# NOVAL OPTICAL METHOD FOR MICROBUBBLES DETECTION IN VIVO

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### Background:

The goal of this study is to evaluate capability of novel optical sensor (Optical Coherence Tomography – OCT) for noninvasive ultra-sensitive detection and quantification of circulating microbubbles in small blood vessels of mice.

### Materials and Methods:

The experiments were performed with mice under anesthesia. The ears and tails were used for 2D and 3D OCT imaging of the blood vessels. The blood vessels were additionally identified using the Doppler analysis. Definity® microbubbles were induced in the up-stream blood flow of the mouse tail artery via direct injection and the blood flow was continuously monitored in the caudal artery of the mouse tail at ~3 cm away from the injection site as well as in the ears. 2D images were continuously acquired at a rate of 20 fps. The resolution of the system was: 8 µm and 12 µm (in-depth and transversal, respectively) for imaging of the blood vessels and 0.01 µm for sensing of the microbubbles.

### Results:

Continuous imaging of the blood vessels demonstrated capability of OCT technology for robust imaging of microbubbles as small as 56 µm, stationary or moving. Stationary air microbubbles were identified as small dark circles that appeared after the injection. Similarly, circular scattering structures that were not observed before injection but were visualized after injection were classified as clusters of the microbubbles.

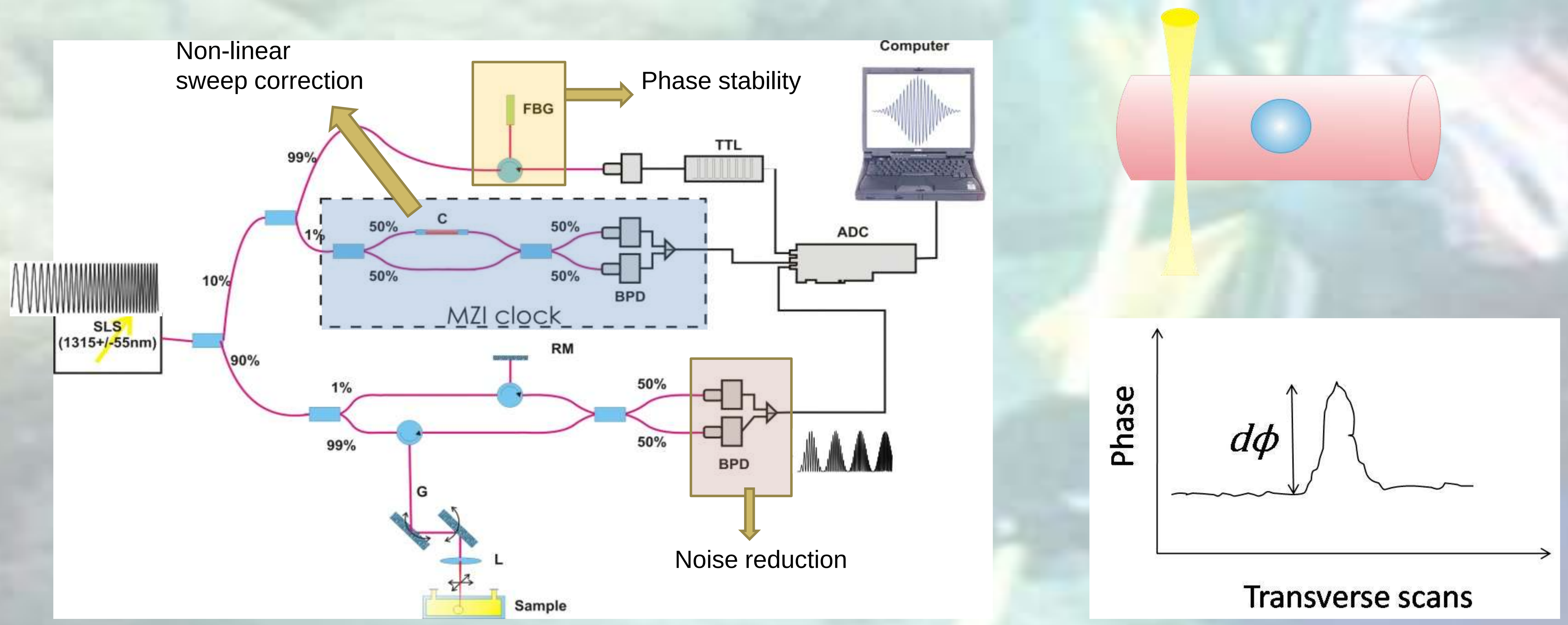


**Figure 1. Experimental setup:** Swept Source Optical Coherence Tomography system. Depth resolution = 8 µm; Transverse resolution = 12µm; Maximum imaging depth = 6 mm (in air); A-line speed = 30 kHz (2D B-mode imaging speed ~100 Hz); Phase stability = 0.01 radians. Microbubbles diameter is calculated using phase information.

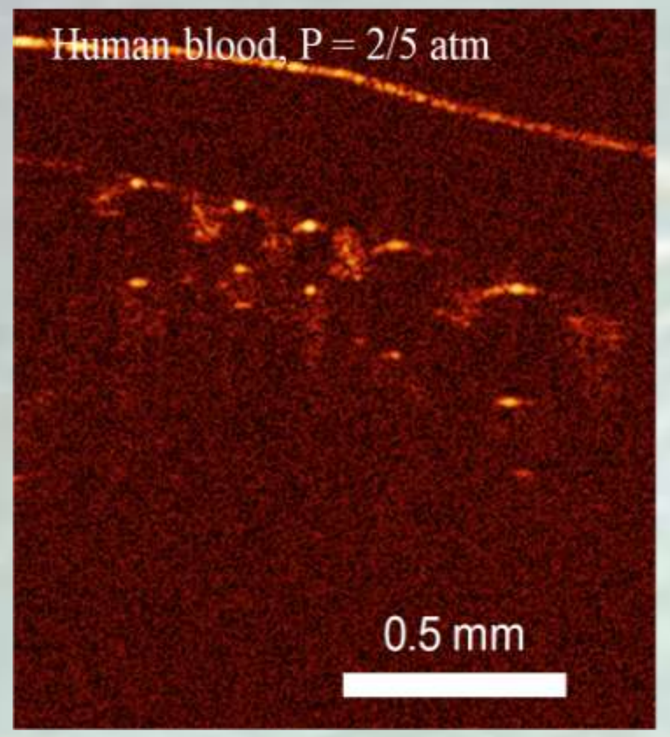


**Figure 2. OCT image of large uBBs**

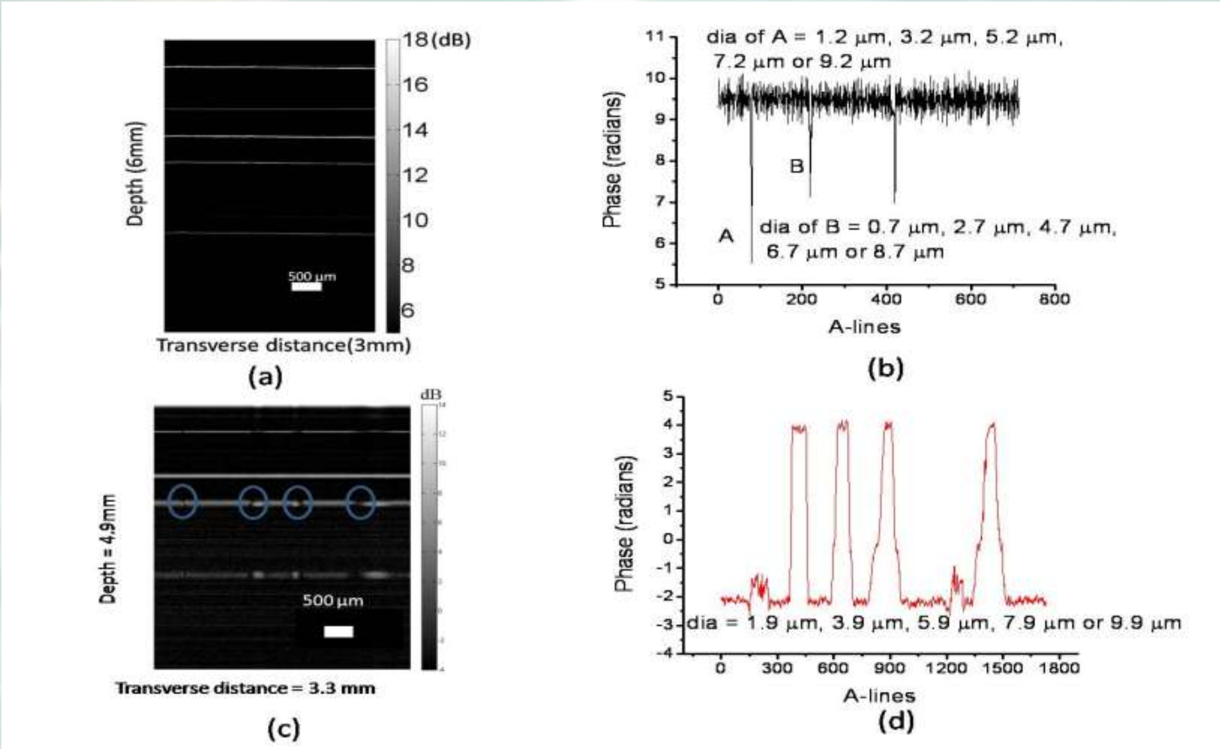


**Figure 3. OCT image and phase response of small uBBs**

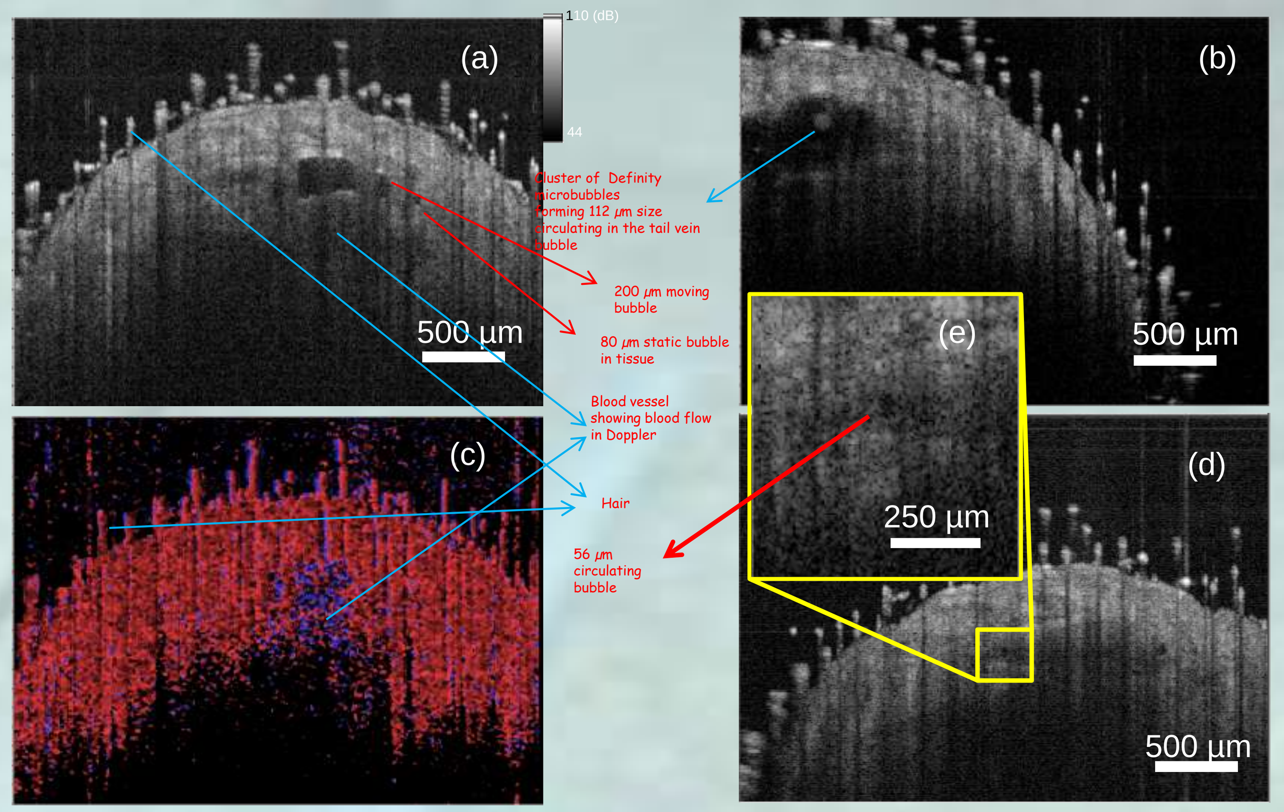


**Figure 4. OCT image and Doppler signal of uBBs in mouse tale *in vivo***

### Discussion and Conclusions:

The developed OCT is capable of imaging, detecting and quantifying of large and small microbubbles in small blood vessels. The results suggest that small microbubbles with diameter beyond imaging capabilities of the system can be detected and quantified using the phase-sensitive analysis. Potentially, microbubbles with sub-micrometer diameters can be detected and quantified using this method.

### Acknowledgments:

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### Selected References:

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[2] R. K. Manapuram, V. G. R. Manne, and K. V. Larin, "Phase-sensitive swept source optical coherence tomography for imaging and quantifying of microbubbles in clear and scattering media," *Journal of Applied Physics,* vol. 105, pp. 102040-10, 2009.
[3] R. K. Manapuram, V. G. R. Manne, and K. V. Larin, "Development of phase-stabilized swept-source OCT for ultra-sensitive quantification of microbubbles," *Laser Physics,* vol. 18, pp. 1080-1086, 2008.