Noninvasive Detection and Assessment of Gas Microbubbles in Blood and Tissues

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ABSTRACT

BACKGROUND: Noninvasive functional imaging, monitoring and quantification of micro bubbles forming in blood and tissues upon rapid changes in barometric pressure are extremely important for effective therapy and diagnostics of several diseases. However, current techniques are unable of imaging and efficient detection of bubbles with diameter less than 50 micrometers. Here we propose novel Optical Coherence Tomography (OCT)-based sensor capable of for real-time, sensitive, accurate, and noninvasive imaging, monitoring, and quantification of microbubbles in skin and whole blood.

METHODS: Experiments were performed with fresh human blood. Once withdrawn (an anticoagulant was added), the blood samples were placed in a specially designed syringe with clear plastic walls. All experiments were performed at 22 °C using a portable fiber-based OCT system (in-depth resolution ~20mkm) with electro-optical peizo fiber-based in-depth scanning system. Continuous OCT imaging of blood optical properties was performed upon application of different negative pressure in the syringe. The acquired images were 450 by 450 pixels. The in-depth scanning was up to 2.2 mm, while the lateral scanning was 2.4 mm.

RESULTS: The OCT imaging was performed at the same position of the syringe before and after application of the negative pressure. Formation of gas bubbles with diameter of 100-200 µm upon application of the negative pressure was clearly detected and assessed. Application of phase-sensitive measurements indicated superior sensitivity of OCT for assessment of changes in refractive index of biofluids (up to 10E-6). These indicate that submicron bubbles could be potentially detected and analyzed in a real-time.

CONCLUSION: Obtained results demonstrate capability of OCT technique to image formation of micro bubbles in whole blood. However, resolution of this system was limited to approximately 20 µm that might be insufficient for detection of small gas bubbles. Currently, we are improving this limit of detection by application of phase-sensitive and spectroscopic methods.

OBJECTIVE

The objective of this research is to develop and apply a novel noninvasive imaging and sensing modality, based on Optical Coherence Tomography (OCT) technique, for real-time, sensitive, and accurate imaging, monitoring, and quantification of microbubbles in circulating blood and tissues. To implement this objective, we are developing a new phase-sensitive spectroscopic OCT system. This OCT-based biosensor will provide unique diagnostic and experimental tool due to its universality (could be applied in many areas of medicine as well as for several imaging and drug delivery projects utilizing microbubbles as a contrast or delivery agent), high in-depth and lateral resolution (up to a few microns), high accuracy (typical OCT signal-to-noise ration exceed 100 dB), high sensitivity (phase-resolved measurements can detect ultra-small changes in samples' refractive index, size, and displacement), and cost (estimated to be in tenths of thousands rather than hundreds of thousands that is typical for MRI or laser scanning confocal microscopy systems). The anticipated outcome from the proposed research is that highly needed SSOCT-based practical solution will be developed for continuous noninvasive imaging, monitoring, and quantification of microbubbles in blood and other tissues with high sensitivity, accuracy, and resolution.

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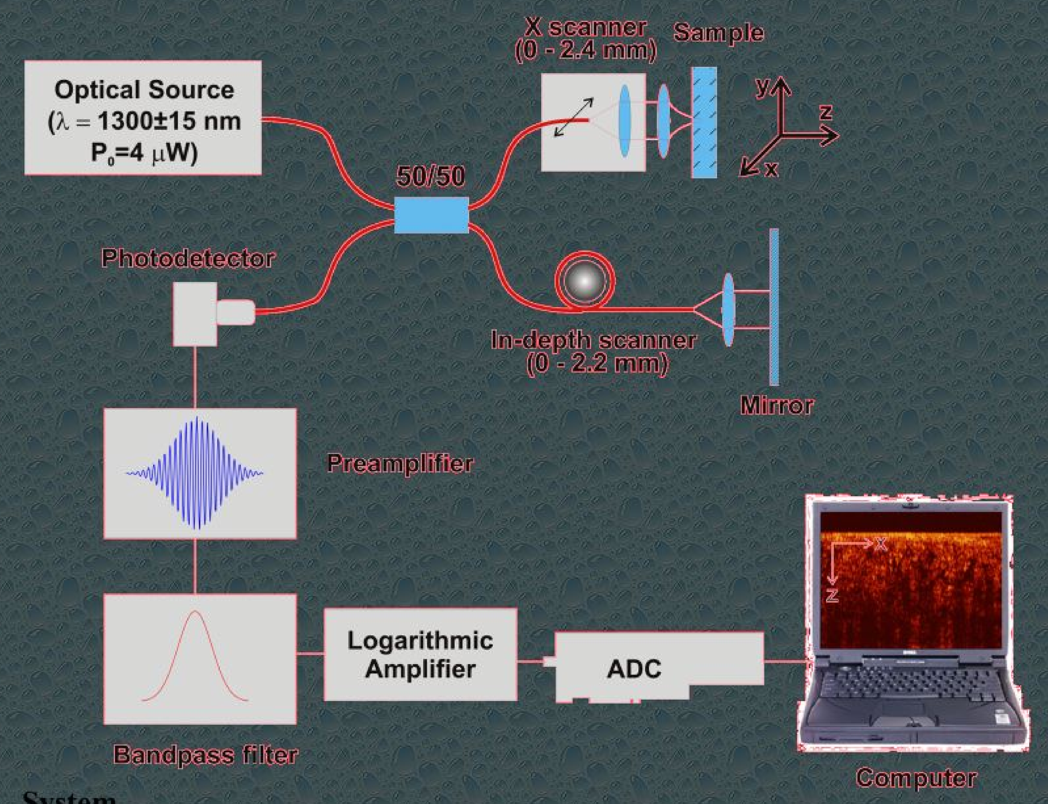
TIME-DOMAIN OCT

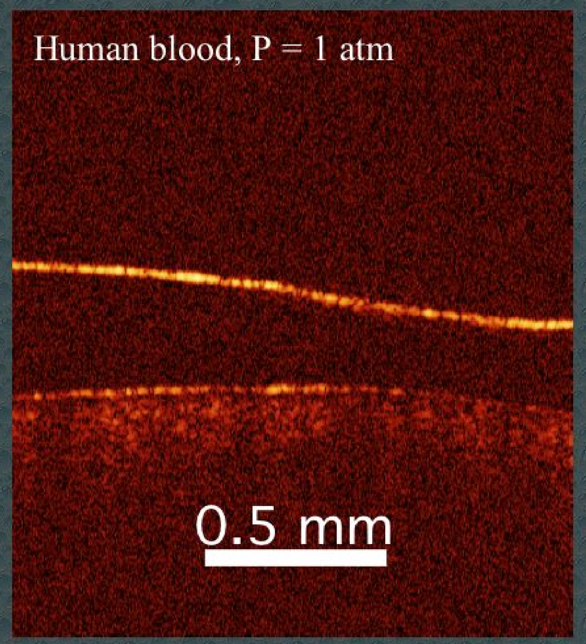


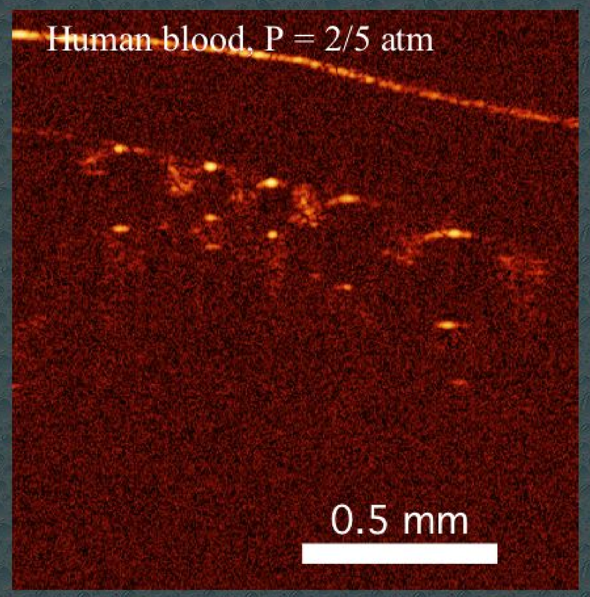
System

- Portable fiber-based TDOCT system – image acquisition speed: 0.25 Hz
- Electro-optical peizo fiber-based in-depth scanning system
- $_0$ = 1310 nm, __ = 30 nm, in-depth resolution ≈ 20 µm
- 2D scanning: 450 by 450 pixels (2.2 by 2.4 mm)
- Only amplitude-based imaging

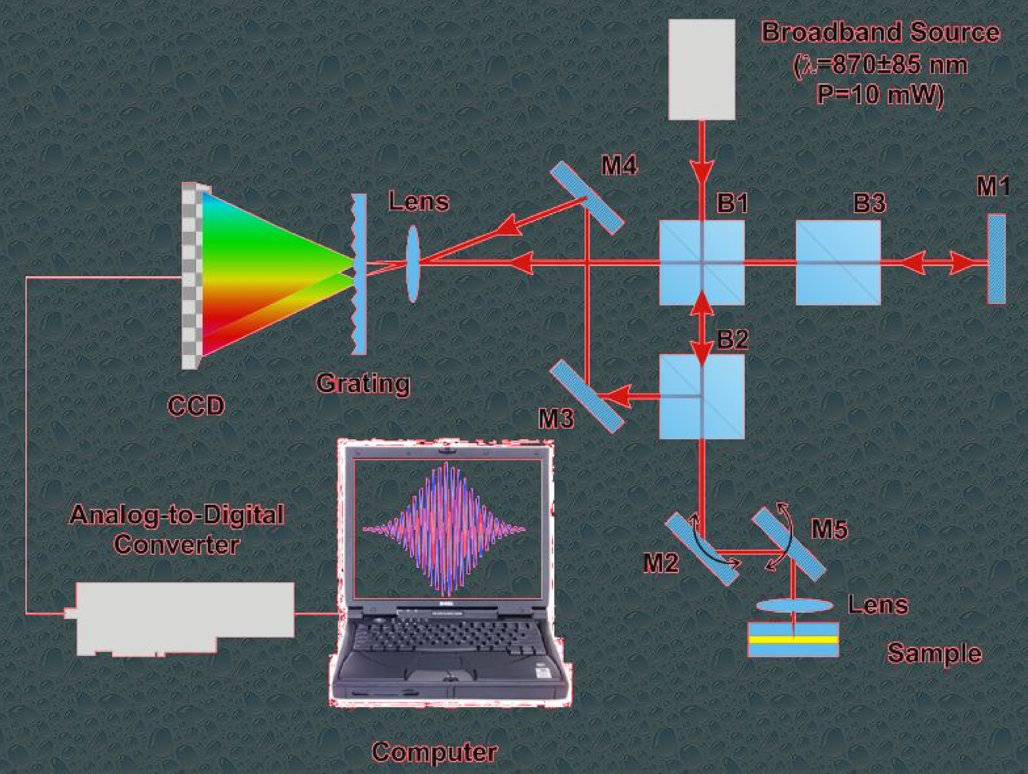
Materials

- Human (donor) blood in a syringe
- 22 °C
- Continuous imaging of blood optical properties was performed upon application of different negative pressure in the syringe.





FOURIER-DOMAIN OCT

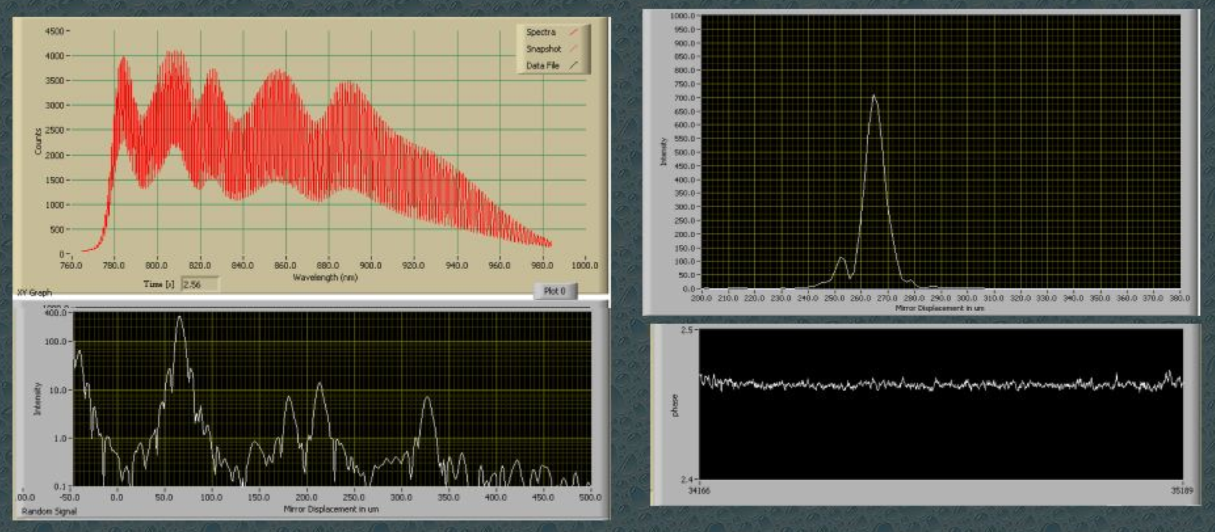


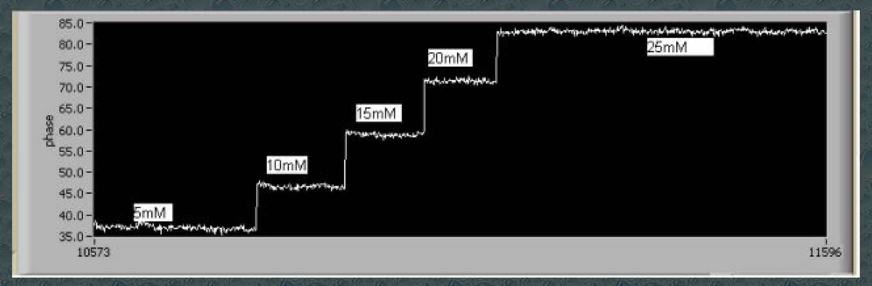
System

- Fourier-Domain OCT system, scanning speed: 30 Hz
- No in-depth mechanical scanning system
- $_0$ = 870 nm, __ = 170 nm, in-depth resolution ≈ 2 µm
- SNR: 130 dB
- z_{max} = 1.26 mm
- Phase-sensitive measurements of the mean refractive index

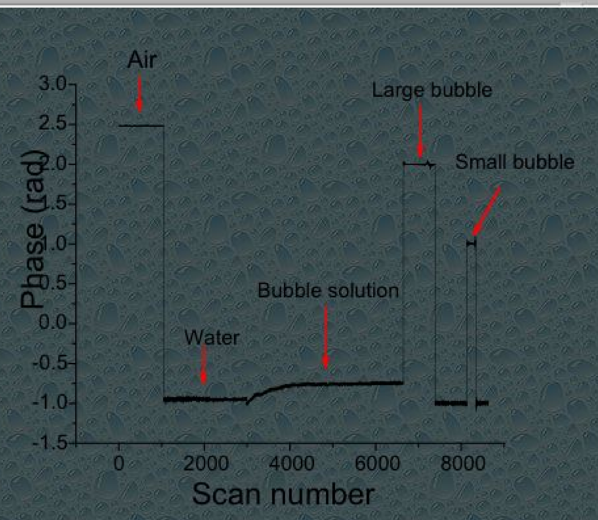
Materials

- TARGESTAR microbubbles: d = 2.5-50 µm
- 22 °C
- Continuous phase-sensitive imaging of 1) glucose of different concentrations and 2) stationary and flow-through microbubbles in 50µm –thick cell.

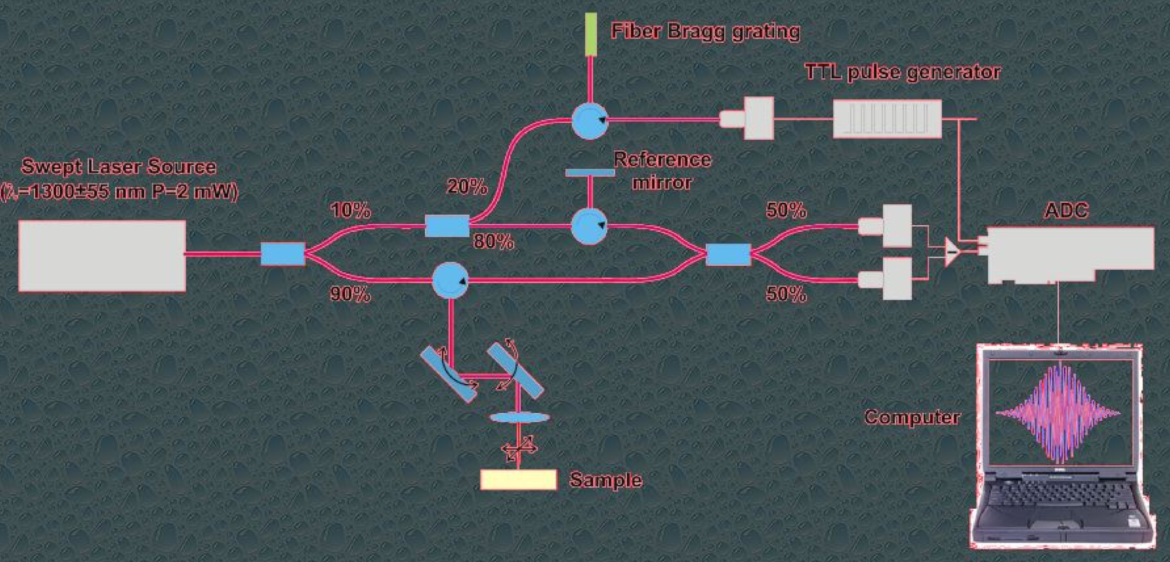




Glucose

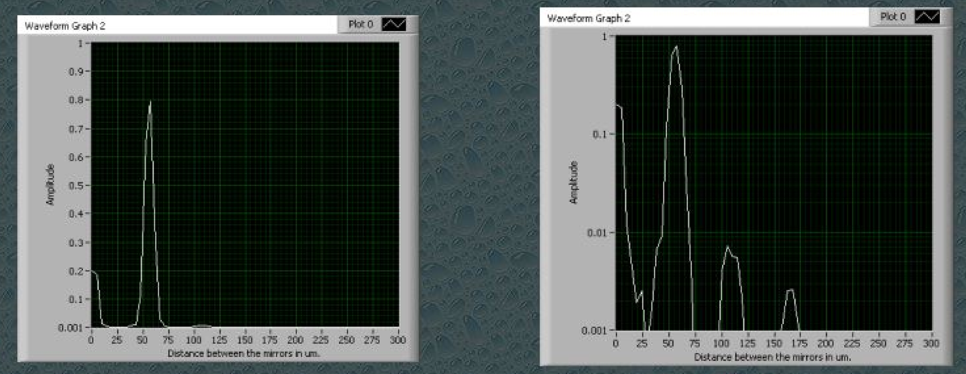


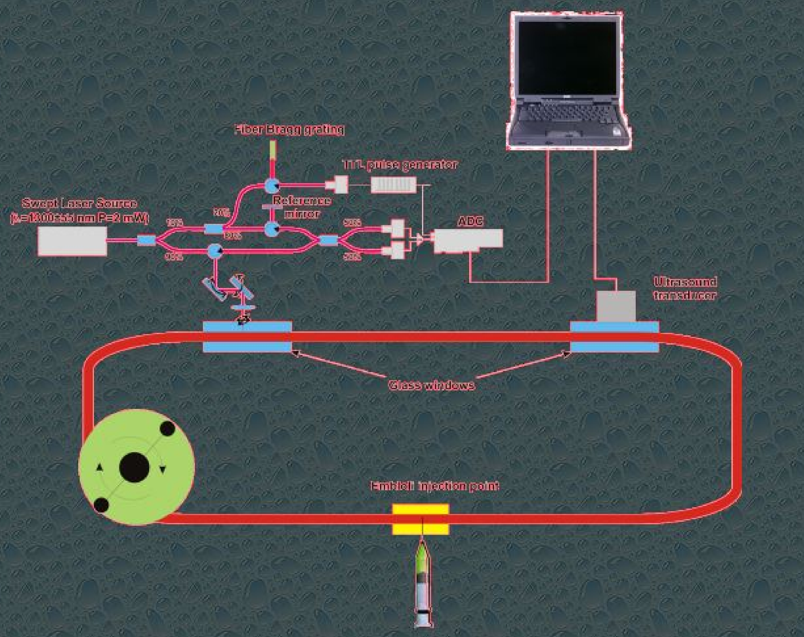
SWEPT-SOURCE OCT (under development)



System

- Swept-Source OCT system - scanning speed: 30 kHz
- No in-depth mechanical scanning system
- $_0$ = 1300 nm, __ = 110 nm, in-depth resolution ≈ 6 µm
- SNR: 114 dB
- z_{max} = 10 mm
- Phase-sensitive measurements of the mean refractive index





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