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# Subepidermal cleft formation as a diagnostic marker for cutaneous malignant melanoma

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This article is dedicated to A. Bernard Ackerman, a master in dermatopathology, a magnificent teacher, and a generous friend.

**Keywords:**
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**Summary** Cleft formation has been postulated as a clue to the histopathological diagnosis of malignant melanoma (MM). The frequency and reliability of clefts as a diagnostic criterion remain to be determined. We reviewed 503 cases of histologically proven MM searching for clefting between the epidermal layer and underlying MM. Cleft was defined as a separation of at least 0.3 mm in length. Conspicuous cleft formation was present in 120 (24%) of 503 MMs. The presence of clefts was not associated with age or sex of the patients, but showed a slight predilection for the back, a slightly higher prevalence in superficial spreading type of MM and for tumors with a Breslow thickness between 1 and 2 mm. Morphologically, clefts could be separated in 3 different types: linear (37.5%), single-nest (10.9%), and multi-nest (51.6%). In comparison, among 939 benign melanocytic lesions including 100 Spitz or Reed nevi, only 9 exhibited clefts longer than 0.3 mm (<1%). One was an atypical compound nevus; all others were Spitz nevi, with the majority exhibiting an arched morphology above 1 or 2 large round nests. The relative frequency of cleft formation allowed a highly significant differentiation between MM and benign melanocytic lesions. Clefts are a reliable diagnostic criterion in favor of MM.


## 1. Introduction

In 1991, Ackerman [1] stated in "Clues to diagnosis in dermatopathology": "An elongated cleft, parallel to the surface of the skin, that separates epidermal keratinocytes from neoplastic melanocytes is a clue to malignant melanoma." As clear as this statement is, it remains unclear how often and how reliably this criterion can be applied for the diagnosis of malignant melanoma (MM). Thus, we examined a spectrum of cases of MM and compared them to benign melanocytic lesions to determine the frequency of occurrence, the morphological appearance, and the extent of cleft formation between the epidermis and underlying melanocytic cells in both classes of lesions.

## 2. Material and methods

A total of 529 MM were retrieved from the files of the Dermatopathology Unit at the Department of Dermatology and Allergy, Technical University Munich, covering a total of 36 637 cases from 1993 to 2001. The original slides were

*Abbreviations:* COE, consumption of the epidermis; LM, lentigo maligna; MIS, melanoma in situ; MM, malignant melanoma; SSM, superficial spreading malignant melanoma.

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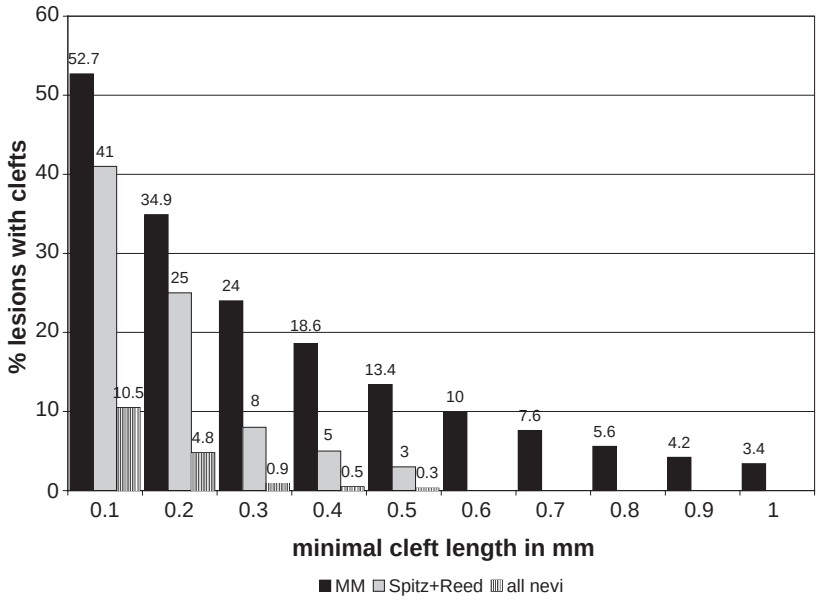


**Fig. 1** Percentage of melanocytic lesions with clefts of at least the indicated length.

reviewed and new sections were prepared when necessary. The slides had been routinely fixed in 3.7% buffered formalin and stained with hematoxylin and eosin. Twenty-six cases had to be excluded from the final study, because they could not be evaluated appropriately (eg, no sections or blocks available, small punch biopsies, smashed or squeezed material, recurrent or metastatic MM, incorrect diagnosis). In addition, 100 cases of Spitz and Reed nevi from the same period and 840 consecutive cases of benign melanocytic nevi except blue nevi from 2001 were selected as a control group. One case of an atypical junctional nevus derived from a 72-year-old patient with melanoma was excluded from the control group, because it was retrospectively diagnosed as lentigo maligna (LM). Thus, 503 primary MM and 939 melanocytic nevi were investigated for the presence or absence of clefts between the melanocytic lesion and the overlying epidermis.

Cleft was defined as a separation between the epidermis and underlying melanocytic cells at the epidermal-dermal junction with a length of at least 0.1 mm. The length was usually measured at a magnification of 100× using an ocular containing a crossline micrometer. Disruptions of the epidermis overlying such separations were not accepted as clefts, as they were interpreted as being caused mainly by mechanical force during technical processing.

Cleft formation was further divided morphologically into 3 different groups designated as linear, single-nest, or multi-nest. Linear clefting was characterized by separation above single melanocytes or small groups located linearly along the epidermal-dermal junction. Single-nest clefts occurred

**Table 1** Distribution of clefts in different anatomical sites and sexes

| Location | MM total (%) | MM with clefts (%) | MM without clefts (%) |
|---|---|---|---|
| Total number | 503 (100) | 120 (100) | 383 (100) |
| Male | 253 (50.3) | 63 (52.5) | 190 (49.6) |
| Female | 250 (49.7) | 57 (47.5) | 193 (50.4) |
| Head | 88 (17.5) | 13 (10.8) | 75 (19.6) |
| Male | 41 (8.2) | 8 (6.6) | 33 (8.6) |
| Female | 47 (9.3) | 5 (4.2) | 42 (11.0) |
| Front | 69 (13.7) | 17 (14.2) | 52 (13.6) |
| Male | 48 (9.5) | 10 (8.4) | 38 (9.9) |
| Female | 21 (4.2) | 7 (5.8) | 14 (3.7) |
| Back | 149 (29.7) | 46 (38.3) | 103 (26.9) |
| Male | 107 (21.3) | 31 (25.8) | 76 (19.9) |
| Female | 42 (8.4) | 15 (12.5) | 27 (7.0) |
| Upper extremity | 75 (14.9) | 18 (15.0) | 58 (15.1) |
| Male | 28 (5.6) | 7 (5.8) | 22 (5.7) |
| Female | 47 (9.3) | 11 (9.2) | 36 (9.4) |
| Lower extremity | 121 (24.1) | 26 (21.7) | 95 (24.8) |
| Male | 28 (5.6) | 7 (5.8) | 21 (5.5) |
| Female | 93 (18.5) | 19 (15.9) | 74 (19.3) |

**Table 2** Cleft formation among different types of malignant melanoma

| MM subtypes (cases) | MM with clefts (%) | MM without clefts (%) |
|---|---|---|
| Total (503) | 120 (23.9) | 383 (76.1) |
| SSM (229) | 65 (28.4) | 164 (71.6) |
| NM (106) | 25 (23.6) | 81 (76.4) |
| LMM (38) | 10 (26.3) | 28 (73.7) |
| ALM (19) | 5 (26.3) | 14 (73.7) |
| MIS (70) | 11 (15.7) | 59 (84.3) |
| LM (39) | 3 (7.7) | 36 (92.3) |
| Others (2) | 1 (50) | 1 (50) |