Thickness, Cross-Sectional Areas and Depth of Invasion in the Prognosis of Cutaneous Melanoma

ALEXANDER BRESLOW,* M.D.

From The George Washington University School of Medicine, Washington, D. C.

CUTANEOUS melanoma is a most unpredictable lesion. The marked variation in prognosis is probably a function of many variables, one of which is the size of the tumor. Though there is a roughly inverse relationship between the diameter of the lesion and survival,[5] very small lesions have recurred or metastasized. One possible reason for the lack of reliability of tumor size in estimating prognosis may be that studies to date have considered size in only two diamensions and have neglected tumor volume. Two melanomas can have the same diameter but differ greatly in thickness because of variation in either depth of invasion or degree of protrusion from the surface of the skin or both. A recent study [2] has shown that prognosis correlates well with staging of the depth of invasion, but there have been no studies relating survival to tumor volume.

To measure tumor volume it is necessary to know the surface area of the tumor, but in this retrospective study we only know the maximal diameters of the lesions. By measuring the maximal thickness of the lesions we can calculate the maximal cross-sectional area, which should be roughly proportional to the volume of the tumor. The depth of invasion was also studied using the criteria for staging of Clark *et al.*[2] to see if maximal cross-sectional area, thickness, stage of invasion, or a combination of these can be of value in assessing the prognosis of cutaneous melanoma. A total of 98 lesions were so studied.

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Reprint requests to: George Washington University Hospital, 901 23rd Street, N. W., Washington, D. C. 20037.

Materials and Methods

The 98 patients in this study were all free of recurrent or metastatic disease and none had satellite nodules when first seen at the George Washington University Hospital. None of the lesions were related to an antecedent lentigo malignum (melanotic freckle of Hutchinson). Their ages ranged from 18 to 80 (average 47). Forty-six were men and 52, women. Sixteen had lesions of the head or neck; 50, of an extremity; and 32, of the trunk.

Following operation 71 remained free of disease for 5 or more years, while 27 developed metastatic or recurrent disease. Patients who died of unknown causes, who died in less than 5 years without melanoma and those lost to follow-up were excluded. Follow-up was 92%.

The maximal diameters of the lesions were measured after fixation in Bouin's solution. Sections were taken through the center of the lesion, and slides prepared and stained with hematoxylin-eosin in the usual manner. One to five slides were prepared from each lesion (usually two).

By means of an ocular micrometer, the maximal thickness of the lesion was measured from the skin surface to the deepest

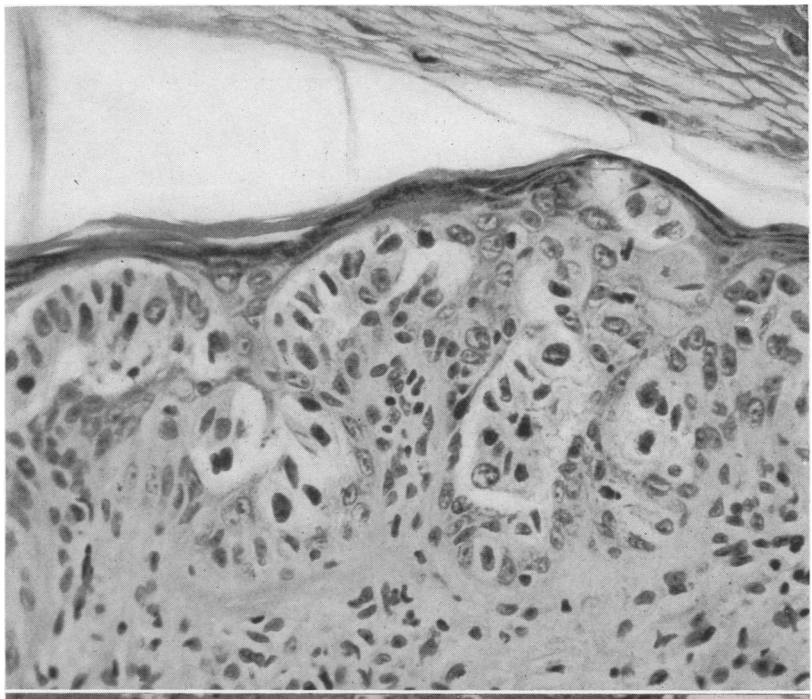

FIG. 1. Stage I melanoma. Malignant melanocytes are confined to the epidermis (H & E, 190×).

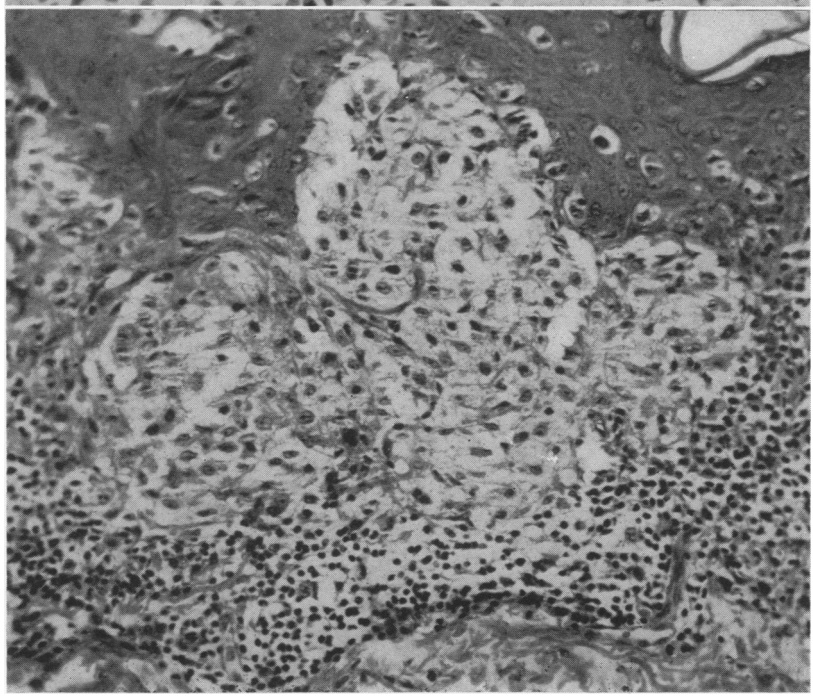

FIG. 2. Stage II melanoma. The papillary dermis is widened and densely inflamed. Malignant melanocytes infiltrate the papillary dermis but do not reach the dense reticular dermis (H & E, 185×).

point of invasion. The maximal cross-sectional area of the lesion was calculated by multiplying the thickness by the maximal diameter of the lesion. The lesions were also staged as to the depth of invasion.[2] By this classification *in situ* lesions are stage I. In stage II the tumor is confined to the loose papillary dermis but does not form a

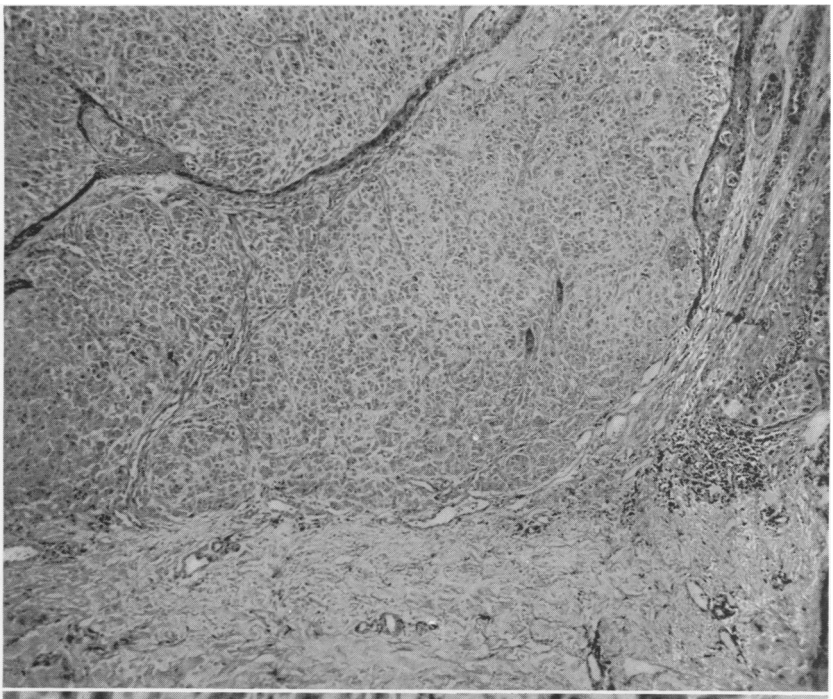

FIG. 3. Stage III melanoma. Malignant melanocytes fill the papillary dermis and abut on the reticular dermis (H & E, 42×).

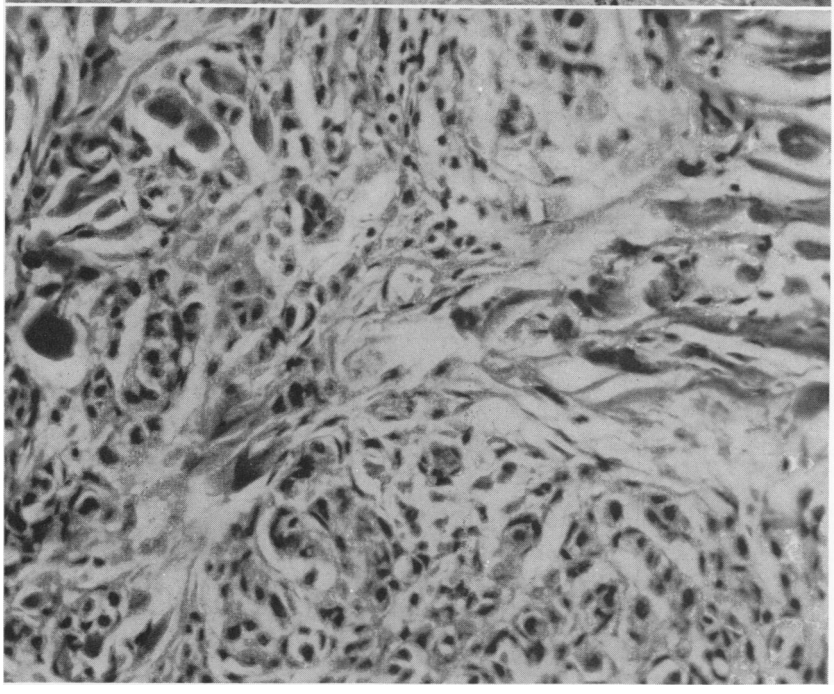

FIG. 4. Stage IV melanoma. Malignant melanocytes infiltrate the reticular dermis (H & E, 250×).

plaque at the junction of the loose papillary and the dense reticular dermis. In stage III the tumor forms such a plaque and usually fills the papillary dermis. In stage IV there is invasion of the reticular dermis, and in V, the subcutaneous fat is involved. These are illustrated in Figures 1–5.

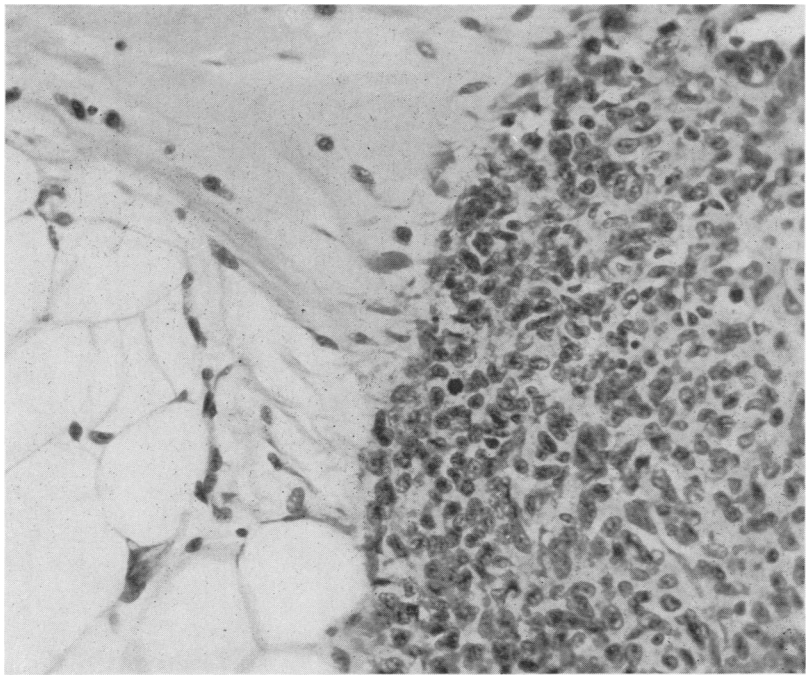

FIG. 5. Stage V melanoma. Malignant melanocytes infiltrate subcutaneous fat (H & E, 250×).

Results

Tumor Size

The distribution of the lesions according to size are seen in Figures 6–8. No patient with a lesion less than 5 mm. in diameter, less than 0.76 mm. in thickness or less than 6.01 mm.^{2} in maximal cross-sectional area subsequently developed recurrent or metastatic disease. Tumor thickness was the most useful measurement, identifying 38 of the 71 patients who remained free of disease. The smallest melanoma which recurred or metastasized was 7 mm. wide, 0.88 mm. thick with a cross-sectional area of 6.16 mm.^{2} The incidence of recurrent or metastatic disease appears to be a function of all three variables and was 100% for lesions over 30 mm. wide or over 5 mm. thick and almost 100% for lesions over 40 mm.^{2} in maximal cross-sectional area. When the patients whose lesions were less than 0.76 mm., in thickness were compared with those whose lesions were over 2.25 mm. thick, there were no significant differences in age, sex or anatomic location of the tumors.

Stage of Invasion

The incidence of recurrent or metastatic disease is also a function of the stage of invasion and our findings (Table 1) are in reasonably good agreement with those of Clark *et al.*[2] No stage I lesions were en-

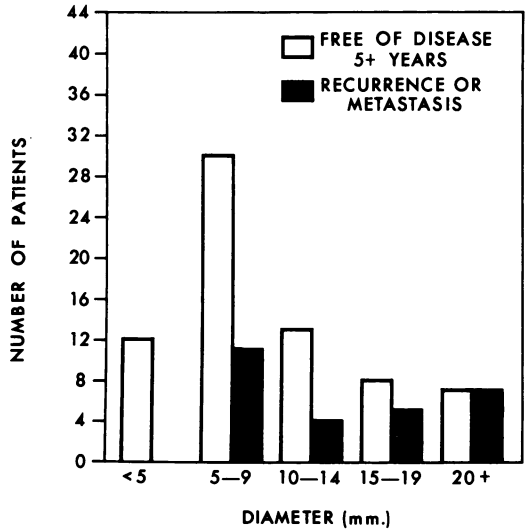

FIG. 6. Diameter of melanomas. None less than 5 mm. recurred or metastasized.

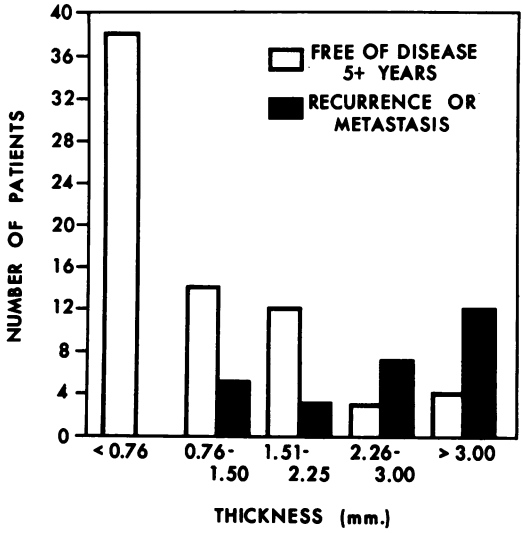

FIG. 7. Maximal thickness of melanomas. None less than 0.76 mm. recurred or metastasized.

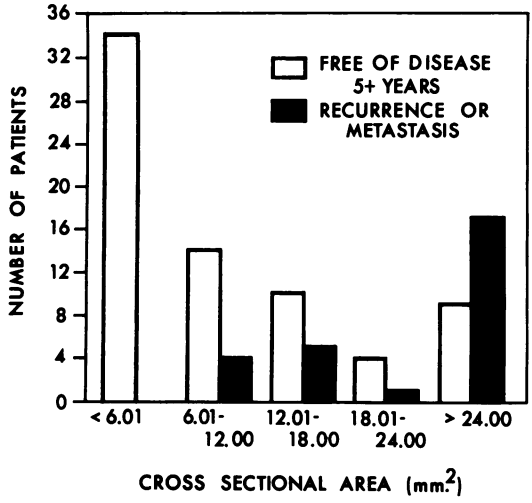

FIG. 8. Maximal cross-sectional area of melanomas. None less than 6.01 mm.^{2} recurred or metastasized.

countered. The prognosis for stage II tumors is excellent with only 1 of 39 patients developing a recurrence or a metastasis.

Simultaneous Evaluation of Size and Stage

In general all measurements of tumor size increased with the stage of invasion, but there was a great deal of overlap (Tables 2–5). For example one stage IV lesion had a maximal cross-sectional area of 6.00 mm.^{2} while one stage II lesion was 22.50 mm.^{2} in maximal cross-sectional area.

Simultaneous evaluation of tumor thickness and stage of invasion is of greater value in assessing prognosis than is either alone. The prognosis for stage II lesions is excellent, and the one lesion that metastasized was over 0.76 mm. in maximal thickness. For patients with stage III lesions six of 13 whose lesions were over 0.76 mm. thick developed recurrence or metastases while all six of those whose lesions were less than 0.76 mm. survived 5 or more years free of disease. Tumor thickness appears to identify those stage II and III lesions with a good prognosis, and a test of partial association in 2 × 2 tables [1, 3] reveals this to be significant at the 0.05 level. By combining stage II lesions with those stage III lesions thinner than 0.76 mm. a group of 45 lesions is identified only one of which recurred or metastasized (2.2%). All stage IV and V lesions were thicker than 0.76 mm.

TABLE 1. *Staging by Depth of Invasion*

Stage	Free of Disease 5+ Years (Number)	Subsequent Recurrences or Metastases	
		Number	%
I	0	0	0
II	38	1	2.6
III	19	6	24
IV	12	16	57
V	2	4	66

Discussion

Prognosis of cutaneous melanoma appears in part to be a function of both tumor size and stage of invasion with tumor thickness the most significant measure of size. Stage II lesions and lesions less than 0.76 mm. in maximal thickness are associated with a favorable prognosis and each identified 38 of 71 patients who remained

TABLE 2. *Measurements for Stage II Lesions*

	Free of Disease 5+ Years	Subsequent Recurrences or Metastases
mm.	Width	
<5	11	0
5–9	14	1
10–14	6	0
15–19	5	0
>19	11	0
mm.	Thickness	
<0.76	32	0
0.76–1.50	6	1
1.51–2.25	0	0
2.26–3.00	0	0
>3.00	0	0
MM^2	Maximal Cross-sectional Area	
<6.01	29	0
6.01–12.00	7	1
12.01–18.00	1	0
18.01–24.00	1	0
>24.00	0	0

TABLE 3. *Measurements for Stage III Lesions*

	Free of Disease 5+ Years	Subsequent Recurrences or Metastases
mm.	Width	
<5	2	0
5–9	7	3
10–14	3	2
15–19	2	1
>19	5	0
mm.	Thickness	
<0.76	6	0
0.76–1.50	6	3
1.50–2.25	4	0
2.26–3.00	2	2
>3.00	1	1
$mm.^2$	Maximal Cross-sectional Area	
<6.01	5	0
6.01–12.00	3	2
12.01–18.00	5	2
18.01–24.00	1	0
>24.00	5	2

TABLE 4. *Measurement for Stage IV Lesions*

	Free of Disease 5+ Years	Subsequent Recurrences or Metastases
mm.	Width	
<5	0	0
5–9	8	6
10–14	4	2
15–19	0	3
>19	0	5
mm.	Thickness	
<0.76	0	0
0.76–1.50	2	1
1.51–2.25	7	3
2.26–3.00	1	3
>3.00	2	9
$mm.^2$	Maximal Cross-sectional Area	
<6.01	1	0
6.01–12.00	3	1
12.01–18.00	4	3
18.01–24.00	1	1
>24.00	3	11

TABLE 5. *Measurement for Stage V Lesions*

	Free of Disease 5+ Years	Subsequent Recurrences or Metastases
mm.	Width	
<5	0	0
5–9	1	1
10–14	0	0
15–19	1	1
>20	0	2
mm.	Thickness	
<0.76	0	0
0.76–1.50	0	0
1.51–2.25	0	0
2.26–3.00	1	0
>3.00	1	4
$mm.^2$	Maximal Cross-sectional Area	
<6.01	0	0
6.01–12.00	0	0
12.01–18.00	0	0
18.01–24.00	1	0
>24	1	4

free of disease for 5 or more years. Only 1 stage II lesion, 1.00 mm. thick, subsequently metastasized. When both criteria are applied, 45 patients whose lesions were either stage II or were stage III but thinner then 0.76 mm. are identified and only 1, the thick stage II lesion subsequently metastasized. These criteria are, of course, not absolute and one can expect on occasion to find a lesion less than 0.76 mm. in maximal thickness which will recur or metastasize. I have seen such lesions at the National Cancer Institute, but they are rare. Patients at the Cancer Institute are highly selected, and these small lethal melanomas must represent a very small per cent of lesions operated upon.

These criteria may be helpful in selecting patients for prophylactic lymph node dissection. Though some reports strongly advocate prophylactic node dissection whenever possible,[5, 7, 8] some question the value of this procedure for small superficial lesions.[5, 6] It would seem reasonable to exclude all patients with stage II lesions as well as those with stage III lesions thinner than 0.76 mm. from this procedure. Thirty-five of our 98 patients underwent prophylactic node dissection. All 12 who were in this favorable group had negative nodes including the patient with the lethal stage II lesion who died of hematogenous metastases.

Summary

From a retrospective study of 98 cutaneous melanomas it was found that both tumor thickness and stage of invasion are of value in assessing prognosis. By combining these two criteria it was possible to identify a group of 45 patients only one of whom developed recurrent or metastatic disease. These criteria may be of value in selecting patients for prophylactic lymph-node dissection.

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