3-D OptoAcoustic Tomography for preclinical research in small animals

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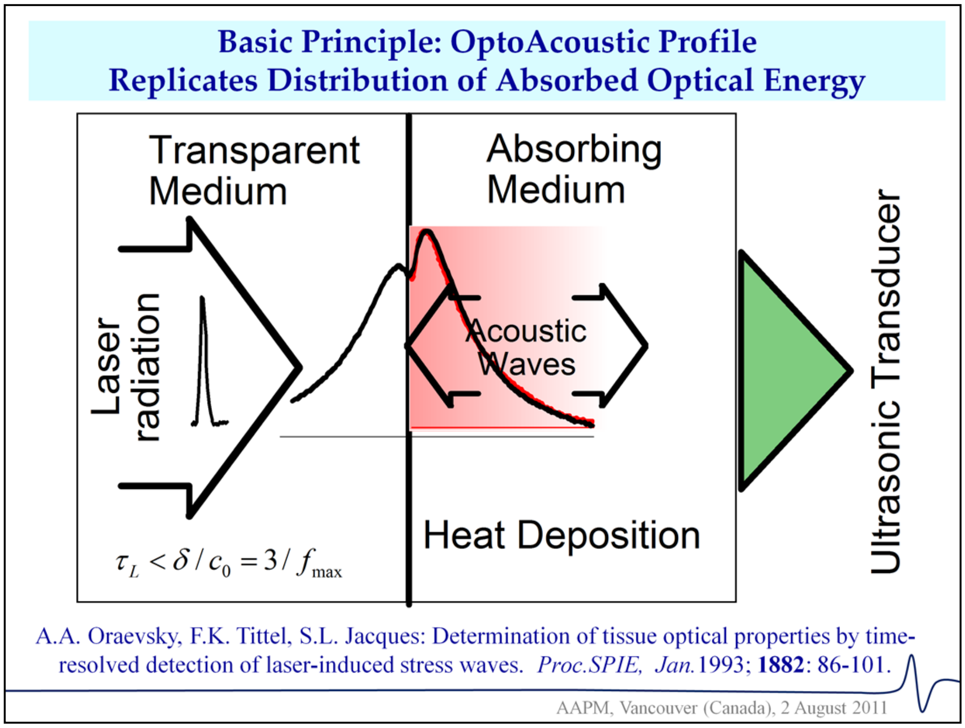
AAPM, Vancouver (Canada), 2 August 2011



Fundamental Principle of Optoacoustic Imaging I:
Pressure Profile Replicates Distribution of Absorbed Optical Energy
under conditions of temporal pressure confinement upon optical energy deposition

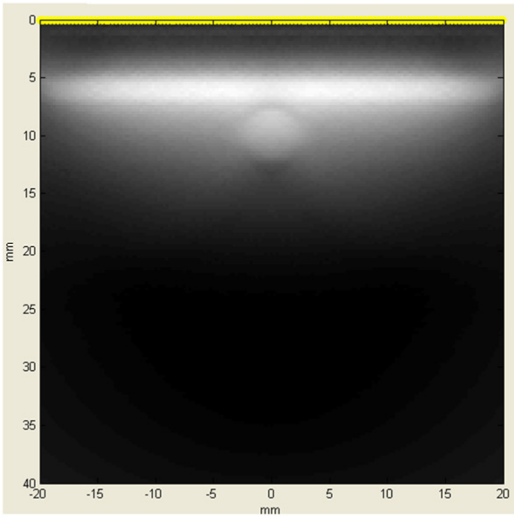
Consequence #1: optical pulse duration must be much shorter than the time it take for acoustic pressure (ultrasound) to escape the voxel to be resolved, t_L<<d/c_s

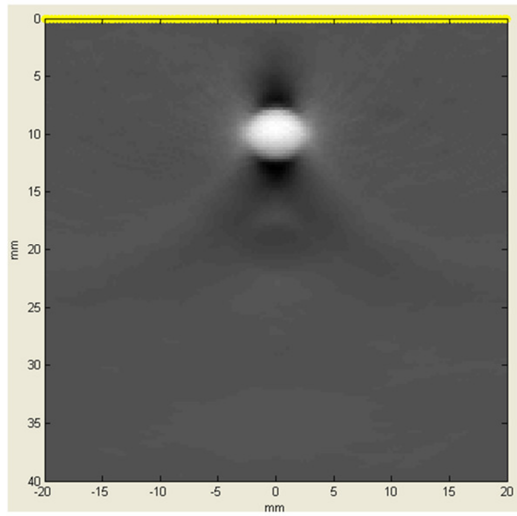
and

Consequence #2: maximum efficiency of optoacoustic pressure can be achieved und illumination conditions of temporal pressure confinement

Fundamental Principle of Optoacoustic Imaging II –
detection system, including ultrasonic transducer must be sensitive
within a ultrawide band of ultrasonic frequencies in order to detect
the OA signals without distortion and enable quantitative information.

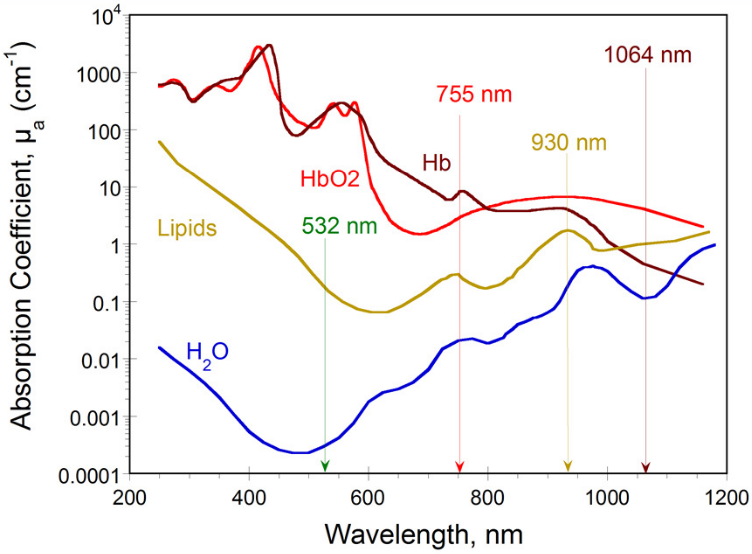
Processing of OptoAcoustic Images Using Principal Component Analysis (PCA)





Principal Component Analysis (PCA) can be used to remove contribution of absorbed optical energy in the tissue surrounding the object of interest.

Optimization of Laser Wavelength optical absorption contrast vs penetration depth in tissue



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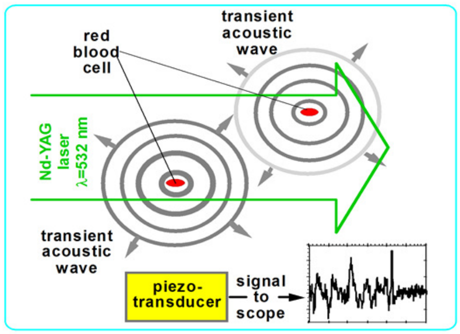
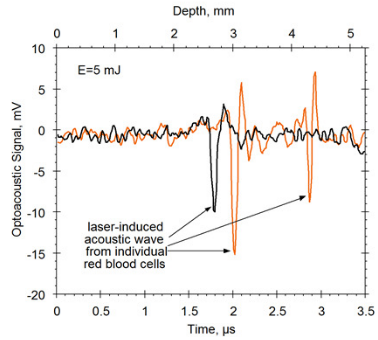
Hemoglobin and Oxyhemoglobin of blood are the two main chromophores (absorbing molecules) of biological tissues in the near-infrared spectral range. Water and lipids (fats) provide background absorption. The thin melanin layer slightly filters NIR light incident on skin.

Optoacoustic Detection of Erythrocytes

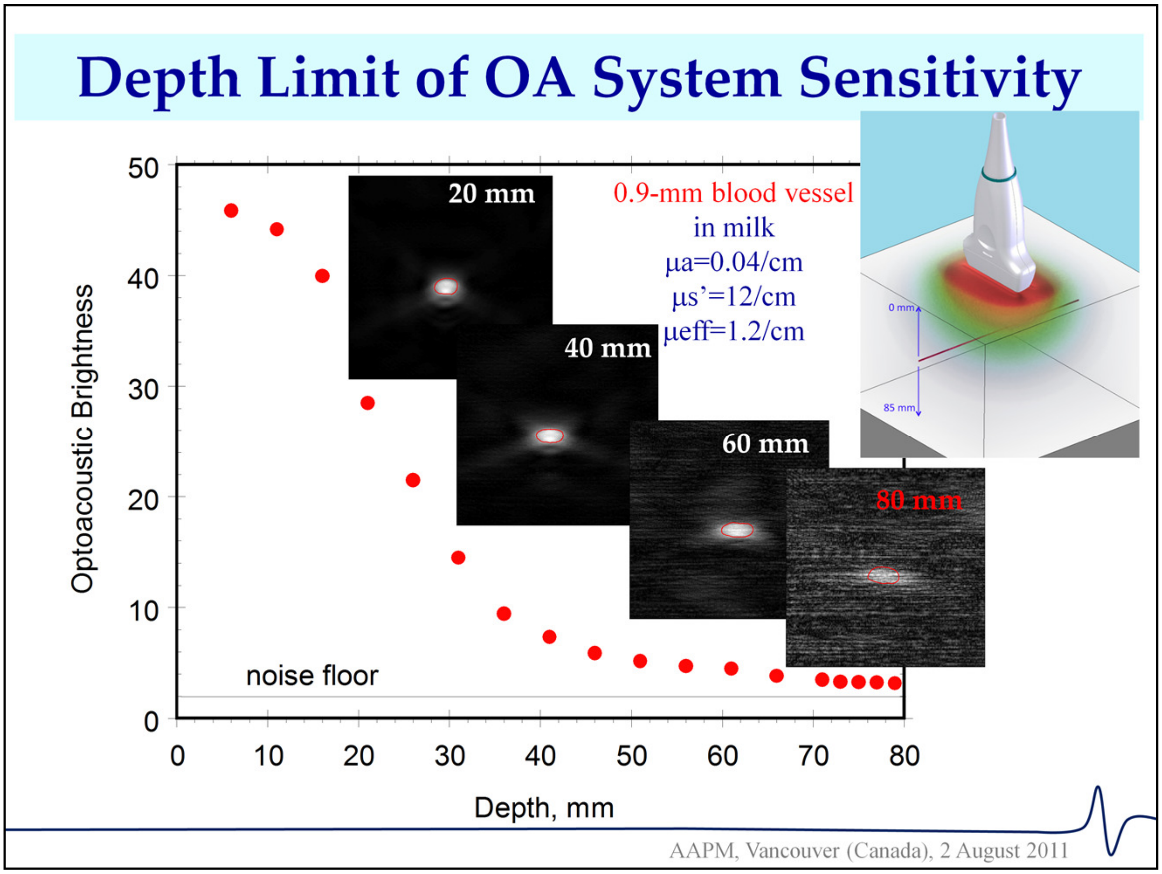




Demonstration of a single blood cell detection in tissue like phantom

A.A. Oraevsky, E.V. Savateeva, Karabutov, V.G. Andreev et al: "Optoacoustic imaging of blood for visualization and diagnostics of breast cancer", *Proc. SPIE* 2002; **4619**: 81-94.

Optoacoustic sensitivity is very high allowing detection of single red blood cells in a tissue like medium (milk).



Due to high detection sensitivity the imaging depth for blood vessels in biological tissue-like medium exceeds 70 mm.

Fundamental OptoAcoustic Equation

Observed Pressure

Spatial Distribution of Heat

Dirac's Function

Time

$$p'(\vec{r},t)=\frac{\Gamma}{4\pi c_0^2}\int_{V'}\frac{\frac{\partial}{\partial t}[Q(\vec{r}')\delta(t-\left|\vec{r}-\vec{r}'\right|/c_0)}{\left|\vec{r}-\vec{r}'\right|}d\vec{r}';\ \left|\vec{r}-\vec{r}'\right|=c_0t$$

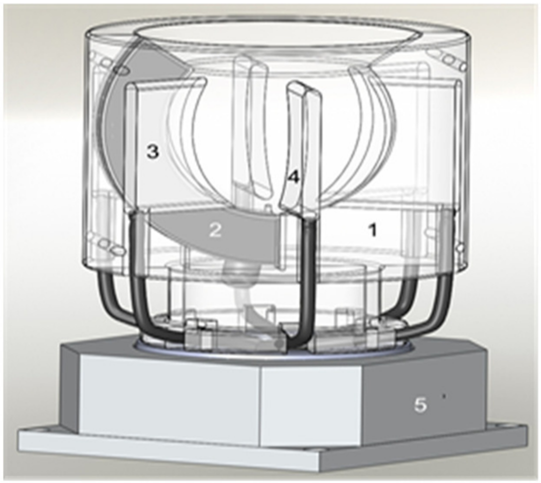
Transducer Position

Speed of Sound

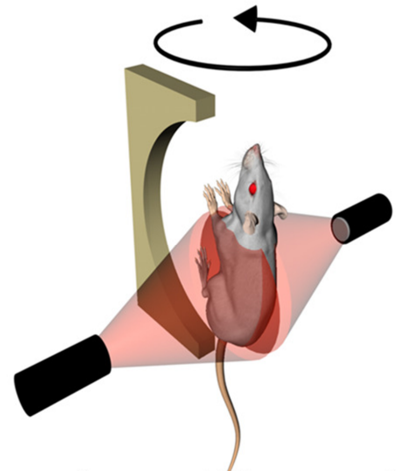
Position of Absorbing Point

This equation has rigorous solution only with complete data set, such as in the case when the object of imaging is completely surrounded by optoacoustic detectors (transducers).

OAT of the Whole Animal Body



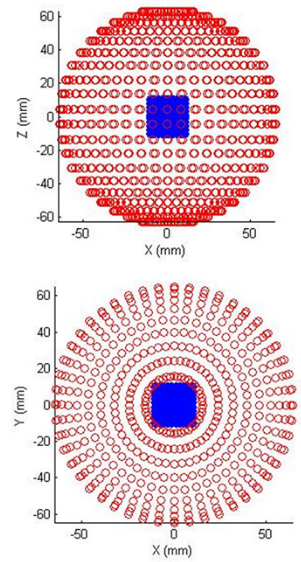
1. Imaging module chamber
2. Transducer array
3. Front Fiberoptic illuminator
4. Ortho Fiberoptic illuminator
5. Rotation step motor stage

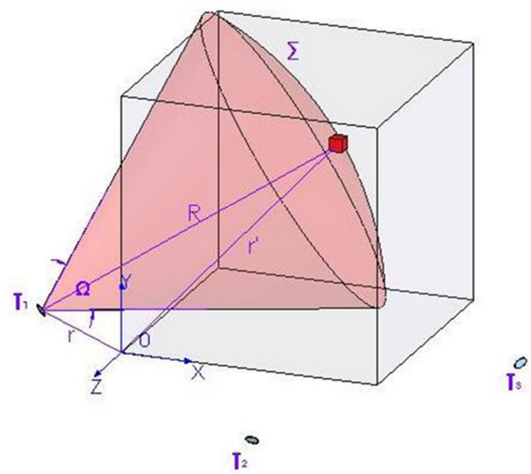


64 transducers x150 steps = 9600
Imaging Time: 20 sec to 4 min
Image Reconstruction: 20 sec (1sec)

H.-P. Brecht, R. Su, M. Fronheiser, S. A. Ermilov, A. Conjusteau, A. A. Oraevsky: "Whole body three-dimensional optoacoustic tomography system for small animals", *Journal Biomedical Optics*, 2009; **14**(6), 0129061.

3D Spherical Reconstruction





Weighing for higher density of transducers at poles $\overline{S}_i = \frac{2\ \pi\ \ r\cos\beta}{N_{Tr}} S_i$

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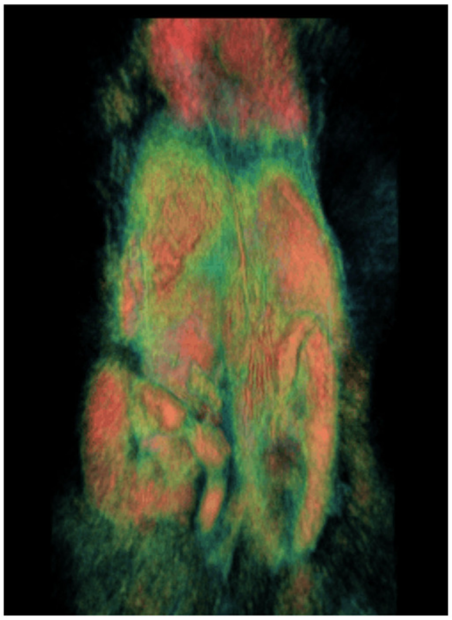
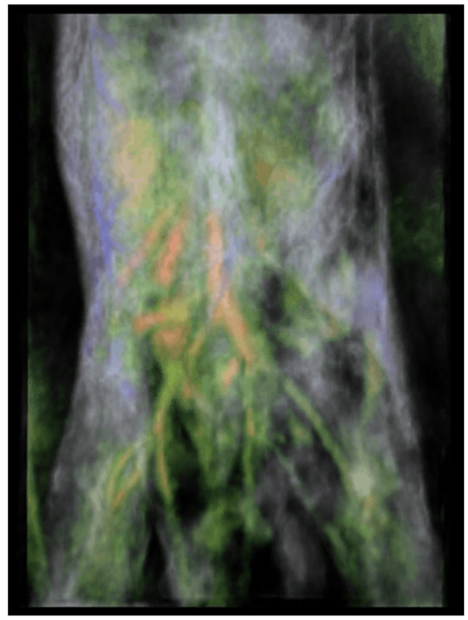
Image reconstruction is made through back-projection of each measured sample of filtered optoacoustic signals onto a spherical surface with radius equal to the product of time of the sample detection and the speed of sound.

The reconstructed image is then normalized to the density of detectors on the sphere comprised of virtual transducers produced by rotating arc-shaped array.

Whole body 3D OptoAcoustic Tomography



Organs and Vessels



Mouse Skin and Internal Tissues

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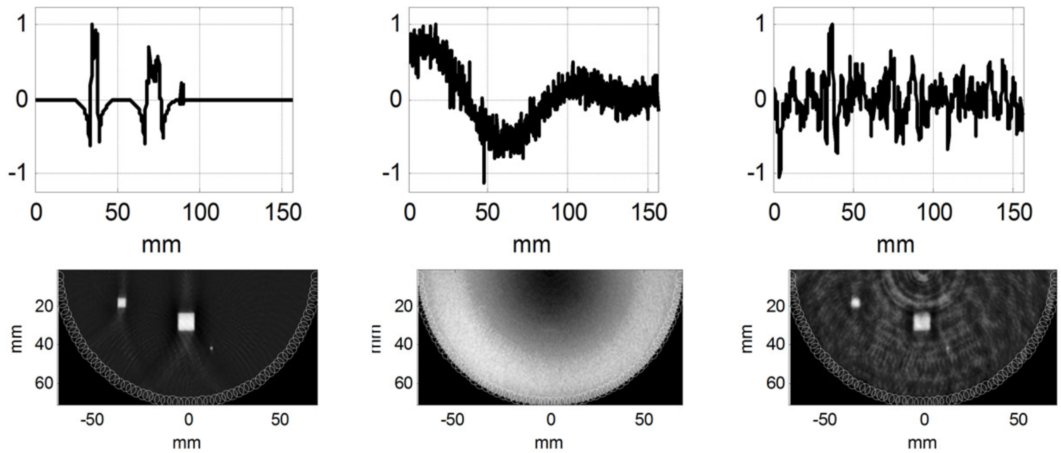
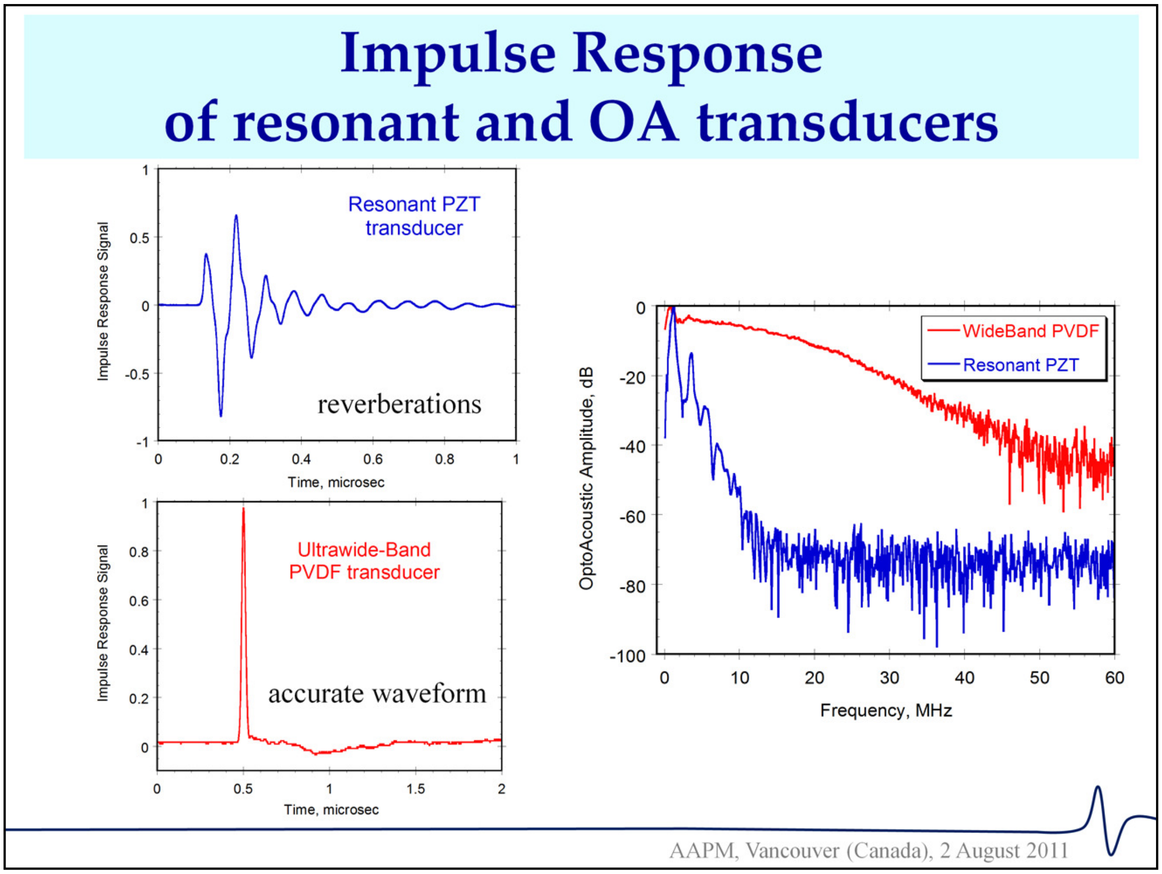
Initially reconstructed image is rich of information,
but hard to interpret due to opacity of the 3D volume.

Wavelet transform filter for OA Signal Recovery from SNR<<1



A.A. Oraevsky, S.A. Ermilov, A. Conjusteau et al: Laser optoacoustic tomography of layered tissues: signal processing, *Proc. SPIE* **1997**; 2979: 59-70.

Filtering with multiscale wavelet filters permits significant increase of the signal-to-noise ratio and also conversion (through integration) of the bipolar pressure signals into molopolar energy signals.



Deconvolution of the system's impulse response helps to restore original signals and improve accuracy of quantitative information.

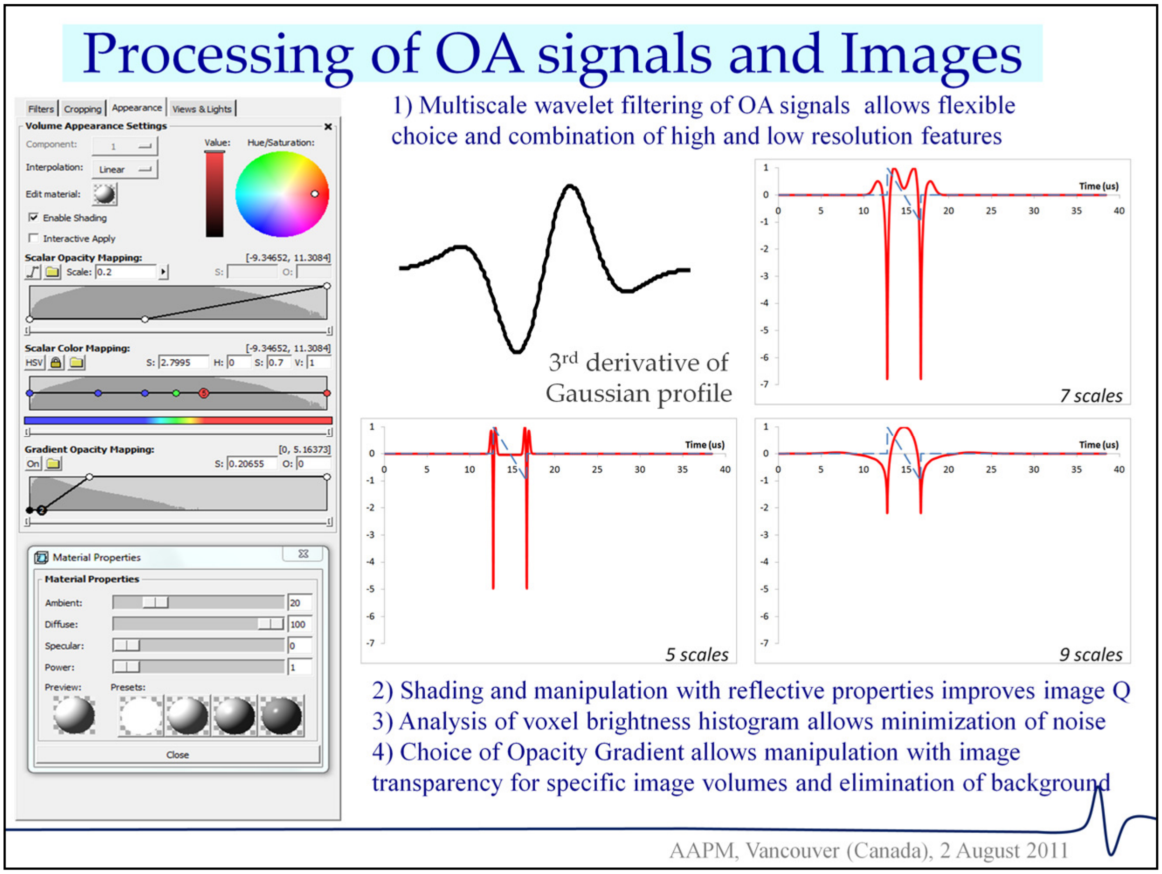
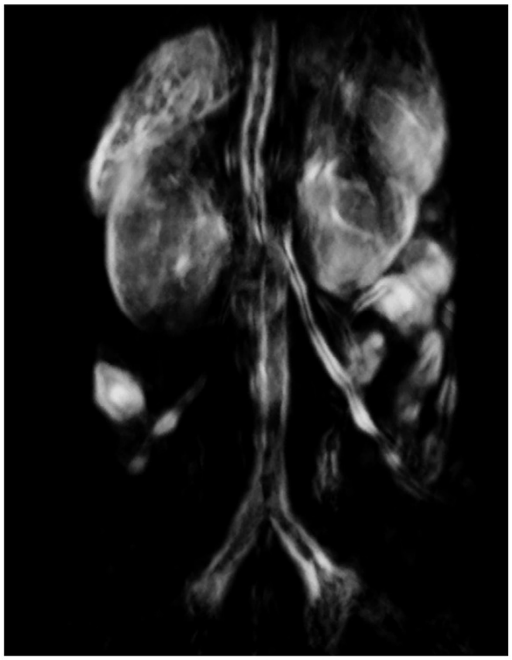
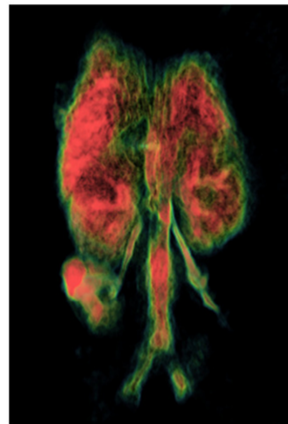


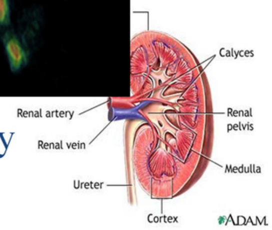
Image post-processing allows one to visualize objects of interest within the animal body (such as organs or blood vessels).

Details of Internal Organs and Vasculature



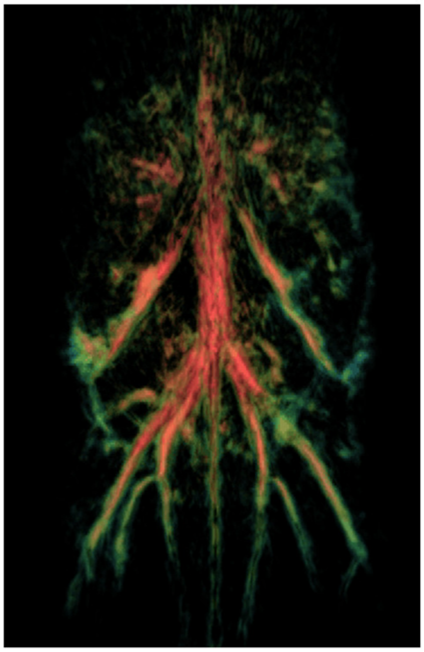


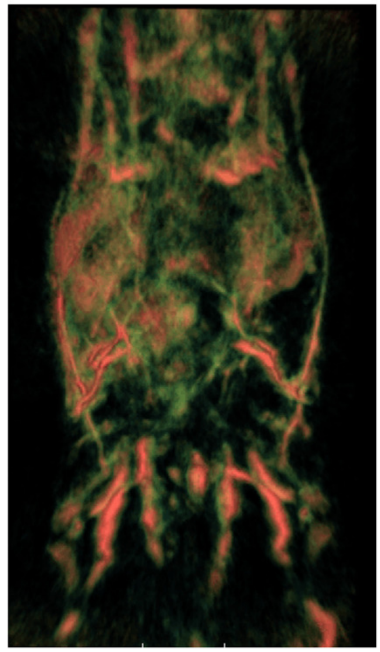
Kidney



Images of internal organs can be obtained by filtering high ultrasonic frequencies out and keeping lower frequencies.

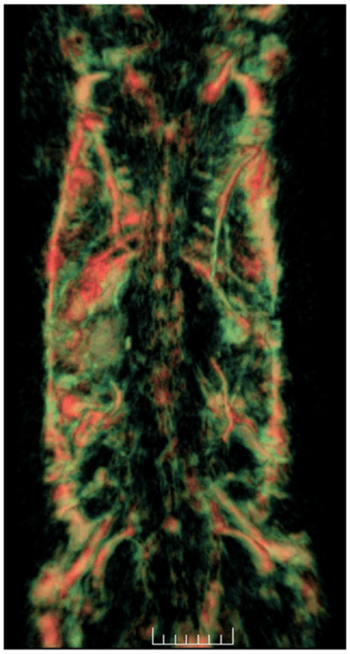
Mouse Circulation (Vascular System)

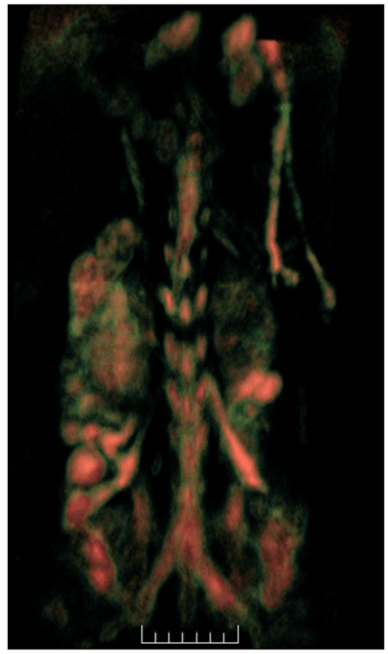




Optoacoustic tomography is ideally suitable for imaging vasculature.
It is the only imaging technology that can provide quantitative
Information regarding concentrations of Hemoglobin and Oxyhemoglobin
With high resolution through the entire animal body.

OptoAcoustic Tomography of Hard Tissues





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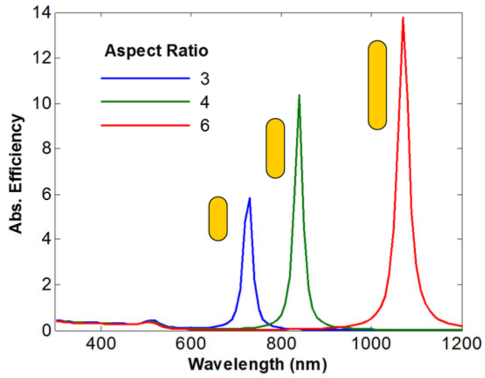
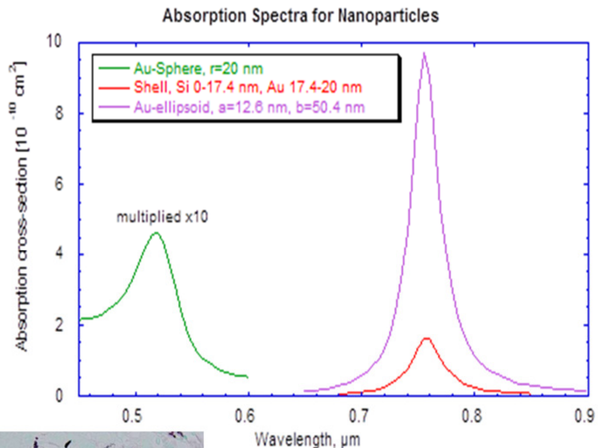
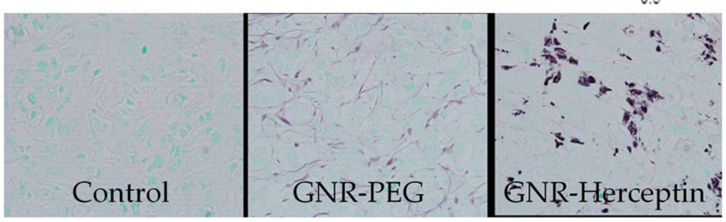
Even bones, spine, ribs and joints can be visualized on
optoacoustic images based on signals detected from microvasculature.

Gold NanoRods (GNR) OptoAcoustic Contrast Agent

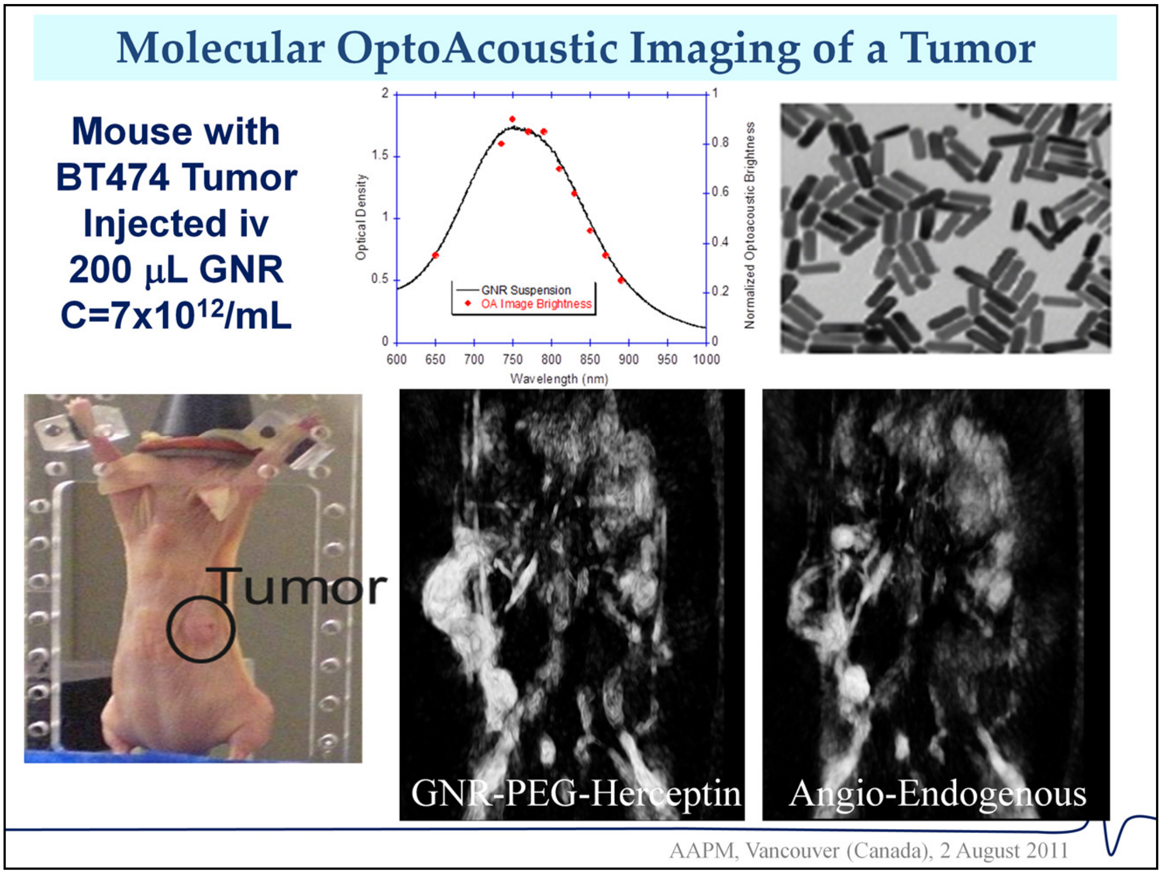






Targeting GNR to cancer cells

Exogenous contrast agents, such as gold nanorods strongly absorbing in the near-infrared spectral range, can be used to target and visualize location of specific molecular receptors in the body.



Mouse was injected with gold nanorods conjugated with antibodies specific to molecular receptors HER2 in the cancer cells

Horizons: Applications of 3D OAT

- **From today's preclinical research:**
- **Quantitative Functional Imaging**
  - Measurement of [Hb] and [HbO] (hematocrit) in tissues and blood vessels, assessment of heart function and blood flow.
  - Assessment of tumor angiogenesis, Angiography, Detection and characterization of stroke and traumatic injury of the brain
- **Quantitative Molecular Imaging**
  - Measurement of distributions of protein-receptors in cells
  - Visualization of gene expression and enzymatic activity

- **To Tomorrow's clinical applications:**
  - Diagnostic imaging of cancer
  - Diagnostics of vascular diseases
  - Kinetics of drug distribution and physiological processes in the body

Arrays of OptoAcoustic Transducers:
- Andre Conjusteau, PhD

Analog and Digital Electronics
- Ketan Mehta, MEE

FiberOptics and Microscopy
- Dmitri Tsybouski, PhD

Firmware and Software

Ketan Mehta, Bryan Clingman

Modeling, Math-Physics, Tomography
- Sergey Ermilov, PhD,
- Slava Nadvoretsky, PhD,
- Mark Anastasio, PhD

Cancer Biology, Animal Studies
- Richard Su, PhD candidate,
- Anton Liopo, PhD

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