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Cutaneous melanoma: methods of biopsy and definitive surgical excision

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ABSTRACT: The proper method of biopsy and definitive surgical excision of cutaneous melanoma is vital for optimal patient outcome. Clearly, the present authors' understanding of the pathophysiology of cutaneous melanoma continues to change at a rapid pace. Indeed, as the present authors' research efforts begin to expose some of the mysteries of melanoma, so do they begin to better understand the intricacies of this dreaded cancer. This article will highlight methods of biopsy for melanoma and the management of the primary tumor. The present authors review current recommendations for excision margins for the primary tumor, usefulness of lymphoscintigraphy, timing of definitive surgical excision, and issues unique for head and neck melanoma.

KEYWORDS: cutaneous melanoma, head and neck melanoma, margins of excision, punch biopsy, shave biopsy

Choice of biopsy technique

Early diagnosis of cutaneous melanoma is critical for decreasing morbidity and mortality related to this potentially lethal cancer. For years, clinicians have relied upon the American Academy of Dermatology (AAD) ABCDE criteria for detecting melanomas early in the course of disease. Yet the naked eye can produce the correct diagnosis in only about 65% of cases (1–6). Accuracy can be improved to 80–85% with imaging tools such as epiluminescence microscopy (ELM) and serial total body photography (TBP), but ultimately, most clinicians prefer biopsy of suspicious lesions to reliance on clinical examination for decision making (7,8). The clinician bears ultimate responsibility for the patient's management and welfare, and histopathologic assessment is the "gold standard" for distinguishing among banal nevomelanocytic and melanocytic nevi, dysplastic melanocytic nevi, and melanoma.

The National Institutes of Health (NIH) consensus and the AAD treatment guidelines for melanoma recommend excisional biopsy as the technique of choice for diagnosis of suspicious pigmented lesions (1–3). For suspected melanoma, an excisional biopsy with 1–2 mm margins into the subcutaneous fat is designed to remove the entire lesion for an unencumbered histopathologic examination. Breslow's microscopic tumor thickness dictates the normal skin margins for tumor re-excision and subsequent steps along the staging algorithm (9,10). Other histopathologic factors that may be of prognostic significance for melanoma include presence of vertical growth phase tumor (versus radial growth phase alone), fibrotic regression, ulceration, and mitotic rate, among others. Obvious advantages for complete removal of a biopsied lesion include elimination of sampling error and minimizing the possibility of false-positive or false-negative results (11).

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Some authorities advocate excisional biopsies with 0.5-cm margins for lesions highly suspicious for in situ melanoma to spare patients the morbidity of a second surgical procedure (12,13). The clinical accuracy for diagnosis of melanoma of any invasiveness is only in the range of 65–80%. Thus, it may be preferable to defer wider excision until the histopathologic diagnosis is rendered and the exact nature of the lesion is defined to reduce excessive scarring for benign lesions (13,14). Excisional biopsies have obvious limitations in the case of large melanomas and those lesions located on the face or ears. The goal is to minimize the risk of cosmetic disfigurement accompanying a biopsy that shows a benign lesion not requiring complete excision (15,16). Excisional biopsies can also be a source of morbidity when performed on the fingers, legs, scalp, and other areas with poor skin mobility for primary wound closure. Wounds closed under tension are more likely to separate and become infected as a result, adding to morbidity and patient discomfort. In such cases, incisional biopsy techniques may be advisable.

The advantage of an incisional biopsy is most obvious in establishing the diagnosis of lesions that are very large or located in cosmetically sensitive areas, without the need to remove the entire specimen. As a rule, the thickest portion of the tumor should be biopsied, avoiding areas that appear to be crusted, ulcerated, or necrotic. These latter areas tend to underestimate the true Breslow microscopic depth of tumor invasion. Additionally, areas of blue or gray discoloration in plaques and nodules tend to offer a better estimate of maximum melanoma thickness.

One should always be cognizant that not all melanomas have a “classic” appearance. Many tumors are difficult to diagnose both clinically and histopathologically. Moreover, sampling error is a feared pitfall for the choice of incisional biopsy. Sampling error may result in false-negative results in addition to the potential underestimation of the true Breslow microscopic tumor depth (14).

There has always been a concern that performing an incisional biopsy may result in the dislodging of melanoma cells into the circulation, possibly resulting in the development of metastatic disease. However, Lederman et al. examined this theoretical risk and found no difference in 5-year survival rates between patients initially diagnosed by incisional versus excisional biopsy, regardless of Breslow microscopic thickness (18).

Salopek et al. conducted a survey of biopsy practices of lesions suspected to be melanoma and concluded that excisional biopsy, which includes subcutaneous fat, is the most commonly used method, favored by 68% of clinicians (1). However, there is anecdotal evidence from recently trained dermatologists that saucerization biopsies, which include reticular dermis but not necessarily subcutaneous fat, are being performed more frequently. A saucerization biopsy is performed with a single-edged razorblade held in a semicurved position. The razorblade offers the advantage of being flexible and therefore easy to use in areas difficult to access, such as the interdigital web and auricular concha. Instilling local anesthesia under the lesion produces a wheal that elevates the lesion above the plane of surrounding skin and facilitates sampling of the epidermis, upper dermis, and even deep reticular dermis and subcutaneous fat. A saucerization is essentially a modified shave biopsy that samples the deeper dermis and is achieved by pinching the skin around the lesion while curving the razorblade.

A potential drawback of the saucerization biopsy method is the danger of transecting the base of the lesion. For this reason, physicians are encouraged to examine the base of the biopsy specimen for any remaining pigmentation and to obtain additional deeper tissue if pigment is seen. Another consideration is that saucerization biopsy sites heal by secondary intention, resulting in depressed and occasionally hypopigmented scars. The time necessary for re-epithelialization varies directly with the size of the defect and the amount of vascularization. Thus, lesions located on the lower extremities tend to be slower to heal, and patient acceptance of saucerization biopsies is lower than biopsy techniques that do not leave an open wound. However, although infrequently utilized, suture material may be used to close saucerization biopsies to prevent large wounds. The reality and demands of a busy medical practice sometimes make it impractical to biopsy pigmented lesions utilizing an elliptical excision and suture closure, especially if the threshold for biopsy is sufficiently low and lesions are relatively small. For this reason as much as any other, saucerization and punch biopsies are widely used.

The main benefit of a punch biopsy is that the specimen can be accurately measured for true depth of invasion in the site sampled (14). The defect is closed primarily, with faster healing than those left to heal by secondary intention. The cosmetic appearance is generally superior to shave or saucerization biopsies, and the scars are usually thin and short in length, with varying degrees of hypopigmentation. Multiple punch biopsies of

Table 1. Cutaneous melanoma: survival rate in patients who develop local recurrence after excision

Reference	Primary tumor microscopic thickness	Rate of local recurrence (%)	5-year survival rate (%)	10-year survival rate (%)
Ng et al. (28)	< 1 to > 4 mm	7	61	–
Dong et al. (29)	0.76 to 4.0 mm	–	51	35
Soong et al. (30)	< 1 to > 4 mm	5	41	37
Urist et al. (31)	0.76 to 4 mm	5	50 (3-yr.)	20
Reintgen et al. (32)	0.76 to 4 mm	–	55	–
Kalady et al. (33)	< 1 mm	15	60	45

large lesions not amenable to excisional biopsy are a potentially useful approach.

The principle drawback of the punch biopsy is the limited sampling of a relatively large lesion, resulting in misdiagnosis. Dermatopathologists recognize the importance of examining overall architecture in addition to evaluating cytological features of the tumor (17). The presence of asymmetry, lack of circumscription, and scattered atypical melanocytes throughout the epidermis and adnexal epithelium, essential for the diagnosis of melanoma, may not be fully appreciated in a punch biopsy sample. In some cases, sampling error may even be responsible for missing the pathologic lesion, resulting in a false-negative diagnosis.

Excision margins

The surgical treatment of melanoma begins and ends with proper management of the primary lesion. When diagnosed early, more than 90% of all primary melanomas can be cured with surgical excision alone. The majority of cutaneous melanomas can be excised and closed primarily, generally with elliptical incisions, with the long axis of the ellipse directed toward the regional nodal basin. Removal of an appropriate margin of normal skin during the excision of a primary melanoma is fundamental to minimizing the most important potential complication associated with surgical excision, namely, local tumor persistence. Local recurrence of disease may in fact be caused by lack of adequate surgical margins, with resulting persistence of malignant cells from the primary melanoma itself, or may be a result of microscopic satellites that exist beyond the margins of excision. It is often impossible to differentiate between local persistence and metastasis. Development of local recurrence, generally defined as tumor recurring within 2 cm of the surgical scar, has been associated with a dismal prognosis. Approximately 40–60% of all patients who develop local recurrence of melanoma die of their disease (Table 1).

It was once thought that excision of primary melanoma required very wide margins. For decades, a 3–5-cm margin of normal surrounding skin was recommended, with the majority of patients requiring a skin graft in order to cover the large wound defect. This extensive surgical procedure required hospitalization and was associated with significant postoperative complications such as wound infection and skin graft necrosis. Still, given the high cure rate associated with wide excision for localized melanoma, any effort to reduce excision margins was based on results of clinical trials.

Prospective randomized trials have been conducted to assess the optimal minimal surgical margins for melanoma. The Intergroup Melanoma Trial addressed the efficacy of 2-cm margins compared to 4-cm margins for melanomas 1–4 mm in thickness (19). Results indicated a local recurrence rate of 0.8% for patients who had 2-cm margins, compared to 1.7% for those who had 4-cm margins (difference not statistically significant). There was, however, a significant difference in the number of skin grafts needed, with 46% of the 4-cm margin group requiring a skin graft, compared to 11% of the 2-cm margin group. Analysis of this trial at a 10-year follow-up revealed no significant differences in local recurrence rate, disease-free survival, or overall survival (20). Results of this trial suggest that a 2-cm margin is safe and effective, compared to a 4-cm margin, for primary melanomas between 1 and 4 mm tumor thickness, with a marked decrease in the need for skin grafting. Two other trials have examined 2-cm versus 5-cm margins for primary melanomas < 2.00 mm thick, with both studies showing no difference in local recurrence rate or overall survival (21,22).

Several randomized trials have established that primary tumor thickness dramatically influences the likelihood of local recurrence (Table 2). One of

Table 2. Prospective clinical trials evaluating surgical margins for primary cutaneous melanoma

WHO study (Veronesi et al.) (23)
• 612 patients with lesions < 2 mm tumor thickness
• Randomized between 1-cm margin or 3-cm margin
• 1-cm margin was safe for melanoma lesions < 1-mm thick
Intergroup Melanoma Study (Balch et al.) (19)
• All patients with primary melanomas from 1 to 4 mm tumor thickness
• Total of 486 patients randomized to either 2-cm or 4-cm margins
• 2 cm margin adequate, with low recurrence rate and less morbidity
UK Melanoma Study Group (Thomas et al.) (26)
• All patients with melanomas > 2.00 mm tumor thickness
• Total of 900 patients randomized to 1- vs. 3-cm margins
• 1-cm margin associated with a greater risk of regional recurrence
• No significant difference in overall survival

the first trials to address this issue was the World Health Organization (WHO) Melanoma Group study by Veronesi et al. (23). This trial prospectively randomized patients with primary melanomas ≤ 2.00 mm in Breslow's thickness to 1-cm versus 3-cm surgical margins (23). There were no local recurrences among patients with primary melanomas < 1.00 mm tumor thickness, regardless of whether a 1- or 3-cm margin was taken. In those patients whose primary melanoma was between 1 and 2 mm in tumor thickness, there were four local recurrences, all occurring within the group allocated to 1-cm margins. However, there were no differences in disease-free or overall survival. This trial has been updated with 15 years of follow-up, confirming an absence of difference in disease-free or overall survival (24). This study strongly suggests that a surgical excision margin of 1 cm is safe and provides excellent local control for melanomas < 1.00 mm in thickness. Further reduction in surgical margins to less than 1 cm for invasive melanoma should probably not be undertaken outside a clinical trial in the usual case.

Data addressing the recommended surgical margins for thick melanomas (> 4 mm) previously had been based on retrospective analyses and extrapolation from studies of intermediate thickness melanomas, but prospective randomized trial data are now available. A multi-institutional retrospective review of surgical margins and prognostic factors in patients with thick primary melanomas (> 4 mm) is available for 278 patients (23). According to this study, there was no difference in local recurrence rate, disease-free survival, or overall survival if margins larger than 2 cm were taken (25). Recently, Thomas et al. prospectively examined excision margins for melanomas at least 2 mm thick (26). In this study, median tumor thickness was 3 mm, and patients were randomized to either 1- or 3-cm margins of excision. The authors found that a 1-cm margin of excision for melanomas at least 2 mm thick was associated with a significantly greater risk of combined locoregional recurrence when compared to a 3-cm margin; local recurrence rates examined separately were not different between the two groups. Although there was no difference between the groups in either melanoma-specific or overall survival, it has been suggested, based on this and other studies, that there may be a reduced overall survival associated with excision margins 1 cm or less for melanomas at least 2 mm thick.

Current recommendations for excision margins

The data cited previously provide a basis for surgical guidelines that are safe, well tolerated, and associated with very low local-regional recurrence rates, especially in thin and intermediate thickness melanomas. Strategies that rely on more narrow excision margins, including reliance on the pathologist's report that the margin for the initial biopsy is tumor free, may offer economic savings and reduced morbidity but may result in higher rates of local recurrence. There is evidence to suggest that a one-stage excision (excisional biopsy only) results in an inferior outcome when compared to a two-stage excision (excisional biopsy, followed by wider re-excision). This issue has been addressed by McKenna et al. who performed a retrospective observational study comparing these two groups in terms of disease-free, recurrence-free, and overall survival (27). This study found that those patients treated with excision alone were older and had thicker melanomas and a

Table 3. Primary cutaneous melanoma: recommendations for excision margins

Location of primary melanoma	Primary tumor thickness	Recommended excision margins
Trunk, proximal extremity	Melanoma in situ	5 mm
	≤ 1.00 mm	1 cm
	> 1.00 mm–2.00 mm	1–2 cm
	> 2.00	2 cm
Head/neck, distal extremity	Melanoma in situ	5 mm
	≤ 1.00 mm	1 cm
	> 1.00 mm	At least 1 cm

higher proportion of lentigo maligna melanomas, head and neck melanomas, and ulcerated lesions. Additionally, 52% of all patients in the one-stage group received an excision margin less than 1 cm, even though over one-half of the patients in this group had a Breslow thickness of > 1.00 mm. Overall survival, disease-free survival, and recurrence-free survival were significantly better in the two-stage excision and re-excision group compared to the one-stage excision group.

Ng et al. also addressed the same issue by analyzing 1155 patients who had their primary melanoma excised (28). There were 84 (7%) local recurrences overall, with a total of 33 of these 84 (39%) patients dying of melanoma. The 5-year survival for patients with local recurrence was 59%, compared to 86% for those without a local recurrence ($p < 0.0001$). Other studies examining local tumor recurrence and its impact upon long-term survival have yielded similar results (29–32). Even patients with thin melanomas (≤ 1 mm in thickness) deserve an appropriate surgical margin, as recurrence does occur even in this group and is often a harbinger of very poor prognosis and outcome (33). Recommendations for excision margins for primary cutaneous melanoma are outlined in Table 3.

Fascia: to remove or not to remove

Removal of the deep fascia as part of the definitive excision of primary cutaneous melanoma has been regularly performed by most surgeons. The rationale has been that single melanoma cells might be attached to fascia, and thus by not removing the fascia the chances of local recurrence would be higher. Conversely, other surgeons believed that the deep fascia contributed to the "last defense" against possible metastasis by providing a mechanical barrier. This issue has been addressed by Kenady et al., who assessed recurrence rates in patients who had the deep fascia removed as part of their surgery, compared to those who did not (34). Although a trend was shown to favor those patients in whom the fascia was removed, the incidence of subsequent recurrence, site of recurrence, and overall survival were not statistically significant between the two groups. These findings have been confirmed in a study by Sondergaard et al., who analyzed 1469 patients with primary cutaneous melanoma and found that removal of the deep fascia did not influence prognosis (35). Removal of the muscular fascia is generally associated with minimal morbidity and should probably be performed for thick melanomas to ensure tumor-free deep margins.

Time interval between biopsy and definitive re-excision

The current surgical management of primary cutaneous melanoma usually involves a diagnostic biopsy to confirm the diagnosis, followed by the appropriate surgical excision based on tumor thickness. The time between original biopsy and re-excision should generally occur within 4–6 weeks. McKenna et al. examined the time interval between diagnostic biopsy and definitive wide excision in patients with primary cutaneous melanoma (36). In their analysis, patients had a surgical interval that ranged from 1 to 468 days, with the median time interval of 30 days between procedures. This study found no difference in any of the groups in overall, disease-free, or recurrence-free survival. At the present authors' institution, it is standard practice to review slides from the original biopsy to confirm the diagnosis and to determine tumor thickness and other prognostic features. The average time from first consultation to surgery is usually less than 3 weeks.

Pregnancy may require special considerations. A patient in the last trimester of pregnancy is often best served by a conservative excision of the primary melanoma with narrow margins. This

procedure can be performed safely with low doses of a local anesthetic such as 1% lidocaine, without the need for general anesthesia or local epinephrine. Sentinel lymphadenectomy and definitive wide excision is then performed after delivery of the child. The present authors have used this approach successfully in a number of patients and have observed no increase in local or regional tumor recurrence. This issue is worth additional study

Lymphoscintigraphy

Sentinel lymph node biopsy is widely utilized for surgical staging of clinically node-negative patients with melanoma. Regardless of whether an individual practitioner performs, or even advocates, sentinel node biopsy, it is possible that the patient may desire this procedure based on prior knowledge and recommendations. Whenever possible, definitive wide excision should be performed at the time of lymphatic mapping to accurately localize the draining lymph nodes for sentinel node biopsy, if that staging procedure is indicated. In many (but not all) cases, lymphatic mapping and sentinel lymphadenectomy can still be performed successfully after a prior wide excision of the tumor. Leong et al. recently addressed this issue in 168 consecutive cases of primary melanoma (37). Of the 168 cases, 65 patients were referred for lymphatic mapping after the wide local excision had been performed, with an equivalent number of patients receiving concurrent wide excision and mapping (37). They found that accurate identification of sentinel nodes was identical in the two groups, with 2.1 sentinel nodes removed in the group who previously had a wide excision compared to two nodes in the concurrent excision group. Overall, there was no difference in relapse-free or overall survival, and there was only a single case of a false-negative lymphatic mapping for a patient who previously underwent a wide excision of a truncal melanoma that was closed with a rotational flap. Similar findings were noted by Karakousis et al., who also found that only 1 of 26 patients had a false-negative sentinel lymph node biopsy, and this patient had previously undergone a flap rotation to close the primary excision defect (38). Thus, it is recommended that lymphatic mapping and sentinel lymphadenectomy not be performed in patients who have had a complex reconstruction that may preclude accurate identification of the exact location of the primary tumor and may create distortion of lymphatic flow.

Head and neck melanoma

Excision of the primary tumor

The present authors attempt to follow the excision margin guidelines that have been outlined, but in the head and neck and other aesthetic and functionally sensitive areas, the margins of resection often need to be adjusted. In general, the larger the tumor-free margin, the lower the local recurrence rate. Surgical treatment of the primary tumor on the head and neck areas includes planning of excision and reconstruction simultaneously. The amount of normal skin margin excised is important in determining the type of reconstruction. Surgical excision and reconstruction must include an adequate margin of surrounding skin that will provide the lowest local recurrence rate and still attain an acceptable aesthetic and functional result (39).

Primary tumor excisions over lymph node-bearing areas of the parotid gland and neck require special considerations. A pre-auricular vertical incision with subsequent development of an anterior cervico-facial flap is used to expose the parotid gland and preauricular and upper neck infra-auricular lymph nodes. Upper neck transverse incisions and mid-neck posterior vertical incisions are used to expose the cervical lymph node basin.

Reconstruction of wound defects

Methods of reconstruction of wound defects for the head and neck areas following excision depend on location and size of the defect, functional and aesthetic requirements, and preexisting medical conditions. Once the primary tumor resection is completed with adequate tumor-free margins, attention is directed toward maximizing reconstruction of the surgical defect. Split-thickness-skin grafts, full thickness skin grafts, local flaps, regional flaps, muscle flaps, and free flaps may be required. Reconstruction should be staged, if necessary, using allograft, skin substitutes, or biologic dressings. Details of reconstruction for surgical defects of the head and neck are beyond the scope of this text.

References

1. Salopek TG, Slade JM, Marghoob AA, et al. Management of cutaneous malignant melanoma by dermatologists of the American Academy of Dermatology. I. Survey of biopsy practices of pigmented lesions suspected as melanoma. J Am Acad Dermatol 1995: **33**: 441–450.

2. Kanzler MH, Mraz-Gernhard S. Primary cutaneous malignant melanoma and its precursor lesions: diagnostic and therapeutic overview. J Am Acad Dermatol 2001: **45**: 260–276.
3. Thomas L, Tranchand P, Berard F, Secchi T, Colin C, Moulin G. Semiological value of ABCD criteria in the diagnosis of cutaneous pigmented tumors. Dermatology 1998: **197**: 11–17.
4. Weinstock MA. Early detection of melanoma. JAMA 2000: **284**: 886–889.
5. Nachbar F, Stolz W, Merkle T, et al. The ABCD rule of dermatoscopy. High prospective value in the diagnosis of doubtful melanocytic skin lesions. J Am Acad Dermatol 1994: **30**: 551–559.
6. McGovern TW, Litaker MS. Clinical predictors of malignant pigmented lesions. A comparison of the Glasgow seven-point checklist and the American Cancer Society's ABCD of pigmented lesions. J Dermatol Surg Oncol 1992: **18**: 22–26.
7. Argenziano G, Soyer H. Dermoscopy of pigmented skin lesions – a valuable tool for early diagnosis of melanoma. Lancet Oncol 2001: **2**: 443–449.
8. Argenziano G, Fabbrocini G, Carli P, De Giorgi V, Sammarco E, Delfino M. Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. Comparison of the ABCD rule of dermatoscopy and a new seven-point checklist based on pattern analysis. Arch Dermatol 1998: **134**: 1563–1570.
9. Breslow A. Prognostic factors in the treatment of cutaneous melanoma. J Cut Pathol 1979: **6**: 208–212.
10. Clark WH Jr, Elder DE, Guerry D, 4th, et al. Model predicting survival in stage I melanoma based on tumor progression. J Natl Cancer Inst 1989: **81**: 1893–1904.
11. Farmer ER. Why a skin biopsy? Arch Dermatol 2000: **136**: 779–780.
12. Herlyn M, Ferrone S, Ronai Z, Finerty J, Pelroy R, Mohla S. Melanoma biology and progression. Cancer Res 2001: **61**: 4642–4643.
13. Johnson TM, Sondak VK. Melanoma margins: the importance and need for more evidence-based trials. Arch Dermatol 2004: **140**: 1148–1150.
14. Landthaler M, Braun-Falco O, Leitl A, Konz B, Holzel D. Excisional biopsy as the first therapeutic procedure versus primary wide local excision of malignant melanoma. Cancer 1989: **64**: 1612–1616.
15. Levi F, Randimbison L, La Vecchia C, Te VC, Franceschi S. Prognostic factors for cutaneous malignant melanoma in Vaud, Switzerland. Int J Cancer 1998: **78**: 315–319.
16. Macy-Roberts E, Ackerman AB. A critique of techniques for biopsy of clinically suspected malignant melanomas. Am J Dermatopathol 1982: **4**: 391–398.
17. Roses D. Biopsy technique for suspected melanoma. Pigment Cell Res 1985: **7**: 8–17.
18. Lederman JS, Sober AJ. Does biopsy type influence survival in clinical stage I cutaneous melanoma? J Am Acad Dermatol 1985: **13**: 983–987.
19. Balch CM, Urist MM, Karakousis CP, et al. Efficacy of 2-cm surgical margins for intermediate thickness melanomas (1–4 mm). Results of a multi-institutional randomized surgical trial. Ann Surg 1993: **218**: 262–267.
20. Balch CM, Soong SJ, Ross MI, et al. Long-term results of a prospective trial comparing 2 cm vs. 4 cm excision margins for 740 patients with 1–4 mm melanomas. Ann Surg Oncol 2001: **8**: 101–108.
21. Khayat D, Rixe O, Martin G, et al. Surgical margins in cutaneous melanoma (2 cm versus 5 cm for lesions measuring less than 2.1 mm thick). Cancer 2003: **97**: 1941–1946.
22. Cohn-Cedermark G, Rutqvist LE, Andersson R, et al. Long term results of a randomized study by the Swedish Melanoma Study Group on 2 cm versus 5 cm resection margins for patients with cutaneous melanoma with a thickness of 0.8–2.0 mm. Cancer 2000: **89**: 1495–1501.
23. Veronesi U, Cascinelli N, Adamus J, et al. Thin stage I primary cutaneous malignant melanoma: comparison of excision with margins of 1 or 3 cm. N Engl J Med 1988: **318**: 1159–1162.
24. Santinami M, Maurichi A, Patuzzo R, Pennacchioli E, Cascinelli N. Impact of clinical trials on the treatment of melanoma. Surg Oncol Clin N Am 2001: **10**: 935–947.
25. Heaton KM, Sussman JJ, Gershenwald JE, et al. Surgical margins and prognostic factors in patients with thick (> 4 mm) primary melanoma. Ann Surg Oncol 1998: **5**: 322–328.
26. Thomas JM, Newton-Bishop J, A'Hern R, et al. Excision margins in high-risk malignant melanoma. N Engl J Med 2004: **350**: 757–766.
27. McKenna DB, Lee RJ, Prescott RJ, Doherty VR. A retrospective observational study of primary cutaneous malignant melanoma patients treated with excision only compared with excision biopsy followed by wider local excision. Br J Dermatol 2004: **150**: 523–530.
28. Ng AK, Jones WO, Shaw JH. Analysis of local recurrence and optimizing excision margins for cutaneous melanoma. Br J Surg 2001: **88**: 137–142.
29. Dong XD, Tyler D, Johnson JL, DeMatos P, Seigler HF. Analysis of prognosis and disease progression after local recurrence of melanoma. Cancer 2000: **88**: 1063–1071.
30. Soong S, Harrison RA, McCarthy WH, Urist MM, Balch CM. Factors affecting survival following local, regional, or distant recurrence from localized melanoma. J Surg Oncol 1998: **67**: 228–233.
31. Urist MM, Balch CM, Soong SJ, Shaw HM, Milton GW, Maddox WA. The influence of surgical margins and prognostic factors predicting the risk of local recurrence in 3445 patients with primary cutaneous melanoma. Cancer 1985: **55**: 1398–1402.
32. Reintgen DS, Cox C, Slingluff CL, Seigler HF. Recurrent malignant melanoma: the identification of prognostic factors to predict survival. Ann Plast Surg 1992: **28**: 45–49.
33. Kalady MF, White RR, Johnson JL, Tyler DS, Seigler HF. Thin melanomas: predictive lethal characteristics from a 30-year clinical experience. Ann Surg 2003: **238**: 528–535.
34. Kenady DE, Brown BW, McBride CM. Excision of underlying fascia with a primary malignant melanoma: effect on recurrence and survival rates. Surgery 1982: **92**: 615–618.
35. Sondergaard K, Schou G. Therapeutic and clinicopathological factors in the survival of 1469 patients with primary cutaneous malignant melanoma in clinical stage I. A multivariate regression analysis. Virchows Arch A Pathol Anat Histopathol 1985: **408**: 249–258.
36. McKenna DB, Lee RJ, Prescott RJ, Doherty VR. The time from diagnostic excision biopsy to wide local excision for primary cutaneous malignant melanoma may not affect patient survival. Br J Dermatol 2002 July: **147**: 48–54.
37. Leong WL, Ghazarian DM, McCready DR. Previous wide local excision of primary melanoma is not a contraindication for sentinel lymph node biopsy of the trunk and extremity. J Surg Oncol 2003: **82**: 143–146.
38. Karakousis CP. Therapeutic lymph node dissection in malignant melanoma. Ann Surg Oncol 1998: **5**: 473–482.
39. Cruse CW, Wells KE, Reintgen DS. Treatment of the primary in malignant melanoma of the skin. Ann Plast Surg 1992: **28**: 22–25.