Volumetric tissue monitoring of structure and function based on optical coherence tomography

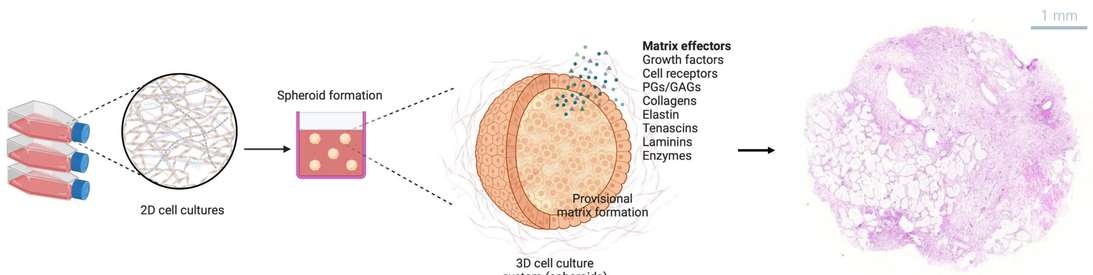
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INTRODUCTION

Extended, volumetric tissues, such as spheroids, organoids and printed compounds of cell-laden biomaterials attract an increasing interest in tissue engineering, pharmacology and in-vitro drug testing but challenge the established light microscopy techniques due to their increased thickness. While modern techniques such as light-sheet fluorescence and confocal multiphoton microscopy are typically limited to penetration depths of up to 100 µm, optical coherence tomography (OCT) is an interferometric imaging modality, which measures the depth-resolved backscattering of near-infrared light at more than 1 mm in dense scattering tissue.

Thin (<10 µm) samples with transparent, cellular structure	Extended (~100 µm) samples with dense cellular structures	Thick tissue (>200 µm) with dense, scattering media
Wide-field or laser-scanning microscopy	Confocal multiphoton light-sheet microscopy	Optical coherence tomography

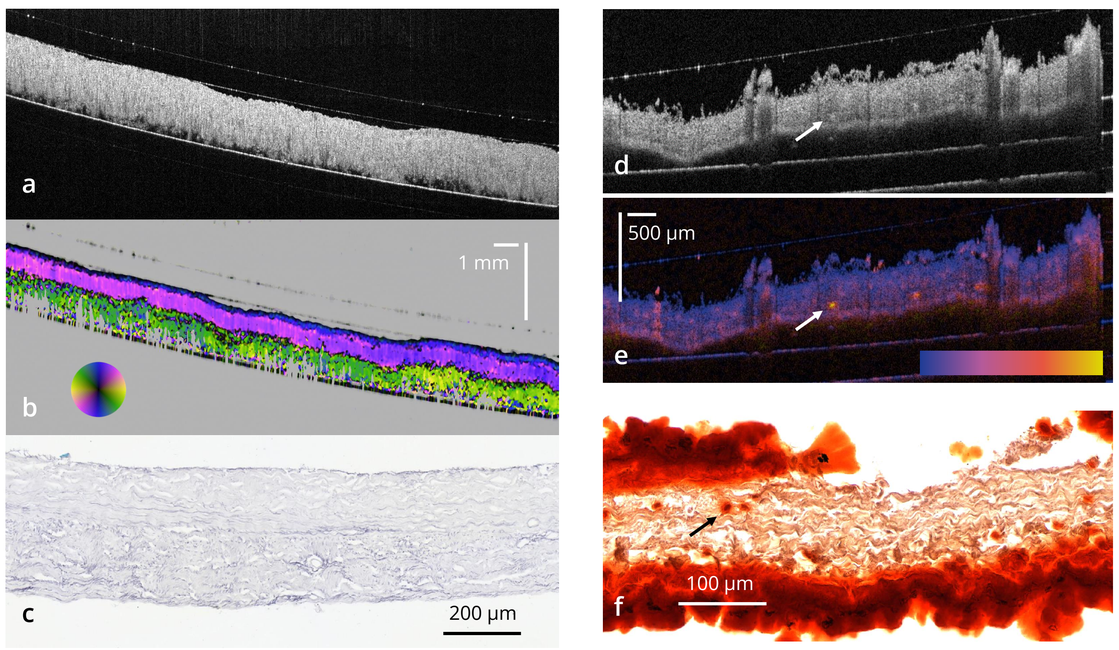


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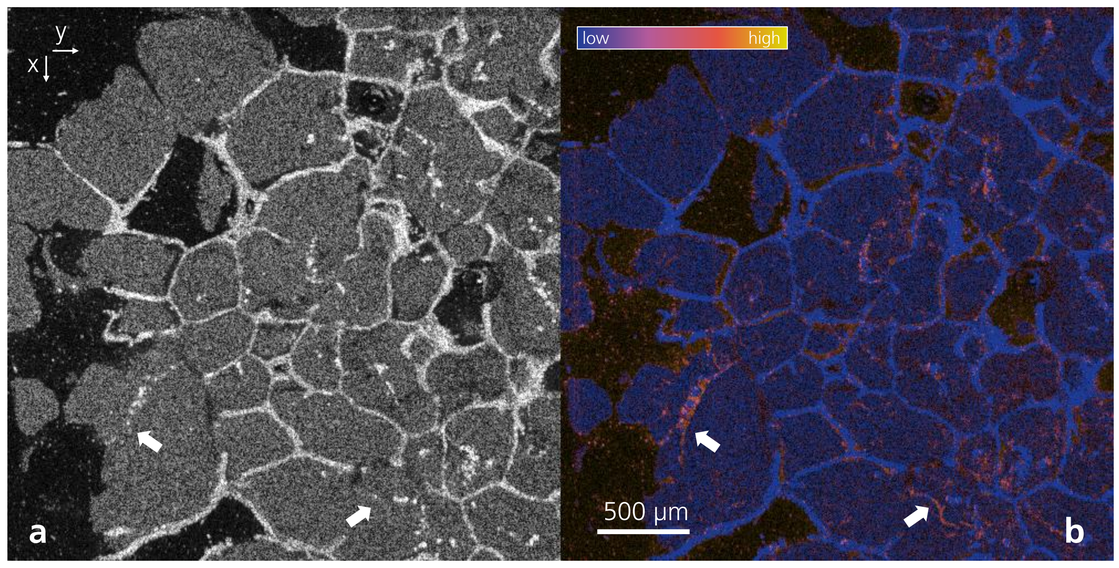
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MULTIPLE CONTRAST OPTIONS

While conventional OCT is based on the intensity of the back-scattered light, different functional extensions have been developed, which provide additional contrast based on the physical properties of the interference signal. To distinguish tissues based on the polarimetric signatures, polarization-sensitive OCT [1] uses an enhanced detection scheme to resolve the effects of birefringence, depolarization or diattenuation in organized structures.



Polarization-sensitive OCT. Cross sections of fixed bovine pericardium (a-c) and calcified porcine pericardium (d-f) show characteristic features in PS-OCT intensity (a,d), optic axis orientation (b) and DOP (e) compared to histology (c: EvG, f: A). Centers of presumed micro calcification are indicated (arrows). As the histology of the bovine pericardium (c) is from another sample than PS-OCT (a,b), thicknesses are not directly comparable (from [2]).

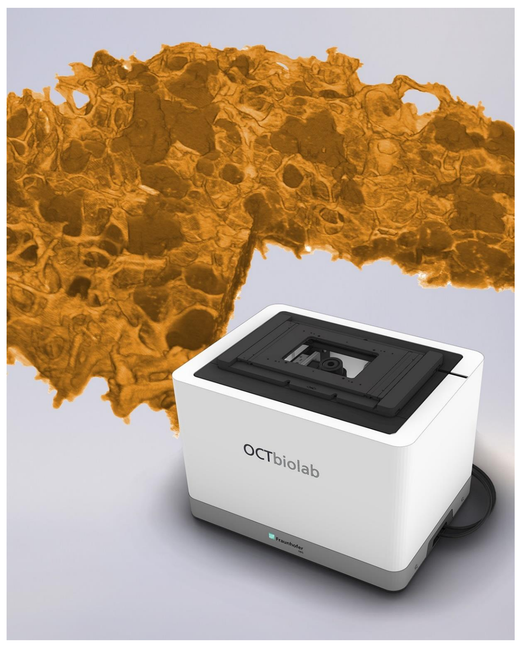


Dynamic OCT. To resolve tissue activity in a cultivated precision-cut lung slice (provided by Fraunhofer ITEM, Hannover), multiple cross sections were acquired at the same position. The enface slice shows the averaged intensity (a) and the speckle variance (b), indicating living cells (arrows).

In case of living samples, speckle dynamics in the OCT images can be used as an additional contrast for cell motility and tissue metabolism. When acquiring multiple images from the same position, speckle changes over time are resolved by calculating the variance or Fourier transform of the sequence. Recent work suggests that this approach can be used to not only identify cellular activity but also developed into a quantitative tool for in-vitro monitoring of drug applications or variations of culture conditions.

OUTLOOK

We have developed OCTbiolab, a novel imaging system based on OCT that enables rapid, label-free exams of live tissues in different sizes and conditions. Based on time-resolved speckle dynamics and polarized light, the OCT contrast is further enhanced to track not only volumetric growth but also necrotic, vascular or extra-cellular matrix (ECM) changes over time, thus providing quantitative metrics on the same sample for improved assay throughput and reduced variability in tissue engineering. In collaboration with partners from preclinical and clinical research, this device shall be tested in the future.



OCTbiolab

- Imaging similar to an inverted microscope for multiwell plates
- Motorized and automated scanning and data acquisition
- Compatible with different microplate sizes and bottoms
- Automated OCT data acquisition and processing for different samples and resolutions
- Multiple contrast methods available
- AI-based 3D segmentation for fast insights

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1 Golde et al., "Detection of carious lesions utilizing depolarization imaging by polarization sensitive optical coherence tomography," Journal of Biomedical Optics, vol. 23, no. 07, p. 1, 2018.
2 Golde et al., "Refined validation of aortic valve pathology and pericardium replacement using polarization-sensitive OCT," Proc. SPIE 13837, 2026.

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