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Are the neck malignant melanomas different from the ones affecting the head? Clinicopathologic, dermoscopic and prognostic findings

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Abstract

Background: Malignant melanomas of the head and neck are usually considered as a unique entity in comparison to other body sites. However, no characterization of neck melanoma has been performed so far, despite the clear anatomic and histological differences. **Aim:** We investigated clinical, demographic, histological and dermoscopic differences between face, scalp and neck melanoma. **Materials and methods:** A retrospective analysis of medical and histologic records from 116 melanomas of the head and neck area collected between January 2003 and January 2008 was performed. Body site, gender, age, number of lesions, age at first melanoma diagnosis, size, Clark level, association with nevi, presence or absence of mitoses and/or ulceration, presence of synchronous and/or metachronous melanoma were recorded. Moreover, digital dermoscopy images of 92 melanomas of the head and neck area were analyzed for main dermoscopic patterns and lesion diameter. **Results:** Significant differences in Breslow thickness, ex-naevo origin and tumor size among neck and face-scalp melanomas were observed. Neck MM patients were younger than those with MM of face and scalp. In contrast to scalp and face, no patient died from neck melanoma. Dermoscopic patterns were similar to those of trunk-limbs MM, and no lesion showed a lentigo maligna pattern which was observed in most lesions of the face. **Conclusion:** Melanomas of the neck must be distinguished from face and scalp melanomas because of younger age, different dermoscopic patterns and ex-naevo origin and better prognosis. These data should be taken into account both from an epidemiological and clinical point of view.

Introduction

Head and neck Malignant Melanomas (MMs) are usually considered a unique entity with common clinico-pathological features with respect to MMs of other body sites. Several studies analyzed MMs of this anatomic macro-region, including the scalp, the face, and the neck in comparison with other body sites (1,2). The main reason for this melanoma categorization is that head and neck are more heavily exposed to UV radiation than any other body site and that the surgical approach is customarily performed by head and neck surgeons, who treat these lesions without differentiating the specific anatomic locations.

Some studies highlighted the differences between MMs of the scalp and of face/neck (1) showing a 5 year overall survival rate of 81.8% for face and neck and 66.7% for the scalp, as well as specific dermoscopic patterns for scalp tumors (3). However, to the best of our knowledge, no specific evidence regarding the neck versus the facial localization is reported in literature. It is recognized that between neck and face skin there are clearly evident anatomic and cyto-architectural differences, concerning the peculiar vascular and lymphatic drainage patterns, the dermal-epidermal junction, the dermis and hair follicles size and density (4). Less data are available for the clinico-pathologic, dermoscopic, and prognostic features of melanocytic lesions differentiating these two contiguous but different anatomic regions.

Lentigo maligna melanoma (LMM), for which delayed diagnosis is common due to its inconspicuous presentation at an early stage, represents the most common type of melanoma on the face. Clinically, the well-known “ABCD rule” cannot be applied to facial lesions (5). From a dermoscopic point of view it is known that this efficient non-invasive technique increases the rate of correct melanoma diagnosis by using criteria involving different patterns and/or structures for melanocytic lesions (6), which are site specific for three distinct anatomic locations: head (including scalp and face), trunk/limbs and palmo-plantar region (7). MMs of the face do not show the classical dermoscopic findings typically observed elsewhere on the skin (8). Stolz et al. described four steps of LMM invasion of the hair follicles observed by dermoscopy (9). In this study we analyzed the clinico-

pathologic, dermoscopic, and prognostic differences between head, scalp and neck malignant melanoma.

Materials and methods

This study was carried out at the Department of Dermatology of the University of Modena and Reggio Emilia based on a retrospective analysis of 116 MMs of the head and neck area recorded between January 2003 and January 2008. The study design, criteria for inclusion and therapeutic protocol were approved by the ethical committee of the same University. Patients' clinical data, such as anatomic distribution, gender, age, number of lesions, age at first melanoma diagnosis, size, Clark level, association with nevi, presence or absence of mitoses and/or ulceration, presence of synchronous and/or metachronous melanoma were tabulated via medical records. Patients were classified in according with the American Joint Committee on Cancer (AJCC) staging system basing on the characteristics of the first lesion (10,11).

The inclusion criteria for head and neck melanoma were:

- patients of both genders older than 18 years, Caucasian race, with at least one melanoma in the head and neck area clinically diagnosed and histologically proven;
- availability of medical records with complete demographic, clinical and radiological procedures performed at diagnosis and repeated every 12 months during follow-up;
- patients with at least three years of follow-up.

Exclusion criteria encompassed:

- patients with pigmented lesions localized on mucosal surfaces (oral mucosa, nasal mucosa);
- patients with recurrences, in transit, and distant metastases or unknown primary melanomas;
- patients with incomplete histopathological data.

Dermoscopy

Dermoscopic images were recorded by means of a digital videomicroscope (FotoFinder, TeachScreen software GmbH, Bad Birnbach, Germany), using a 20- and a 50-fold magnification. The instrument

and the calibration method have already been described elsewhere (12). Images were examined by 3 expert dermoscopists for classification into main dermoscopic patterns (12-17). The lesion was definitely attributed to a group when at least two observers agreed.

Atypical pseudonetwork, the lentigo maligna main pattern, was defined by Schiffner et al. for the diagnosis of facial melanoma, as the presence of asymmetric pigmented hair follicular openings, rhomboidal structures, annular-granular structures, black dots within the hair follicle or destruction of the hair follicles (Figure 1 and 2) (17). The reticular-globular pattern included lesions with the contemporary presence of network and globules, whereas when structureless areas coexisted with globules, we adopted the term homogeneous-globular (Figure 3a). In the group with island, we comprised lesions containing a well circumscribed lesion area, showing a uniform dermoscopic pattern, differing from the one present in the rest of the lesion (14). Amelanotic pattern included lesions without recognizable pigmented structures (15). The flat-nodular pattern (Figure 3b) was recognized in lesions showing a nodular component and some areas at the periphery where an atypical pseudonetwork was identifiable (15). Finally, an aspecific pattern was attributed to MMs not categorized in other subgroups. Differences between MMs of face, scalp and neck were studied employing demographic and dermoscopic data.

Data analysis

A statistical analysis was carried out using the Statistical Package for the Social Science (SPSS), Version 9.02 for Windows®. Data were expressed as mean and standard deviation (SD). Differences between in the different groups were calculated by Kruskal-Wallis test. *P*-values below 0.05 for all tests were considered statistically significant.

Results

During the study period January 2003 - January 2008, 1256 patients were diagnosed with melanoma in different body areas at the Department of Dermatology of the University of Modena. A subgroup of 116 patients were diagnosed with MMs in the head and neck area, comprising 93 patients with melanoma of the face, 13 patients with melanoma of the scalp and 10 patients with melanoma of the

neck. As regards face involvement, the most affected site was the cheek (28.4%) followed by the zygomatic area (13.7%) and the forehead (7.8%), while 13 (11.2%) MMs were localized on the scalp and 10 (8.6%) in the neck area.

Demographic data for each patient subgroup are described in Table 1. The estimated overall 10-year survival rate (according to the method of Kaplan-Meier) was calculated for the three different anatomical areas (Figure 4).

Patients affected by MMs of the neck area were significantly younger, with a mean age at diagnosis of 62.6 ± 11.8 years (CI 54.2-71.03). Instead, patients with MMs localized on the face were significantly older, with a mean age at diagnosis of 73.9 ± 11.5 years (CI 71.6-76.2).

Thickness and diameter of lesions were significantly different between scalp MMs and lesions of the face and neck. Lesions with a Breslow's thickness >4 were more frequently present among scalp MMs compared to face and neck MMs. The percentage of lesion with mitoses was higher on the face, while the mean number of mitoses was higher for scalp lesions.

An *ex-naevo* origin was observable in 13.92% of lesions on the face, in 14.29% of scalp lesions, and in 50% of neck lesions. As concerning the staging, patients were assigned to the AJCC classification on the basis of characteristics of the first melanoma (Table 2). Of 13 MMs located on the scalp, 5 (38.5%) were stage IIB compared to face (5.38%) and neck (0%) MMs.

Positive sentinel lymph nodes were more frequently present in 4 (30.8%) patients with melanoma of the scalp. Melanoma was a significant cause of death among patients with a scalp localization.

Multiple primary MMs were diagnosed only in 6 patients with melanoma localized in the face area: in 4 patients they were synchronous while in 2 patient metachronous.

Dermoscopic images were available for face MMs in 71 cases, for scalp MMs in 11 cases, and for neck ones in 10 subjects. Table 3 illustrates the dermoscopic, clinical and histological aspects of 82 face/scalp MMs, whose dermoscopic images were available, according to thickness. The following main dermoscopic patterns were recognized in face and scalp MMs: atypical pseudonetwork (67 cases), flat-nodular (9 cases), amelanotic (2 cases), reticular-globular (one case), homogeneous-

globular (one case), island (one case) and aspecific (one case). When subdividing face and scalp MMs according to thickness range, diameter did not significantly vary according in the different subgroups, whereas main dermoscopic patterns were differently distributed. The lentigo maligna (atypical pseudonetwork) pattern was observable in most MMs thinner than 2 mm. Among MMs in situ, one lesion was amelanotic and another one showed the contemporary presence of network and globules; thin invasive MMs (<1 mm) showed an amelanotic aspect in one case, the presence of structureless pigmentation and globules in one case and an island pattern in one case. All lesions 1-2 mm thick showed the lentigo maligna pattern, whereas thicker ones presented a flat-nodular pattern in 9 cases and an aspecific one in one case.

Neck MMs displayed reticular (2 cases), reticular-globular (2 cases), homogeneous (2 cases), multicomponent (1 case), globular-structureless (1 case), dermoscopic island (1 cases) and aspecific (1 case) main patterns. No neck melanoma showed a lentigo maligna pattern.

Discussion

The analysis of the clinic and pathological differences between MMs of the face and of the neck revealed that the latter localization is quite uncommon and associated to better prognosis, when compared to the face, although the effective reasons of such evidence are still unclear. Our data confirm that neck and scalp MMs predominate in men (2); the reason of this observation may be that men are often bald-headed and tend to have shorter hair than women with a relative more intensive neck exposure to UV radiation. In contrast to what previously described (18) patients with neck melanoma tend to be younger than those with MMs arising on the face/scalp, independent of the histologic subtype.

It is already well known that scalp tumors have the worst prognosis compared to their counterparts in other localizations (1-3). However, in contrast to scalp melanoma, the prognosis of neck melanoma may be influenced by different factors which can have an critical impact on the prognosis, i.e. the easier detection on glabrous skin and the different lymphatic and vascular drainage patterns involved in the growth and spreading patterns. In particular, previous studies demonstrate that cutaneous

lymphatic drainage pathways display anatomic variations among patients, especially in the head and neck area (19-21). It is important to note that more than 40% of MMs of the anterior and posterior lower neck show discordancy from clinically predicted lymphatic drainage showing multiple, varied and asymmetric lymphatic drainage patterns possibly associated to higher metastatic potential (22). However, our data do not confirm literature observations regarding the worse prognosis of neck melanoma.

While sun exposure may plays an equivalent role in the development of face and neck MMs, differences in early detection and prognosis could be related to peculiar anatomic features of neck skin, which is similar to other body sites', but very different from facial skin. In fact, the latter is distinguished by a flat dermal-epidermal junction and hair follicles of higher size and density (4) possibly responsible for the higher density of vascular and lymphatic structures, as well as for a higher mitotic activity in the basal layer, that might anticipate tumor invasion and the transition from horizontal to vertical growth.

Dermoscopic patterns vary according to skin site. For face and acral lesions peculiar dermoscopic patterns have been identified, showing striking differences with respect to those employed for diagnostic analysis of lesions located on trunk and limbs. These differences rely on the anatomic characteristics of facial skin presenting a higher size and density of pilosebaceous units (4). Schiffner et al. first described the evolving lentigo maligna pattern in facial melanoma underlying its peculiar mode of growth (17). However, to the best of our knowledge other peculiar dermoscopic patterns of face and scalp MMs, especially referring to their vertical growth phase, have not been described so far. In this study we showed that most facial MMs maintain the lentigo maligna pattern until they reach the thickness of 2 mm. Above this threshold, a so called flat-nodular pattern is observable, characterized by a flat component often presenting a rhomboidal structure, and a vertical component showing structureless pigmentation. In most of these lesions the characteristic melanoma features observable in MMs at other skin sites are not identifiable, and this may correspond to a peculiar biological behavior of MMs of face and scalp, also supported by a higher rate of lesions starting *de-*

novo and not related to a malignant transformation of a nevus. On the contrary, neck MMs present a variety of dermoscopic patterns such as those found in malignant melanocytic lesions located at other skin sites, and accordingly, their age of onset and *ex-naevo* origin reflects the one of non-head MMs. Scientific literature usually reports head and neck MMs as an unique entity; this creates a methodological and clinical bias since the two locations might give rise to tumors with different biological behavior. As a consequence, epidemiologic data obtained from medical records including both melanoma sites may be prejudiced, and patients are followed with the same treatment and follow-up protocols. We suggest therefore that MMs of the face should be equalized to its scalp counterpart for diagnosis and surveillance, and that neck MMs should be assimilated to those of trunk-limbs ones. In particular, the very poor prognosis of scalp melanoma as well as face tumors must be taken into account in order to better differentiate detection processes, surgical management and follow-up strategies.

Conclusions

The main evidences of this single-institution study can be summarized as following:

1) Although scientific literature has stressed the differences between MMs of the scalp and other head-neck locations, the characterization of neck melanoma is still not clear. We conclude that melanoma of the neck represent a distinct entity from the clinic-pathological, dermoscopic and prognostic features and should therefore be separated by its facial counterpart in the clinical assessment and management.
2) The anatomical peculiarities of the cutaneous districts are reflected in the related dermoscopic patterns. As a consequence, the skin of the neck does not present the same dermoscopic features as the face and scalp but rather those of the trunk.
3) The very poor prognosis of scalp melanoma as well as face tumors must be taken into account in order to better differentiate detection processes, surgical management and follow-up strategies.

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Table 1. Clinical, histological and dermoscopic characteristics of scalp, face and neck melanomas

	Face	Scalp	Neck	Face *vs* Scalp	Face *vs* Neck	Scalp *vs* Neck	*P*-value (Kruskal-Wallis test)
Patients (%)	93 (80.2%)	13 (11.2%)	10 (8.6%)	<0.001	<0.001	<0.001	<0.0001
Female	39 (41.9%)	4 (30.8%)	2 (20%)	>0.05	>0.05	>0.05	0.3
Male	54 (58.1%)	9 (69.2%)	8 (80%)	>0.05	>0.05	>0.05	0.3
Age	73.9 ± 11.5 (CI 71.6-76.2)	68.5 ± 16.9 (CI 58.2-78.7)	62.6 ± 11.8 (CI 54.2-71.03)	>0.05	<0.05	>0.05	0.02
Thickness (mm ± SD)	0.6 ± 1.4 (CI 0.3-0.9)	3.9 ± 4.5 (CI 1.2-6.6)	0.6 ± 0.9 (CI 0.02-1.2)	>0.05	>0.05	>0.05	0.04
Diameter (mm ± SD)	15.3 ± 8 (CI 13.6-16.9)	21.3 ± 13.8 (CI 12.9-29.7)	14.6 ± 7.4 (CI 9.3-19.9)	>0.05	>0.05	>0.05	0.43
Lesions with mitoses	13 (11.2%)	7 (6.01%)	2 (1.7%)	<0.01	>0.05	>0.05	<0.003
Mean number of mitoses	0.6 ± 3.4 (CI 0.03-1.4)	6.6 ± 13.9 (CI 1.8-15)	1 ± 2.8 (CI 1-3)				
Ex-naevo/*de-novo*	13.92%	14.29%	50%	>0.05	<0.01	>0.05	0.007
Clark level							
I	51 (54.8%)	0 (0%)	3 (30%)	<0.001	>0.05	>0.05	0.0006
II	29 (31.2%)	2 (15.4%)	4 (40%)	>0.05	>0.05	>0.05	0.4
III	7 (7.5%)	1 (7.7%)	2 (20%)	>0.05	>0.05	>0.05	0.4
IV	6 (6.5%)	1 (7.7%)	1 (10%)	>0.05	>0.05	>0.05	0.3

V	4 (4.3%)	5 (38.5%)	0 (0%)	<0.001	>0.05	<0.01	<0.0001
Breslow's thickness							
MIS	51 (54.8%)	3 (23.1%)	3 (30%)	>0.05	>0.05	>0.05	0.04
≤1.00	33 (35.5%)	3 (23.1%)	6 (60%)	>0.05	>0.05	>0.05	0.2
1.01-2.00	6 (6.5%)	0 (0%)	0 (0%)	>0.05	>0.05	>0.05	0.5
2.01-4.00	2 (2.2%)	0 (0%)	1 (10%)	>0.05	>0.05	>0.05	0.3
>4.00	5 (5.3%)	6 (46.2%)	0 (0%)	<0.001	>0.05	<0.001	<0.0001
Sentinel lymph nodes							
Positive	1 (1.1%)	2 (15.4%)	1 (10%)	<0.05	>0.05	>0.05	0.02
Negative	5 (5.3%)	2 (15.4%)	0 (0%)	>0.05	>0.05	>0.05	0.3
Not done	88 (94.6%)	9 (69.2%)	9 (10%)	<0.01	>0.05	>0.05	0.009
Multiple primary melanomas							
Synchronous	0 (0%)	4 (30.8%)	0 (0%)	<0.001	>0.05	<0.001	0.0001
Metachronous	0 (0%)	2 (15.4%)	0 (0%)	<0.001	>0.05	<0.05	0.0003
5-years overall survival	89 (95.7%)	9 (64.3%)	10 (100%)	<0.05	<0.001	<0.001	<0.0001

Table 2. Clinical staging of all melanoma lesions

Stage at initial diagnosis	Face	Scalp	Neck	Face *vs* Scalp	Face *vs* Neck	Scalp *vs* Neck	*P*-value (Kruskal-Wallis test)
0	49 (42.2%)	4 (3.4%)	2 (1.7%)	>0.05	>0.05	>0.05	0.06
IA	27 (23.3%)	3 (2.6%)	7 (6.03%)	>0.05	>0.05	>0.05	0.1
IB	9 (7.8%)	0 (0%)	0 (0%)	>0.05	>0.05	>0.05	0.3
IIA	2 (1.7%)	0 (0%)	0 (0%)	>0.05	>0.05	>0.05	0.8
IIB	5 (4.3%)	5 (4.3%)	0 (0%)	<0.001	>0.05	<0.01	0.0002
IIC	0 (0%)	0 (0%)	0 (0%)	0	0	0	0
IIIA	1 (0.09%)	1 (0.09%)	1 (0.09%)	>0.05	>0.05	>0.05	0.11
IIIB	0 (0%)	0 (0%)	0 (0%)	0	0	0	0
IIIC	0 (0%)	0 (0%)	0 (0%)	0	0	0	0
IV	0 (0%)	0 (0%)	0 (0%)	0	0	0	0
Unknown	0 (0%)	0 (0%)	0 (0%)	0	0	0	0

Table 3. Dermoscopic, clinical and histological aspects of 82 face/scalp melanomas according to thickness

Thickness (mm) (mean ± SD)	Age (years) (mean ± SD)	Gender (male/total)	Site (cheek/total)	Diameter (mm) (mean ± SD)	Lentigo maligna	Flat-nodular	Amelanotic	Reticular-globular	Homogeneous-globular	Island	Aspecific	Total
0	71.97 ± 8.81	21/39	24/39	14.34 ± 7.09	37	0	1	1	0	0	0	39
0.01-1 (0.40 ± 0.20)	76.27 ± 9.84	15/28	28/28	18.55 ± 10.39	25	0	1	0	1	1	0	28
1.01-2 (1.34 ± 025)	83.4 ± 7.57	3/5	2/5	12.78 ± 3.26	5	0	0	0	0	0	0	5
>2.01 (6.11 ± 1.68)	67.4 ± 23.44	8/10	8/10	15.17 ± 1.05	0	9	0	0	0	0	1	10
0-9	73 ± 11.84	47/82	62/82	15.78 ± 8.2	67	9	2	1	1	1	1	82

71 face melanomas including: cheek (44), nose (9), forehead (8), temple (4), ear (4), and lower lid (2)

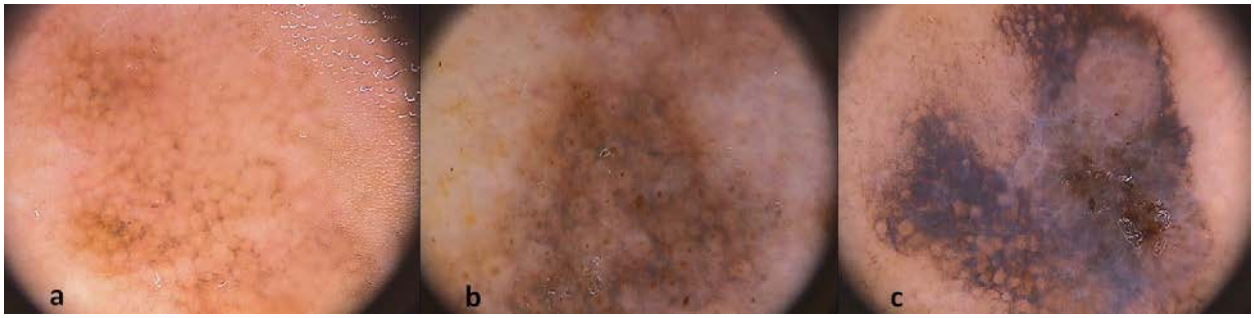

Figure 1. Lentigo maligna progression as assessed by dermoscopy (FotoFinder, 20-fold magnification): a) light brown pigmentation around follicular openings; b) dark brown and grey-blue rhomboidal structures around hair follicles; c) besides rhomboidal structures, homogeneous grey-blue pigmentation occluding hair follicle openings can be seen along with a nodular component.

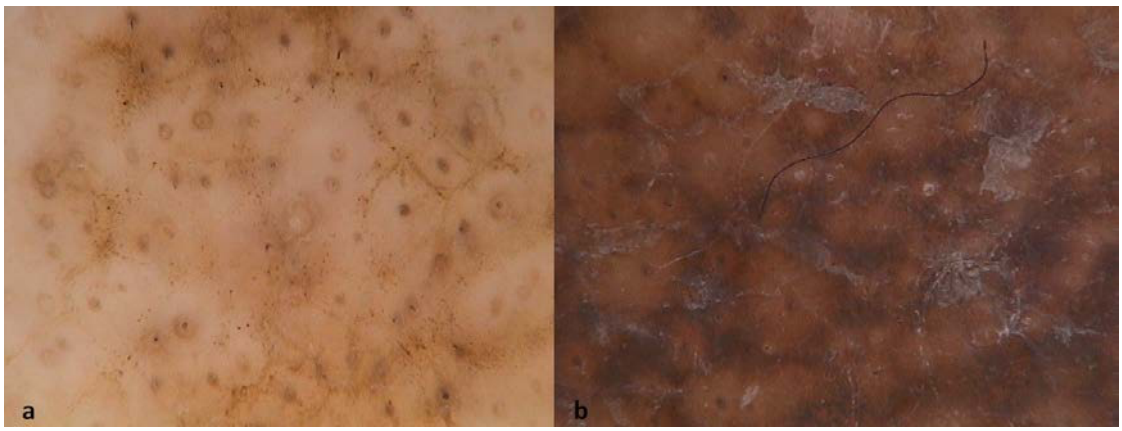

Figure 2. Lentigo maligna progression as assessed by high magnification dermoscopy (FotoFinder, 50-fold magnification): a) follicular openings appear as target structures with a perifollicular halo surrounding a small dot in the centre; light brown and dotted rhomboidal structures around hair follicles are also visible; b) dark brown and grey-blue rhomboidal structures centered by gray-blue hair follicles and homogeneous grey-blue pigmentation.

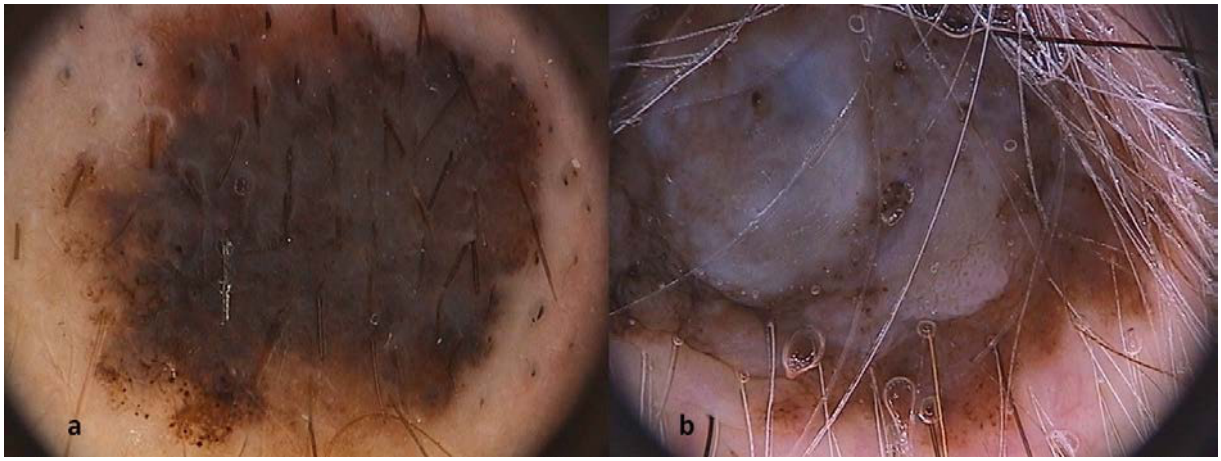

Figure 3. Melanoma of the face/scalp: a) the homogeneous-globular pattern in a melanoma on the cheek; b) the flat-nodular pattern in a melanoma on the scalp.

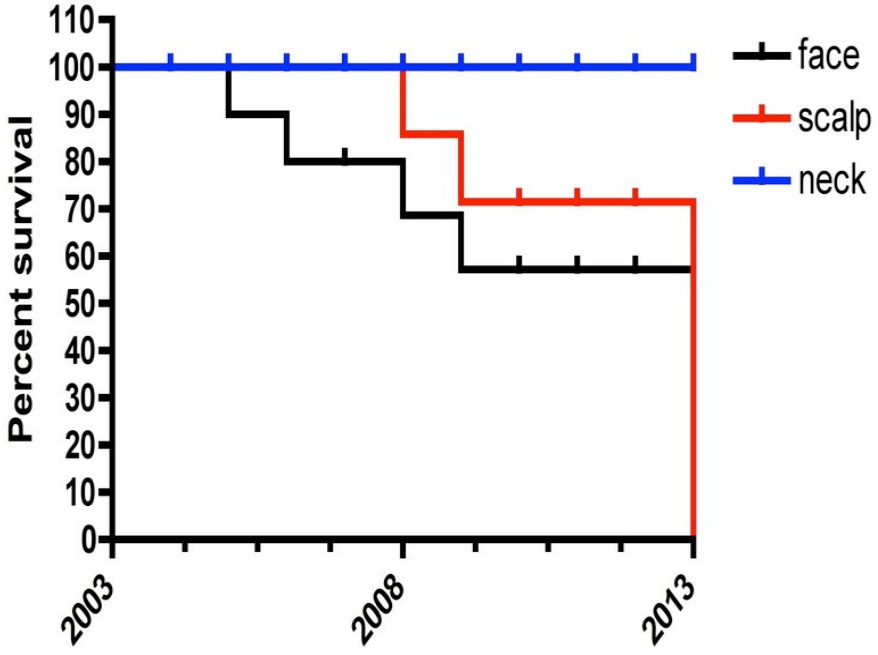

Figure 4. Kaplan-Meier 10-year overall survival estimated for different anatomical areas: face, scalp and neck.