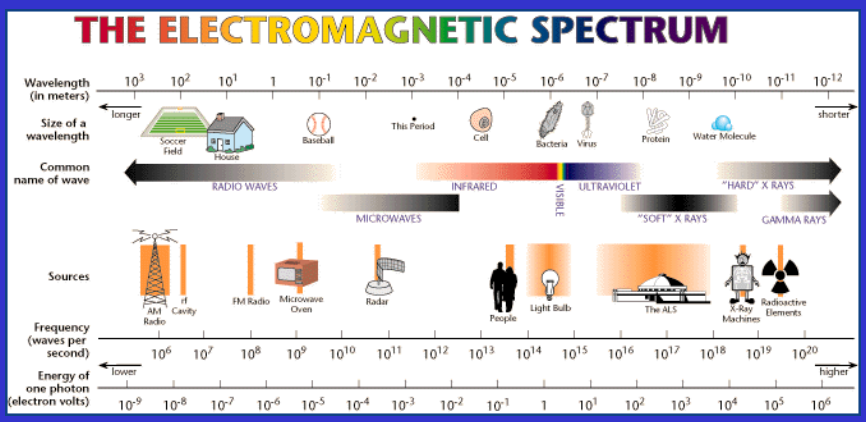
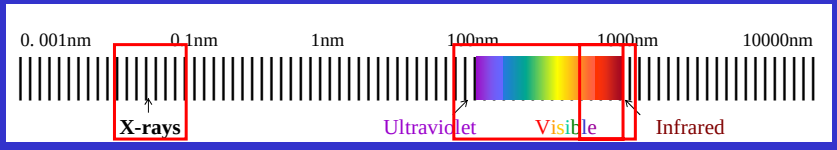
Lighting up the brain – a 25 year journey from basic science to commercial instrument

D.T. Delpy

Engineering & Physical Sciences Research Council

The Electromagnetic spectrum





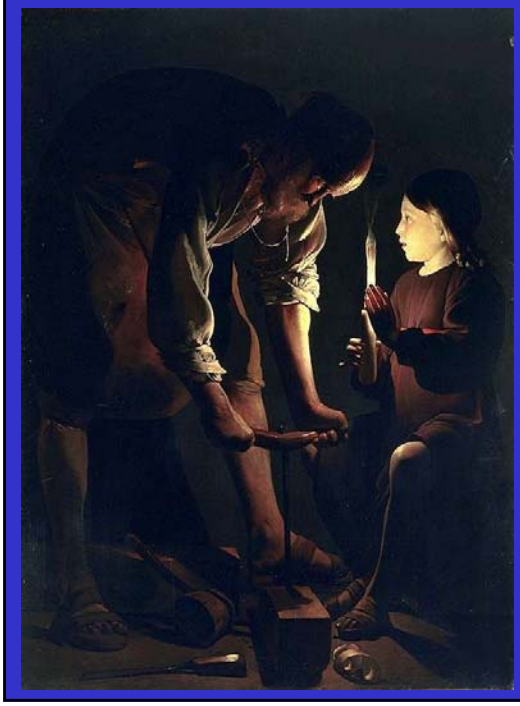
Looking inside the body from the outside: the transparency of tissue

fetus

hydrocephalus

‘ If a candle was held behind his head, or the sun happened to be behind it, the cranium appeared semi-transparent and this was more or less evident until he attained his fourteenth year’

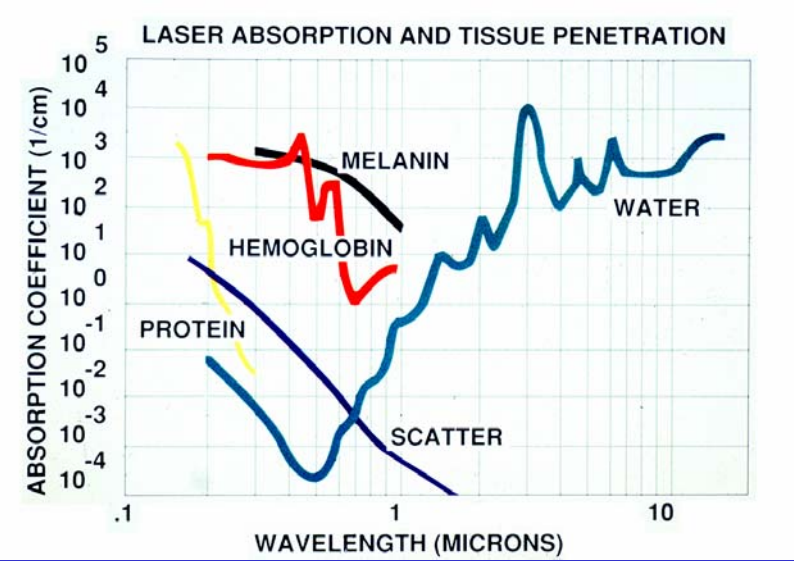
Richard Bright, Guy’s Hospital, on a patient with hydrocephalus, 1831.



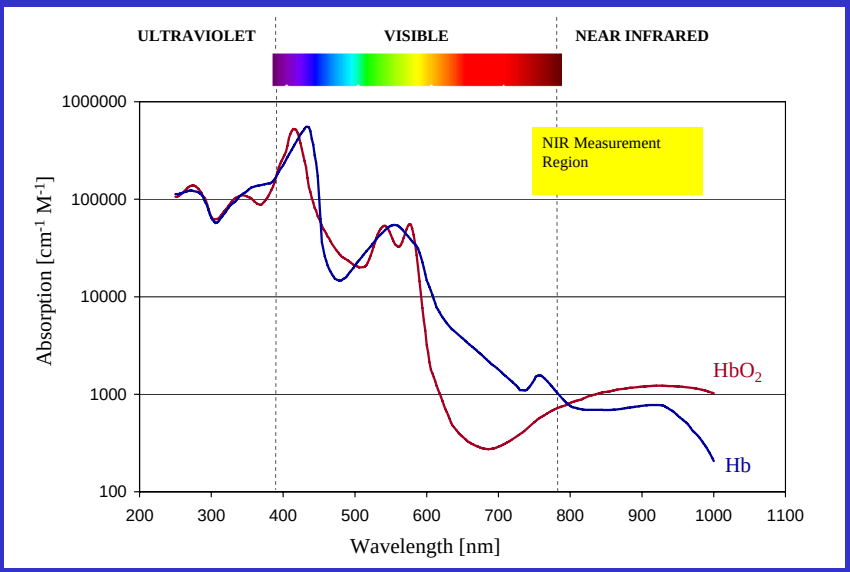
Early Optical imaging?

Georges de La Tour
1593-1652
Christ with St. Joseph in the Carpenter's Shop
c. 1640

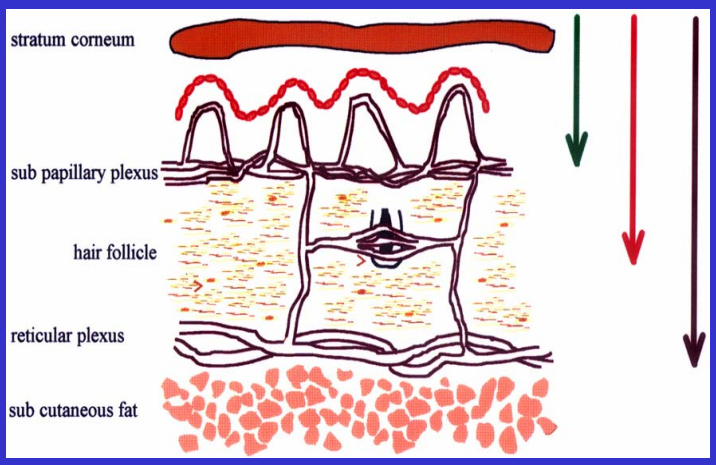
The absorption of light by major tissue chromophores



The Absorption Spectrum of blood



The effect of wavelength on the distance light will penetrate into the skin



Multispectral imaging: 700 - 900 nm range

700nm

800nm

900nm

Blood vessel visualisation with the “Veinviewer”

From about 1978, increased focus on neonatal brain oxygenation and metabolism

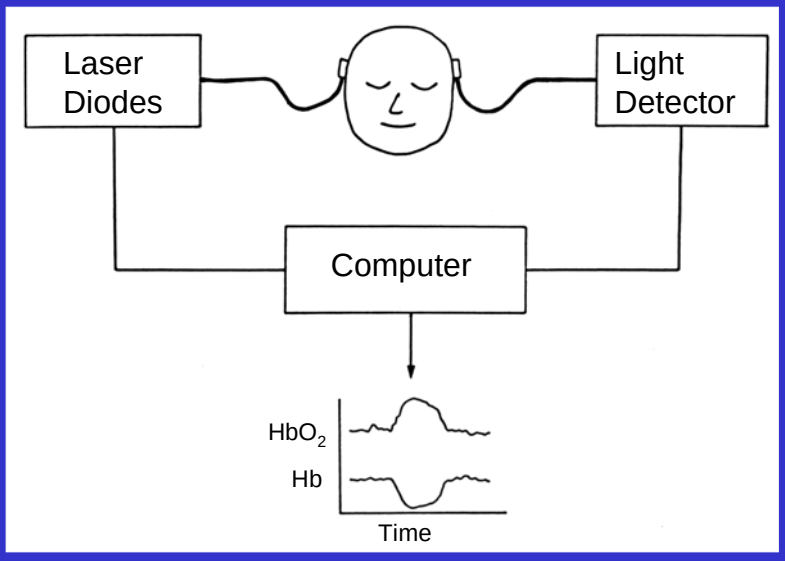
Methodologies:

- 31P NMR Spectroscopy
- Near Infrared Spectroscopy

Doug Wilkie

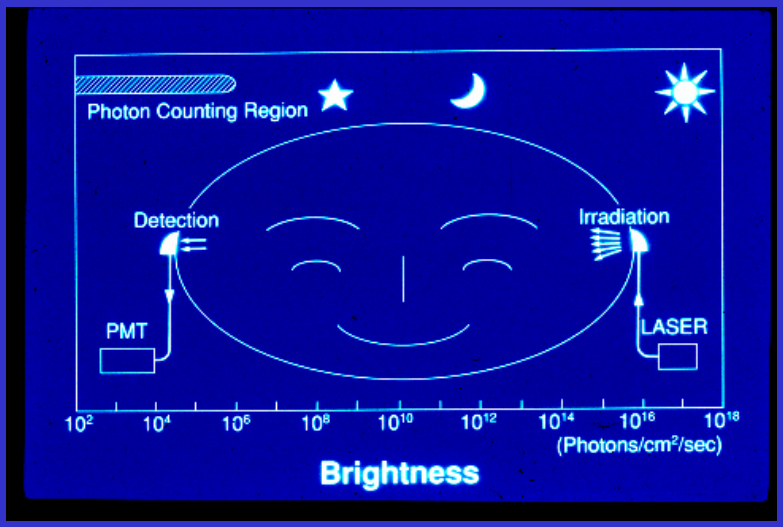
Frans Jobsis van der Vliet

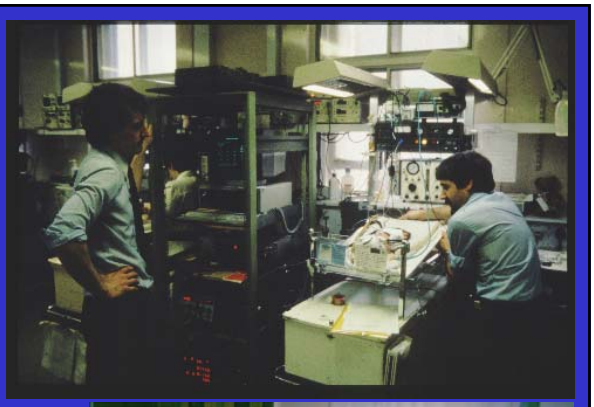
Looking deeper into tissue: Near Infrared Spectroscopy (NIRS) -
Note: Any tissue can be studied. e.g. muscle, brain, the breast



Note: we need to know how far the light has travelled – see later!!

Light levels in Near Infrared Spectroscopy





- Original NIRS system developed by Mark Cope
- First Baby studies
- Relaxation after successful study

Impending disaster – funder withdraws:

Along comes Hamamatsu Photonics to the Rescue

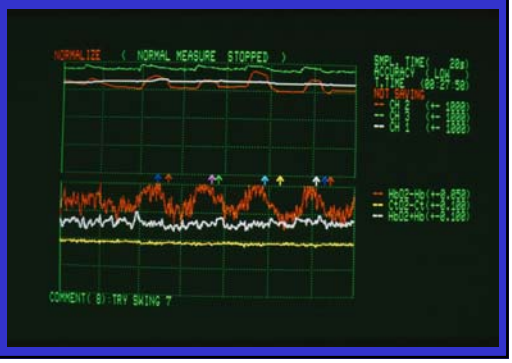
Instrument design is thirsty work!

The NIRO1000 (can you guess the origin of the number?)

(Included the rather unwisely named POX mode of operation)

Early baby study

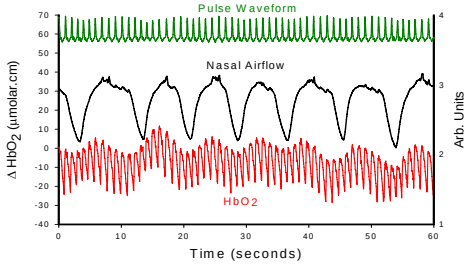
(note who the workers are)



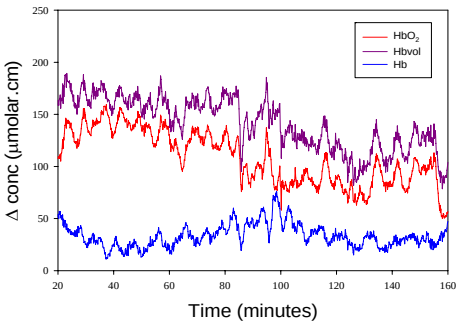
Delpy forced to wear a suit and tie!!

What does NIRS show? What are its advantages?

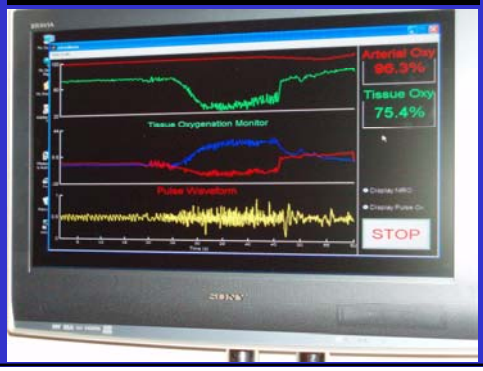
Cerebral NIR Respiratory and Cardiac Oscillations



Long term Cerebral NIR Oscillations



Near Infrared muscle exercise studies

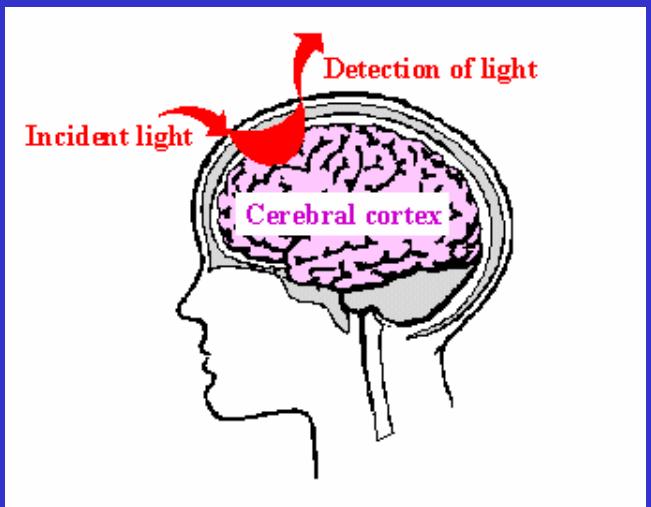


Fifth and sixth generation NIRS instruments

NIRO200
and
NIRO100

Pretty well everyone in European NIRS (about 1992)

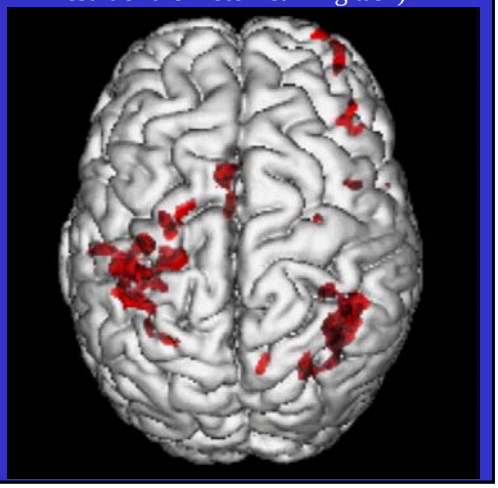
Localising NIRS measurements through careful positioning of the light source and detector



An aside: Watching the brain think with functional Magnetic Resonance Imaging (fMRI)

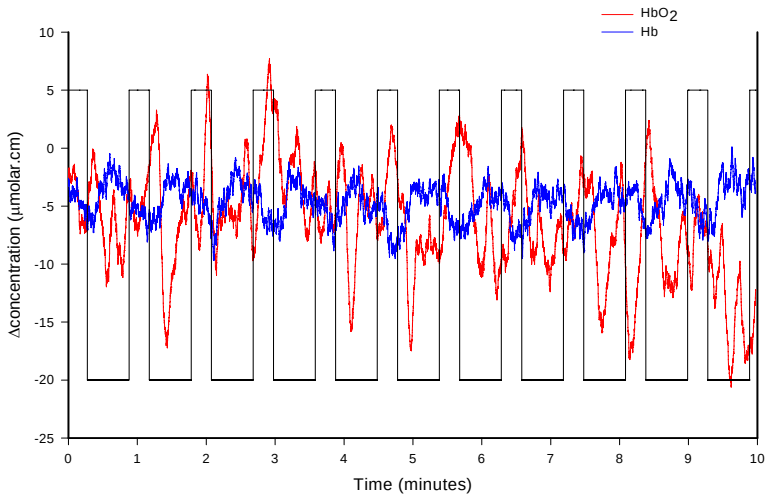
Ordinary MR image of the brain

fMRI images of the brain showing activation changes during 40 minutes of motor learning (red areas show where Hb has changed as a result of the motor learning task)

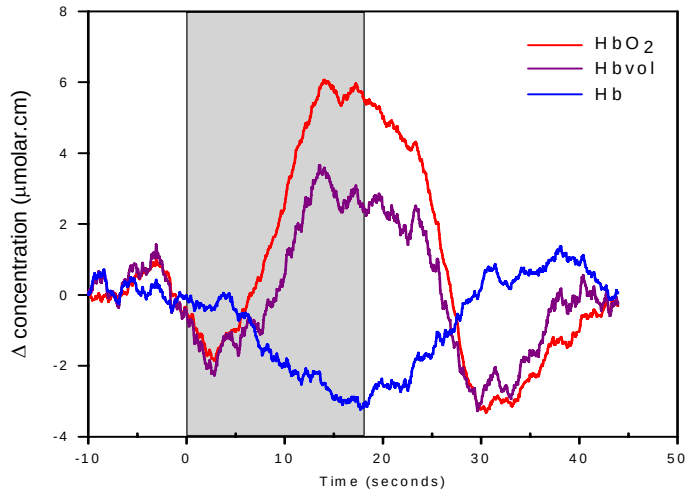


Functional NIRS – watching the visual cortex at work (the checker board pattern flashes then stops)

Functional NIRS of the infant visual cortex – the raw signals

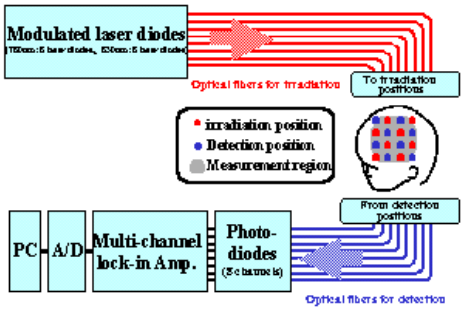


Functional NIRS of the infant visual cortex – the averaged signal



Mapping the activity on the whole surface of the brain:

The principles of NIRS Topographic Brain Imaging



Hitachi Medical System

UCL System

The patient interface

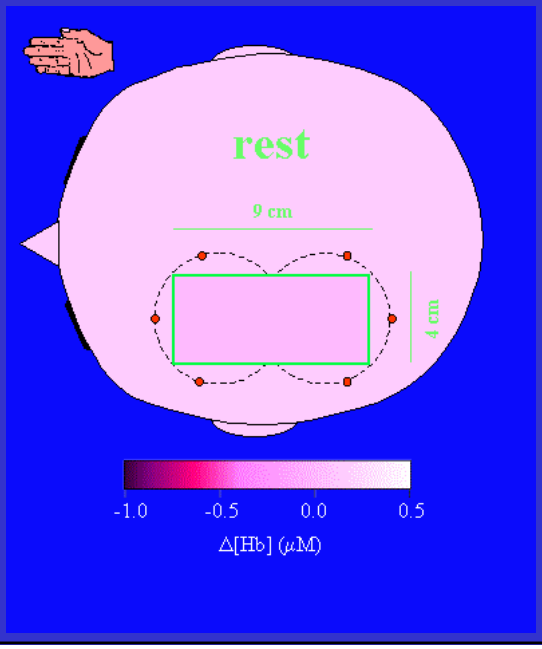
Optical Topography signals in the adult

Motor Cortex activation movie

Hb signal change.

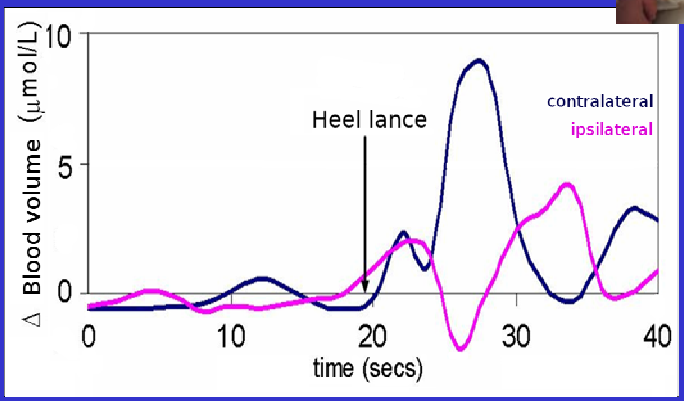
(160 mS per acquisition)

(Franceschini et al 2001)



Optical Topography signals in the infant

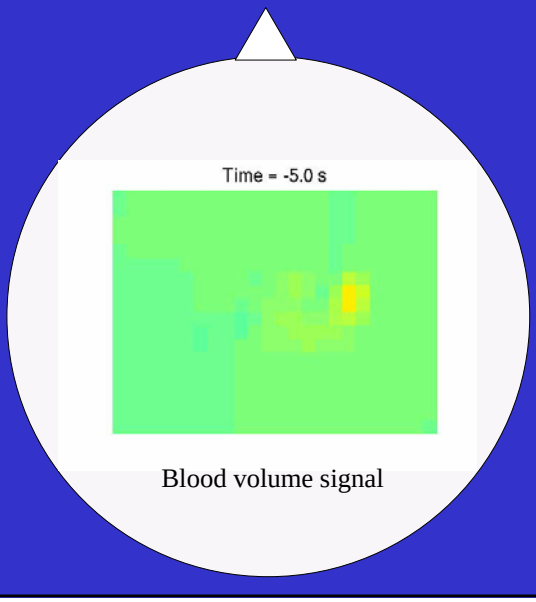
Cortical pain responses to a heel prick in infants (blood volume signal)



Slater et al (2006)

Optical Topography signals in the infant

Cortical pain responses to a heel prick in infants (2)

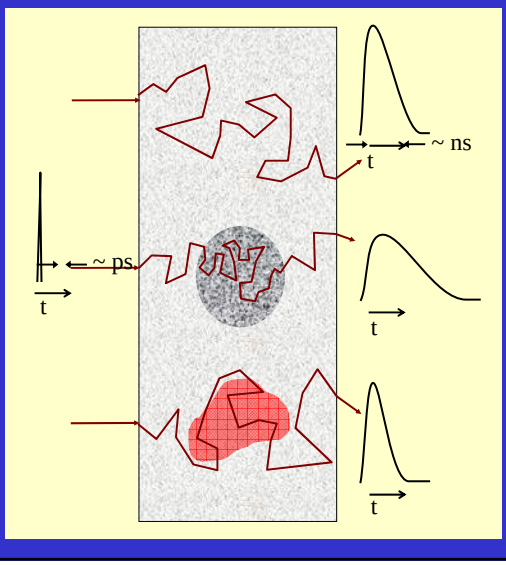


Time resolved measurements to separate the effects of absorption from scatter

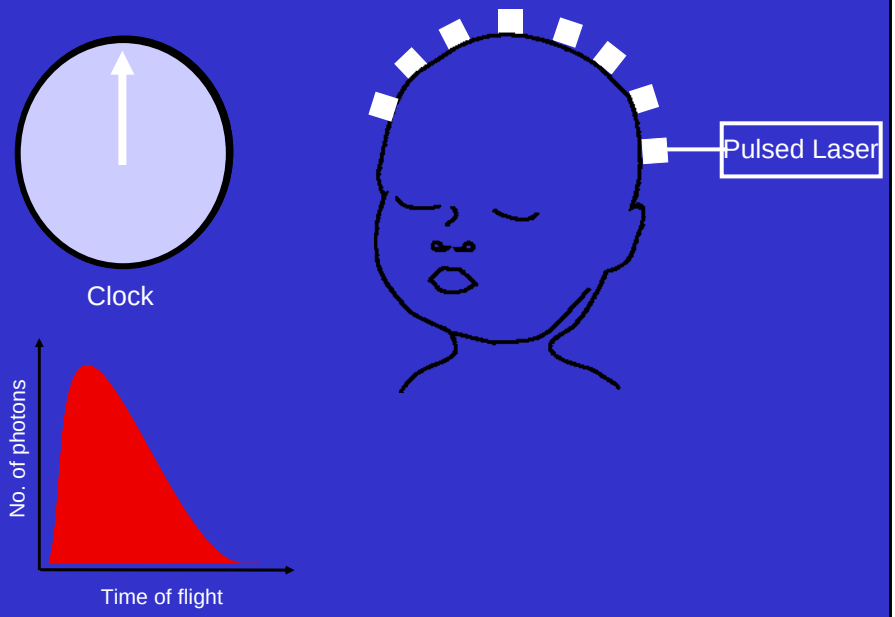
The (temporal) Impulse Response Function of tissue to a pulse of laser light can be used to distinguish between the effects of scatter *and* absorption.

It also allows us to know the optical pathlength from the mean time of flight

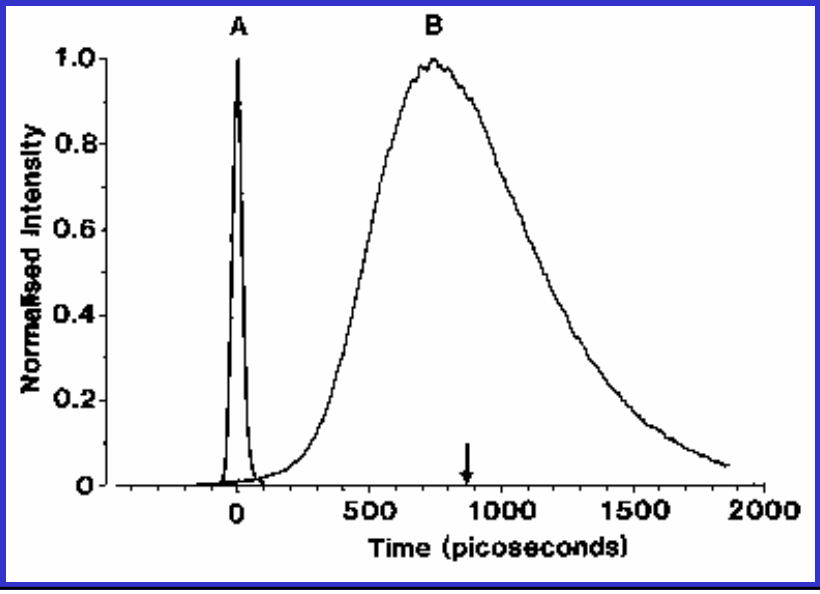
Finally it allows us a better estimate on where the light has travelled and hence permit tomographic (i.e. full 3D) imaging



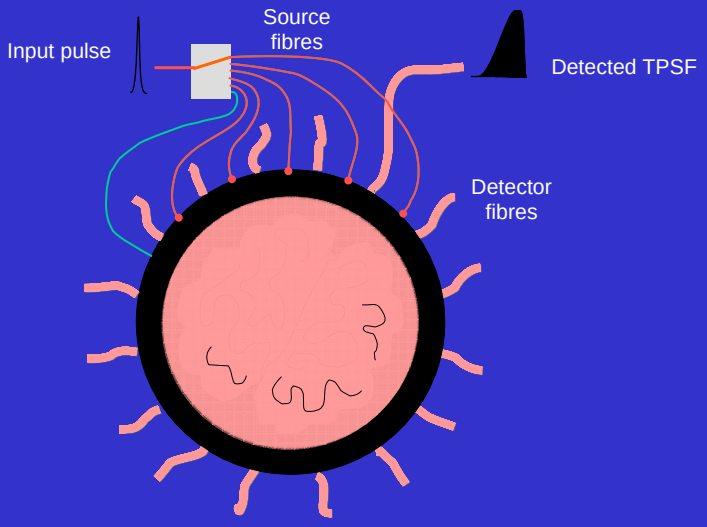
Time Resolved Measurement Principles



Time of Flight Measurement of Optical Pathlength across the Baby Head – 5cm source/detector spacing



The principles of time resolved measurements for optical tomography

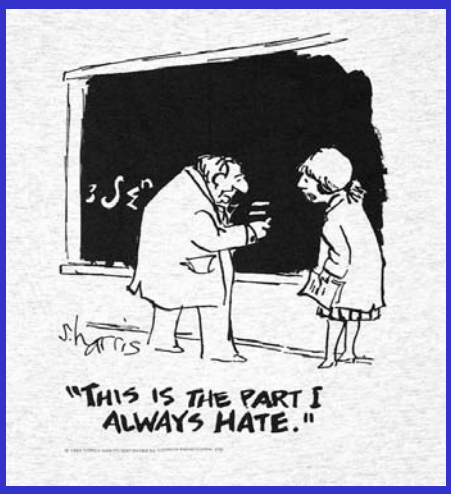


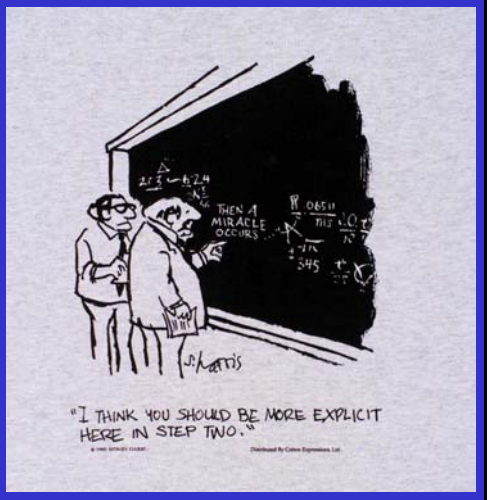
NB. All measurements are made at two different NIR wavelengths

The MONSTIR imaging system

Multi-channel **O**pto-electronic **N**ear-infrared **S**ystem for **T**ime-resolved **I**mage **R**econstruction

The realisation dawns that we need to do some maths!





Tomographic image reconstruction requires knowing where the detected light has travelled

Intensity and time of flight photon distributions are calculated using TOAST

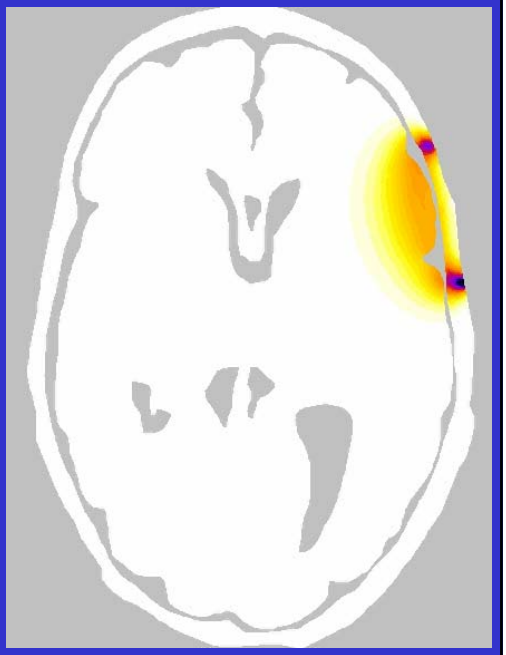
Time resolved

Optical

Absorption &

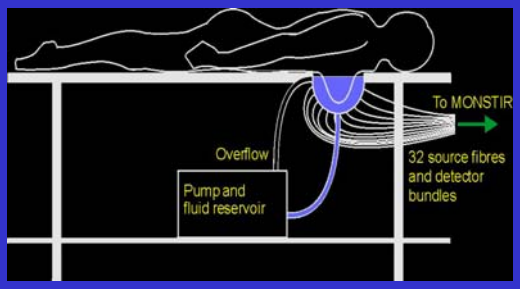
Scattering

Tomography



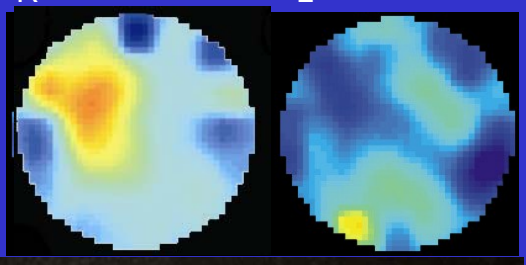
NIRS tomography applied to the breast: Imaging the extra blood volume and different blood oxygenation in tumours

The optical mammography scanning table (note no breast compression)

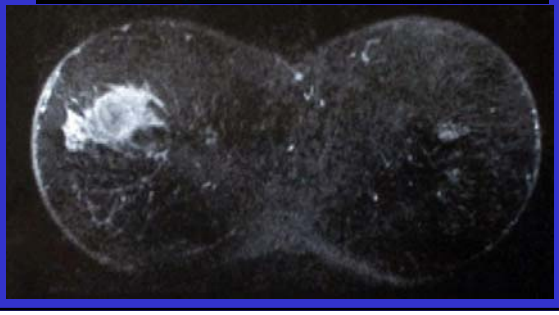


optical mammography results: Invasive ductal grade III carcinoma (48-year-old subject)

R L



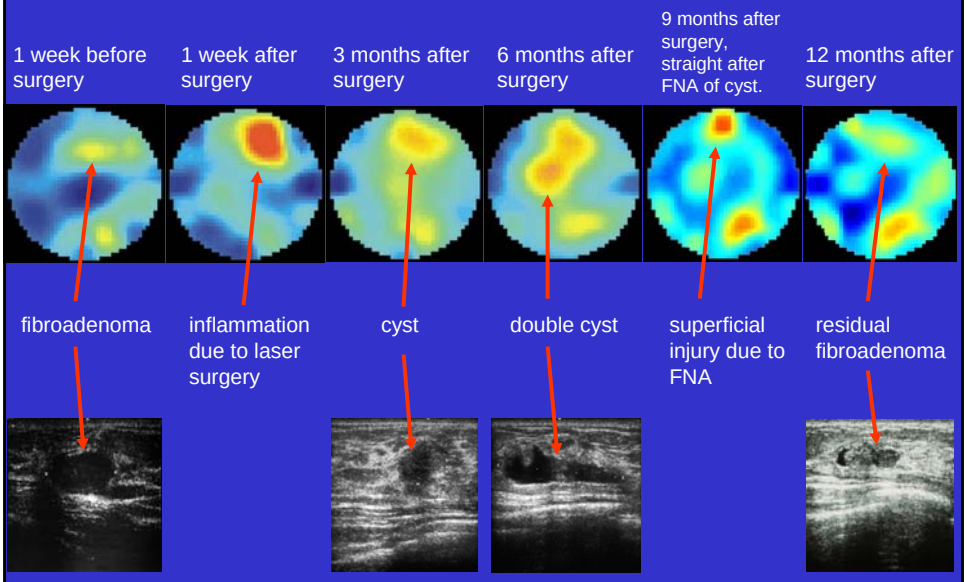
Optical tomography images



Magnavist enhanced MRI image

Interstitial laser photocoagulation treatment of fibroadenoma

26-year-old subject

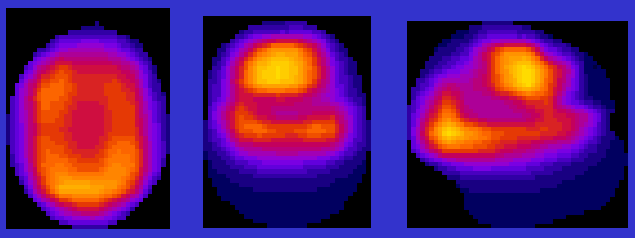


NIRS Optical tomography of the infant brain - the “Creche Helmet”

A baby undergoing an optical tomography study

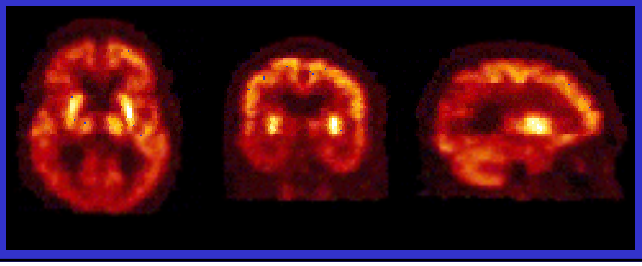
Optical Tomography images of the normal infant brain

Optical image: 32-week female infant



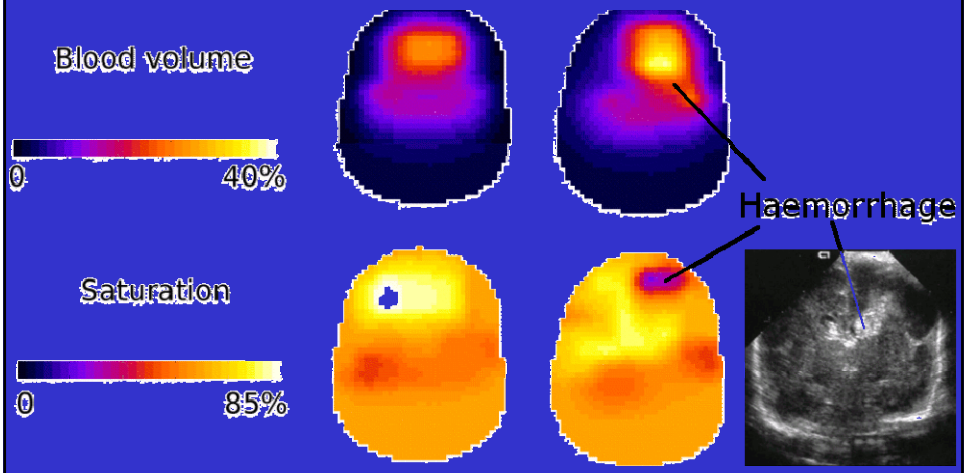
Anatomical slices of pre-term brain

Positron Emission Tomography (PET) image: of adult brain



Optical Tomography images of the abnormal infant brain

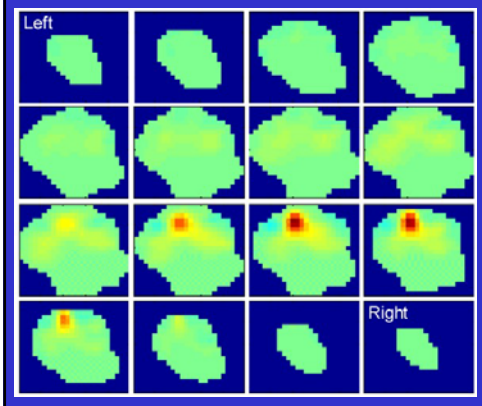
Static imaging of haemorrhage



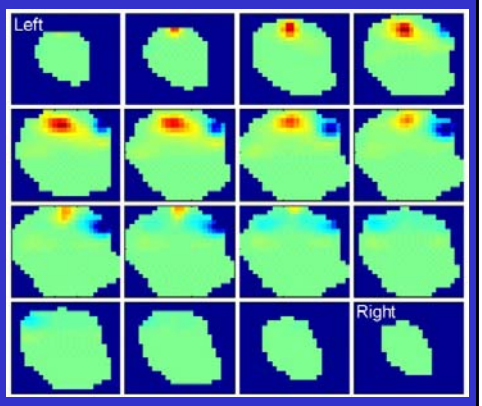
Motor Cortex Activation in Infants

Tomographic mapping of functional activation of the motor cortex in the neonate

(Sequential sagittal slices displayed from a full 3D image)



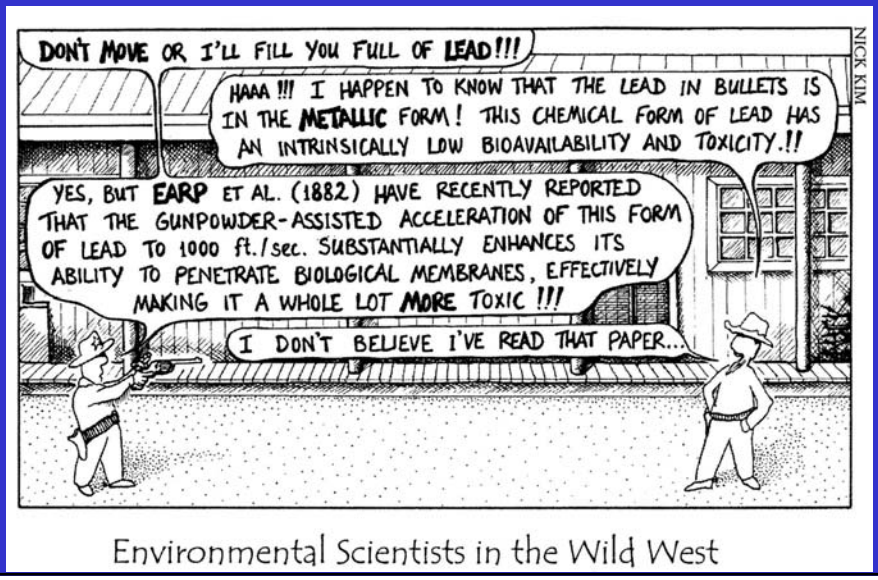
Passive movement of Left Arm



Passive movement of Right Arm

Lessons learned:

(1) Don't restrict yourself to your own area – you never know what you will learn that is relevant



Environmental Scientists in the Wild West

Lessons learned:
(2) Pick good people to work with, give them their head and stand back

Contributors:

Clive Aldridge
Simon Arridge
Topun Austin
Tiziano Binzoni
Tony Bishop
Tara Bland
Gilberto Branco
David Brown
Guy Brown
Tim Cheatle
Chris Cooper
Mark Cope
Kate Costeloe
Gergely Csibra
Brian Davidson
Mauren de Souza
Roberto de Blasi
Geofrey De Visscher
Enrico De Vita
Hamid Dehghani
Michael Douek
Arlene Duncan
David Edwards
Hamid El-Desoky
Louise Enfield
Matthias Essenpries
Nick Everdell
Marco Ferrari
Mike Firbank
Laure Gendron
Adam Gibson Felix Gora
Cornelia Hagman
David Hall
Pat Hamilton
Sally Harkins
Jem Hebden
Julian Henty
Elizabeth Hillman
Mutsu Hiraoka
Veronica Hollis
Peter Hope
Ian Hutchinson
Mark Johnson
David Jennions
Peck Koh
Jan Laufer
Ting Lee
Terence Leung
Tim Lovell
Dave Kirkby
Matthias Kohl
Ivo Kwee
Steve Matcher
Judith Meek
Aladangady Narendra
Eiji Okada
Huw Owen-Reece
Christos Panagiotou
Donald Peebles
Caroline Reid
Os Reynolds
Clare Richardson
Ged Ridgeway
Florian Schmidt
Martin Schweiger
Alex Seifalian
Rebecca Simpson
Martin Smith
Roger Springett
Ilias Tachtsidis
Martin Tisdall
Ian Tullis
Tharshan Vaithianathan
Piet van der Zee
Koen van Rossem
Russell Watson
Kevin Wells
Susan Wray
John Wyatt
Roza Yusof
Giovanni Zaccanti

Funders:

Action Medical Research
BBSRC
EPSRC
European Union
Hamamatsu Photonics KK
Hitachi Medical Ltd
MRC
Royal Society
Swiss National Science Foundation
Wellcome Trust
Wolfson Foundation

…and many many others!

The End!

(or a new beginning at EPSRC)