Imaging oxygenation by near-infrared optical tomography based on SPAD image sensors

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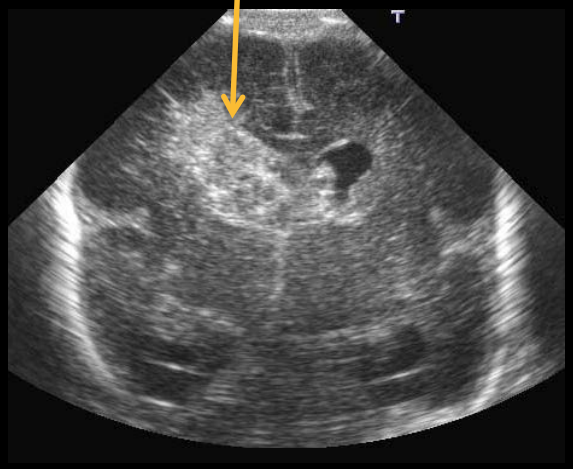
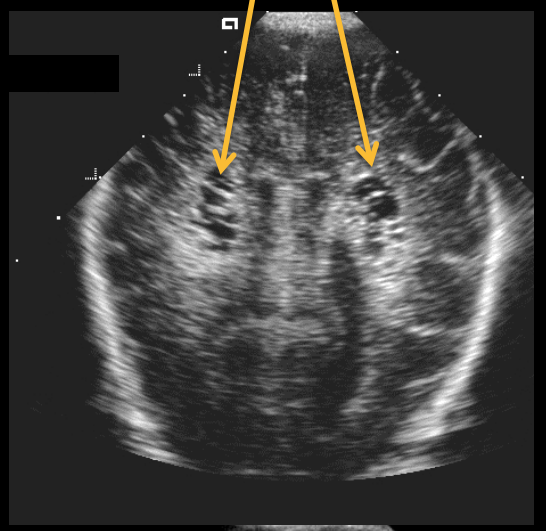
Brain lesions in preterm infants

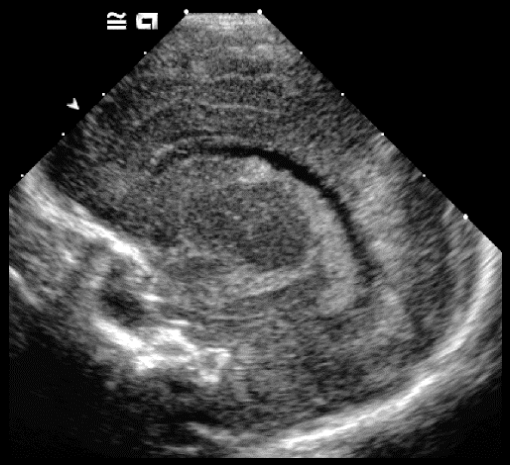
Healthy

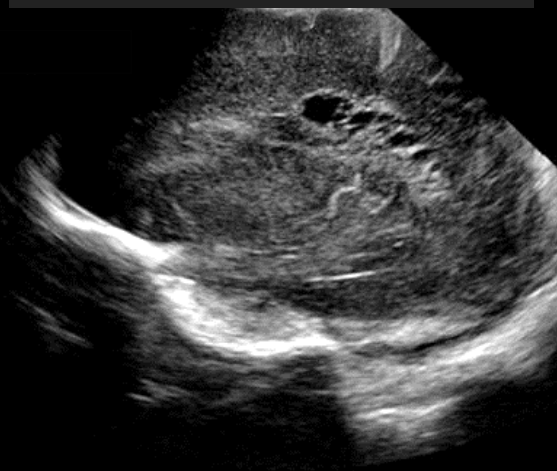
Bleeding due to hypoxia

Cysts due to hypoxia/ischemia









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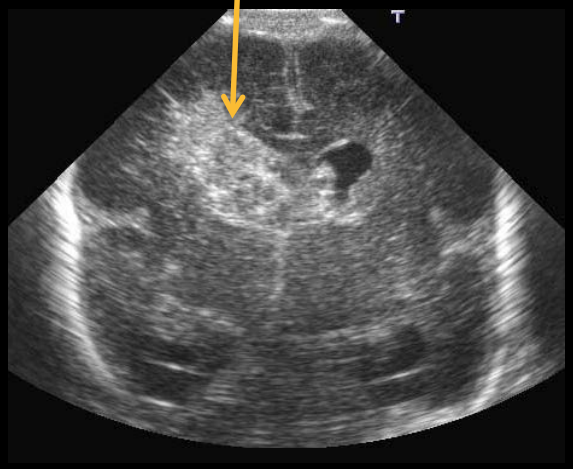

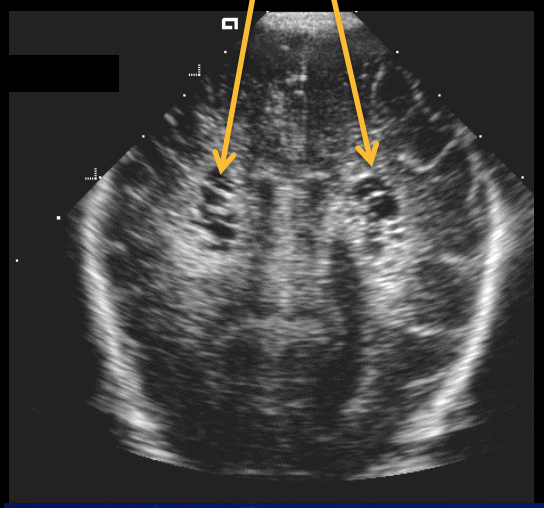

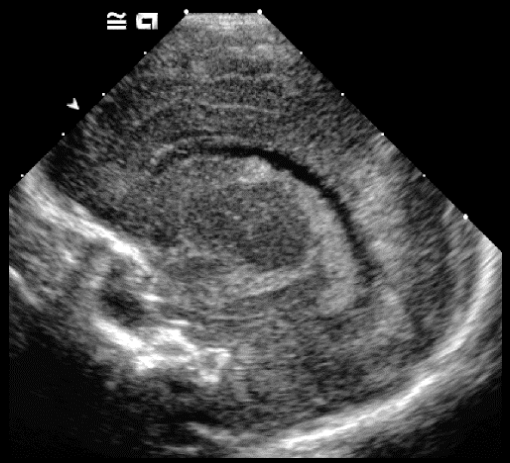

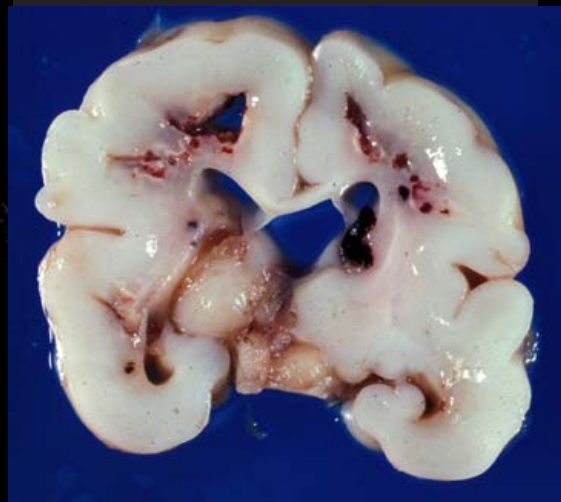

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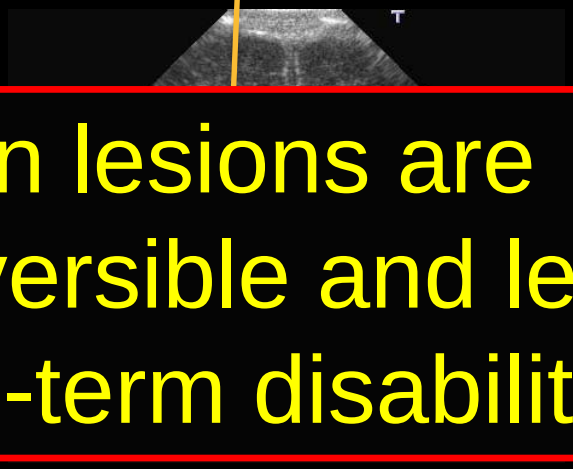
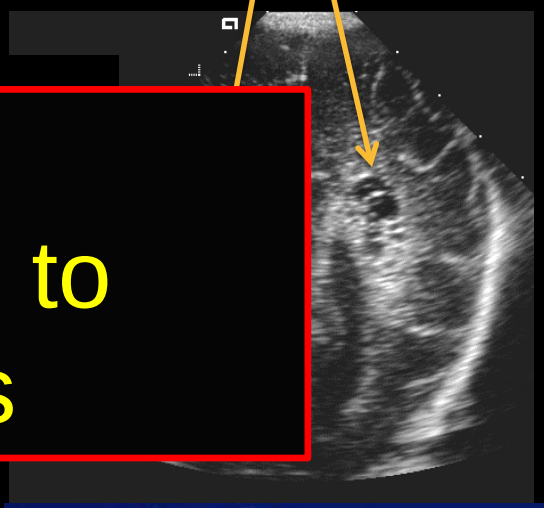
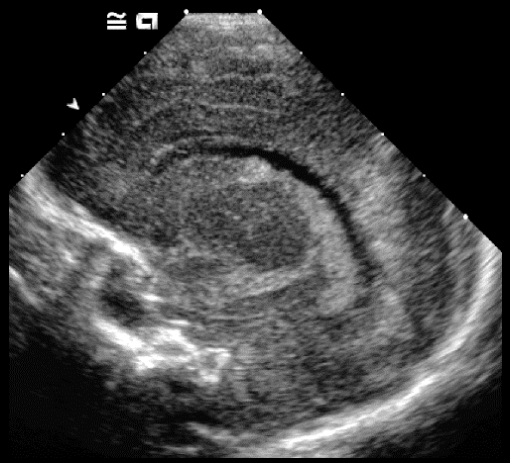
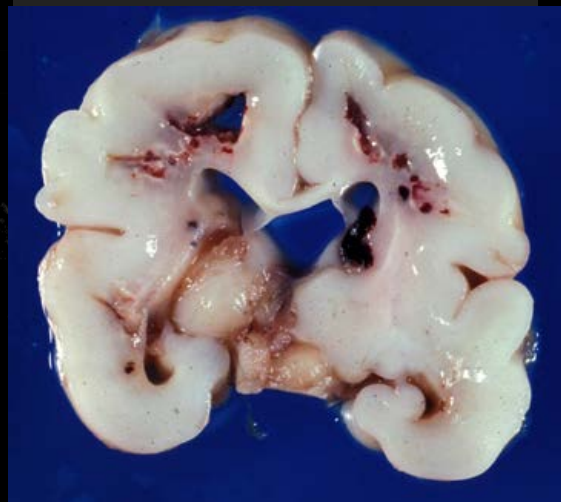




Brain lesions are irreversible and lead to long-term disabilities





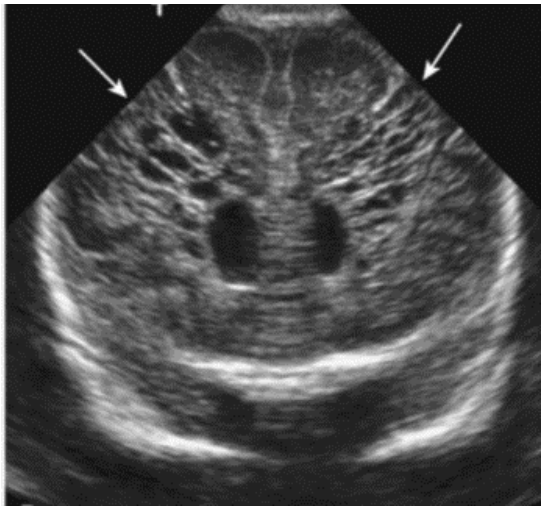
Clinical situation today

1st days of life

hypoxia invisible

3 weeks

22nd day of life

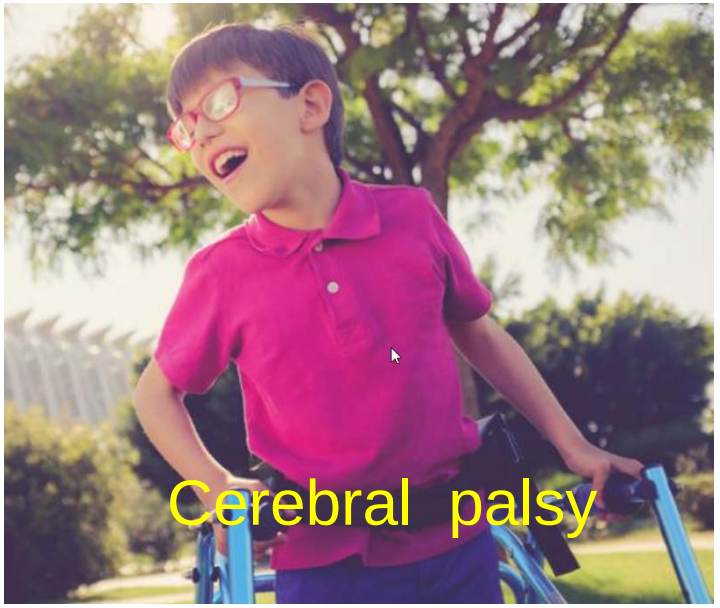


cysts due to hypoxia at ≤72h

- Brain damage occurs during first 72h of life due to **hypoxia/ischemia**
- Hypoxia cannot be measured → not treated
- White matter injury visible only once tissue decays (day 21) → too late
- Irreversible brain damage → life-long disability
- **If hypoxia was detected, → prevention possible**

High clinical need to prevent brain lesions

- 900 preterm infants / year in CH (23 - 32 weeks gestation)
- 15 millions worldwide
- 80% survivors
- 50% significant cognitive delay
- 40% behavioural problems
- 25% cerebral palsy



➡ Lifelong and severe socio-economical burden

How to prevent life-long disability:

- Needed:
  - Quantitative oxygenation imaging
  - At bedside

Modality	Oxygenation	Quantitative	Non-ionizing	Bed-side	Continuous	
CT	No	-	No	No	No	risky transport
PET	No	-	No	No	No	
MRI	No	-	Yes	No	No	
EEG	No	-	Yes	Yes	Yes	routine techniques
Ultrasound	No	-	Yes	Yes	(Yes)	
Optoacoustic	Yes	No	Yes	Yes	(Yes)	research
NIROT	Yes	Yes	Yes	Yes	Yes	**choice**

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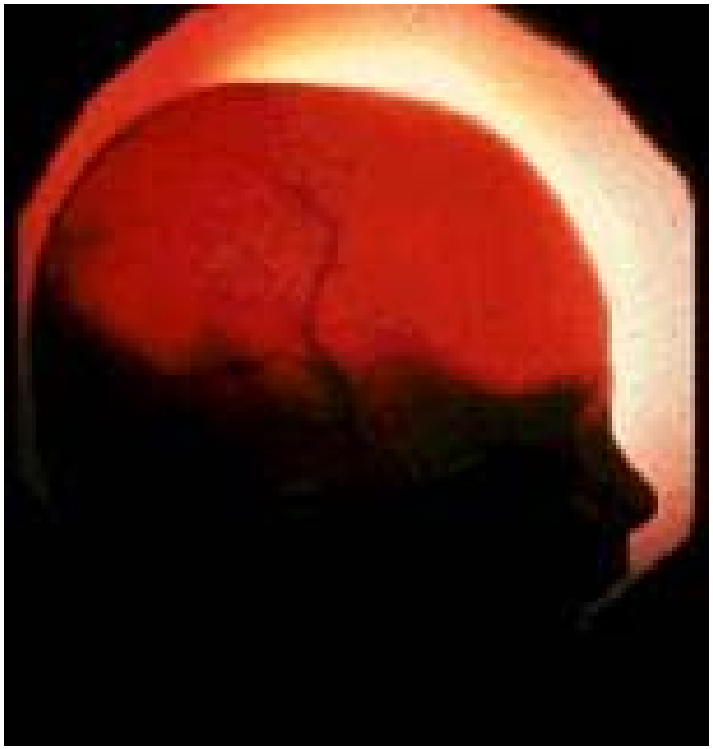
NIRS and NIROT

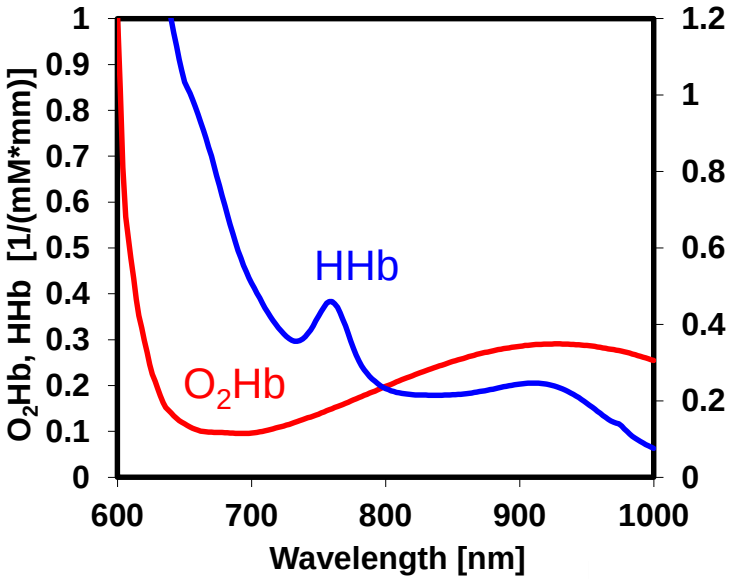


Transillumination of whole head

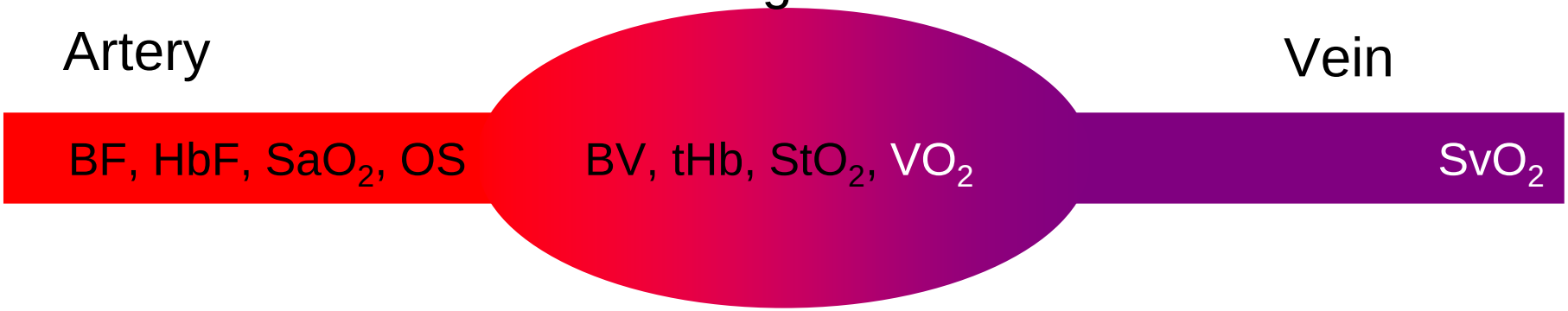
Contrast: Oxy-, deoxyhemoglobin

Oxygenation $StO_2 = O_2Hb / (O_2Hb + HHb)$

Quantitative, non-invasive, harmless, frequently repeatable



Oxygenation

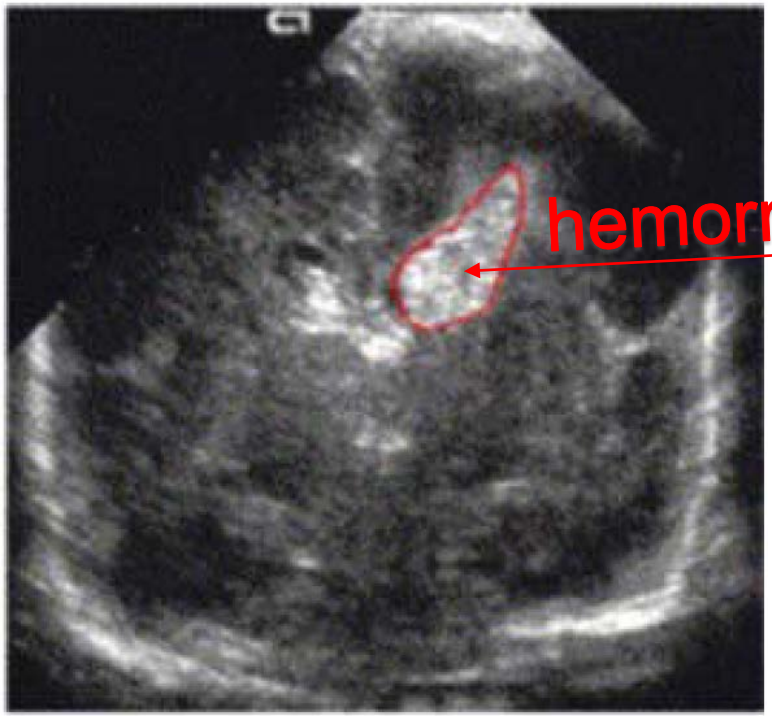


Blood volume BV in [ml/100g] or total hemoglobin concentration [tHb µmol/l]
Blood flow BF in ml/100g/min or hemoglobin flow HbF [µmol/(l*min)]
Arterial, venous or tissue oxygen saturation SaO_2, SvO_2, StO_2 [%]
O_2 delivery DO_2 [µmol/(l*min)] $DO_2 = HbF * SaO_2$
O_2 consumption VO_2 [µmol/(l*min)] $VO_2 = HbF * (SaO_2 - SvO_2)$
Tissue oxygen saturation StO_2 [%]= 0.25 * SaO_2 + 0.75 * SvO_2 ~ SvO_2

$$\mathbf{StO_2 = SaO_2 - 0.75 * VO_2 / HbF}$$

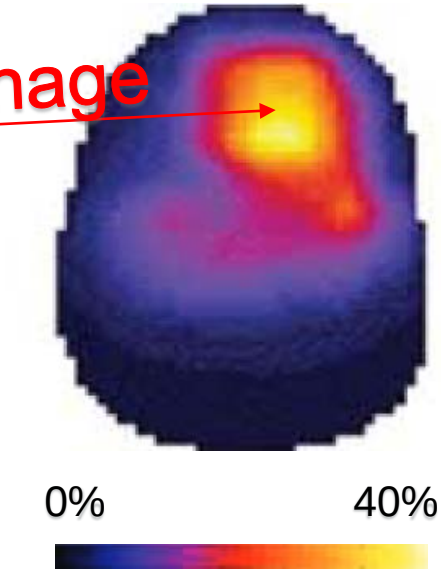
$$\mathbf{tHb = a * HbF^{\beta} \text{ where } 0.28<\beta<0.38}$$

State of the art in NIROT



Blood volume

StO_2



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State of the art in NIROT

- Spatial resolution ~1cm
- ≤32 PMT detectors
- Bulky systems
- NOT UPSCALABLE

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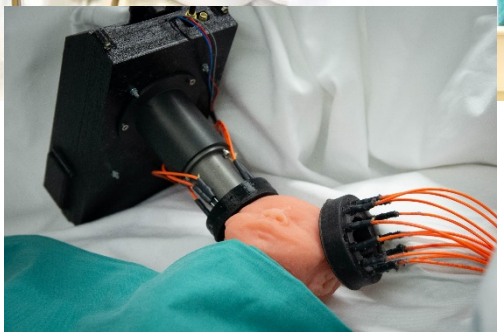
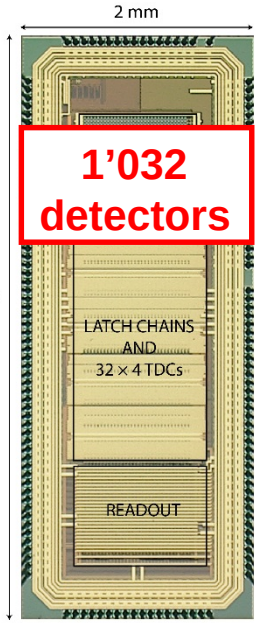
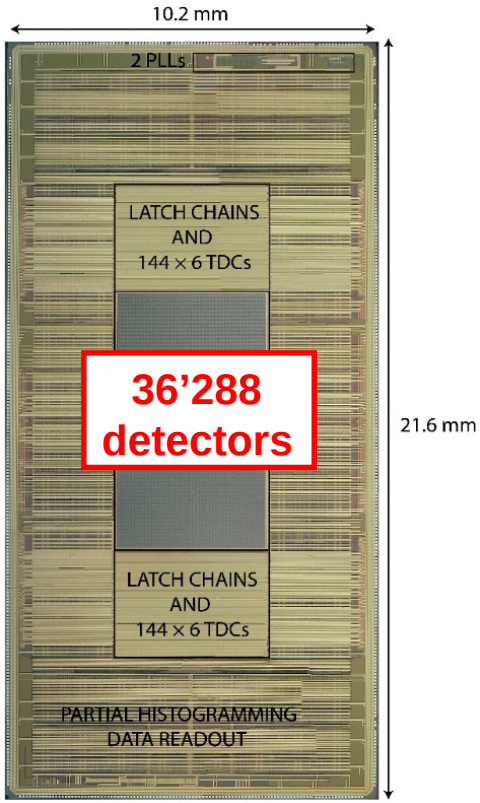
Our approach: NIROT Pioneer





Piccolo
32 × 32
SPAD image sensor
128 timestamps per frame)



Ocelot
144 × 252
SPAD image sensor
(1726 timestamps per frame)

- **Single-photon SPAD time-resolved picosecond camera**
- **~1000 x more detectors than state of art**

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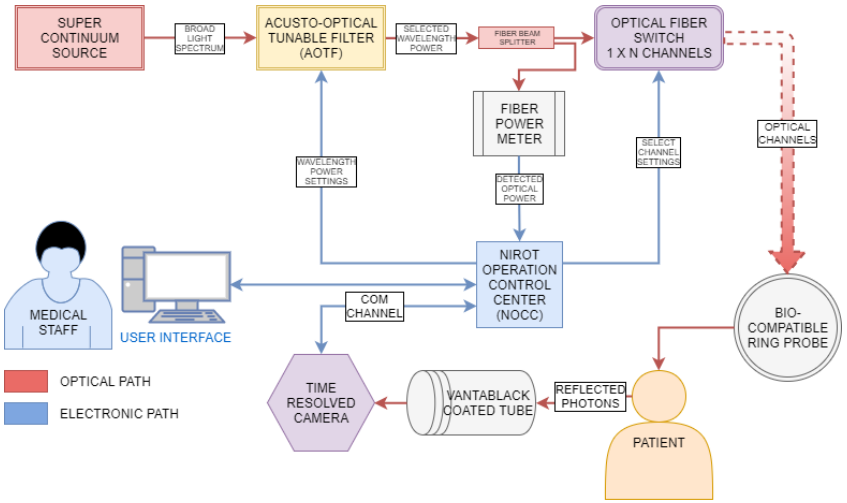
Ocelot and Piccolo

	Ocelot	Piccolo
Array size	144 X 252	32 X 32
DCR Hz	60	141
Fill-factor %	28	28
Peak PDP (500nm) %	40	40
PDP NIR (800nm) %	12	12
Microlenses CF	2.97	2.97
PDE (800nm) %	10	10
Max. excess bias V	5.5	5.5
No. of TDCs	1728	128
TDC LSB ps	48.9 or 65.1	48.9
FWHM timing response (ps)	116	116
1/0 bandwidth Gbps	11.5 Gbps	5.12
Max. throughput Gphotons/s	6 Gphoton/s (includes compression)	0.224
Die area mm^2	10.3 mm x 21.6 mm	2.0 mm x 5.0mm

Schematic of the Pioneer system



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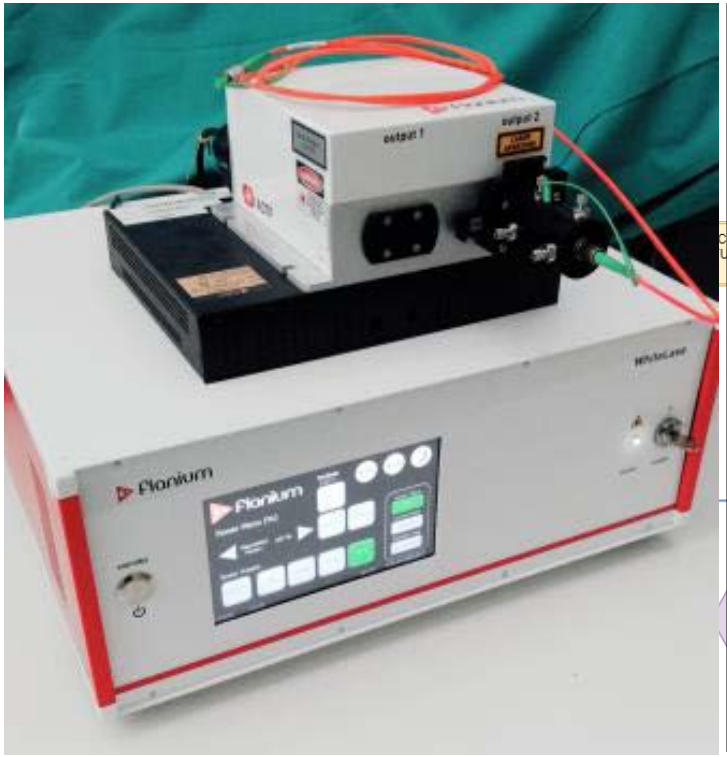
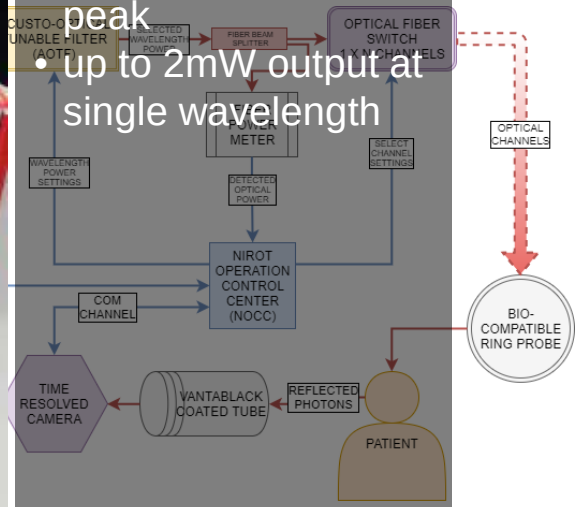


Fianium WL-450-8
- 8W total output
- 650-950nm range
- ~5-10nm FWHM peak
- up to 2mW output at single wavelength



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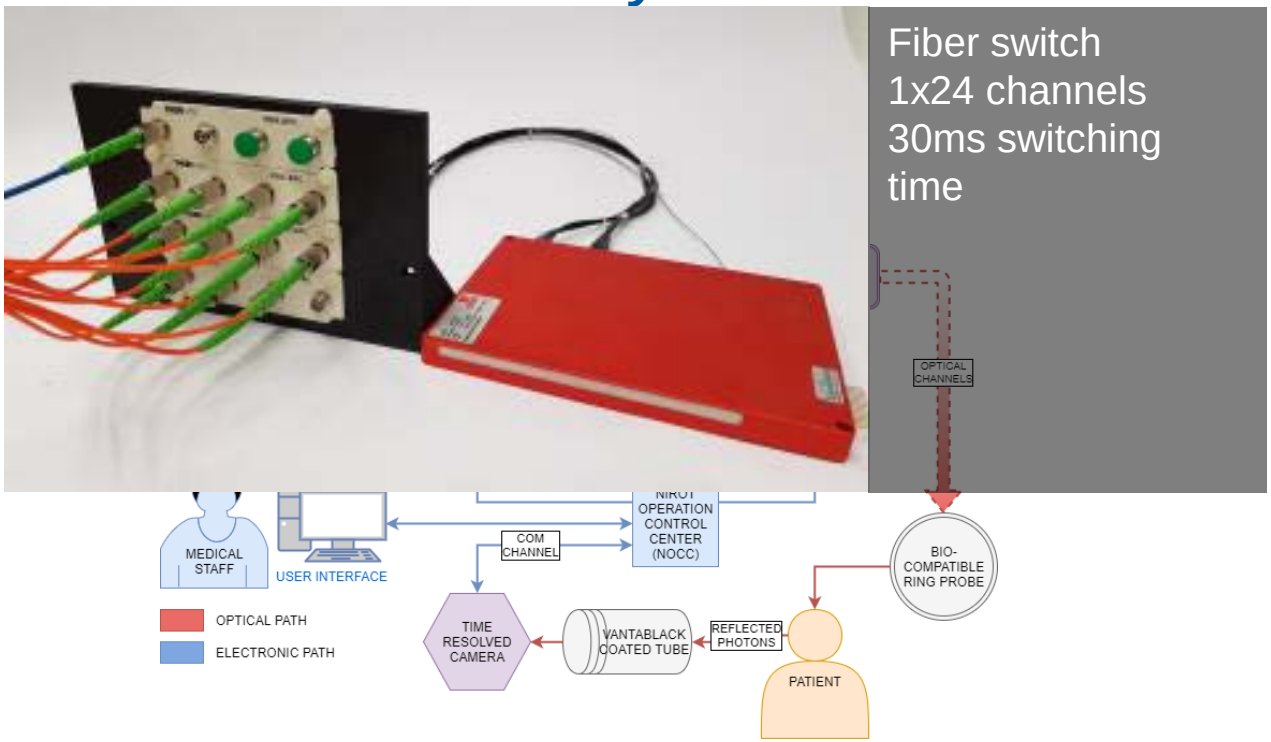
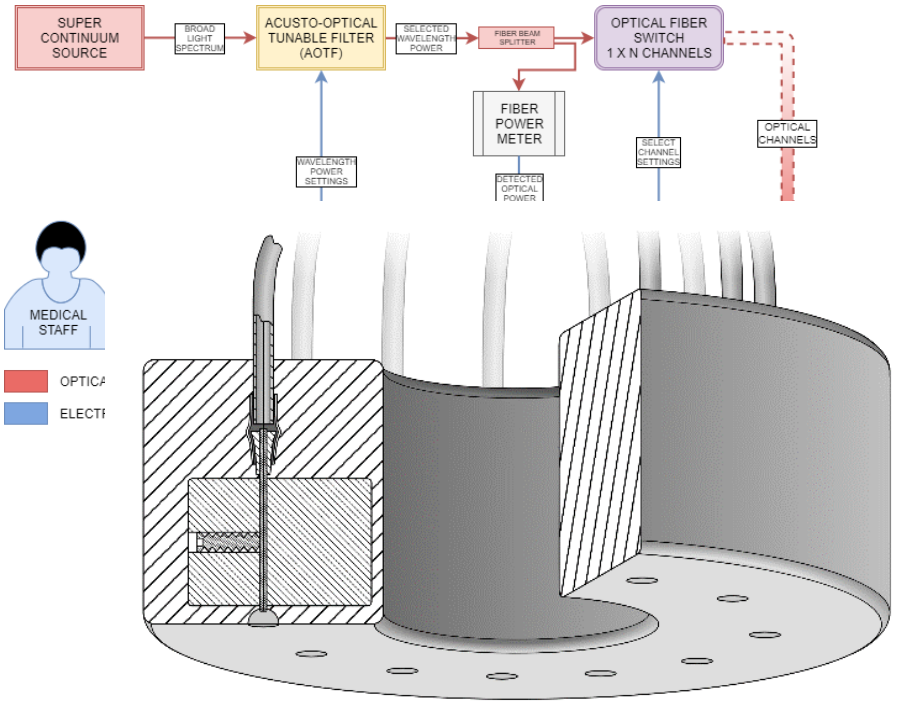


Schematic of the Pioneer system

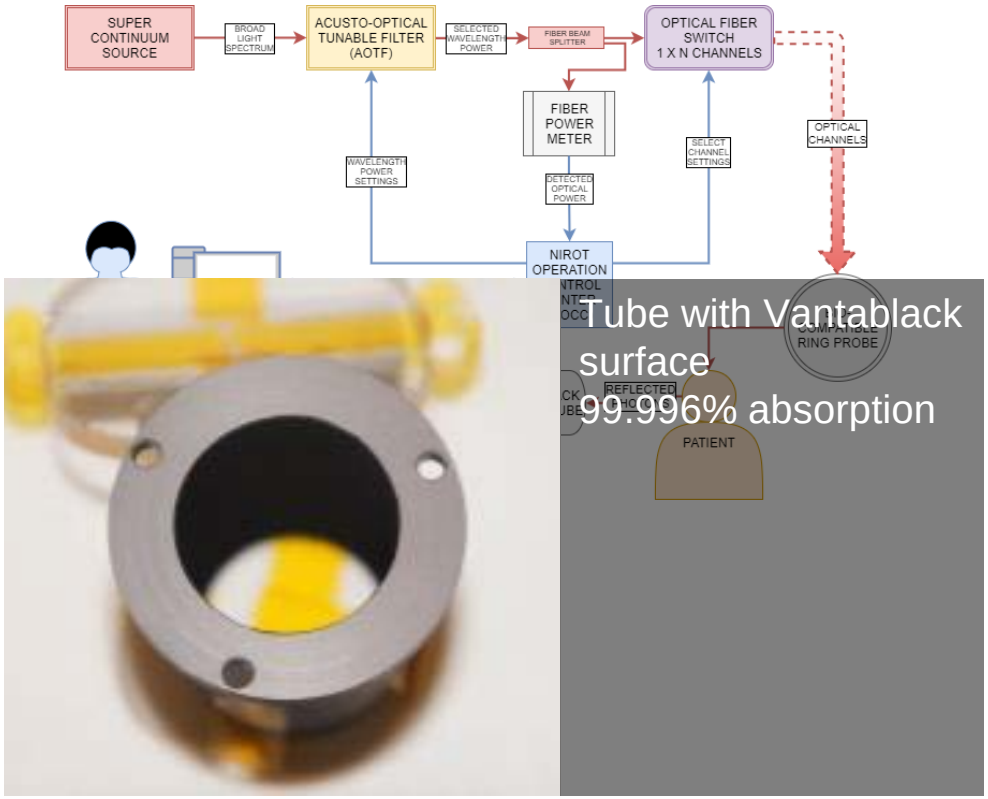
Y-fiber splitter with power meter
98/2 splitting ratio

Schematic of the Pioneer system



Source ring
- 11 optical sources
- biocompatible
- 25mm FoV

Schematic of the Pioneer system



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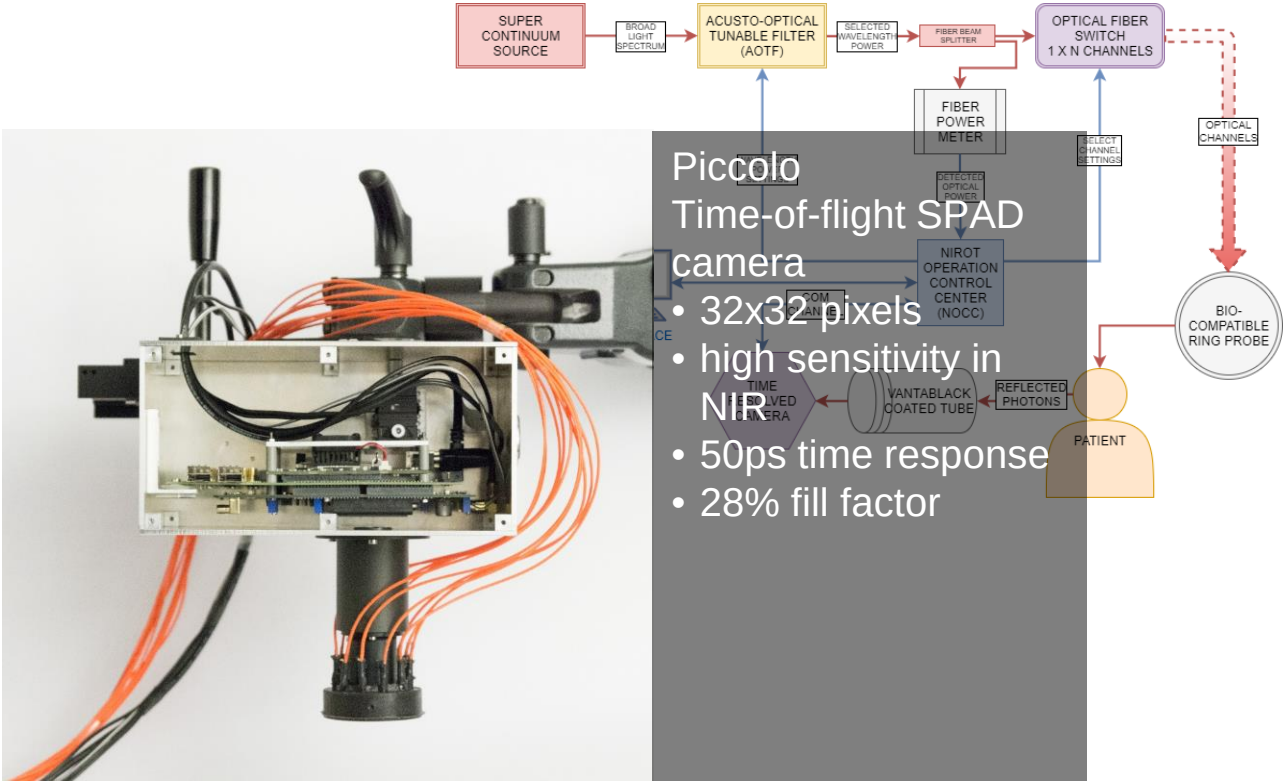
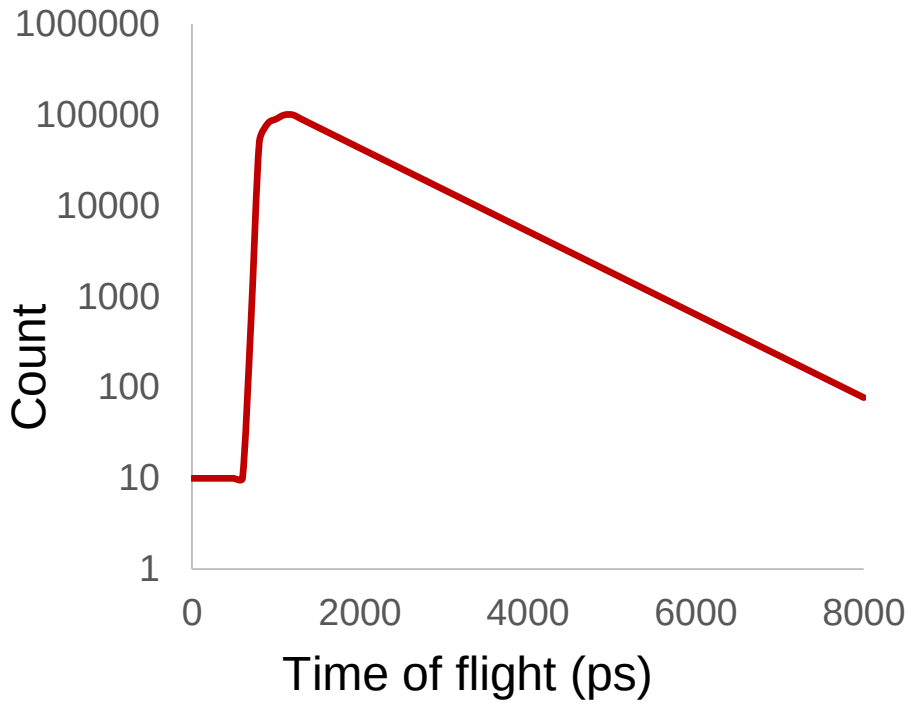
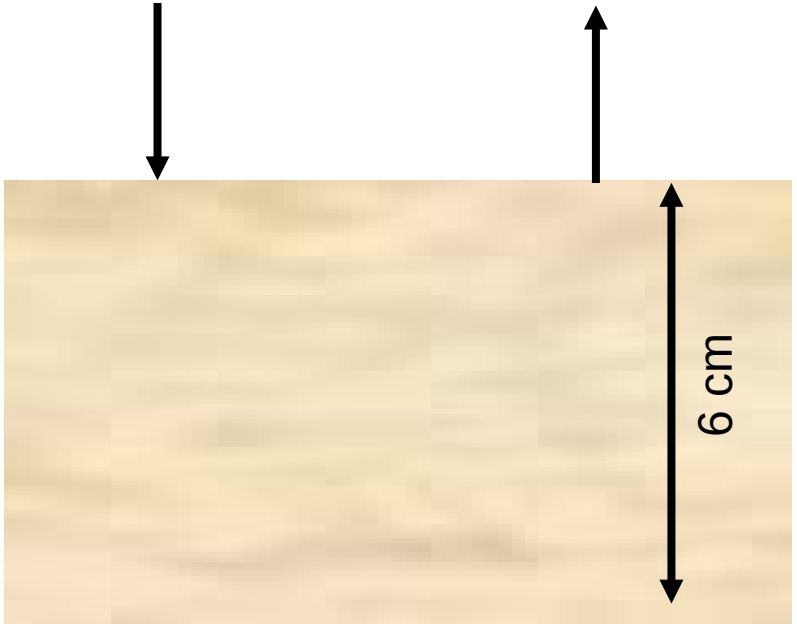


Picosecond timing resolution

- Depth reachable and clinical usefulness
  - 6cm for gated SPAD, ~zero distance





Tosi A et al. Opt Exp 2011;19:10735-46

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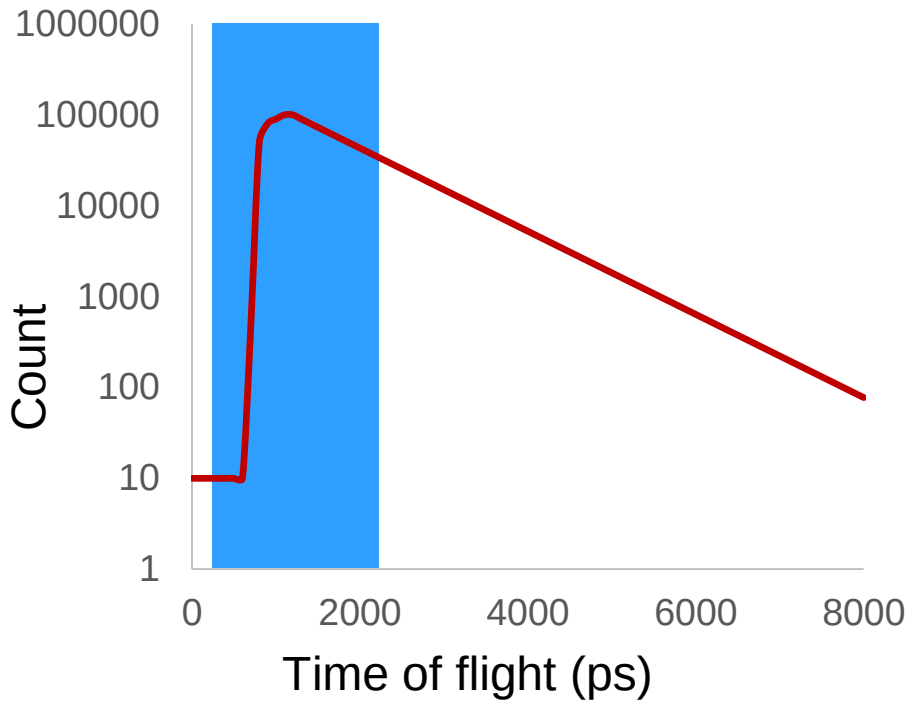

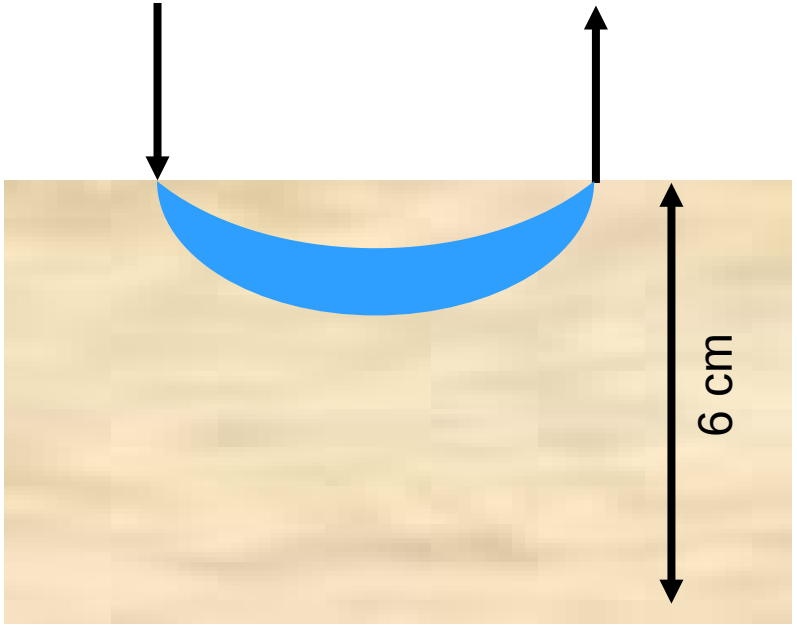

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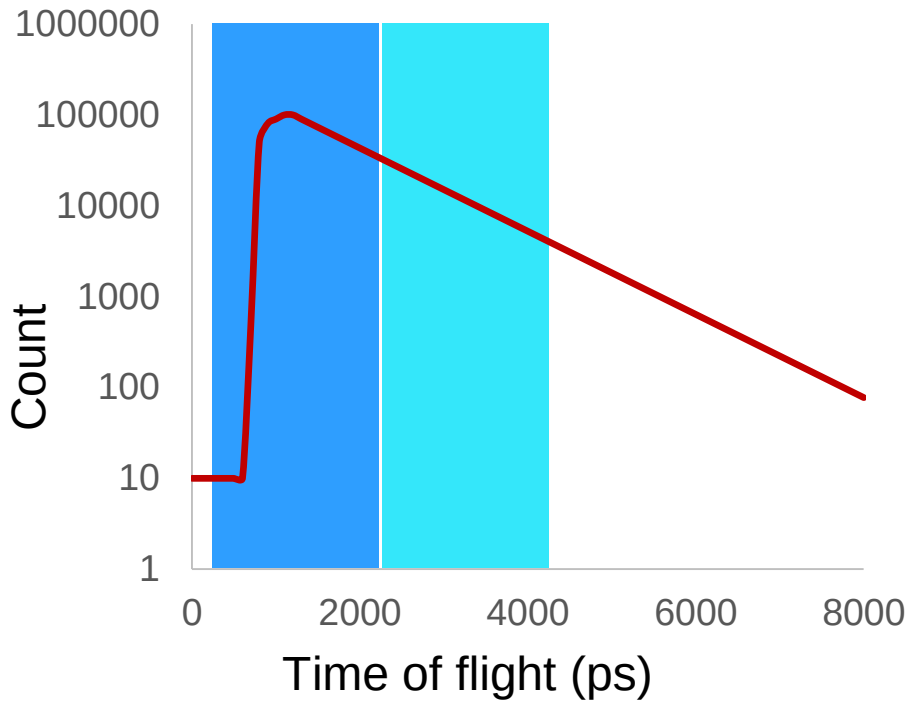

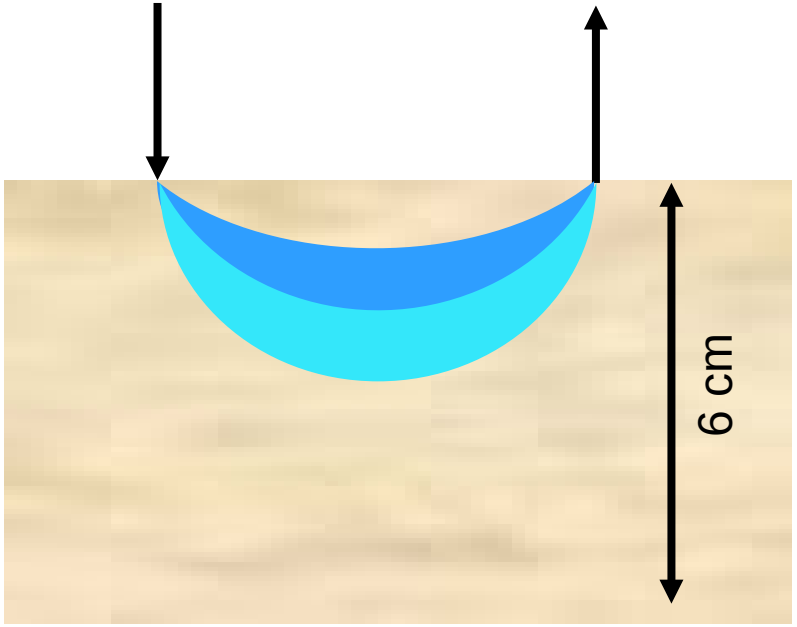

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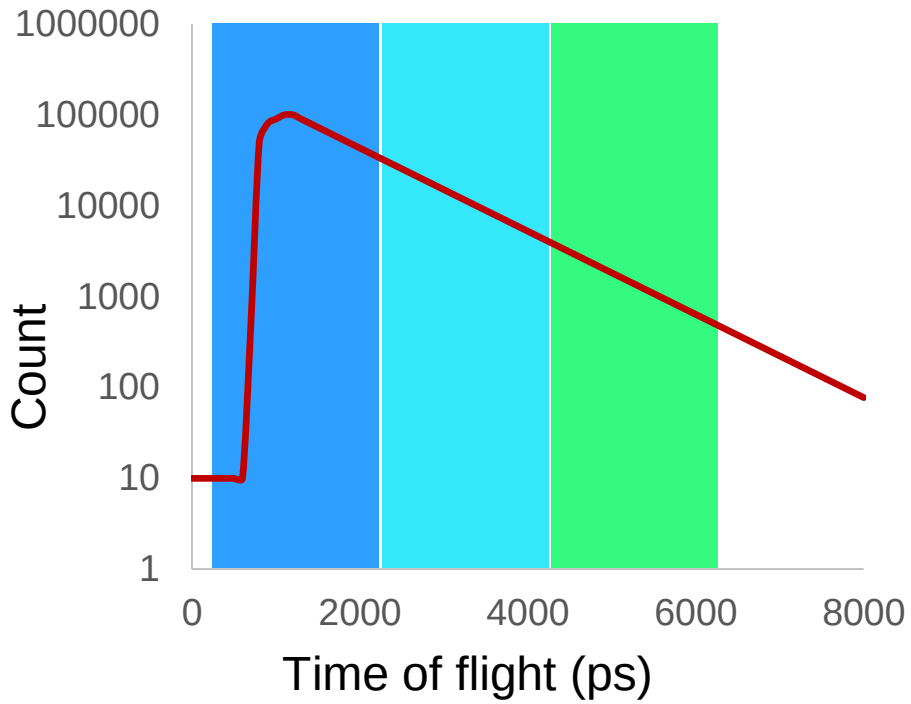

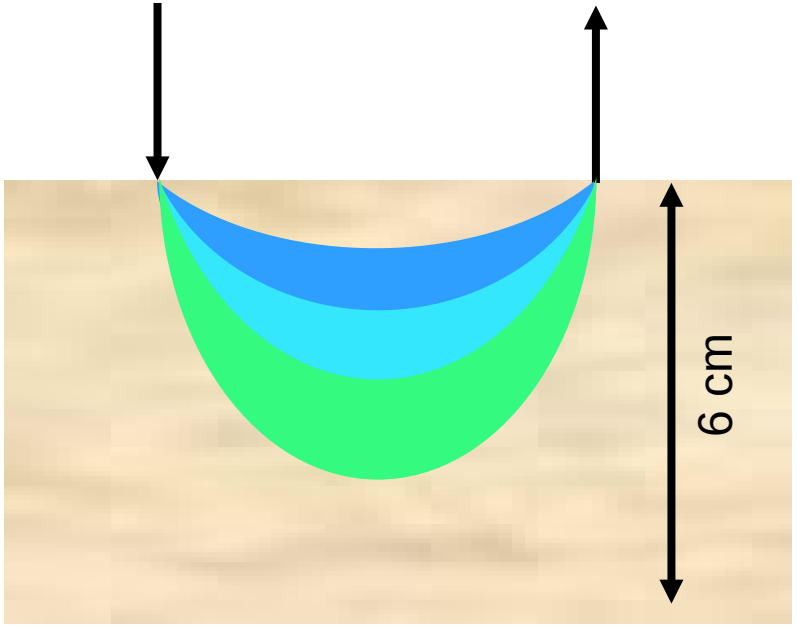

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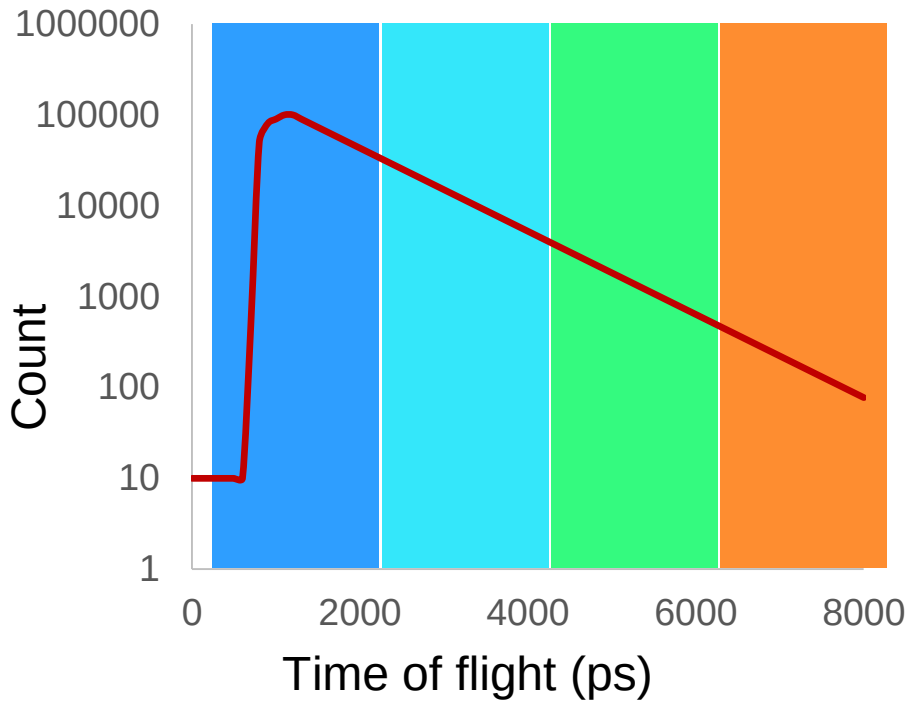

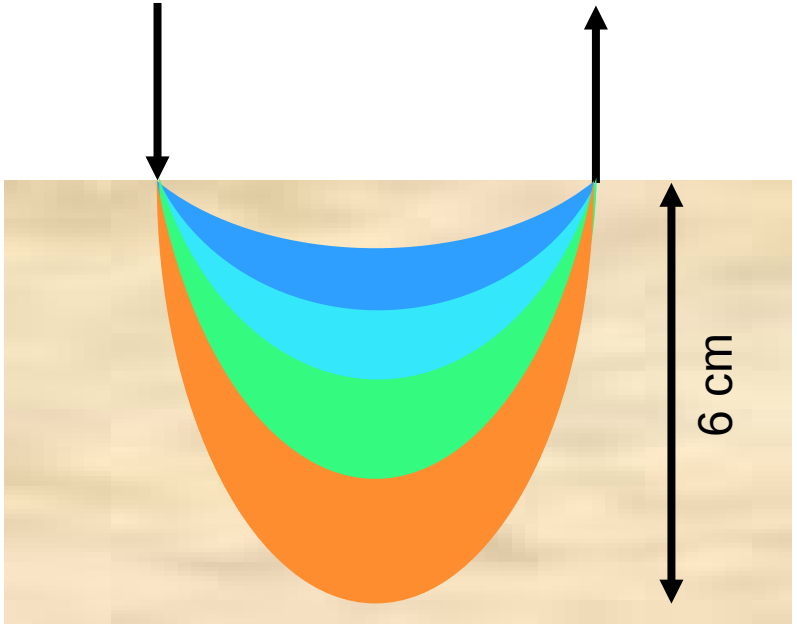

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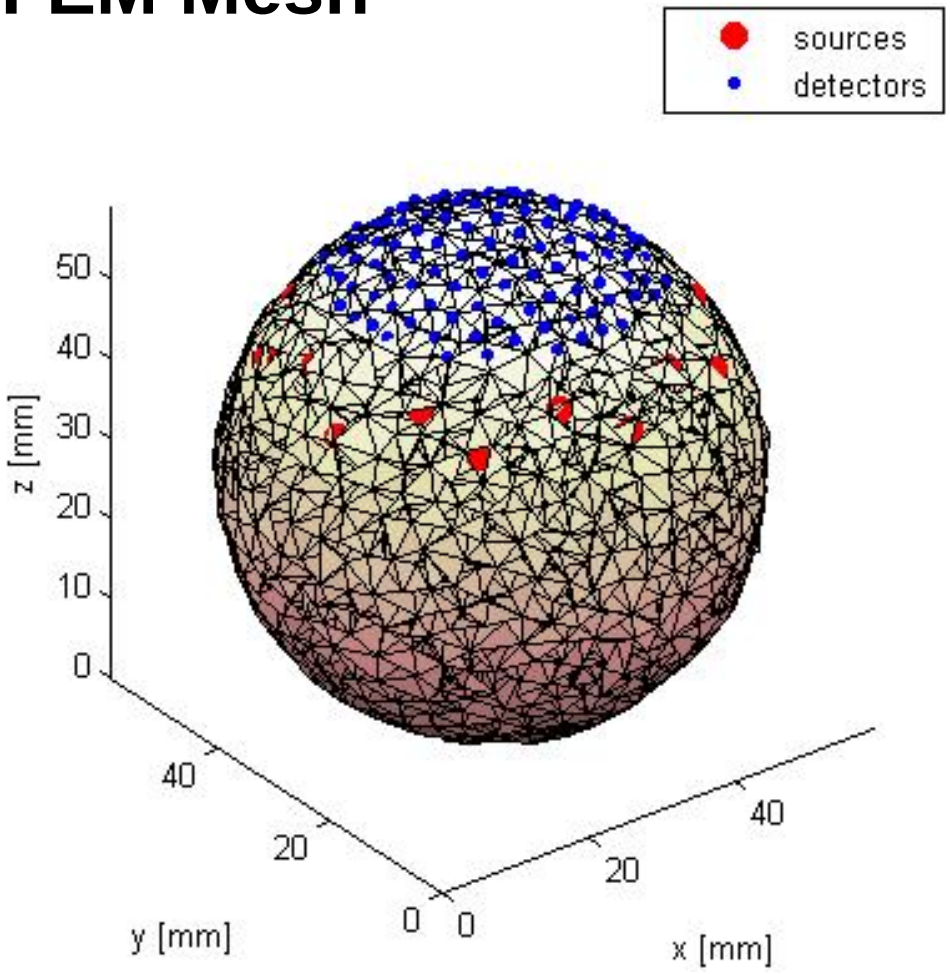
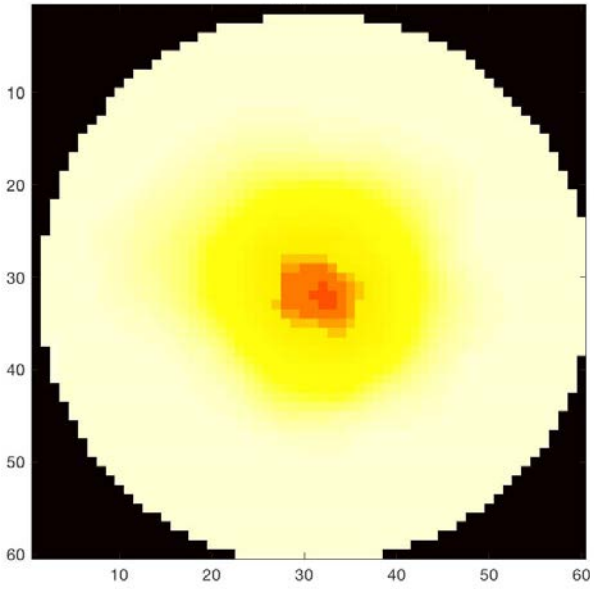
Simulation results

FEM Mesh



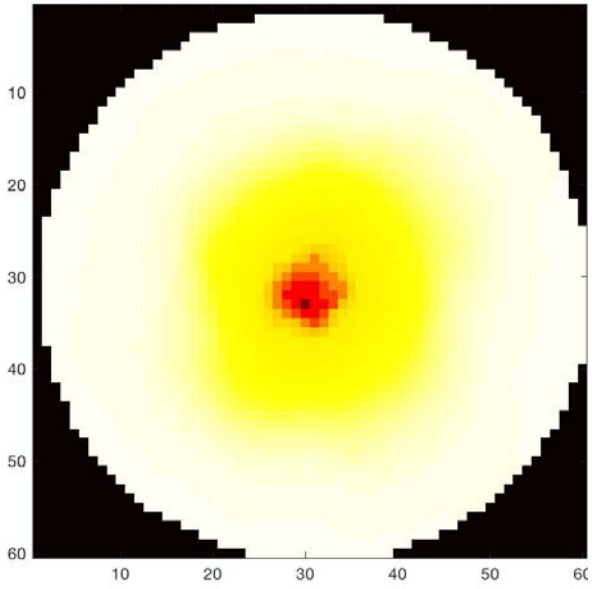
Simulation results

Ischemia 1.8mm Ø



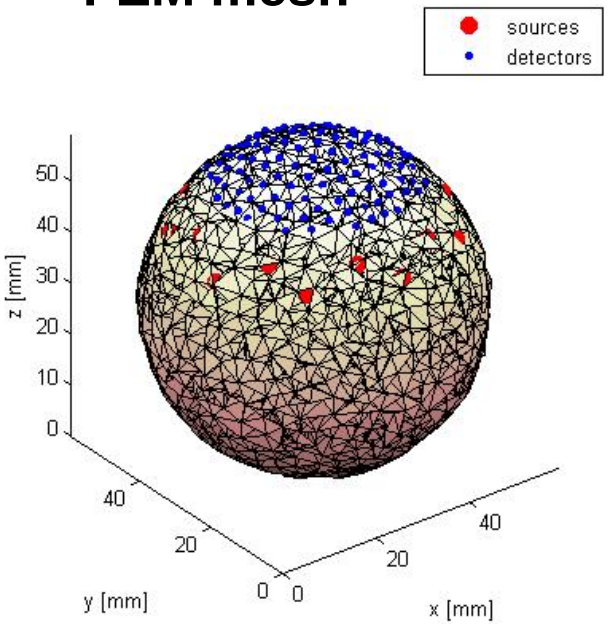
Contrast factor 250%

Bleeding 1.8mm Ø



Contrast factor 5000%

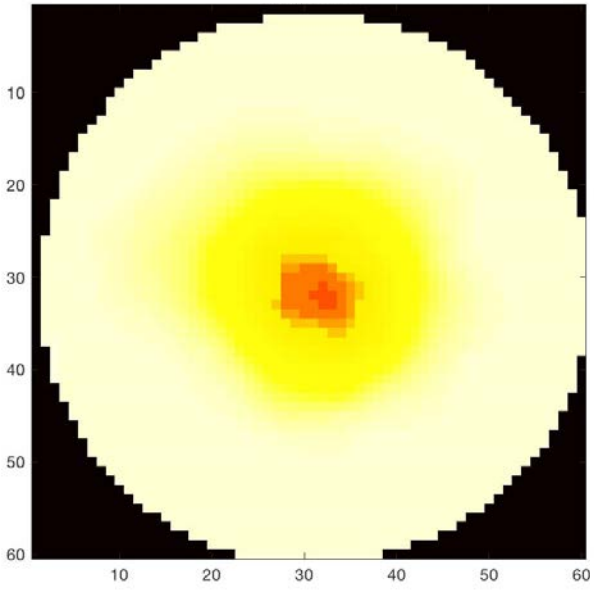
FEM mesh



Lesions of 1.8mm diameter detectable

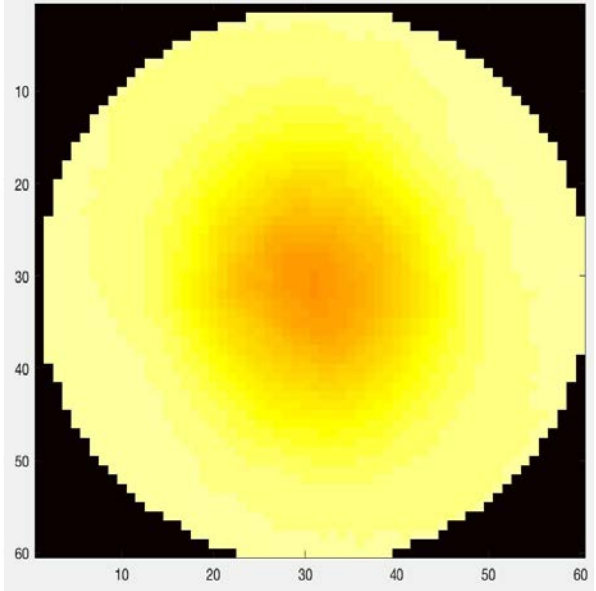
Simulation results

Ischemia 1.8mm Ø



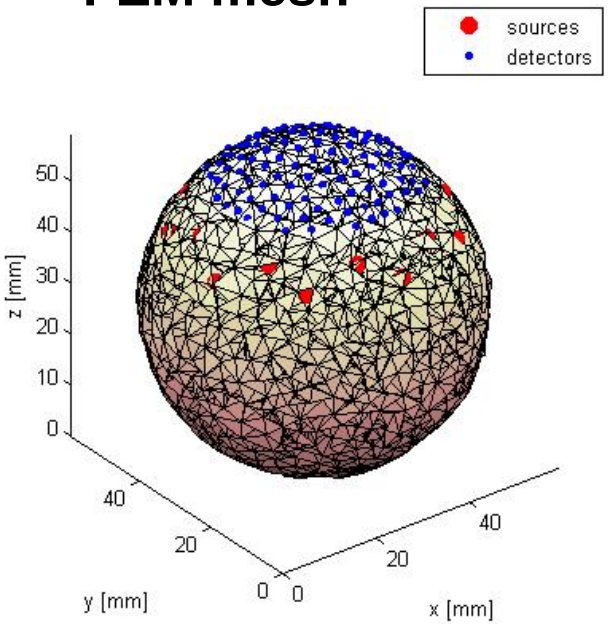
116 detectors

Ischemia 1.8mm Ø



32 detectors

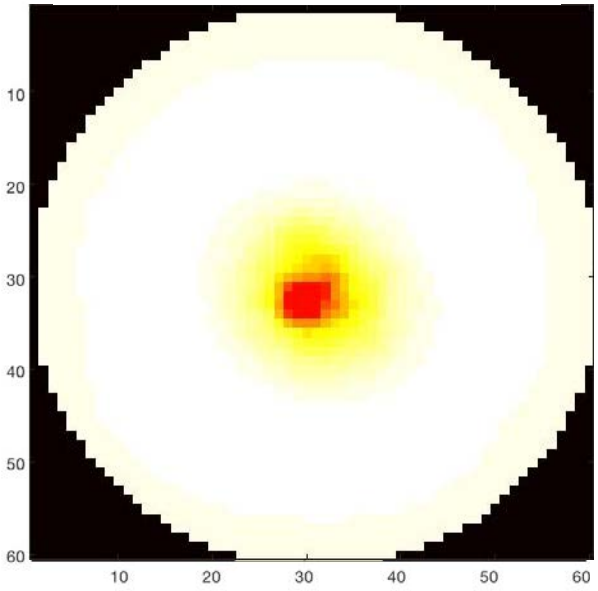
FEM mesh



Number of detectors increases the resolution

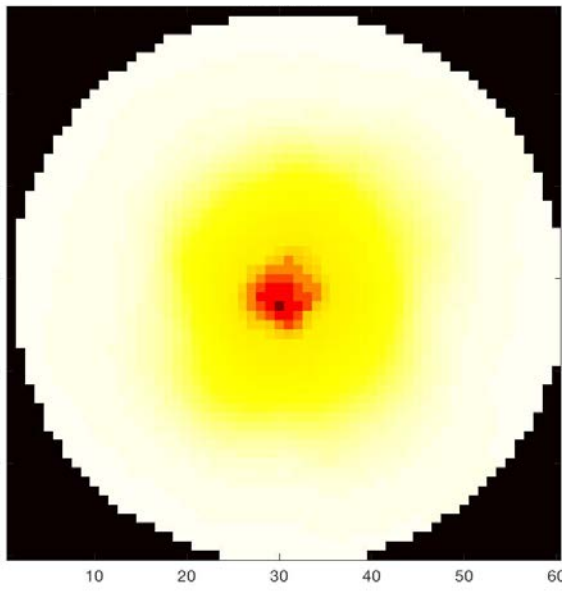
Experiment vs. simulation results

Bleeding 1.8mm Ø



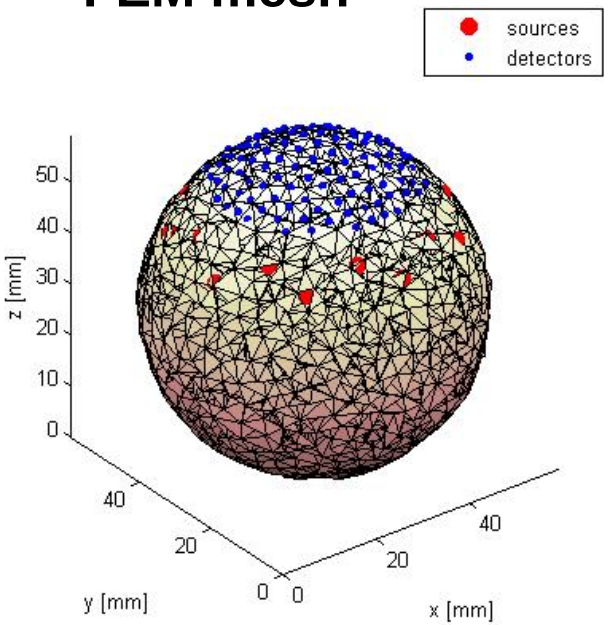
Experiment

Bleeding 1.8mm Ø



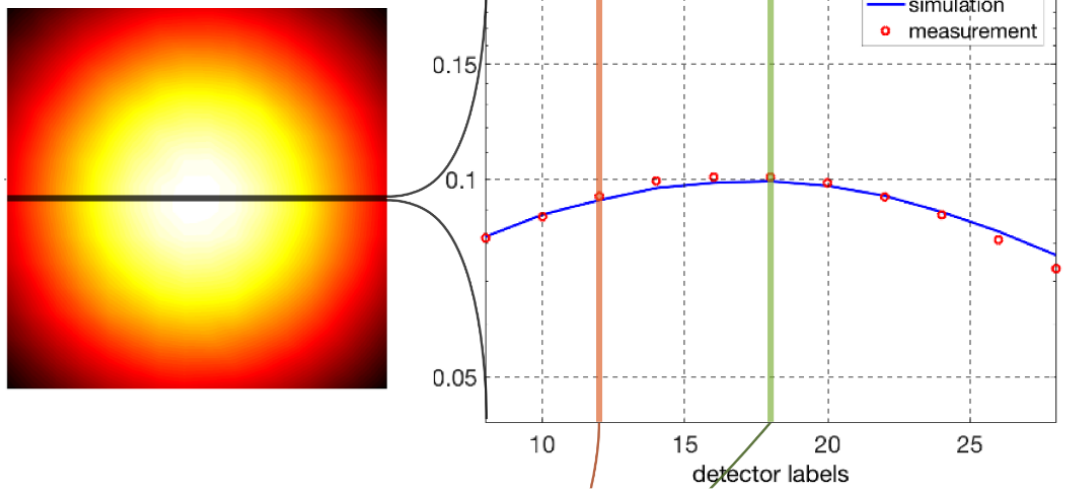
Simulation

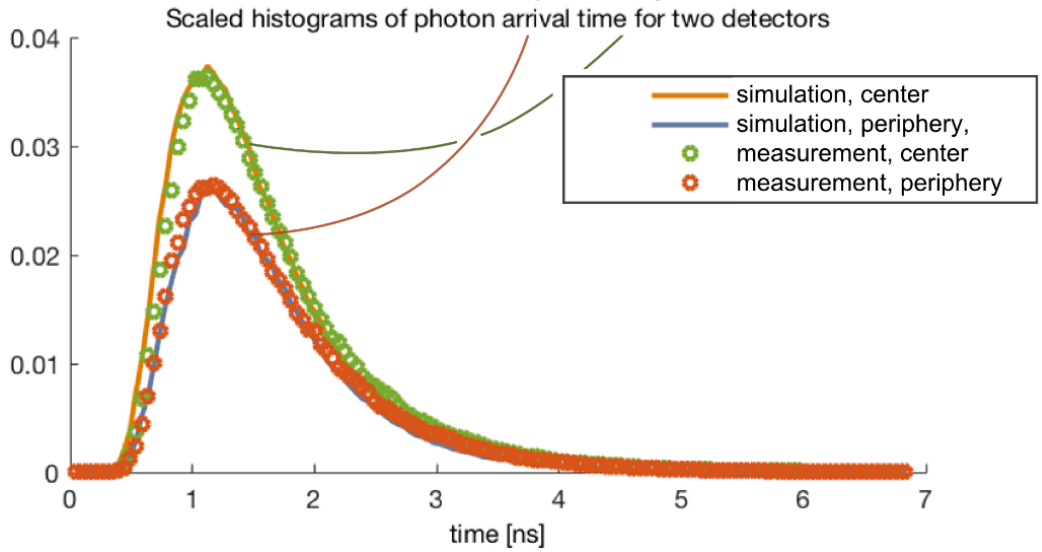
FEM mesh

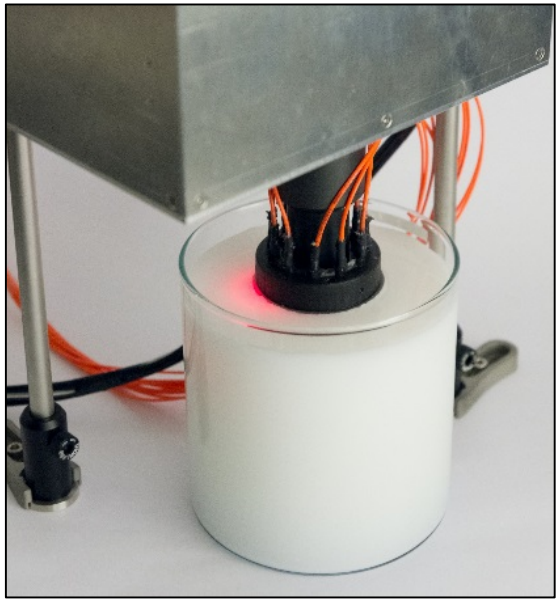


Experiment and simulations agree

Phantom results







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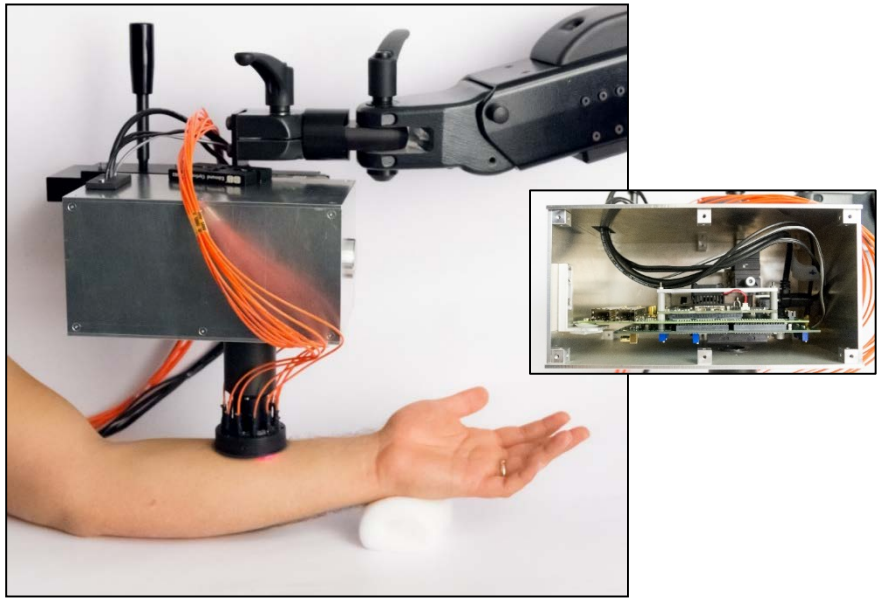
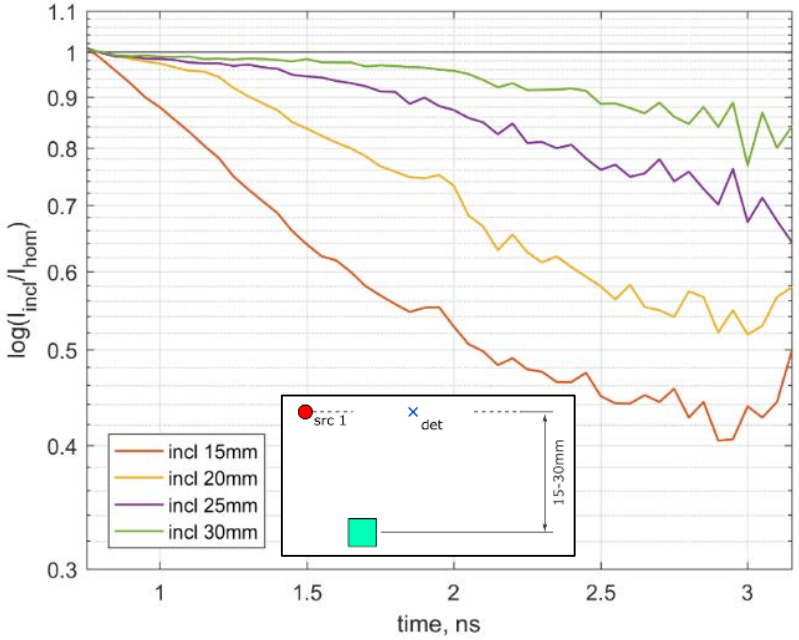
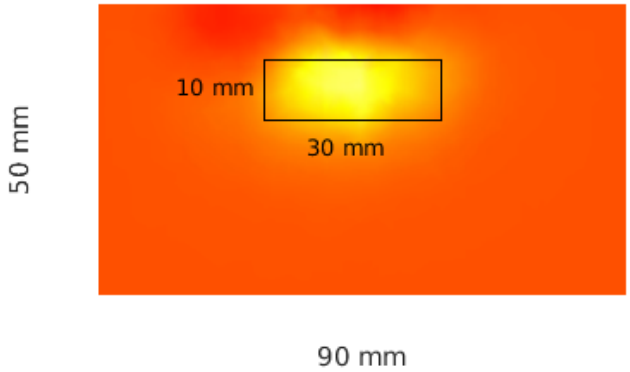
HR-NIROT prototype & results







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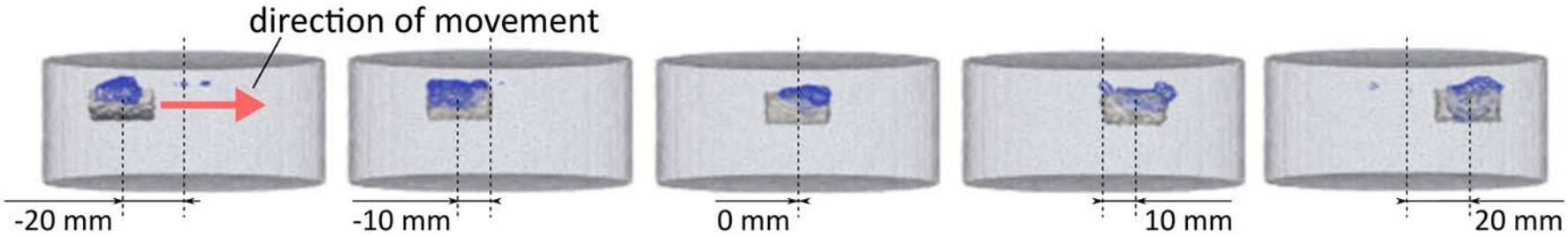
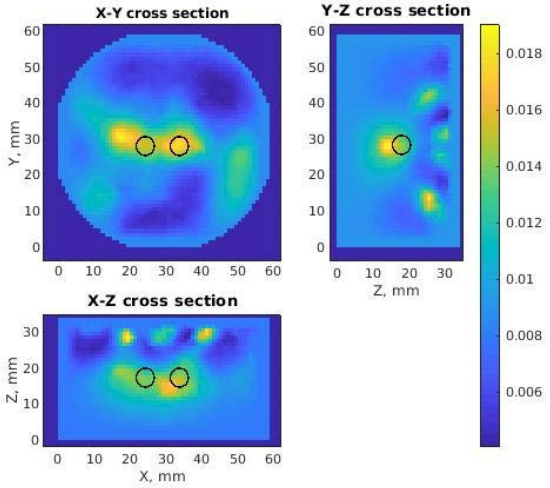
Phantom validation: Speed





Case 1: resolution
Two spheres Ø = 5 mm
lateral distance = 5 mm
depth = 15 mm

Tracking objects
0.2 second acquisition / source

When it comes to clinics …

- Moles and hair are difficult to model
- Instrumental response function is non-trivial to decouple

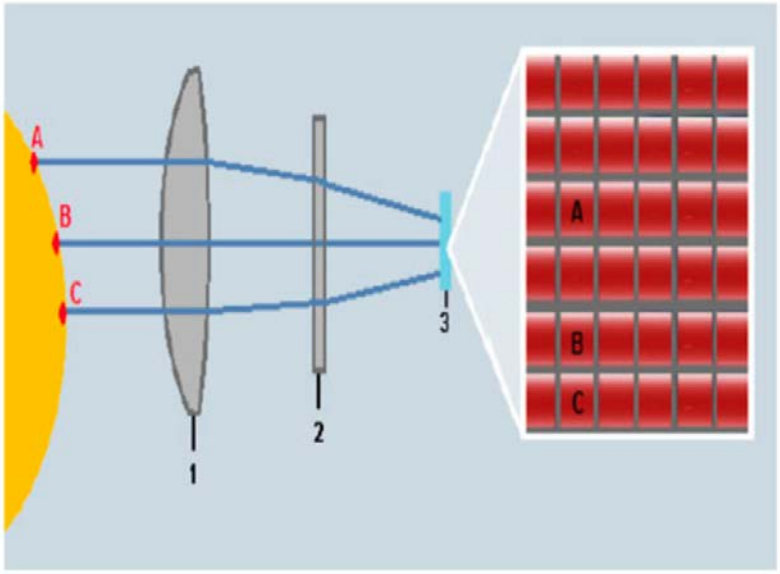
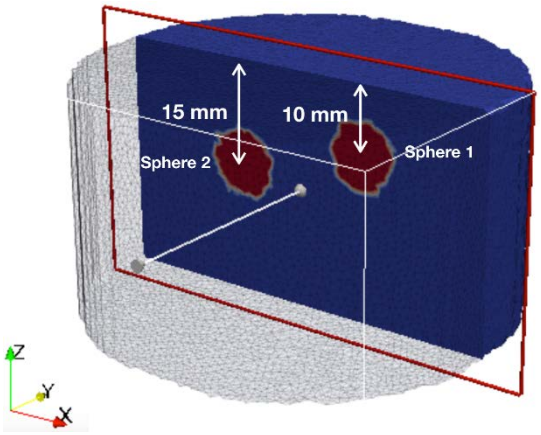


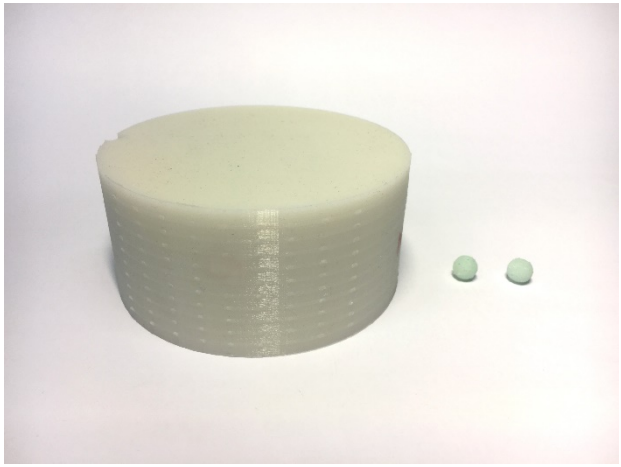
Fig.1 Three rays A, B and C are projected from the object to the SPAD array.

- Methods needed to tackle noise: Calibration methods

J. Jiang, M. Wolf, and S. Sanchez Majos, “Fast reconstruction of optical properties for complex segmentations in near infrared imaging,” J. Mod. Opt. 64, 732–742 (2017).

Phantom experiment





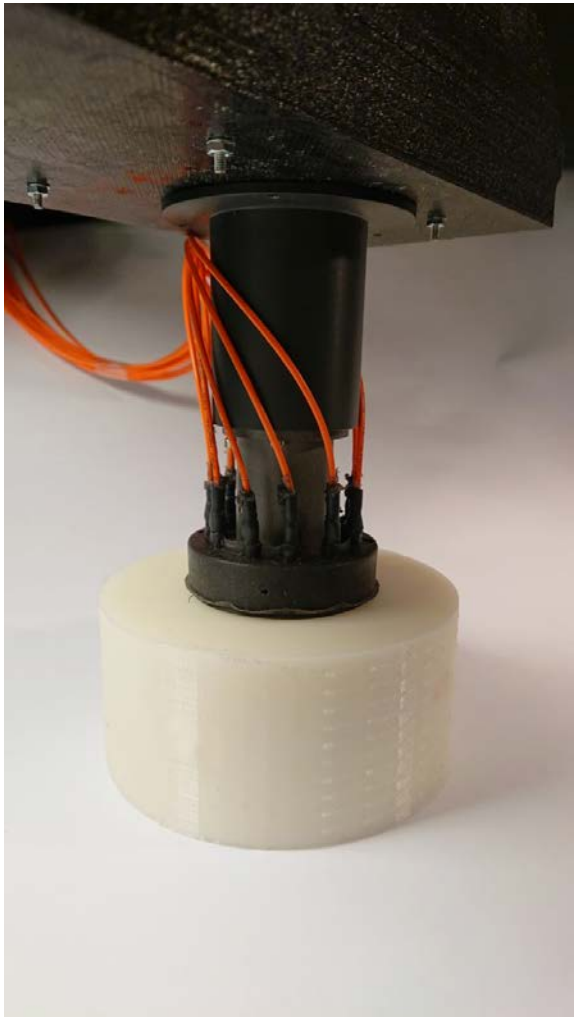
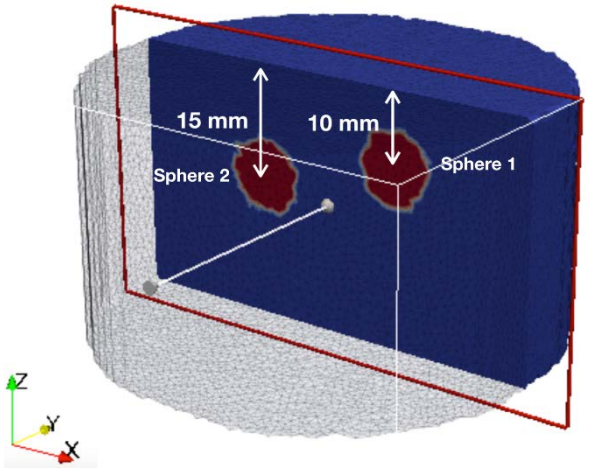


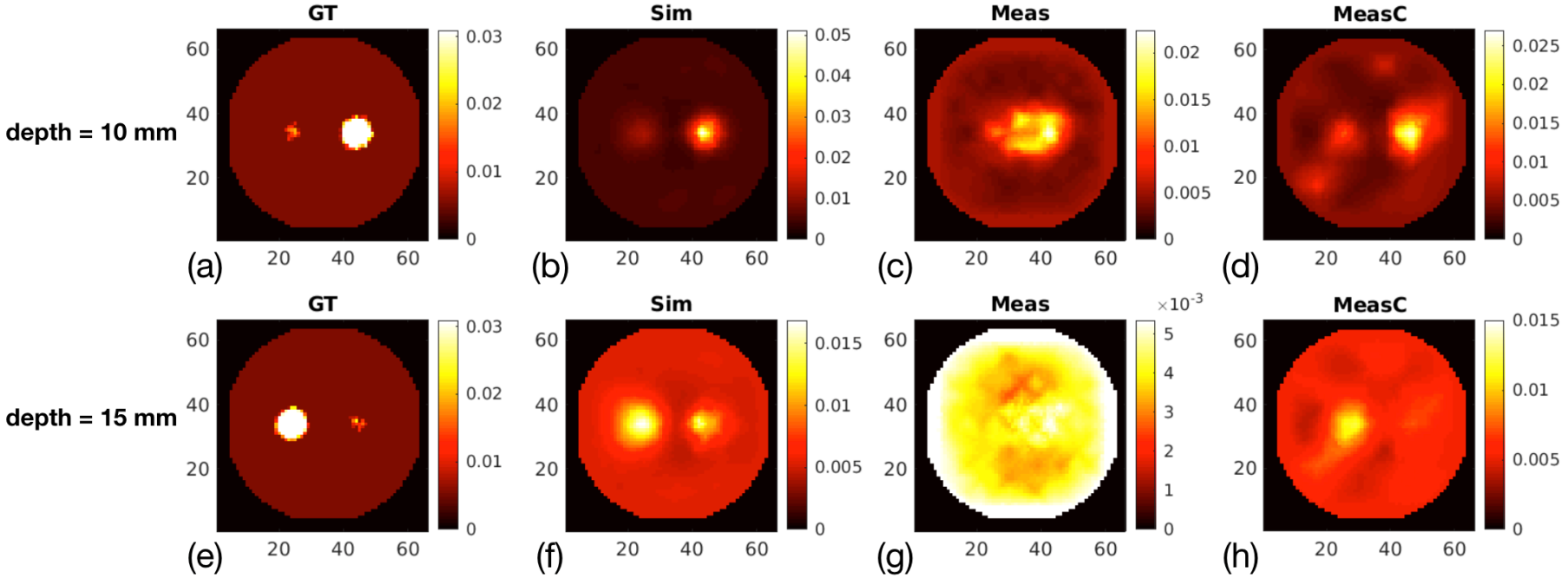
Table 1. Optical properties of the silicone phantom

optical properties	μ_a $[mm^{-1}]$		μ_s' $[mm^{-1}]$	
wavelengths	689 nm	725 nm	689 nm	725 nm
bulk	0.0053	0.0055	0.9	0.86
sphere 1	0.031	0.025	1.06	1.01
sphere 2	0.031	0.025	1.06	1.01

Results
image reconstruction (1)

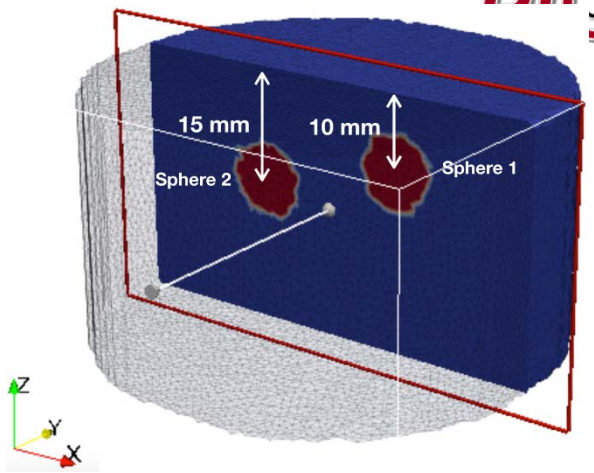
689 nm

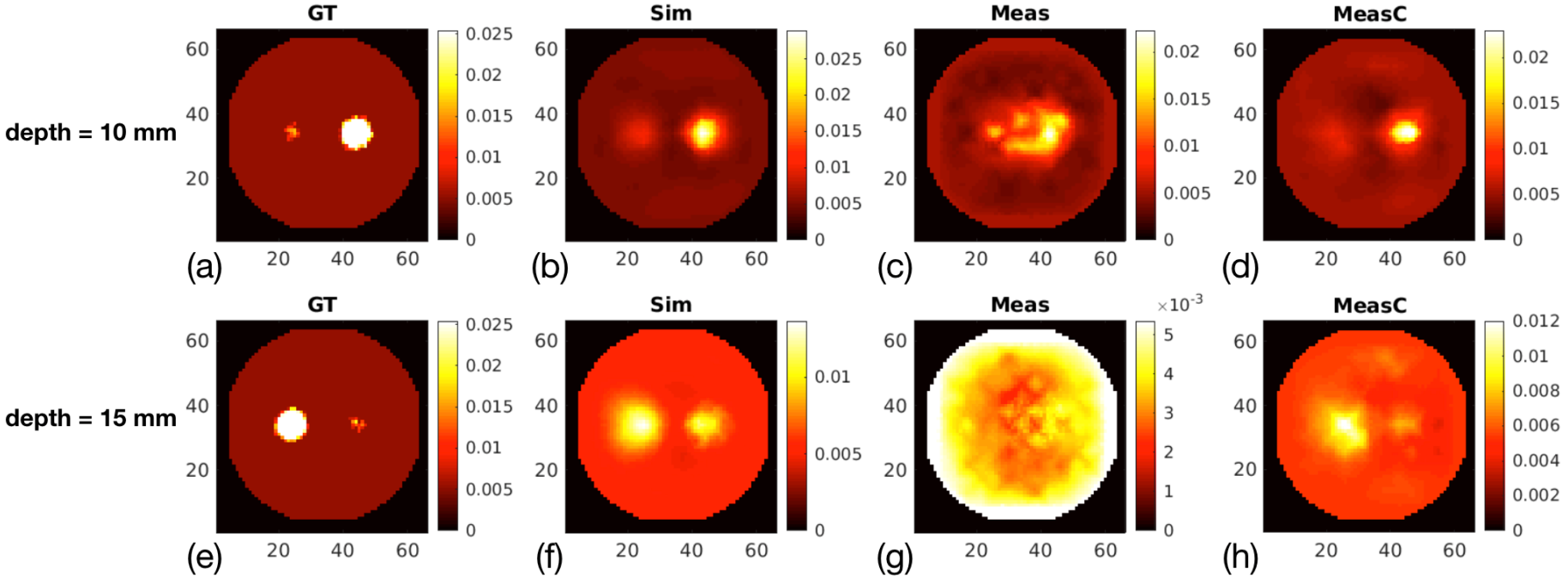




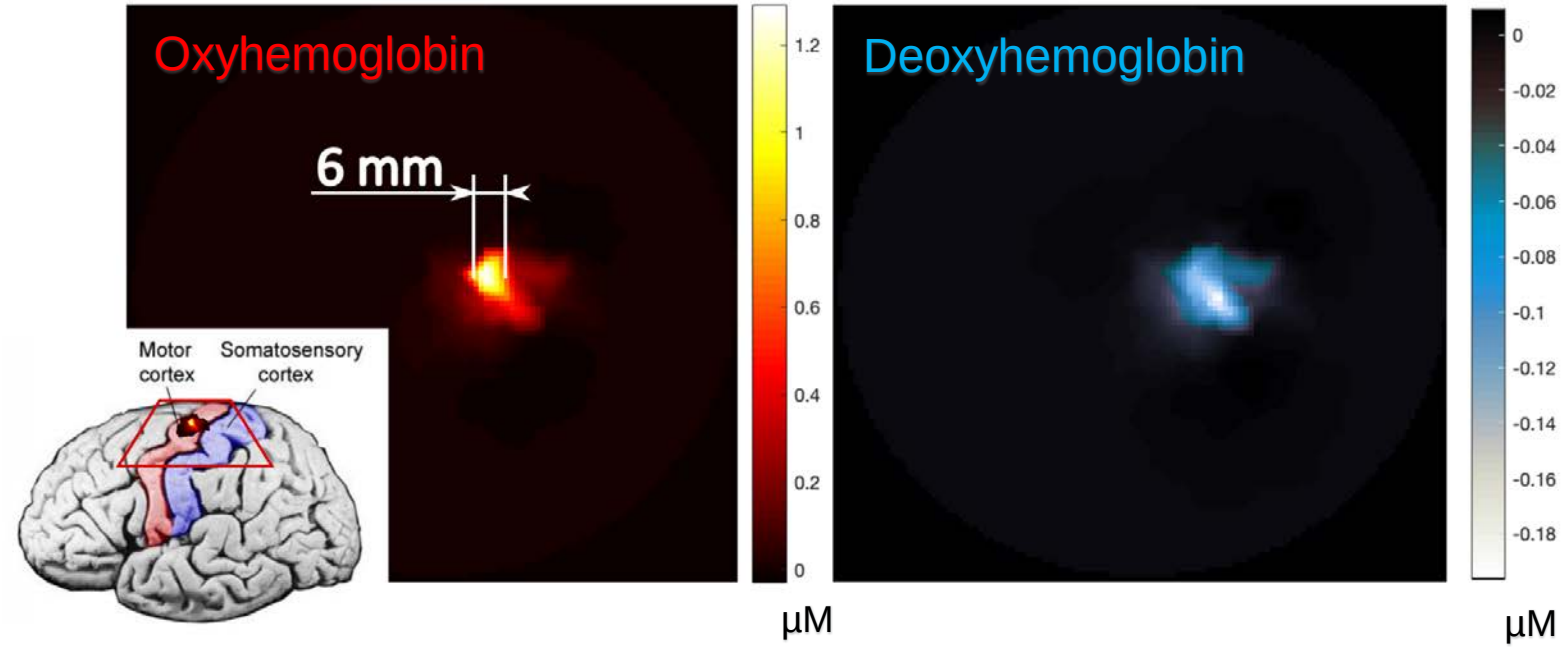
Results
image reconstruction (2)

725 nm





Motor activation in adult subject



- Stimulus: Fingertapping exercise
- 3D tomographic images
- Activation visible in 2cm depth

➢ Demonstrates brain imaging.

Conclusions NIROT

Technological

- ✓ A new NIROT concept
- ✓ First test successful

Societal/Clinical

- ✓ 10% preterm birth rate
- ✓ Prevention & efficient therapy
- ✓ Reduced mortality & life-long disability

Outlook

- ✓ First in vivo studies
- ✓ Ocelot image sensor

PiOneer

Thank you!

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