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Optical coherence tomography imaging of non-melanoma skin cancer undergoing photodynamic therapy reveals subclinical residual lesions

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Abstract
Background: Photodynamic therapy with methyl aminolaevulinate (MAL—PDT) is a widely used non-invasive treatment modality for non-melanoma skin cancer (NMSC). The outcome of MAL—PDT is usually primarily evaluated clinically. Optical coherence tomography (OCT) is a non-invasive imaging technology based on interferiometry. OCT has been proven to provide high accuracy in identifying NMSC lesions and performing thickness measurements of thin tumours.
Objectives: To describe the OCT morphology in in-vivo NMSC lesions during MAL—PDT treatment and to investigate the use of OCT in evaluating the response of MAL—PDT treated NMSC lesions.
Methods: A total of 18 biopsy-proven basal cell carcinomas and actinic keratoses were monitored by OCT during 2 sessions of MAL—PDT treatment. At 3-months follow-up the patients were assessed both by OCT and clinically. If the clinical and OCT evaluation came to different conclusions on recurrence of the lesion, patients were followed more closely at clinical appointments for up to one year after the PDT treatment.
Results: All lesions displayed at least one OCT characteristic before MAL—PDT treatment. At 3 months follow-up, recurrence was suspected clinically in 5/18 cases, with OCT in 7/18 cases. OCT correctly identified all of the partial responses also found by the clinical examinations. In both cases where recurrence was only found in OCT, this was subsequently confirmed by histology.

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Conclusions: Our study suggests that OCT identified 29% more recurrences than clinical examination alone. OCT can detect subclinical residual NMSC lesions after MAL—PDT treatment and may therefore be an accurate tool for early detection of residual lesional tissue.

Introduction

Currently, non-invasive therapies are established treatments of non-melanoma skin cancers (NMSC) such as actinic keratosis (AK), Bowen's disease and basal cell carcinoma (BCC). Photodynamic therapy (PDT) with methyl aminolaevulinate (MAL) is a widely used non-invasive treatment modality for NMSC offering clinically significant response rates and superior cosmetic outcomes [1,2]. The outcome of MAL—PDT is usually primarily evaluated clinically and by dermoscopy. If an incomplete response or recurrence is suspected, a skin biopsy and subsequent histopathological evaluation of the lesion will most often be performed. A good cosmetic outcome has been described as a feature of MAL—PDT treatment and therefore skin biopsies appear to be an inexpedient invasive practice for evaluating treated lesions. Consequently, it is speculated that non-invasive monitoring and evaluation of PDT treated NMSC using optical coherence tomography (OCT) imaging may be a useful alternative [3]. OCT is a non-invasive imaging technology based on interferometry [4]. OCT is a dynamic tool providing real-time, cross-sectional images of skin structures; in vivo to a depth of around 2 mm. Previous studies have reported high accuracy in distinguishing lesions from normal skin and providing thickness measurements of thin NMSC tumours [5—7]. This implies that OCT may potentially be utilised to monitor and evaluate the efficacy of treatments, especially of skin tumours [3,8,9]. In this study we aim to describe the OCT morphology of in vivo NMSC lesions during PDT treatment and to investigate the use of OCT in evaluating the response of PDT treated NMSC lesions.

2 Materials and methods

2.1 Patients

The study was performed at the Department of Dermatology, Roskilde Hospital, according to the Helsinki Declaration. A total of 23 consecutive patients diagnosed with either BCC or AK were included in the study (6 AK patients and 17 BCC patients, respectively). A total of 5 patients did not complete the 3-month follow-up examinations and were therefore excluded from the study, leaving a total of 18 evaluable patients: 4 AK patients and 14 BCC patients. All diagnoses were based on histopathology.

2.2 Treatment protocol

Patients were OCT-imaged during the MAL—PDT treatment process. OCT-images of lesions and adjacent normal skin were acquired at baseline, before and after MAL—PDT treatments, and at 3-months follow-up. OCT-imaging and image analysis were performed by the same investigators (LT and CB) throughout the study.

Lesions were curettaged lightly (only superficial debulking of tumours in order to enhance photosensitizer penetration) and a 1 mm thick layer of the topical photosensitizer methyl aminolevulinat (Metvix®, Galderma Nordic) was applied to the lesion and to a rim of approximately 10 mm adjacent normal skin. The photosensitizer was left under a light-blocking occlusive dressing for 3 h and any residual was removed from the surface with saline. Lesions were subsequently exposed to standard 630 nm red light emitting diode (LED) light for a total of 8 min (Aktilite CL16/128, PhotoCure ASA®; dose: 37 J/cm^2). All lesions received two sessions of PDT 7 days apart.

At 3-months follow-up the patients were assessed both by OCT and clinically by a doctor at the Department of Dermatology, Roskilde Hospital. The clinical and OCT assessments were not performed by the same doctor. The conclusions from the clinical examination remained unknown to the doctor performing the OCT imaging at the time of the OCT evaluation. If the clinical and OCT evaluation came to different conclusions on recurrence of the lesion, patients were followed more closely for up to one year according to the clinical decision of the treating physician in order to provide realistic data for assessing the utility of OCT in a routine setting. If the suspicion of recurrence persisted, a skin sample was taken from the treated area and examined by histopathology.

2.3 Optical coherence tomography

Skin morphology was studied using the VivoSight OCT (Michelson Diagnostics Ltd., UK), a swept-source Fourier-domain OCT system with a 7.5 μm lateral and 10 μm vertical resolution. The laser operates at a center wavelength of 1300 nm and the probe is placed directly on the skin without the use of gel or oil. Images were captured in real-time as sequences of video data that was subsequently reviewed and stored as single images. ImageJ software was used to analyse the OCT images. Two investigators (LT and CB) carried out the analyses of the results. The OCT morphology of lesions before, during and after MAL—PDT treatment was described and the OCT image dept was measured. In accordance with former studies of OCT morphology of NMSC lesions, the following OCT criteria for BCC and AK were used [5,10—12]:

(i) disruption of normal layered skin architecture (BCC and AK),
(ii) thickening of epidermis (BCC and AK),
(iii) oval signal-poor structures surrounded by white stroma corresponding to BCC tumour lobules (BCC),
(iv) white streaks in the upper epidermis corresponding to dense, hyperkeratotic areas (AK).