

# Stage I Melanoma of the Skin: the Problem of Resection Margins

W.H.O. COLLABORATING CENTRES FOR EVALUATION OF METHODS OF  
DIAGNOSIS AND TREATMENT OF MELANOMA\*

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**Abstract**—*The importance of the width of resection margins in the treatment of primary malignant melanoma of the skin was evaluated on the basis of 593 stage I patients collected by the W.H.O. Collaborating Centres for Evaluation of Methods of Diagnosis and Treatment of Melanoma. The chances of cure of these patients were reduced with increasing thickness ( $P < 0.001$ ), while survival was not influenced by the size of resection margins ( $P = 0.66$ ).*

*Local recurrences, as first sign of relapse of the disease, were observed in 25 patients (4.2%). The percent of recurrences increased from 1.1 to 5.8% with increasing thickness and decreased from 10.8 to 3.0% with increasing margins of resection. This last trend was probably due to a different ratio of thick/thin tumors in various groups of resection margins, because the increase of local recurrences with decreasing margins was no more significant considering patients with maximum thickness equal or less than 2 mm and more than 2 mm. The rate of local recurrences was significantly lower ( $P < 0.025$ ) in patients with maximum thickness no more than 2 mm.*

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The authors do not draw final conclusions on this matter because the number of patients with 'narrow' excision is too limited and because surgeon's choice of treatment may bias the results.

A prospective randomized trial is proposed to evaluate whether or not 'narrow' excision may be considered the treatment of choice of thin ( $\leq 2$  mm) cutaneous melanoma.

## INTRODUCTION

THE QUESTION of the optimal size of the resection margin in cutaneous melanomas has troubled surgeons for many years. In 1907 Handley [1] recommended a 2.5 cm margin, but this was based on a study of the distribution of tumor in the lymphatics surrounding cutaneous metastases, not primary tumors. Pringle [2] also suggested a 'wide' excision as the treatment of choice in this disease. Pack *et al.* [3] and Lund and Ihnem [4] reported 5-yr survival rates of 50% and 44% respectively in large numbers of patients submitted to radical surgery with 'wide' margins. Wilson [5] stressed the importance of 'wide' excision in a study of 50 patients. The 5-yr survival rate was 24% for 21 patients treated with an excisional biopsy as compared to 41% for 29 patients treated with 'wide' margins or amputation. Similar results were obtained by Lehman *et al.* [6]. Olsen [7] found the same rate of local recurrence, regardless of the size of the resection margins, but found a higher metastatic rate for patients treated with 'narrow' margin. She concluded that a wide excision with a 5 cm margin might not be necessary in all cases.

In recent years it became evident that melanomas differ in histologic type, level of invasion, maximal thickness and consequently, in prognosis [8-12] and there were attempts to use this information as a guide to the selection of the optimal resection margin. Everall and Dowd [13] suggested varying the size of the resection margin depending on the level of invasion. Breslow and Macht [14] reported that all 62 patients with tumors less than 0.76 mm thick, were alive and free of disease for 5 or more yr with resection margins which ranged from 0.1 to 5.5 cm with 32% of the patients having no more than 1 cm margin. Balch *et al.* [8] reported no recurrences in 36 patients with primary tumors thinner than 0.76 mm, irrespective of the size of the resection margin. In 30% of the cases the margin was less than 3 cm.

In this retrospective study we shall evaluate the importance of tumor thickness and the size of the resection margin in relation to the rate of local recurrence as well as to survival.

## MATERIALS AND METHODS

### Patients

From September 1, 1967 to January 1, 1975, 593 cases were collected by the W.H.O. Collaborating Centres for Evaluation of Methods of Diagnosis and Treatment of Melanoma. Patients had a single primary tumor without clinical evidence of metastatic disease, were treated only by surgical excision with the width of the resection margin recorded by the surgeon. Patients were followed for at least 3 yr and good histologic slides of the tumors were available for review.

Out of 593 patients, 159 were male and 434 female (male/female ratio was 0.37). Distribution by sex and age is given in Table 1. The prognostic criteria considered were: sex, age, site of origin, histologic type according to Clark *et al.* [10] and McGovern *et al.* [11], and maximum tumor thickness according to Breslow [9]. The performance of elective regional node dissection was not considered because the policy of the Group is not to perform prophylactic node dissection in head and neck and trunk cases and because it was shown in a previous paper that elective node dissection does not modify the prognosis of stage I melanoma of the extremities [15]. Levels of invasion [10] were not considered because this criterion had a very limited value in the assessment of prognosis as compared to maximum thickness as shown in a previous study [16] and confirmed by others [8]. Tumor thickness was evaluated in five clusters with 1 mm increments: the correlation between thickness and death rate is linear [16] no matter how subgroups are defined.

The excision margin was defined as the width of unaffected skin beyond the grossly visible lesion, and was reported by the surgeons in centimeters. A separate group of 210 stage II cases with 11 local recurrences was used in the analysis of the correlations of thickness and size of margin to the local recurrence rate, but were not, of course, used to calculate survival data. The patients were divided into sub-groups with respect to tumor thickness with a separation at 2 mm because patients with tumors no more than 2 mm thick had a much better prognosis than those

Table 1. Distribution by sex and age of 593 patients previously untreated with clinically uninvolved regional lymph nodes

Age	Sex		Total
	Male	Female	
≤13	1	—	1
14-23	3	8	11
24-33	18	35	53
34-43	33	92	125
44-53	30	108	138
54-63	35	104	139
64-73	28	56	84
≥74	11	31	2
Total	159	434	593

with thicker tumors. Table 2 shows that cases are reasonably well distributed in these two sub-groups and this did not vary significantly with respect to site, sex or age. Data for resection margins are shown in Table 3. The number of patients treated with a surgical margin of no more than 1 cm was small (36). Within this sub-set all prognostic criteria, except the site of origin, are balanced. When the site of origin is considered, only one case of the trunk has been treated with a narrow excision. This distribution is a result of the policy of surgical treatment followed by the members of the group: the minimum distance from the borders of primary melanoma was more frequently observed in head and neck and extremities, while in the trunk the ma-

jority of cases had an excision of 4 cm or more (61.6%). However since site of origin is not significantly related to survival (Table 4) this unbalanced distribution does not bias the comparison. The other prognostic criteria are balanced in these two groups. In particular it does not seem that maximum thickness has been used as a guide for selecting the resection margins. The width of resection margin and maximum tumor thickness in the assessment of prognosis was measured in order to study their relationship to the incidence of local recurrences and survival. Incidence of local recurrences was evaluated by means of a multifactorial analysis on polichotomous data [17] and survival by Cox's regression model with censored data [18]. Trends were tested by correlation coefficients.

## RESULTS

Patients without clinically uninvolved nodes and with tumors no more than 2 mm thick had a 10-yr survival of about 80%. Increased thickness reduced survival to about 60% for patients with tumors thicker than 4 mm (Fig 1). Females were found to have a better prognosis than males. Site of origin of the primary tumor did not influence prognosis in these patients. Lentigo maligna melanoma had a better prognosis than did superficial spreading or nodular melanomas (Table 4) and had a higher percentage of tumors ≤2 mm than did the other types. The significant

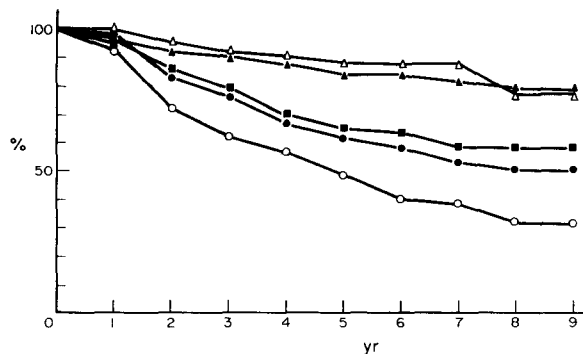
Table 2. Distribution of cases according to maximum tumor thickness and prognostic criteria

	≤2.00 mm	≥2.01 mm	Total
Sex			
Male	58 (36.5)	101 (63.5)	159
Female	171 (39.3)	263 (60.7)	434
Age (yr)			
4-33	21 (32.3)	44 (67.7)	65
34-63	168 (41.7)	234 (58.3)	402
≥64	40 (31.7)	86 (68.3)	126
Site			
Head and neck	30 (30.9)	67 (69.1)	97
Extremities	138 (38.0)	225 (62.0)	363
Trunk	61 (45.9)	72 (54.1)	133
Histologic type			
Lentigo	29 (72.5)	11 (27.5)	40
S.S.M.	146 (54.3)	123 (45.7)	269
N.M.	41 (16.7)	205 (83.3)	246

Percentages given in parentheses

Table 3. Distribution of cases by resection margins and prognostic criteria

Prognostic criteria	Resection margins	≤ 1 cm	≥ 2 cm	P value
Sex				
Male		11 (30.5)	148 (33.6)	NS
Female		25 (69.5)	245 (66.4)	
Age (yr)				
≤ 33		3 (8.4)	62 (11.6)	NS
34–63		24 (66.6)	378 (66.7)	
≥ 64		9 (25.0)	117 (21.7)	
Site				
Head and neck		17 (47.2)	80 (14.4)	<0.001
Limbs		18 (50.0)	345 (61.9)	
Trunk		1 (2.8)	132 (23.7)	
Histologic type				
Lentigo maligna		6 (17.6)	34 (6.6)	NS
Superficial spreading		14 (41.2)	255 (48.9)	
Nodular		14 (41.2)	232 (44.5)	
Thickness (mm)				
≤ 1		6 (16.7)	81 (14.5)	NS
1.01–2		6 (16.7)	136 (24.4)	
2.01–3		3 (8.3)	116 (20.9)	
3.01–4		8 (22.2)	83 (14.9)	
≥ 4.01		13 (36.1)	141 (25.3)	

Fig. 1. Survival of 593 cases  $N_0$  according to maximum tumor thickness.  $P < 0.001$ .

- ( $\triangle$ ) 0.0–1.0 mm (87 cases);  
 ( $\blacktriangle$ ) 1.01–2.0 mm (142 cases);  
 ( $\blacksquare$ ) 2.01–3.0 mm (119 cases);  
 ( $\bullet$ ) 3.01–4.0 mm (91 cases);  
 ( $\circ$ ) 4.01 mm and above (154 cases).

prognostic criteria are well balanced among the different resection margins groups and for this reason the comparison is possible. The analysis of survival according to resection margins and maximum tumor thickness is shown in Table 5: the resection margins were divided into five groups by 1 cm increments and tumor thickness by increments of 1 mm.

Survival was not influenced by the size of the resection margins ( $P = 0.66$ ) while the chances of cure are reduced with increasing thickness ( $P < 0.001$ ). Since survival seems not to be related to the resection margins, local recurrences by width of excision and maximum thickness were evaluated.

Table 6 gives the incidence of local failures by these two criteria: only 25 out of the 593 patients (4.2%) had a local recurrence as first sign of relapse of the disease. The Chi-square analysis indicates that neither resection margins nor tumor thickness seem to influence the rate of local recurrences: the  $P$  values are 0.16 and 0.22, respectively. However, this table shows trends of association between tumor thickness, width of excision and frequency of local recurrences. The percentage of recurrences increases from 1.1 to 5.8% with increasing thickness and decreases from 10.8 to 3.0% with increasing margins of resection. The  $T$ -test on this last trend is significant:  $-3.79$  ( $P = 0.032$ ). To evaluate whether or not the last trend is related to a different ratio of thin/thick tumors in the various groups of resection margins, cases were divided into two groups of thickness, less or equal to 2 mm and more than 2 mm. (Table 7). The analysis of

Table 4. Survival of patients with stage I malignant melanoma according to sex, site, histologic type of primary

	No. of patients	5-yr survival (%)	9-yr survival (%)
Sex			
Male	159	56.32	42.3
Female	434	72.10	62.6
Site			
Head and neck	97	67.36	59.3
Extremities	363	70.0	58.7
Trunk	133	62.74	52.7
Histologic type			
L.M.M.	40	94.2	79.9
S.S.M.	269	71.4	61.2
N.M.	246	61.2	49.8

Table 5. Analysis of survival according to maximum tumor thickness and resection margins

		$\beta$	S.E.	$\lambda$ (death/yr)	P	$\chi^2$
Resection margins (cm)	1.	-2.26	0.21	0.104	0.66	2.41
	2.	-2.38	0.19	0.092		
	3.	-2.51	0.12	0.081		
	4.	-2.71	0.24	0.066		
	5.	-2.36		0.094		
Thickness (mm)	1.	-3.61	0.27	0.027	<0.001	68.7
	2.	-3.44	0.20	0.032		
	3.	-2.51	0.15	0.081		
	4.	-2.34	0.16	0.096		
	5.	-1.86		0.155		

Table 6. Frequency of local recurrences according to maximum tumor thickness and margins of resection

Thickness (mm)	0.01-1.00	1.01-2.00	2.01-3.00	3.01-4.00	$\geq 4.01$	Total
Margins (cm)						
1.	0/6	1/6	1/3	1/8	1/13	4/36
2.	0/12	1/14	1/7	0/6	3/21	5/60
3.	0/31	1/50	3/53	1/41	4/75	9/250
4.	0/6	1/17	0/10	0/8	0/7	1/48
$\geq 5$	1/32	0/55	2/46	2/28	1/38	6/199
Total	1/87	4/142	7/119	4/91	9/154	25/593

Table 7. Frequency of local recurrences by maximum thickness and margins of resection

Thickness (mm) $\leq 2$	$\geq 2$	Total
Margins (cm)		
1	1/12 3/24	4/36
2	1/26 4/34	5/60
3	1/81 8/169	9/250
4	1/23 0/25	1/48
$\geq 5$	1/87 5/112	6/199
Total	5/229 20/364	25/593

these sub-sets indicates that the  $T$ -test values are not significant within cases with maximum thickness less or equal to 2 mm ( $T = -1.94$ ) ( $P = 0.146$ ) and more than 2 mm ( $T = 2.55$ ) ( $P = 0.083$ ). The Fisher's exact test on the contrary shows that the frequency of local recurrences is significantly lower in patients with maximum thickness of 2 mm. ( $P < 0.025$ ). The data for 36 local recurrences from combined stage I and II patients is shown in Table 8. The correlation coefficient between tumor thickness and local recurrences is  $+0.935$  ( $P < 0.01$ ).

## DISCUSSION

Practically all the authors are strongly convinced that wide excision (3–5 cm) is always necessary. However some [8, 13, 14] suggest narrow excision (1 cm margins) in selected cases and others [12] suggest wide excision leaving open the possibility of a more limited surgery without fixing definite rules.

If one is to use a narrow resection margin in selected cases of melanoma one must be certain that this does not increase the incidence of local recurrence or the mortality

rate. In this study the size of resection margin did not influence the mortality rate (Table 5).

The evaluation of the frequency of local recurrences is rather difficult because this number is limited if only stage I cases are used. Even then it seems reasonable to conclude, that the frequency is more related to tumor thickness than to resection margins (Table 7) because the  $T$  values are not significant within the two groups of thickness, while the frequency of local recurrences is significantly lower in patients with tumor thickness no more than 2 mm.

If one uses data for both stage I and II cases, the correlation between thickness and the local recurrence rate is very close and is highly statistically significant. It is valid to include stage II cases because there is no evidence that nodal metastases cause local wound recurrences. A measure of the difficulty of this evaluation is also given by other reports. Olsen [7] in a review of 1300 cases of malignant melanoma of the skin found 6% of local recurrences after wide or narrow excision or radiation therapy, but she found a higher frequency of distant metastases after narrow excision or radiation therapy. Elias *et al.* [19] had opposite results: local excision with primary closure of surgical wound is related to a frequency of local recurrences four times higher than the one observed in patients submitted to wide excision and skin grafting. Regional lymphnode and distant metastases had the same incidence in the two groups. It is not possible to draw final conclusion on the matter of optimal resection margins from the results of the present analysis because: (1) the number of cases submitted to narrow excision is limited (40 cases); (2) the surgeon's choice of treatment may bias the results. However, since it has been shown that cases with maximum tumor thickness no more than 2 mm

Table 8. Frequency of local recurrences by maximum thickness and resection margins in 803 patients with malignant melanoma (clinical stage I and II)

Resection margins (cm)	Maximum thickness (mm)					Total
	0–1	2	3	4	>4	
1	0/6	1/6	1/5	1/9	1/14	4/40
2	0/14	1/19	1/9	0/6	4/28	6/76
3	0/40	1/75	5/73	3/58	9/134	18/380
4	0/6	1/22	0/17	0/11	0/15	1/71
>5	1/32	0/61	2/33	2/34	2/56	7/236
	1/98	4/183	9/157	6/118	16/247	36/803

have an excellent prognosis, (Fig. 1) that the frequency of local recurrence is low and not related to margins of resection in this group (Table 7) one may plan a randomized pro-

spective clinical trial to evaluate whether or not narrow excision may be considered the treatment of choice of thin cutaneous melanoma.

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