# Prognostic Predictors of Thin Melanoma in Clinico-Pathological Practice

The latest reviews on thin melanoma (TM) continue to consider it a melanoma within 1 mm in thickness, but no consensus exists as to which patients with TM are at risk for lymph node metastases (1). Numerous studies have evaluated the impact of various predictors (Breslow thickness, Clark level, ulceration, regression, vascular invasion, mitotic activity, location, sex) for nodal disease in melanoma, but the conclusions have not been homogenous (2,3). For this reason, we read the paper by Homolak *et al.* with great interest, where the authors examine the sentinel lymph node biopsies (SLNB) of 184 patients affected by melanoma of thickness less than 1.5 mm, defined as thin (4). SLNB was positive in 22 patients (12%), and 30 patients (7.65%) developed metastatic disease. The group of thinnest tumors (<0.50 mm) had the highest proportion of positive nodes (33%); the group of thickest tumors (1.26-1.50 mm) had the highest proportion of patients with metastatic disease (23%). The authors divided TM into 5 groups: 1) <0.50 mm (15 patients, 5 with positive SLNB); 2) 0.50-0.75 mm (18 patients, 3 with positive SLNB); 3) 0.76-1.00 mm (67 patients, 7 with positive SLNB); 4) 1.01-1.25 mm (45 patients, 4 with positive SLNB); 5) 1.26-1.50 mm (36 patients, 3 with positive SLNB). The current staging system of the American Joint Committee on Cancer (AJCC) uses Breslow thickness as the primary attribute, and up to 1 mm thick melanoma is defined as 'thin' because it shows a good prognosis after surgical excision, with a 10-year survival rate of 85-90% in case of a tumor-free margin of at least 1 cm (5). Based on our experience, this limit should be maintained at 1 mm because TM includes four main histological subtypes, which reflect specific biological attitudes: the

**Table 1.** The malignant melanocytic lesions of the skin can be subdivided, according to Breslow thickness, into thin melanoma (≤1 mm) or thick melanoma (>1 mm). The intra-epidermal radial growth phase and the micro-invasive radial growth phase without regression of thin melanoma are devoid of tumorigenic potential, while the micro-invasive radial growth phase with regression is burdened by an uncertain metastatic potential. The early invasive vertical growth phase of thin melanoma and the subcategories of the invasive vertical growth phase of thick melanoma all show tumorigenic potential, directly correlated to the depth of invasion and mitogenicity (pTis, pT1, pT2, pT3, pT4 and a/b specifications are adapted from the American Joint Committee on Cancer (AJCC) staging system)

| THIN MELANOMA<br>BRESLOW THICKNESS ≤1 mm | THICK MELANOMA<br>BRESLOW THICKNESS >1 mm |
|---|---|
| Intra-epidermal radial growth phase (*in situ*, **pTis**) | Invasive vertical growth phase >1 mm ≤2 mm (**pT2**) |
| Micro-invasive radial growth phase without regression (**pT1**) | Invasive vertical growth phase >2 mm ≤3 mm (**pT3**) |
| Micro-invasive radial growth phase with regression (**pT1**) | Invasive vertical growth phase >3 mm ≤4 mm (**pT3**) |
| Early (≤1 mm) invasive vertical growth phase (**pT1**) | Invasive vertical growth phase >4 mm (**pT4**) |

**a** and **b** specifications are assigned based on ulceration and thickness
**a:** without ulceration at any thickness and thin melanoma thickness < 0.8 mm
**b:** without ulceration and thin melanoma thickness > 0.8 mm ≤ 1 mm
**b:** with ulceration at any thickness of thin or thick melanoma

intra-epidermal (*in situ*) radial growth phase (RGP), the non-tumorigenic micro-invasive radial growth phase without regression, the micro-invasive radial growth phase with regression (>75%) of uncertain tumorigenic potential, and the tumorigenic early (≤1 mm) invasive vertical growth phase (VGP) (6-10). This proposed sub-typing fits better with the AJCC staging system, as elucidated below and in Table 1: intra-epidermal radial growth phase (pTis), micro-invasive radial growth phase without regression (pT1), micro-invasive radial growth phase with regression (pT1), early invasive vertical growth phase (pT1), invasive vertical growth phase >1 mm, ≤2 mm (pT2), invasive vertical growth phase >2 mm, ≤4 mm (pT3), invasive vertical growth phase >4 mm (pT4). The *in situ* RGP and micro-invasive RGP without regression are biologically indolent if completely removed, and SLNB is not necessary in these cases (6). In micro-invasive RGP with regression, performing SLNB is prudent, in particular if accompanied by high mitotic rates, while it is mandatory in early invasive VGP (7). Therefore, the prognostic predictors of nodal and distant metastases require further research in the four above-mentioned histological subtypes of thin melanoma.

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