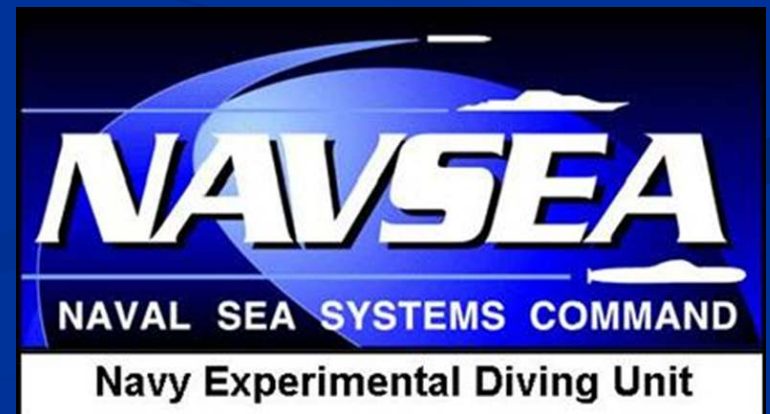


NOVAL OPTICAL METHOD FOR MICROBUBBLES DETECTION IN VIVO

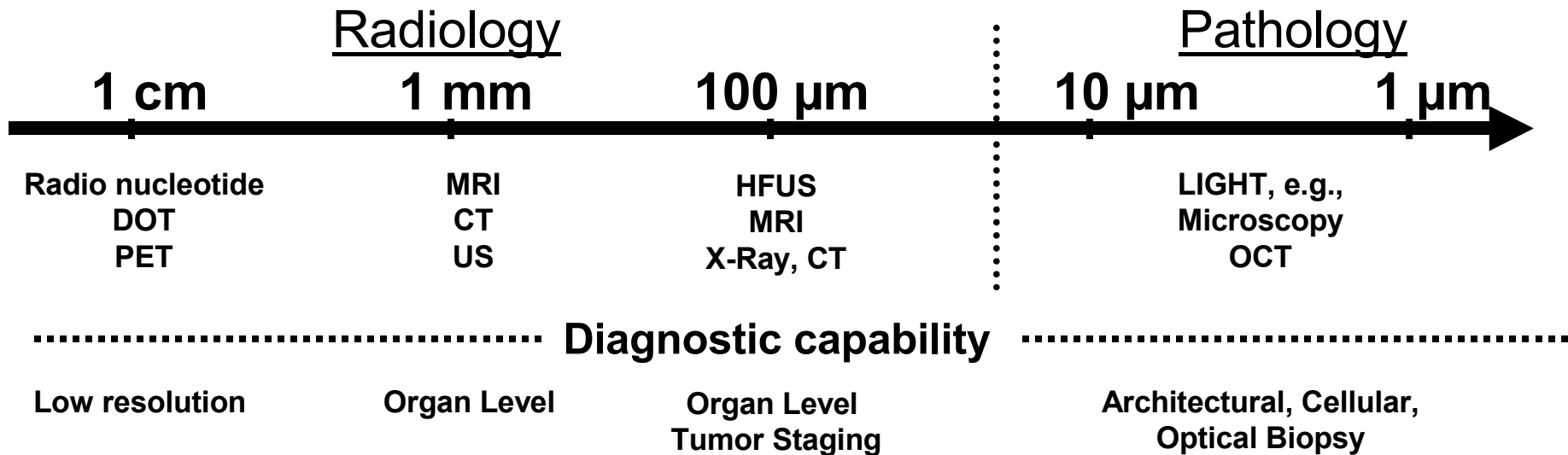
Sobakin AS¹, Manapuram RK², and Larin KV²

¹Department of Pediatrics, University of Wisconsin-Madison, WI, 53590 USA

²Department of Biomedical Engineering, University of Houston, TX, 77204 USA



Optics in Medicine



Histopathology is the golden standard
especially for cancer diagnosis

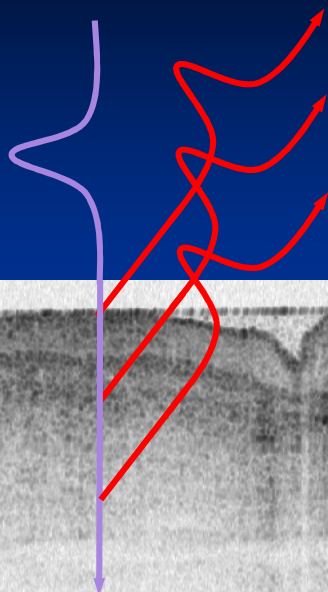
Only optical technique approach cellular resolution

DOT: Diffuse Optical Tomography; PET: Positron Emission Tomography;
MRI: Magnetic Resonance Imaging; CT: Computed Tomography; US: Ultra Sound;
HFUS: High Frequency Ultra Sound; OCT: Optical Coherence Tomography.

OCT

- **Optical coherence tomography (OCT)**
 - three-dimensional imaging technique with ultrahigh spatial resolution even in highly scattering media,
 - based on measurements of the reflected light from tissue discontinuities;
 - e.g. the epidermis-dermis junction,
 - based on interferometry;
 - involves interference between the reflected light and the reference beam.

Optical Coherence Tomography

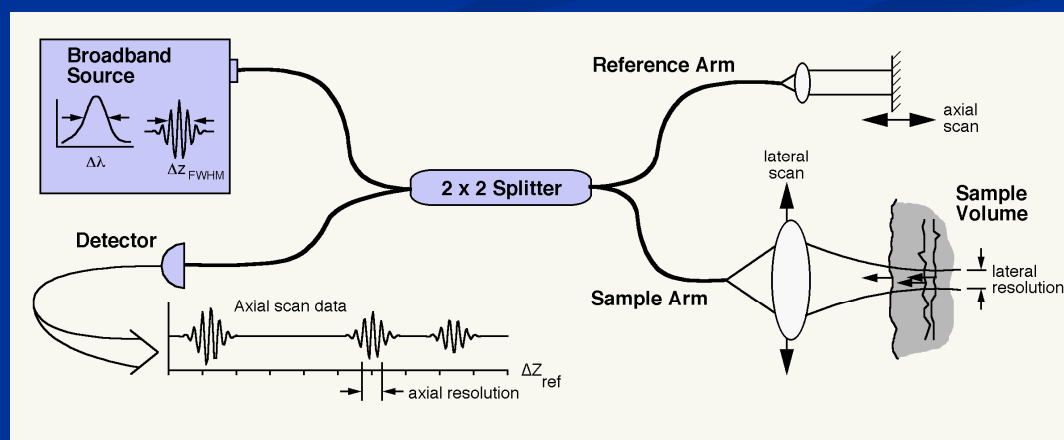


OCT is analogous to ultrasound imaging
Uses infrared light in stead of sound

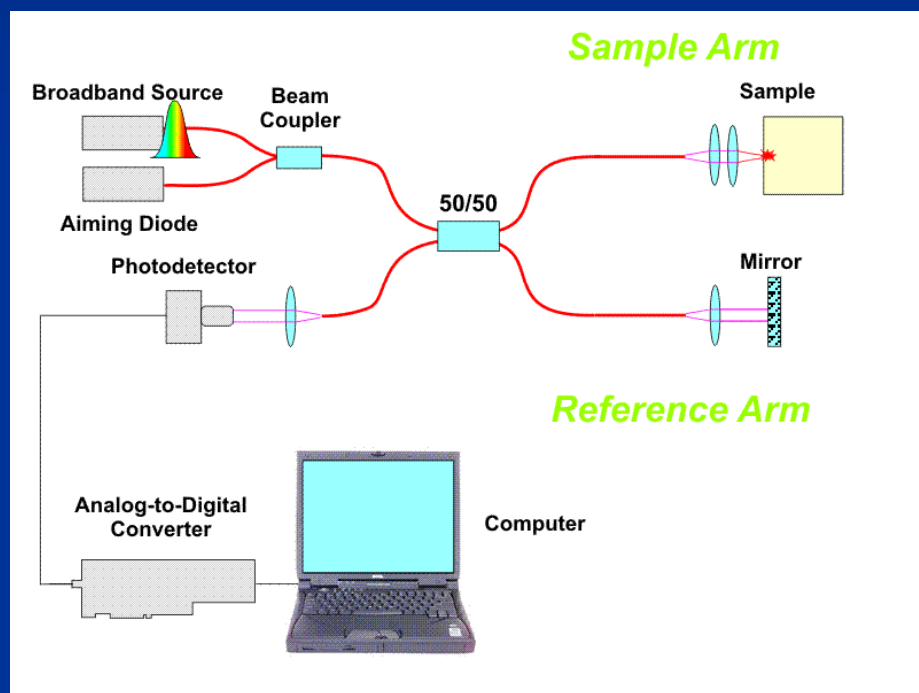
Speed of sound ~ 1480 m/sec (in water)
Speed of light $- 3 \times 10^8$ m/sec

Human skin
5 mm wide x 1.6 mm deep
Resolution: 10-30 μ m

Interferometry
is used to measure
small time delays
of scattered photons

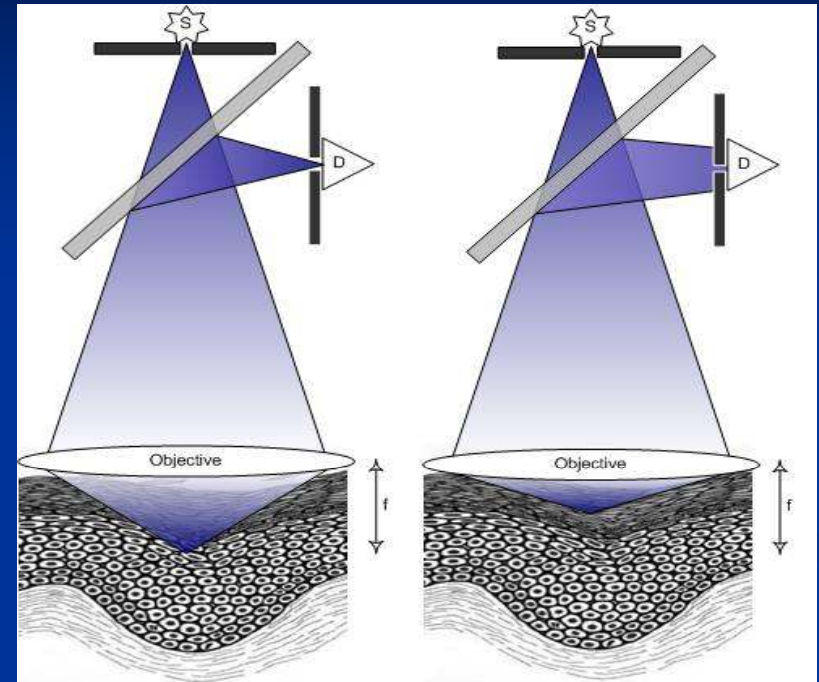
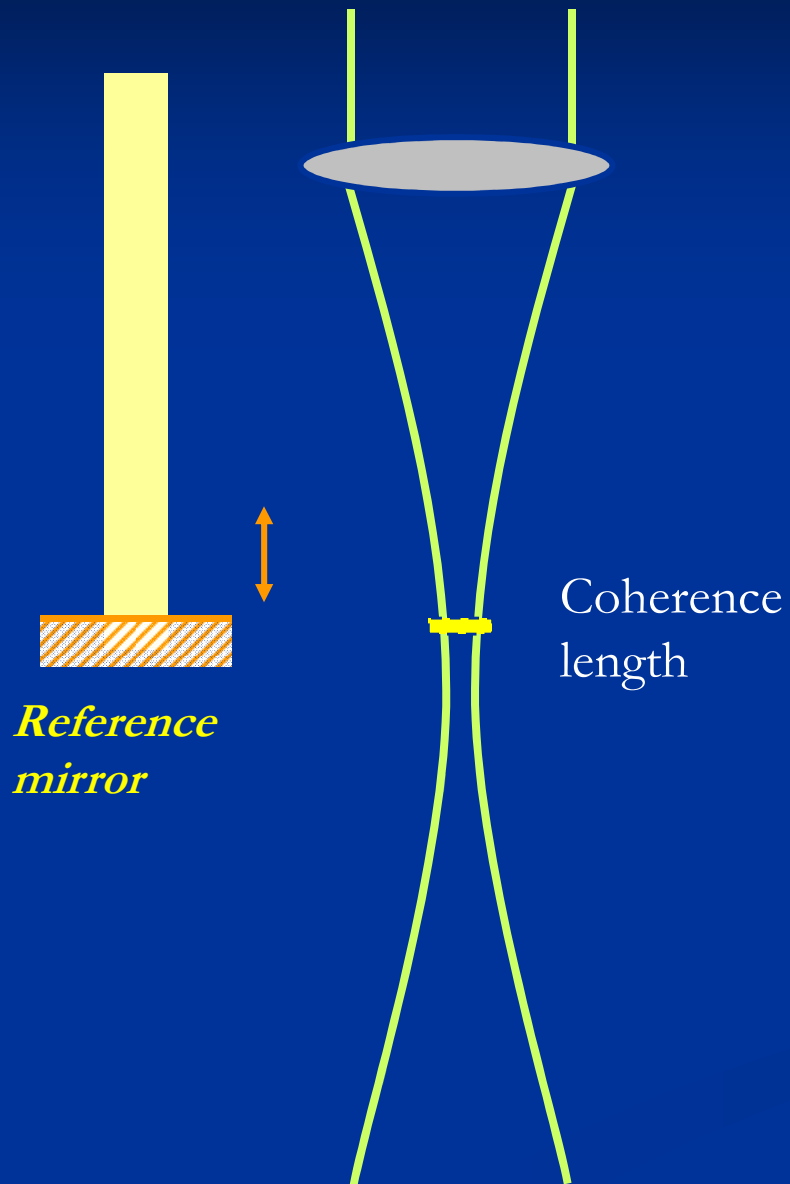


Optical coherence tomography

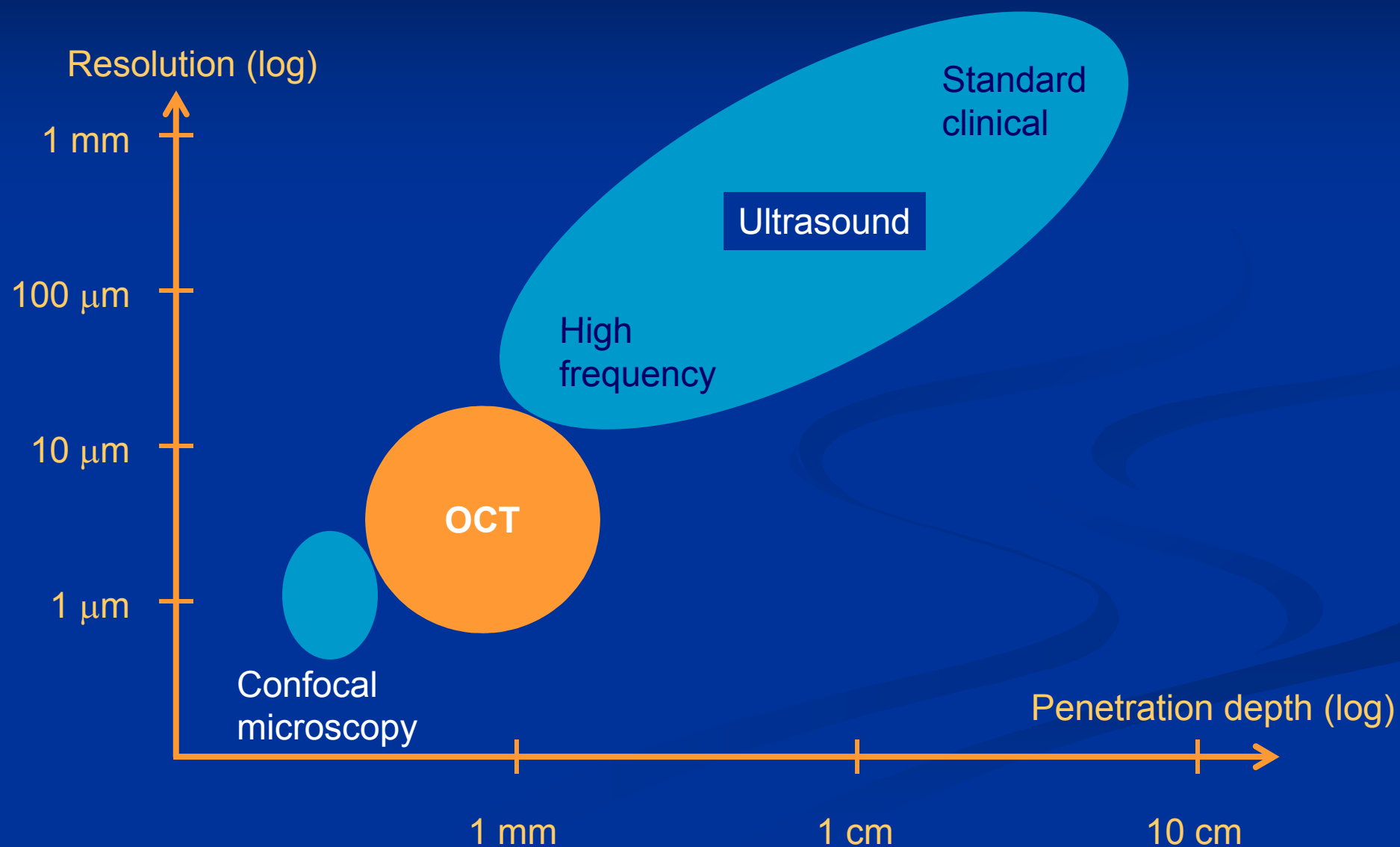


- three-dimensional imaging technique with ultrahigh spatial resolution even in highly scattering media,
- based on measurements of the reflected light from tissue discontinuities;
 - e.g. the epidermis-dermis junction,
- based on interferometry;
 - involves interference between the reflected light and the reference beam.

OCT vs. CM



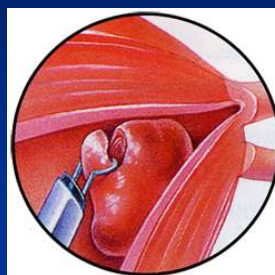
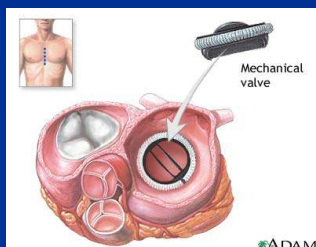
OCT vs. Standard Imaging



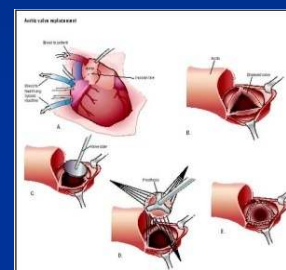
Bubbles Detection In a blood stream

Risks of bubbles

Cardiac valve replacement

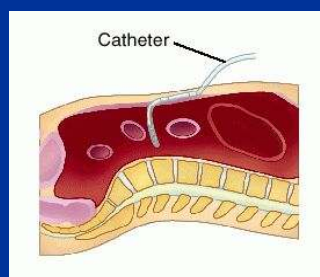


Operative hysteroscopy

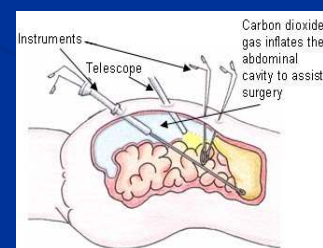


Cardio pulmonary bypass

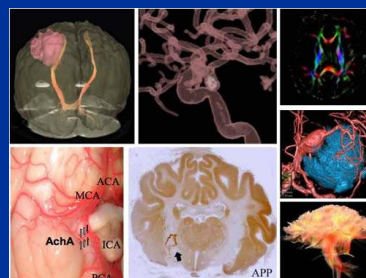
Risks of micro bubble generation



Central venous line insertion

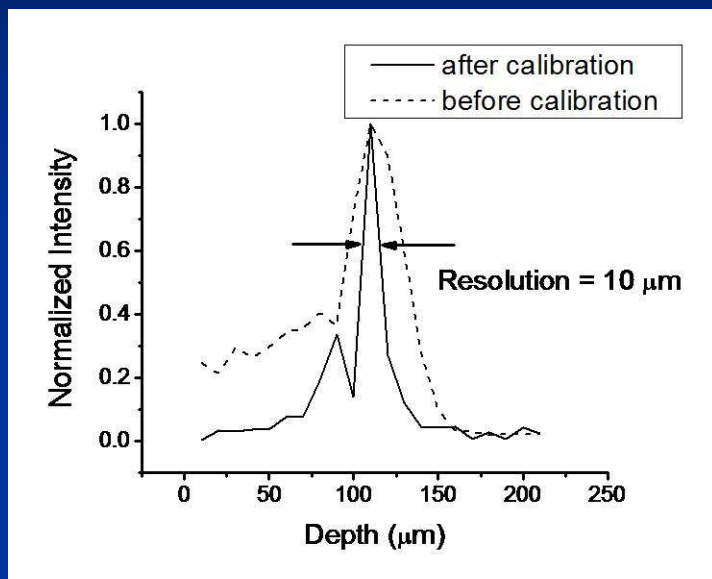


Laser ablation and laparoscopic surgery



Neurosurgery

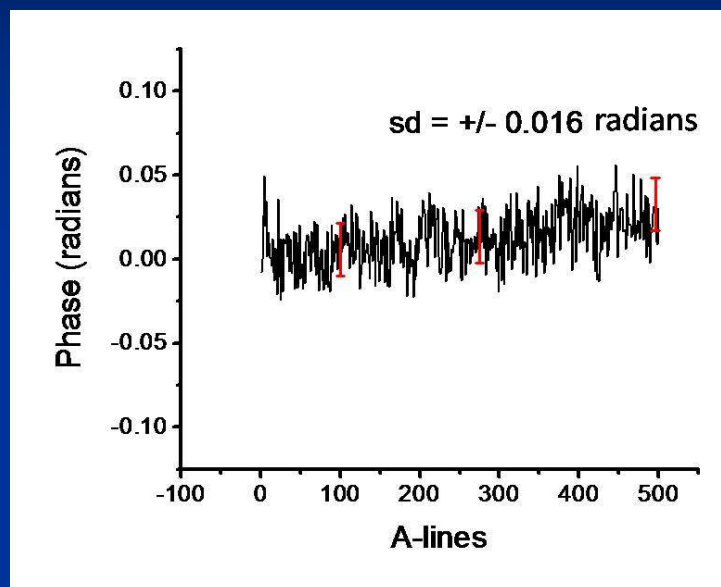
System characteristics



Depth resolution = 6 μm

Transverse resolution = 15 μm

Maximum imaging depth = 6 mm



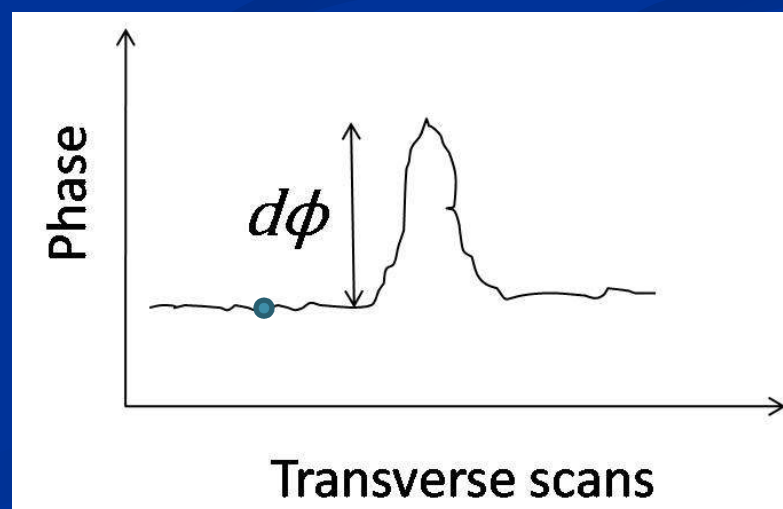
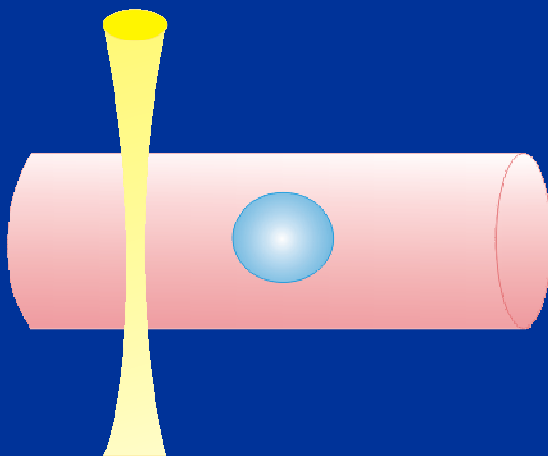
Imaging speed = 30 kHz

Phase stability = 0.01 radians

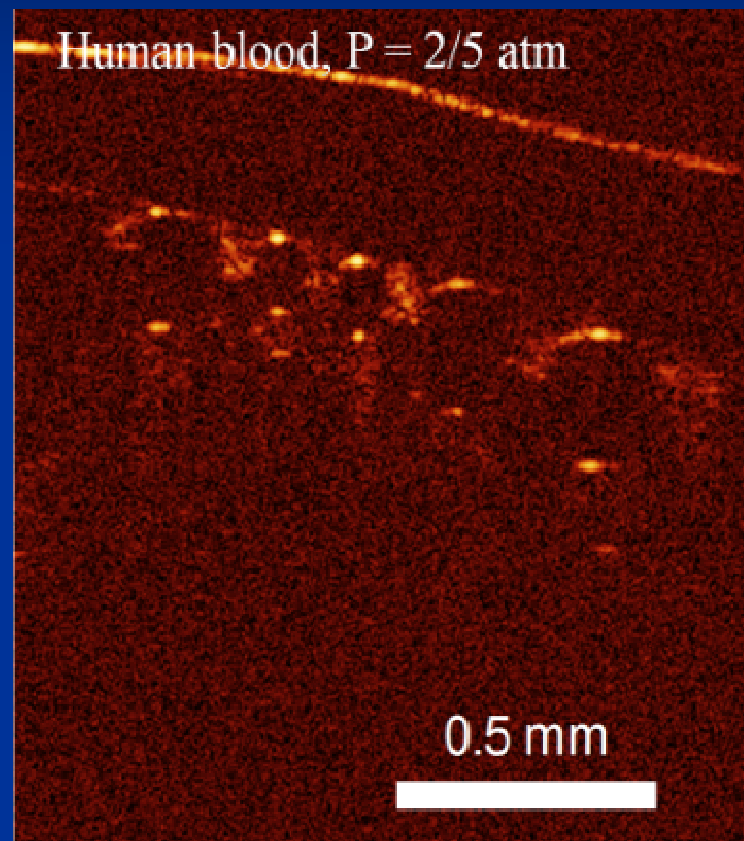
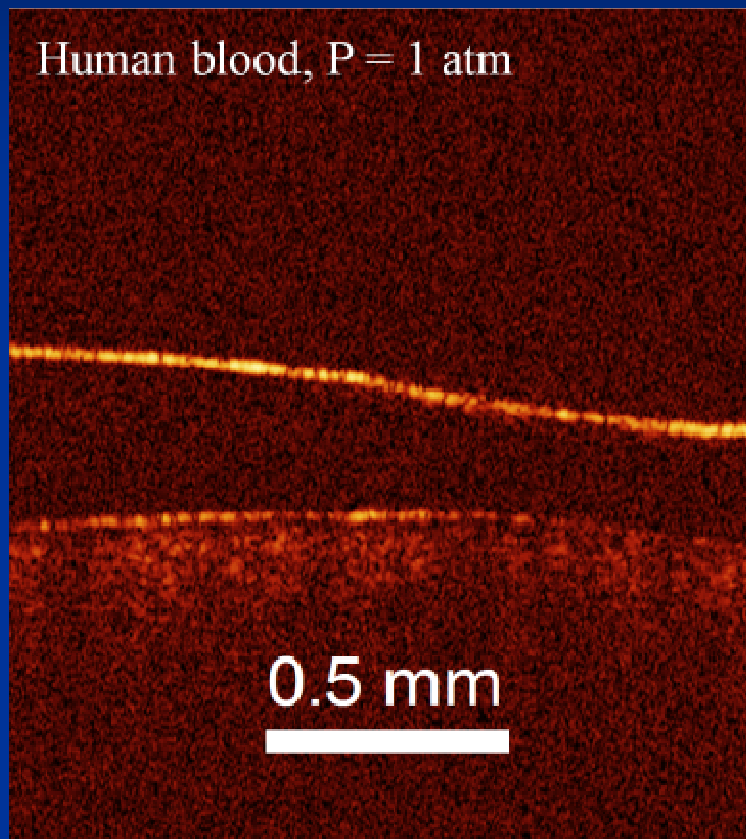
Microbubble Detection

Principle: The bubbles induce changes in refractive index that is reflected in temporal Phase response.

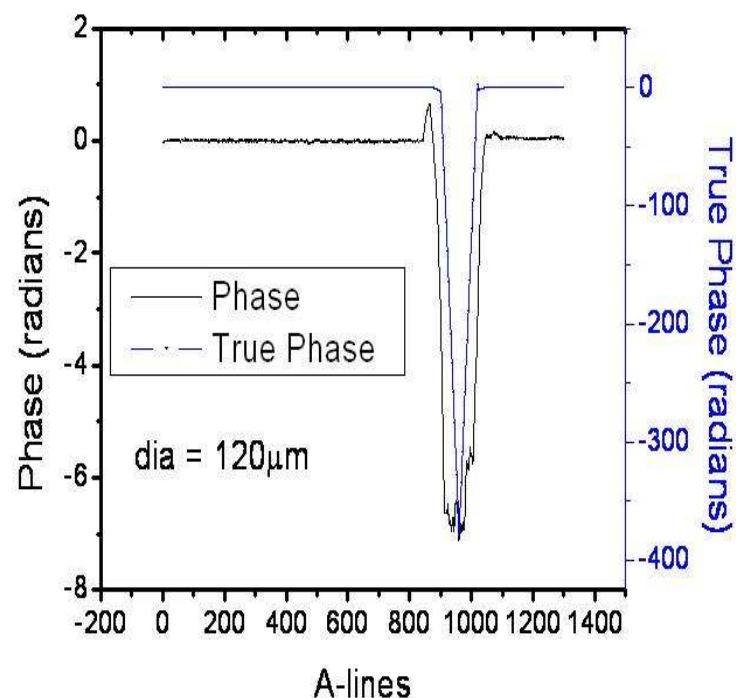
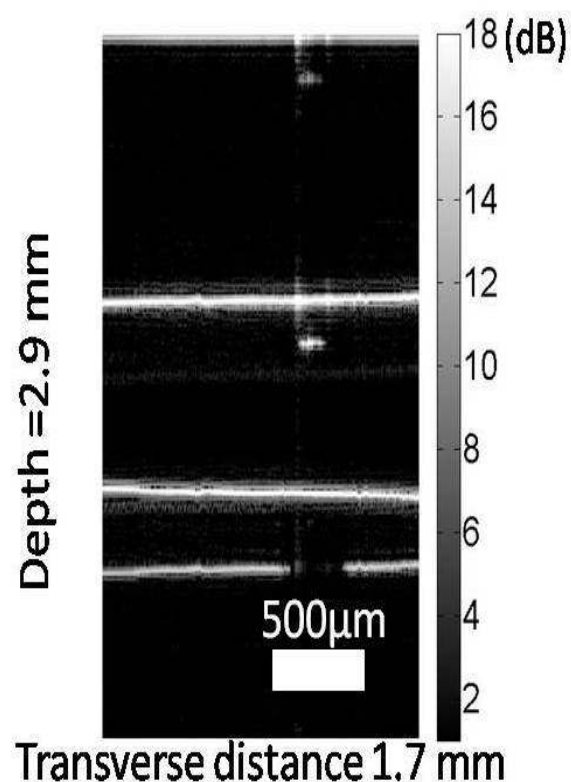
$$d = \frac{1}{(n_{tissue} - n_{bubble})} \frac{\lambda}{4\pi} \delta\phi$$



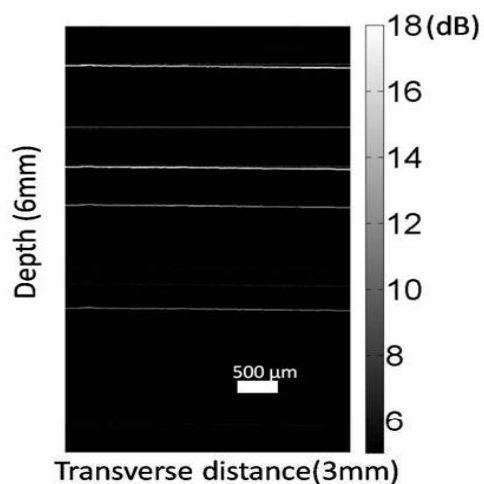
Detection of Large Microbubbles



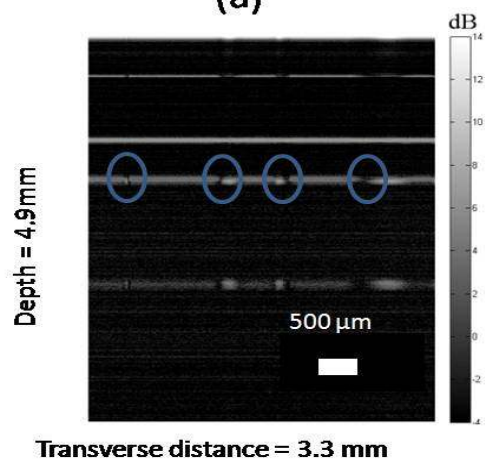
Detection of Large Microbubbles in transparent media



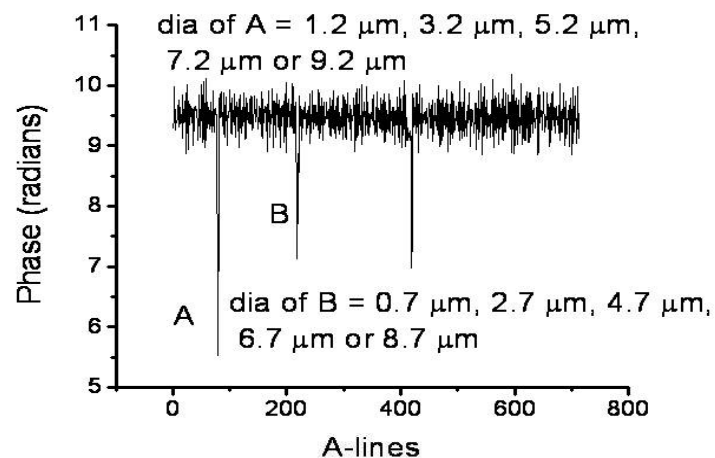
Detection of Small Microbubbles



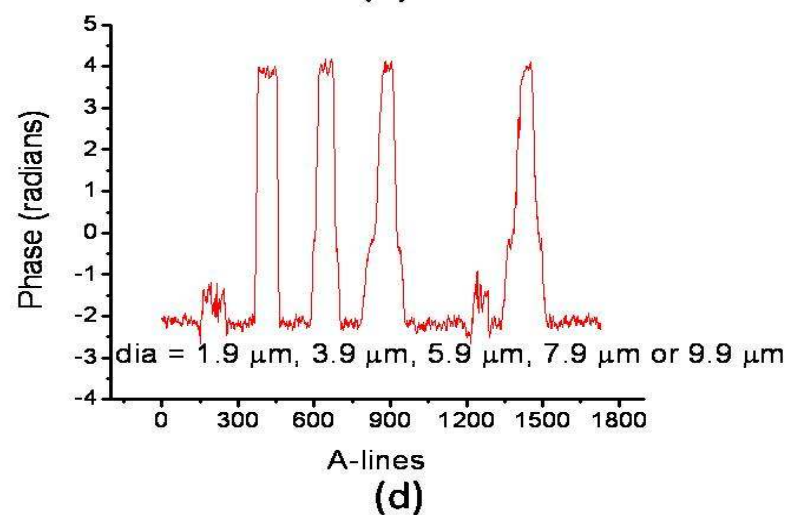
(a)



(c)

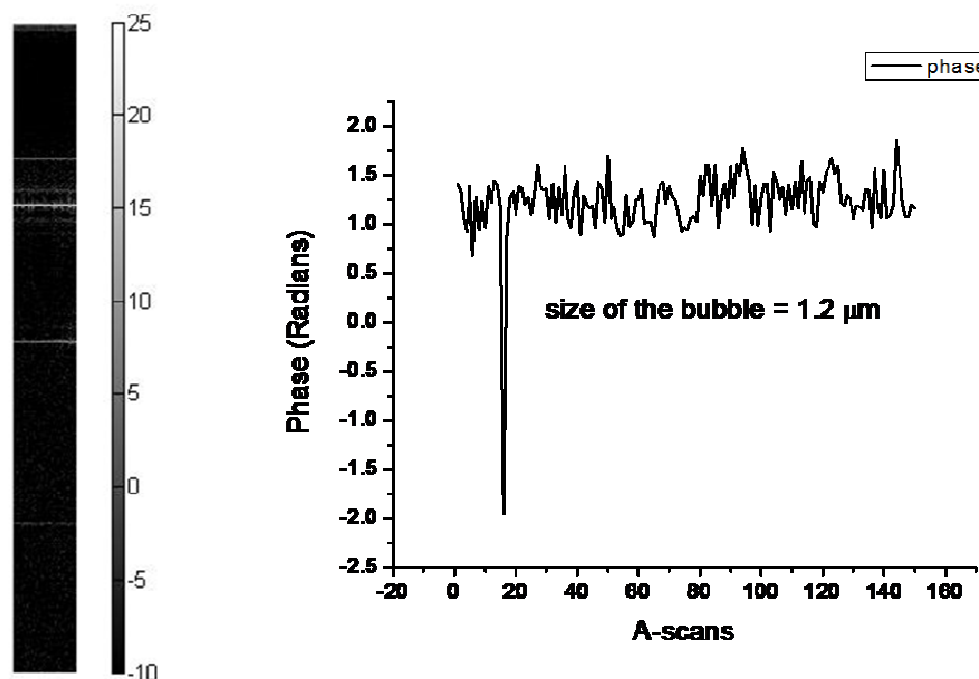


(b)



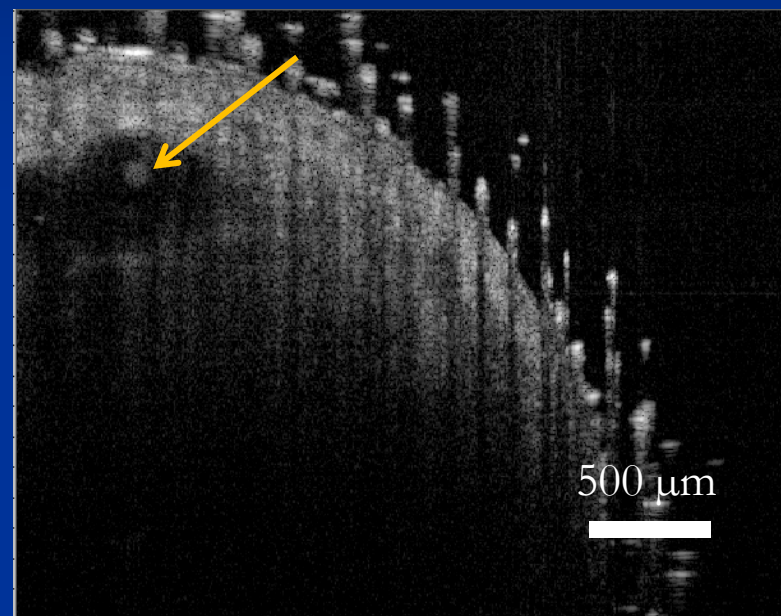
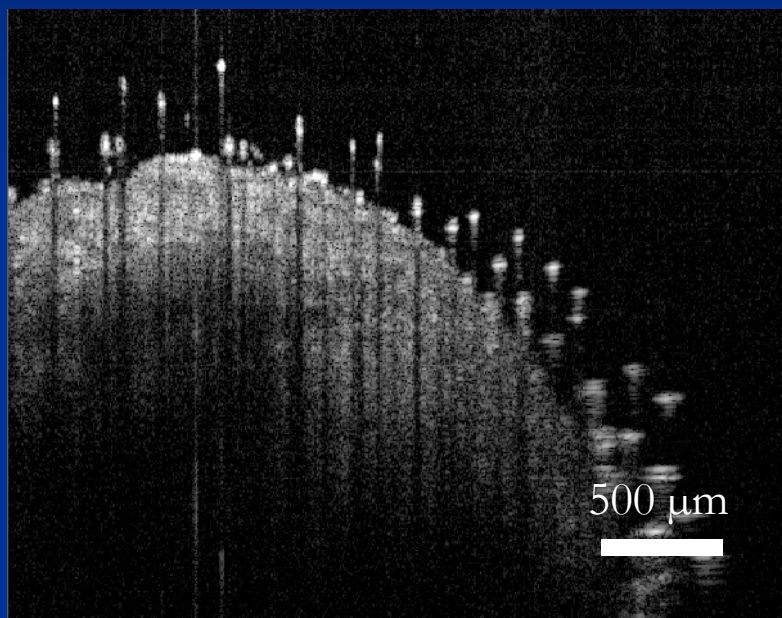
(d)

Detection of Small Microbubbles in blood



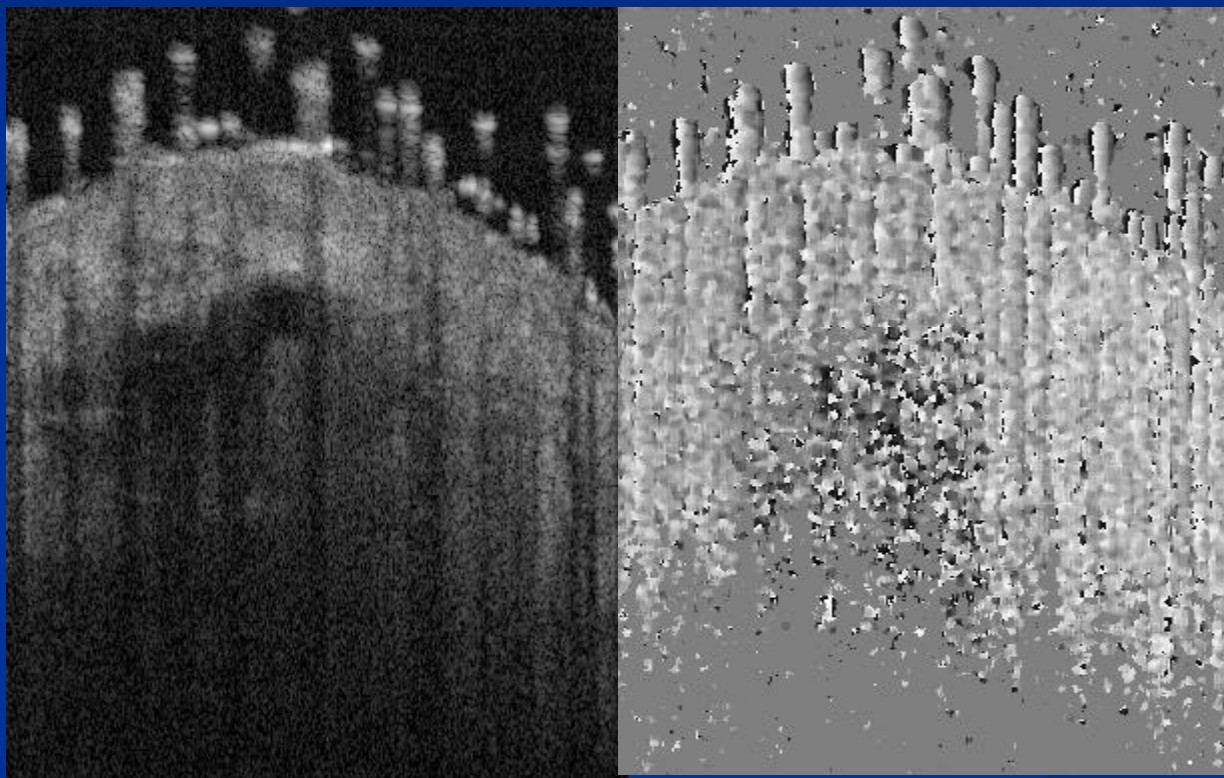
Manapuram, et al: *Journal of Applied Physics*, 2009

Detection of Definity bubbles in mouse tail *in vivo*



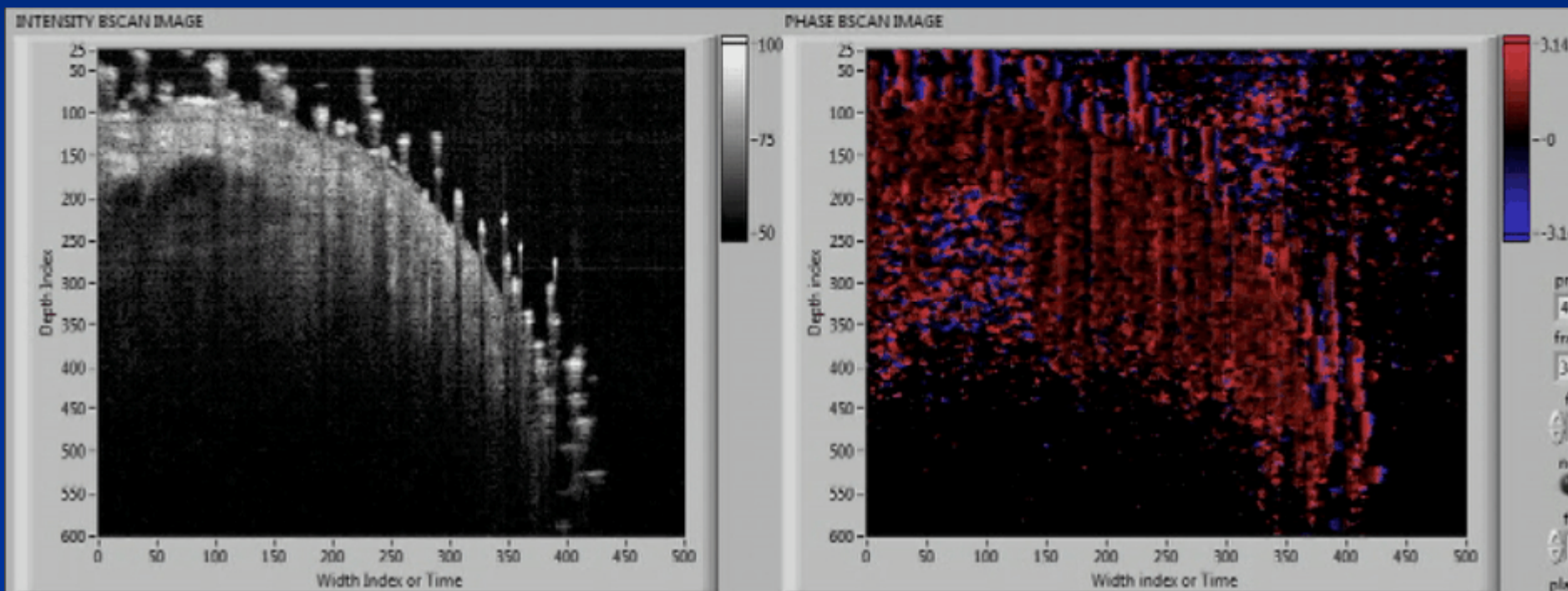
Before and After injection of Definity

Moving Definity bubbles in mouse tail *in vivo*



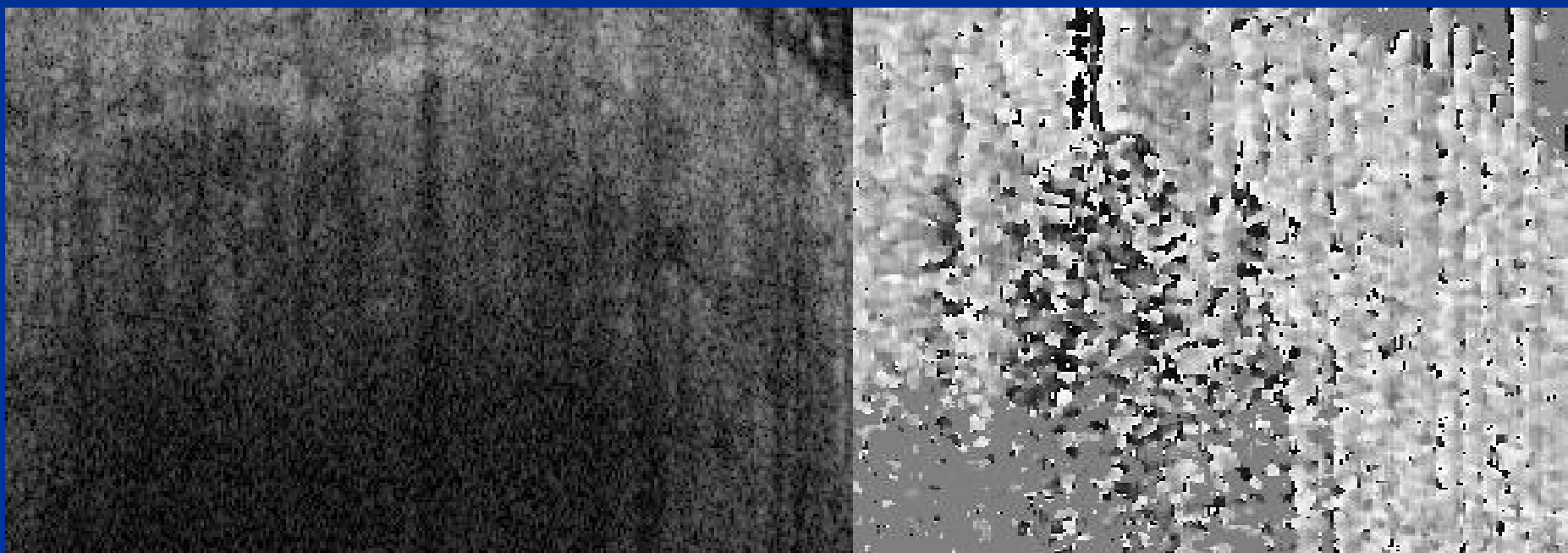
Manapuram, et al: *unpublished*

Moving Definity bubbles in mouse tail *in vivo*



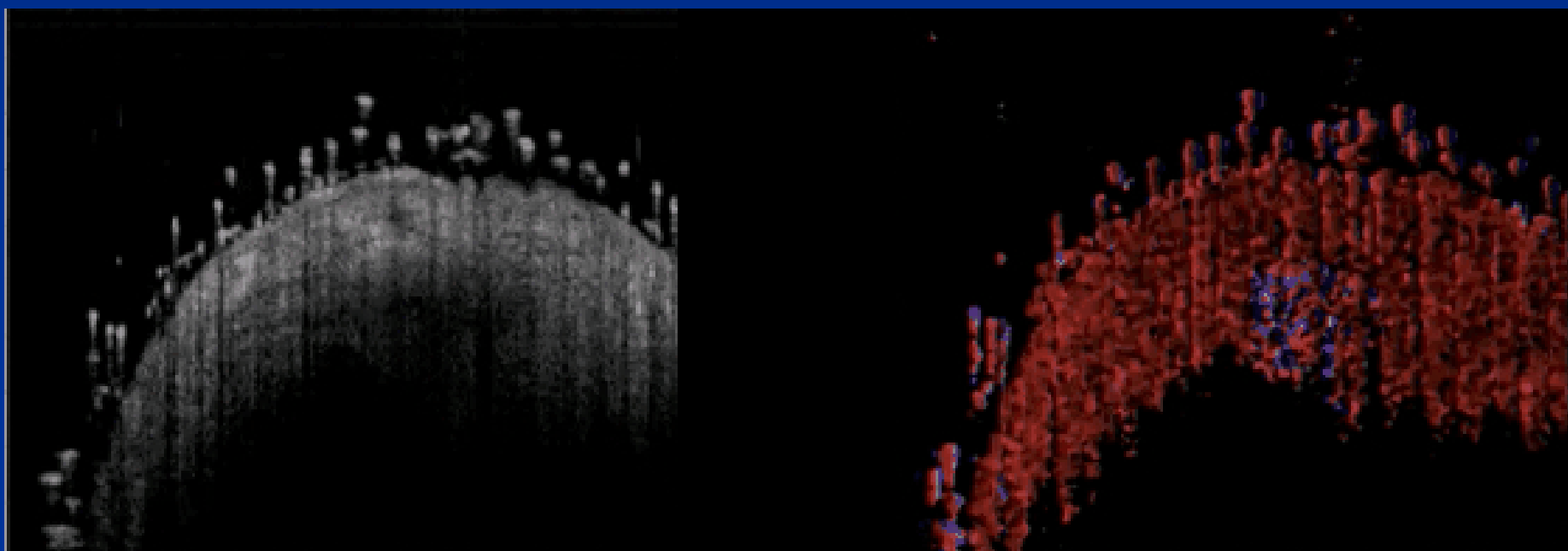
Manapuram, et al: *unpublished*

Moving air bubbles in mouse tail *in vivo*



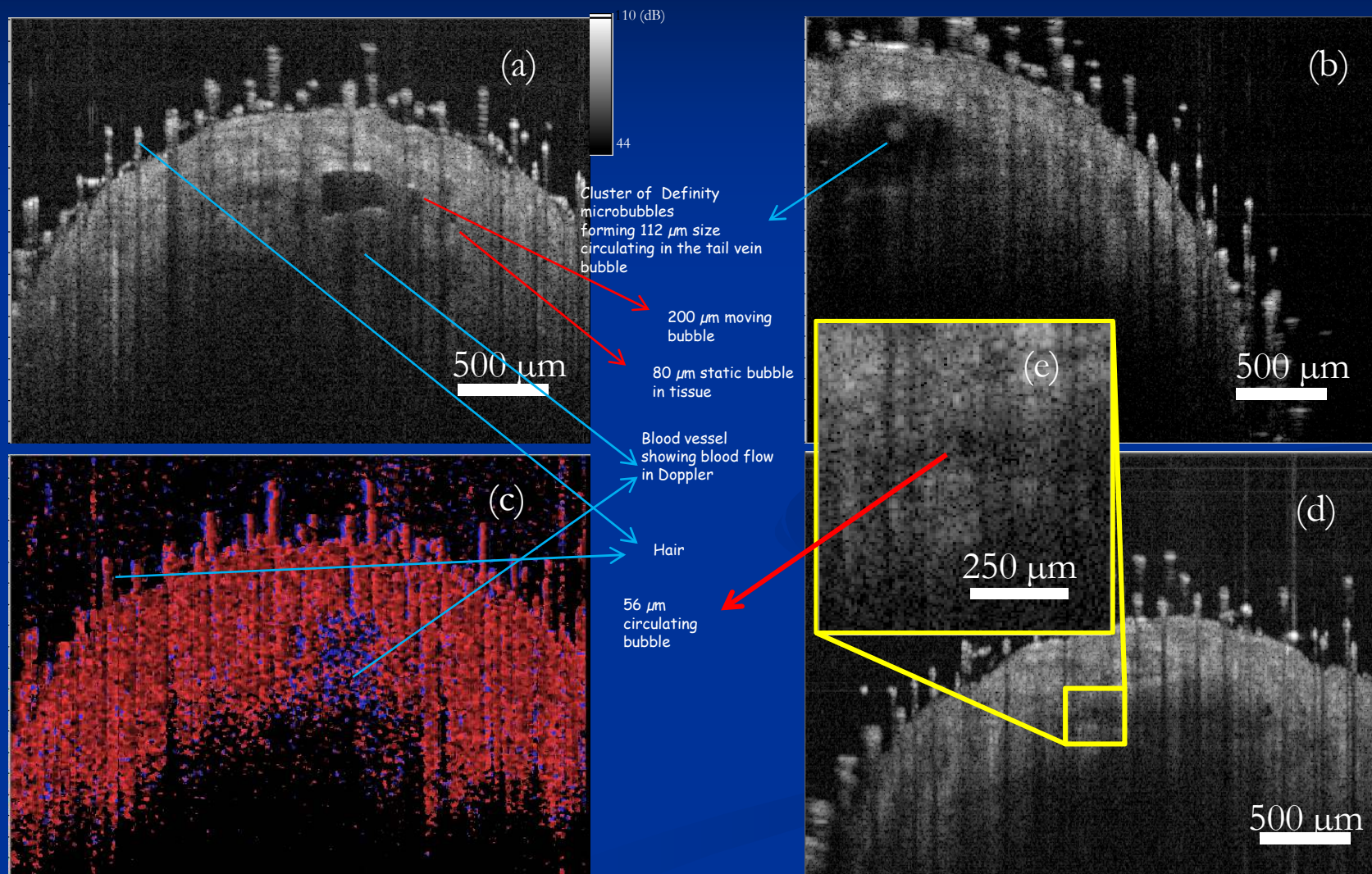
Manapuram, et al: *unpublished*

Moving air bubbles in mouse tail *in vivo*



Manapuram, et al: *unpublished*

Detection of air bubbles in mouse tail *in vivo*



CONCLUSIONS

- Microbubbles of diameters $> 10 \mu\text{m}$ could be detected *in vitro* by both structural imaging and phase response and diameters $< 10 \mu\text{m}$ in the phase response.
- By noninvasively detecting the microbubbles when they are very small, early diagnosis of diseases associated with Decompression sickness, barotrauma etc., could be possible.