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Saratov Fall Meeting 2006

Optical Technologies in Biophysics and Medicine VIII

Valery V. Tuchin
Editor

26–29 September 2006
Saratov, Russia

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The CID number appears on each page of the manuscript. The complete citation is used on the first page, and an abbreviated version on subsequent pages.

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MANAGEMENT IN BIOPHOTONICS RESEARCH AND EDUCATION

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Oral Session V: Seminar on Telemedicine - Opportunities, Applications, Prospects
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Alexander B. Pravdin, Saratov State University (Russia)

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Internet Plenary Session
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Discussion via Internet
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Introduction

The Annual International Multidisciplinary School for Young Scientists and Students on Optics, Laser Physics and Biophysics X, Saratov Fall Meeting (SFM-06) was held in Saratov, Russia, 26–29 September 2006, with about 600 participants from Russia, FSU countries, USA, Canada, Europe, and Asia. It included the wide range of the modern problems of fundamental and applied optics, laser physics, photonics, and biomedical optics.

SFM-06 also contained ten international workshops and seminars:

- ***Optical Technologies in Biophysics and Medicine VIII*** (Valery V. Tuchin, Chair), SPIE Proc. 6535
- ***Coherent Optics of Ordered and Random Media VII*** (Dmitry A. Zimnykov, Chair), SPIE Proc. 6536
- ***Laser Physics and Photonics VIII*** (Leonid A. Melnikov and Vladimir L. Derbov, Chairs), SPIE Proc. 6537
- ***Spectroscopy and Molecular Modeling VII*** (Valentin I. Berezin, Lev M. Babkov, and Michael D. Elkin, Chairs), SPIE Proc. 6537
- ***Electromagnetics of Microwaves, Submillimeter and Optical Waves IV*** (Michael V. Davidovich, Chair), SPIE Proc. 6537
- ***English as a Communicative Tool in the Scientific Community V*** (Vladimir L. Derbov, Svetlana V. Eremina, and Alexander B. Pravdin, Chairs), SPIE Proc. 6537
- ***Management of High Technologies Commercialization III*** (Valery V. Tuchin, Chair), SPIE Proc. 6535
- ***Luminescence II*** (Vyacheslav I. Kochubey and Sergey N. Shtykov, Chairs), SPIE Proc. 6537
- ***Nanostructures and Nanoparticles: Fabrication, Properties, and Applications II*** (Nikolai G. Khlebtsov, Chair), SPIE Proc. 6536
- ***Telemedicine: Opportunities, Applications, Prospects*** (Irina L. Maksimova, Alexander B. Pravdin, Chairs), SPIE Proc. 6535

The main organizers of the Saratov Fall Meeting are Saratov State University (SSU), Research-Educational Institute of Optics & Biophotonics at SSU, and Research-Educational Center on Nonlinear Dynamics and Biophysics of CRDF and Ministry of Education and Science RF (REC-006).

The main goal of the school, workshops, and seminars is to inform young researchers and students in the field of recent developments and applications of laser and optical technologies in medicine and biology, coherent optics of random and ordered media, material and environmental sciences, nonlinear dynamics of laser systems, laser spectroscopy, and molecular modeling. The primary focus was the discussion of fundamentals and general approaches of description of coherent, low-coherent, polarized, spatially and temporally modulated light interactions with inhomogeneous absorbing media, photonic crystals, tissue phantoms, and various types of tissues in vitro and in vivo. Such effects as static and dynamic light scattering, Doppler effect, optoacoustic and optothermal interactions, mechanical stress, photodynamic effect, etc., were also considered. On this basis the variety of laser and optical technologies for medical diagnostics, therapy, surgery, and light dosimetry, as well as for spectroscopy of random and ordered media, were presented.

SFM-06 was organized as morning plenary sessions, afternoon lecture and oral sessions, and evening poster presentations. The original oral reports and posters were presented by the junior scientists and students. Plenary lectures were listened to with great interest and were discussed by the audience.

Plenary and invited lectures and oral and poster presentations covered a wide area of topics including tissue optics, spectroscopy and imaging, controlling of optical properties of tissues, as well as biophysical and photo-chemical aspects of photo and laser therapy.

One main aspect of Saratov Fall Meetings is the one-day Internet session. In 2006 this session included the plenary lecture "High-resolution photoacoustic tomography" by Lihong V. Wang from the Washington University in St. Louis (USA).

Participants from USA, Russia, Austria, Australia, Bulgaria, Canada, Finland, Germany, Ireland, UK, Slovakia, Canada, China, Portugal, Italy, Japan, Ukraine, Belarus, Switzerland, Denmark, Spain, Singapore, the Netherlands, Poland, India, and other countries have placed their papers on the meeting website: http://optics.sgu.ru/SFM/, which was available during the meeting and will be available for a whole year up to the next meeting. Among the invited Internet lecturers were well-recognized experts in the fields of biomedical optics and light scattering: Steven L. Jacques (USA), S. Fantini (USA), Sean J. Kirkpatrick (USA), R. K. Wang (USA), Hong Liu (USA), Wei Chen (USA), Omar S. Khalil (USA), K. M. Meek (UK), J. Lademann (Germany), M. Hoffmann (Germany), O. Minet (Germany), Colin J. R. Sheppard (Singapore), A. K. Asundi (Singapore), A. Kishen (Singapore), Qingming Luo (China), P. K. Gupta (India), Christoph K. Hitzenberger (Austria), A. Kowalczyk (Poland), Vitali A. Tougbaev (South Korea), and O. V. Angelsky (Ukraine). A three-hour on-line Internet discussion was held on papers presented in the Internet session via a chat moderated by Alexander Priezzhev. Many of the presented Internet papers are published in this conference volume.

SFM-06 has gathered about 600 participants; a great number of presented materials are the result of collaboration between research groups from different countries supported by international scientific programs such as CRDF, INTAS, Royal Society and others.

The major portion of this volume includes papers presented in the workshop on Optical Technologies in Biophysics and Medicine VIII. However, a few of the most interesting papers (paper numbers 30, 44, 72, and 73) presented in the workshops on Management of High Technologies Commercialization III and Telemedicine: Opportunities, Applications, Prospects also are published in the volume.

This year SFM was held a few months after the XII Conference on Laser Optics in St. Petersburg (26–30 June 2006) with the Workshop on Lasers in Biomedical Diagnostics and Laser Tomography of Biomedical Objects (co-chairs, V. V. Lubimov, A. M. Sergeev, and V. V. Tuchin), with topics related to SFM-06. This opportunity allowed us to invite a few papers presented in the St. Petersburg Workshop to be published in this volume. These papers are numbers 75, 76, 77, and 78.

This year is also very important for organizers of the meeting, because 60 years ago the Chair of Optics of Saratov State University was organized by our teacher, Professor Mark L. Katz. We have dedicated SFM-06 to the memory of Professor Mark L. Katz on the 100th anniversary of his birth and the 60th anniversary of the Chair of Optics, founded by him in 1946. We are very proud that our Chair is recognized as a host of many international conferences and schools including SFM. We are very thankful to our numerous friends all over the world who sent us their congratulations and best wishes.

It is a great pleasure and privilege for the chair of SFM to thank all of the authors for their contributions to SFM-06, especially to the Internet lecturers for their exciting presentations, and to Alexander Priezzhev, a moderator of the Internet sessions for the last nine years, for his talent and impressive moderation.

The organizers of SFM are grateful to all of the sponsoring organizations and programs that supported this meeting very effectively: SPIE Russia Chapter, Executive Director Edmund Akopov; Russian Foundation for Basic Research; U.S. Civilian Research & Development Foundation for the Independent States of the Former Soviet Union (CRDF), grant REC-006 and mini-grant on the conference support; and Volga Region Center of New Information Technologies.

I would like to thank Elina Genina and Ivan Fedosov for their help with the preparation of this volume.

Valery V. Tuchin

High-resolution Photoacoustic Tomography

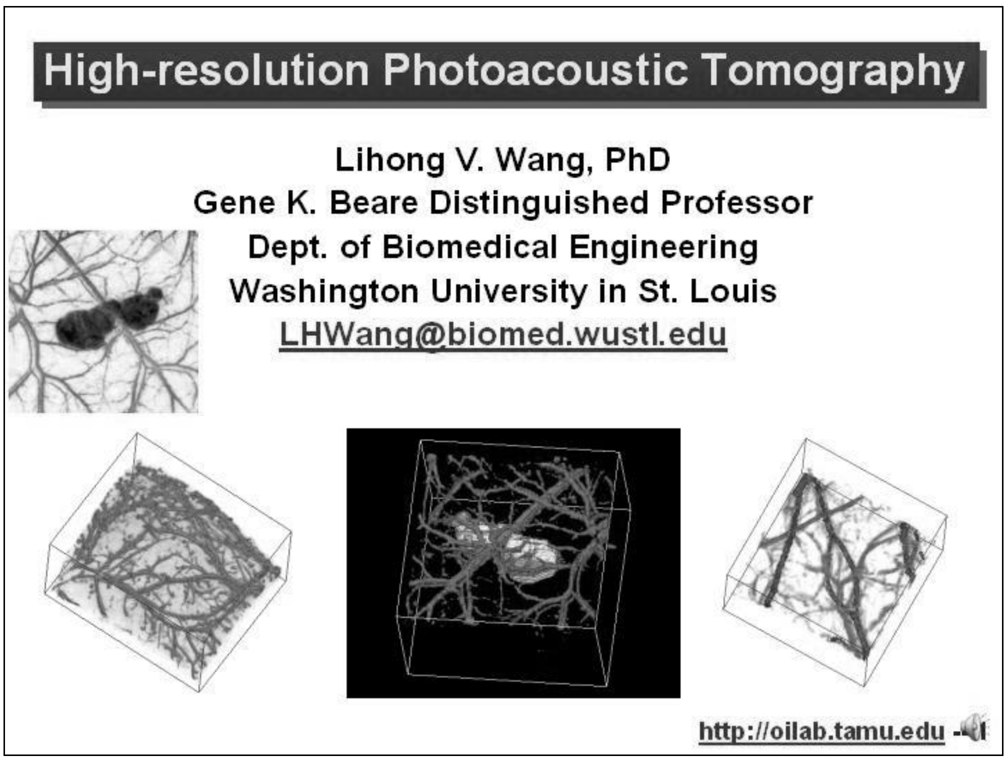
Lihong V. Wang, Gene K. Beare

Dept. of Biomedical Engineering Washington University in St. Louis

ABSTRACT

Novel photoacoustic tomography techniques, including, orthogonal-mode photoacoustic tomography, reflection-mode photoacoustic microscopy and deeply penetrating RF-based thermoacoustic tomography are presented.

Keywords: photoacoustic tomography, photoacoustic microscopy



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- **S. Hu**
- **X. Jin**
- **R. Kothapalli**
- **C. Kim**
- **G. Ku**
- **C. Li**
- **L. Li**
- **Y. Li**
- **K. Maslov**
- **E. Smith**
- **K. Song**
- **L. Song**
- **M. Todorovic**
- **X. Xu**
- **X. Yang**
- **R. Zemp**
- **H. Zhang**
- **S. Zhou**

SELECTED FORMER LAB MEMBERS

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- D. Feng, MS
- J. Hollmann
- S. Jiao, PhD
- J. Li, PhD
- M. Li, PhD
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- M. Xu, PhD
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- X. Zhao, MS

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Credits to Collaborators

- Texas A&M University (Animal study):
  - G. Stoica, DVM
- UT MD Anderson Cancer Center (Clinical study & molecular contrast agents):
  - M. Duvic, MD
  - B. Fornage, MD
  - K. Hunt, MD
  - C. Li, PhD
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- Nanospectra (Nanoshells):
  - P. O'Neal, PhD
  - J. Schwartz, PhD

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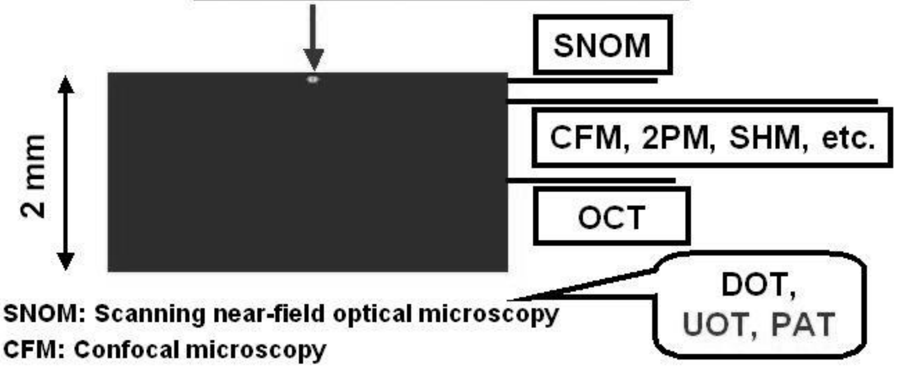
Outline

- Motivation
- Orthogonal-mode photoacoustic tomography
- Reflection-mode photoacoustic microscopy
- Deeply penetrating RF-based thermoacoustic tomography
- Summary

Motivation for Optical Imaging

- Safety — Non-ionizing radiation: photon energy is ~2 eV.
- Physics — Related to the molecular conformation of tissue.
- Optics — High intrinsic contrast:
  - Optical absorption: Angiogenesis, hyper-metabolism, apoptosis, necrosis, and exogenous contrast agents.
  - Optical scattering: Size of cell nuclei.
  - Optical polarization: Collagen, muscle fibers.
  - Spectroscopy: Wavelength multiplexing
- Physiology — Functional imaging of physiological parameters:
  - Oxygen saturation of hemoglobin
  - Total hemoglobin concentration (related to blood volume)
  - Enlargement of cell nuclei
  - Denaturation of collagen
  - Blood flow (Doppler)
- Physiology — Molecular imaging (exogenous contrast agents).
- ….

Challenges in Optical Imaging



- SNOM: Scanning near-field optical microscopy
- CFM: Confocal microscopy
- 2PM: Two-photon microscopy
- SHM: Second harmonic microscopy
- OCT: Optical coherence tomography
- DOT: Diffuse optical tomography
- UOT: Ultrasound-modulated optical tomography
- PAT: Photoacoustic tomography

Simulation software available from http://oilab.tamu.edu

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Outline

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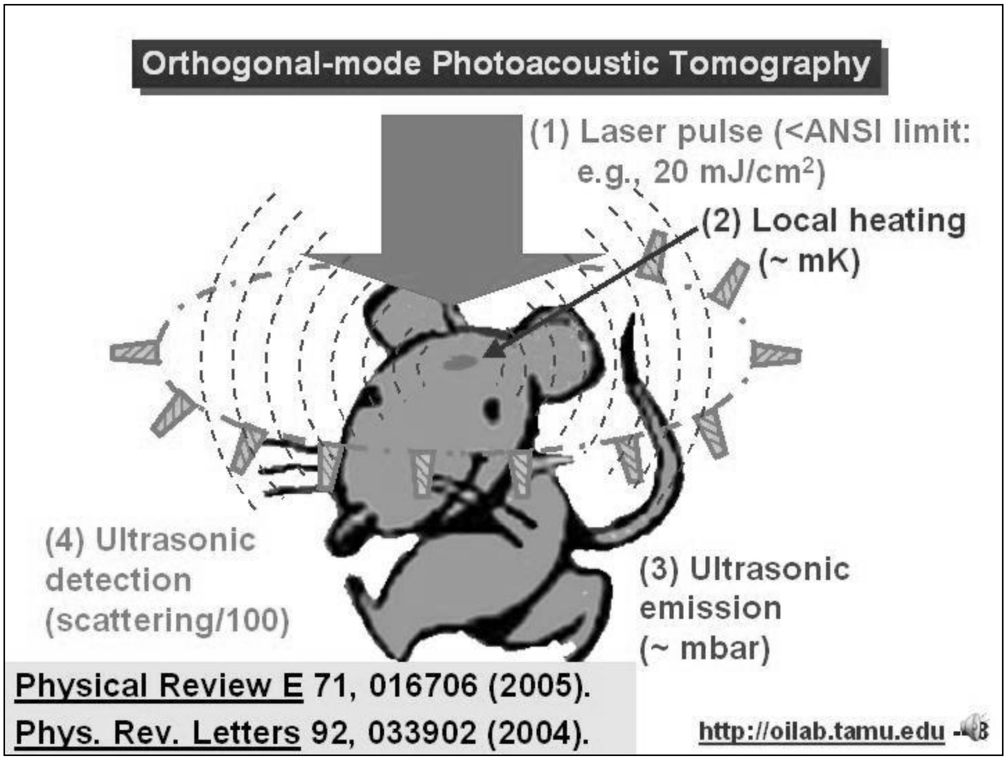
Orthogonal-mode Photoacoustic Tomography
(1) Laser pulse (<ANSI limit: e.g., 20 mJ/cm²)
(2) Local heating (~ mK)
(3) Ultrasonic emission (~ mbar)
(4) Ultrasonic detection (scattering/100)
Physical Review E 71, 016706 (2005).
Phys. Rev. Letters 92, 033902 (2004).
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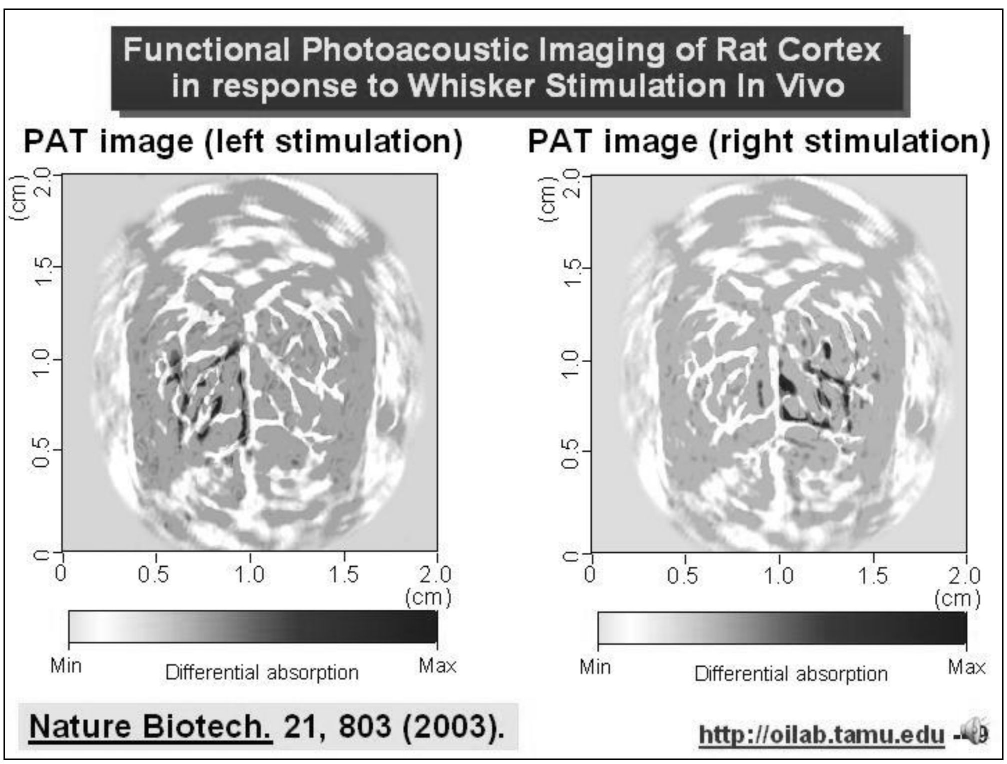
Functional Photoacoustic Imaging of Rat Cortex in response to Whisker Stimulation In Vivo
PAT image (left stimulation)
PAT image (right stimulation)
(cm)
0
0.5
1.0
1.5
2.0
Min
Differential absorption
Max
Nature Biotech. 21, 803 (2003).
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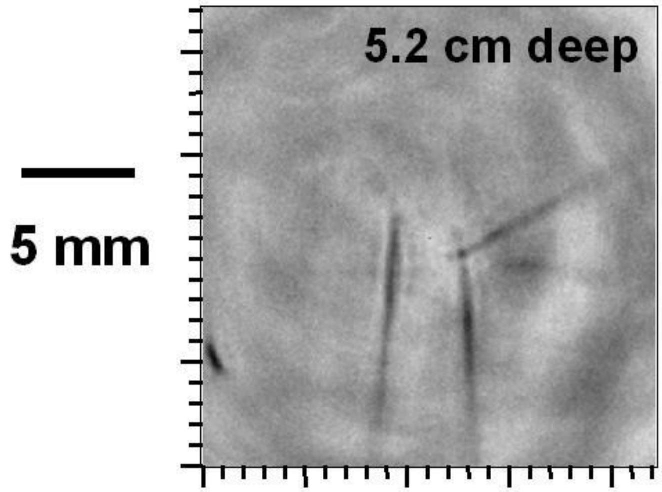
Deeply Penetrating Photoacoustic Tomography with NIR Excitation & ICG Contrast



Optics Letters 30, 507 (2005).

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Outline

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- Deeply penetrating RF-based thermoacoustic tomography
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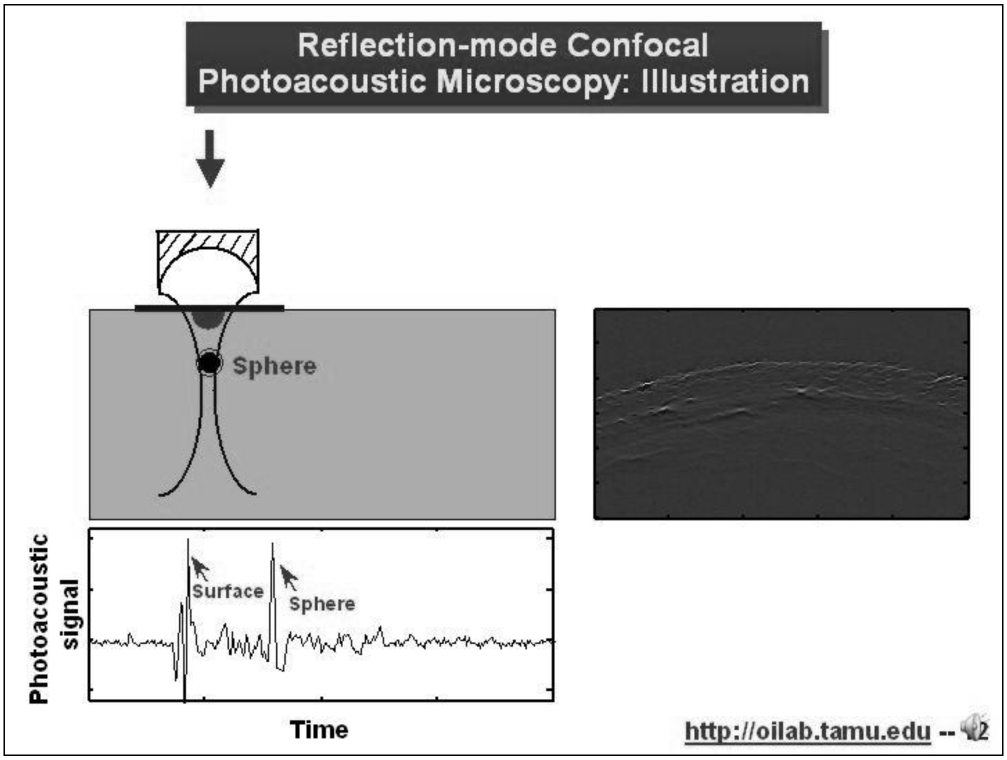
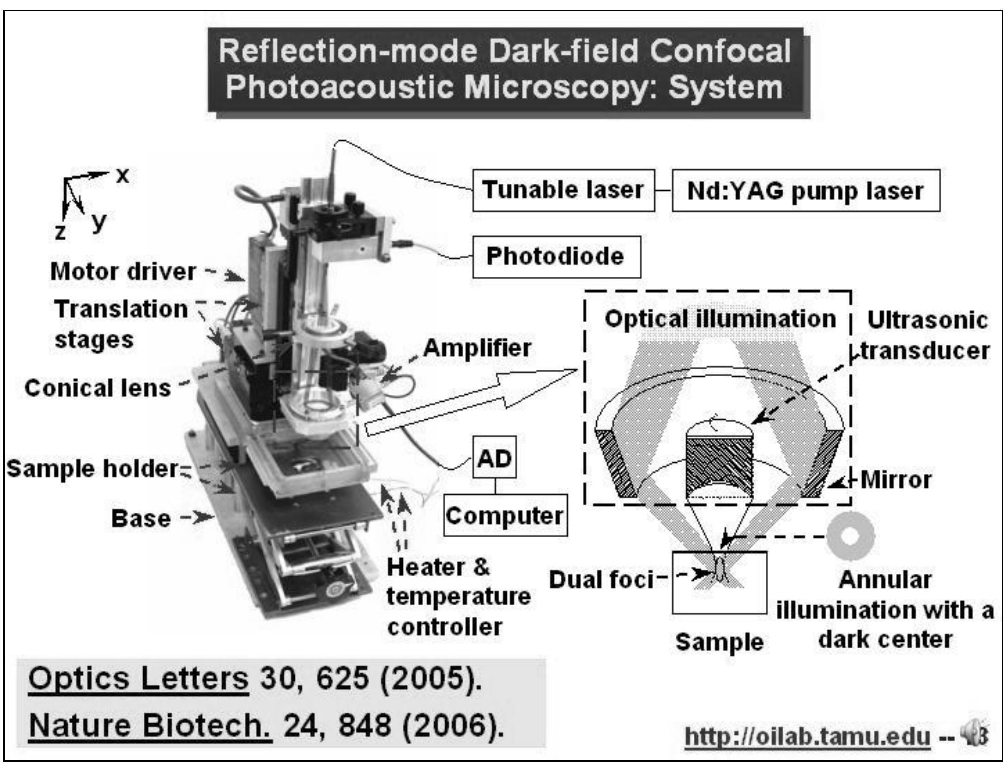

Reflection-mode Confocal Photoacoustic Microscopy: Illustration
Sphere
Photoacoustic signal
Surface
Sphere
Time
http://oilab.tamu.edu --


Reflection-mode Dark-field Confocal Photoacoustic Microscopy: System
x
y
z
Tunable laser
Nd:YAG pump laser
Photodiode
Motor driver
Translation stages
Conical lens
Amplifier
Sample holder
Base
AD
Computer
Heater & temperature controller
Optical illumination
Ultrasonic transducer
Mirror
Dual foci
Sample
Annular illumination with a dark center
Optics Letters 30, 625 (2005).
Nature Biotech. 24, 848 (2006).
http://oilab.tamu.edu --

System Parameters

- Laser
  - Tunability: 570-770 nm
  - Repetition rate: 10 Hz
  - Pulse width: 6.5 ns
  - Optical fiber: 0.6 mm diameter
  - Energy per pulse: 0.2 mJ
  - Energy density at focus: ~6 mJ/cm^2 <20 mJ/cm^2 (ANSI safety limit)
- High-frequency ultrasound transducer
  - Center frequency: 50 MHz
  - Nominal bandwidth: 70% of 50 MHz
  - NA: 0.44

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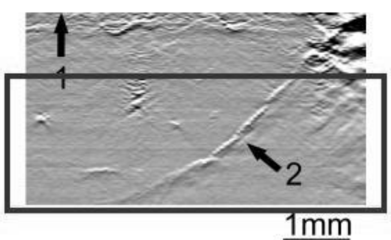
Imaging Depth and Resolution



B-scan of a black double-stranded cotton thread embedded in rat

- Imaging depth: ~3 mm
- Axial resolution: ~15 microns
- Depth/resolution: ~200 pixels

- Lateral resolution: ~45 microns
- Acquisition time: 2 μs/A-scan
- No signal averaging

Optics Letters 30, 625 (2005).

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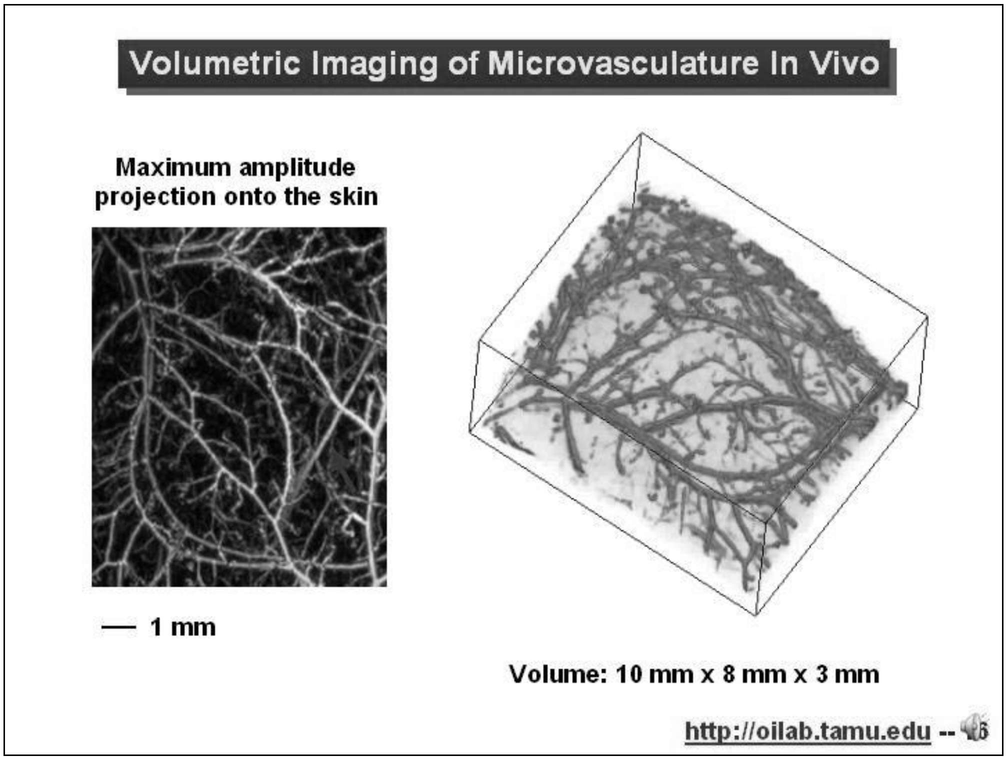
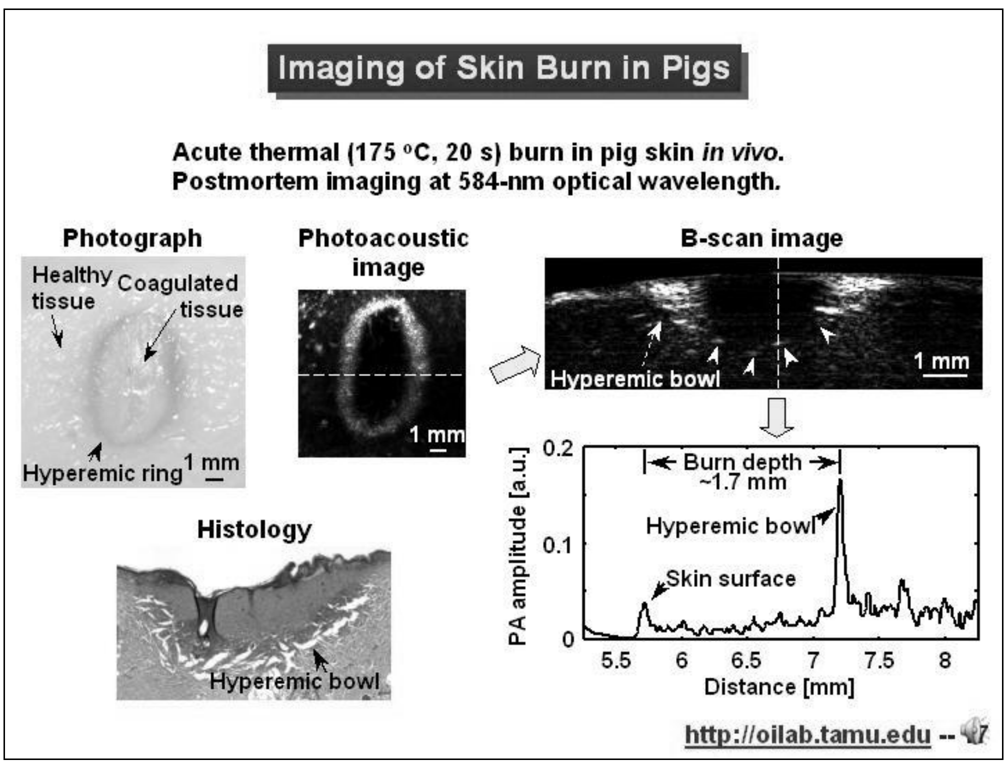
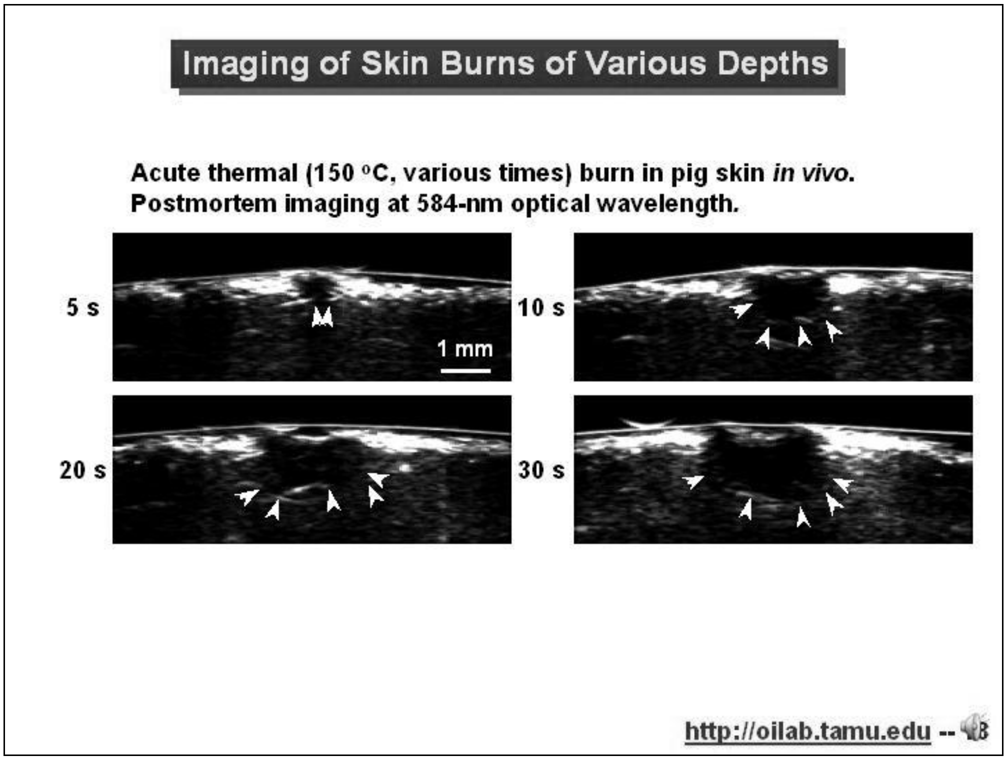
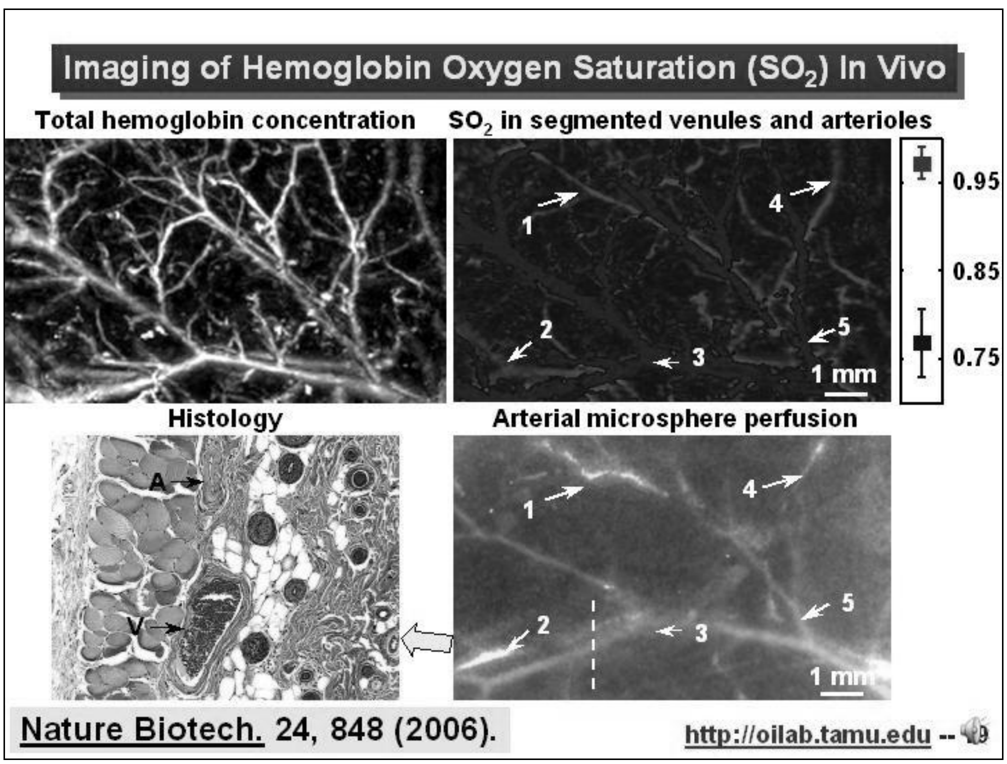
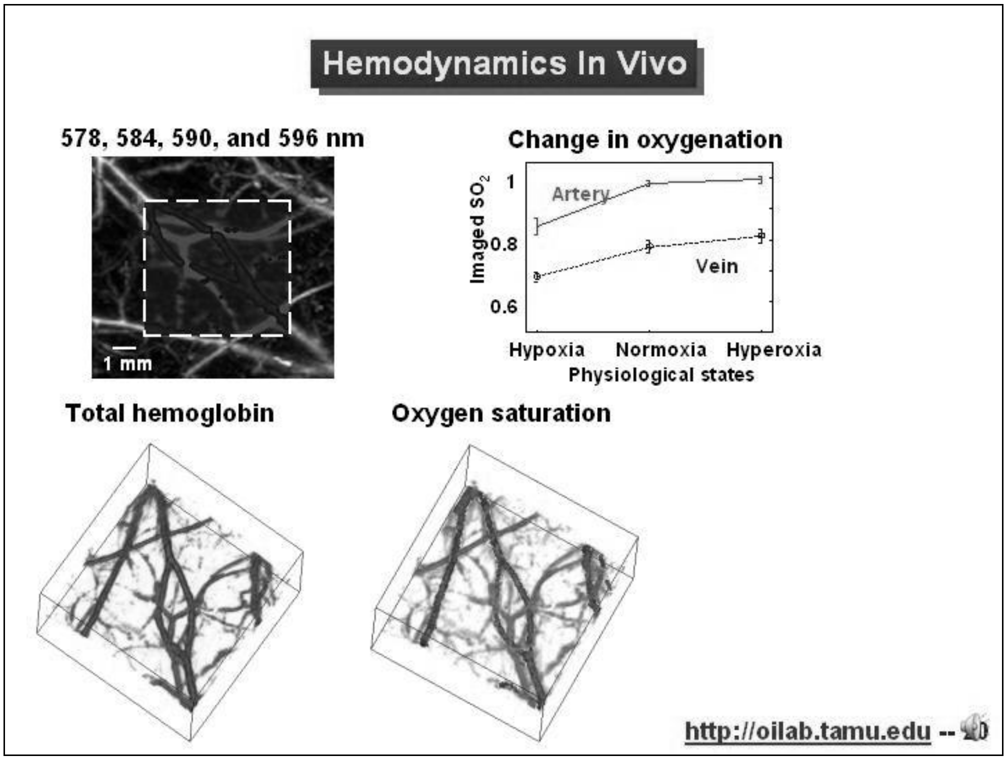

Volumetric Imaging of Microvasculature In Vivo
Maximum amplitude
projection onto the skin
1 mm
Volume: 10 mm x 8 mm x 3 mm
http://oilab.tamu.edu --
6


Imaging of Skin Burn in Pigs
Acute thermal (175 °C, 20 s) burn in pig skin *in vivo*.
Postmortem imaging at 584-nm optical wavelength.
Photograph
Healthy tissue
Coagulated tissue
Hyperemic ring
1 mm
Photoacoustic image
1 mm
B-scan image
Hyperemic bowl
1 mm
Burn depth ~1.7 mm
Hyperemic bowl
Skin surface
PA amplitude [a.u.]
0.2
0.1
0
5.5
6
6.5
7
7.5
8
Distance [mm]
Histology
Hyperemic bowl
http://oilab.tamu.edu --
7


Imaging of Skin Burns of Various Depths
Acute thermal (150 °C, various times) burn in pig skin in vivo.
Postmortem imaging at 584-nm optical wavelength.
5 s
10 s
1 mm
20 s
30 s
http://oilab.tamu.edu --


Imaging of Hemoglobin Oxygen Saturation (SO2) In Vivo
Total hemoglobin concentration
SO2 in segmented venules and arterioles
1
2
3
4
5
1 mm
0.95
0.85
0.75
Histology
A
V
Arterial microsphere perfusion
1
2
3
4
5
1 mm
Nature Biotech. 24, 848 (2006).
http://oilab.tamu.edu --


Hemodynamics In Vivo
578, 584, 590, and 596 nm
1 mm
Change in oxygenation
Imaged SO2
1
0.8
0.6
Artery
Vein
Hypoxia
Normoxia
Hyperoxia
Physiological states
Total hemoglobin
Oxygen saturation
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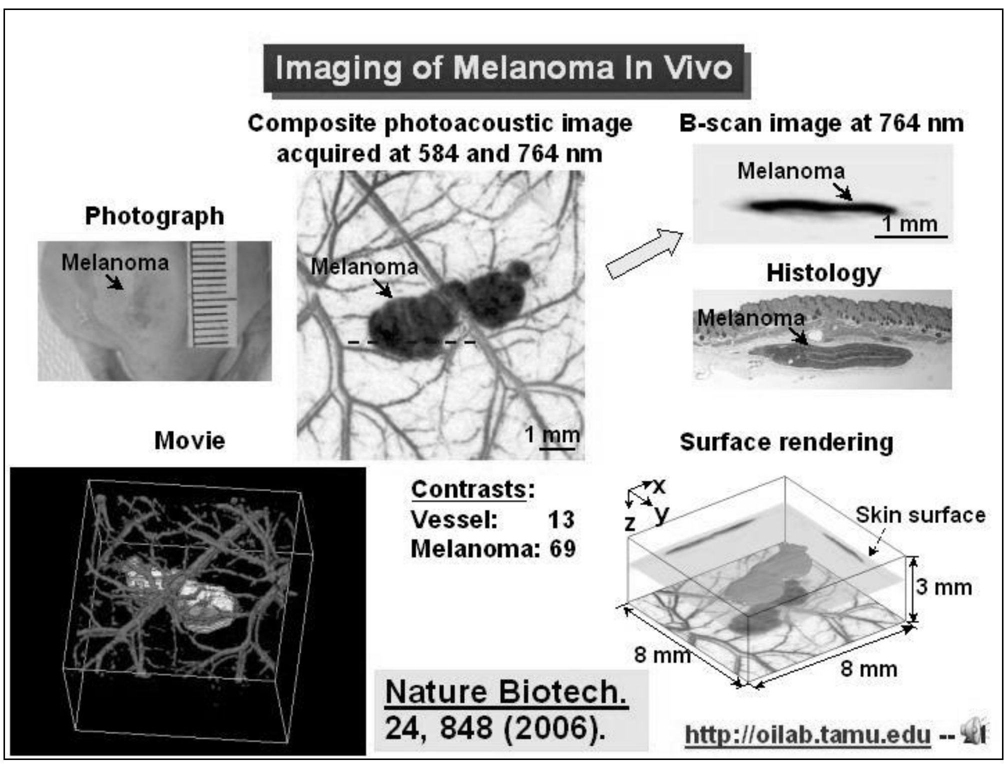
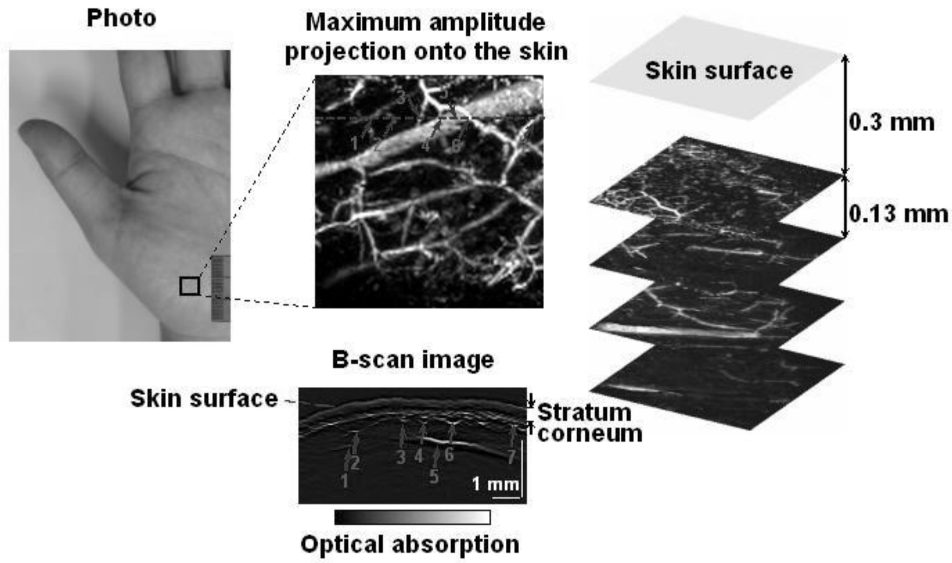

Imaging of Melanoma In Vivo
Composite photoacoustic image acquired at 584 and 764 nm
B-scan image at 764 nm
Melanoma
1 mm
Photograph
Melanoma
Melanoma
1 mm
Histology
Melanoma
Movie
Surface rendering
Contrasts:
Vessel: 13
Melanoma: 69
x
z
y
Skin surface
3 mm
8 mm
8 mm
Nature Biotech.
24, 848 (2006).
http://oilab.tamu.edu --

Imaging of Human Palm In Vivo



Nature Biotech. 24, 848 (2006).

Modern High-resolution Optical Microscopy

Modality	Year	Depth	Depth / Resolution	Contrast
Confocal microscopy	1970s	~0.5 mm	> 100	Scattering, fluorescence
Two-photon microscopy	1990s	~0.5 mm	> 100	Fluorescence
Optical coherence tomography	1990s	~1 mm	> 100	Scattering, polarization
Dark-field confocal photoacoustic microscopy	2005*	~3 mm, scalable	> 100	Absorption

* Optics Letters 30, 625 (2005).

Outline

- Motivation
- Orthogonal-mode photoacoustic tomography
- Reflection-mode photoacoustic microscopy
- Deeply penetrating RF-based thermoacoustic tomography
- Summary

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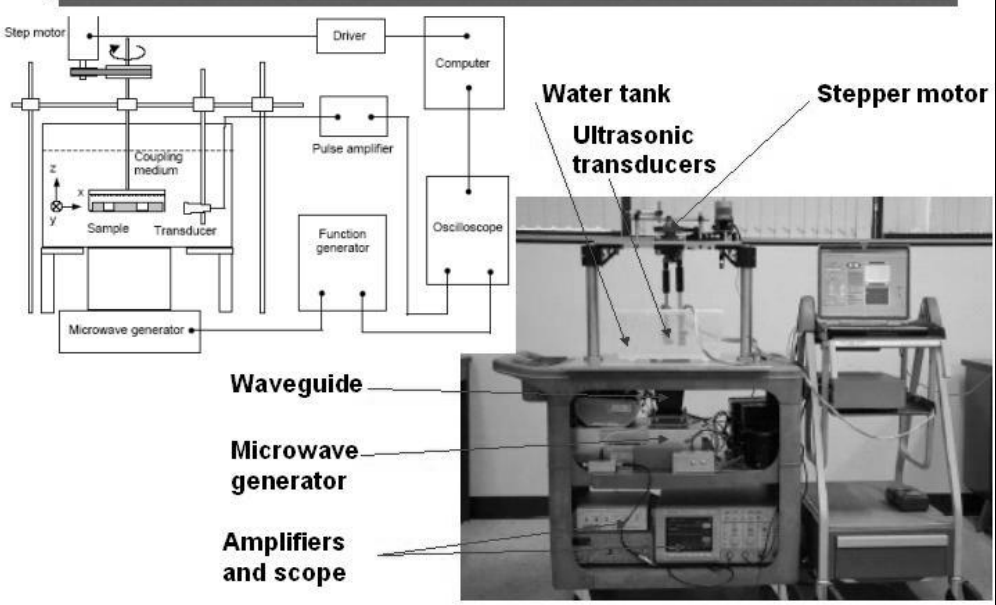
Experimental System for Thermo-acoustic Tomography



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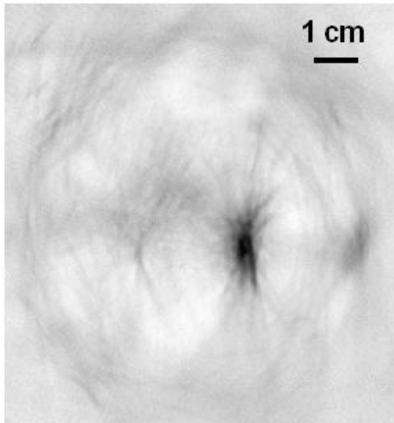
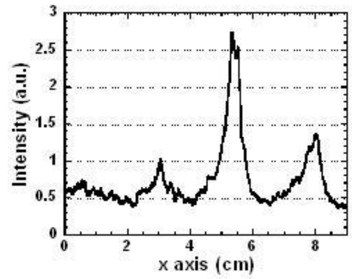
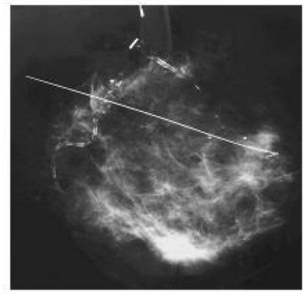
Thermo-acoustic Image of a Mastectomy Specimen







- 11 cm diam. X 9 cm thick
- ~5:1 contrast
- Invasive lobular carcinoma

Tech. in Cancer Res. & Treatment 4, 559 (2005).

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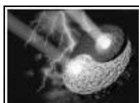

Summary

- Physically combining ultrasonic and electromagnetic waves (light & RF) provides
  - improved spatial resolution compared with optical/RF imaging.
  - new contrast mechanisms compared with ultrasound imaging.
- Spatial resolution is determined by the ultrasonic parameters.
- Spatial resolution is scalable with the ultrasonic parameters.
- Contrast is provided by the electromagnetic properties.
- Deep (~cm) tissue imaging can be achieved.
- Speckle artifacts do not exist.
- Functional imaging can be accomplished with endogenous contrast.
- Molecular imaging can be accomplished with exogenous contrast agents.
- Non-ionizing radiation is used.
- Costs are comparable with those of ultrasound systems.

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Funding Sources

ACTIVE

- NIH
  - R01 CA106728
  - R01 NS46214 (BRP)
  - R33 CA094267
  - R01 CA092415
  - R01 EB000712
- NIST

RECENTLY COMPLETED

- NIH
  - CA83760
  - CA71980
  - CA68562
  - EB000319
- NSF
- US Army
- Whitaker Foundation

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