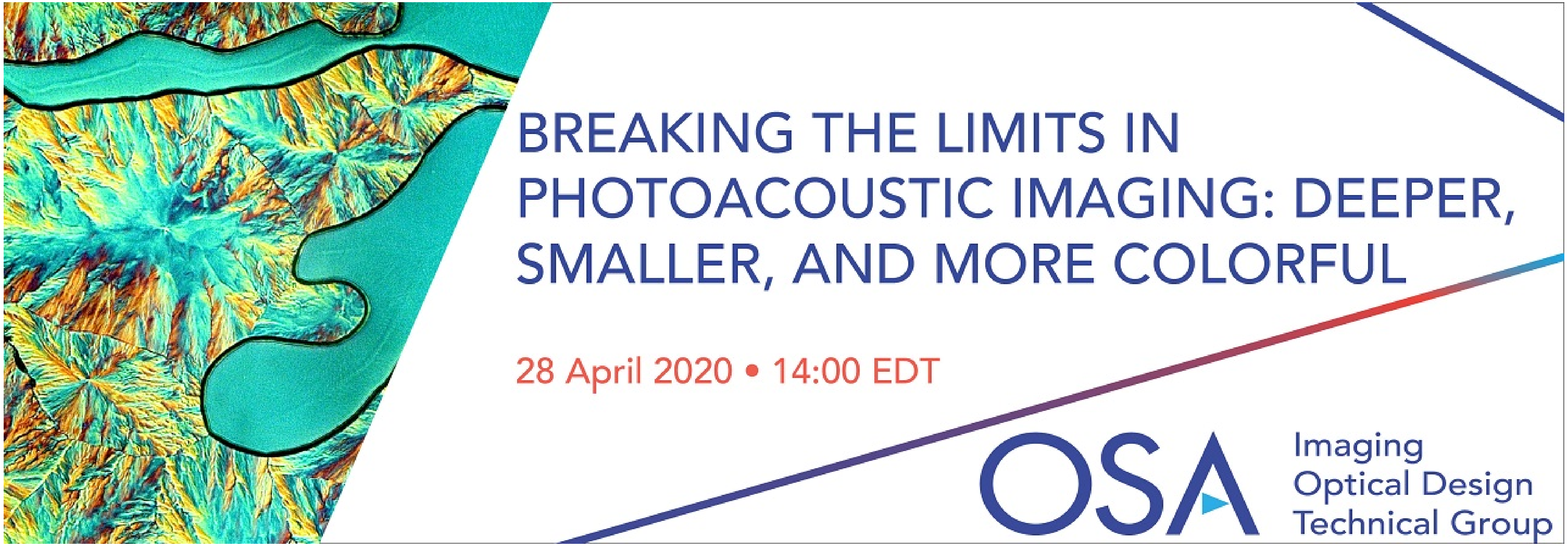

# Breaking the Limits in Photoacoustic Imaging: Deeper, Smaller, and More Colorful

Junjie Yao, Duke University

# The OSA Imaging Optical Design Technical Group Welcomes You!



# The OSA Imaging Optical Design Technical Group

This group encompasses the design and characterization of traditional optical systems utilizing lens design, geometric ray-tracing, and physical optics modeling.

The evolution and development of design codes and software to assist in designing components and systems are included here.

Typical applications include astronomical telescopes, microscopes, cameras, stray light, and adaptive optics.

# Technical Group Leadership 2020

Chair
Dr. Maryna L. Meretska

Vice Chair
Dr. Xusan Yang

Social Media Officer
Dr. Marie-Anne Burcklen

Event Officer
Dr. Sarmishtha Satphaty

# Our Technical Group at a Glance

## Our Focus

- “Physics of nonlinear optical materials, processes, devices, & applications”
- 2000 members

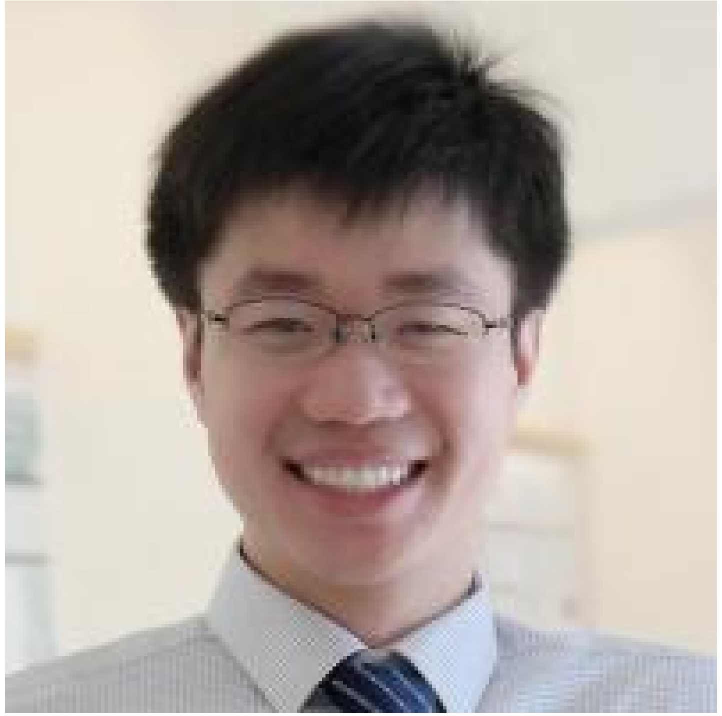
## Our Mission

- To benefit *YOU*
- Webinars, social media, publications, technical events, business events, outreach
- Interested in presenting your research? Have ideas for TG events? Contact us at: TGactivities@osa.org.

## Where To Find Us

- Website: https://www.osa.org/fd
- Facebook: https://www.facebook.com/groups/OSAImagingOpticalDesign/
- LinkedIn: https://www.linkedin.com/groups/8113351/

# Today's Webinar



## Breaking the limits in photoacoustic imaging: deeper, smaller, and more colorful


## Dr. Junjie Yao

Assistant Professor at the Department of Biomedical Engineering
at Duke University, USA
junjie.yao@duke.edu

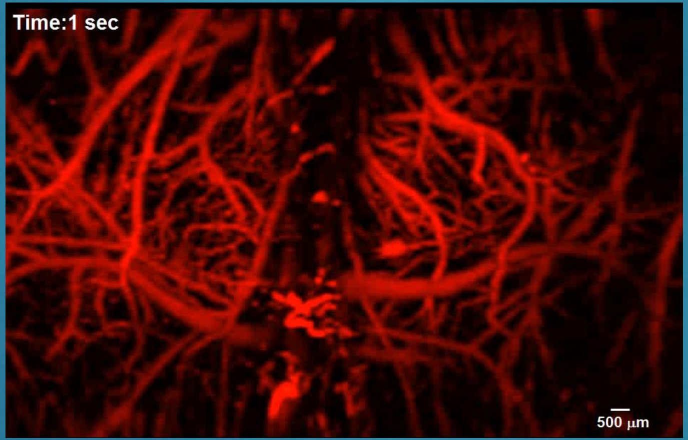

## Speaker's Short Bio:

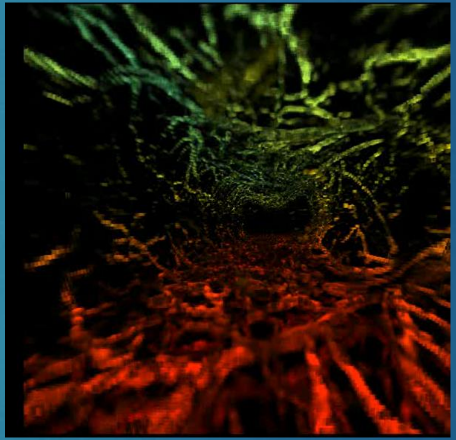
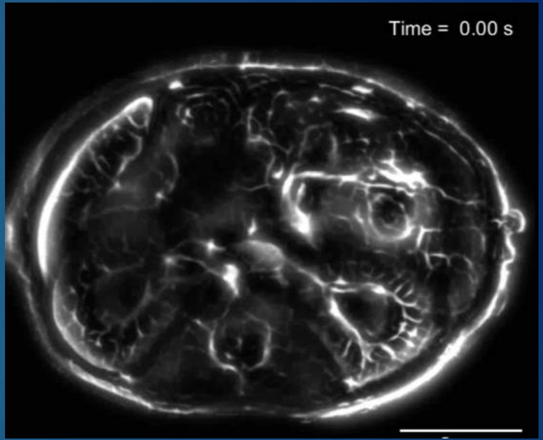
Graduation in Physics at Tsinghua University, China
Ph.D. degree from Washington University, USA

Imaging
Optical Design
Technical Group

From Light to Sound

# Breaking the Limits in Photoacoustic Imaging: Smaller, Deeper, and More Colorful




**Junjie Yao, Ph.D.**
Assistant Professor
Biomedical Engineering
Duke University

**OSA**
**April 28th, 2020**

https://photoacoustics.pratt.duke.edu/

# Acknowledgements

Collaborators

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Ulrike Hoffmann (Duke)
Wei Yang (Duke)
Vlad Verkhusha (AEC)
Jeff Chan (UIUC)
Yun Jing (NCSU)

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Maomao Chen
Qiangzhou Rong
Xiaoyi Zhu
Hannah Humayun

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NIH R01 NS115581 (Yao)
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NIH R21 EB027304 (Jiang and Yao)
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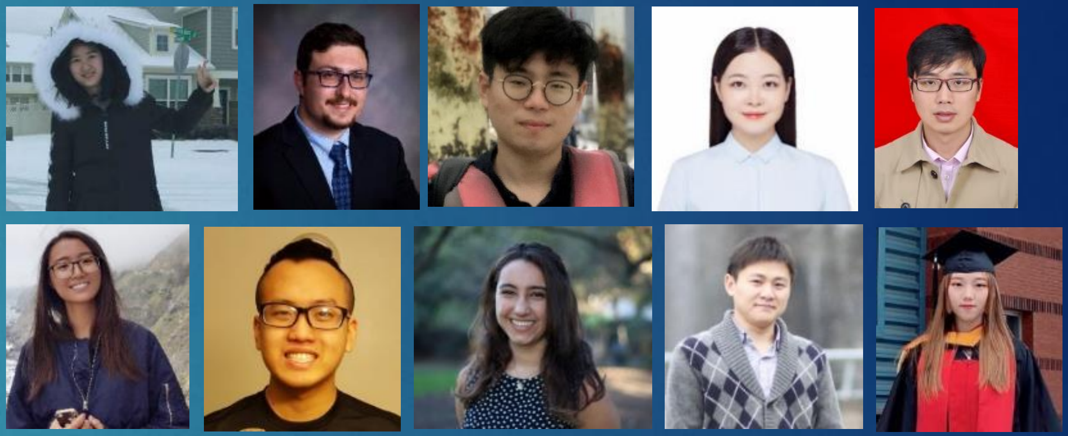
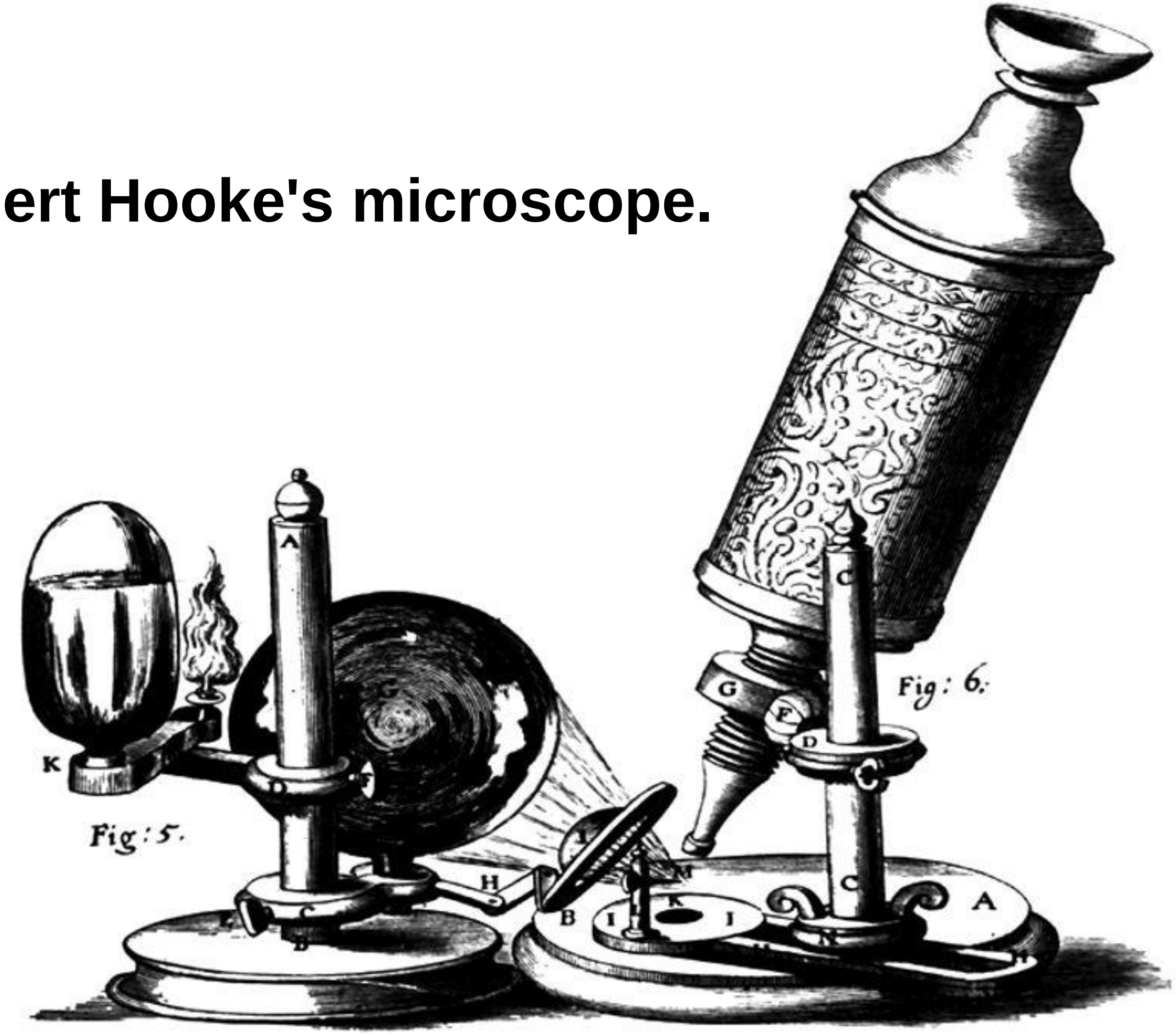
Duke DIBS incubator grant (Yao)



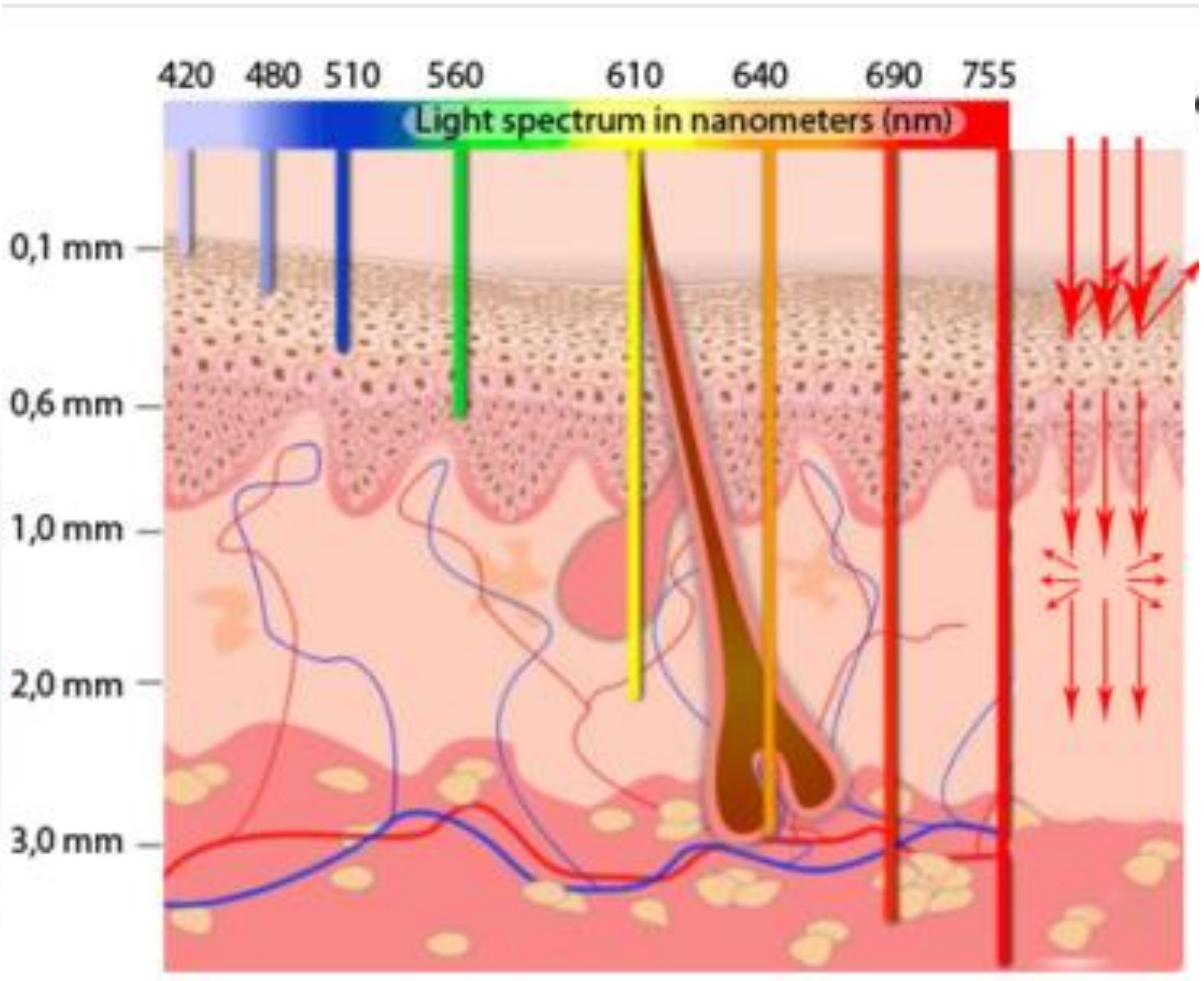
# More than 300 years, optical imaging stays similar!

**1665 - Robert Hooke's microscope.**

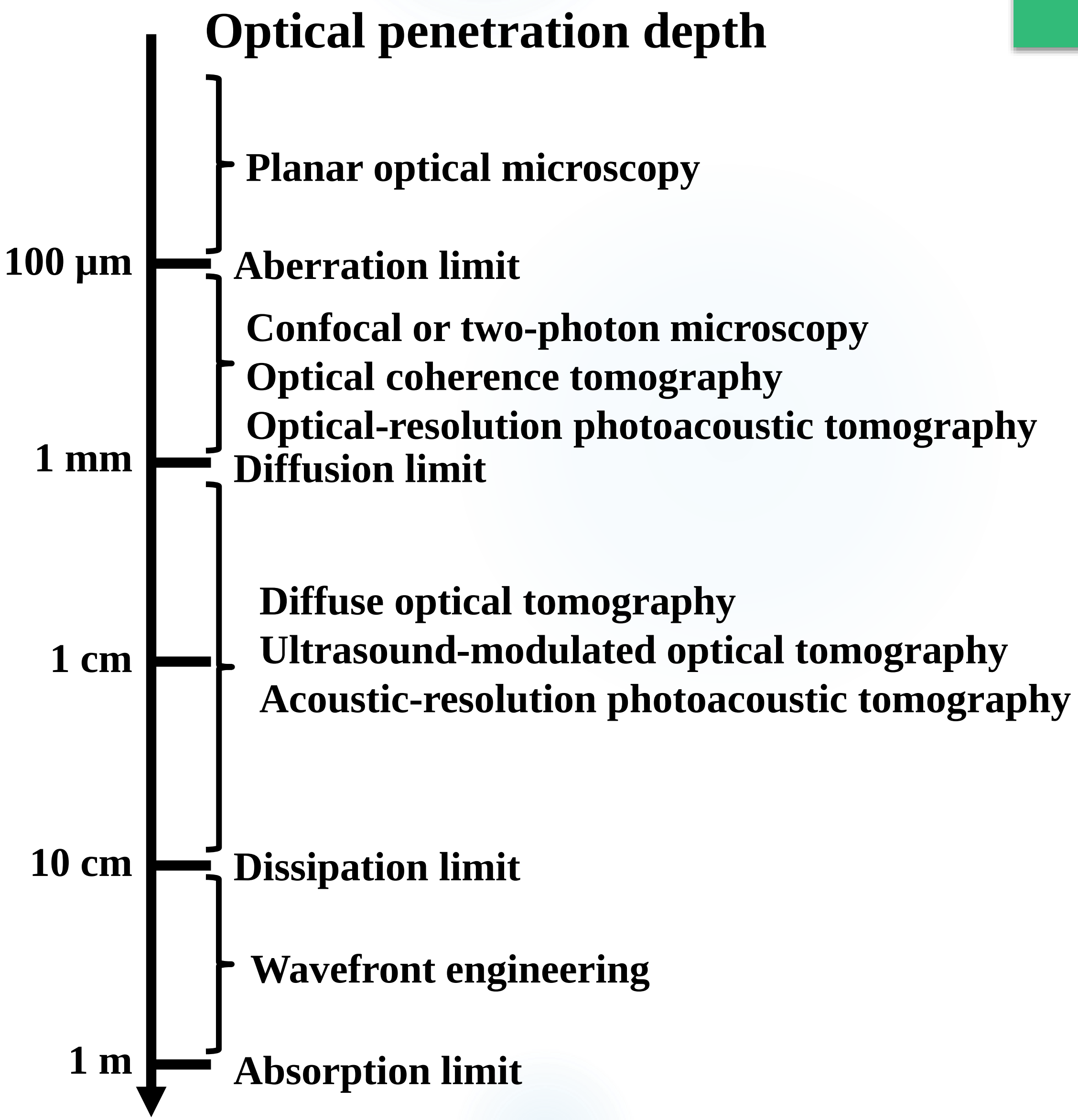


# When light meets tissue: scattering and absorption






*The propoagation of light of different wavelengths in the tissues.*

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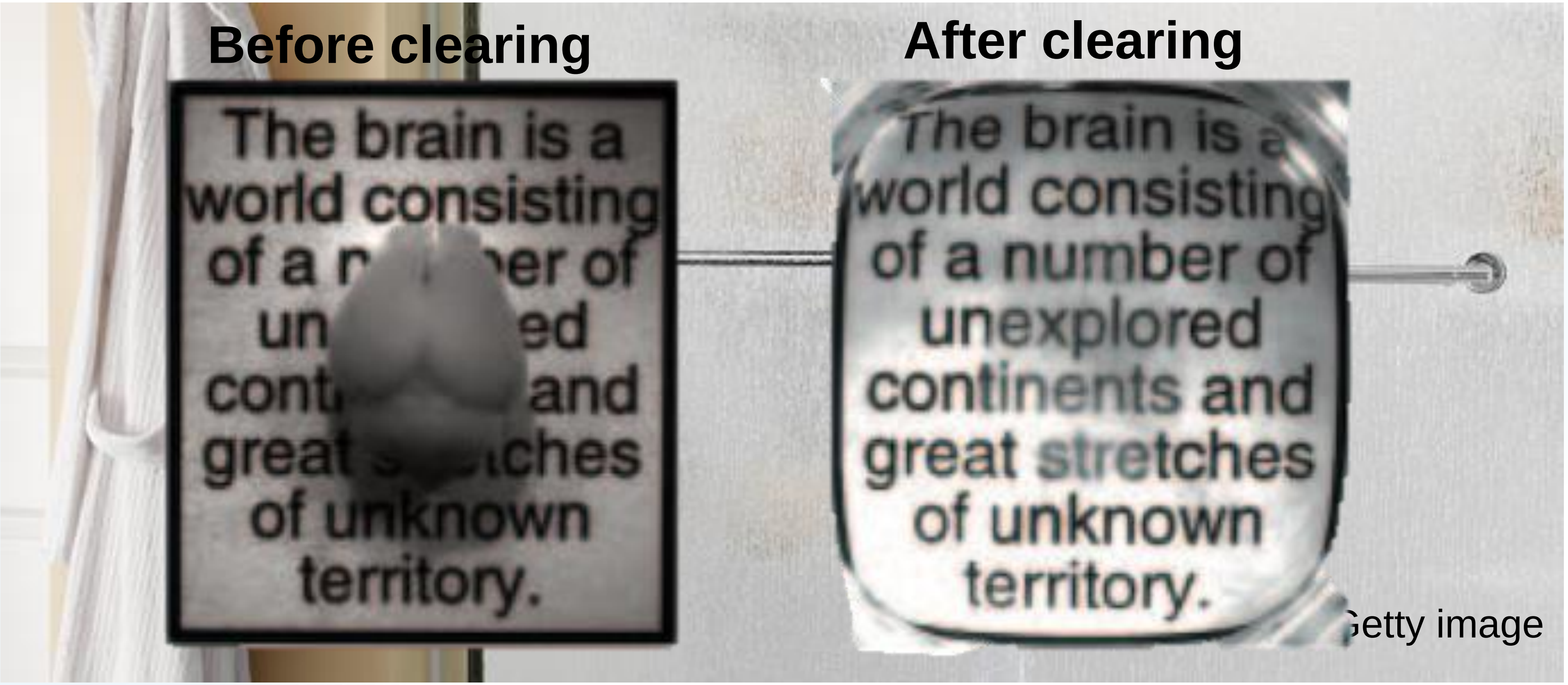
# Light is like life, going in all directions

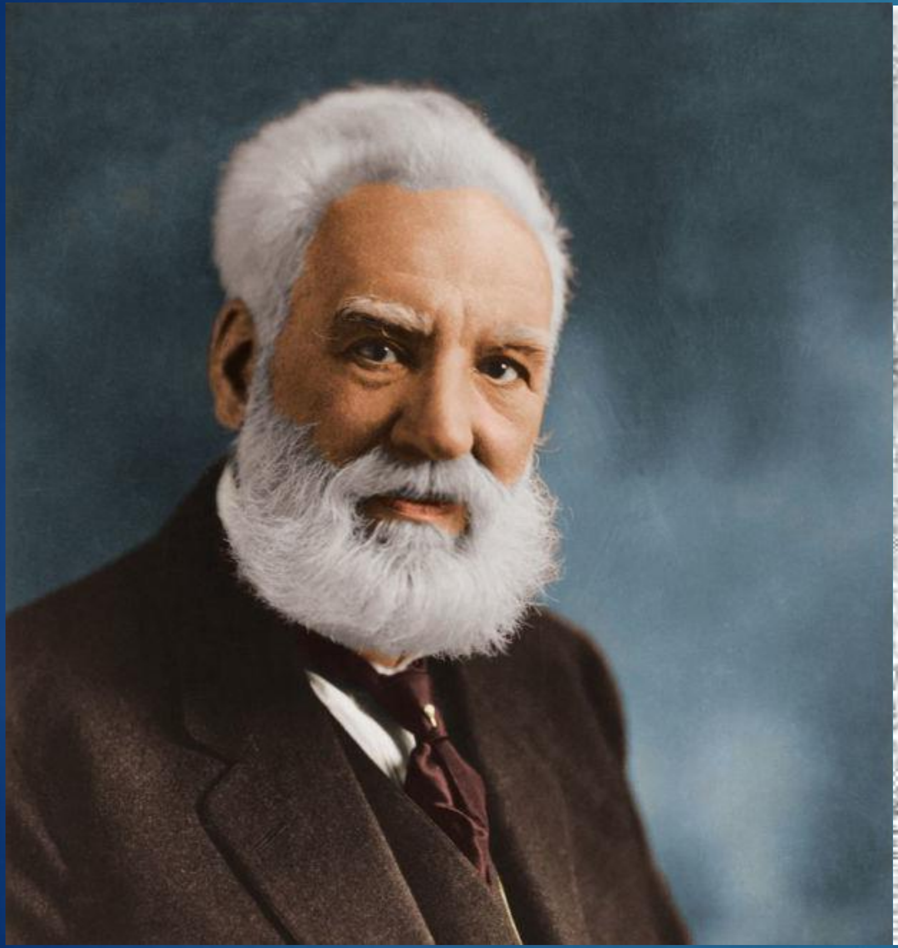


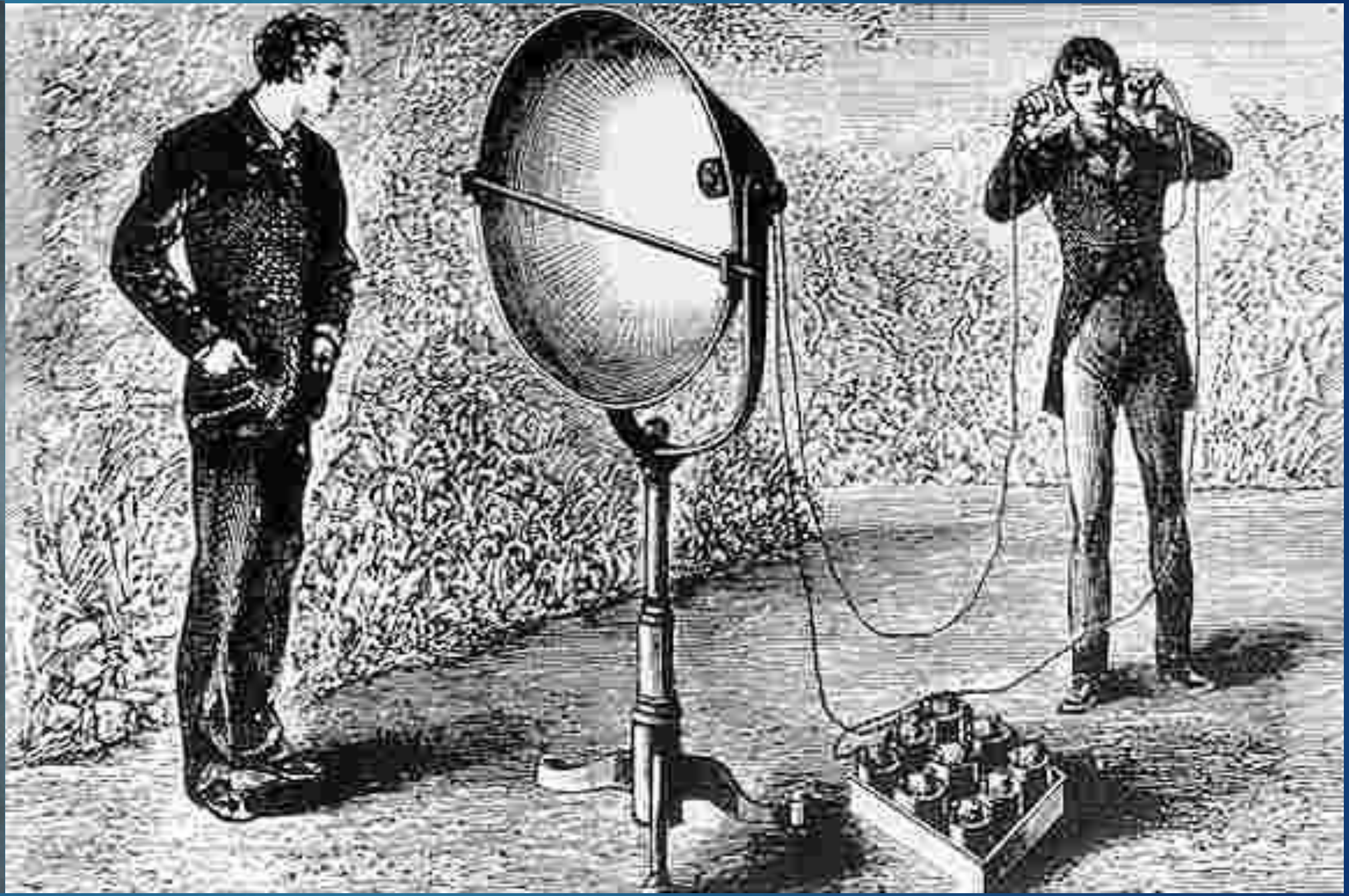



Nature, 497, 332–337

# Photoacoustic effect: Listening to absorbed light

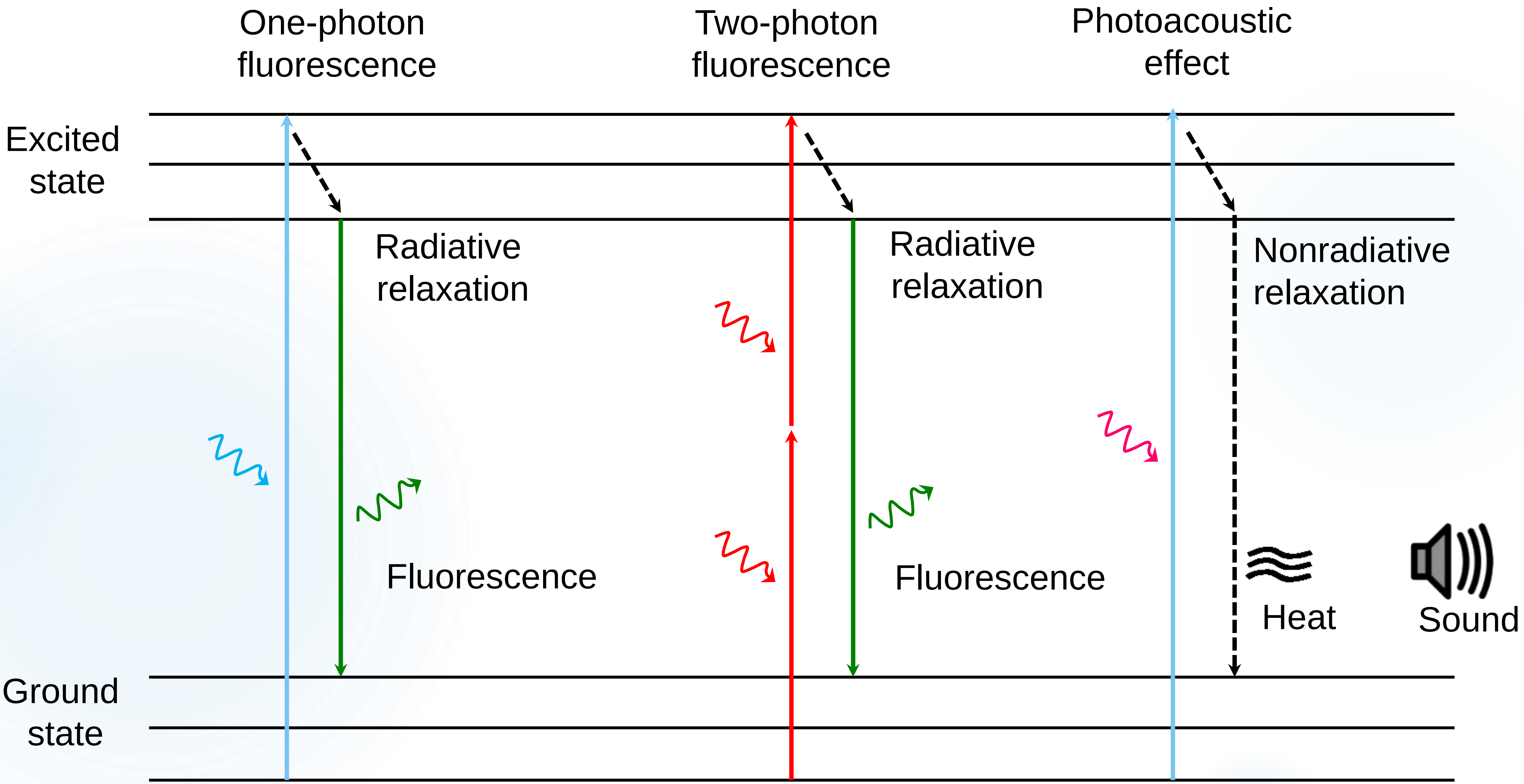






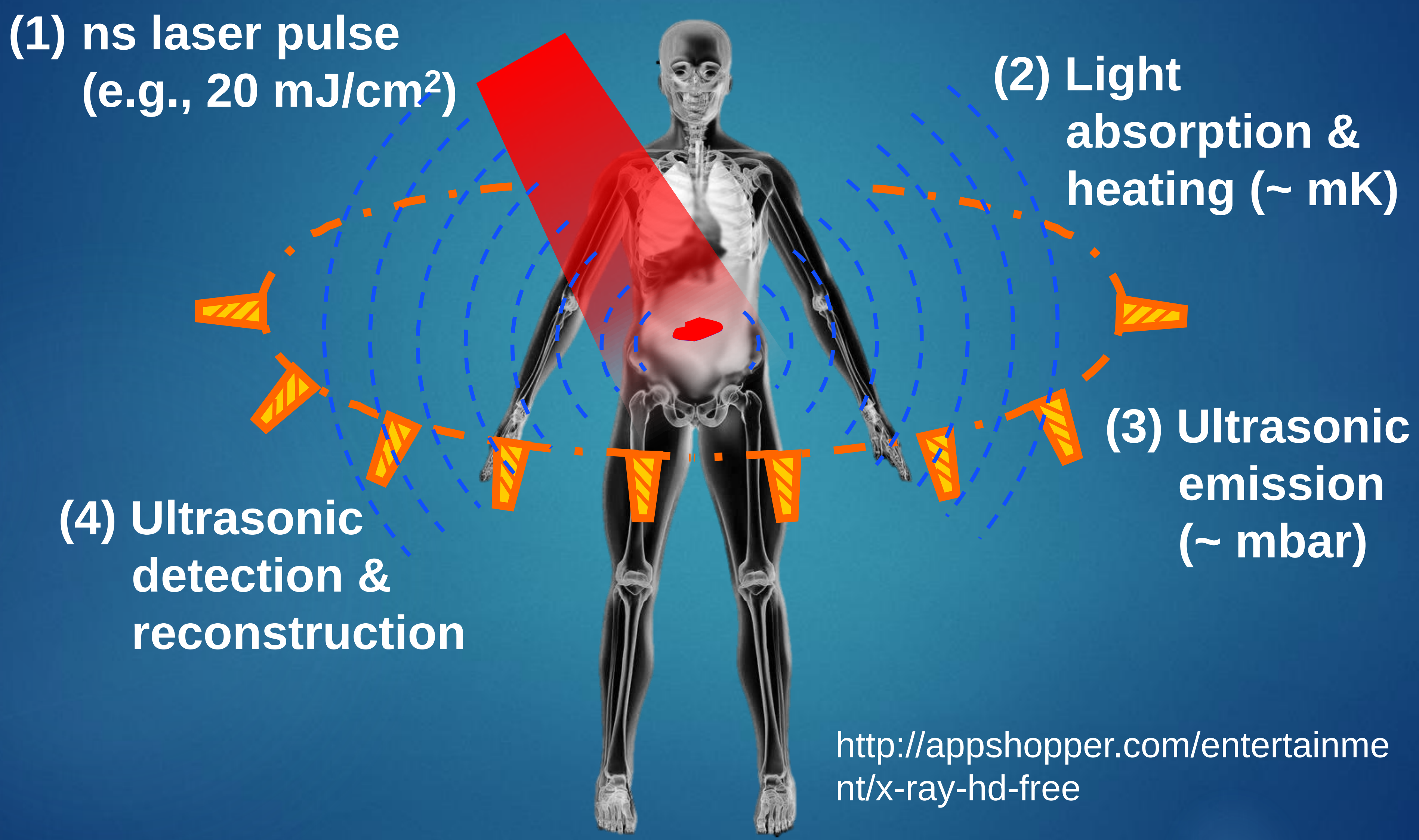
# When light is absorbed, it is fluorescence and/or heat





# Photoacoustic tomography: from energy to image



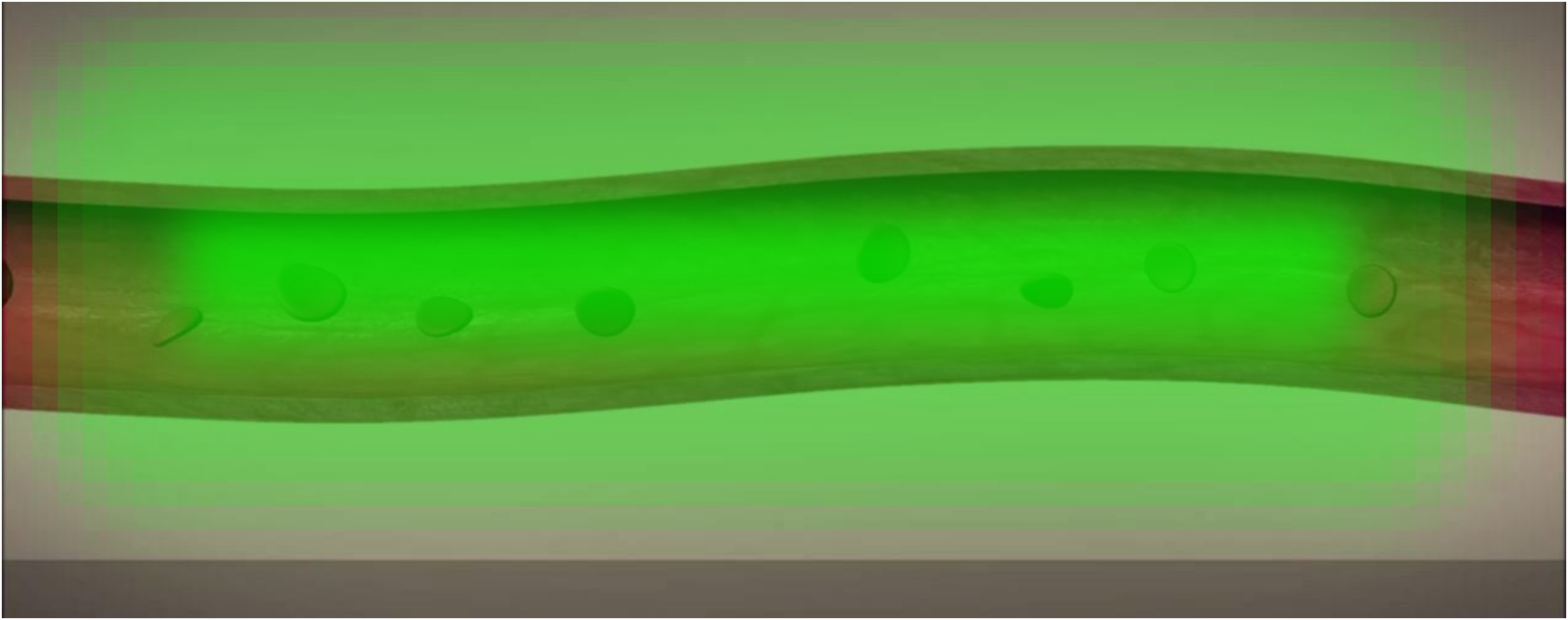



http://appshopper.com/entertainment/x-ray-hd-free

J Yao et al., Nature Methods 13(8), 2016

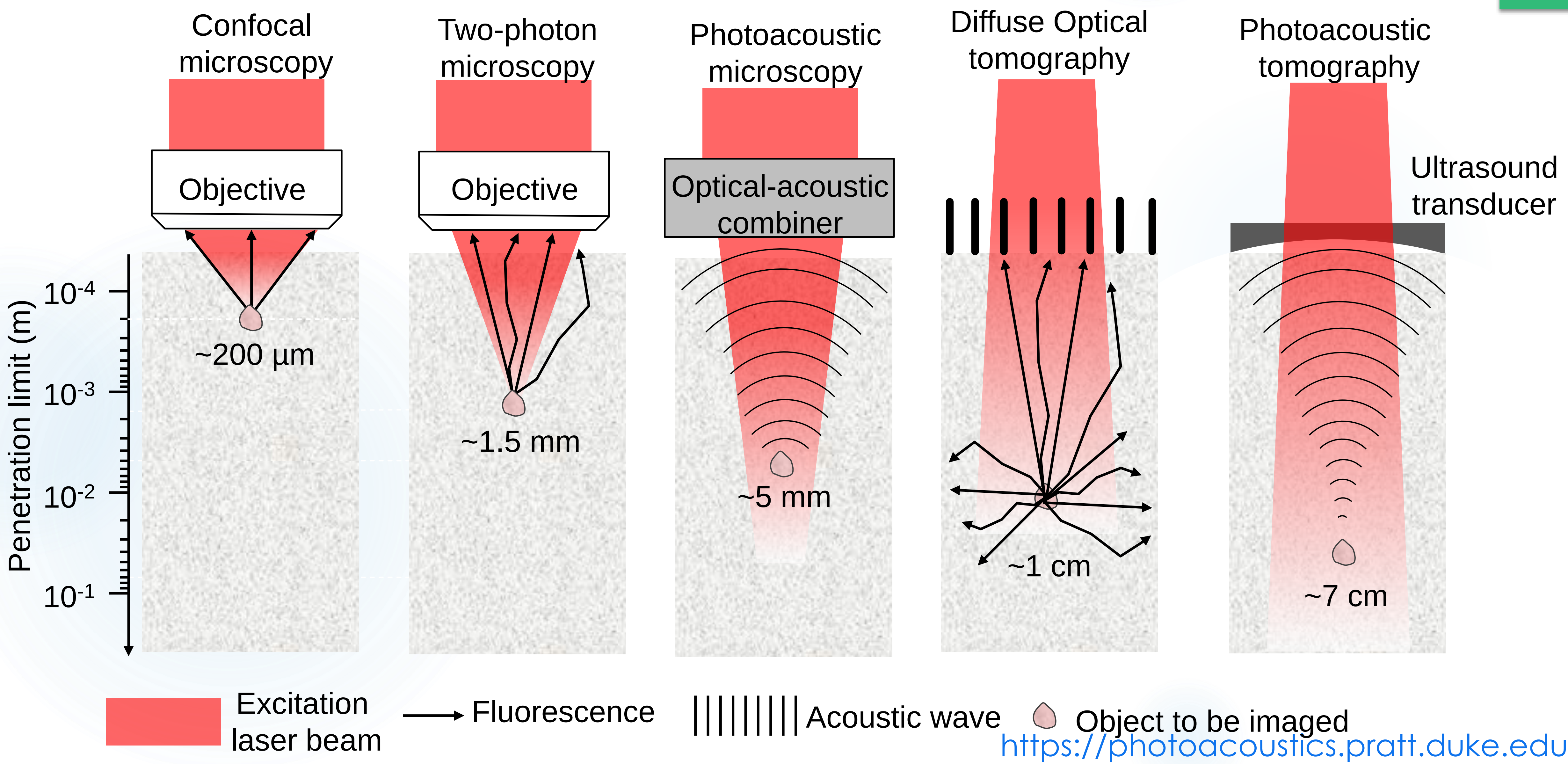
# Photoacoustic imaging: Listening to light whispering in tissues





Reference: Canon Inc.

# Optical imaging of the tissue: from shallow to deep

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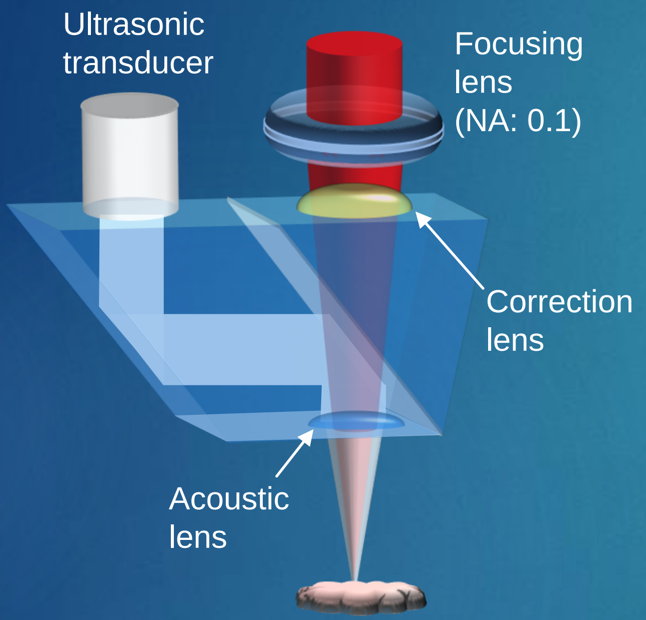
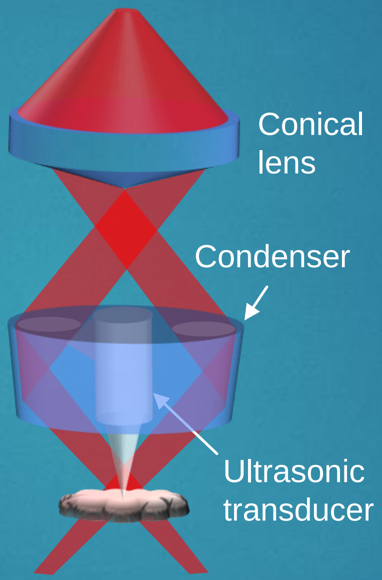
# Implementations of photoacoustic tomography

**Optical-resolution photoacoustic microscopy**



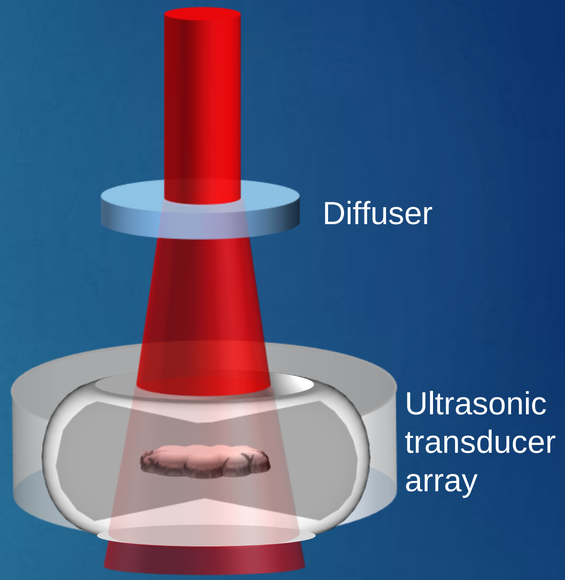

Resolution: 0.2-10 µm
Penetration: 1-2 mm

**Acoustic-resolution photoacoustic microscopy**




Resolution: 15-50 µm
Penetration: 3-10 mm

**Photoacoustic computed tomography**



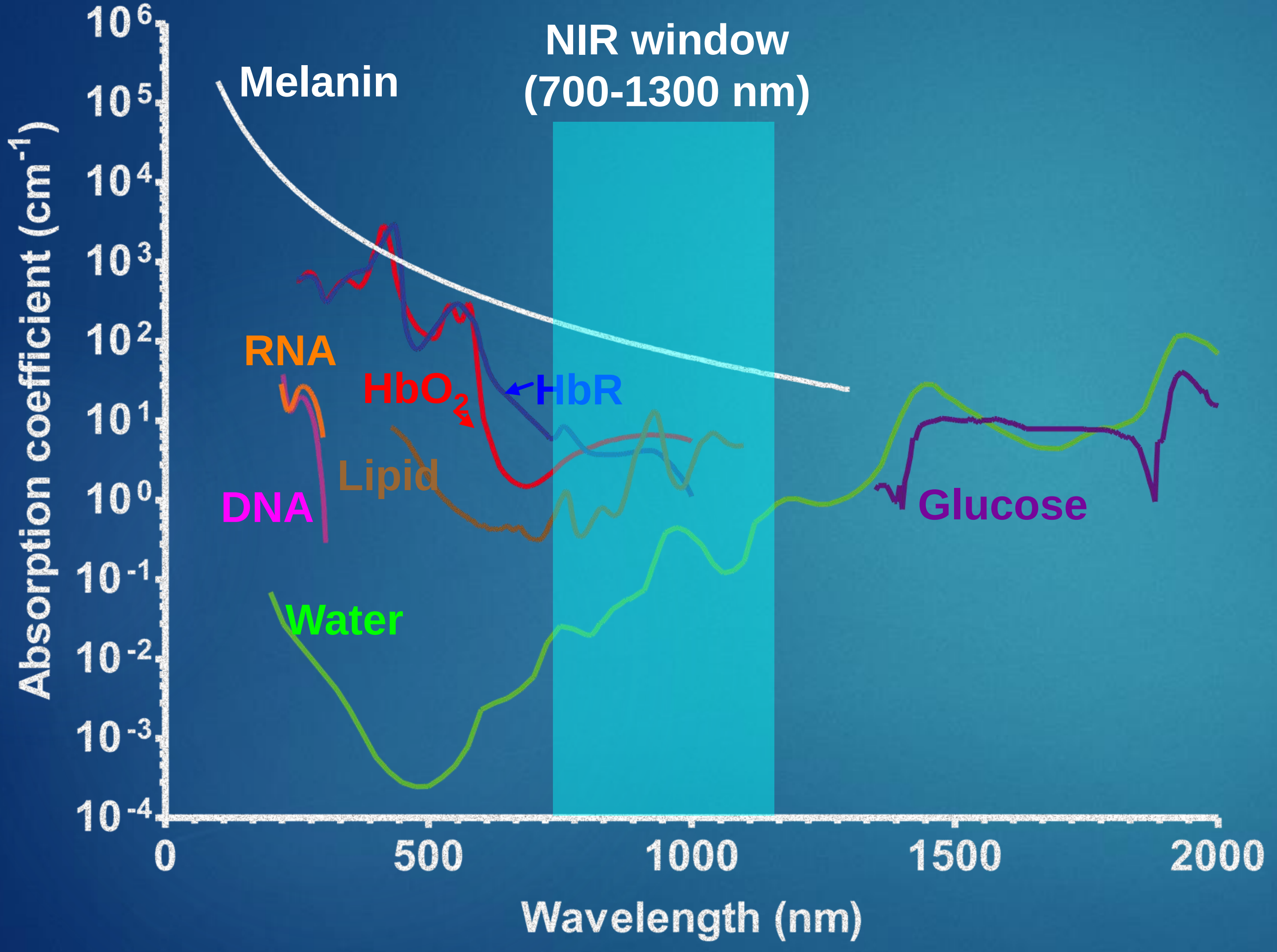

Resolution: 100-500 µm
Penetration: 10-100 mm

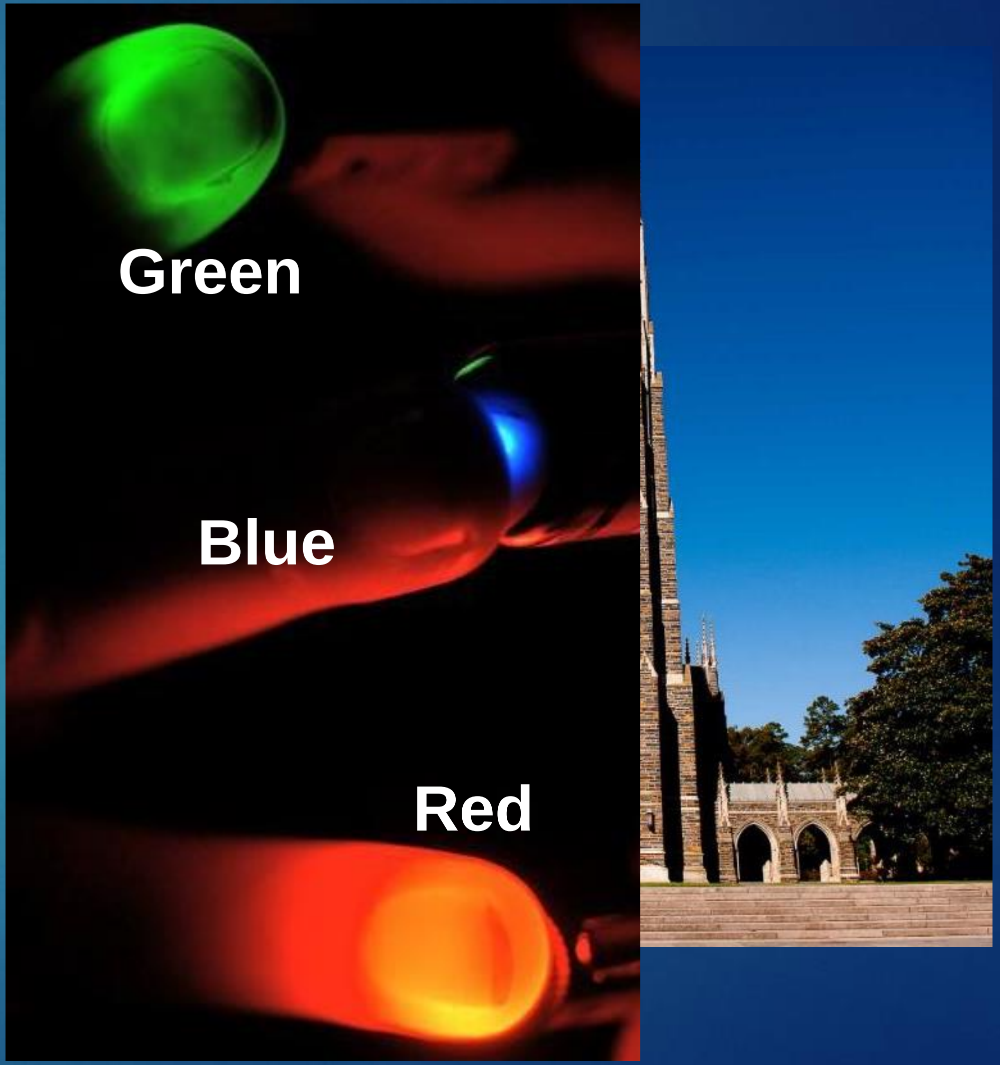
Laser beam | Acoustic wave | Object to be imaged

J Yao et al., Nature Methods 13(8), 2016

https://photoacoustics.pratt.duke.edu/

# Endogenous contrast for photoacoustic imaging




J Yao and L Wang, Laser Photon Rev, 7(5), 2013.

# Exogenous contrast for photoacoustic imaging

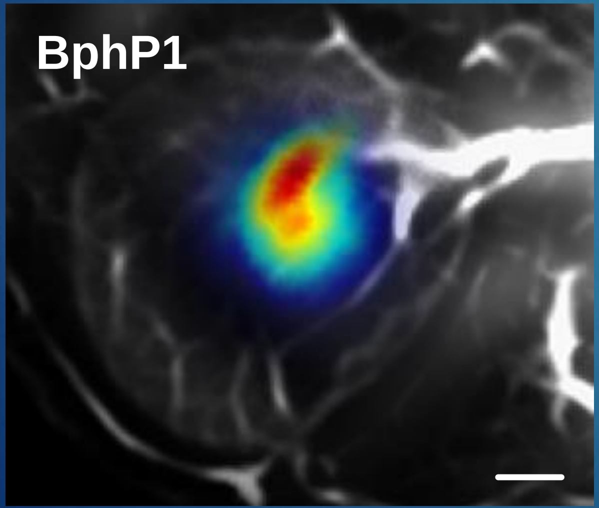
**Size (nm)**

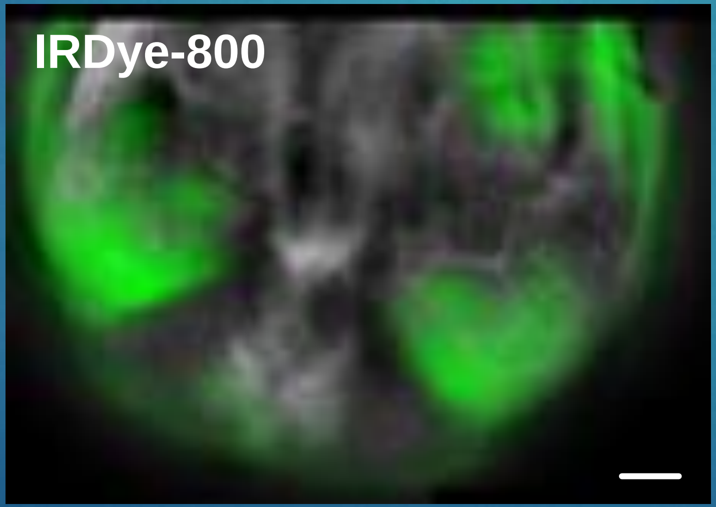
1 | 5 | 10 | 50 | 100 | 1000

**Reporter gene products** | **Organic dyes** | **Nanoparticles/Quantum dots**

$10^6$ | $10^3$ | $10^0$ | $10^{-3}$

**Sensitivity (nM)**





J Yao et al., Nature Methods 13(8), 2016

# Duke photoacoustic-imaging Lab in 3 years!

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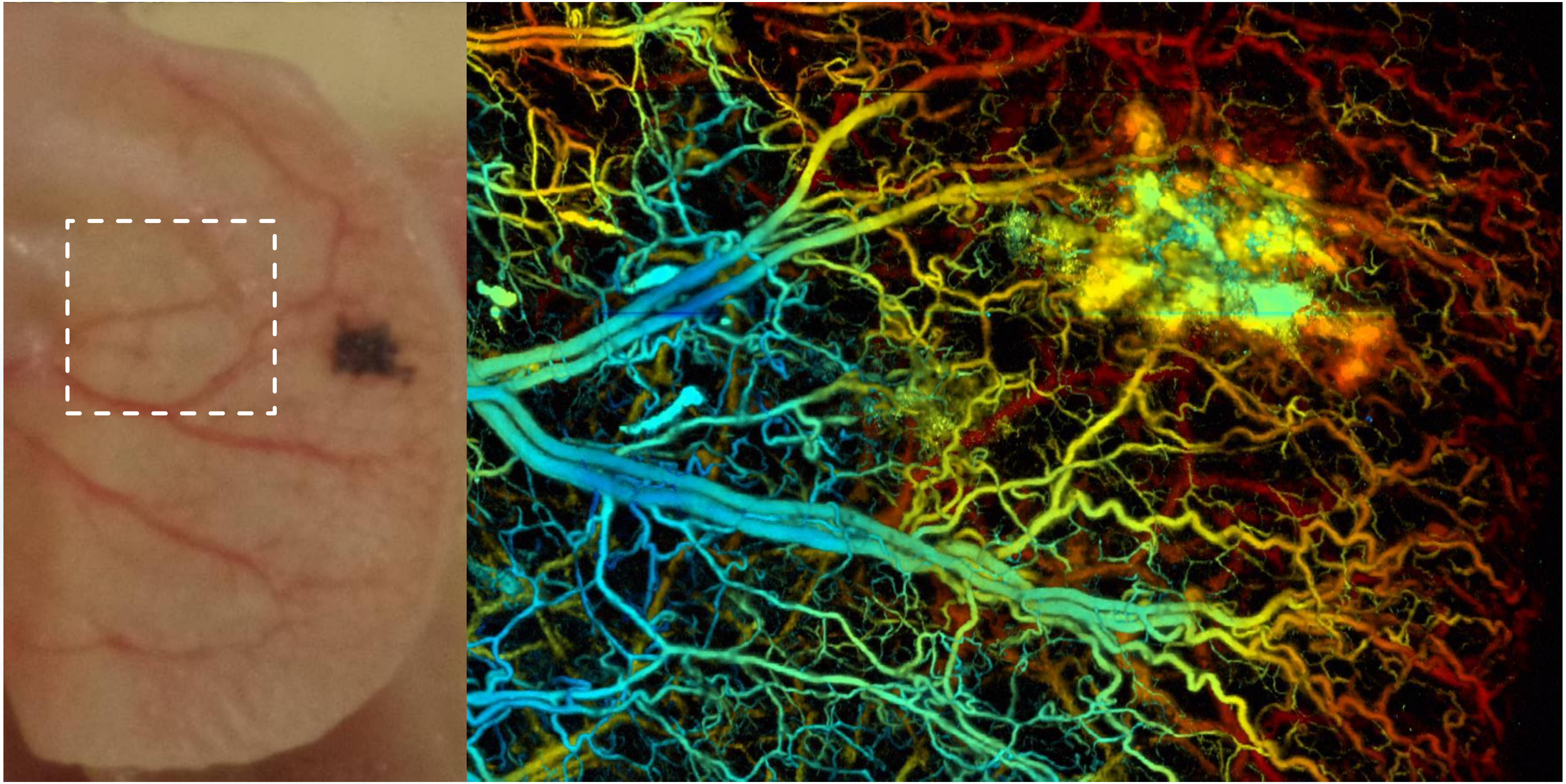
# Example 1: High-resolution photoacoustic microscopy





J Yao et al. Optics Letters, 35(9), 2010

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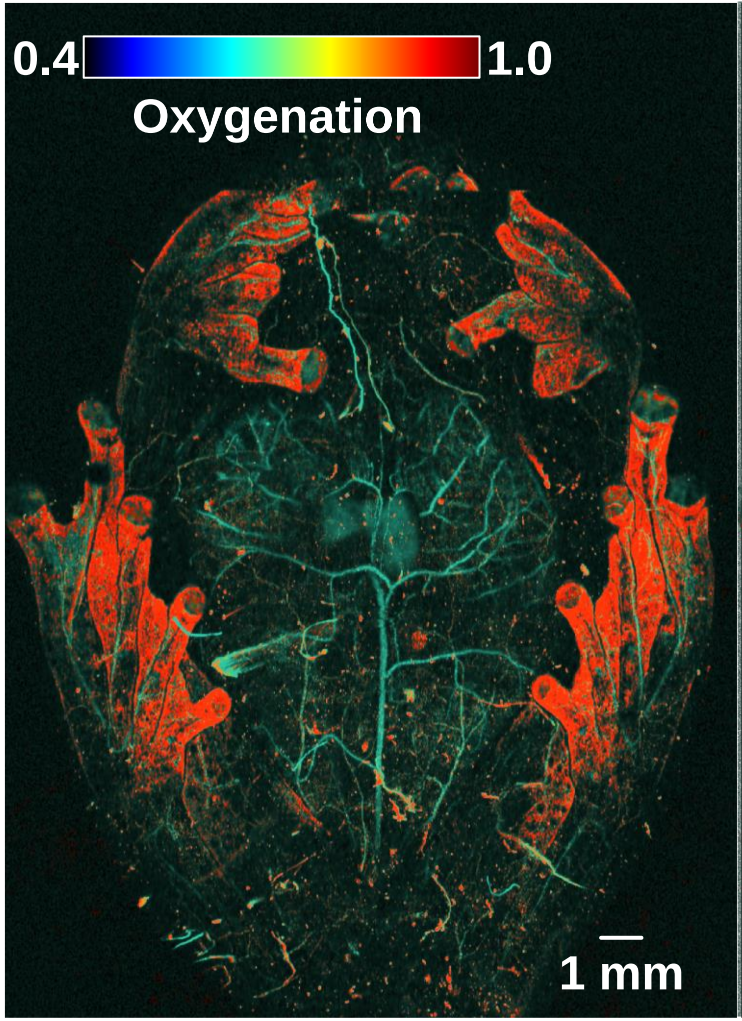
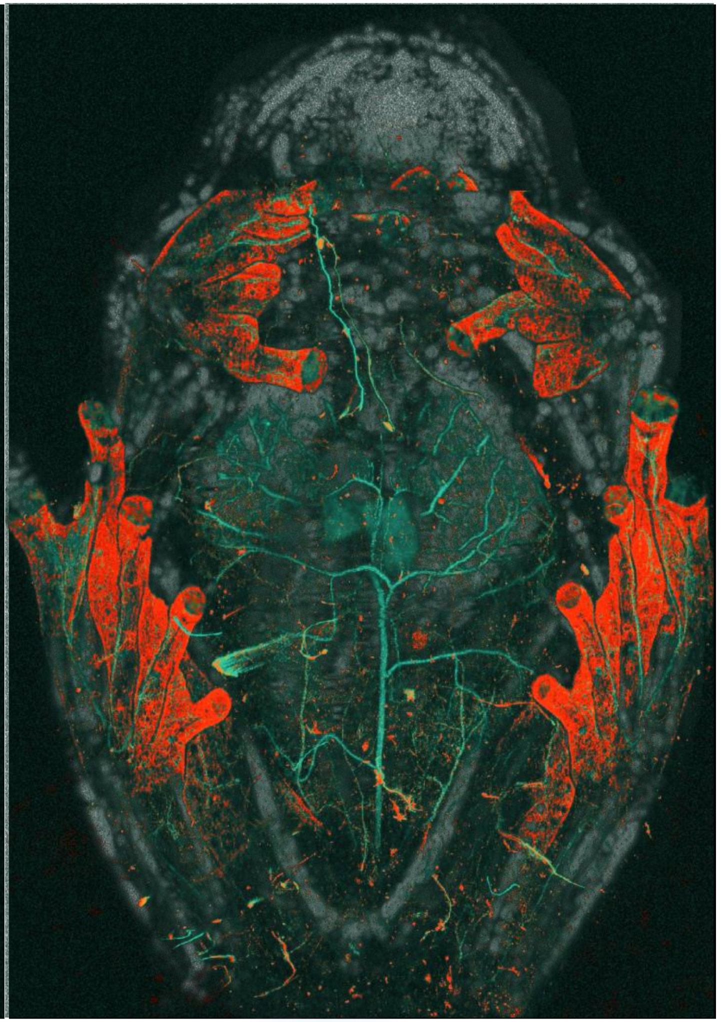
# Photoacoustic microscopy of glass frog in resting/active states



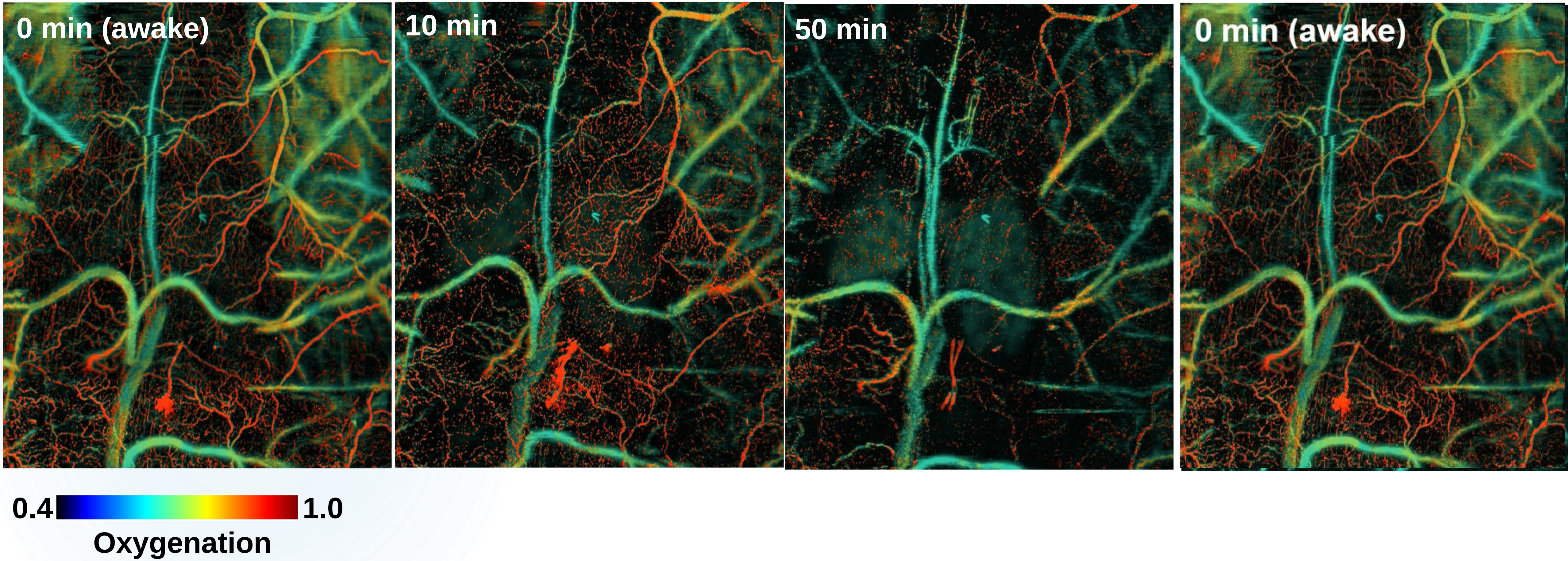
**H. Fleischmanni** | **Oxygenation map (PAM)** | **Anatomy (US imaging)**



**Unpublished, Duke Photoacoustic Lab; Collaborator, Carlos Taboada**

# Monitoring blood 'storage' of glass frog from awake to asleep

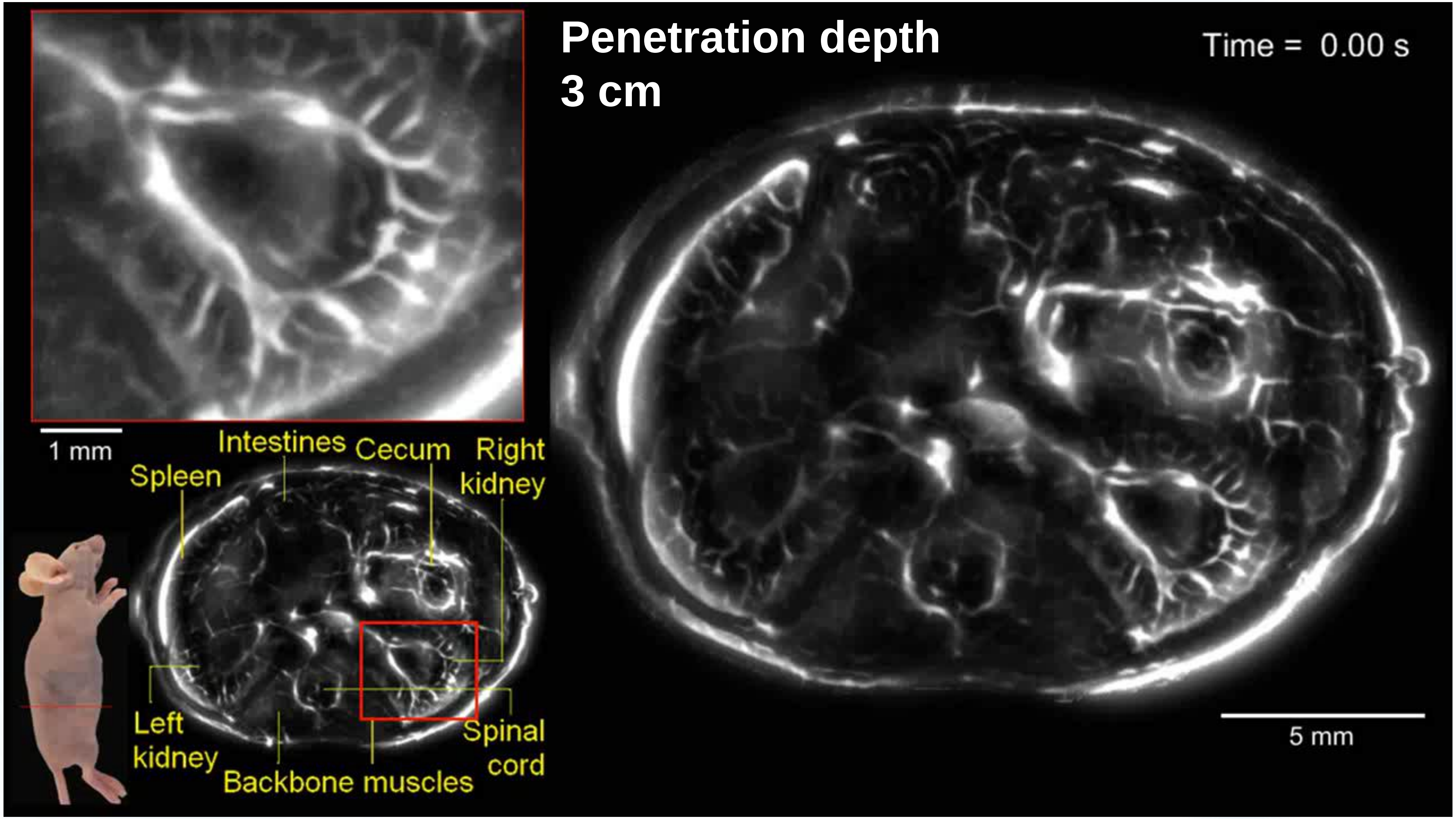



Unpublished, Duke Photoacoustic Lab; Collaborator, Carlos Taboada

https://photoacoustics.pratt.duke.edu/

# Example 2: Whole-body small-animal photoacoustic tomography

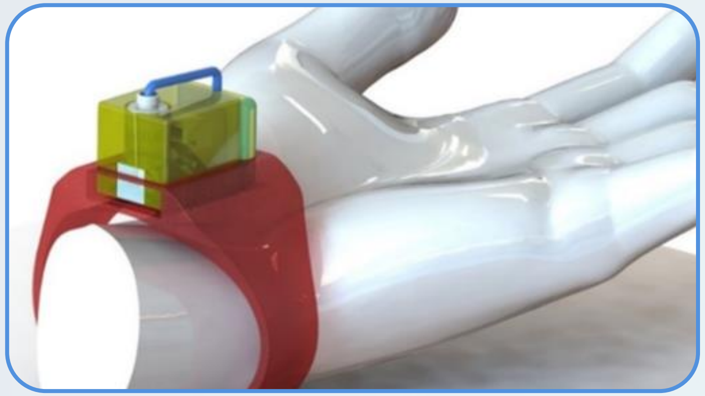


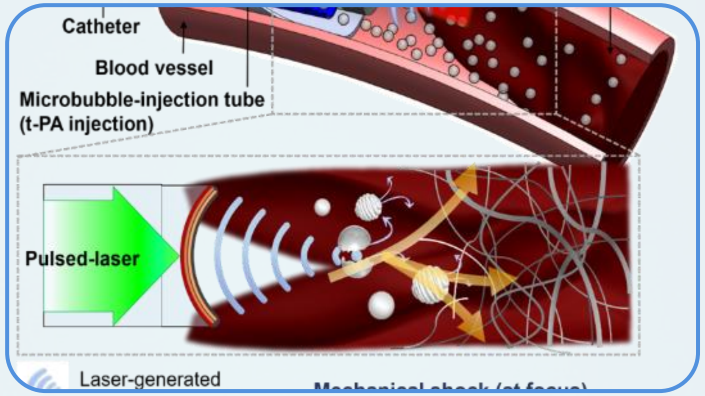


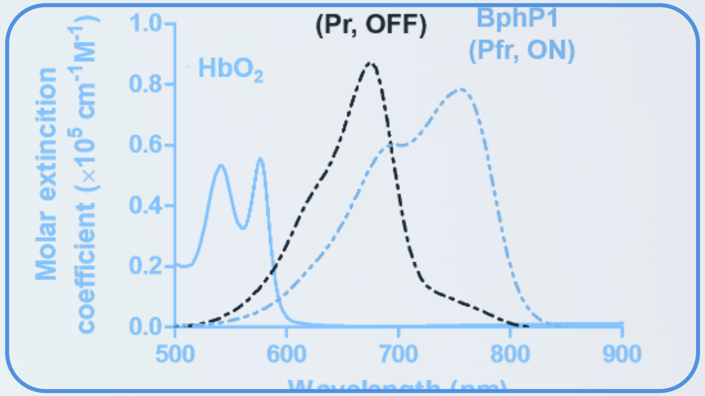

L Li, J. Yao et al. Nature Biomedical Engineering, 1, 0071 (2017)

https://photoacoustics.pratt.duke.edu/

# Our missions at Duke PI-Lab





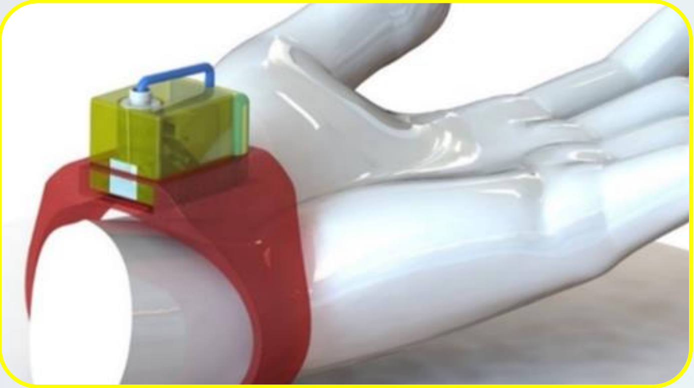

**Smaller** for high throughput

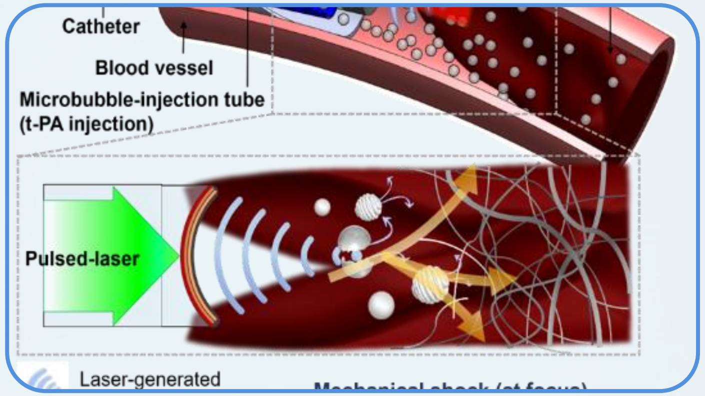
**Deeper** for clinical impact

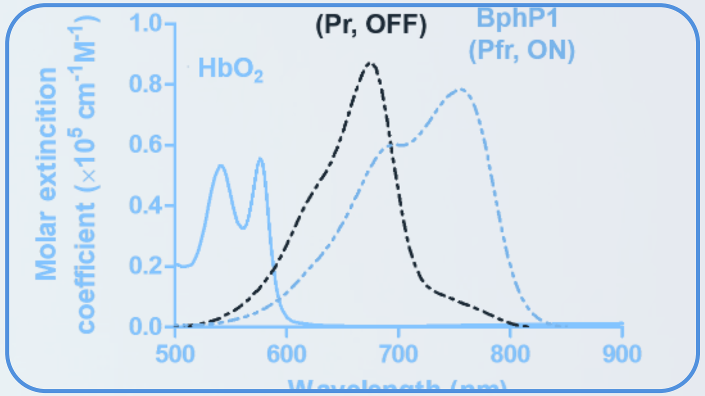
**Colorful** for molecular sensitivity

# Our missions at Duke PI-Lab







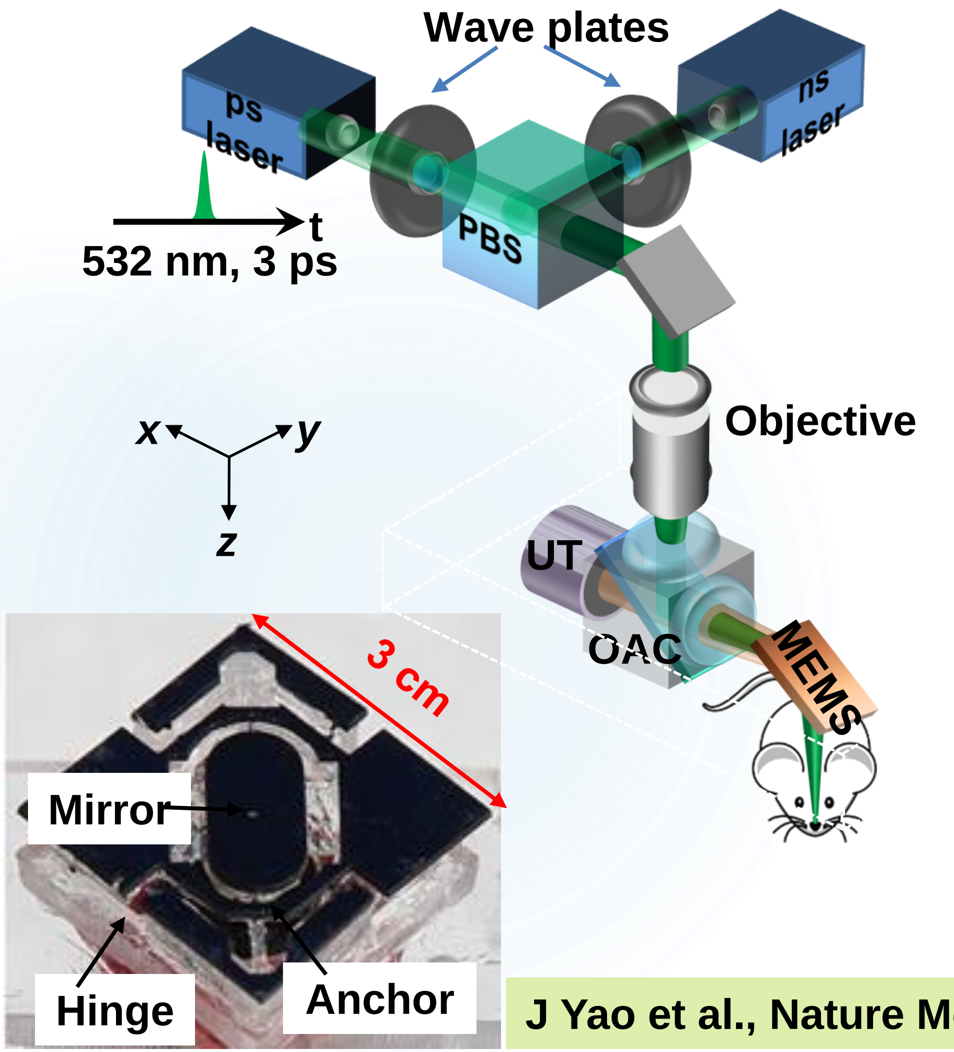



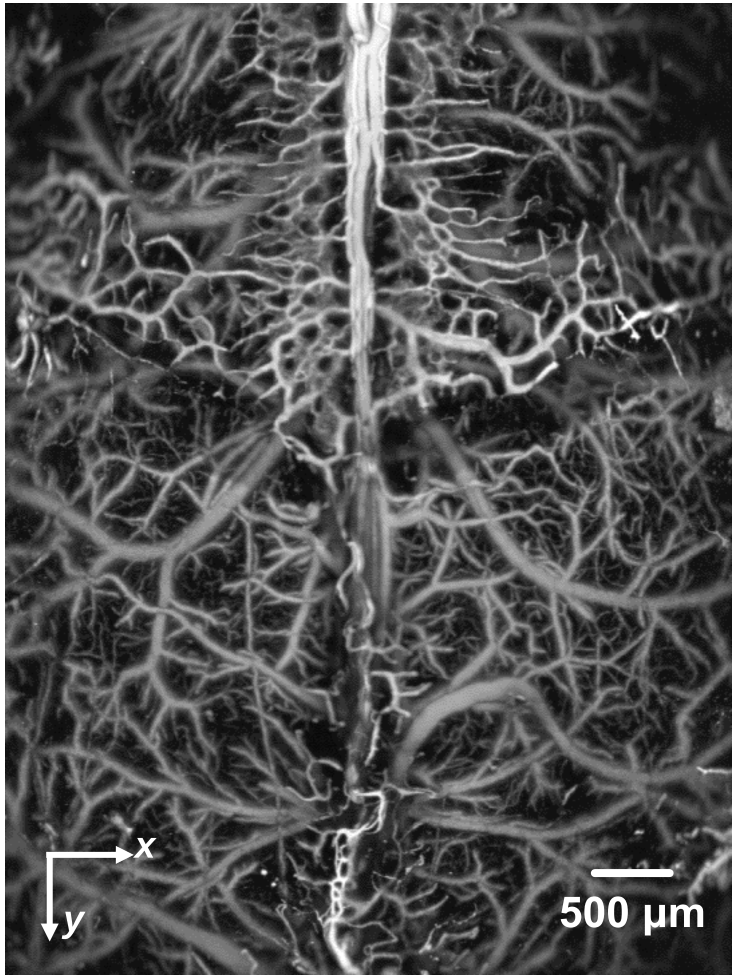

**Smaller** for high throughput

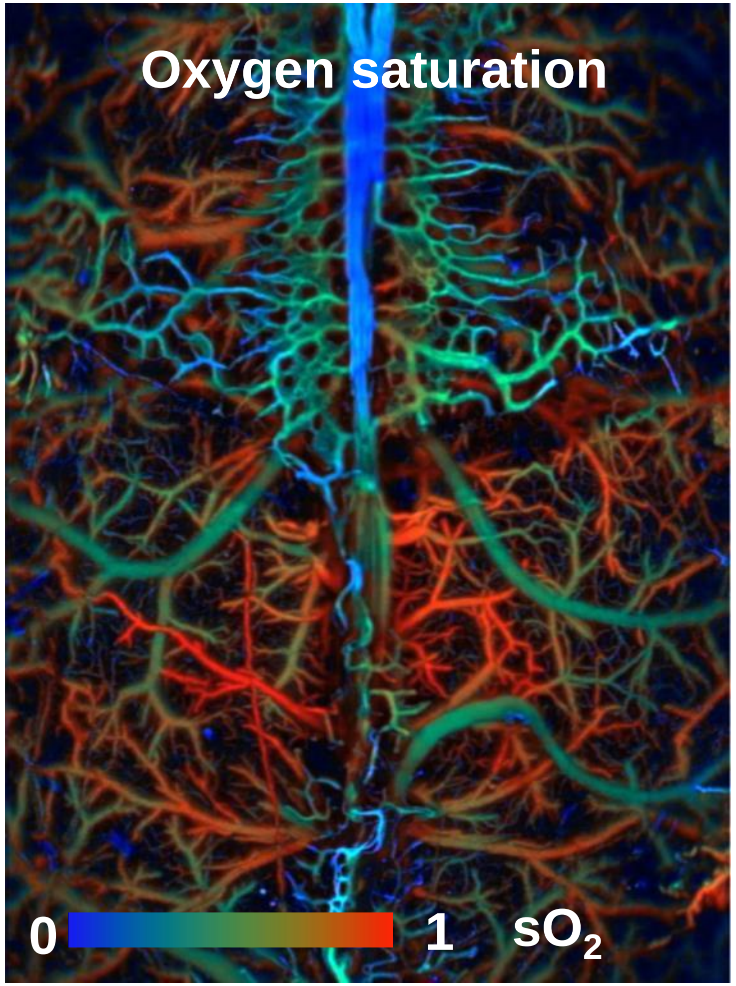
**Deeper** for clinical impact

**Colorful** for molecular sensitivity

# High-speed MEMS-based benchtop photoacoustic imaging



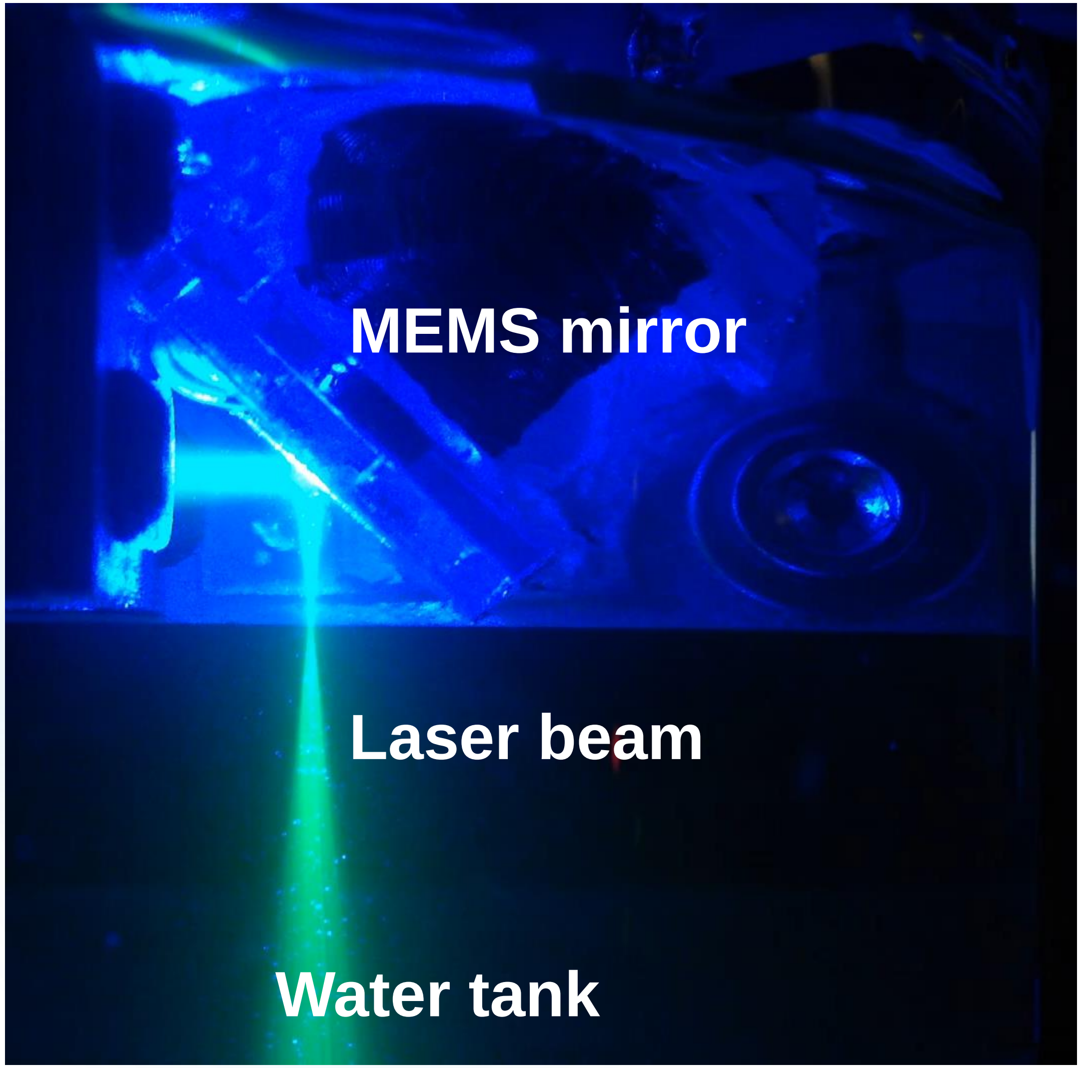



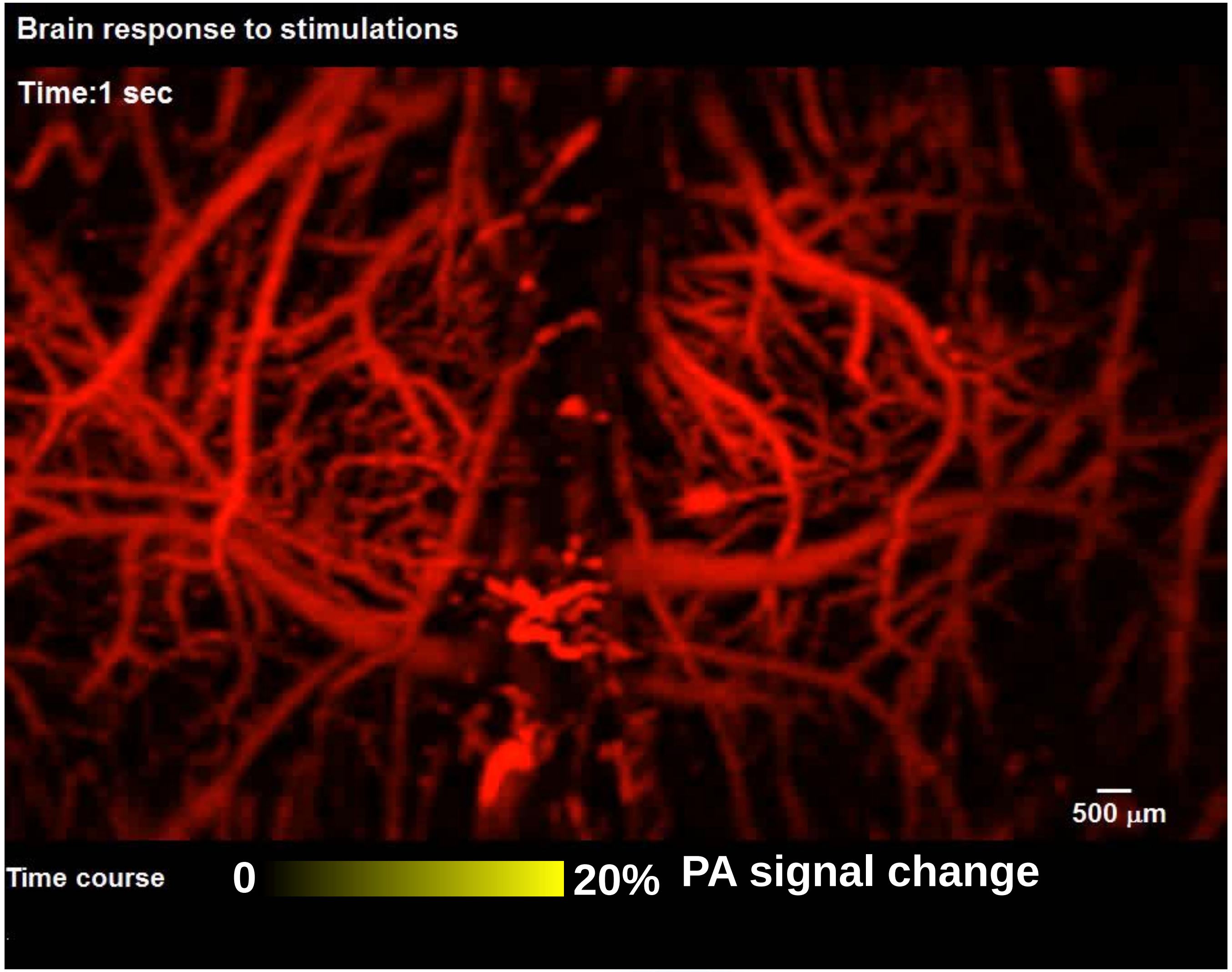

J Yao et al., Nature Methods, 2015, 12 (5), 407-410

https://photoacoustics.pratt.duke.edu/

# MEMS-based benchtop PAM of brain's hemodynamic response



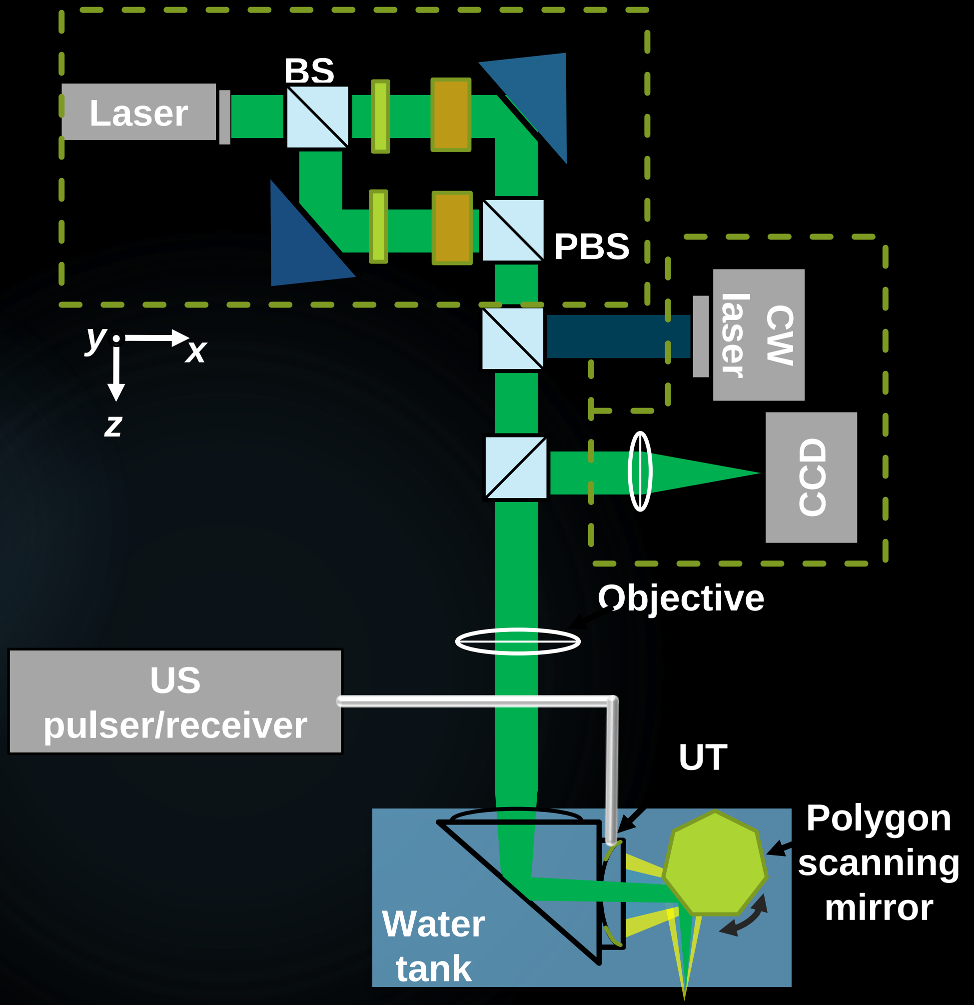


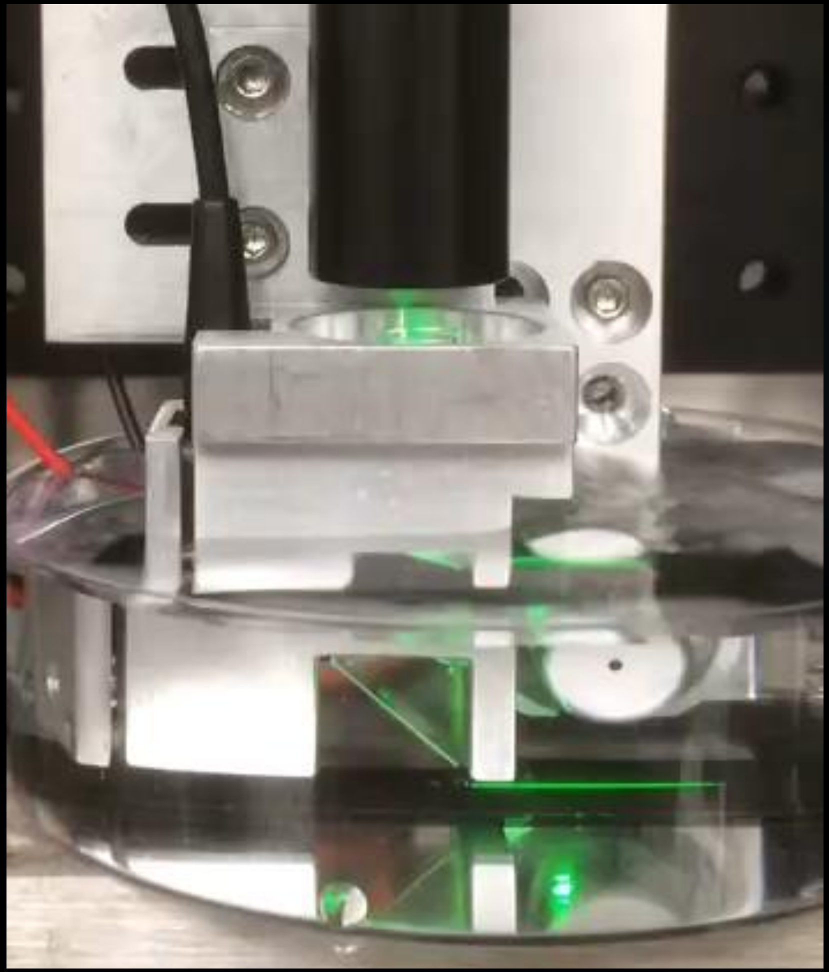




J Yao et al., Nature Methods, 2015, 12 (5), 407-410

https://photoacoustics.pratt.duke.edu/

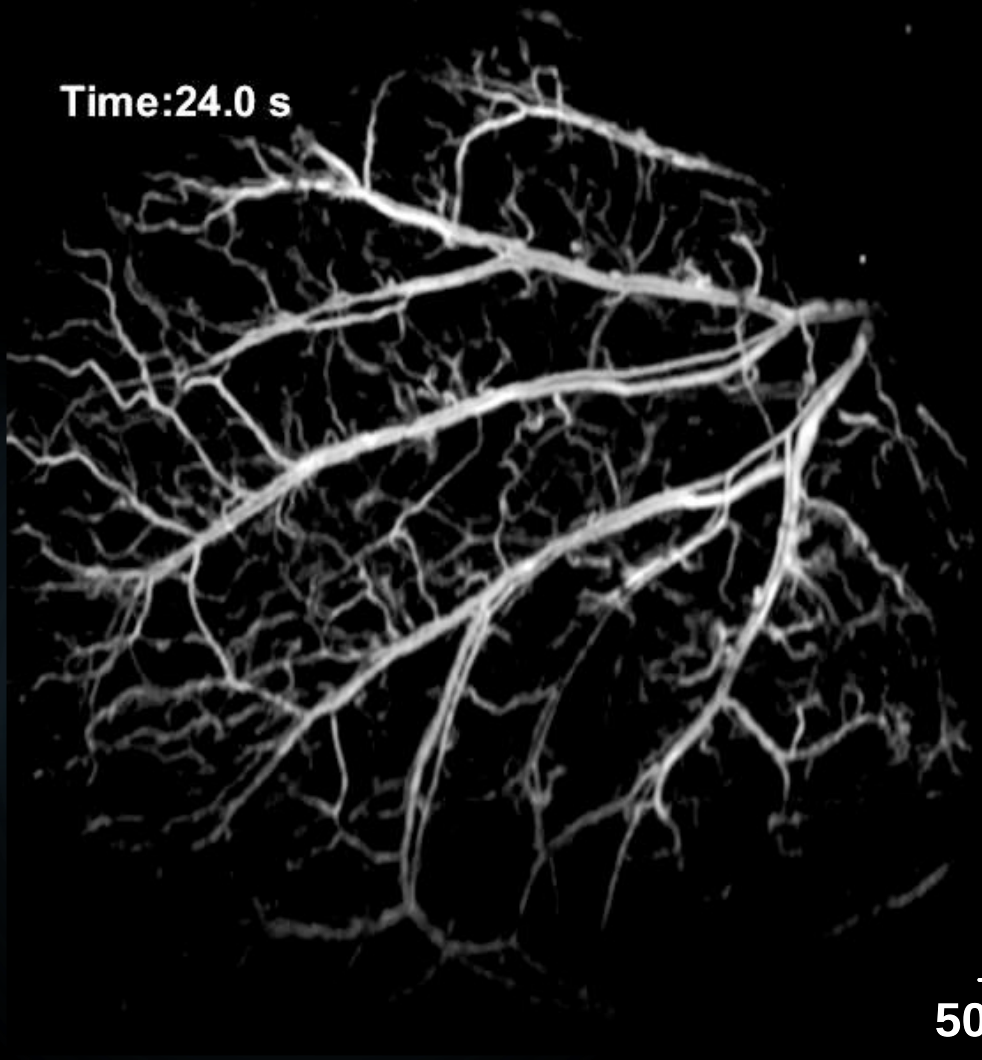
# Polygon-scanner PAM with ultrawide scanning range of 10 mm

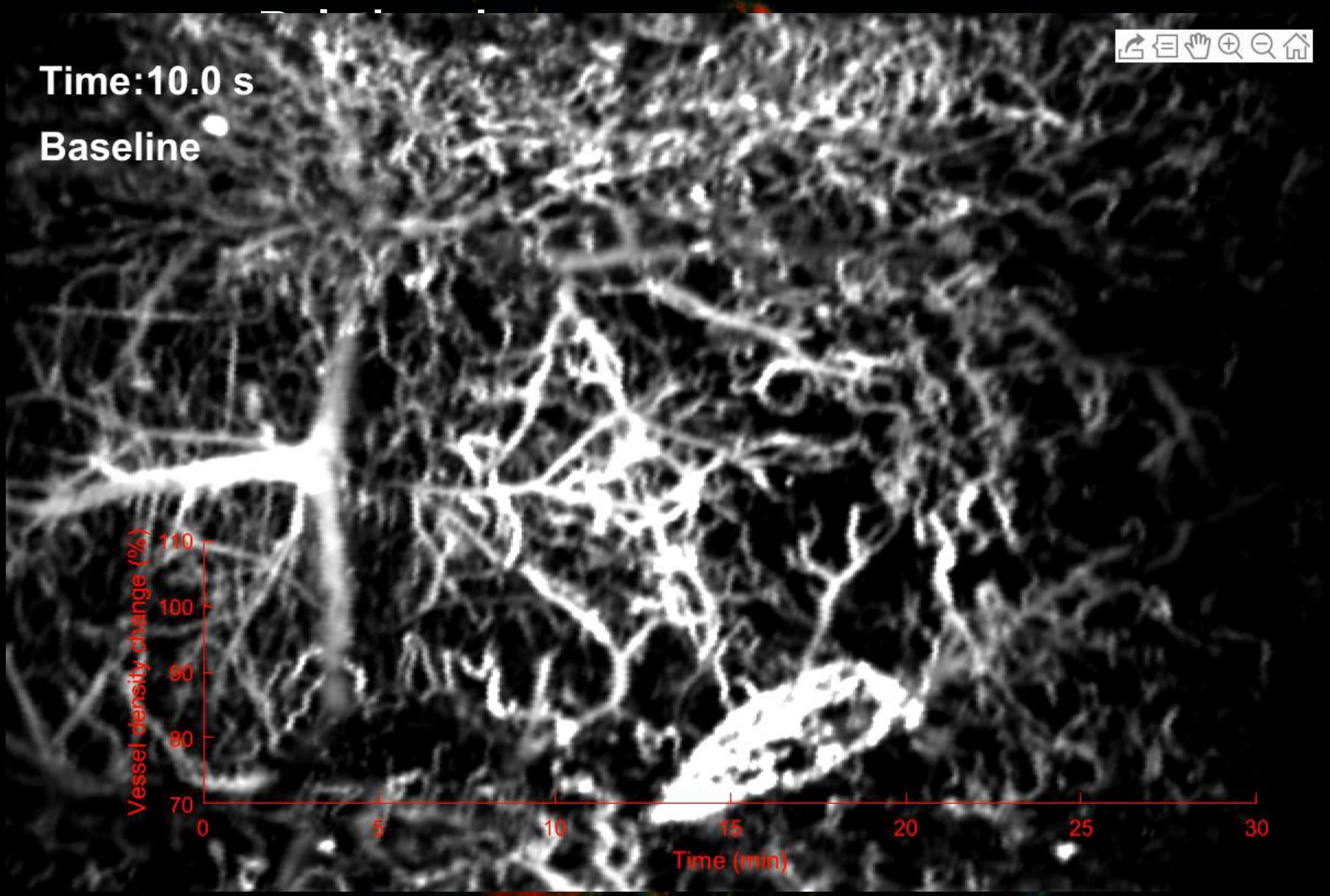


Unpublished, Duke Photoacoustic Lab

# Vessel constrictions induced by Epinephrine in skin and brain

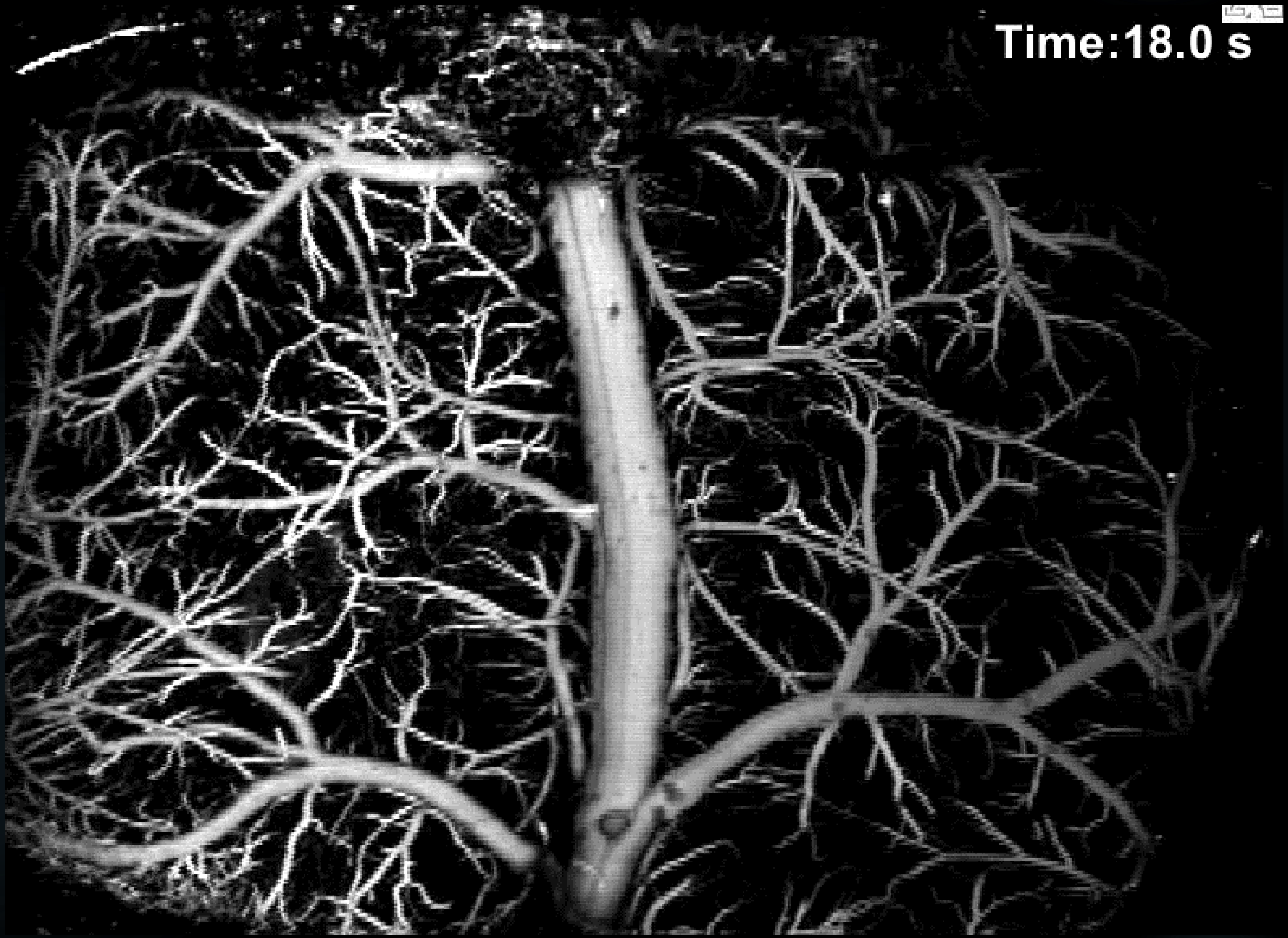



Lan et al., BOE, 2018, 9(10), 4689-4701

# Brain microvasculature hemodynamics induced by Cardiac Arrest

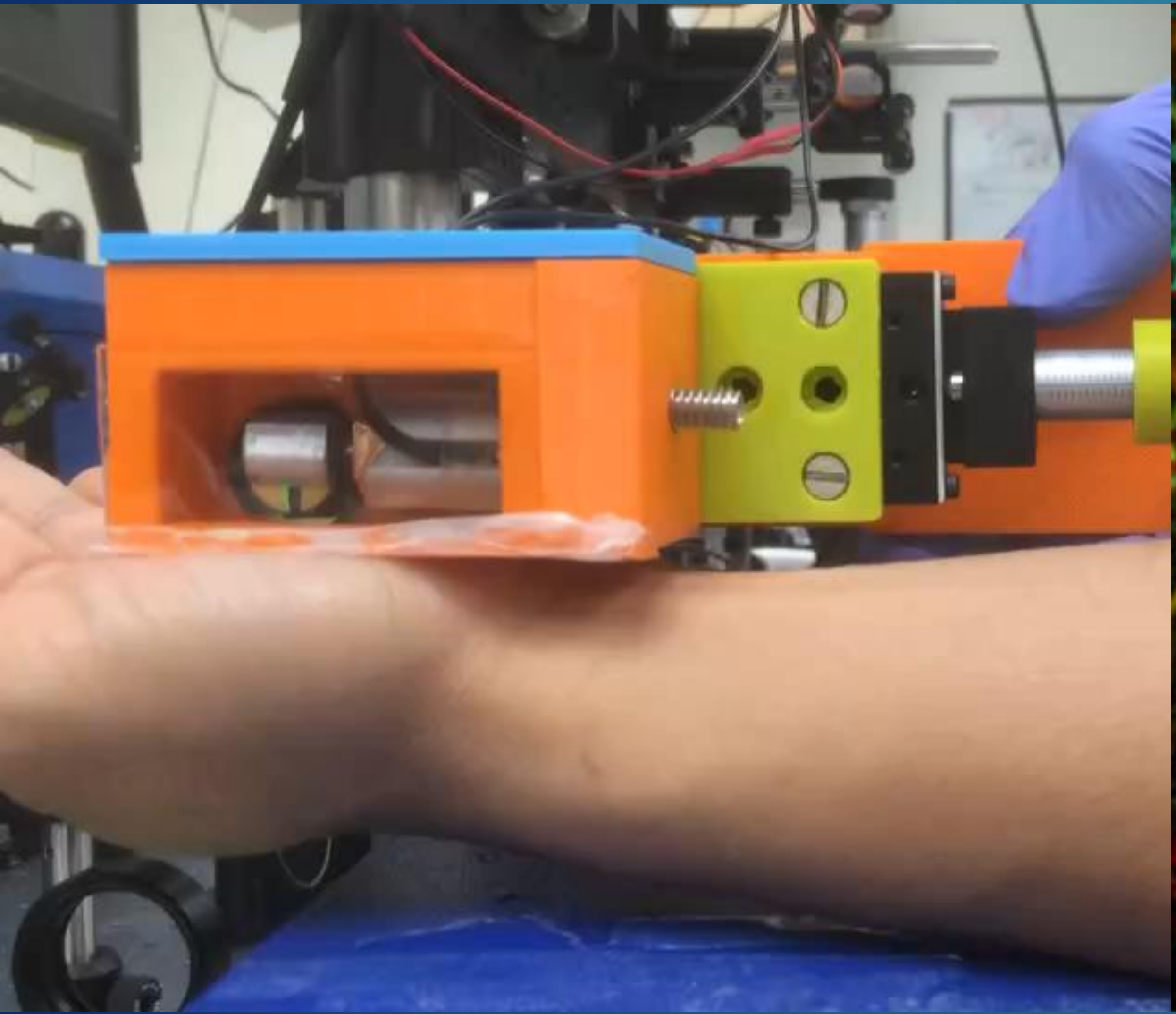


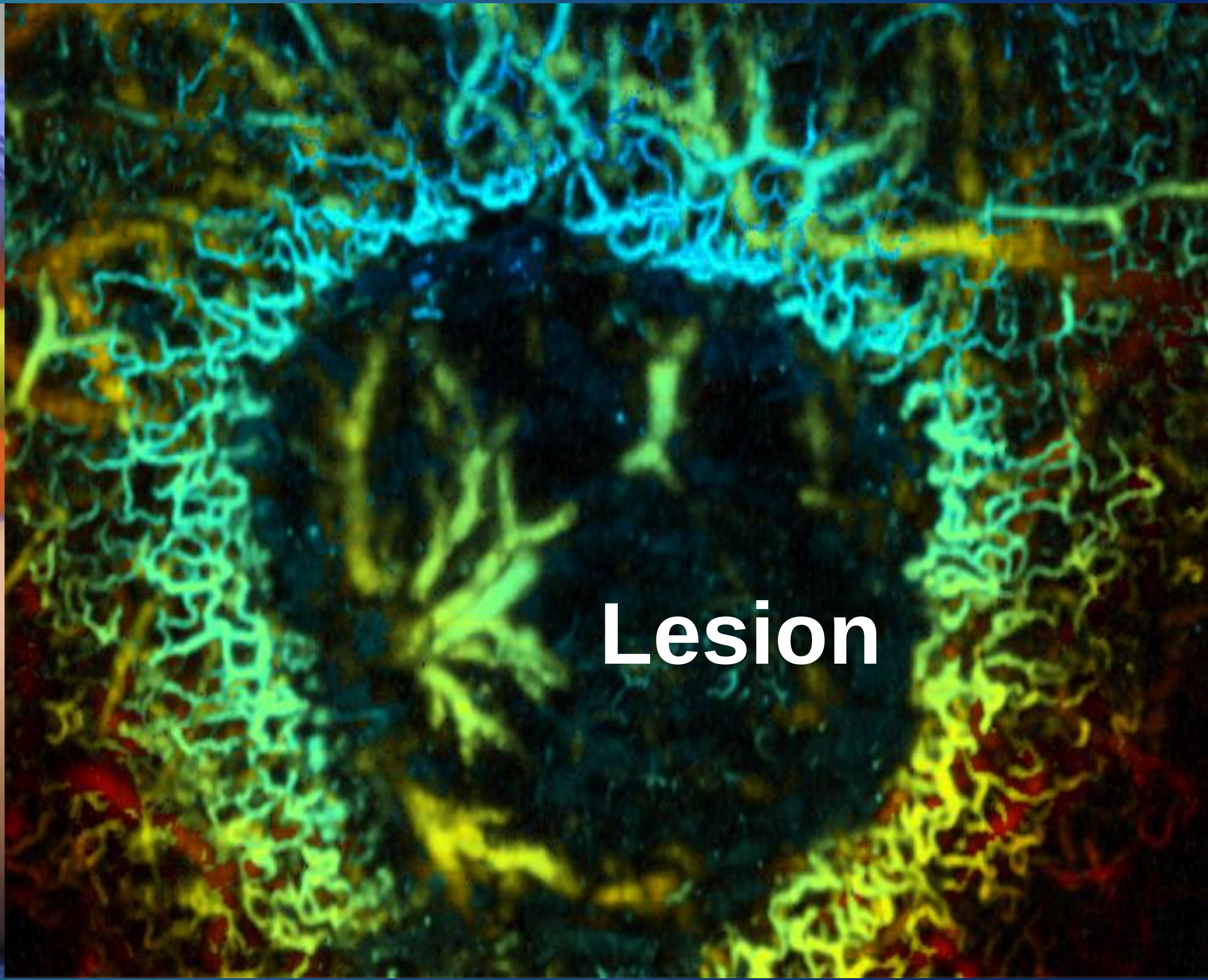



Unpublished, Duke Photoacoustic Lab

# Handheld photoacoustic microscopy for skin lesion imaging








Unpublished, Duke Photoacoustic Lab

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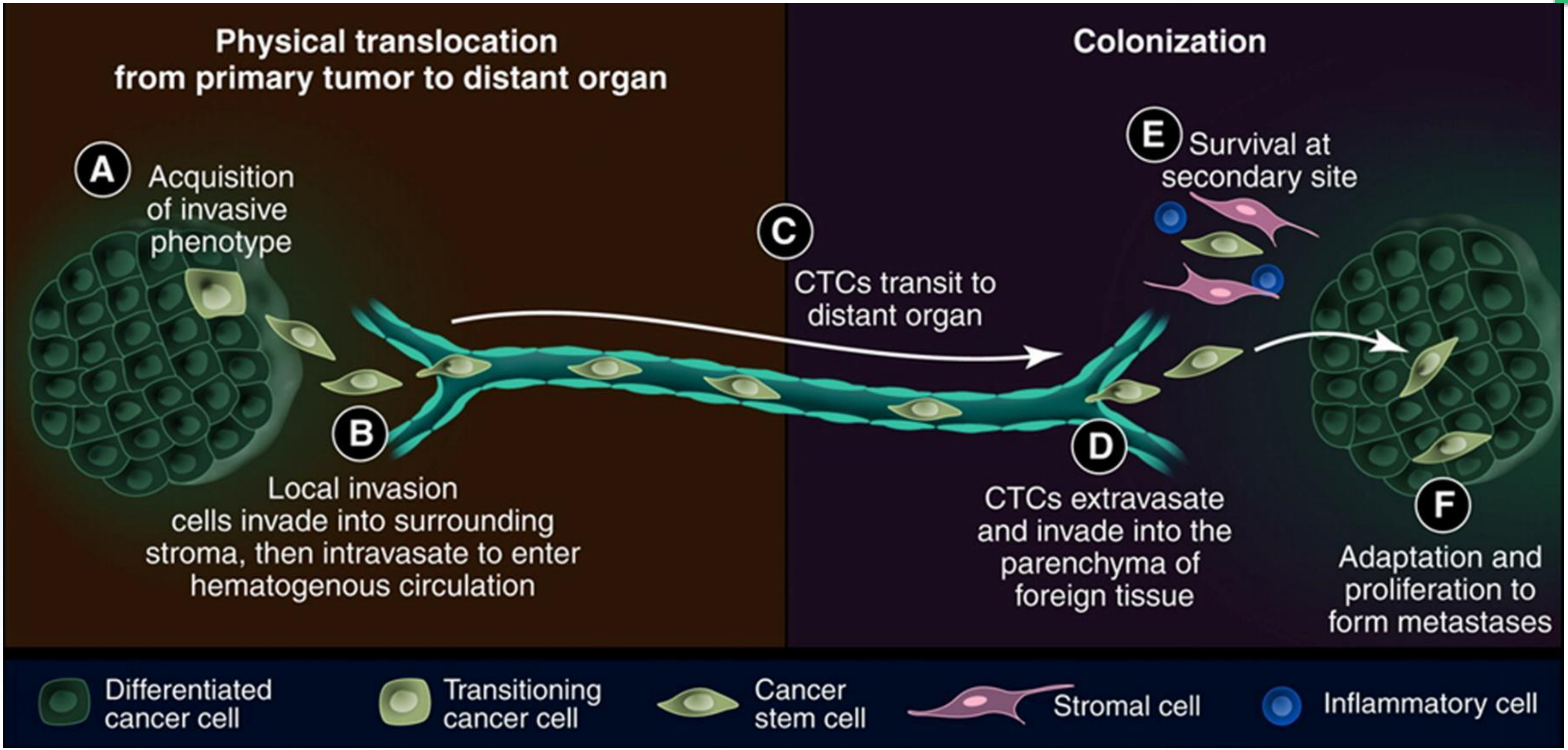
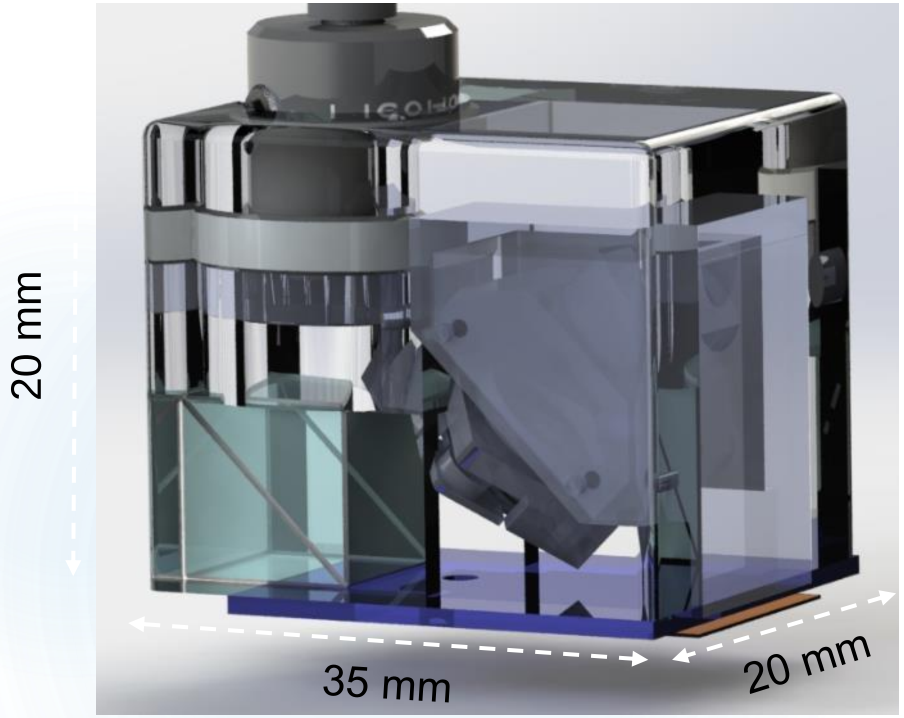
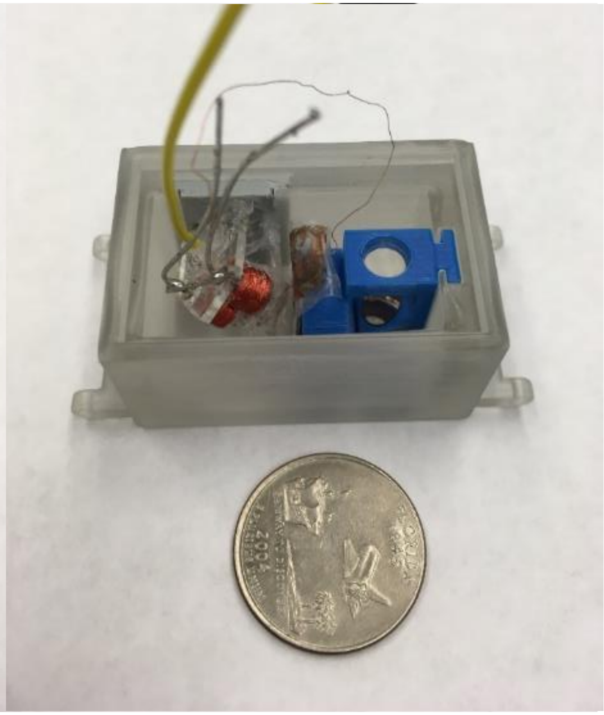
# Label-free wearable photoacoustic imaging and treatment of circulating melanoma cells

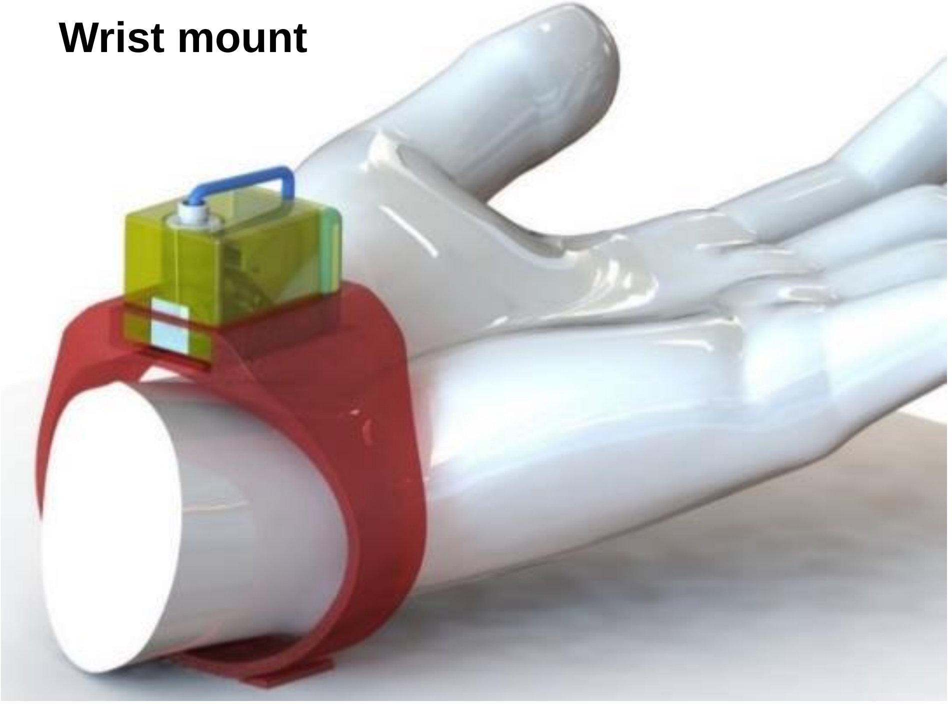




# Wearable photoacoustic watch for circulating melanoma detection during immune therapy






**Unpublished, Duke Photoacoustic Lab**

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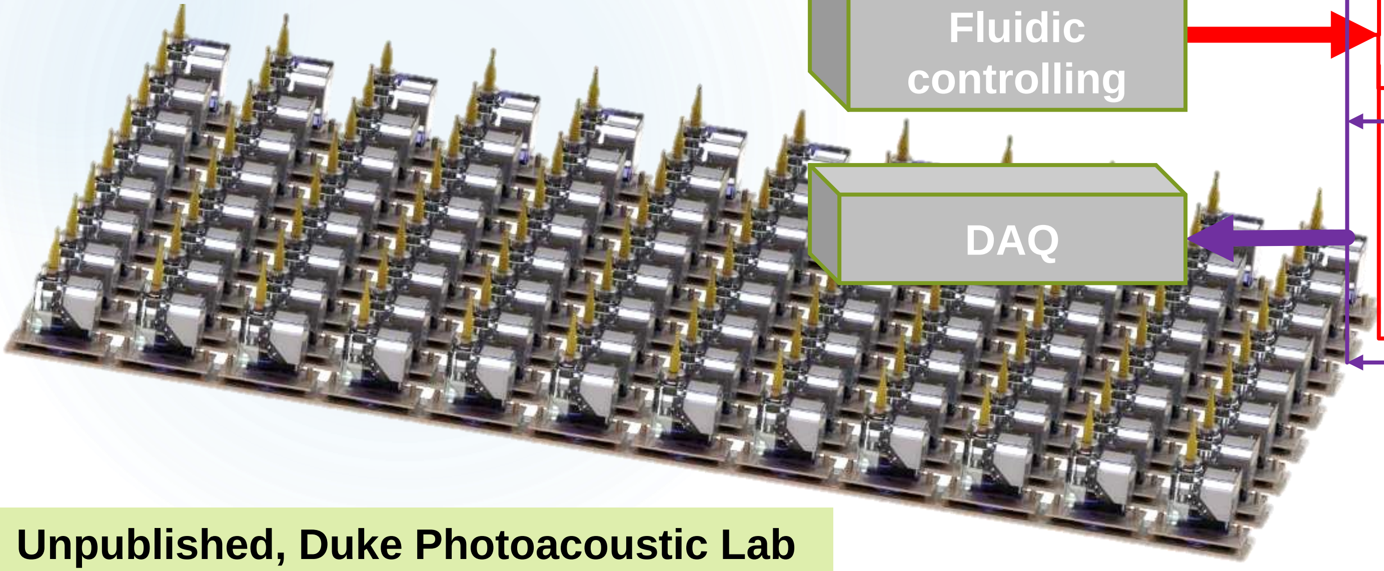
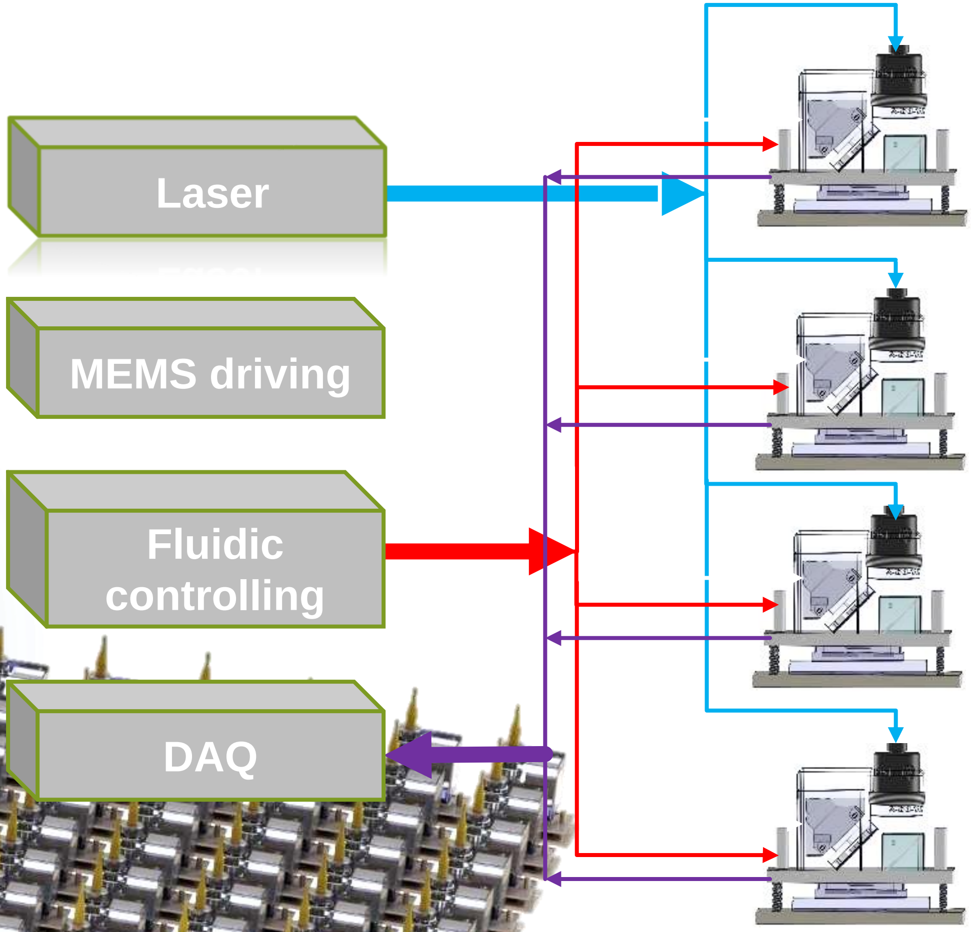
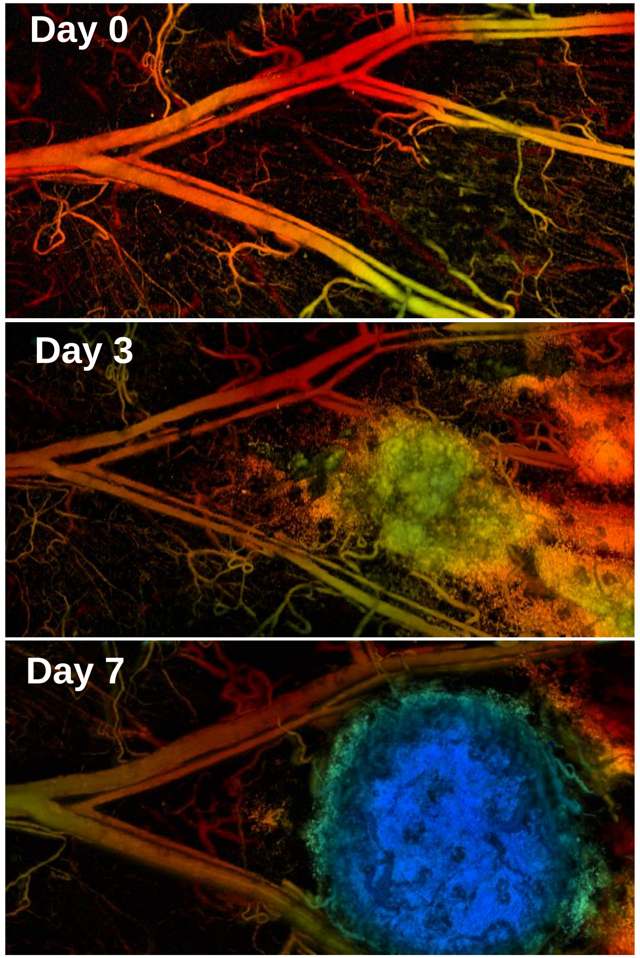
# Multiplexing the miniaturized photoacoustic imaging

Single PA unit



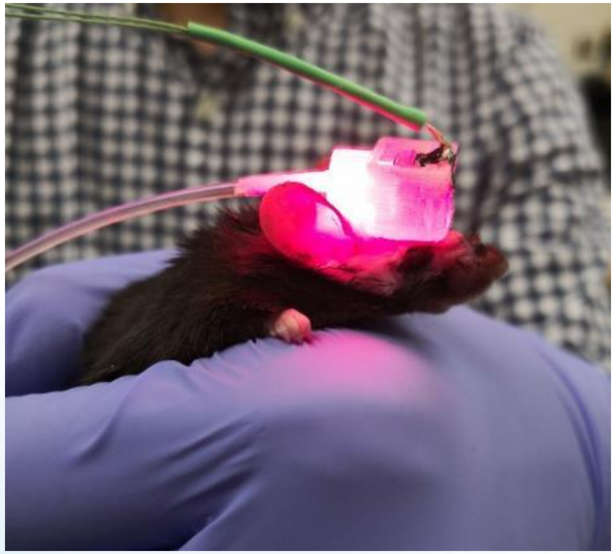


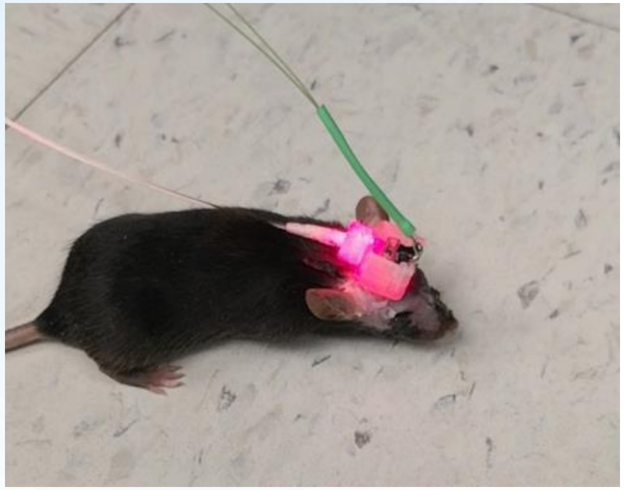



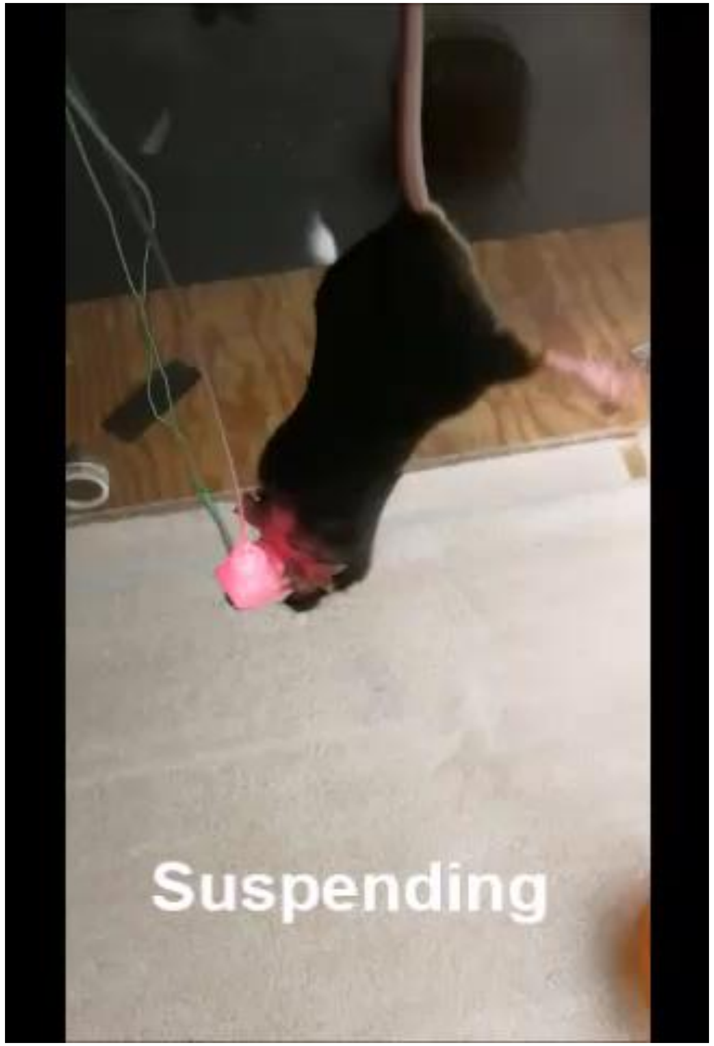

Unpublished, Duke Photoacoustic Lab

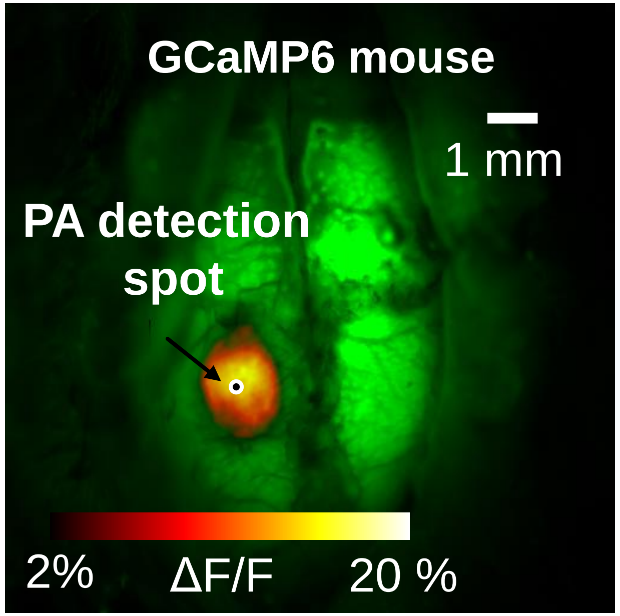
https://photoacoustics.pratt.duke.edu/

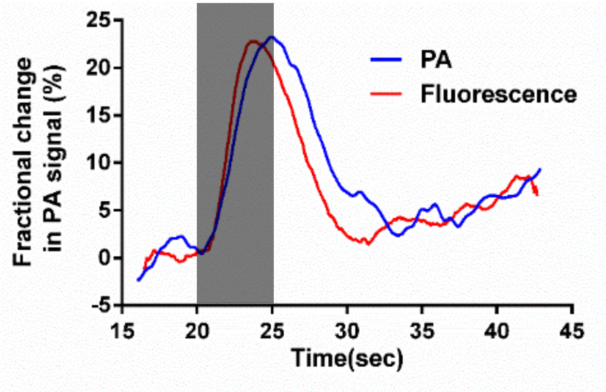
# Head-mounted photoacoustic imaging of neural activities on freely-behaving aged animals







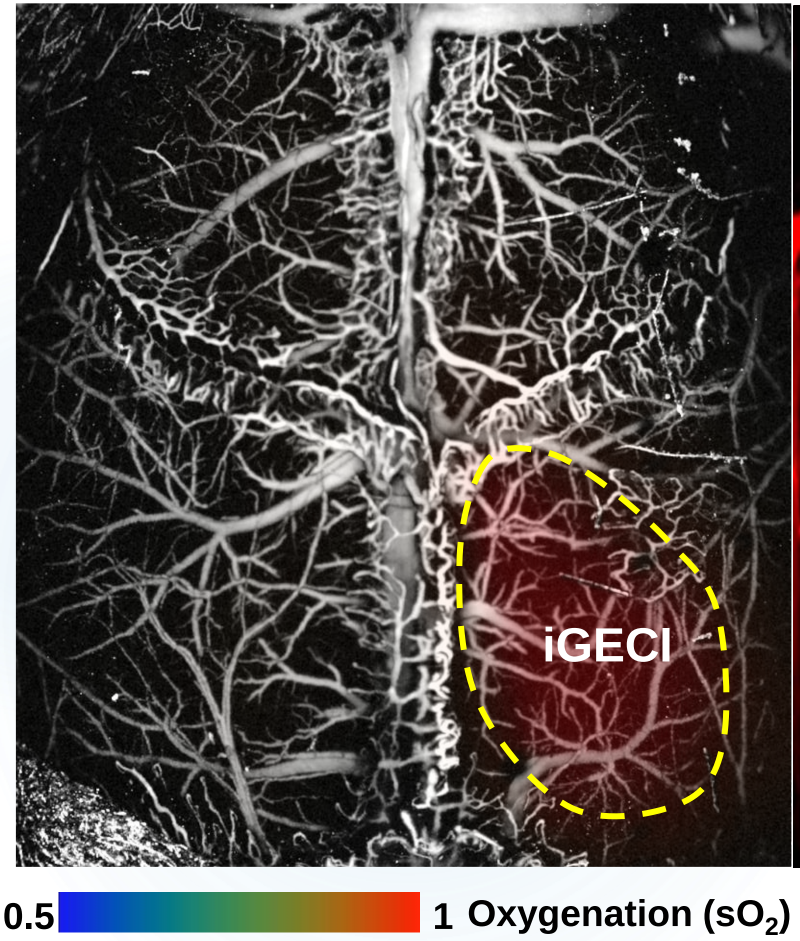




**Unpublished, Duke Photoacoustic Lab**

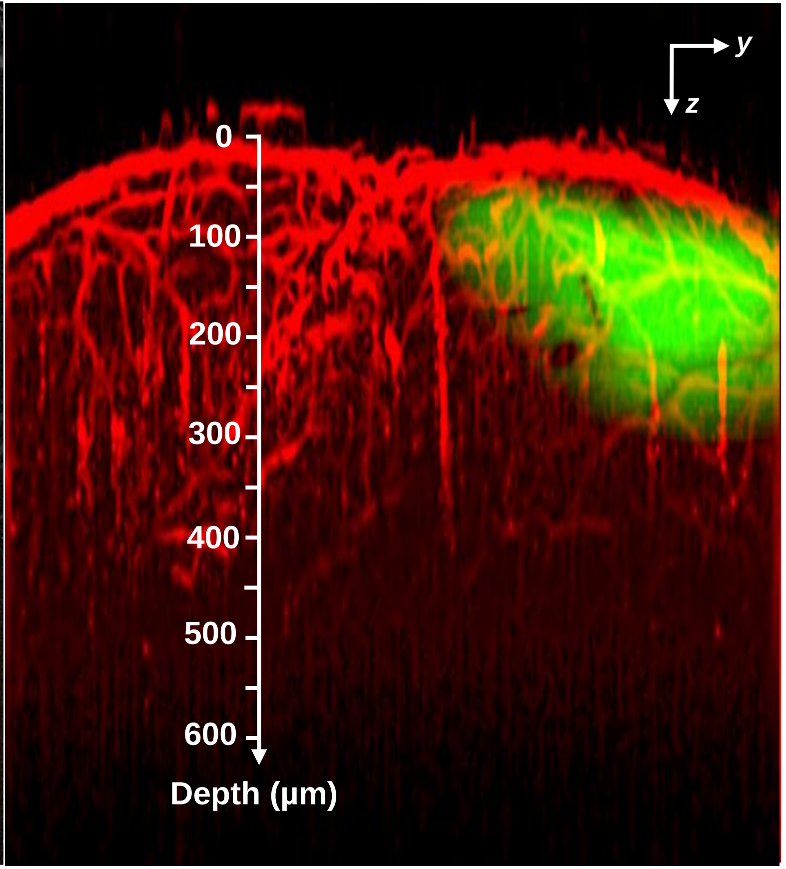
https://photoacoustics.pratt.duke.edu/

# PAM/Fluorescence imaging of near-infrared calcium indicator (iGECI, ex: 670 nm)

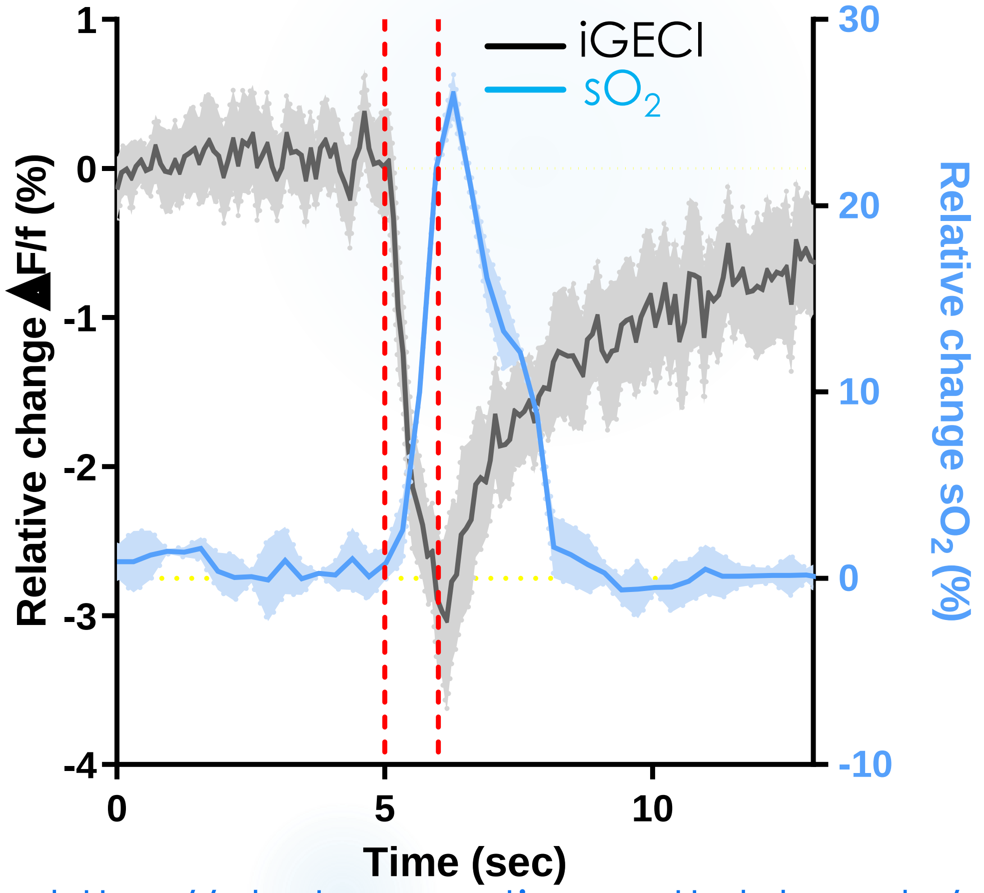
**Blood oxygenation (PAM)**




**iGECI (fluorescence)**




**Paw stimulation**




**Nature Biotechnology, under review. Collaborator, Vlad Verkhusha**

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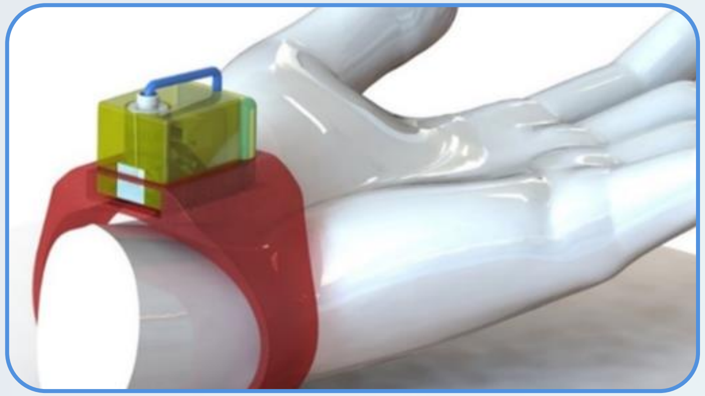
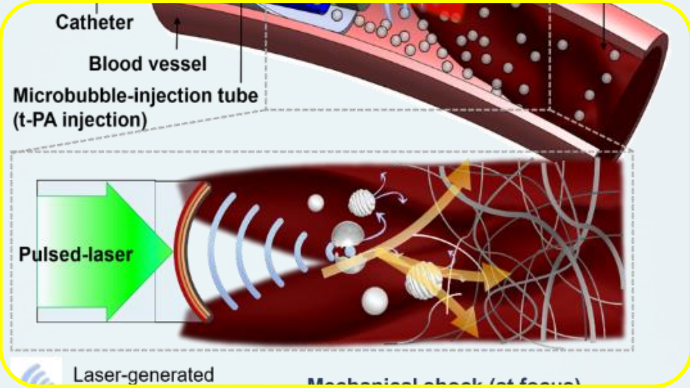
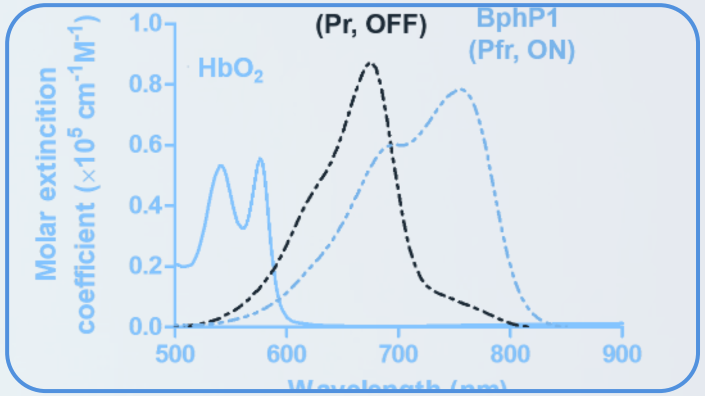
# Our missions at Duke PI-Lab






**Smaller** for high throughput

**Deeper** for clinical impact

**Colorful** for molecular sensitivity

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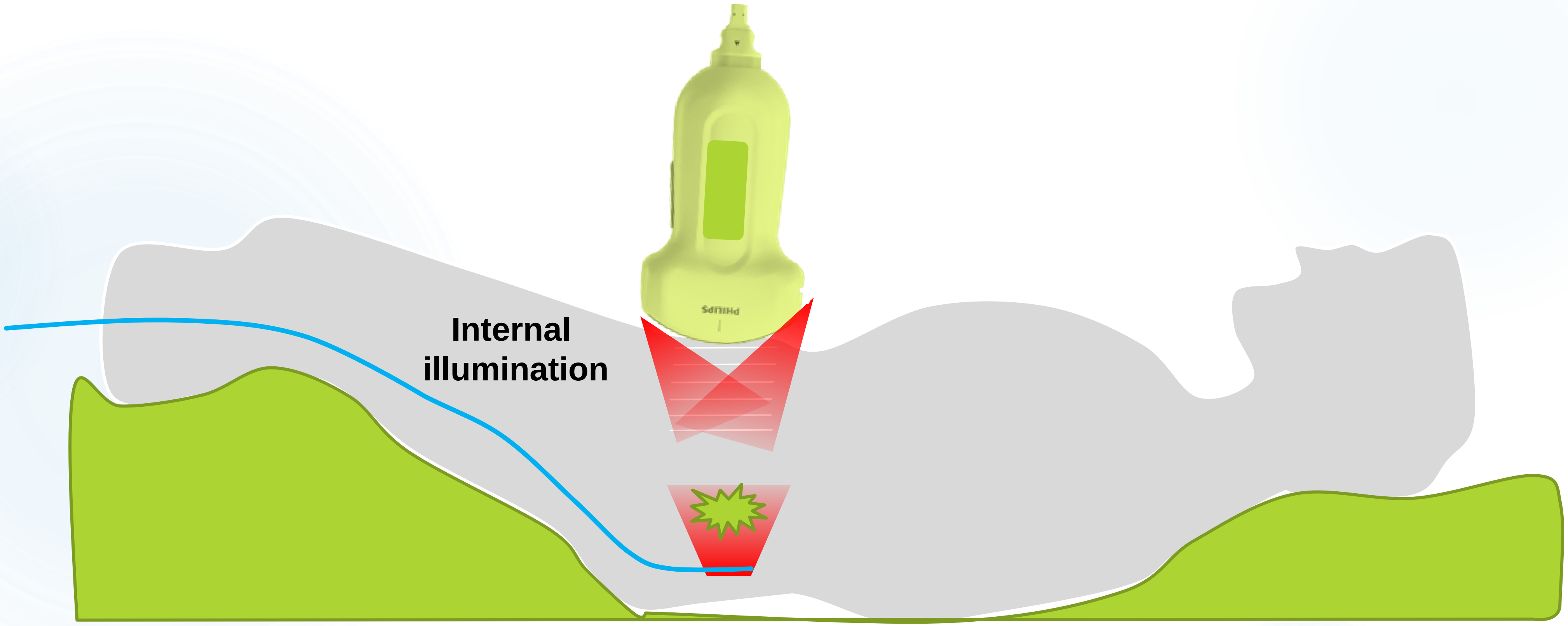
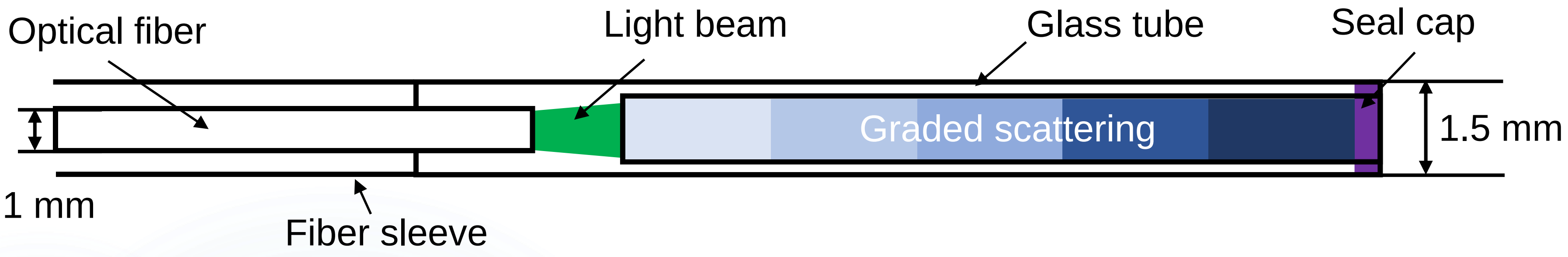
# Lighting up from inside: Super-deep PAT with internal light

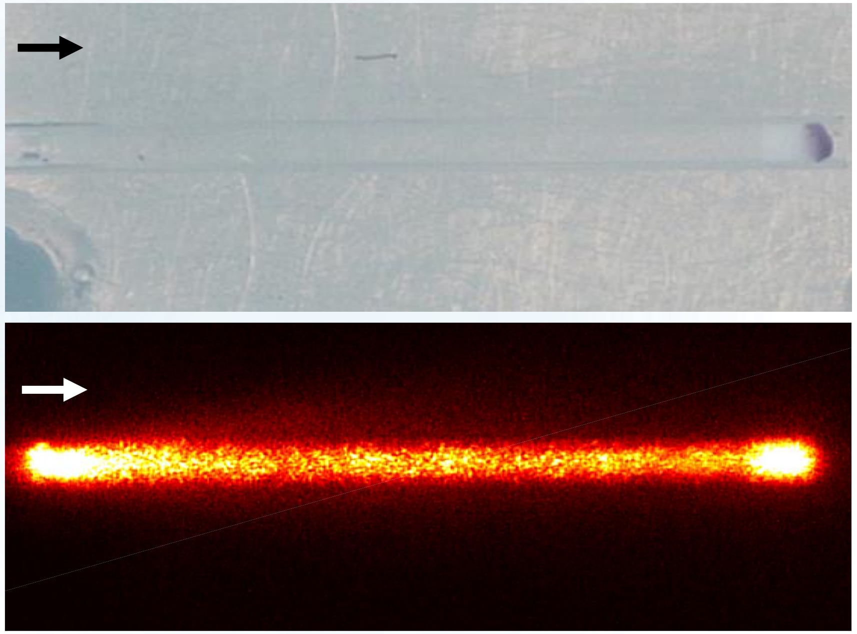
- Human whole-body imaging needs a penetration of more than 10 cm
- Photon penetration is limited to about 5 cm by optical attenuation

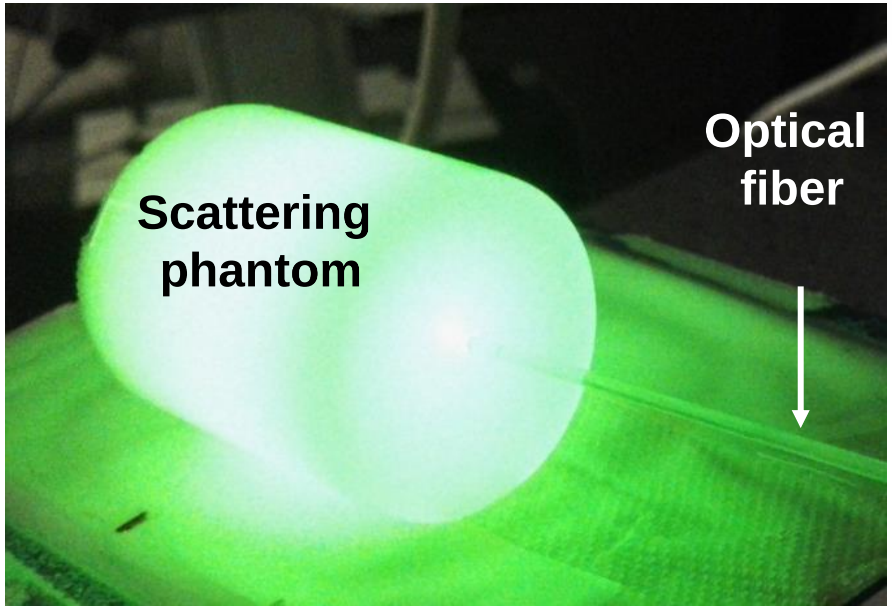


# A graded-scattering based optical fiber diffuser

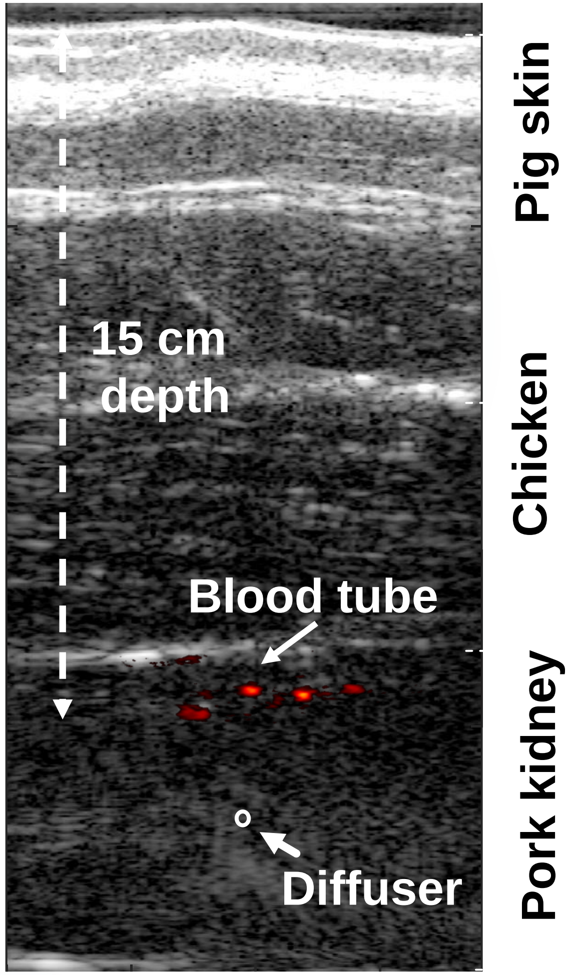







Tissue phantom




Li et al., IEEE transactions on medical imaging, 2019

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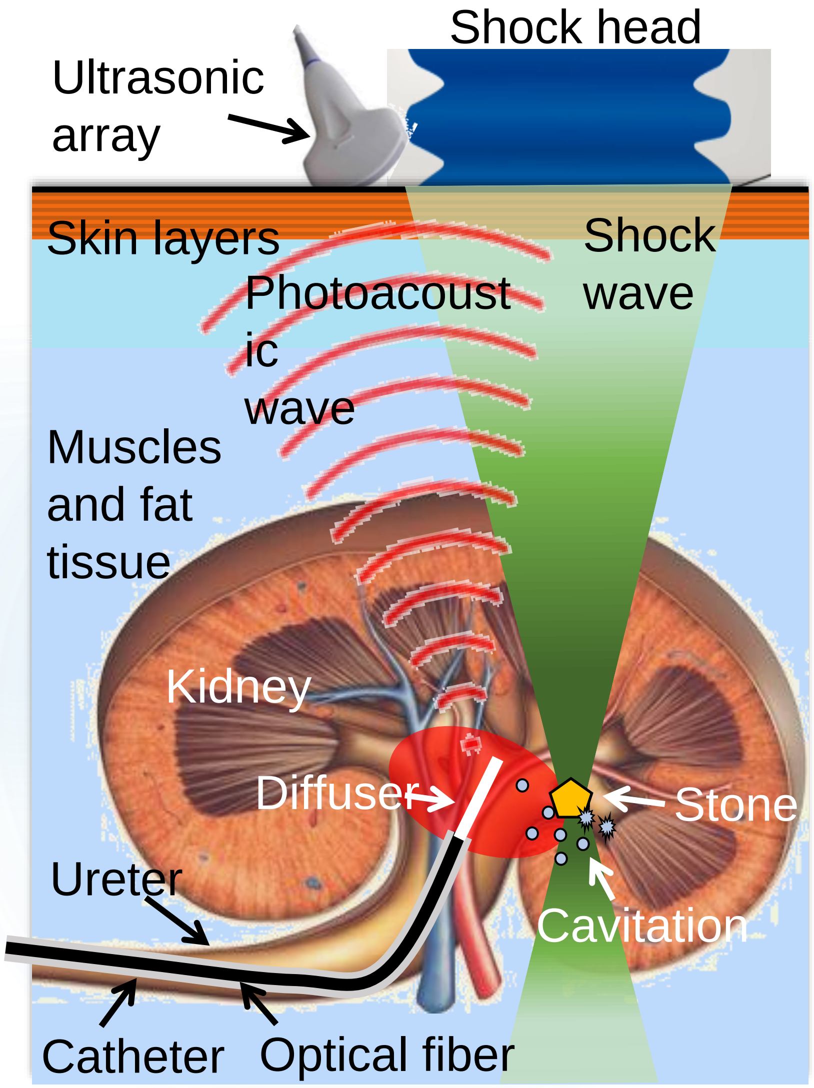
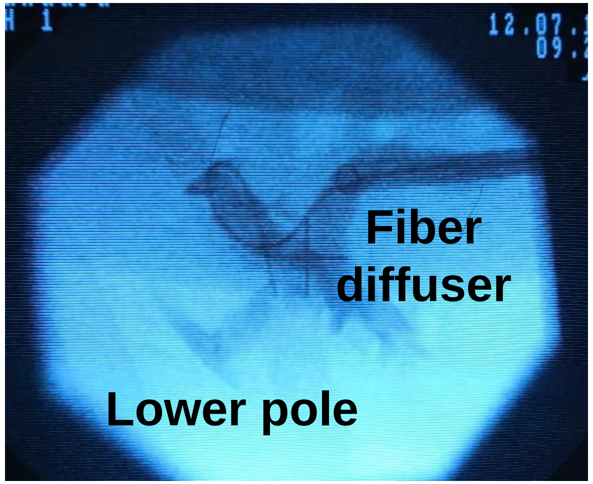
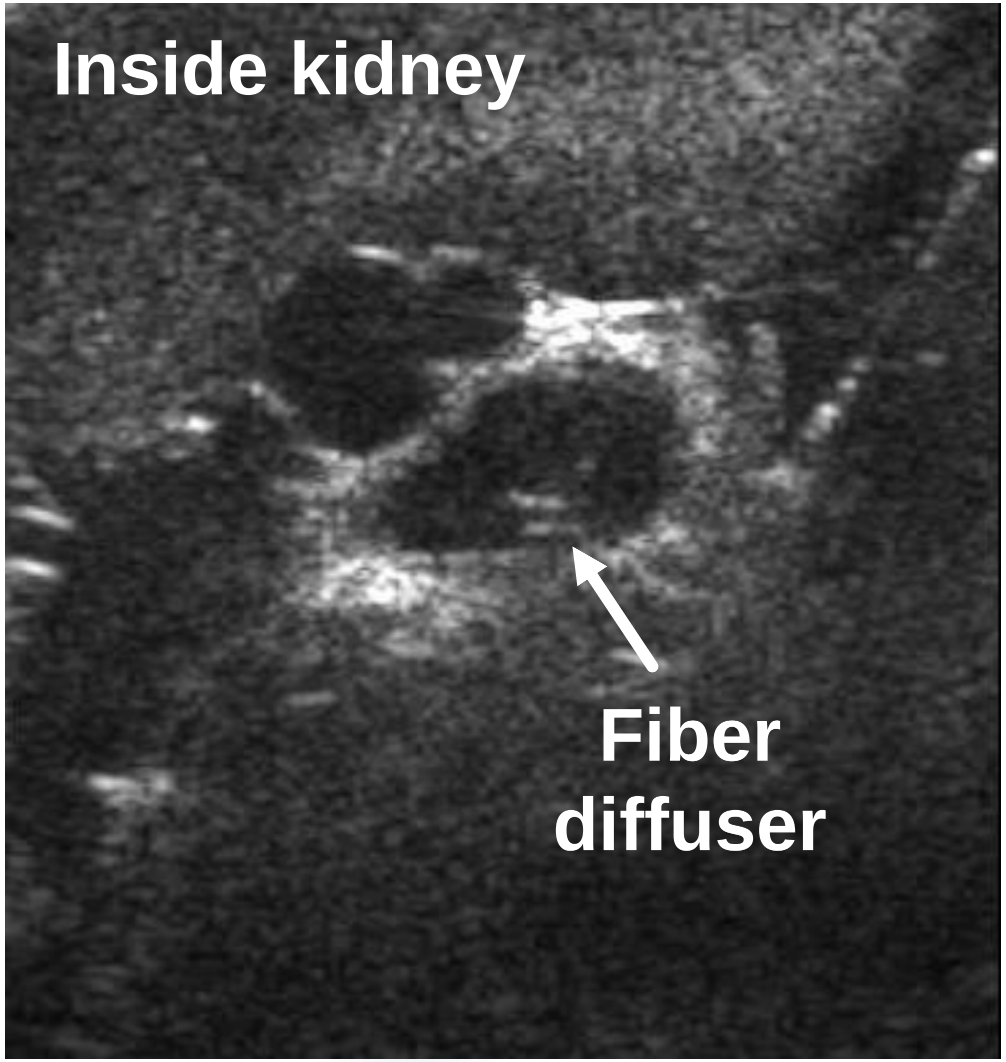
# Deep PAT with internal light illumination in pig models during shockwave treatment

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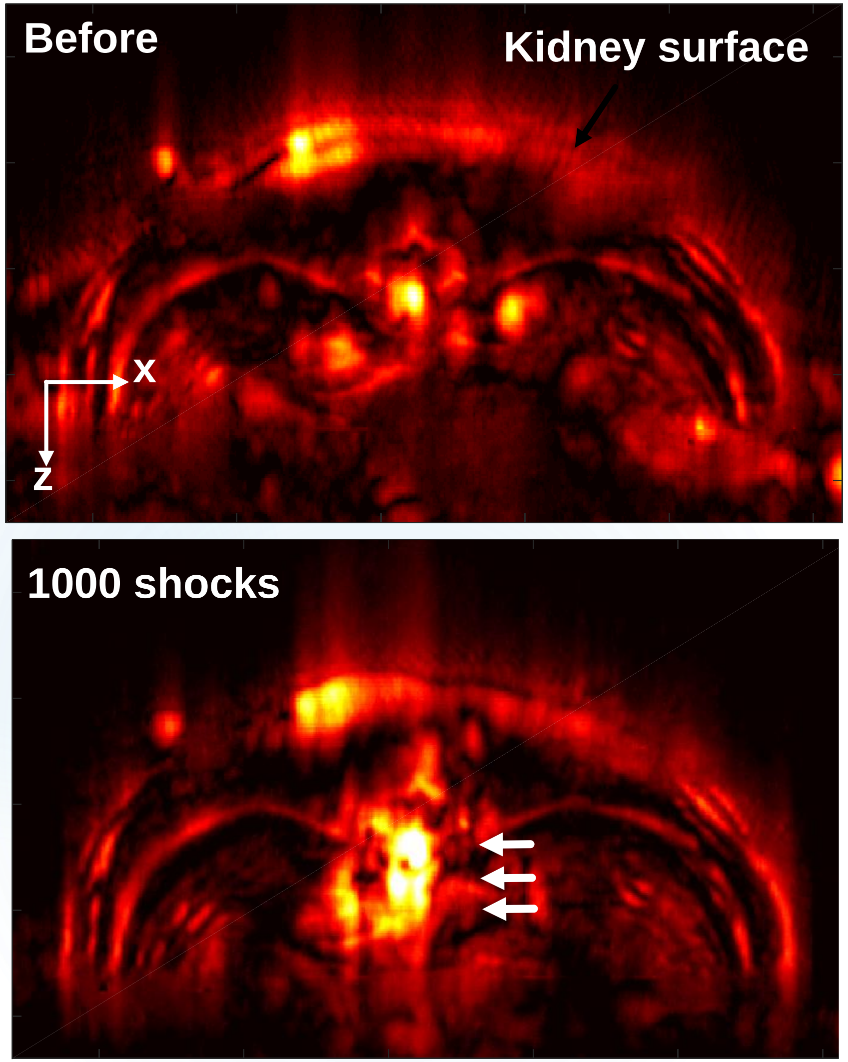
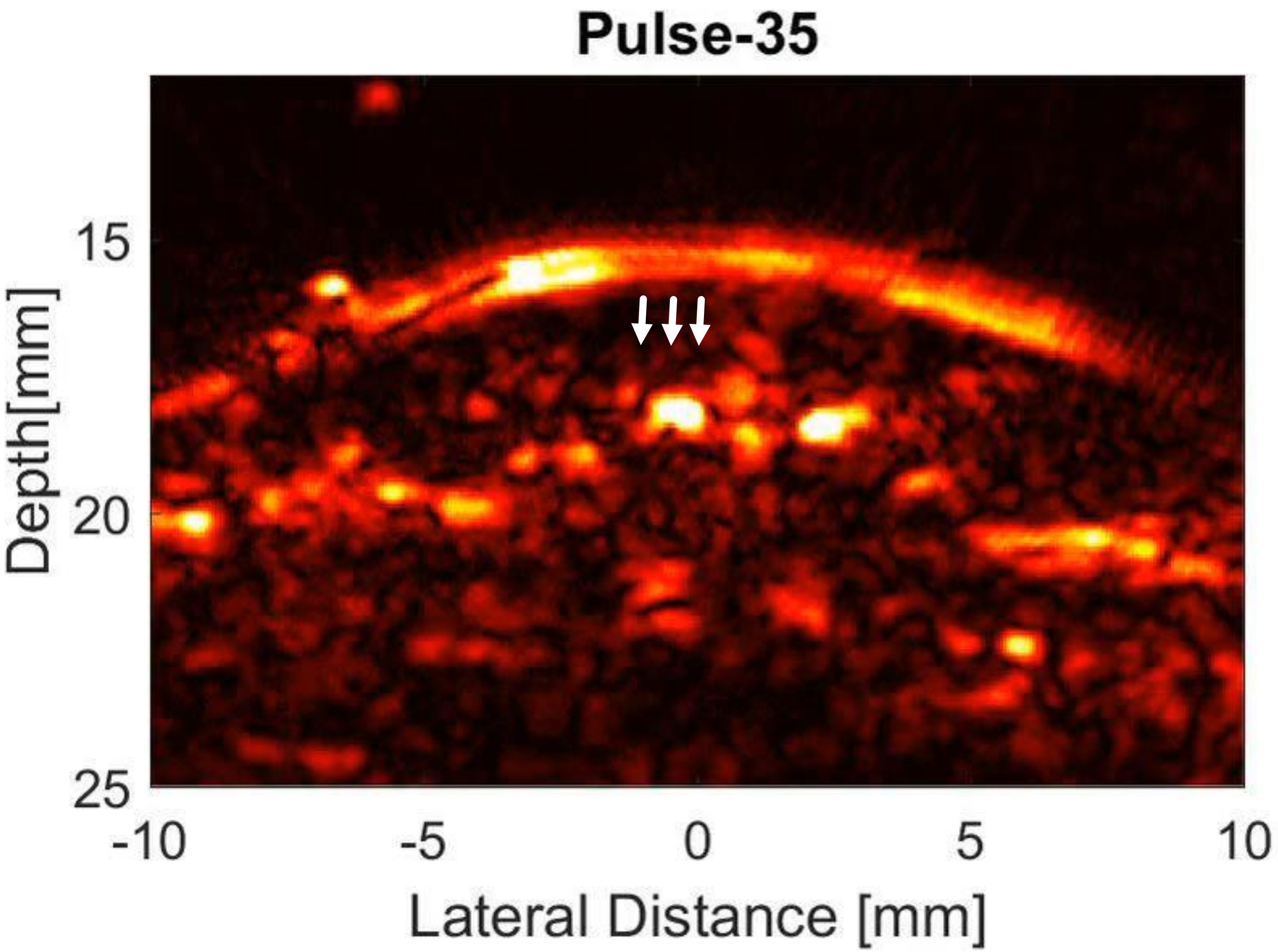
# Deep PAT with internal light illumination in pig models during shockwave treatment



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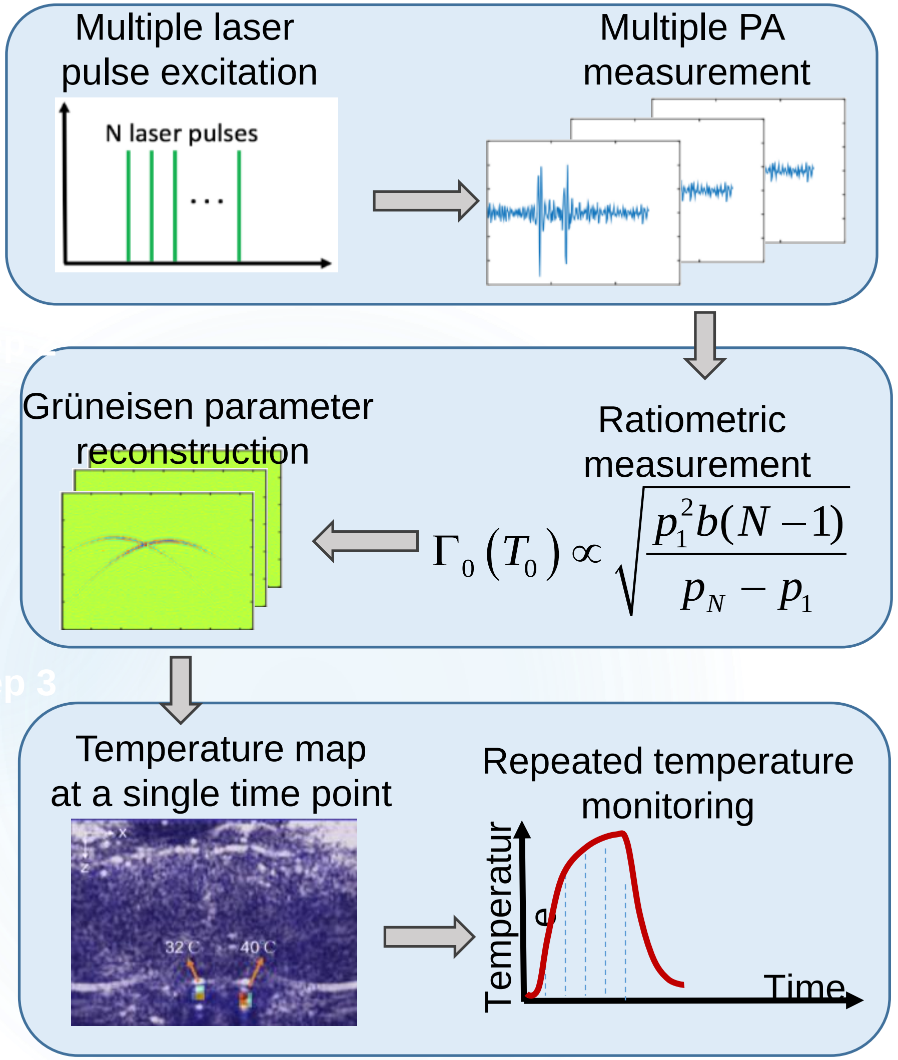
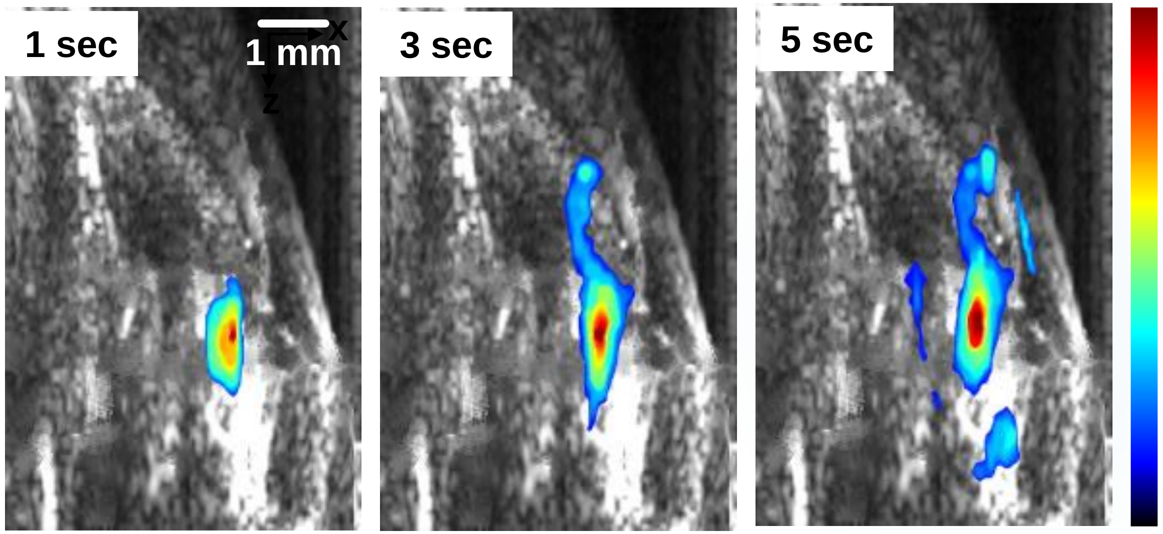
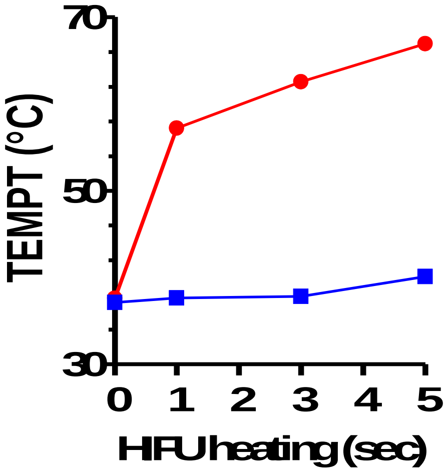
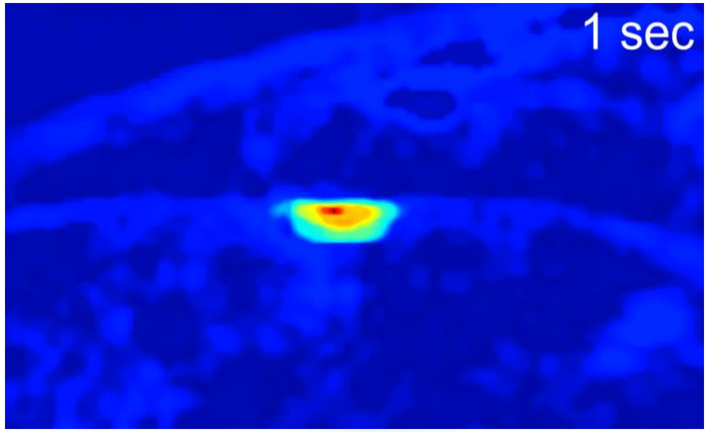
# Thermal-memory-based PAT (TEMPT) of temperature during focused ultrasound therapy




Zhou, et al., Optica, 2019, 6(2), 198-205

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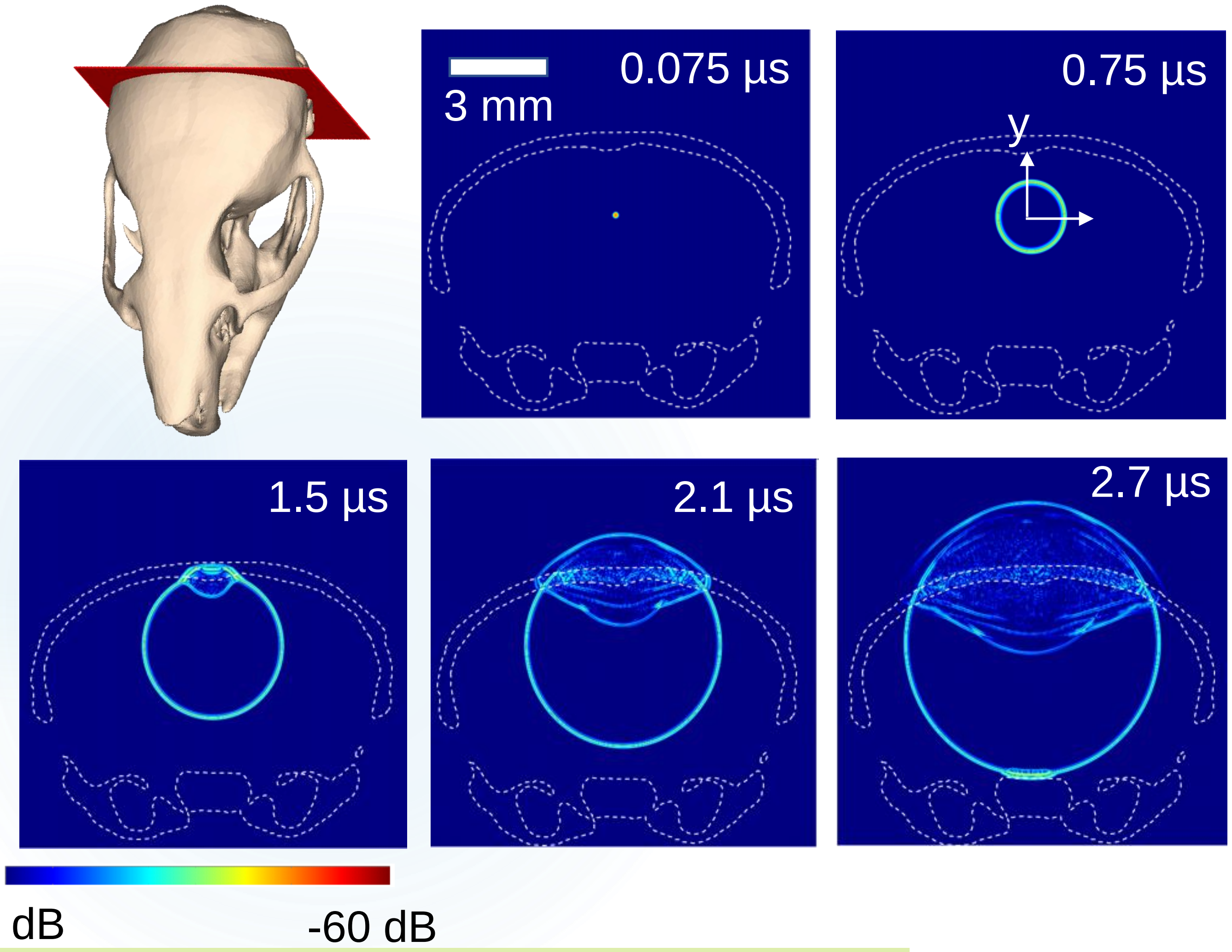
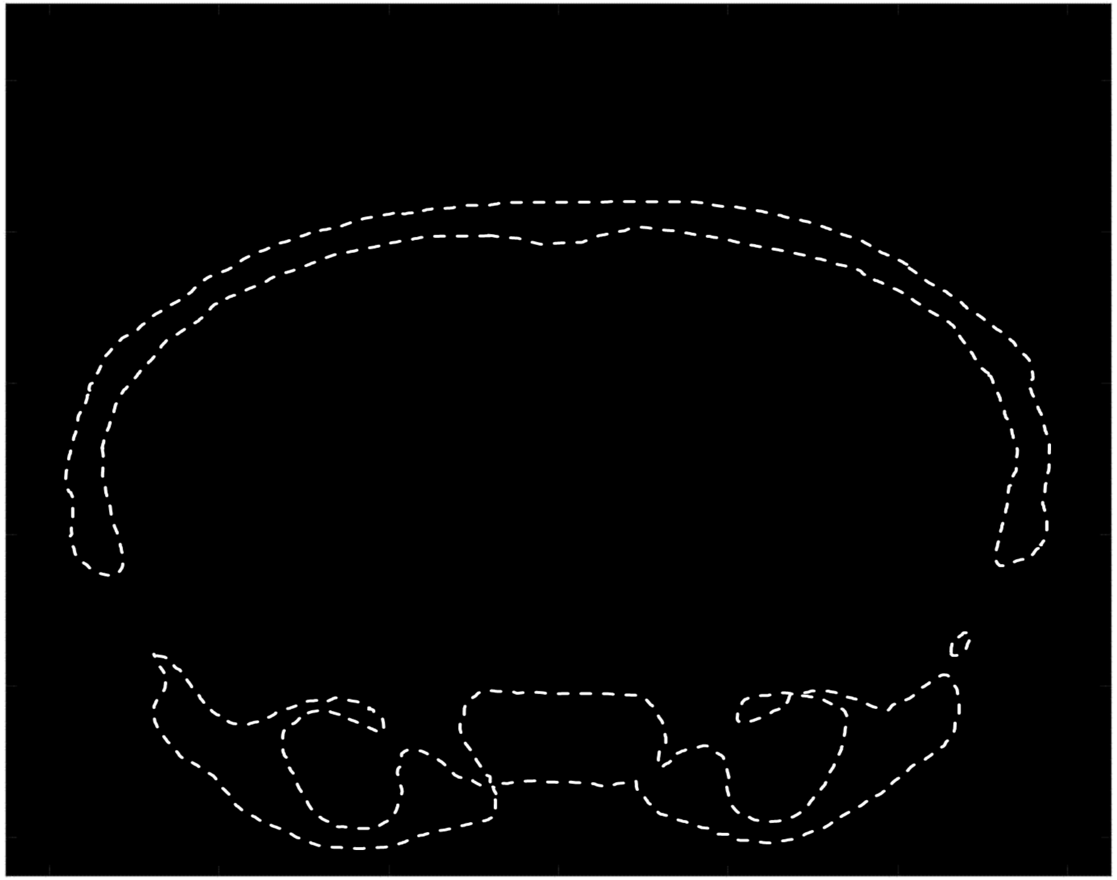
# Correcting the skull's aberration to ultrasound waves



## Skull's acoustic distortion



**Liang, et al., J of Biophotonics, 2019, e201800466**

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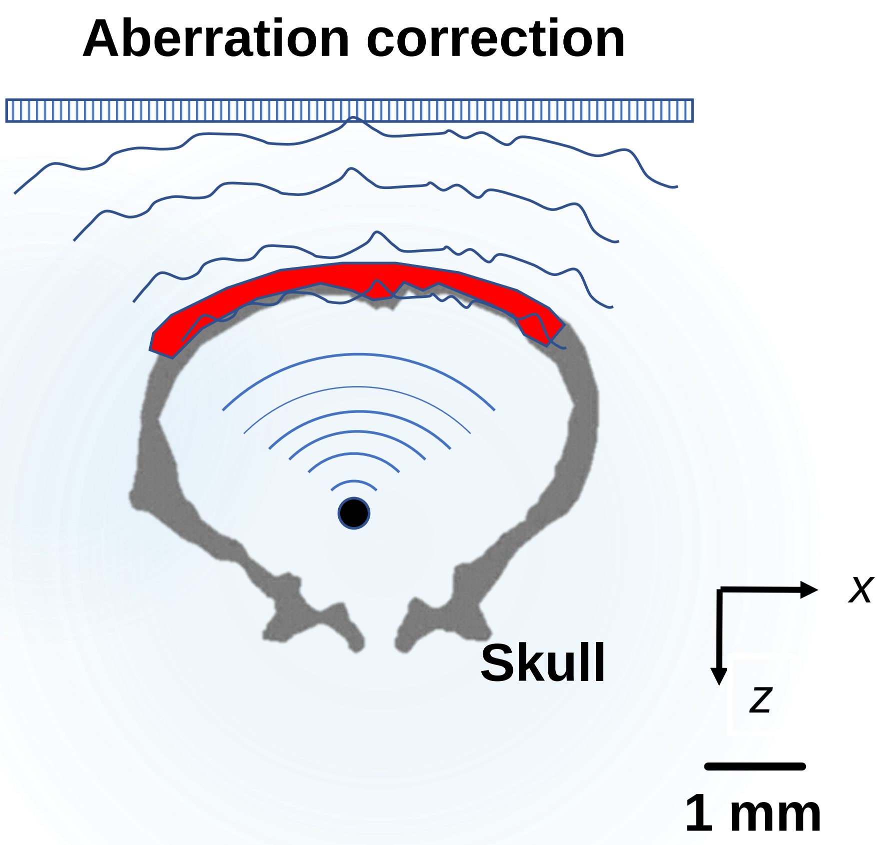
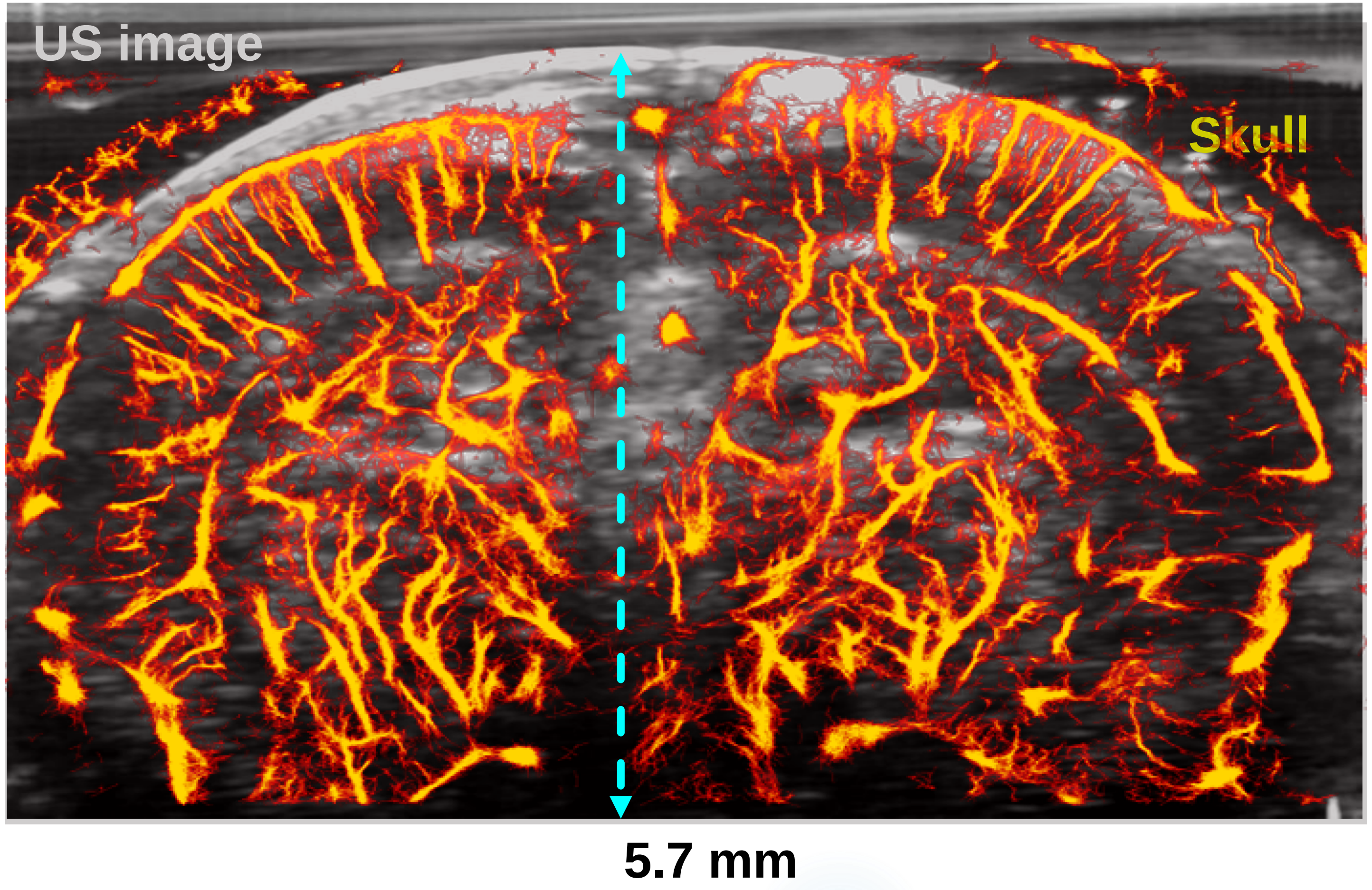
# Correcting the skull's aberration to ultrasound waves




Liang, et al., J of Biophotonics, 2019, e201800466

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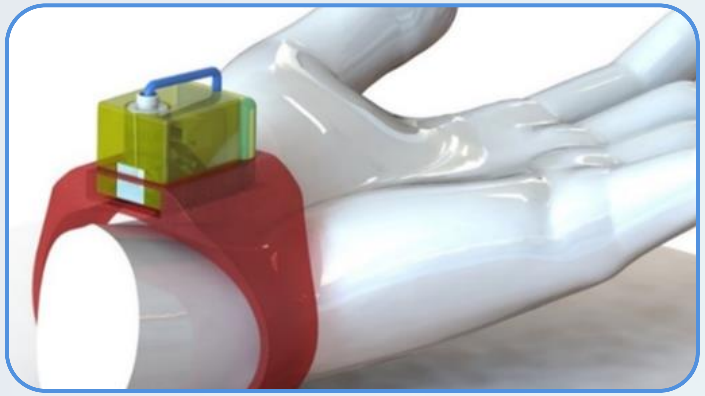
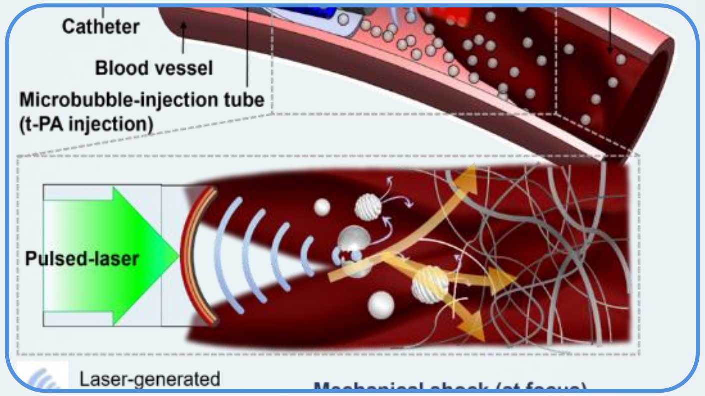
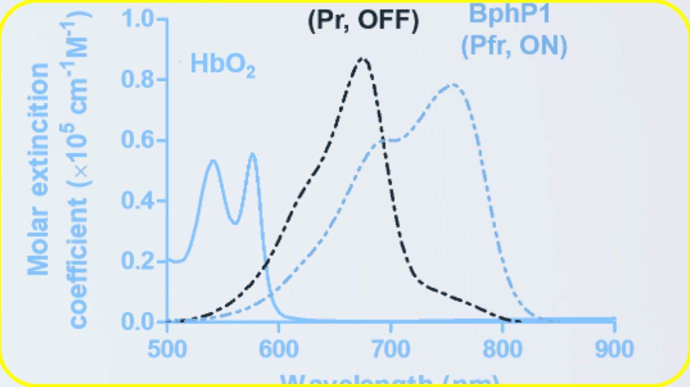
# Our missions at Duke PI-Lab



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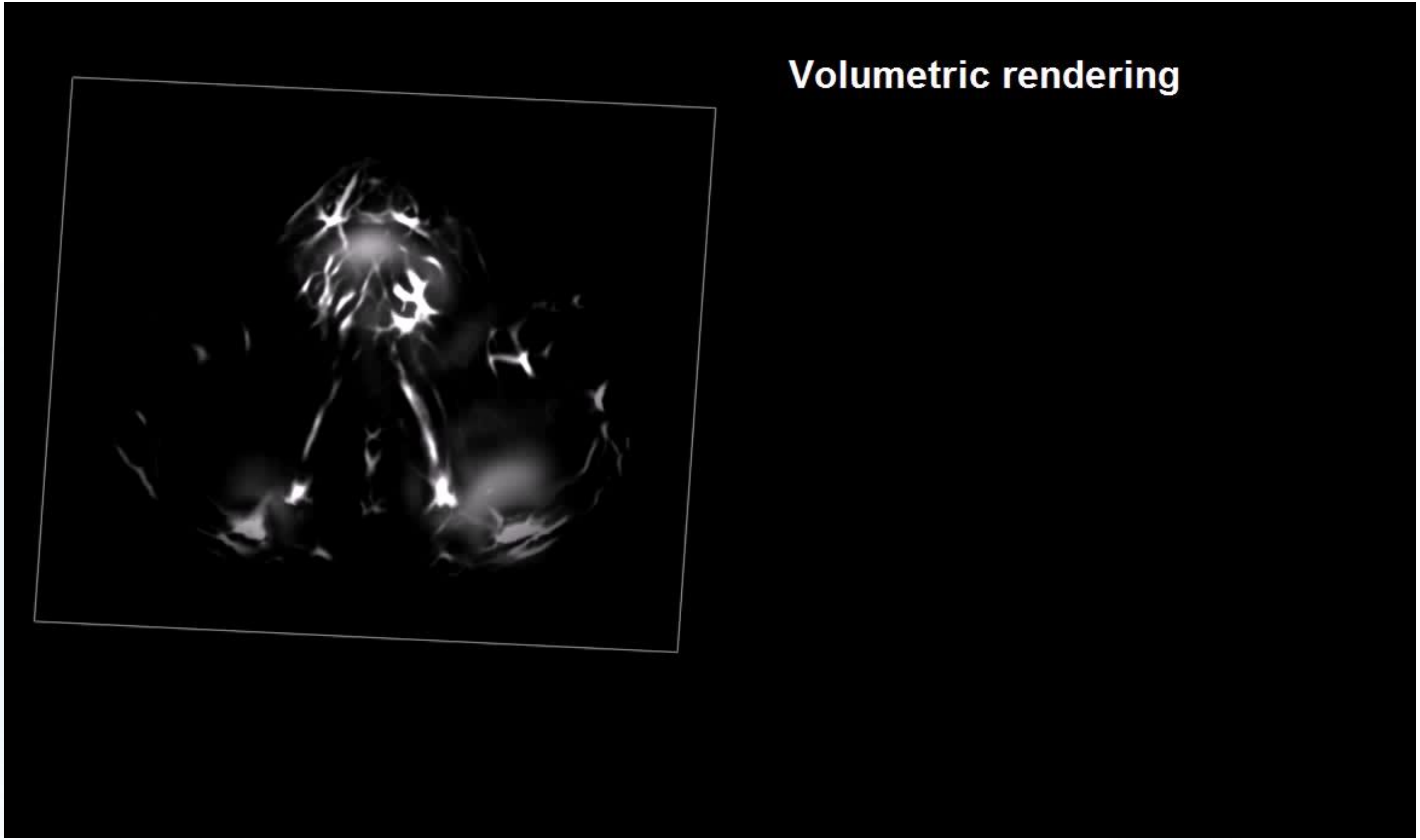
# Overwhelming endogenous biomolecules in deep-tissue PAT



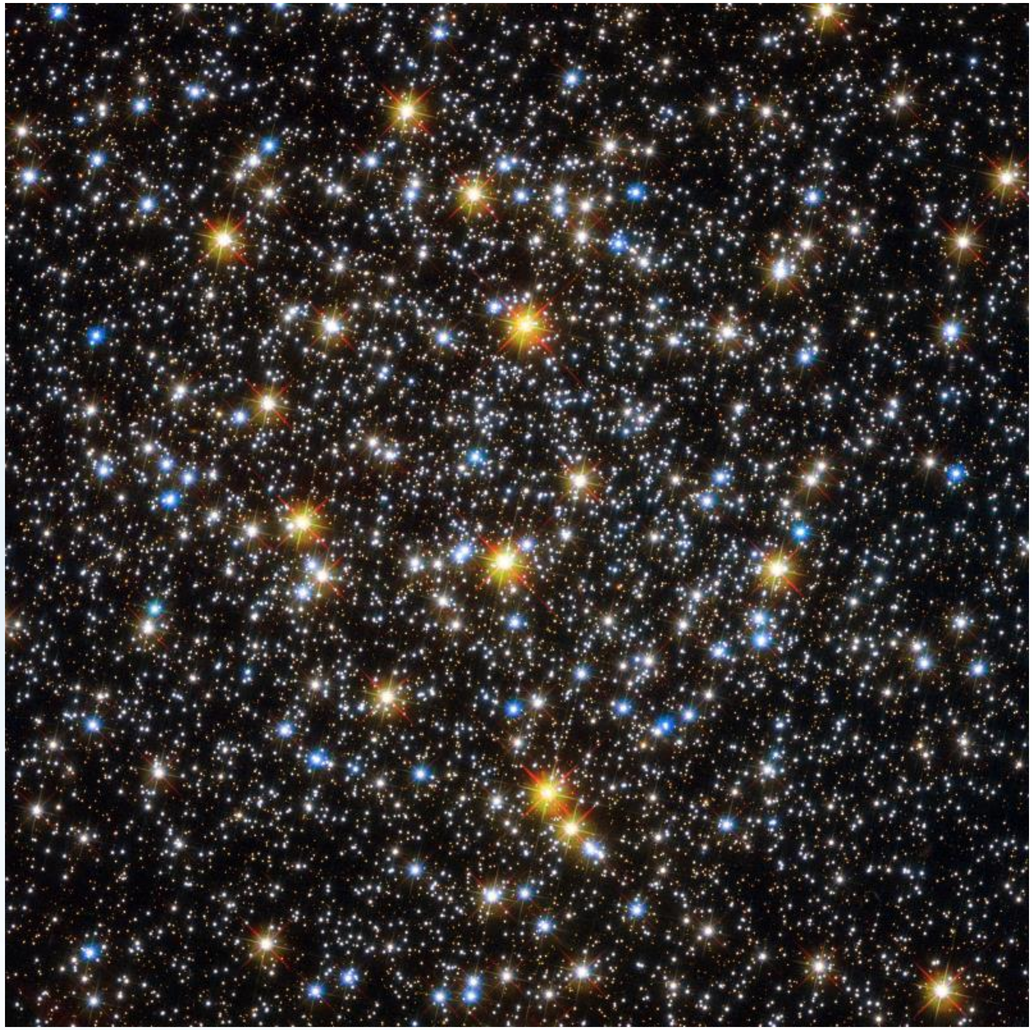



J Yao et al., Nature Methods, 13 (1), 2016

https://photoacoustics.pratt.duke.edu/

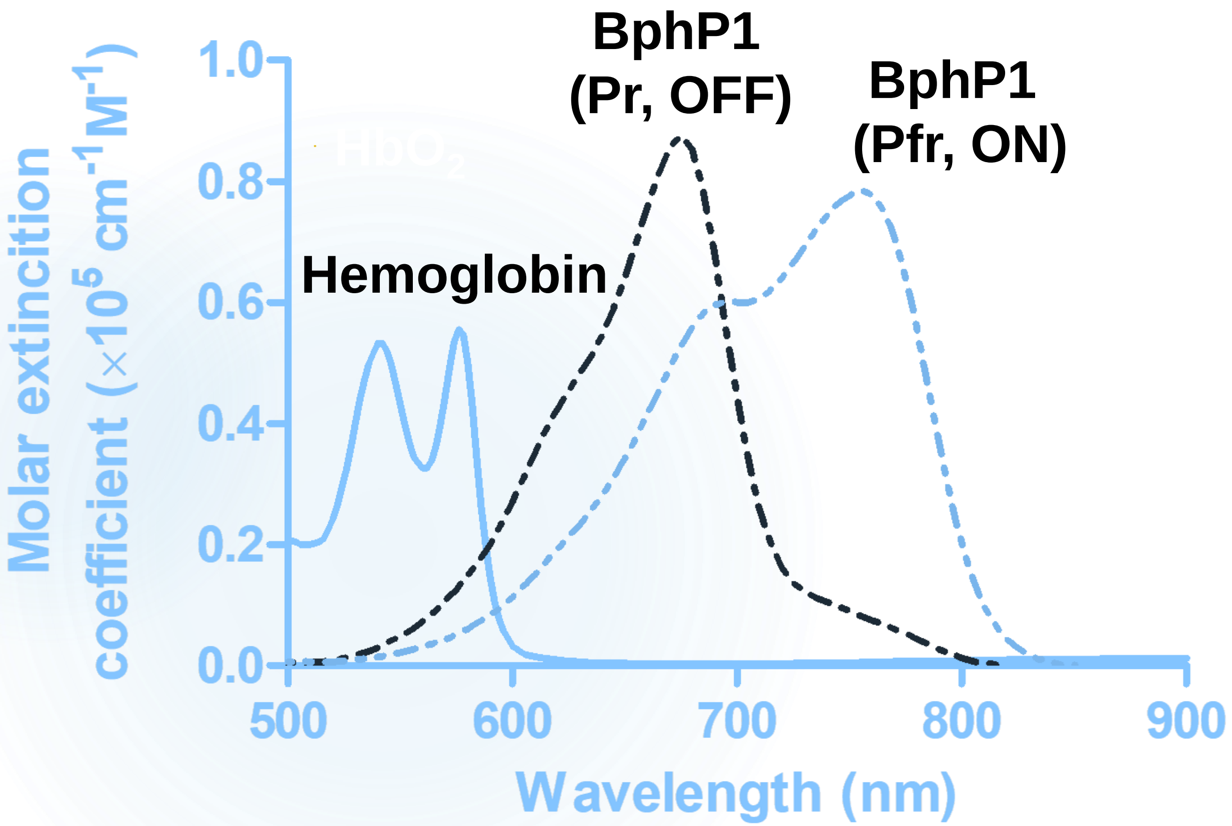
# Weak molecular signals are overwhelmed by strong background blood signals

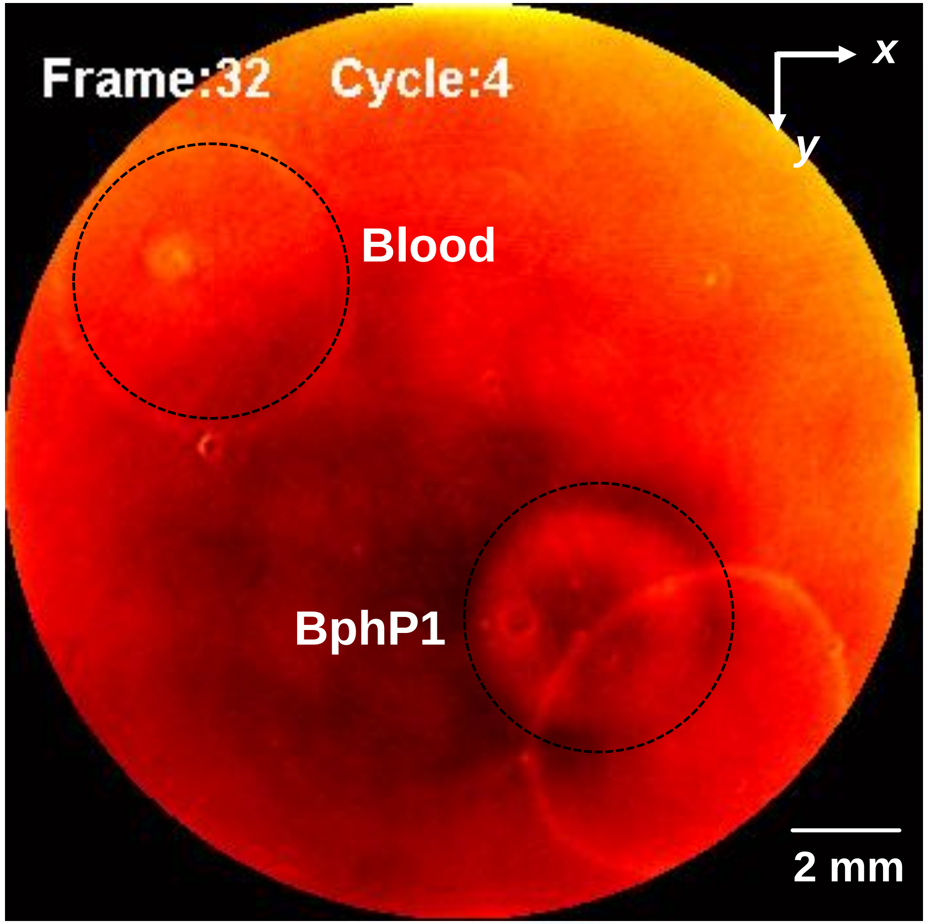




www. nasa. gov

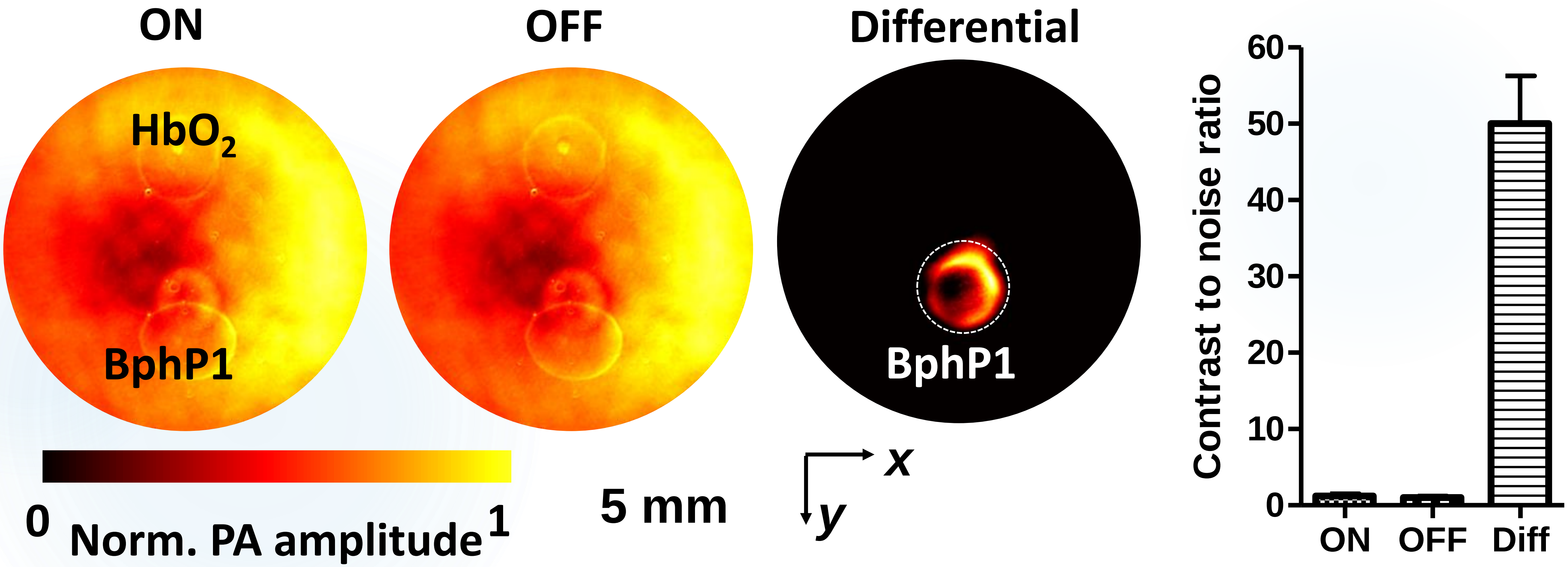
# Photoswitchable non-fluorescent NIR bacterial phytochrome BphP1



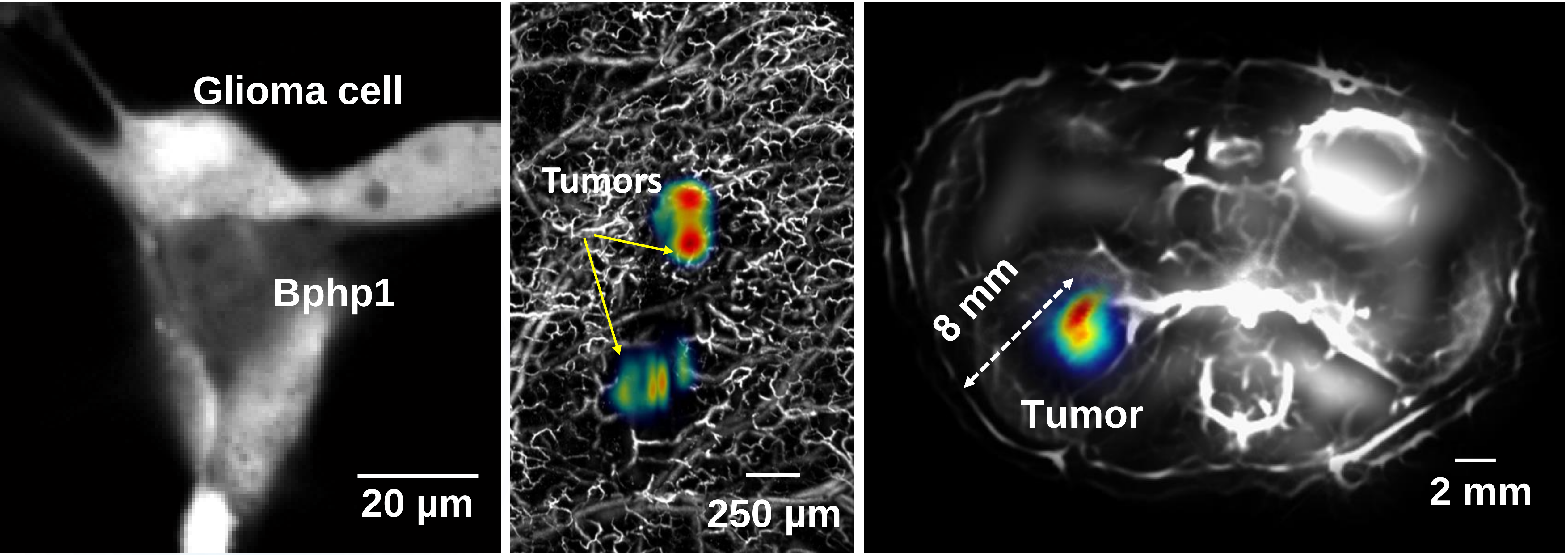

J Yao et al., Nature methods 13 (1), 67-73 (2016)

# Differential PAT of BphP1: improved contrast and sensitivity




J Yao et al., Nature methods 13 (1), 67-73 (2016)

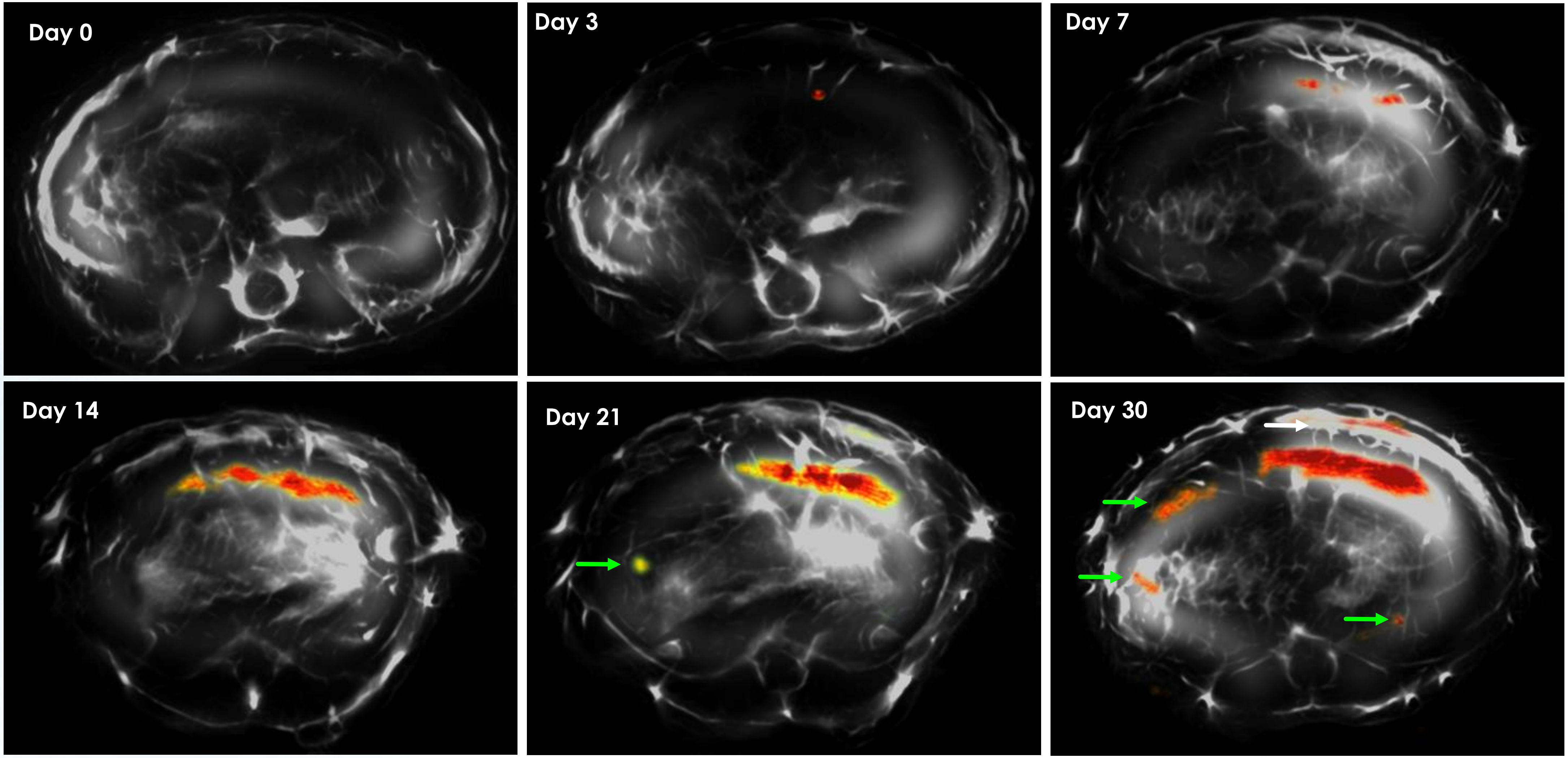
# Multi-scale differential PAT: from single cells to whole-body




J Yao et al., Nature methods 13 (1), 67-73 (2016);

# Longitudinal RS-PACT of cancer metastasis in mouse liver



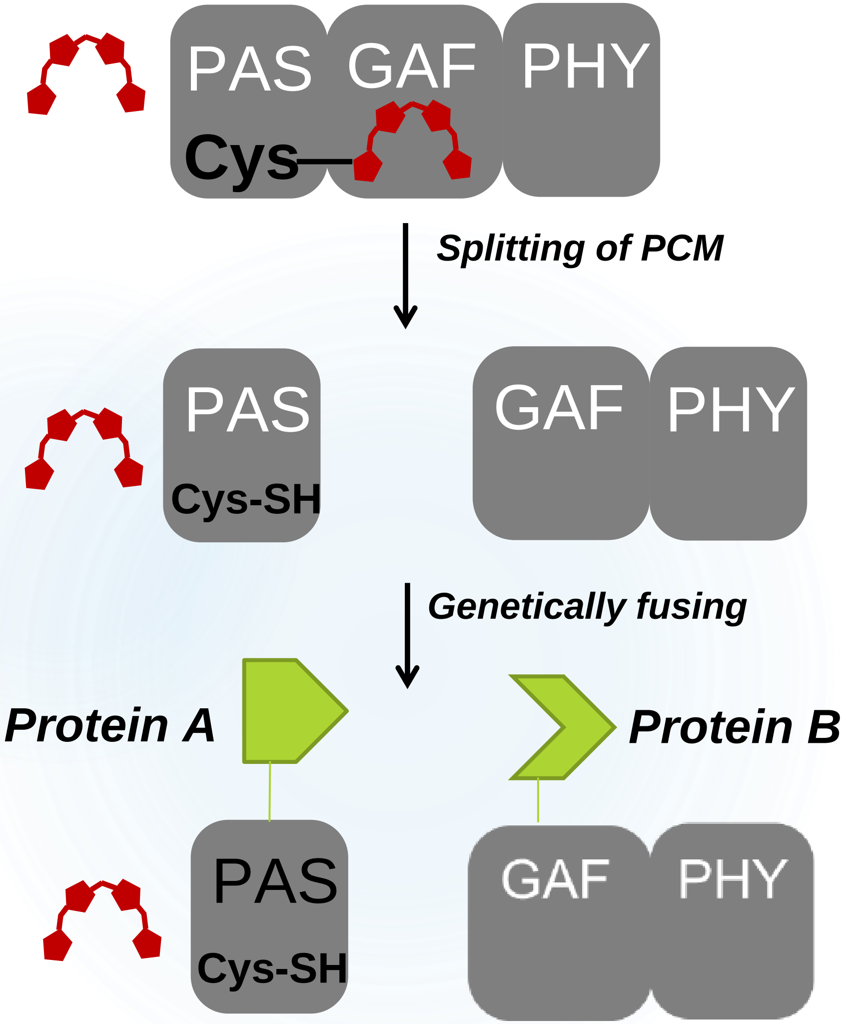


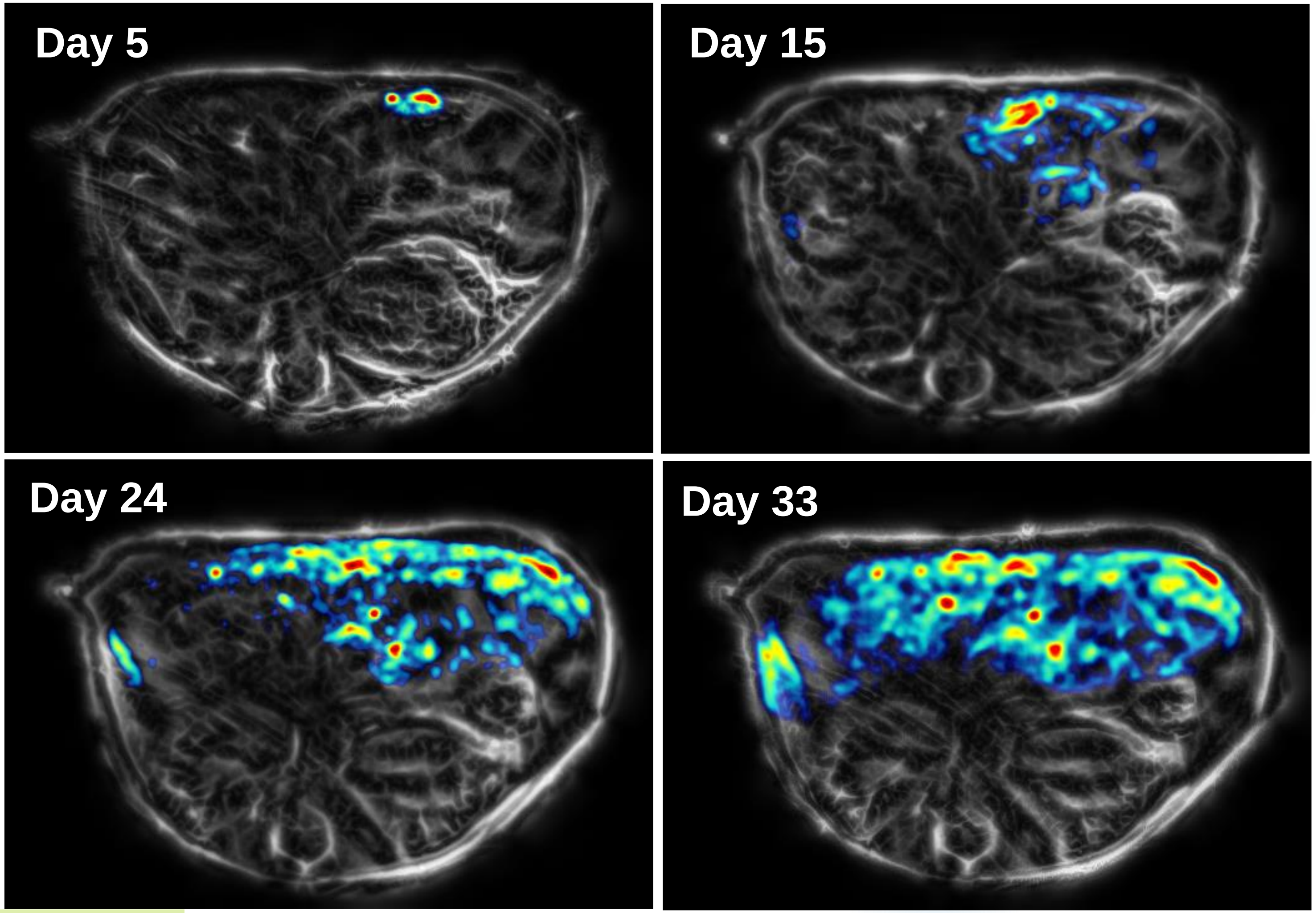

**Detection sensitivity: 200 cancer cells at 10 mm depth**

J Yao et al., Nature methods 13 (1), 67-73 (2016);

# Imaging protein-protein interactions by using a split version of BphP






Lei Li et al., Nature communication, 9, 2734 (2018)

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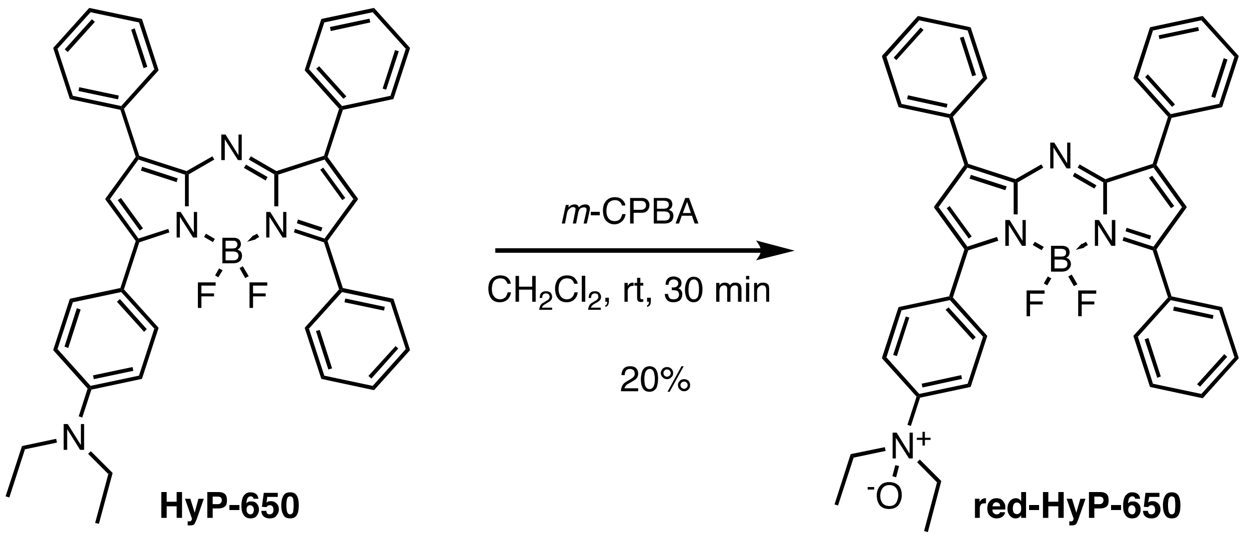
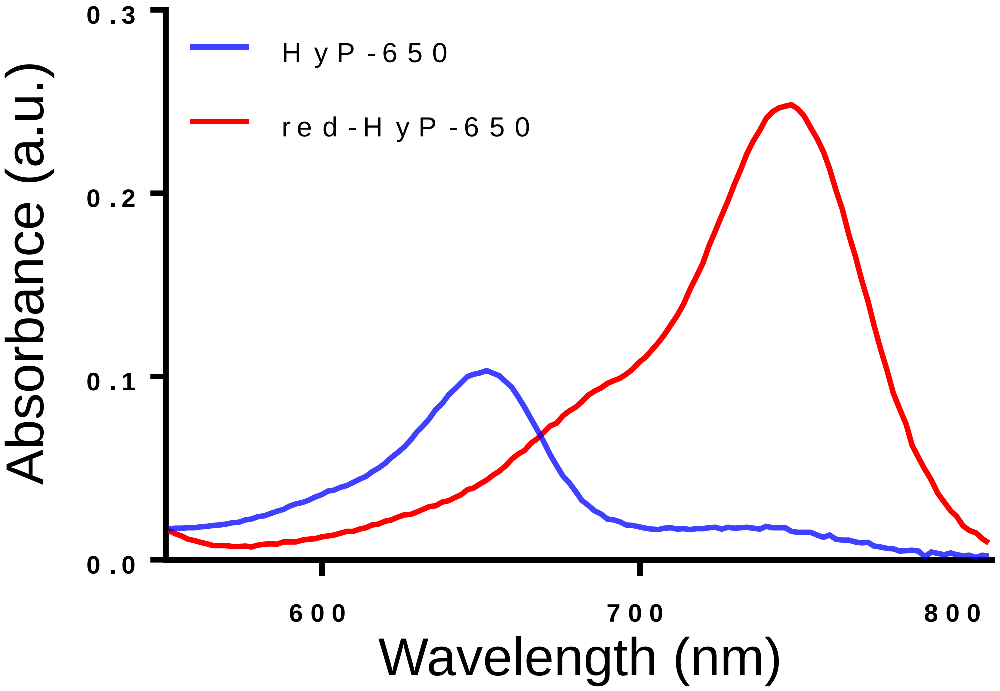
# Bio-switchable hypoxia-sensitive dye Hyp-650




Chen et al., Optics Letters, 44(15), 2019; Collaborator, Jeff Chan, UIUC

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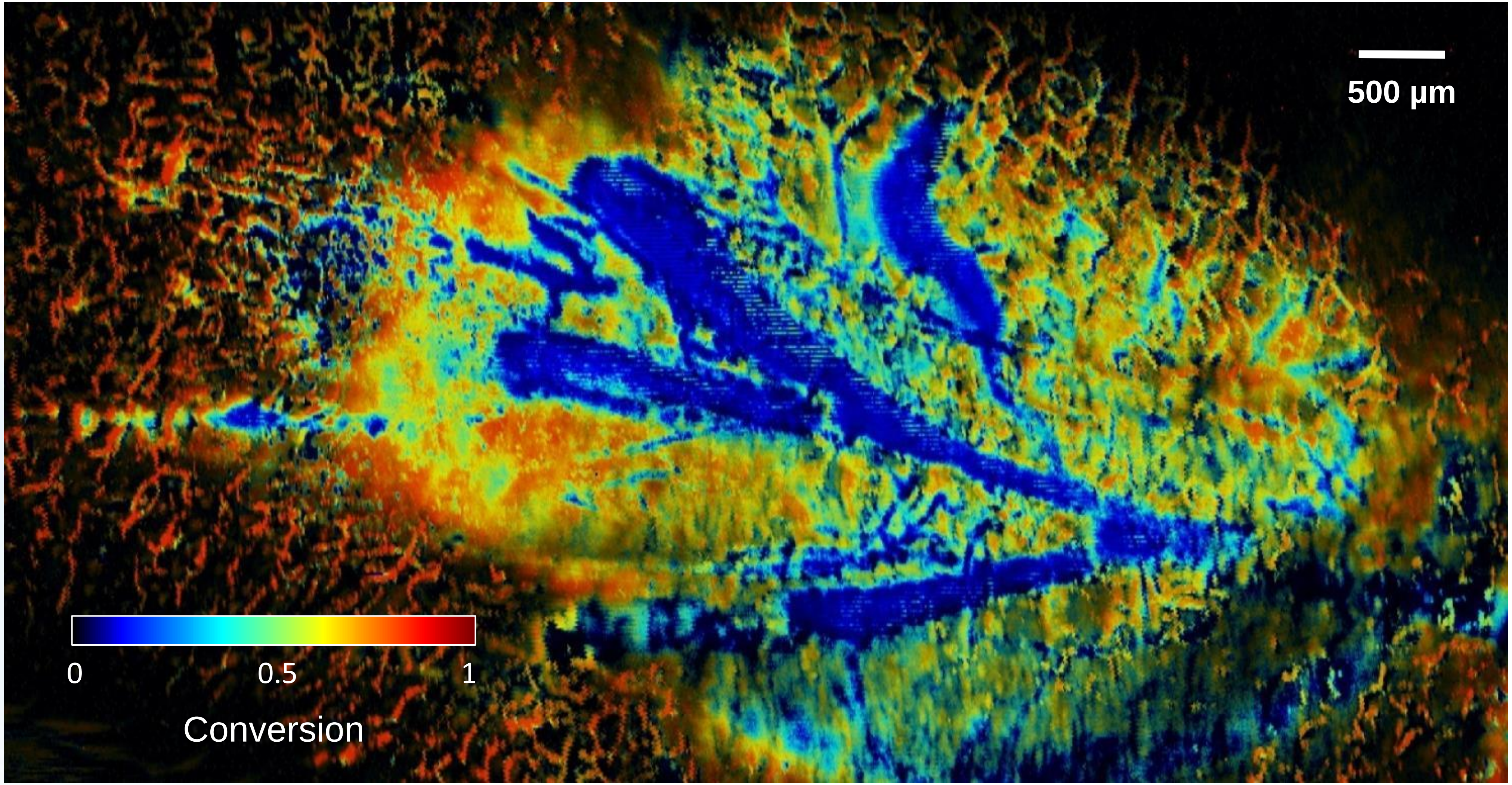
# Quantify the tissue's hypoxia under ischemia




Chen et al., Optics Letters, 44(15), 2019; Collaborator, Jeff Chan, UIUC

# Conclusions

- Photoacoustic imaging is intrinsically sensitive to tissue's functional molecular information, based on optical absorption contrast
- A variety of functional and molecular probes (endogenous or exogenous) can be imaged by photoacoustic imaging, with high sensitivity and deep penetration
- Photoacoustic-imaging-specific functional molecular imaging strategies and toolkits have been developed and applied in life science
- Clinical translation of photoacoustic imaging is on the horizon and will bring its unique impact to the medical imaging playground.

# Welcome to visit us at Duke PI-Lab