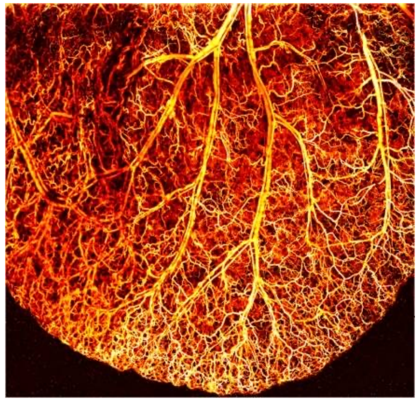
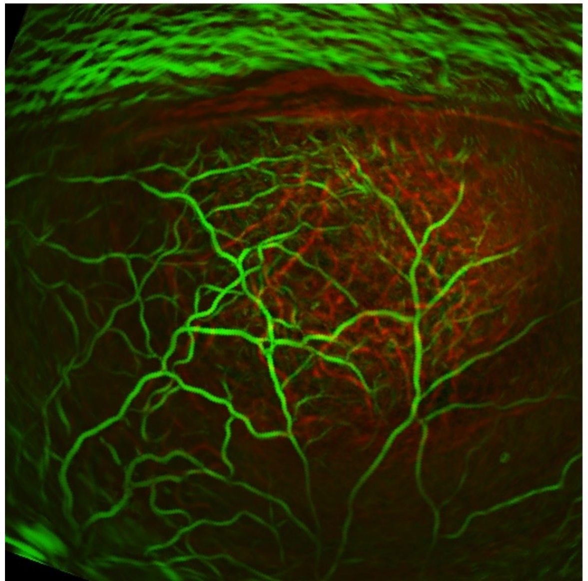
Photoacoustic, Light-Speed, and Quantum Imaging

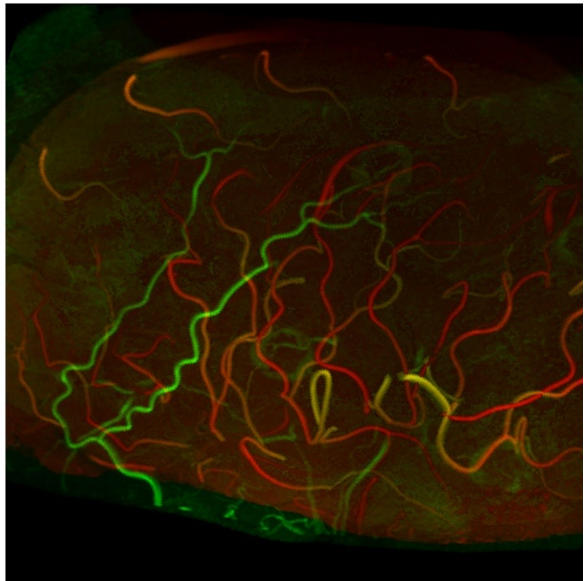


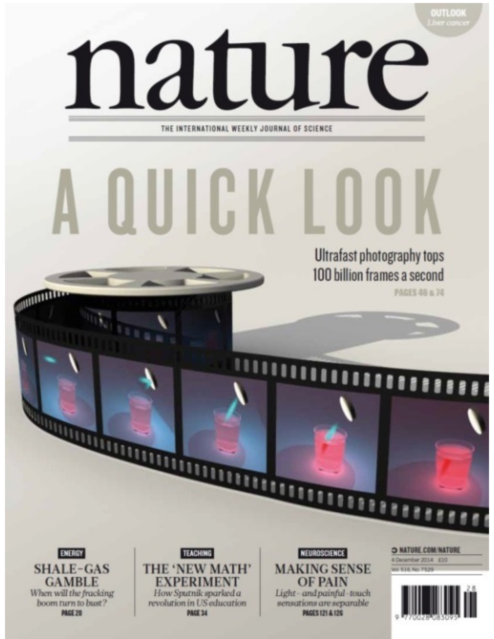
Lihong V. Wang, Ph.D., Bren Professor
Caltech Optical Imaging Laboratory (COIL)
Andrew and Peggy Cherng Department of Medical Engineering &
Department of Electrical Engineering
California Institute of Technology (Caltech), Pasadena

Photoacoustic computed tomography



7-Tesla magnetic resonance imaging





OUTLOOK
Liver cancer

nature
THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

A QUICK LOOK

Ultrafast photography tops
100 billion frames a second
PAGES 46 & 74

ENERGY
SHALE-GAS GAMBLE
When will the fracking boom turn to bust?
PAGE 28

TEACHING
THE 'NEW MATH' EXPERIMENT
How Sputnik sparked a revolution in US education
PAGE 34

NEUROSCIENCE
MAKING SENSE OF PAIN
Light- and painful-touch sensations are separable
PAGES 121 & 126

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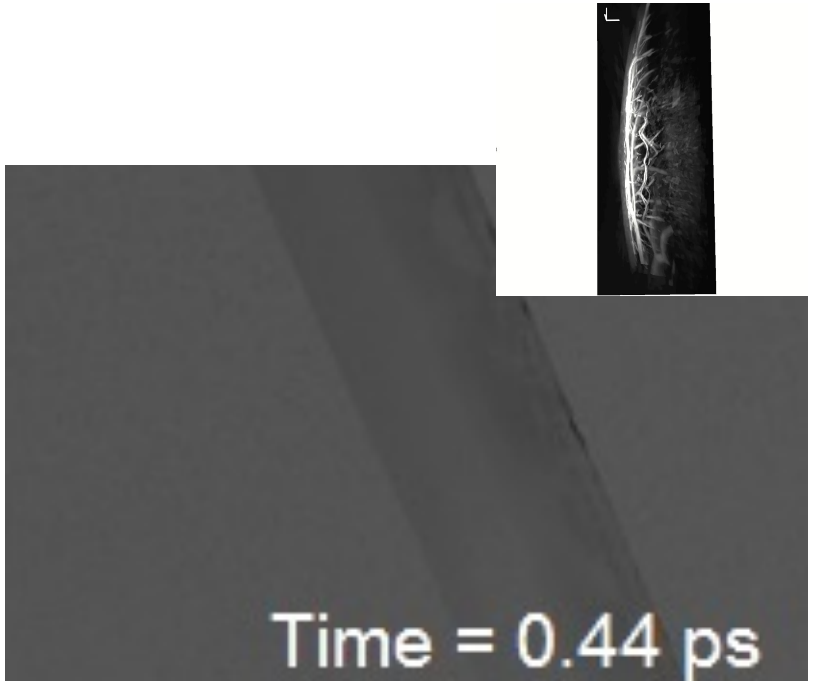
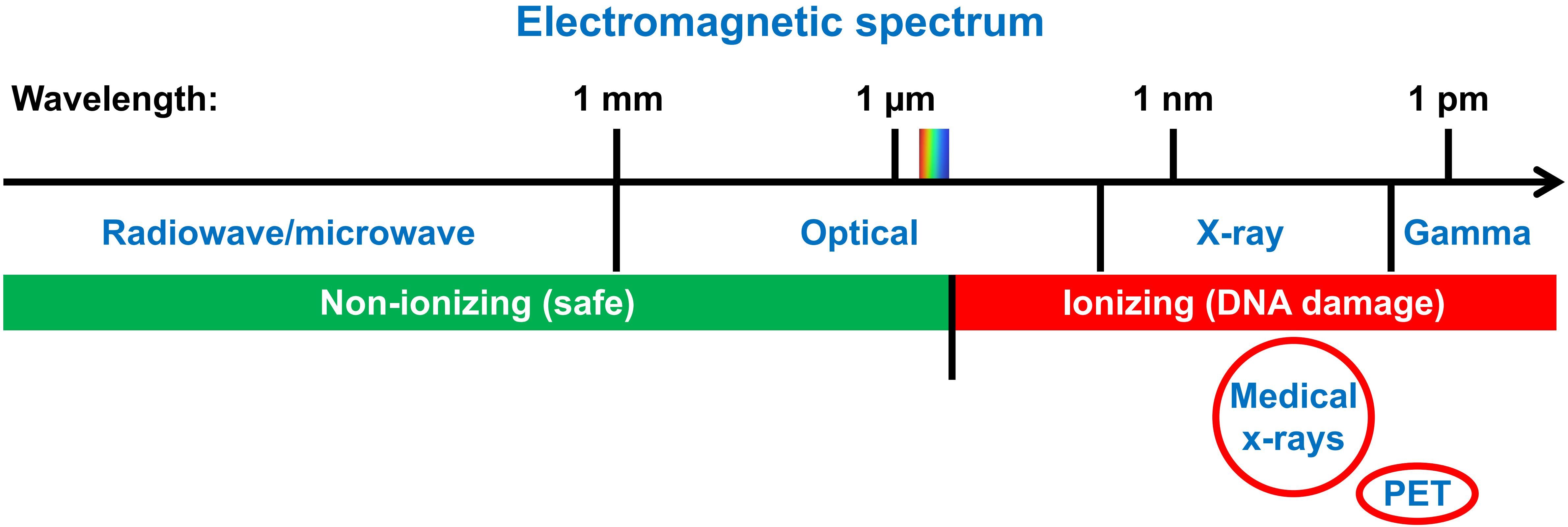
4 December 2014 £10
Vol. 516, No. 7529



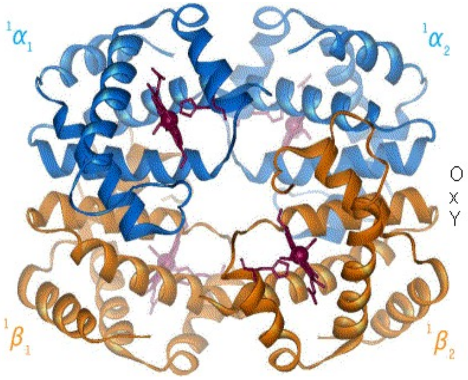
Molecular Specificity of Optical Imaging

- **Light-matter interaction uniquely positioned at the molecular level**



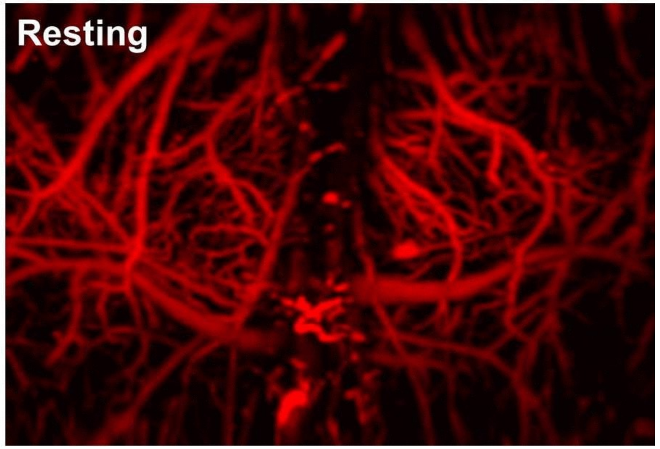
Molecular Specificity of Optical Imaging

- Light-matter interaction uniquely positioned at the molecular level
- Fundamental role of molecules in biology and medicine
- *In vivo* functional imaging analogous to functional MRI
- *In vivo* metabolic imaging analogous to PET
- *In vivo* molecular imaging of gene expressions or disease markers
- *In vivo* label-free histologic imaging of cancer without excision

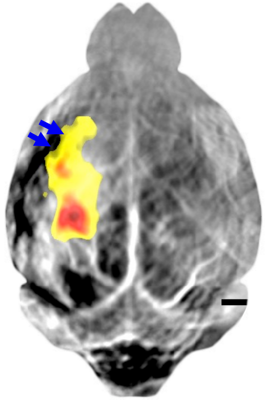


Oxy- & deoxy-hemoglobins

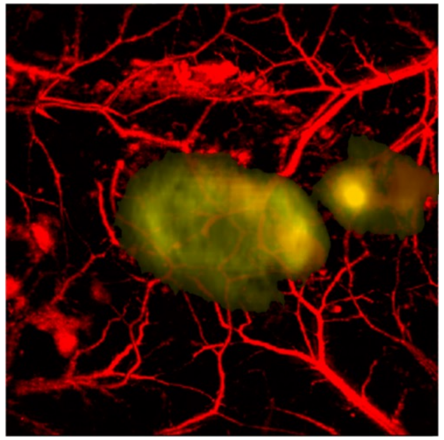
Source: Wikipedia



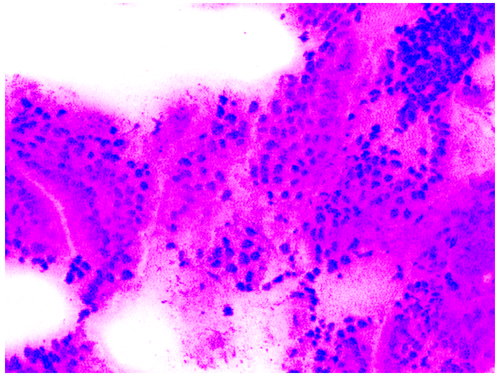
Brain activation



Glucose uptake



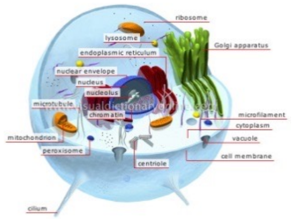
Melanoma hallmark



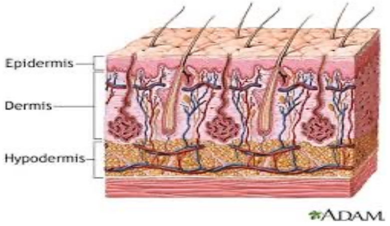
Photoacoustic microscopy of cell nuclei

Challenges in Optical Penetration

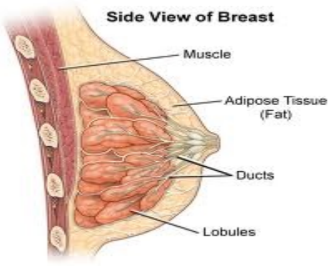
Cell



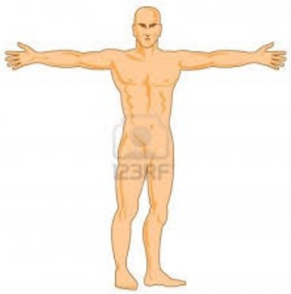
Skin

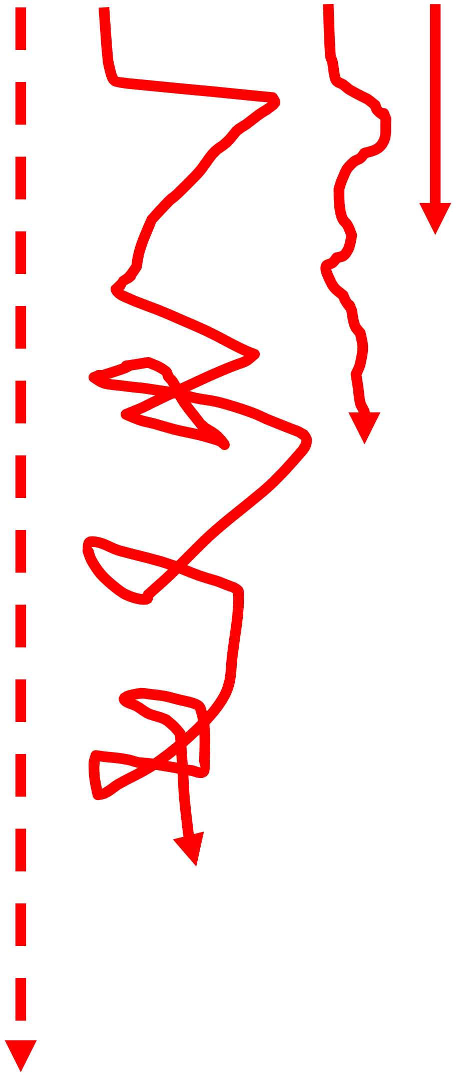


Organ

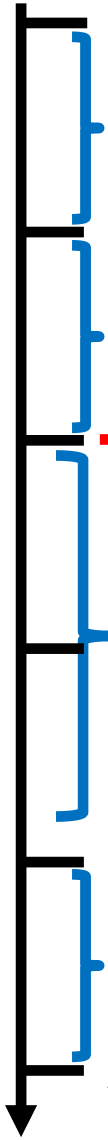


Human





Depth



10 µm

Classical planar optical microscopy

100 µm — ~~Aberration limit:~~ 1/scattering coefficient

Confocal or two-photon microscopy
Optical coherence tomography

1 mm — ~~Diffusion limit:~~ 10/scattering coefficient

Photoacoustic tomography

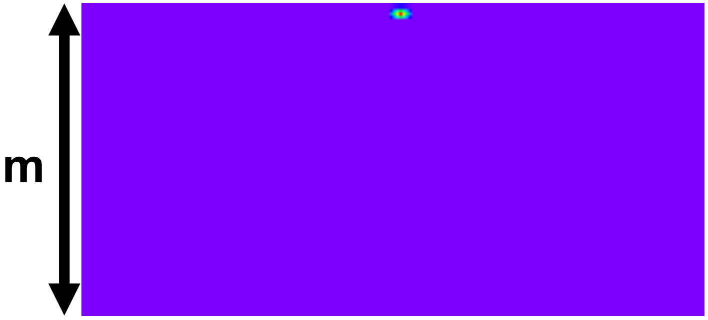
1 cm

10 cm — Dissipation limit: 10/attenuation coefficient

?

1 m — Absorption limit: 10/absorption coefficient

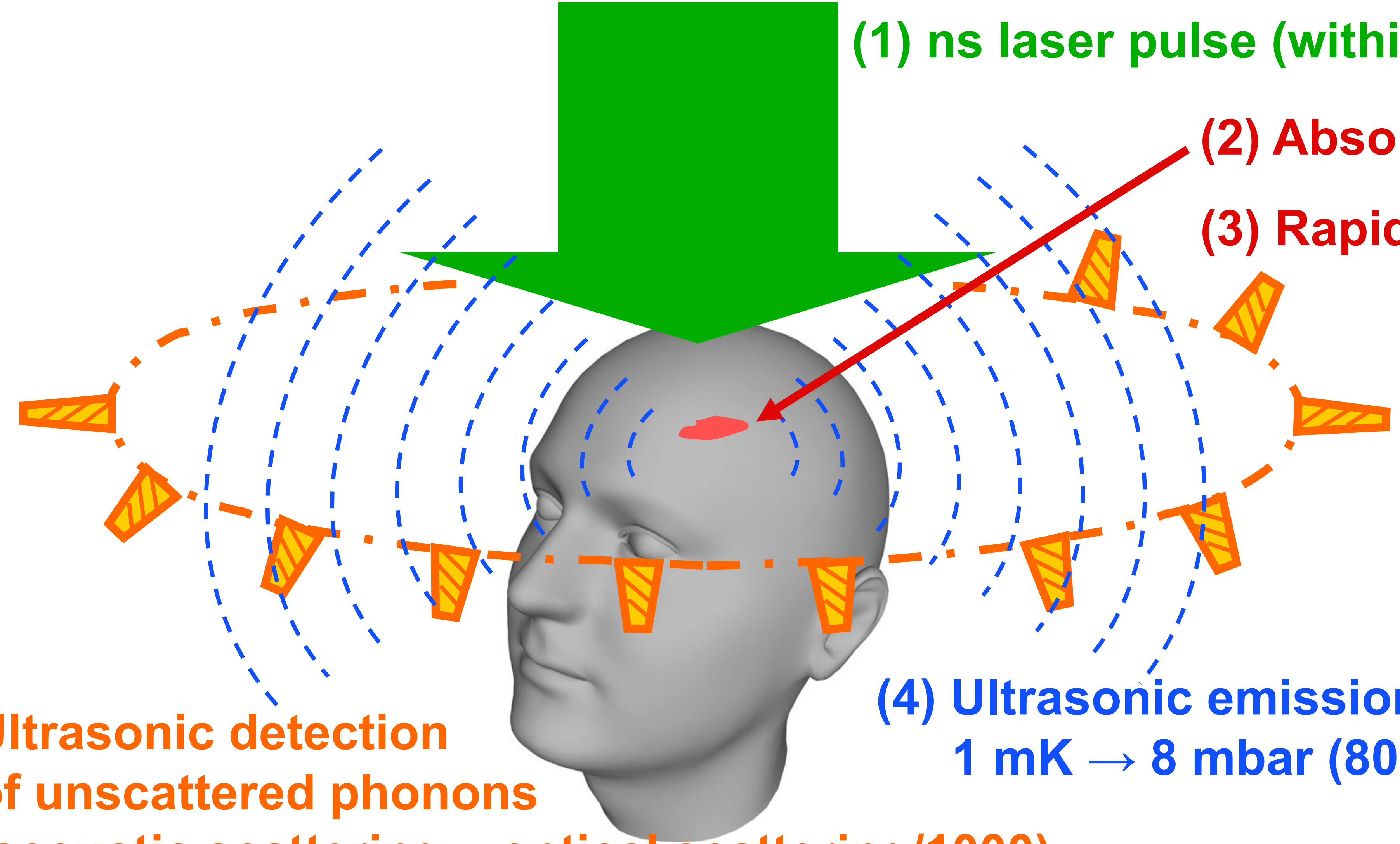
Photon propagation



LV Wang, HI Wu, *Biomedical Optics* (Wiley, 2007); LV Wang, JJ Yao, *Nature Methods* 13, 627, 2016

COILab.Caltech.edu

Photoacoustic Computed Tomography:
Deep Penetration with Optical Contrast and Ultrasonic Resolution



(1) ns laser pulse (within safety limit)

(2) Absorption of photons

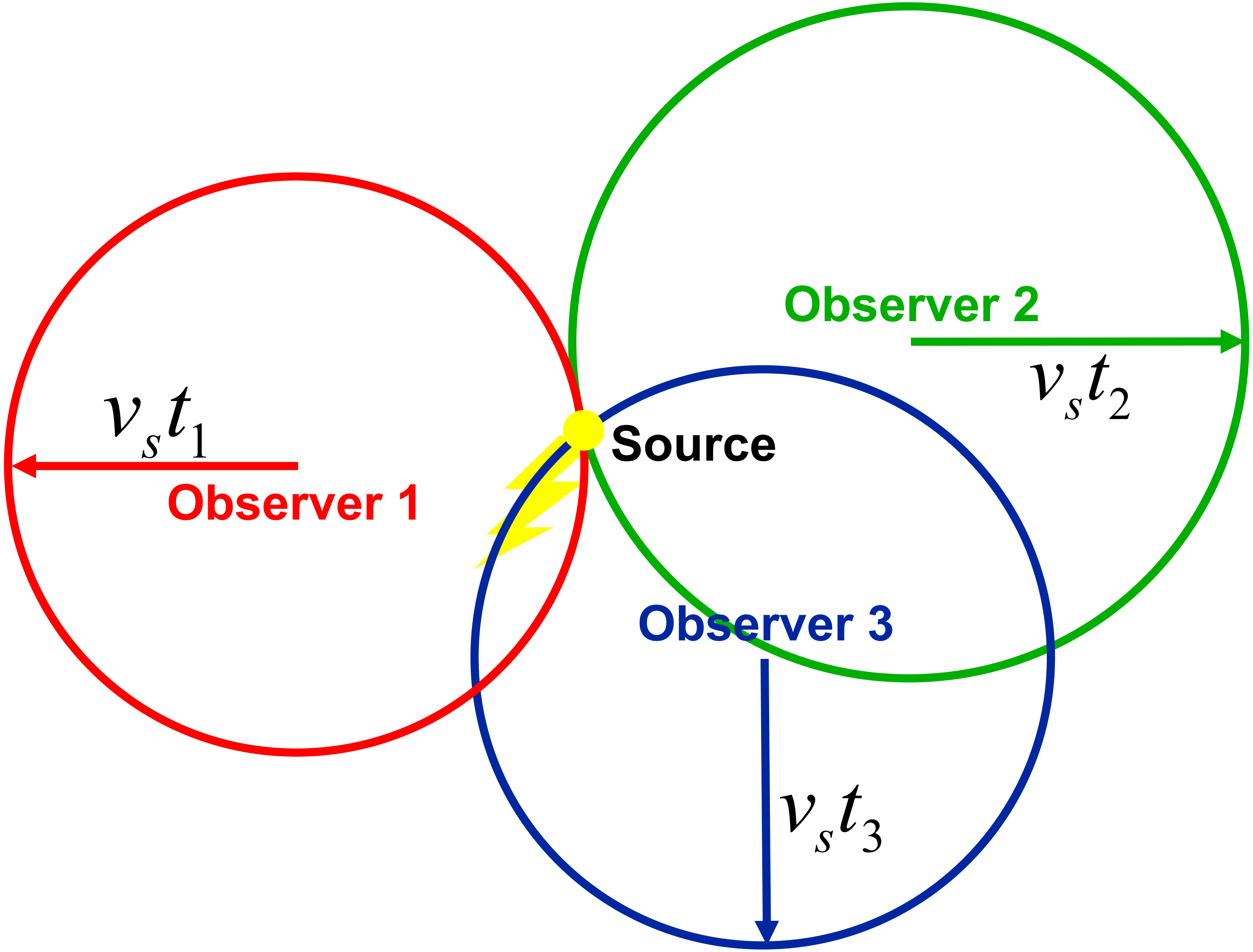
(3) Rapid heating (~ mK)

(4) Ultrasonic emission:
1 mK → 8 mbar (800 Pa), detectable

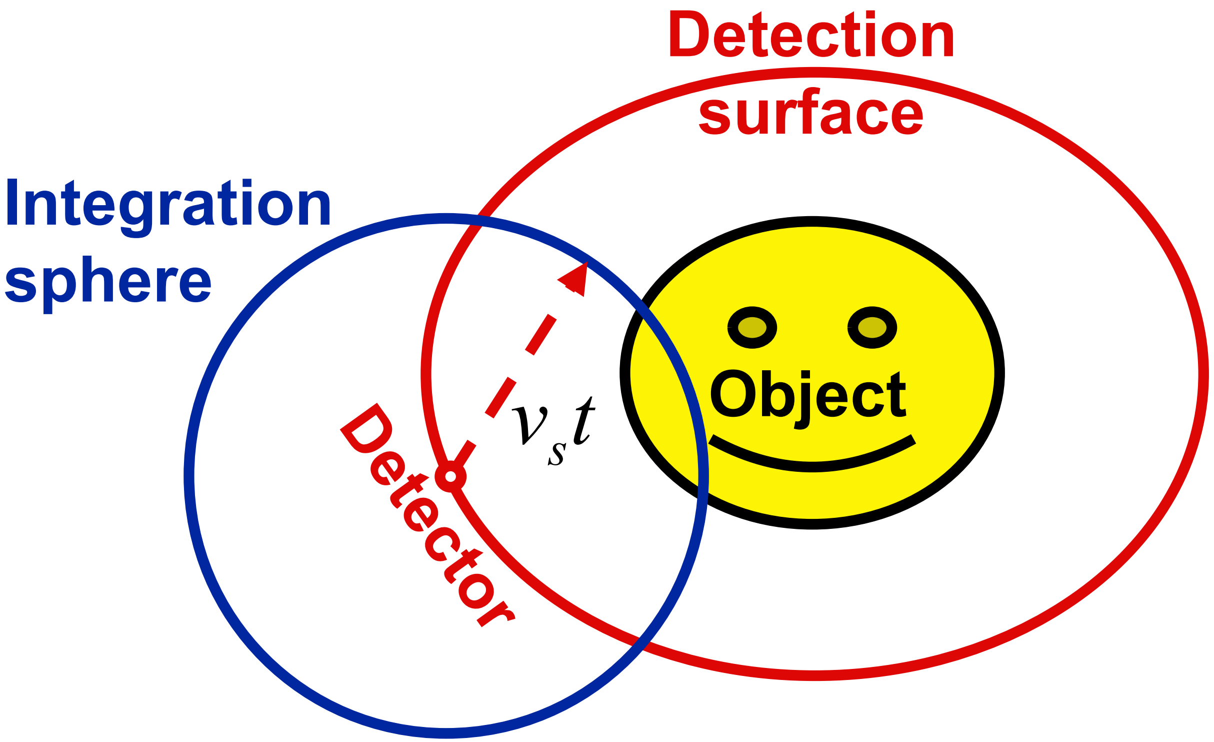
(5) Ultrasonic detection
of unscattered phonons
(acoustic scattering ~ optical scattering/1000)

X Wang, Y Pang, G Ku, G Stoica, LV Wang, *Nature Biotech* 21, 803, 2003

Imaging of a Single Sound Source by Triangulation



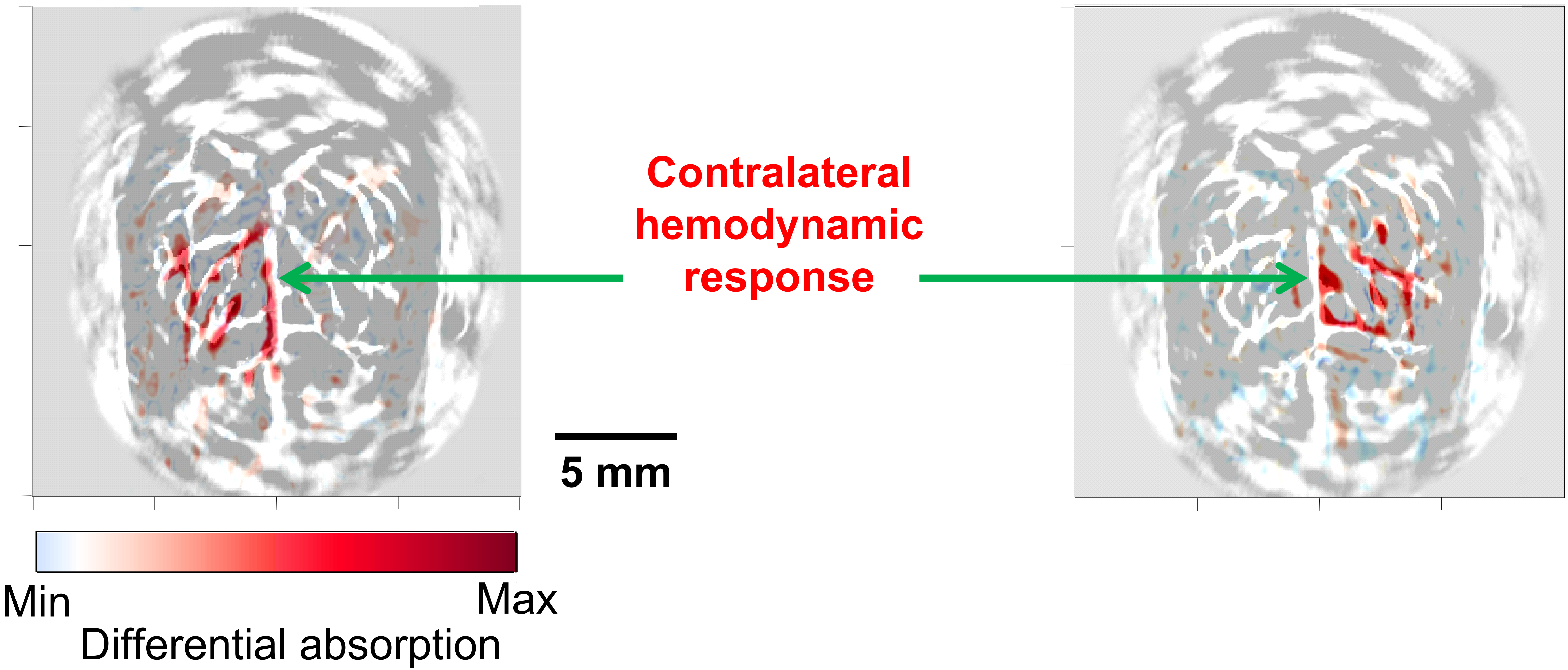
Inverse Spherical Radon Transformation: Universal Backprojection



M Xu, LV Wang, *Phys Rev E* 71, 016706, 2005
Y Xu, LV Wang, *Phys Rev Lett* 92, 033902, 2004

$$\underbrace{\boldsymbol{p}_0(\boldsymbol{r})}_{\text{Optical contrast}} = \frac{2}{\Omega_0}\int \left[\left(\underbrace{1}_{\text{Beam forming}} - \underbrace{t\frac{\partial}{\partial t}}_{\text{High-frequency filtering}}\right) p(\boldsymbol{r}_0, t)\right]_{\underbrace{t=\frac{|\mathbf{r}-\mathbf{r}_0|}{v_s}}_{\text{Delay}}} \underbrace{d\Omega_0}_{\text{Solid angle}}$$

First Functional (Also First *In Vivo*) Photoacoustic Tomography in Small Animals with Intact Scalp and Skull



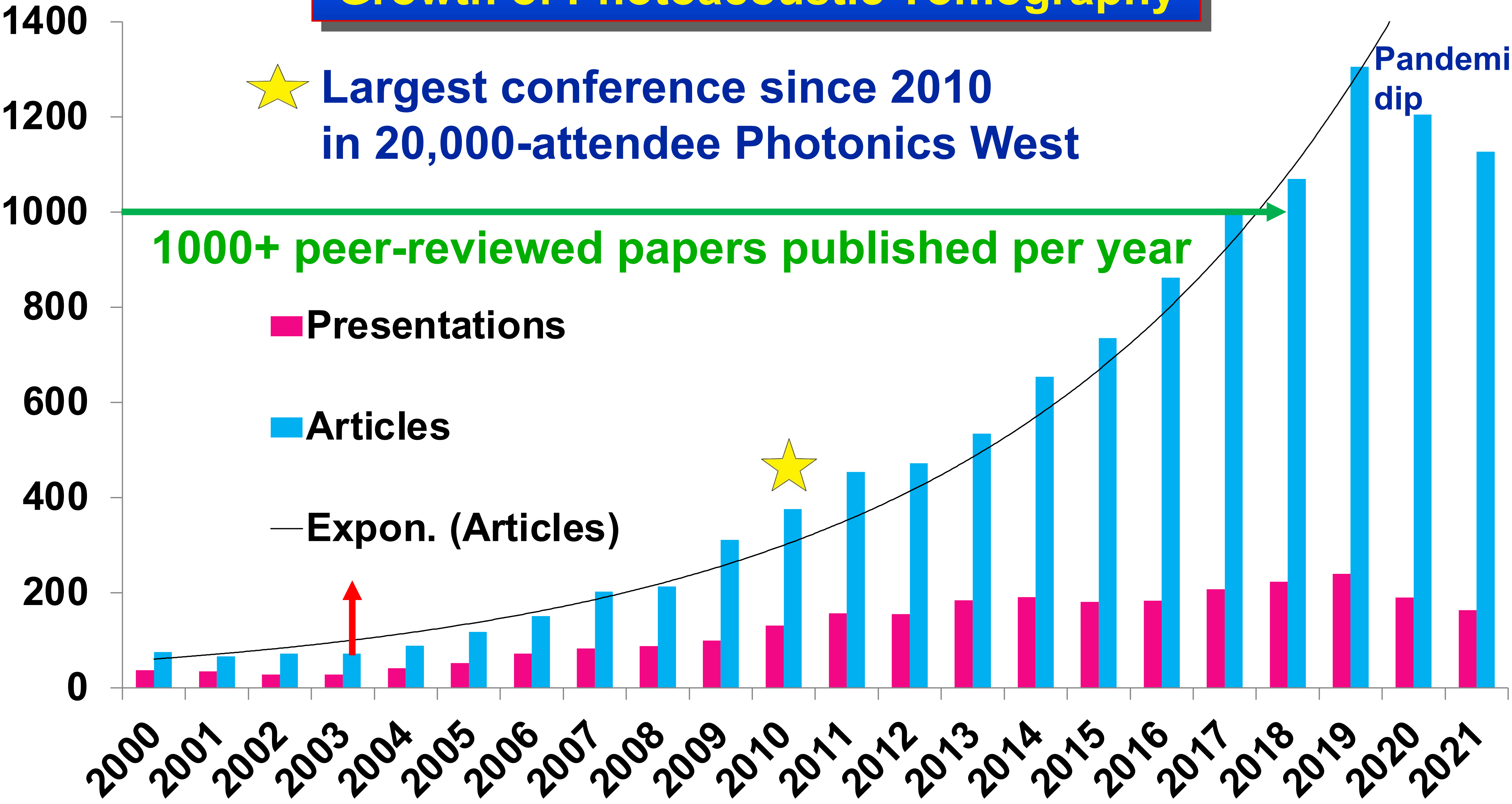
Left-whisker stimulation

Right-whisker stimulation

Contralateral hemodynamic response

X Wang, Y Pang, G Ku, G Stoica, LV Wang, *Nature Biotech* 21, 803, 2003

Growth of Photoacoustic Tomography



★ Largest conference since 2010 in 20,000-attendee Photonics West

1000+ peer-reviewed papers published per year

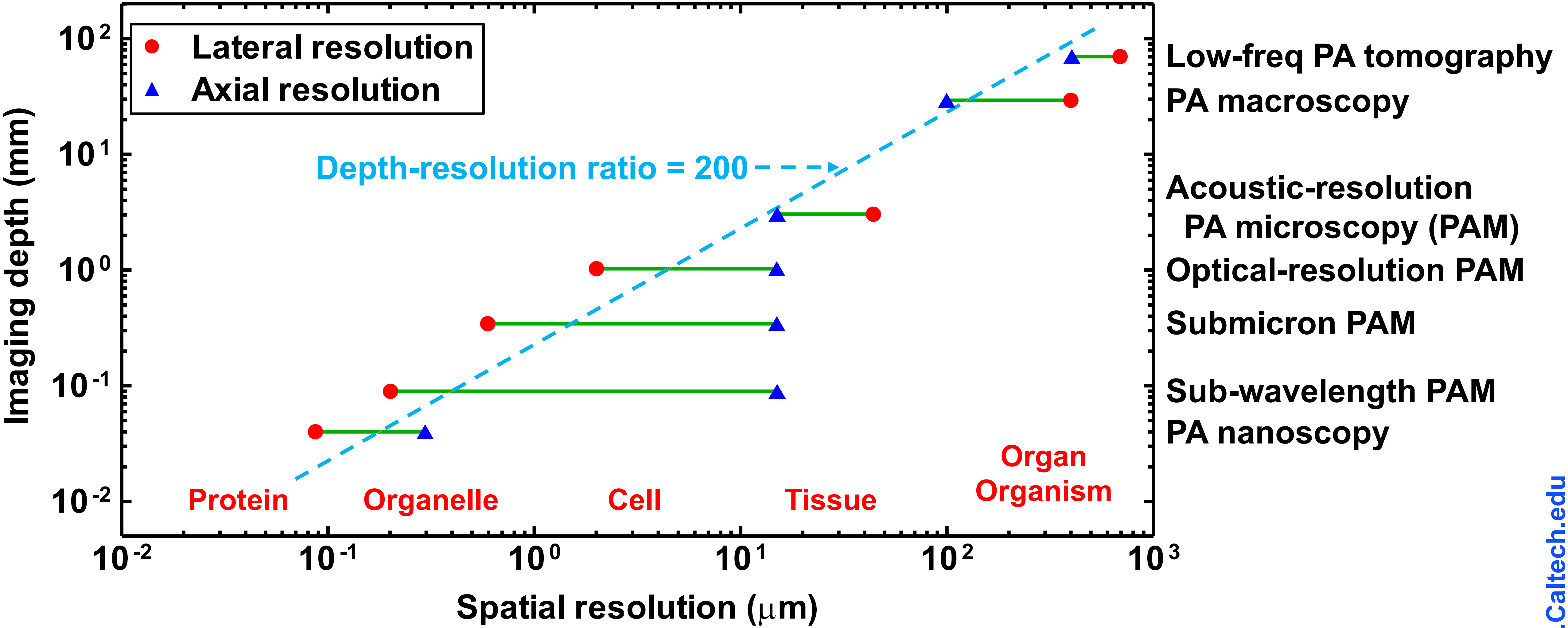
Pandemic dip

Commercialization of Photoacoustic Tomography

1. CalPACT [*e]
2. Canon
3. Cyberdyne
4. Endra [*c]
5. Fuji VisualSonics
6. illumiSonics
7. iThera (2021 CE mark approval)
8. Kibero
9. Luxonus (2023 Japanese PMDA approval)
10. MicroPhotoAcoustics [*e]
11. Mindray
12. OptoSonics
13. PA Imaging
14. PhotoSound
15. Photothermal Spectroscopy [*p]
16. PreXion
17. Seno Medical (2021 FDA approval) [*c]
18. TomoWave
19. Union Photoacoustic Technologies [*e]
20. Verasonics
21. Vibronix
22. Anonymous [*p]

[*c] Consultant, past
[*e] Equity & patent holder
[*p] Patent holder

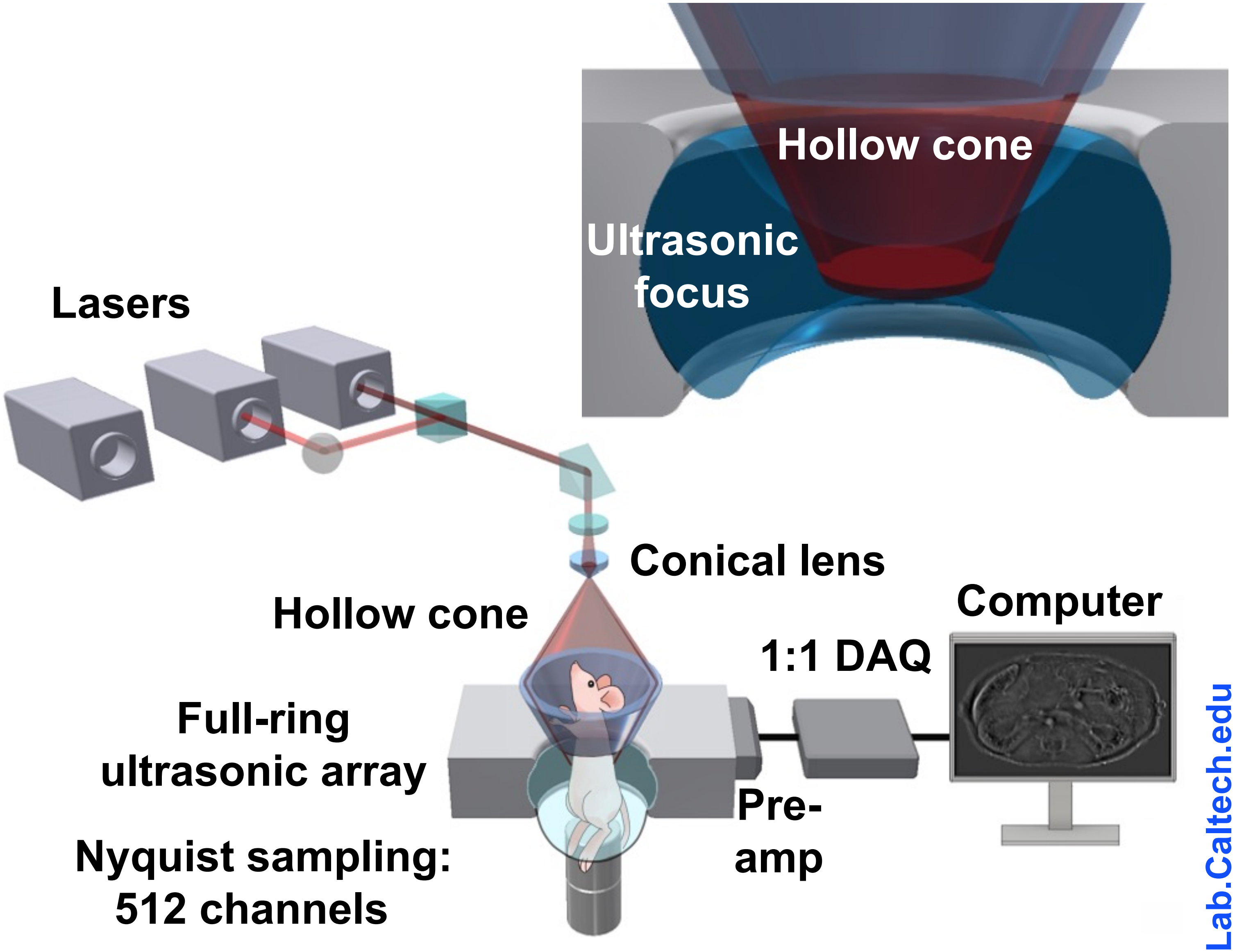
Omniscale *In Vivo* Photoacoustic (PA) Tomography with Consistent Contrast



- Omniscale biological research from organelles to small-animal organisms
- Translation of microscopic lab discoveries to macroscopic clinical practice

LV Wang, S Hu, *Science* 335, 1458, 2012; LV Wang, *Nature Photon* 3, 503, 2009

Single Impulse Panoramic Photoacoustic Computed Tomography



Hollow cone

Ultrasonic focus

Lasers

Conical lens

Computer

Hollow cone

1:1 DAQ

Full-ring ultrasonic array

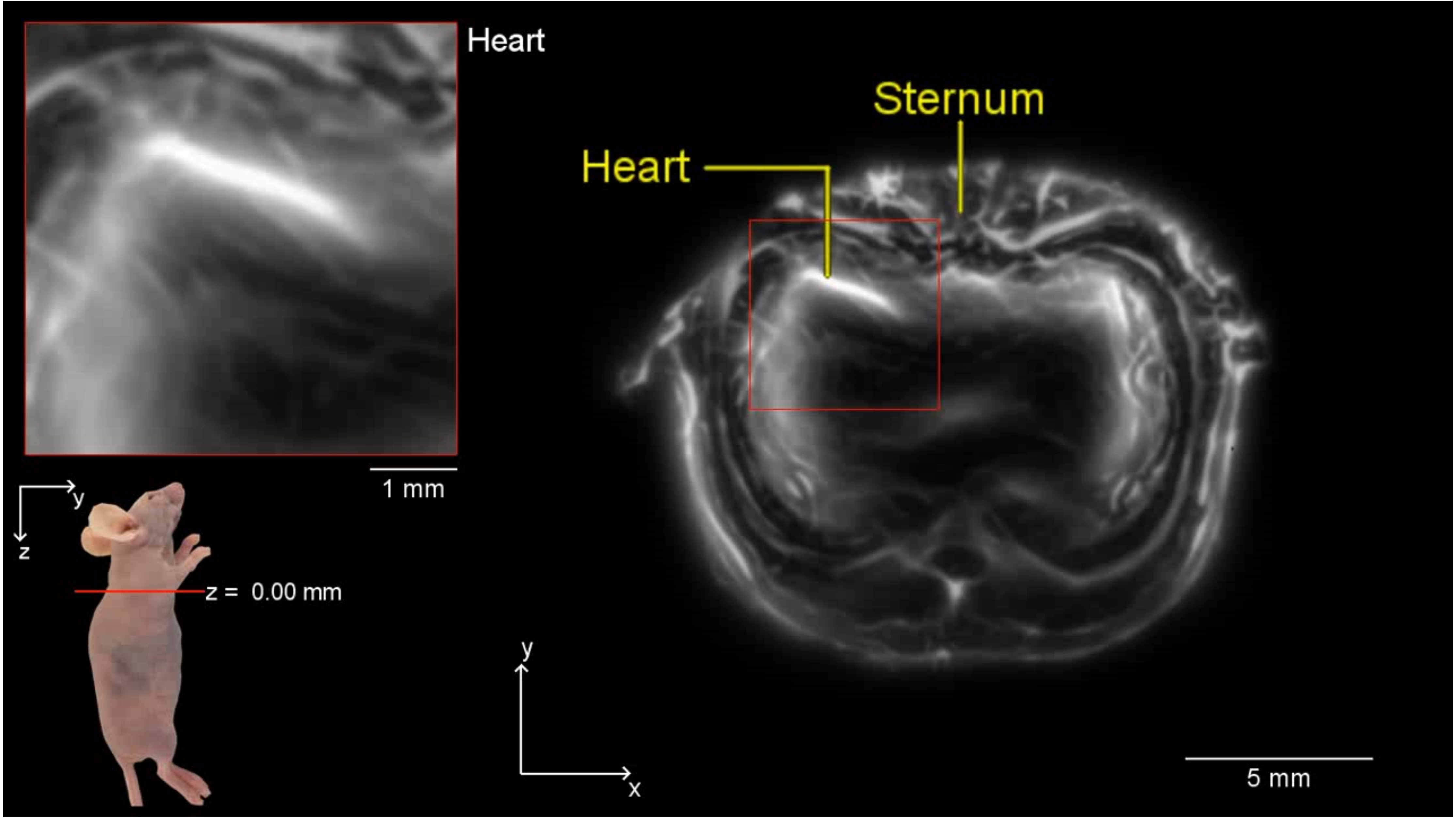
Pre-amp

Nyquist sampling: 512 channels

Trunk imaging

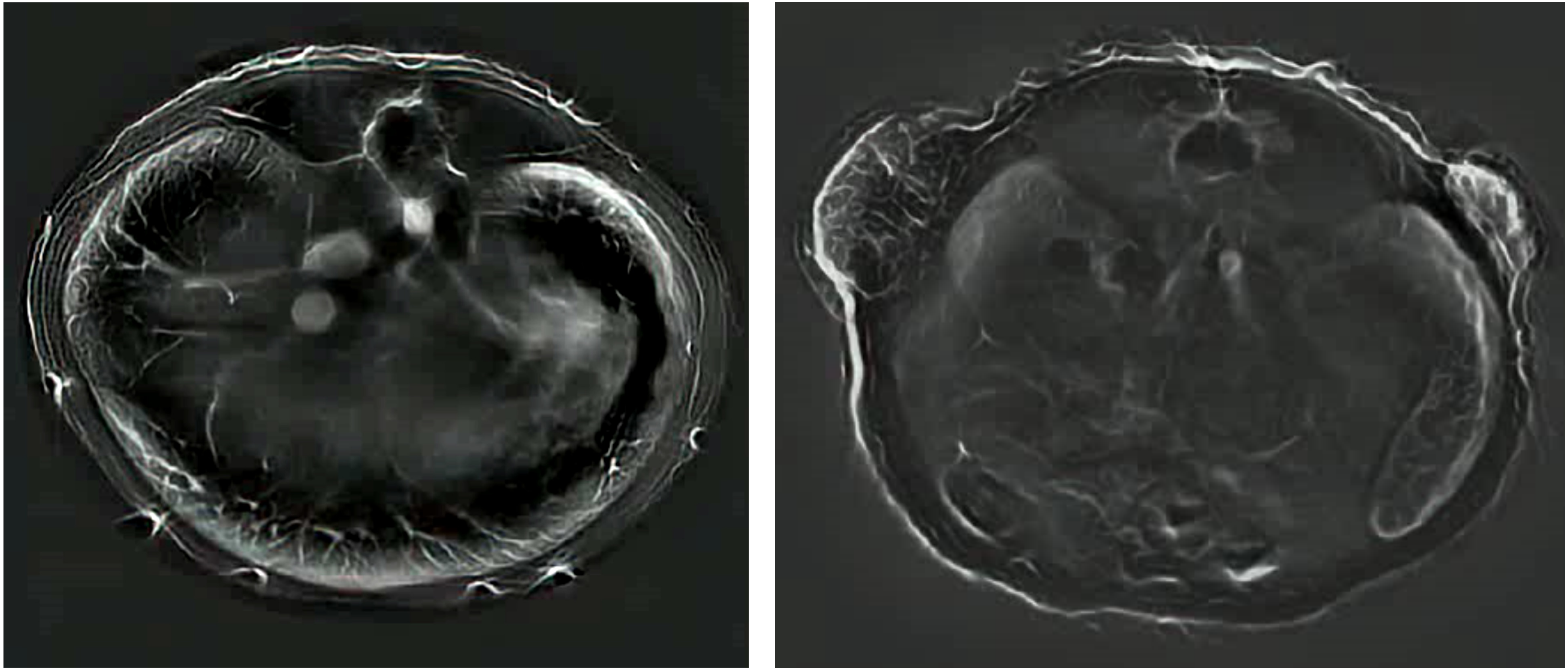
[L Li, LR Zhu, C Ma, L Lin], JJ Yao, LD Wang, K Maslov, RY Zhang, WY Chen, JH Shi, LV Wang, *Nature BME* 1, 0071, 2017

50 Hz Frame-Rate Whole-Body Photoacoustic CT of Mice *In Vivo*



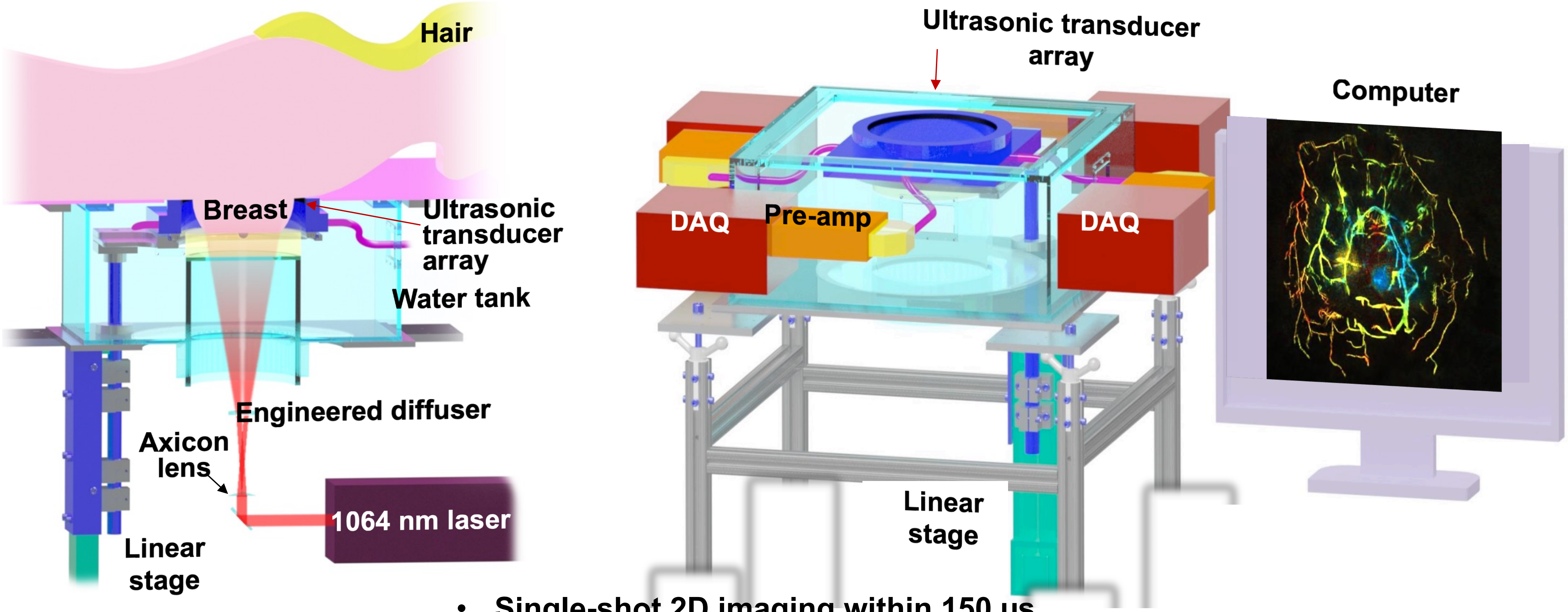
[L Li, LR Zhu, C Ma, L Lin], JJ Yao, LD Wang, K Maslov, RY Zhang, WY Chen, JH Shi, LV Wang, *Nature BME* 1, 0071, 2017

Commercialized Whole-Body Photoacoustic Computed Tomography System



CalPACT, LLC and Union Photoacoustic Technologies, Ltd.; Conflict of Interest

Single Breath-Hold Panoramic Photoacoustic Computed Tomography of Human Breasts: Schematic of the Equipment

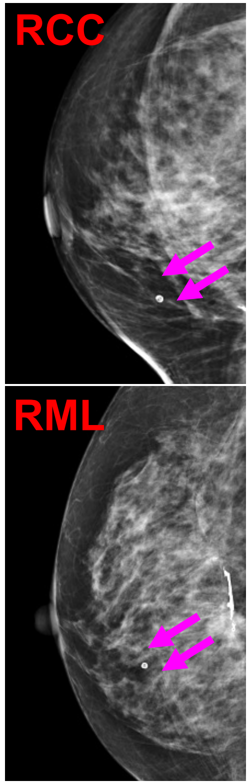


- Single-shot 2D imaging within 150 μs
- Single-breath-hold 3D imaging within 15 s
- Smallest imaged-vessel diameter of 258 μm
- One-way penetration of ~4 cm

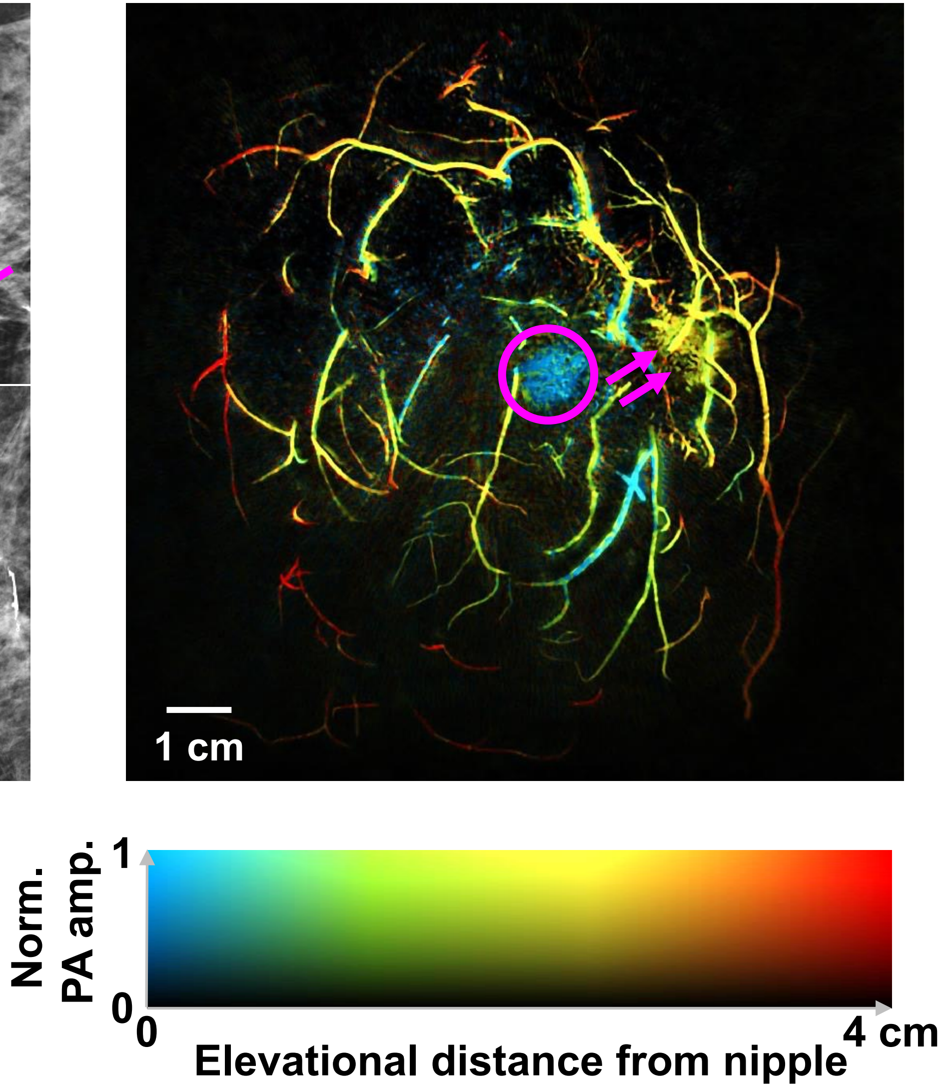
[L Lin, P Hu, J Shi], CM Appleton@WUSTL, K Maslov, L Li, R Zhang, LV Wang, *Nature Comm* 9, 2352, 2018

Photoacoustic Tomo/Elastography of a Radiographically Dense Human Breast

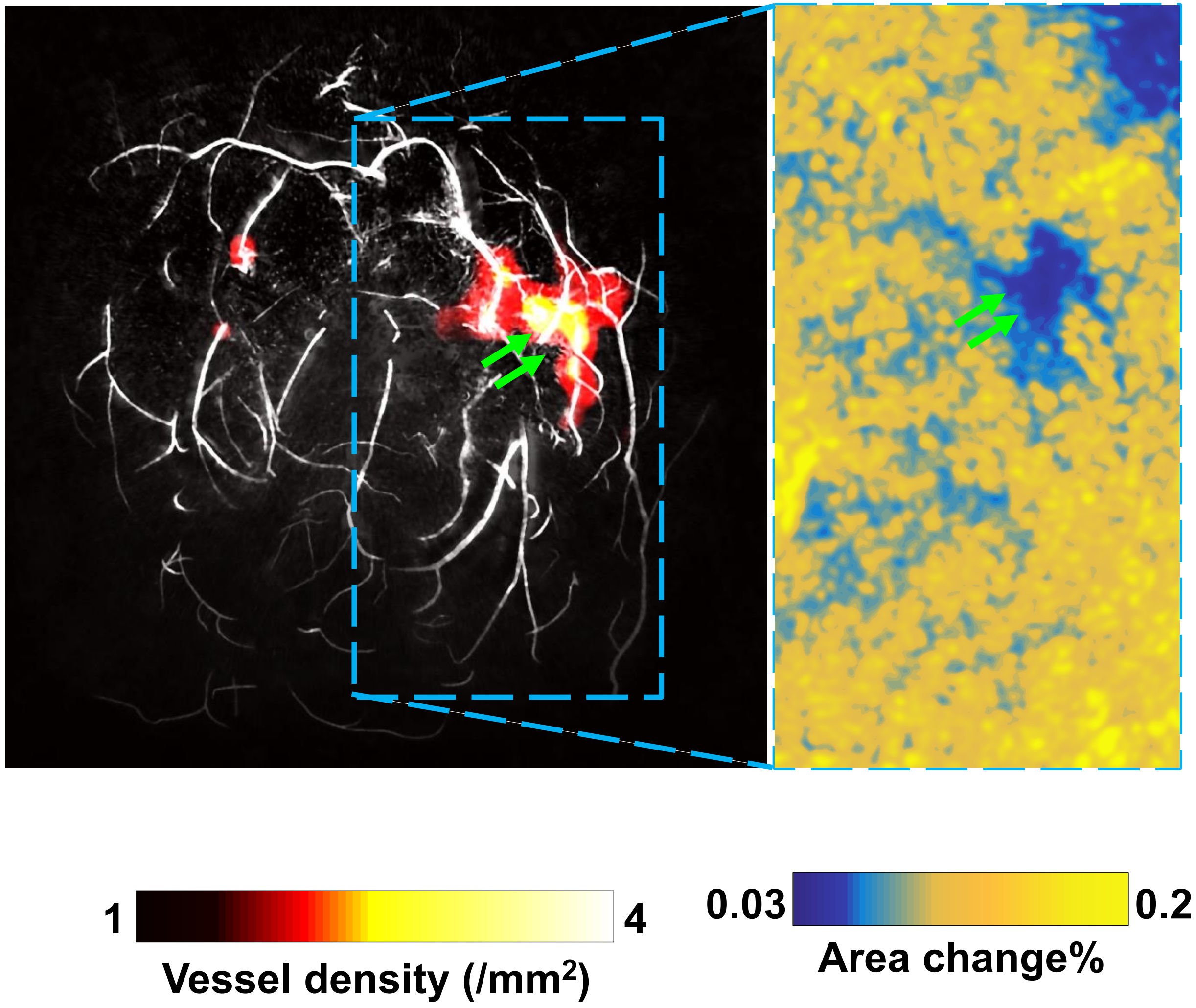
X-ray mammograms



Patient 6 (Invasive ductal carcinoma, age 69)



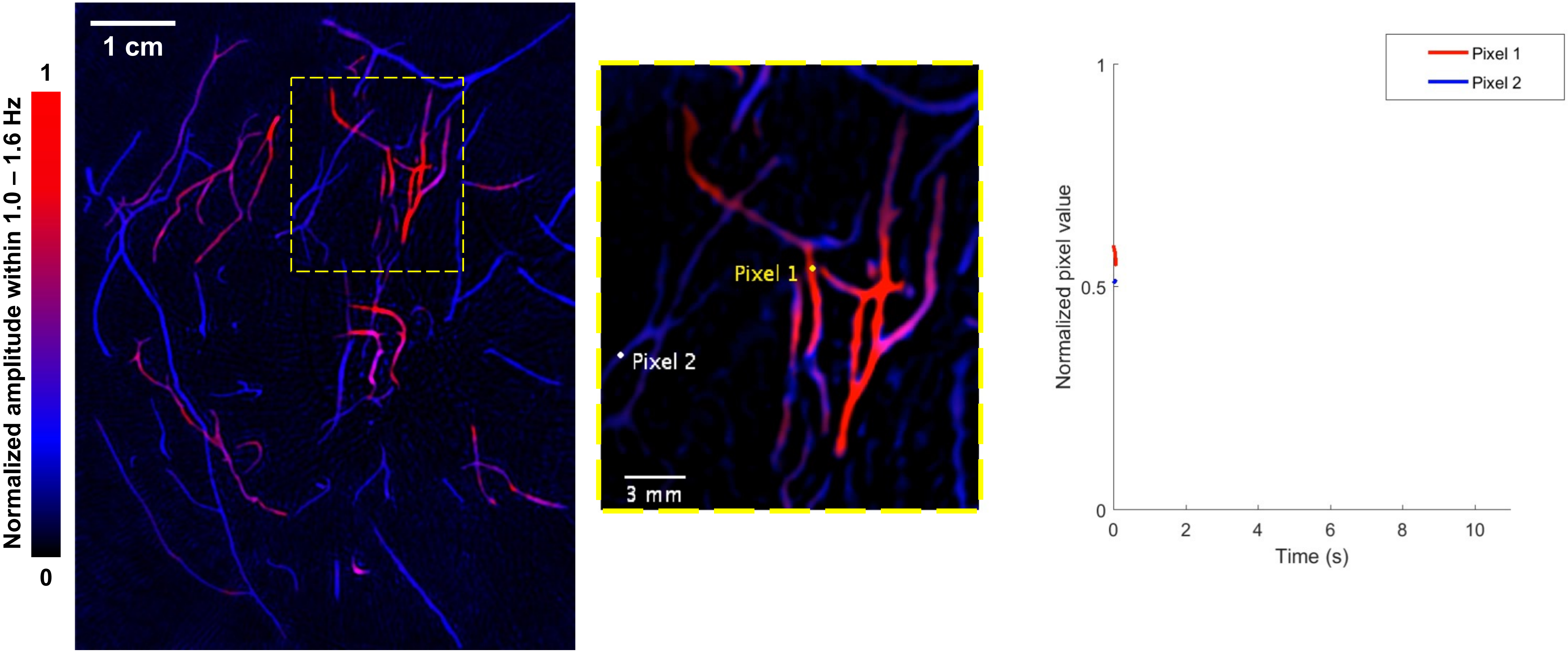
Elastography



[L Lin, P Hu, J Shi], CM Appleton@WUSTL, K Maslov, L Li, R Zhang, LV Wang, *Nature Comm* 9, 2352, 2018

Arterial and Venous Photoacoustic Mapping in Human Breasts

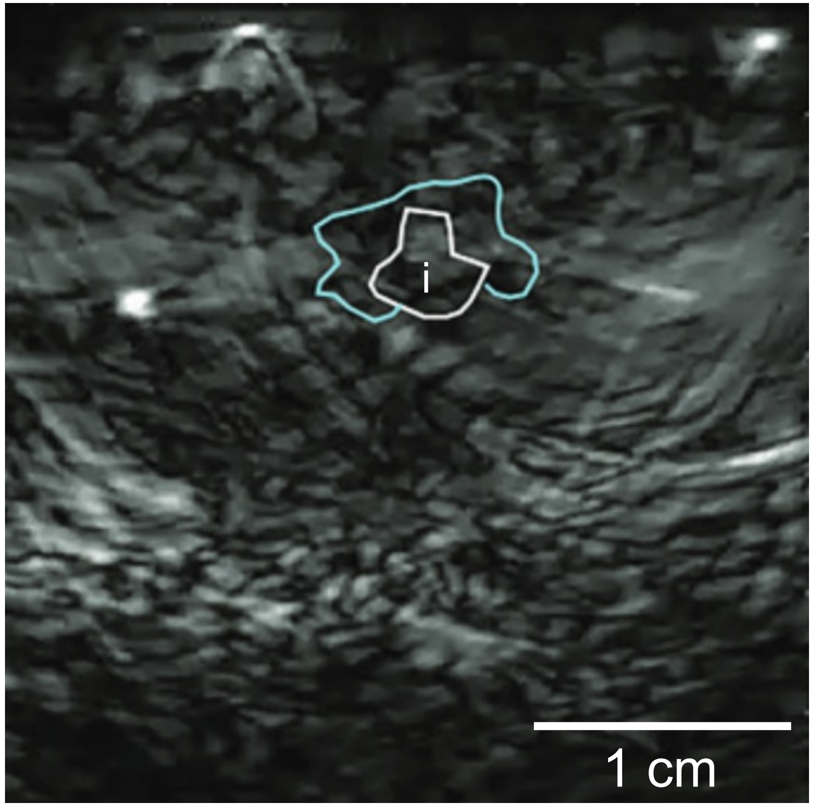
Heartbeat encoded arterial network



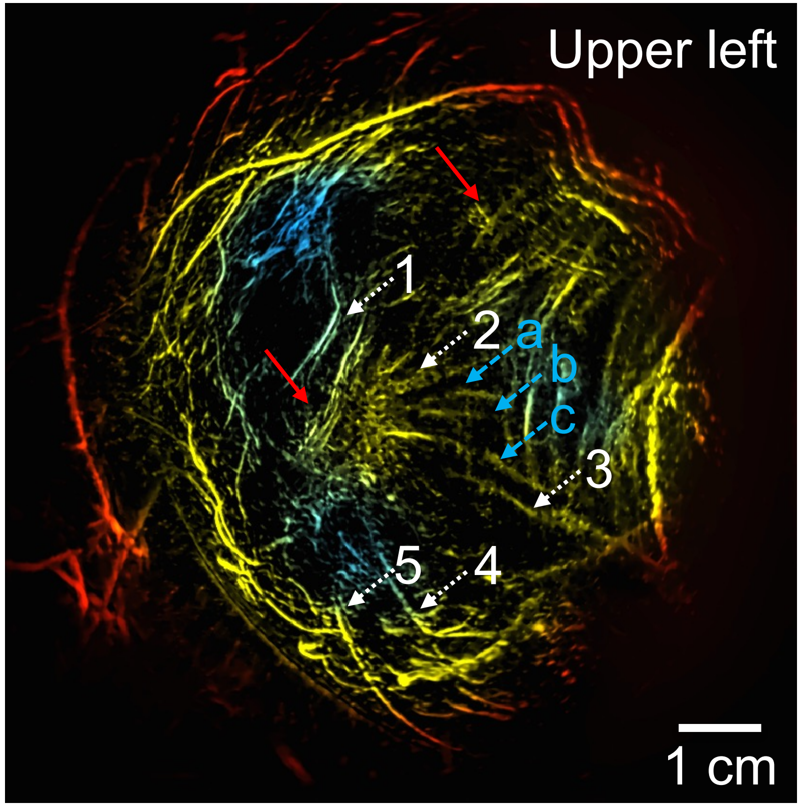
[L Lin, P Hu, J Shi], CM Appleton@WUSTL, K Maslov, L Li, R Zhang, LV Wang, *Nature Comm* 9, 2352, 2018

Label-Free Photoacoustic Imaging vs Gadolinium-Contrast MRI

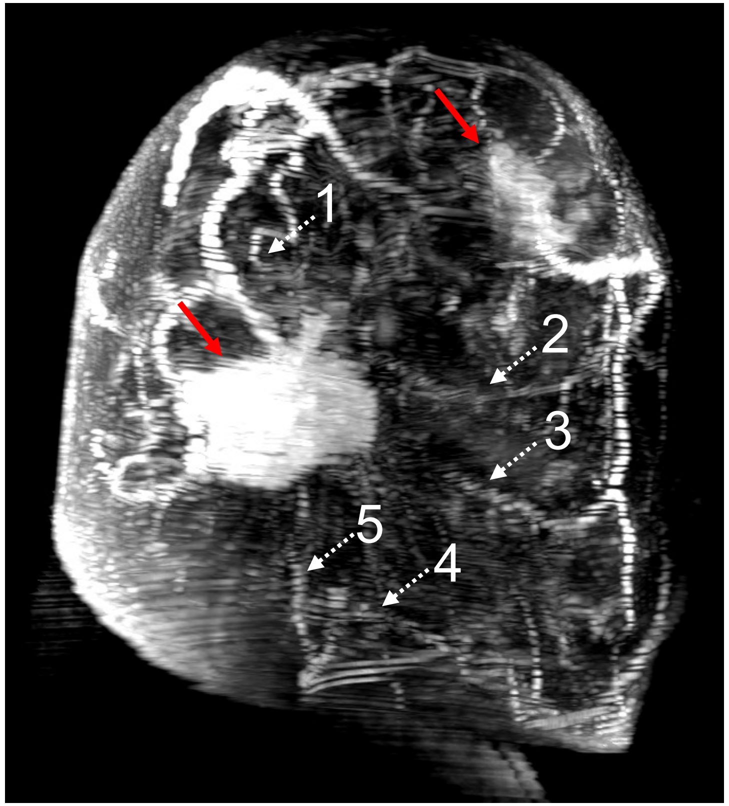
FDA-approved PAT



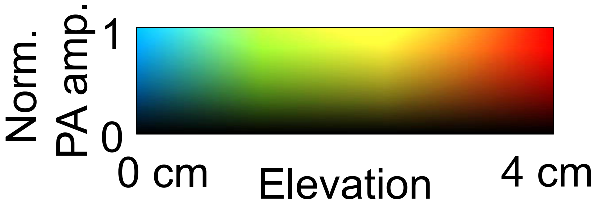
Caltech label-free PACT



Gadolinium-contrast MRI

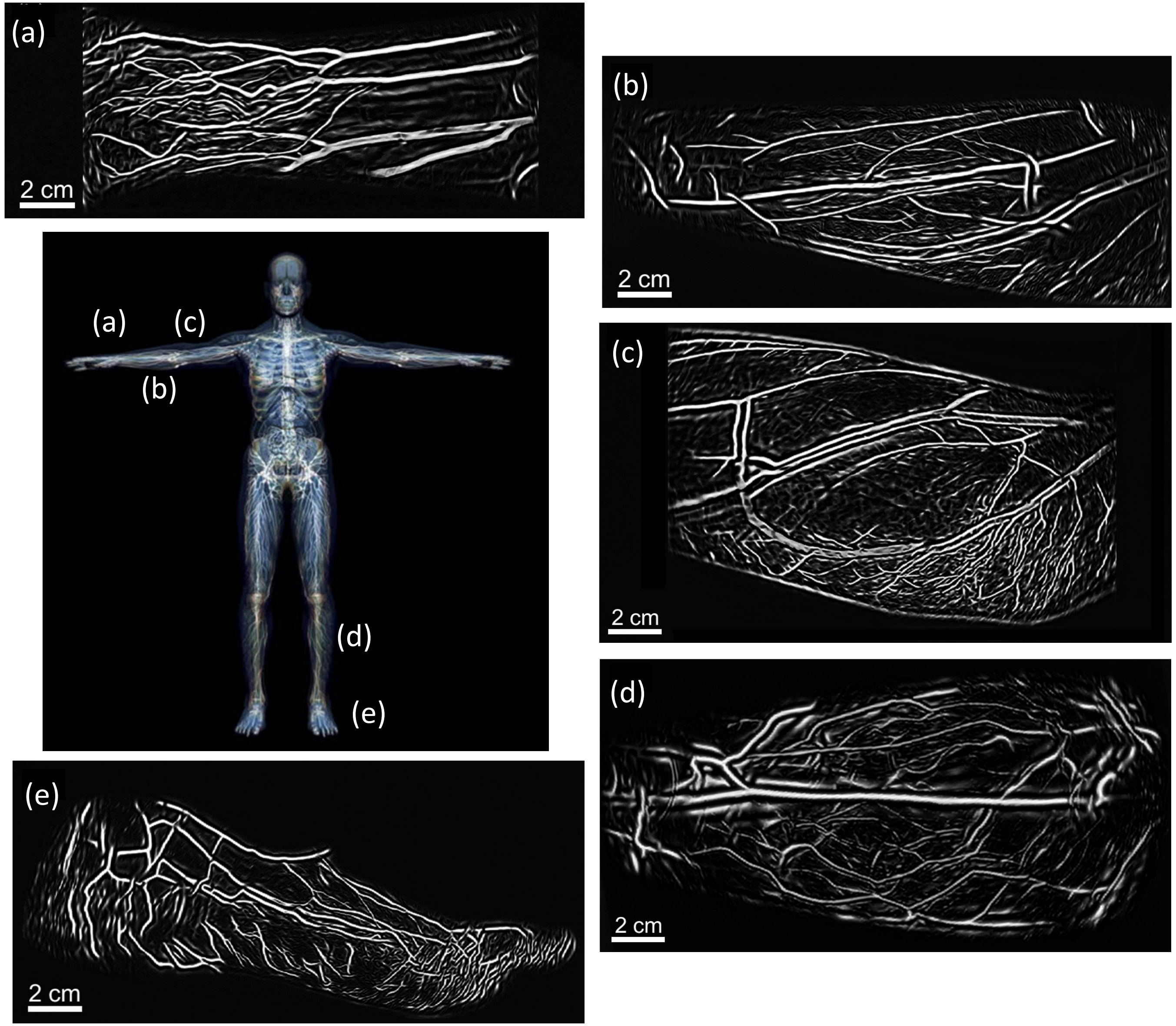


- **Solid arrows: tumors**
- **1–5: vessels detected by both PACT and MRI**
- **a–c: vessels detected by PACT only**



Left: EI Neuschler, R Butler, CA Young, LD Barke, ML Bertrand, M Böhm-Vélez, ..., BE Dogan, Radiology (2018).
Xin Tong, Li Lin, Yilin Luo, Peng Hu, [Armine Kasabyan, Marta Invernizzi, Lily Lai, Lisa Yee]@COH, LV Wang, *unpublished*

Photoacoustic Imaging of Human Extremities: Arm and Leg

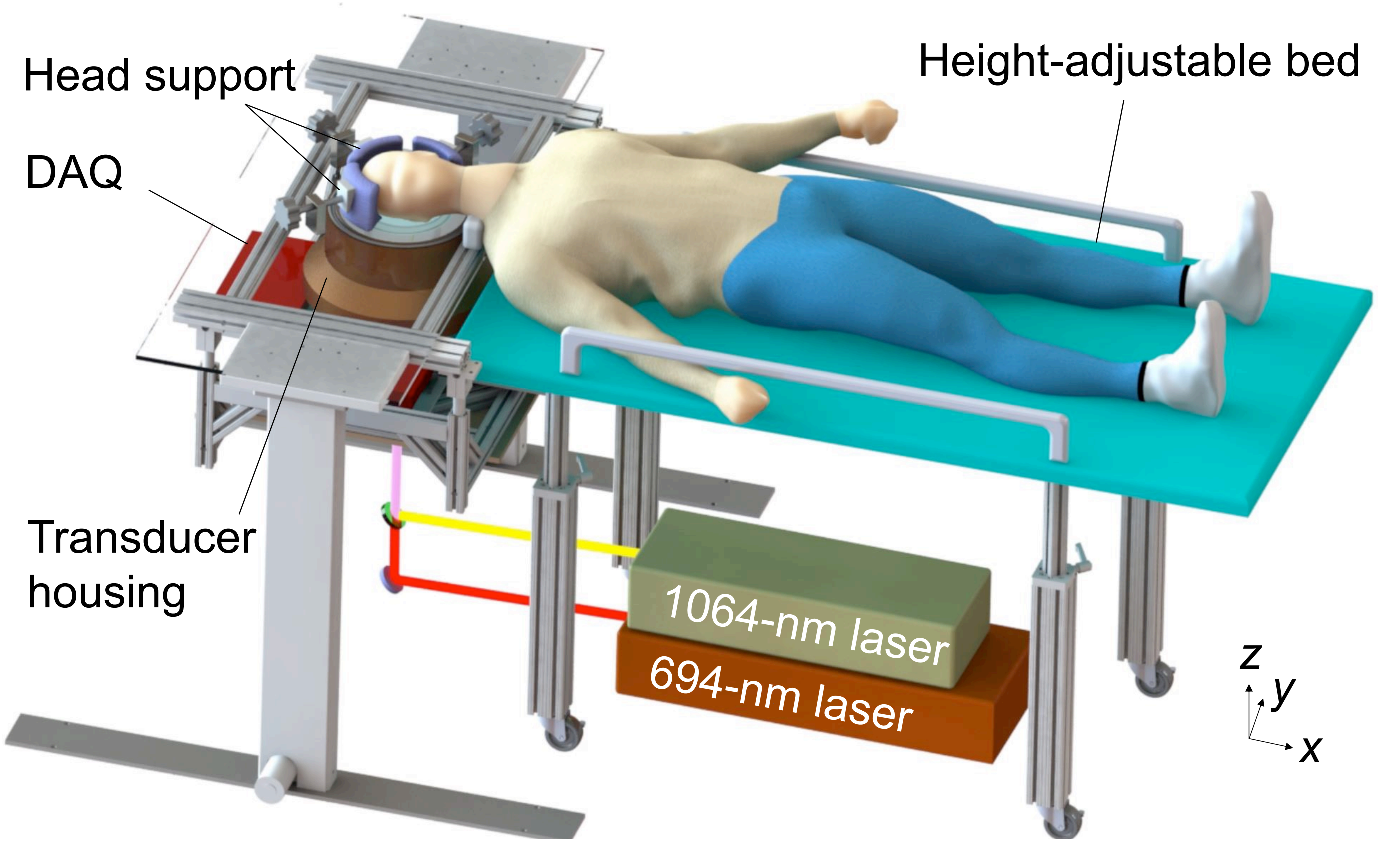


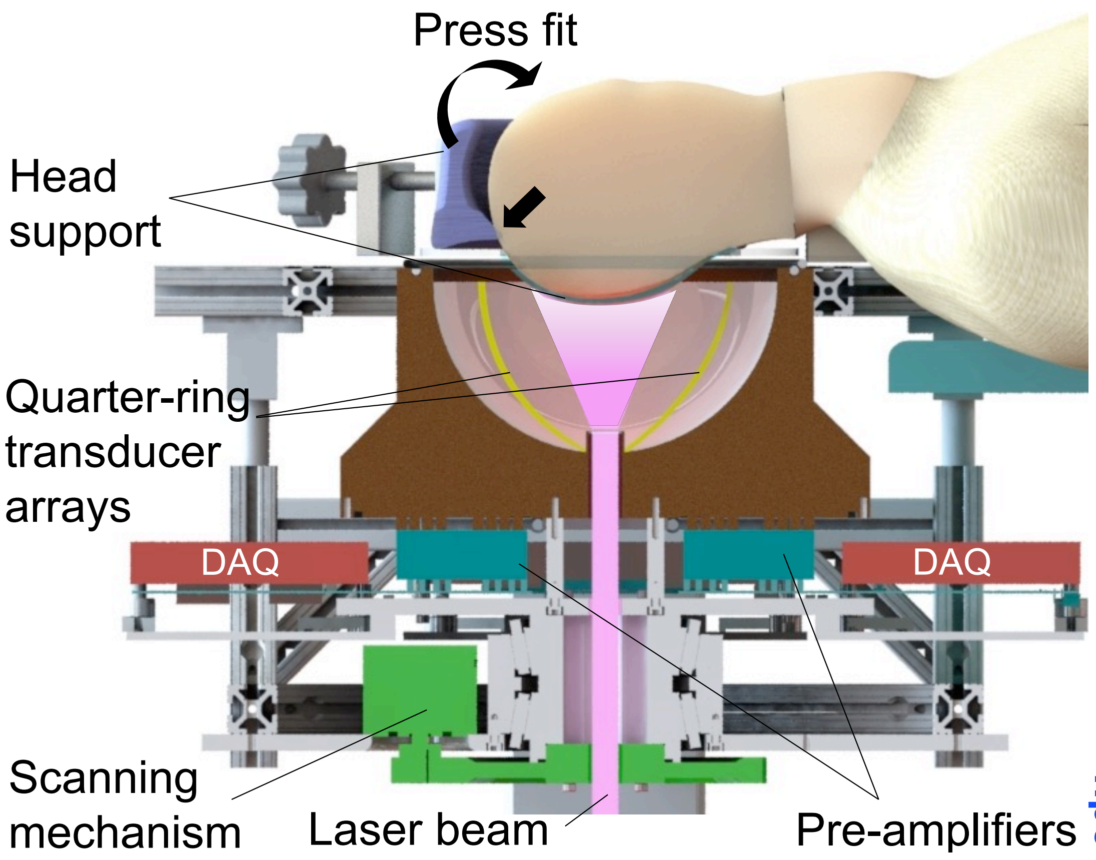
Potential applications

- **Screen/diagnose diabetic foot**
- **Diagnose vascular obstructions**
- **Assist in vascular surgery**
- **Monitor postop revascularization surgery**
- **Monitor perfusion**

P Wray, L Lin, P Hu, LV Wang, *J Biomed Opt* 24, 026003, 2019

Human Breast/Brain Photoacoustic Tomography

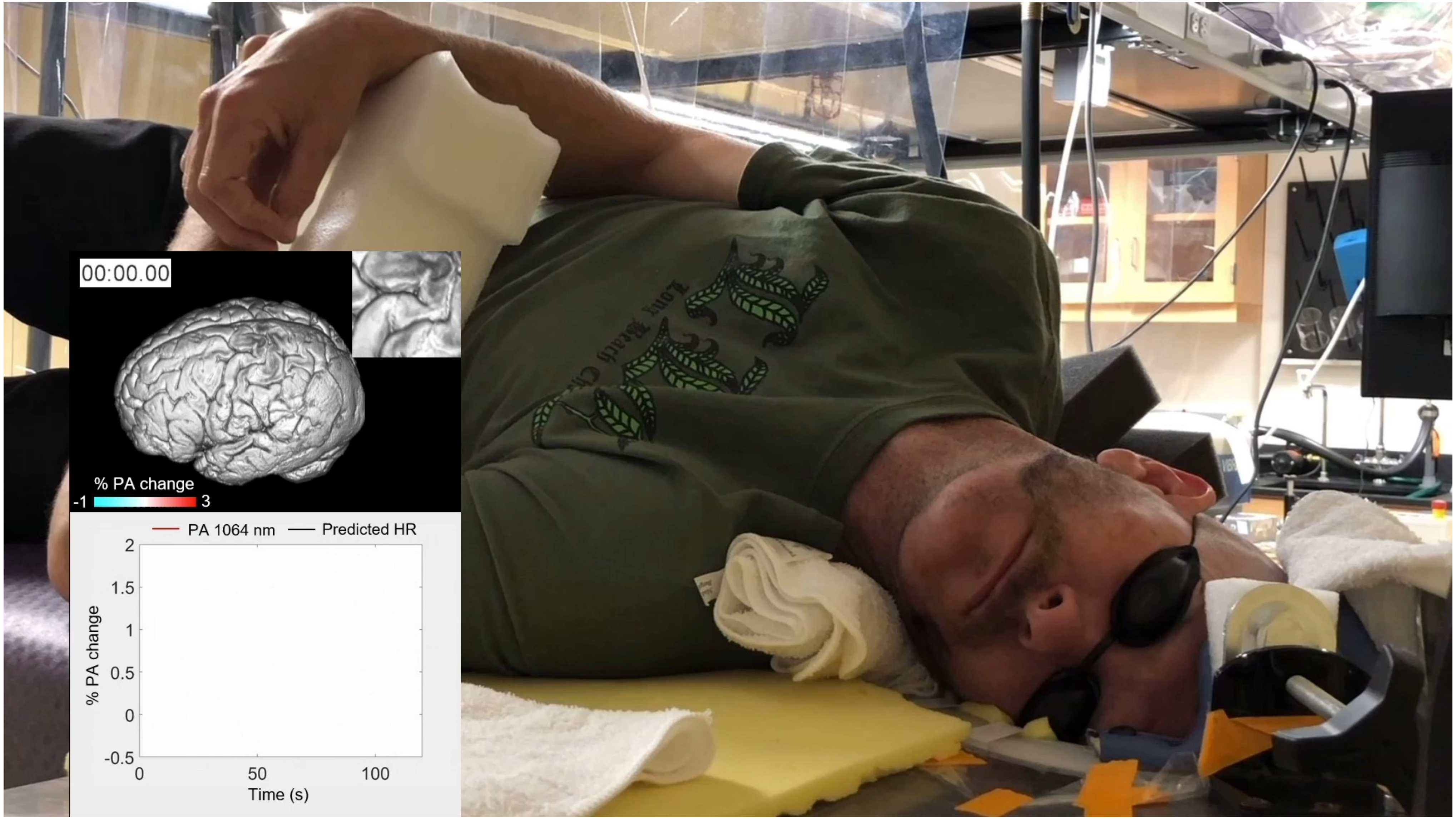




- **1024 ultrasonic channels**
  - **Anatomic mode (10 s 3D)**
  - **Function mode (2 s 3D)**
- **Dual laser wavelengths**
  - **1064 nm, 10 Hz (HbO_2 dominant)**
  - **694 nm, 1 Hz (HbR dominant)**

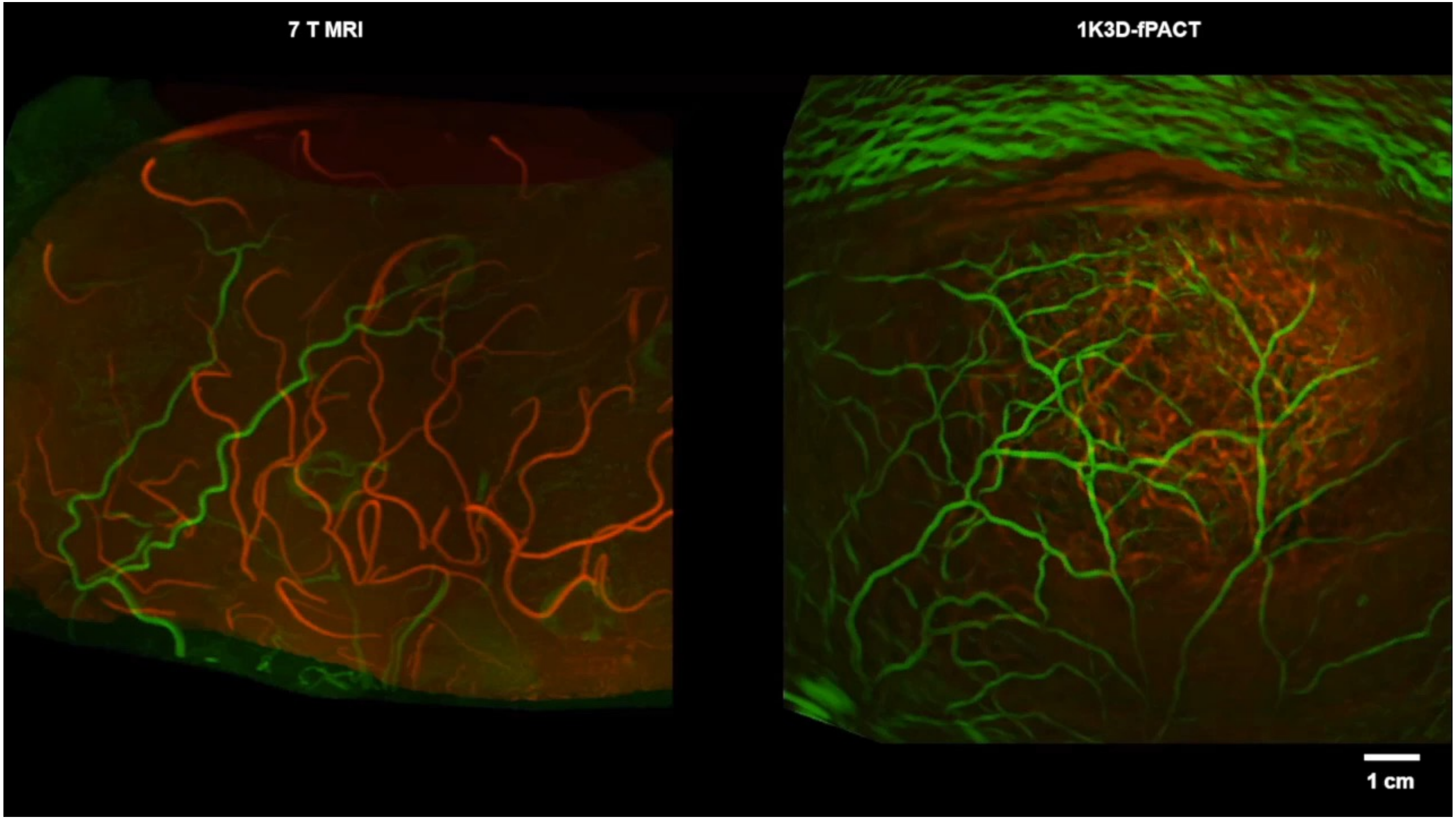
[S Na, J Russin, L Lin, X Yuan], P Hu, KB Jann, L Yan, K Maslov, J Shi, DJ Wang, CY Liu@USC, LV Wang, *Nature BME, 2021* (https://doi.org/10.1038/s41551-021-00735-8)

First Functional Photoacoustic Tomography of Human Brains



[S Na, J Russin, L Lin, X Yuan], P Hu, KB Jann, L Yan, K Maslov, J Shi, DJ Wang, CY Liu@USC, LV Wang, *Nature BME* 6, 584, 2022

First Functional Photoacoustic Tomography vs 7-T fMRI of Human Brains



[S Na, J Russin, L Lin, X Yuan], P Hu, KB Jann, L Yan, K Maslov, J Shi, DJ Wang, CY Liu@USC, LV Wang, *Nature BME* 6, 584, 2022

Functional PACT vs fMRI of Cortical Human Brains

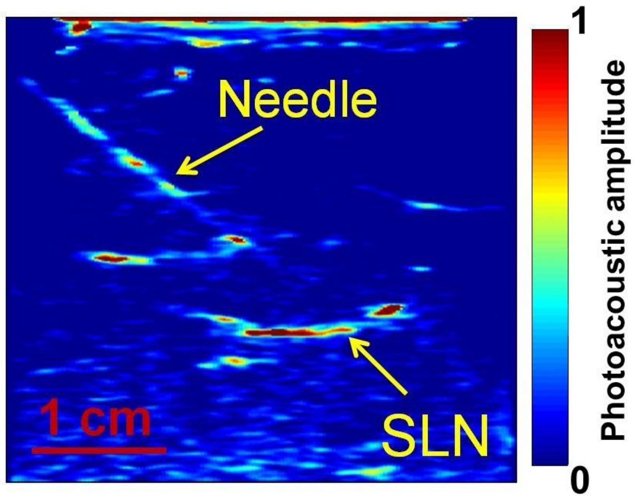
	fPACT	fMRI
Contrast	HbR, HbO_2, [sO_2, HbT]	HbR
Response time	sO_2: 6.5 ± 0.6 s; HbT: 6.1 ± 0.7 s	BOLD: 7.8 ± 0.6 s
Background	Low	High
Linearity	Yes	No
Portability	Yes	No
Platform	Open	Closed
Acoustic noise	Low	High
Cost	Lower	High ($10M + $150K/year)
Magnet	No	Yes

HbR: deoxyhemoglobin; HbO_2: oxyhemoglobin
HbT: total hemoglobin; sO_2: O_2 saturation
BOLD: blood oxygenation-level dependent signal

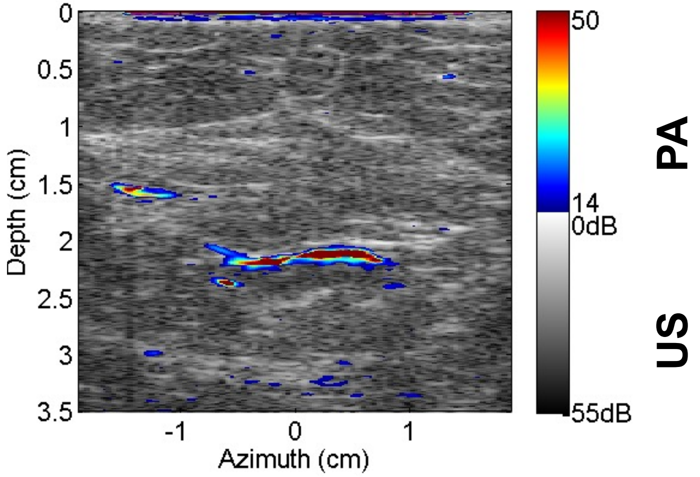
In Vivo Photoacoustic Tomography of Sentinel Lymph Node (SLN) in Humans for Breast Cancer Staging

Concept

Photoacoustic



Photoacoustic + Ultrasonic

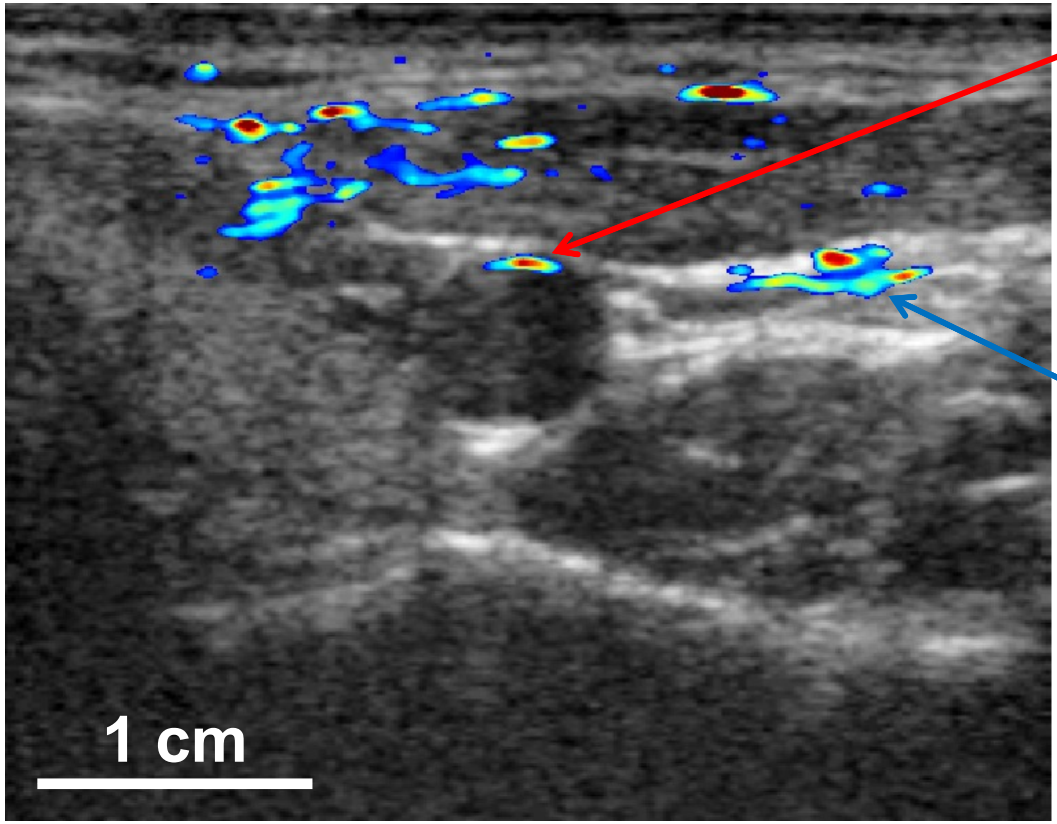


1. Inject dye into the breast
2. Image the SLN with optical contrast from the dye
3. Sample the SLN by photoacoustically guided needle biopsy
4. Examine the specimens for cancer

A Garcia-Uribe, T Erpelding@Philips, K Maslov, C Appleton, J Margenthaler, LV Wang, *Sci Rep* 5, 15748, 2015

In Vivo Functional Photoacoustic Imaging of Oxygen Saturation (sO_2) in Humans Co-Registered with Ultrasonic Imaging

Photoacoustic + ultrasonic imaging

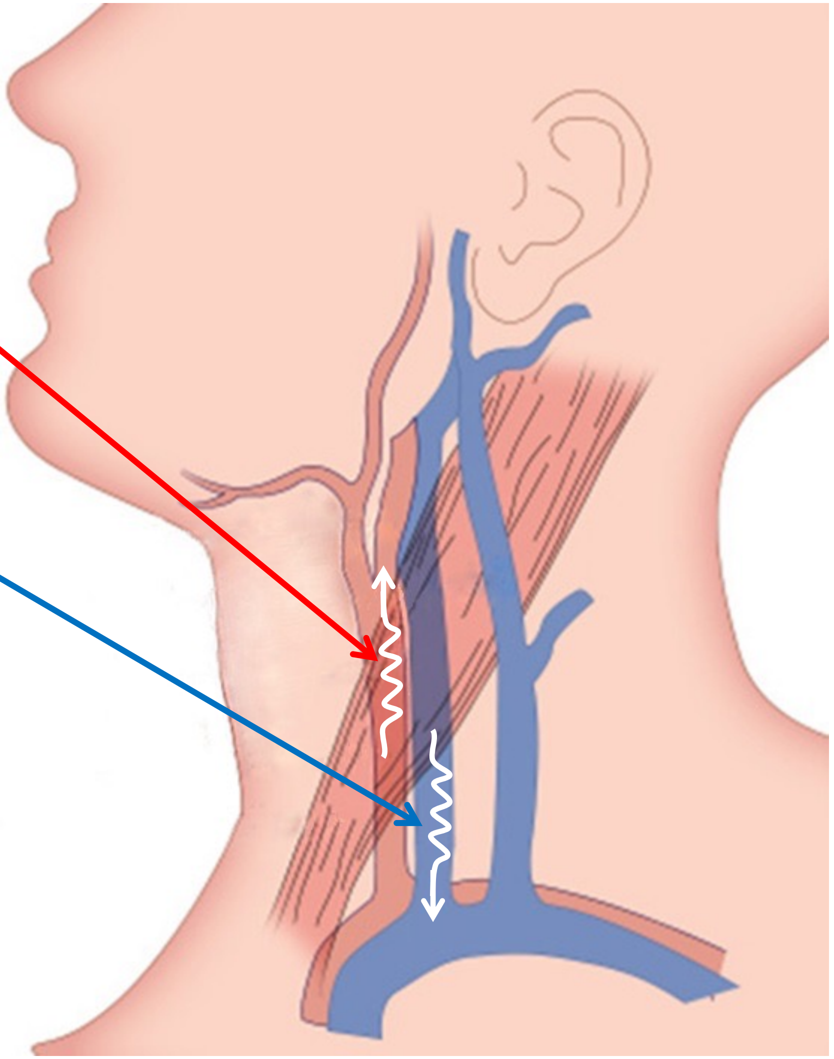


Common carotid artery: 96%

Internal jugular vein: 66%

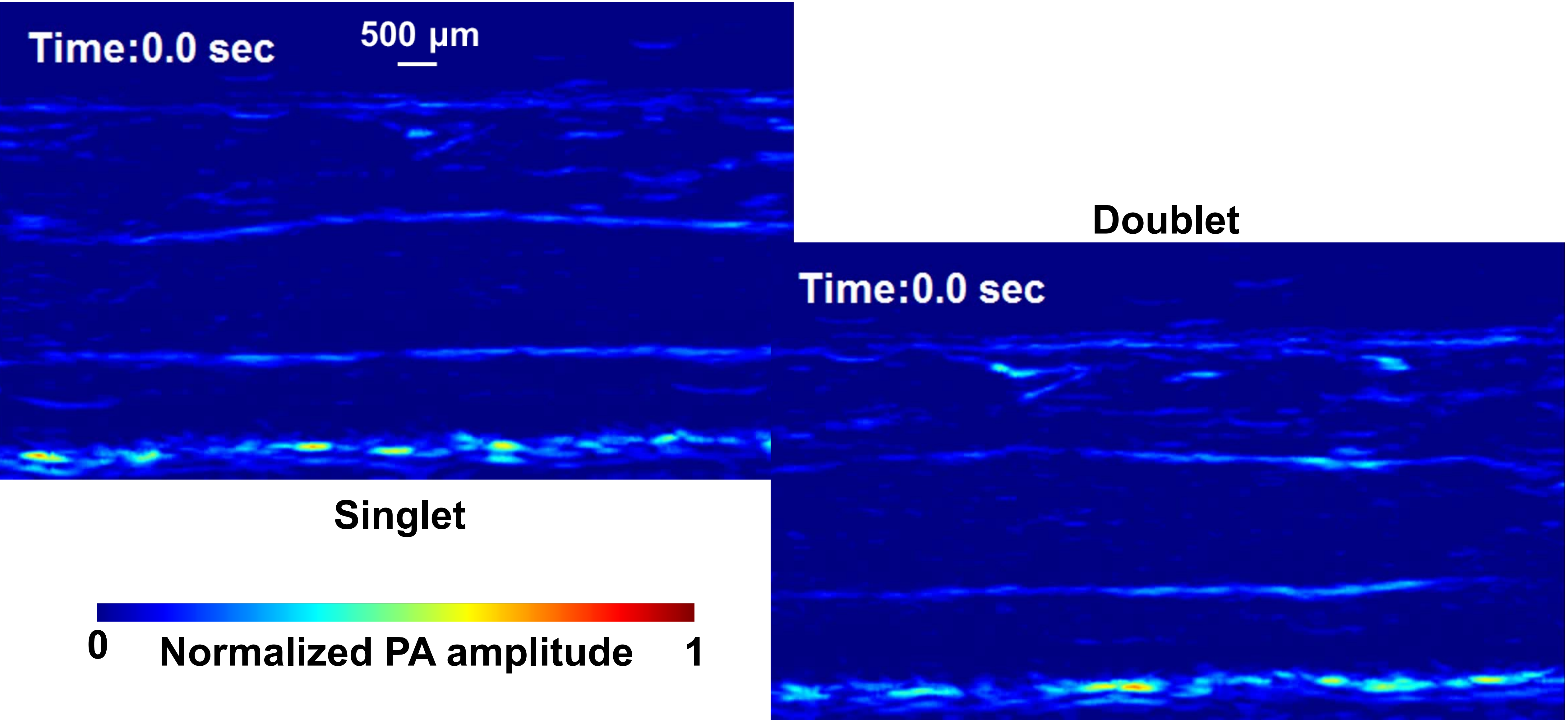
Average (N = 7): 72% ± 7%

Normal: 60%-75%



A Garcia-Uribe, T Erpelding@Philips, [K Reddy, A Sharma]@WUSTL, LV Wang, *arXiv* 2303.10775, 2023

In Vivo Photoacoustic Microscopy of Single Circulating Tumor Cells in Humans

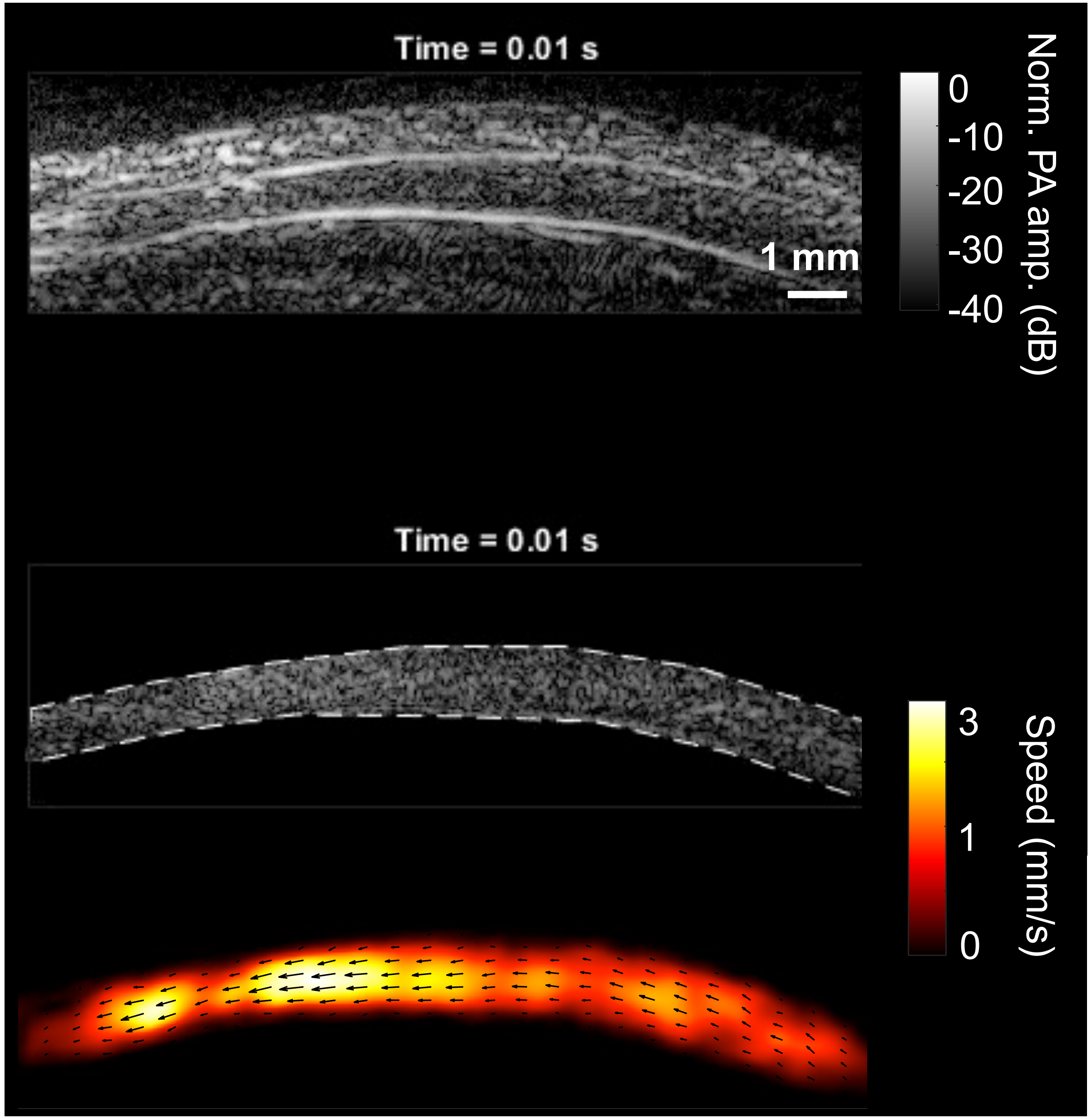


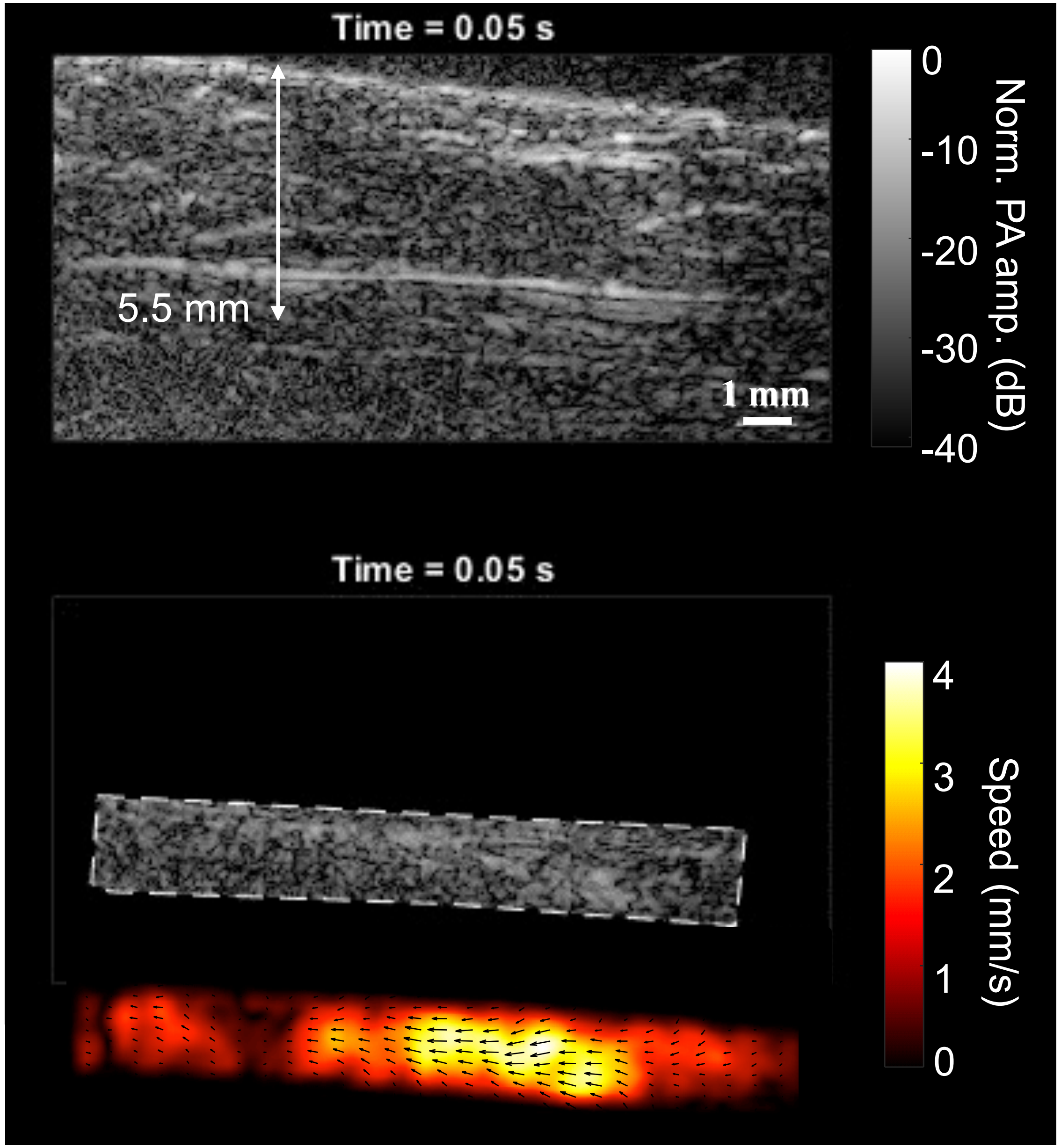
Singlet

Doublet

PF Hai, Y Qu, Y Li, L Zhu, L Shmuylovich, L Cornelius@WUSTL, LV Wang,
***J Biomed Optics* 25, 036002, 2020**

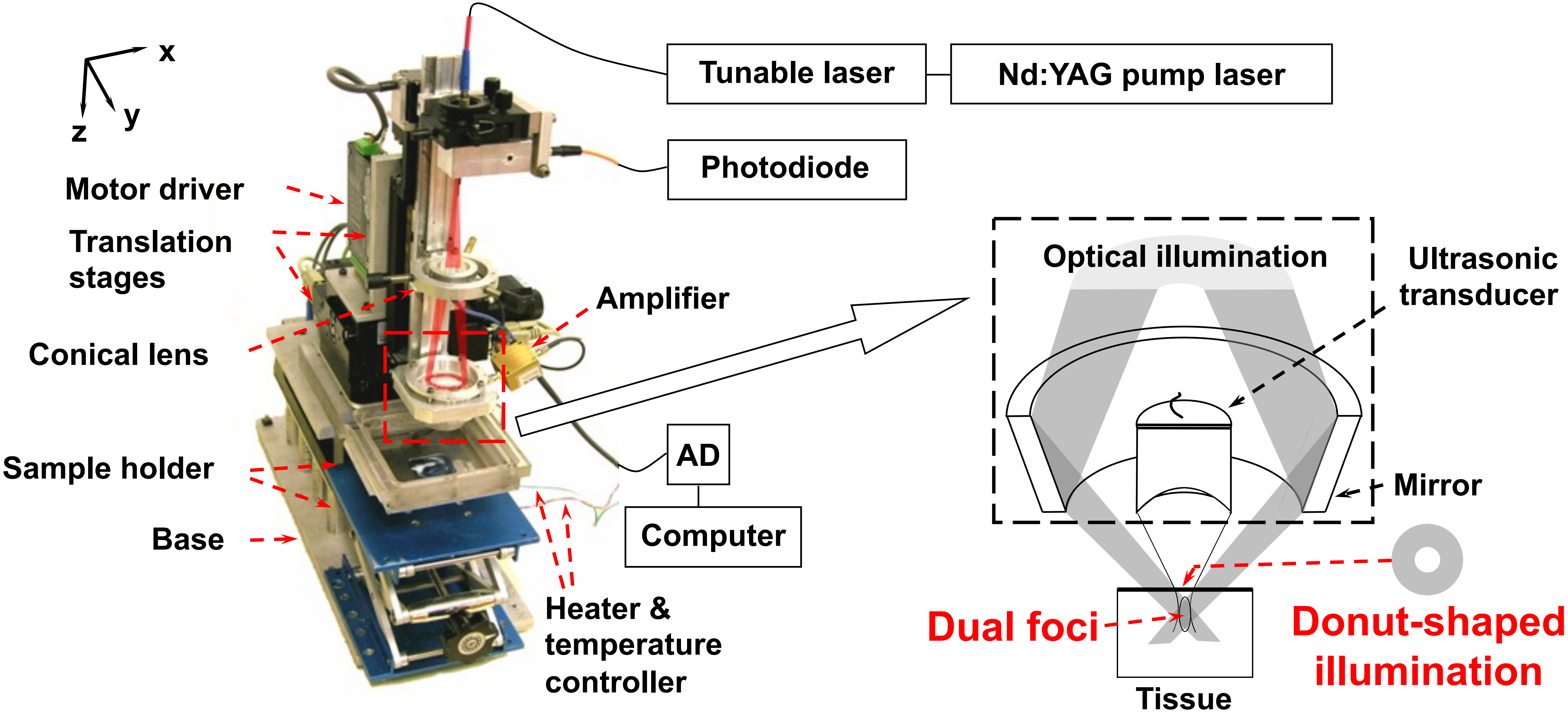
In Vivo Human Photoacoustic Vector Tomography Beyond Optical Diffusion Limit





[Y Zhang, J Olick-Gibson], A Khadria, LV Wang, Nature Biomedical Engineering, in press

First 3D Photoacoustic Microscope



K Maslov, G Stoica, LV Wang, *Optics Lett* 30, 625, 2005

H Zhang, K Maslov, G Stoica, LV Wang, *Nature Biotech* 24, 848, 2006; *Nature Protoc* 2, 797, 2007

Wave of Single-Impulse–Stimulated Single-Vessel Response in Mouse Brains

Loop 1

532 & 558 nm wavelengths

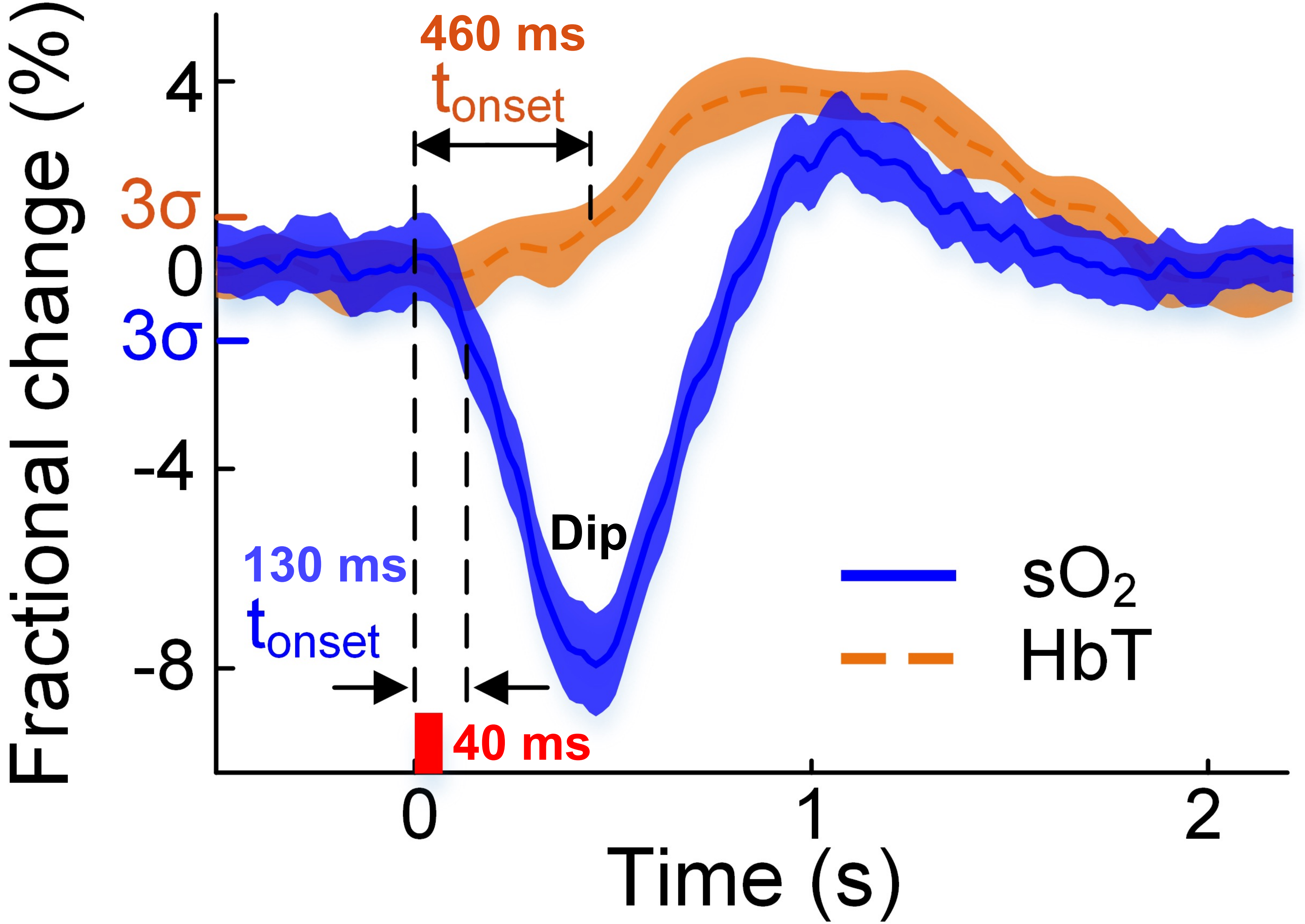
1 MHz 1D imaging rate

sO_2: oxygen saturation of hemoglobin

HbT: total concentration of hemoglobin

Y He, J Shi, K Maslov, R Cao, LV Wang, *J Biomed Optics* 25, 066501, 2020

Single-Impulse–Stimulated Fast Initial Dip in Single Capillaries of Mouse Brains

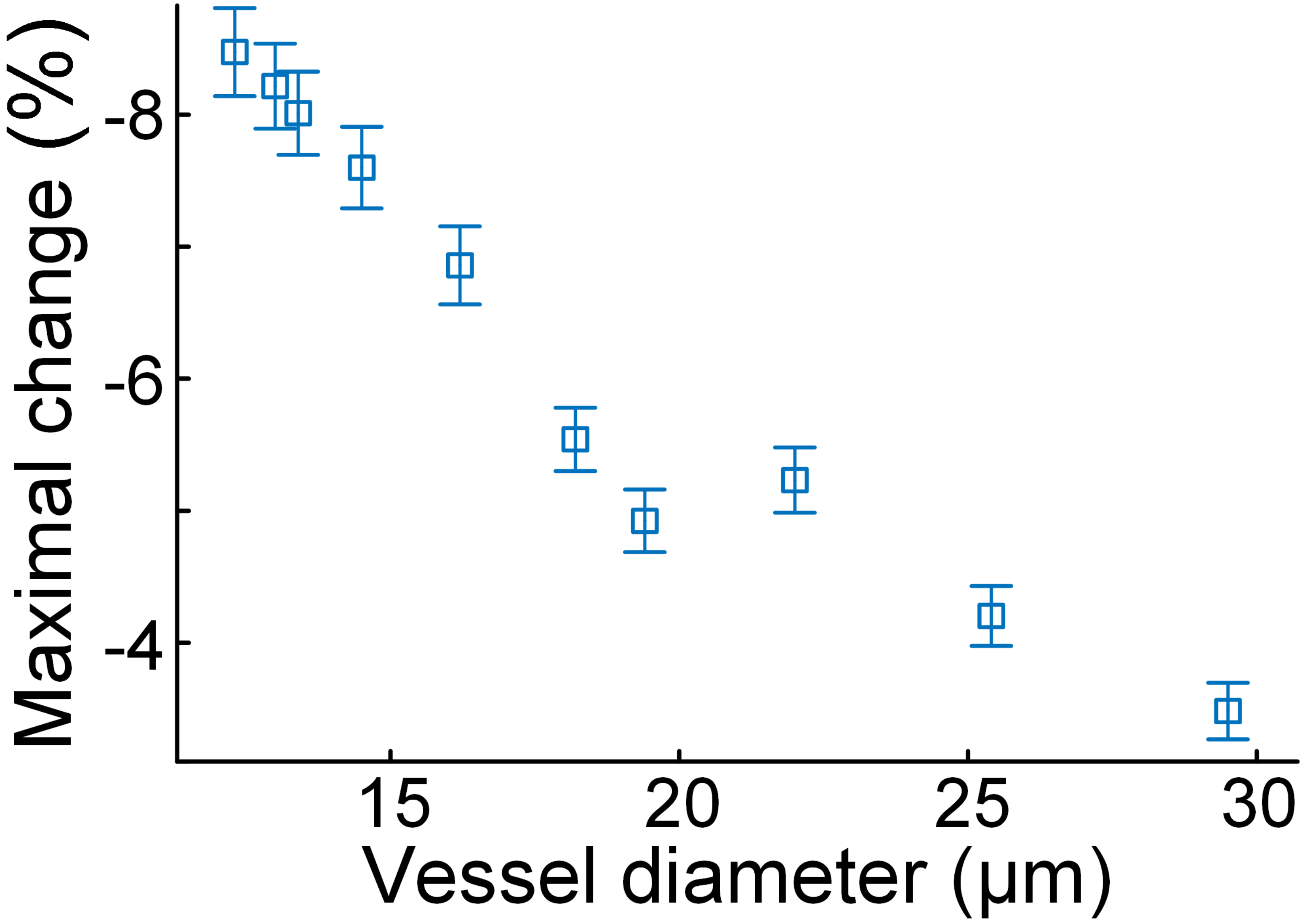


sO_2: oxygen saturation of hemoglobin

HbT: total concentration of hemoglobin

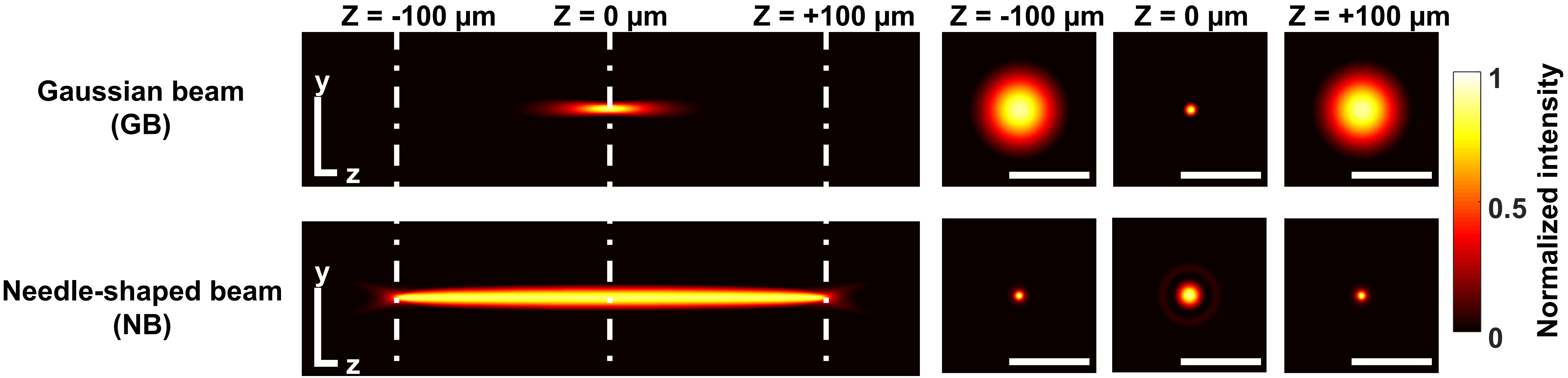
Y He, J Shi, K Maslov, R Cao, LV Wang, *J Biomed Optics* 25, 066501, 2020

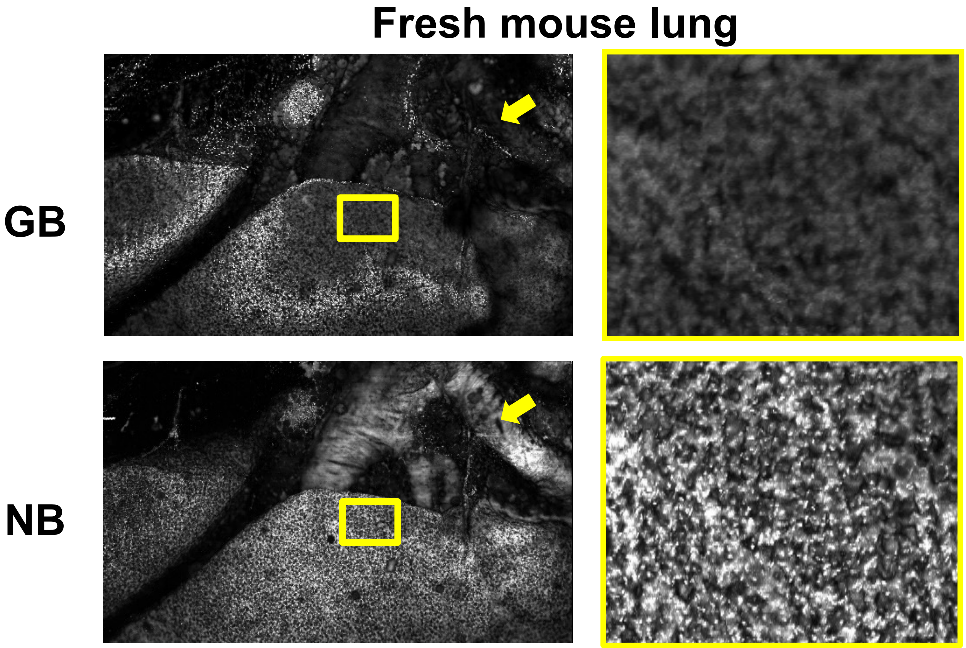
Single-Impulse–Stimulated Fast Initial Dip in Single Vessels of Mouse Brains: Dependence on Vessel Diameter

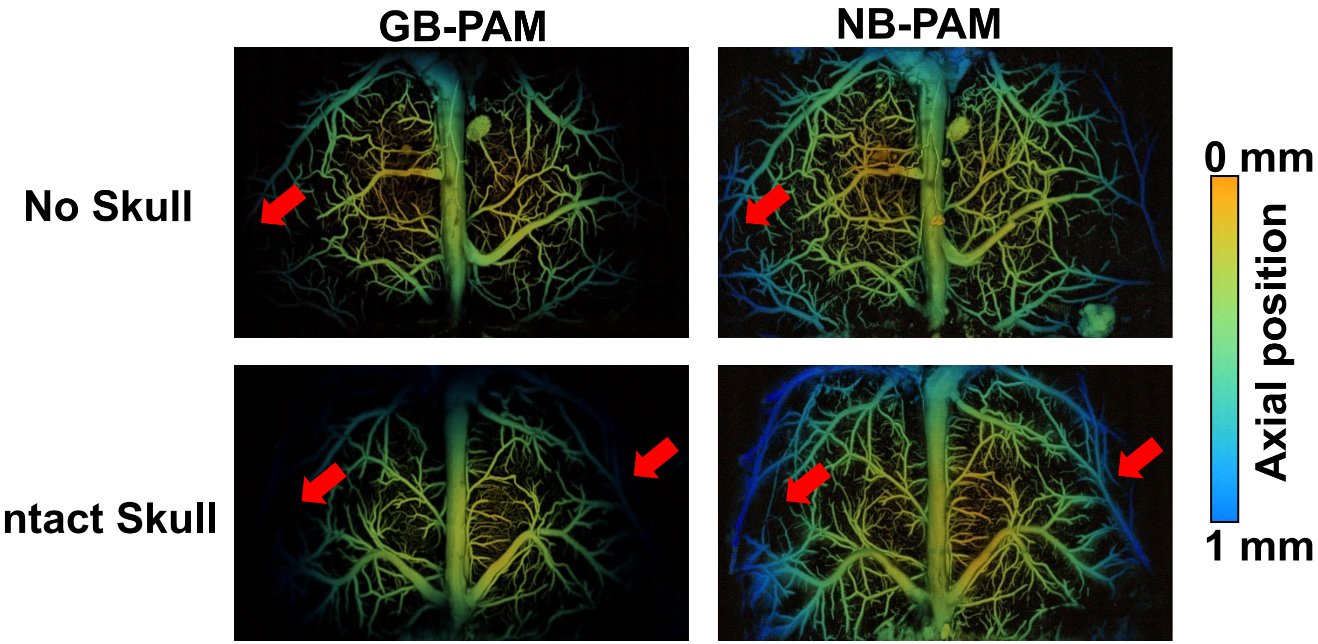


Y He, J Shi, K Maslov, R Cao, LV Wang, *J Biomed Optics* 25, 066501, 2020

Needle-Shaped Beam Photoacoustic Microscopy

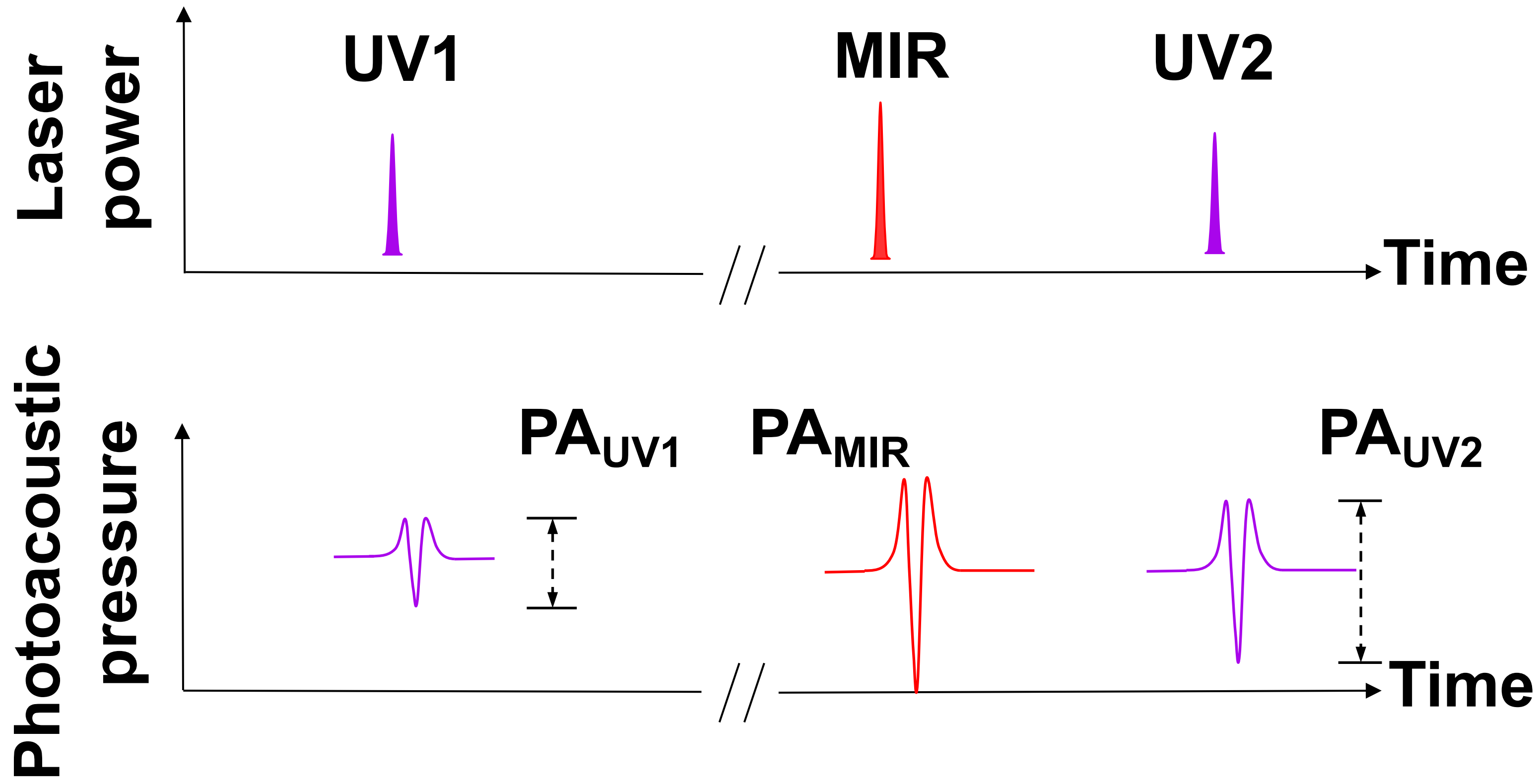


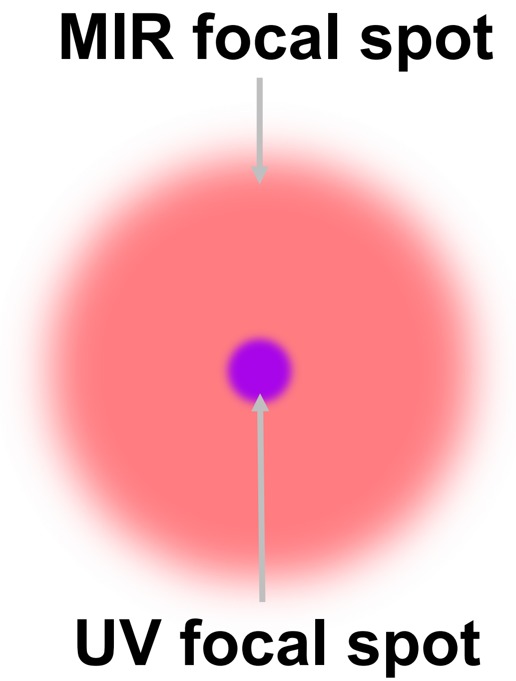




[R Cao, J Zhao], L Li, L Du, Y Zhang, Y Luo, L Jiang, S Davis, Q Zhou, A de la Zerda, LV Wang, *Nature Phot* 17, 89, 2023

Ultraviolet-Localized Mid-Infrared (MIR) Photoacoustic Microscopy (ULM-PAM) for High-Resolution, High-Contrast Imaging of Fresh Biological Samples





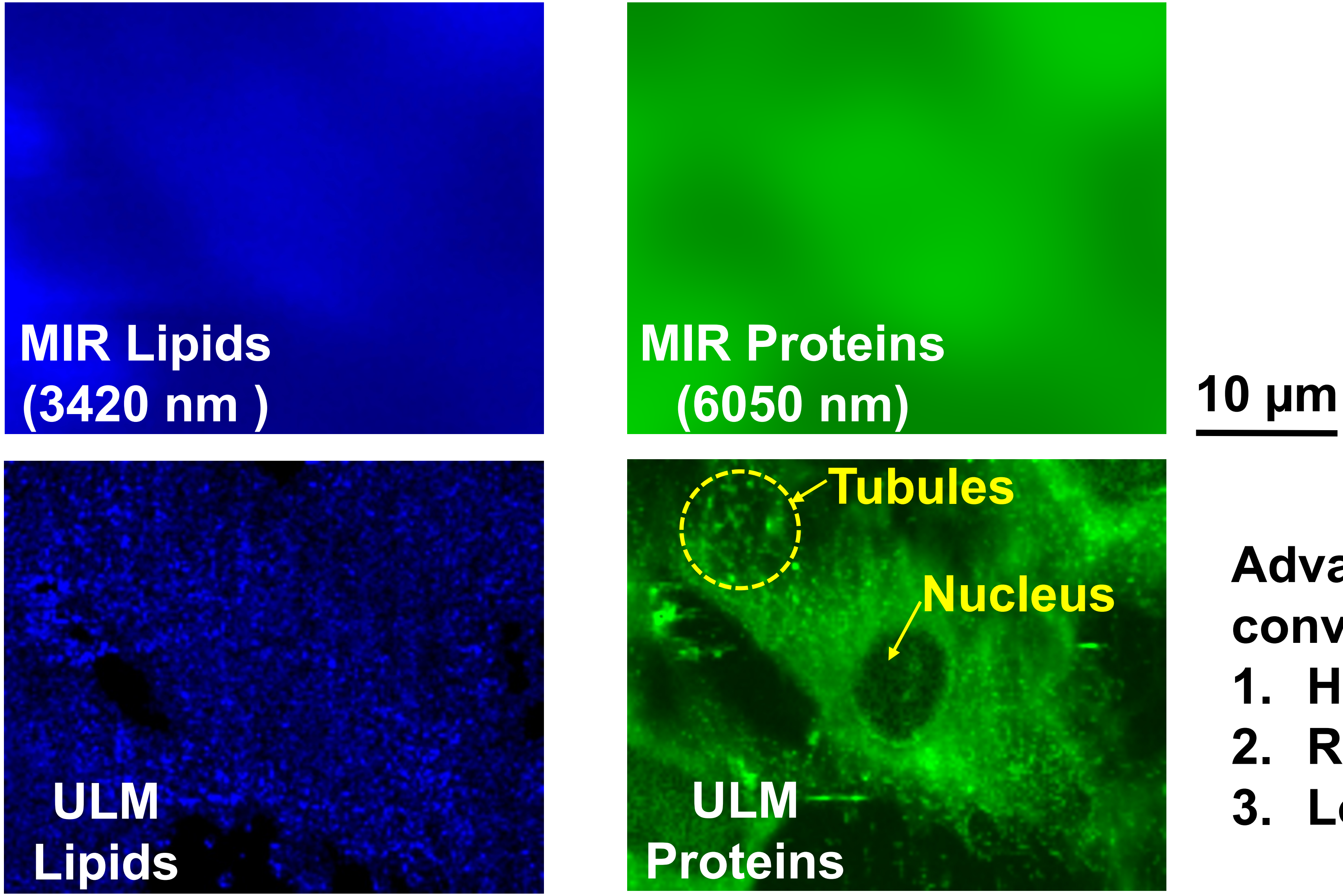
$$\%\Delta PA = (PA_{UV2} - PA_{UV1})/PA_{UV1} \propto \text{Absorption at MIR}$$

Conventional MIR imaging:

1. Low spatial resolution
2. Transmission mode
3. High water background

J Shi, T Wong, Y He, L Li, R Zhang, C Yung, J Hwang@NIST, K Maslov, LV Wang, *Nature Phot* 13, 609, 2019. Grueneisen relaxation: L Wang, C Zhang, LV Wang, PRL 113 174301, 2014

Ultraviolet-Localized Mid-Infrared Photoacoustic Microscopy (ULM-PAM) of Lipids, Proteins, and Nucleic Acids in Fresh Fibroblast Cells



Advantages over conventional MIR imaging:

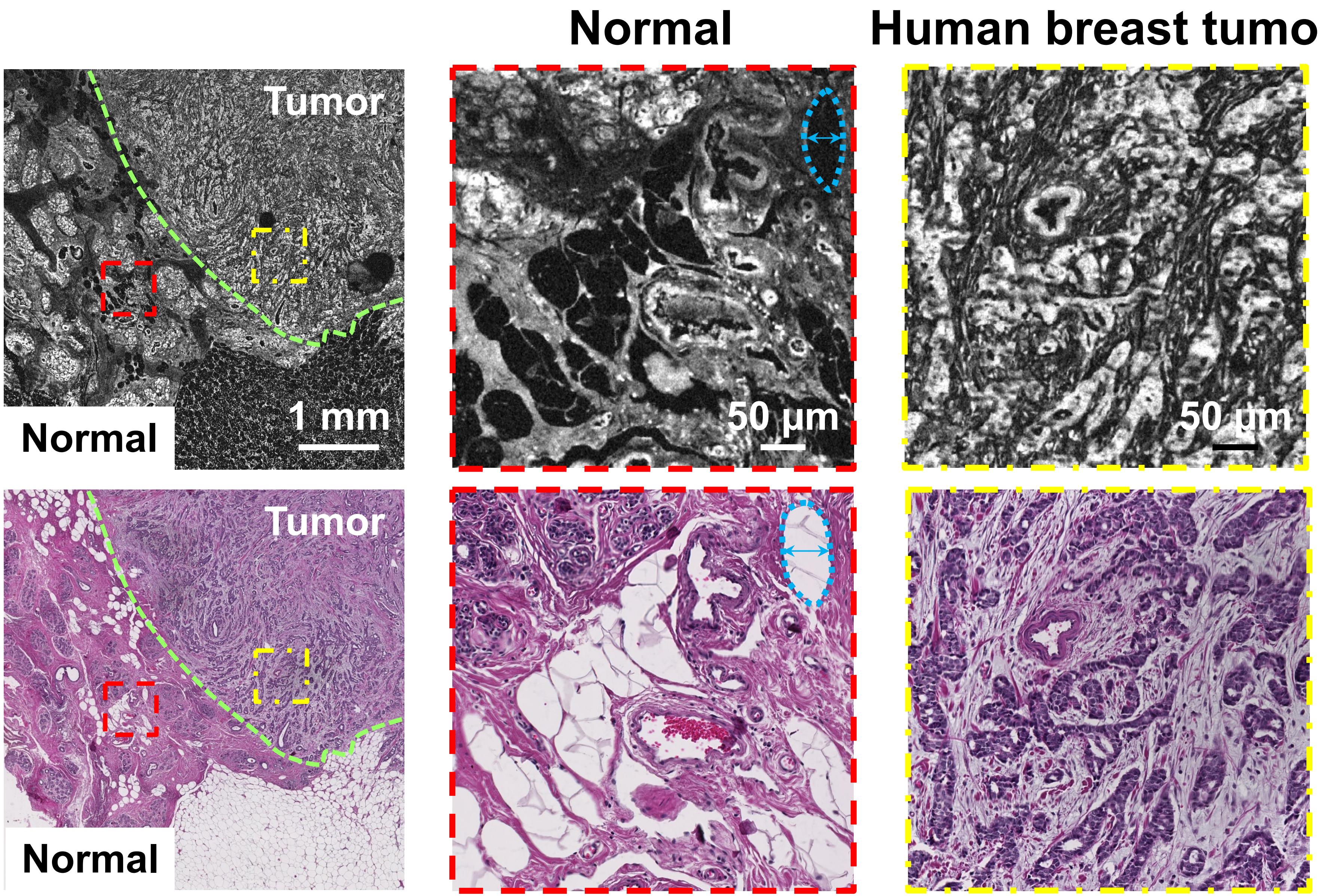
1. High spatial resolution
2. Reflection mode
3. Low water background

J Shi, T Wong, Y He, L Li, R Zhang, C Yung, J Hwang@NIST, K Maslov, LV Wang, *Nature Phot* 13, 609, 2019

Label-Free Photoacoustic Histology by Imaging DNA & RNA in Cell Nuclei

Photoacoustic microscopy without staining

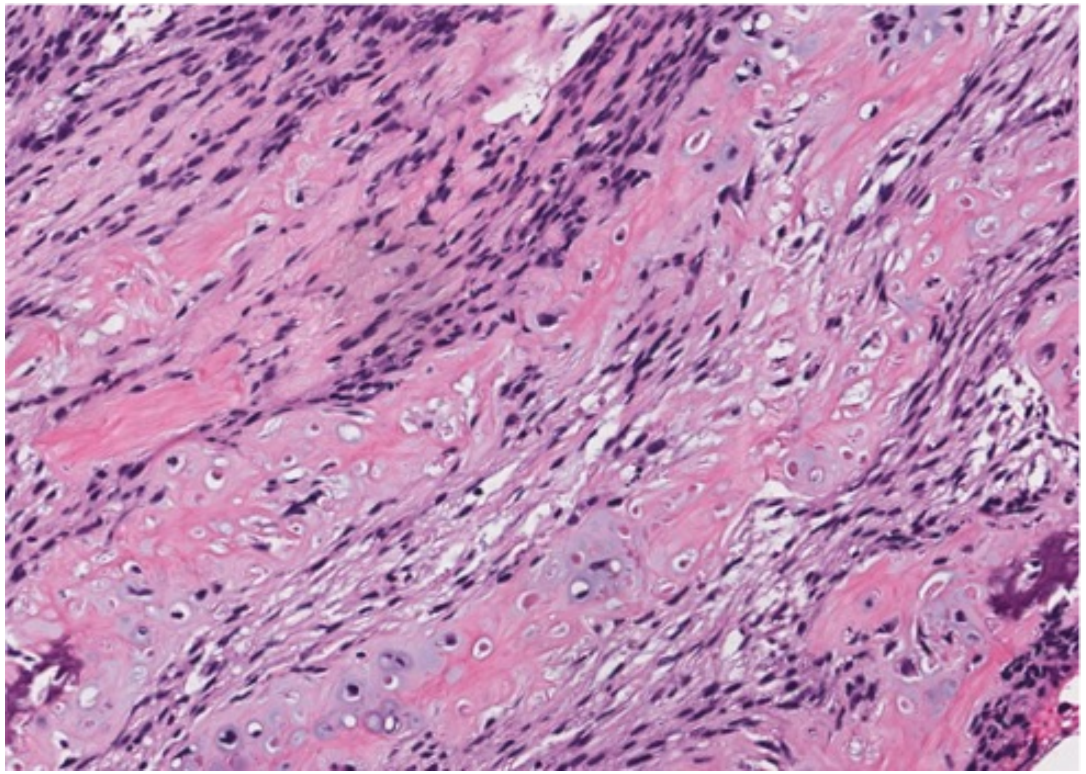
Histology with hematoxylin-eosin staining



TTW Wong, RY Zhang, P Hai, C Zhang, MA Pleitez, [RL Aft, DV Novack]@WUSTL, LV Wang, *Science Adv* 3, e1602168, 2017

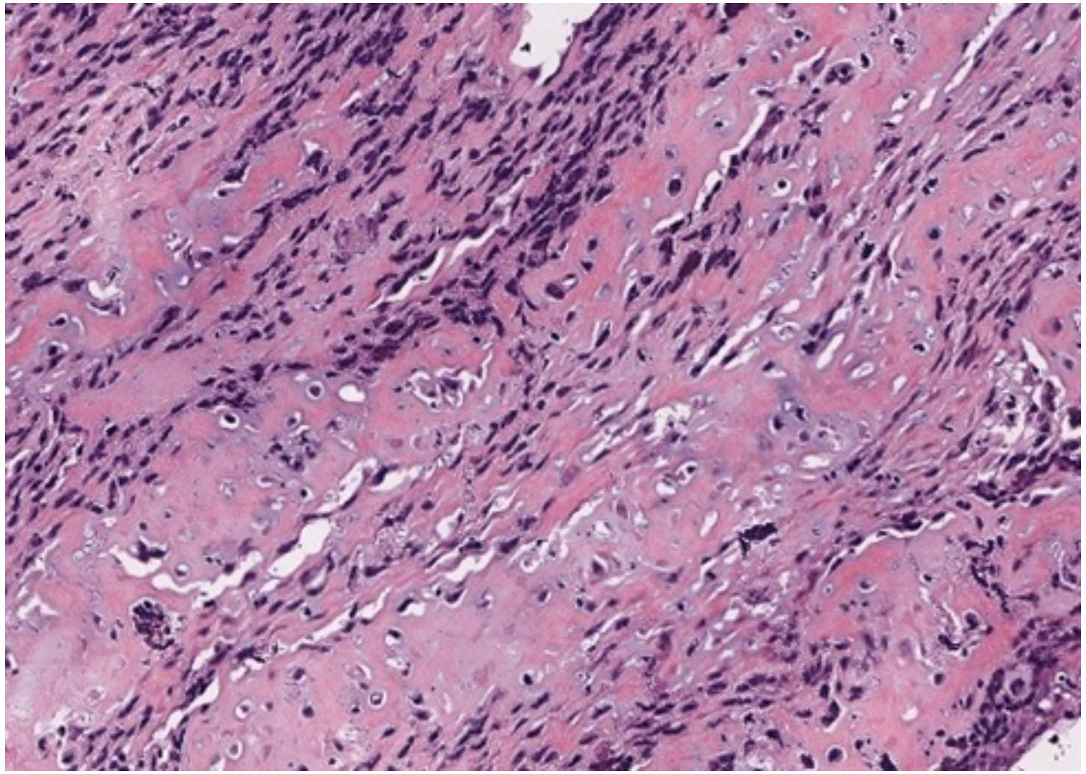
Decalcification-Free and Label-Free Photoacoustic Histology of Bone Specimens by Imaging DNA & RNA in Cell Nuclei

Histology with calcification and hematoxylin & eosin staining (1–7 days)



100 µm

Photoacoustic microscopy without decalcification or staining (<11 minutes)

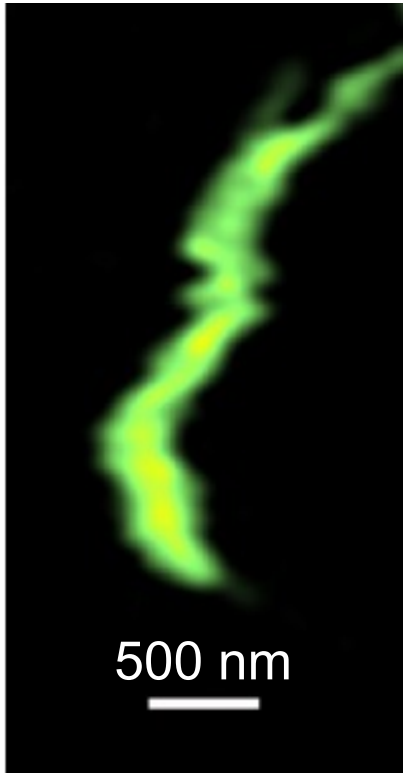


Reduce margin from 20 to 2 mm

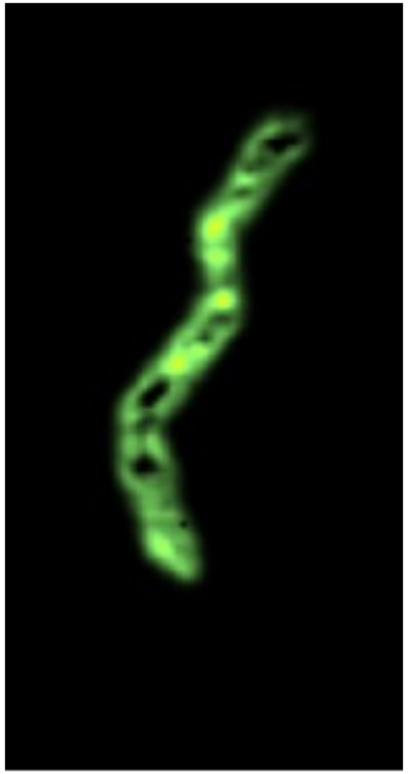
Rui Cao, Scott Nelson, Samuel Davis, Yu Liang, Yilin Luo, Yide Zhang, Brooke Crawford @UCLA, and Lihong V. Wang, *Nature BME* (2022)

Label-Free Photoacoustic (PA) Nanoscopy of a Mitochondrion with Sub-Organelle Resolution: Beat Optical Diffraction Nonlinearly

PA microscopy
(Resolution: 234 nm)

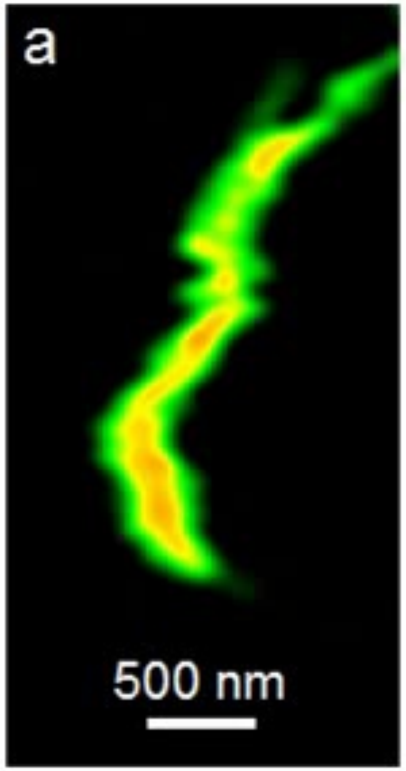


PA nanoscopy
(Resolution: 90 nm)

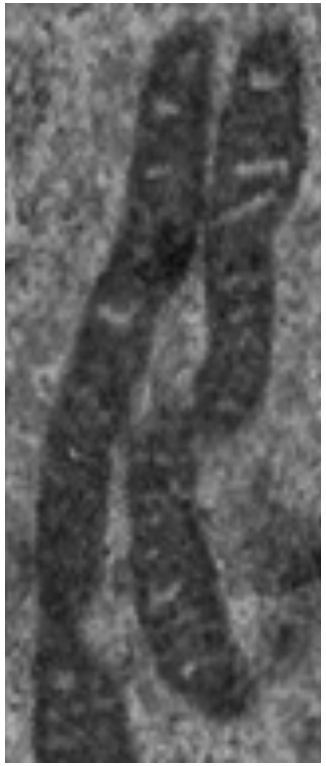


Comparison

Conventional PAM

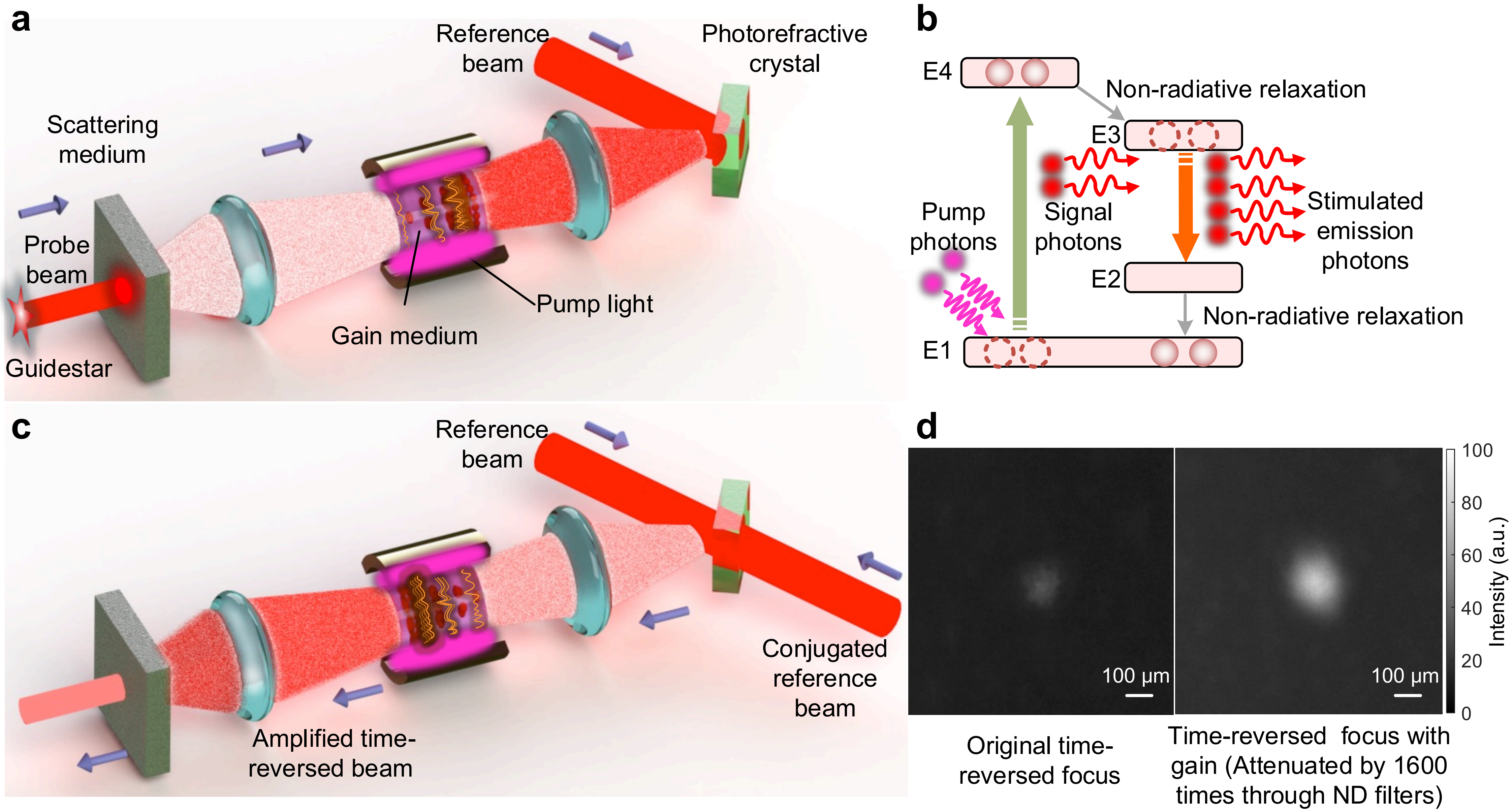


Electron microscopy



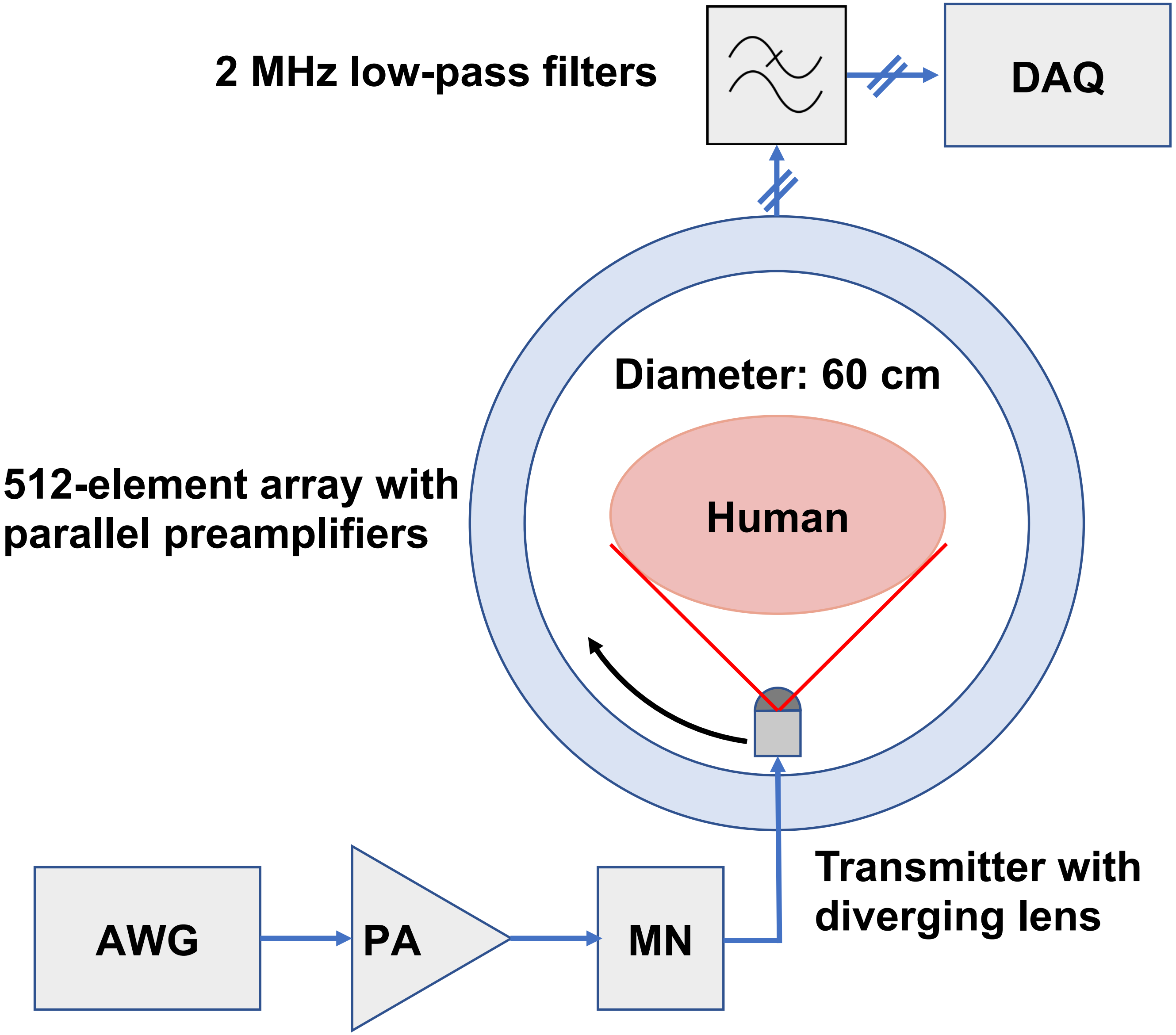
A Danielli, K Maslov, A Garcia-Uribe, A Winkler, CY Li, LD Wang, Y Chen, G Dorn, LV Wang, *J Biomed Optics* 19, 086006, 2014; Collaboration: G Dorn;
J Yao, LD Wang, CY Li, C Zhang, LV Wang, *Phys Rev Lett* 112, 014302, 2014

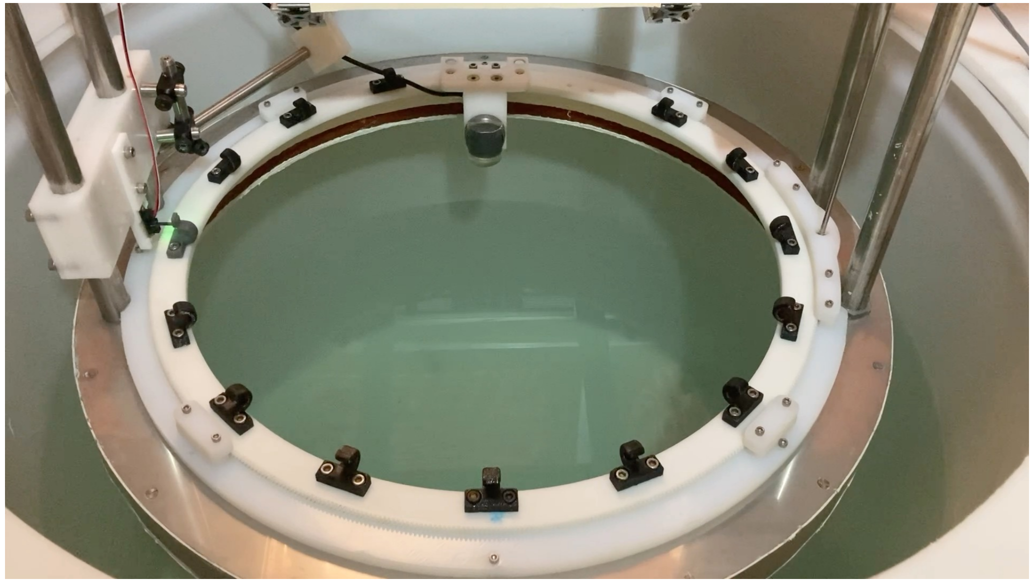
High-gain and High-speed Wavefront Shaping Through Scattering Media



Z Cheng, C Li, A Khadria, Y Zhang, LV Wang, *Nature Phot,* accepted, 2023

First Whole-Body Human Ultrasound Tomography System

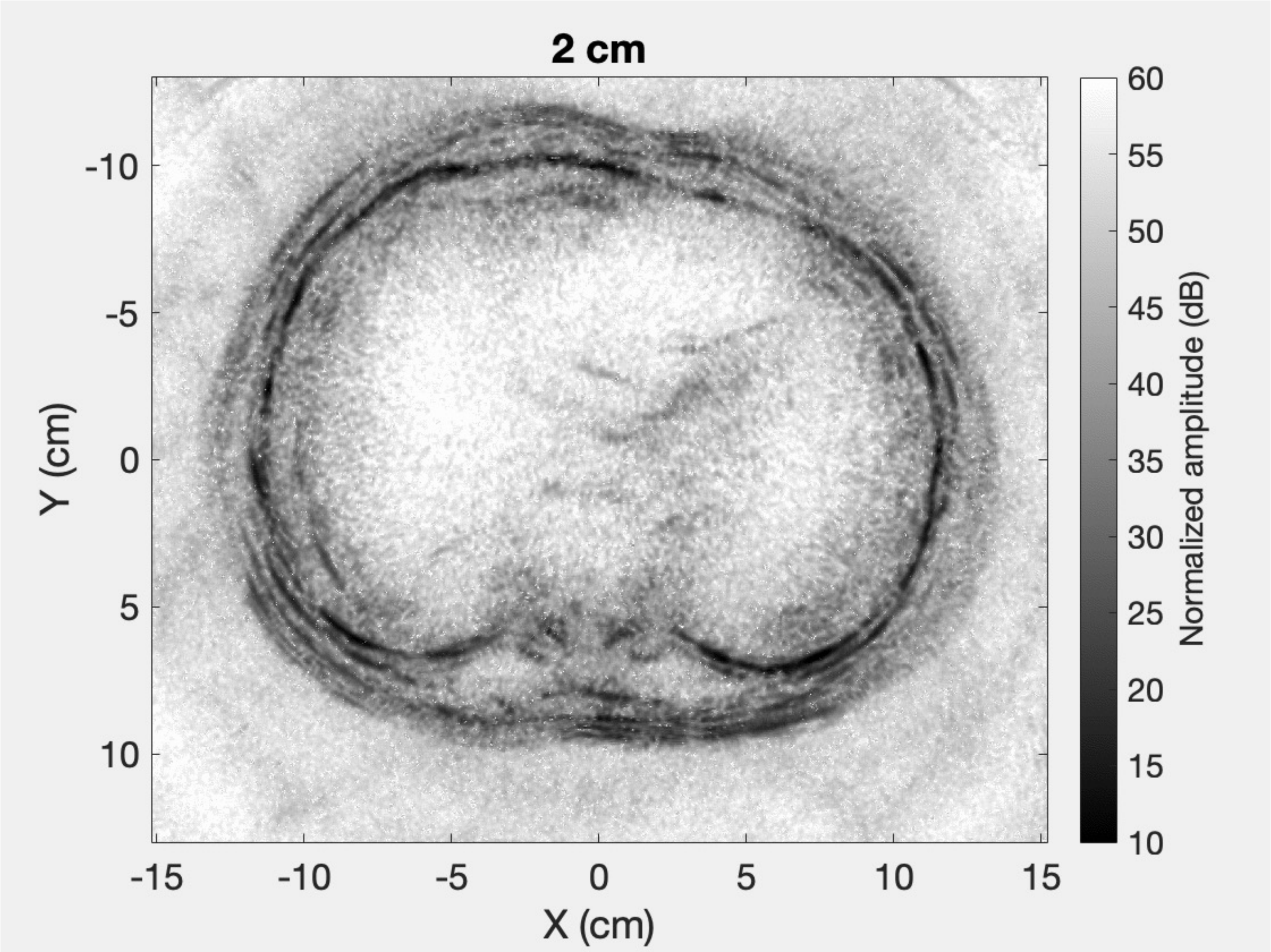


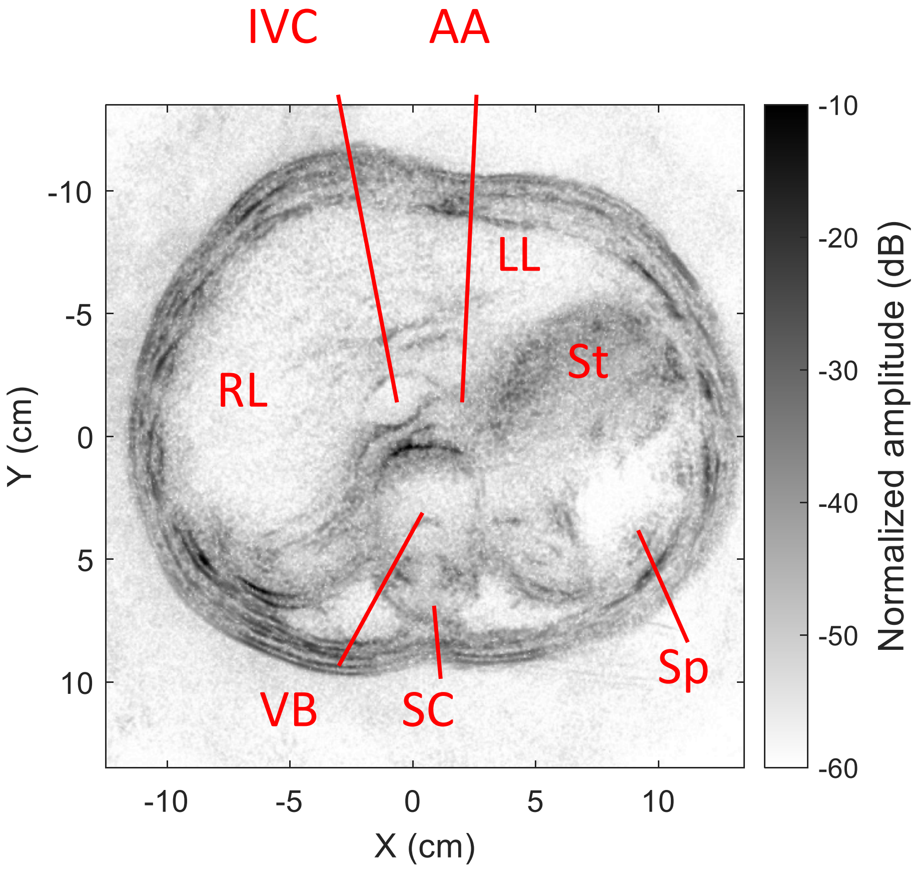


AWG: arbitrary waveform generator
PA: power amplifier
MN: matching network
DAQ: data acquisition

DC Garrett, J Xu, G Ku, LV Wang, arXiv:2307.00110

First Whole-Body Human Ultrasound Tomography Images



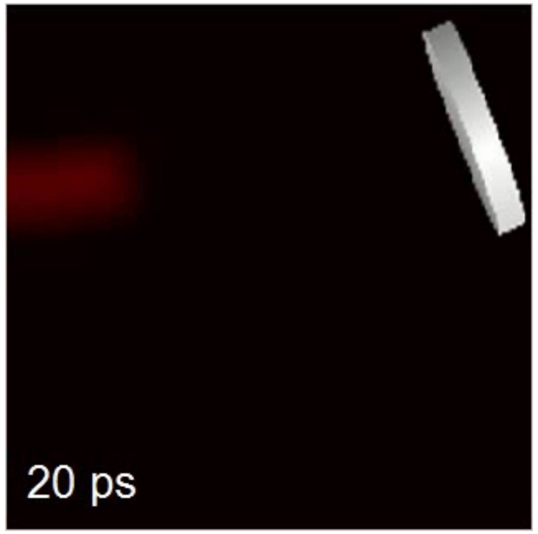


IVC: inferior vena cava	**AA: abdominal aorta**
RL: right lobe of liver	**LL: left lobe of liver**
St: stomach	**Sp: spleen**
VB: vertebral body	**SC: spinal cord**

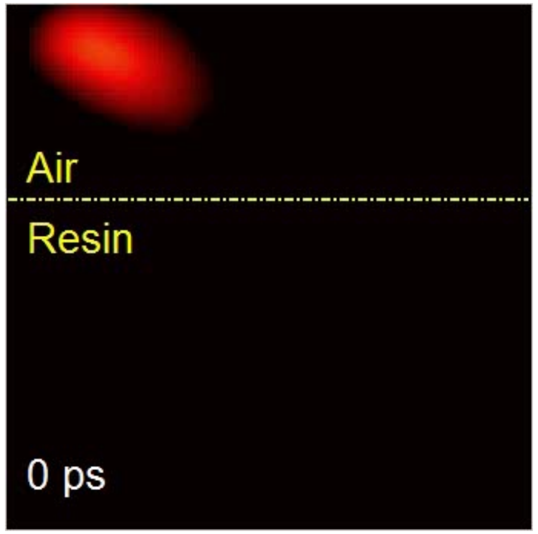
DC Garrett, J Xu, G Ku, LV Wang, arXiv:2307.00110

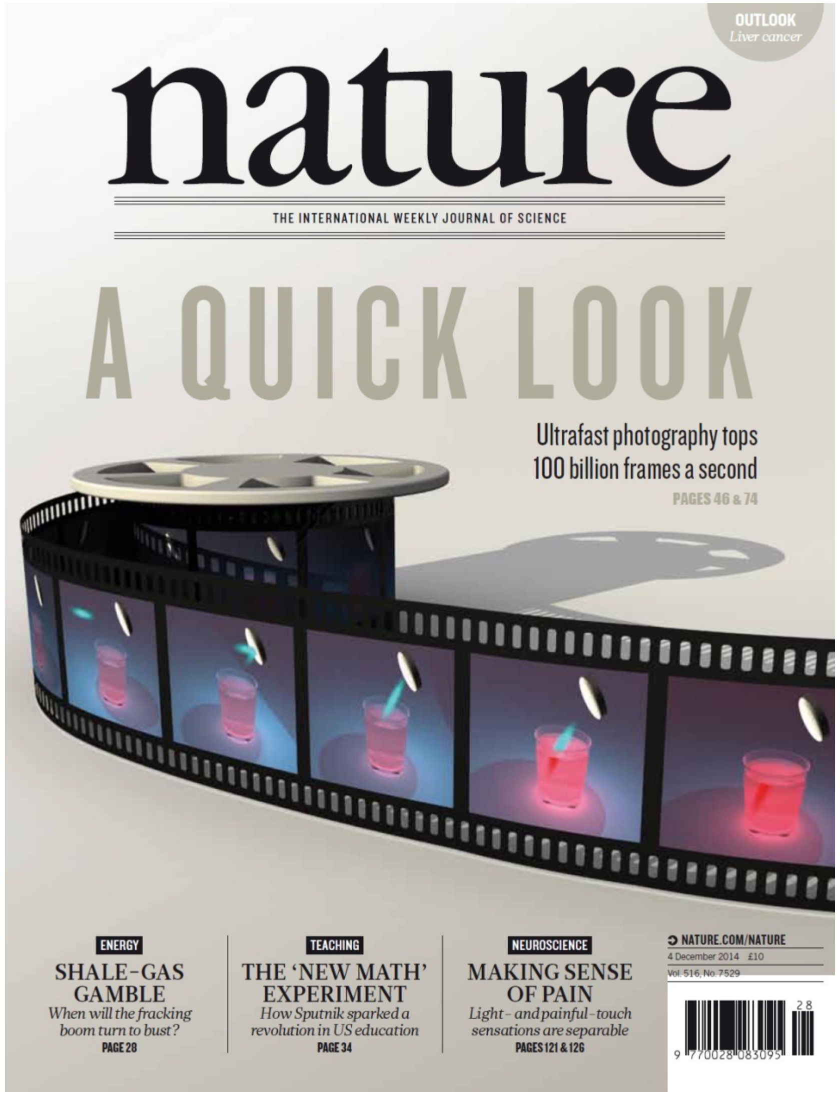
Watch a Flying Laser Pulse with Single-Shot Compressed Ultrafast Photography at 100 Billion Frames/Second

Reflection



Refraction





OUTLOOK
Liver cancer

nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

A QUICK LOOK

Ultrafast photography tops 100 billion frames a second
PAGES 46 & 74

ENERGY
SHALE-GAS GAMBLE
When will the fracking boom turn to bust?
PAGE 28

TEACHING
THE ‘NEW MATH’ EXPERIMENT
How Sputnik sparked a revolution in US education
PAGE 34

NEUROSCIENCE
MAKING SENSE OF PAIN
Light- and painful-touch sensations are separable
PAGES 121 & 126

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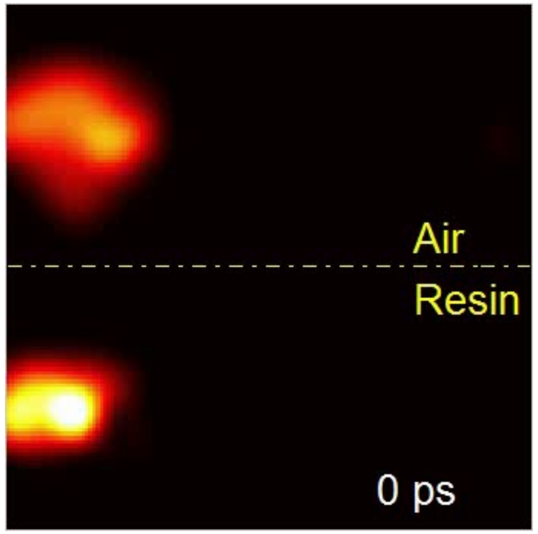
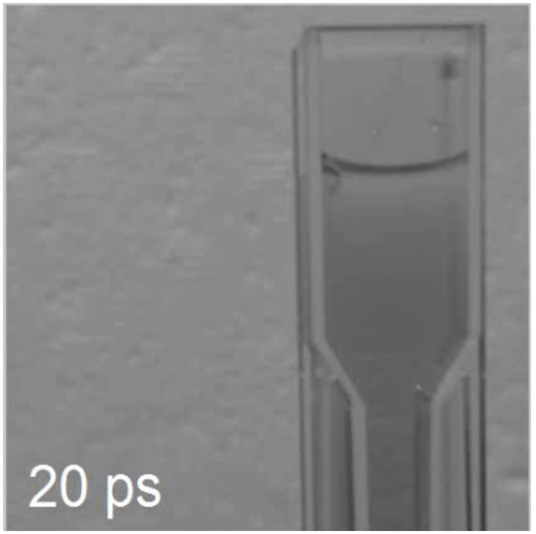
Vol. 516, No. 7529

Racing



Fluorescence

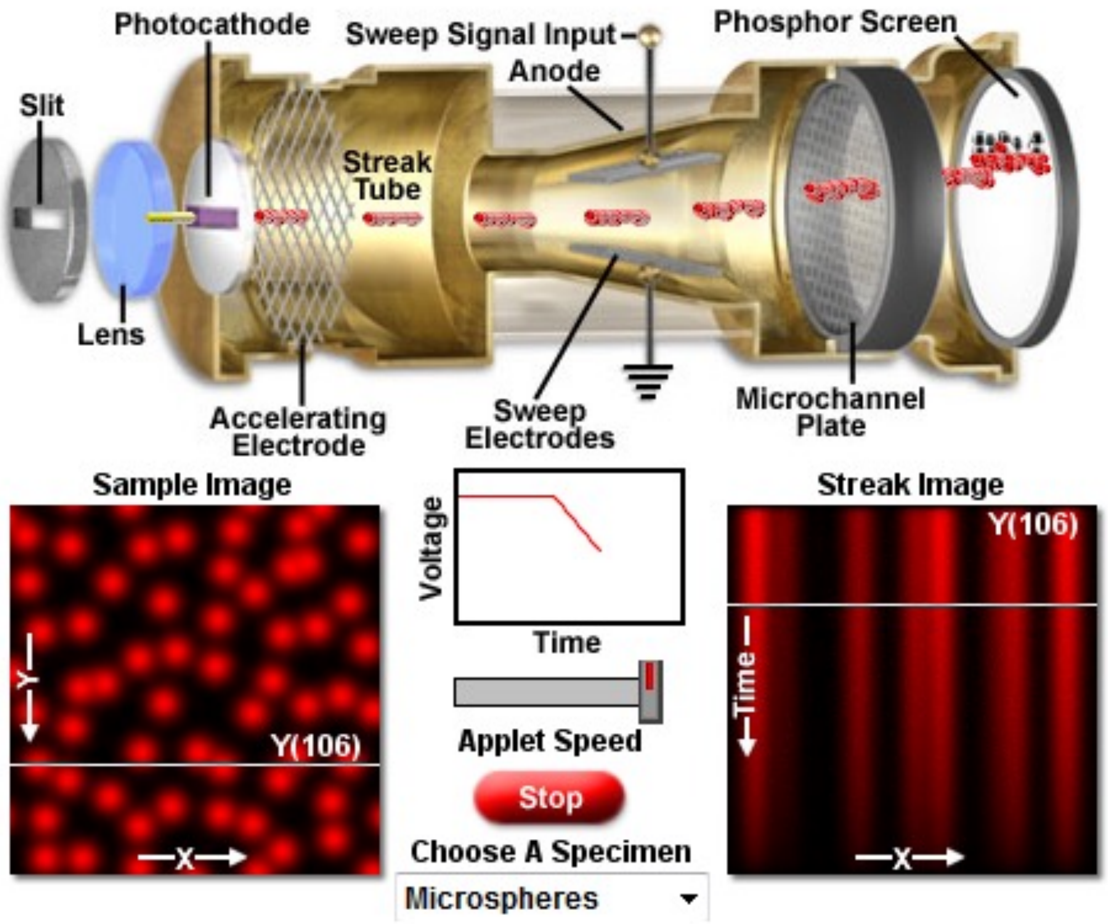


10 mm

[L Gao, J Liang], C Li, LV Wang, *Nature* 516, 74, 2014

Video slowdown: 10 billion X

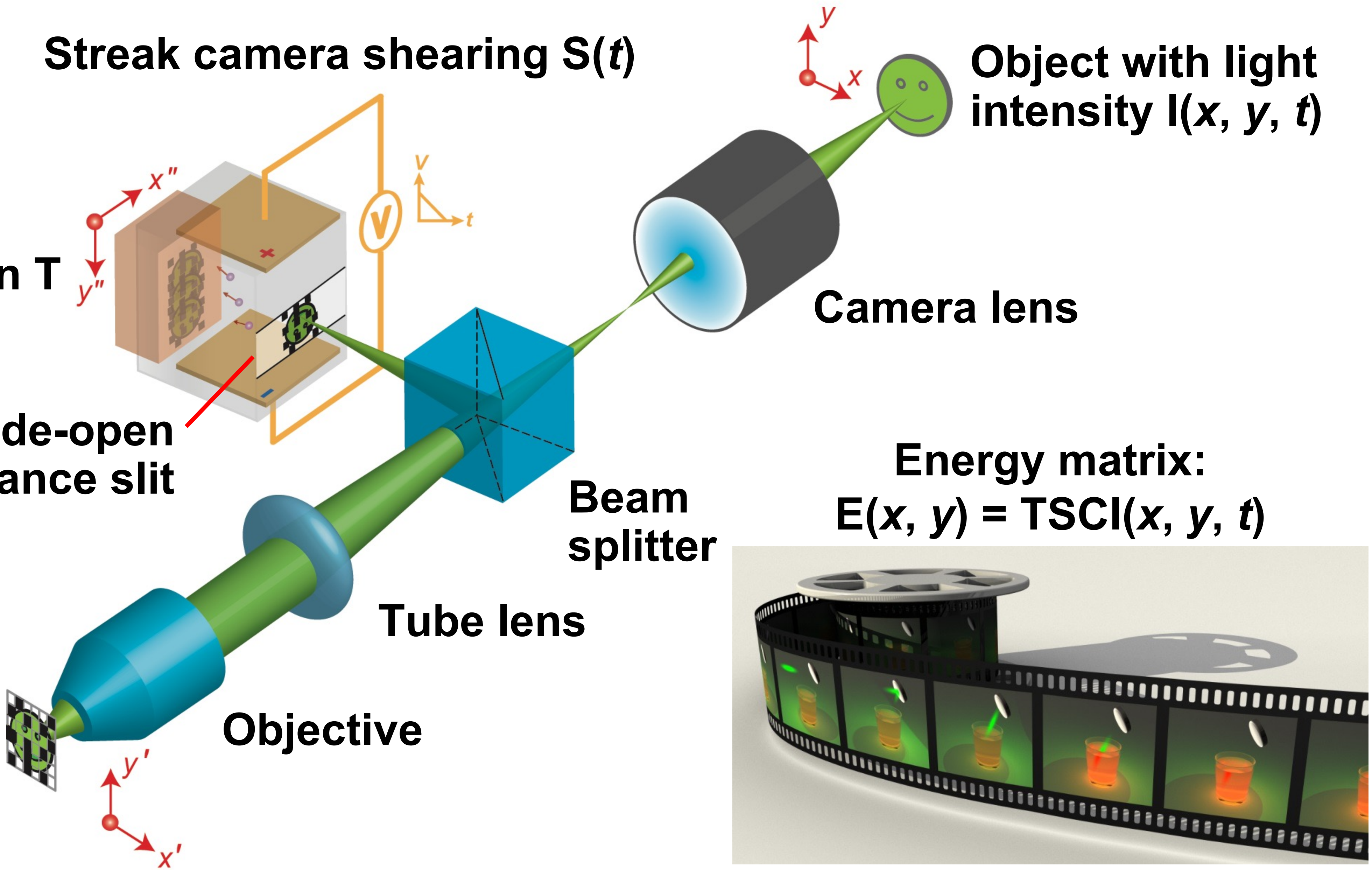
Multi-Shot 2D Imaging using a Streak Camera



- Scanning is required along the axis that is perpendicular to the entrance slit
- The event itself must be repeatable

http://hamamatsu.magnet.fsu.edu/tutorials/java/streakcamera/

Single-Shot Compressed Ultrafast Photography: 100 Billion Frames per Second



Streak camera shearing S(*t*)

Object with light intensity I(*x*, *y*, *t*)

CCD integration T

Camera lens

Wide-open entrance slit

Beam splitter

Tube lens

Objective

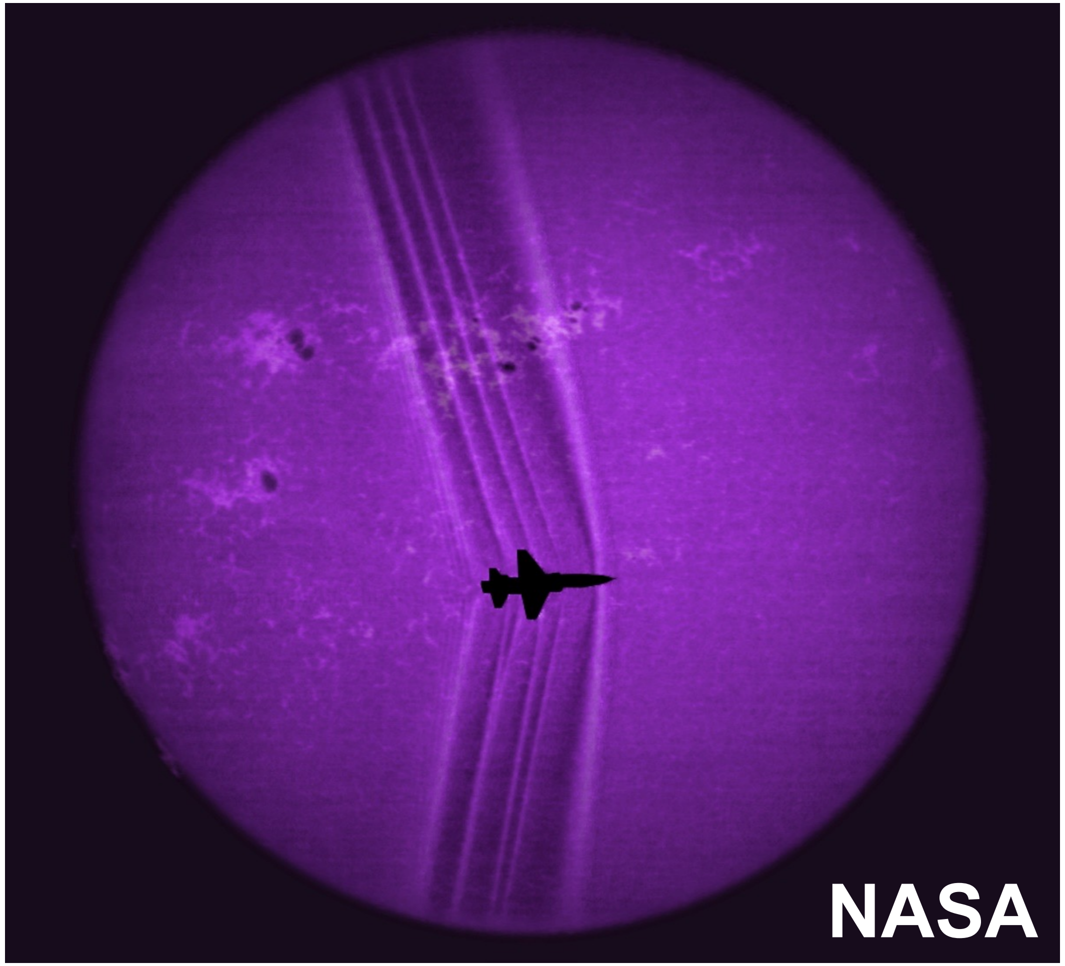
Digital micromirror device coding C(*x*, *y*)

Energy matrix:
E(*x*, *y*) = TSCI(*x*, *y*, *t*)

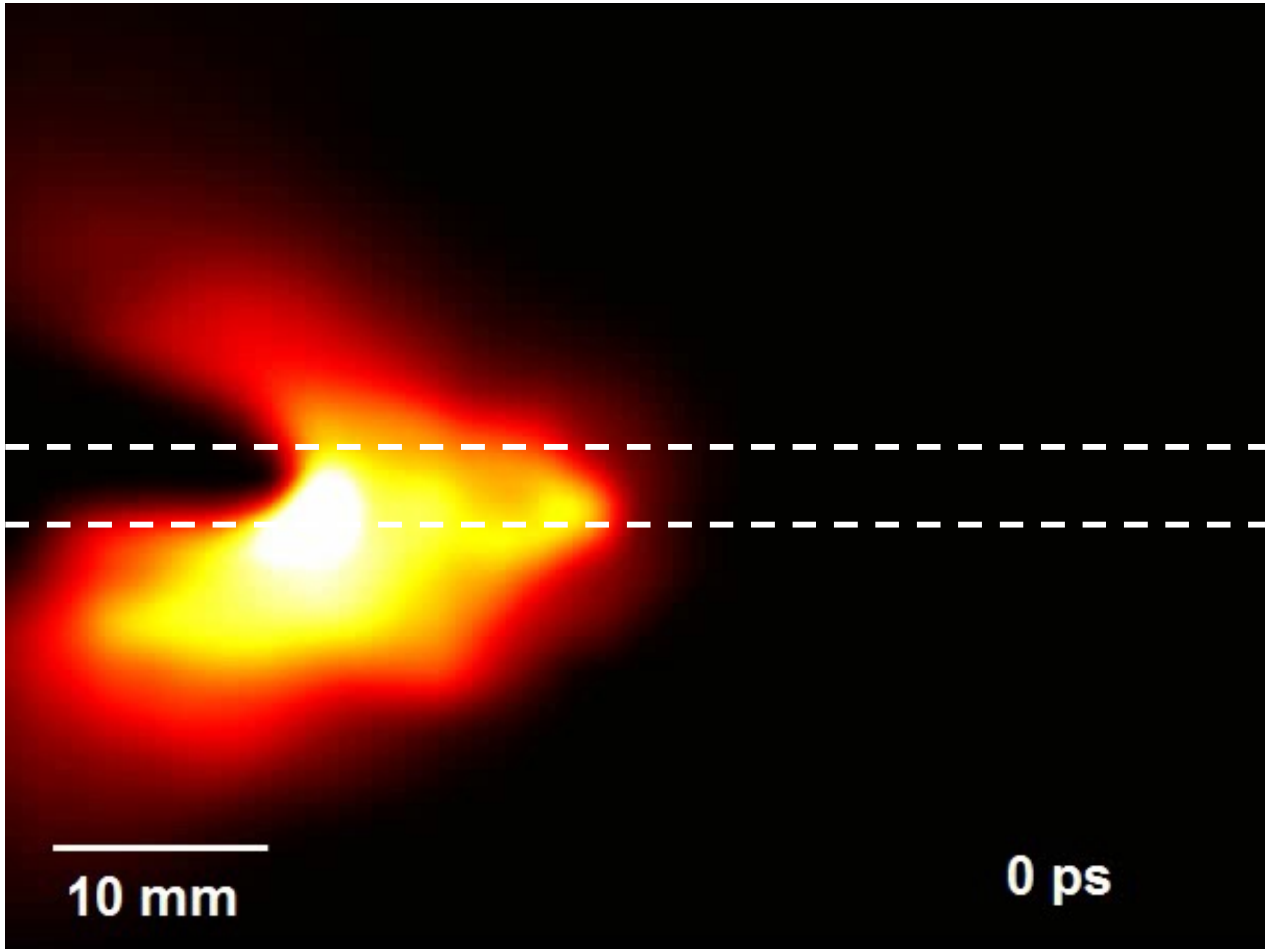
[L Gao, J Liang], C Li, LV Wang, *Nature* 516, 74, 2014; Comments by B Pogue, *Nature* 516, 46

Watch a Flying Superluminal Mach Cone with Single-Shot Compressed Ultrafast Photography at 100 Billion Frames/Second

Supersonic Mach cone (Sonic Boom)

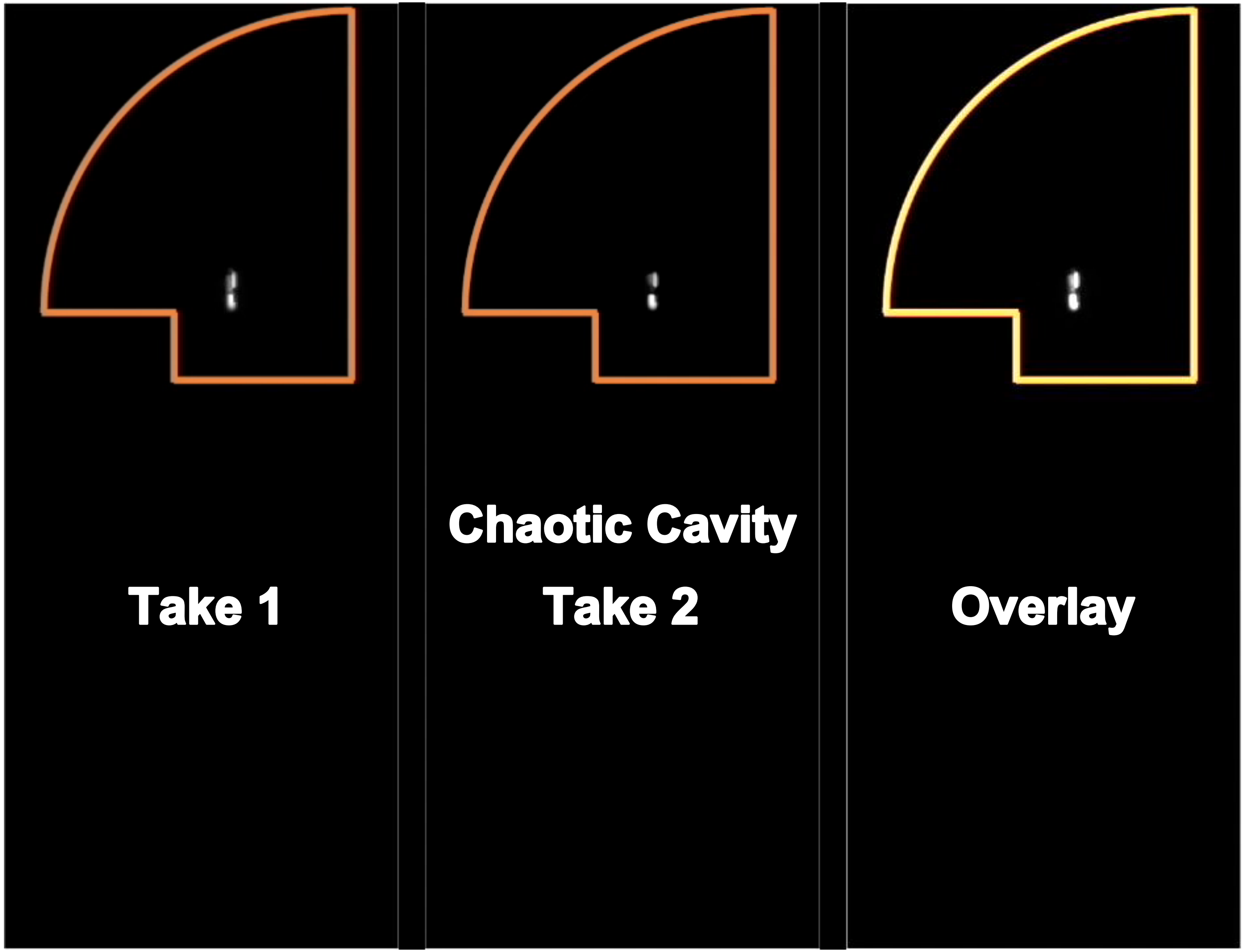


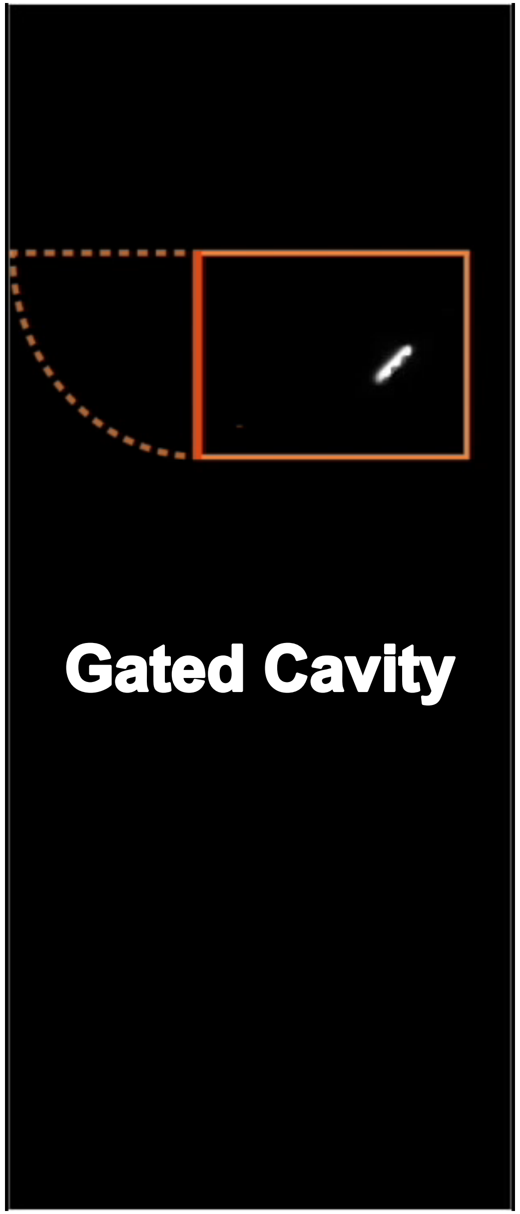
Superluminal Mach cone (Optical Boom)



[J Liang, C Ma, L Zhu], YJ Chen, L Gao, LV Wang, *Science Adv* 3, e1601814, 2017

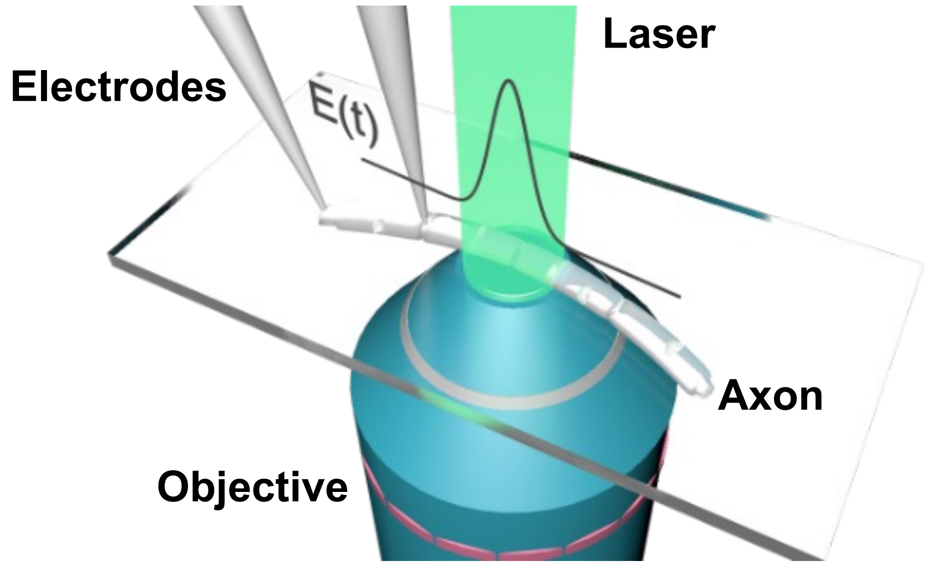
Real-Time Imaging of a Bouncing Photon Packet in a Chaotic Cavity

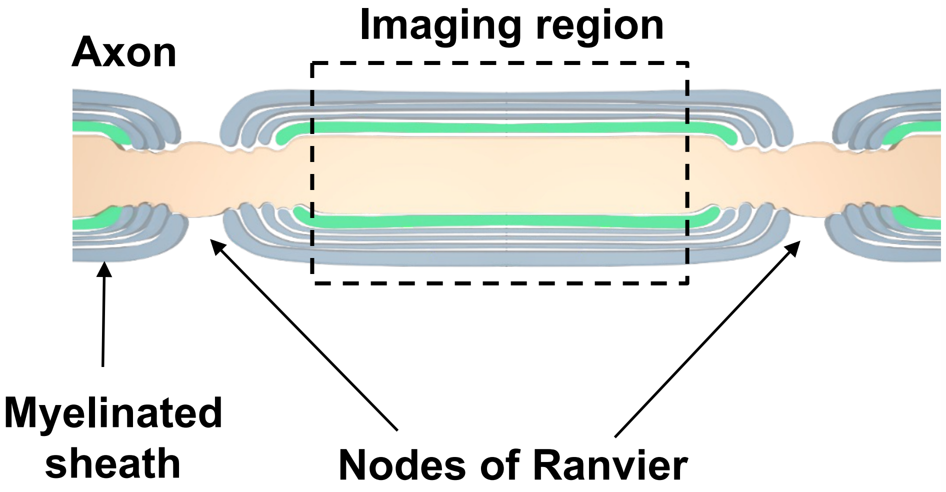


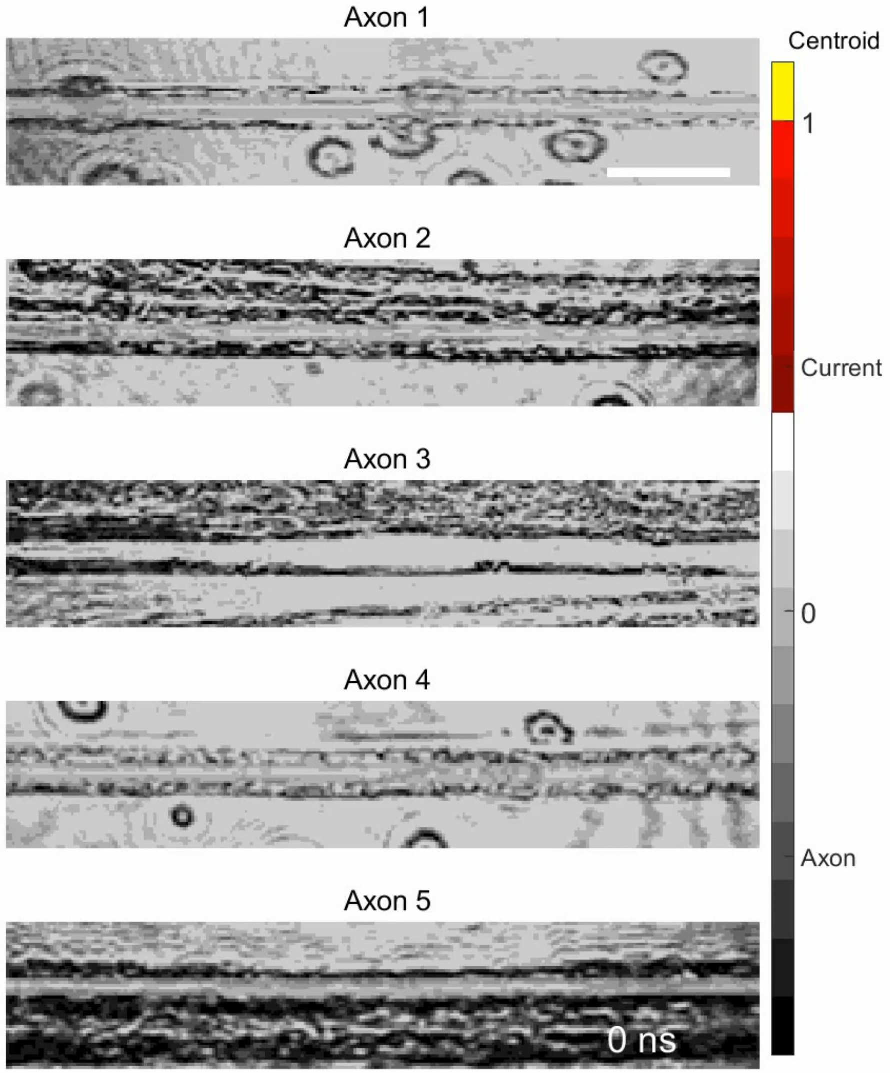


[L Fan, X Yan], H Wang@USC, LV Wang, *Science Adv* 7, eabc8448, 2021

Compressed Ultrafast Photography of Electrical Pulses along Myelinated Axons







Speed: 100 m/s

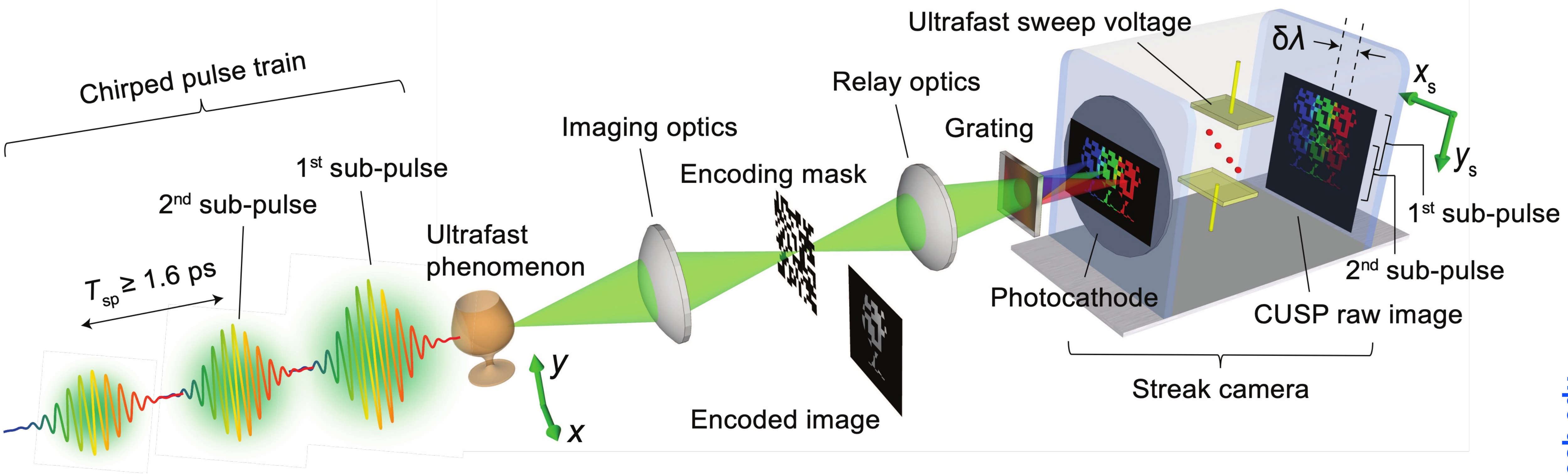
Phase sensitivity: 20 µrad

Step: 50 ns

20 µm

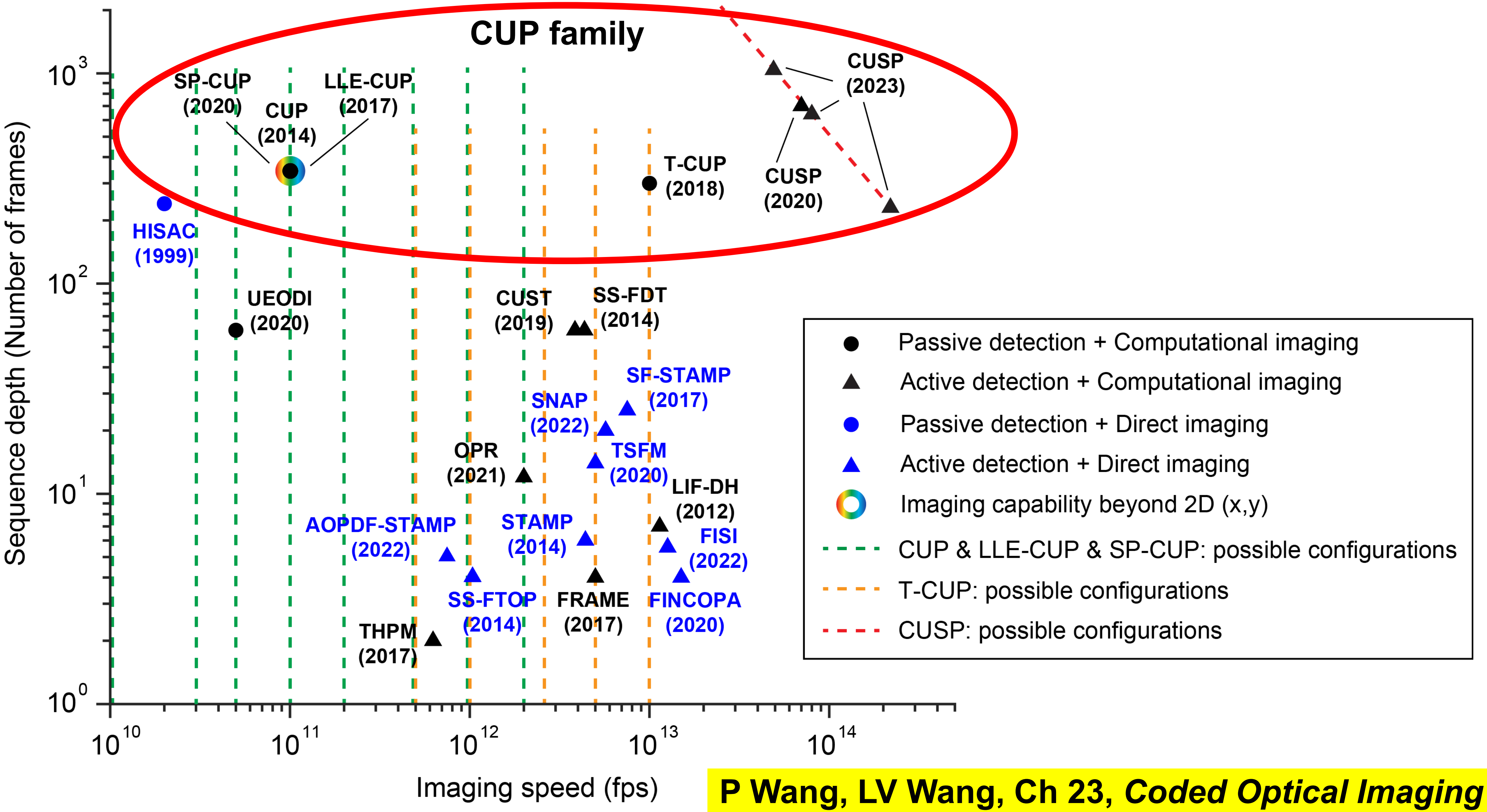
[Y Zhang, B Shen], T Wu, J Zhao, JC Jing, P Wang, K Sasaki-Capela, WG Dunphy, D Garrett, K Maslov, W Wang, LV Wang, *Nature Comm* 13, 5247, 2022

Compressed Ultrafast Spectral Photography (CUSP): 219 THz



P Wang, LV Wang, *Adv Science* 10, e2207222, 2023: 219 THz
P Wang, J Liang, LV Wang, *Nature Comm* 11, 2091, 2020: 70 THz

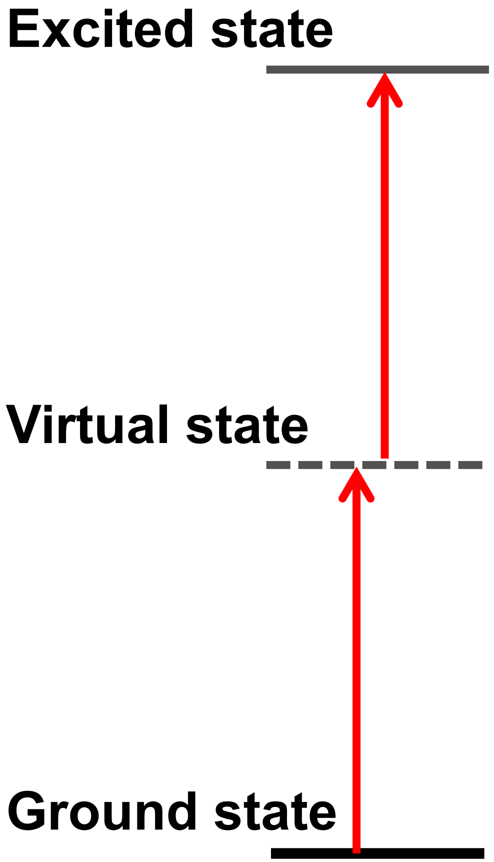
Comparison of Single-Shot Ultrafast Optical Imaging Techniques



P Wang, LV Wang, Ch 23, *Coded Optical Imaging*

Standard Quantum Limit vs Heisenberg Limit with N Photons

Two-photon excitation



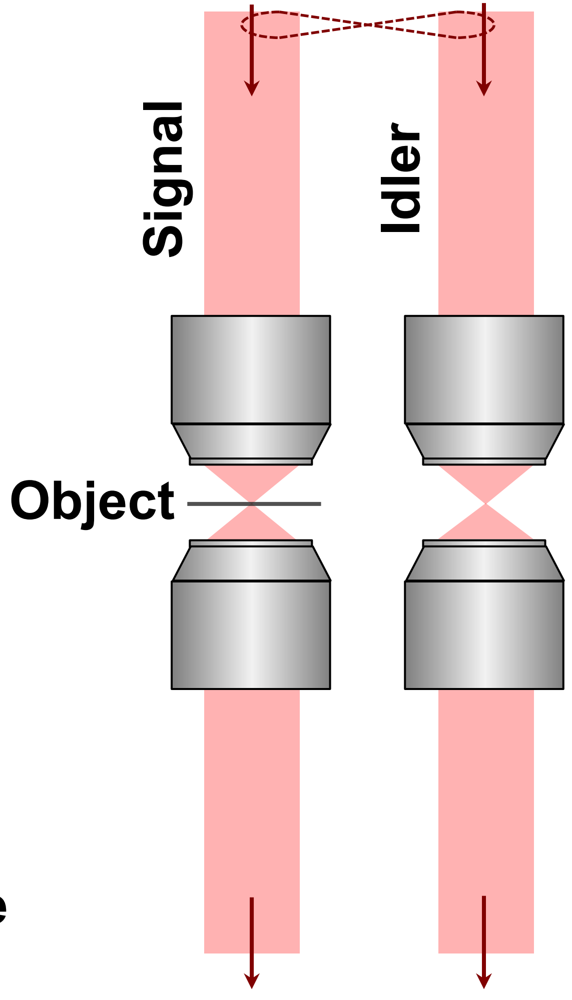
Excited state

Virtual state

Ground state

- Spatial resolution at the standard quantum limit $\propto 1/\sqrt{N}$
    - The standard quantum limit is achieved with a regular light source such as a laser
    - Examples: two-photon microscopy, PALM/STORM
    - Intuitively, N statistically independent photons average the spatial standard error down by $\sqrt{N}$ times according to the central limit theorem
- Spatial resolution at the Heisenberg limit $\propto 1/N$
    - The Heisenberg limit is achieved with an entangled-photon source such as a spontaneous parametric down conversion (SPDC) source
    - Intuitively, N entangled photons behave like one with N times greater momentum or shorter wavelength.

Entangled photon pair



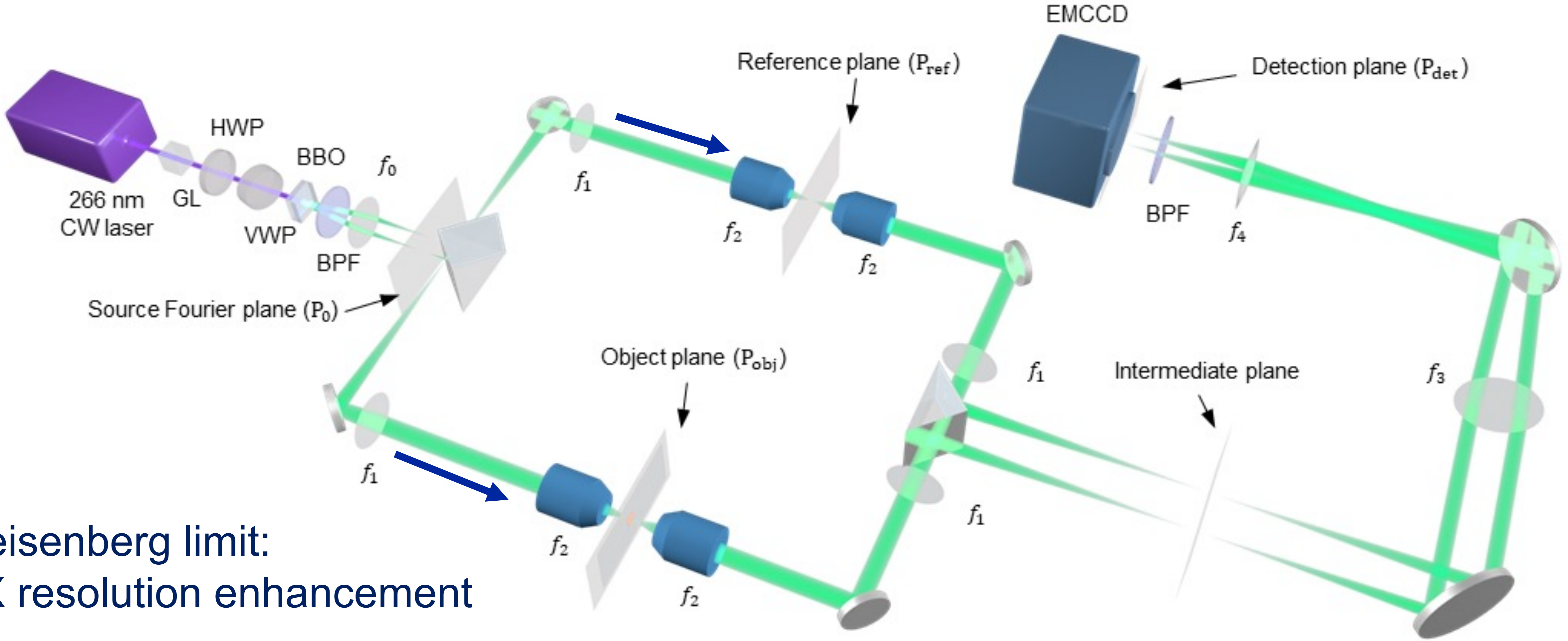
Signal

Idler

Object

Coincidence counts

Quantum Microscopy of Cells using Entangled Photon Pairs

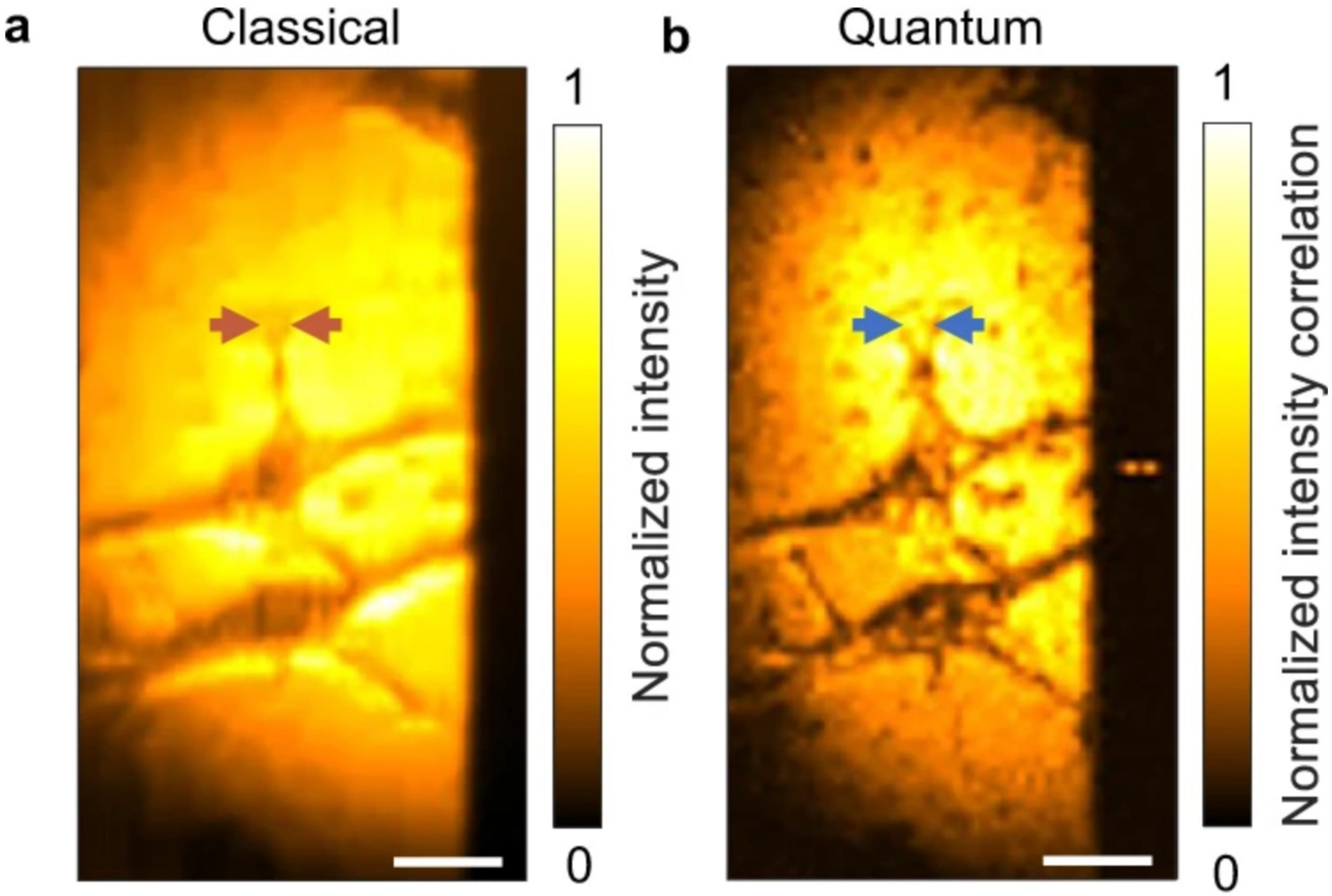


Heisenberg limit:
2X resolution enhancement

CW, continuous wave. GL, Glan-Laser polarizer. HWP, half-wave plate. VWP, variable wave plate. BBO, β-barium borate crystals. BPF, 532 nm bandpass filter. PBS, polarizing beam splitter. EMCCD, electron multiplying charge-coupled device camera. P_0, the Fourier plane of the BBO crystal.

[Z He, Y Zhang, X Tong], L Li, LV Wang, *Nature Comm* 14, 2441, 2023

Quantum Microscopy of HeLa Cells using Entangled Photon Pairs



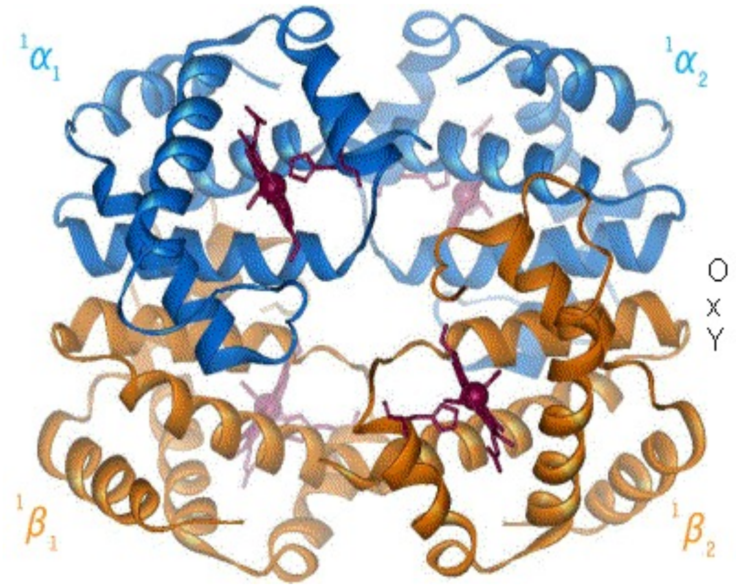
[Z He, Y Zhang, X Tong], L Li, LV Wang, *Nature Comm* 14, 2441, 2023

Scale bars, 20 μm

Rich Optical Contrasts and Multiscale Imaging from Organelles to Patients

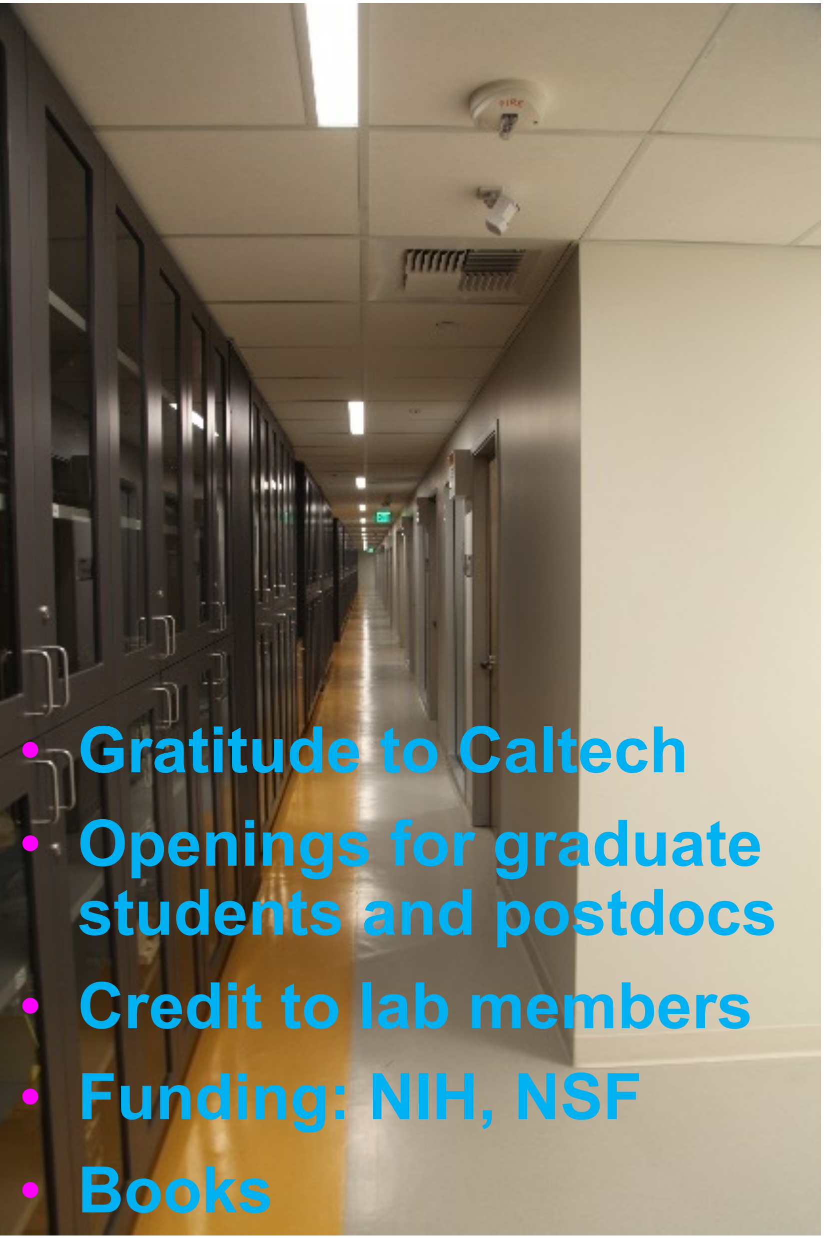
- **Diverse molecules interacting with light at chosen wavelengths**
  - *Nucleic acids: DNA, RNA*
  - *Carbohydrates: Glucose, cellulose*
  - *Lipids: Fat, myelin*
  - *Proteins: Oxy/deoxy/met/carboxy-hemoglobin, myoglobin, cytochromes*
  - *Other endogenous molecules: Melanin, bilirubin, water*
  - *Exogenous absorbers: Dyes, nanoparticles*
- ***In vivo* functional imaging: blood oxygenation/perfusion, brain activity**
  - *Concentration of hemoglobin (angiogenesis)*
  - *Oxygen saturation of hemoglobin (hyperoxia/normoxia/hypoxia)*
  - *Blood flow (Doppler effect)*
- ***In vivo* metabolic imaging**
  - *Metabolic rate of oxygen (hyper-metabolism)*
  - *Glucose uptake via glucose analogs*
- ***In vivo* molecular imaging**
  - *Biomarkers: Integrin, VEGF, HER2*
  - *Reporter genes: LacZ, iRFP, tyrosinase*
- ***In vivo* label-free histologic imaging**
  - *Cell nuclei*
  - *Cytoplasm*

Oxygen binding to hemoglobin



Picture: Wikipedia

Further Information



- Gratitude to Caltech
- Openings for graduate students and postdocs
- Credit to lab members
- Funding: NIH, NSF
- Books

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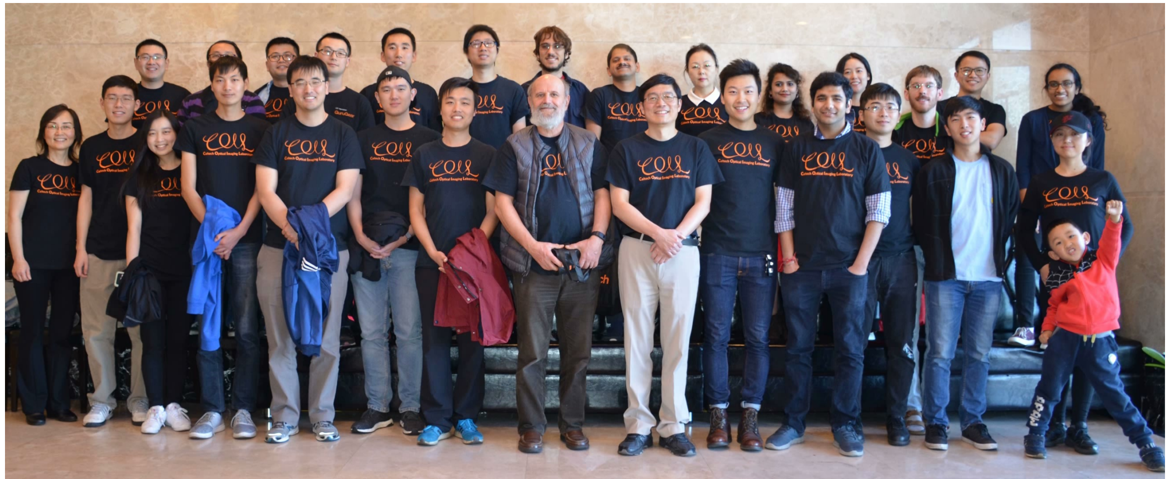

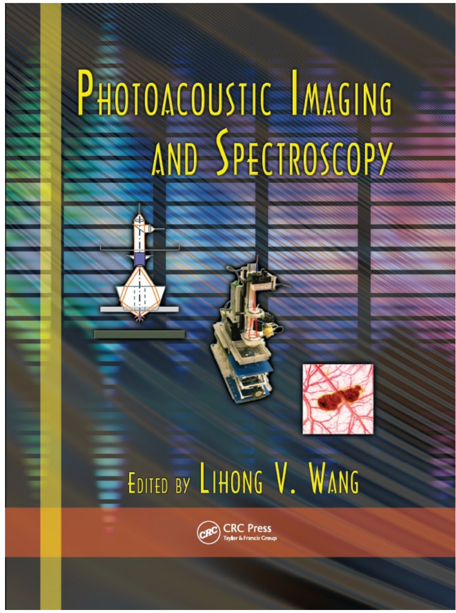

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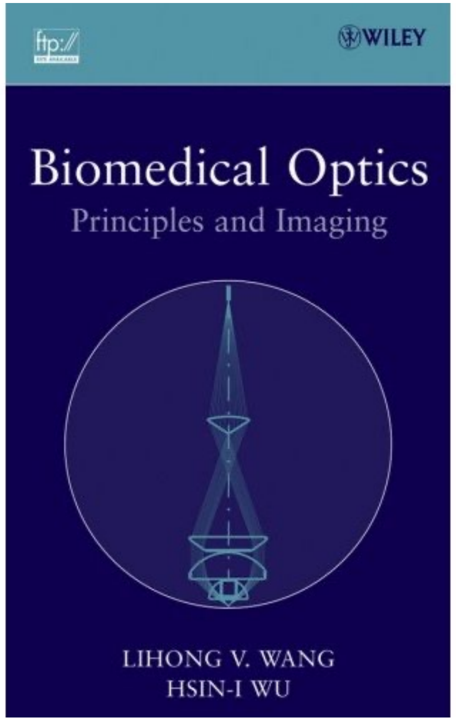

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Biomedical Optics

Principles and Imaging

LIHONG V. WANG
HSIN-I WU