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MULTIMODAL OPTOSPECTRAL INVESTIGATION OF MELANOCYTIC SKIN LESIONS: A CORRELATION STUDY USING OPTICAL COHERENCE TOMOGRAPHY AND DERMOSCOPY

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Abstract. Optical coherence tomography (OCT) is one of the best options, in terms of skin penetration depth and resolution, for skin lesion diagnosis. This study reports on the use of OCT for the *in vivo* imaging analysis of 67 melanocytic skin lesions in 34 patients. The OCT results have been compared with the dermoscopy – the standard non-invasive, visible-light-based skin imaging technique. The variations of the OCT imaging correlate with the dermoscopic pattern and presence of dermoscopic structures, like globules, blotches and regression areas. Our study shows that OCT is a promising non-invasive imaging technique for the diagnosis of skin lesions and in combination with dermoscopy, it could complement and extend the morphologic information obtained *in vivo* and could offer the premise for new diagnostic approaches.

Key words: optical coherence tomography, *in vivo* imaging, skin cancer, dermoscopy.

1. INTRODUCTION

Optical coherence tomography (OCT) is an emergent technique of medical imaging diagnosis, which uses the interference of infrared radiation (900–1500 nm) with living tissues, in order to allow the non-invasive, high resolution, two- or three-dimensional, cross-sectional visualization of microstructural morphology of living tissue structures [1, 2]. Introduced in medical practice in the field of ophthalmology [3] and cardio-vascular surgery, this technique also gave promising results in the analysis of the skin structure in clinical setting [4]. This technique allows direct imaging of superficial tissue morphology at depths of up to 2 mm, resolution equivalent to a low-power microscope; therefore it represents a promising tool for non-invasive evaluation, early detection and monitoring of various benign and malignant skin lesions [5–9]. Up to present however, there are

no definitive morphologic diagnostic criteria for OCT in skin pathology. Intensive research efforts are dedicated to correlate the morphologic aspects obtained with OCT with the classic standard of histopathology and with other validated or developing imaging methods [7, 10, 11].

In this context the diagnosis characteristic of OCT in melanocytic nevi (moles) was studied, in comparison with dermoscopy, which is the standard optical *in vivo* imaging technique for skin, especially for this type of lesions. We aimed to correlate the morphologic features of melanocytic lesions obtained through the two imaging techniques and to explore which morphological structures influence the performance of OCT in visualizing this type of lesions.

2. METHODS

2.1. OPTICAL COHERENCE TOMOGRAPHY

OCT measurements were performed with a Thorlabs OCP930SR Spectral Radar OCT device. The device uses a superluminescent diode operating at a wavelength of about 930 nm. The light radiation is split by an interferometer into two beams directed one onto a mirror (reference beam) and the other onto the skin surface (sample beam). Back-scattered photons are then recombined to interfere with the light source, providing information about the path length distribution of the sample beam, due to optical inhomogeneities of the tissue, to obtain spatial morphological information. Measurement of the interference pattern indicates the position of different absorbent or reflective skin tissue components, such as cell membranes or melanin (the dark pigment within cells, responsible for the color of moles) which provide the contrast in the images. The OCT scanning device has a spectral bandwidth of 100 nm, yielding a typical imaging depth of ~1.6 mm, 20 μm lateral resolution and a 6.2 μm axial resolution. Bidimensional images (B-scans) of vertical sections through the skin were acquired at 8 fps, maximum image width of 6 mm and image size of 512 rows. The duration of the scan acquisition was 5 to 10 seconds. The scans were performed through the mid part of the largest diameter of the lesions. In order to optimize optical coupling of the probe with the uneven and mobile surface of the skin, a contact gel was applied to the skin. The gel layer was visible through all our images as a bright line at skin surface. The acquired images were stored as jpg-files for further analysis and comparative studies.

2.2. DERMOSCOPY

Dermoscopy is an optical analysis technique, using a source of visible light coupled with a magnification lenses system, which allows the examination of skin lesions in vivo, with an improved accuracy of diagnosis. Parafin oil is used as

immersion medium, at the interface between the device's objective and the skin, in order to optically eliminate the superficial layers of the skin and allow deeper visualization. The dermoscopic images are bidimensional, en-face images of skin lesions, that are captured and stored by a computer system with a color video camera used at a magnification of × 20 (FotoFinder, TechScreen Software GmbH, BadBirnbach, Germany), with integrated software for pictures management and follow-up. Images of all lesions were taken at 20 fold magnification and stored as jpg files for further analysis.

2.3. SUBJECTS

The study enrolled consecutive patients with melanocytic skin lesions (MSL) presenting in the Dermatology Clinic of Elias Emergency University Hospital in the period February 2012-November 2012. Only flat lesions were included in the study, as OCT system performance in elevated lesions is reduced [11, 12]. Lesions with marked scaling or crusting were excluded from the study. Further inclusion criteria consisted of: age over 18 years, informed consent, both OCT and dermoscopy images available, clear diagnosis of MSL clinically and dermoscopically, established by 2 independent clinical experts.

A total number of 67 melanocytic skin lesions (MSL) in 34 patients (21 women and 13 males, with a median age of 44 years) were included in the study. Sixty lesions in 27 patients were diagnosed as various types of benign nevi, and the other 7 lesions were histopathologically confirmed as malignant melanoma. We compared the OCT images with the corresponding dermoscopy photographs. To ascertain accuracy of correlation between the OCT and dermoscopic evaluations, all lesions were analyzed using the same positioning, *i.e.* on the center of the lesion and parallel with the longest axis of the lesion.

Statistical analysis was performed with the JMP v.10 software, SAS Inc. Univariate analysis of distribution of categorical and ordinal variables across groups was performed through contingency analysis, by means of chi-square test. A value of $p < 0.05$ was considered statistically significant through all analyses.

3. RESULTS

Some dermoscopic patterns and features of lesions are presented as example in Fig. 1 corresponding to a reticular pattern (A) and (C), globular pattern – globules (B), and mixed pattern (D). For reticular and mixed pattern blotches (B), pigment network (P), regression areas (R) and peripheral streaks (S) are indicated.

The parameters analyzed in dermoscopy images are presented in Table 1 and included the main elements of dermoscopic diagnosis established for melanocytic lesions [14, 15]: the dermoscopic patterns of the lesions – reticular, globular,

homogeneous or combined; the intensity of lesion pigmentation (1=light brown, 2 = brown, 3 = dark brown, 4 = black), the symmetry, the presence of clear-cut margins, the presence of architectural details like dots/globules, blotches, streaks, regression areas, blue-white veil, vascular structures, and typical or atypical pigment network.

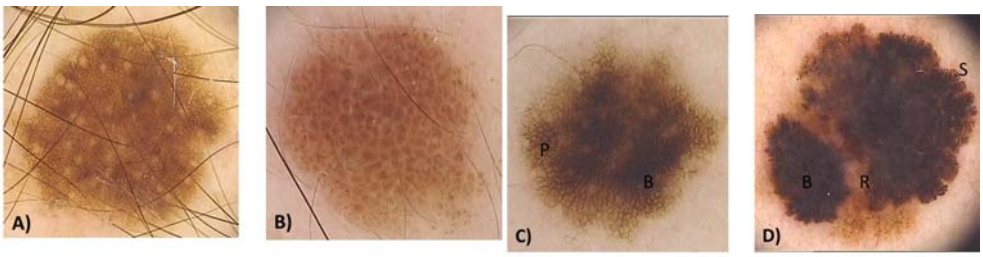

Fig. 1 – Dermoscopic aspect of melanocytic lesions:
A) reticular pattern; B) globular pattern; globules; C) reticular pattern; D) mixed pattern
B = blotches, P = pigment network, R = regression areas, S = peripheral streaks.

Table 1

Dermoscopic characteristics of analyzed melanocytic lesions (Total MSL = 67)

Dermoscopic features	**Number of lesions**	**% of lesions**
Pattern		
reticular	29	43.28
globular	3	4.48
homogeneous	3	4.48
combined	32	47.76
Color		
light brown	19	28.36
brown	29	43.28
dark brown	18	26.87
black	1	1.49
Margins		
clear	33	49.25
blurry	34	50.75
Symmetric lesion	37	55.22
Vascular structures visible	16	23.88
Dots/globules present	44	65.67
Blotches present	35	52.24
Streaks present	6	8.96
Blue-gray structures present	9	13.43
Regression present	8	11.94
Pigment network present	54	80.60
Type of pigment network		
typical	26	38.81
atypical	28	41.79

Most MSL had reticular or combined dermoscopic patterns (43.28% and 47.76%), with only 4.48% globular and 4.48% homogeneous patterns. The pigment was brown in 43.28% of cases and light brown in 28.36% of cases. 80.60% of lesions had a visible pigment network, with almost similar rates of typical and atypical features (41.79% *versus* 38.81%).

The OCT image of healthy skin layered structure can be seen in Fig. 2. The epidermis was slightly less signal-intense. The dermo-epidermal junction (DEJ) was clearly visible, signal-intense, and had a normal sinusoid aspect. The subjacent upper (papillary) dermis was more signal intense than the epidermis, relatively homogenous and containing dark, echo-poor, ovoid or elongated, branched spaces corresponding to blood vessels. In the deeper (reticular) dermis the signal faded. The parameters analyzed in OCT images were in agreement with previous case reports [1, 11, 13] and are presented in Table 2. They included the: visible stratification of skin layers, the clarity of the limit between dermis and epidermis (dermo-epidermal junction), the presence and localisation of dark, well circumscribed round-oval structures (clusters), the intensity of shadow in the dermis (1 = no shadow, 2 = light shadow, 3 = intense shadow, 4 = very intense shadow), lesion symmetry, clarity of lesion's margins, modified signal of epidermis compared with healthy skin.

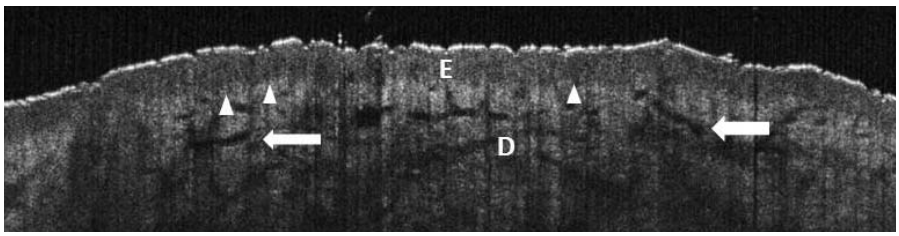

Fig. 2 – OCT aspect of normal skin E = epidermis, D= dermis, arrow heads= dermo-epidermal junction; arrow= branched dark structures corresponding to blood vessels in dermis.

Table 2

OCT characteristics of analyzed melanocytic lesions (Total MSL = 67)

OCT features	**Number of lesions**	**% of lesions**
Clear stratification of skin layers	39	58.21
Clear visualization of the dermo-epidermal junction	20	29.85
Elongated epidermal ridges	31	46.27
Dark clusters		
Present	40	59.70
Absent	27	40.30
Clusters localization		
Dermo-epidermal junction	18	26.87
Dermis	9	13.43
Mixed (dermis & junction)	13	19.40

Table 2 (continued)

Shadow within dermis		
Almost no shadow	5	8.77
Light shadow	18	31.58
Intense shadow	31	54.39
Very intense shadow	3	5.26
Lesions margins*		
Clearly visible	21	37.50
Blurry	35	62.50
Vascular structures in the skin		
Less than in normal skin	8	17.39
Same as in normal skin	29	63.04
More than in normal skin	9	19.57
Symmetry*	30	44.78
Modified epidermis	40	59.70
*in 10 lesions margins and symmetry could not be exactly determined, as lesions dimensions surpassed the field of the OCT probe		

OCT also allowed the visualization of elements typical for melanocytic lesions, and which have a correspondent in the classical histopathologic examination (Fig 3): elongation and accentuation of the finger-shaped aspect of the dermo-epidermal junction; irregular, variable scattering of the signal due to the melanin pigment accumulated in the lesions, dark ovoid-round shapes (clusters) corresponding to groups of melanocytic cells, loaded with pigment, distributed along the jonction or deeper in the dermis.

3.1. OCT SIGNAL SCATTERING

Signal scattering due to melanin presence in the melanocytic nevi was an important aspect of OCT analysis of these lesions. It resulted in a dark shadow of variable intensity partially obscuring the structures in the upper dermis and at the junction. In our study, the intensity of dermal shadowing in OCT images correlated, statistically significant, with the presence of globules and blotches in the dermoscopic images. Intense shadow (scores 3 and 4) was present in 62% of lesions with blotches on dermoscopy and in 52.63% of lesions with dots and globules. Also, darker shadow (score > 3) in OCT was seen mostly in lesions without visible pigment network on dermoscopy ($p < 0.05$) and with blurry margins.

There was no statistically significant correlation between the over-all lesion colour detected in dermoscopy and the intensity of the shadow present in the OCT images, with 34.32% of cases having similar scores.

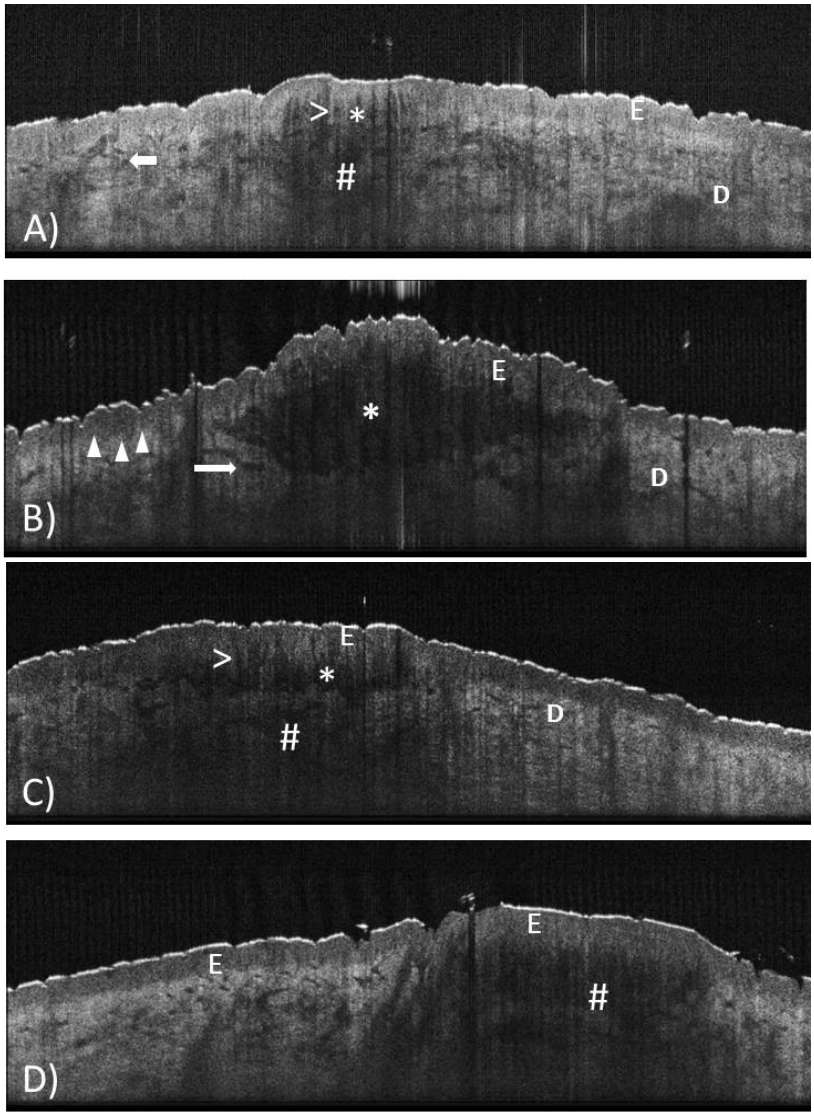

Fig. 3 – OCT aspects of melanocytic lesions. E = epidermis, D= dermis, arrow heads= dermo-epidermal junction, *=dark clusters; arrow= branched dark structures corresponding to blood vessels in dermis; # shadow obscuring subjacent dermal structures:

A) jonctional nevus; elongated epidermal ridges, small dark clusters at the dermo-epidermal junction; shadow obscuring partially subjacent dermal structures;

B) dermal nevus; dark agglomerated clusters in the deeper dermis;

C) compound nevus; elongated epidermal ridges, small dark clusters at the dermo-epidermal junction and in the superficial dermis; shadow obscuring partially subjacent dermal structures;

D) intense shadow, lesion obscured.

3.2. VISIBILITY OF SKIN STRATIFICATION AND OF DERMO-EPIDERMAL JUNCTION

In 39 lesions (58.21%) the skin stratification was clearly visible in OCT. Skin layering was most frequently observed in lesions with reticular pattern (56.41%), less frequently in those with combined pattern (38.46%) and in only 5.12% of those with homogeneous dermoscopic patterns ($p < 0.05$). Visibility of skin layering in OCT was also a feature of lesions without blotches, streaks, blue-gray areas or regression in dermoscopy ($p < 0.05$)**.**

The DEJ was clearly detectable in 20 lesions (29.85%), 70% with reticular pattern, 25% with combined pattern and 5% with globular pattern ($p = 0.01$). A clearly visible DEJ was associated, statistically significant, with the dermoscopic pattern, and with the absence of blotches and blue-gray areas in dermoscopy. 70% of MLS without blotches and over 90% of lesions without blue grey areas or regression have a clear DEJ compared to only 30% and less than 5% of lesions, when such structures are dermoscopically identifiable ($p < 0.05$). DEJ tended to be more often clearly defined in brown colored lesions (55% compared to 25% in light brown and 20% in dark brown lesions) ($p = 0.059$).

3.3. MODIFIED EPIDERMIS AND CLUSTERS

Elongated epidermal ridges visible in OCT were statistically significant correlated with the dermoscopic pattern; they were more frequently seen in reticular (56.25%) and homogenous pattern (9.37%), and were absent in globular pattern lesions ($p < 0.05$). In OCT images, changes of thickness or signal intensity of the epidermis, compared to normal adjacent skin were visible in nevi with reticular (51.22%) and mixed (36.59%) dermoscopic pattern and in lesions without regression (82% of lesions) ($p < 0.05$).

There was a statistically significant correlation between the presence of globular dermoscopic structures (dots, globules, blotches, streaks) and presence and localization of clusters in OCT ($p = 0.006$). Dermoscopic globular structures were more frequently associated with junctional and compound clusters (85% *vs* 15% dermal clusters).

The color intensity in dermoscopy varied with the localization of OCT clusters, the most intense color (3 – dark brown) was associated with the presence of junctional clusters ($p < 0.05$). In OCT images, the presence of visible clusters correlated with a visible dermal-epidermal stratification, with a clear DEJ and with lower ($< = 2$) shadow intensity ($p < 0.05$ for all comparisons).

Symmetry was concordant in both dermoscopy and OCT images in 76% of analyzed lesions ($p < 0.05$). The sharpness of lesion margins was concordant between OCT and dermoscopy in half of cases; none of the dermoscopic aspects

could be significantly associated with the margins quality in OCT. Vascularisation of the lesions, visible in OCT images was more or equal as in normal skin in MSLs without blotches on dermoscopy.

4. DISCUSSION

OCT and dermoscopy are complementary opto-spectral methods of visualizing the skin *in vivo*: dermoscopy provides en-face colored images, resulting from the superposing of colors and shapes of cell groups across the horizontal skin layers, while the OCT provides black-white images of vertical sections through the skin, resulting from differences of layers' textures and signal transmission. As such, it is of great interest to study these methods in parallel, in order to establish the elements of concordance or of complementarity between them that would help design future better diagnosis techniques.

OCT images in our study revealed dark clusters with jonctional or dermal localization, corresponding to the histopathological hallmark of nests of melanocytic cells, as reported in other studies [9, 11]. We found out that the presence and disposition of these clusters correlated significantly with the aspects seen in dermoscopy, under the form of dermoscopic pattern and dermoscopic structures (blotches, globules etc.).

The scattering of the OCT signal by the melanin in the MSL and the consequent shadowing of the dermis is an important issue constraining the use of OCT in the analysis of these lesions [7, 9, 11, 12]. Our results showed that the intensity of signal scattering and shadow was less influenced by the overall melanin quantity of the lesion, reflected in the overall color score in dermoscopy, but rather by the distribution of pigment and the particular architecture of pigmented cells aggregates (the morphological equivalent of dermoscopic dots/globules and blotches).

In our study the reticular dermoscopic pattern was significantly associated with clearer visibility of DEJ in OCT and visible changes of epidermis, including elongated epidermal ridges. This is in line with other studies, which showed that the dermo-epidermal junction and epidermal changes are visible by OCT in junctional nevi but may lack in compound nevi [11]. Junctional nevi are characterized by single or small nests of pigmented nevocytes present at the dermo-epidermal junction [9, 10], and usually correspond to the reticular pattern seen in dermoscopy. In change, globular and homogeneous dermoscopy patterns are more often the dermoscopical equivalents of larger, deeper nests of pigmented melanocytes [15–17]. This could explain the less visibility of skin layering and dermo-epidermal demarcation of these patterns in OCT.

To our knowledge this is the first prospective study performing a statistical analysis, on a conveniently-sized sample, of the correlations between OCT and

dermoscopic aspects of melanocytic lesions. Earlier studies allowed only qualitative analysis on smaller case series [5, 9, 11].

The limitations of our analysis include the relative small size of the sample that did not allow for further stratification of nevus subtypes. Technical limitations included the limited skin penetration depth associated with the 930 nm OCT wavelength, the motion artifacts and the limited size of the OCT probe field, preventing the proper investigation of larger lesions.

5. CONCLUSIONS

This study presents the first statistical analysis of the correlations between OCT and dermoscopic aspects of melanocytic lesions. OCT revealed important diagnosis elements for skin lesions that are normally identified in histopathology examination, like the margins, the changes in epidermis and the presence and location of the nests of melanocytic cells that make up these lesions. The morphologic aspects as well as the visibility and quality of OCT imaging correlated well with the dermoscopic pattern, and with the presence of dermoscopic features such as dots, globules, blotches or the pigment network.

Our study showed that OCT is a promising non-invasive imaging technique for the diagnosis of melanocytic skin lesions. Its combination with other imaging modalities, such as dermoscopy, could complement and extend the morphologic information obtained in vivo, and could offer the premise for new diagnostic approaches.

These results have a particular relevance for the medical practice, since benign moles are frequent and their prompt differentiation from a beginning malignant lesion – the deadly melanoma – is a crucial and difficult task for the dermatologist, with heavy consequences for the patient. Further studies, at larger samples, under the control of histopathology are useful to establish the precise role of OCT and of the further developments of this technique in the diagnostic algorithms in the medical practice.

REFERENCES

1. A. Tycho, P. Andersen, L. Thrane and G.B.E. Jemec, *Optical coherence tomography in dermatology*, J. Serup, G.B.E. Jemec, G. Grove (Eds.), *Handbook of Non-Invasive Methods and the Skin* (ed. 2), Boca Raton, FL, CRC Press, 2006, 1055.
2. J. Welzel, *Optical coherence tomography in dermatology: a review*, Skin Res. Technol., **7**, 1–9 (2001).
3. J.G. Fujimoto, M.E. Brezinski, G.J. Tearney, S.A. Boppart, B. Bouma, M.R. Hee, J.F. Southern and E.A. Swanson, *Optical biopsy and imaging using optical coherence tomography*, Nat. Med., **1**, 970–972 (1995).
4. J. Welzel, E. Lankenau, R. Birngruber and R. Engelhardt, *Optical coherence tomography of the human skin*, J. Am. Acad. Dermatol., **37**, *6*, 958–963 (1997).

5. T. Hinz, L.K. Ehler, H. Voth, I. Fortmeier, T. Hoeller, T. Hornung and M.H. Schmid-Wendtner, *Assessment of tumor thickness in melanocytic skin lesions: comparison of optical coherence tomography*, *20 MHz, ultrasound and histopathology*, Dermatology, **223**, 161–168 (2011).
6. M. Mogensen, H.A. Morsy, L. Thrane and G.B. Jemec, *Morphology and epidermal thickness of normal skin imaged by optical coherence tomography*, Dermatology, **217**, 14–20 (2008).
7. T. Gambichler, V. Jaedicke and S. Terras, *Optical coherence tomography in dermatology: technical and clinical aspects*, Arch. Dermatol. Res., **303**, 457–473 (2011).
8. PJ. Tadrous, *Methods for imaging the structure and function of living tissues and cells: optical coherence tomography*, J. Pathol., **191**, 115–119 (2000).
9. T. Gambichler, P. Regeniter, G. Bechara, A. Orlikov, R. Vasa, G. Moussa, M. Stucker, P. Altmeyer and K. Hoffmann, *Characterization of benign and malignant melanocytic skin lesions using optical coherence tomography in vivo*, J. Am. Acad. Dermatol., **57**, 629–637 (2007).
10. M. Boone, G.B. Jemec and V. Del Marmol, *High-definition optical coherence tomography enables visualization of individual cells in healthy skin: comparison to reflectance confocal microscopy*, Exp. Dermatol., **21**, *10*, 740–744 (2012).
11. V. de Giorgi, M. Stante, D. Massi, L. Mavilia, P. Cappugi and P. Carli, *Possible histopathologic correlates of dermoscopic features in pigmented melanocytic lesions identified by means of optical coherence tomography*, Exp. Dermatol., **14**, *1*, 56–59 (2005).
12. A.M. Forsea, E.M. Carstea and G. Pavelescu, *Clinical application of optical coherence tomography for the imaging of non-melanocytic cutaneous tumors: a pilot multi-modal study*, J. Med. Life, **3**, *4*, 381–389 (2010).
13. E. Sattler, R. Kästle and J. Welzel, *Optical coherence tomography in dermatology*, J. Biomed. Opt., **18**, *6*, 061224 (2013).
14. R. Hofmann-Wellenhof, A. Blum, I.H. Wolf, D. Piccolo, H. Kerl, C. Garbe and H.P. Soyer, *Dermoscopic classification of atypical melanocytic nevi (Clark nevi)*, Arch. Dermatol., **137**, *12*, 1575–1580 (2001).
15. G. Argenziano, H.P. Soyer, S. Chimenti, R, Talamini et al., *Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet*, J. Am. Acad. Dermatol., **48**, *5*, 679–693 (2003).
16. I. Zalaudek, M. Manzo, G. Ferrara and G. Argenziano, *New classification of melanocytic nevi based on dermoscopy*, Expert Rev. Dermatol., **3**, *4*, 477–489 (2008).
17. J. Malvehy, S. Puig, G. Argenziano, A.A. Marghoob, H.P. Soyer and International Dermoscopy Society Board members, *Dermoscopy report: proposal for standardization. Results of a consensus meeting of the International Dermoscopy Society*, J. Am. Acad. Dermatol., **57**, *1*, 84–95 (2007).