Contrast-Detail Analysis for Hyperspectral Imaging

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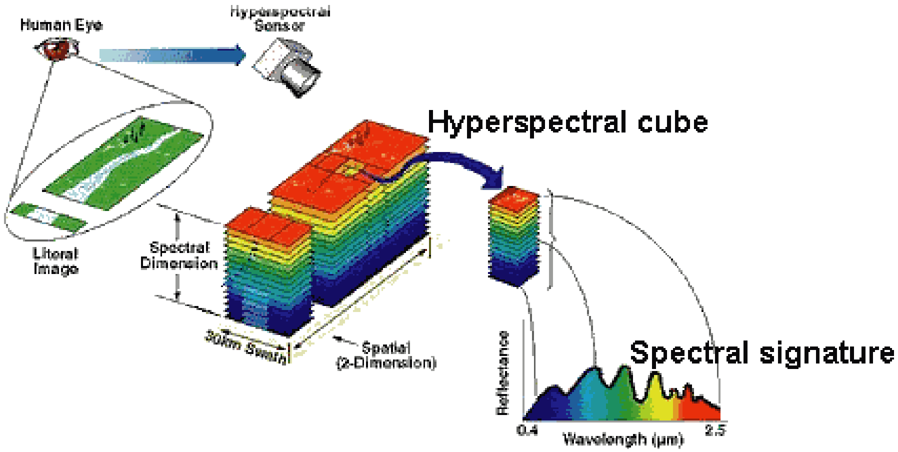
Hyperspectral Reflectance Imaging (HRI)



- Hyperspectral Imaging takes images at different wavelength, therefore it records the spectrum at each pixel.

- Both spatial and biochemical information

- It is now being applied to biomedical imaging, because of the distinct absorption spectra of some molecules in the visible-NIR:

Target	Application
✓ Hemoglobin	Tissue Oximetry, skin lesion detection
✓ Dyes	Molecular imaging of cancer
✓ Some metal nanoparticles	Molecular imaging of cancer

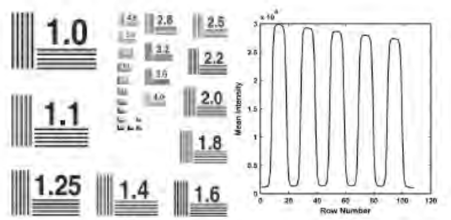
- Standardized phantom-based test methods are needed to characterize HRI systems for biomedical applications

Phantoms for Medical Imaging

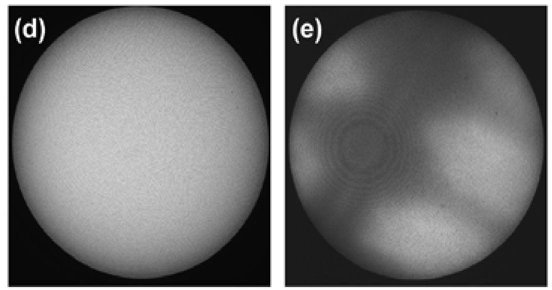
- Phantom-based test methods form the foundation of numerous guidance documents and international standards for established imaging modalities.

Basic Tests:

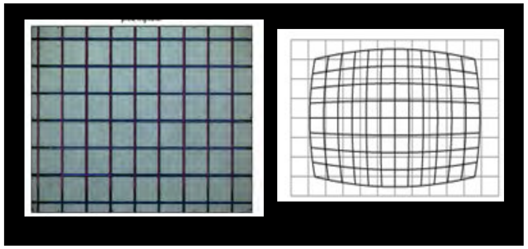
Resolution: NBS 1963A target, USAF target



Illumination / detection uniformity



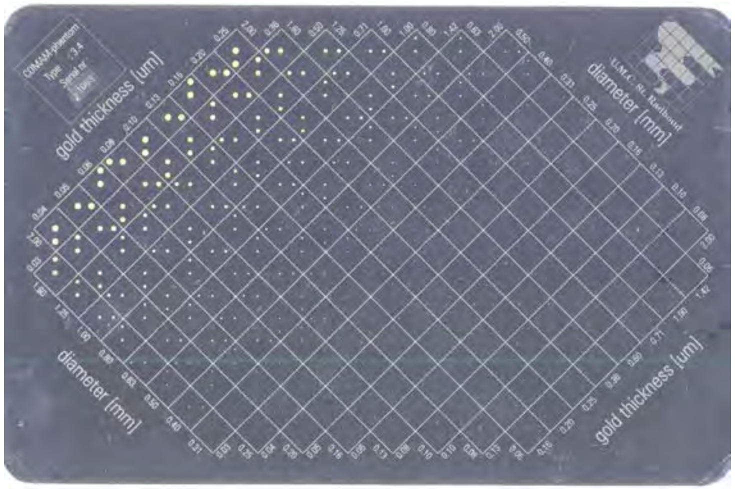
Distortion



Sellors J Acquir Immune Defic Syndr,37:160, 2004

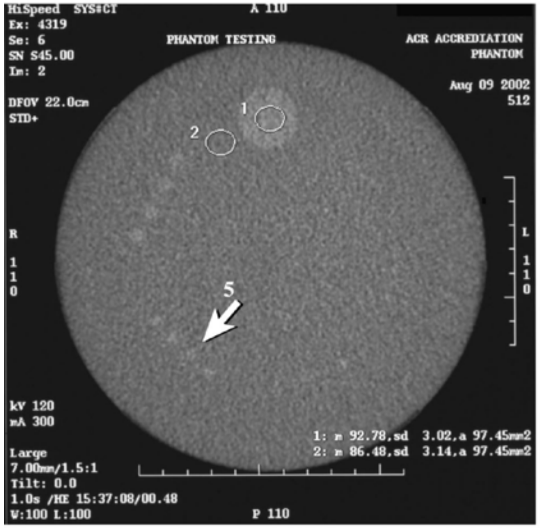
Task-based Tests:

Contrast-detail mammography (CDMAM) phantom



Thomas et al., Med. Phys. 32 .3., 807

Low contrast detection (LCD) CT phantom



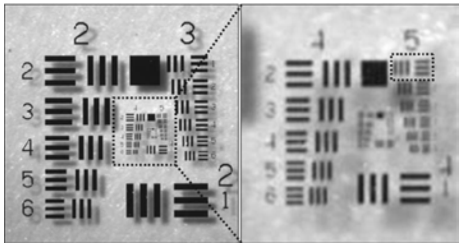
McCollough et al., Medical Physics, Vol. 31, 2004

Phantom-based Methods for HRI

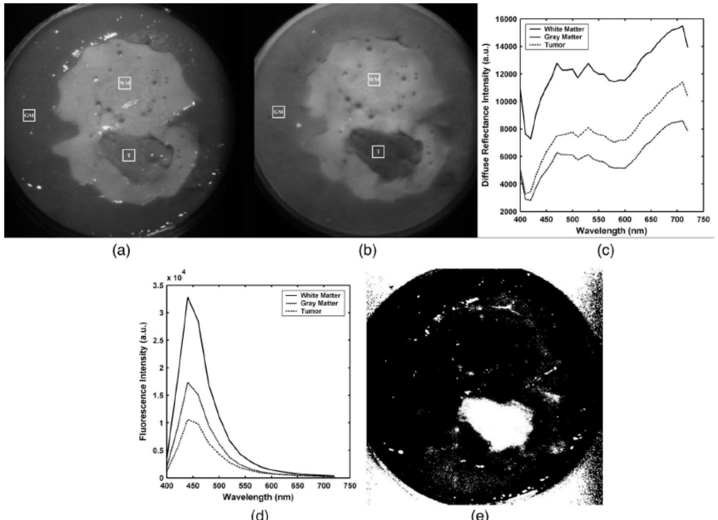
- Phantom-based test methods for assessing HRI are being studied, but standardized task-based methods have not been established

Bar chart test for resolution

D. Roblyer et al., J. Biomed. Opt. 132:024019, 2008

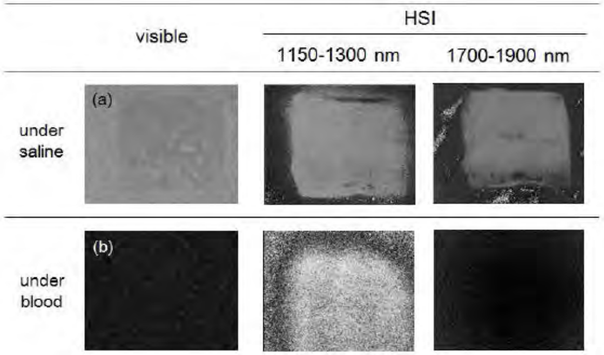


Brain tissue phantom for spectral imaging of brain tumor
Bovine hemoglobin, polystyrene microspheres in gelatin



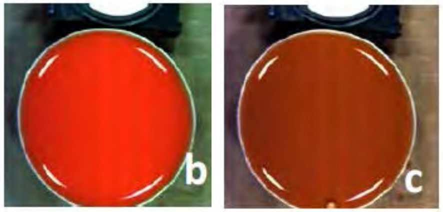
SC Gebhart, Applied Optics, 46:1896

Atherosclerotic Tissue Phantom for HRI
bovine fat inside biological tissue phantom, under saline or blood



K. Ishii et al., Proc. SPIE 87980Z, 2013

Blood Phantom with Different Oxygenation Level
Porcine whole blood, India ink, powdered milk solution



RX. Xu et al., Biomed. Opt. Exp. 3:1433, 2012

Overall Goals

- Enable optimal standardized testing/inter-comparison of biophotonic imaging devices (preclinical, clinical) for device developers and users

- Enhance ability to rapidly, objectively and quantitatively evaluate innovative devices in an optically realistic and least-burdensome manner

Specific Objectives

- Fabricate tissue phantoms based on 3D printing and PDMS molding with subsurface channels

- Characterize phantom
  - Optical properties
  - Morphology, using 3D imaging approaches

- Demonstrate utility of tissue phantoms with subsurface channels for HRI-based detection of contrast agents

- Identify detectability at varied
  - Inclusion size, contrast agent concentration, inclusion depth

I. Phantom Fabrication and Characterization

3D printing

PDMS molding

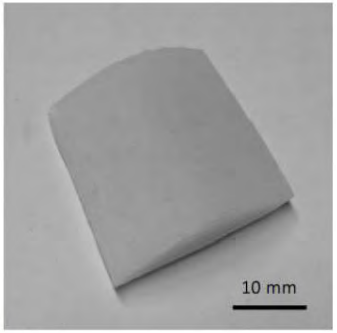
II. Phantom tests for HRI system

3D Printing of Tissue Phantoms

- "3-D printing…has the potential to revolutionize the way we make almost everything" *President Barack Obama, State of the Union Address, February 12, 2013*
  - This includes tissue phantoms!
- Rapid prototyping with 3D printer allows arbitrary geometries
- Simple, fast, and reliable
- Easy distribution of standard designs to users

Application of 3D printing in phantom fabrication for bioimaging

- Curvature correction in spatial frequency domain imaging



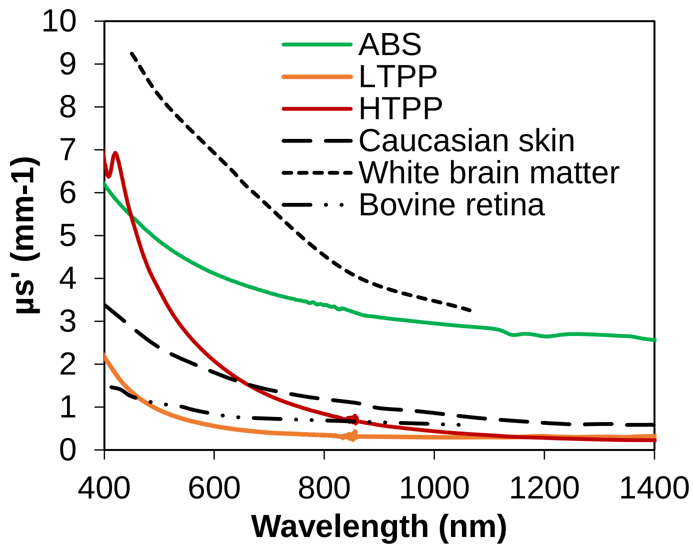
T. Nguyen, et al., Biomed Opt Express ***3****, 1200-1214 (2012).*

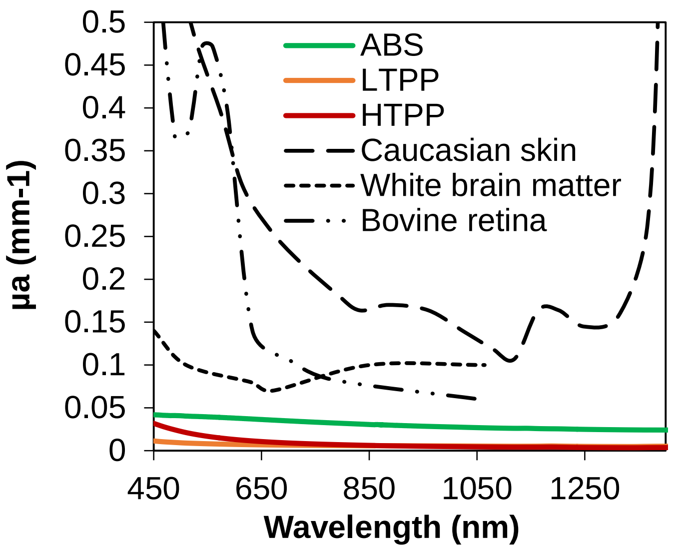
- Microwave breast imaging

M. J. Burfeindt, et al., IEEE Antennas 367 Wireless Propagat. Lett. 11, 1610 (2012).

Optical Properties of 3D-printed Polymer Samples

- Measured by Integrating Sphere – Inverse Adding Doubling (IAD)
- Sample: printed thin sheet (0.6 mm thickness)
  - Thermal plastic:
    - •Acrylonitrile Butadiene Styrene (ABS)
  - Photopolymers:
    - •polypropylene-like, low turbidity photopolymer (LTPP)
    - •resin-like, high turbidity photopolymer (HTPP)





Reference:

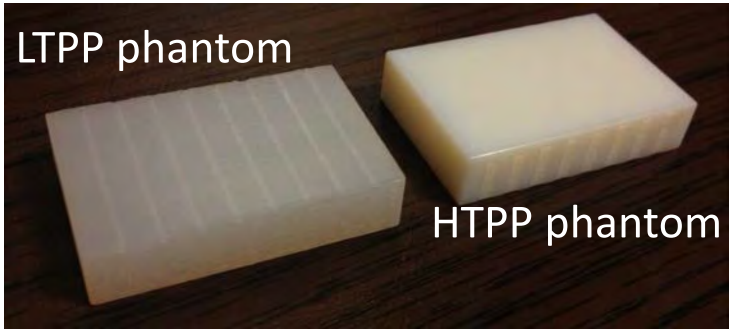
Caucasian skin: *E. K. Chan, et al., Selected Topics in Quantum Electronics, IEEE,Journal of 2, 943-950 (1996).*

White brain matter: *A. Yaroslavsky, et al., Phys Med Biol. 47, 2059-2073 (2002).*

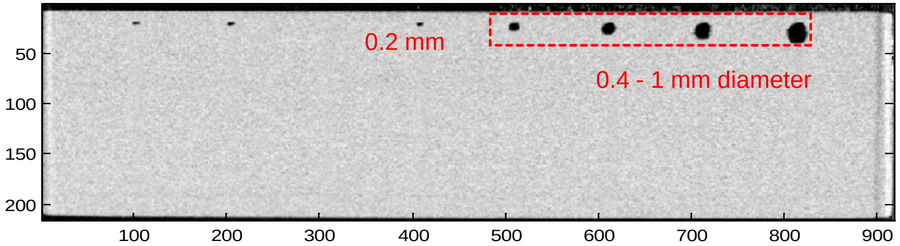
Bovine retina: *M. Hammer, et al., Phys Med, Biol 40, 963-978 (1995).*

3D printed phantoms

(Objective30, Objet Geometries Ltd. Billirica, MA)
Build layer of 28 µm, with 100 µm accuracy

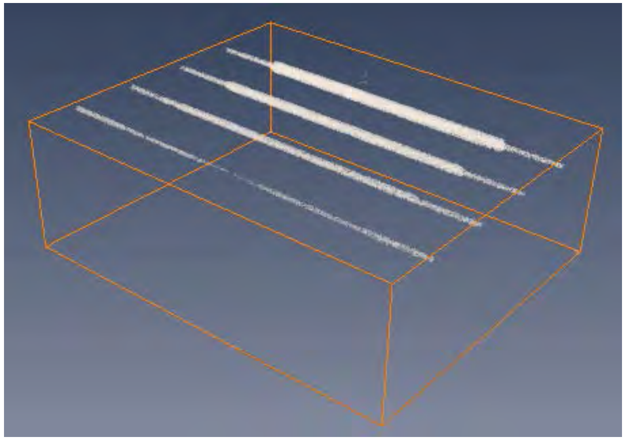


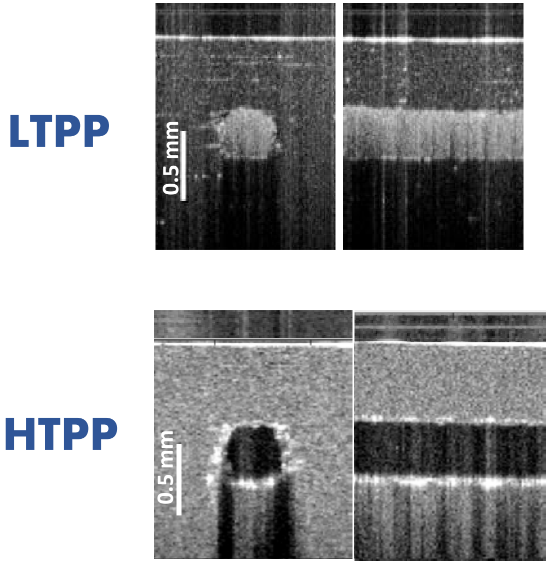
MicroCT Scan
Voxel size ~49 µm



Varied channel size: 0.4-1.5 mm
Varied channel depth: 0.3-2 mm

MicroCT Scan





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PDMS molding

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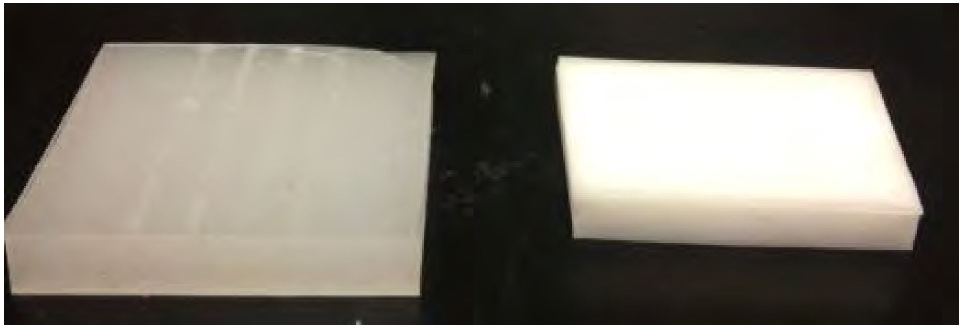
Polydimethylsiloxane (PDMS) Phantoms

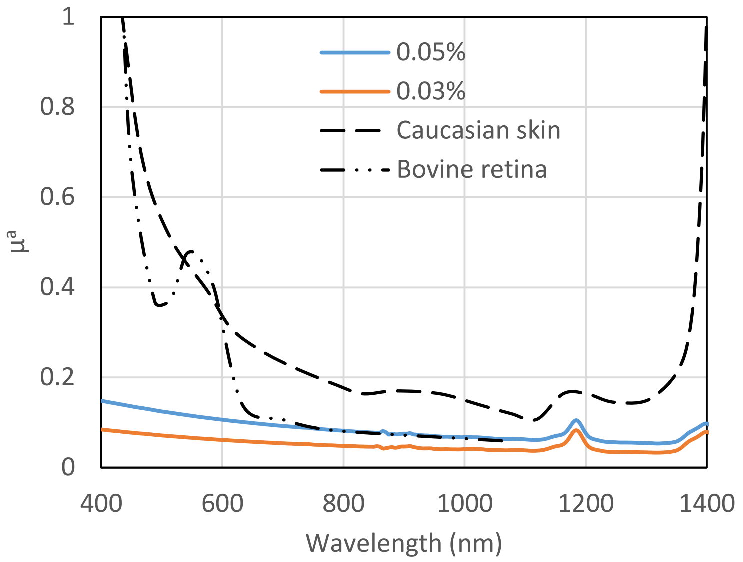
- For molding- and photolithography-based fabrication
- Easy molding / curing
- PDMS is optically clear, and, in general, inert, non-toxic, and non-flammable
- Can be mixed with absorber/scatterers to tune the optical property

PDMS phantoms

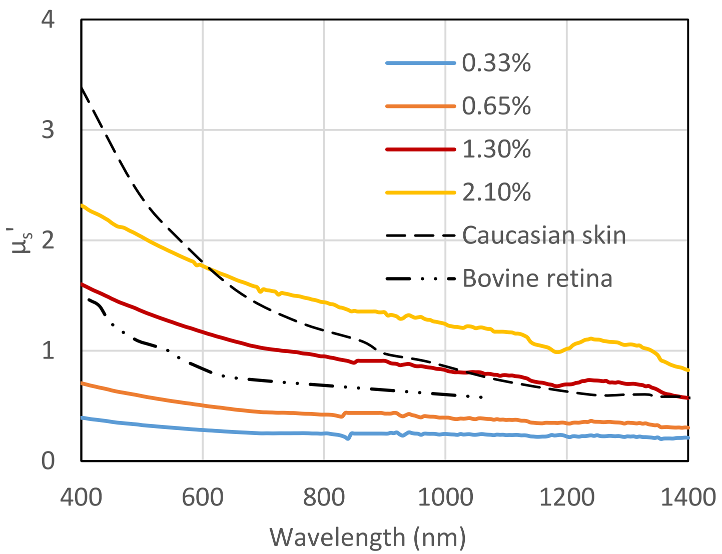


Tuning Optical Properties by Adding Absorber and Scatterer

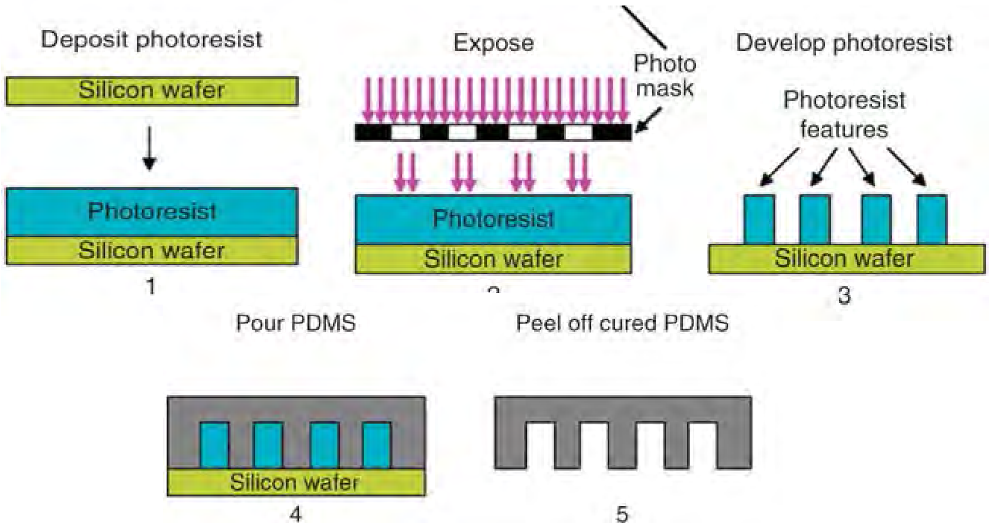
India ink for tuning μ_a

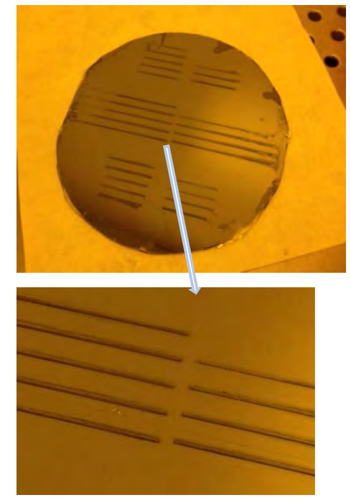


$BaSO_4$ powder for tuning μ_s'



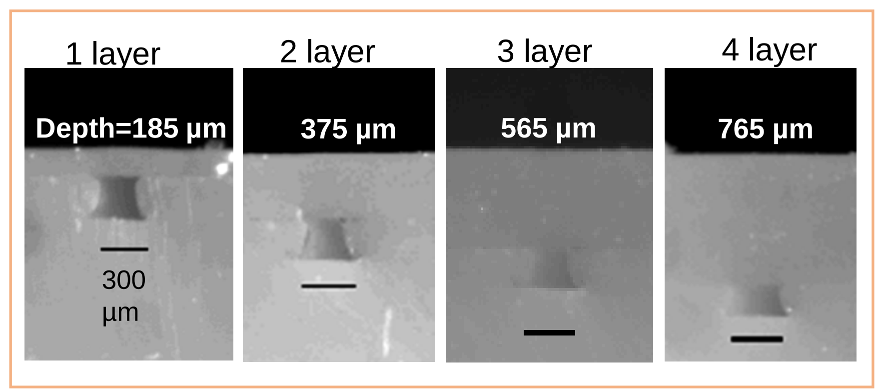
Photolithography for Sub-mm Channel Mold



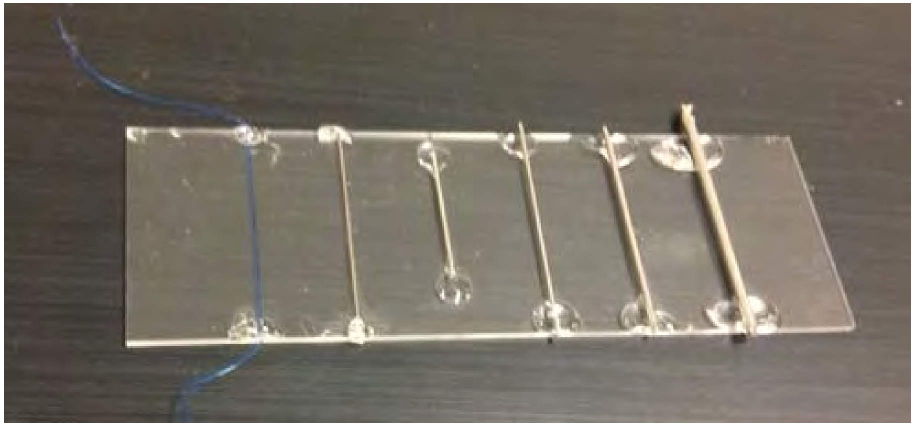


Derek L Englert, et al., Nature Protocols ***5****, 864 - 872 (2010).*

- Varied channel depth
  - Spinning coating of PDMS, layer-by-layer, to make the top layer above **rectangular** channels
  - Depth=0.19, 0.57, 0.95, 1.5, 1.9 mm



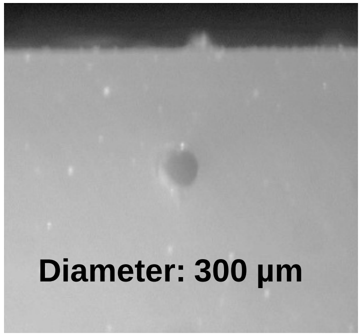
Needle-based Mold for Sub-mm Channel

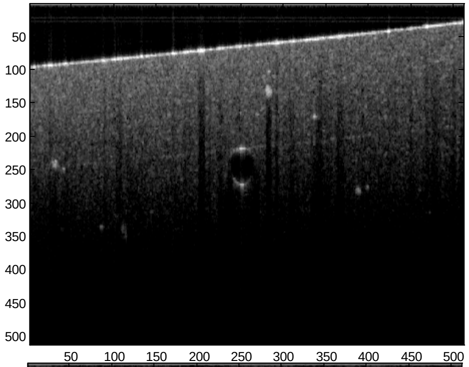


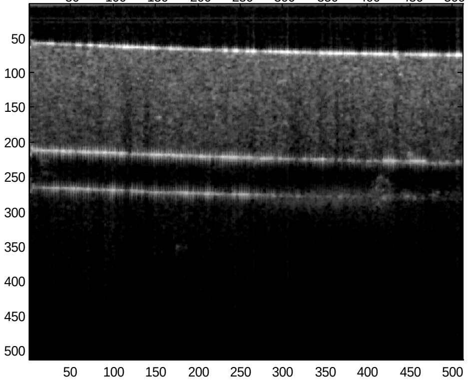
Needles and medical suture wires as mold for PDMS phantom with varied channel size

0.1 – 1.5 mm in diameter

Cylindrical channels







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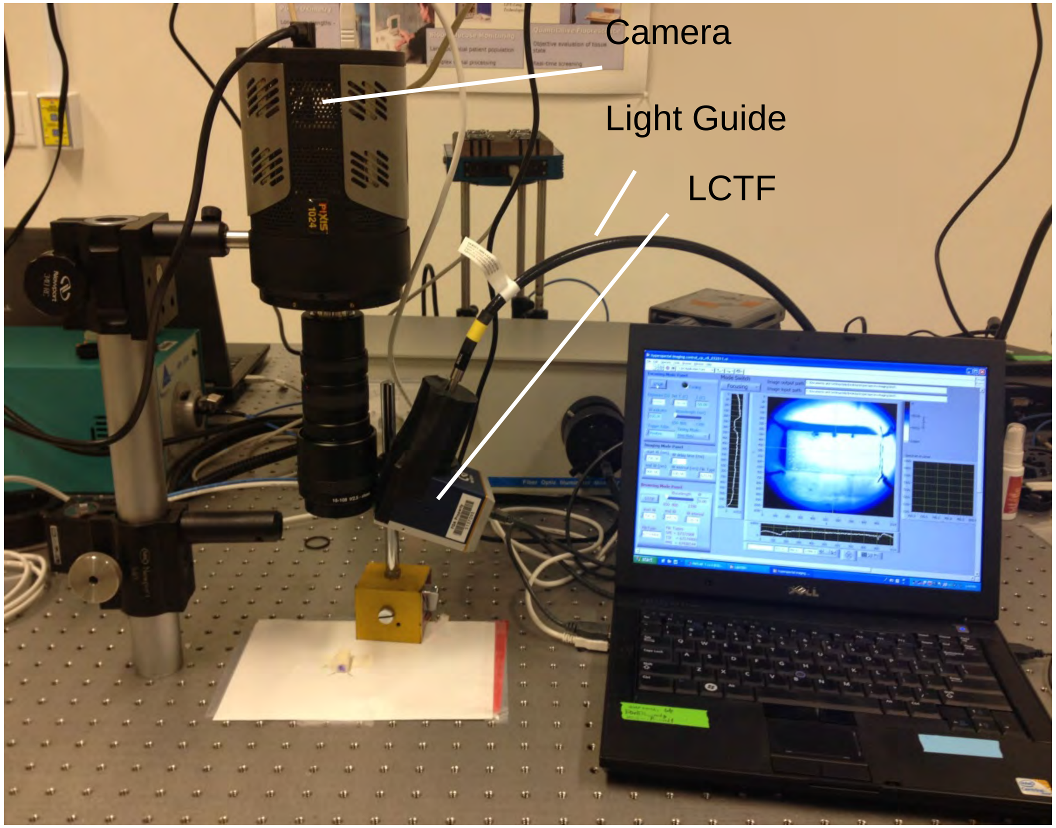
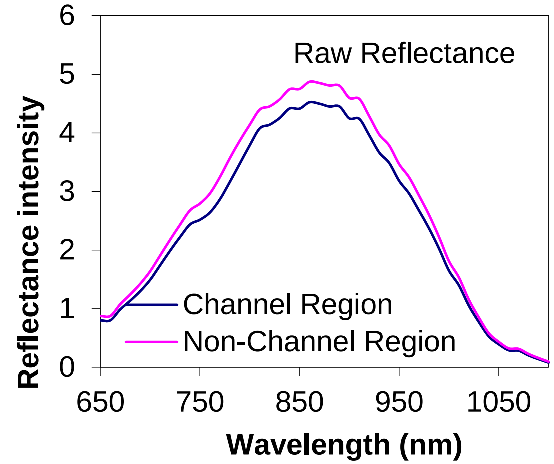
Hyperspectral Reflectance Imaging System at FDA





- Light Source: 100W Quartz Tungsten-Halogen fiber-optic light source (Oriel Instruments)
- Light Guide: Liquid light guide, 5 mm diameter.
- Collimating Probe: Beam size 22-25 mm

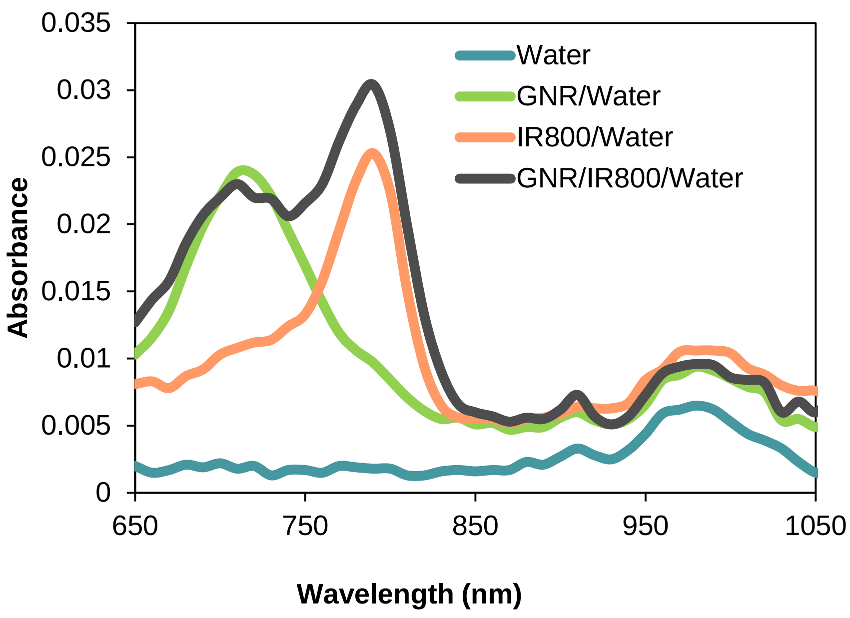
- Liquid Crystal Tunable filter (LCTF): Near infrared range (650-1100 nm), bandwidths of 7-10 nm (Varispec, CRI, Inc.)
- Camera: High sensitivity visible-NIR CCD camera (Princeton Instruments) with a Macro Video Zoom Lens (18-108 f/2.5, Edmund Optics)
- Computer with LabView software interface

Spectral Unmixing Algorithm

Absorbance was calculated according to Beers Law:

$$A(\lambda) = -\log [\, I(\lambda) / I^0(\lambda) \,]$$

Where I is the measured reflectance at channel region, and I^0 is the reflectance at non-channel region.



- Total absorbance at each wavelength is a linear sum of the absorption by each components.

- When the components of the system and their extinction coefficients are known, the amount of each components can be solved from the measured absorbance using **Non negative linear least square fitting**

$$\min_x \|C \cdot x - d\|_2^2, \text{ where } x \geq 0.$$

- **C** is a matrix of extinction coefficients for each component
- **x** is the abundance of each component to be solved
- **d** is measured absorbance for each pixel.

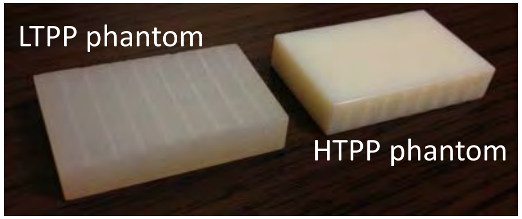
HRI System Characterization:

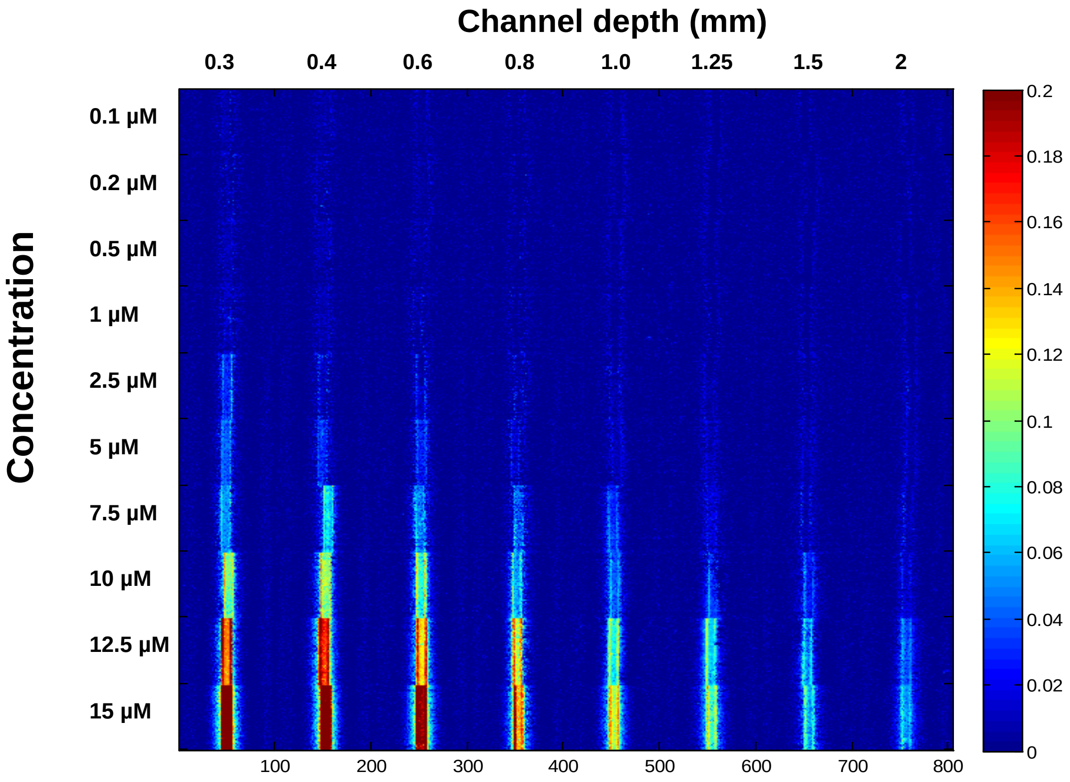
Detectability as a function of *depth* and *dye concentration*

In 3D printed HTPP phantom

With IR800 (Peak=770 nm), where phantom μs'=1.1 /mm

Composite false color map of multi-depth phantom images



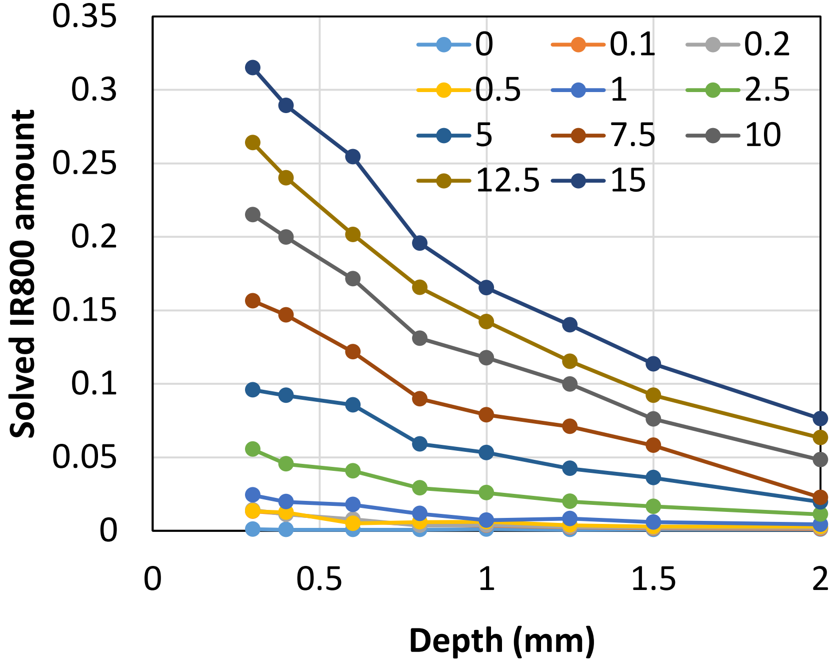


- *Each row derived from an HRI data volume (phantom with all channels at same concentration)*
- *Color shows solved IR800 abundance*

HRI System Characterization:

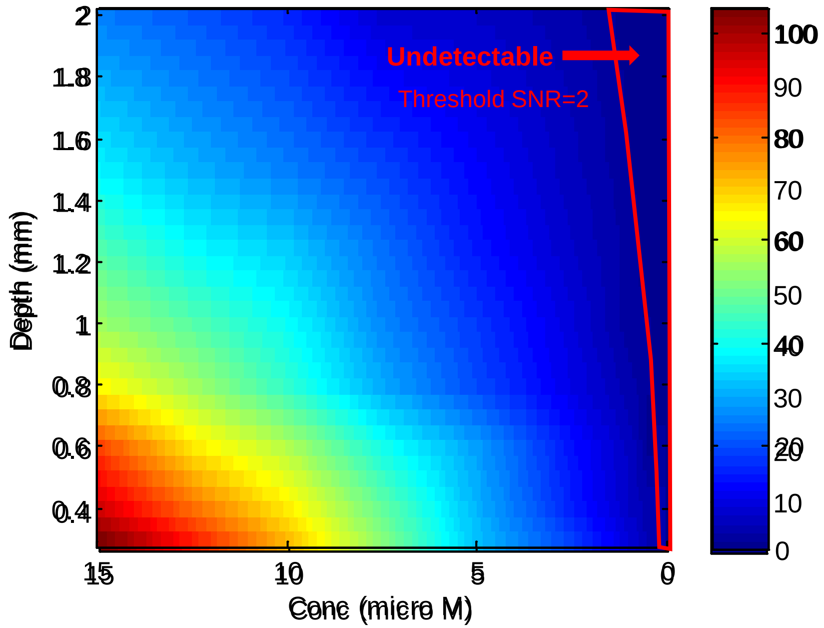
Detectability as a function of *depth* and *dye concentration*

In 3D printed HTPP phantom, channel size 0.5 mm



Contrast map

SNR: Signal/STD of non-channel region



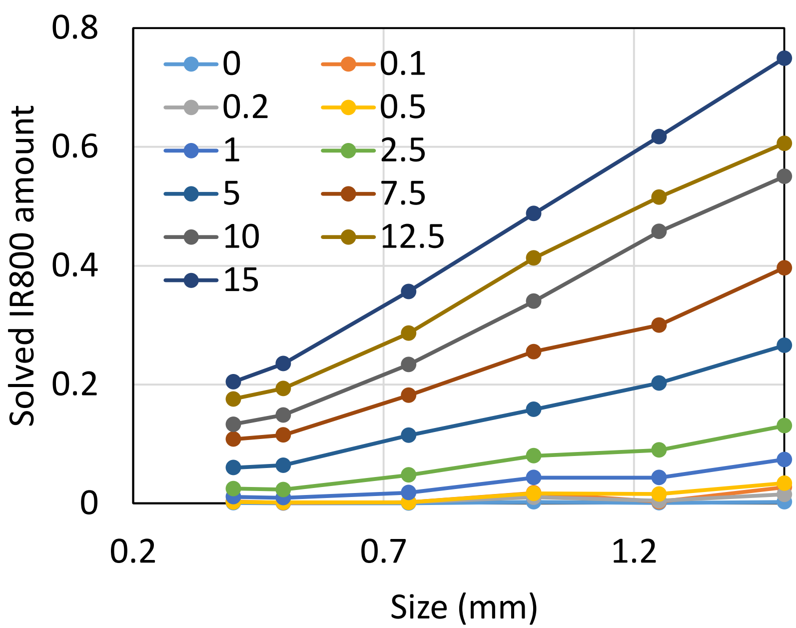
- With threshold is SNR=2, the minimum detectable concentrations are:
  0.5 μM for 1 mm deep channel;
  1.4 μM for 2 mm deep channel;

- All channels are detectable in at least part of the tested concentration range
- Deeper channels are needed to identify non-detectable depth

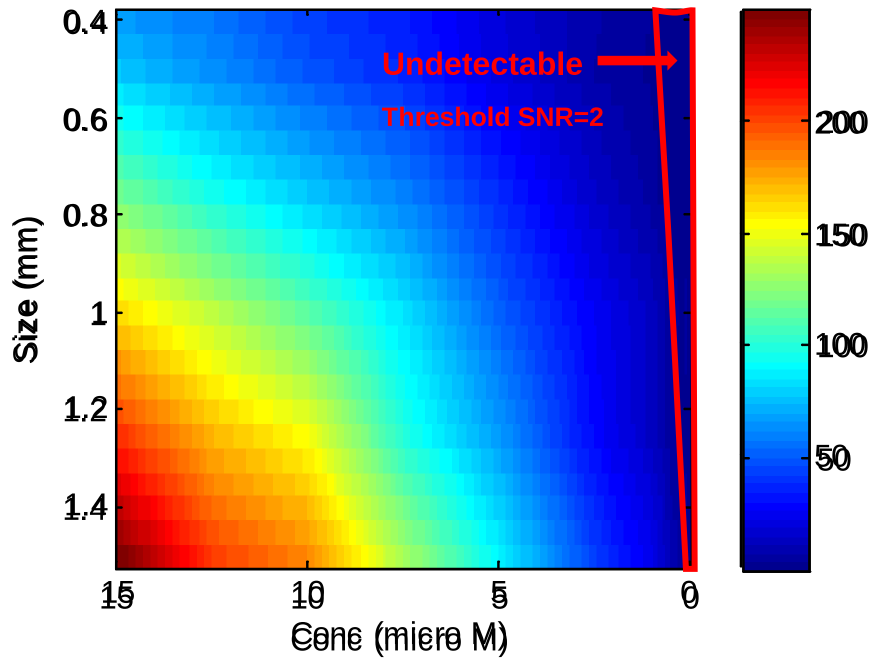
HRI System Characterization:

Detectability as a function of *size* and *dye concentration*

In 3D printed HTPP phantom, channel depth 0.5 mm



Contrast-Detail Map



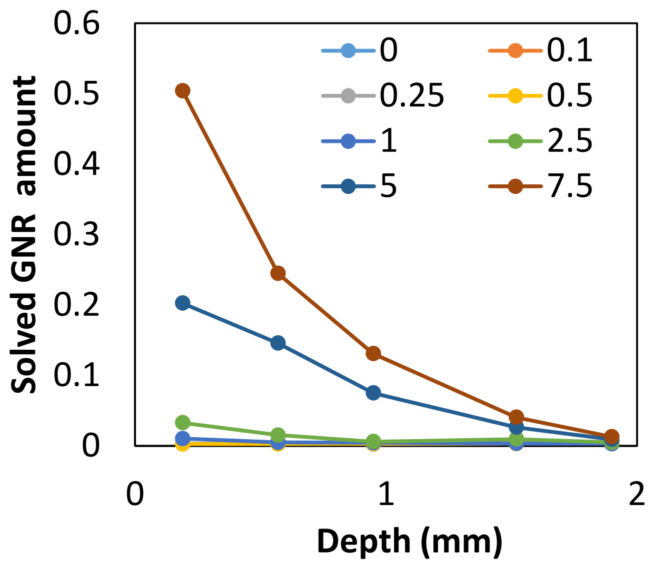
- With threshold SNR=2, the minimum detectable concentration is 0.9 μM for 0.4 mm channel
- Smaller channels are needed to identify minimum detectable size

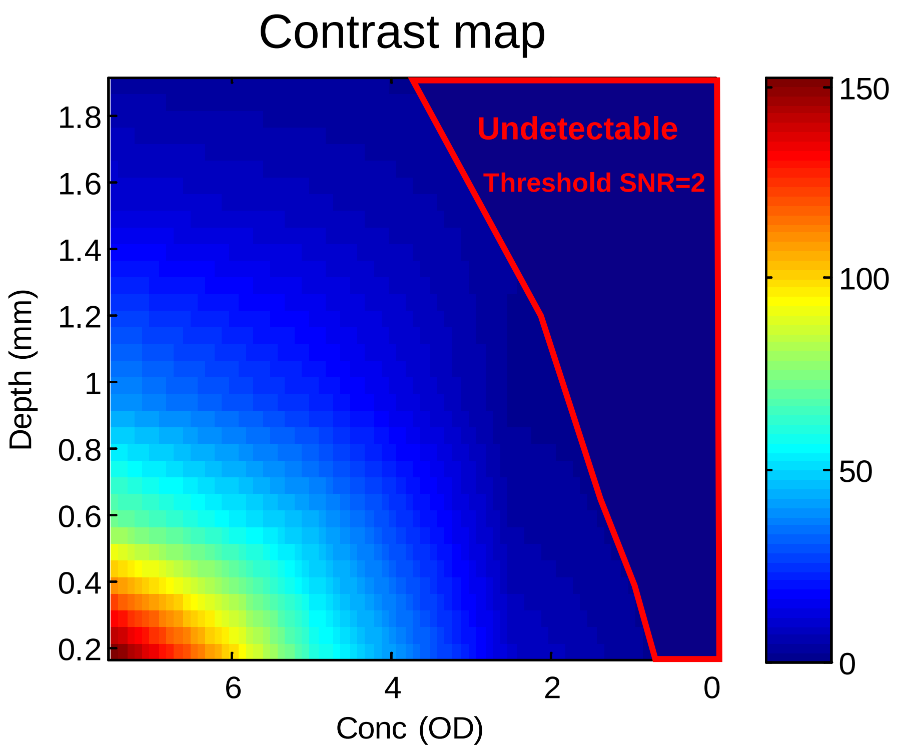
HRI System Characterization:

Detectability as a function of *depth* and *dye concentration*

In PDMS (w/ 2.1% $BaSO_4$) phantom, square channels, 0.3 x 0.3 mm

With Gold nanorods (Peak=720 nm), where phantom μs'=1.5 /mm





- For 1.8 mm channel, the minimum detectable conc. is 3.5 OD

Conclusions

- Well-designed turbid phantoms with sub-surface channels should be useful for determining contrast-detail relationship, maximum penetration depth, and minimum detectable dye concentration for HRI systems.
- More phantoms needed to determine maximum detection depth and minimum detection size for all dye concentrations.
- 3D-printing holds promise as a simple, fast, and flexible way of fabricating biophotonic phantoms with sub-surface features
    - ✓Materials with biologically relevant $\boldsymbol{\mu_s}'$ and low $\boldsymbol{\mu_a}$ available
- PDMS molding provides phantoms with smooth texture and tunable optical properties

Future Work

- ➢*In vitro* tissue validation
- Improve realism of phantoms
    - 3D printed phantoms
        - Adjust absorption and scattering
        - Print realistic structures (vessel-image-based)
    - PDMS: Add absorber to matrix

Acknowledgements

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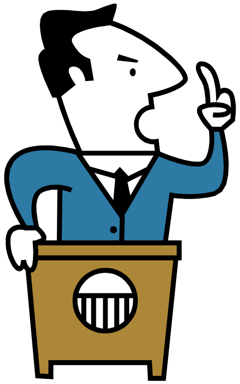
- University of Maryland Center for Excellence in Regulatory Science and Innovation (CERSI)

•Dr. Maureen Dreher for her help with micro-CT imaging



Thank you!

Comments and questions?

Composite false color map of multi-depth phantom images