

Thin Melanoma: A Generic Term Including Four Histological Subtypes of Cutaneous Melanoma

Today, the scientific community is focusing on the prognostic significance of different histological subtypes of thin melanoma (1). The current staging system for melanoma of the American Joint Committee on Cancer (AJCC) uses Breslow thickness as the primary attribute: melanomas with up to 1 mm thickness is defined as thin, because they present a good prognosis after surgical excision, with a 10-year survival rate of 85-90% in case of a tumor-free margin ≥ 1 cm (2). There is a significant interaction between mitotic rate and Breslow depth, so the predictive value of the mitotic rate on sentinel lymph node (SLN) positivity can be dependent on Breslow thickness (3). Cutaneous melanoma generally evolves through three clearly discernible progression stages. At first, transformed melanocytes proliferate above the epidermal basement membrane (the *in situ* or epidermal radial growth phase); they then invade the papillary

dermis (the micro-invasive radial growth phase); and subsequently acquire the capacity to grow as a well-known malignant tumor (the invasive vertical growth phase). More specifically, micro-invasive melanoma is a non-tumorigenic radial growth phase of cutaneous melanoma, which invades the superficial dermis without forming a tumor nodule or papule, in absence of regression (3). In contrast, the micro-invasive radial growth phase of cutaneous melanoma with regression will rarely metastasize and, for this reason, the lesion should be recognized and could also be categorized as a 'micro-invasive radial growth phase of uncertain tumorigenic potential' (4). The early vertical growth phase of tumorigenic melanoma is characterized by the presence of a cell cluster in the dermis that is larger than the largest cluster in the epidermis (5). This feature is typical of tumorigenicity, while the mitogenicity is documented by the observation of

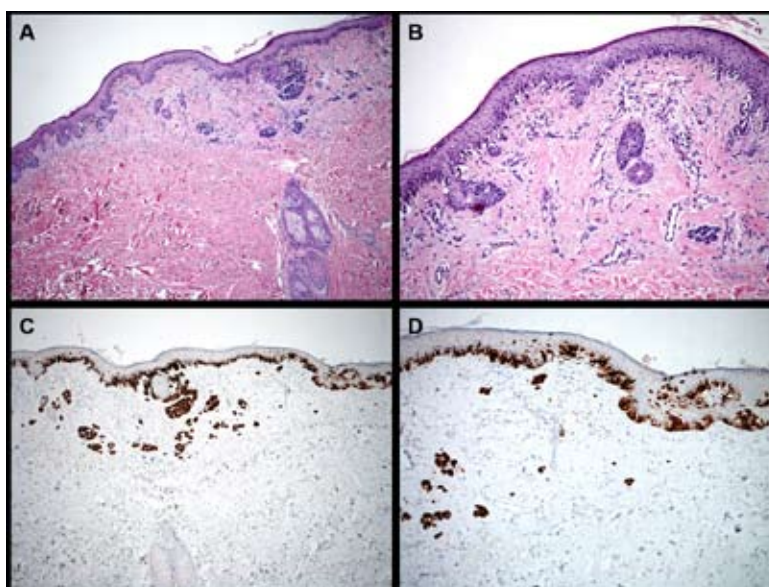


Figure 1. (a) Micro-invasive radial growth phase of cutaneous melanoma with regression (hematoxylin and eosin, $\times 4$). (b) The diffuse presence of regression (hematoxylin and eosin, $\times 10$) confers uncertain tumorigenic potential to the lesion. The immunohistochemistry of melan-A (clone A103, prediluted; Ventana, Roche) clearly shows the superficial nests of dermal microinvasion (c) (hematoxylin and eosin, $\times 4$) and the epidermal pagetoid diffusion (d) (hematoxylin and eosin, $\times 10$).

mitotic figures in dermal melanoma cells (5,6). The early vertical growth phase and the radial growth phase with regression have a statistical chance of distant metastases (7). Therefore, thin melanoma includes four main histological subtypes, which reflect a specific biological behavior: the *in situ* epidermal radial growth phase, the non-tumorigenic micro-invasive radial growth phase, the micro-invasive radial growth phase with regression of uncertain tumorigenic potential, and the tumorigenic early vertical growth phase. In conclusion, thin melanoma can be considered a generic term and its subtypes should be histologically distinguished beyond its site of origin (acral versus non-acral) because they have different prognostic relevance.

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