Clinical Practice Guidelines for Melanoma
Douglas Reintgen, MD, et al
H. Lee Moffitt Cancer Center & Research Institute

These clinical practice guidelines for melanoma have been developed at H. Lee Moffitt Cancer Center & Research Institute under the direction of Douglas Reintgen, MD, Program Leader of the Cutaneous Oncology Program, and the following program members: Frank Glass, MD; Neil Fenske, MD; C. Wayne Cruse, MD; David Rapaport, MD; Jane Messina, MD; Karen E. Wells, MD; Ronald DeConti, MD, and Jan Marshburn, MPH. Algorithms are provided for melanoma screening and diagnosis, staging, stage III and IV management, and recurrence. Follow-up guidelines are also included.

Melanoma Screening and Diagnosis

Individuals with a personal or family history of melanoma or dysplastic nevi have a 10- to 100-fold increased relative risk of melanoma\(^1\) and are eligible for screening. Those with skin phenotypes I and II (fair skin, blond or red hair, blue eyes, freckles), those raised in the sunbelt, and those with a past history of other skin cancers also have an increased relative risk of melanoma.\(^2\) Patients with a family or personal history of dysplastic nevus, with early-onset melanoma, or who are members of a melanoma-prone family are screened for the dysplastic nevus syndrome\(^3\) and/or the p16 gene mutation.\(^4\) The initial screening for the p16 gene mutation will occur in the proband identified with melanoma. If the mutation is found, screening will be offered to family members. A total body skin examination performed by trained personnel identifies 90% of melanomas.\(^5\)

An excisional biopsy technique is used for suspicious lesions, and an incisional biopsy technique of the most nodular part of the lesion is used for lesions greater than 2 cm in diameter. Lesions that are found to be benign and dysplastic are followed, if the margins of excision are clear. The diagnosis of melanoma requires wide local excision (WLE), depending on the size.

Melanoma Staging

In order to ensure agreement with the diagnosis and depth of the melanoma, a formal pathology review is required for patients who present with a diagnosis of melanoma. This review has resulted in the remicrostaging of 5% of the melanomas reviewed. If the regional nodes are palpable and suspicious for tumor, fine needle aspiration (FNA) is performed. Those with a positive regional nodal FNA have stage III disease, and management is described in the stage III algorithm.

Patients with melanomas less than 1 mm in tumor thickness are treated with a 1-cm WLE per the World Health Organization trial,\(^6\) followed by observation. Those with melanomas equal to or greater than 1 mm in thickness are treated with a 2-cm WLE as dictated by the Intergroup Melanoma Trial.\(^7\) For tumors greater than 4 mm in thickness, our policy is to use 2-cm margins of excision. Physicians have leeway in the size of the margin of excision for their patients with melanoma in cosmetic-concerned areas of the body (eg, the face) or functional areas of the body (eg, palms and fingers). Clear margins must be obtained.

Patients are offered three choices for the management of the regional nodal basin: (1) observation of the nodes, (2) sentinel node biopsy of all basins at risk for disease,\(^8,9\) or (3) the NCI-sponsored Multicenter Selective Lymphadenectomy Trial,\(^10\) which randomizes patients between WLE of the primary site plus observation of their nodes vs WLE of the primary site, lymphatic mapping, and sentinel lymph node biopsy. If lymphatic mapping is not possible, patients are managed with either observation or elective node dissection.\(^11\) If the biopsy of the sentinel lymph node is positive, the patient has stage III disease and is treated according to the stage III algorithm.

Stage III and Stage IV Disease

A chest radiograph and computed tomography (CT) scan of the abdomen are obtained for patients with proven metastatic melanoma. Magnetic resonance imaging of the head is performed for those with central nervous system symptoms, and a CT scan of the pelvis is obtained for patients with lower extremity or lower abdomen primary sites that demonstrate cutaneous drainage to the groin.\(^12\)

Patients with documented stage III disease and no demonstrable systemic disease undergo therapeutic regional node dissection if the disease is deemed resectable. Unresectable lesions are debulked if possible. Patients with positive margins or extranodal disease following the debulting process or a therapeutic node dissection are considered for adjuvant radiation therapy according to Radiation Therapy Oncology Group protocols.\(^13\) These patients are at risk for systemic recurrence and also are candidates for adjuvant or unresectable stage III protocols.

Patients with stage III disease that has been resected are candidates for adjuvant interferon alfa-2b according to the Eastern Cooperative Oncology Group (ECOG) Trial 1684.\(^14\) Those with stage IV disease with solitary metastases after staging are candidates for surgical resection and adjuvant therapy on research protocols. Patients with a positive resection margin of stage IV disease are candidates for radiation. Those with solitary and isolated metastases to the central nervous system are candidates for corticosteroids, resection, radiation therapy, and perhaps systemic therapy.\(^15\) Patients with solitary metastases also may be treated on stage IV research protocols using DTIC (dacarbazine), the Dartmouth regimen,\(^16\) BOLD (bleomycin, oncovin, lomustine, dacarbazine) chemotherapy,\(^17\) or interferon alfa-2b. Patients with unresectable solitary metastases may be candidates for radiation therapy and/or systemic therapies. Spine metastases are treated with radiation therapy followed by chemotherapy.

Patients with multiple metastases or multiple sites of metastases who are ECOG status 1 and 2 are candidates for stage IV research protocols using interferon alfa-2b plus DTIC, the Dartmouth regimen,\(^16\) or BOLD chemotherapy.\(^17\) Patients with an ECOG performance status worse than 2 receive palliative care.

Recurrence

Local and/or intransit recurrences of extremity melanoma that are confined to the extremity are treated with resection for clear margins and hyperthermic, isolated limb
If the tumor cannot be completely resected, a hyperthermic isolated limb perfusion is performed for palliation. Distant cutaneous or soft-tissue recurrence can be resected. Positive margins can be radiated, or patients can be treated with stage IV protocols or systemic therapies.

Follow-up

Follow-up guidelines for patients with melanoma are presented in the Table. Those with melanoma in situ or thin melanomas are followed with a complete skin examination to detect a second melanoma, which will occur in 5% of the population. Those with intermediate-size melanoma undergo a baseline liver function and a chest radiograph; they are then followed with a physical examination of the local-regional distribution, a complete skin examination, and an evaluation of any symptom that could be a sign of systemic disease. The local-regional physical examination is expected to find 80% of all melanoma recurrences, with the remainder being marked by the appearance of systemic symptoms.

Patients with thick stage II and stage III disease have baseline liver function tests, a chest radiograph, and CT scan of the abdomen for staging. A CT scan of the pelvis is performed for those with metastatic disease to the groin. Patients are followed with a local-regional physical examination, a complete skin examination, and questions for systemic symptoms. Follow-up of patients with unresectable stage III and stage IV disease is guided by research or in-house protocols.

### Follow-up Schedule for Cutaneous Melanoma Patients

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor Characterization</th>
<th>Follow-up Schedule</th>
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<tbody>
<tr>
<td>I</td>
<td>M1 or &gt;0.76 mm</td>
<td>Physical examination is scheduled every 6 months for 2 years, then yearly by the Dermatology Service. No laboratory data or radiographs are obtained. Patients with typical indolent lesions are followed by the Dermatology Service. After 3 years without recurrence or appearance of a second primary melanoma, patients with the &quot;idiopathic&quot; melanoma phenotype have the option of follow-up with the treatment physician or in the Lifetime Cancer Screening Center.</td>
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<tr>
<td>II</td>
<td>0.76 mm to 4.0 mm</td>
<td>Physical examination is scheduled every 6 months for 2 years, then yearly by the General of Plastic Surgery Service. Baseline LFTs and CT scan are obtained at diagnosis. No laboratory data or radiographs are obtained at follow-up unless patient becomes symptomatic. After 3 years of follow-up without recurrence, patient is followed by a local physical.</td>
</tr>
<tr>
<td>III</td>
<td>&gt;4.0 mm, Any T, N1, M0</td>
<td>Physical examination is scheduled every 6 months for 2 years, then yearly by the General of Plastic Surgery Service or the Medical Oncology Service. Baseline LFTs, CT scan of abdomen are obtained at diagnosis. CT scan of liver is performed for patients with skin metastases - any T, N1, M0. Laboratory data and radiographs are repeated for patients with symptoms.</td>
</tr>
<tr>
<td>IV</td>
<td>Any T, any N, M1</td>
<td>Physical examination and follow-up at least every 3 months by Medical Oncology according to the histology of the melanoma or research protocols. Laboratory data and radiographs are obtained according to protocol. Staging may include MRI of the head and CT scan of the chest, abdomen, and pelvis.</td>
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M1 = melanoma in situ
LFT = liver function test
CT = chest radiograph
GI = gastrointestinal
MRI = magnetic resonance imaging

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**Summary Algorithm for Melanoma Screening and Diagnosis**

[Diagram of the summary algorithm is shown here, illustrating the steps from patient presentation for melanoma screening through final biopsy, patient counseling, and detailed follow-up.]
References
