Characterization of benign and malignant melanocytic skin lesions using optical coherence tomography in vivo

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Background: Although optical coherence tomography (OCT) is a promising noninvasive imaging technique for the micromorphology of the skin, OCT has not been studied systematically in skin cancer such as malignant melanoma (MM).

Objective: We sought to visualize and characterize melanocytic skin lesions (MSL) by using OCT in vivo, compare OCT features of benign nevi (BN) and MM, and histologically validate the OCT findings.

Methods: In all, 75 patients with 92 MSL, including 52 BN and 40 MM, were included in this study. MSL were investigated by OCT in vivo and consecutive histology. We compared the OCT images with the corresponding histologic slices of BN and MM. To ascertain accuracy of correlation between OCT images and histologic sections, the excised lesions were tattooed according to the level of OCT scanning. For every MSL, serial histologic slices were prepared.

Results: MM often showed a marked architectural disarray (P = .036) and rarely displayed a clear dermoepidermal border (P = .0031) when compared with BN. OCT of MM infrequently demonstrated a dermoepidermal junction zone with finger-shaped elongated rete ridges as typically seen in BN (P = .011). Compared with BN, the papillary and superficial reticular dermis in MM frequently displayed a more diffuse or patchy reflectivity with loss of the typical bright horizontal linear structures (P = .022). However, more or less large vertical, icicle-shaped structures were the most striking OCT feature of MM, which were not observed in BN ($P < .001$).

Limitations: The diagnostic performance of OCT in the diagnosis of MSL could not be fully determined. Sensitivity and specificity studies also including other skin tumors have not been performed.

Conclusion: In this study, distinct OCT features of MSL could be correlated to histopathologic findings. With regard to the micromorphologic features visualized by OCT, we detected significant differences between BN and MM. These OCT features might serve as useful discriminating parameters of MSL. (J Am Acad Dermatol 2007;57:629-37.)

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Optical coherence tomography (OCT) is an emerging medical diagnostic imaging technique that provides information on the structure and function of biological tissue in vivo with micron resolution. Depending on the scattering properties of tissue and some accepted loss in resolution, a penetration depth of about 1000 μm can be achieved with OCT.[1-3] Prototypes of OCT systems with ultrahigh resolution of about 1 μm have recently been developed; however, a lateral resolution of 10 to 15 μm is more typical in conventional OCT technology.[2] Similarly to conventional histology, OCT is particularly capable to present cross-sectional high-resolution images of structures below

Abbreviations used:

BN: benign nevi
CLSM: confocal laser scanning microscopy
MM: malignant melanoma
MSL: melanocytic skin lesions
OCT: optical coherence tomography

the tissue surface. The method of OCT is being evaluated in several countries, and in some it has already been certified for medical diagnostics, including endoscopic study of mucosae, eg, esophagus, stomach, and uterine cervix.[1]

In vivo differentiation between benign and malignant melanocytic skin lesions (MSL) is one of the most important issues in clinical dermatology. Although reports assessing clinical (naked-eye) diagnosis of malignant melanoma (MM) have shown sensitivity values of 65% to 80%, depending on the expertise of the investigators, the diagnostic sensitivity of epiluminescence microscopy in detecting MM has turned out to be 10% to 27% higher than in clinical diagnosis by the unarmed eye.[4-6] The need for improved diagnostic accuracy in MSL has led to the development of imaging techniques including confocal laser scanning microscopy (CLSM) in vivo,[7,8] high-resolution ultrasound,[9,10] and spectroscopy.[11] Apart from the imaging techniques mentioned above, OCT also appears to be a promising tool for the in vivo investigation of physiologic and pathologic features of human skin.[2] After initial observations of healthy skin[12-14] various inflammatory conditions including psoriasis, contact dermatitis, and physically induced skin alterations such as thermal injury and sunburn[15-17] have so far been studied by means of OCT. However, OCT has not been investigated systematically in skin cancer such as MM. The aim of the current study was to visualize and characterize MSL by using OCT in vivo, to compare OCT features of benign nevi (BN) and MM, and to histologically validate the OCT findings.

METHODS

Patients

This prospective study included 92 MSL in 75 patients, recruited from our pigment lesion clinic. The patients had been scheduled for excision either to rule out MM or for cosmetic reasons. After clinical inspection and dermoscopic assessment, the patients' skin lesions were all subjected to OCT measurements in vivo, full thickness skin excision, and histology. Only MSL with a tumor size of up to 1.5 cm in diameter were included. Lesions with frank ulceration, marked hyperkeratosis, or both were excluded from the study, as both associated crust and scab are known to enhance posterior light attenuation. Non-MSLs were excluded from further evaluation as confirmed on histology. The study was conducted in the light of the Declaration of Helsinki. All those who participated in the investigation signed an informed consent form.

OCT in vivo

OCT works analogously to an ultrasound scanner—the main difference being that ultrasound pulses are replaced by a fiber-optic Michelson interferometer with a low-coherence—length broadband light source. The corresponding short-coherence length permits a spatial resolution in-depth direction of less than 10 μm. The lateral resolution is given by the numeric aperture of the used objective as long as single scattering prevails. Depending on the scattering properties of tissue and some accepted loss in resolution, a penetration depth of about 1 mm can be achieved. The source coherence length and the spot size of the beam focus on the sample determine the depth resolution and lateral image resolution, respectively.[2,3,18] A commercial OCT scanner (SkinDex 300, ISIS optronics GmbH, Mannheim, Germany) was used in this study.[18] A bandwidth $\Delta\lambda = 70$ nm and a center wavelength of $\lambda_0 = 1300$ nm is used. According to the manufacturer's manual, the spatial resolution in the 3-dimensional (3D) measurement modus is 3 (lateral) by 5 (depth) μm^2. Imaging is possible up to a maximum depth of 1 mm. The architecture of the system with 8 parallel scanning channels allows for fast scans. Within 2 seconds a total of 512 scans is acquired along the length of 1 mm in lateral direction and an axial range of 0.9 mm. Echocardiographic signals are digitized with 14 bits amplitude resolution. Before OCT measurement, two closely adjacent waterproof marks were drawn on the surface of interest. At least 3 OCT scans (1- × 0.14-mm scan field) per lesion were obtained between these marks, which were captured with a charge couple device camera (field-of-view of 4.5 mm^2) integrated in the sensor head of the OCT scanner (Fig 1, *A*). The 3-dimensional measurement modus of the OCT scanner with 5-μm interplane distance was used to generate 15 2-dimensional images (B-scan) per 3-dimensional scan.

Histology

After OCT assessment including site marking, the tumors were completely excised under local anesthesia. Then the waterproof marks were tattooed using red stain (Red WAK-HM-4, WAK Chemie, Steinbach, Germany). The excised tissue was then fixed in formalin and embedded in paraffin. Serial