Julia Welzel · Maike Bruhns · Helmut H. Wolff

Optical coherence tomography in contact dermatitis and psoriasis

Abstract Optical coherence tomography (OCT) is a new noninvasive imaging technique. In this study, it was used for the investigation of contact dermatitis and psoriasis. In these common inflammatory skin diseases the value of OCT for quantification and monitoring of the changes in comparison with other bioengineering methods was evaluated. Repeated measurements were performed in healthy volunteers after experimental induction of irritant contact dermatitis and in patients with psoriasis. In the OCT images, the thickness of the epidermis and the signal attenuation coefficient in the upper dermis were evaluated. The changes were compared with measurements of transepidermal water loss, hydration, skin colour and surface roughness, and with high-frequency ultrasound measurements. In irritant dermatitis and psoriasis, thickening of the epidermis was detected and could be monitored over time. The light scattering in the upper dermis was lower than in healthy skin. This was interpreted to be due to the inflammation and oedema, leading to a less-dense arrangement of the collagen fibres. The changes in the OCT images did not significantly correlate with the changes shown by the other methods. OCT is an interesting tool for investigation of inflammatory skin diseases. It is a simple method for determination of epidermal thickness and therefore provides, in addition to other methods, information on the severity of the disease and on treatment effects.

Keywords OCT · Psoriasis · Contact dermatitis · Bioengineering methods

Introduction

Inflammatory skin diseases such as contact dermatitis and psoriasis are common. In most cases, the diagnosis is simple and can be made by the naked eye. In cases of doubt, histological examination of biopsy tissue is used for confirmation. For grading of the diseases, visual scores such as the PASI (psoriasis area and severity index) have been established [5]. They are used for quantification and monitoring of the disease during clinical and experimental studies on therapeutic effects, but are lacking in objectivity and reliability. Using image analysis methods, the affected area can be evaluated with great accuracy [14], but the severity of inflammation at a single location is left unclear. Most of the bioengineering instruments such as measurements of transepidermal water loss (TEWL), hydration and skin colour give information only on changes of the skin function and not on morphological features. Ultrasound at 20 MHz can be used for visualization of the dermis, but the resolution is not high enough to define the epidermis and the differentiation between inflammation and oedema is poor [10, 16]. Besides, a water path has to be used for ultrasound to reduce the impedance difference. This disturbs investigation of the hydration status of the skin. Scales complicate the noninvasive measurements, e.g. when performing erythema determination or sonography, because they lead to total reflection of the signal at the surface. They often have to be removed beforehand which might result in artefacts. Repeated biopsies are invasive and therefore not useful for time-course studies, and besides a repeat biopsy cannot be from the identical area from which the preceding biopsy was taken. Therefore there is a demand for a noninvasive morphological method for studies of treatment effects in inflammatory skin diseases.

Optical coherence tomography (OCT) was developed for investigation of the human eye [9]. It is a noninvasive method using infrared light. The principle is based on interferometry. Two-dimensional images are displayed in real time which are comparable with those from ultrasound but represent optical and not acoustic inhomogeneities of the tissue. The axial and lateral resolution is about 15 µm and much higher than that of 20-MHz ultrasound. The lateral image dimensions are some millimetres with a penetration depth of the signal of about 1 mm. The specifications de-

J. Welzel (✉) · M. Bruhns · H. H. Wolff
Department of Dermatology, University of Lübeck,
Ratzeburger Allee 160, 23538 Lübeck, Germany
Tel.: +49-451-5002515, Fax: +49-451-5002981,
e-mail: welzel@medinf.mu-luebeck.de

pend on the light source and some technical details [2, 11]. The images represent backscattered signals in a negative grey scale where the brightness of the pixels correlates with the signal intensity. The scattering characteristics of skin depend on the composition, size and distribution of particles and play a more important role than absorption. Previous studies have shown that layers such as the stratum corneum and the epidermis as well as adnexal structures and blood vessels can be distinguished in OCT images [6, 13, 18, 20]. The scattering is influenced by the melanin content, the distribution of cells and the orientation and density of the collagen fibres. It is likely that scales, acanthosis of the epidermis and dilation of blood vessels are detectable in OCT images.

In this study, the value of OCT for monitoring inflammatory skin diseases was evaluated. Two common skin diseases, contact dermatitis and psoriasis, were investigated over a period of time. For induction of irritant contact dermatitis, a standard model was used in which sodium lauryl sulphate (SLS) was applied as an irritant. OCT was compared with other established bioengineering methods to interpret and correlate the results as well as to assess the relative importance of this new method.

Subjects and methods

OCT system

For this study, a prototype of the OCT system (Sirius, 4optics, Lübeck, Germany) was used which was developed and constructed at the Medical Laser Center Lübeck. It is a fibre-optic interferometer with a light source at a wavelength of 1300 nm and a coherence length of 15 µm, resulting in an axial and lateral resolution of 15 µm and a penetration depth of the signal of about 1 mm. A compact handpiece allows any skin region of interest to be reached. The two-dimensional images are recorded in real time with a lateral dimension of 4 to 6 mm. In a region of interest of the b-scan image, an average a-scan can be calculated which represents the signal intensities. On the curve, the height of peaks and distances between peaks as well as the attenuation coefficient µ as a function of the slope of the curve can be calculated at different depths. The signal attenuation coefficient µ depends on the degree of scattering and absorption, and represents the decrease in the number of photons which are backscattered. For distance measurements, the values have to be corrected by dividing by the refractive index of skin which is approximately that of water (1.33) because the optical distances are dependent on the medium.

Other noninvasive methods

Measurements of the TEWL were performed using the a Tewameter TM 210 (Courage & Khazaka, Köln, Germany). The hydration of the stratum corneum was determined using a Corneometer CM 820 (Courage & Khazaka). For investigation of skin colour, a Chromameter CR 200 (Minolta, Ahrensburg, Germany) was used. The bioengineering methods were carried out with regard to guidelines for standardization, i.e. at a constant air temperature and humidity after acclimatizing for 15 min. Laser profilometry was performed using a profilometer UB 16 (UMB, Ettlingen, Germany) on silicone replicas of the skin areas using the material Silflo (Flexico, Potters Bar, UK). The replicas were oriented along the body axis. Measurements of a square area of 4×4 mm parallel to the axis were performed. After inversion and alignment, a high-pass filter with a 0.5-mm cut-off was used to minimize artefacts. The roughness parameters Rz (mean depth) and Ra (arithmetic mean) were calculated [19]. For high-frequency ultrasound, a Dermascan C (Cortex, Hadsund, Denmark) was used. It is a 20-MHz ultrasound system which provides images with a resolution of 80 to 200 µm and a detection depth of about 8 mm. The transducer is coupled to the skin by a water path and a gel film. In two-dimensional images, the dermis can be distinguished from the subcutis. Thickness measurements can be performed as well as a calculation of the echodensity.

Subjects

Experimentally induced contact dermatitis was investigated in 15 healthy female volunteers (aged 24 to 27 years) after informed consent had been obtained. The psoriasis group comprised 31 patients (16 female, 15 male; aged 10 to 87 years). After therapy, 18 plaques in 16 patients (9 female, 7 male; aged 10 to 82 years) were monitored. The patients were likewise informed of the intention of the study and gave their informed consent to participate.

Treatments

Contact dermatitis

To the inner forearm, 300 µl of a 0.5% aqueous solution of SLS (Merck, Darmstadt, Germany) was applied with occlusion for 24 h in a polypropylene chamber (diameter 19 mm) fixed with tape. Before irritation, after 1 day 1 h after removal of the chamber, and on days 4 and 7, OCT was performed and TEWL, hydration and skin colour measured. A silicone replica was taken from the area at the same time-points for laser profilometry. The OCT images were evaluated by calculating the epidermal thickness, the intensity of the entrance signal and the signal attenuation in the upper dermis.

Psoriasis

In each patient, a psoriatic plaque and the adjacent healthy skin were investigated before and after therapy by OCT and ultrasound imaging. The patients were treated with various regimens: PUVA bath therapy, topical vitamin D_3 or dithranol, partly combined with UV irradiation. Second measurements were taken when the lesion was cured (no scales, no infiltration, but in some cases with a little reddening remaining). The healing time varied between 8 and 47 days with a mean of 21 days. The OCT images were evaluated by determination of the epidermal thickness and the attenuation coefficient of the upper dermis. In the sonographic images, the thickness and the echodensity of the echolucent band in the upper dermis were calculated.

Statistical analysis

For comparison of the values before and after treatment, the Wilcoxon signed ranks test for matched pairs was used. Significance was assumed at $P \leq 0.05$. The different methods were compared by calculating the Spearman's rank correlation coefficient with significance of $r_s > 0.5$ or < -0.5.

The study and the OCT measurements were reviewed and approved by the local ethics committee. They were in accordance with the revised Declaration of Helsinki.

Results

Irritant contact dermatitis

Occlusive treatment with SLS resulted in a reddening of the skin, followed by dryness, in some cases with scales.

Table 1 Comparison between OCT, physiological parameters and roughness values in irritant contact dermatitis. Values are means±SD, n= 15

Day	OCT thickness epidermis (µm)	OCT signal attenuation, µ, dermis (/cm)	TEWL ($g/m^2 \cdot h$)	Capacitance (IU)	a*	Ra	Rz
0 (before)	123±27	27±15	6.3± 1.9	60.6± 9.7	5.2±1.3	88.8± 4.7	12.7±2.1
1	129±35	26±18	35.7±16.1**	60.6±17.8	8.0±2.1**	114.1±34 *	13.3±2.6
4	145±29	23±10	24.6±11.3**	35.8±16.6**	9.3±3.3**	111.4±46	13.9±3.9
7	145±26*	22±10	17.2± 7.5**	33.6±16.8**	7.4±2.8*	99.4±28.2	14 ±3.1

*$P \leq 0.05$, **$P \leq 0.01$, vs before irritation

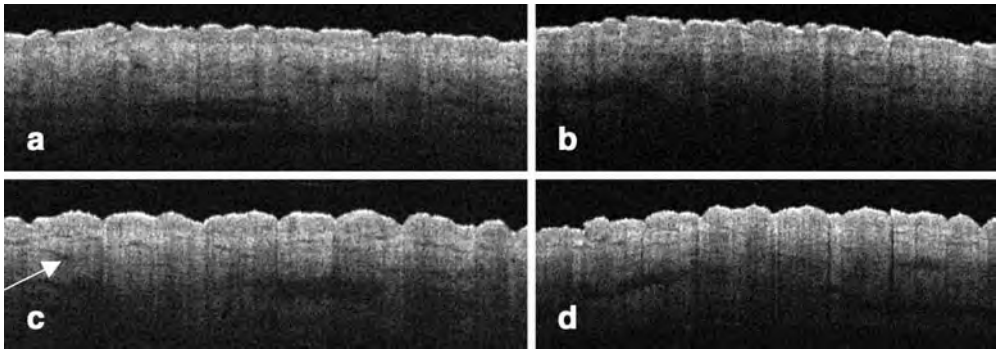

Fig. 1a–d OCT images of healthy forearm skin before irritation (**a**), and 1 day (**b**), 4 days (**c**) and 7 days (**d**) after irritation with SLS. The surface shows larger folds, the entrance signal is more pronounced and the epidermis is thickened. The dermis shows dilated blood vessels (*arrow*). (4×1.8 mm)

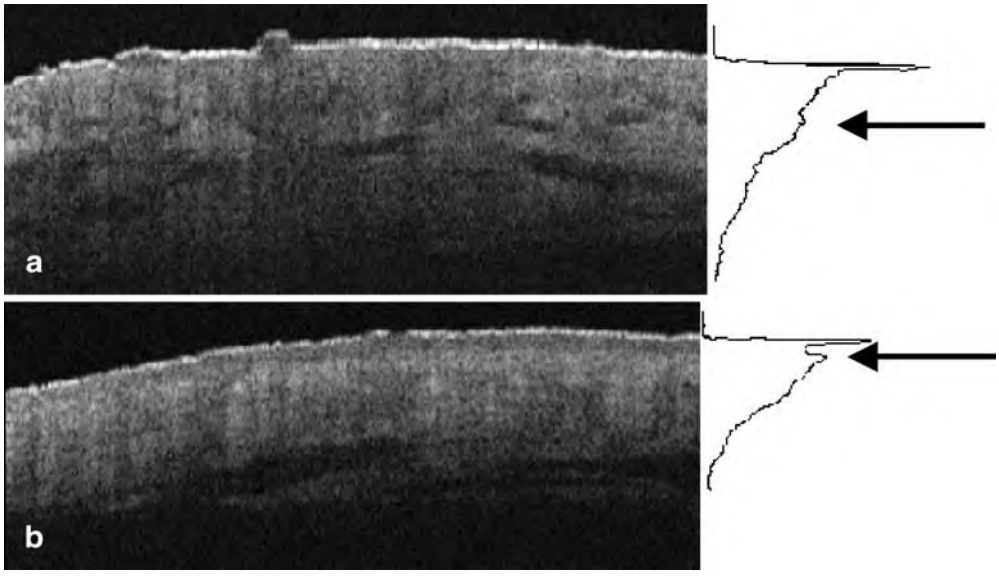

Fig. 2a, b OCT image of psoriatic skin (**a**) and healthy adjacent skin (**b**) of the forearm. The subject and the location are identical to those of Fig. 4. On the right, the average a-scans are shown. In psoriasis, the entrance peak is higher, and the distance to the second intensity peak (*arrows*) which represents the border with the dermis is larger. The signal attenuation in the dermis is lower (4×1.8 mm)

The interindividual variability in the severity of the reaction was high. The irritation induced a significant increase in TEWL and the red value a* showed a maximum after 24 h. Even after 1 week, the values were still higher than before irritation. The hydration values decreased stepwise to a minimum after 1 week. Laser profilometry showed an increase in both roughness parameters Rz and Ra (Table 1).

In the OCT images of healthy skin before irritation, the skin surface showed a homogeneous small entrance signal without interruptions, representing light reflection at the surface. The superficial flat layer below the entrance signal corresponded to the epidermis. The border with the dermis was sharply demarcated, represented by a second intensity peak in the average a-scan. The dermis was more signal-intense with an irregular distribution of pixels and some signal-free longish cavities (Fig. 1a, Fig. 2b). After irritation, the surface showed larger and more irregular folds. The entrance signal was thickened and stronger, and this could be quantified by a significant increase in the relationship between the signal intensity of the entrance peak and the second peak representing the border with the upper dermis. The thickness of the epidermis increased significantly with a maximum after 4 days. In the dermis, dilation of the signal-free cavities was observed (Fig. 1b–d). This was accompanied by a slight decrease in the attenuation coefficient µ, but this did not reach statistical signifi-

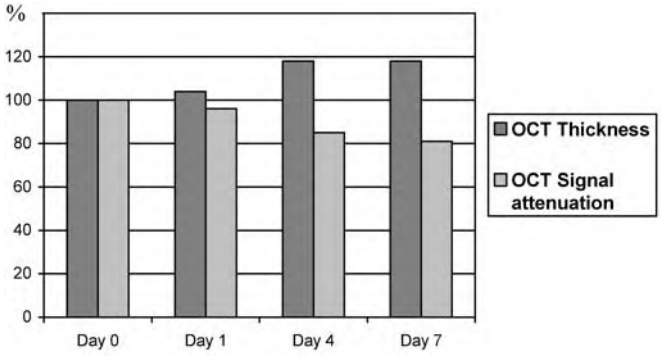

Fig. 3 Changes in the thickness of the epidermis and the signal attenuation coefficient μ in the upper dermis after irritation with SLS (percentage of the starting value before irritation)

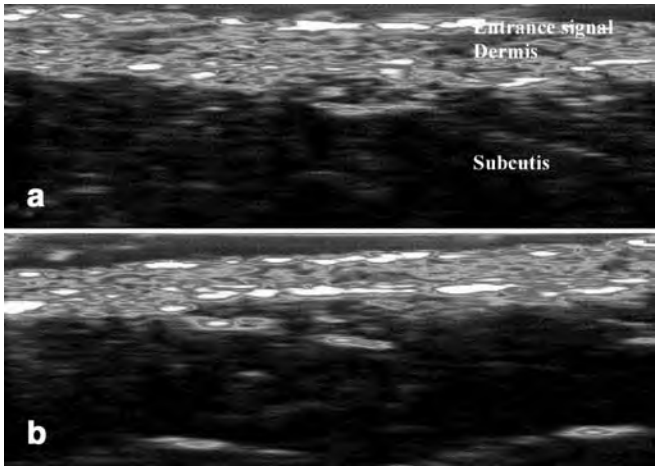

Fig. 4a, b 20-MHz ultrasound of psoriatic skin (**a**) and healthy adjacent skin (**b**) of the forearm. In psoriasis, the entrance signal is slightly more pronounced with some interruptions. The dermis is thickened with some echo-poor areas (12×4 mm)

cance (Table 1, Fig. 3). The degree of epidermal acanthosis or the decrease in attenuation coefficient did not correlate with the changes in the physiological parameters indicating that not all subjects with a pronounced TEWL increase or erythema showed equivalent changes in OCT and vice versa.

Psoriasis

In psoriasis, the ultrasound images showed a thickened entrance signal, some echo-poor areas in the upper dermis and an increase in dermal thickness compared to unaffected adjacent skin (Fig. 4). The variability in the changes was high. In many images, the echodensity of the upper dermis could not be evaluated because of a signal shadow due to total reflection at the surface. The thickness and echodensity of the echolucent band in the upper dermis showed a slight but not significant decrease after therapy.

The OCT images of psoriasis before therapy were markedly different from those of unaffected skin (Fig. 2).

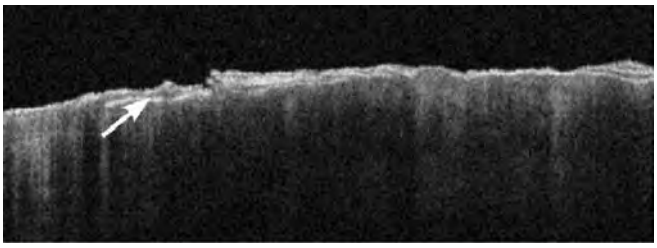

Fig. 5 OCT image of severe scaling in psoriasis. The entrance signal is composed of several parallel layers (*arrow*) (4×1.8 mm)

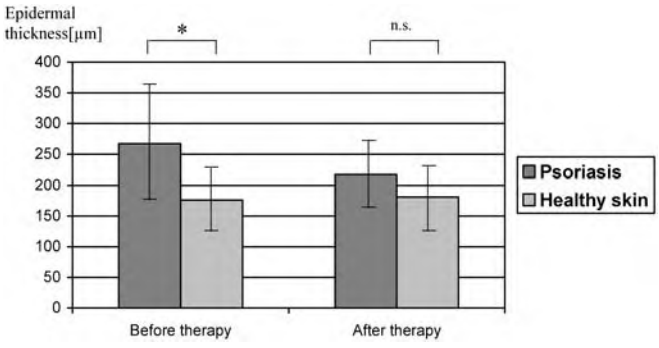

Fig. 6 Distance between the entrance peak and the second peak (μm) before and after therapy. Values are means±SD. The thickness of the epidermis in the psoriatic lesion decreases but does not reach normal values

The entrance signal was significantly thickened and in some cases composed of several parallel layers (Fig. 5). The epidermis showed significant acanthosis (Fig. 6). The second intensity peak was lower and less-defined than in healthy skin. The dermis showed dilated signal-free cavities and significantly lower signal attenuation (Table 2). The changes diminished after therapy and the data approximated those of healthy skin, although they did not reach normal values.

Discussion

In OCT of irritant contact dermatitis, several changes could be observed which correspond to the visible appearance of the eczematous reaction and to changes known from histological investigations.

The skin surface appeared more irregular. Morphological evaluation of skin replicas has shown that roughness increases after irritation [12]. OCT as a two-dimensional cross-sectional imaging method is not directly comparable with profilometry as a method for quantification of surface area characteristics. Besides, a special modification of OCT, the so-called optical coherence radar, can be used for profilometry and provides information on the surface parameters [8]. After irritation, the entrance signal is higher and more enlarged which corresponds to the thickening of the stratum corneum combined with parakeratosis. In healthy forearm skin, the stratum corneum is about 10 μm thick, that is smaller than the resolution of the method,

Table 2 Psoriasis before and after therapy in comparison with healthy adjacent skin. The ratio between the height of the entrance peak and the noise level is without dimensions. The values are means±SD, n=28 (after therapy n=17)

	Before therapy		After therapy	
	Lesional skin	Healthy skin	Lesional skin	Healthy skin
Thickness epidermis (µm)	266.7±94.4*	175.8±49.9	216.5±61.3	180.8±58.1
Entrance peak/noise level	93.6±45.1*	60.7±42.1	63.1±43.5	84.9±37.4
µ dermis (/cm)	29 ± 9*	36 ±15	38 ±17	42 ±16

*$P \leq 0.05$, vs healthy skin

and is therefore not detectable. Nevertheless, the horny layer influences the entrance peak because of the reflectivity of the corneocytes.

In the OCT images after irritation, the distance between the entrance signal and the second intensity peak increased. Previous studies have shown that the second peak corresponds to the upper dermis which is more signal-intense than the epidermis [18]. Thus, the epidermis increased in thickness after irritation. After 1 day, this increase could be explained by swelling due to spongiosis, whereas after 4 and 7 days, the induction of proliferation led to acanthosis that is known from histology. In our previous studies of the histology of irritant contact dermatitis using the same model of experimental irritation and a similar group of subjects [21], an increase in proliferation and a thickening of the epidermis were detected. Therefore we performed these OCT investigations without histology and used our previous data for interpretation.

The decrease in signal attenuation corresponded to the inflammatory reaction which is accompanied by a dilation of vessels, cellular infiltrates and interstitial oedema. These changes influence the density and distribution of the collagen fibres. The light attenuation is mainly dependent on the scattering which is influenced by the size, shape and composition of particles. Light absorption plays a minor role. The regular arrangement of collagen in the dermis leads to a strong light scattering. Any change in the orientation of the fibres or the structural composition of the dermis influences the optical properties. In ultrasound, inflammatory reactions as well as oedema result in a decrease in echodensity due to the less-dense orientation of the collagen [3, 7, 10, 16]. OCT studies of the dermal water content and water distribution using injections of glycerol as a hygroscopic agent have shown that the transparency of the skin increased [17]. This is in accordance with our findings. The inflammatory reaction changed the composition of the dermis with a higher proportion of cellular components and water and a lower density of collagen. A decrease in signal attenuation due to a lower scattering is followed by an increase in signal penetration and detection depth. The absorption coefficient of water is only of importance at larger wavelengths where there is a markedly higher absorption which would reverse this effect [15].

The bioengineering methods revealed well-known changes in functional parameters after irritation which confirmed that the experimental treatment was effective [1, 22]. The comparison of the methods with the OCT findings showed no significant correlation. This might have been due to the great variability of the values and the relatively small sample size. On the other hand, OCT is a morphological method and evaluates different parameters from the functional techniques. It is not necessary that morphological changes such as epidermal acanthosis are accompanied by a disturbance in the skin barrier function. Previous studies of skin biopsies have demonstrated that proliferation after SLS irritation does not correlate with the degree of TEWL increase [21].

For this study, the well-established model of experimental induction of an irritant contact dermatitis was chosen to get a more standardized reaction. Nevertheless, it is likely that our results would be transferable to other eczematous skin diseases such as atopic eczema, because the morphological changes known from histology are comparable.

The OCT images of psoriasis showed similar changes but with some differences. The entrance signal was even more pronounced with parallel layers corresponding to the severe scaling in psoriasis. The irregularity of the stratum corneum with sheets of parakeratosis led to strong reflective zones in the OCT images. Changes in the arrangement, size and shape of corneocytes influenced the optical properties of the stratum corneum by increasing the light scattering. As in contact dermatitis, the epidermis is acanthotic. The second intensity peak was in some cases difficult to detect. This could be explained by the shape of the epidermis-dermis border which has a distinct toothed appearance in psoriasis. The enlarged papillary dermis is mixed with the rete ridges of the epidermis when averaging the a-scan signals which results in a less-defined border. The signal attenuation of the dermis in the psoriatic plaques was lower than in healthy skin due to the inflammatory reaction comparable to that in contact dermatitis. Our OCT investigations of psoriasis were limited to images before and after therapy irrespective of the type of psoriasis or the kind of treatment. It is likely that the degree of inflammation as well as the treatment influence the optical properties of diseased skin. Further studies are necessary to get more detailed information.

The results of the ultrasound investigation demonstrated that this method is problematical for imaging psoriasis. The scales caused artefacts which in many cases prevented evaluation of the dermal morphology. Additionally, the resolution was too poor to distinguish between acanthotic epidermis and inflammation. This is well known

from 20-MHz sonography and led to the development of ultrasound systems using a higher frequency. At 50 to 100 MHz, differentiation between the epidermis and the upper dermis is possible [4]. Compared to OCT, the technique is more complicated. With experimental 100-MHz ultrasound systems, the time for image acquisition is much longer. Because of the high absorption of sound at this frequency, the penetration depth of the signal is limited. Therefore, a depth-scanning technique has to be applied which leads, together with specially constructed transducers, to a higher cost. Additionally, it is not possible to perform the ultrasound measurement without a water path, which is necessary for impedance matching. In contrast, OCT is totally noninvasive. There is no contact with the skin surface and the images can be obtained nearly in real time. In practice OCT allows no detection of single cells. An increase in resolution would be of great interest for the use of OCT in dermatology and is therefore the main target of future development. The integration of novel strong broad-band light sources with a very short coherence length bears the potential to reach microscopic resolution markedly improving the image quality.

In summary, OCT is a promising new method for monitoring inflammatory skin diseases. Structural changes such as epidermal thickness as well as the optical density of the dermis can be visualized which are a part of the characteristic appearance of these diseases. It is a morphological imaging technique comparable with histology but with a lower resolution and a poorer tissue differentiation. OCT has the major advantage of inducing no adverse effects. Therefore, time-course studies as well as an easy quantification of changes are possible. In comparison with other noninvasive methods, OCT provides additional information on morphological changes. It is superior to conventional 20-MHz ultrasound concerning resolution and handling. OCT allows a simple in vivo measurement of epidermal thickness and is therefore a very interesting technique for evaluation of treatment effects such as steroid atrophy.

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