OPTIMAL EXCISION MARGINS FOR PRIMARY CUTANEOUS MELANOMA

Effective Date: February 2013

The recommendations contained in this guideline are a consensus of the Alberta Cutaneous Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.
BACKGROUND

In 2007, in Alberta, there were 461 new cases and 71 deaths resulting from melanoma. In 2015, there will be an estimated 570 new cases and 80 deaths. Although the incidence of melanoma continues to increase (age-standardized incidence rate [ASIR] of 8.1 in 1987 versus ASIR of 12.5 in 2007) in Alberta, survival rates have also increased. Five-year and ten-year survival rates based on TNM classification range from 97% and 93% for patients with T1aN0M0 melanomas to 53% and 39%, respectively for patients with T4bN0M0 melanomas.

Surgical excision remains preferred treatment option for primary cutaneous melanoma. The majority of recommendations for optimal excision margins range from 5 mm to 2 cm, depending on the stage of disease. However, the optimal margins for melanomas of the face and distal extremities are less certain because of the desire to maintain functional and aesthetic aspects of the anatomy. Overall, a conservative approach has been suggested for melanomas in these areas. This guideline aims to define optimal excision margins for melanoma, in general, with special consideration to melanomas of the face and distal extremities.

GUIDELINE QUESTIONS

- What are the optimal excision margins for pTis? pT1? pT2? pT3? pT4 tumours?
- What are the optimal excision margins for melanomas of the distal extremities and face?
- What is the role of Moh’s micrographic surgery in the management of primary cutaneous melanoma? In which patients (e.g. location and type of melanoma) is this procedure appropriate?

DEVELOPMENT PANEL

This guideline was reviewed and endorsed by the Alberta Cutaneous Tumour Team. Members of the Alberta Cutaneous Tumour Team include surgical oncologists, radiation oncologists, medical oncologists, dermatologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Cutaneous Tumour Team and a Knowledge Management Specialist from the Guideline Utilization Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook.

SEARCH STRATEGY

The MEDLINE, EMBASE, and Cochrane databases were searched (1990 through May 2010) for clinical trials and meta-analyses. Search terms included: “excision margins” or “wide excision” or “surgical excision” or “Mohs surgery” AND “primary cutaneous melanoma” with limits of Human and English language. A total of 190 studies were returned, 17 of which were clinical trials.

In addition, the National Guidelines Clearinghouse and individual guideline organizations were searched for practice guidelines relevant to this topic. A total of eight original clinical practice guidelines were identified from the following organizations: the National Health and Medical Research Council (Australia), the National Comprehensive Cancer Network, the BC Cancer Agency, the European Dermatology Forum, the Scottish Intercollegiate Guidelines Network, the German Cancer Society, the American Society of Plastic Surgeons, and the European Society for Medical Oncology.
For the 2013 update of the guideline, PubMed was searched for evidence on optimal excision margins in cutaneous melanoma. The search term “melanoma” was used and results were limited to clinical trials, published through January 2013. Citations were hand-searched for studies pertaining to surgical excision. Following a review of the evidence by the Alberta Cutaneous Tumour Team, no changes to the recommendations were made.

TARGET POPULATION

The recommendations outlined in this guideline apply to adults over the age of 18 years with malignant melanoma. Different principles may apply to pediatric patients.

RECOMMENDATIONS

For staging, please refer to the Appendix.

An initial excision biopsy should first be performed according to recommendations outlined in the CancerControl Alberta guideline, Biopsy of a Suspicious Pigmented Lesion. As well as data from recent clinical trials.

The following recommendations were adapted from existing guidance as well as data from recent clinical trials.

1. Following biopsy, optimal excision margins (from the edge of the melanoma) are as follows:
   - pTis melanoma (in situ): 5 mm margin
   - pT1 melanoma (<1.0 mm): 1 cm margin
   - pT2 melanoma (1.0–2.0 mm): 1–2 cm margin
   - pT3 melanoma (2.0–4.0 mm): 1–2 cm margin
     - A wider margin (2 cm) is optimal, where possible, depending on tumour site and surgeon/patient preference.
   - pT4 melanoma (>4.0 mm): 2 cm margin

2. For melanomas of the distal extremities and face:
   - A minimum surgical margin is normally used (as outlined above) where possible, in order to maintain aesthetic and functional aspects.
     - Partial digital amputation usually incorporates the joint immediately proximal to the melanoma.
     - It should be noted that there is no data from randomized controlled trials to determine the effect of narrower margins on survival or recurrence in melanomas of the face and distal extremities.
   - Radiotherapy may be a good alternative to surgery in elderly patients.
     - It should be noted that radiotherapy does not allow a histological evaluation of the tumour area and the side margins.
   - Topical imiquimod is an experimental, but emerging, therapy that may be highly beneficial for some patients with lentigo maligna.
     - The optimal frequency and duration have yet to be determined.
     - Imiquimod may be best suited for poor operative candidates and those who refuse surgery.
A post treatment biopsy is recommended to confirm destruction of the tumour, as imiquimod will not allow a histological evaluation of the tumour area and the side margins.

3. Mohs micrographic surgery allows for smaller surgical margins and, therefore, may be useful for melanomas on the face and distal extremities.
   - It should be noted that, to date, no randomized controlled trials have compared Mohs micrographic surgery with surgical excision in melanomas of the face and distal extremities; nevertheless, this procedure has demonstrated excellent recurrence-free survival rates in patients with melanoma of the face.
   - Based on data from randomized clinical trials in basal cell carcinoma, Mohs micrographic surgery appears to be tissue sparing and results in fewer recurrences of primary and recurrent disease.

4. If a patient is eligible for sentinel node biopsy (SNB), both the SNB and wide local excision should be performed together, ideally.

DISCUSSION

For suspicious pigmented lesions, a biopsy should be performed in accordance with the CancerControl Alberta guideline, *Biopsy of a Suspicious Pigmented Lesion*. Following biopsy, the margins required for surgical excision of the melanoma vary according to tumour size. For in situ melanomas (pTis), the standard of practice is an excision margin of 5 mm. For tumours <1 mm (pT1), a margin of 1 cm has been recommended. Guidance on the optimal margins for tumours between 1 mm and >4mm (pT2/pT3/pT4) vary between 1 to 2 cm. These recommendations are in accordance with clinical trials that have shown no survival benefit of a 3 to 5 cm margin over a 1 to 2 cm margin. However, the difference between a 1 cm margin and a 2 cm margin, in terms of recurrence and survival outcomes, has not been tested. While a 2 cm margin is considered optimal, especially for tumours on the upper end of the 2.0-4.0 mm range, a 1 cm margin may be used in when a 2 cm margin is not feasible (i.e. for facial melanomas, ocular melanomas, etc.).

For melanomas of the face and digital extremities, a more conservative approach has been suggested, in order to maintain functional and aesthetic aspects of the anatomy. However, there is no data from randomized controlled trials to determine the effect of narrower margins on survival or recurrence in melanomas of the face and distal extremities. As such, alternatives, such as radiotherapy, topical imiquimod, and micrographic surgery have been proposed.

Radiotherapy may be a good alternative in some patients, if surgery is contraindicated. A recent meta-analysis of three studies in which patients with mucosal malignant melanoma of the head and neck were treated with carbon ion radiotherapy (52.8-64 GyE in 16 fixed fractions over 4 weeks; median follow-up of 49.2 months) demonstrated a local control rate of 84.1% with overall and cause-specific survival rates of 27.0% and 39.6%, respectively. However, with radiotherapy alone, there is no opportunity for a histological evaluation of the tumour area and the side margins.

Topical imiquimod may be considered for some patients with lentigo maligna. Some case studies and small trials have shown that treatment with imiquimod can prevent melanoma metastases. A review of eleven case reports and four open-label studies, for a total of 67 patients with lentigo maligna, found that only eight patients failed to respond; of these, two developed lentigo maligna melanoma. However, treatment schedules and regimens varied greatly and the definition of response (i.e. clinical versus
histological) also varied. Moreover, the development of invasive melanoma while receiving imiquimod treatment has also been reported. As such, the use of imiquimod as first line therapy for the treatment of melanoma should be at the discretion of the physician. Imiquimod is not recommended as a potential alternative to surgery for invasive melanomas.

Studies utilizing Mohs micrographic surgery for the treatment of melanomas of the head and neck have shown promising results while creating minimal surgical defect. Bienert, et al. (2003) conducted a phase II study in patients with cutaneous malignant melanoma in situ or invasive melanoma of the face (n=92) and demonstrated a disease-free survival rate of 97% (mean follow up of 33 months) with good correlation between frozen and permanent sections. Bene, et al. (2008) demonstrated similar survival (98.2%) at a mean follow up of 63 months for patients with melanoma in situ and lentigo maligna.

GLOSSARY OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>ASIR</td>
<td>age-standardized incidence rate</td>
</tr>
<tr>
<td>GyE</td>
<td>Gray equivalents</td>
</tr>
<tr>
<td>pT</td>
<td>primary tumour</td>
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</table>

DISSEMINATION

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

MAINTENANCE

A formal review of the guideline will be conducted at the Annual Provincial Meeting in 2015. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

CONFLICT OF INTEREST

Participation of members of the Alberta Cutaneous Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Cutaneous Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.
REFERENCES


34 Fisher GH, Lang PG. Treatment of Melanoma In Situ on Sun-Damaged Skin With Topical 5% Imiquimod Cream Complicated by the Development of Invasive Disease. Archives of Dermatology. 139(7):945-947, July 2003.


# AJCC 2009 (7th Edition) Anatomic Stage Groupings for Cutaneous Melanoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Staging</th>
<th>Pathologic Staging</th>
<th>5-year Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis N0 M0</td>
<td>Tis N0 M0</td>
<td>100%</td>
</tr>
<tr>
<td>IA</td>
<td>T1a N0 M0</td>
<td>IA T1a N0 M0</td>
<td>95%</td>
</tr>
<tr>
<td>IB</td>
<td>T1b N0 M0</td>
<td>IB T1b N0 M0</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td>T2a N0 M0</td>
<td>T1b T2a N0 M0</td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>T2b N0 M0</td>
<td>IIA T2b N0 M0</td>
<td>78%</td>
</tr>
<tr>
<td>IIIB</td>
<td>T3b N0 M0</td>
<td>IIIB T3b N0 M0</td>
<td>65%</td>
</tr>
<tr>
<td>IIIC</td>
<td>T4b N0 M0</td>
<td>IIIC T4b N0 M0</td>
<td>45%</td>
</tr>
<tr>
<td>III</td>
<td>Any T N &gt; N0 M0</td>
<td>IIIA T1-4a N1a M0</td>
<td>66%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IIB T1-4a N2a M0</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IIIC T1-4a N1b M0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>27%</td>
</tr>
<tr>
<td>IV</td>
<td>Any T Any N M1</td>
<td>IV Any T Any N M1</td>
<td>13%</td>
</tr>
</tbody>
</table>

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**Clinical Staging** includes microstaging of the primary melanoma and clinical/radiologic evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.

**Pathologic Staging** includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial (i.e., sentinel node biopsy) or complete lymphadenectomy. Pathologic stage 0 or IA patients are the exception; they do not require pathologic evaluation of their lymph nodes.
### AJCC 2009 (7th Edition) TNM Staging Categories for Cutaneous Melanoma

<table>
<thead>
<tr>
<th>T</th>
<th>Thickness (mm)</th>
<th>Ulceration Status/Mitoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
| T1 | ≤ 1.00        | a: without ulceration and mitosis < 1/mm²  
|    |               | b: with ulceration or mitoses ≥ 1/mm²     |
| T2 | 1.01-2.00     | a: without ulceration       |
|    |               | b: with ulceration          |
| T3 | 2.01-4.00     | a: without ulceration       |
|    |               | b: with ulceration          |
| T4 | > 4.00        | a: without ulceration       |
|    |               | b: with ulceration          |

<table>
<thead>
<tr>
<th>N</th>
<th>Number 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: micrometastasis⁹      
|    |                           | b: macrometastasis¹⁰     |
| N2 | 2-3                       | a: micrometastasis⁹      
|    |                           | b: macrometastasis¹⁰     
|    |                           | c: in transit metastases/satellites without metastatic nodes |
| N3 | 4+ metastatic nodes, or matted nodes, or in transit metastases/satellites with metastatic nodes | |

<table>
<thead>
<tr>
<th>M</th>
<th>Site</th>
<th>Serum LDH (lactate dehydrogenase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastases</td>
<td>not applicable</td>
</tr>
<tr>
<td>M1a</td>
<td>Distant skin, subcutaneous or nodal metastases</td>
<td>Normal</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 metastases</td>
<td>Elevated</td>
</tr>
</tbody>
</table>

⁹Micrometastases are diagnosed after sentinel lymph node biopsy.

¹⁰Macrometastases are defined as clinically detectable nodal metastases confirmed pathologically.