth
  - Ulceration
  - Vascular invasion
  - Microsatellite lesions
Prognostic Factors:
Nodal metastases

- Single most powerful predictor of recurrence and survival
- Occurs in 15-20% of patients
- Decreases survival by 40%-50% independent of other prognostic factors

- Increases with increasing tumor thickness

<table>
<thead>
<tr>
<th>Thickness</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thin (T1)</td>
<td>&lt; 1.0mm</td>
</tr>
<tr>
<td>Intermediate (T2)</td>
<td>1.01-2.0 mm</td>
</tr>
<tr>
<td>Intermediate (T3)</td>
<td>2.01-4.0 mm</td>
</tr>
<tr>
<td>Thick (T4)</td>
<td>&gt; 4.0 mm</td>
</tr>
</tbody>
</table>
Risk Of Nodal Metatasis

Rationale for ELND

![Graph showing risk of regional and distant metastasis based on melanoma thickness.]

- % Risk: <0.76, 0.76-1.5, 1.5-4, >4
- Melanoma Thickness: Regional, Distant

Balch 1980
Rationale for ELND

Balch 1979
Impact of Nodal Metastases

5 ys 83% vs 49%
P<0.0001

Martin et al
Impact of N Stage

Survival by node group

- No nodes
- One node
- Two or Three nodes
- Four or more nodes

<table>
<thead>
<tr>
<th>Survival</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>No nodes</td>
<td>408</td>
<td>399</td>
<td>311</td>
<td>237</td>
<td>189</td>
<td>143</td>
<td>119</td>
</tr>
<tr>
<td>One node</td>
<td>168</td>
<td>155</td>
<td>103</td>
<td>71</td>
<td>58</td>
<td>46</td>
<td>34</td>
</tr>
<tr>
<td>Two or Three nodes</td>
<td>84</td>
<td>69</td>
<td>45</td>
<td>30</td>
<td>19</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Four or more nodes</td>
<td>56</td>
<td>32</td>
<td>15</td>
<td>10</td>
<td>8</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>
Mortality

• Mortality is typically related to the development of distant metastases

• Goals of management are
  – Locoregional control
  – Prevention of systemic disease
    • Adjuvant immunotherapy &/or chemotherapeutic agents
    • May have significant side effects
    • Expensive
Management

• Wide local excision of primary
• Neck management
  – Watch & wait policy
  – Elective lymph node dissection
  – Sentinel node biopsy & nodal management
Treatment of Primary Melanoma

• Wide local excision

... But How Wide?
Margins – Randomised trials

- 5cm historical margins

French Co-operative Group, 1985
2cm vs 5cm margin for melanoma $\leq$ 2mm

NO DIFFERENCE

Khayet et al, Cancer 2003
Margins – Randomised trials

- Intergroup Melanoma Committee
  - Compared 2 v 4 cm margins for MM 1 to 4 mm
  - No significant difference in LR, ITM, survival
  - Fewer SSG, shorter hospital stays
  - Concluded 2 cm safe for intermediate thickness MM


No evidence to say that a margin > 1cm improves survival
Summary of margins trials

- No overall survival nor local recurrence advantage for margin >2cm
- No overall survival advantage for margin >1cm
- No RCT data for ALM and subungual melanoma
- Optimal margins for T3 primaries not certain
Guidelines for excision margins

Melanoma

• In-situ
• 0 to 1.0 mm
• 1.0 to 4.0 (minimum 1 cm)
• >4.0

Margin

5 mm
1 cm (minimum maximum
minimum 2 cm

Consider other pathological features

– satellitosis,
– lymphatic invasion,
– desmoplasia,
– neurotropism
Various Melanomas
Excision margins - Head and Neck

T < 1mm
• 1cm margin

T > 1mm
• As wide a margin up to 2cm that can be
  • closed without graft / complicated flap or
  • significant disfigurement
• If a graft or flap is required for the
  • minimum margin – take the recommended
  • margin (ie 2cm)
Prognostic Factors

Tumour thickness
Ulceration
Clark level
Histological type
Cell type
Primary site
Regression
Mitoses
Lymphocytic infiltration
Vertical maturation grade
Blood vessel invasion
Lymphatic space invasion

Ploidy
S-Phase
DR-1 Expression
DNA index
HSP expression
HLA-DR staining
p53 mutations
CAM expression
Protease expression
Migration-associated molecule
Angiogenesis-related factor
Oncogene expression
Oestrogen receptor expression
Cytokine, growth factor expression
# Prognosis of Melanoma Based on Tumor Thickness

<table>
<thead>
<tr>
<th>Tumor thickness</th>
<th>Sample Size</th>
<th>10-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&lt; 1.00 mm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level II</td>
<td>975</td>
<td>94.8</td>
</tr>
<tr>
<td>Level III</td>
<td>688</td>
<td>84.7</td>
</tr>
<tr>
<td>Level IV</td>
<td>450</td>
<td>88.6</td>
</tr>
<tr>
<td>Level V</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>1.01-2.00 mm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level II</td>
<td>49</td>
<td>78.5</td>
</tr>
<tr>
<td>Level III</td>
<td>425</td>
<td>75.8</td>
</tr>
<tr>
<td>Level IV</td>
<td>713</td>
<td>72.4</td>
</tr>
<tr>
<td>Level V</td>
<td>12</td>
<td>65.6</td>
</tr>
<tr>
<td><strong>2.01-4.00 mm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level II</td>
<td>18</td>
<td>50.9</td>
</tr>
<tr>
<td>Level III</td>
<td>237</td>
<td>53.8</td>
</tr>
<tr>
<td>Level IV</td>
<td>562</td>
<td>60.4</td>
</tr>
<tr>
<td>Level V</td>
<td>55</td>
<td>37.3</td>
</tr>
<tr>
<td><strong>&gt; 4.00 mm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level II</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Level III</td>
<td>44</td>
<td>36.5</td>
</tr>
<tr>
<td>Level IV</td>
<td>194</td>
<td>38.6</td>
</tr>
<tr>
<td>Level V</td>
<td>132</td>
<td>38.8</td>
</tr>
</tbody>
</table>

Ten-Year Survival Rates in Patients with Melanoma by Tumor Thickness and Ulceration

(n = 4568)

<table>
<thead>
<tr>
<th>Thickness, mm</th>
<th>No Ulceration</th>
<th>Ulceration</th>
<th>10-year survival rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.01 – 1.00</td>
<td>2017 (95.5)</td>
<td>96 (4.5)</td>
<td>92.0</td>
</tr>
<tr>
<td>1.01 – 2.00</td>
<td>944 (78.8)</td>
<td>255 (21.2)</td>
<td>77.7</td>
</tr>
<tr>
<td>2.01 – 4.00</td>
<td>500 (57.4)</td>
<td>372 (42.6)</td>
<td>59.5</td>
</tr>
<tr>
<td>&gt; 4.00</td>
<td>146 (38.1)</td>
<td>238 (61.9)</td>
<td>54.5</td>
</tr>
</tbody>
</table>

Management of the Primary

- Wide local excision of Primary
  - Margin analysis of the paraffin block
  - No frozen section
- Delayed Reconstruction
  - Margin Status
  - Management of the Neck
- Neck Management
  - Watch & wait policy
  - Elective lymph node dissection
  - Sentinel node biopsy & nodal management
Superficial lesions
(<0.76mm thick)

• **Excision:**
  – 1 cm margin down to fascia

• **N0 neck:**
  – SLNB not indicated
  – Elective neck dissection not indicated
Intermediate lesions (0.76-3.99mm thick)

- Excision
  - 1-2 cm margin down to fascia
- N0 neck:
  - SLNB
- N1-N3 neck:
  - neck dissection +/- superficial parotidectomy
  +/- chemotherapy
  +/- interferon α-2b etc.
Deep lesions (>4.0mm thick)

• Excision -- 2 cm margins down to fascia
• N0 neck:
  – elective neck dissections not indicated
• N1-N3 neck: neck dissection
  +/- superficial parotidectomy
  +/- chemotherapy
  +/- interferon α-2b
## Summary of Management

<table>
<thead>
<tr>
<th>MELANOMA</th>
<th>DEPTH</th>
<th>MARGIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>pTis melanoma</td>
<td>in situ</td>
<td>5mm</td>
</tr>
<tr>
<td>pT1 melanoma</td>
<td>&lt;1.0 mm</td>
<td>1cm</td>
</tr>
<tr>
<td>pT2 melanoma</td>
<td>1.0-2.0 mm</td>
<td>1-2cm</td>
</tr>
<tr>
<td>pT3 melanoma</td>
<td>2.0-4.0 mm</td>
<td>1-2cm</td>
</tr>
<tr>
<td>pT4 melanoma</td>
<td>&gt;4.0 mm</td>
<td>2cm</td>
</tr>
</tbody>
</table>
Management of The Neck In Melanoma
Prognostic Factors

- Tumour thickness
- Ulceration
- Clark level
- Histological type
- Cell type
- Primary site
- Regression
- Mitoses
- Lymphocytic infiltration
- Vertical maturation grade
- Blood vessel invasion
- Lymphatic space invasion

Lymph node status

- Ploidy
- S-Phase
- DR-1 Expression
- DNA index
- HSP expression
- HLA-DR staining
- p53 mutations
- CAM expression
- Protease expression
- Migration-associated molecule
- Angiogenesis-related factor
- Oncogene expression
- Oestrogen receptor expression
- Cytokine, growth factor expression
Impact of nodal metastases
5 Year survival 83% vs 49%

Martin et al

5 yrs 83% vs 49%
P<0.0001
Current Node Management

- SNB offered to
  - 1mm or greater
  - <1mm + ulceration, high MR, (younger age)
- SNB +ve
  - Offered participation in MSLT II, or
  - TLND, extent based on lymphatic mapping
- Clinically N+
  - Confirm diagnosis FNA, systemic staging
  - TLND, selective if appropriate
- pN+
  - Considered for adjuvant XRT
  - Offered adjuvant systemic therapy trials
To \( snB \)
or
not to
\( snB \)…?
Melanoma

CLINICAL STAGE

Stage 0 in situ
Stage IA, IB (≤0.75 mm thick, any features)\textsuperscript{h}
Stage IA (0.76–1.0 mm thick, no ulceration, mitotic rate 0 per mm\textsuperscript{h})

WORKUP\textsuperscript{c,d}

- H&P
- Routine imaging/lab tests not recommended
- Imaging (CT scan, PET/CT, MRI) only to evaluate specific signs or symptoms
- H&P
- Routine imaging/lab tests not recommended
- Imaging (CT scan, PET/CT, MRI) only to evaluate specific signs or symptoms

PRIMARY TREATMENT

- Wide excision\textsuperscript{k}
- Discuss and consider sentinel node biopsy\textsuperscript{j}
- Wide excision\textsuperscript{k} (category 1)

ADJUVANT TREATMENT

- Wide excision\textsuperscript{k} (category 1) with sentinel node biopsy\textsuperscript{j} (category 2B)
- Sentinel node negative
- Sentinel node positive

See Stage III Workup and Primary Treatment (ME-4)
See Follow-Up (ME-7)
Melanoma

CLINICAL STAGE

Stage IB
(0.76–1.0 mm thick with ulceration or mitotic rate ≥1 per mm²)
or
Stage IB or II (>1 mm thick, any feature, N0)

WORKUP c,d

- H&P
- Routine imaging/laboratory tests not recommended
- Imaging (CT scan, PET/CT, MRI) only to evaluate specific signs or symptoms

PRIMARY TREATMENT

Discuss and offer sentinel node biopsy l,m

Wide excision k (category 1)

Sentinel node negative

Sentinel node positive

Wide excision k (category 1) with sentinel node biopsy l

ADJUVANT TREATMENT

If Stage IB, IIA:
Clinical trial (if available) or Observation

Stage IIB, IIC:
Clinical trial (if available) or Observation or Interferon alfa (category 2B) See Stage III Workup and Primary Treatment (ME-4)

Follow-Up (ME-7)

---

k In general, SLNB is not recommended for primary melanomas ≤0.75 mm thick, unless there is significant uncertainty about the adequacy of microstaging. For melanomas 0.76 to 1.0 mm thick, SLNB may be considered in the appropriate clinical context. In patients with thin melanomas (≤1.0 mm), apart from primary tumor thickness, there is little consensus as to what should be considered “high-risk features” for a positive SLN. Conventional risk factors for a positive SLN, such as ulceration, high mitotic rate, and LVI, are very uncommon in melanomas ≤0.75 mm thick. When present, SLNB may be considered on an individual basis.

l Microsatelitosis, when present in the initial biopsy or wide excision specimen, defines at least N2c and at least stage III disease. SLN status does have prognostic significance in these patients, with a positive SLN upstaging a patient to N3, stage IIIc. However, the importance of SLNB in the management and outcome of these patients has not been clearly defined. Regardless of SLN status, these patients should be managed as stage III in discussions of workup, adjuvant therapy, and follow-up.

---
Neck Management: Watch & wait

• In situ melanoma

• Thin melanoma < 1mm & less than Clark level III and no adverse pathologic features
  – Risk of nodal metastasis <2%

• Thick melanoma > 4mm
  – Some debate as to whether to offer SLNB
Elective Lymph Node Dissection

- No strong evidence in favour of performing ELND in clinically node negative patients with H & N melanoma

- ND unnecessary in > 80% patients

- Clinical prediction of lymphatic dissemination is unreliable
  - Discordancy rate as high as 14%
  - Lymphatic draining patterns vary
Sentinel Lymph Node Biopsy

- Introduced by Cabanas in 1977
- Popularized by Morton 1990
- Staging and therapeutic procedure
  - Increases sensitivity to detect regional metastasis
  - Halts regional progression of disease.
  - Selects patients who might benefit from:
    - Further regional therapy
    - Systemic adjuvant therapy
Role of Sentinel Lymph Node Biopsy

- Popularized by Morton for Melanoma

- Rationale
  - Metastases occur through specific lymphatic channels to involve sentinel nodes as first site of spread
  
  - If the SLN is negative, the assumption is that rest of the regional nodes are very likely to be free of disease as well
"Sentinel Node" - Definition

- "First draining lymph node on the direct drainage pathway from the primary tumor site"
  
  Morton

- "Any lymph node receiving direct drainage from a primary lesion site"
  
  Uren et al
Indications

- > 1 mm depth, any Clark level
- < 1 mm depth with Clark level IV, V or ulceration
- > 4 mm depth with no adverse risk features
  - Controversial
Sentinel node biopsy
Who should undergo SLN Biopsy?

Summary Indications

- 1-4 mm thick
- ? Thin Melanomas
  - Ulcerated
  - Clark level IV or V
  - Mitoses- > 1/mm²
- ? Thick Melanomas
Contraindications

- Clinically or radiographic lymph node metastases
- Tumors > 4 to 5 cm
- Disruption of lymphatic drainage
  - Prior extensive surgery
  - Extensive local flaps
  - Previous radiation to H & N
- Pregnancy and breast-feeding
- Allergy to dye
SLNB Technique

• Morning of Procedure:
  – Injection of primary site with radiolabelled sulfur colloids (technetium-99m)
  – Planar Lymphoscintigraphy (15 min – 1 hour)
• Inject tumour with blue dye (15 min)
• Wide Local Excision of Primary Site
• Use lymphoscintigraphy imaging, Gamma Probe and visualized blue dye to identify sentinel node
Sentinel Node Technique

Primary Tumor

Sentinel Node

Regional Lymph Nodes

Lymphatic Channel
Pre-operative Details

- Dynamic Lymphatic mapping is performed
- Multiple peripheral intradermal injections of Tc-99 Sulfur Colloid 40mBq within 12 hrs of surgery
  - Choice of radiocolloid
- Uptake sites labeled on skin surface
SLNB Technique

45 Min. RLAT

50 Min. LLAT

1 mCi TC Sulfur Colloid
SLNB Technique

• SLN serially section by pathology
  – As oppose to a single cut through the node

• Immunohistochemistry
  – S-100
  – Melan-A
  – HMB-45
Hybrid Imaging with SPECT/CT

Lymphoscintigraphic Imaging

• Higher diagnostic reliability
  – Anatomic correlation
  – Higher specificity

• Better image quality
  – Due to CT attenuation correction

Sebaceous cell carcinoma of left upper eyelid: Planar imaging (D) demonstrated only 1 node, whereas SPECT/CT demonstrated 4 nodes, possibly because of slight delay in imaging time. Level IIA (A), level IIB (B), and preauricular (C) lymphatic chains are shown.
Hybrid Imaging with SPECT/CT Lymphoscintigraphic Imaging

• Higher diagnostic reliability
  – Anatomic correlation
  – Higher specificity

• Better image quality
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Sebaceous cell carcinoma of left upper eyelid: Planar imaging (D) demonstrated only 1 node, whereas SPECT/CT demonstrated 4 nodes, possibly because of slight delay in imaging time. Level IIA (A), level IIB (B), and preauricular (C) lymphatic chains are shown.
Intra-operative technique
2-3 cm incision(s) made over previously identified areas
In line with incision that would be used for ND &/or parotidectomy
Isosulfan blue (<1cc) is injected into the dermis at the biopsy margins
Dye colored lymph nodes are identified.
Hand held gamma probe is used to localize the hottest sites.

Using a combination of Isotope mapping, hand held gamma probe and intraoperative blue dye SLN identified in >98% of cases.
SLN shows radioactive uptake exceeding a 10:1 ratio of ex vivo to resection bed count or a 3:1 ratio of in vivo to resection bed count.

10% rule: Keep looking until bed count < 10% of initial in situ count.

Formalin fixation and Permanent Sections
Special micro-sectioning
SPECT-CT for SLNB

- Single Photon Emission CT
- Primarily H&N melanoma
- Improves anatomic location of SLN
  - EJ vs IJ
  - Levels IIA vs IIB vs VA
  - Parotid nodes
  - Suboccipital nodes
- Shortens operative time
- Proper placement of incision
If SNB positive…

- Neck dissection and consideration for systemic therapy +/- clinical trial
Management of +ve SN

- Therapeutic dissection
  - Based on pattern of drainage at LSG
    - Only 20% will have additional +ve nodes

- Is CLND-Complete Lymph node dissection necessary?
  MSLT II
Why is Head and Neck site different from all other sites?

- Cosmetic issues in the head and neck

- Technically challenging
  - Complex anatomy:
    - nerves and vessels at risk
    - Intraparotid nodes
  - Incision(s) need to be planned based on potential for neck dissection

- Radionucleotide overlap between primary and drainage
Arguments Against SNB

- Micromets may be clinically irrelevant

- False negative rates
  - Can still have regional recurrence following SNB and SNB w/ND
  - Drainage not predictable
  - Number of sentinel nodes generally greater than elsewhere- may miss

- ?? Survival benefit
Summary

• SNB improves locoregional control of head and neck melanoma

• Sentinel-node biopsy has staging and prognostic value in patients with intermediate thickness melanoma

• But there is no clear survival benefit
Current Role for SNB

- To identify patients with poor prognosis that can be offered adjuvant immunotherapy and/or chemotherapeutic agents
  - Very limited benefit
- Or to be enrolled in a clinical trial investigating systemic therapies
Final Trial Report of Sentinel-Node Biopsy versus Nodal Observation in Melanoma

MSLT-1: Rationale

• Phase 3 Trial to assess the role of SNLBx in melanoma staging (identification of occult nodal metastases)

• Why?
  – Authors were unsatisfied with the other options:
    • Lymphadenectomy (procedure related risk)
    • Observation

• Results previously reported but only for intermediate thickness melanomas at 5 years (2006)
Stratification and randomization of all patients

60% of patients assigned to wide excision and sentinel-node biopsy

Sentinel-node positive: Immediate complete lymphadenectomy

Sentinel-node negative: Nodal observation

Nodal recurrence: Complete lymphadenectomy

No nodal recurrence: Continued nodal observation

Follow-up for systemic recurrence and survival (10 yr)

40% of patients assigned to wide excision and nodal observation

Nodal recurrence: Complete lymphadenectomy

No nodal recurrence: Continued nodal observation
Outcomes

• **Primary**
  – Melanoma Specific Survival (DSS)

• **Secondary**
  – Disease Free Survival (DFS)
Primary Outcome (DSS)

A Melanoma-Specific Survival

<table>
<thead>
<tr>
<th></th>
<th>Intermediate-Thickness Melanomas</th>
<th>Thick Melanomas</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of Events/Total No.</strong></td>
<td><strong>Rate (%)</strong></td>
<td><strong>Rate (%)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Yr 5</strong></td>
<td><strong>Yr 10</strong></td>
</tr>
<tr>
<td>OBS</td>
<td>97/500</td>
<td>85.7±1.6</td>
</tr>
<tr>
<td>SNB</td>
<td>125/770</td>
<td>86.6±1.3</td>
</tr>
<tr>
<td></td>
<td>67.5±4.5</td>
<td>64.4±4.6</td>
</tr>
<tr>
<td></td>
<td>67.0±3.7</td>
<td>58.9±4.1</td>
</tr>
</tbody>
</table>

Hazard ratio, 0.84 (95% CI, 0.64–1.09)
P = 0.18

Hazard ratio, 1.12 (95% CI, 0.76–1.67)
P = 0.56
Secondary Outcome (DFS)

C  Disease-free Survival

**Intermediate-Thick Melanomas**

<table>
<thead>
<tr>
<th></th>
<th>OBS</th>
<th>SNB</th>
<th>Rate (Yr 5)</th>
<th>Rate (Yr 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Events/Tot. No.</td>
<td>161/500</td>
<td>199/770</td>
<td>72.7±2.1</td>
<td>64.7±2.3</td>
</tr>
<tr>
<td></td>
<td>Yr 5</td>
<td>Yr 10</td>
<td>Yr 5</td>
<td>Yr 10</td>
</tr>
<tr>
<td>OBS</td>
<td>77.8±1.6</td>
<td>71.3±1.8</td>
<td>43.7±4.7</td>
<td>40.5±4.7</td>
</tr>
<tr>
<td>SNB</td>
<td>77.8±1.6</td>
<td>71.3±1.8</td>
<td>43.7±4.7</td>
<td>40.5±4.7</td>
</tr>
</tbody>
</table>

Disease-free Survival

Disease-free Survival

**Thick Melanomas**

<table>
<thead>
<tr>
<th></th>
<th>OBS</th>
<th>SNB</th>
<th>Rate (Yr 5)</th>
<th>Rate (Yr 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Events/Tot. No.</td>
<td>68/171</td>
<td>80/173</td>
<td>43.7±4.7</td>
<td>40.5±4.7</td>
</tr>
</tbody>
</table>

Hazard ratio, 0.76 (95% CI, 0.62–0.94)
P=0.01

Hazard ratio, 0.70 (95% CI, 0.50–0.96)
P=0.03
MSLT – I Conclusions

• “Our long-term results confirm that sentinel-node biopsy correctly determines the pathologic status of the nodal basin in 96% of cases and is the most powerful **prognostic indicator**.”

• “These long-term results clearly validate the use of sentinel-node biopsy in patients with intermediate-thickness or thick primary melanomas. The procedure provides accurate and important staging information, **enhances regional disease control, and, among patients with nodal metastases, appears to improve melanoma-specific survival substantially.””
Bias

- Despite the consistent strength of the data from the MSLT-I, there has been some reluctance to accept the results of comparisons between node-positive patients in the biopsy group and those in the observation group, because of concern about ascertainment (surveillance) bias. Latent-subgroup analysis methods were used to address this statistical consideration.
Sentinel Lymph Node Biopsy for Melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Joint Clinical Practice Guideline

Sandra L. Wong, Charles M. Balch, Patricia Hurley, Sanjiv S. Agarwala, Timothy J. Akhurst, Alistair Cochran, Janice N. Cornier, Mark German, Theodore Y. Kim, Kelly M. McMasters, R. Dirk Noyes, Lynn M. Schuchter, Matthew E. Valicenti, Donald L. Weaver, and Gary H. Lyman

Recommendations

SLN biopsy is recommended for patients with intermediate-thickness melanomas (Breslow thickness, 1 to 4 mm) of any anatomic site; use of SLN biopsy in this population provides accurate staging. Although there are few studies focusing on patients with thick melanomas (T4; Breslow thickness, > 4 mm), SLN biopsy may be recommended for staging purposes and to facilitate regional disease control. There is insufficient evidence to support routine SLN biopsy for patients with thin melanomas (T1; Breslow thickness, < 1 mm), although it may be considered in selected patients with high-risk features when staging benefits outweigh risks of the procedure. Completion lymph node dissection (CLND) is recommended for all patients with a positive SLN biopsy and achieves good regional disease control. Whether CLND after a positive SLN biopsy improves survival is the subject of the ongoing Multicenter Selective Lymphadenectomy Trial II.
“There is consensus that the procedure should be discussed and offered to patients with primary melanomas greater than 1.0 mm thick.”

For melanomas 0.76 to 1.0 mm thick, SLNB should be discussed and considered. The discussion about SLNB in this group of patients should include the recognition that the yield of a positive SLNB is low and the clinical significance of a positive SLN is modest.

- Ulceration
- High mitotic rate
- Lymphovascular invasion
MSLT – II

• SLN+ randomized to:
  – Completion lymphadenectomy
  – Observation

• Outcomes
  – Primary: DSS
  – Secondary: DFS and Recurrence at 10 years

• Estimated completion date 2022
Completion Dissection or Observation for Sentinel-Node Metastasis in Melanoma

- S. Schneebaum, J.E. Gershenwald, C.E. Ariyan, D.C. Desai, L. Jacobs, K.M. McMasters, A. Gesierich, P. Hersey,
A. Disease-free Survival

B. Survival without Nodal Recurrence

C. Distant Metastasis–free Survival

D. Cumulative Rate of Non-sentinel-Node Metastasis.

MSLT II - Conclusions

Immediate completion lymph-node dissection:

• Increased the rate of regional disease control

• Provided prognostic information

But

Did not increase melanoma-specific survival among patients with melanoma and sentinel-node metastases.
Completion Dissection or Observation for Sentinel-Node Metastasis in Melanoma

**Conclusions:**

- Immediate completion lymph-node dissection increased the rate of regional disease control and provided prognostic information but did not increase melanoma-specific survival.
- among patients with melanoma and sentinel-node metastases. (Funded by the National Cancer Institute and others; MSLT-II ClinicalTrials.gov number, NCT00297895.)
Management of the PN+ Neck Surgery: What levels to dissect
**NCCN Guidelines Version 2.2016**

**Melanoma**

<table>
<thead>
<tr>
<th>CLINICAL/PATHOLOGIC STAGE</th>
<th>WORKUP</th>
<th>PRIMARY TREATMENT</th>
<th>ADJUVANT TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage III (sentinel node positive)</td>
<td>Consider baseline imaging for staging (category 2B) and to evaluate specific signs or symptoms (CT scan, PET/CT, MRI)</td>
<td>Discuss and offer complete lymph node dissection</td>
<td>Clinical trial or Observation or Interferon alfa or High-dose ipilimumab (category 2B)</td>
</tr>
<tr>
<td>Stage III (clinically positive node[s])</td>
<td>• FNA preferred, if feasible, or core, incisional, or excisional biopsy</td>
<td>• Recommend baseline imaging for staging and to evaluate specific signs or symptoms (CT scan, PET/CT, MRI)</td>
<td>Clinical trial or Observation or Interferon alfa or High-dose ipilimumab (category 2B) or Biotherapy (category 2B) and/or Consider RT to nodal basin in selected high-risk patients based on location, size, and number of involved nodes, and/or macroscopic extranodal extension (category 2B)</td>
</tr>
</tbody>
</table>

---

*See Principles of Surgical Margins for Wide Excision of Primary Melanoma (ME-B).*

*Mutational analysis is recommended if patients are being considered for either routine treatment or clinical trials, but is not recommended for patients with cutaneous melanoma who are otherwise NED.*

*CLND contributes to staging. Its impact on regional disease control and overall survival is the focus of ongoing clinical trials. Factors that predict non-sentinel lymph node.*
Nodal Burden vs Outcome

![Graph showing survival rate vs time for different nodal burden categories.](image)
ROLE OF RADIOTHERAPY

◆ 36 patients N+ cMMHN
  ◆ 20 primary
  ◆ 16 recurrent
◆ N+ with local excision of LN only + XRT
◆ 5 yr actuarial regional control 93%
◆ 5 yr actuarial DFS 59%

PRINCIPLES OF RADIATION THERAPY FOR MELANOMA

Consider RT in the following situations:¹

PRIMARY DISEASE
• Adjuvant treatment in selected patients with factors including, but not limited to deep desmoplastic melanoma with narrow margins, extensive neurotropism, or locally recurrent disease.

REGIONAL DISEASE²
• Adjuvant treatment in selected patients following resection of clinically appreciable nodes (category 2B)³ if
  ‣ Extranodal tumor extension AND/OR
    ◊ Parotid: ≥1 involved node, any size of involvement
    ◊ Cervical: ≥2 involved nodes and/or ≥3 cm tumor within a node
    ◊ Axillary: ≥2 involved nodes and/or ≥4 cm tumor within a node
    ◊ Inguinal: ≥3 involved nodes and/or ≥4 cm tumor within a node
• Palliative
  ‣ Unresectable nodal, satellite, or in-transit disease

METASTATIC DISEASE
• Brain metastases (See NCCN Guidelines for Central Nervous System Cancers)
  ‣ Stereotactic radiosurgery either as adjuvant or primary treatment
  ‣ Whole brain radiation therapy, either as adjuvant (category 2B) or primary treatment⁴
• Other symptomatic or potentially symptomatic soft tissue and/or bone metastases²
Adjuvant RT

- **Aim**: improves regional control without unacceptable complications
- ? survival benefit
- Indications based on histopathological findings
Published data on role of adjuvant RT

• Only randomized data: Creagan et al. 1978
  - 56 pts
  - Sx vs Sx + RT (unusual split course)
  - Trend toward better DFS
  - No comment on locoregional control
TROG 96.06: Single arm phase II trial of adjuvant radiotherapy after lymphadenectomy

- 234 patients
- Radiotherapy: 48 Gy in 20 fraction given 5 days per week
- Lymph node field relapse rate 7%
- Late grade 3 toxicity (fibrosis, lymphoedema)
  - Axilla 9%
  - Groin 19%

Burmeister et al., ANZ J Surg 72: 344-48; 2002

Burmeister et al., Radiotherapy and Oncology 81: 136-42; 2006
Time to LN field relapse by arm

- **RT**: Green line
- **Obs**: White line

- **P = 0.005**
- **HR = 0.47, 95% CI = 0.28 to 0.81**

**Number at risk:**

- **RT**: Obs 122, 66, 44, 24, 10, 6, 3, 0
- **Obs**: 126, 68, 36, 22, 7, 4, 1, 0

**Years from randomisation: 0, 1, 2, 3, 4, 5, 6, 7**

**Hazard ratio 95% CI:**

- **0.25**, **0.5**, **1**, **2**, **4**

---

2017 International Federation of Head and Neck Oncological Societies
No significant difference in relapse free survival (2 yr 44% vs 38%, p=0.53)
No significant difference in overall Survival (2yr 55% vs 67%, p=0.14)
### NCCN Guidelines Version 2.2016 Melanoma

#### CLINICAL/PATHOLOGIC STAGE

| Stage III (sentinel node positive) | Consider baseline imaging for staging (category 2B) and to evaluate specific signs or symptoms (CT scan, PET/CT, MRI) | Discuss and offer complete lymph node dissection

| Stage III (clinically positive node[s]) | FNA preferred, if feasible, or core, incisional, or excisional biopsy | Recommend baseline imaging for staging and to evaluate specific signs or symptoms (CT scan, PET/CT, MRI) | Wide excision of primary tumor (category 1) + complete therapeutic lymph node dissection | Consider RT to nodal basin in selected high-risk patients based on location, size, and number of involved nodes, and/or macroscopic extranodal extension (category 2B)

#### WORKUP

1. **Stage III (sentinel node positive)**
   - Consider baseline imaging for staging (category 2B) and to evaluate specific signs or symptoms (CT scan, PET/CT, MRI).
   - Discuss and offer complete lymph node dissection.

2. **Stage III (clinically positive node[s])**
   - FNA preferred, if feasible, or core, incisional, or excisional biopsy.
   - Recommend baseline imaging for staging and to evaluate specific signs or symptoms (CT scan, PET/CT, MRI).

#### PRIMARY TREATMENT

- **Wide excision of primary tumor (category 1)** + complete therapeutic lymph node dissection.

#### ADJUVANT TREATMENT

- Clinical trial or Observation or Interferon alfa or High-dose ipilimumab (category 2B)

- Clinical trial or Observation or Interferon alfa or High-dose ipilimumab (category 2B) or Biochemotherapy (category 2B) and/or Consider RT to nodal basin in selected high-risk patients based on location, size, and number of involved nodes, and/or macroscopic extranodal extension (category 2B)

---

*See Principles of Surgical Margins for Wide Excision of Primary Melanoma (ME-B).

*Mutational analysis is recommended if patients are being considered for either routine treatment or clinical trials, but is not recommended for patients with cutaneous melanoma who are otherwise NED.

*CLND contributes to staging. Its impact on regional disease control and overall survival is the focus of ongoing clinical trials. Factors that predict non-sentinel lymph node involvement are the focus of ongoing clinical trials.*
CONCLUSIONS

- A new era in systemic treatment for advanced stage melanoma
  - Targeted therapy: BRAF and MEK mutations
    - Some remarkable responses but resistance develops rapidly
  - Immunotherapy
    - Targets PD-1 and CTLA 4
    - 30% response, durable remissions in some patients
    - Need predictive biomarkers
    - Expensive
  - In the future patients at high risk will receive biomarker driven combinatorial therapy
Adjuvant Therapy

• Chemotherapy
  – Dacarbazine (DTIC)

• Interferon
  – 1% survival benefit approx

• Immunotherapy

• Postoperative Radiation Therapy
Conclusions

• Adjuvant RT improves nodal control
• Acceptable early toxicities
• No overall survival benefit
• Await QoL and lymphoedema data
Conclusions

- Nodal status most significant predictor of disease free and overall survival
- SNB standard of care
- Better outcomes with therapeutic dissection for microscopic disease, but era of ELND over
- Therapeutic dissection may be selective
- Surgery remains the mainstay of regional metastatic melanoma treatment
CONCLUSIONS

• Challenging disease with early metastasis
• Imperative for accurate staging
  – Pre-op: pathology, nodal staging
  – Intra-op: WLE + SLNB
  – Post-op: Pathologic staging, margin status, reconstruction