The Frequency of Local Recurrence and Microsatellites as a Guide to Reexcision Margins for Cutaneous Malignant Melanoma

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A retrospective study was undertaken of local, regional, and distant recurrences in 346 patients with primary melanomas of tumor thickness less than 1.0 mm that were excised with margins of normal skin varying between 0.1 cm and 5.0 cm or more. Prospective histopathologic examination of 284 melanomas for the presence of microsatellites was also performed and their effect upon the frequency of local recurrence was studied. Margins of excision did not influence the frequency of local, regional, or distant metastases. Four recurrences of *in situ* superficial spreading melanoma occurred, however, when very narrow margins of excision (0.5 cm or less) were employed. Microsatellites were uncommon with tumors less than 3.0 mm in thickness (2.8% of all tumors of less than 3.0 mm in thickness, taken together), but relatively frequent in association with thicker tumors (37%). Melanomas with microsatellites were associated with a greater frequency of local clinical metastasis than those without (14% *vs.* 3%). Removal of more than 1.0 cm of normal skin around a melanoma of less than 1.0 mm in thickness does not further reduce rates of recurrence of any type. The use of margins of 0.5 cm or less for melanomas with a radial growth phase does appear to result in an increased frequency of local recurrence of the primary melanoma with an epidermal *in situ* component. These recurrences can be prevented by the removal of 1.0 cm of normal skin around such a melanoma. Microsatellites constitute a risk factor for local recurrence, but are a relatively uncommon phenomenon at tumor thickness less than 3.0 mm.

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FOR SOME DECADES, WIDE LOCAL EXCISION, with margins of 3.0 to 5.0 cm and more, has been the form of local surgery recommended for the treatment of malignant melanoma.[1] The historic background for this procedure has generally been attributed to W. Sampson Handley, who, in the Hunterian Lectures of 1907, reported his autopsy observations of the mode of spread of malignant melanoma.[2] Based on his observations of the centrifugal lymphatic spread of melanoma around nodal metastases in the inguinal region of a patient whose primary melanoma had occurred over the Achilles tendon, Handley recommended an operation that was somewhat different from the procedure that has generally been performed since then. He described an operation in which "about an inch" of normal skin from the edge of the tumor is removed and about 3 inches of subcutaneous fat, deep fascia, and underlying muscle are taken around the tumor.

Several studies have demonstrated that wide excision margins fail to favorably affect survival,[3-8] and some conclude that there is no association between excision margins and survival.[4,6,8,9] A number of authors have questioned the value of wide local excision,[3,7,9-16,20] and recommended the use of narrower (1.0–2.0 cm) excision margins for melanomas that are less than 0.76 mm in maximum thickness.[3-5,9,11,12,17] Similar margins have also been recommended for selected melanomas in the 0.76–1.50 mm thickness range.[9,15] Despite the large number of papers containing recommendations on the subject, we are unaware of any published study that has examined a sufficient number of patients with low-risk melanoma and narrow excision margins to warrant a firm conclusion regarding the most appropriate margins of excision in these patients.

Two theoretic reasons for excision of a margin of normal skin around a melanoma have been cited.[5,17] The first relates to a "field effect" and applies only to tumors with a radial growth phase (superficial spreading, lentigo maligna, and acral lentiginous melanoma). These types of melanoma have a propensity to recur as *in situ* melanoma in the immediate vicinity of the primary site. The occurrence of local *in situ* melanoma as a field change is best illustrated in lentigo maligna, the form of

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TABLE 1. *Tumor Distribution by Site for Patients with Tumor Thickness Less Than 1.0 mm*

Site	No.	%
Scalp	12	3.5
Forehead	4	1.2
Face	21	6.0
Neck	18	5.2
Shoulders	34	9.8
Chest	27	7.8
Abdomen	29	8.3
Back	81	23.3
Upper arm	41	11.8
Forearm	11	3.2
Leg	44	12.6
Buttock	1	0.3
Genitalia	2	0.6
Thigh	23	6.6

melanoma that also has the greatest tendency to radial growth. Such *in situ* recurrences may subsequently lead to a further invasive melanoma. The second reason for removal of a margin of normal skin around a primary melanoma is that small groups of tumor cells may occur adjacent to the main tumor mass in the surrounding tissue (microsatellites). These microsatellites may remain following a narrow excision or reexcision and later present as a local metastasis or serve as a source of distant metastasis if this has not already occurred.

In order to investigate the question of the most appropriate margin of excision with respect to these two possible modes of local recurrence we studied 1) the types and frequencies of local recurrence in a group of 346 patients with melanomas less than 1.0 mm in thickness, whose tumors had been excised with a variety of excision margins, and 2) the frequency of microsatellitosis in association with 284 malignant melanomas of all tumor thicknesses.

Materials and Methods

The records of 406 patients with malignant melanomas measuring less than 1.0 mm in thickness, who were accessioned prospectively and followed in the Melanoma Clinic, University of California San Francisco between 1971 and 1983, were examined. For the purposes of the study the excision margin was taken from the pathology reports, and the measurement abstracted was the shortest

TABLE 2. *Tumor Distribution by Type for Tumors of Thickness Less Than 1.0 mm and for Tumors of All Thickness Measurements Taken Together*

Tumor Type	% of 346 Tumors Less Than 1.0 mm	% of 1441 Tumors of All Thickness
SSM*	92.8	59.0
LM†	3.2	4.9
NM‡	1.2	19.9
Unclassified	2.9	13.1

* Superficial spreading melanoma.
† Lentigo maligna melanoma.
‡ Nodular melanoma.

TABLE 3. *Margins of Reexcision by Thickness Grouping*

Margins of Reexcision (cm)	Thickness < 0.76 mm		Thickness 0.76–1.0 mm	
	No.	%	No.	%
0.1–0.9	43	16.4	8	9.5
1.0–1.9	101	38.5	29	34.5
2.0–2.9	58	22.1	26	31.0
3.0–3.9	30	11.5	9	10.7
4.0–4.9	19	7.3	10	11.9
5.0+	11	4.2	2	2.4
Totals	262	100.0	84	100.0

distance from the border of the tumor or from the scar of the previous biopsy to the edge of the reexcision specimen. The excision margins referred to in this report are those that were taken at a definitive reexcision procedure, following a complete excisional biopsy and careful histologic assessment of serial sections through the primary lesion. Sixty patients having missing data with regard to excision margins were excluded from the study, leaving a total of 346 cases. Microstaging had been performed in all cases by a single pathologist (R.W.S.). Follow-up time varied from 1 to 140 months, and the median time of follow-up was 46.37 months. Of 346 patients, 57% were female and 43% were male, a result consistent with the fact that female patients have a lesser mean tumor thickness.[18]

Population data, including tumor location, tumor type, and distribution of margins taken for tumors of thickness measurement less than 0.76 mm (76% of cases) and 0.76 to 1.0 mm (24% of cases), are shown in Tables 1 to 3. It can be seen that 71% of the tumors occurred in high-risk sites (the trunk and the head and neck). Ninety-three per cent of the tumors were of the superficial spreading type, and only one per cent were of the nodular type in this range of thickness. Comparative data are listed for the total population of 1441 patients with melanomas of all thicknesses. Margins of 0.1 to 0.9 cm were taken in 16% of cases and margins of 1.0 to 1.9 cm in 40% of cases.

Local recurrences were classified as local cutaneous with an *in situ* component, local metastasis (satellitosis), or in-transit metastasis (a metastasis arising in the lymphatic channels between the site of the primary melanoma and the regional lymph nodes). Local metastasis was defined as recurrence within 5.0 cm of the excision scar and without the presence of an epidermal *in situ* component. Recurrences at other sites were also recorded and classified as regional lymph node, visceral, and distant cutaneous metastasis (Table 4).

The pathology relating to a separate group of 284 consecutive patients was examined prospectively for the presence or absence of microsatellitosis. The definition used for miscrosatellitosis was that of Day et al.,[15] which defines "microscopic satellites" as "discrete tumor nests greater than 0.05 mm in diameter, that were separated

from the main body of the tumor by normal reticular dermal collagen or subcutaneous fat." These cases were grouped by thickness; less than 1.0 mm, 1.0–1.9 mm, 2.0–2.9 mm, and 3.0 mm or greater. Thickness could not be assessed in 12 cases as a result of a partial biopsy technique that interfered with the measurement. The incidence of local metastasis over the period of follow-up (mean follow-up period 2.35 years) was compared between the groups with and without microsatellitosis.

Results

Rates of Recurrence Versus Margins of Excision

The recurrence rates in the period of follow-up for each excision margin interval are listed in Table 4. It can be seen that the recurrence rate remains low for these thin tumors regardless of the margin of excision and is not significantly affected by the size of the excision margins. The highest rate of recurrence (7.8%) occurred in the group with excision margins of 0.1 to 0.9 cm and all of these were of the local cutaneous type with an *in situ* component present. Three recurred following narrow excision for treatment of *in situ* melanoma (atypical melanocytic hyperplasia) and had recurred with an associated invasive component. The margins of initial excision had been 0.5 cm or less in each case, and none had had a reexcision performed. These were the only cases in the study that were initially diagnosed as *in situ* melanoma. They were discovered because invasive melanoma subsequently developed, and were included because we believe that they illustrate an important form of local recurrence. No metastatic recurrences were seen in the 0.1 to 0.9 cm group of patients, and no recurrences with an *in situ* component were seen outside this group.

The remaining excision margin intervals from 1.0 cm to greater than 5.0 cm were found to have 10 recurrences. There was one local metastasis (satellite recurrence), one in-transit recurrence, one regional lymph node recurrence, and the remaining seven recurrences were to visceral organs.

The overall recurrence rate (*i.e.*, for all excision margins) for melanomas measuring less than 0.76 mm in thickness was 2.3%, and for those measuring 0.76 to 1.0 mm in thickness, 8.3%.

Microsatellites

The results of examination of 284 biopsies of melanoma for the presence of microsatellites are presented in Table 5. It can be seen that there were no microsatellites seen in association with 93 melanomas that were less than 1.0 mm in thickness. The frequency of microsatellites remained low for tumors that were less than 3.0 mm in thickness. However, for tumors 3.0 mm or more in thickness, the frequency of microsatellites was markedly higher (37%). The mean thickness for those tumors in which microsatellites were found was 4.1 mm, and for those in which microsatellites were absent the mean thickness was 1.7 mm. In order to examine recurrence rates in these groups, the effect of thickness was minimized by studying only those patients with tumor thickness greater than or equal to 3.0 mm, resulting in two groups of similar mean thickness (5.0 mm with microsatellitosis and 4.4 mm without). The overall recurrence rate (local and distant) in both groups was 59%. However, the frequency of local recurrence was greater in 22 patients with microsatellites than in 38 patients without microsatellites (14% *vs.* 3%).

TABLE 4. *Type and Frequency of Recurrences by Excision Margin Interval for Melanomas Less Than 1.0 mm in Thickness*

Margins of Excision (cm)	# Recurrences/ # Patients	Rate of Recurrence (%)	Initial Site of Recurrence
0.1–0.9	4/51	7.8	4 local cutaneous with *in situ* component
1.0–1.9	3/130	2.3	2 visceral 1 local metastasis
2.0–2.9	2/84	2.4	2 visceral
3.0–3.9	2/39	5.1	1 in-transit 1 visceral
4.0–4.9	2/29	6.9	1 regional lymph node 1 visceral
5.0+	0/13	0	Nil

Discussion

Thin Melanomas

The results of this study confirm the conclusions drawn by other investigators from the study of smaller numbers of patients having thin melanomas; namely, that conservative excision of these tumors does not adversely affect the rate of recurrence of melanoma or survival of the patient.[3–5,9,12,16,17] We have shown a uniformly low rate of recurrence, regardless of margins of excision, for melanomas less than 1.0 mm in thickness.

The distinction between *in situ* recurrence with or without an invasive component and local metastasis (satellitosis) was drawn by Olsen,[7] who confined her study to those patients with true local metastasis. This is an important distinction and one that has not been considered in the majority of studies of local recurrence reported in the literature. The highest recurrence rate in

TABLE 5. *Frequency of Occurrence of Microsatellites by Interval of Tumor Thickness*

Thickness Range (mm)	Total No. Tumors Examined	No. with Micro-satellitosis	% Micro-satellitosis
<1.0	91	0	0
1.0–1.9	91	2	2.2
2.0–2.9	34	4	11.7
≥3.0	60	22	36.7

our series (7.4%) was for excision margins of less than 0.9 cm and was entirely attributable to local recurrences with an *in situ* component. Three of these four cases had developed supervening, invasive, superficial spreading malignant melanoma following an excision with narrow margins for treatment of atypical melanocytic hyperplasia without subsequent reexcision. The thickness measurements of these tumors were 0.65 mm, 0.85 mm, and 1.8 mm, respectively.

A study performed by Breslow and Macht[17] demonstrated no recurrences, over 5 years of follow-up, in a group of 62 patients with melanomas less than 0.76 mm in thickness. Of these cases, 20 had resection margins of 1.0 cm or less.

The cases of *in situ* recurrence reported by us emphasize the need for the excision of a small but adequate margin of normal skin around a melanoma with the potential for radial growth. We would therefore recommend a margin of not less than 1.0 cm around any *in situ* or invasive melanoma, it being unusual for nodular melanomas to be biopsied and diagnosed when less than 1.0 mm in thickness. In view of the relative ease of obtaining an excision margin of 1.0 cm around most melanomas, it would seem unnecessary to make special provision for narrower margins in these cases in which there is absence of radial growth and, therefore, in which *in situ* recurrence may be less likely.

Thicker Melanomas

There is now ample evidence from several studies with large numbers of patients[4,6,8] (and from studies with smaller numbers[3,5]) that conservative excision margins for melanoma of all thicknesses do not adversely affect survival. There is also evidence from the same studies that narrow excision margins for thicker melanomas may result in a higher incidence of local metastasis. The rationale that has been stated to explain this apparent paradox is that microsatellites are present in the skin surrounding the primary melanoma and remain following a conservative reexcision.[5–7] These microsatellites later present as local recurrences, but do not adversely influence survival because distant spread has already occurred at the time the microsatellites themselves were seeded.[5,9]

Of 284 patients examined for the presence of microsatellites, we found these to be present in 30 (11%). None were present in association with tumors less than 1.0 mm in thickness, and the frequency remained low in association with tumors less than 3.0 mm in thickness. The percentage of tumors greater than or equal to 3.0 mm in thickness exhibiting microsatellitosis was markedly higher (37%). Our findings are similar to those of Elder et al.[5] who found no microsatellites in association with 82 tumors less than 2.25 mm in thickness, and a 22% incidence of microsatellitosis in 23 tumors greater than 2.25 mm in thickness. Day et al.[15] found an incidence of microsatellites of 4.6% for tumors of thickness 0.76 to 1.5 mm, 23.4% for tumors of thickness 1.51 to 3.99 mm, and 63.5% for tumors greater than or equal to 4.0 mm in thickness. Although different thickness intervals have been used by these authors, a similar association between microsatellitosis and tumor thickness is evident in each of the studies.

Tumors greater than 3.0 mm in thickness, with microsatellitosis, were associated with a greater frequency of local clinial metastasis than those without (14% *vs.* 3%) despite an identical overall recurrence rate of 59% in the two groups. This trend was evident despite a relatively short mean period of follow-up (2.35 years) and may become more marked with continuing follow-up.*

The data suggest that microsatellitosis does not become a major risk factor for local recurrence until tumor thickness reaches 3.0 mm. The greater frequency of local recurrence in association with the presence of microsatellitosis lends support to the concept of this phenomenon as a precursor of local clinical metastasis. The similar overall recurrence rates in the groups with and without microsatellites suggest that, while microsatellites are precursors of local metastasis, they are markers of high metastatic potential in general, rather than precursors of distant metastasis.

The Problem of Overtreatment

There is now a concensus among authors who have recently examined the subject that conservative excision margins are appropriate for thin melanomas that have a good prognosis.[3–6,9–12,16,17] It is true for most body sites that removal of a conservative (1.0–2.0 cm) margin of normal skin around the site of a primary melanoma will permit a primary closure that can generally be performed as an office procedure without hospitalization of the patient. Margins of 3.0 to 5.0 cm will generally require hospitalization of the patient and a skin graft or skin flap repair. In the latter case, the patient is exposed to the risks of a general anesthetic, the added complications associated with these procedures, the expense of 4 to 8 days in hospital, and a more prolonged recovery period, which may preclude work or recreational activities for 3 to 6 weeks. Cassileth et al. have recently drawn attention to the continuing psychologic impact of the depressed scar, which is usually associated with split thickness skin grafts, and those providing follow-up care to large numbers of melanoma patients will recognize this to be a common complaint.[14] We would therefore argue strongly against the use of wide reexcision

* The reason for this short mean period of follow-up is that this prospective study of microsatellitosis was not begun until 1979 and all patients in the study have been diagnosed and have commenced follow-up since that time.

(3.0–5.0 cm) for the treatment of melanomas less than 1.0 mm in thickness.

Excision Margins

The data presented here confirm the adequacy of removal of 1.0 cm of normal skin adjacent to the tumor for treatment of malignant melanoma measuring 1.0 mm or less in thickness. The local recurrences of *in situ* melanoma following narrow excision with a margin of 0.5 cm or less emphasize the need for removal of an adequate margin of normal skin around even preinvasive lesions.

The results suggest that histologic microsatellitosis at the primary site does not become a major risk factor for local clinical metastasis until a tumor thickness of 3.0 mm is reached. The most appropriate excision margin for tumors of thickness 1.0 to 3.0 mm remains ill-defined. Our current policy is to vary excision margins for this thickness interval from 1.0 to 3.0 cm according to tumor thickness and other clinical[18] and histopathologic[19] risk factors that have previously been identified.

For tumors of thickness measurement 3.0 mm or greater, we recommend an excision margin of 3.0 cm if anatomic factors permit and if such a margin can be obtained without significant disfigurement. Results from the only large studies published to date (including tumors of all thicknesses) from the World Health Organisation[4] (593 patients), the New York University–Massachusetts General Hospital Clinical Co-operative Group[6] (598 patients), and the University of Munich[8] (588 patients) do not demonstrate a decrease in local recurrence rate by the use of excision margins of greater than 3.0 cm. In these studies, increases in local recurrence rates were found when excision margins were reduced below 2.0 cm, 1.5 cm, and 3.0 cm, respectively, and these increases were observed only in intermediate- and high-risk melanomas. In an earlier study of 456 patients reported by Olsen,[7] in which cases were not stratified by thickness, no relationship between excision margin and rate of local metastasis could be demonstrated. Among 79 patients with excision margins of 5.0 cm or greater, Olsen found a rate of local metastasis of 13%, similar to that found for each of the five lesser excision margin intervals from 0.0 to 5.0 cm. The removal of more than a 3.0 cm margin of clinically normal skin appears to confer no added benefit to the patient,[6–8,11] and we argue that wider reexcisions for treatment of melanoma of any thickness cannot be justified.

We wish to emphasize that studies of large numbers of patients[4,6,8] have demonstrated no relationship between margins of excision and survival. We conclude, therefore, that conservative margins of excision can be justified for thick melanomas (3.0 mm or more in thickness), and should be used, where wider margins of excision would result in serious cosmetic deformity or functional impairment of important anatomic structures. Examples of sites where such considerations frequently apply are the face (especially the periorbital region) and the anogenital region. When conservative margins of excision are to be used for treatment of melanomas that measure 3.0 mm or more in thickness, a regime of close follow-up should be pursued in any case, in view of the greater risk of systemic as well as local metastasis. While the phenomenon of local metastasis does not appear to add to the mortality associated with melanoma, it is important that such recurrences be detected early in order to minimize the resulting morbidity.

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