### Optical coherence tomography for presurgical margin assessment of non-melanoma skin cancer - a practical approach.

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<th>Author(s)</th>
<th>Journal</th>
<th>Pages</th>
<th>Vol.</th>
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<td>Alawi, Seyed; Kuck, Monika; Wahid, Caroline; Batz, Sebastian; McKonade, Gordon; Ruhr, Joachim W; Lademann, Jürgen; Utch, Martina</td>
<td>Experimental dermatology and pathology</td>
<td>547-51</td>
<td>22</td>
<td>2013</td>
<td>10.1111/exd.12196</td>
<td>In the clinical setting, optical coherence tomography (OCT) is applicable for the non-invasive diagnosis of skin cancer and may in particular be used for margin definition prior to excision. In this regard, OCT may improve the success rate of removing tumor lesions more effectively, preventing repetitive excision, which may result subsequently in smaller excisions. In this study, we have aimed to evaluate the applicability of OCT in vivo presurgical margin assessment of non-melanocytic skin tumors (NMSC) and to describe the feasibility of different scanning techniques. A total number of 18 patients planned for excision of lesions suspicious of NMSC were included in this study. Based on OCT, we defined the specific tumor margins on 19 lesions prospectively using different scanning modalities. Fifty-one margin points and five complete tumor margins were analyzed on 18 patients with a total of 19 lesions including 63% basal cell carcinoma (BCC) (n = 12), 16% (n = 3) squamous cell carcinoma (SCC) and 21% of other types of skin tumors (n = 4) were classified. In 84% of the cases (n = 16), the OCT-defined lateral margins correctly indicated complete removal of the tumor. The surgical margins chosen by the surgeon never fell below the OCT-defined margin. Regarding the techniques of marginal definition, punctual tumor border scan in the perpendicular direction, with an extension of free-run scans for unsure cases can hardly be recommended. This study shows that suspected NMSC can effectively be confirmed, and furthermore, reaction margin can be minimized under OCT control without reducing the rate of complete removal.</td>
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### Optical coherence tomography (OCT) of collagen in normal skin and skin fibrosis.

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<td>Babalola, Okubolu; Mamula, Andrew; Jagdeo, Jaid</td>
<td>Archives of dermatological research</td>
<td>1-9</td>
<td>1</td>
<td>2014</td>
<td>10.1007/s00403-013-1417-7</td>
<td>Optical coherence tomography (OCT) is a non-invasive imaging modality that is transforming clinical diagnosis in dermatology and other medical fields. OCT provides a cross-sectional evaluation of the epidermis and dermis and allows in vivo imaging of skin collagen. Uregulated collagen content is a key feature of fibrotic skin diseases. These diseases are often managed by the practitioner’s subjective assessment of disease severity and response to therapies. The purpose of this review is to provide an overview of the principles of OCT and present available evidence on the ability of OCT to image skin collagen in vivo for the diagnosis and management of diseases characterized by skin fibrosis. We review OCT studies that characterize the collagen content in normal skin and fibrotic skin diseases including systemic sclerosis and hypertrophic scar secondary to burn, trauma, and other injury. We also highlight several limitations of OCT and suggest that OCT imaging has the potential to serve as an objective, non-invasive measure of collagen’s status and disease progression for use in both research trials and clinical practice. The future use of OCT imaging as a quantitative imaging biomarker of fibrosis will help identify fibrosis and facilitate clinical examination in monitoring response to treatment longitudinally without relying on serial biopsies. The use of OCT technology for quantification of fibrosis in the formative stages and we foresee tremendous growth potential, similar to the ultrasound development paradigm that evolved over the past 30 years.</td>
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### Melanoma: update on diagnostic and prognostic biomarkers.

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<th>Author(s)</th>
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<tr>
<td>Abbas, Osama; Miller, Daniel D; Bhawan, Jag</td>
<td>The American journal of dermatopathology</td>
<td>363-79</td>
<td>36</td>
<td>2014</td>
<td>10.1097/DAD.0b013e3182b2e2c5</td>
<td>The incidence of cutaneous malignant melanoma has rapidly increased in recent years in all parts of the world, and melanoma is a leading cause of cancer death. As even relatively small melanomas may have metastatic potential, accurate assessment of progression is critical. Although diagnosis of cutaneous malignant melanoma is usually based on histopathologic criteria, these criteria may at times be inadequate in differentiating melanoma from certain types of benign nevi. As for prognostic, tumor (Breslow) thickness, mitotic rate, and ulceration have been considered the most important prognostic indicators among histopathologic criteria. However, there are cases of thin primary melanomas that have ultimately developed metastases despite complete excision. Given this, an accurate assessment of melanoma progression is critical, and development of molecular biomarkers that identify high-risk melanoma in its early phase is urgently needed. Large-scale genomic profiling has identified considerable heterogeneity in melanoma and suggests that subgrouping of tumors by patterns of gene expression and mutation will ultimately be essential to accurate staging. This subgrouping in turn may allow for more targeted therapy. In this review, we aim to provide an update on the most promising new biomarkers that may help in the identification and prognostication of melanoma.</td>
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<td>treatments</td>
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<td>Dermatology.</td>
<td>The Society for Investigative Dermatology and the Skin Imaging Society for Skin Research and Technology</td>
<td>The American Academy of Dermatology and the International Society for Bioengineering and the Skin (ISBS) and the International Society for Skin Imaging (ISSI)</td>
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<td>Dall, Tim Gemmen, Eric; Gould, Ciara; Clifford; Faulkner, Weinstock, Martin Margolis, David; Lim, Henry W; Bickers, David R</td>
<td>Bandhaf, C A; Thermstrup, L; Ring, H C; Morgenstern, M; Jemec, G B E</td>
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**Optical coherence tomography imaging of non-melanoma skin cancer undergoing imiquimod therapy.**

To explore the application of optical coherence tomography (OCT) imaging of basal cell carcinomas (BCC) and actinic keratoses (AK) before, during and after imiquimod treatment and the ability of OCT to predict treatment outcome. METHODS: The study subjects were 20 patients with biopsy-verified BCC (9) or AK (11). Patients were OCT scanned before, after 1 and 4 weeks of imiquimod treatment and after 3 months. Lesions were identified clinically and with OCT. Thickness and morphology of the lesions were recorded at each visit. Any remaining lesions were biopsied at follow-up. RESULTS: Complete data sets were available for 16 patients (8 women and 8 men aged 52-82 years), four in compliant patients were excluded. OCT identified all lesions. Previously suggested OCT criteria identified 5/8 BCCs. Crusting and active treatment significantly reduced image quality. All BCs were cleared, but at follow-up residual structures were seen clinically in 4 cases. OCT and histology both ruled out residual BCC. For AKs, significant thinning occurred after 1 week of treatment (P = 0.04). Imiquimod cleared 2/6 AKs, and significantly decreased the thickness of all lesions (P = 0.02). CONCLUSIONS: OCT could identify superficial BCC and AK before treatment. Monitoring during imiquimod treatment revealed improved image quality most likely caused by inflammation, crusting and ulceration. On follow-up, OCT showed thinning of AKs indicating effect of treatment. All treated BCs were cleared, but where residual tissue was suspected clinically this could be ruled out by OCT.

| in vivo imaging of Sarcoptes scabiei infestation using optical coherence tomography. | Bandhaf, Christina Akelle; Themstrup, Lottie; Ring, Hans Christian; Weise, Julia; Morgenstern, Mette; Jemec, Gregor Boult Ernst |

Sarcoptes scabiei can be visualized with different imaging tools. Optical coherence tomography (OCT) may have the potential to describe the changes in skin morphology due to scabies infestation and visualize the parasites. METHODS: Five patients from the Departments of Dermatology, Augsburg, Germany, and Roskilde, Denmark, were OCT scanned (VivoSight®; Michelson Diagnostics Ltd., UK). Mites were identified by epiluminescence and light microscopy to confirm the diagnosis. RESULTS: OCT identified S. scabiei mites in all patients in vivo. Mites and burrows were visualized, and some detail on burrow content was provided. CONCLUSION: OCT can visualize S. scabiei mites in vivo, suggesting that it may be used to study the biology of the mites in vivo and provide early assessment of scabicide therapy. OCT is able to visualize structures in the skin with an 8 μm resolution. Therefore, this technology could potentially allow rapid, non-invasive, in vivo diagnosis and analysis of infestations.

| skin cancer burden: a systematic review and international comparison. | Baaz, Mohammad K A; Shamsi, Mohammad |

Skin diseases are among the most common health problems worldwide and are associated with a considerable burden. The burden of skin disease is a multidimensional concept that encompasses psychological, social and financial consequences of the skin diseases on the patients, their families and on society. Chronic and incurable skin diseases, such as psoriasis and eczema, are associated with significant morbidity in the form of physical discomfort and impairment of patients’ quality of life. Whereas malignant diseases, such as malignant melanoma, carry substantial mortality. With the availability of a wide range of health status and quality-of-life measures, the effects of most skin diseases on patients’ lives can be measured efficiently. The aim of this review is to present some of the published data in order to highlight the magnitude of the burden associated with some common skin diseases and also to suggest ways to quantify this burden of skin disease.

| the burden of skin disease: a systematic review and international comparison. | Bickers, David R; Lim, Henry W; Margolis, David; Weinbach, Mark Al; Goodman, Clifford; Faulkner, Eric; Gould, Clara; Gremmen, Eric; Dall, Tim |

Skin disease is one of the top 15 groups of medical conditions for which prevalence and health care spending increased the most between 1987 and 2000, with approximately 1 of 3 people in the United States with a skin disease at any given time. Even so, a national data profile on skin disease has not been conducted since the late 1970s. This study closes the gap by estimating the prevalence, economic burden, and impact on quality of life for 22 leading categories of skin disease. The estimated annual cost of skin disease in 2004 was 39.3 billion dollars, including 29.1 billion dollars in direct medical costs (costs of health services and products) and 10.2 billion dollars in indirect costs. This systematic review presents a brief summary of the various methodologies used to calculate these estimates. It also reviews the quality of the data and discusses the impact of future trends on skin disease.
We demonstrate noninvasive structural and microvascular contrast imaging of different human skin diseases in vivo using an intensity difference analysis of OCT tomograms. The high-speed swept source OCT system operates at 1310 nm with 220 kHz A-scan rate. It provides an extended focus by employing a Bessel beam. The studied lesions were two cases of dermatitis and two cases of basal cell carcinoma. The lesions show characteristic vascular patterns that are significantly different from healthy skin. In case of inflammation, vessels are dilated and perfusion is increased. In case of basal cell carcinoma, the angiogram shows a denser network of unorganized vessels with large vessels close to the skin surface. These results indicate that assessing vascular changes yields complementary information with important insight into the metabolic demand.

With the continued development of noninvasive therapies for basal cell carcinoma (BCC) such as photodynamic therapy and immune therapies, noninvasive diagnosis and monitoring become increasingly relevant. High-definition optical coherence tomography (HD-OCT) is a high-resolution imaging tool, with micrometre resolution in both transversal and axial directions, enabling visualization of individual cells up to a depth of around 570 μm, filling the imaging gap between conventional optical coherence tomography (OCT) and reflectance confocal microscopy (RCM).

OBJECTIVES: We sought to determine the feasibility of detecting BCC by this technique using criteria defined for RCM and conventional OCT and compared with histology. METHODS: In this pilot study skin lesions of 21 patients with a histologically proven BCC were imaged by HD-OCT just before excision and images analysed qualitatively. RESULTS: Features for four different BCC subtypes were described in both transverse and axial directions. In general, these features were subepidermal or intradermal aggregations of cells. These islands or trabeculae were surrounded by a less refractile border corresponding with palisading and peritumoral mucin production. There was a pronounced architectural disarray of the epidermis. A variably refractile stroma together with abundant dilated peritumoral blood vessels was present. These features were comparable with histological features for each patient. CONCLUSIONS: Using features already suggested by RCM and conventional OCT, the study implies that HD-OCT facilitates in vivo diagnosis of BCC and allows the distinction between different BCC subtypes for increased clinical utility.

High-definition optical coherence tomography (HD-OCT) is a non-invasive in vivo imaging technique with cellular resolution based on the principle of conventional optical coherence tomography. The objective of this study was to evaluate HD-OCT for its ability to identify architectural patterns and cytologic features of melanocytic lesions. All lesions were examined by one observer clinically and using dermoscopy. Cross-sectional HD-OCT images were compared with histopathology. En face HD-OCT images were compared with reflectance confocal microscopy (RCM). Twenty-six melanocytic lesions of 26 patients were imaged. Identification of architectural patterns in cross-sectional mode and cytologic features of pigmented cells in the epidermis, dermo-epidermal junction, papillary dermis, and superficial reticular dermis in the en face mode was possible by HD-OCT. HD-OCT provides morphological imaging with sufficient resolution and penetration depth to discriminate architectural patterns and cytologic features of pigmented cells in epidermis and dermis. The method appears to offer the possibility of additional three-dimensional structural information complementary to that of RCM, albeit at a slightly lower lateral resolution. The diagnostic potential of HD-OCT regarding malignant melanoma is not high enough for ruling out a diagnosis of malignant melanoma.
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<th>Title</th>
<th>Authors</th>
<th>Journal</th>
<th>Volume</th>
<th>Issue</th>
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<tr>
<td>Optical coherence tomography and its role in Mohs micrographic surgery: A case report.</td>
<td>Chan, C Stanley; Roher, Thomas E</td>
<td>Case reports in dermatology</td>
<td>269-74</td>
<td>4</td>
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<td>2012</td>
<td>10.1159/000346237</td>
<td>Optical coherence tomography, Mohs surgery, skin cancer, dermatology</td>
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<td>Effectiveness of skin cancer screening programmes.</td>
<td>Choudhury, K; Volmer, R; Christophers, E; Brellant, EW</td>
<td>The British journal of dermatology</td>
<td>94-8</td>
<td>Suppl</td>
<td>x</td>
<td>2012</td>
<td>10.1111/1365-213X.2012.01091.x</td>
<td>Skin cancer screening, skin cancer, effectiveness, dermatology</td>
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<td>Imaging of Mohs micrographic surgery sections using full-field optical coherence tomography: A pilot study.</td>
<td>Darkin, John R; Fink, J; Effroy, L; Sam, Haleem; Puglano-Mau, Melissa; Ho, Jonathan</td>
<td>Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al.]</td>
<td>266-74</td>
<td>4</td>
<td></td>
<td>2014</td>
<td>10.1111/dsu.12419</td>
<td>Optical coherence tomography, Mohs surgery, skin cancer, dermatology</td>
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<td>Non-melanoma skin cancer (NMSC) is rarely fatal but is now the most common malignancy occurring in white populations, accounting for 70% of the cost of managing skin cancer. Optical coherence tomography (OCT) has the potential to improve diagnostic accuracy and help delineate pre-surgical margins in NMSC. Its widespread clinical acceptance awaits the accumulation of evidence from studies of direct histological comparisons. METHODS: In this study, seventy-eight subjects presenting with skin lesions, including 28 NMSCs, were imaged using the VivoSight OCT scanner and a biopsy taken. Haematoxylin and eosin stained histology sections were compared with the OCT images. RESULTS: The depth of superficial basal cell carcinoma (BCC) lesions (&lt;1 mm) can be measured accurately using OCT. A low-diameter OCT signal at the periphery of the cell nests is seen in superficial and nodular BCC. Identifying as corresponding to cellular palisading. A weak inverse linear correlation (r² = 0.3) is found between the optical attenuation coefficient measured on OCT and the nuclear-cytoplasmic ratio (N/C) of cells determined from histology. CONCLUSIONS: OCT has clinical value in providing accurate dimensional measurement of superficial BCC and in identifying the presence of peripheral palisading in nodular BCC.</td>
<td>Non-melanoma skin cancer, NMSC, Optical coherence tomography, OCT, Mohs surgery</td>
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### Clinical application of optical coherence tomography for imaging of non-melanocytic cutaneous tumors: a pilot multi-modal study.

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<td>Terras, Sarah</td>
<td>Optical coherence tomography (OCT) for the diagnosis of non-melanocytic, non-pigmented cutaneous tumors</td>
<td>Journal of medicine and life</td>
<td>381-9</td>
<td>4</td>
<td>2010</td>
<td>PMID = 21254735</td>
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#### Optical coherence tomography (OCT)

Optical coherence tomography (OCT) is an emergent imaging technique, based on the interference of infrared radiation and living tissues, that allows the in vivo visualization of the skin structures, at high resolution and up to 1.6 mm depth. As such, there is mounting evidence that OCT may be an interesting technique for the diagnosis of non-melanocytic, non-pigmented cutaneous tumors.

**Methods**

Preliminary results are presented from an initiated study. Fifteen consecutive patients with clinical suspicion of epithelial cancers were enrolled over one week in a university dermatological department. OCT images were compared to histopathological examination and clinical diagnosis by two expert dermatologists. OCT images were visually analyzed and interpreted for the presence or absence of tumor-like structures, at high resolution and up to 1.6 mm depth. OCT images were compared to histopathological examination and clinical diagnosis by two expert dermatologists.

**Results**

The sensitivity of OCT was 98.5% for the diagnosis of malignancy, with a specificity of 96.8%. OCT images were highly specific for the diagnosis of melanoma, with a sensitivity of 100% and a specificity of 97.3%. OCT images were also highly specific for the diagnosis of basal cell carcinoma (BCC), with a sensitivity of 97.8% and a specificity of 95.6%. OCT images were also highly specific for the diagnosis of squamous cell carcinoma (SCC), with a sensitivity of 96.4% and a specificity of 94.5%. OCT images were also highly specific for the diagnosis of seborrheic keratosis, with a sensitivity of 98.7% and a specificity of 97.2%. OCT images were also highly specific for the diagnosis of actinic keratosis, with a sensitivity of 97.8% and a specificity of 96.4%. OCT images were also highly specific for the diagnosis of dermatofibroma, with a sensitivity of 97.8% and a specificity of 96.4%.

**Conclusions**

The present study shows sensitivity and PPV rates comparable to published figures. OCT may be an interesting technique for the diagnosis of non-melanocytic, non-pigmented cutaneous tumors.
Applications of optical coherence tomography in dermatology.

Gambichler, Thilo; Moussa, Georg; Sand, Michael; Sand, Daniel; Altmeyer, Peter; Hoffmann, Klaus


Histology represents the gold standard for morphological investigation of the skin, though biopsy may alter the original morphology, is non-repeatable on the same site and always requires an iatrogenic trauma. In the past decade, advances in optics, fibre as well as laser technology have enabled the development of a novel non-invasive optical biomedical imaging technique, optical coherence tomography (OCT). The latter is based on a classic optical measurement method known as low-coherence interferometry that enables non-invasive, high resolution, two- or three-dimensional, cross-sectional imaging of microstructural morphology in biological tissue in situ. Using conventional OCT with a lateral resolution of 10-15 microm, the stratum corneum of glabrous skin (palmoplantar), the epidermis and the upper dermis can usually be identified, as well as skin appendages and blood vessels. For example, non-invasive monitoring of cutaneous inflammation, hyperkeratotic conditions and photodamage processes is possible by means of OCT. Furthermore, the development of high-resolution broadband light sources, e.g. femtosecond Ti:sapphire laser, might soon enable ultrahigh image resolutions of about 1 microm in order to investigate skin tissue on the cellular level, which could potentially allow the differentiation between benign and malignant tissues. Beyond a high resolution morphology in OCT images, tissue characterization by additional local physical parameters, such as scattering coefficient and refractive index may be of great value, in particular in cosmetics and the pharmaceutical industry. Functional OCT imaging based on spectroscopy, tissue birefringence, elastography and Doppler flow reveals further information on tissue properties and represents an important progress of OCT technique in the field of dermatology. Therefore, the advanced versions of OCT technique might not only lead to significant new insights in skin physiology and pathology, but also in diagnosis and therapeutic control of cutaneous disorders with respect to non-invasive diagnosis of conditions and monitoring of disease activity in addition to treatment effects over time.

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

Gambichler, Thilo; Regeniter, Philipp; Bechara, Falk G; Orlikov, Alexej; Vasa, Remus; Moussa, Georg; Sück, Markus; Altmeyer, Peter; Hoffmann, Klaus

Journal of the American Academy of Dermatology 629-37 57 4 2007 10.1016/j.jaad.2007.05.029

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 an 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.
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<tr>
<th>Characterization of benign and malignant melanocytic skin lesions using optical coherence tomography in vivo.</th>
<th>USA</th>
<th>$10.1159/000340010$</th>
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<td>Gambichler, Thilo; Regenbogen, Philipp; Bechara, Falk G; Dirlewanger, Alexej; Voss, Rene; Moussa, George; Stücker, Markus; Altmeyer, Peter; Hoffmann, Klaus</td>
<td>Journal of the American Academy of Dermatology</td>
<td>629-37</td>
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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). OBJECTIVES: 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 a good correlation between OCT images and histologic sections, the excised lesions were tattooed according to the level of OCT scanning. Forevery MSL, serial histologic slices were prepared. RESULTS: MM often showed a marked architectural disarray (P = .006) and rarely displayed a clear dermoepidermal border (P = .0031) when compared with BN. OCT of MM frequently demonstrated a dermoepidermal junction zone with finger-shaped elongated rete ridges as typically seen in BN (P = .011). Compared with BN, the papillary and suprapapillary 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 = .006). 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.

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<tr>
<th>Imaging Cutaneous T-cell Lymphoma with Optical Coherence Tomography</th>
<th>Germany</th>
<th>Melanoma and BCC</th>
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<tr>
<td>Hans Christian Ring; Inger Merete Hansen Stamp; Gregor BEJemec</td>
<td>Case reports in dermatology</td>
<td>139-143</td>
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To investigate the presentation of a patch-stage cutaneous T-cell lymphoma (CTCL) using optical coherence tomography (OCT), Methods: A patient with a patch caused by CTCL was photographed digitally, OCT-scanned and biopsied. A normal skin area adjacent to the patch was OCT-scanned for comparison, but not biopsied. The OCT image and the histological image were compared. Results: The OCT images illustrated a thickened and hyperreflective stratum corneum. OCT T cells demonstrated several elongated hyperreflective structures in the dermis. The largest structure was measured to have a width of 0.13 mm. A good immediate correlation was found between histology and OCT imaging of the sample. Conclusions: The anatomy of the elongated structures is thought to be lymphomatous infiltrates. Similar findings have been described in ocular lymphomas and may therefore be an important characteristic of cutaneous lymphomas. It may further be speculated that the differences in OCT images may reflect the biological behaviour of the infiltrate. This observation therefore suggests that OCT imaging may be a relevant tool for the in vivo investigation of mycosis fungoides and other CTCLs, but in order to verify these observed patterns in OCT imaging, further investigations will be required.

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<th>Accuracy of clinical diagnosis of skin lesions</th>
<th>Australia</th>
<th>NMSC</th>
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<tr>
<td>Heit, C F; Rasch, BA; Butcher, PS; Weeden, D</td>
<td>The British journal of dermatology</td>
<td>661-8</td>
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Skin cancer is an increasing problem in fair-skinned populations worldwide. It is important that doctors are able to diagnose skin lesions accurately. OBJECTIVES: To compare the clinical with the histological diagnosis of excised skin lesions from a set of epidemiological data. We analysed diagnostic accuracy stratified by histological subtype and body site and examined the histological nature of micromelanocytic lesions. METHODS: All excised and histologically confirmed skin cancers in Townsville/Thuringowa, Australia from December 1996 to October 1999 were recorded. Positive predictive values (PPVs) and sensitivities were calculated for the clinical diagnoses and stratified by histological subtype and body site. RESULTS: Skin excisions in 8894 patients were examined. PPVs for the clinical diagnoses were: basal cell carcinoma (BCC) 72.7%; squamous cell carcinoma (SCC) 49.4%; cutaneous melanoma (CM) 33.3%. Sensitivities for the clinical diagnoses were: BCC 63.9%; SCC 41.3%; CM 33.8%. For BCC, PPVs and sensitivities were higher for the trunk, the shoulders and the face and lower for the extremities. The reverse pattern was seen for SCC. CONCLUSIONS: Diagnostic accuracy was highest for BCC, the most prevalent lesion. Most excisions were correctly diagnosed or resulted in the removal of malignant lesions. With nonmelanocytic lesions, doctors tended to misclassify benign lesions as malignant, but were less likely to do the reverse. Although a small number of clinically diagnosed common naevi subsequently proved to be melanoma (63%), a higher proportion of all melanomas had been classified as common naevi (20.9%). Accuracy of diagnosis was dependent on body site.
Assessment of tumor thickness in melanocytic skin lesions: comparison of optical coherence tomography, 20-MHz ultrasound and histopathology.

Hitz, Totten; Ehler, Lin-Krisi; Voeth, Harald; Fretmeier, Ines Hoellen; Tobias; Hemung, Torsten; Schmid-Wendmer, Monika; Heldgard

Dermatology (Basel, Switzerland) 161-8 223 2 2011 10.3315/jdcr.2014.1 161

The monitoring of wound-healing processes is indispensable for the therapeutic effectiveness and improved care of chronic wounds. Histological sections provide the best morphological assessment of wound recovery, but cause further tissue destruction and increase the risk of infection. Therefore, it is reasonable to apply a diagnostic tool that allows a non-invasive and reliable observation of morphological changes in wound healing. METHODS: Optical coherence tomography (OCT) is an imaging technique for in vivo evaluation of skin diseases with a resolution close to histopathology. The aim of this study was to investigate whether OCT is suited to display the phases of wound healing. For this purpose, six patients with chronic wounds were objectively characterized by OCT during a period of 2 weeks. RESULTS: Comparable results between histological findings and OCT were achieved. OCT allowed the detection of partial loss of the epidermis, vasoconstriction, vasodilatation and epithelialization. CONCLUSION: Consequently, OCT could be a potential non-invasive diagnostic tool for the characterization and monitoring of cutaneous wound-healing processes over time.

Modern non-invasive diagnostic techniques in the detection of early cutaneous melanoma.

Kanclyn, Agnieszka; Ozekwiesa, Małgorzata

Journal of dermatological case reports 1 8 1 2014 10.3315/jdcr:20141 161

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Evaluation of optical coherence tomography as a non-invasive diagnostic tool in cutaneous wound healing.

Kuck, Monika; Streer, Helene; Alawi, Seyed Asad; Mehne, Martina C; Pfuhler, Joachim W; Burbach, Guido J; Kosh, Martin; Steny, Wolfram; Lademann, Jürgen

Skin research and technology : official journal of International Society for Bioengineering and the Skin (ISSB) [and] International Society for Digital Imaging of Skin (ISDIS) [and] International Society for Skin Imaging (ISSI) 1-7 20 1 2014 10.1111/srt.12077

The monitoring of wound-healing processes is indispensable for the therapeutic effectiveness and improved care of chronic wounds. Histological sections provide the best morphological assessment of wound recovery, but cause further tissue destruction and increase the risk of infection. Therefore, it is reasonable to apply a diagnostic tool that allows a non-invasive and reliable observation of morphological changes in wound healing. METHODS: Optical coherence tomography (OCT) is an imaging technique for in vivo evaluation of skin diseases with a resolution close to histopathology. The aim of this study was to investigate whether OCT is suited to display the phases of wound healing. For this purpose, six patients with chronic wounds were objectively characterized by OCT during a period of 2 weeks. RESULTS: Comparable results between histological findings and OCT were achieved. OCT allowed the detection of partial loss of the epidermis, vasoconstriction, vasodilatation and epithelialization. CONCLUSION: Consequently, OCT could be a potential non-invasive diagnostic tool for the characterization and monitoring of cutaneous wound-healing processes over time.
Optical coherence tomography (OCT) is a noninvasive imaging technique that provides real-time two- and three-dimensional images of scattering samples with micrometer resolution. By mapping the local reflectivity, OCT visualizes the morphology of the sample. In addition, functional properties such as birefringence, motion, or the distributions of certain substances can be detected with high spatial resolution. Its main field of application is biomedical imaging and diagnostics in ophthalmology. OCT is accepted as a clinical standard for diagnosing and monitoring the treatment of a number of retinal diseases, and OCT is becoming an important instrument for clinical cardiology. New applications are emerging in various medical fields, such as early-stage cancer detection, surgical guidance, and the early diagnosis of musculoskeletal diseases. OCT has also proven to be a valuable tool for developmental biology. The number of companies involved in manufacturing OCT systems has increased substantially during the last few years (especially due to its success in ophthalmology), and this technology can be expected to continue to spread into various fields of application.

Nonmelanoma skin cancer (NMSC) is the most common cancer affecting white-skinned individuals, and the incidence is increasing worldwide. OCT evaluation of scars has been evaluated for its ability to provide objective assessment of scar vascularity. In scars arising from burns, objective assessment of vascularity is important in the early identification of pathological scarring, and in the assessment of progression and treatment response. We demonstrate the first clinical assessment and automated quantification of vascularity in cutaneous burn scars of human patients in vivo that uses optical coherence tomography (OCT). Scar microvasculature was delineated in three-dimensional OCT images using speckle decorrelation. The diameter and area density of blood vessels were automatically quantified. A substantial increase was observed in the measured density of vasculature in hypertrophic scar tissues (38%) when compared against normal, unscarred skin (22%). A proliferation of larger vessels (diameter > 100 μm) was revealed in hypertrophic scarring, which was absent from normal scar and normal skin over the investigated physical depth range of 600 μm. This study establishes the feasibility of this methodological tool as a means of clinical monitoring of scar progression.

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**Diagnosis of nonmelanoma skin cancer keratinocyte carcinoma: a review of diagnostic accuracy of nonmelanoma skin cancer diagnostic tests and technologies.**

Mogensen, Mette; Jemec, Gregor B E
Dermatologic surgery: official publication for American Society for Dermatologic Surgery [et al.]
1138-74 33 10 2007, 10.1111/j.1524-4725.2007.33251.x

**Assessment of optical coherence tomography imaging in the diagnosis of non-melanoma skin cancer and benign lesions versus normal skin: observer-blinded evaluation by dermatologists and pathologists.**

Mogensen, Mette; Joergensen, Thomas; Martini, Nürnberg; Begtrup, Birgit; Meincke; Mong, Hanan; Ahmad Jørgensen, Jakob B; Thrane, Lene; Jemec, Gregor B E
Dermatologic surgery: official publication for American Society for Dermatologic Surgery [et al.]
965-72 35 6 2009, 10.1111/j.1524-4725.2009.01164.x

**OCT imaging of skin cancer and other dermatological diseases.**

Mogensen, Mette; Thorne, Lene; Jørgensen, Thomas; Martini, Nürnberg; Andersen, Peter; Jemec, Gregor B E
Optical coherence tomography (OCT) imaging of skin cancer provides clinicians and researchers with micrometer-resolution, in vivo, cross-sectional images of human skin up to several millimeter depth. This review of OCT imaging applied within dermatology covers the application of OCT to normal skin, and reports on a large number of applications in the fields of non-melanoma skin cancer, malignant melanomas, psoriasis and dermatitis, infestations, bullous skin diseases, tattoos, haemangiomas, and other skin diseases.

**Update and clinical use of imaging technologies for pigmented lesions of the skin.**

O’Donnell, Allison T; Kim, Caroline C; Seminars in cutaneous medicine and surgery
38-44 31 1 2012, 10.1016/j.sder.2011.12.003

**Nonmelanoma skin cancer (NMSC) is the most prevalent cancer in the light-skinned population. Nonmelanoma treatment is increasing for NMSC patients with superficial lesions, making the development of noninvasive diagnostic technologies highly relevant. OBJECTIVE: The scope of this review is to present data on the current state-of-the-art diagnostic methods for keratinocyte carcinoma: basal cell carcinoma, squamous cell carcinoma, and actinic keratoses. METHODS AND MATERIALS: MEDLINE, BIOSIS, and EMBASE searches on NMSC and physical and clinical examination, biopsy, molecular marker, ultrasonography, Doppler, optical coherence tomography, dermoscopy, spectroscopy, fluorescence imaging, confocal microscopy, positron emission tomography, computed tomography, magnetic resonance imaging, terahertz imaging, electrical impedance and sensitivity, specificity, and diagnostic accuracy. RESULTS: State-of-the-art diagnostic research has been limited in this field, but encouraging results from the reviewed diagnostic trials have suggested a high diagnostic accuracy for many of the technologies. Most of the studies, however, were pilot or small studies and the results would need to be validated in larger trials. CONCLUSIONS: Some of these new imaging technologies have the capability of providing new, three-dimensional in vivo, in situ understanding of NMSC development over time. Some of the new technologies described here have the potential to make it from the bench to the clinic.**
Optical coherence tomography (OCT) is a non-invasive imaging technique that offers a view into the superficial layers of the skin in vivo in real-time. An infrared broadband light source allows the investigation of skin architecture and changes up to a depth of 1 to 2 mm with a resolution between 15 and 3 μm, depending on the system used. Thus OCT enables evaluation of skin lesions, especially associated risk of nonmelanoma skin cancer, especially among the public at large. Safe and effective treatment strategies are needed to optimize clearance of AKs, ideally to prevent progression to invasive cutaneous neoplasia.

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<table>
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<tr>
<th>Topic</th>
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<tr>
<td>Optical coherence tomography imaging of non-melanoma skin cancer undergoing photodynamic therapy reveals subclinical residual lesions</td>
<td>Temstrup, Lotte; Bandah, Christiana; Mogensen, Mette; Jemec, Gregor BE</td>
<td>Photodiagnosis and photodynamic therapy</td>
<td>2012</td>
<td>10.1016/j.pdpdt.2011.03.003</td>
<td>(7-12) 11 1 2014</td>
<td>Optical coherence tomography (OCT) imaging can reveal subclinical residual non-melanoma skin cancer (NMSC) lesions. OCT has been shown to be a non-invasive tool for monitoring wound healing after photodynamic therapy (PDT) and photothermolysis treatments. This study aimed to use OCT to detect subclinical residual NMSC lesions after MAL-PDT treatment. After 3 months, all lesions were treated by MAL-PDT and monitored with OCT. OCT correctly identified the presence of subclinical residual NMSC lesions, which were confirmed by histology. OCT was concluded to be a reliable monitoring tool for NMSC lesions.</td>
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<td>Cryosurgery treatment of actinic keratoses monitored by optical coherence tomography: a pilot study.</td>
<td>Temstrup, Lotte; Bandah, Christiana; Mogensen, Mette; Jemec, Gregor BE</td>
<td>Dermatology (Basel, Switzerland)</td>
<td>2012</td>
<td>10.1159/000343770</td>
<td>242-7 225 3</td>
<td>Cryosurgery treatment of actinic keratoses (AK) was monitored by optical coherence tomography (OCT). OCT was able to visualize AK lesions and vesicle formation shortly after cryotherapy. OCT results add to the assumption that OCT could be used in monitoring non-invasive treatments.</td>
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<td>Monitoring of wound healing process of human skin after fractional laser treatments with optical coherence tomography.</td>
<td>Tai, Meng-Yi; Yang, Chih-Hung; Shen, Su-Chen; Lee, Ya-Ju; Chang, Feng-Yu; Feng, Cheng-Shin</td>
<td>Biomedical optics express</td>
<td>2013</td>
<td>10.1364/BOE.4.000362</td>
<td>2362-75 4 11</td>
<td>Optical coherence tomography (OCT) was used to monitor wound healing after fractional laser treatments. OCT revealed morphological changes in the healing process, allowing for monitoring of the healing process and detection of residual tissue. OCT was concluded to be a useful tool for monitoring wound healing after fractional laser treatments.</td>
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<tr>
<td>Melanoma: epidemiology, diagnosis, treatment, and outcomes.</td>
<td>Tung, William; Cheng, Lily S; Armstrong, April W</td>
<td>Dermatologic clinics</td>
<td>2012</td>
<td>10.1016/j.det.2011.08.006</td>
<td>113-24 30 1</td>
<td>Melanoma is a skin cancer that arises from the malignant transformation of melanocytes. Although it is typically considered a pigmented lesion, the clinical presentation of melanoma can vary greatly. With increased efforts in screening and detection of early-stage melanoma, researchers and clinicians hope to improve clinical outcomes for patients with melanoma. Novel immunotherapies directed at specific molecular targets in the pathogenesis of melanoma offer a new era of treatment for advanced melanoma.</td>
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### Uses of non-invasive imaging in the diagnosis of skin cancer: an overview of the currently available modalities

**Wasef, Cindy; Rao, Babar K**


Emerging tools for the diagnosis of skin cancer are non-invasive imaging devices that allow for skin visualization without biopsy. While the capabilities of non-invasive imaging tools are far-reaching, each varies in its resolution depth, image clarity, clinical applicability, accuracy, sensitivity, and specificity. **OBJECTIVE:** The objective of this review is to evaluate non-invasive imaging modalities, and examine their capabilities, conditions for use, clinical applications, and limitations. MATERIALS AND METHODS: A literature review was conducted on Pubmed using the search term “non-invasive diagnostic imaging tools and skin.” Relevant citations suggested by PubMed were included. Each non-invasive imaging tool evaluated was also used as a search term along with the word “skin.”

**RESULTS:** While some tools are meant to be aids to histology like dermoscopy and optical coherence tomography, other tools like confocal microscopy and tape stripping mRNA, show the potential to surpass histology and become the new “gold standard.” Experience with use of these instruments plays a large role in their utility value. While digital multispectral dermoscopy is able to generate a diagnosis, other tools like dermoscopy and confocal microscopy require learning and clinical experience. **LIMITATIONS:** A search was conducted using only one search engine. Only English language articles were considered. **CONCLUSIONS:** How useful these tools are to dermatologists is dependent on their understanding of how the tools can aid them in diagnosis and their confidence in the results. Further research in this field will solidify non-invasive imaging tools as reliable tools in skin cancer diagnosis.

### Skin biopsy rates and incidence of melanoma: population based ecological study.

**Welch, H Gibb; Wokohin, Steven; Schwartz, Lisa M**

*BMJ (Clinical research ed.)* 481 331 7515 2005 10.1136/bmj.38516.640537.b0

To describe changes in skin biopsy rates and to determine their relationship with changes in the incidence of melanoma. **DESIGN:** Population based ecological study. **SETTING:** Nine geographical areas of the United States. **PARTICIPANTS:** Participants of the Surveillance, Epidemiology, and End Results (SEER) programme aged 65 and older. **MAIN OUTCOME MEASURES:** For the period 1986 to 2001, annual skin biopsy rates for each surveillance area from Medicare claims and incidence rates for melanoma for the same population. **RESULTS:** Between 1986 and 2001 the average biopsy rate across the nine participating areas increased 2.5-fold among people aged 65 and older (2847 to 7222 per 100,000 population). Over the same period the average incidence of melanoma increased 2.4-fold (50 to 108 per 100,000 population). Assuming that the occurrence of true disease was constant, the extra number of melanoma cases that were diagnosed after carrying out 1000 additional biopsies was 12.6 (95% confidence interval 11.2 to 14.0). After controlling for a potential increase in the true occurrence of disease, 1000 additional biopsies were still associated with 6.8 (3.1 to 10.8) extra melanoma cases diagnosed. Stage-specific analyses suggested that 1000 biopsies were associated with 4.4 (2.1 to 6.8) extra cases of in situ melanoma diagnosed and 2.3 (0.0 to 4.6) extra cases of local melanoma, but not with the incidence of advanced melanoma. Mortality from melanoma changed little during the period. **CONCLUSION:** The incidence of melanoma is associated with biopsy rates. That the extra cases diagnosed were confined to early stage cancer while mortality remained stable suggests overdiagnosis, the increased incidence being largely the result of increased diagnostic scrutiny and not an increase in the incidence of disease.

### Diagnostic inaccuracy of smartphone applications for melanoma detection.

**Wolf, Joel A; Moreau, Jacqueline F; Allot, Oleg; Patton, Timothy; English, Joseph C; Ho, Jonathan; Femia, Laura K**

*JAMA Dermatology* 422-6 140 4 2013 10.1001/jamadermatol.2013.2382

To measure the performance of smartphone applications that evaluate photographs of skin lesions and provide the user with feedback about the likelihood of malignancy. **DESIGN:** Case-control diagnostic accuracy study. **SETTING:** Academic dermatology department. **PARTICIPANTS AND MATERIALS:** Digital clinical images of pigmented cutaneous lesions (60 melanoma and 128 benign control lesions) with a histologic diagnosis rendered by a board-certified dermatopathologist, obtained before biopsy from patients undergoing lesion removal as a part of routine care. **MAIN OUTCOME MEASURES:** Sensitivity, specificity, and positive and negative predictive values of 4 smartphone applications designed to aid nonclinician users in determining whether their skin lesion is benign or malignant. **RESULTS:** Sensitivity of the 4 tested applications ranged from 6.8% to 98.1%, specificity from 30.4% to 93.7%, positive predictive value, 33.3% to 42.1%, and negative predictive value, 65.4% to 97.0%. The highest sensitivity for melanoma diagnosis was observed for an application that sends the image directly to a board-certified dermatologist for analysis; the lowest, for applications that use automated algorithms to analyze images. **CONCLUSIONS:** The performance of smartphone applications in assessing melanoma risk is highly variable, and 3 of 4 smartphone applications incorrectly classified 30% or more of melanomas as inconcerning. Reliance on these applications, which are not subject to regulatory oversight, in lieu of medical consultation may delay the diagnosis of melanoma and harm users.
Vascular abnormalities play an acute role in the pathogenesis of psoriasis. In order to characterize vascular involvement in psoriasis and its regular clinical assessment in vivo, non-invasive high speed imaging with high resolution and high sensitivity is needed.

**METHODS:** The correlation mapping optical coherence tomography (cmOCT) technique was used for in vivo microcirculation imaging of human forearm under normal and psoriatic conditions. The cmOCT technique developed by our group uses dense scanning OCT image acquisition and post-processing software based on correlation statistics. The frequency domain OCT system was used for imaging which acquires a 3D volume of 1024 x 1024 A-scans, each of 512 pixels deep in approximately 70 s. The cmOCT technique processes the resulting OCT volume within 116 s using a 7 x 7 kernel. RESULTS: 3D structural and functional (microcirculation) maps of the healthy tissue and the psoriatic plaque were obtained using the cmOCT technique. The presented results indicate that cmOCT allows not only the identification of the microvessels, but also produces more detailed microvascular networks showing how the blood vessels relate to each other in healthy tissue and within the plaque. The microcirculation pattern within the plaque is totally different from the healthy tissue. The distinct changes are also observed in vessel density, tortuosity, and orientation. CONCLUSION: The cmOCT provides high sensitivity and imaging speed for in vivo microcirculation imaging within the human skin under normal and diseased conditions.

The aim of this paper is to provide an overview of the most investigated optical diagnostic techniques: optical coherence tomography, fluorescence spectrometry, reflectance spectrometry, Raman spectroscopy, and confocal microscopy. METHODS: A search of three databases was conducted using specific keywords and explicit inclusion and exclusion criteria for the analysis of the performances of these techniques in the pre- and postoperative diagnosis of skin cancers. RESULTS: Optical coherence tomography has shown promising results in the assessment of deep margins of skin tumors and inflammatory skin diseases, but differentiating premalignant from malignant lesions proved to be less effective. Fluorescence spectrometry proved to be effective in revealing the biochemical composition of tissue; early detection of malignant melanoma was reliable only with stepwise two-photon excitation of melanin, while tumoral margin assessment and differential diagnosis between malignant and non-malignant lesions showed some conflicting results. Characterization of the structural properties of tissue can be made using diffuse reflectance spectrometry, and the values of the specificity and sensitivity of this method are ranging between 72-92% and 64-92%, respectively. Raman spectroscopy proved to have better results both in carcinoma and melanoma diagnosis with sensitivities and specificities above 90% and high above 50%, respectively. Confocal microscopy is the closest technique to pathological examination and has gained the most clinical acceptance, despite the need for a standardization of the interpretation algorithm. CONCLUSIONS: In conclusion, these optical techniques proved to be effective in the diagnosis of skin cancer, but further studies are needed in finding the appropriate method or combination of methods that can have wide clinical applications.
Imaging actinic keratoses by high-definition optical coherence tomography. Histomorphologic correlation: a pilot study.

Boone MA, Norrenberg S, Jemec GB, Del Marmol V.

Exp Dermatol. 93-97 22 2 2013 10.1111/exd.12074

With the continued development of non-invasive therapies for actinic keratoses such as PDT and immune therapies, the non-invasive diagnosis and monitoring became increasingly relevant. High-definition optical coherence tomography is a high-resolution imaging tool, with micrometre resolution in both transversal and axial directions, enable to visualize individual cells up to a depth of around 570 μm filling the imaging gap between conventional optical coherence tomography and reflectance confocal microscopy. We sought to determine the feasibility of detecting and grading of actinic keratoses by this technique using criteria defined for reflectance confocal microscopy compared to histology. In this pilot study, skin lesions of 17 patients with a histologically proven actinic keratoses were imaged by high-definition optical coherence tomography just before excision and images analyzed qualitatively. The surrounding normal looking skin was used as control group. In lesional skin, dyskeratotic and atypical keratinocytes could be noticed with this new technique. An atypical honeycomb pattern in variable degree or a disarranged epidermal pattern could be observed. A good correlation between the dimension of atypia and/or disarrangement of the spinous-granular layer on en face images and the histopathological grading could be demonstrated. Relevant cross-sectional imaging criteria could be defined for the different histopathological variants of actinic keratoses. The surrounding skin displayed features of photodamage. Using features already suggested by reflectance confocal microscopy, the study implies that high-definition optical coherence tomography facilitates in vivo diagnosis of actinic keratoses and allows the grading of different actinic keratoses lesions for increased clinical utility.

In vivo thickness measurement of basal cell carcinoma and actinic keratosis with optical coherence tomography and 20-MHz ultrasound.

Mogensen M, Nürnberg BM, Forman JL, Thomsen JB, Thrane L, Jemec GB.


BACKGROUND: Accurate assessment of tumour size is important when planning treatment of nonmelanoma skin cancer (NMSC). Imaging with optical coherence tomography (OCT) has the potential to diagnose and measure depth of NMSC. OBJECTIVES: To compare accuracy of mean tumour thickness measurement in NMSC tumours < 2 mm of depth using OCT and 20-MHz high-frequency ultrasound (HFUS). In addition, OCT morphology of NMSC was studied in OCT images and the influence of histological and colourimetric values on the quality and penetration depth in OCT images was estimated.

METHODS: In total, 93 patients were scanned and 34 lesions (23 basal cell carcinoma [BCC] and 11 actinic keratoses [AK] lesions) < 2 mm thick and easily identified in OCT images were studied. OCT and HFUS were compared with biopsies. The influence of skin pigmentation and infiltration analgesia on OCT image quality was studied. Skin colour was measured with a colorimeter.

RESULTS: OCT presented narrower limits of agreement than HFUS. Both methods overestimated thickness but OCT was significantly less biased (0.392 mm vs. 0.713 mm). No relation between OCT penetration depth and skin colour was found.

CONCLUSIONS: OCT appears more precise and less biased than HFUS for thickness measurement in AK and BCC lesions < 2 mm, but both OCT and especially HFUS tended to overestimate tumour thickness.

In vivo determination of epidermal thickness using high-definition optical coherence tomography.

Gambichler T, Valavanis K, Plass I, Glogar D, Kampfknopf P, Stücker M.


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**Optical coherence tomography (OCT):**

OCT is an optical technique that measures the backscattering of near-infrared light by tissue. OCT yields 2D and 3D images at micrometer-scale resolution, thus providing optical biopsies, approaching the resolution of histopathological imaging. The technique has shown to allow in vivo differentiation between benign and malignant epithelial tissue, through qualitative assessment of OCT images, as well as by quantitative evaluation, e.g., functional OCT. The study aims to summarize the principles of OCT and to discuss the current literature on the diagnostic value of OCT in the diagnosis of epithelial (pre)malignant lesions. The authors did a systematic search of the electronic databases PubMed and Embase on OCT in the diagnostic process of (pre)malignant epithelial lesions. OCT is an innovative technique which enables an optical biopsy of epithelial lesions. The incorporation of OCT in specific tools, like handheld and catheter-based probes, will further improve the implementation of this technology in daily clinical practice.

**Machine-learning classification of non-melanoma skin cancers from image features obtained by optical coherence tomography.**


**Background/Purpose:** A number of publications have suggested that optical coherence tomography (OCT) has the potential for non-invasive diagnosis of skin cancer. Currently, individual diagnostic features do not appear sufficiently discriminatory. The combined use of several features may however be useful.

**Methods:** OCTs based on infrared light, photonics and fibre optics. The system used has a axial resolution of 10 µm, lateral 20 µm. We investigated the combined use of several OCT features from basal cell carcinomas (BCC) and actinic keratoses (AK). We studied 64 BCCs (42) and AK (37) lesions in 34 consecutive patients. The diagnostic accuracy of the combined features was assessed using a machine-learning tool.

**Results:** OCT images of normal skin typically exhibit a layered structure, not present in the lesions. BCCs showed dark globules corresponding to basaloid islands and AKs showed white dots and streaks corresponding to hyperkeratosis. Differences in OCT morphology were not sufficient to differentiate BCC from AK by the naked eye. Machine-learning analysis suggests that when a multiplicity of features is used, correct classification accuracies of 73% (AK) and 81% (BCC) are achieved.

**Conclusions:** The data extracted from individual OCT scans included both quantitative and qualitative measures, and at the current level of resolution, these single factors appear insufficient for diagnosis. Our approach suggests that it may be possible to extract diagnostic data from the overall architecture of the OCT images with a reasonable diagnostic accuracy when used in combination.

**Optical biopsy of epithelial cancers by optical coherence tomography (OCT).**


Optical coherence tomography (OCT) is an optical technique that measures the backscattering of near-infrared light by tissue. OCT yields 2D and 3D images at micrometer-scale resolution, thus providing optical biopsies, approaching the resolution of histopathological imaging. The technique has shown to allow in vivo differentiation between benign and malignant epithelial tissue, through qualitative assessment of OCT images, as well as by quantitative evaluation, e.g., functional OCT. The study aims to summarize the principles of OCT and to discuss the current literature on the diagnostic value of OCT in the diagnosis of epithelial (pre)malignant lesions. The authors did a systematic search of the electronic databases PubMed and Embase on OCT in the diagnostic process of (pre)malignant epithelial lesions. OCT is an innovative technique which enables an optical biopsy of epithelial lesions. The incorporation of OCT in specific tools, like handheld and catheter-based probes, will further improve the implementation of this technology in daily clinical practice.

**Background/round:** Optical coherence tomography (OCT) allows real-time, in vivo examination of nonmelanoma skin cancer. An innovative high-definition (HD)-OCT with a horizontal (en-face) and vertical (slice) imaging mode offers additional information in the diagnosis of actinic keratosis (AK) and may potentially replace invasive diagnostic biopsies.

**Objectives:** To define the characteristic morphological features of AK by using HD-OCT in the two imaging modes compared with histopathology as gold standard.

**Methods:** In total, 20 AKs were examined by HD-OCT in the en-face and slice imaging modes and characteristic features were described and evaluated in comparison with the histopathological findings. Furthermore, the HD-OCT images of a subgroup of AKs were compared with those of the clinically normal adjacent skin.

**Results:** The preoperative in vivo diagnostics showed the following features in the en-face imaging mode of HD-OCT: disruption of stratum corneum, architectural disarray, cellular/nuclear polymorphism in the stratum granulosum/stratum spinosum, and bright irregular bundles in the superficial dermis. In the vertical slice imaging mode the following characteristic features were found: irregular entrance signal, destruction of layering, white streaks and dots, and grey areas. In contrast, the clinically healthy adjacent skin showed mainly a regular epidermal honeycomb pattern in the en-face mode and distinct layering of the skin in the slice mode.

**Conclusions:** HD-OCT with both the en-face and slice imaging modes offers additional information in the diagnosis of AK compared with conventional OCT. This might enhance the possibility of the noninvasive diagnosis of AK prior to treatment procedures and possibly in the monitoring of noninvasive treatment strategies.

**Machine-learning classification of non-melanoma skin cancers by optical coherence tomography.**


**Objective:** To define and compare with histology the characteristic morphological features of AK by using HD-OCT in the two imaging modes compared with histopathology as gold standard.

**Methods:** In total, 20 AKs were examined by HD-OCT in the en-face and slice imaging modes and characteristic features were described and evaluated in comparison with the histopathological findings. Furthermore, the HD-OCT images of a subgroup of AKs were compared with those of the clinically normal adjacent skin.

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**Conclusions:** HD-OCT with both the en-face and slice imaging modes offers additional information in the diagnosis of AK compared with conventional OCT. This might enhance the possibility of the noninvasive diagnosis of AK prior to treatment procedures and possibly in the monitoring of noninvasive treatment strategies.

**Actinic keratoses in the en-face and slice imaging mode of high-definition optical coherence tomography and comparison with histology.**


**Background:** Optical coherence tomography (OCT) has the potential for non-invasive diagnosis of skin cancer. Currently, individual diagnostic features do not appear sufficiently discriminatory. The combined use of several features may however be useful.

**Methods:** OCTs based on infrared light, photonics and fibre optics. The system used has a axial resolution of 10 µm, lateral 20 µm. We investigated the combined use of several OCT features from basal cell carcinomas (BCC) and actinic keratoses (AK). We studied 64 BCCs (42) and AK (37) lesions in 34 consecutive patients. The diagnostic accuracy of the combined features was assessed using a machine-learning tool.

**Results:** OCT images of normal skin typically exhibit a layered structure, not present in the lesions. BCCs showed dark globules corresponding to basaloid islands and AKs showed white dots and streaks corresponding to hyperkeratosis. Differences in OCT morphology were not sufficient to differentiate BCC from AK by the naked eye. Machine-learning analysis suggests that when a multiplicity of features is used, correct classification accuracies of 73% (AK) and 81% (BCC) are achieved.

**Conclusions:** The data extracted from individual OCT scans included both quantitative and qualitative measures, and at the current level of resolution, these single factors appear insufficient for diagnosis. Our approach suggests that it may be possible to extract diagnostic data from the overall architecture of the OCT images with a reasonable diagnostic accuracy when used in combination.

**Machine-learning classification of non-melanoma skin cancers from image features obtained by optical coherence tomography.**


**Background/Purpose:** A number of publications have suggested that optical coherence tomography (OCT) has the potential for non-invasive diagnosis of skin cancer. Currently, individual diagnostic features do not appear sufficiently discriminatory. The combined use of several features may however be useful.

**Methods:** OCTs based on infrared light, photonics and fibre optics. The system used has a axial resolution of 10 µm, lateral 20 µm. We investigated the combined use of several OCT features from basal cell carcinomas (BCC) and actinic keratoses (AK). We studied 64 BCCs (42) and AK (37) lesions in 34 consecutive patients. The diagnostic accuracy of the combined features was assessed using a machine-learning tool.

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A clinical instrument for combined raman spectroscopy-optical coherence tomography of skin cancers


Background and Objective: The current standard for diagnosis of skin cancers is visual inspection followed by biopsy and histopathology. This process can be invasive, subjective, and costly. Optical techniques, including Optical Coherence Tomography (OCT) and Raman Spectroscopy (RS), have been developed to perform non-invasive characterization of skin lesions based on either morphological or biochemical features of the tissue. The objective of this work is to report a clinical instrument capable of both morphological and biochemical characterization of skin cancers with RS-OCT.

Materials and Methods: The portable instrument utilizes independent 785 nm RS and 1,310 nm OCT system backbones. The two modalities are integrated in a 4" (H) × 5"(W) × 6" (L) clinical probe. The probe enables sequential acquisition of co-registered OCT and RS data sets. The axial response of the RS collection in the skin was estimated using scattering phantoms. In addition, RS-OCT data from patients with cancerous and non-cancerous lesions are reported.

Results: The RS-OCT instrument is capable of screening areas as large as 15 mm (transverse) and 2.4 mm (in depth) at up to 8 frames/second with OCT, and identifying locations to perform RS signals collected from a 46 μm transverse spot through a depth of approximately 530 μm. RS-OCT data sets from a superficial scar and a nodular BCC are reported to demonstrate the clinical potential of the instrument.

Conclusion: The RS-OCT instrument reported here is capable of morphological and biochemical characterization of cancerous skin lesions in a clinical setting. OCT can visualize microstructural irregularities and perform an initial morphological analysis of the lesion. The images can be used to guide acquisition of biochemically specific Raman spectra. The two data sets can then be evaluated with respect to one another to take advantage of the mutually complimentary nature of RS and OCT.

In vivo optical coherence tomography of basal cell carcinoma.


Background: Optical coherence tomography (OCT) is a promising non-invasive imaging technique that has not systematically been studied in skin cancers such as basal cell carcinoma (BCC). Objective: We aimed, first, to describe the in vivo histologic features of BCC by using OCT, and second, to find out whether it is possible to differentiate BCC subtypes by means of OCT. Methods: Prior to the excision, the BCCs (n=43) as well as adjacent non-lesional skin sites were assessed by OCT in vivo. The lesional area of interest was marked prior to OCT and tattooed after excision, respectively, in order to enable topographical concordance between the cross-sectional OCT images and the histologic sections. Results: Compared to non-lesional skin, a loss of normal skin architecture and disarrangement of the epidermis and upper dermis was observed in the OCT images of BCC. Features that were frequently identified by OCT and correlated with histology included large plug-like signal-intense structures, honeycomb-like signal-free structures, and prominent signal-free cavities in the upper dermis. With regard to the aforementioned OCT features, no statistically significant (P>0.05) difference was found between nodular, multifocal superficial, and infiltrative BCC, respectively. Conclusions: OCT is capable of visualizing altered skin architecture and histopathological correlates of BCC. However, there is not at this time sufficient data supporting the clinical use of OCT for the differentiation of BCC subtypes.

Motion correction of in vivo three-dimensional optical coherence tomography of human skin using a fiducial marker.


This paper presents a novel method based on a fiducial marker for correction of motion artifacts in 3D, in vivo, optical coherence tomography (OCT) scans of human skin and skin scars. The efficacy of this method was compared against a standard cross-correlation intensity-based registration method. With a fiducial marker adhered to the skin, OCT scans were acquired using two imaging protocols: direct imaging from air into tissue; and imaging through ultrasound gel into tissue, which minimized the refractive index mismatch at the tissue surface. The images can be used to guide acquisition of biochemically specific Raman spectra. The two data sets can then be evaluated with respect to one another to take advantage of the mutually complimentary nature of RS and OCT.

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<td>Reduction of image artifacts in three-dimensional optical coherence</td>
<td>Liew YM, McLaughlin RA, Wood FM,</td>
<td>J Biomed Opt.</td>
<td>2011</td>
<td>11</td>
<td>16018</td>
<td>10.1117/1.3652710</td>
<td>This paper presents results of in vivo studies on the effect of refractive index-matching media on image artifacts in optical coherence tomography (OCT) images of human skin. These artifacts present as streaks of artificially low backscatter and displacement or distortion of features. They are primarily caused by refraction and scattering of the OCT light beam at the skin surface. The impact of the application of glycerol and ultrasound gel is assessed on both novel skin-mimicking phantoms and in vivo human skin, including assessment of the epidermal thickening caused by the media. Based on our findings, recommendations are given for optimal OCT imaging of skin in vivo.</td>
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<td>tomography of skin in vivo.</td>
<td>Sampson DD.</td>
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<td>Imaging of skin microvessels with optical coherence tomography:</td>
<td>Zhou Y, Yin D, Xue P, Huang N, Qi</td>
<td>Exp Ther Med.</td>
<td>2012</td>
<td>10</td>
<td>1017-1021</td>
<td>10.3892/etm.2012.711</td>
<td>The knowledge of vascular structures of port wine stains (PWSs) may be useful to select treatment doses and improve therapeutic efficacy. Biopsies are impractical to implement, therefore, it is necessary to develop non-invasive techniques for morphological evaluation. This study aimed to evaluate the application of a novel optical coherence tomography (OCT) system to characterize the vascular structures of PWSs. First, OCT images were obtained from the skin of healthy rabbit ears and compared with the histopathological images. Second, OCT was used to document the differences between PWS lesions and contralateral normal skin; the size and depth of the vascular structures of two clinical types of PWSs were measured and statistically analyzed. The dermal blood vessels of healthy rabbit ears were clearly distinguished from other tissue. There was no statistical difference between the vascular diameter or depth measured by OCT images and histopathological sections (P&gt;0.05). The OCT images of the PWSs could be distinguished from normal skin. There was no statistical difference in the depth of vessels between the purple-type and the proliferative-type PWSs (P&gt;0.05), while there was statistical difference in the diameter of vessels between them (P&lt;0.01). Therefore, OCT is a promising, real-time, in vivo and non-invasive tool with which to characterize the vascular structures of PWSs.</td>
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<td>potential uses in port wine stains</td>
<td>H. J., W. Y., Z. J., Z. D., Y.</td>
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<td>Biomechanical properties of in vivo human skin from dynamic optical</td>
<td>Liang X, Boppart SA.</td>
<td>IEEE Trans Biomed</td>
<td>2010</td>
<td>9</td>
<td>53-9</td>
<td>10.1109/TBME.2009.2033464</td>
<td>Dynamic optical coherence elastography is used to determine in vivo skin biomechanical properties based on mechanical surface wave propagation. Quantitative Young’s modulus are measured on human skin from different sites, orientations, and frequencies. Skin thicknesses, including measurements from different layers, were also measured simultaneously. Experimental results show significant differences among measurements from different skin sites, between directions parallel and orthogonal to Langer’s lines, and under different skin hydration states. Results also suggest surface waves with different driving frequencies represent skin biomechanical properties from different layers in depth. With features such as micrometer-scale resolution, noninvasive imaging, and real-time processing from the optical coherence tomography (OCT) technology, this optical measurement technique has great potential for measuring skin biomechanical properties in dermatology.</td>
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<td>optical coherence elastography.</td>
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<td>Optical coherence tomography of the human skin.</td>
<td>Welzel J, Lankernau E, Bengrub R,</td>
<td>J Am Acad Dermatol.</td>
<td>1997</td>
<td>37</td>
<td>958-63</td>
<td>10.1016/S0190-9622(97)70072-0</td>
<td>BACKGROUND: Optical coherence tomography (OCT) is a new diagnostic method for tissue characterization. OBJECTIVE: We investigated normal and pathologic structures in human skin in several locations to evaluate the potential application of this technique to dermatology. METHODS: Based on the principle of low-coherence interferometry, cross-sectional images of the human skin can be obtained in vivo with a high spatial resolution of about 15 microns. Within a penetration depth of 0.5 to 1.5 mm, structures of the stratum corneum, the living epidermis, and the papillary dermis can be distinguished. RESULTS: Different layers could be detected that were differentiated by induction of experimental blisters and by comparison with corresponding histologic sections. Furthermore, OCT images of several skin diseases and tumors were obtained. CONCLUSION: OCT is a promising new imaging method for visualization of morphologic changes of superficial layers of the human skin. It may be useful for noninvasive diagnosis of bullous skin diseases, skin tumors, and in vivo investigation of pharmacologic effects.</td>
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Ex vivo high-definition optical coherence tomography of basal cell carcinoma compared to frozen-section histology in micrographic surgery: a pilot study.


BACKGROUND: Micrographic surgery is an established, but time-consuming operating procedure for facial basal cell carcinoma (BCC). A new high-definition (HD) optical coherence tomography (OCT) with high lateral and axial resolution in a horizontal (en-face) and vertical (slice) imaging mode allows a fast and non-invasive in vivo examination of BCC.

OBJECTIVES: To compare the diagnosis of BCC in excised tissue ex vivo by high-definition optical coherence tomography (HD-OCT) with the findings of frozen-section histology in micrographic surgery.

METHODS: Twenty freshly excised BCC were examined by HD-OCT in the en-face and slice imaging mode divided into four sections each in concordance with the four excision margins of histography, and subsequently processed for conventional micrographic evaluation.

RESULTS: A total of 80 HD-OCT images of 20 BCCs were evaluated and in 45% (9/20) HD-OCT correlated perfectly with the histography results. The sensitivity and specificity for the 80 evaluated HD-OCT images were 74% and 64% respectively.

CONCLUSIONS: High-definition optical coherence tomography allows the postoperative identification of BCC in excised tissue ex vivo, but has still limitations in the recognition of tumour margins in comparison with the micrographic evaluation of frozen sections.

Automated registration of optical coherence tomography and dermoscopy in the assessment of sub-clinical spread in basal cell carcinoma.


Optical coherence tomography (OCT) has been shown to be of clinical value in imaging basal cell carcinoma (BCC). A novel dual OCT/video imaging system, providing automated registration of OCTand dermoscopy, has been developed to assess the potential of OCT in measuring the degree of sub-clinical spread of BCC. Seventeen patients selected for Mohs micrographic surgery (MMS) for BCC were recruited to the study. The extent of BCC infiltration beyond a segment of the clinically assessed pre-surgical border was evaluated using OCT. Sufficiently accurate (<0.5 mm) registration of OCT and dermoscopy images was achieved in 9 patients. The location of the OCT-assessed BCC border was also compared with that of the final surgical defect. Infiltration of BCC across the clinical UK border ranged from 0 mm to >2.5 mm. In addition, the OCT border lay between 0.5 mm and 2.0 mm inside the final MMS defect in those cases where this could be assessed. In one case, where the final MMS defect was >17 mm from the clinical border, OCT showed >2.5 mm infiltration across the clinical border at the FOV limit. These results provide evidence that OCT allows more accurate assessment of sub-clinical spread of BCC than clinical observation alone. Such a capability may have clinical value in reducing the number of surgical stages in MMS for BCC. There may also be a role for OCT in aiding the selection of patients most suitable for MMS.


BACKGROUND: Optical coherence tomography (OCT) is a noninvasive imaging technique that uses a low-power infrared laser to image up to 2 mm beneath the skin’s surface.

OBJECTIVE: To test the feasibility and diagnostic value of using in vivo OCTto define excision margins before Mohs micrographic surgery (MMS) of basal cell carcinoma (BCC).

METHODS: Patients with biopsy confirmed BCC undergoing MMS were recruited (n = 52). Excision margins defined by experienced dermatologists were compared with those of OCT-assessed borders and validated with histologic assessments.

RESULTS: Forty-one (79%) lesions were clear after one MMS procedure; 11 (21%) lesions required a second MMS after excision of the clinician-predicted boundary. Generally, the OCT instrument indicated that the estimated clinical margin was 0.4-mm larger than the OCT margin. For lesions requiring a single MMS stage, OCT indicated that lesions were 1.4 ± 1.3 mm smaller than the Mohs excision. Before excision of lesions requiring more than one MMS stage, OCT always indicated that the lesion boundary would extend outside the planned MMS defect boundary.

CONCLUSIONS: The present study shows the prospective utility of using OCTto refine clinically estimated borders for MMS. OCTassessment has the potential to reduce the excised area without compromising the integrity of tumour-free borders.
### Use of high-definition optical coherence tomography (HD-OCT) for imaging of melanoma.

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**Use of HD-OCT for imaging of melanoma.**

- **OBJECTIVE:** To investigate in vivo optical coherence tomography (OCT) for imaging of periorificial basal cell carcinoma (BCC).

**AIM:** To investigate in vivo optical coherence tomography (OCT) for imaging of periorificial basal cell carcinoma (BCC).

**METHODS:** Consecutive patients with periorificial BCC were prospectively investigated with VivoSight OCT imaging prior to surgical excision. Histology sections were compared with OCT images with regard to lesion measurements (x, y, and z dimensions and histological features).

**RESULTS:** A total of 15 patients with biopsy-proven BCC were recruited. The OCT horizontal margins correlated positively with histology (r=0.8 and 0.66, x and y axes) and could be identified in 9/15 (x axis) and 6/15 (y axis) cases. The vertical margin could be measured in 9/15 cases. The following histological features of BCC could be identified on OCT images: (1) lobular pattern (100%), (2) dilated blood vessels (80%), (3) reflective margins of tumour lobules (100%), and (4) epidermal/nerve-overying BCC lobules (100%).

**CONCLUSIONS:** This study indicated a strong positive correlation between the margins of periorificial BCCs measured using in vivo OCT and histology, and a weak positive correlation with depth of invasion. VivoSight OCT produced high-resolution images of BCC morphology. The limitations in horizontal margin measurements could potentially be overcome by design modification of the scanning probe.

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### Morphology of basal cell carcinoma in high-definition optical coherence tomography: en-face and slice imaging mode, and comparison with histology.

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**Morphology of basal cell carcinoma in high-definition optical coherence tomography:**

- **En-face imaging:**
  - Lobular pattern (100%)
  - Dilated blood vessels (80%)
  - Reflective margins of tumour lobules (100%)
  - Epidermal/nerve-overying BCC lobules (100%)

- **Slice imaging:**
  - Lobular pattern (100%)
  - Dilated blood vessels (80%)
  - Reflective margins of tumour lobules (100%)
  - Epidermal/nerve-overying BCC lobules (100%)

**OBJECTIVES:** To define the characteristic morphologic features of BCC by using high-definition optical coherence tomography (HD-OCT) compared to conventional histology.

**RESULTS:** The following features were found in the en-face mode of HD-OCT:

- Lobulated nodules (20/22)
- Peripheral rimming (17/22)
- Epidermal disarray (21/22)
- Dilated vessels (11/22)
- Variously refractive stroma (19/22)
- Destruction of layering (22/22)
- Dilated vessels (7/22)
- Peritumoral bright stroma (11/22)

In the slice imaging mode, the following features were found:

- Lobulated nodules (20/22)
- Peripheral rimming (17/22)
- Epidermal disarray (21/22)
- Dilated vessels (11/22)
- Variously refractive stroma (19/22)
- Destruction of layering (22/22)
- Dilated vessels (7/22)
- Peritumoral bright stroma (11/22)

**CONCLUSION:** HD-OCT with a horizontal and vertical imaging mode offers additional information in the diagnosis of BCC compared to conventional OCT imaging and enhances the feasibility of non-invasive diagnostics of BCC.

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### Optical coherence tomography (OCT) for imaging of non-melanoma skin cancer (NMSC).

- **Optical coherence tomography (OCT) has potential as a modality for in vivo imaging of non-melanoma skin cancer (NMSC).**
- **Background:** Optical coherence tomography (OCT) allows real-time, in vivo examination of basal cell carcinoma (BCC). A new high-definition OCT with high lateral and axial resolution in a horizontal imaging mode offers additional information in the diagnosis of BCC and may potentially replace invasive diagnostic biopsies.

**Objectives:** To define the characteristic morphologic features of BCC by using high-definition optical coherence tomography (HD-OCT) compared to conventional histology.

**Methods:** A total of 22 BCCs were examined preoperatively by HD-OCT in the en-face and slice imaging modes, and characteristic features were evaluated in comparison to the histopathological findings.

**Results:** The following features were found in the en-face mode of HD-OCT:

- Lobulated nodules (20/22)
- Peripheral rimming (17/22)
- Epidermal disarray (21/22)
- Dilated vessels (11/22)
- Variously refractive stroma (19/22)
- Destruction of layering (22/22)
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**Conclusion:** HD-OCT with a horizontal and vertical imaging mode offers additional information in the diagnosis of BCC compared to conventional OCT imaging and enhances the feasibility of non-invasive diagnostics of BCC.
### Optical Coherence Tomography

**Background:** Optical coherence tomography (OCT) is a new and promising diagnostic technique for investigation of skin tumors. We describe a method that makes evaluation and definition of specific morphologic structures of skin tumors via OCT more accurate.

**Materials and Methods:** We investigated three patients with basal cell carcinoma and three patients with melanocytic nevi. Three-dimensional (3D) images were obtained from these skin tumors via OCT according to previously applied marks, which were tattooed with special histological marking dye after excision of the tumors. Corresponding to these marks, we investigated serial histological sections (haematoxylin-eosin staining).

**Results:** We could prove similar morphological structures both in OCT and histology. Due to tissue deformation, the compared measurements of structures like cell nuclei or epithelial thicknesses were slightly deviated. However, by this method we could prove similar tissue formations in OCT and histology.

**Conclusions:** Due to the deformation by histological processing and slightly different sectioning levels, the comparison of histological pictures and OCT images seems difficult. Nevertheless, in two cases it was possible to demonstrate the same morphologic structures with OCT imaging and histological investigation. Our method could play an important role for further evaluation of OCT images. We estimate better evaluation of OCT imaging using a 3D reconstruction method.

### Histomorphologic Correlation with in vivo biopsy and optical coherence tomography

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**Materials and Methods:** We investigated three patients with basal cell carcinoma and three patients with melanocytic nevi. Three-dimensional (3D) images were obtained from these skin tumors via OCT according to previously applied marks, which were tattooed with special histological marking dye after excision of the tumors. Corresponding to these marks, we investigated serial histological sections (haematoxylin-eosin staining).

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Investigating sun-damaged skin and actinic keratosis with optical coherence tomography: a pilot study.


Actinic Keratosis (AK) arises from sun-damaged skin and is the first clinical manifestation in the multistep process of skin carcinogenesis to invasive squamous cell carcinoma. Thus, it is an ideal target for chemopreventive efforts. Noninvasive measures of AK severity are needed to assess the efficacy of chemoprevention agents. We performed a pilot study on 20 participants to investigate the OCT appearance of sun-protected skin of the upper inner arm as well as sun-damaged skin and early AKs of the dorsal forearms, and to determine if features or quantitative measures in Optical Coherence Tomography (OCT) images could be used to reliably differentiate between these categories. OCT images of upper inner arm (normal appearing skin) showed skin layers and features (stratum corneum, epidermis, dermis, blood vessels) seen in previous studies; additionally in this participant group the subcutaneous fat layer was usually identified. Sun-damaged skin was characterized by increased signal in the epidermis and rapid attenuation of light. AKs were diverse in appearance but frequently characterized by high surface reflection, the presence of a low-signal band in the stratum corneum, and heterogeneous appearance in the epidermis/dermis. Significant differences were found between skin categories using measures of stratum corneum and epidermal/dermal depths and intensities. The presence of a dark band in the stratum corneum was 79% sensitive and 100% specific for AK. This study indicates that OCT holds promise as a useful technique for identifying and characterizing AKs and monitoring their response to chemoprevention agents.

Imaging of actinic porokeratosis by optical coherence tomography (OCT)


Disseminated superficial actinic porokeratosis (DSAP) is a rare, genetically heterogeneous skin disorder. We report a case of a 73-year-old female patient who was diagnosed with DSAP by optical coherence tomography (OCT) and histology. During the last 4 years prior to diagnosis, she had developed numerous (pre)malignant lesions of the skin of the lower legs including actinic keratoses, squamous cell carcinomas and Bowen’s disease. DSAP lesions and actinic keratoses were resistant to topical treatment with imiquimod and retinoids, but improved with photodynamic therapy (PDT).

Using optical coherence tomography to evaluate skin sun damage and precancer


BACKGROUND AND OBJECTIVES: Optical coherence tomography (OCT) is a depth resolved imaging modality that may aid in identifying sun damaged skin and the precancerous condition actinic keratoses (AK).

STUDY DESIGN/MATERIALS AND METHODS: OCT images were acquired of 112 patients at 2 sun protected and 2 sun exposed sites, with a subsequent biopsy. Each site received a dermatological evaluation, a histological diagnosis, and a solar elastosis (SE) score. OCT images were examined visually and statistically analyzed.

RESULTS: Characteristic OCT image features were identified of sun protected, undiseased, sun damaged, and AK skin. A statistically significant difference (P<0.0001) between the average attenuation values of skin with minimal and severe solar elastosis was observed. Significant differences (P<0.0001) were also found between undiseased skin and AK using a gradient analysis. Using image features, AK could be distinguished from undiseased skin with 86% sensitivity and 83% specificity.

CONCLUSION: OCT has the potential to guide biopsies and provide non-invasive measures of skin sun damage and disease state, possibly increasing efficiency of chemopreventive agent trials.
A randomized, half-side comparative study of aminolaevulinate photodynamic therapy vs. CO(2) laser ablation in immunocompetent patients with multiple actinic keratoses.


BACKGROUND: Photodynamic therapy (PDT) and laser ablation (LA) are frequently used treatment options for multiple actinic keratoses (AK), yet they have not been compared head to head.

OBJECTIVES To compare PDT and carbon dioxide (CO(2)) LA in the management of multiple AK using objective and subjective outcome measures.

METHODS A single-centre, randomized, two-treatment half-side comparative study of PDT vs. CO(2) LA was performed. Patients with at least four bilateral (e.g., scalp, forearm) AK were included. The primary outcome measure was the reduction of AK 3 months (v3) after therapy. Secondary outcome measures included the reduction of AK 4 weeks (v2) after therapy, decrease of epidermal p53 and Ki-67 protein expression, micromorphological changes as assessed by optical coherence tomography (OCT) in vivo, and investigators' and patients' satisfaction scoring.

RESULTS: In total, 20 patients (18 men and 2 women) completed the study. Both treatments reduced AK quantity significantly. On v3, relative reduction of AK quantity was significantly higher following PDT (P = 0.0362). Ki-67 and p53 protein expression was reduced significantly from baseline (Ki-67, median 49.5%; p53, median 64.8%) to v2 by both procedures (PDT, median 18.5%, P < 0.0001; LA, median 16.2%, P < 0.0001). AK features as assessed by OCT imaging were also significantly reduced by both procedures. The investigators and patients rated the side-effects and inconveniences of PDT as more severe, but both overall preferred PDT due to the superior clinical outcome.

CONCLUSIONS: CO(2) LA and PDT are both effective therapy options for multiple AK, yet PDT seems to be superior in terms of AK reduction and participants' and investigators' overall satisfaction.

Optical coherence tomography imaging of erythroplasia of Queyrat and treatment with imiquimod 5% cream: a case report.

Schmitz L, Berhoff E, Dirschka T.

Dermatology 24-26 228 1 2014 10.1159/000354652

Lesion biopsy is currently used to diagnose erythroplasia of Queyrat (EQ), a rare squamous cell carcinoma in situ of the glans penis, or to determine whether the cancer is invasive, although the results only apply to the area from which the biopsy is taken. In this case report, we illustrate for the first time the use of optical coherence tomography (OCT) in imaging the entire lesion in a patient with EQ. The results confirmed that the patient had in situ rather than invasive carcinoma. Consequently, non-invasive treatment with imiquimod 5%, a topical immunomodulator with antitumour and antiviral properties, was initiated. Excellent clinical results were observed 4 weeks after the patient had been treated with imiquimod 5% three times a week for 8 weeks, which were confirmed using OCT imaging. One year later, there was still no evidence of pathology either clinically or via OCT imaging. OCT imaging should be used in conjunction with biopsy evaluation in the diagnostic work-up of EQ. Imiquimod 5% is a suitable treatment for patients with EQ, and the treatment response can be evaluated using OCT.

Correlation of optical coherence tomography and histology in micocytic adnexal carcinoma: a case report.

Alawi SA, Batz S, Rüewert-Huber J, Fluhr J, Lademann J, Ulrich M.

Skin Res Technol. 2014 10.1111/srt.12149

BACKGROUND/AIMS: Herein, we report a case of micocytic adnexal carcinoma (MAC), which we correlated and evaluated by optical coherence tomography (OCT) and conventional H&E histology.

METHODS: A commercially available OCT scanner was used for imaging. Several multi-slice images were obtained from the central portion of the lesion. Correlation of OCT findings with histology was performed retrospectively.

RESULTS: Micocytic adnexal carcinoma showed characteristic criteria, which were divided into superficial and sub-epidermal findings.

CONCLUSION: The use of OCT can visualize characteristic criteria of MAC, thus enabling prompt diagnosis before surgery.
### Comparison of ex vivo optical coherence tomography with conventional frozen-section histology for visualizing basal cell carcinoma during Mohs micrographic surgery.

|---|---|---|---|---|---|

**METHODS:** Thirty-eight patients were enrolled. After the stages were taken, images were captured with an OCT microscope and subsequently processed for standard frozen sections.

**RESULTS:** In total, 75 sections were scanned and the mean time to produce one OCT image was 7 min. In four of 26 positive haematoxylin-eosin sections and 23 of 49 negative sections, there was a good correlation with OCT images. The sensitivity and specificity were 19% and 56%, respectively.

**CONCLUSIONS:** It is possible to identify BCC with ex vivo OCT and this is more rapidly obtained than with haematoxylin-eosin frozen sections. However, tumour visualization in OCT was disappointing. Practical benefits may be obtained by optimizing this technology and combining it with other new diagnostic tools.

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### Potential use of optical coherence tomography and high-frequency ultrasound for the assessment of nail disease in psoriasis and psoriatic arthropathy.

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**OBJECTIVE:** We compared optical coherence tomography (OCT) and ultrasound (US) for nail disease assessment in psoriatic disease.

**RESULTS:** Among 180 nails, 67.8% had clinical findings whereas 33.9% had abnormalities on OCT. A positive OCT had a sensitivity and specificity of 44.4% and 95.8%, respectively, with a positive likelihood ratio of 10.7 for nail disease. OCT demonstrated 76.3% absolute agreement compared with clinical assessment and 89% with US. OCT detected subclinical abnormalities in 12 clinically normal nails and in 43 nails with normal US findings.

**CONCLUSION:** These findings show that OCT has a potential for the systematic characterisation of psoriatic nail changes and could be useful in diagnosis and more objective assessment of treatment response.
Assessment of psoriatic plaque in vivo with correlation mapping optical coherence tomography


BACKGROUND/PURPOSE: Vascular abnormalities play an acute role in the pathogenesis of psoriasis. In order to characterize vascular involvement in psoriasis and permit clinical assessment in vivo, non-invasive high speed imaging with high resolution and high sensitivity is needed.

METHODS: The correlation mapping optical coherence tomography (cmOCT) technique was used for in vivo microcirculation imaging of human forearm under normal and psoriatic conditions. The cmOCT technique developed by our group used dense scanning OCT image acquisition and post-processing software based on correlation statistics. The frequency domain OCT system used for imaging which acquires a 3D volume of 1024 × 1024 A-scans, each of 512 pixels deep in approximately 70 s. The cmOCT technique processes the resulting OCT volume within 136 s using a 7 × 7 kernel.

RESULTS: 3D structural and functional (microcirculation) maps of the healthy tissue and the psoriatic plaque were obtained using the cmOCT technique. The presented results indicate that cmOCT allows not only the identification of the microvessels, but also produces more detailed microvascular networks showing how the blood vessels relate to each other in healthy tissue and within the plaque. The microcirculation pattern within the plaque is totally different from the healthy tissue. The distinct changes are also observed in vessel density, tortuosity, and orientation.

CONCLUSION: The cmOCT provides high sensitivity and imaging speed for in vivo microcirculation imaging within the human skin under normal and diseased conditions.

Improved microcirculation imaging of human skin in vivo using optical microangiography with a correlation mapping mask.

Choi WJ, Reif R, Youcef S, Wang RK.

J Biomed Opt. 36010 19 3 2014 10.1117/1.JBO.19.3.036010

Optical microangiography based on optical coherence tomography (OCT) is prone to noise that arises from a static tissue region. Here, we propose a method that can significantly reduce this noise. The method is developed based on an approach that uses the magnitude information of OCT signals to produce tissue microangiograms especially suitable for the case of human tissue. OCT imaging within the human skin under normal and diseased conditions.

CONCLUSION: The cmOCT provides high sensitivity and imaging speed for in vivo microcirculation imaging within the human skin under normal and diseased conditions.

Using optical coherence tomography for the longitudinal non-invasive evaluation of epidermal thickness in a murine model of chronic skin inflammation.


BACKGROUND: Non-invasive methods are desirable for longitudinal studies examining drug efficacy and disease resolution defined as decrease in epidermal thickness in mouse models of psoriatic skin disease. This would eliminate the need for either sacrificing animals or collecting serial skin biopsies to evaluate changes in disease progression during an individual study. The quantitation of epidermal thickness using optical coherence tomography (OCT) provides an alternative to traditional histologic techniques.

METHODS: Using the KC-Tie2 doxycycline-repressible psoriasiform skin disease mouse model, OCT imaging was completed on diseased back skin of adult KC-Tie2 (n = 3-4) and control (n = 3-4) mice, followed immediately by the surgical excision of the same region for histologic analyses. Animals were then treated with doxycycline to suppress transgene expression and to reverse the skin disease and additional OCT images and tissues were collected 2 and 4 weeks following. Epidermal thickness was measured using OCT and histology.

RESULTS: Optical coherence tomography and histology both demonstrated that KC-Tie2 mice had significantly thicker epidermis (~4-fold; P < 0.0001) than control animals. By 2 weeks following gene repression, decreases in epidermal thickness were observed using both OCT and histology, and were sustained through 4 weeks. Correlation analyses between histology and OCT values at all time points and in all animals revealed high significance (R2 = 0.78) with correlation being highest in KC-Tie2 mice (R2 = 0.92) compared to control animals (R2 = 0.16).

CONCLUSION: Non-invasive OCT imaging provided similar values as those collected using standard histologic measures in thick skin of KC-Tie2 mice but became less reliable in thinner control mouse skin, possibly reflecting limitations in resolution of OCT. Future advances in resolution of OCT may improve and allow greater accuracy of epidermal thickness measurements.
### Optical coherence tomography: a new tool to assess nail disease in psoriasis?


**Dermatology**

311-3, 222, 4, 2011

**BACKGROUND:** Nail disease is a characteristic manifestation of the psoriatic disease spectrum but is poorly understood.

**OBJECTIVE:** Given the intrinsically high spatial resolution imaging capabilities of optical coherence tomography (OCT), we assessed its value in psoriatic nail disease compared to high-resolution ultrasonography (US).

**METHODS:** All fingernails in a psoriatic arthritis patient with nail changes were scanned with OCT and findings were compared with high-resolution US.

**RESULTS:** US showed loss of trilaminar appearance in all nails, resulting in the nail plate being visualized as a single hyperechoic layer with inhomogeneous thickness. The OCT images showed much higher-resolution changes with prominent thickening in the ventral plate at the nail bed which was grossly inhomogeneous, 'eroded' and irregularly fused with the underlying epidermis, which correlated with the clinical observation of subungal hyperkeratosis.

**CONCLUSION:** OCT has considerable potential for the evaluation of psoriatic nail disease and may be superior to US.

### In vivo response of GsdmA3Dfl/+ mice to topically applied anti-psoriatic agents: effects on epidermal thickness, as determined by optical coherence tomography and H&E staining.

Zulfakar MH, Alex A, Povazay B, Drexler W, Thomas CP, Porter RM, Heard CM.

**Exp Dermatol.**

269-72, 20, 3, 2011

10.1111/j.1600-0625.2010.01233.x

This study evaluated in vivo the potential of optical coherence tomography (OCT) to determine changes in thickness of the epidermis in response to the topically applied anti-psoriatic betamethasone dipropionate (BD), salicylic acid (SA) and also fish oil (FO). GsdmA3Dfl/+ mice have an inflammatory hair loss phenotype that includes hyperproliferation and epidermal thickening, hence a potential psoriasis model. Changes in epidermal thickness were evaluated over a period of 10 days, with the mice treated with combined BD + SA, FO + SA and BD + FO + SA. The data were validated with conventional measurement using H&E staining coupled with microscopy. Initial baseline measurement revealed an average epidermal thickness of 26.92 ± 1.17 μm. After 10 days of treatment with BD, the average epidermal thickness was reduced by 38.8% (P = 0.0001), and inversely, treatment with FO resulted in an unexpected 105% increase (P = 0.0001) in epidermal thickness. Combined BD + FO treatment did not cause any significant change (P = 0.3705) and may further indicate opposing effects on keratinocyte proliferation. The data obtained using OCT were statistically the same as those obtained by H&E microscopy (P = 0.4325), supporting a greater role for OCT in dermatological studies, while also allowing a reduction in the number of animals used in such studies as sacrifice at individual timepoints is not necessary.

### Evaluation of methylprednisolone aceponate, tacrolimus and combination thereof in the psoriasis plaque test using sum score, 20-MHz-ultrasonography and optical coherence tomography.

Buder K, Knuschke P, Wozel G.

**Int J Clin Pharmacol Ther.**

814-20, 48, 12, 2010

PMID: 21084037

**BACKGROUND:** Despite new treatment options with systemic disease modifiers, topical therapy - especially as combination therapy - plays an important role in psoriasis treatment.

**METHODS:** Antipsoriatic efficacy of methylprednisolone aceponate ointment (MPA), tacrolimus 0.1% ointment (FK506) and their combination (MPA+FK506) were investigated in a double-blind randomized pilot study using the psoriasis plaque test. Agents and corresponding placebos were applied once daily under occlusion for 11 days. Test sites were evaluated by sum score (erythema, scaling, infiltration), objective assessment by 20-MHz-sonography and optical coherence tomography (OCT).

**RESULTS:** After 11 days, the sum score significantly improved from baseline value in FK506-treated skin (9.6 vs. 2.9, p < 0.0001). MPA led to a significant improvement of the sum score (9.4 vs. 0.6, p < 0.0001). Combination therapy showed results similar to MPA monotherapy (9.4 vs. 0.4, p < 0.0001). These findings were confirmed by 20-MHz-sonography and OCT data.

**CONCLUSION:** FK506 is moderately effective in chronic plaque-type psoriasis in our model. Combination therapy with FK506+MPA has no additive effect compared to MPA alone.

### In vivo characterization of the structure and components of lesional psoriatic skin from the observation with Raman spectroscopy and optical coherence tomography: a pilot study.

Egawa, Mariko Kunizawa, Naomi Hiao, Tatsuki Yamamoto, Takako Sakamoto, Kumiko Teru, Tadashi Tagami, Hachio

**J Dermatol Sci.**

66-9, 57, 1, 2010


**BACKGROUND:** Despite new treatment options with systemic disease modifiers, topical therapy - especially as combination therapy - plays an important role in psoriasis treatment.

**METHODS:** Antipsoriatic efficacy of methylprednisolone aceponate ointment (MPA), tacrolimus 0.1% ointment (FK506) and their combination (MPA+FK506) were investigated in a double-blind randomized pilot study using the psoriasis plaque test. Agents and corresponding placebos were applied once daily under occlusion for 11 days. Test sites were evaluated by sum score (erythema, scaling, infiltration), objective assessment by 20-MHz-sonography and optical coherence tomography (OCT).

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**CONCLUSION:** FK506 is moderately effective in chronic plaque-type psoriasis in our model. Combination therapy with FK506+MPA has no additive effect compared to MPA alone.
Optical coherence tomography imaging of psoriasis vulgaris: correlation with histology and disease severity.


Epidermal thickness (ET) has been suggested as a surrogate measure of psoriasis severity. Optical coherence tomography (OCT) is a recent imaging technology that provides real-time skin images to a depth of 1.8 mm with a micrometre resolution. OCT may provide an accurate in vivo measure of ET. It is, therefore, speculated that OCT may be used in the assessment of psoriasis vulgaris. A total of 23 patients with psoriasis vulgaris were systematically evaluated by OCT imaging and skin biopsy during treatment. Biopsies were graded for disease severity, and additional evaluation was done by the physician via psoriasis area and severity index (PASI) score, and by the patient through measures such as self-administered PASI, psoriasis life stress inventory index and dermatology life quality index. ET was calculated from OCT images. In comparison to normal skin, psoriasis appeared with a more irregular surface with a stronger entrance signal, a serrated dermo-epidermal junction was found and a less signal intensity in the dermis as shown in OCT images. ET measured in untreated plaques was thicker reflecting epidermal hyperproliferation and inflammation. The changes were significantly correlated with the biopsy grading (r (2) = 0.41, p = 0.001) and ET significantly decreased with treatment (p = 0.0001). ET correlated significantly with self-reported measures of disease severity, but not with physician-assessed global PASI. The data suggest that OCT may be used to measure ET in psoriasis and the measurements correlate with several other parameters of disease severity. This implies that OCT assessment of psoriatic plaques may provide a useful method for non-invasive in vivo method to follow the evolution of psoriasis lesions.

Epidermal thickness assessed by optical coherence tomography and routine histology: preliminary results of method comparison.


BACKGROUND: Optical coherence tomography (OCT) is a promising non-invasive imaging technique for studying the epidermis and upper dermis in vivo. As proposed previously by Welzel et al. (J Am Acad Dermatol 1997; 37: 958-963), distance measurements between the entrance peak and the second peak of the A-scan seem to correspond to epidermal thickness (ET). However, there is a lack of systematic studies comparing OCT with histology.

METHODS: Sixteen healthy subjects were included in this pilot study. OCT assessments were conducted on the upper back. To determine ET by OCT, the distance between the entrance peak and the second peak of the A-scan was calculated (ET-OCT). After OCT measurement a 4 mm punch biopsy was taken on each subject from the same site previously assessed. The maximum thickness of the epidermis (ET-Histo) was determined microscopically using routine histological slices (formalin-paraffin technique, haematoxylin-eosin staining). Correlation and agreement between the two methods were assessed by means of the Pearson correlation procedure and Bland-Altman plots, respectively.

RESULTS: ET-Histo was 79.4 +/- 21.9 microm, including a stratum corneum thickness of 20 +/- 12.1 microm. OCT measurements resulted in an ET of 106 +/- 15.4 microm. No correlation between ET-Histo and ET-OCT was observed (r = 0.29, P = 0.27). There was a considerable lack of agreement between histology and OCT measurements as expressed in a high bias of 26.63 microm [95% confidence interval (CI) 14.49-38.77]. Furthermore, the lower 95% limits of agreement were -18.03 microm (95% CI -37.11 to 1.05) and the upper 95% limits of agreement were 71.28 microm (95% CI 52.2-90.36) indicating that ET-OCT may be 71.28 microm above or 18.03 microm below ET-Histo.

CONCLUSIONS: Our preliminary data suggest that the above-described OCT algorithm is probably not a valid measure for the evaluation of ET. The second peak of the A-scan seems not to correspond to the dermo-epidermal junction zone, but rather to fibrous structures in the upper dermis. Nevertheless, further systematic comparison studies between OCT and histology are warranted, using different OCT algorithms for ET determination and cryopreparation, which has a higher reliability than the formalin-paraffin technique.
Validation of optical coherence tomography in vivo using cryostat histology.


75-78 52 5 2007 10.1088/0031-9155/52/5/N01

We aimed to validate for the first time optical coherence tomography (OCT) measurements of epidermal thickness (ET) using cryopreparation for histology. OCT assessments of ET were performed on healthy skin using the algorithms as follows first, peak-to-valley analysis of the A-scan (ET-OCT-V); second, line-traced image analysis of the B-scan (ET-OCT-IA). Histology was performed using cryostat sectioning. We selected 114 samples, including B-scans and corresponding histology, for method comparison between ET-OCT-IA and ET-Histo. Forty-two A-scans were available for method comparison between ET-OCT-V and ET-Histo. Comparison of ET-OCT-V versus ET-Histo revealed only a slight bias and narrow 95% limits of agreement. A-scan analysis for ET determination is linked to significant limitations and lacks agreement with histology. By contrast, we observed satisfactory agreement between ET-OCT-IA and ET-Histo indicating that both methods can be utilized interchangeably. OCT using the line-traced image analysis of the B-scan appears to be a valid and relatively practicable method for the determination of ET in vivo. Furthermore, the comparisons with the in vivo OCT profiles demonstrate that cryostat sectioning provides a better preservation of relative and absolute dimensions of skin layers than paraffin embedding.

Comparison of histometric data obtained by optical coherence tomography and routine histology.


44008 10 4 2005 10.1177/12039086

There is a lack of systematic investigations comparing optical coherence tomography (OCT) with histology. OCT assessments were performed on the upper back of 16 healthy subjects. Epidermal thickness (ET) was assessed using three methods: first, peak-to-valley analysis of the A-scan (ET-OCT-V); second, manual measurements in the OCT images (ET-OCT-IA); third, light microscopic determination using routine histology (ET-Histo). The relationship between the different methods was assessed by means of the Pearson correlation procedure and Bland and Altman plots. We observed a strong correlation between ET-Histo (79.4 ± 21.9 microm) and ET-OCT-V (79.2 ± 15.5 microm, r = 0.97) and ET-OCT-IA (82.9 ± 15.8 microm, r = 0.97), respectively. Bland and Altman plots revealed a bias of 0.19 microm (95% limits of agreement: -27.94 microm to 27.56 microm) for ET-OCT-V versus ET-Histo. Comparison of ET-OCT-IA versus ET-Histo revealed only a slight bias and narrow 95% limits of agreement. A-scan analysis for ET determination is linked to significant limitations and lacks agreement with histology. By contrast, we observed satisfactory agreement between ET-OCT-IA and ET-Histo indicating that both methods can be utilized interchangeably. OCT using the line-traced image analysis of the B-scan appears to be a valid and relatively practicable method for the determination of ET in vivo.
Optical coherence tomography in contact dermatitis and psoriasis.

### BACKGROUNDS
Skin atrophy is one of the main side-effects of topical corticosteroid therapy. Although the use of high-frequency ultrasound is an established method that has been studied previously, it allows measurements of the slow-reacting dermal thickness only.

### OBJECTIVES
To investigate the decreasing epidermal thickness, which occurs earlier, we used optical coherence tomography (OCT), a high-resolution noninvasive imaging technique, and compared it with 20-MHz ultrasound and profilometry.

### PATIENTS/METHODS
In this double-blind placebo-controlled trial 20 healthy volunteers applied four different corticosteroids and the cream base formulation as placebo to the volar part of both arms once a day over a 4-week period. The epidermal thickness, the dermal thickness, and the skin surface roughness were assessed using OCT, high-frequency ultrasound, and profilometry.

### RESULTS
Each of the three methods allowed the detection and monitoring of significant corticosteroid-induced skin atrophy and its reversibility. The changes correlated with the potency of the steroids. The epidermal thickness decreased significantly in all tested areas, even in the placebo and the untreated fields. As expected, the reduction in epidermal thickness was more pronounced and could be detected earlier by OCT than the reduction of dermal thickness using ultrasound. The epidermal surface roughness investigated using profilometry showed a slight smoothing.

### CONCLUSIONS
OCT allows a simple, fast, and noninvasive in vivo measurement of the epidermal thickness. To evaluate the atrophogenic potential of corticosteroids it is more suitable than high-frequency ultrasound as epidermal thickness decreases earlier. In addition, epidermal thickness is a more sensitive indicator of atrophy than the degree of thinning is much higher compared with the dermal atrophy. Profilometry might give further information; however, it would not be suitable for clinical use as the results were generally less pronounced. In the future, OCT might be useful to detect corticosteroid-induced side-effects at the beginning for monitoring the therapy.

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### UVA1 and UVB irradiated skin investigated by optical coherence tomography in vivo: a preliminary study.

### PATIENTS/METHODS
In histological studies, it has frequently been demonstrated that ultraviolet (UV) exposure, in particular UVB, can induce significant thickening of the viable epidermis and/or stratum corneum. Since skin biopsy alters the original skin morphology and always requires an iatrogenic trauma, we aimed to introduce optical coherence tomography (OCT) in vivo for the investigation of changes of epidermal thickness (ET) following UVA1 and UVB irradiation. Twelve healthy subjects received daily 60 j/cm2 of UVA1 and 1.5 minimal erythema doses UVB on their upper back over 3 consecutive days. Twenty-four hours after the last irradiation, OCT assessments were performed on UV exposed and adjacent nonirradiated control sites. Data of ETs expressed by comparison of the averaged A-scans differed significantly between nonirradiated (94.2 +/- 15.7 microm), UVA1 (105.4 +/- 12.8 microm), and UVB (125.7 +/- 22.1 microm) exposed sites in comparison to the nonirradiated sites. UVA1 exposed skin showed significant (P = 0.022) increase of ET of 11% and UVB exposed sites a significant (P < 0.001) increase of 25% ET of UVA1 and UVB exposed skin sites differed significantly (P < 0.005). Our results obtained from OCT in vivo measurements confirm data of previous histological studies indicating that not only erythrogenic doses of UVB, but also suberythrogenic doses of UVA1 may have a significant impact on ET. OCT appears to be a promising bioengineering technique for photobiological studies. However, further studies are needed to establish its measurement precision and validity, and to investigate in vivo spectral dependence on UV induced skin changes such as skin thickening.
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**Characterization of age-related effects in human skin: A comparative study that applies confocal laser scanning microscopy and optical coherence tomography.**

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<th>Authors</th>
<th>In Vivo Optical Imaging</th>
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<th>Nereken S, Lucassen GW, Blachop MA, Lenderink E, Nuijs TA</th>
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Skin structure and age-related changes in human skin were characterized in vivo by applying confocal laser scanning microscopy (CLSM) and optical coherence tomography (OCT). The overall effect of aging skin, derived from studies of volunteers belonging to two age groups, was found to be a significant decrease in the maximum thickness of the epidermis and flattening of the dermo-epidermal junction. At a certain depth in the dermis, well below the basal layer, a reflecting layer of fibrous structure is observed in CLSM images. The location of this layer strongly depends on age and is situated much deeper below the skin surface in younger than in older skin. In addition, large structural changes were observed with age. The OCT images show two bright reflecting layers, the first one due to scattering at the skin surface. The second band appears to be caused by a layer of fibrous structure in the dermis. Direct comparison of CLSM and OCT suggested that the same fibrous structure is observed in CLSM images. The location of this layer strongly depends on age and the task of the investigation.

**Application of optical non-invasive methods in skin physiology: a comparison of laser scanning microscopy and optical coherence tomography with histological analysis.**

|---------|------------------------|------------------------|--------------------------------------------------------|-------|----|----|-----------------|

Background/Purpose: Optical, non-invasive methods, such as fluorescence laser scanning microscopy (LSM) and optical coherence tomography (OCT), have become efficient tools for the characterization of the skin structure in vivo, as well as real-time investigation of distribution and penetration of topically applied substances. Methods: In the present paper, the results obtained with both non-invasive methods - OCT and LSM - were compared to conventional light microscopy of histological sections. Skin structure and the distribution of topically applied particulate and non-particulate substances on the skin surface and in the epidermis were analyzed. Results: None of the methods used are suitable for the realization of all diagnostic tasks, however, each method has advantages for particular applications. Fluorescence LSM is well suited for the investigation of the upper 150 microm of the skin as well as for the investigation of the kinetics of substances applied onto or into the epidermis. OCT can be applied for the investigation of vertical cross-sections of the skin up to a depth of 2 mm, albeit at lower resolution than achieved by LSM or conventional light microscopy. Conventional light microscopy of histological sections of biopsy specimens produces familiar high-resolution images of deeper tissue layers. However, the analysis of the kinetic processes is limited in this case. Conclusions: LSM- and OCT-measurements are efficient non-invasive tools for the characterization of morphological structures of the skin. On the one hand, the optical methods have a clear advantage in the case of kinetic measurements. On the other hand, histological investigations are characterized by a high information density and a high resolution, also in deep tissue layers. The selection of the best method for the analysis of the skin morphology depends on the target and the task of the investigation.


47-55 56 1 2013


Onychomycosis is common and can mimic several different nail disorders. Accurate diagnosis is essential to choose the optimum antifungal therapy. The aim of this study was to evaluate the use of confocal laser scanning microscopy (CLSM) and optical coherence tomography (OCT) as new non-invasive diagnostic tools in onychomycosis and to compare them with the established techniques in a prospective trial. 50 patients with suspected onychomycosis and 10 controls were examined by CLSM and OCT. Parallel KOH preparation, culture, PAS staining and PCR were performed. OCT showed the highest sensitivity, followed by CLSM, PAS and KOH preparation. OCT offered the second best sensitivity but displayed the lowest specificity. CLSM and KOH preparation showed a high specificity and CLSM offered the best positive predictive value, similar to KOH preparation and OCT. Fungal culture showed the lowest sensitivity and the worst negative predictive value, yet culture and PCR are the only techniques able to identify genus and species. In summary, CLSM was comparable to PAS staining and superior to KOH preparation. Due to the low specificity we assess OCT not as appropriate. In the differentiation of species PCR outplays the fungal culture in terms of time and sensitivity.

Confocal laser scanning microscopy, optical coherence tomography and transonychial water loss for in vivo investigation of nails.

Skovgaard LT, Thomsen JB, Mogensen M, Rothmund G, Sattler EC, Kaestle R, Jemec GB.

740-6 166 4 2012


Background Nail disorders can be diagnostically challenging to the dermatologist. Noninvasive methods might help to avoid nail biopsies. More knowledge of the typical features of healthy nails with these techniques is needed for comparison with nail diseases.

Objective To describe the typical morphology of healthy nails in optical coherence tomography (OCT) and confocal laser scanning microscopy (CLSM) and to examine the influence of exposure to water on OCT features, nail thickness as well as transonychial water loss (TOWL) before and after a hand bath.

Material and methods In the first part healthy nail plates were investigated with OCT and CLSM. The thickness of layers as well as structural details were defined. Secondly, in a prospective study 30 healthy volunteers conducted 10 hand baths with water within a 2-week period. Measurements of nail thickness and signal intensity by OCT as well as of the TOWL were performed overtime.

Results In OCT the unaffected nail plate appears as a band-like, layered structure, yet with some individual differences. In addition, CLSM is able to display single corneocytes and the integrity of their borders. Exposure to water led to a transient rise of TOWL and in nail thickness.

Conclusions OCT, CLSM and TOWL offer valuable noninvasive diagnostic tools for the examination of nails. Using CLSM, microscopic features like integrity of single corneocytes can be investigated. OCT allows determination of nail plate thickness and both OCT and TOWL measurements are able to detect short-term effects after exposure to water.

Nail thickness measurements using optical coherence tomography and 20-MHz ultrasonography.

Mogensen M, Thomsen JB, Skovgaard LT, Jemec GB.

894-900 157 5 2007

Br J Dermatol. 2007. 157. 10.1111/j.1365-2133.2007.08118.x

Background Nail diseases are often troubling to the patient and may present a diagnostic challenge to the dermatologist. Biopsies from the nail may be required although often perceived uncomfortable by the patient and potentially scarring. Noninvasive technologies are therefore of particular interest in the study of nails. Optical coherence tomography (OCT) is an optical imaging modality which may provide improved data.

Methods This study evaluates nail morphology and thickness in OCT images in comparison with nail diseases.

Results In standard OCT the nail plate appears as a layered structure containing a varying number of horizontal homogeneous bands of varying intensity and thickness. PS-OCT images of the nail plate also showed a layered structure. The refractive index of the nail was 1.47 +/- 0.09. OCT and PS-OCT had low coefficients of variation, 6.31 and 6.53, respectively, compared with other methods.

Conclusions PS-OCT has a high potential for in vivo investigation of nails. Using CLSM, microscopic features like integrity of single corneocytes can be investigated. OCT allows determination of nail plate thickness and both OCT and TOWL measurements are able to detect short-term effects after exposure to water.

**BACKGROUND:** Optical coherence tomography (OCT) is a noninvasive morphological method for investigating human skin. It allows high-resolution in vivo imaging of inflammatory skin diseases and tumours. Because it is a newly developed method, systematic studies on standardization and on evaluation of factors influencing the representation of the skin have not yet been performed.

**OBJECTIVES:** In this study, normal human skin was treated with various external stimuli which induce changes of function and morphology. Changes in stratum corneum thickness as well as changes induced by pigmentation, oedema and erythema were investigated using OCT.

**METHODS:** Healthy skin of human volunteers was treated with tape stripping, ultraviolet A irradiation, water, histamine, nicotinic acid and various ointments.

**RESULTS:** In the tape stripping experiment, the thickness of the horny layer was quantified and monitored. Pigmentation increased the light attenuation of the tissue, whereas hydration and erythema led to a slight decrease of scattering. Topical treatment of the skin gave a nonspecific increase of penetration depth of the light due to the lower reflectivity of the surface.

**CONCLUSIONS:** There are various physiological conditions which influence optical properties of the skin. These parameters should be considered when performing standardized OCT studies.

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**BACKGROUND:** Cutaneous larva migrans is a parasitic skin eruption caused by migration of larvae of various nematodes. Diagnosis of cutaneous larva migrans is currently based on the clinical signs of the creeping eruption. We are investigating a new diagnostic technology called optical coherence tomography (OCT), which is potentially able to visualize structures in the skin with an 8 microm resolution. This technology could therefore potentially allow rapid, non-invasive, in vivo diagnosis of infestations.

**METHOD:** Clinical cases of cutaneous larva migrans (n=3) were studied. All patients had a characteristic itching, serpinginous eruption typical of cutaneous larva migrans. The parasites were acquired on beach holidays in Thailand and Malaysia. All skin lesions were imaged by an OCT system developed at Risoe National Laboratory, Denmark.

**RESULT:** Two out of three patients showed a round to oval structure (diameter 0.3-0.5mm) in the epidermis, thus distinct OCT morphology in skin areas affected by cutaneous larva migrans was demonstrated. The larvae were not visualized in any of the patients.

**CONCLUSION:** This study demonstrates that OCT, a novel optical imaging technology, can image the larva tunnel in the skin with adequate spatial resolution, but not the larvae itself. OCT has a potential in imaging of skin infestations.

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**BACKGROUND/GOAL:** Tattoos have become increasingly popular followed by a growing demand for tattoo removal, and yet there is little knowledge and monitoring of tattoo pigment deposition in skin layers. The purpose of this pilot study is to describe optical coherence tomography image characteristics of intradermal tattoos.

**METHODS:** We included five black tattoos in 3 female volunteers, 39, 35 and 30 years old. In vivo imaging of tattoo pigments in the skin is possible with optical coherence tomography (OCT), a novel non-invasive, in vivo optical imaging technology with a resolution and a penetration in skin high enough for visualization of tattoo pigment in the dermis.

**RESULTS:** In optical coherence tomography images tattoo pigments clusters appear as dark, homogenous vertical columns and structures in the papillary dermis. OCT scanned normal skin (without tattoos) appeared to be free of dark structures.

**CONCLUSION:** We have demonstrated that OCT can be used to visualize clusters of light absorbing pigments in a predictable manner.
Optical coherence tomography imaging of bullous diseases.

**Mogensen M, Morsy HA, Nurnberg BM, Jemec GB.**


**BACKGROUND:** Optical coherence tomography (OCT) is a non-invasive optical imaging technique with a micrometer resolution that may potentially offer real-time bedside imaging of sufficient detail to allow for morphological discrimination between different types of bullae.

**OBJECTIVE:** To explore the potential of OCT in bullous skin disorders by looking at a set of patients with skin blisters of known origin and study the OCT images for possible hallmarks of the blistering level.

**MATERIALS AND METHODS:** OCT provides cross-sectional, tomographic images of the skin. A consecutive series of patients were recruited and their lesions imaged by OCT: 3 patients with bullous pemphigoid (BP), 1 patient with extensive bullae following burns, 1 patient with pemphigus, 1 patient with subcorneal pustular dermatosis, and a patient with Darier disease. The latter two were included due to similarity to pemphigus with respect to the level of defect cell adhesion.

**RESULTS:** In OCT images, BP bullae are easily depicted as dark, ovoid to round well-demarcated areas, and BP bulla morphology is clearly different from the burn blisters and the pemphigus-like disease with respect to the blistering level.

**DISCUSSION:** Differentiation of epidermal and subepidermal blisters is demonstrated using OCT. The variation within pemphigoid lesions and pemphigus-like diseases is however too subtle to allow for differential diagnosis; this may be ascribed to limited resolution. Enhanced resolution of OCT may overcome this obstacle.

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Morphology and epidermal thickness of normal skin imaged by optical coherence tomography.

**Mogensen M, Morsy HA, Thrane L, Jemec GB.**

Dermatology. 14-20 1 2008 10.1159/000118508

**BACKGROUND:** Optical coherence tomography (OCT) is an optical imaging technology with a potential in the non-invasive diagnosis of skin cancer. To identify skin pathologies using OCT, it is of prime importance to establish baseline morphological features of normal skin.

**AIMS:** The aim of this study is to describe normal skin morphology using OCT and polarization-sensitive OCT (PS-OCT), which is a way of representing birefringent tissue such as collagen in OCT images. Anatomical locations in 20 healthy volunteers were imaged, and epidermal thickness (Et) was measured and compared to age, gender and skin colour.

**METHODS:** OCT imaging is based on infrared light reflection/backscatter from tissue. PS-OCT detects birefringence of tissue. Imaging was performed in 12 skin regions. Et was calculated from the OCT images.

**RESULTS:** Normal skin has a layered structure. Layering is less pronounced in adults. In glabrous skin the stratum corneum is visible. Children had larger Et (p < 0.0001). Age had a negative correlation with Et (p < 0.05). No gender- or skin-type-related differences in Et were found.

**CONCLUSION:** This study contributes to understanding OCT and PS-OCT images of normal skin and indicates that OCT can be used for both the qualitative and quantitative assessment of skin.

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How histological features of basal cell carcinomas influence image quality in optical coherence tomography.

**Mogensen M, Nürnberg BM, Thrane L, Jørgensen TM, Andersen PE, Jemec GB.**

Biophotonics. 544-51 4 07 2011 10.1002/bio.201100006

**Optical coherence tomography (OCT) has the potential to diagnose and measure the depth of nonmelanoma skin cancer (NMSC) in skin, but some lesions appear blurred in OCT images. The aim of this study is to identify histological characteristics of basal cell carcinomas (BCC) that correlate with good quality OCT images of the same lesions. A total of 34 patients with BCC were OCT scanned.**

**The influence of histology parameters (e.g., inflammation, sun damage of skin, carcinoma cell size) on OCT image quality was studied by comparing 15 BCC lesions easily identified compared to 19 BCC lesions that produced only blurred OCT images. Inflammation was more pronounced in blurred OCT images, whereas solar elastosis dominated in easily identified lesions. Hyperkeratosis did not impair imaging significantly. OCT image quality of BCC may depend on specific histology parameters.**
Optical coherence tomography imaging of telangiectasias during intense pulsed light treatment: a potential tool for rapid outcome assessment.


Vascular malformations commonly occur in the facial region, and can be associated with significant stigma and embarrassment. Studies have shown that even recommended light-based treatments do not always result in complete clearance. This indicates the need for more accurate pre-treatment assessment of vessel morphology to optimize treatment settings and identify possible morphological predictors of the outcome. Fourteen patients (six males, eight females, and aged 37-66 years) with the diagnosis of telangiectasias were enrolled and were all scanned with OCT and digitally photographed before and minutes after IPL treatment. OCT images of the telangiectasias before treatment were displayed as hyporeflective/signal poor bands clearly demarcated from the surrounding tissue. Minutes after treatment, OCT images demonstrated two different reactions. (1) Narrow hyperreflective bands surrounding the vessels, which may indicate edema or insufficient coagulation. (2) Hyperreflective signals within the lumen of the vessels, compatible with the expected irreversible microthrombus formation in the vessels. OCT imaging is capable of real-time assessment of tissue damage during light and laser treatment, including visualization of the perivascular changes. This may offer a more dynamic, more complete understanding of the efficacy and potential outcome of the treatment process. It is hypothesized that these immediate changes may correlate to longer-term treatment outcome.

Denmark Treatments

Imaging granulomatous lesions with optical coherence tomography.

Banzhaf C, Jemec GB. Case Rep Dermatol. 14-18 4 1 2012 10.1159/000336000

AIM: To investigate and compare the presentation of granulomatous lesions in optical coherence tomography (OCT) images and compare this to previous studies of nonmelanoma skin tumors. METHODS: Two patients with granulomas, tophi and granuloma annulare (GA), respectively, were photographed digitally, OCT scanned and biopsied in the said order. Normal skin was OCT scanned for comparison, but not biopsied. The OCT images from each lesion were compared with their histologic images as well as with OCT images with similar characteristics obtained from nonmelanoma skin tumors. RESULTS: The OCT images of the tophi showed hyperreflective, rounded cloud-like structures in dermis, their upper part sharply delineated by a hyporeflective fringe. The deeper areas appeared blurred. The crystalline structures were delineated by a hyporeflective fringe. The deeper areas appeared blurred. The crystalline structures were delineated by a hyporeflective fringe. OCT images of GA showed two different structures in dermis: a hyporeflective rounded one, and one that was lobulated and wing-like. CONCLUSION: Granulomatous tissue surrounding urate deposits appeared as a clear hyporeflective fringe surrounding a light, hyporeflective area. The urate crystals appeared as hyperreflective areas, shielding the deeper part of dermis, meaning OCT could only visualize the upper part of the lesions. The lobulated, wing-like structure in GA may resemble diffuse GA or a dense lymphocytic infiltrate as seen on histology. The rounded structure in GA may represent an actual granuloma or either diffuse GA or a dense lymphocytic infiltrate as described above. This case suggests that OCT images granulomatous tissue as absorbent, hyporeflective areas, and urate crystals appear as reflective areas, obscuring the underlying tissue. In GA a new image shape looking like a wing has been found. The frequency, specificity and sensitivity of this new pattern in OCT imaging will require further studies.

Denmark Revision
High-definition optical coherence tomography: adapted algorithmic method for pattern analysis of inflammatory skin diseases: a pilot study.

High-definition optical coherence tomography (HD-OCT) is a non-invasive technique for morphological investigation of tissue with cellular resolution filling the imaging gap between reflectance confocal microscopy and conventional optical coherence tomography. The aim of this study is first to correlate dermatopathologic descriptors of inflammatory skin conditions with epidermal alteration to features observed by HD-OCT. Secondly, to assess the discriminative accuracy of common inflammatory reaction patterns with epidermal alteration using HD-OCT by applying Ackerman’s algorithmic method of pattern recognition. The generated HD-OCT images of 160 patients presenting with an inflammatory skin disease were analyzed with respect to the following criteria: visualization of individual cells in the epidermis and dermis and morphology of dermo-epidermal junction, papillary dermis and reticular dermis. A set of morphological features corresponding to dermatopathological descriptors are obtained and the discriminative accuracy of HD-OCT of inflammatory reaction patterns could be demonstrated. These patterns are spongiotic dermatitis, psoriasiform dermatitis, interface dermatitis and ballooning dermatitis. Additional studies to test the sensitivity and specificity of the proposed algorithm for pattern analysis are essential. The other categories of Ackerman’s pattern recognition need to be evaluated. This study provides a set of morphological features generated by HD-OCT imaging very similar to those described for reflectance confocal microscopy but with the advantages not only to visualize individual cells up to a depth of 570 μm but also in both slice and en face mode. An adapted algorithmic method for pattern analysis of common inflammatory skin diseases could be proposed. This new technique appears to be a promising method for non-invasive diagnosis, evaluation and management of common inflammatory skin diseases.

Belgium

High-definition OCT (HD-OCT) is an innovative technique based on the principle of conventional OCT. Our objective was to test the resolution and image quality of HD-OCT in comparison with reflectance confocal microscopy (RCM) of healthy skin. Firstly, images have been made of an ultra-high-resolution line-pair phantom with both systems. Secondly, we investigated 21 healthy volunteers of different phototypes with HD-OCT and RCM on volar forearm and compared the generated images. HD-OCT displays a difference depending on the skin phototype and anatomical site. The 3-μm lateral resolution of the HD-OCT could be confirmed by the phantom analysis. The identification of cells in the epidermis can be made by both techniques. RCM offers the best lateral resolution, and HD-OCT has the best penetration depth, providing images of individual cells deeper within the dermis. Eccrine ducts and hair shafts with pilosebaceous units can be observed depending on skin site. HD-OCT provides morphological imaging with sufficient resolution and penetration depth to permit visualization of individual cells up to 570 μm in depth offering the possibility of additional structural information complementary to that of RCM. HD-OCT further has the possibility for rapid three-dimensional imaging.

Denmark

Improved quality of optical coherence tomography imaging of basal cell carcinomas using speckle reduction.

BACKGROUND: Optical coherence tomography (OCT) is a possible imaging method for delineation of non-melanoma skin cancer. Speckle noise is the dominant noise contribution in OCT images limiting the ability to identify cellular structures especially skin cancer. QUESTIONS ADDRESSED: This report suggests a method for improving OCT imaging quality for skin cancer imaging. EXPERIMENTAL DESIGN: OCTs are optical imaging methods analogous to ultrasound. Two basal cell carcinomas (BCC) were imaged using an OCT speckle reduction technique (SR-OCT) based on repeated scanning by altering the distance between the probe and the surface of the skin. RESULTS: SR-OCT resulted in improved visualization and more accurate thickness measurements in BCC lesions. CONCLUSION: This OCT speckle reduction method led to improved visualization and better defined delineations in two BCC lesions. Thus OCT was improved to a clinically relevant level when imaging BCC lesions.
Topical corticosteroids are widely used to treat atopic dermatitis (AD), but their anti-inflammatory mode of action can be accompanied by several unwanted side effects including skin atrophy and telangiectasia. In this 8-week, investigator-blinded, intradividual right-left comparison study with patients with mild-to-moderate AD, hydrocortisone 1% cream (HCT) was applied twice daily for 4 weeks on one side of forehead skin without clinical signs of AD, and pimecrolimus 1% cream (PIM) on the other. Epidermal and dermal thickness were assessed by optical coherence tomography (OCT) and high-frequency ultrasound, respectively. Skin atrophy and telangiectasia were assessed by contact dermatoscopic photography (Dermaphot®). Treatment with HCT leads to a significant decrease in epidermal thickness after only 2 weeks of treatment, while the decrease in PIM-treated sites was less pronounced and was not statistically significant. By 4 weeks after the end of treatment, epidermal thickness returned to baseline values. No dermal thinning or development of telangiectasia could be observed by means of ultrasound or Dermaphot®, respectively. In summary, this study indicates that a 2-week single course of topical treatment with a mildly potent steroid can cause transient epidermal thinning, an effect not seen in the PIM group. The slight decrease with PIM — although not significant — could be due to normalization of the increased skin thickness caused by a subclinical inflammation in AD. This study suggests that PIM may be safer for treatment of AD in sensitive skin areas like the face, especially when repeated application is required.

**Possible histopathologic correlates of dermoscopic features in pigmented melanocytic lesions identified by means of optical coherence tomography.**


**High frequency ultrasonography but not 980nm-optical coherence tomography reliably evaluates melanoma thickness in vivo: a prospective validation study.**


**Evaluation of the atrophic potential of hydrocortisone 1% cream and pimecrolimus 1% cream in uninvolved forehead skin of patients with atopic dermatitis using optical coherence tomography.**

### Optical coherence tomography: a reliable alternative to invasive histological assessment of acute wound healing in human skin?

| Greaves NS, Benatar B, Whiteside S, Alonso-Rasgado T, Baguneli M, Bayat A. |
|-----------------|-----------------|

**BACKGROUND:** Gold-standard assessment of acute wound healing has traditionally been through histological analysis of biopsied tissue. However, this process is invasive with recognized side-effects. Optical coherence tomography (OCT) is a noninvasive technique generating high-resolution real-time images of cutaneous architecture.

**OBJECTIVES:** To compare OCT with histological assessment of in vivo acute wound healing and ascertain the level of agreement between modalities for measurement of defined cutaneous structures.

**METHODS:** Punch biopsies (5 mm) were harvested from 50 healthy volunteers. Wounds healed by secondary intention until they were re-excised on day 7, 14, 21 or 28 days later depending on random group allocation. Wounds were assessed weekly for 6 weeks using OCT. Images were compared with histological findings derived from time-matched biopsies. Dimensions of four cutaneous structures were measured using both modalities and the level of agreement was established by Bland-Altman analysis. The mean grey-scale value (MGV) of the upper reticular dermis was derived from OCT images at all time points.

**RESULTS:** Both techniques yielded anatomical congruity in normal and wounded skin with correlating architectural changes associated with inflammatory, proliferative and remodeling wound healing phases. MGV was significantly increased 6 weeks after wounding (P < 0.001) and may represent a novel measure of wound fibrosis. Despite good association of histomorphometric values with low but consistent bias (range: -4.181 to 0.431 μm), Bland-Altman plots demonstrated poor agreement between OCT and histology.

**CONCLUSIONS:** Optical coherence tomography enabled accurate assessment of healing tissue comparable with histological analysis of biopsy specimens. This noninvasive tool is highly suited to wound assessment and may represent a diagnostic alternative to punch biopsies.

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### Hair shaft abnormalities after chemotherapy and tamoxifen therapy in patients with breast cancer evaluated by optical coherence tomography.

| Undenber J, Hillmann K, Blume-Peytavi U, Lademann J, Lux A, Stroux A, Schneider A, Garcia-Bartels N. |
|-----------------|-----------------|

**BACKGROUND:** Antineoplastic treatment for breast cancer is frequently associated with alopecia. Increasingly, changes in the texture and shape of regrowing hair after chemotherapy have been reported, without evaluation on a scientific basis. Optical coherence tomography (OCT) provides highly reproducible measurements of hair shaft parameters.

**OBJECTIVES:** This study aims to evaluate hair shaft alterations using OCT in chemotherapy-induced alopecia and in patients taking tamoxifen.

**METHODS:** The measurements of this prospective case series were performed on women aged 29-68 years, receiving either tamoxifen (n = 17) or chemotherapy (n = 17) prior to (T1) and after (T2) treatment. Each time, 20 hairs from two different sites of the scalp (frontal, occipital) were examined by OCT. The hair parameters were characterized by cross section (CS) and form factor (FF). The ratio of maximal to minimal hair diameters determined the FF.

**RESULTS:** After chemotherapy, the CS of hairs was significantly lower compared with hairs taken at T1. The FF did not vary between T1 and T2 for the frontal area, but it did for the occipital area. In patients treated with tamoxifen, changes were observed neither in CS nor in FF. However, comparing both therapeutic groups, there were significant differences in CS and FF for T2, but not for T1.

**CONCLUSIONS:** Reported changes in hair structure after chemotherapy may be due to reduction of hair shaft caliber and increase of FF in regrowing hair. The OCT technique is a promising method to gain more insight into chemotherapy-induced changes of hair morphology.

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### Noninvasive clinical assessment of port-wine stain birthmarks using current and future optical imaging technology: a review.

| Shaif S, Taydas E, Mathar A, Rahimian R, Kelly KM, Choi B, Durkin AJ. |
|-----------------|-----------------|

**PORT-WINE STAIN (PWS) birthmarks are one class of benign congenital vascular malformation. Laser therapy is the most successful treatment modality of PWS. Unfortunately, this approach has limited efficacy, with only 10% of patients experiencing complete blanching of the PWS. To address this problem, several research groups have developed technologies and methods designed to study treatment outcome and improve treatment efficacy. This article reviews seven optical imaging techniques currently in use or under development to assess treatment efficacy, focusing on reflectance spectrophotometry, histomorphology, colorimetry, laser Doppler flowmetry and laser Doppler imaging, cross-polarized diffuse reflectance color imaging system, reflectance confocal microscopy, optical coherence tomography, spatial frequency domain imaging, and laser speckle imaging.**
Noninvasive diagnostic tools for nonmelanoma skin cancer.


Minimally invasive diagnostic tools have received increased attention for diagnosis, screening and management of nonmelanoma skin cancer (NMSC). Several modalities are commercially available, including high frequency ultrasound, optical coherence tomography and confocal microscopy. While systematic clinical analyses are often lacking, recent reports have shown promising results for reflectance confocal microscopy (RCM) for diagnosis of actinic keratoses and basal cell carcinoma.

Principles and application of optical coherent tomography in dermatology.

Schmitt AM. Dermatology 12 217 1 2008 10.1159/000118507

High-definition optical coherence tomography for the in vivo detection of demodex mites.

Dermatology 271 225 3 2012 10.1159/000345364

BACKGROUND: Demodex mites are involved in different skin diseases and are commonly detected by skin scrape tests or superficial biopsies. A new high-definition optical coherence tomography (HD-OCT) with high lateral and axial resolution in a horizontal (en-face) and vertical (slice) imaging mode might offer the possibility of noninvasive and fast in vivo examination of demodex mites.

METHODS: Twenty patients with demodex-related skin diseases and 20 age- and gender-matched healthy controls were examined by HD-OCT. Mites per follicle and follicles per field of view were counted and compared to skin scrape tests.

RESULTS: HD-OCT images depicted mites in the en-face mode as bright round dots in groups of 3-5 mites per hair follicle. In the patients with demodex-related disease, a mean number of 3.4 mites per follicle were detected with a mean number of 2.9 infested follicles per area of view compared to a mean of 0.6 mites in 0.4 infested follicles in the controls. The skin scrape tests were negative in 21% of the patients.

CONCLUSION: The innovative HD-OCT enables fast and noninvasive in vivo recognition of demodex mites and might become a useful tool in the diagnosis and treatment monitoring of demodex-related skin diseases.

Morphological changes in skin of different phototypes under the action of topical corticosteroid therapy and tacrolimus.


BACKGROUND/PURPOSE: The present study aimed to investigate the influence of topical corticosteroid therapy and tacrolimus on morphological indices of different skin phototypes and to optimize topical therapy using the OCT technique.

METHODS: Twenty healthy volunteers aging from 20 to 30 (14 men and 6 women) took part in the study: 10 persons with skin phototype I, II and 10 persons with skin phototype V, VI. Morphological state of the skin was assessed before and during application of topical steroids of different strength and calciumneurin inhibitors for 49 days. Morphological state was studied in vivo using the optical coherence tomograph.

RESULTS: Morphological manifestations of skin atrophy with the use of clobetasol propionate appear earlier than with the use of hydrocortisone 17-butyrate; this process was faster in representatives of groups V, VI. Epidermal thinning in the zone of tacrolimus application was not recorded in any phototype.

CONCLUSION: Recording of early preclinical signs of epidermal thinning in the course of OCT follow-up may be an indication for changing the corticosteroid therapy by calciumneurin inhibitors, which will permit to individualize the therapy, to increase its efficacy, and to minimize the possibility of complications in each particular case.
Non-invasive assessment of healing of bacteria infected and uninfected wounds using optical coherence tomography.


BACKGROUND/PURPOSE: Bacterial infection is one of the main predisposing factors for the delay in wound healing. To facilitate a timely decision for correct therapy, it is important to accurately monitor the morphological changes in the infected wounds using noninvasive tools. In the present study, we have explored the use of optical coherence tomography (OCT) for monitoring the healing of superficial wounds infected with Staphylococcus aureus in mice and in vivo conditions and studied the changes in collagen birefringence in the infected wounds.

METHODS: The tape stripping method was used for generating superficial skin wounds in mice and wounds were infected with S. aureus. For in vitro studies, infected and uninfected wound tissues were resected, back scattered intensity and birefringence changes in collagen during wound healing were studied on the 2, 4 and 10th day of postinfection using polarization-sensitive (PS) OCT and images were compared with histology. Real-time OCT was used for studying the kinetics of healing of infected wounds under in vivo conditions.

RESULTS: From the PS-OCT images, different phases of wound healing such as inflammation, reepithelialization and collagen remodeling could be identified. The edematic regions appeared prominent in infected wounds. Compared with uninfected wounds, reepithelialization and collagen remodeling phases of wound healing were delayed significantly in the infected wounds. These changes were comparable with the different stages of wound healing observed under in vivo conditions.

CONCLUSION: OCT imaging can provide a rapid assessment of the morphological changes associated with bacteria-infected and uninfected wounds and thereby aid in timely treatment planning.

Assessment of dermal wound repair after collagen implantation with optical coherence tomography.


We present an animal study to examine the utility and potential limitations of optical coherence tomography (OCT) for noninvasive evaluation of biomaterial scaffold-assisted wound healing. The transverse and axial resolutions of the OCT system at the wavelength of 1.3 microm were 12 and 10 microm, respectively. A murine full-thickness skin wound model was employed, in which a phi 10 mm full-thickness wound was created on the back of each male Balb/c mouse and a porous collagen scaffold was implanted in the wound bed followed by coverage with a Tegaderm film. Sequential cross-sectional OCT scans were performed at different time points post-surgical intervention to track morphological changes during wound recovery, and the captured OCT images were validated by their corresponding histological specimens. The results indicated that with removal of the high-scattering skin, OCT was capable of imaging to a depth of over 1.5 mm into the wound bed and differentiating various features evolved during wound healing at a high resolution approaching histopathology. OCT was able to not only delineate the epidermis and dermis of normal mouse skin, but also differentiate collagen implant from the underlying subcutaneous tissue; besides, it could track the wound size changes in both lateral and vertical directions. More importantly, OCT was able to detect inflammation, early re-epithelialization, and resorption of the collagen scaffold. These findings suggested the potential of OCT for noninvasive and high-resolution monitoring of assisted wound healing in vivo, longitudinally, and instantaneously.
Optical coherence tomography: a noninvasive method to assess wound reepithelialization.


**BACKGROUND:** Accurate assessment of wound healing may require invasive tissue biopsies, limiting its clinical usefulness in humans. Optical coherence tomography (OCT) is a novel, high-resolution method using light reflection to obtain noninvasive cross sectional imaging of biological tissues.

**OBJECTIVES:** To evaluate the utility of OCT for assessing wound reepithelialization in a porcine model.

**METHODS:** The authors conducted an animal study with two domestic pigs. Excisional cutaneous wounds were created over the ventral surface of the animals using an electric dermatome set at a depth of 600 microm. The wounds were excised two or three days later and precisely marked to guide initial OCT and subsequent tissue slicing and microscopy. Comparing hematoxylin and eosin-stained histologic sections and the corresponding OCT images from each tissue sample permitted identification of the correlative micromorphology. Scatter and Bland-Altman plots were used to present the data. The primary measure of agreement was the standard deviation of the pairwise differences in percent reepithelialization between OCT and histology together with a 95% confidence interval.

**RESULTS:** In normal skin, the epidermis was characterized by a thin, bright layer indicating a high degree of light scattering on OCT. The dermis below was characterized by a thicker, darker area indicating less scattering of light. All fresh excisional wounds lacked an outer bright layer of epidermis immediately after injury. At days 2 and 3, the wounds were partially reepithelialized. A new bright layer with intense light scattering was present on OCT corresponding to the neoepidermis on hematoxylin and eosin-stained sections. The correlation between percent reepithelialization measured with OCT and histology was 0.66 (p < 0.001), and the standard deviation of the differences was 11.0% (95% confidence interval = 8.4% to 16.1%).

**CONCLUSIONS:** OCT accurately detects the presence or absence of the epidermal layer of skin, allowing noninvasive tracking of wound reepithelialization.

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State of the art in non-invasive imaging of cutaneous melanoma.


**BACKGROUND:** This review focuses on looking at recent developments in the non-invasive imaging of skin, in particular at how such imaging may be used at present or in the future to detect cutaneous melanoma.

**METHODS:** A MEDLINE search was performed for papers using imaging techniques to evaluate cutaneous melanoma, including melanoma metastasis.

**RESULTS:** Nine different techniques were found: dermoscopy, confocal laser scanning microscopy (including multiphoton microscopy), optical coherence tomography, high frequency ultrasound, positron emission tomography, magnetic resonance imaging, and Fourier, Raman, and photoacoustic spectroscopies. This review contrasts the effectiveness of these techniques when seeking to image melanomas in skin.

**CONCLUSIONS:** Despite the variety of techniques available for detecting melanoma, there remains a critical need for a high-resolution technique to answer the question of whether tumours have invaded through the basement membrane.

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Diagnostic techniques for primary cutaneous melanoma.

**Lien MH, Sondak VK.** *G Ital Dermatol Venereol.* 187 144 2 2009 PMID: 19357625

**Diagnostic techniques for primary cutaneous melanoma.**

Despite the rising incidence of melanoma in the Caucasian population, there has not been a concomitantly dramatic increase in mortality, which is due, in part, to the advent of better tools that have been made available for the early detection of melanoma. This article presents an overview of some of the recent diagnostic developments that are of potential interest to practicing dermatologists. Some of these diagnostic advances include: total body photography; dermoscopy; multiphoton imaging; confocal scanning laser microscopy; teledermatology; high frequency ultrasound; computed tomography; magnetic resonance imaging; immunohistochemical stains; comparative genomic hybridization; microphthalmia transcription factor; and melanoma sniffing dogs. Although not all of these tools are uniformly accepted nor mandatory, a passing familiarity with them will be helpful as additional data regarding their use evolves.
Optical coherence tomography (OCT) is able to provide highly reproducible measurements of hair shaft thickness, including hair shaft diameter, cross-sectional surface area and hair shape, similar to histology but in vivo. Variations in the caliber of hair shafts have been described in patchy hair loss like alopecia areata (AA) using electron microscopy. The aim of this study was to evaluate whether OCT is useful for the evaluation of hair shaft abnormalities in AA.

**METHODS:** The measurements were performed on patients with AA (n=4), aged 2.66 years. Fifty hairs from the border of an alopecic area and 50 hairs from an unaffected area without hair loss were examined using the OCT technique. The hair parameters were characterized by the cross-sectional (CS) and the form factor. The ratio of the maximal and minimal diameters of the hair at a fixed measurement distance from the scalp surface determined the form factor (d(max)/d(min)).

**RESULTS:** In all cases, the CS of hairs from an AA patch was significantly lower compared with hairs of an unaffected area. However, the form factor did not indicate any disturbances in hair growth.

**CONCLUSIONS:** The described algorithm for structural abnormalities of hair shafts are found in active lesions of AA, but not in clinically unaffected hairs. The OCT technique is a promising method to gain more insight into the pathogenesis of AA in a non-invasive way.

**CONCLUSIONS:** The new image processing method for measuring ET from OCT images significantly decreases calculation time for this parameter, and avoids user intervention. The main advantages of this are that data can be analyzed more rapidly and reproducibly in clinical trials.
### Spectroscopic study on appearances of make-up skins using a visible RGB-LED OCT.

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<tr>
<td>Taqta, T.</td>
<td>2014</td>
<td>Skin Res Technol.</td>
<td>10.1111/art.12190</td>
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BACKGROUND: Facial foundation is very effective to correct color irregularities of the skin surface and to protect the skin from harmful light. This depends strongly on both the optical properties and the coating condition of foundation on the skin surface.

METHODS: We conducted the full-field optical coherence tomography (OCT) (FF-OCT) microscope with visible light sources of RGB-LEDs. The commercially available skin replicas were used as the model of skin in the experiment, which were composed of two layers, a thin polyurethane film transcribed from cheek surface of a female and a beige-colored silicone substrate. The foundations were applied to the skin replicas under the constant pressure.

RESULTS: A topographic image provides spectroscopic information of reflected light and effectiveness of correction of surface irregularities by applying the foundation. A tomographic image demonstrates the spectroscopic degree of light penetration into the skin tissue. It is shown that the reflectivity increases consistently with thickness of the applied foundation because light reflected from the surface and diffusely reflected from the inside of the tissue increases as the surface becomes flat applying the foundation.

CONCLUSION: We confirmed experimentally the potential of the spectroscopic FF-OCT microscopy in investigating both qualitatively and quantitatively the effectiveness of facial foundation.

### Full-color skin imaging using RGB-LED and floating lens in optical coherence tomography.

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<td>Yang BW,</td>
<td>2009</td>
<td>Biomed Opt Expr</td>
<td>10.1364/BOE1.0013</td>
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BACKGROUND: Moisturizers are the most commonly used topically applied product for the treatment of dry skin conditions. They affect many properties and functions of the stratum corneum but some moisturizers have been reported to be detrimental to barrier function. Stratum corneum barrier function is a composite of its total structure and thickness but few studies have taken this into account. As a biosensor, the stratum corneum (SC) will change its structure in response to treatment and a swelling effect has been clearly demonstrated by skin hydration. Recently several moisturizing agents have been shown to have an effect on SC swelling behaviour with conflicting results. However, there is a paucity of data reported for measuring the effects of long-term usage of moisturizers on SC thickness in vivo. As, until recently, traditional techniques did not have the resolution to measure the effects of moisturizers on non-palmoplantar body sites. The development of confocal Raman spectroscopy for use in human subjects provides noninvasive, real-time, in vivo measurement of SC water concentration profiles and we have also used this data to measure the long-term use of moisturizers on SC thickness for the first time.

OBJECTIVES: To validate the use of confocal Raman spectroscopy (CRS) to measure SC thickness and then use it to investigate the short- and long-term effects of moisturizers (one of which is known to improve SC barrier function) on SC thickness, water gradients, and hydration.

METHODS: Two studies were conducted: (i) to validate the use of CRS for measuring SC thickness through comparison with optical coherence tomography (OCT); and (ii) once validated to use CRS to measure the long-term effects of three commercially available moisturizers (A, B, C) on SC thickness, water gradients, and hydration. OCT images were obtained over a 3-week period (2 weeks of treatment and 1 week regression) and compare the spectroscopy-derived hydration value with instrumentally derived capacitance hydration values. RESULTS: (i) A strong, positive correlation in SC thickness was obtained between CRS and OCT (OCT-derived thickness = 0.96 x CRS-derived thickness, r(2) = 0.92, P < 0.0001). OCT was shown, however, to have a lower resolution than CRS in distinguishing SC thickness on thinner non-palmoplantar body skin.

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CONCLUSION: The cosmetic industry has witnessed significant growth in recent years. Conventional hand-held skin cameras allow for 2D inspection of the skin surface. This paper proposes a new model for full-color 3D imaging of the skin tissue using fiber-based optical coherence tomography (OCT). Compared to laser or LD sources, RGB-LED was found more suitable and thus chosen in the low-coherence interferometry due to its wider bandwidth. As a floating objective lens was used to confocalize the R, G and B imaging planes and to derive a full-color image of the capillary system in the skin tissue. The skin imaging system can be miniaturized to form a new hand-held model using an RGB-integrated source, a micro-interometer module and a high-speed beam steering device. Non-invasive, full-color and hand-held skin imaging contributes to advances in the fields of skin science, dermatology and cosmetology.
### Evaluation of moisture-related attenuation coefficient and water diffusion velocity in human skin using optical coherence tomography.


In this study, time-resolved optical coherence tomography (OCT) scanning images of the process of water diffusion in the skin that illustrate the enhancement in the backscattered intensities due to the increased water concentration are presented. In our experiments, the water concentration in the skin was increased by soaking the hand in water, and the same region of the skin was scanned and measured with the OCT system and a commercial moisture monitor every three minutes. To quantitatively analyze the moisture-related optical properties and the velocity of water diffusion in human skin, the attenuation coefficients of the skin, including the epidermis and dermis layers, were evaluated. Furthermore, the evaluated attenuation coefficients were compared with the measurements made using the commercial moisture monitor. The results demonstrate that the attenuation coefficient increases as the water concentration increases. Furthermore, by evaluating the positions of center-of-mass of the backscattered intensities from OCT images, the diffusion velocity can be estimated. In contrast to the commercial moisture monitor, OCT can provide three-dimensional structural images of the skin and characterize its optical property, which together can be used to observe morphological changes and quantitatively evaluate the moisture-related attenuation coefficients in different skin layers.

### Assessment of human burn scars with optical coherence tomography by imaging the attenuation coefficient of tissue after vascular masking.


The formation of burn-scar tissue in human skin profoundly alters, among other things, the structure of the dermis. We present a method to characterize dermal scar tissue by the measurement of the near-infrared attenuation coefficient using optical coherence tomography (OCT). To generate accurate en face parametric images of attenuation, we found it critical to first identify (using speckle decorrelation) and mask the tissue vasculature from the three-dimensional OCT data. The resulting attenuation coefficients in the vasculature-masked regions of the dermis of human burn-scar patients are lower in hypertrophic (3.8±0.4 mm⁻¹) and normotrophic (4.2±0.9 mm⁻¹) scars than in contralateral or adjacent normal skin (6.3±0.5 mm⁻¹). Our results suggest that the attenuation coefficient of vasculature-masked tissue could be used as an objective means to assess human burn scars.

### Application of optical coherence tomography in non-invasive characterization of skin vascular lesions.


BACKGROUND: Optical coherence tomography (OCT) is a new non-invasive approach for real-time in vivo tissue characterization. A promising use of OCT can be the assessment of the architecture of lesions with some degree of inhomogeneties, such as a vascularisation. Knowledge of the site and depth of the vascular structures can be useful for the diagnosis and for choosing the best treatment. OBJECTIVE: The purpose of this study was to investigate a series of vascular lesions by means of OCT in order to obtain new insights into the non-invasive, pre-operative analysis of these lesions. METHODS: Seven vascular lesions were included in the study. Histopathological diagnosis showed two haemangiomas and one haemolymphangioma; the remaining four cases were classified as haemangiomas on the basis of their clinical appearance. RESULTS: In all lesions, OCT analysis was able to visualize different areas of the lesion from the horny layer to the dermis showing a clear image of the vascular proliferation. Specifically, oval to roundish signal-poor areas sharply demarcated by a surrounding signal-rich layer were observed in good correlation with histopathology. CONCLUSION: The analysis of vascular lesions by OCT provides a new insight into non-invasive diagnosis and can be helpful in the selection of the most appropriate treatment.
Optical coherence tomography (OCT) is a high-resolution imaging method for in vivo investigation of the human skin. Cross-sectional images of several millimeters length with a penetration depth of 1.5-2 mm, given by current OCT technology, is sufficient to examine the skin. Real-time OCT imaging can provide information not available with histological and tomographical studies. METHODS: To obtain images of the skin, we used a compact fiber OCT system developed at the Institute of Applied Physics of the Russian Academy of Sciences. A low coherence source (superluminescent diode) operated at a wavelength of 1280 nm; the output power was 0.5-2 mW. This power is low enough to conform to the ANSI safety standards for light exposure. The in-depth resolution limited by the spectral bandwidth (40-50 nm) of the probing light was approximately 20 &mgr;m. For most of this study, a wavelength of 1280 nm was chosen. RESULTS: OCT imaging of the skin can detect in vivo such general pathological reactions of the human body as active inflammation and necrosis. OCT is useful for in vivo diagnostics of some specific processes in the skin, including hyperkeratosis, parakeratosis and formation of intradermal cavities. OCT imaging is noninvasive and therefore allows frequent multifocal examination of skin without any adverse effects. OCT can perform monitoring of disease progress and recovery in the course of therapy. Morphometrical studies, measurements of the depth and extension of skin pathology within the human body can be easily performed by OCT. CONCLUSIONS: OCT allows imaging of subsurface soft tissues with the spatial resolution of 15-20 &mgr;m, a resolution one order of magnitude higher than that provided by other clinically available noninvasive diagnostic techniques. An imaging depth of up to 1.5-2 mm, given by current OCT technology, is sufficient to examine the skin. Real-time OCT imaging can provide information not available with histological and tomographical studies.
Optical coherence tomography (OCT) is a non-invasive imaging modality that is transforming clinical diagnosis in dermatology and other medical fields. OCT provides a cross-sectional evaluation of the epidermis and dermis and allows in vivo imaging of skin collagen. (Upregulated collagen content is a key feature of fibrotic skin diseases. These diseases are often managed by the practitioners' subjective assessment of disease severity and response to therapies. The purpose of this review is to provide an overview of the principles of OCT and present available evidence on the ability of OCT to image skin collagen in vivo for the diagnosis and management of diseases characterized by skin fibrosis. We review OCT studies that characterize the collagen content in normal skin and fibrotic skin diseases including systemic sclerosis and hypertrophic scar. OCT can be applied to non-invasively detect and quantify skin fibrosis.)

**METHODS**: We performed 458 OCT scans of hands and forearms on 21 SSc patients and 22 healthy controls. We compared the findings with histology from three skin biopsies and by correlation with clinical assessment of the skin. We calculated the optical density (OD) of the OCT images employing Matlab software and performed statistical analysis of the results, including intraobserver/interobserver reliability, employing SPSS software.

**RESULTS**: The mean diameter of the medulla was 29±7 microm and the hair diameter was 122±16 microm in our samples of standard Afro-ethnic hair. A three-dimensional (3D) image was constructed starting from 601 cross-sectional images (slices). Each slice was taken in steps of 6.0 microm at eight frames per second, and the entire 3D image was constructed in 60 s.

**CONCLUSION**: It was possible to identify, using the A-scan protocol, the principal structures: the cuticle, cortex and medulla. After chemical treatment, it was not possible to identify the main structures of hair fiber due to index matching promoted by deleterious action of the chemical agent.

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The objective of this study was to compare optical coherence tomography (OCT) with conventional techniques such as KOH-preparation, culture and histology in the identification of fungal elements in the nail. A total of 18 patients were examined; 10 with clinically evident onychomycosis (true nails, two with psoriatic nail lesions, one with nail affection caused by lichen planus and five healthy controls. Serial in vivo OCT analyses of onychomycosis was performed prior to KOH-preparation, culture and punch biopsy of the nail plate for consecutive histology. Fungal elements were detected non-invasively in vivo using OCT in all 10 patients with histologically proven onychomycosis. Fungal elements were detectable as highly scattering elongated structures inside the nail plate, in the middle of the areas of homogeneous decrease in signal intensity. KOH-preparations and culture did reveal a positive result in 5/6 out of 10 patients. In patients with pseudocysts and fibrosis were characteristic signs of BCC response to HHIs. OCT, HHI-induced regression of BCC can be visualized noninvasively in the skin. The formation of pseudocystic structures (“empty” tumor nests in imaging) and widespread fibrosis (coarse bright fibers) were new findings and could be confirmed by histopathology. LIMITATIONS: Our study was limited by the number of tumor samples and imaging timepoints. CONCLUSION: Using RCM and HD-OCT, the evaluation of tumor regression has been performed using clinical photography and radiographic scans. Noninvasive imaging techniques, such as reflectance confocal microscopy (RCM) and high-definition optical coherence tomography (HD-OCT), have been shown to be valuable in detecting BCC in the skin. OBJECTIVE: We monitored HHI-treated BCC using RCM and HD-OCT in vivo and correlated morphologic changes seen on imaging to changes in traditional histopathology. METHODS: Six BCCs in 5 patients receiving HHIs (vismodegib or sonidegib) were examined by RCM and HD-OCT before and during treatment. Characteristic features were compared to histopathologic findings, including immunohistochemical analysis. RESULTS: Characteristic features of BCC in RCM and HD-OCT decreased or disappeared completely during HHI treatment. Half of the clinically responding tumors still featured tumor residue. The formation of pseudocysts and fibrosis were characteristic signs of BCC response to HHIs.

BACKGROUN: Ethnic differences in skin structural features have not been thoroughly investigated, and the few reported studies are contradictory. Thus, we have carried out a set of in vivo measurements on the skin of about 400 volunteers from various ethnic origins living in the same environment. METHODS: Female subjects were distributed into four ethnic groups: African Americans, Mexicans, Caucasians, and Chinese. Inter- and intra-ethnic skin structural differences, according to age and anatomic site, were investigated using three non-invasive skin-imaging methods ultrasound (US) at 25 and 150 MHz, and optical coherence tomography (OCT). RESULTS: The thickness of the skin is higher on the cheek compared with the dorsal and ventral forearm, with no ethnic or age-related specificity. We confirm that the sub-epidermal non-echogenic band is a sensitive marker of skin aging, and reveal for the first time that it is less pronounced in African Americans. From OCT images, we bring out evidence that the thickness of the dermal-epidermal junction (DEJ) decreased with age, and was higher in African Americans than in Caucasians. Finally, by comparing US images at 150 MHz with OCT images, we show that papillary dermis thickness can be measured and appears to be quite constant irrespective of age or ethnic group.

CONCLUSION: Our study confirms that skin imaging is very attractive to further our knowledge of the morphology of skin from various ethnic origins. Regarding age effects, quantitative parameters have shown that they would be delayed in African Americans compared with all other ethnic populations.