ORIGINAL PAPER

THE IMPORTANCE OF HIGH DEFINITION OPTICAL COHERENCE TOMOGRAPHY IN THE ACCURATE DIAGNOSIS OF BASAL CELL CARCINOMA

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Abstract. *High definition optical coherence tomography (HD-OCT) is a non-invasive imaging technique, with significant relevance in different area, mainly ophthalmology. In recent years OCT has become a promising tool also for the in vivo evaluation and diagnosis of different skin diseases, especially skin cancers. HD OCT can be used as a reliable diagnosis method that provides useful information on the architecture of cutaneous layers and sometimes on cellular morphology in the epidermis and other structures of the skin. Our work brings new information about the value of HD-OCT in describing in vivo pattern of basal cell carcinoma, one of the most frequent non-melanocytic skin cancers, compared with histopathology and dermoscopy.*

Keywords: *high-definition optical coherence tomography, dermoscopy, diagnosis, non-melanocytic skin cancer.*

1. INTRODUCTION

OCT (optical coherence tomography) is an innovative non-invasive imaging technique, based on the principle of conventional optical coherence tomography but with the property to carry out optical imaging up to 570 um deep within highly scattering media such as the skin; OCT permits visualization of single cells in their 3-D microarchitectural context, as shown in recent studies, therefore images captured by OCT can be sufficiently detailed to enable identification of architectural and morphological criteria for different types of non-melanocytic skin tumors such as BCC and AK [1-5].

OCT has the advantage, together with dermoscopy and other imaging techniques (confocal microscopy) to establish a correct diagnosis and to follow up treatment efficiency of suspicious skin lesions, therefore replacing unnecessary skin biopsies and reducing costs [6-10].

Basal cell carcinoma is one of the most frequent NMSC, especially in Caucasians and its higher incidence is growing year by year. There are recent studies that have highlighted that there is also an age drop regarding the onset of this skin cancer with a higher frequency between 40-50 years old individuals. Although its development is related with different environmental factors, chronic UV exposure has the most relevant contribution, as BCC often appears in skin damaged anatomical sites [11-15].

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The aim of this study was to show the sensitivity of OCT as a non-invasive imaging technique, in establishing morphological features of BCC and BCC subtypes compared with dermoscopy and histopathological examination.

2. MATERIALS AND METHODS

58 lesions that clinically suggested BCC were included in this study; in 55 lesions the histopathological examination confirmed diagnostic criteria for solid/ infiltrative BCC (29 cases) and superficial BCC in 26 cases. In the rest of the cases, the histopathological examination of biopsy specimens revealed diagnostic features of actinic keratosis and other benign tumors and they were excluded.

Biopsy specimens were obtained from 30 patients, 17 women and 13 men, with ages between 35 and 83 years old, many of them with more than 1 BCC, one of the patients having a total number of 9 BCCs, and also 1 patient with a melanoma and a BCC, all excised and histopathologically confirmed. The patients were I-III Fitzpatrick skin type and the lesions were located in different anatomical sites, most of them on the face and upper trunk. Signed informed consent was obtained in every case (Table 1).

Table 1. Patient and tumor characteristics.

Total number of patients	30	17 women	Aged	35- 83 years old	
		13 men			
Total number of tumors	58	**Solid / infiltrative BCC**		**Superficial BCC**	**Other tumors**
		29		26	3
BCC anatomical sites	**Head / Face / Neck**	**Trunk**	**Upper limbs**	**Lower limbs**	
	25	25	2	3	
Patients skin type	**Fitzpatrick I**	**Fitzpatrick II**		**Fitzpatrick III**	
	8	13		37	

Clinical appearance of the lesions was recorded using a Cannon HD camera, and all were subsequently analyzed using digital dermoscopy with the aid of Fotofinder System (Medicam 1000). Before surgical removal, the tumors were evaluated and pictures of lesional, peritumoral and healthy skin were captured, using an OCT - Skintell System (Agfa HealthCare, Belgium) [16].

High definition OCT, although it is based on the interference of infrared radiation with living tissue, the same principle as conventional OCT, was recently demonstrated to be an useful in vivo imaging technique for the diagnosis of different type of skin tumors. High definition OCT scanners have better advantages than conventional OCT; the lateral and axial resolution of 3 um exceeds the resolution of OCT with a reported lateral and axial resolution of 10 up to 25 μm, respectively 5 to 10 μm [3]. In addition to that, the system is capable of capturing 2 types of images in real time – slice image and en face image, as well as three dimensional acquisitions [2]. Many images can be captured using a hand probe and an optical gel that is put in contact with the lesional skin as coupling medium. Unfortunately the field of view in the en face mode is 1.8 x 1.5 and it is better to center the probe in the mid part of the lesion for a better accuracy of the diagnosis. The captures are subsequently transferred to a computer and are recomposed in an OCT image using a blue or greyblack scale [2].

3. RESULTS AND DISCUSSION

The histopathological examination is considered the gold standard for this type of skin cancers [17-20]. Common features can be found in the histopathological examination, like the islands of basaloid cancer cells with specific pallisanding arrangement at the borders, with monomorphic hyperchromatic nuclei, variable numbers of mitoses and apoptotic cells. The tumor is usually surrounded by stroma and inconstant edema with fluctuating polymorphic inflammatory infiltrate. Other notable changes are actinic alteration of the epidermis; solar elastosis with basophile degenerated dermis, increased and enlarged blood vessels. Depending of the subclinical type of the BCC we can find also ulceration, focal pigmentation, areas with squamous differentiation, desmoplastic reaction, tumoral necrosis, different stages of local invasion etc.

All BCCs were histopathologically analyzed with hematoxilyn eosin staining. Precise features were found in all lesions, like nests of basaloid cells, with pallisading disposition of the cells at the periphery and haphazard arrangement in the center, clefting (separation of tumor cells from the surrounding stroma), proeminent vascularity.

Solar elastosis was noticed in all lesions and also polymorphic inflammatory infiltrate – abundant in 34 (61.81%) tumors and moderate in 21 (38.18%) tumors. Deep dermal invasion was observed in 20 (36.36%) lesions and invasion of the hypodermis in 2 (3.63%) lesions (Fig. 1).

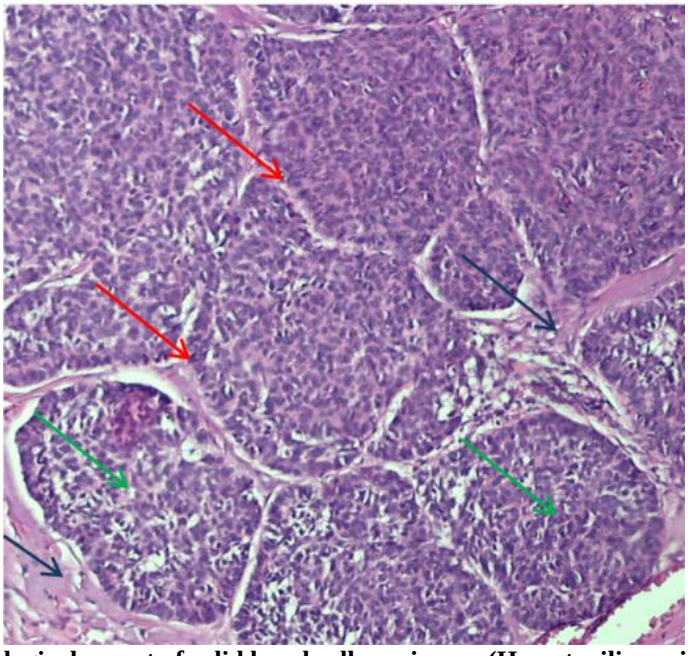
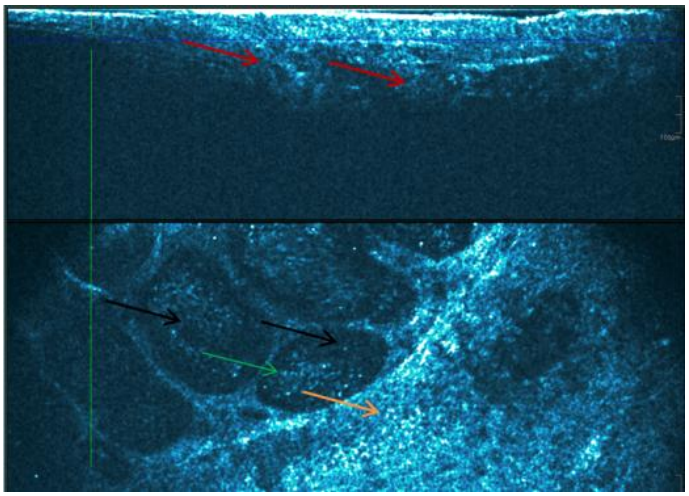


Figure 1. Histopathological aspect of solid basal cell carcinoma (Hematoxilin eosin stain) showing the tumoral islands (green arrows), the specific pallisading at the periphery of the tumoral nests (red arrows), the peritumoral stroma (dark blue arrows).

CT of the lesions showed compatible features with those seen in histopathology (Fig. 2). With the aid of OCT we were able to see the tumor islands in almost all the cases.

In the solid type BCC the OCT images revealed in most of the cases (76%) noticeable architectural disarray of the epidermis, tumoral islands with lobular structures in connection with the epidermis, dermis and adnexal structures.



a

b

Figure 2. OCT 3 D capture: a) vertical image of solid BCC showing epidermal disarray with unclear dermo-epidermal junction because of the invasive tumoral islands in the dermis (red arrows); b) OCT en face image of solid BCC showing the tumoral nodules (black arrows) and refractile stroma (yellow arrow); the islands of tumoral cells can be noted with the intercede areas of low reflactility; inside the tumoral island the cells appear more reflactile (green arrow).

Regarding the peritumoral area, proeminent or moderate inflammatory infiltrate was seen in most of the lesions (63%), as for the vascular aspect, increased number of vessels were seen as high density hyporeflective holes (small fine holes and branched vessels/holes) in 54 % of the cases (Fig. 3 and Table 2).

Table 2. OCT findings and HP examination of tumors / Total and Split ratio of the analyzed tumors depending of the OCT (slice) and Histopathology findings.

	HD-OCT – vertical (slice)			Histopathology		
	SI – BCC*	**S – BCC****	**Total**	**SI – BCC***	**S – BCC****	**Total**
Epidermal disarray	20 (68.97%)	22 (84.62%)	42 (76.36%)	26 (89.66%)	26 (100.00%)	51 (94.55%)
Tumoral islands	21 (72.41%)	20 (76.92%)	41 (74.55%)	29 (100.00%)	26 (100.00%)	55 (100.00%)
a)connected to the epidermis	10 (47.62%)	13 (65.00%)	23 (41.82%)	23 (88.46%)	26 (100.00%)	49 (89.09%)
b) located in the dermis	11 (52.38%)	7 (35.00%)	18 (32.73%)	29 (100.00%)	26 (100.00%)	55 (100.00%)
Peritumoral area -refractile stroma	20 (68.97%)	12 (46.15%)	32 (58.18%)	20 (68.97%)	14 (53.85%)	34 (61.82%)
Peritumoral area -proeminent inflammatory infiltrate	21 (72.41%)	14 (46.15%)	35 (63.64%)	21 (72.41%)	16 (61.53%)	37 (67.27%)
Vascular pattern	18 (62.07%)	12 (46.15%)	30 (54.55%)	27 (93.10%)	24 (92.31%)	51 (92.73%)

** SI – BCC represents „Solid / Infiltrative BCC"; ** S – BCC represents „Superficial BCC"*

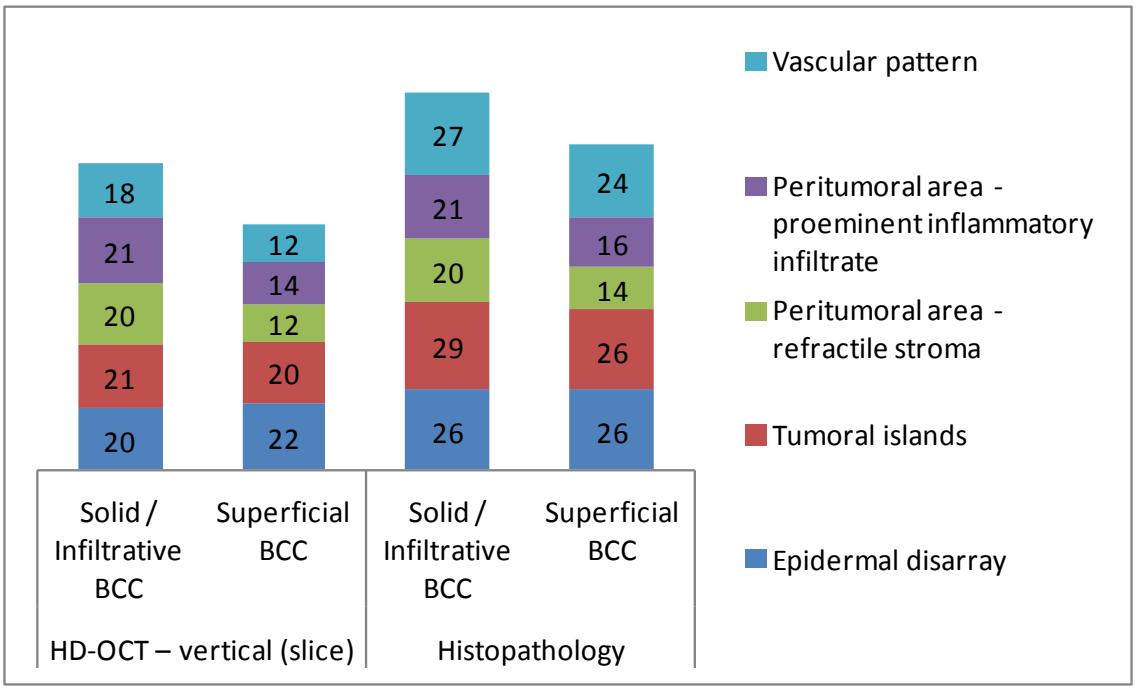


Figure 3. Graphic representations OCT findings and HP examination of tumors (total number of cases identified).

OCT is an important diagnostic tool for non melanocytic skin cancer [21-27]. Many important histopathological features were comparable with the OCT findings in our study regarding the aspects of BCCs. The presence of tumoral islands and lobular structures, regardless of their localization was one of the most proeminent features found in our study. Epidermal disarray was also one notable feature found in almost all cases of BCCs both in vertical and in the en face mode of OCT (Fig. 4 and Table 3).

Table 3. Aspects of HD OCT (en face) and Dermocopy in BCC / Total and Split ratio of the analyzed tumors depending of the OCT and Dermoscopy aspects.

HD-OCT – Horizontal (en-face mode)	SI – BCC*	S – BCC**	Total	Dermoscopy	SI – BCC*	S – BCC**	Total
Epidermal alterations	20 68.97%	22 84.62%	42 72.73%	Scale	10 34.48%	16 61.54%	26 47.27%
				Small Ulcerated areas	28 96.55%	24 92.31%	52 94.55%
Tumoral islands	20 68.97%	20 76.92%	40 72.73%	Blue ovoid nests and pigmented globules	24 82.76%	20 76.92%	44 80.00%
Peritumoral area- abnormal refractile stroma	21 72.41%	20 76.92%	41 74.55%	White areas – fibrosis	18 62.07%	10 38.46%	28 50.91%
Vascular aspects Increased vascularisation	18 62.07%	12 46.15%	30 54.55%	Tipical vascular pattern with branched arborizing vessels	27 93.10%	26 100.00%	53 96.36%

** SI – BCC represents „Solid / Infiltrative BCC"; ** S – BCC represents „Superficial BCC"*

The alteration of the normal distribution of the epidermal layering could be seen in 52% of the superficial BCCs together with subepidermal clusters of tumoral aggregates. Both the en face and the vertical OCT images offered details about the surrounding area of the tumors, like the presence of refractile stroma with abundant inflammatory infiltrate in 74% of the cases; the type of the inflammatory infiltrate could not be identified compared to the histopathology exam, that showed in most of the cases the presence of polymorphic inflammatory infiltrate, with the predominance of lymphocytes and in some cases with the presence of melanophages.

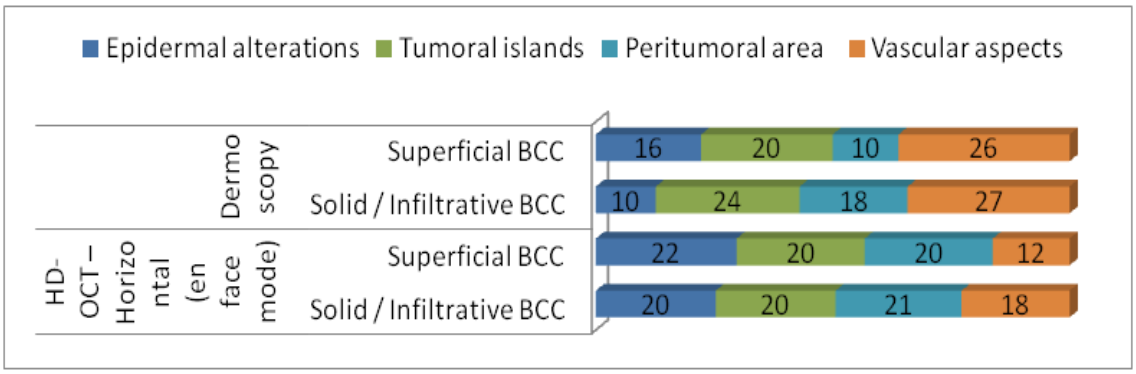


Figure 4. Graphic representations OCT findings and Dermosocpy examination of tumors (total number of cases identified).

Increased vascularisation with the same pattern (small holes/branched vessels) were also visible in most lesions and can be an important architectural aspect of BCC seen in dermoscopy and also in OCT scanning; they can be identified in both the en face and vertical mode of OCT, mainly as high density hyporeflective holes (small fine holes), and sometimes dilated /enlarged in some areas (branched vessels/holes). The same pattern with typical arborizing / branched vessels, were seen in almost all cases- 96% of both superficial and infiltrative BCC on dermoscopy.

Blue ovoid nests /pigmented globules are the most specific dermoscopy pattern of BCCs and were present in almost all cases of the analyzed tumors. On the other hand the OCT scanning is not reliable in differentiating this type of pigmented structures, the pigmented globules cannot be identified individually. When analyzed with OCT in the en face mode, the tumoral islands with the pallisading specific ring of tumoral cells with high reflective margins, were clearly seen in 72% of cases but the presence of the pigment could not be identified as clearly as it was with the means of dermoscopy.

In the en face OCT imaging, the islands of tumoral cells can be noted with the intercede areas of low reflactility (darker streaks) especially in the solid type of BCC; inside the tumoral islands, the cells can appear more reflactile, and may have a monomorphic aspect in shape. The described OCT features and characteristics of this type of non melanocytic skin cancer come to complete other several studies, up to present [1, 2, 28, 29].

4. CONCLUSIONS

OCT has a higher resolution and offers superior details when compared with dermoscopy, but a clear distinction between the subtypes of BCC and the real depth of the lesions was not possible in all cases. Therefore it is reccomended to perform biopsy and histopathological examination when one cannot find explicit features of BCC.

The gold standard diagnosis on a morphological and architectural level of BCC remains the conventional excisional biopsy with subsequent histology. On the other hand OCT results showed many compatible features with the histology aspects of BCCs and BCC subtypes and it can be reefered to as a useful tool for the non-invasive diagnosis of this type of tumors.

However additional studies to confirm the sensitivity and specificity of the features described in this study, on a larger number of tumors, are necessary to confirm the findings of the present one.

REFERENCES

[1] Boone, M.A. et al., *J. Eur. Acad. Dermatol. Venereol.*, **29**(9), 1771, 2015.
[2] Boone, M.A. et al., *Br. J. Dermatol.*, **167**(4), 856, 2012.
[3] Markowitz, O. et al., *J. Clin. Aesthet. Dermatol.*, **8**(10), 14, 2015.
[4] Maier, T. et al., *J. Eur. Acad. Dermatol. Venereol.*, **27**(1), e97, 2013.
[5] Malvehy, J., *J. Eur. Acad. Dermatol. Venereol.*, **29**(S1), 3, 2015.
[6] Markowitz, O. et al., *J. Dermatol. Res. Therapy*, **2016**, 24, 2016.
[7] Jemec, E.B. et al., *Arch. Dermatol. Res.*, **307**, 1, 2015.
[8] Gambichler, T. et al., *J. Dermatol. Sci.*, **45**(3), 167, 2007.
[9] Bechara, F.G. et al., *Skin Res. Technol.*, **10**(3), 169, 2004.
[10] Gambichler, T. et al., *Br. J. Dermatol.*, **170**(6), 1358, 2014.
[11] Neale, R.E. et al., *J. Am. Acad. Dermatol.*, **56**(3), 380, 2007.
[12] Nemer, K.M., *Dermatol. Surg.*, Doi: 10.1097/DSS0000000000001541, 2018.
[13] S. Van Hattem et al., Br. J. Dermatol., 161(4), 840 – 845 (2009).
[14] R.I. Greinert, Pathobiology, 76(2), 64 – 81 (2009).
[15] A.G. Marzuka et al., Yale J. Biol. Med., 88(2), 167 – 179 (2015).
[16] ***** Optical Coherence Tomography News, *AGFA Healthcare Releases SKINTELL an OCT Dermatology Product*, available online at http://www.octnews.org/articles/3177636/agfa-healthcare-releases-skintell-an-oct-dermatolo/, accessed May 7th 2018.
[17] Firnhaber, J.M., *Am. Fam. Physician.*, **86**(2), 161, 2012.
[18] Mogensen, M., *J. Biophotonics*, **4**(7-8), 544, 2011.
[19] Coleman, A.J., *Skin Res. Technol.*, **19**(1), e10, 2013.
[20] Mogensen, M. et al., *SPIE Proceedings*, **7372**, 73721U, 2009.
[21] Ulrich, M., *Br. J. Dermatol.*, **173**(2), 428, 2015.
[22] Ulrich, M. et al., *Br. J. Dermatol.*, **157**(S2), 56, 2007.
[23] Hussain, A.A. et al., *Arch. Dermatol. Res.*, **307**(1), 1, 2015.
[24] Jensen, L.K. et al., *SPIE Proceedings*, **5140**, 160, 2003.

[25] Wahrlich, C. et al., *J. Eur. Acad. Dermatol. Venereol.*, **29**(8), 1562, 2015.
[26] Aneesh, A. et al., *Imag. Med.*, **3**(6), 653, 2011.
[27] Ulrich, M. et al., *Br. J. Dermatol.*, **171**(3), e20, 2014.
[28] Olmedo, J.M. et al., *J. Am. Acad. Dermatol.*, **55**(3), 408, 2006.
[29] Mogensen, M. et al., *SPIE Proceedings*, **6627**, 662708, 2007.