

The International Classification of Diseases for Oncology Integrated with the Melanoma Histogenetic Model

Mezinárodní klasifikace nemocí pro onkologii integrovaná s histogenetickým modelem melanomu

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Malignant melanoma can be defined, quite simply, as a malignant neoplasm derived from melanocytes; however, there is great histological and, consequently, clinical variability from case to case [1]. In order to try to overcome this intrinsic difficulty, various classification systems have been proposed over the years; in this regard, the World Health Organization (WHO) introduced its notorious classification about half a century ago [2]. Currently, the International Classification of Diseases for Oncology (ICD-O), provided by the WHO International Agency for Research on Cancer (IARC), distinguishes the *in situ* forms from invasive ones, recognising among these four main morphological subtypes – nodular melanoma, superficial spreading melanoma, lentigo maligna

melanoma and acral lentiginous melanoma [3]. The ICD-O classification includes further morphological codes, such as balloon cell melanoma, regressing melanoma, amelanotic melanoma, melanoma in junctional nevus, melanoma in precancerous melanosis, desmoplastic melanoma, neurotropic melanoma, mucosal lentiginous melanoma, melanoma in giant pigmented nevus / congenital melanocytic nevus, mixed epithelioid and spindle cell melanoma, epithelioid cell melanoma, spindle cell melanoma (not otherwise specified), spindle cell melanoma (type A), spindle cell melanoma (type B) and malignant blue nevus [3]. Alongside a strictly morphological classification, a histogenetic model, based on the concept of tumour progression, is regaining ground [4,5]. In

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Tab. 1. Melanoma progression model.

The non-tumorigenic radial growth phase encompasses the intraepidermal lesions, namely lentigo maligna and *in situ* melanoma, and the microinvasive forms, that means ultra-thin melanoma and the vast majority of thin melanoma. Only a small quota of thin melanoma, burdened by an aggressive biological behavior, shows an early tumorigenic vertical growth phase. Contrariwise, a late tumorigenic vertical growth phase is constantly present in all thick and ultra-thick melanoma.

Melanoma progression model

non-tumorigenic radial growth phase (RGP)	tumorigenic vertical growth phase (VGP)
intraepidermal RGP	early VGP
microinvasive RGP	late VGP

fact, at the onset, a melanoma is characterised by a non-tumorigenic radial growth phase (RGP), inside the epidermis (intraepidermal) or within the papillary dermis (microinvasive), devoid of metastatic potential, which may be followed, early or late, by a tumorigenic vertical growth phase (VGP), with deeper extension in the dermis or beyond, nodular confluence, mitotic activity and

metastatic capacity (tab. 1). The unique exception to this is represented by nodular melanoma, in which either RGP is rapidly overrun by VGP or the tumour arises directly from dermal melanocytes [6]. Today, the Breslow depth remains the single most important prognostic factor for clinically localised primary melanoma – it allows the identification of melanoma as ultra-thin (≤ 0.5 mm), thin (≤ 1 mm), thick (> 1 mm) or ultra-thick (> 6 mm) [7,8]. The systematic application of the histogenetic model to the Breslow depth explains the debated reason why some thin melanoma behave aggressively, because they possess an early tumorigenic VGP inside them [9]. Moreover, any diagnostic report should also be accompanied by further well-known microstaging attributes, such as Clark level, mitotic count, lymphovascular invasion, perineural in-

filtration, ulceration, satellitosis, tumour infiltrating lymphocytes and, if available, sentinel lymph node status [10,11]. In conclusion, we believe that a renewed histogenetic approach to melanoma diagnosis deserves a wide scientific dissemination, for a better clinical management of individual cases in the era of personalised medicine.

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