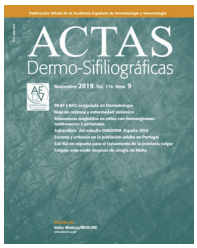
ACTAS Dermo-Sifiliográficas 112 (2021) 922–923

ACTAS
Dermo-Sifiliográficas

Full English text available at
www.actasdermo.org



RESIDENT'S FORUM

Calculated Tumor Area and Breslow Density: Two New Prognostic Features in the Staging of Melanoma☆

FR -Área tumoral calculada y densidad de Breslow, dos nuevos parámetros pronósticos en la evaluación histológica del melanoma

X. Bosch-Amate,[a] P. Vargas-Mora,[b] D. Morgado-Carrasco[a,*]

[a] *Departamento de Dermatología, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain*
[b] *Departamento de Dermatología, Facultad de Medicina, Universidad de Chile, Santiago, Chile*

KEYWORDS
Melanoma;
Breslow thickness;
Biomarker;
Breslow density;
Tumor area;
Prognostic factors

PALABRAS CLAVE
Melanoma;
Índice de Breslow;
Biomarcador;
Densidad de Breslow;
Área tumoral;
Factores pronósticos

Breslow thickness (Fig. 1A) is one of the main prognostic factors in cutaneous melanoma and forms the basis of the American Joint Committee on Cancer (AJCC) TNM staging system. Although newly developed molecular assays are available for establishing prognosis in melanoma, their use is limited by their high cost. Histology thus remains the cornerstone for prognostic assessment.

It has been proposed that tumor volume may have greater prognostic relevance than Breslow thickness in melanoma.[1] In a recent publication, Saldanha et al.[2] described the results of a retrospective study of 1239 patients with primary cutaneous melanoma (median Breslow thickness, 0.9 mm; interquartile range, 0.5-2 mm) and analyzed the prognostic value of calculated tumor area (CTA). CTA is a 2-dimensional measurement of the area occupied by melanoma in the area of maximum invasion (where Breslow thickness is measured) (Fig. 1B). The measurements were obtained using conventional hematoxylin-eosin–stained sections and took less than 1 minute in most cases. Interobserver agreement (intraclass correlation coefficient) was 0.99, indicating almost perfect agreement. Cox proportional hazards regression showed superior prognostic performance for CTA compared with Breslow thickness (hazard ratio, 1.70; 95% CI, 1.43-2.03; $P < .001$) after adjusting for Breslow thickness, ulceration, age, mitotic count, and microscopic satellites. Melanomas stratified by CTA showed a wider separation of survival curves than those stratified by Breslow thickness based on the criteria in the 8th edition of the AJCC Cancer Staging Manual (AJCC-8). In addition, significant heterogeneity was observed for CTA in lesions with the same T classification, suggesting that CTA subgrouping might result in improved prognostic accuracy.

Saldanha et al.[3,4] had previously assessed the prognostic value of Breslow density in melanoma. In a retrospective series of 970 cases of melanoma with a median Breslow thickness of 0.9 mm, they used conventional histologic sec-

☆ Please cite this article as: Bosch-Amate X, Vargas-Mora P, Morgado-Carrasco D. FR -Área tumoral calculada y densidad de Breslow, dos nuevos parámetros pronósticos en la evaluación histológica del melanoma. Actas Dermosifiliogr. 2021;112:922–923.

* Corresponding author.
E-mail address: danielmorgado@yahoo.com.ar (D. Morgado-Carrasco).

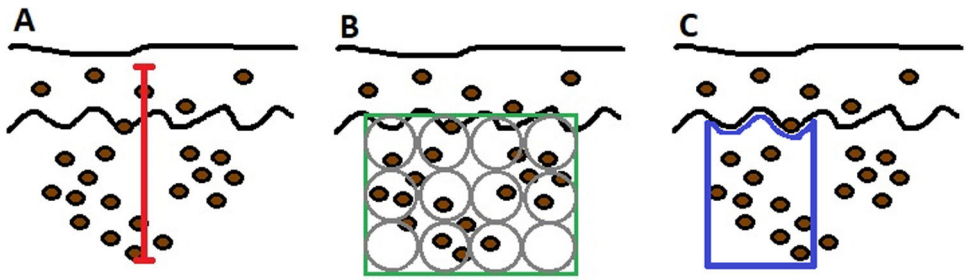


Figure 1 Schematic representation of Breslow thickness, calculated tumor area, and Breslow density din melanoma.
A, Breslow thickness, mm. B, Calculated tumor area (CTA). To calculate CTA, construct a box in the Breslow thickness measurement area that includes the entire invasive melanoma and estimate the percentage of the area occupied by invasive cells. Measure the height and width of the box (mm) using the microscope objective lens diameter. The formula for calculating CTA is height × width × proportion. For example, if the objective measures 5 mm, the box (as shown in the Fig.) measures 3 lenses high and 4 lenses wide, and the area occupied by tumor cells is 20%, the CTA would be 15 × 20 × 20/100 = 60 mm^2. C, Breslow density. To calculate Breslow density, at the ×10 magnification, construct a window in the Breslow measurement area, the bottom of which is limited by the deepest melanoma cell and the top of which is limited by the basement membrane. The width is determined by the width of the magnification field. Horizontally move the window to the area of the dermis with the highest density of melanoma, whilst keeping the deepest melanoma cell within the window. The proportion of the dermis occupied by melanoma cells is expressed with a precision of 5% (for scores < 5% or > 95%, use a precision of 1%).

tions to estimate the proportion of the dermis occupied by tumor cells in a 2-mm area in which Breslow thickness had been measured (Fig. 1C). Median Breslow density was 60% (interquartile range, 15%-85%). After adjusting for conventional prognostic factors, the authors found that Breslow density was a significant predictor of overall survival, metastasis-free survival, and melanoma-specific survival. It also explained melanoma-specific survival better than Breslow thickness, and its explanatory capacity was even higher when Breslow thickness and density were combined. High Breslow density (> 65%) upstaged the AJCC-8 T category from ''a'' to ''b'' in 27% of cases, showing its potential as an additional staging factor.

CTA and Breslow density are noteworthy for their simplicity and reproducibility. They may be potentially useful as risk markers in thin melanomas, and could even help select optimal candidates for sentinel lymph node biopsy, although further research is needed. It will be difficult to depart from the paradigm of Breslow thickness, although it is reasonable to assume that 2-dimensional measurements probably provide a better measure of tumor burden and metastatic potential. Digital pathology will soon occupy a prominent place in melanoma staging and could further simplify measurement of CTA and Breslow density.

Funding

None.

Conflicts of Interest

None.

References

1. Voss B, Wilop S, Jonas S, el-Komy MHM, Schaller J, von Felbert V, et al. Tumor volume as a prognostic factor in resectable malignant melanoma. Dermatology (Basel). 2014;228:66–70.
2. Saldanha G, Yarrow J, Elsheikh S, O'Riordan M, Uraiby H, Bamford M. Development and initial validation of calculated tumor area as a prognostic tool in cutaneous malignant melanoma. JAMA Dermatol. 2019;155:890–8.
3. Rashed H, Flatman K, Bamford M, Teo KW, Saldanha G. Breslow density is a novel prognostic feature in cutaneous malignant melanoma. Histopathology. 2017;70:264–72.
4. Saldanha G, Yarrow J, Pancholi J, Flatman K, Teo KW, Elsheik S, et al. Breslow density is a novel prognostic feature that adds value to melanoma staging. Am J Surg Pathol. 2018;42:715–25.