In vivo optical imaging : revealing endogeneous optical contrast at depth

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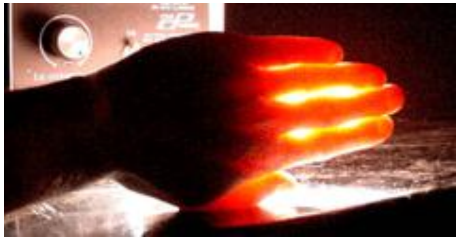
Why using optical imaging *in vivo* ?

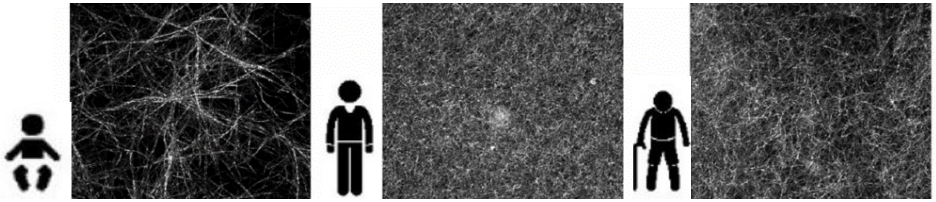
✓ Near infra-red light penetrates into tissue



✓ Interactions between light and tissue through:

Absorption

Scattering : micro-structure



Collagen structure at different stage of life

✓ Spectral information can discriminate tissue components

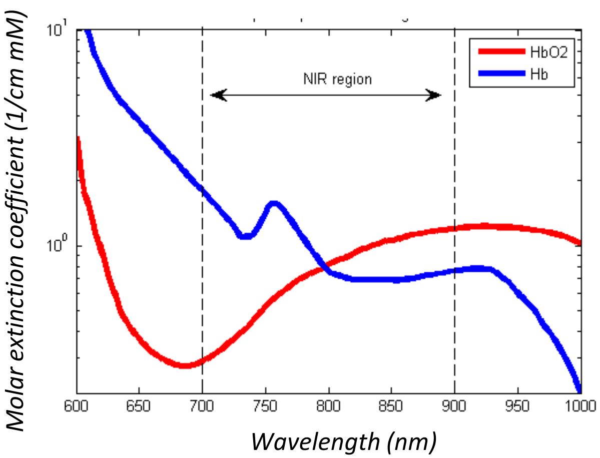
Hemoglobin, melanin, lipid, water …

➔ **bring anatomical, functional and molecular information**

Information provided by optical properties *in vivo*

Absorption:

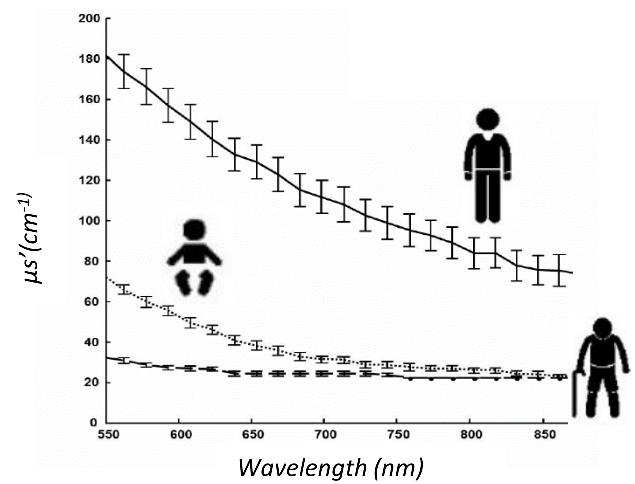
- **Hemodynamic parameter** (Oxy/Deoxy Hemoglobin, SO2, blood volume,…)
- **Chromophores concentrations** (Hemoglobin, Melanin, Water, Lipid, …)



Scattering :

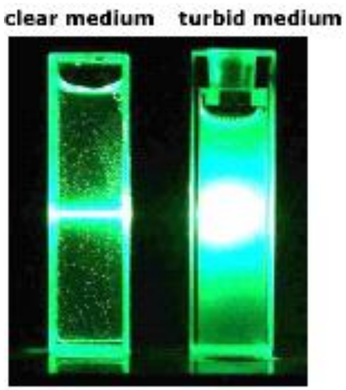
- **Tissue structure** (muscle, fat, tumoral structure, collagen modification..)

➔ **Application:** Monitoring in space and time for diagnostic or observation



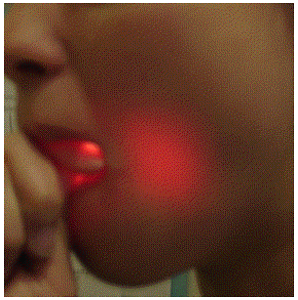
Optical imaging and Photoacoustic imaging

Light/tissue interactions contain anatomical, functional and molecular information



BUT

- Can we **achieve imaging of endogenous optical contrast at depth** in strongly scattering tissues ?
- **Can we separate absorption from scattering ?**

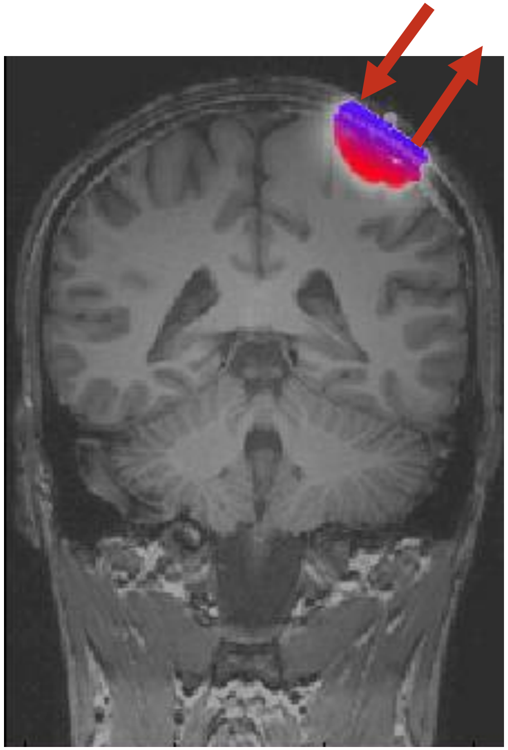


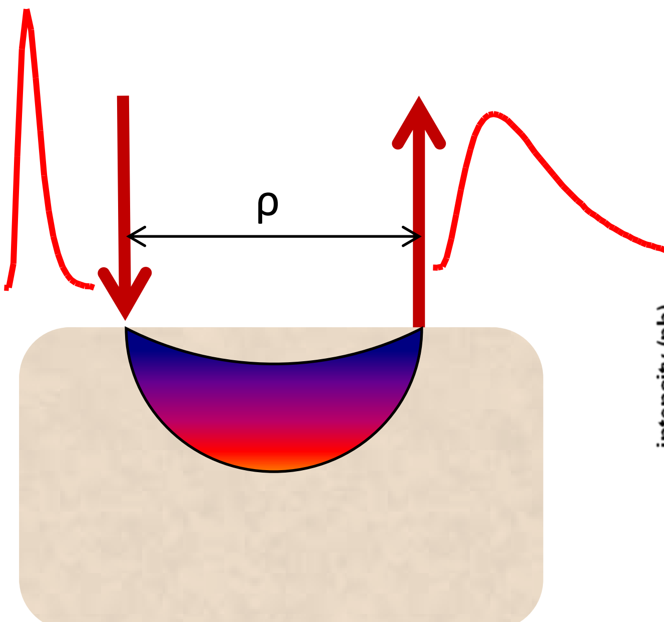
✓ Diffuse optics

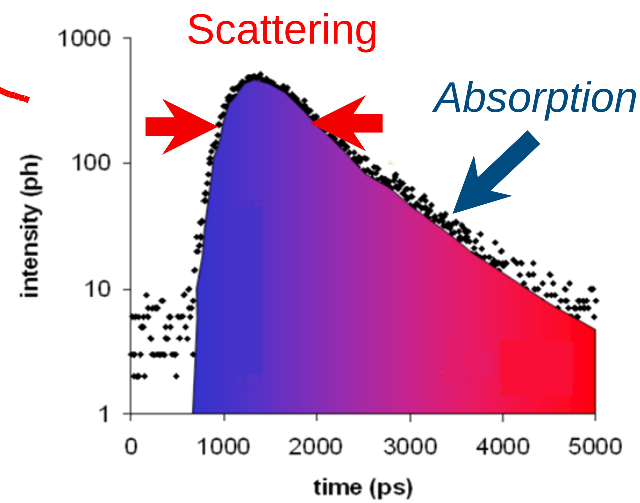
✓ Photoacoustics

Endogenous Optical imaging – Time-resolved approach

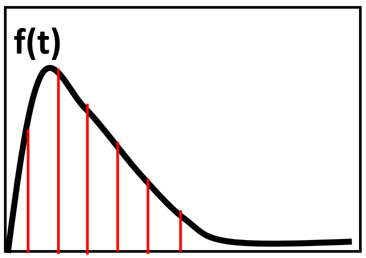
- **Why time-resolved measurements?**
- separation of effects due to scattering from those due to absorption
- «time encodes depth»



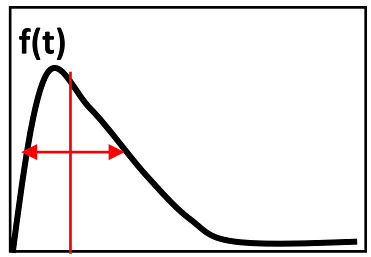




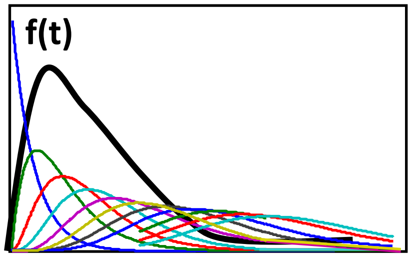
- **Time-selection of detected photons**



Temporal sampling

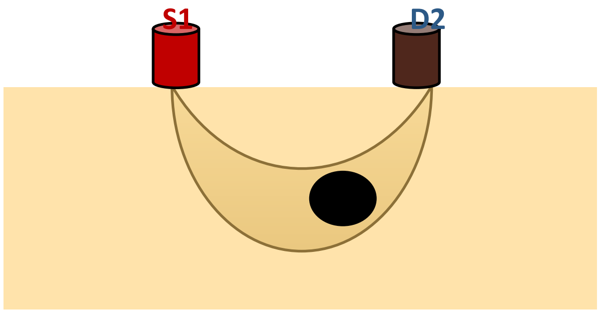


Temporal moment

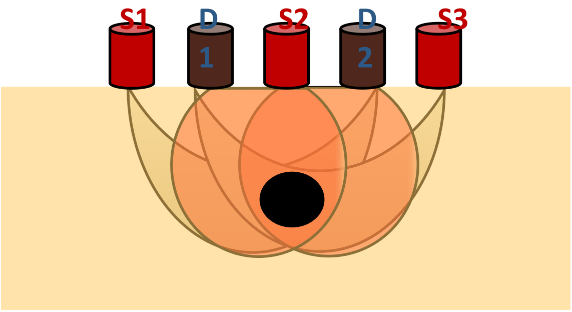


Temporal window

- **Acquisition protocol**



Time-resolved - Diffuse optical Spectroscopy
TR-DOS

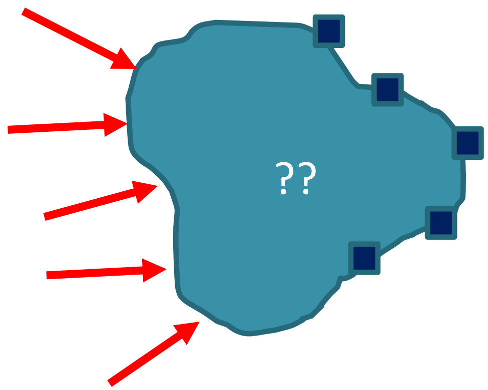


Time-Resolved – Diffuse Optical Tomography

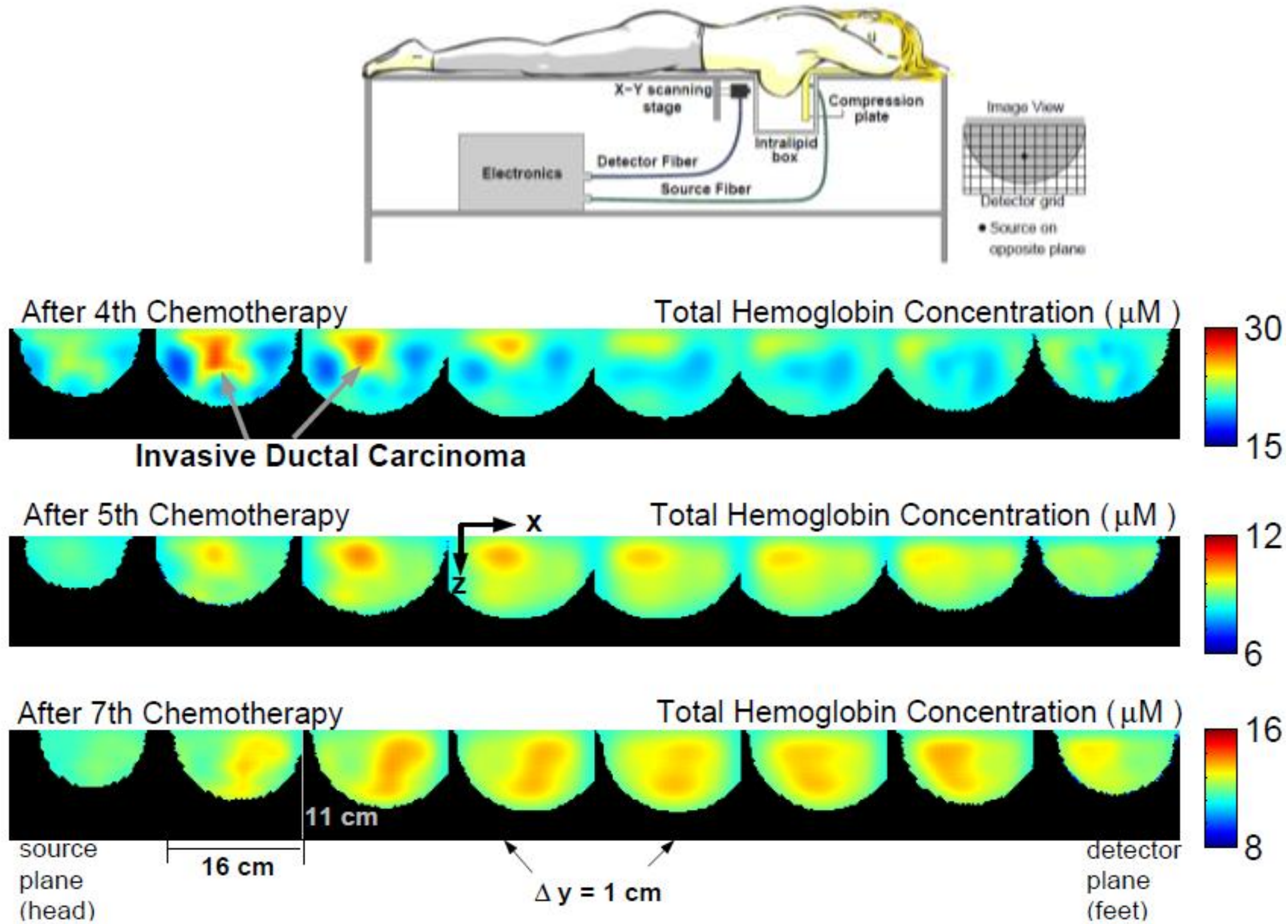
TR-DOT

➢**Absolute quantification of absorption and diffusion**

- **Time-Resolved Optical Diffuse Tomography: TR-DOT**



A.G. Yodh J Biomed Opt. 2009 Mar-Apr;14(2):024020: 1–18.



?? Unkown Optical properties

Detection point

Excitation point

Optical Imaging : Technical implementations

- **Time-resolved instrumentation**

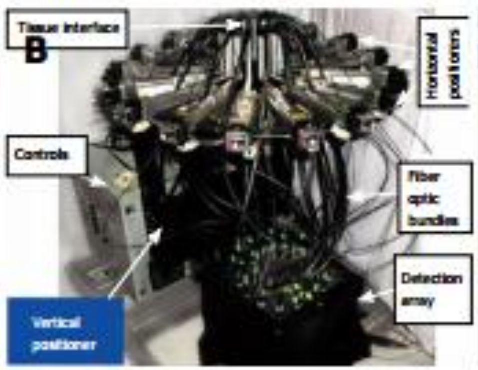
? ?

- **Frequency-Domain instrumentation**

Instrumentation complexity	**TD > FD**
Level of information per source-detector pair	**TD > FD**

- **Different acquisition geometries**

FD - DOT
Parallel Plate



FD - DOT
Ring-Type

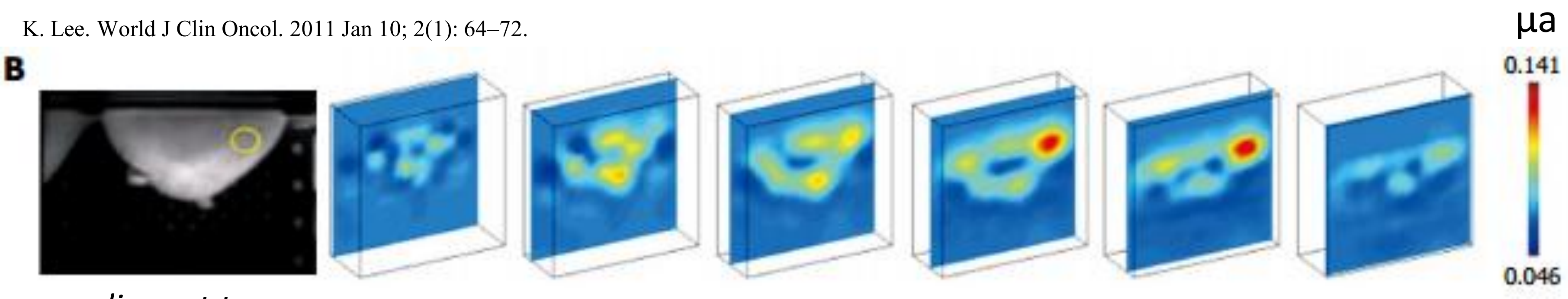
FD - DOT
Hand-Held

TR-DOT
Transmission type

K. Lee. World J Clin Oncol. 2011 Jan 10; 2(1): 64–72.

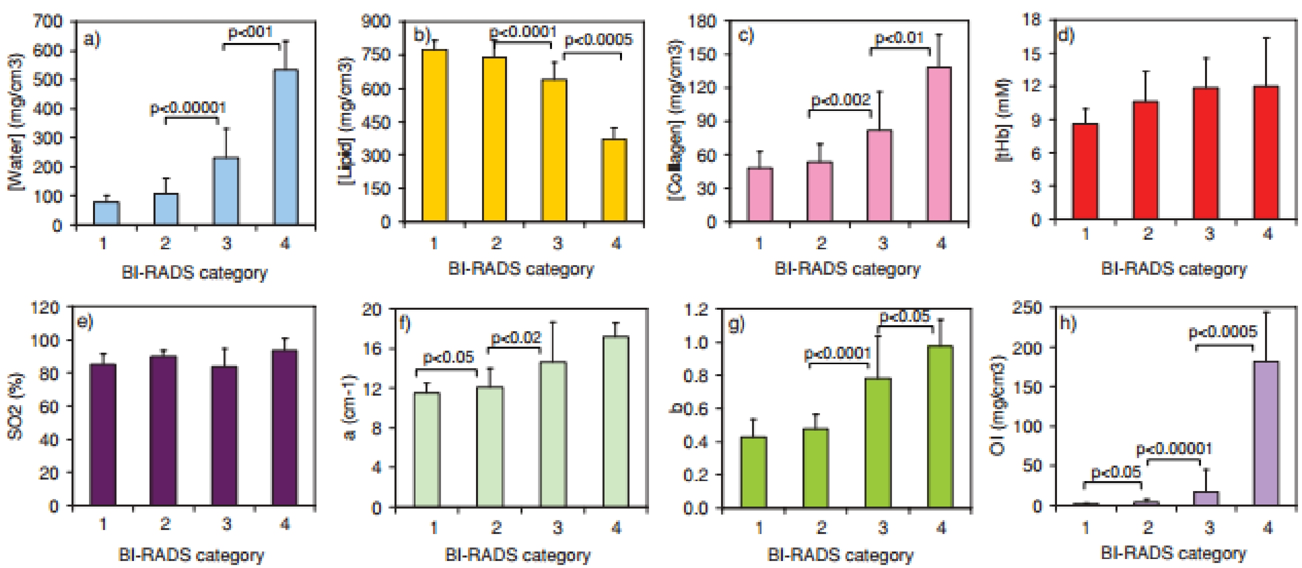
Mammography

K. Lee. World J Clin Oncol. 2011 Jan 10; 2(1): 64–72.



malignant tumor

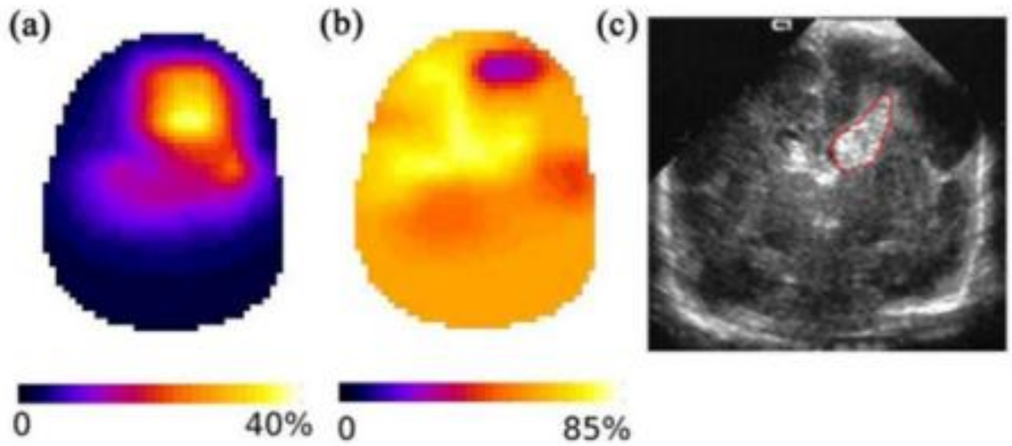
P. Taroni. JBO, **2010**, 15(6)



Optical Imaging : Applications

Brain: Example of neonates

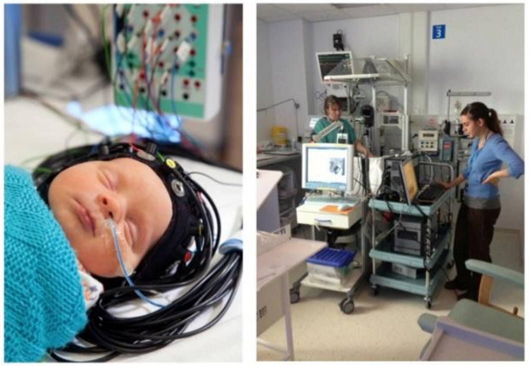
Hebden JC. European Radiology 2007 17(11):2926–2933



% Blood volume

% Blood oxygen saturation

L. Dempsey Proc. SPIE 953818, ECBO (July 16, 2015)



TR-DOT

Whole-head functional brain imaging of neonates at cot-side using time-resolved diffuse optical tomography

Other application in BRAIN

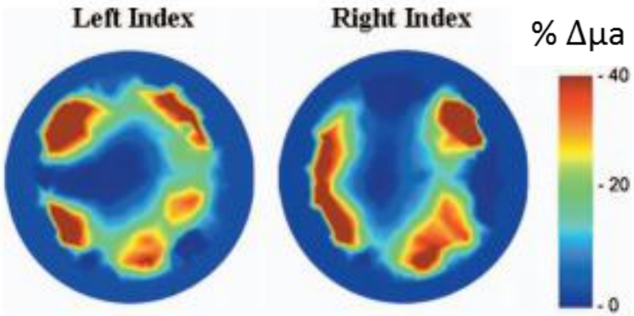
- *traumatic brain injury (TBI)*
- *subarachnoid hemorrhage (SAH)*
- *ischemic stroke*
- *sleep apnea and other sleep disorders*
- *intraoperative brain monitoring*

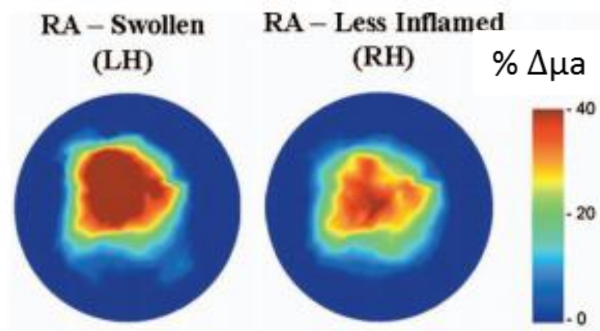
Other applications: Functional respons

- Tomography of finger joint physiology and disease

M.Lasker. JBO 2015, 12(5)

CW-DOT

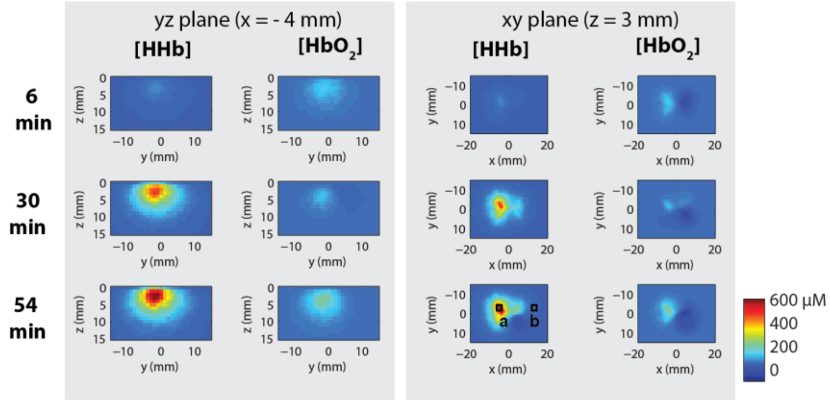




- Flaps monitoring

L. DiSieno Proc. SPIE 9538, ECBO (July 16, 2015)

FD-DOT
➔ Depth



- Liebert / Hebden/etc…

Synthesis

	Diffuse optics TR-DOT	Photoacoustics
Image contrast	**Absorption** and **scattering**	
Spatial resolution	From ~ mm at surface to ~ cm in depth *depending on the number of source/detector pairs, depth and (μa,μs')*	
Penetration depth	~ 2.5 cm more in case of diffusing medium (breast)	
Temporal resolution	From ~s (spectroscopy) to ~min (optical fibers helmet) *depending on the number of source/detector pairs, depth and (μa,μs')*	
Accessible organs	All externally or endoscopy Brain + monitoring	
Typical contrast agents	**Indocyanine green**	

Photoacoustic imaging: a multiwave modality

Biological tissue

Optical excitation ⇨  ⇨ **Ultrasound detection**

Photoacoustic effect

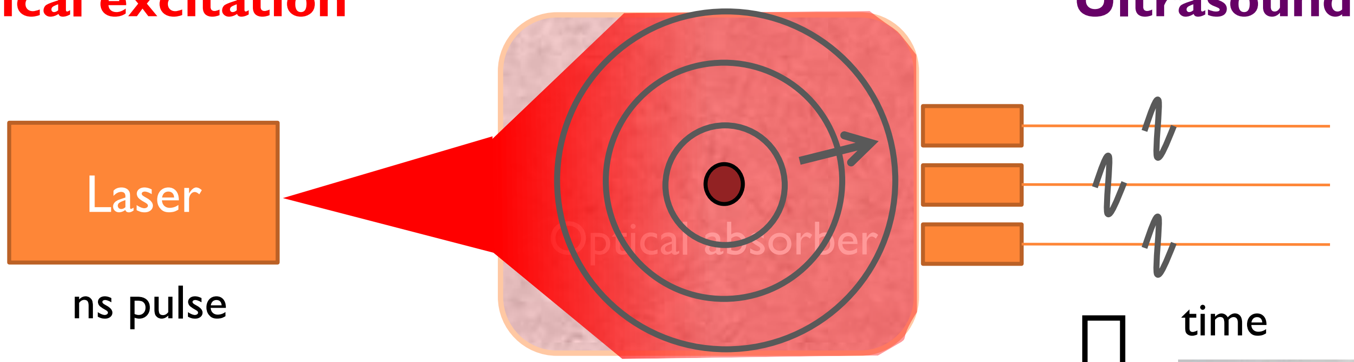
Optical contrast

Ultrasound resolution

Spatial resolution : < 1 mm at cm-depth

Photoacoustic imaging : principle

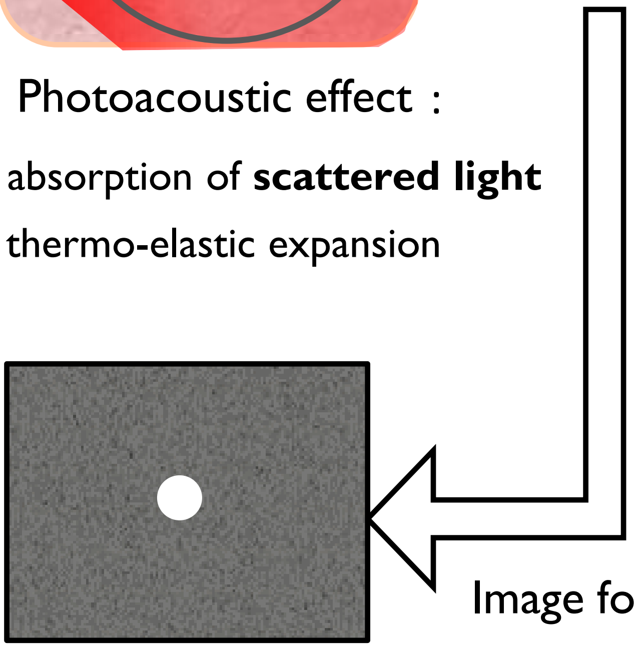
Optical excitation | Biological tissue | **Ultrasound detection**



Photoacoustic effect :

Optical absorption of **scattered light**

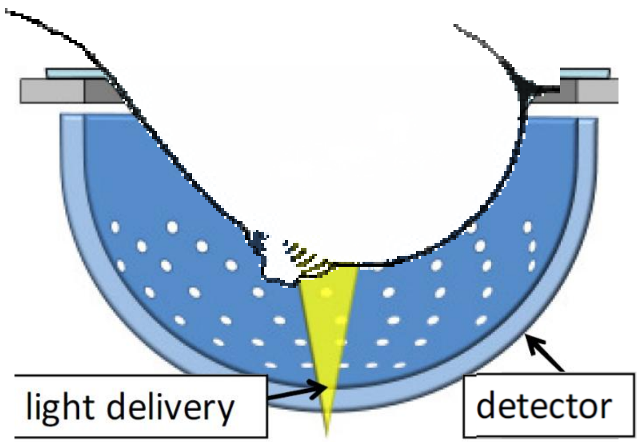
+ thermo-elastic expansion



Ratio penetration depth / resolution ~ 200

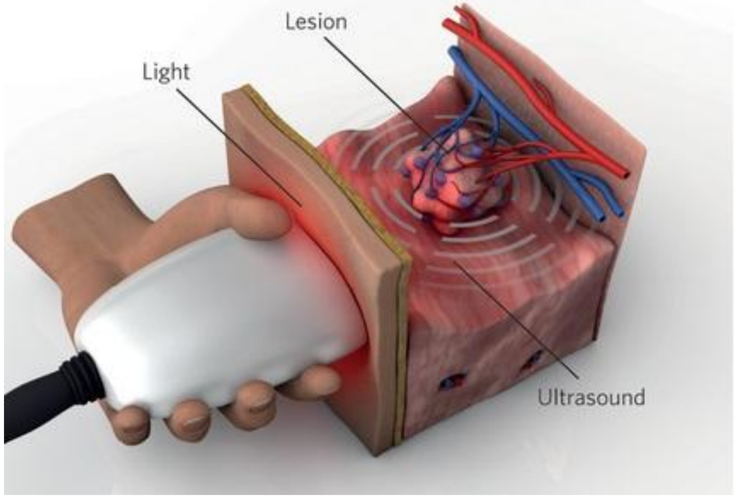
Photoacoustic imaging : Technical implementations

Tomographic detection



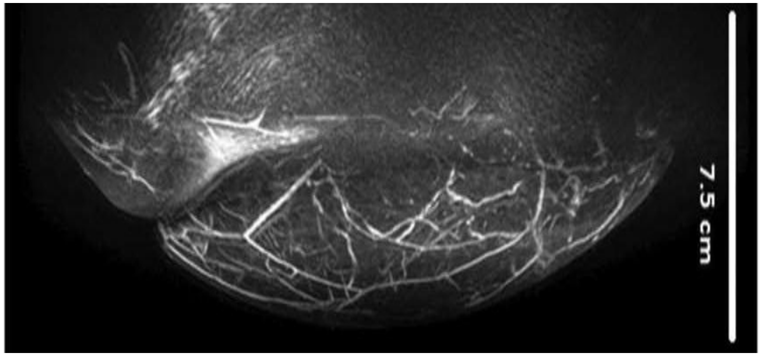
Optosonics Inc., Endra Inc.

Hand-held detector array



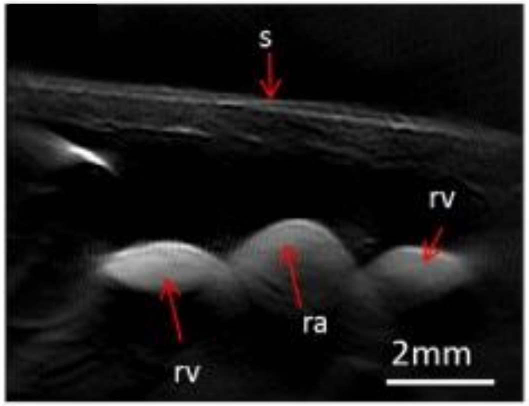
Taruttis A. and Ntziachristos V., Nat. Photo. 9, 2015

Human breast



Kruger R. et al, Med. Phys. 40 (11), 2013

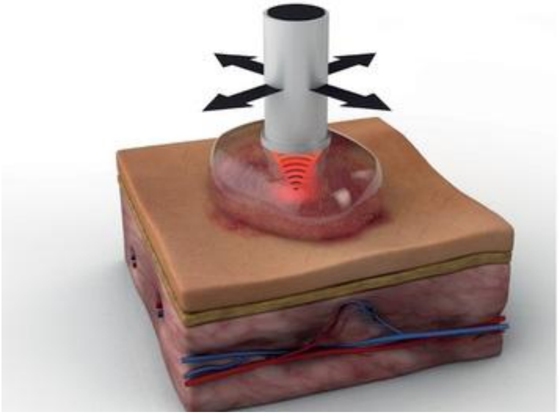
Human wrist



Buehler R. et al, Opt. Let. 38 (9), 2013

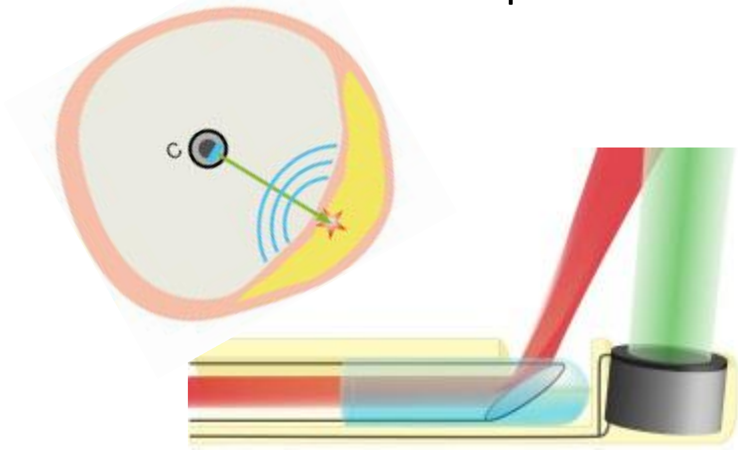
Photoacoustic imaging : Technical implementations

Scanning mode

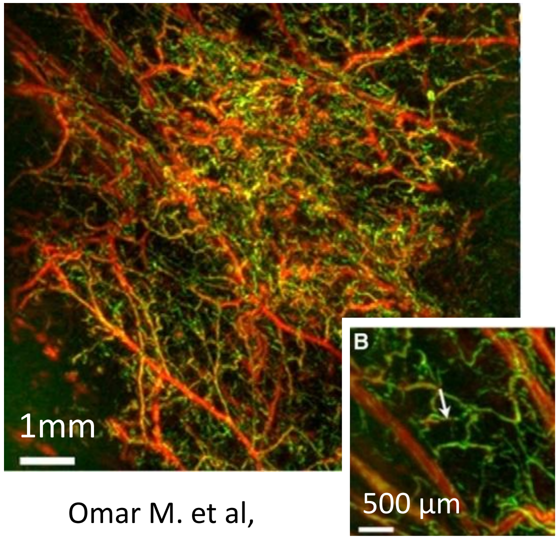


Taruttis A. and Ntziachristos V., Nat. Photo. 9, 2015

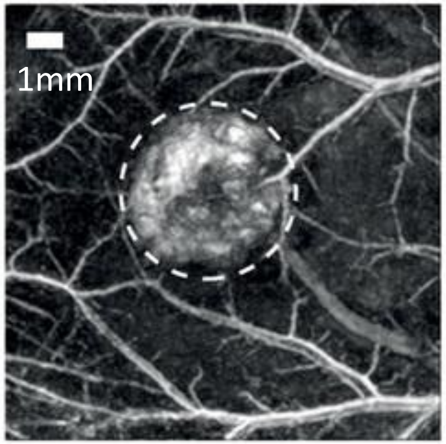
Endoscope



Sub-cutaneous tumors

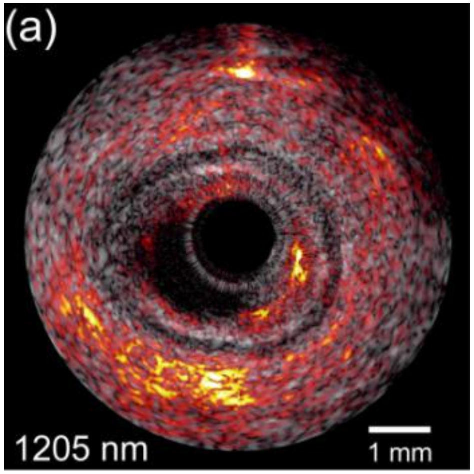


Omar M. et al,
Neoplasia, 7, 2015



Laufer et al,
J. Bio. Opt., 17(5), 2012

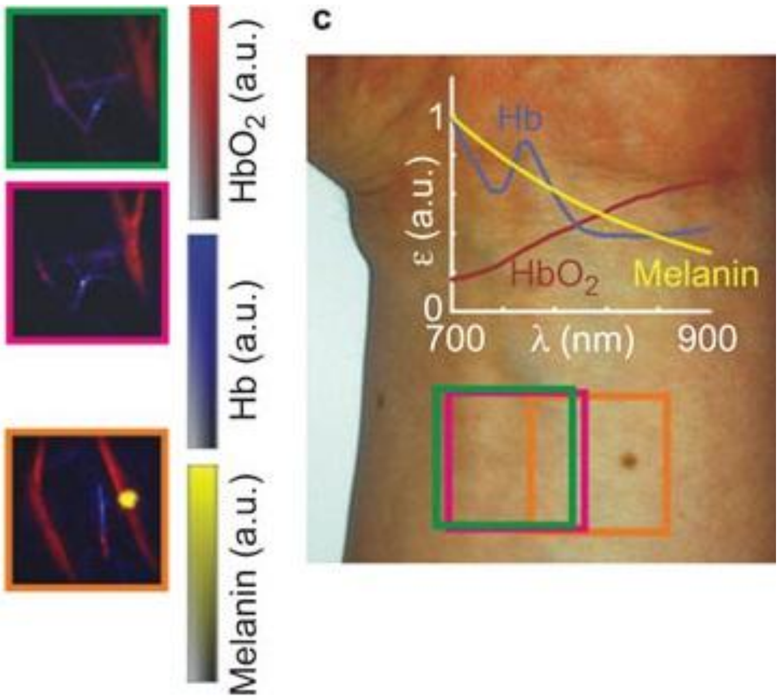
Coronary artery with plaque



Jansen K. et al, Opt. Exp., 21 (18), 2013

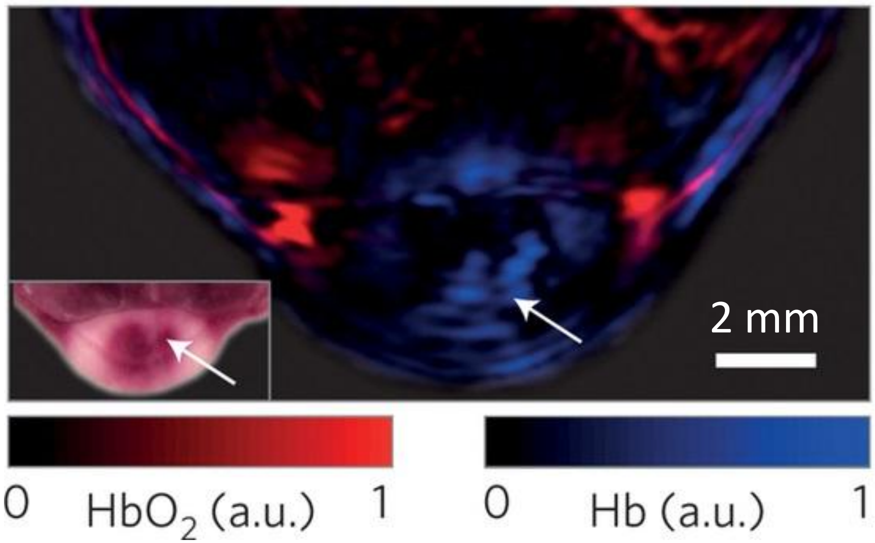
Photoacoustic imaging : blood oxygenation

Human wrist



Deán-Ben XL. and Razansky D., Light Sci Appl, 3, 2014

Subcutaneous tumor

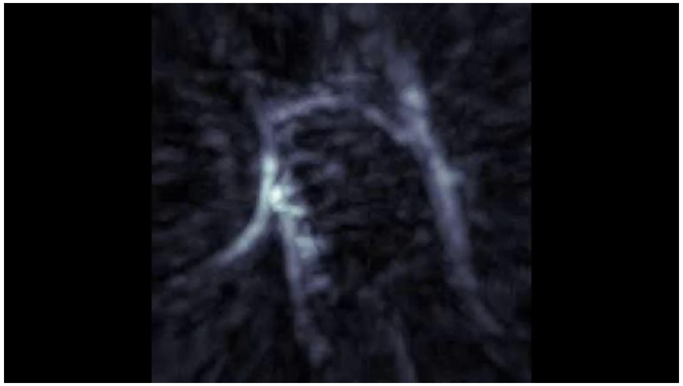


Herzog E. et al, Radiology, 38 (9), 2012

Photoacoustic imaging : applications for endogenous contrast

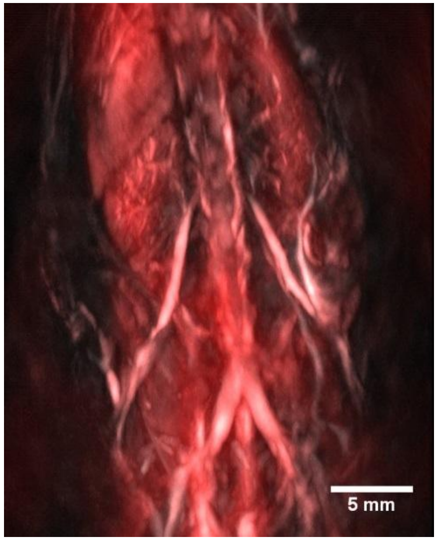
- ✓ Angiography and perfusion

Human forearm



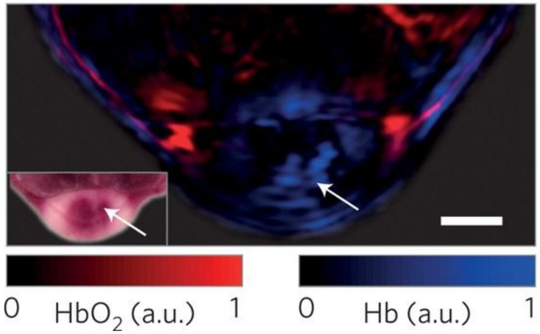
Deán-Ben XL. and Razansky D., Photoacoustics 1 (3-4), 2013

Mouse

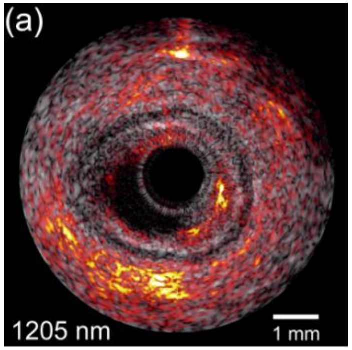


Gateau J. et al, Medical Phys. 40 (1), 2013

- ✓ Tumor heterogeneity and hypoxia



Herzog E. et al, Radiology, 38 (9), 2012



Jansen K. et al, Opt. Exp., 21 (18), 2013

- ✓ Atheroma: vulnerable plaques

Synthesis

	Diffuse optics TR-DOT	Photoacoustics
Image contrast		**Absorption**
Spatial resolution		< 1 mm ~ penetration depth/200 *depending on the number and distribution of detectors*
Penetration depth		Max. 4 cm
Temporal resolution		0.01 – 10 images/s *depending on the number of detectors*
Accessible organs		All externally or endoscopy except brain (adults) and lungs
Typical contrast agents		**Methylene blue, Indocyanine green, Gold nanoparticles**

Conclusion

Both diffuse optical imaging and photoacoustic imaging techniques :

- are **non-invasive** and **non-ionizing**
- can reveal **endogenous contrast** with anatomical and functional information **at cm-depth** in tissue *in vivo*
- report results in **real-time** (depending on the set-up).
- may be **bedside** and allow **longitudinal** studies.
- **Applications** : mapping blood oxygenation, tumor, hemorrhage, vulnerable plaque … *+ molecular contrast agents.*
- are complementary:
  - **Photoacoustics:** spatial resolution and depth
  - **Diffuse optics:** scattering and monitoring ability

Comparison of the methods

	Diffuse optics TR-DOT	Photoacoustics
Image contrast	**Absorption** and **scattering**	**Absorption**
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