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Pigmented skin lesions assessment with OCT

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Objective diagnosis on site, in real time is still a challenge for skin lesions, specifically pigmented skin lesions. Different optical tools are currently under development or in process for clinical implementation in order to assist diagnostic procedures. Some of the techniques applied are diffuse reflectance spectroscopy, fluorescence spectroscopy, even confocal fluorescence microscopy. They provide information about biochemical and morphological alterations in the tissue, but no insight on an important for successful treatment parameter- the thickness of the lesion. However, another optical modality could "shine light" on that matter – optical coherence tomography.

Optical coherence tomography (OCT) has been an established tool for diagnosis in ophthalmology; however, its application as imaging modality in dermatology requires more work in creating guidelines for its application.

The objective of this work is to elaborate on specifying peculiarities of pigmented lesions, specifically malignant melanoma, observed through OCT imaging.

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1.Introduction

Skin cancer is one of the most widly spread diseases worldwide. Newly registered cases of non - melanoma skin cancer and malignant melanoma are increasing every year.[1] Early detection of all cutaneous neoplasia is challenging due to similarities in their visual manifestation. The accurate and timely treatment is essential for the achievement of high survival rates. [2,3] Several optical techniques have been applied in recent years for early diagnosis of skin lesions in real time, reducing the necessity of biopsy. Most of those techniques provide information about biochemical and morphological changes in the tissue [4-6]. However, one of the important diagnostically valuable parameters is the thickness of the lesion.

Diagnostic modalities based on the detection of fluorescence signal are some of the most promising in the field of optical diagnostics. However, there is a demand for enhancement of the current techniques and one of the approaches for improvement of fluorescence spectroscopy for diagnostics is through detailed investigation of spectral pecularities of pathological tissue's fluorescence. A very detailed information on the fluorescence properties of biological tissue could be obtained through its investigation with fluorescence spectroscopy performed with excitation – emission matrices (EEM). An EEM is a three-dimensional plot, which provides the means for comprehensive analysis of biological samples without the need for application fluorescent markers. [7] On the other hand, Optical coherence tomography (OCT) is a novel non – invasive method, which works on the principle of Michelson interferometer. It allows 2 or 3 – dimensional cross – sectional as well as en - face sectional images in real time of the microstructural morphology of biological tissue. [8] Therefore, the technique enables visualization of changes that occur in the lesions and interpretation of cutaneous anatomy.

In the current study ex vivo samples of benign, dysplastic, and malignant pigmented cutaneous lesions are investigated using OCT imaging modalities to elaborate on specifying peculiarities that may offer additional diagnostic information compared to other techniques. Moreover, it would allow a more detailed analysis of the lesion and would contribute to better differentiation between dysplastic and malignant ones.

1.1 Methods and Materials

Examination of ex vivo cutaneous lesions was accomplished using FluoroLog 3 spectrofluorometer (HORIBA JY, France) and spectral domain OCT (SD- OCT) system from Thorlabs.

For the fluorescence measurements an additional module with optical fiber was used, since the samples vary in size and shape. The excitation, provided by a xenon lamp, was set in the range of 280 - 440 nm with increment of 10 nm. The detected signal was corrected for the excitation intensity and was in the range of 300 - 800 nm with increment of 1 nm. The face of the optical fiber was in contact with the sample, without added pressure and the fiber was in normal geometry.

The OCT experimental set – up includes SD- OCT base unit, OCTP-PS User-Customizable PS OCT Scanner, OCT-STAND with OCT-XYR1 and computer. The base unit contains a 1300nm super luminescent laser diode providing over 100 nm of spectral bandwidth. The SLD

allows the base units to achieve high imaging depth of 3.5 mm and axial resolution of up to 5.5 μm.

All the samples used in the present investigation were surgically excised at University Hospital "Tsaritsa Yoanna - ISUL" and stored in safe – keeping modified Krebs solution to be investigated with different types of optical modalities. Measurements were performed no longer than two hours after the excision, in order to be as close as possible to the in vivo conditions. All patients received and signed informed consent, as per the regulations of the local Ethics committee.

1.2 Results

The results obtained for a few different types of lesions, investigated through both techniques are presented in the following figures:

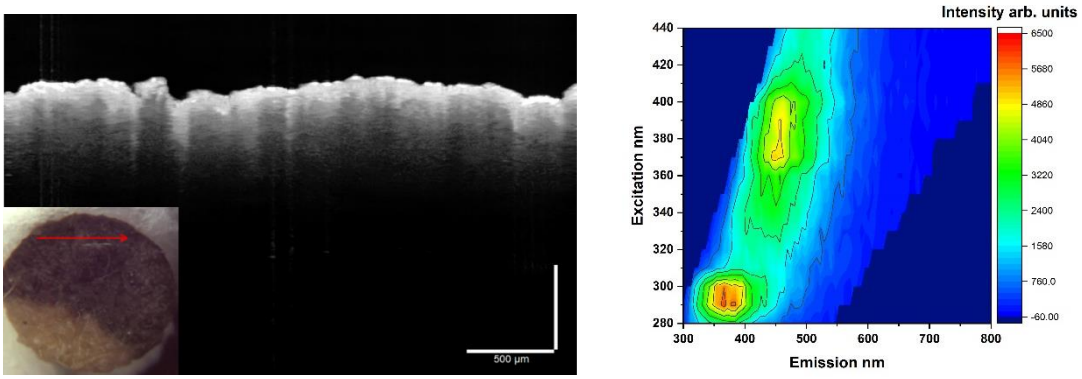

Figure 1. OCT images and EEM of Dysplastic melanocyte nevus.

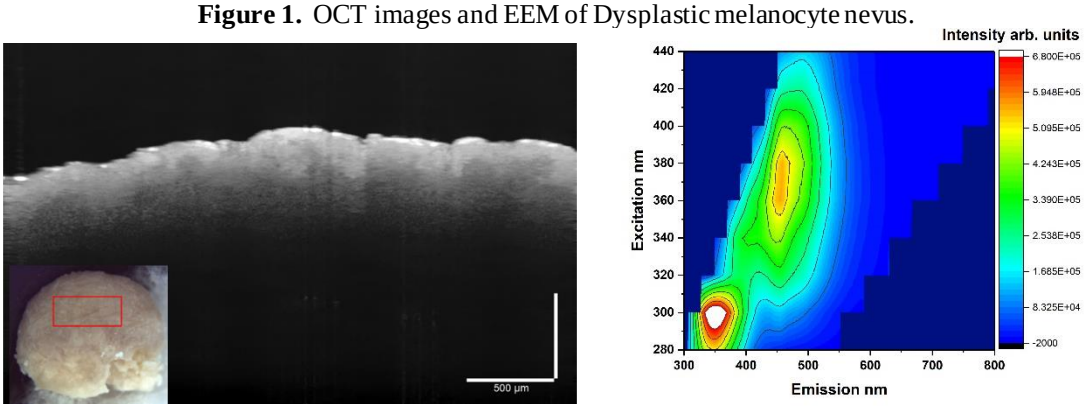

Figure 2. OCT images and EEM of Basal cell carcinoma.

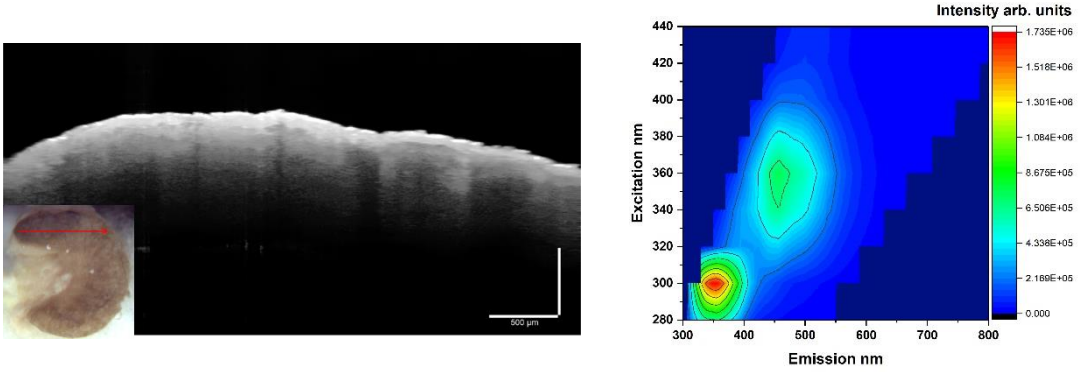

Figure 3. OCT images and EEM of Basal cell carcinoma/ Squamous cell carcinoma.

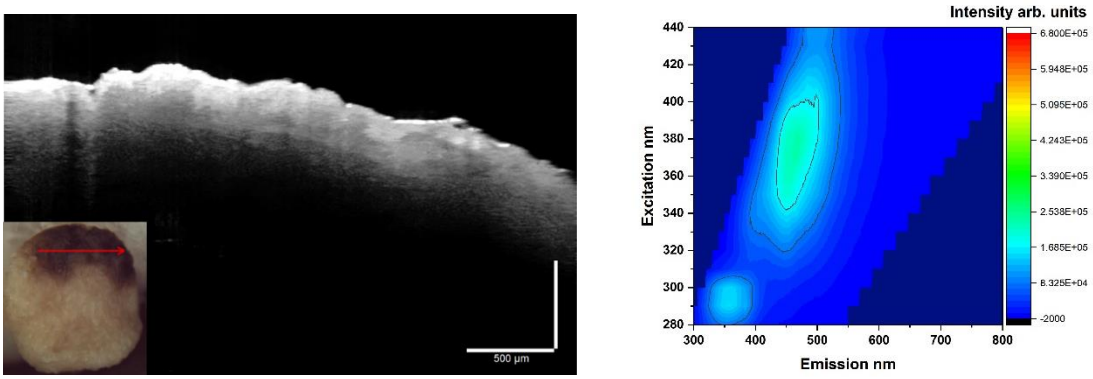

Figure 4. OCT images and EEM of Malignant melanoma.

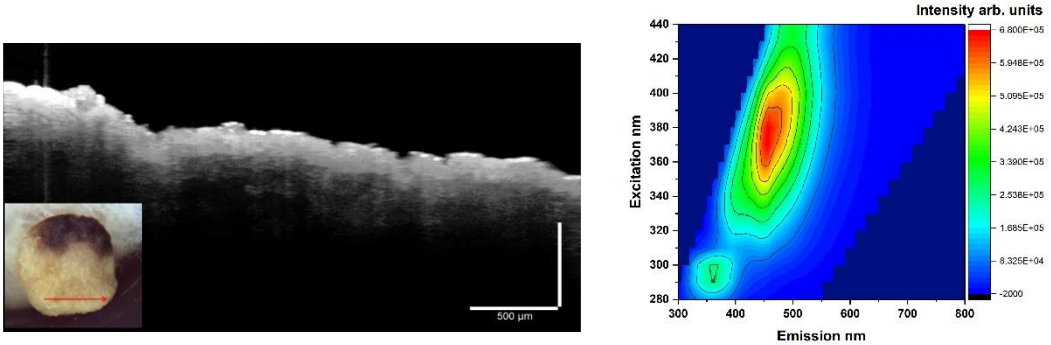

Figure 5. OCT images and EEM of the healthy part of Malignant melanoma.

Endogenous fluorophore	*Tryptophan Tyrosine*	*Collagen Elastin*	*Collagen cross-links*	*NADH*
Excitation maximum [nm]	290 – 300	290, 320	340, 360	340 - 380
Emission maximum [nm]	330 - 400	340, 400	400, 440	450 – 500

Table 1. Excitation and emission maximums of typical endogenous fluorophores in tissue [9,10].

1.3 Discussions

OCT images demonstrate abnormal thickening of the viable epidermis layer in the case of visualization of pathologies, mostly in the case of malignant melanoma. Infiltration of the superficial into deeper skin layers, from the epidermis into the dermis, could be determined in the OCT images of dysplastic melanocyte nevus, basal cell carcinoma and malignant melanoma. The observed surface roughness also changes in correlation with lesion development. Further analysis of OCT images through image processing algorithms could provide quantification parameters for differentiation between cancerous and healthy skin.

EEM of dyspastic melanocyte nevus and BCC demonstrate higher fluorescence intensity from amino acids tyrosine and tryptophan rather than stuctural proteins, collagen, elastin and collagen cross – links. On the other hand, healthy part of the MM have exactly the opposite fluorescent intensity – lower from amino acids and higher from proteins. The most significant difference was observed for MM's fluorescence. It has overall lower intensity of fluorescence due

to melanin absorption. Also, the distortion of the fluorescence signal from the dysplastic nevus could be attributed to the melanin content. [11]

1.4 Conclusions

Dispite the fact that fluorescence spectroscopy provides quantitative information about collagen presence in the investigated tissue samples, it gives no further enlightenment on the alterations in the tissue architecture. OCT provides the opportunity for visual non-invasive assessment and direct translation of standard histology diagnostic peculiarities for lesion identification. On the other hand, fluorescence spectroscopy gives more information about biochemical and metabolic alterations in the tissue. Both techniques could be used repeatedly without affecting the treated area, which gives the opportunity to monitor suspicious pathologies and treatment results.

However, in order to establish diagnostic procedure based on OCT and fluorescence characteristic of skin pathologies and extensive amount of samples both ex vivo and in vivo should be thoroughly evaluated.

In particular, combination between OCT and fluorescence spectroscopy could be an useful noninvasive novel diagnostic modality for skin cancer diagnosis and can improve the currenct diagostic tools such as dermatoscopy, thus will be avoid unnesessary biopsies.

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