# *Tumor Thickness, Level of Invasion and Node Dissection in Stage I Cutaneous Melanoma*

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**From a retrospective study of 97 and a prospective study of 41 Stage I cutaneous melanomas, it was found that tumor thickness is a better measure of prognosis than is the level of invasion of the tumor. The chance of developing recurrent disease appears to be directly proportional to tumor thickness. Prophylactic lymph node dissection doubled the rate of survival for patients with lesions greater than 1.50 mm thick but had no effect on those with thinner lesions. Thirty-nine per cent of the patients had lesions less than 0.76 mm thick and all survived free of disease for 5 or more years. Six per cent of the tumors that recurred or metastasized were in an intermediate range of 0.76-1.50 mm thick, and no discriminant could be found to separate these 9 lesions with a bad prognosis from the remaining 18 in this group.**

THE ROLE OF PROPHYLACTIC lymph node dissection in the treatment of patients with Stage I cutaneous melanoma is still under debate.[3,4] A probable explanation for the persistence of this debate is the marked heterogeneity of cutaneous melanoma with variation in size, type of lesion and level of invasion, any of which might alter the prognosis and subsequent need for prophylactic node dissection. In 1969 Clark et al.[2] separated melanomas into nodular, superficial spreading and lentigo maligna types and demonstrated that the nodular was the most and the lentigo maligna the least malignant. They also defined four levels of invasion of the dermis and subcutaneous fat and found that prognosis, independent of treatment, was inversely related to the level of invasion. These levels are commonly used to select patients for prophylactic node dissection, restricting such treatment to patients with level III to V lesions. In 1970 we[1] showed that tumor thickness is a reliable measure of prognosis in cutaneous melanoma and this has recently been confirmed by Hansen and McCarten[5] and Wanebo et al.[9] The former group also found that prophylactic node dissection is of value when used for patients with melanomas 1.50 mm or thicker but not for patients with thinner lesions.

In this study we would like to add a prospective group of 41 patients to our original retrospective series of 97 patients and to compare the usefulness of tumor thickness with Clark's level of invasion in selecting patients for prophylactic lymph node dissection.

## Materials and Methods

All patients in this study were 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 of the lentigo malignum type. Their ages ranged from 14 to 79 years (average 39). Twenty were men and 21 women. Seven had lesions of the head and neck; 14 of an extremity; and 20 of the trunk.

Following operation, 17 remained free of disease for 5 or more years, while 24 developed metastatic or recurrent disease. Patients who died of unknown causes, who died in less than 5 years without melanoma and those lost to followup were excluded from the study. Followup was 87% for the prospective group, 92% for the retrospective group and 91% for the combined series. After the publication of our original paper, we discovered that one of the patients with a level IV, 2.50 mm thick lesion had died 5.5 years after surgery, supposedly of a primary bronchogenic carcinoma. Despite repeated attempts, we

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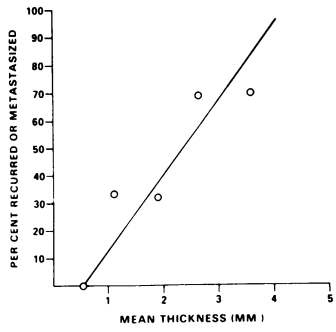


FIG. 1. Percent of patients with recurrent or metastatic disease is plotted against mean tumor thickness of groups from 0-0.75 to 3.01-3.75 mm thick. The correlation coefficient is 0.931 (P = 0.022).

have not been able to obtain the slides from the autopsy and have excluded this case from the study.

The entire lesion was studied if it was small, and several sections were taken through the center of the lesion if it was large. Sections were fixed in neutral formalin, and slides prepared and stained with hematoxylin-eosin in the usual manner.

By means of an ocular micrometer, the maximal thickness of the lesion was measured in several slides from the top of the granular cell layer to the deepest point of invasion. If the lesion was ulcerated, the ulcer base over the deepest point of invasion was used rather than the top of the granular cell layer. The level of invasion was measured by the method of Clark et al.[2]

## Results

In Fig. 1, the percentage of cases with recurrent or metastatic disease is plotted against mean tumor thickness for groups of melanomas in a series from 0-0.75 mm to 3.01-3.75 mm. The correlation coefficient is 0.931, which indicates a very strong correlation. This is significant at the 0.022 level.

The distribution of tumor thickness and the clinical results for the combined series are shown in Fig. 2. Most

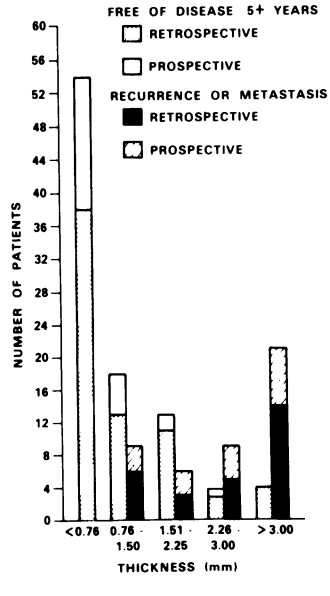


FIG. 2. The distribution of lesions according to tumor thickness. Patients surviving free of disease for 5 or more years are shown in the clear and stippled columns. Those developing recurrent or metastatic diseases are shown in the black and cross-hatched columns. All with lesions less than 0.76 mm thick survived free of disease.

TABLE 1. *Results of Prophylactic Node Dissections Based on Maximal Tumor Thickness. Patients Free of Disease 5+ Years.*

| Thickness | LN Dissection | No LN Dissection |
|---|---|---|
| <0.76 | 10/10 (100%) | 44/44 (100%) |
| 0.76-1.50 | 7/10 (70%) | 12/17 (70%) |
| >1.50 | 14/22 (64%) | 11/35 (31%) |

Node dissection doubled the survival rate for patients with lesions greater than 1.50 mm thick (P<0.03) but not for those with thinner lesions.

of the therapeutic failures were due to lymph node or hematogenous metastases. Only 4 developed local wound recurrences and 3 of these subsequently died of hematogenous metastases. The fourth is alive and free of disease at 11 years. In 7 cases metastatic tumor was found in clinically negative nodes removed during prophylactic node dissections. The results for the prospective series can be superimposed on the retrospective series. On the basis of tumor thickness, there appears to be three populations of patients with melanoma. The first are those with lesions less than 0.76 mm thick and all have done well. The second is a group of 27 patients with lesions 0.76-1.50 mm thick. Despite the small size of these lesions, 9 developed metastases. Last is a group of 57 patients with lesions thicker than 1.50 mm. As can be seen in Table 1, it is this group that is most likely to benefit from prophylactic lymph node dissection. For this group node dissection doubled the survival rate (P<0.03). By contrast, elective node dissections did not alter the survival rate for patients with lesions less than 1.51 mm thick. Three patients with thick lesions and one with a thin lesion had positive nodes and are free of disease at five or more years. Of the 8 patients with thick lesions who died despite node dissection, 5 had negative nodes. For comparable patients with thin lesions, three had negative nodes.

The slides of the nine lesions, 0.76-1.50 mm thick, which metastasized, were compared to those of the 18 that did not. The results are shown in Table 2. The maximal cross-sectional area is the product of the maxi-

TABLE 2. *Analysis of Melanomas 0.76-1.50 mm Thick*

| | Free of Disease 5+ Yrs | Recurred or Metastasized |
|---|---|---|
| Mean Thickness | 1.22 | 1.01 |
| Mean Maximal Cross-sectional Area | 14.0 | 12.4 |
| Nodular | 2 | 0 |
| Sup. Spread | 16 | 9 |
| Level II | 7 | 2 |
| Level III | 7 | 5 |
| Level IV | 4 | 2 |
| Proph. Node Dissection | 6 | 3 |
| Mitoses/10 HPF | 2.4 | 1.5 |
| Inflammation | Same | Same |

No discriminant separated the 9 lesions which recurred or metastasized from the 18 lesions which did not.

TABLE 3. *Clinical Results and Distribution of Lesions According to Clark's[2] Levels of Invasion*

| Level | Recurred or Metastasized | | |
|---|---|---|---|
| | Retrospective | Prospective | Total |
| | (97) | (41) | (138) |
| II | 1/39 | 1/15 | 4% |
| III | 7/25 | 5/11 | 33% |
| IV | 16/27 | 8/12 | 61% |
| V | 4/6 | 3/3 | 78% |

mal thickness and the maximal diameter of the lesion. No discriminant could be found to explain the difference between the two groups.

The data for the levels of invasion are shown in Table 3. The results for the retrospective and prospective series are in reasonably good agreement and, as expected, the rate of recurrence increased as the levels of invasion became deeper.

The distribution of tumor thickness within each of these levels is shown in Table 4. There is great heterogeneity especially within levels III and IV. Of the 14 patients with level III lesions treated with prophylactic node dissection, 11 survived free of disease for 5 or more years (78%) as compared to 15 of the 22 not so treated (68%). For those with level IV lesions the comparable figures are 9 of 17 for the treated group (53%) and 8 of 22 for those not treated (36%). The difference between the treated and untreated groups are not statistically significant. No patients with level V lesions were treated with prophylactic node dissections. For level II lesions survival was over 90% for both treatment groups.

## Discussion

Tumor thickness and level of invasion of cutaneous melanoma are independent variables which are relatively congruent in levels II and V but not in levels III and IV. Though most level II lesions are thin and all level V lesions are thick, there is great variation in thickness for levels III and IV and this has recently been confirmed by others.[5,9] Since the chance of developing recurrent disease appears to be directly proportional to tumor thickness and the mean survival following surgery appears to be inversely proportional to tumor thickness,[5] this heterogeneity within levels III and IV is a serious defect if the level of invasion is to be used to guide treatment. If the suggestion that all patients with level III to V melanomas should be treated with elective node dissection is followed, and if our patient population is not unique, the following can be expected:

1. Seventeen per cent of patients with level II lesions will not be treated with node dissection but will have lesions 0.76-1.50 mm thick. Though this is in the range for which the value of elective node dissection is still to be proven, one such patient had positive nodes and is alive and free of disease at more than 5 years.

2. Twenty-five per cent of patients with level III lesions will have unnecessary node dissections with lesions less than 0.76 mm thick. We have yet to see such a lesion recur or metastasize.

3. If one wishes to limit node dissections to patients with lesions greater than 1.50 mm thick, for whom node dissections are of proven value, 29% of patients with level III to V lesions will be treated unnecessarily.

Another serious problem in using Clark's levels of invasion is the difficulty in differentiating between an advanced level II and a level III lesion. The difference is somewhat subjective, and several pathologists have commented on this problem.[7,8,9] In one collaborative study,[8] agreement among the pathologists could only be achieved after instruction by Dr. Clark. By contrast, measurement of tumor thickness is objective, and good agreement among pathologists is to be expected.

TABLE 4. *Distribution of Tumor Thickness For Each of Clark's Levels of Invasion[2]*

| Level | | Free of Disease 5 Yrs | Recurred or Metastasized |
|---|---|---|---|
| II | <0.76 | 45 (7)* | 0 |
| | 0.76-1.50 | 7 (3) | 2 (1) |
| III | <0.76 | 9 (3) | 0 |
| | 0.76-1.50 | 7 | 5 (3) [1]† |
| | 1.51-2.25 | 4 (3) | 1 |
| | 2.26-3.00 | 3 (2) | 4 (1) |
| | >3.00 | 1 (1) | 2 (1) [1] |
| IV | <0.76 | 0 | 0 |
| | 0.76-1.50 | 4 (2) | 2 |
| | 1.51-2.25 | 9 (3) | 5 (3) [1] |
| | 2.26-3.00 | 0 | 6 (1) |
| | >3.00 | 2 (2) | 11 (6) [4] |
| V | 2.26-3.00 | 1 | 0 |
| | >3.00 | 1 | 7 |

*Number treated with prophylactic node dissection.
†Number with positive nodes in prophylactic dissection.
There is great heterogeneity within each group, especially in levels III and IV. The number of patients treated with prophylactic node dissection is indicated in parentheses. The number of patients with positive nodes in prophylactic dissections is shown in brackets.

For these reasons, we believe that tumor thickness rather than the level of invasion should be used to select patients for prophylactic node dissection. It is clear that patients with lesions less than 0.76 mm thick should not be subjected to node dissection while those with lesions greater than 1.50 mm should be so treated. The indications for node dissection for the group with lesions 0.76-1.50 mm thick are still obscure and the treatment will continue to depend on the intuition of the surgeon, perhaps influenced by the distance between the lesion and the nearest group of lymph nodes. We are aware of the hazards of using data from retrospective nonrandomized studies to guide therapy, but this is all we have at the present time. Clearly a cooperative prospective study of randomized patients is needed to prove the value of prophylactic node dissection in cutaneous melanoma. From the data at hand, this study should be limited to patients with lesions thicker than 0.75 mm.

In a retrospective study of 151 melanomas at Memorial-Sloan Kettering Cancer Center, Wanebo et al.[9] found three melanomas less than 0.76 mm which metastasized. Two were subungual lesions, which are uncommon and were not encountered in our study. One was a cutaneous level II lesion 0.60 mm thick. In a review of all primary cutaneous melanomas at the National Cancer Institute in 1969, we found one lethal level II lesion 0.45 mm thick. Very thin lethal cutaneous melanomas are very rare and are most likely to be seen at very large referral centers.

Hansen and McCarten,[5] in a retrospective study of 154 melanomas (50 of head and neck, 36 of trunk and 68 of extremities), also found tumor thickness to be of greater value than level of invasion in selecting patients for prophylactic node dissection. They report that prophylactic lymph node dissection is of value for melanomas 1.50 mm or thicker but not for thinner lesions. Seventy-seven per cent of treated patients survived free of disease for an average of 8 years as compared to 43% for the untreated group ($P<0.01$). Though their overall study included patients with lentigo maligna melanoma, a group we excluded because of its low degree of malignancy, none of the patients in their treated group of thick melanomas had such a lesion.[6]

They only encountered one lethal melanoma less than 1.50 mm thick, while we found 9. This may reflect differences in the rates at which rural Canadians and urban white Washingtonians seek medical care. The more lethal thin melanomas may have metastasized before the patients saw the physicians, thus excluding these patients from the stage I group under study.

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