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CLINICAL SIGNIFICANCE OF MORPHOMETRIC MEASUREMENTS OF MELANOMA METASTATIC TO SINGLE SENTINEL LYMPH NODES

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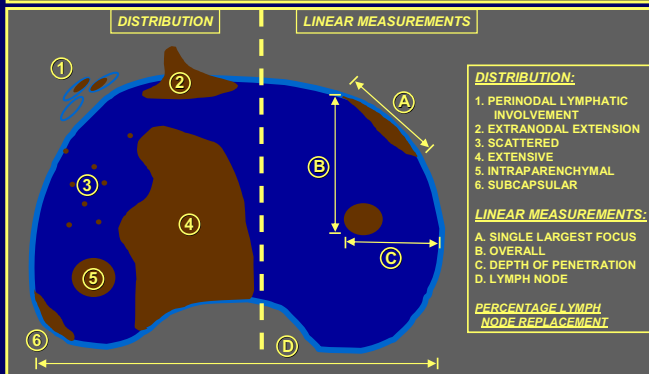


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BACKGROUND

- > Sentinel lymph node (SLN) biopsy is a common procedure for staging patients with melanoma of >1 mm thickness.
- > Immunohistochemistry for S100 protein and HMB45 facilitates examination of SLNs by highlighting small deposits of melanoma.
- > Previous studies suggest that morphometric features of metastatic deposits may play a role in predicting the clinical behavior of malignancies and help guide treatment.
- > The goal of this study is to explore the relationship between morphometric features of metastatic deposits of melanoma in single SLNs and clinical relapse.

FIGURE 1. SCHEMATIC OF MORPHOMETRIC FEATURES



METHODS

- > S100 protein and HMB45 immunostained sections of SLNs from 122 patients with melanoma and a single, positive SLN were reviewed.
- > Eleven morphometric features were each scored by two pathologists (RY and CC; figure 1).
- > Univariate and multivariate statistical analyses were used to evaluate the relationship between disease relapse and (1) morphometric features and (2) routine clinical features (location of primary melanoma, Breslow depth, etc).

TABLE 1. CORRELATION BETWEEN MORPHOMETRIC FEATURES AND DISTANT RELAPSE (HMB45)^a

	DISEASE FREE	DISTANT RELAPSE	UNI-VARIATE P VALUE	MULTI-VARIATE P VALUE	RELATIVE RISK (CONFIDENCE INTERVAL)
AGE (YEARS)	50.0	51.7	0.59	0.73	1.00 (0.97 - 1.03)
FEMALE	26 (76.5%)	8 (23.5%)	0.27	0.47	0.65 (0.21 - 2.02)
BRESLOW DEPTH	4.04	3.17	0.16	0.95	ND
<5% SLN REPLACEMENT ^c	47 (79.7%)	12 (20.3%)	0.01	0.02	0.21 (0.06 - 0.72)
<10% SLN REPLACEMENT ^c	51 (73.9%)	18 (26.1%)	0.17	ND	ND
DEPTH OF PENETRATION (mm)	1.20	1.85	0.04	0.11	1.75 (0.88 - 3.46)
INTRAPARENCHYMAL DEPOSITS ONLY	3 (33.3%)	6 (66.7%)	0.01	0.02	7.65 (1.39 - 42.29)
HEAD AND NECK PRIMARY	4 (28.6%)	10 (71.4%)	<0.001	0.01	7.57 (1.73 - 33.09)

TABLE 2. CORRELATION BETWEEN MORPHOMETRIC FEATURES AND DISTANT RELAPSE (S100 PROTEIN)^b

	DISEASE FREE	DISTANT RELAPSE	UNI-VARIATE P VALUE	MULTI-VARIATE P VALUE	RELATIVE RISK (CONFIDENCE INTERVAL)
<5% SLN REPLACEMENT ^c	57 (77.0%)	17 (23.0%)	0.01	0.054	2.50 (0.99 - 6.36)
<10% SLN REPLACEMENT ^c	63 (75.0%)	21 (25.0%)	0.02	0.48	0.65 (0.19 - 2.19)
DEPTH OF PENETRATION (mm)	1.14	1.78	0.02	0.11	1.15 (0.89 - 2.79)
INTRAPARENCHYMAL DEPOSITS ONLY	10 (55.6%)	8 (44.4%)	0.18	ND	ND
HEAD AND NECK PRIMARY	4 (26.7%)	11 (73.3%)	<0.001	0.004	7.25 (1.89 - 27.96)

^aClinical and morphometric features are listed on the left side of the table. The number and percentage of disease free patients and patients with distant relapse are listed. Age, Breslow depth, and depth of penetration are reported as a mean. ND = not determined.

^bData for age, sex, and Breslow depth are similar for both HMB45 and S100 protein data and show no statistically significant correlation with distant relapse.

^cMultivariate analysis for <5% lymph node replacement and <10% lymph node replacement is performed separately due to the expected association between the two features.

RESULTS

- > Metastatic deposits stained positively for S100 protein in 98% of cases and for HMB45 in 84% of cases.
- > There were 41 (34%) relapses of any type and 37 (31%) distant relapses (excludes local recurrences).
- > By *univariate* analysis, statistically significant features include: percentage of SLN replacement by melanoma (<1% and <5%), depth of melanoma deposits relative to the SLN capsule, and intraparenchymal deposits in the absence of subcapsular deposits (tables 1 and 2).
- > By *univariate* analysis, <10% SLN replacement by melanoma is correlated with a decreased incidence of relapse by S100 protein data, but not by HMB45 data (tables 1 and 2).
- > By *multivariate* analysis, head and neck primary site is associated with an increase in distant relapse (71.4% relapse rate, p=0.01), as are intraparenchymal deposits in the absence of subcapsular deposits (66.7% relapse rate, p=0.02; tables 1 and 2).
- > By *multivariate* analysis, a low percentage of SLN replacement by melanoma (<5%) is associated with a decreased incidence of distant relapse (20.3% relapse rate, p=0.02; table 1).

CONCLUSIONS

- > Certain morphometric features of metastatic deposits of melanoma in SLNs are associated with clinical relapse.
- > A small volume (<5%) of melanoma and intraparenchymal deposits in the absence of subcapsular deposits are independently correlated with the incidence of distant relapse.
- > Head and neck primary melanomas are independently correlated with an increased incidence of relapse.
- > These findings may help predict clinical behavior and have therapeutic implications in patients with single, positive SLNs.