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Erstveröffentlichung in / First published in:

European Conferences on Biomedical Optics. Munich, 2017. Bellingham: SPIE, Vol. 10416
{Zugriff am: 23.05.2019}.

DOI: <https://doi.org/10.1117/12.2286073>

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SPIE.

Event: European Conferences on Biomedical Optics, 2017, Munich, Germany

3D handheld endoscope for optical coherence tomography of the human oral mucosa *in vivo*

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Abstract: The early non-invasive diagnosis of epithelial tissue alterations in daily clinical routine is still challenging. Since optical coherence tomography (OCT) shows the potential to differentiate between benign and malignant tissue of primal endothelium, OCT could be beneficial for the early diagnosis of malignancies in routine health checks. In this research, a new handheld endoscopic scanning unit was designed and connected to a spectral domain OCT system of our workgroup for the *in vivo* imaging of the human oral mucosa.

1. Introduction

Endoscopic optical coherence tomography (EOCT) enables the non-invasive, contactless, *in vivo* optical imaging of subsurface scattering tissue with high spatial resolution in combination with endoscopic optics for the investigation of body cavities and hollow organs accessible through natural orifices or minimal invasive access. Developments over the last decade tend to offer EOCT probes with a very small diameter in the form of catheter-based solutions for intravascular, bronchial as well as gastrointestinal diagnosis [1-4] and rigid needle-like probes for intra-tissue investigations in cancer diagnosis [5] both in forward- and side-imaging configuration. While side-facing systems realize 2D and 3D imaging by translation and rotation of the endoscopic probe, forward-facing devices are including additional mechanical scanning units for the beam deflection, making a miniaturized probe challenging under the claim of a broad field of view (FOV) and a suitable numerical aperture for OCT imaging over a large range of depth. In this research study, we would like to present our newest development of a rigid handheld endoscopic device for spectral domain optical coherence tomography in the 800 nm wavelength range (Fig. 1) to image the human oral mucosa *in vivo*. Therefore, we have modified our established handheld 3D OCT scanner head by an endoscopic optics device and a fiber-coupled reference arm applicable with any light source and standalone spectrometer designed for OCT in the 800 nm wavelength band. Advantageously, the endoscopic optics, considered as an attachment to the scanner head, can be cleaned and sterilized in the daily hospital routine. Thus, this device is one contribution to a multitude of promising and highly demanded developments in EOCT.

Fig. 1. Schematic of the principle EOCT setup. SLD: 5 mW superluminescent diode (SLD) with $\lambda_{\text{center}} = 835 \text{ nm}$, OC: optical circulator, FC: fiber coupler, C1,C2: collimators, GS: galvanometer scanner, M: mirror, L1-L4: lenses, EO: endoscopic optics, PC: polarization controller, RM: reference mirror, spectrometer: line rate of 11.88 kHz.

2. Specification of the rigid endoscopic optics

The scanning endoscopic OCT probe consists of a collimator for light coupling, two galvanometer scanners for 3D imaging, transmission optics to realize the endoscopic application and an objective lens for OCT imaging as well as glass fibers for VIS illumination. In contrast to a previous development, a fiber-coupled Michelson interferometer is realized. The pure endoscopic transfer optics in combination with ocular and objective is based on an afocal optics with a lateral resolution of $\Delta x = 62.5 \mu\text{m}$ at a working distance of $WD \sim 49 \text{ mm}$ according to the transition point between Fresnel and Fraunhofer diffraction for a center wavelength of $\lambda_{\text{center}} = 580 \text{ nm}$ (Fig. 2a). Therefore, reduction of the endoscopic distal beam width, and with this the increase of the lateral resolution, is achieved by adapting the optics of the basic scanner head for light coupling into the endoscopic part. As a result, a lateral resolution of $\Delta x = 12.4 \mu\text{m}$ at $WD \sim 7.5 \text{ mm}$ and $\lambda_{\text{center}} = 580 \text{ nm}$ was measured (Fig. 2b), which corresponds to $\Delta x = 17.8 \mu\text{m}$ for the NIR wavelength range with $\lambda_{\text{center}} = 835 \text{ nm}$. The measurement of the FWHM of the sample beam by using the designed proximal optics, a SLD with $\lambda_{\text{center}} = 835 \text{ nm}$ and the VIS camera at the distal end confirms the estimated lateral resolution with $\Delta x = 17.4 \mu\text{m}$.

Fig.2. (a) Lateral resolution of $\Delta x = 62.5 \mu\text{m}$ of the pure endoscopic optics using the USAF resolution test target at $WD \sim 49 \text{ mm}$ in combination with a proximal VIS camera focused to infinity. (b) By adapting the proximal optics for light coupling, $\Delta x = 12.4 \mu\text{m}$ is achieved at $WD \sim 7.5 \text{ mm}$ and $\lambda_{\text{center}} = 580 \text{ nm}$. (c) Measurement of $\Delta x = 17.4 \mu\text{m}$ by using identical coupling optics as in (b) with the modification of $\lambda_{\text{center}} = 835 \text{ nm}$ and a VIS camera at the distal end for detection.

For the determination of the field of view (FOV) in dependency on WD, a millimeter paper test chart (mm-chart) was used, detecting $FOV \sim 11 \text{ mm}$ at $WD \sim 7.5 \text{ mm}$ and $FOV \sim 14.5 \text{ mm}$ at $WD \sim 10 \text{ mm}$, respectively. As expected, a linear relationship was found between FOV and WD shown in Fig. 3c.

Fig. 3. (a,b) Endoscopic VIS images are detected of a millimeter paper test chart (mm-chart), illuminated by integrated glass fibers, for measuring the linear relation between FOV and WD (c). At the favorable WD of 5 to 10 mm, FOV ranged from 8.3 to 14.5 mm (c).

3. Performance of the EOCT system with telecentric scanning

The 3D forward-viewing telecentric endoscopic scanner head with fiber-coupled reference arm was characterized using an established spectral domain OCT system of our workgroup [6]. First, the signal-to-noise-ratio (SNR) was measured on a glass substrate surface (-14 dB reflector). Due to the endoscopic optics (EO) in the sample arm and missing additional glass substrates in the reference arm (Fig. 1), a numerical dispersion compensation is applied to the image data [7]. The SNR is determined between the peak of the A-scan of the glass substrate surface and the noise baseline. At optimum power settings in the reference arm, a SNR of ~88 dB at 20 % of the respective maximum scanning depth is achieved. Using the same data set, the measured free-space axial resolution as the full-width at half maximum (FWHM) of the A-scan peak amounts to 11.7 μm , which is 6 % higher than without endoscopic optics and numerical dispersion compensation. The result of the telecentric configuration by means of an additional lens L2 (cp. Fig. 1) is presented on the example of a mm-chart at WD ~ 6 mm resulting in FOV ~ 4.8 mm as shown in Fig. 4.

Fig. 4. (a) OCT cross-sectional and (b) enface image of the telecentric scanned mm-chart. (c) Corresponding image of the VIS camera.

First *in vivo* imaging is presented at the human fingertip, where the epidermal layers, the stratum corneum and the subjacent stratum granulosum can be differentiated (cp. Fig. 5a,b). Moreover, the results of the EOCT imaging of the healthy human buccal mucosa at two different zones of the cheek is presented in Fig. 5c and 5d. There, Fig. 5c shows exemplarily the posterior part and Fig. 5d the anterior part of the buccal mucosa.

Fig. 5. (a) Telecentric endoscopic imaging of the human fingertip utilizing the full telecentric scanning range or rather (b) a smaller section with increased lateral resolution. (c,d) *In vivo* EOCT imaging of the healthy human buccal mucosa at different zones of the cheek. Scale bar in (c) and (b) corresponds to 300 μm .

Additionally, representative OCT measurements of the healthy oral mucosa of the tongue and soft palate are exemplarily imaged with the developed OCT endoscope. The result of the lingual mucosa measured at the inferior surface of the tongue is presented in Fig. 6a1. EOCT imaging of the soft palate and the palatoglossal arch are exemplarily presented in Fig. 6b1,c1 and 7a1,b1.

Fig. 6. (a,a1) Healthy lingual mucosa of the inferior surface of the tongue imaged in contact mode by means of an additional contact piece. (b,b1,c,c1) Healthy oral mucosa of the soft palate also imaged in contact mode by E OCT imaging.

Fig. 7. Results of the E OCT imaging of the soft palate towards the buccal mucosa of a healthy volunteer performed in contact mode.

4. Conclusion and Outlook

In this research, we have developed a 3D forward-imaging endoscopic device usable for optical coherence tomography in the 800 nm wavelength range. The new E OCT scanner head with fiber-coupled reference arm allows telecentric imaging of scattering structures with variable WD and sufficiently large FOV. In combination with an existing high power and high resolution OCT system of our workgroup and the implementation of the dispersion encoded full range algorithm, the E OCT scanner will be used in a clinical study for the qualitative morphological and functional imaging of human healthy and altered oral mucosa.

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