Short-Term and Long-Term Management of Melanoma

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Abstract: Without consensus guidelines for surveillance in patients with resected melanoma, much debate exists on the appropriate short-term and long-term management of melanoma. When discussing surveillance, it is also important to keep in mind the long-term impact of ongoing surveillance in terms of improved survival, patient quality of life, cost effectiveness, and exposure to risks associated with certain surveillance methods. Most studies recommend frequent follow-up visits with dermatologic surveillance to detect potentially curable recurrence, especially resectable locoregional recurrences. Surveillance laboratory tests and chest x-rays (CXR) can have limited value while producing a relatively high false-positive rate. Lymph node ultrasonography is a valuable imaging modality in patients with equivocal lymphatic nodal basin physical examinations. In patients with early stages of melanoma, the benefit of routine surveillance imaging studies is questionable; however, close surveillance with detailed medical history and physical examination is necessary, with special attention to regional recurrences every 3–12 months, depending on the American Joint Committee on Cancer (AJCC) stage category the patient falls into and the risk of recurrence. In Stage III or greater, more frequent surveillance in the form of more frequent physical examination, laboratory tests based on symptomatology, and cross-sectional imaging


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may be indicated because of the higher risk of recurrence in this population. CT, MRI, and/or PET/CT are often a component of the overall follow-up for these high-risk patients. Additional studies are needed to better define the role of surveillance in the asymptomatic patient with resected melanoma.

**Key words:** Management; Melanoma; Surveillance; Survival

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## Introduction

In the absence of consensus guidelines for surveillance in patients with resected melanoma, much debate exists on the appropriate short-term and long-term management of melanoma (1). When discussing surveillance, it is also important to keep in mind the long-term impact of ongoing surveillance in terms of improved survival, patient quality of life, cost effectiveness, and exposure to risks associated with certain surveillance methods (2). Some studies recommend frequent follow-up visits with abundant use of radiographic imaging and laboratory review, while others question the value of these strategies altogether (3, 4).

According to the National Comprehensive Cancer Network (NCCN), the lifetime risk of developing a second primary melanoma approaches 4–8%; therefore, lifetime dermatological surveillance is recommended (1). However, follow-up recommendations vary worldwide and guidelines are disparate. Lifelong surveillance is important because of the risk of (i) second primary melanomas, (ii) locoregional recurrence, (iii) late recurrence, and (iv) other cutaneous malignancies. The risk of local recurrence is greatest in the first 5 years after diagnosis, especially in thick and ulcerated tumors (5). Locoregional recurrence of melanoma is defined as recurrence at the site of the primary lesion, regionally in the draining lymph node basin, or in between. Satellite and in-transit metastases are differentiated by their distance from the primary site, with satellite lesions occurring within 2 cm and in-transit metastases occurring more than 2 cm from the primary lesion. Both satellite and in-transit metastases are considered Stage III B (without regional nodal metastases) or Stage III C (with regional nodal metastases) disease. (American Joint Committee on Cancer 7th edition) (6).

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## Dermatological Surveillance

### TOTAL CUTANEOUS EXAMINATION

Dermatologic surveillance includes a total-body skin examination, palpation of the primary site and surrounding area for local recurrences, satellitosis, in-transit metastases, and a thorough regional lymph node basin examination. In addition, a review of systems should include questions about new or changing lesions, weight loss, fatigue, headache, new back pain, and any new symptoms that have persisted. Patients should be counseled to adhere to sun-protective measures and perform skin self-examinations.

Regular skin surveillance with monthly self-examination and total cutaneous examinations (TCEs) by a dermatologist increases the chances of detecting
melanomas when they are thinner, thereby reducing morbidity and mortality. However, there are no controlled trials evaluating TCE on melanoma mortality. Berwick et al. describes an association between regular skin self-examination and reduction in the risk of developing advanced melanoma, reducing melanoma mortality by 63% (7). De Giorgi et al. studied 802 patients retrospectively and found that 36% of melanomas were discovered during annual TCEs by dermatologist and 33% were discovered by patients. Additional analysis showed that self-detection was linked with a greater probability of having a thicker melanoma (8).

In 1987, a follow-up protocol at the Yale Melanoma Unit was devised to improve the detection of recurrence in patients with Stage I–Stage III melanoma. The protocol included a patient education program and a standardized follow-up schedule. A retrospective evaluation of 419 patients treated from January 1988 to December 1994 revealed that of the 78 patients with disease recurrence, 44% had clinical symptoms initially detected by the patients and 56% of recurrences were detected by physician-directed surveillance examinations (9). Most recurrences were found within the first (47%) or second (32%) year of follow-up. The study results recommended the following surveillance guidelines: (i) Stage I, annually; (ii) Stage II, every 6 months for years 1–2 and annually thereafter; (iii) Stage III, every 3 months for year 1, every 4 months for year 2, and every 6 months for years 3–5; (iv) at year 6 and beyond, all patients should have surveillance annually, due to the risk of late recurrence and/or multiple primaries (9).

Garbe et al. prospectively analyzed 2008 patients within a single institution in Germany. A total of 233 metastatic recurrences and 62 second primary melanomas were discovered during the 25-month study period. Over 70% of recurrences were found on scheduled follow-up examinations and 17% of all recurrences were first discovered by the patients. Physical examination diagnosed 50% of recurrences and the remaining 50% were identified radiographically (10). Garbe et al. also classified recurrences as early or late in terms of development. Patients diagnosed in the early phase had significantly more favorable odds of recurrence-free and overall survival than those in a late phase.

The Scottish Melanoma Group found that almost half (47%) of recurrences were first observed by the patient, with only 26% initially detected on follow-up (11). A recent German nationwide study prospectively analyzed 668 patients from 67 centers, of whom 96% were in regular melanoma surveillance. Of the patients, 118 (11.1%) had tumor progression and the rate of progression increased with stage. However, it was higher in Stage IIIC than Stage IIIA and Stage IIIB (54.2% vs. 42.9% and 43.6%, respectively). Median progression-free survival (PFS) of Stage IIIC patients was 34.5 months. The rate of progression was highest in Stage IV disease (63.6%, median PFS 5.3 months). In years 3 and 4 of surveillance, 55.6% of locoregional and 60% of distant metastases were detected on regular follow-up. Only 33.3% of locoregional metastases were patient detected, although 47.2% were described as being clinically visible and 22.2% palpable. Overall, the authors questioned the benefit of frequent follow-up visits in the low-risk patient group, especially since most recurrences were locoregional and amenable to visual or palpation by the patient. Consequently, the authors recommend reducing melanoma follow-up in low-risk melanoma patients and increasing patient education in terms of how to perform self-examinations (12).
The German Cancer Society and German Dermatologic Society guidelines are stage and Breslow specific and include examination by TCE every 6 months for 5 years in Stage I with ≤1 mm thickness, every 3 months for 5 years in Stage I and Stage II with >1 mm thickness, and every 3 months for the first 3 years for Stage III. For years 6–10, the TCE is every 12 months in Stage I with ≤1 mm thickness, every 6 months in Stage I and Stage II with >1 mm thickness, and every 6 months for Stage III (10).

The Swiss guidelines are stage specific and consist of a TCE every 3 months for years 1–3, every 6 months for years 4–5, and then every 6–12 months for years 6–10 in Stage I (T2N0)–IIB patients. In Stage IIC–Stage III, TCE should be performed every 3 months for years 1–5, then every 6 months for years 6–10. They recommend individualized follow-up in patients with Stage IV disease (13).

The European Society for Medical Oncology (ESMO) guidelines do not follow a staging system but provide general recommendations for monitoring patients at risk for recurrent and new disease. The guidelines recommend that for low-risk thin melanomas imaging is not recommended and for high-risk patients (i.e., those with thick primary tumors or recent tumor resection), computed tomography (CT) and/or PET scans are suggested for earlier detection of relapse. The ESMO also recommends patient education regarding sun avoidance and lifelong regular self-examinations of the skin and peripheral lymph nodes (14).

The American Academy of Dermatology (AAD) recommends TCE at least annually and possibly every 3–12 months based on tumor stage, history of multiple melanomas, presence of atypical nevi, family history of melanoma, patient anxiety, and the patient’s ability to recognize signs and symptoms of a disease. The AAD also recommends patient education on monthly self-skin and self-lymph node examinations (15).

The British Association of Dermatologists (BAD) follow-up recommendations for in situ melanomas are self-examination with no additional follow-up required. For Stage IA melanomas, they recommend TCE 2–4 times a year for the first year. For Stage IB to Stage IIIA melanomas, the BAD guidelines recommend a TCE every 3 months for 3 years, and then every 6 months for 2 years. For Stage IIIB and Stage IIIC and resected Stage IV melanomas, the BAD guidelines recommend evaluation every 3 months for 3 years, then every 6 months for the next 2 years, and then annually for the next 5 years. For unresected Stage IV melanomas, follow-up should be done on an individualized basis. In addition, they do not have specific guidelines for lab work or imaging (16).

Guidelines for the Management of Melanoma in Australia and New Zealand (GMMANZ) emphasize the importance of self-examinations in patients properly trained to detect recurrent disease. Along with this cost-effective measure, patients with Stage I melanoma should undergo TCE every 6 months for 5 years from a health care professional of their choice. Patients with Stage II and Stage III disease should have a TCE every 3–4 months for 5 years and annually thereafter. The guidelines recommend ultrasound (US) by an experienced US technician as the only imaging modality in patients with advanced disease. They do not have any specific recommendations for Stage IV disease. In addition, more frequent visits are recommended in patients with extensive disease, many atypical nevi, a family history of melanoma, and those with difficulty performing a self-evaluation.
GMMANZ also emphasizes the importance of evaluating individual patient needs in developing a follow-up schedule (17).

According to NCCN guidelines, the recommended follow-up is annually for Stage 0 and every 6–12 months for the first 5 years for Stage IA–Stage IIA. For Stage IIB–Stage IV, follow-up is recommended every 3–6 months for the first 2 years, then every 3–12 months for the next 3 years, and then annually starting after 6 years (1). The AAD guidelines for follow-up of resected melanoma states that no clear data regarding follow-up interval exist and that annual examinations with self-examination at regular intervals are necessary (15). As it can be seen, there is no international consensus on surveillance guidelines. Table 1 summarizes the major recommendations for follow-up examinations currently published.

<table>
<thead>
<tr>
<th>Organization</th>
<th>Stage/Breslow thickness</th>
<th>History and physical</th>
<th>Imaging</th>
<th>Lab values</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCCN (National Comprehensive Cancer Network)</td>
<td>Stage 0</td>
<td>Annual for life</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stage IA–Stage IIA</td>
<td>Every 3–12 months for 5 years, then annually unless clinically indicated</td>
<td>None</td>
<td></td>
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<tr>
<td></td>
<td>Stage IIB–Stage IV</td>
<td>Every 3–6 months for 2 years, then Every 3–12 months for 3 years, then annually unless clinically indicated</td>
<td>CXR, CTC/A/P ± PET/CT Every 3–12 months and annual brain MRI, or as clinically indicated</td>
<td></td>
</tr>
<tr>
<td>ESMO (European Society for Medical Oncology)</td>
<td>Thin/low risk</td>
<td>No specific recommendations</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thick/high risk</td>
<td>No specific recommendations</td>
<td>CTC/A/P ± PET/CT</td>
<td></td>
</tr>
<tr>
<td>AAD (American Academy of Dermatology)</td>
<td>N/A</td>
<td>H and P at least annually, possibly Every 3–12 months</td>
<td>Not recommended in asymptomatic patients Imaging not recommended after 5 years in high-risk patients</td>
<td>None</td>
</tr>
</tbody>
</table>

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### TABLE 1 Guidelines for Follow-Up (Continued)

<table>
<thead>
<tr>
<th>Organization</th>
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<th>History and physical</th>
<th>Imaging</th>
<th>Lab values</th>
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</thead>
<tbody>
<tr>
<td>BAD (British Association of Dermatologists)</td>
<td>In situ Stage IA</td>
<td>Self-exam, H and P Every 3–6 months for 1 year</td>
<td>None</td>
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</tr>
<tr>
<td>Stage IA–Stage IIIA</td>
<td>H and P Every 3 months for 3 years, then Every 6 months for 2 years</td>
<td>None</td>
<td></td>
<td></td>
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<tr>
<td>Stage IIIB–Stage IV (resected)</td>
<td>H and P Every 3 months for 3 years, then Every 6 months for 2 years</td>
<td>Consider CT</td>
<td></td>
<td></td>
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<tr>
<td>Stave IV (unresected)</td>
<td>As needed</td>
<td>No specific guidelines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>German Cancer Society and German Dermatologic Society</td>
<td>Stage I &lt; 1 mm</td>
<td>H and P Every 6 months for the first 5 years, then Every 6–12 months for the next 5 years until year 10</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Stage I and Stage II &gt;1 mm</td>
<td>H and P Every 3 months for the first 5 years, then Every 6–12 months for the next 5 years until year 10</td>
<td>Lymph Node US Every 6 months for years 1–5 Abdominal US and CXR on individual basis</td>
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<tr>
<td>Stage III</td>
<td>H and P Every 3 months for 5 years, and then Every 6 months for the next 5 years until year 10</td>
<td>Lymph Node US Every 3–6 months for years 1–5 Abdominal US and CXR on individual basis</td>
<td>S100β level every 3–6 months for years 1–5</td>
<td></td>
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<tr>
<td>Stage IV</td>
<td>Abdominal US and CXR or CT, MRI, or PET Every 6 months for years 1–5</td>
<td>Abdominal US and S100β level every 3–6 months for years 1–5</td>
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Total cutaneous photography (TCP) was initially described in 1988 by William Slue as a method of taking total-body photographs to document dysplastic nevi. These photos are then reviewed and compared at subsequent follow-up examinations. Detection of thin malignant melanomas in a curable stage is enhanced by utilizing these baseline photographs (18). Currently, TCP has evolved into a system involving digital photography-based mole mapping. Patients at high risk with multiple nevi can use the photographs to assist in self-examinations. Feit et al. reported an increase in the melanoma diagnosis rate with the use of this technique. Moreover, they reported that melanomas identified with the assistance of TCP are

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</tr>
</thead>
<tbody>
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<td>Swiss guidelines</td>
<td>Stage I (T2N0)–IIB</td>
<td>H and P Every 3 months for years 1–3; Every 6 months for years 4–5, and then Every 6–12 months for years 6–10</td>
<td>Lymph Node US Every 6–12 months for years 1–5</td>
<td>S100β Every 6–12 months for years 1–5</td>
</tr>
<tr>
<td></td>
<td>Stage IIC–Stage III</td>
<td>H and P Every 3 months for years 1–5, then Every 6 months for years 6–10</td>
<td>Lymph Node US Every 6 months for years 1–5</td>
<td>S100β Every 6 months for years 1–5</td>
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<tr>
<td></td>
<td>Stage IV</td>
<td>Individualized follow-up</td>
<td></td>
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<tr>
<td>GMMANZ (Guidelines for the Management of Melanoma in Australia and New Zealand)</td>
<td>Stage I</td>
<td>H and P Every 6 months for 5 years</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Stage I and Stage III</td>
<td>H and P Every 3–4 months for 5 years, and annually thereafter</td>
<td>Lymph Node US in advanced disease</td>
<td></td>
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<tr>
<td></td>
<td>Stage IV</td>
<td>No guidelines</td>
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generally thin melanomas (19). Barriers to the increased use of TCP include the cost, which tends not to be covered by insurances, having the photos available during physical examinations, and a medical-legal concern for the potential of these photographs to be used in malpractice suits (20).

### Laboratory Tests

The two potential tumor markers that exist for melanoma include lactate dehydrogenase (LDH) and S100β. LDH is found throughout the body and is expressed by a multitude of cancers and nonmalignant etiologies; however, it is unsuitable for use in screening for or diagnosis of melanoma. Persistent or recurrent elevations of LDH after treatment of melanoma may indicate residual or recurrent disease. Another marker is serum protein S100β which was first described in 1980 in cultured melanoma cells and is an immunohistochemical marker of pigmented skin lesions.

Finck et al. reported 121 Stage II and 58 Stage III patients where high levels of LDH indicated recurrence with a sensitivity and specificity of 72 and 97%, respectively. As an indicator of liver metastasis, LDH had a sensitivity and specificity of 95 and 82%, respectively, in Stage II melanoma, and 86 and 57%, respectively, in Stage III melanoma. An elevated LDH was the first indication of recurrent disease in 11/88 (12.5%) Stage II patients. The mean survival following LDH elevation was 5.9 months. It was concluded that monitoring LDH can provide useful information in the postoperative follow-up of patients with melanoma (20). Other reports have documented an association between serum levels of LDH and prognosis in patients with Stage IV melanoma; however, the prognostic value of LDH in patients with Stage I–Stage III melanoma is very limited as it is rarely elevated (21).

In a retrospective analysis of 261 patients with a regimented follow-up schedule, 145 evaluable patients developed recurrent melanomas. A total of 99 patients (68%) developed clinical symptoms that initiated a workup for recurrence. Physical examination of asymptomatic patients led to the diagnosis of recurrent disease in 37 patients (26%). The other nine patients (6%) with recurrent disease had abnormal CXR. Laboratory results were never a sole indicator of recurrent disease. They concluded blood analyses and CXR have limited value in the follow-up of patients with resected intermediate-risk and high-risk melanomas (22).

Garbe et al. evaluated 1492 patients of which 2719 blood tests (including blood count, erythrocyte sedimentation rate, renal function, liver enzymes, LDH, and S100β) were performed annually in the earlier stages and twice yearly in patients with more advanced stage melanoma. Blood tests were rarely the first sign of metastasis, and a diagnosis was made in only three patients after the detection of an elevated LDH. In patients developing metastasis, LDH and alkaline phosphatase (AP) were found to be elevated in 16.4 and 12.5%, respectively. Both percentages were significantly higher than in patients without metastasis (4.2% for LDH and 3.5% for AP, \( P < 0.0001 \)). Half of these patients with Stage II and Stage III disease expressed serum protein S100β and it was elevated in approximately 50% of patients with distant metastasis. In patients with locoregional recurrence, only a few were found to have an elevated protein S100β (10).
Routine blood tests contribute to the detection of metastasis in a very small subset of patients. Nevertheless, increasing values of both markers, LDH and serum protein S100β, may be the first sign of recurrence. Future investigations are needed to clarify whether protein S100β is a suitable substitute for the other blood values or whether it should be used as a supplementary examination method. Currently, use of laboratory tests in the surveillance of earlier stage melanoma is not recommended.

**Imaging**

Currently, there are no formal imaging guidelines for surveillance in patients with resected melanomas. According to the NCCN, additional radiological imaging is only recommended based on symptoms (1). CXR, CT, and/or positron emission tomography/CT (PET/CT) are considered optional and should be tailored to the stage and discretion of the physician (1). Guidelines recommend “considering” radiological studies every 4–12 months in Stage IIB or greater (1). Published guidelines for the management of cutaneous melanoma in the United Kingdom, the Netherlands, and Australia do not recommend routine radiological investigations; however, German guidelines recommend cross-sectional imaging every 6 months for Stage IIC or greater for the first 3 years after resection. Swiss guidelines recommend annual CXRs for the first 5 years in patients with Stage I/Stage II disease, and PET/CT or CT in the follow-up of Stage III patients (22, 23).

**CHEST X-RAY**

A common site of distant spread for melanoma is to the lungs. Surveillance CXRs have a high number of false-positive and false-negative findings. Morton et al. studied the accuracy of surveillance CXRs and the impact on survival by evaluating the extent of distant disease, time to detection, and treatment in those with CXR-detected compared with symptomatic pulmonary metastases. A total of 108 high-risk patients were followed with CXR every 6 months for 8 years and then annually until 10 years. A total of 23 out of 108 (21%) high-risk patients developed pulmonary metastases but only 10% were detected by CXR. Sensitivity and specificity of surveillance CXRs were 48 and 78%, respectively, with a high false-positive rate. Only 3 of the 23 (13%) cases of identified pulmonary metastases were amenable to surgical intervention (22). Leiter et al. showed a benefit in the use of CXR only in Stage III disease. This study prospectively followed 1969 patients and only 10 of the 204 relapses were discovered by CXR. The majority (7/10) of recurrences were in patients with Stage III disease (24). Brown et al. reported a low sensitivity of 7.7% and a specificity of 96.5%. In a trial of 1235 patients, 210 relapses occurred, 38 of which were detected by CXR. In order to detect these 38 recurrences, a total of 4218 (38/4218, 0.9%) x-rays were performed with a 129 (3.1%) false-positive rate. Isolated pulmonary metastases amenable to resection were found in only 3 of the 38 patients (25).

In conclusion, CXR does not dependably identify pulmonary metastases, nor has it lead to earlier detection of pulmonary metastases. In most series, when pulmonary metastases are detected, they are generally unresectable. Frequent CXR
surveillance can cause unnecessary patient anxiety, given high false-positive rates as well as the significant medical costs involved.

**LYMPH NODE ULTRASONOGRAPHY**

Ultrasonography examines the surgical scar of the primary tumor, the in-transit area, the locoregional lymph nodes, and potentially further lymph node basins. However, its utility is user dependent. Lymph node US has been debated in terms of its efficacy in early detection of locoregional lymph node metastases (25, 26). According to a meta-analysis by Bafounta et al. of 6642 patients and 18,610 paired palpation and US examinations, US had a higher discriminatory power (odds ratio 1755; 95% CI 726–4238) than did palpation (21 [4–111]; \( P = 0.0001 \)). Furthermore, positive-likelihood ratios were 41.9 for ultrasonography and 4.55 for palpation; negative-likelihood ratios were 0.024 and 0.22, respectively. This group concluded that US detects lymph node invasion more accurately than palpation and should therefore probably be used routinely in patients with melanoma (27). In addition, Garbe et al. reported 71% early detection compared to 48% early detection for all examination methods (10).

On the other hand, Chai et al. reviewed 325 patients with melanoma who underwent US before sentinel lymph node biopsy (SLNB) from 2005 to 2009. A total of 471 basins were examined with US. Only six patients (1.8%) avoided SLNB by undergoing US-guided fine-needle aspiration of involved nodes, followed by therapeutic lymphadenectomy. Overall, sensitivity of US was 33.8%, specificity 85.7%, positive predictive value 36.5%, and negative predictive value 84.2%. Sensitivity and specificity improved somewhat with increasing Breslow depth. Sensitivity was highest for the neck, but specificity was highest for the inguinal lymph nodes. The authors concluded that routine preoperative US in clinically node-negative melanoma is impractical because of its low sensitivity, but selected patients with thick or ulcerated lesions may benefit. However, because of variable lymphatic drainage patterns, preoperative US without lymphoscintigraphic localization will provide incomplete evaluation in many cases (28). These data can be extrapolated for patients in the follow-up setting given the low sensitivity of US in clinically node-negative patients.

Machet et al. from France performed US follow-up for 373 patients for melanomas with thick melanomas, greater than 1.5 mm, every 6 months and every year for thin melanomas, less than 1.5 mm. In total, 1909 US examinations combined with clinical examination were analyzed. Node biopsy was performed in 65 patients and demonstrated melanoma metastases in 54. Sensitivity of clinical examination and US examination was 71.4 and 92.9%, respectively. Specificity of clinical examination and US examination was 99.6 and 97.8%, respectively. Despite this apparent superiority of US examination over palpation, only 7.2% of the patients really benefited from US examination (earlier lymph node metastasis detection or avoidance of unnecessary surgery), while 5.9% had some deleterious effect from US examination such as unnecessary stress caused by repetitive US and excision of benign lymph nodes. This French group confirmed the greater sensitivity of US examination to clinical examination in the diagnosis of nodal metastases from cutaneous melanoma. However, they concluded that the role of US in routine follow-up is still questionable since only a very small
proportion of patients (1.3%) benefited from adding US to clinical examination. A large prospective randomized clinical trial would be needed to study the efficacy of US (29).

While lymph node ultrasonography has been studied, neither the NCCN nor the AAD include this technique in their recommendations. The NCCN states lymph node US may be considered in patients with an equivocal physical examination, in patients who were offered SLNB but refused, or patients with positive sentinel lymph nodes who did not receive complete lymph node dissections (1). German melanoma guidelines however do recommend lymph node ultrasonography every 6 months in Stage IB to Stage IIB and every 3 months for Stage IIC or greater (23).

COMPUTED TOMOGRAPHY/MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) can more readily detect cerebral metastases over CT and PET/CT (30). MRI has proven to be more sensitive and specific in the detection of soft tissue and osseous metastases as well (31), but there is no strong data directly comparing MRI to CT in osseous metastasis (32). Whole-body CT is a sensitive procedure, which allows for the detection of metastases as small as 2–4 mm (31). In a study by Romano et al., 72% of asymptomatic distant metastases were discovered by CT scans (3), while other trials yielded detection rates of 15–28% (10). During follow-up of patients with Stage IV disease and in cases of suspected metastasis, CT plays a pivotal role. More than 50% of recurrences in asymptomatic Stage III patients are detected by the patient or by examinations; therefore, cross-sectional imaging screening should only be performed in high-risk patients (3, 10, 33). CT has a higher sensitivity compared to MRI in the diagnosis of small pulmonary metastases (66.9 vs. 2.9%, \( P < 0.0001 \)) and should be considered (31). Drawbacks to CT are its limited soft tissue contrast, cost, and radiation exposure.

POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY

PET/CT displays the uptake of radioactively labeled glucose in metabolically active areas. In a meta-analysis evaluating imaging modalities in surveillance of melanoma patients, PET/CT revealed a high sensitivity (80%) and specificity (87%) in the detection of distant metastases, higher than conventional CT (51 and 69%, respectively) (26). Rinne et al. studied 100 patients prospectively and found an increase in sensitivity from 20 to 71.4% when comparing conventional diagnostic techniques to PET/CT (30). The NCCN recommends considering PET/CT every 4–12 months in Stage IIB or higher melanoma patients (1). According to the AAD, surveillance imaging studies in asymptomatic patients have low yield for detection of metastases and are associated with high false-positive rates (15). Overall, a general recommendation on imaging procedures cannot be made based on current data as the studies included inhomogeneous patients groups and are characterized by low evidence levels. In addition, the safety of CT and PET/CT is of significant concern since large-population-based studies have shown an increased risk of cancer with cumulative radiation exposure from repeat CT and PET/CTs (34, 35).
Conclusion

The major benefit of dermatological surveillance is the detection of potentially curable recurrence, especially resectable locoregional recurrences. Surveillance laboratory tests and CXRs can have limited value while producing a relatively high false-positive rate. Lymph node ultrasonography is a valuable imaging modality in patients with equivocal lymphatic nodal basin physical examinations. In patients with early stages of melanoma, the benefit of routine surveillance imaging studies is questionable, and we do not generally perform this at our institution; however, close surveillance with detailed medical history and physical examination is necessary, with special attention to regional recurrences every 3–12 months, depending on the AJCC stage category the patient falls into and the risk of recurrence. In Stage III or greater, more frequent surveillance in the form of more frequent physical examination, laboratory tests based on symptomatology, and cross-sectional imaging may be indicated because of the higher risk of recurrence in this population. CT, MRI, and/or PET/CT are often a component of the overall follow-up for these high-risk patients. Additional studies are needed to better define the role of surveillance in the asymptomatic patient with resected melanoma.

Conflict of interest: The authors declare no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

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