Sclerodermiform basal cell carcinomas vs. other histotypes: analysis of specific demographic, clinical and dermatoscopic features

C. Conforti,1,* M.A. Pizzichetta,1,2 S. Vichi,1 F. Toffolutti,3 D. Serraino,3 N. Di Meo,1 R. Giulfrida,4 T. Deinlein,5 J. Giacomel,6 C. Rosendahl,7 J.Y. Gourhant,8 I. Zalaudek1

1Dermatology Clinic, Maggiore Hospital, University of Trieste, Trieste, Italy
2Department of Medical Oncology-Preventive Oncology, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Aviano, Italy
3Unit of Cancer Epidemiology, Centro di Riferimento Oncologico di Aviano, IRCCS, Aviano, Italy
4Department of Clinical and Experimental Medicine, Dermatology Section, University of Messina, Messina, Italy
5Department of Dermatology, Medical University of Graz, Graz, Austria
6Skin Spectrum Medical Services, Como, WA, Australia
7School of Clinical Medicine, The University of Queensland, Brisbane, QLD, Australia
8Centre de Dermatologie, Nemours, France
*Correspondence: C. Conforti. E-mail: claudioconforti@yahoo.com

Abstract

Background Among the various types of basal cell carcinoma, the sclerodermiform variant has a high risk of recurrence and local invasiveness. A systematic description of the dermatoscopic features associated with specific body localization is lacking.

Objectives To describe the clinical and dermoscopic features of sclerodermiform basal cell carcinoma (BCC) according to localization in the body confronting with superficial and nodular types.

Methods Clinical and dermoscopic images of sclerodermiform, nodular and superficial BCCs were retrospectively evaluated to study the location in the various body districts, maximum diameter, clinical appearance of the lesion, features of edges and presence or absence of specific dermatoscopic criteria of BCCs.

Results We examined 291 histopathologically proven BCCs showing that in nodular BCCs, classical arborizing vessels were more frequently found in the body macro-area (trunk and limbs; n = 46, 97.9%) than in the head/neck area (n = 43, 82.7%); within sclerodermiform BCCs, short arborizing vessels were found more frequently in the head/neck district (n = 35, 49.3%) than in the body (n = 6, 23.1%; P-value 0.02); within nodular BCCs, multiple blue-grey dots and globules were more frequently found on the trunk (n = 23, 48.9%) than in the head/neck district (n = 12, 23.1%; P-value 0.01). In sclerodermiform BCCs, ulceration was found more frequently in the head/neck district (n = 38, 53.5%) than in the body (n = 4, 15.4%; P-value > 0.01), and in superficial BCCs, ulceration was found more frequently in the head/neck district (n = 5, 38.5%) than in the body (n = 8, 9.8%; P-value 0.02).

Conclusion Our study shows that superficial BCC are found frequently in the head/neck district dermoscopically characterized by ulceration and arborizing vessels; nodular BCCs are more frequently found in the body than in the head/neck district, and the dermoscopic pattern is characterized by the combination of three features: (i) classical arborizing vessels, (ii) multiple blue-grey dots and (iii) globules. Instead, sclerodermiform BCC is preferentially located in areas at high-moderate risk of recurrence; if pink-white areas and/or fine arborizing vessels are seen, clinicians should consider this diagnosis. Furthermore, location-specific dermatoscopic criteria have been described.

Received: 14 January 2020; Accepted: 21 April 2020

Conflicts of interest
None.

Funding source
None.
Introduction
Basal cell carcinoma (BCC) is a slow-growing and mostly locally invasive tumour, and its incidence is increasing worldwide. Among BCCs, different histotypes with aggressive growth patterns can be distinguished, of which sclerodermiform BCC (sdBCC) is one of the most important variant, presenting a higher risk of local invasiveness, perineural invasiveness and distant metastasis than subtypes with non-aggressive growth patterns, such as nodular (nBCC) and superficial BCC (sBCC), which show a significantly lower risk of such events. Dermatoscopy is a fundamental tool for the diagnosis and management of BCC; frequent criteria for the diagnosis are ulceration, arborizing vessels, ovoid nests and many others that help to differentiate a pigmented BCC (pBCC) from a non-pigmented BCC and, within non-pigmented BCC, can allow to distinguish between a nodular, superficial or morphoeform subtype; to date, sdBCC remains a difficult lesion to diagnose, as it appears clinically as a slow-growing, skin-coloured plaque, which the patient interprets as something harmless; in addition, vascular dermatoscopic patterns typically develop in an advanced stage, which makes the early diagnosis of sdBCC complex. SdBCC is also a difficult lesion to treat because it is characterized by deep tissue destruction, subclinical extension, as well as high rates of local recurrence and poor prognosis if treatment is not started at an early stage. The aim of this study is to obtain a better characterization of sdBCC from a demographic, clinical and dermoscopic point of view compared to non-aggressive histotypes. This knowledge will enable the clinicians to diagnose these lesions earlier, differentiate them from other clinical histological subtypes and skin neoplasms, and consequently choose targeted therapies, reducing the risk of recurrence and improve the patient’s quality of life.

Material and methods
A retrospective observational analysis was conducted on three groups of patients, affected, respectively, by nodular, superficial or sclerodermiform BCC, for a total of 291 patients:

1 Ninety-seven patients who had suffered excision of sdBCC in 2016 at the Dermatological Clinic of Graz (Austria), Perth or Capalaba (Australia).
2 Ninety-nine patients who suffered excision of nBCC between January and March 2019 at the Dermatological Clinic of Trieste (Italy).
3 Ninety-five patients with sBCC, histologically confirmed by skin biopsy, who underwent MAL-PDT between March 2018 and March 2019 at the Dermatological Clinic of Trieste.

Patients from Trieste, Graz, Perth and Capalaba were identified through authorized records of the respective centres; the clinical and dermatoscopic image was then taken from an authorized image storage database. All dermatoscopic images were acquired with a polarized light dermatoscope, in non-contact mode, associated with a camera. The following data were collected for each patient and then entered in an Excel table: sex and age of the patient, histotypes of BCC, location in the various body districts, maximum diameter expressed in mm, clinical appearance of the lesion, edges, presence/absence of dermatoscopic criteria of BCCs.

For the statistical analysis, descriptive statistics were used to compare histotypes according to demographic, clinical and dermoscopic features. Chi-square test or Fisher’s exact test or Kruskal–Wallis test were used, when appropriate, to assess the association between histotypes and clinical features. Unconditional logistic regression models were used to estimate odds ratio (OR) and their corresponding 95% confidence intervals (CIs) in order to explore the dermoscopic features associated with histotypes. Variables that were statistically significant in the univariate analysis were included in the multivariate model. We performed a hierarchical cluster analysis based on dermoscopic features/demographic, clinic and dermatoscopic features to generate three clusters; Ward’s clustering method was used. Chi-square test was used to evaluate the association between histotypes and clusters. All tests are two-tailed and were considered statistically significant for P-values below 0.05.

Results
Within the study population, the M/F ratio was found to be 1.8 : 1 for nBCCs, 1.4 : 1 for sdBCC and 1.2 : 1 for sBCCs, showing a higher incidence in men than in women; however, no statistically significant correlation between sex and histotype was found (P = 0.37). Regarding the median age at diagnosis, a statistically significant difference was found between sdBCC and sBCC [67 (55–78) years vs 73 (60–79) years; P = 0.02] and between sdBCC and nBCC [67 (55–78) years vs 76 (69–81) years; P < 0.01].

Clinical characteristics of collected BCC are summarized in Table 1. The macro-area of the head/neck district was more frequently involved in sdBCC than in nBCC and sBCC; the most frequently area affected by nBCCs was the periauricular region, followed by the nose, cheek and forehead. Instead, the trunk macro-area was more frequently affected by sBCC compared to nBCC and sdBCC while the limb macro-area was more frequently affected by sBCC compared to sdBCC and nBCC; the differences were statistically significant (P < 0.01; Table 1).

It is interesting to highlight that for sBCC, the most frequently affected region was the nose followed mainly by the cheek and the periauricular zone; in sBCC, the most frequently area involved was the neck followed by the periauricular region and the cheek (Table 1).

The distribution of BCC by dermatoscopic characteristics and histotype is summarized in Table 2. Within nBCCs, classical arborizing vessels were more frequently found in the body macro-area (trunk and limbs; n = 46,
**Table 1** Distribution of clinical features based on histotype

| Clinical features | Histotype                  | P-value‡ |
|-------------------|----------------------------|----------|
|                   | Nodular (n = 99)          | Sclerodermiform (n = 97) | Superficial (n = 95) |
|                   | n (%)                     | n (%)    | n (%)    |
| **Location**      | Head/neck                 | Scalp    | Forehead |
|                   | 52 (52.5)                 | 1 (1.0)  | 8 (8.1)  |
|                   | Scalp                     | 1 (1.0)  | 9 (9.3)  |
|                   | Periauricular              | 12 (12.1)| 12 (12.4)|
|                   | Periorbicular              | 1 (1.0)  | 6 (6.2)  |
|                   | Nose                      | 11 (11.1)| 16 (16.5)|
|                   | Cheek                     | 10 (10.1)| 15 (15.5)|
|                   | Perioral                  | 5 (5.1)  | 6 (6.2)  |
|                   | Neck                      | 4 (4.0)  | 3 (3.1)  |
|                   | Trunk                     | 33 (33.3)| 11 (11.3)|
|                   | Extremities               | 14 (14.1)| 15 (15.5)|
| **Clinical aspect** | Macule                    | 0 (0.0)  | 18 (18.6)|
|                   | Papule                    | 48 (48.5)| 10 (10.3)|
|                   | Plaque                    | 17 (18.3)| 39 (40.2)|
|                   | Nodule                    | 32 (34.4)| 0 (0.0)  |
|                   | Ulceration                | 2 (2.1)  | 30 (30.9)|
| **Edges**         | Well defined              | 77 (77.8)| 17 (17.5)|
|                   | Poorly defined            | 22 (22.2)| 80 (82.5)|
| **Median of maximum diameter in mm (IQR)** | 8 (6–11) | 7 (6–9) | 12 (9–14) |

Regarding the maximum diameter, there is a statistically significant difference between superficial and sclerodermiform (P-value 0.02) and between superficial and nodular (P-value < 0.01).

IQR, interquartile range.

‡The clinical aspects variable had 6 missing values in the group of nodular BCCs; †Pearson chi-squared test; §Test calculated on head/neck, trunk and limb macro-area frequencies by histotype; ¶Kruskal–Wallis test.

**Table 2** Distribution of dermatoscopic characteristics by site and histotype

| Dermoscopic features | Histotypes                  | P-value† |
|----------------------|----------------------------|----------|
|                      | Nodular (n = 52)           | Sclerodermiform (n = 71) | Superficial (n = 13) |
|                      | Head/neck (n = 47)         | Trunk (n = 26) | Head/neck (n = 82) |
|                      | n (%)                     | n (%)    | n (%)    | n (%)    |
| Classical arborizing vessels | Present | 43 (82.7) | 0 (0.0) | 13 (100.0) |
|                      | Absent                    | 9 (17.3)  | 71 (100.0)| 2 (2.4)  |
| Short arborizing vessels | Present | 5 (9.6)  | 35 (49.3) | 0 (0.0) |
|                      | Absent                    | 47 (90.4) | 36 (50.7) | 10 (76.9) |
| Multiple blue-grey dots and globules | Present | 12 (23.1) | 3 (4.2) | 0 (0.0) |
|                      | Absent                    | 40 (76.9) | 68 (95.8) | 13 (100.0) |
| Ulceration | Present | 13 (25.0) | 38 (53.5) | 5 (38.5) |
|                      | Absent                    | 39 (75.0) | 33 (46.5) | 8 (9.8)  |

†Pearson chi-squared test, unless otherwise specified; ‡Fisher’s exact test.
97.9%) than in the head/neck macro-area (n = 43, 82.7%); the difference was statistically significant (P = 0.02).

Within sdBCC, short arborizing vessels were found more frequently in the head/neck district (n = 35, 49.3%) than in the body (n = 6, 23.1%); the difference was statistically significant (P = 0.02).

Within nBCCs, multiple blue-grey dots and globules were more frequently found on the trunk (n = 23, 48.9%) than in the head/neck district (n = 12, 23.1%); the difference was statistically significant (P = 0.01). As far as sclerodermiform and superficial BCCs are concerned, on the contrary, no statistically significant correlation between the dermatoscopic multiple blue-grey dots and globules and the localization in the different macro-areas was found.

In sdBCC, ulceration was found more frequently in the head/neck district (n = 38, 53.5%) than in the body (n = 4).

**Table 3** Uni- and multivariate analyses of dermoscopic features of sclerodermiform basal cell carcinoma vs. other histotypes

| Dermoscopic features | Histotype | Univariate | Multivariate |
|----------------------|-----------|------------|-------------|
|                      | sdBCC (n = 97) | nBCC + sBCC (n = 194) |              |              |
| Classical arborizing vessels | Present | 1 (1.0) | 91 (46.9) | 0.01 (0.00-0.09) | <0.01 | 0.01 (0.00-0.11) | <0.01 |
| | Absent | 96 (99.0) | 103 (53.1) |              |              |              |              |
| Fine arborizing vessels | Present | 55 (56.7) | 48 (24.7) | 3.98 (2.37-6.68) | <0.01 | 5.17 (2.59-10.34) | <0.01 |
| | Absent | 42 (43.3) | 146 (75.3) |              |              |              |              |
| Short arborizing vessels | Present | 41 (42.3) | 83 (42.8) | 0.98 (0.60-1.60) | 0.93 |              |              |
| | Absent | 56 (57.7) | 111 (57.2) |              |              |              |              |
| Large blue-grey ovoid nests | Present | 0 (0.0) | 20 (10.3) |              | – | – | – |
| | Absent | 97 (100.0) | 174 (89.7) |              |              |              |              |
| Multiple blue-grey dots and globules | Present | 5 (5.2) | 35 (18.0) | 0.25 (0.09-0.65) | <0.01 | 1.93 (0.45-8.24) | 0.37 |
| | Absent | 92 (94.8) | 159 (82.0) |              |              |              |              |
| Focused dots | Present | 4 (4.1) | 22 (11.3) | 0.34 (0.11-1.01) | 0.05 |              |              |
| | Absent | 93 (95.9) | 172 (88.7) |              |              |              |              |
| Concentric structures | Present | 0 (0.0) | 11 (5.7) |              | – | – | – |
| | Absent | 97 (100.0) | 183 (94.3) |              |              |              |              |
| Spoke-wheel areas | Present | 0 (0.0) | 9 (4.6) |              | – | – | – |
| | Absent | 97 (100.0) | 185 (95.4) |              |              |              |              |
| Leaf-like areas | Present | 1 (1.0) | 9 (4.6) | 0.21 (0.03-1.72) | 0.15 |              |              |
| | Absent | 96 (99.0) | 185 (95.4) |              |              |              |              |
| Ulceration | Present | 42 (43.3) | 45 (23.2) | 2.53 (1.50-4.26) | <0.01 | 8.42 (3.63-19.55) | <0.01 |
| | Absent | 55 (56.7) | 149 (76.8) |              |              |              |              |
| Small erosions | Present | 27 (27.8) | 64 (33.0) | 0.78 (0.46-1.34) | 0.37 |              |              |
| | Absent | 70 (72.2) | 130 (67.0) |              |              |              |              |
| Pink-white areas | Present | 82 (84.5) | 89 (45.9) | 6.45 (3.47-11.97) | <0.01 | 4.26 (1.72-10.51) | <0.01 |
| | Absent | 15 (15.5) | 105 (54.1) |              |              |              |              |
| Short white streaks | Present | 12 (12.4) | 24 (12.4) | 1.00 (0.48-2.10) | 1.00 |              |              |
| | Absent | 85 (87.6) | 170 (87.6) |              |              |              |              |

sdBCC, superficial basal cell carcinoma; sdBCC sclerodermiform basal cell carcinoma; nBCC nodular basal cell carcinoma; OR, odds ratio; CI confidence interval

© 2020 European Academy of Dermatology and Venereology
In our study, the M/F ratio was found to be >1 for all three histotypes, showing a higher incidence in men than in women, according to what reported in literature. From the available data, BCCs in all their variants are more common in the 6th, 7th and 8th decade of life, with a higher incidence in men than in women (M/F = 1.5–2 : 1). Some studies, however, have shown a younger age of onset for superficial BCC and a relative increase in incidence in women compared to other histotypes.2,3

In terms of BCC location, the head/neck district was more frequently involved in sclerodermiform BCCs and to a lesser extent in nodular BCCs, while trunk and limbs were more frequently involved in superficial BCCs as reported by other authors.3,4

Within the head/neck district, the most affected areas in sdBCC were the nose, cheek and periauricular region; the periorbital region was significantly more frequently involved in sdBCC than in the other two histotypes. The nose, periauricular region and periorbital region belong to H area, which is considered an area at high risk of recurrence, while the cheek is part of M area, which is associated with moderate risk of recurrence.5,6

Our data show that sdBCC, already considered at high risk of recurrence, is preferentially located in areas at high-moderate risk of recurrence, so an early diagnosis and targeted therapy can reduce the high rates of local recurrence and improve the prognosis of patients.7

With regard to lesion edges, these appeared more frequently poorly defined in sclerodermiform BCCs and more frequently well defined in nodular and superficial BCCs. It should be noted that a BCC with poorly defined edges is considered at high risk of recurrence; therefore, the importance of early diagnosis and correct therapy to reduce the risk of local recurrence and distant metastasis in sdBCC is confirmed.

In this study, the median of the maximum lesion diameter was found to be greater in sBCC than in the other two histotypes; this can be explained by the fact that sBCC is preferentially located on the trunk and limbs, therefore in less visible areas, so it is often noticed later.
Dermoscopy has shown to improve the diagnostic accuracy for basal cell carcinoma. Numerous dermoscopic criteria have been described in literature, including arborizing vessels, ulceration, blue-grey globules, maple leaf-like structure, blue-ovoid nests and spoke-wheel structures.8,9

In our population, classical arborizing vessels were found more frequently in nBCCs, fine arborizing vessels were more frequent sdBCC, while short arborizing vessels were found more frequently in sBCCs and our results are in accordance with literature data.10

In our study, large blue-grey ovoid nests, multiple blue-grey dots and globules and focused dots were found more frequently in nodular BCCs, while concentric structures, spoke-wheel areas and leaf-like areas were found more frequently in sBCCs. In

| Table 4 Uni- and multivariate analyses of dermoscopic features of superficial basal cell carcinoma vs. other histotypes |
|---------------------------------------------------------------|
| **Dermoscopic features** | **Histotype** | **sdBCC + nBCC (n = 196)** | **Univariate** | **Multivariate** |
| | | sBCC (n = 95) | sdBCC + nBCC (n = 196) | OR (95% CI) | P-value | OR (95% CI) | P-value |
| Classical arborizing vessels | Present | 2 (2.1) | 90 (45.9) | 0.03 (0.01-0.11) | <0.01 | 0.02 (0.00-0.13) | <0.01 |
| | Absent | 93 (97.9) | 106 (54.1) | | | | |
| Fine arborizing vessels | Present | 21 (22.1) | 82 (41.8) | 0.40 (0.23-0.69) | <0.01 | 0.20 (0.09-0.43) | <0.01 |
| | Absent | 74 (77.9) | 114 (58.2) | | | | |
| Short arborizing vessels | Present | 73 (76.8) | 51 (26.0) | 9.43 (5.32-16.74) | <0.01 | 3.28 (1.56-6.88) | <0.01 |
| | Absent | 22 (23.2) | 145 (74.0) | | | | |
| Large blue-grey ovoid nests | Present | 0 (0.0) | 20 (10.2) | | | | |
| | Absent | 95 (100.0) | 176 (89.8) | | | | |
| Multiple blue-grey dots and globules | Present | 0 (0.0) | 40 (20.4) | | | | |
| | Absent | 95 (100.0) | 156 (79.6) | | | | |
| Focused dots | Present | 6 (6.3) | 20 (10.2) | 0.59 (0.23-1.53) | 0.28 | | |
| | Absent | 89 (93.7) | 176 (89.8) | | | | |
| Concentric structures | Present | 6 (6.3) | 5 (2.6) | 2.57 (0.77-8.66) | 0.13 | | |
| | Absent | 89 (93.7) | 191 (97.4) | | | | |
| Spoke-wheel areas | Present | 8 (8.4) | 1 (0.5) | 17.93 (2.21-145.53) | <0.01 | 23.64 (0.86-653.37) | 0.06 |
| | Absent | 87 (91.6) | 195 (99.5) | | | | |
| Leaf-like areas | Present | 8 (8.4) | 2 (1.0) | 8.91 (1.86-42.84) | <0.01 | 12.76 (1.31-123.96) | 0.03 |
| | Absent | 87 (91.6) | 194 (99.0) | | | | |
| Ulceration | Present | 13 (13.7) | 74 (37.8) | 0.26 (0.14-0.50) | <0.01 | 0.15 (0.06-0.36) | <0.01 |
| | Absent | 82 (86.3) | 122 (62.2) | | | | |
| Small erosions | Present | 41 (43.2) | 50 (25.5) | 2.22 (1.32-3.72) | <0.01 | 2.87 (1.34-6.12) | 0.01 |
| | Absent | 54 (56.8) | 146 (74.5) | | | | |
| Pink-white areas | Present | 74 (77.9) | 97 (49.5) | 3.60 (2.06-6.29) | <0.01 | 1.24 (0.48-3.19) | 0.65 |
| | Absent | 21 (22.1) | 99 (50.5) | | | | |
| Short white streaks | Present | 18 (19.0) | 18 (9.2) | 2.31 (1.14-4.68) | 0.02 | | |
| | Absent | 77 (81.0) | 178 (90.8) | | | | |

CI confidence interval; nBCC nodular basal cell carcinoma; OR, odds ratio; sBCC, superficial basal cell carcinoma; sdBCC sclerodermiform basal cell carcinoma.

Dermoscopy has shown to improve the diagnostic accuracy for basal cell carcinoma. Numerous dermoscopic criteria have been described in literature, including arborizing vessels, ulceration, blue-grey globules, maple leaf-like structure, blue-ovoid nests and spoke-wheel structures.8,9

In our population, classical arborizing vessels were found more frequently in nBCCs, fine arborizing vessels were more frequent sdBCC, while short arborizing vessels were found more frequently in sBCCs and our results are in accordance with literature data.10

In our study, large blue-grey ovoid nests, multiple blue-grey dots and globules and focused dots were found more frequently in nodular BCCs, while concentric structures, spoke-wheel areas and leaf-like areas were found more frequently in sBCCs. In
2010, Zalaudek et al.\textsuperscript{11} highlighted the presence of different pigmentation patterns between superficial and nodular BCCs: the criteria indicating the presence of melanin at the dermo-epidermal junction (leaf-like areas, spoke-wheel areas, concentric structures and focused dots) are brown and are characteristic of superficial BCCs, while those indicating the presence of melanin at the dermis level (large blue-grey ovoid nests and multiple blue-grey dots and globules) are blue or grey and are characteristic of nodular BCCs.

Focused dots are more frequently present in superficial BCCs, but they can still be found in all subtypes, including nodular BCCs, as microscopically they correspond to the deposition of melanin along the dermo-epidermal junction and/or to the presence of melanophages in the papillary and reticular dermis.\textsuperscript{12}

### Table 5 Frequencies of demographic, clinical, dermoscopic features and histotypes in cluster analysis

| Clusters | Cluster 1 (n = 116) | Cluster 2 (n = 131) | Cluster 3 (n = 38) | P-value |
|----------|---------------------|---------------------|-------------------|---------|
| Histotype† | nBCC | 87 (75.0) | 5 (3.8) | 1 (2.6) | <0.01 |
|           | sdBCC | 19 (16.4) | 70 (53.4) | 8 (21.1) | |
|           | sBCC | 10 (8.6) | 56 (42.7) | 29 (76.3) | |

**Demographic features**

- **Sex**
  - Male: 74 (63.8) | 71 (54.2) | 22 (57.9) |
  - Female: 42 (36.2) | 60 (45.8) | 16 (42.1) |
- **Median age**: 75 | 70 | 77 |

**Clinical features**

- **Location**
  - Head/neck: 54 (46.6) | 45 (34.4) | 34 (89.5) |
  - Trunk: 52 (44.8) | 36 (27.5) | 3 (7.9) |
  - Extremities: 10 (8.6) | 50 (38.2) | 1 (2.6) |
- **Clinical aspect**
  - Macule: 18 (15.5) | 58 (44.3) | 0 (0) |
  - Papule: 49 (42.2) | 3 (2.3) | 0 (0) |
  - Plaque: 16 (13.8) | 70 (53.4) | 0 (0) |
  - Nodule: 32 (27.6) | 0 (0) | 0 (0) |
  - Ulceration: 1 (0.9) | 0 (0) | 38 (100) |
- **Edges**
  - Well defined: 92 (79.3) | 61 (46.6) | 6 (15.8) |
  - Poorly defined: 24 (20.7) | 70 (53.4) | 32 (84.2) |
- **Median of maximum diameter in mm**: 9 | 9 | 7 |

**Dermoscopic features**

- Classical arborizing vessels: 81 (69.8) | 7 (5.3) | 1 (2.6) |
- Fine arborizing vessels: 33 (28.4) | 53 (40.5) | 13 (34.2) |
- Short arborizing vessels: 29 (25.0) | 69 (52.7) | 24 (63.2) |
- Large blue-grey ovoid nests: 20 (17.2) | 0 (0) | 0 (0) |
- Multiple blue-grey dots and globules: 37 (31.9) | 3 (2.3) | 0 (0) |
- Focused dots: 21 (18.1) | 4 (3.1) | 0 (0) |
- Concentric structures: 11 (9.5) | 0 (0) | 0 (0) |
- Spoke-wheel areas: 9 (7.8) | 0 (0) | 0 (0) |
- Leaf-like areas: 10 (8.6) | 0 (0) | 0 (0) |
- Ulceration: 29 (25.0) | 18 (13.7) | 38 (100) |
- Small erosions: 24 (20.7) | 54 (41.2) | 10 (26.3) |
- Pink-white areas: 24 (20.7) | 116 (88.5) | 29 (76.3) |
- Short white streaks: 7 (6.0) | 25 (19.1) | 4 (10.5) |

nBCC nodular basal cell carcinoma; sBCC, superficial basal cell carcinoma; sdBCC, sclerodermiform basal cell carcinoma.

†Histotype was not included in Cluster Analysis.
It is interesting to note that in our analysis large blue-grey ovoid nests are also absent in sdBCC as well as in sBCC. Ulceration was more frequently found in sdBCC and to a lesser extent in nBCCs; in contrast, small erosions were more frequently found in sBCCs. From literature data, ulceration typically characterizes nBCCs, while small erosions are associated with sBCCs. Our results confirm this evidence and show that ulceration can also be found with some frequency in sdBCC, especially when these are diagnosed at an advanced stage. Pink-white areas were more frequently found in sdBCC, less in sBCCs; short white streaks, which can only be seen with polarized light dermoscopy, were detected more frequently in sBCCs.

Pink-white areas and short white streaks indicate dermal fibrosis or fibrotic tumour stroma and have been described primarily in the context of superficial BCC. Our work shows that pink-white areas can also be found with some frequency in sdBCC, as they microscopically correspond to dermal fibrosis, which histologically characterizes this histotype.

From our analysis, regarding the distribution of some dermoscopic characteristics in relation to the site and histotype, some practical interesting results emerge:

1. In nBCCs, classical arborizing vessels and multiple blue-grey dots and globules were more frequently found in the body than in the head/neck district.
2. Sclerodermiform BCCs present more frequently on the head/neck area; if pink-white areas or fine arborizing vessels are seen, clinicians should consider this diagnosis, especially in high-risk zones such as nose, cheek and periauricular zone.
3. In sdBCC and sBCCs, ulceration was found more frequently in the head/neck district than in the body.

Our study can be compared with an extensive monocentric study by Suppa et al., in which authors investigated the dermoscopic variability of BCCs in relation to clinical subtype and anatomical localization. They showed that facial BCCs were more frequently characterized by classical arborizing vessels and ulceration than BCCs located elsewhere in the body, while trunk BCCs were more frequently characterized by leaf-like areas, short arborizing vessels, small erosions, concentric structures and spoke-wheel areas than BCCs located elsewhere. The dermoscopic variability of BCC in relation to anatomical location is an area that has yet to be explored in dermoscopy. The anatomical differences of the skin in different areas of the body, as well as the different photodamage patterns in different body positions, could hypothetically explain this dermoscopic variability and could suggest new specific body site-specific treatments; based on our findings, we propose to treat with cryotherapy sBCC throughout the body while resorting to surgery for nBCC and sdBCC. In doubtful cases, during the clinical routine, it is useful to perform one or more punch biopsies to define the extent of a sdBCC especially before a large excision on the face in which Mohs’ surgery is also of considerable importance to limit local recurrences. When available, reflectance confocal microscopy (RCM) helps in the non-invasive differential diagnosis of the sdBCC allowing to easily observe some suggestive criteria of BCC such as keratinocyte atypia, epidermal streaming, ulceration and tumour island. Moreover, it has recently been demonstrated that optical coherence tomography is another method that can be used for the early diagnosis of BCC and its diagnostic performance did not depend on the lesion’s anatomical location. In conclusion, our study, although there is a lack of follow-up patient data, which is the main limitation of the research, represents a starting point for future retrospective and prospective studies to investigate the clinical and dermoscopic variability of BCC presentation.

References
1. Conforti C, Corneli P, Harwood C, Zalaudek I. Evolving role of systemic therapies in non-melanoma skin cancer. Clin Oncol (R Coll Radiol) 2019; 31: 759–768.
2. Lallas A, Apalla Z, Argenziano G et al. The dermoscopic universe of basal cell carcinoma. Dermatol Pract Concept 2014; 4: 11–24.
3. Cameron MC, Lee E, Hibler BP et al. Basal cell carcinoma: epidemiology; pathophysiology; clinical and histological subtypes; and disease associations. J Am Acad Dermatol 2019; 80: 303–317.
4. McCormack CJ, Kelly JW, Dorevitch AP. Differences in age and body site distribution of the histological subtypes of basal cell carcinoma. A possible indicator of differing causes. Arch Dermatol 1997; 133: 593–596.
5. Muzic JG, Schmitt AR, Wright AC et al. Incidence and trends of basal cell carcinoma and cutaneous squamous cell carcinoma: a population-based study in Olmsted County, Minnesota, 2000 to 2010. Mayo Clin Proc 2017; 92: 890–898.
6. Peris K, Fargnoli MC, Garbe C et al. Diagnosis and treatment of basal cell carcinoma: European consensus-based interdisciplinary guidelines. Eur J Cancer 2019; 118: 10–34.
7. Husein-ElAhmed H. Sclerodermiform basal cell carcinoma: how much can we rely on dermoscopy to differentiate from non-aggressive basal cell carcinomas? Analysis of 1256 cases. An Bras Dermatol 2018; 93: 229–232.
8. Conforti C, Guiffrida R, Vezzoni R, Resende FSS, di Meo N, Zalaudek I. Dermoscopy and the experienced clinicians. Int J Dermatol 2020; 59: 16–22.
9. Conforti C, Guiffrida R, Retsos,  di Meo N, Zalaudek I. Two controversies confronting dermoscopy or dermoscopy: nomenclature and results. Clin Dermatol 2019; 37: 597–599.
10. Lallas A, Argenziano G, Zendri E et al. Update on non-melanoma skin cancer and the value of dermoscopy in its diagnosis and treatment monitoring. Expert Rev Anticancer Ther 2013; 13: 541–558.
11. Zalaudek I, Kreusch J, Giacomel J, Ferrara G, Catricala C, Argenziano G. How to diagnose nonpigmented skin tumors: a review of vascular structures seen with dermoscopy: part I. Melanocytic skin tumors. J Am Acad Dermatol. 2010; 63: 361–374; quiz 375–6.
12. Lallas A, Apalla Z, Ioannides D et al. Dermoscopy in the diagnosis and management of basal cell carcinoma. Future Oncol 2015; 11: 2975–2984.
13. Suppa M, Micantonio T, Di Stefano A et al. Dermoscopic variability of basal cell carcinoma according to clinical type and anatomic location. J Eur Acad Dermatol Venereol 2015; 29: 1732–1741.
Dermoscopy of basal cell carcinoma vs. superficial and nodular histotypes

14 Longo C, Borsari S, Pampea R et al. Basal cell carcinoma: the utility of in vivo and ex vivo confocal microscopy. J Eur Acad Dermatol Venereol 2018; 32: 2090–2096.

15 Holmes J, von Braunmühl T, Berking C et al. Optical coherence tomography of basal cell carcinoma: influence of location, subtype, observer variability and image quality on diagnostic performance. Br J Dermatol 2018; 178: 1102–1110.

16 Giuffrida R, Conforti C, Di Meo N, Deinlein T, Guida S, Zalaudek I. Use of noninvasive imaging in the management of skin cancer. Curr Opin Oncol 2020; 32: 98–105.