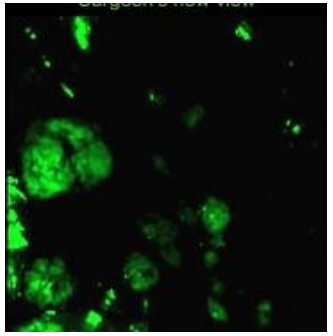
U.S. FOOD & DRUG ADMINISTRATION

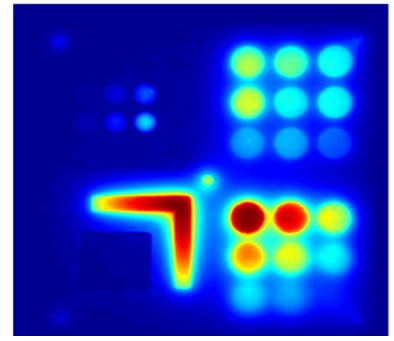
Performance Standardization of Emerging Biophotonic Imaging and Sensing Technologies

NIST/NIBIB Symposium on Medical Metrology and Standards for American Healthcare and Commerce









T. Joshua Pfefer, PhD

Division of Biomedical Physics

Office of Science and Engineering Laboratories

Center for Devices and Radiological Health

U.S. Food and Drug Administration

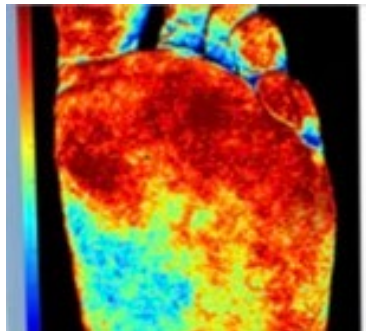
The opinions and conclusions stated in this work are those of the authors and do not represent the official position of the Food and Drug Administration. The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the Food and Drug Administration or the Department of Health and Human Services.

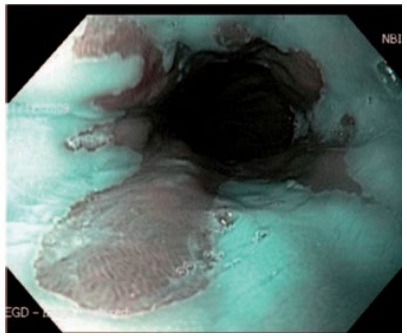
Biophotonic Technologies

- Since the 1980's light-based devices have become ubiquitous tools in medicine
- FDA has cleared/approved a wide range of *in vivo* imaging and sensing technologies

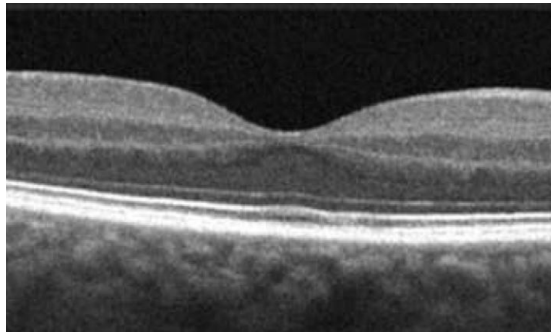

Pulse oximetry

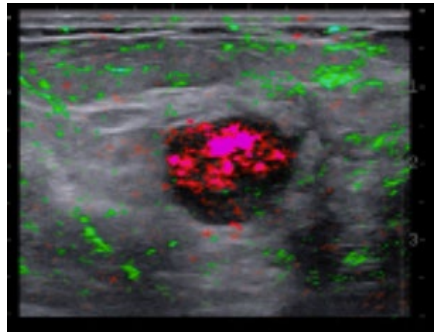

Cerebral oximetry

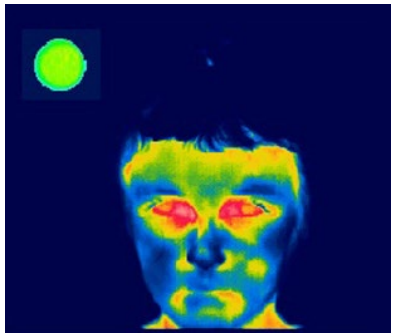

Hyperspectral imaging

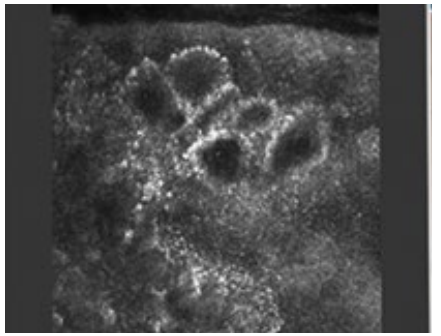

Narrow band imaging

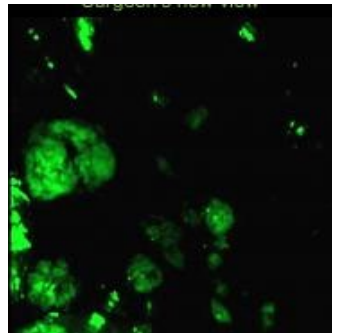

Wearables/PPG


Optical coherence tomography (OCT)


Photoacoustic imaging

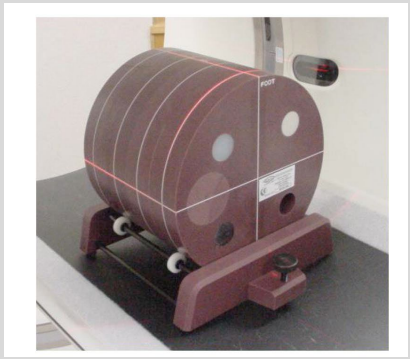

Thermography

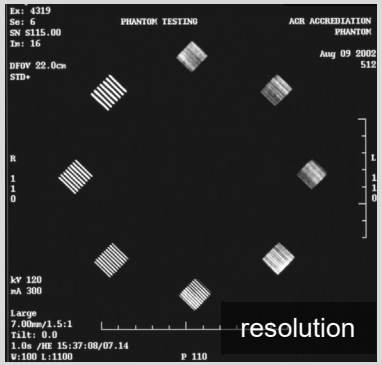

Confocal imaging


Fluorescence imaging

Medical Image Quality Standards

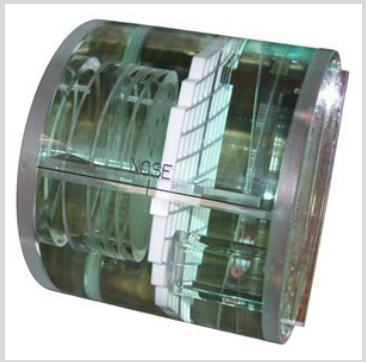
X-ray Computed Tomography (CT)

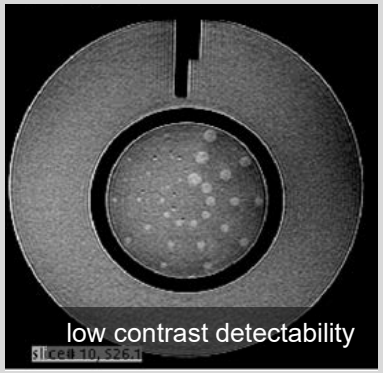




McCullough et al., Med Phys 2004

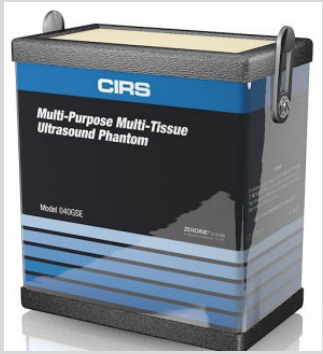
Magnetic Resonance Imaging (MRI)

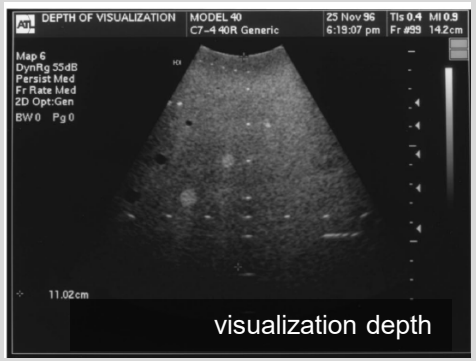




AAPM Report 100, 2010 (ACR Phantom)

Ultrasound

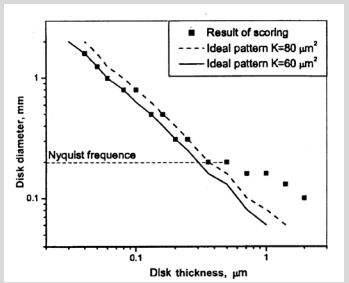




Goodsitt et al., Med Phys 1998

Mammography





Thomas et al, Med Phys 2005

- Review of >100 consensus documents *Palma-Chavez et al., J Biomed Opt 2021*
  - Performance characteristics
  - Materials
  - Methods – measurement and calculation
  - Metrics
- *Can these methods be adapted for biophotonics?*



Chronology of Biophotonic Device Standardization

- Increasing interest over past 10-15 years
- Driven in part by NIST, NIH/NCI, FDA-organized meetings & publications (2011+)
- Published consensus documents with test methods
  - Endoscopy (1997, 2020 – ISO/IEC)
  - IR Thermography (2009, 2017 – ISO/IEC)
  - Pulse oximetry (2011, 2017, 2026 – ISO/IEC)
  - Optical coherence tomography (2015, 2024 – ISO/IEC)
  - Functional near-IR spectroscopy (2015, 2025 – ISO/IEC)
  - Cerebral oximetry (2021 – ISO/IEC)
  - Photoacoustics (2022 – IPASC)
  - Fluorescence imaging (2024 – AAPM)

FDA Regulatory Science Tools (RSTs)



- Tissue phantoms, computational models, lab test methods
- Streamline device development, pre-clinical testing, and regulatory testing
- Reduce developer burden of designing *ad hoc* test methods for safety and performance
- Not intended to replace Guidance or Standards; not qualified as Medical Device Development Tools

- RST Catalog web site contains over 140 entries
- Many of the tools in this presentation are described in detail in the Catalog
- Some of these tools have also been incorporated in the *NIST/NIBIB Medical Phantom Library*

U.S. FOOD & DRUG ADMINISTRATION

Biophotonic Device Test Methods

White Light Imaging

Clinical Indications



GI Endoscopy



Tele-Dermatology

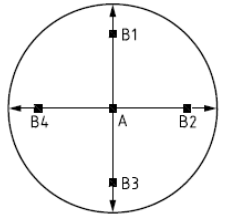
Garud et al., Ther Adv Gastro 2010; *Suresh et al., OSA Continuum 2019*

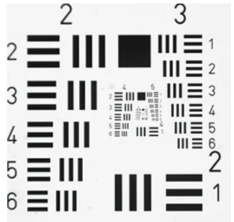
ISO 8600-5 Optics and photonics — Medical endoscopes and endotherapy devices —

Part 5: Determination of optical resolution of rigid endoscopes with optics

Second edition 2020-10

- Spatial resolution
- Distortion
- Field of view
- Image quality targets





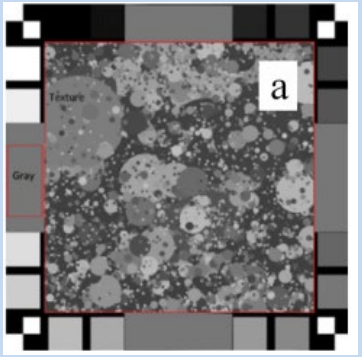
Test Method Research @ FDA (Q Wang)

- Endoscopic imaging
  - Updated test methods (e.g., distortion)
  - Modifications for novel device designs (e.g., capsules)

Wang et al., Sensors 2024



- Mobile phone imaging
  - Texture reproduction accuracy test method
  - Dead leaves target
  - Assess denoising algorithms

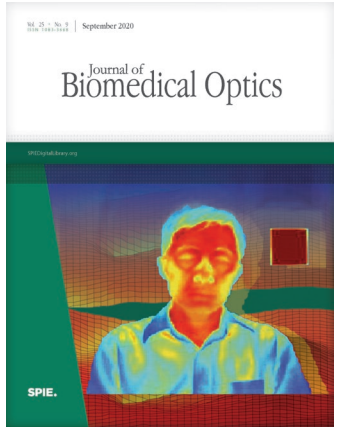


Suresh et al., OSA Continuum 2019

Infrared Thermographic Imaging

Clinical Indications

- Fever detection
- Pandemic response (COVID)
- Hospital triage
- Public screening



IEC 80601-2-59

Edition 2.0 2017-09

Medical electrical equipment –
Part 2-59: Particular requirements for the basic safety and essential performance of screening thermographs for human febrile temperature screening

ISO/TR 13154 First edition 2009-04-01

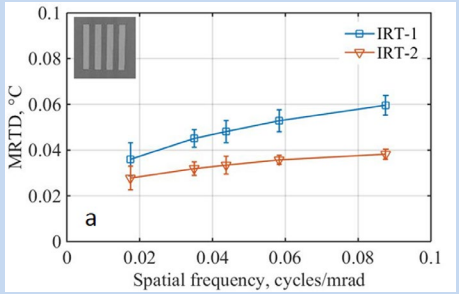
Medical electrical equipment — Deployment, implementation and operational guidelines for indentifying febrile humans using a screening thermograph

Test Method Research @ FDA (Q Wang)

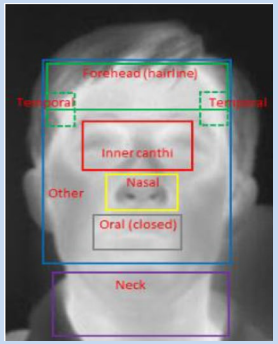
- Practical methods for implementing standards
  - Uniformity
  - Stability
  - Drift

Ghassemi et al., PLoS One 2018

- Minimum resolvable temperature difference (MRTD)



- Clinical study to standardize measurement and processing protocols



Zhou et al., JBO 2020

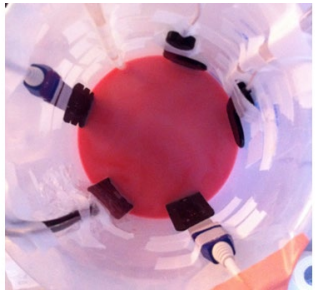
Cerebral Oximetry

Clinical Indications

- Measurement of blood oxygenation in frontal cortex
- Surgical and NICU monitoring



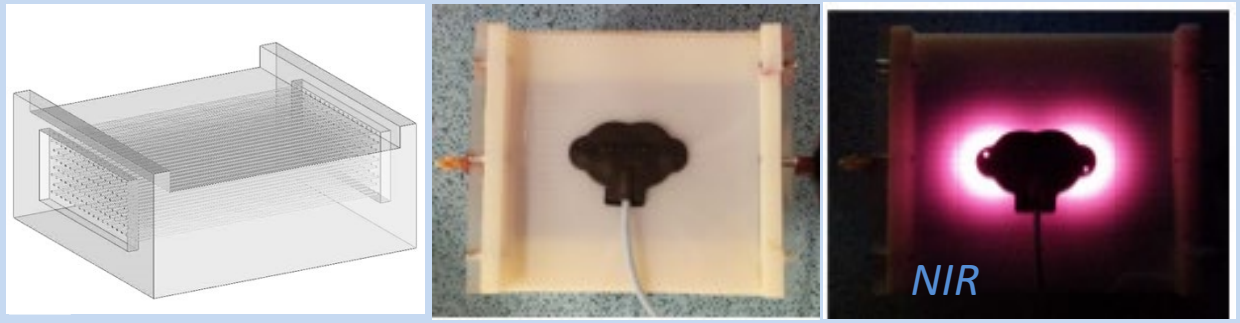
Medical electrical equipment —
ISO 80601-2-85:2021
Particular requirements for basic safety and essential performance of cerebral tissue oximeter equipment



- Dynamic liquid oximetry phantom (Wolf, U of Zurich) *Hyttel-Sorensen et al., Biomed Opt Express 2013*
- StO_2 - Root mean square error, mean bias, precision

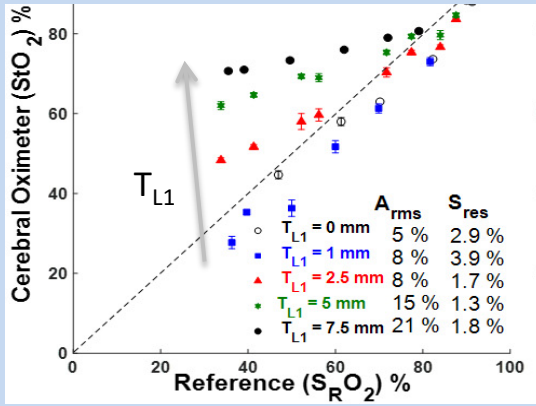
Test Method Research @ FDA (J Pfefer): 3D-printed channel array phantoms for saturation measurement accuracy

Testing adult and neonatal clinical probes



Afshari et al., Biomed Opt Express 2019

Effect of patient anatomy: Extra-cerebral tissue (T_{L1})



Pulse Oximetry

Clinical Indications

- Arterial blood oxygenation - "5th vital sign"
- Anesthesiology, pulmonology, EMS, etc
- Home use, wearables



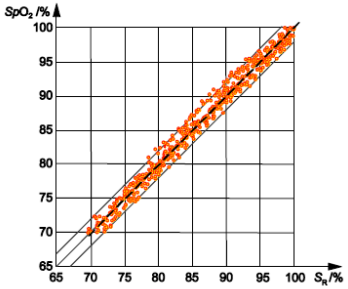
ISO 80601-2-61

Third edition
2026-04

Medical electrical equipment —

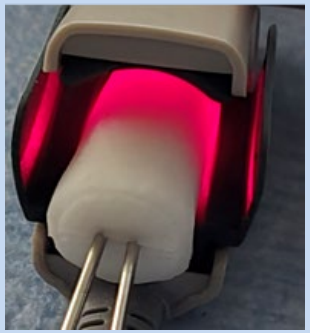
Part 2-61:
Particular requirements for basic safety and essential performance of pulse oximeter equipment

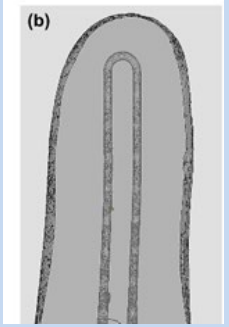
- No phantom testing
- Electronic functional tester
- Larger clinical studies (n≥24)
- Robustness to skin pigmentation



Test Method Research @ FDA (S Vasudevan): Mock cardiovascular flow loop w/tunable pressure waveform, SaO_2

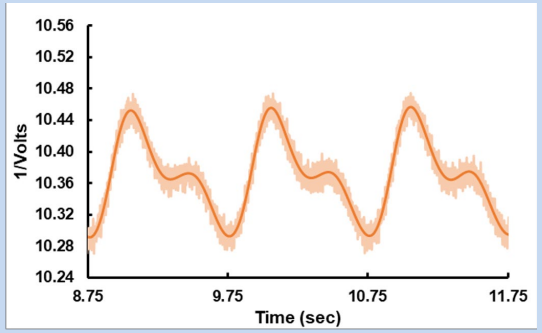
Finger phantom



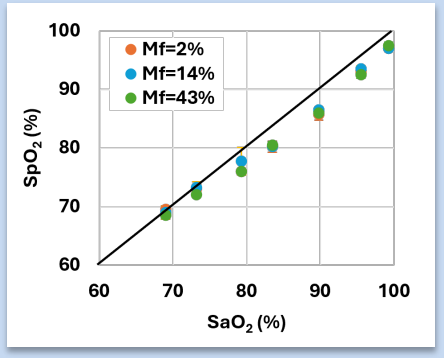


3D-printed molding

PPG waveform



Saturation accuracy

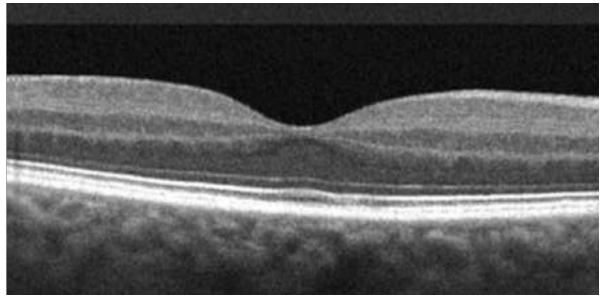


Lee et al., (submitted)

Optical Coherence Tomography

Clinical Indications

- Retinal
- Intravascular



ISO 16971-1

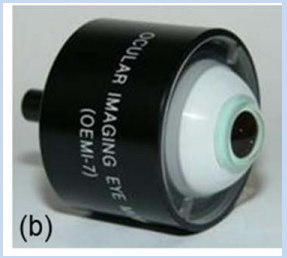
First edition
2024-11

Ophthalmic instruments — Optical coherence tomograph for the posterior segment of the human eye

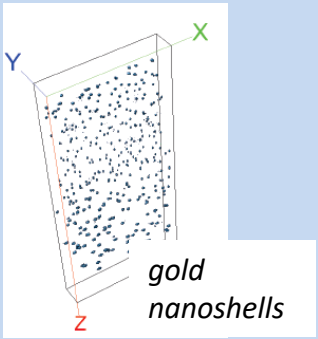
- Transverse resolution: knife edge, microbeads
- Axial resolution: glass plate
- Sensitivity, roll-off: glass plate
- Co-registration of fundus and OCT scan

Test Method Research @ FDA (A Agrawal)

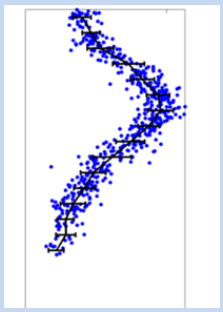
Model eye



Resolution/PSF



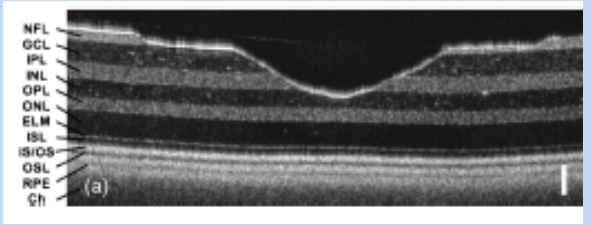
Uniformity



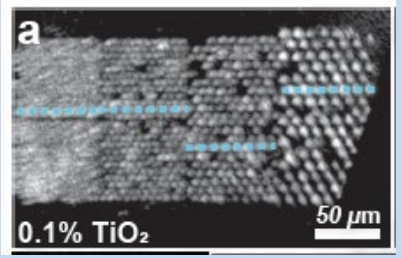
Agrawal et al., Biomed Opt Exp 2012; Fouad et al., Biomed Opt Exp 2014

Anthropomorphic Phantoms

Registration/segmentation, spatial measurement accuracy



OCT retina phantoms *Baxi et al., JBO 2014; Agrawal et al., IOVS 2016*

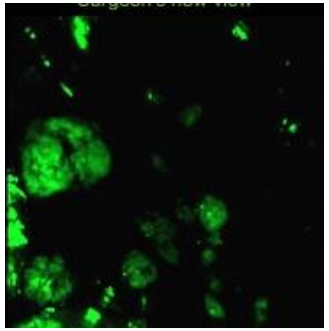


AO-OCT retinal cone phantom *Lamont et al., Opt Mat Exp 2020*

Contrast-enhanced Fluorescence Imaging

Clinical Indications

- Vascular, lymph imaging
- Fluorescence-guided surgery: tumor/margin, nerves, vessels
- Molecular imaging



Van Dam et al., Nature Medicine 2011

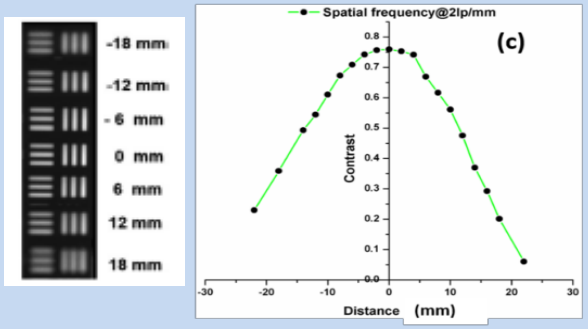
AMERICAN ASSOCIATION of PHYSICISTS IN MEDICINE

Prof. Brian Pogue

AAPM Task Group Report 311: Guidance for performance evaluation of fluorescence-guided surgery systems (2024)

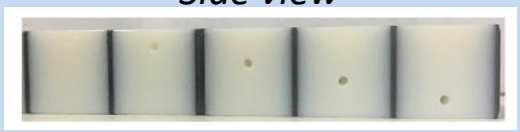
Test Method Research @ FDA (J Pfefer)

Depth of Field

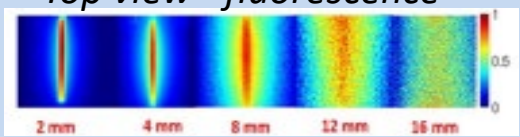


Detection Depth

Side view

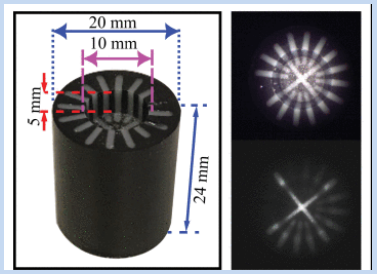


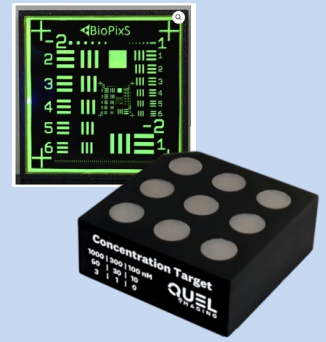
Top view - fluorescence



Kanniyappan et al., Med Phys 2019

Towards Commercialization



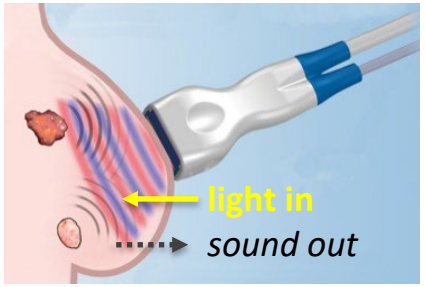


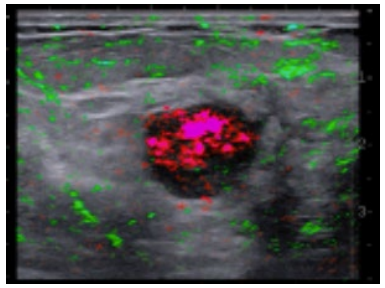
Tenditnaya et al., IEEE Trans Med Imag 2024 (Gorpas - Munich)

Photoacoustic Imaging

Clinical Indications

- Oximetry and vascular imaging
- Breast cancer detection



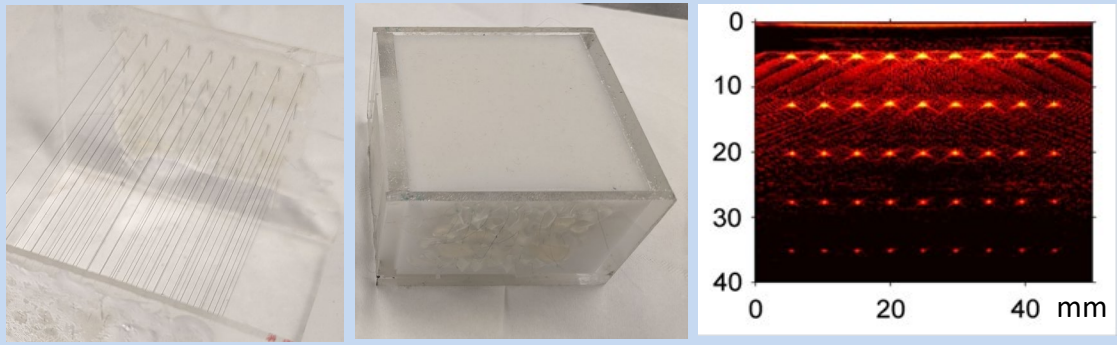


IPASC
International Photoacoustic Standardisation Consortium

Consensus documents on tissue phantoms, image quality, saturation measurement accuracy, etc. (Bohndiek, U of Cambridge, UK)

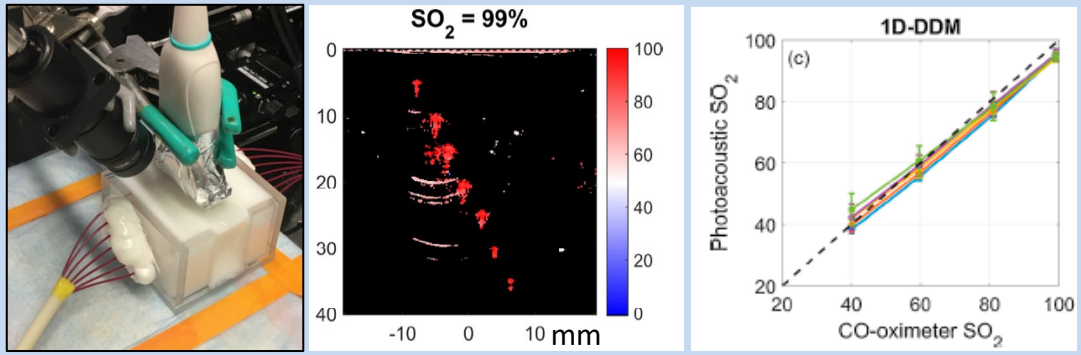
Test Method Research @ (W Vogt): Breast phantoms with relevant optical, acoustic properties

Filament inclusions: Spatial resolution, imaging depth



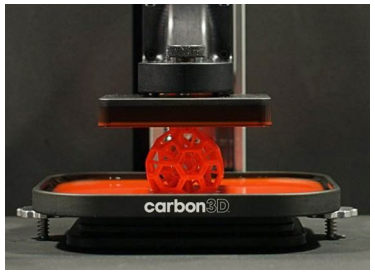
Vogt et al., J Biomed Opt 2017

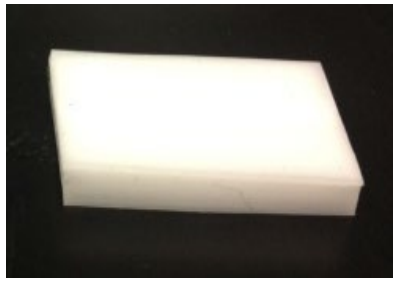
Tube inclusions: Blood oxygenation accuracy

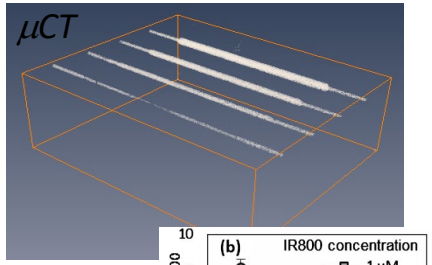


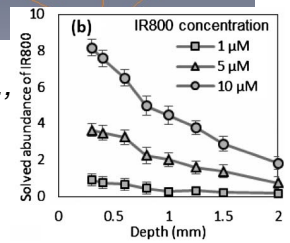
Vogt et al., Biomed Opt Exp 2019; Zhou et al., Photoacoustics 2020

3D-Printed Tissue Phantoms

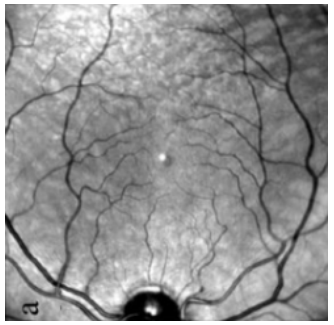




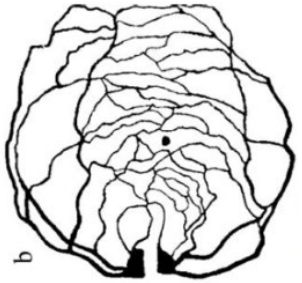




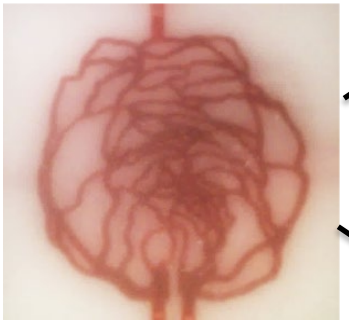
Wang et al., Opt Lett 2015



Fundus image of retina

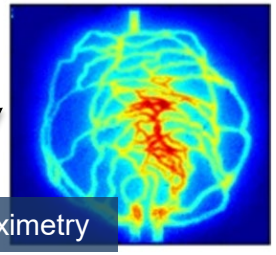


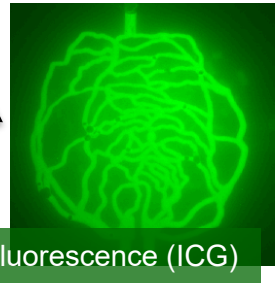
CAD Model



3D-Printed Phantom
(w/ Hb solution)

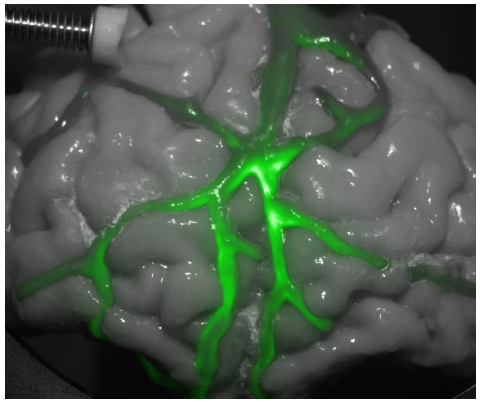
Ghassemi et al.,
J Biomed Opt 2015





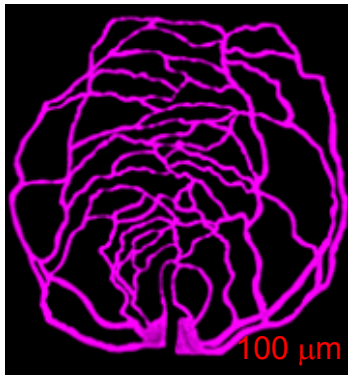
Ghassemi et al.,
IEEE TBE 2017





MRI-derived forebrain phantom
Liu et al., Biomed Opt Exp 2018

- Use of additives to customize optical properties
- Multi-material printing
- Dissolvable molds



High res 2-photon printing
Horng et al., Opt Lett 2021

U.S. FOOD & DRUG ADMINISTRATION

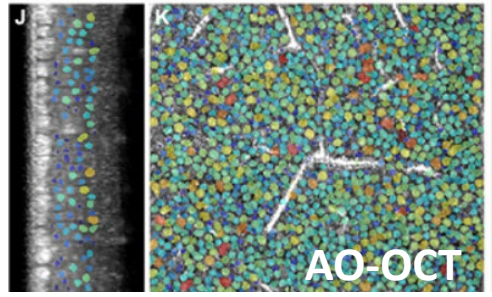
Wrap-Up: Research Needs

Biophotonics Standardization Needs: General

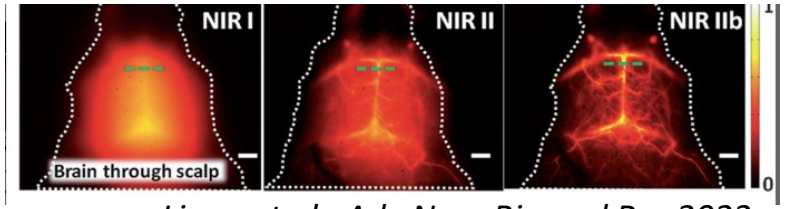
- Accurate data on physical properties of tissue
  - Optical
  - Acoustic
  - Mechanical
  - Thermal
- Tissue mimicking materials (TMMs)
  - Absorption and scattering of blood across visible, NIR
- High-precision referencing of blood oxygenation (CO-oximeters, blood gas analyzers)

Biophotonics Standardization Needs: Emerging Areas

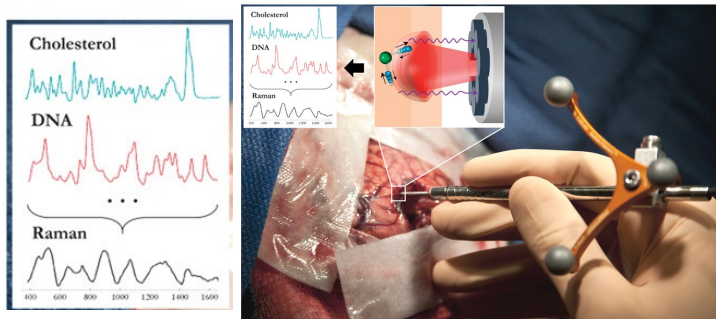
- Photoacoustics (PA)
  - Optical-acoustic-relevant TMMs for different tissue types
  - Test methods for confounding factors, melanin
- High resolution imaging
  - Adaptive optics (OCT), PA microscopy, multi-photon
- Fluorescence imaging
  - NIR-II window (1000 nm-1700 nm)
  - Time-resolved fluorescence
- Raman spectroscopy
  - TMMs relevant to different tissue types



Hammer et al., IOVS 2023



Liang et al., Adv NanoBiomed Res 2022



Jermyn et al., Sci Trans Med 2020

Conclusions

- Major strides have been made in biophotonic device performance standardization over the past decade
  - Updating/modernizing existing standards
  - Developing new standards for emerging clinical technologies
- FDA has generated a wide range of RSTs to advance public health
- Given wide range of biophotonic modalities, maximum research impact may come from cross-cutting topics
- Modality-specific research needed for more prevalent devices

*For more discussion of standardization in Biophotonics, join us at **SPIE Photonics West BiOS** for **Design and Quality for Biomedical Technologies XX** – Jan. 30-31, 2027 in San Francisco, CA*

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