Romanian Reports in Physics **71**, 601 (2019)

HIGH-RESOLUTION OPTICAL COHERENCE TOMOGRAPHY FOR THE DIAGNOSIS OF ACTINIC KERATOSIS

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Received March 19, 2018

Abstract. Actinic keratosis (AK) are considered precursors of invasive squamous cell carcinoma and for this reason early correct diagnosis and treatment is necessary. As these lesions often appear in sun exposed areas, mainly the upper body (head, neck, face), minimum or non-invasive diagnosis techniques are preferred, like optical coherence tomography (OCT). The aim of this study is to find typical morphological characteristics of AK using the OCT technique and to guide the clinician to distinguish between AK's and normal skin or from other cutaneous lesions. A total of 25 lesions from 15 patients that clinically and dermoscopically suggested AK were included in this study; OCT using Skintell was performed for all lesions. OCT examination offers morphological information that is helpful in differentiating AK from healthy skin and from its closest clinical imitators. This work brings information about the value of OCT in describing *in vivo* patterns of AK. These findings can relate and extend previous research on these types of lesions. Further studies on a larger samples of cases, correlated with histopathological results are warranted in this direction.

Key words: optical coherence tomography (OCT), non-invasive imaging, actinic keratosis (AK), epidermal disarray, dermis, dermo-epidermal junction.

1. INTRODUCTION

Optical Coherence Tomography (OCT) is an established method for the investigation of skin morphology that was proposed in the early 1990s. Since its development it has been mainly used as a diagnostic tool in ophthalomology. In time, it has been succesfully applied in other medical fields, such as cardiology, gastroenterology, as well as dermatology [1–5].

OCT uses low-coherence interferometry to produce a two-dimensional (2D) image of optical scattering from superficial and deep skin structures. It has longitudinal and lateral spatial resolutions of a few micrometers [6]. Swept Source (SS) OCT has been developed to provide improved lateral and axial resolution, and it appears to be superior to conventional Time Domain (TD) OCT imaging.

It allows both horizontal (*en-face* mode) and conventional vertical (slice mode) and also the 3D imaging of the skin [7].

OCT is presently considered a potential adjunct to the histopathological assessment of skin tissue specimens, since it is non-invasive and can give immediate results. In the past decade, several functional extensions of OCT have emerged, such as Doppler OCT, polarization sensitive OCT, optical coherence elastography, spectroscopic OCT or molecular imaging OCT.

The incidence of non-melanoma skin cancer is rising world wide. As AKs are considered precursor lesions of potential invasive squamous cell carcinoma, early diagnosis and treatment of these lesions is imperative. Research is continuously developing minimally invasive treatment modalities for this pathology, therefore it is reasonable also to have non-invasive diagnostic methods and follow up techniques of treatment response, and this is where OCT may be extremely useful.

Up to present there are several studies that describe OCT characteristics of AKs in both horizontal and vertical modes [1, 3–5], based on the capability of OCT to generate high resolution *in vivo* images of the skin, up to mid dermal layers. It can be used in association with other imaging methods like dermoscopy, high frequency ultrasound, or confocal microscopy.

In clinical practice, OCT has been employed to identify the morphological characteristics of various diseases, including skin cancers and inflammatory skin disorders. In pre-cancerous lesions like AK, non-invasive diagnostic tools such as OCT may be especially useful, as these lesions often appear in cosmetically sensitive areas like the face and scalp. In these settings, skin biopsies have many disadvantages including pain, scarring, risk of infection or sampling error. OCT imaging does not cause trauma and has no side effects; this technique allows for the evaluation of *in vivo* skin structure, therefore substantial work has been done up to present, in order to identify OCT features in various diseases of the skin and especially in malignant or pre-malignant lesions. No preparation or aid are necessary to perform OCT imaging. The system is mobile and may be used on any skin site. A flexible hand piece is positioned on the lesion that is intended to be analyzed using clear ultrasound gel [8–10]. The area is immediately visualized and can be evaluated directly during the examination. Also the aquired images may be stored for later assessment.

2. EXPERIMENTAL

The SS OCT system uses infrared laser optics, it is a 1300 nm (central wavelength) setup, claiming a penetration depth of 1 mm, imaging an area of 1.8 mm × 1.5 mm with an optical resolution of 3 microns (both lateral and axial). The speed is remarkable as it takes barely 1 s to make a 1 GB 3D image. The penetration depth

of up to 1 mm is typical for OCT and it is limited by the absorption and scattering in the tissue, and not to the quality of the OCT system, although in air it can be enhanced by the quality of the SS [11, 12].

In this study 25 AK were investigated using the commercially available OCT system described in [13]. 15 patients (Fitzpatrick II–III), aged between 48 and 87 years were considered. The group included 8 women and 7 men. Most lesions were located on the scalp and face – 16 lesions, and the rest were situated in the upper anterior trunk – 9 lesions. The lesions were evaluated clinically and dermoscopically before using OCT. Several images (slice, *en face* and 3D) of the lesional and perilesional skin were captured using the Skintell System (Agfa Healthcare) [13]. Many of the included patients had more than one lesion with the same clinical features, mainly in the same anatomical area, close to each other; in this cases the biopsy and the histopathological examination were performed only to one selected lesion. The results came with the confirmation of the actinic keratosis (keratinocyte intraepithelial neoplasia – KIN II–III) and the patients were treated in consequence. No further onchological therapies were necessary.

3. RESULTS AND DISCUSSION

Boon *et al.* findings indicated that OCT is able to identify subclinical AKs and also provides a good correlation between histopathological AK variants and corresponding OCT images, allowing the potential *in-vivo* diagnosis and grading of AK [14, 15]. Mogensen *et al.* analyzed 39 AKs using OCT and polarisation sensitive OCT, reporting a 79–94% sensitivity and a 85–96% specificity in differentiating normal skin from skin lesions in general [3].

Another study by Mogensen *et al.* evaluated 11 AKs with less than 2 mm depth [4]. Results showed that OCT overestimated tumor thickness, but it is more precise than 20 MHz high frequency ultrasound in measuring the maximal thickness of AK. Regarding the morphological characteristics of lesions, OCT images showed comparable results with histological findings like disruption of skin layers and focal thickening of the epidermis [4].

Other features described in AKs were hyperkeratotic scale, polygonal nucleated cells in the stratum corneum (parakeratosis), and stratum corneum disruption. All lesions demonstrated round blood vessels in the superficial dermis and perivascular inflamation [4].

In this study the vertical slice imaging of AKs analyzed revealed an irregular entrance signal, lack of distinct layering, white streaks, dots and grey areas, corresponding to hyperkeratosis. The abnormal layering of the epidermis was visibile in almost all 23 lesions (Fig. 1).

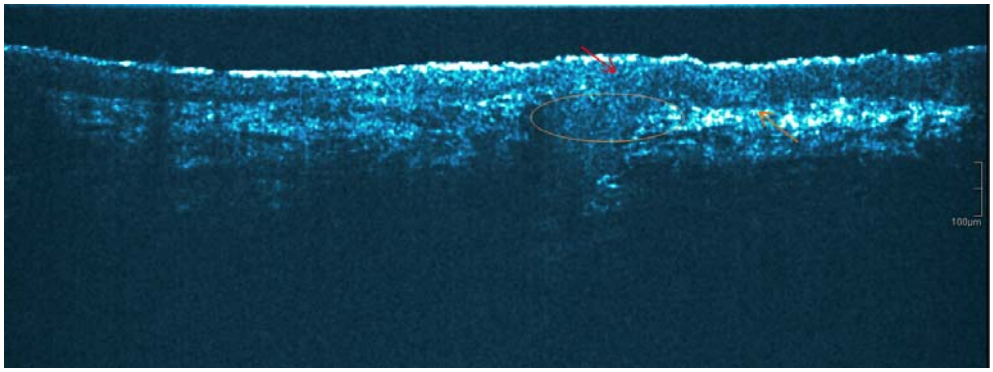

Fig. 1 – High-resolution OCT image from a patient with AKs, showing abnormal layering, irregular thickening of epidemis (red arrow), flat dermo epidermal junction (DEJ) and not outlined (yellow circle and arrow) (Color online).

Boone *et al.* described OCT images of 17 AKs, trying to investigate whether it correlates with the three grading KIN scale of the histopathological examination. There was a good correlation between the dimension of the atypia and of the disarrangements of the spinous/granular layer observed in the *en face* mode and the histopathological AK KIN grading.

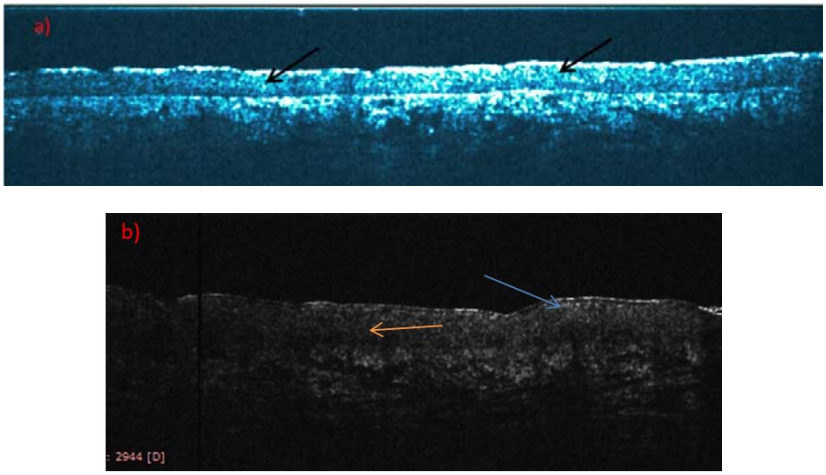

Fig. 2 – High-resolution OCT image of normal skin, a) showing normal layering, with regular epidermis (black arrows), b) normal aspect of stratum corneum (blue arrow), continuous and clear DEJ (yellow arrow) (Color online).

KIN I AKs showed a mildly atypical honeycomb pattern in the lower third of the epidermis; KIN II AKs had an atypical honeycomb pattern involving the lower two thirds of the epidermis, and full thickness disarranged epidermal pattern was observed in AKs KIN III [14, 15]. In our study diskeratotic and atypical keratinocytes

were visible mainly in KIN II and III AKs. In the healthy skin, OCT vertical imaging reveals distinct layering of the epidermis – stratum corneum, and dermis (Fig. 2).

The *en face* OCT investigation in this study displayed disruption of the stratum corneum, architectural disarray in the epidermis and atypical honeycomb pattern in almost all lesions. Stratum granulosum and spinosum presented cellular and nuclear polymorphism and the superficial dermis contains bright irregular bundles coresponding to solar elastosis. These aspects were visible especially in KIN II and III Aks, as the histopathological examination also concluded (Fig. 3).

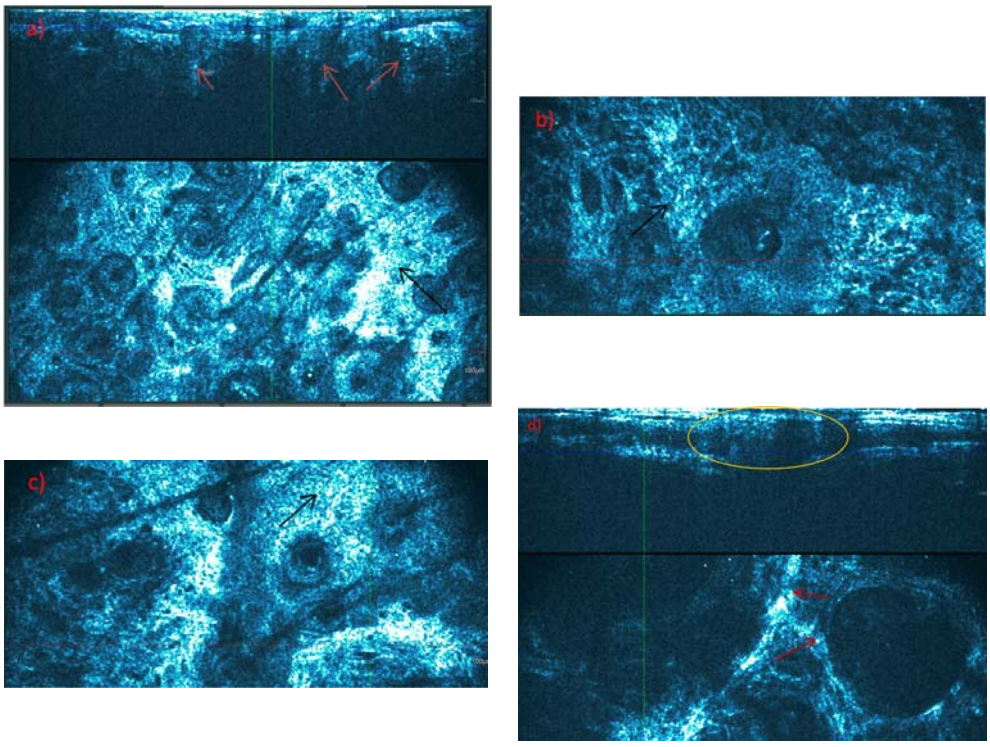

Fig. 3 – a) 3D OCT image of AKs showing architectural disarray, absence of a clear demarcation between dermis and epidermis, elongation and broadening of the rete ridges is present (red arrows); b) & c) atypical honeycomb pattern (keratinocytes are more irregular and brighter and the nuclei are less visible – black arrows); d) 3D image of AK showing in the center absence of clear DEJ (orange circle) and honeycomb aspect with irregular cells (red arrows) (Color online).

Normal skin imaging reveals no interruption of the stratum corneum and a regular honeycomb pattern in the stratum granulosum and spinosum.

In a large study performed by Korde *et al.* [16], 123 AKs were analysed by OCT imaging and compared to normal skin in 112 patients. Results showed heterogenous

images of AK lesions, with the most prominent feature being a dark band in the stratum corneum, which appears to be associated with hyperkeratosis.

The presence of scaling and an abnormal stratum corneum was also visible in most of the AKs analyzed in our study (Fig. 4).

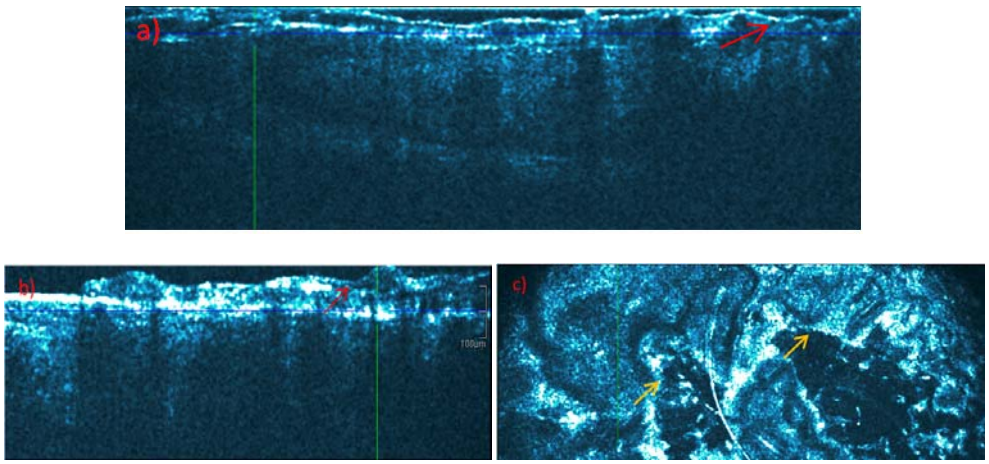

Fig. 4 – B-scan OCT images of AK a) & b) showing a inhomogeneous stratum corneum, irregular and scaling (red arrows); c) *en face* OCT image showing scaling (orange arrows) (Color online).

Other characteristics found in our study were increased epidermal thickness often exhibited bright horizontal reflections due to flaking within the keratinized region. Vertical shadowing from skin flakes was also common.

Mayer *et al.* investigated 20 lesions clinically suspicious of AKs. The images were evaluated starting from the stratum corneum through the epidermis and upper dermis, with the hand piece placed preferentially in the center of the lesions and in the adjacent healthy skin [17].

The clinically healthy adjacent skin showed stratum corneum without interruption, regular epidermal honeycomb pattern in the straum granulosum and spinosum, reticulated mesh work in the upper dermis – in the *en face* mode, as well as distinct layering of the skin – in the slice (B-scans) mode. In this slice mode, AKs were found to display a disruption of the typical layering of the epidermis and dermis (100%), white streaks, dots (95%) and grey areas corresponding to hyperkeratosis (90%).

The *en face* mode of OCT allowed the visualisation of cellular and nuclear polymorphism, diskeratosis (large dark roundish bodies with bright irregular centres) and acantholysis (dark blurry spaces), which have not been described with conventional OCT. Therefore, Mayer *et al.* study proved that the morphological alterations of AKs, could be visualized with OCT, allowing supplementary information on celullar changes in the *en face* mode [17].

4. CONCLUSIONS

AKs are described in OCT imaging in most of previously published studies as being relatively easy to be distinguished from the normal skin, as they are characterised in vertical mode imaging/B-scans by abnormal layering, with thickening of the epidermis and with a visible but disrupted stratum corneum. Also, the *en face* mode of OCT reveals features that are correlated with the histological analysis of the lesions – parakeratosis and distruction of the epidermal structure [18–20].

OCT provides useful information on cellular morphology in the epidermis and on the architecture of cutaneous layers, and could be used in association with other imaging techniques like reflectance confocal microscopy and high frequency ultrasound, to extensively analyze skin lesions in a non-invasive manner, obtaining results close to the gold standard of histopathological examination [15, 19–22].

SS-OCT makes evaluation of normal and pathological skin morphology possible, allowing for the visualisation of architectural changes and cellular features in combined horizontal and vertical mode, with improved resolution compared to TD OCT, for example.

The current study revealed important morphological features present in OCT that can help to distinguish AK's from normal skin – both for B-scans and in *en face* mode. One can thus remark the presence of hiperkeratosis alternating with parakeratosis, an atypical honeycomb pattern and full disarranged epidermal architecture, especially in KIN III AK's.

Diagnosing skin malignant and premalignant lesions as early as possible and in a non-invasive manner remains a challenge for the dermatologist. In conclusion, OCT proves to be a key benefit in this endeavour, with improved resolution compared to the conventional method by combining horizontal and vertical modes. It represents a non-traumatic and time-efficient method for investigating a large number of skin conditions: cutaneous tumors or inflammatory lesions; further reasearch on its applications is warranted [14, 15, 23–28].

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