'ELITEAM'- ESTABLISHMENT OF THE ELI INSTITUTE AT THE UNIVERSITY OF SZEGED: FOUNDATION OF INTERDISCIPLINARY RESEARCH IN THE FIELD OF LASERS AND THEIR APPLICATIONS

MICROCIRCULATION IMAGING WITH LIGHT AND SOUND

TÁMOP-4.2.2.D-15/1/KONV-2015-0024 project

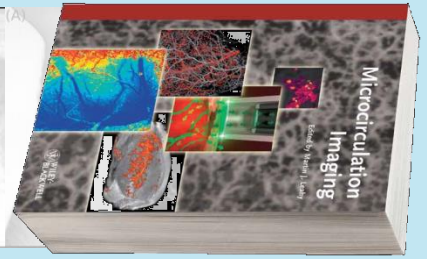
SZÉCHENYI 2020

HUNGARIAN GOVERNMENT

European Union
European Social Fund

INVESTING IN YOUR FUTURE

TOMI
Tissue optics & microcirculation imaging



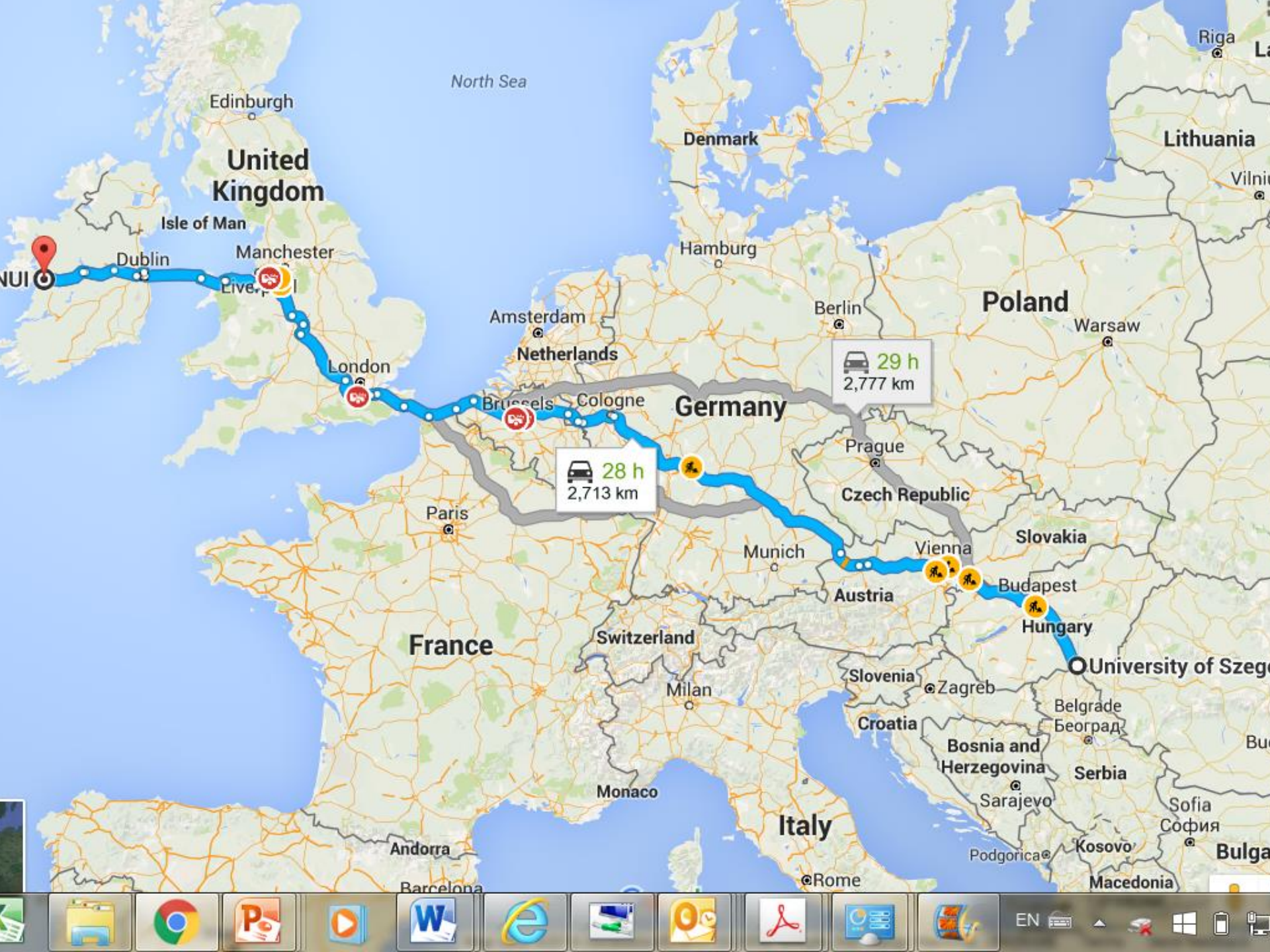
Microcirculation Imaging with Light and Sound

04/07/2016

Prof. Martin J. Leahy
Chair of Applied Physics, NUI Galway
Scientific Director, NBIP Ireland

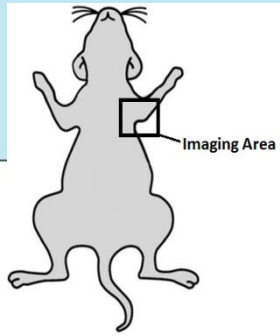
NUI Galway
OÉ Gaillimh

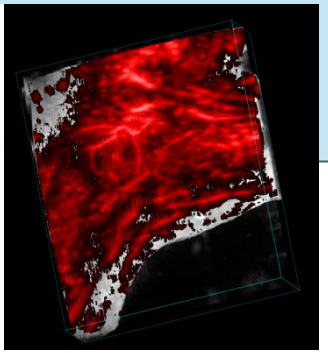
NBIPI

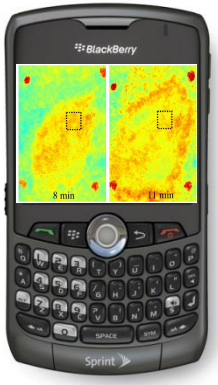

North Sea
Edinburgh
United Kingdom
Isle of Man
Dublin
Manchester
London
Amsterdam
Netherlands
Brussels
Cologne
Germany
Hamburg
Denmark
Berlin
Poland
Warsaw
Lithuania
Riga
29 h
2,777 km
28 h
2,713 km
Prague
Czech Republic
Paris
Munich
Vienna
Slovakia
Austria
Budapest
Hungary
France
Switzerland
Slovenia
Zagreb
Milan
Croatia
Belgrade
Bosnia and Herzegovina
Serbia
Sarajevo
Monaco
Italy
Andorra
Barcelona
Rome
Podgorica
Kosovo
Macedonia
Sofia
EN

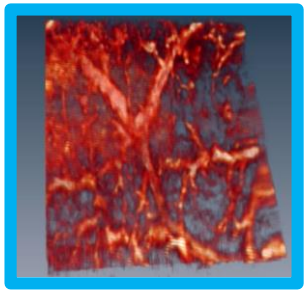
Microcirculation Imaging Techniques – TOMI lab

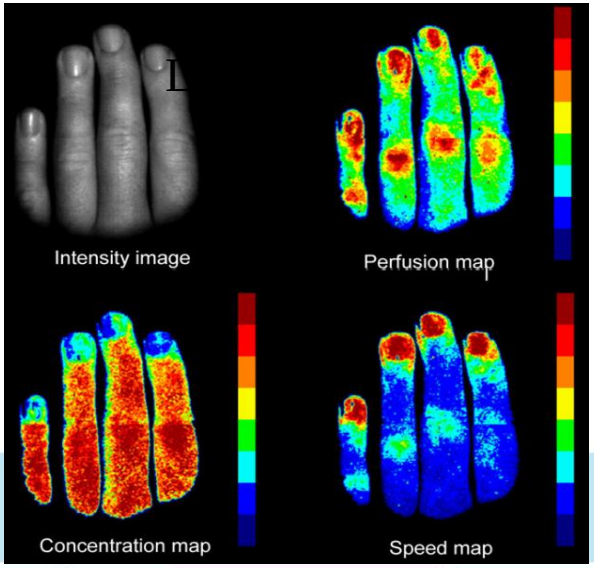
- Laser Doppler perfusion imaging (LDPI)
- Laser speckle contrast imaging (LSCI)
- Tissue viability imaging (TiVi)
- Photoacoustic Imaging (PAI)
- Optical coherence tomography (OCT)

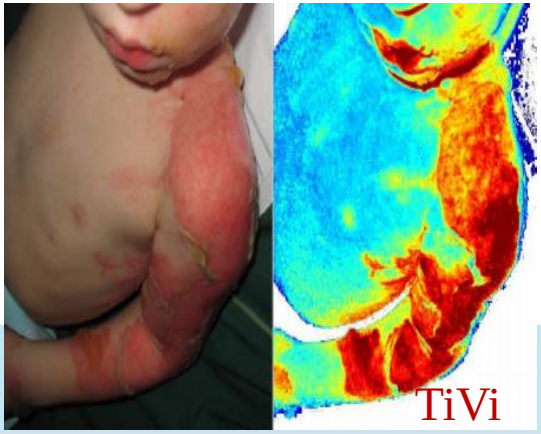


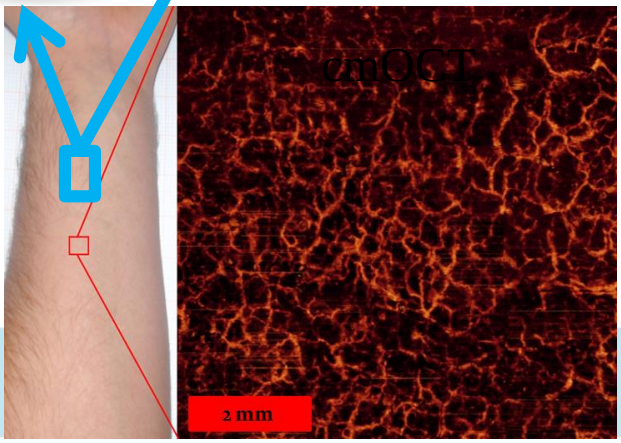


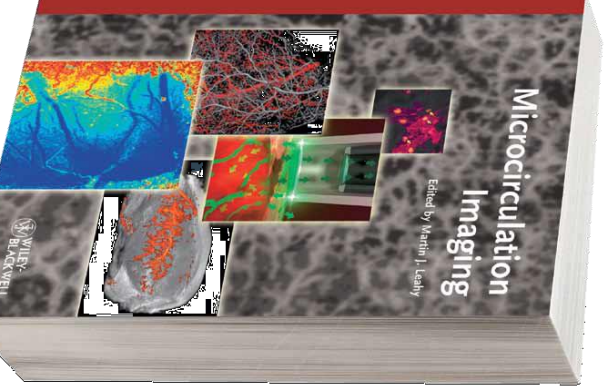












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Tissue optics & microcirculation imaging

A Historical Perspective of Imaging of the Skin and Its Gradual Uptake for Clinical Studies, Inclusive of Personal Reminiscences of Early Days of Microcirculation Societies Terence J. Ryan and Martin J. Leahy

Sidestream Dark-Field (SDF) Video Microscopy for Clinical Imaging of the Microcirculation Dan M. J. Milstein, Rick Bezemer and Can Ince

Clinical Applications of SDF Videomicroscopy Daniel De Backer and Jean-Louis Vincent

Laser Doppler Flowmetry Ingemar Fredriksson, Marcus Larsson and Tomas Strömberg

Toward Assessment of Speed Distribution of Red Blood Cells in Microcirculation Adam Liebert, Stanislaw Wojtkiewicz and Roman Maniewski

Fast Full-Field Laser Doppler Perfusion Imaging Wiendelt Steenbergen

Speckle Effects in Laser Doppler Perfusion Imaging Wiendelt Steenbergen

Laser Speckle Contrast Analysis (LASCA) for Measuring Blood Flow J. David Briers, Paul M. McNamara, Marie Louise O'Connell and. Martin J. Leahy

Tissue Viability Imaging Jim O'Doherty, Martin J. Leahy and Gert E. Nilsson

Optical Microangiography: Theory and Application Ruikang K. Wang and Hrebesh M. Subhash

Photoacoustic Tomography of Microcirculation Song Hu and Lihong V. Wang

Fluorescence and OCT Imaging of Microcirculation in Early Mammalian Embryos Irina V. Larina, Mary E. Dickinson and Kirill V. Larin

High Frequency Ultrasound for the Visualization and Quantification of the Microcirculation F. Stuart Foster

Studying Microcirculation with Micro-CT Timothy L. Kline and Erik L. Ritman

Imaging Blood Circulation Using Nuclear Magnetic Resonance Christian M. Kerskens, Richard M. Piech and James F. M. Meaney

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Microcirculation Imaging Reviews

Daly, S. M. and Leahy, M. J., 2013. 'Go with the flow': A review of methods and advancements in blood flow imaging. *J. Biophoton.* 6 (3) 217–255. doi:10.1002/jbio.201200071.

DOI:10.1111/micc.12284

Invited Review

An Updated Review of Methods and Advancements in Microvascular Blood Flow Imaging

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*Department of Applied Physics, Tissue Optics and Microcirculation Imaging, National University of Ireland, Galway, Ireland; †Royal College of Surgeons in Ireland, Dublin, Ireland

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Received 17 January 2016; accepted 17 April 2016.

Classics of Scientific Method

THE DISCOVERY OF THE CIRCULATION OF THE BLOOD

Charles Singer

1922

PLATE VIII

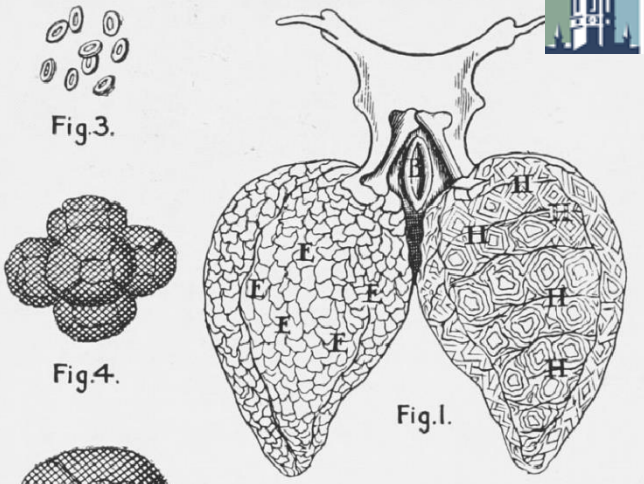


Fig.1.

Fig.3.

Fig.4.

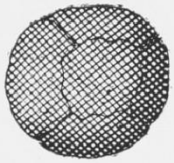


Fig.5.

Fig.6.

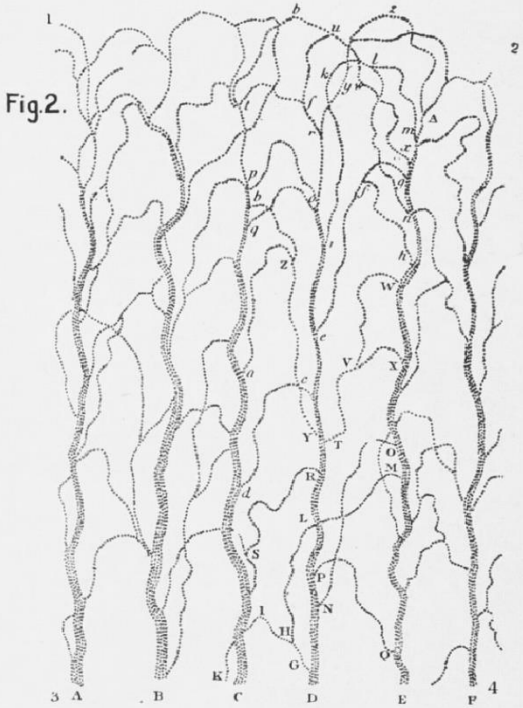
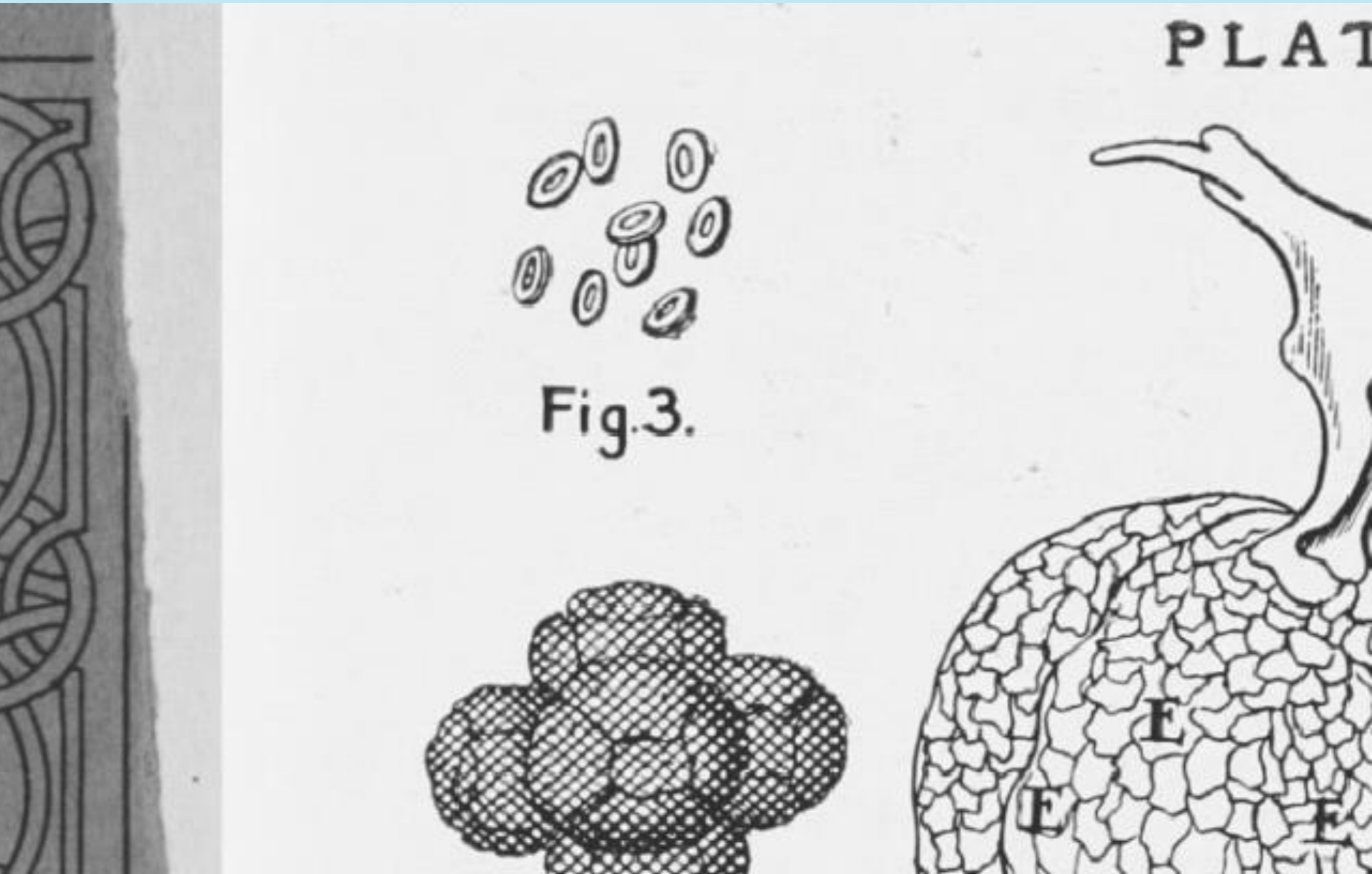


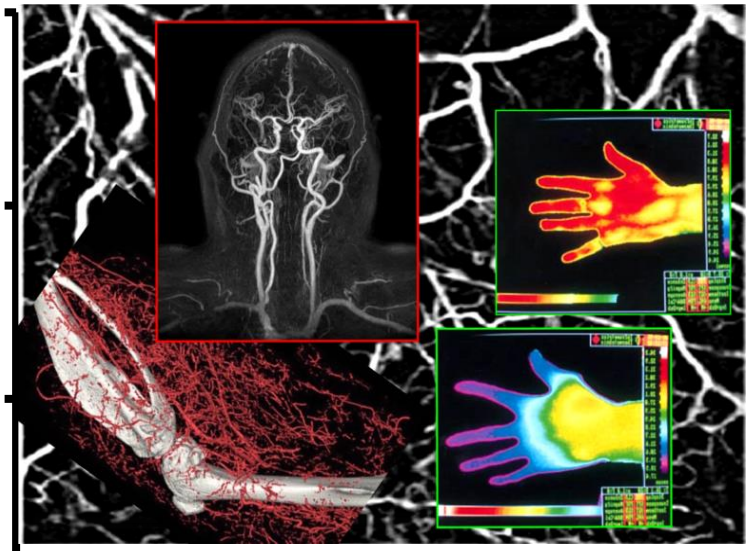
Fig.2.

FIG. 1. LUNG OF FROG, MAGNIFIED, SHOWING CAPILLARIES. From MALPIGHI.
FIG. 2. CAPILLARY NETWORK IN TAIL OF EEL. From LEEUWENHOEK. A, C, E are Veins, and B, D, F are Arteries.
FIG. 3. RED BLOOD CORPUSCLES OF SALMON. From LEEUWENHOEK.
FIGS. 4 AND 5. HUMAN RED BLOOD CORPUSCLES. From LEEUWENHOEK.
FIG. 6. HUMAN RED BLOOD CORPUSCLES DRAWN FROM THE OBJECT UNDER A MODERN MICROSCOPE.

Leeuwenhoek



Microcirculation



All fields

Physical Sciences

Total Publications per year

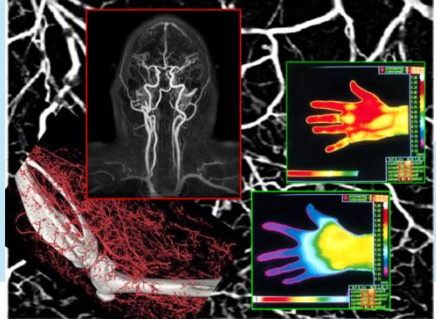
In Physical Science Journals

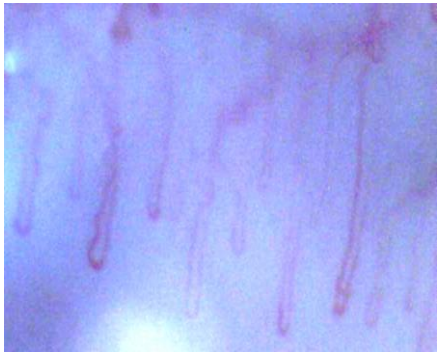
2500
2000
1500
1000
500
0

350
300
250
200
150
100
50
0

1960
1970
1980
1990
2000
2010

Microcirculation





Motivation

- **Microcirculation serves key functions within the body:**
  - **Exchange nutrients and metabolic waste to body**
  - **Regulate body temperature.**
  - **Regulate blood pressure.**

- **Structural changes associated with disease**
  - **Diabetes**
  - **Raynaud's syndrome**
  - **Cancer**

Sidestream dark-field (SDF) imaging

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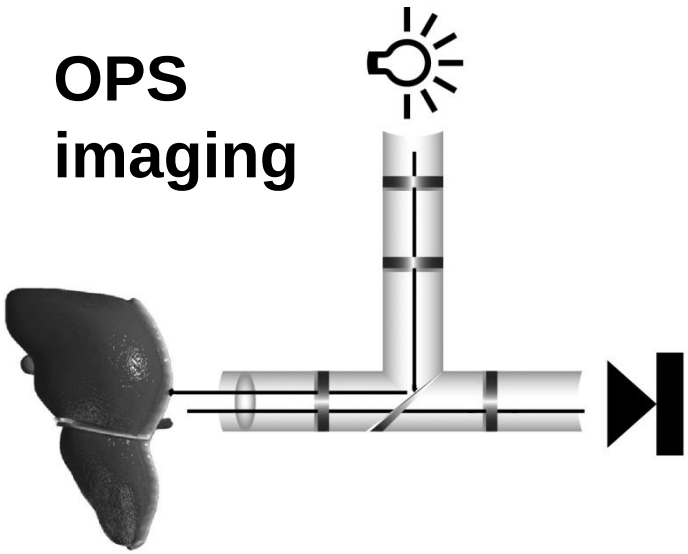
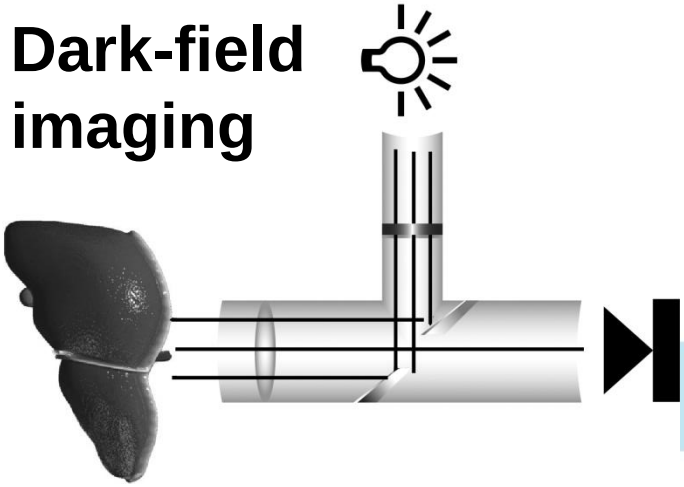
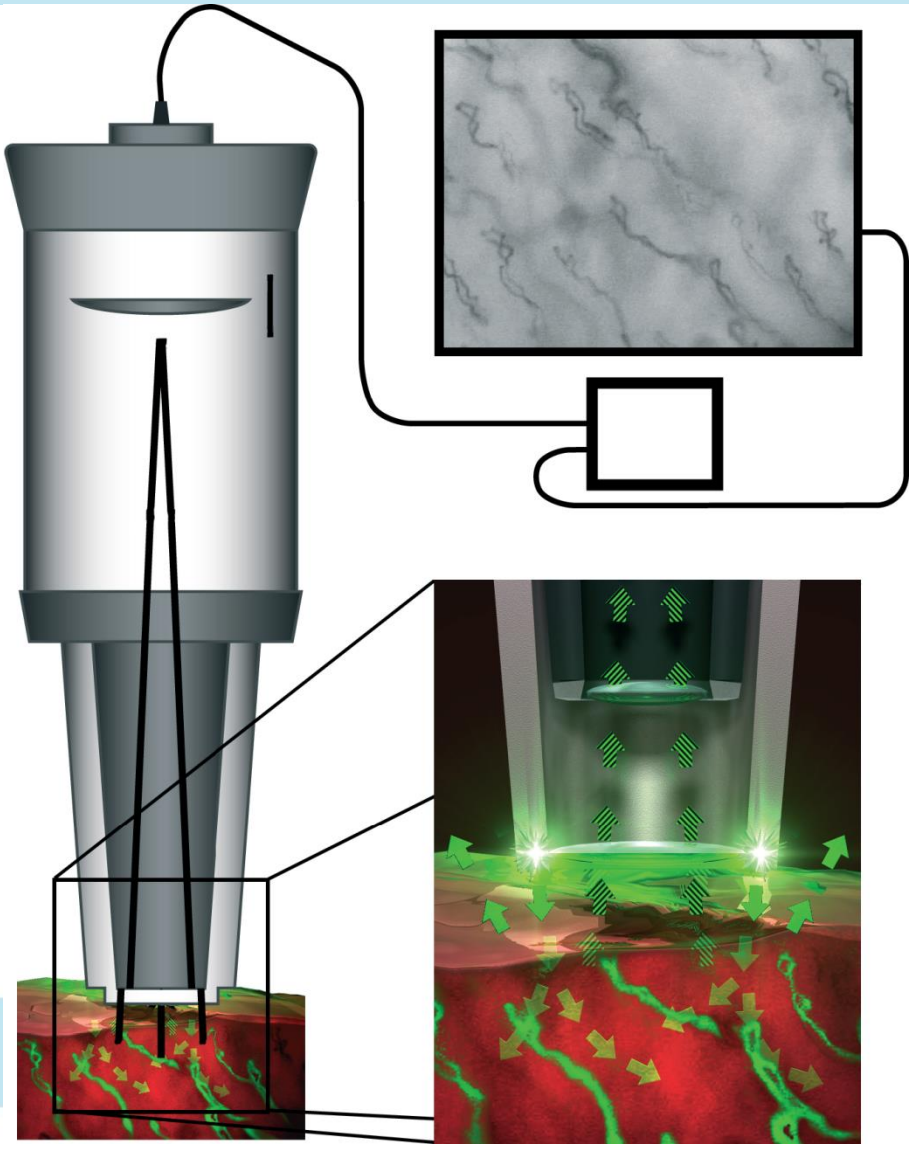
OPS imaging



Dark-field imaging





Heidelberg Scanning Laser Ophthalmoscope

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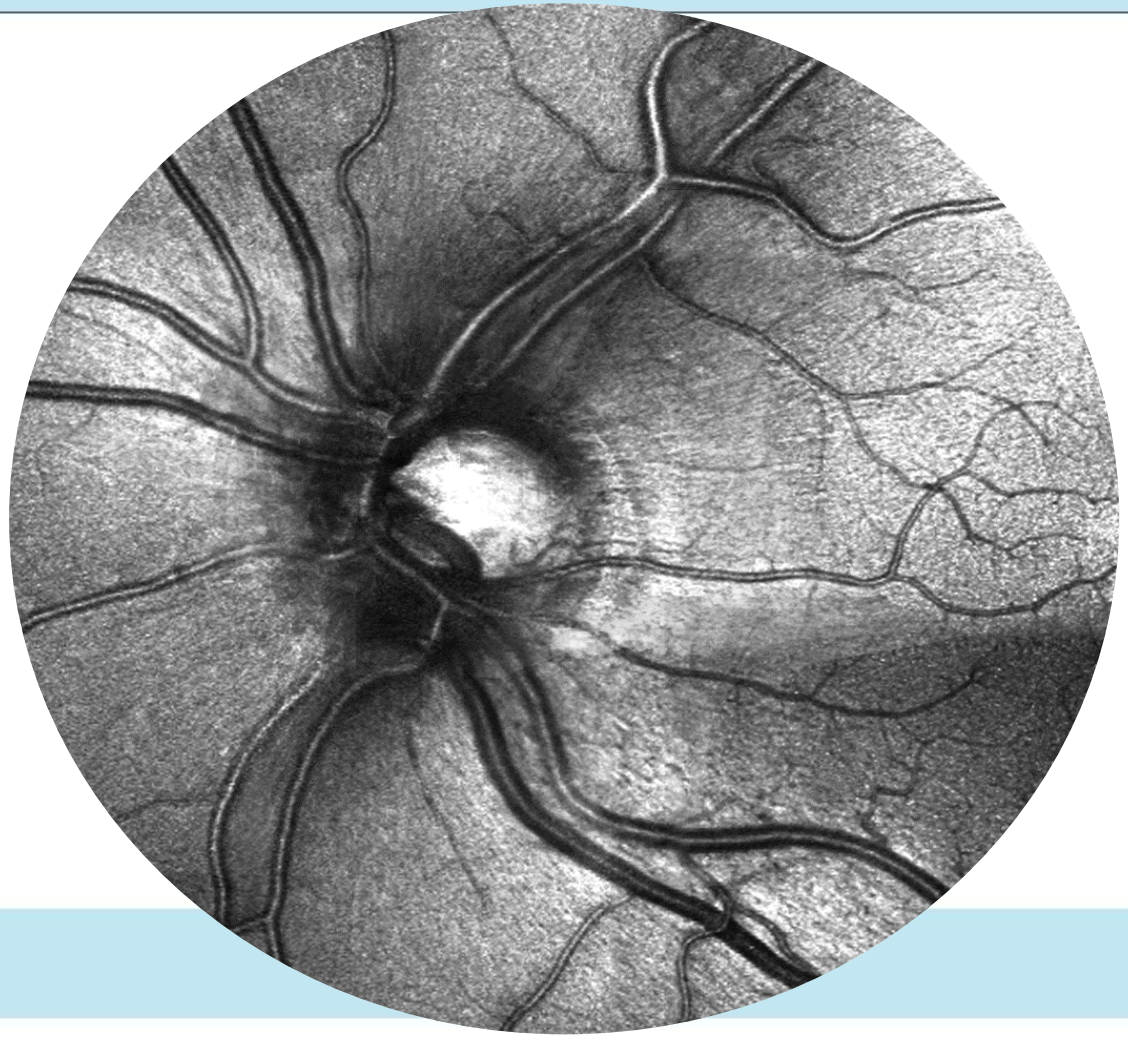
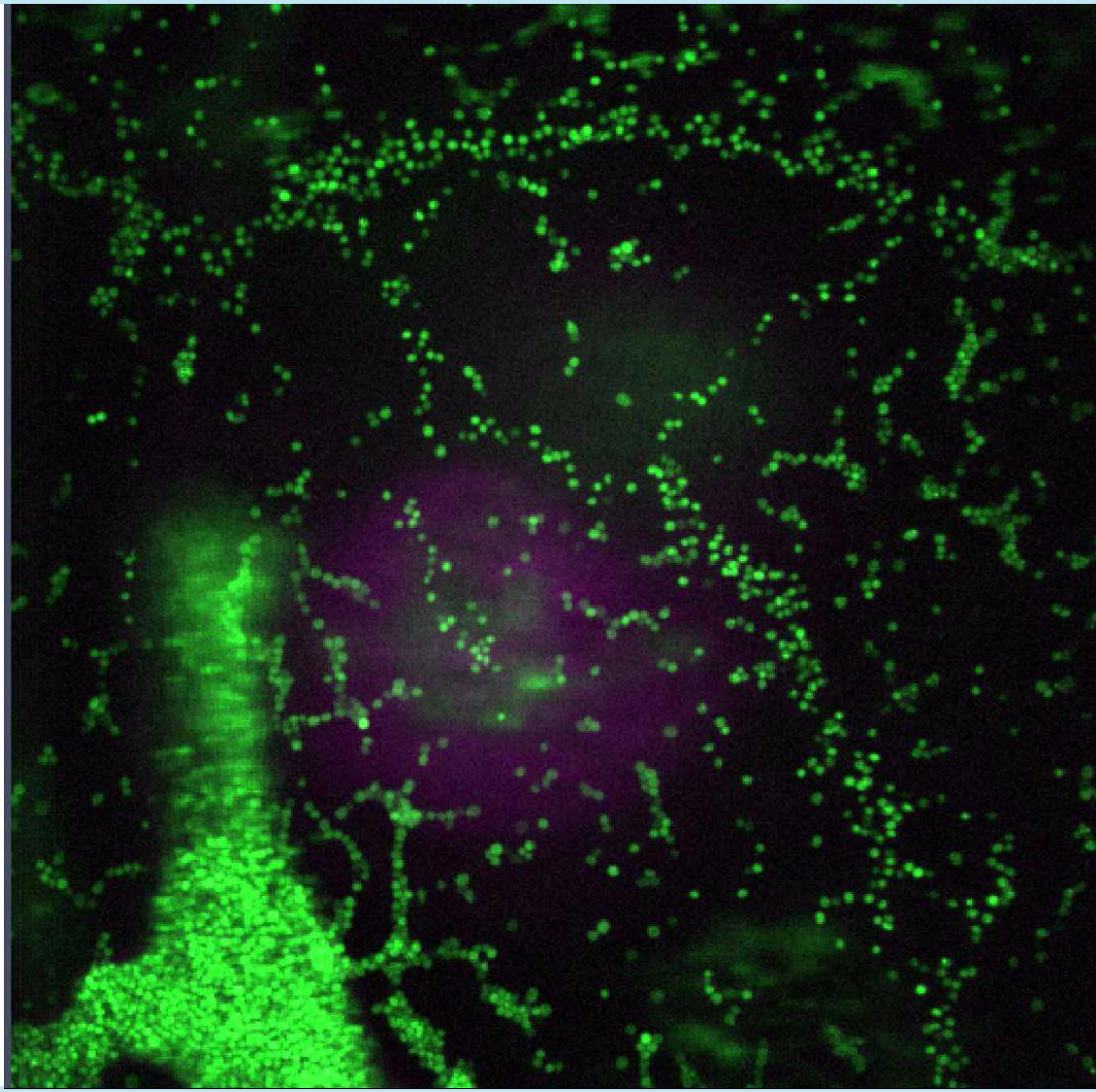
Microvessel diameter measurement for endothelial function assessment



NUI Galway
OÉ Gaillimh

Confocal Microscopy

- Wonderful, but
- Toxic
- Severely depth limited
  - c. 100 μm



Courtesy of Prof. Larina

Laser Doppler and Combretastatin

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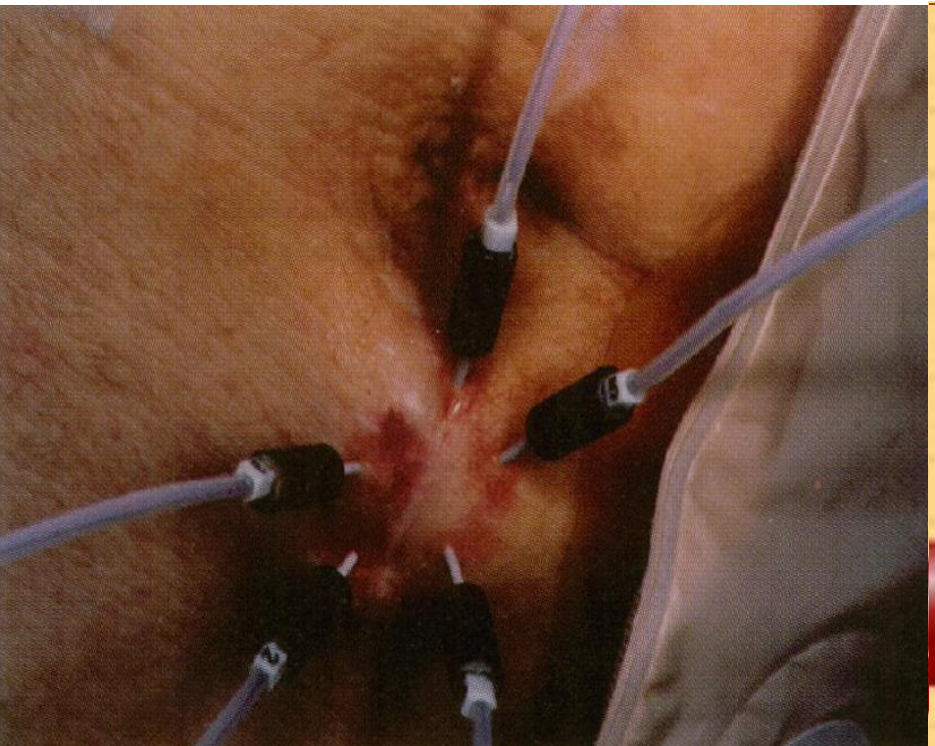
Tissue optics & microcirculation imaging

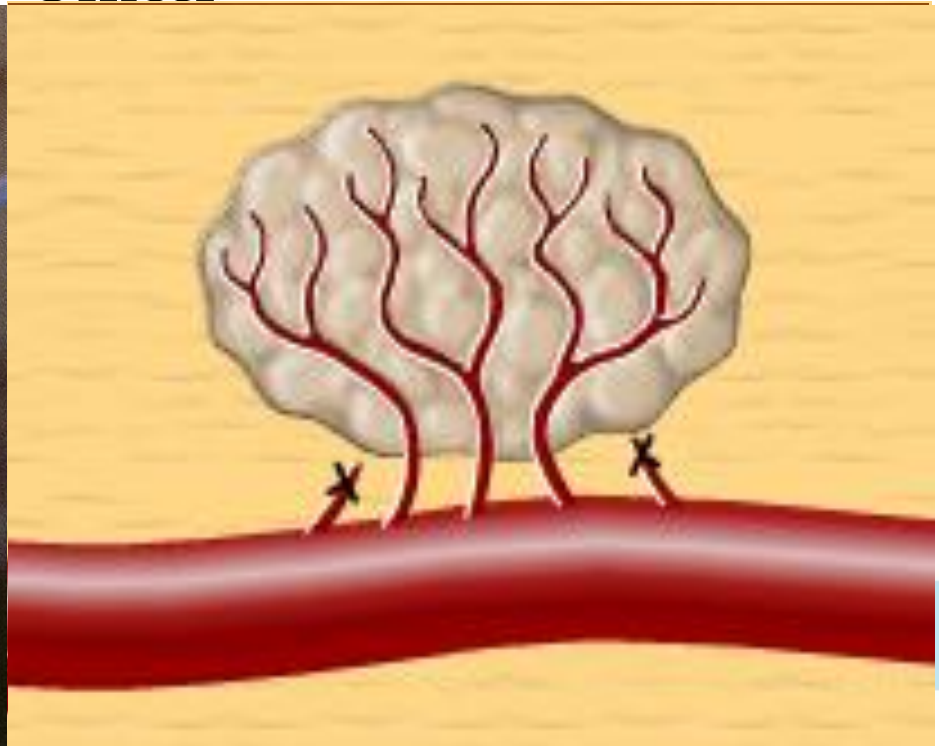
OXFORD OPTRONIX

Martin Leahy, DPhil
Director of R&D



Dai Chaplin, Ph.D.
Head of Research and Development & Chief Scientific Officer

OXIGENE

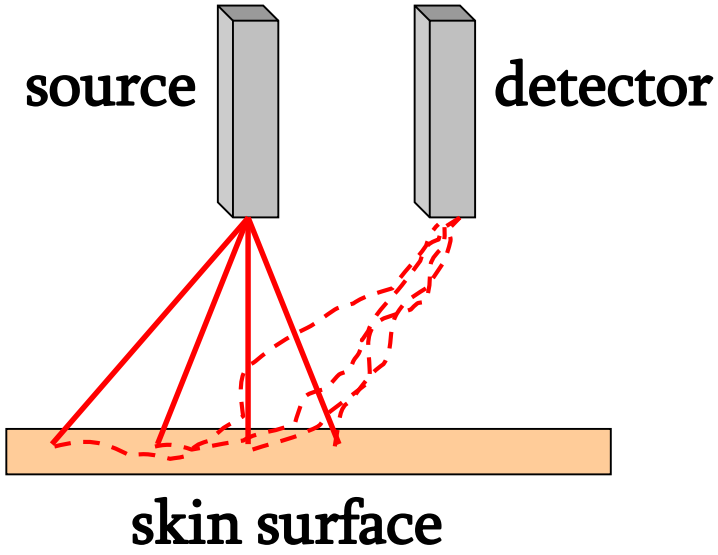


British Journal of Cancer 74, 260 – 263 (1996)

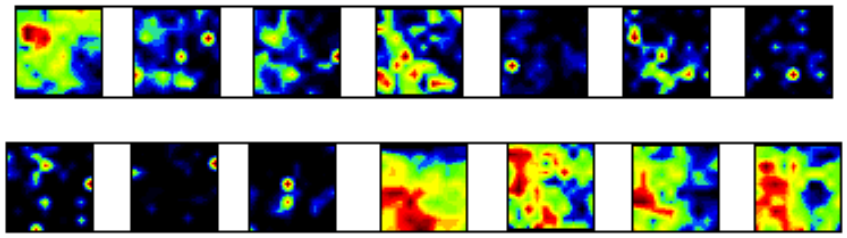
Microcirculation Techniques

Sequential raster scanning of tissue creating a colour coded "perfusion" image of underlying vasculature

Cannot monitor real-time changes in microvasculature



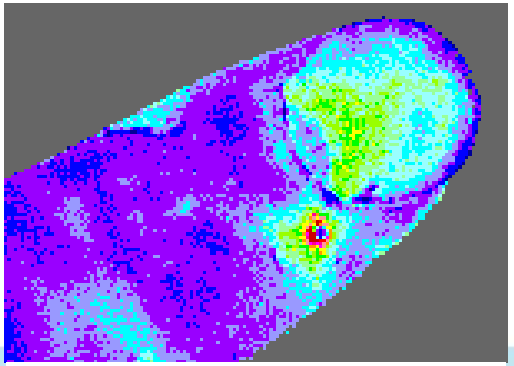
Example during brachial artery occlusion



Leahy, M.J., de Mul, F.F.M, Nilsson, G.E., and Maniewski, R
Principles and Practice of the laser Doppler perfusion technique,
TECHNOLOGY AND HEALTH CARE, pp 143-162 7, 1999

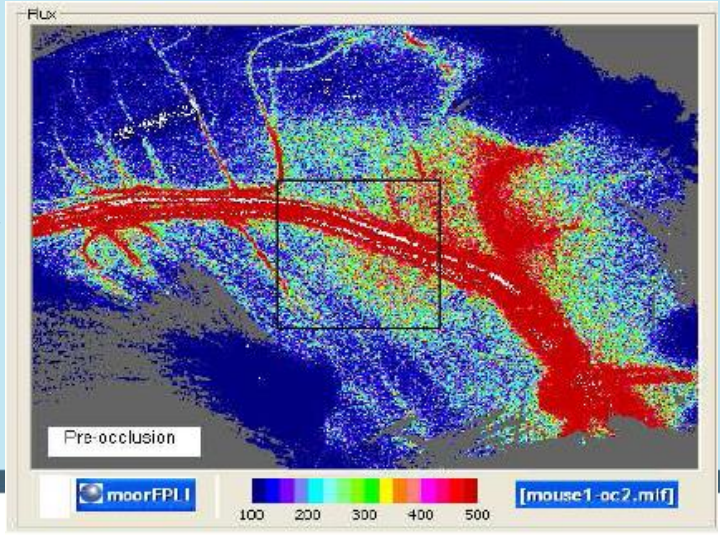
Laser Speckle

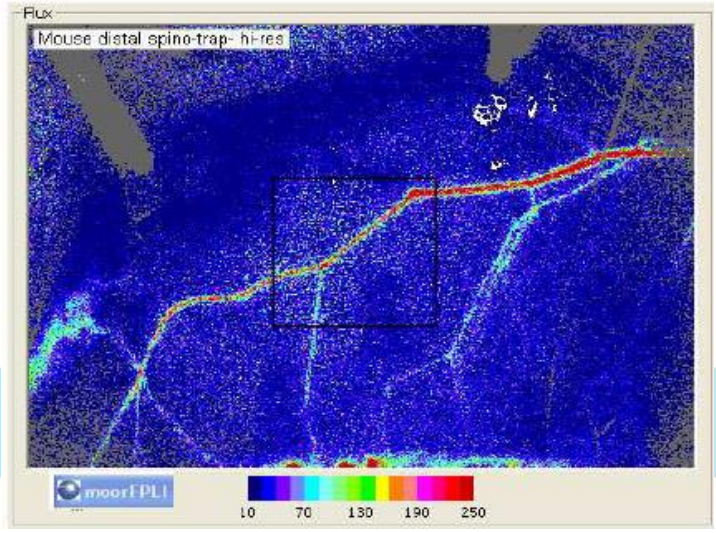
- The line scanner generates quite good images that look like ordinary LDPI images - a new image can be generated every 10 second or faster.
- “the image acquisition times are much shorter - 50 x 64 pixels in 5 seconds!”
- The **FLPI** unit generates real-time images (or close to real time)
- What the images really display? -

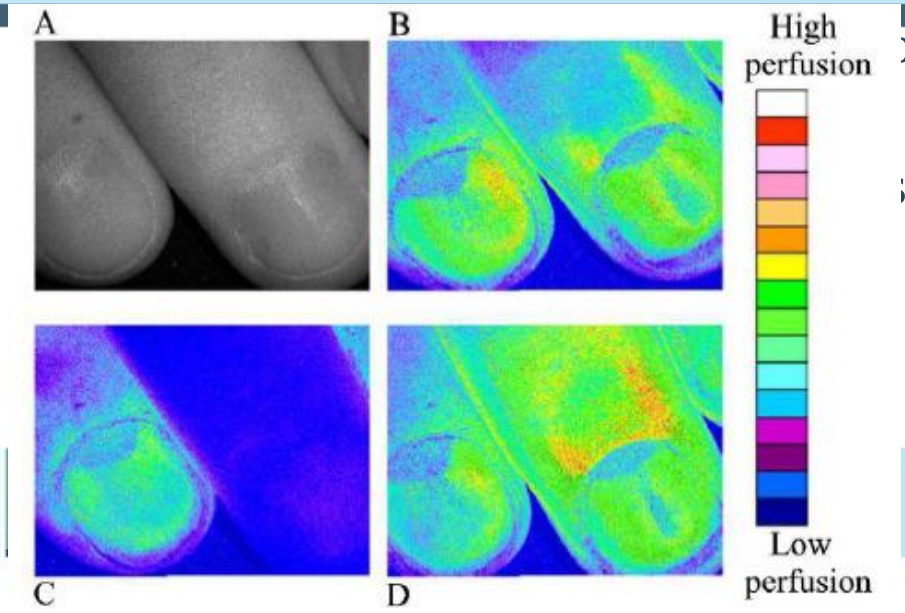


Laser Speckle Imaging

- First commercial medical imager in 2007 (Moor Instruments)
- Known limitations:
  - Studies limited to exposed tissues (shallow imaging depth due to laser power density and $P(\omega)$
  - Biological zero







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Light penetration

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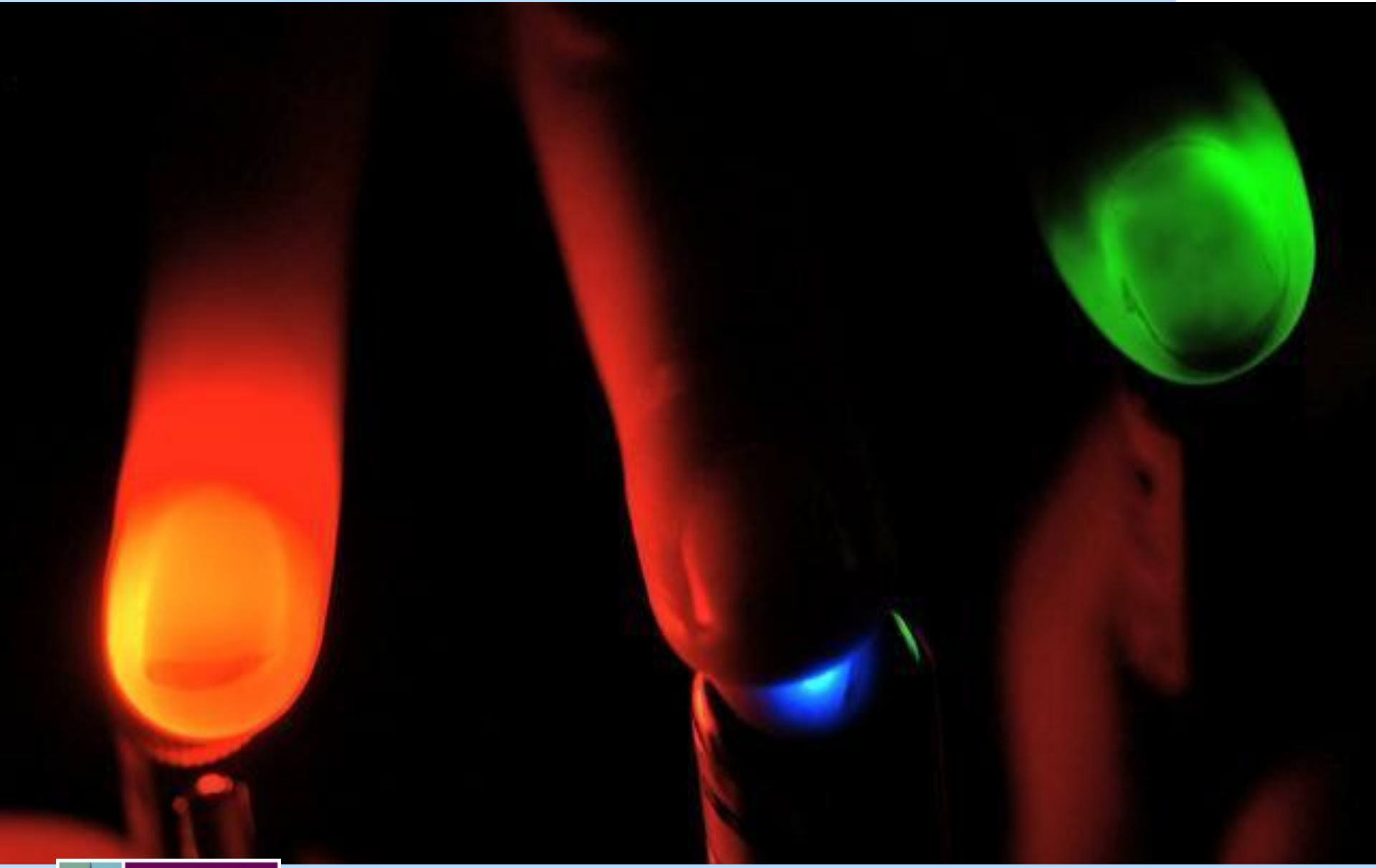
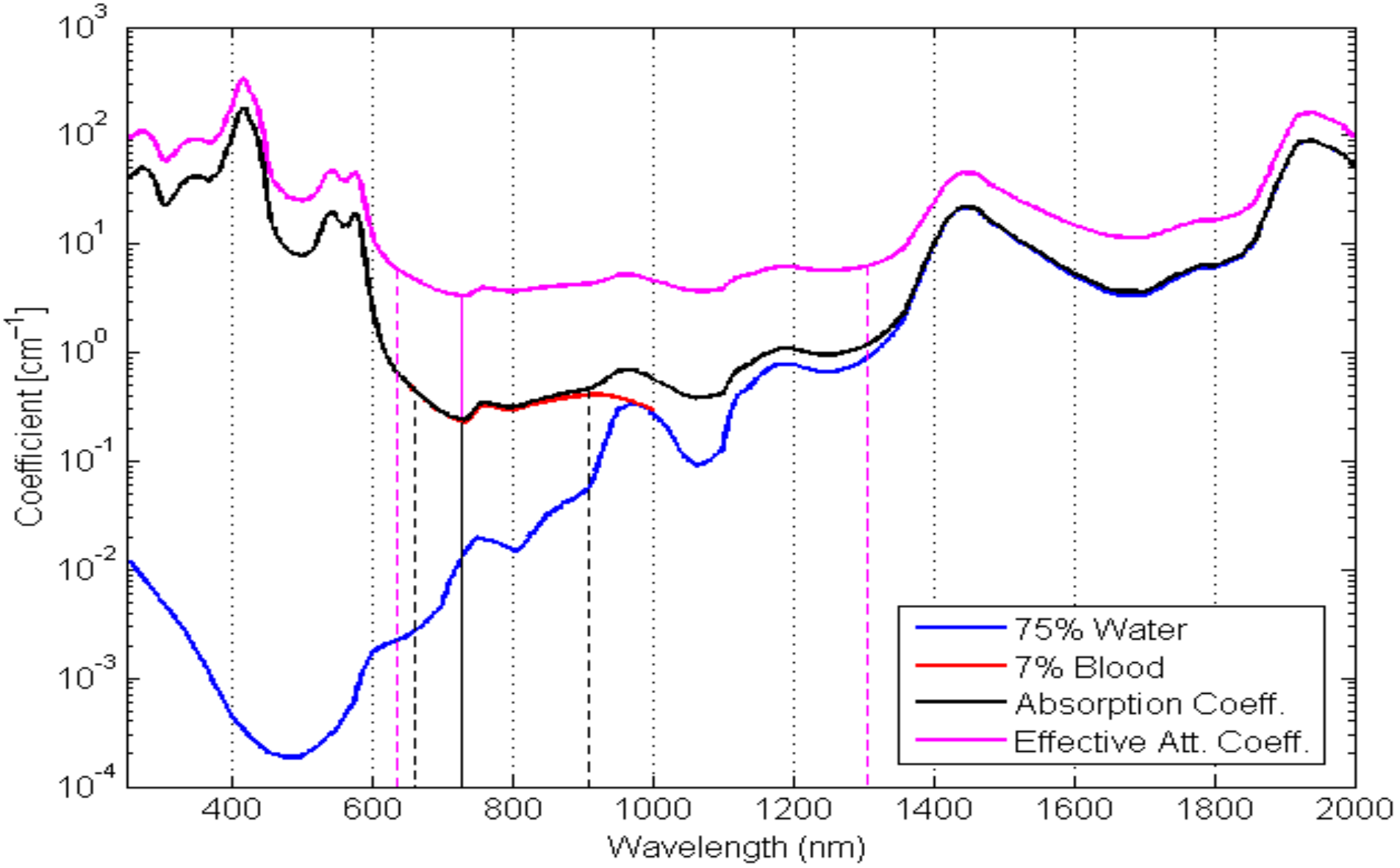


NUI Galway

Image from www.biophonticsWorld.com

National University of Ireland, Galway

Breast tissue



NUI Galway
OÉ Gaillimh

Wheels Bridge

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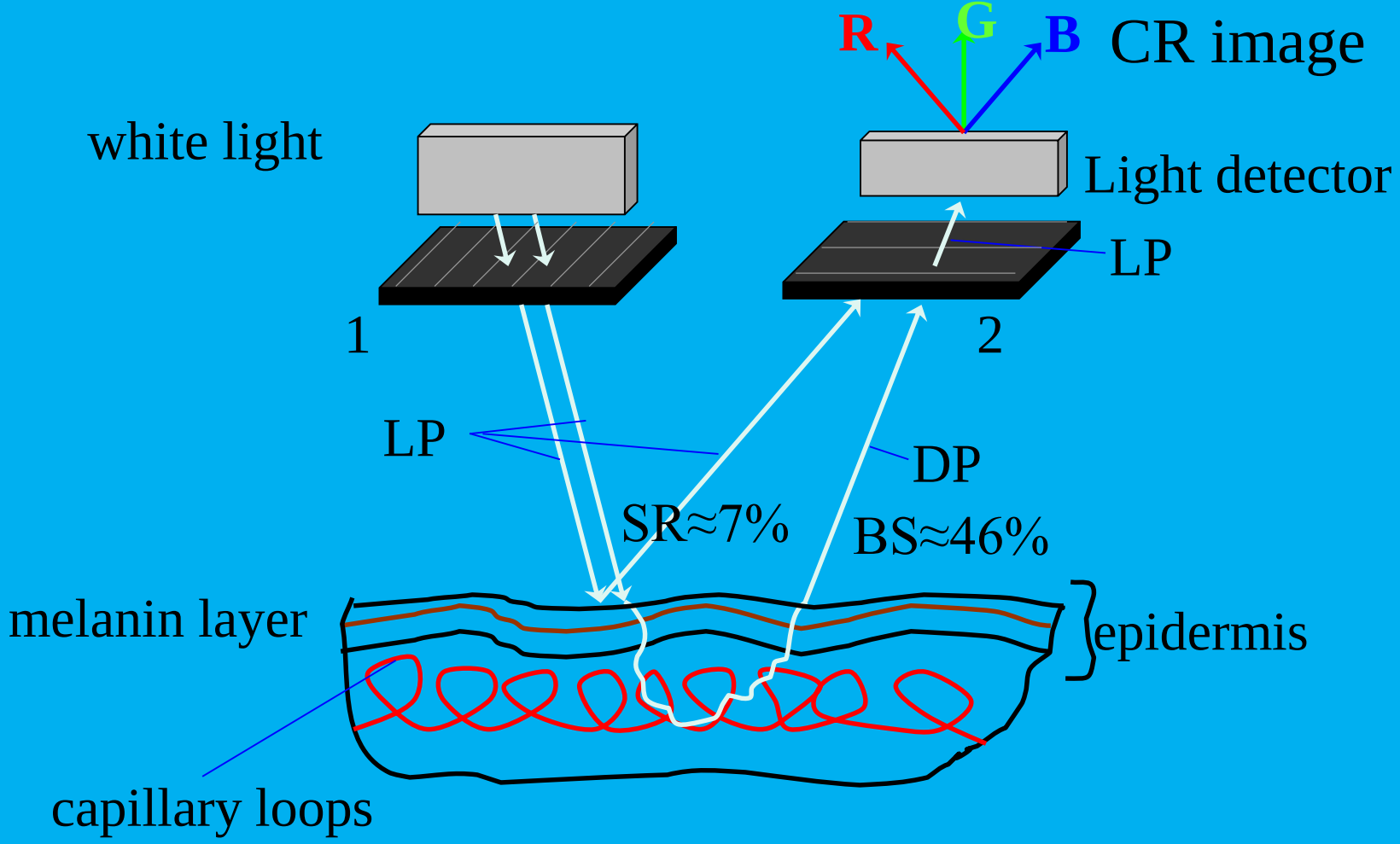
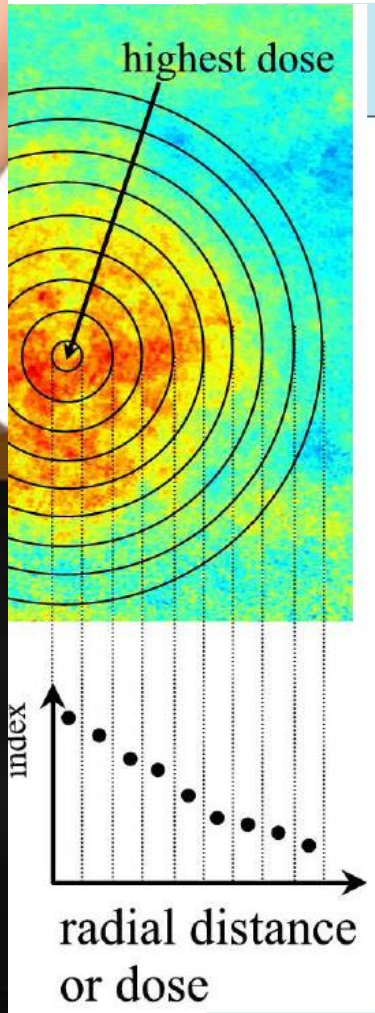
How TiVi Works



1,2 = polarisers LP= Linear Polarised DP= Depolarised SR = surface reflection BS = backscattered CR = cross polarised

Skin Res and Tech – **13** (4) 2007; *Opt-Elect Rev* **16**, 2008.; *J. Biomed. Opt.* **14** (3) 2009; *J. Biophotonics*, **3**, 2010; *Arch Derm Res* **303** (2)

nemal



O'Doherty, J., *et al.*, 2011 .*Arch Derm Res (2010)*

Commercially available mHealth devices

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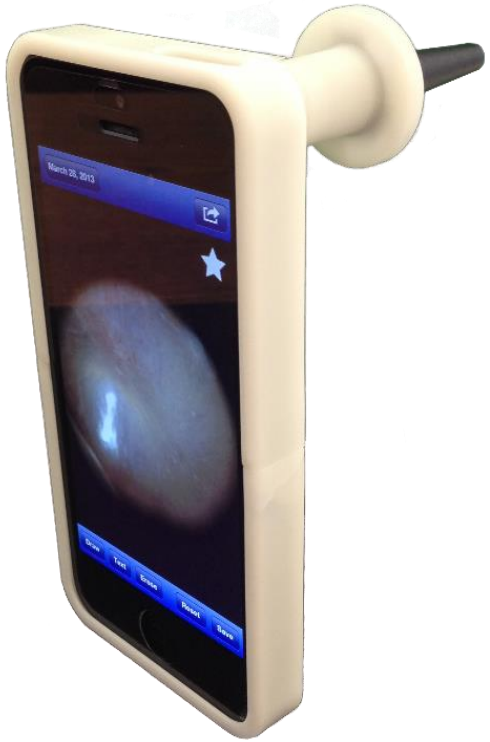
Otoscope

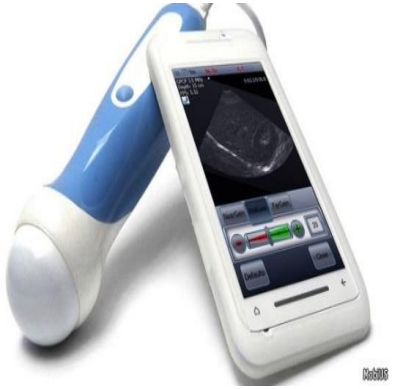


Dermascope

Ophthalmoscope

Microscope

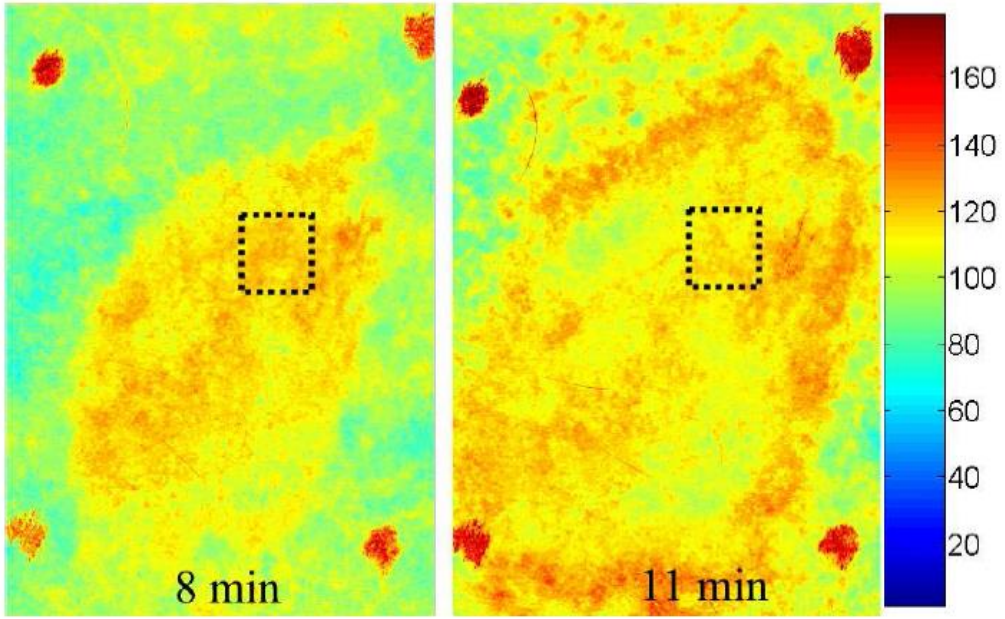
Ultrasound

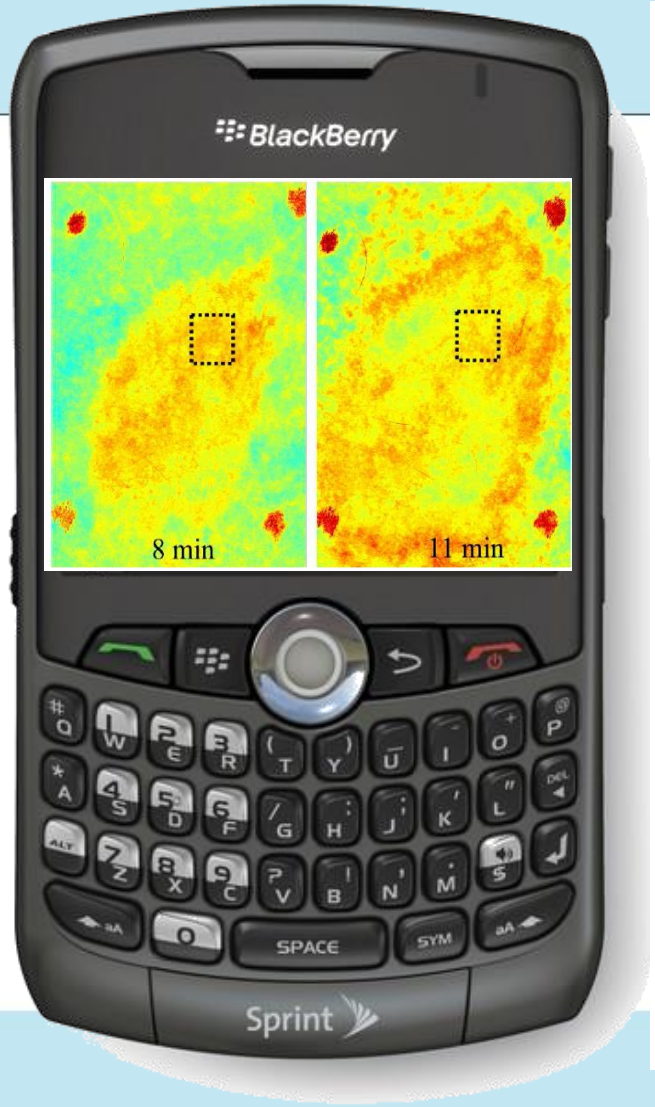


Mobile platform

Swelling reduces TiVi index value

18% reduction in averaged value of dashed box while the edges increase





J. Biophotonics 1–4 (2010) / DOI 10.1002/jbio.201000050.
J. Physiological Measurement (2010)

Mobile platform

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J. Biophotonics 1–4 (2010) / **DOI** 10.1002/jbio.201000050

Journal of
BIOPHOTONICS

LETTER

Cellular phone-based photoplethysmographic imaging

Enock Jonathan and Martin J. Leahy*

Tissue Optics and Microcirculation Imaging (TOMI) Facility, National Biopho
Department of Physics, University of Limerick, Ireland

Received 4 April 2010, revised 3 August 2010, accepted 3 August 2010
Published online 6 September 2010

Key words: photoplethysmography, biophotonics, optical imaging, cel

We present study results on visible light reflection photoplethysmographic (PPG) imaging with a mobile cellular phone operated in video imaging mode. PPG signal components around 0.1 Hz attributed to the sympathetic component of the heart rate, 1 Hz as the heart rate and 2 Hz as heart rate high order harmonic were quantified on the index finger of a healthy volunteer. The green channel reported PPG signals throughout the sampled area. The blue and red channel returned plethysmographic information, but the signal strength was highly position specific. Our results obtained with a cellular phone as the data acquisition device are encouraging, especially in the broad context of personal or home-based care and the role of cellular phone technology in medical imaging.

Cellu

Spectral signature of Haemoglobin

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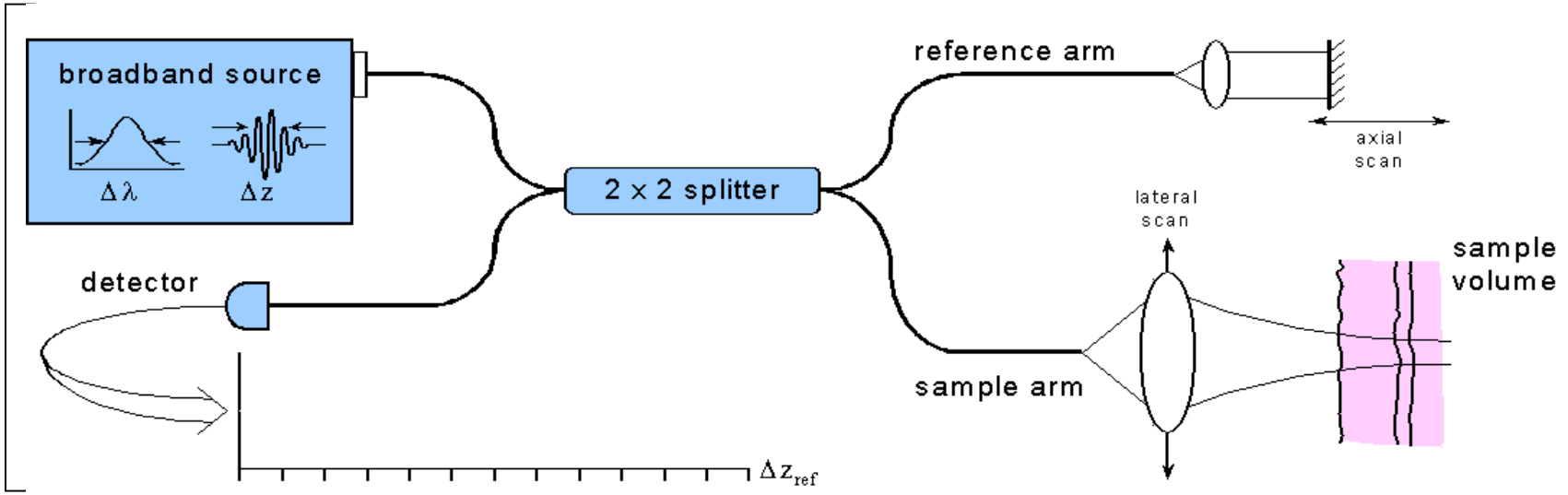
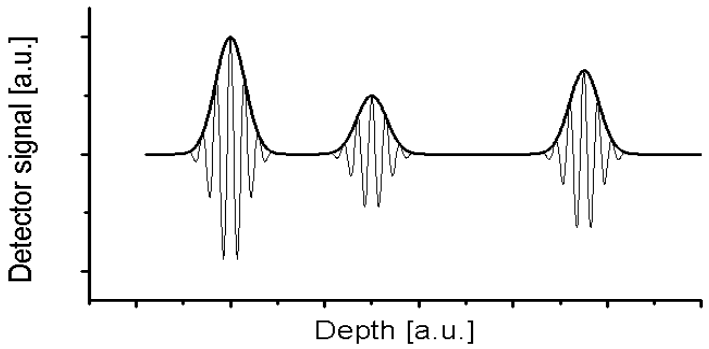
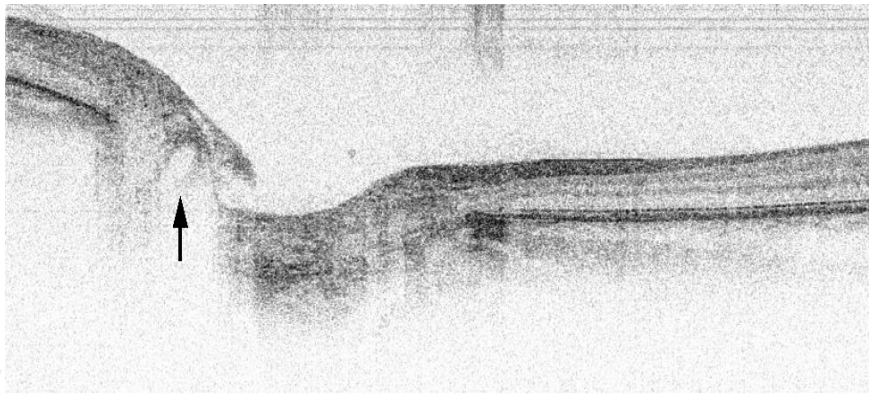
Optical Coherence Tomography





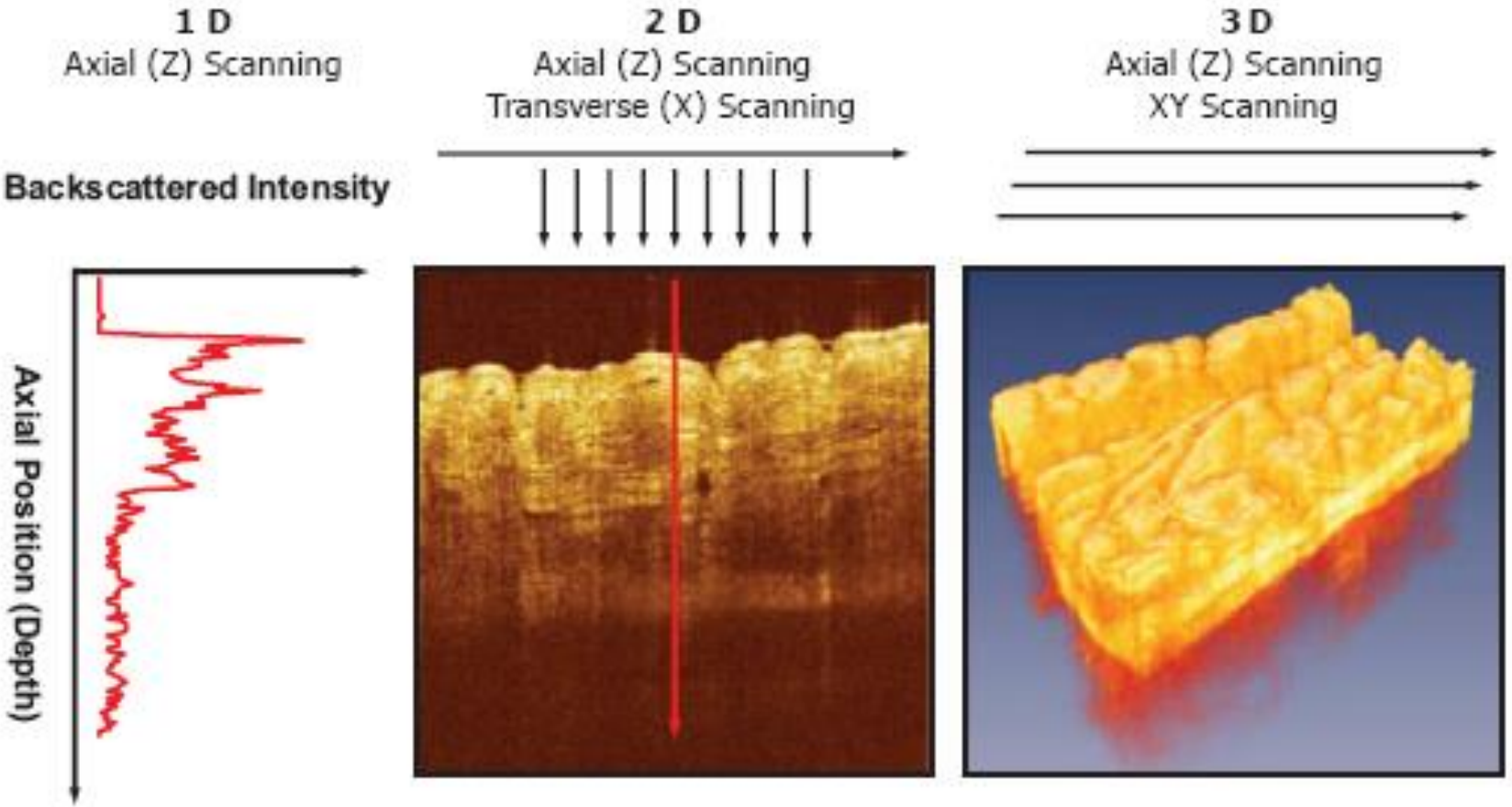
B-Scan

A-line



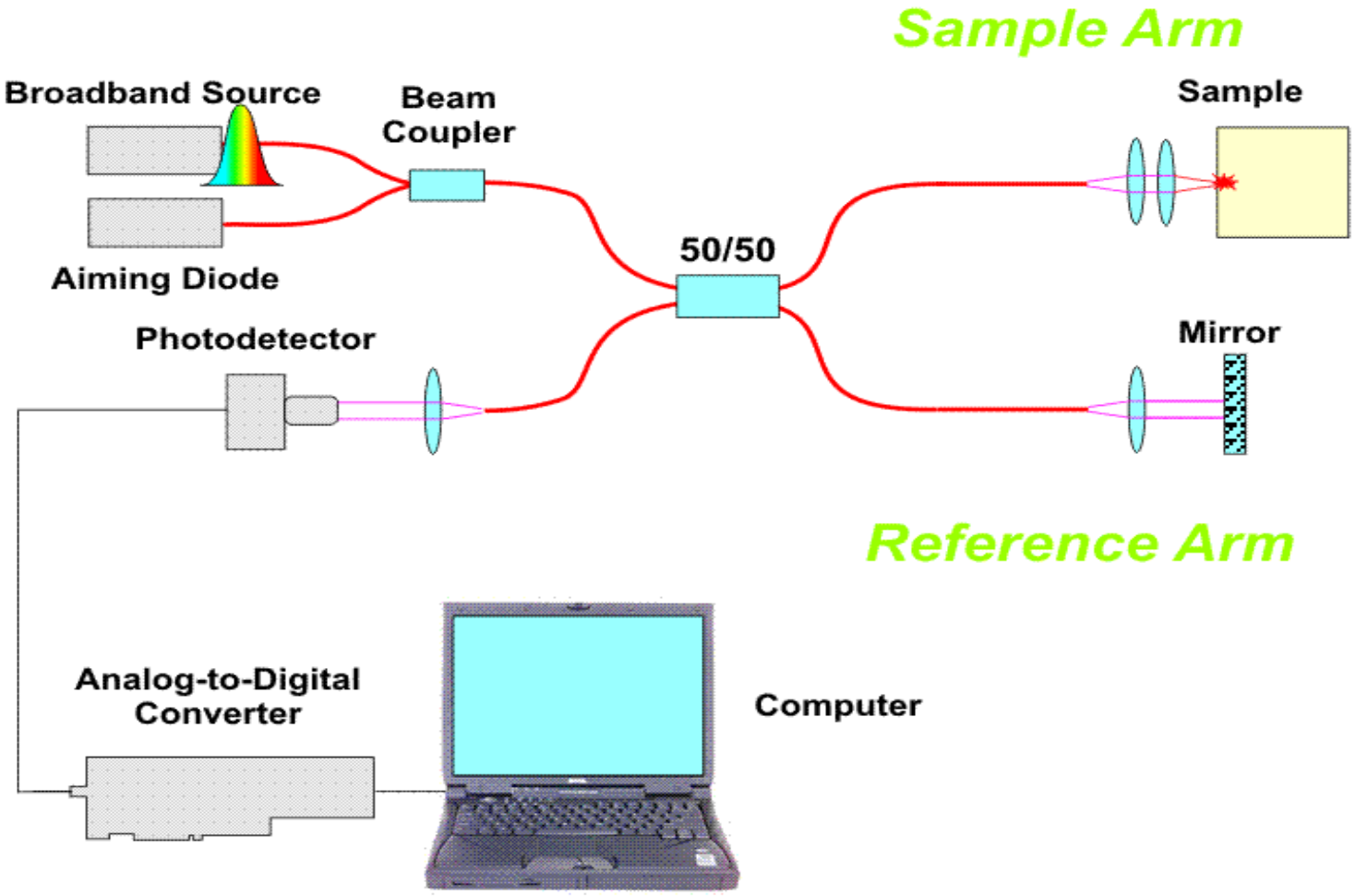
Courtesy of Johannes de Boer

OCT: optical analogue of pulsed-wave ultrasound



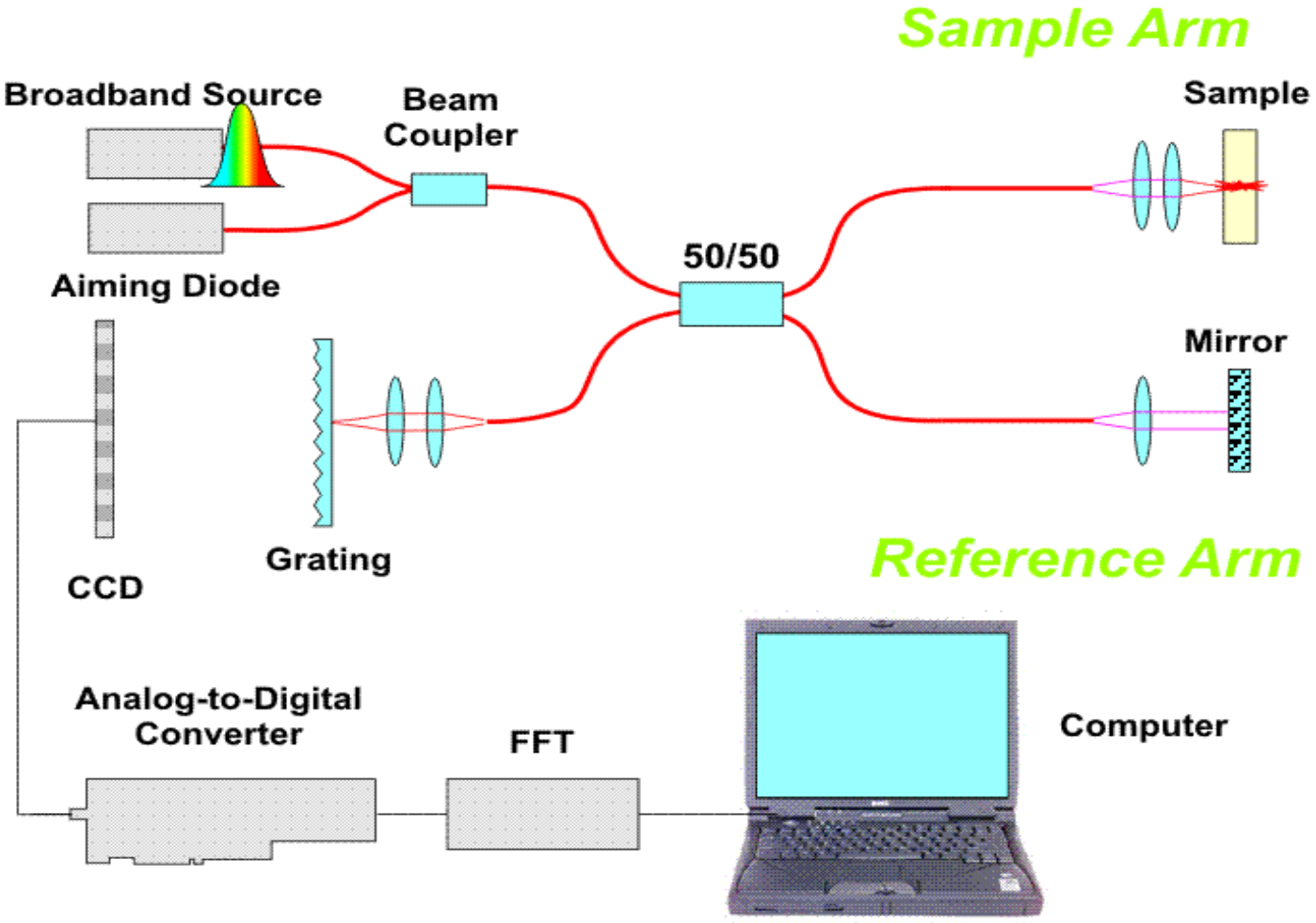
J. Fujimoto, 2008

Time-Domain OCT



Slides from de Boer and Larin

Fourier-Domain OCT



Slides from de Boer and Larin

Photonics and the UNESCO Year of Light 2015

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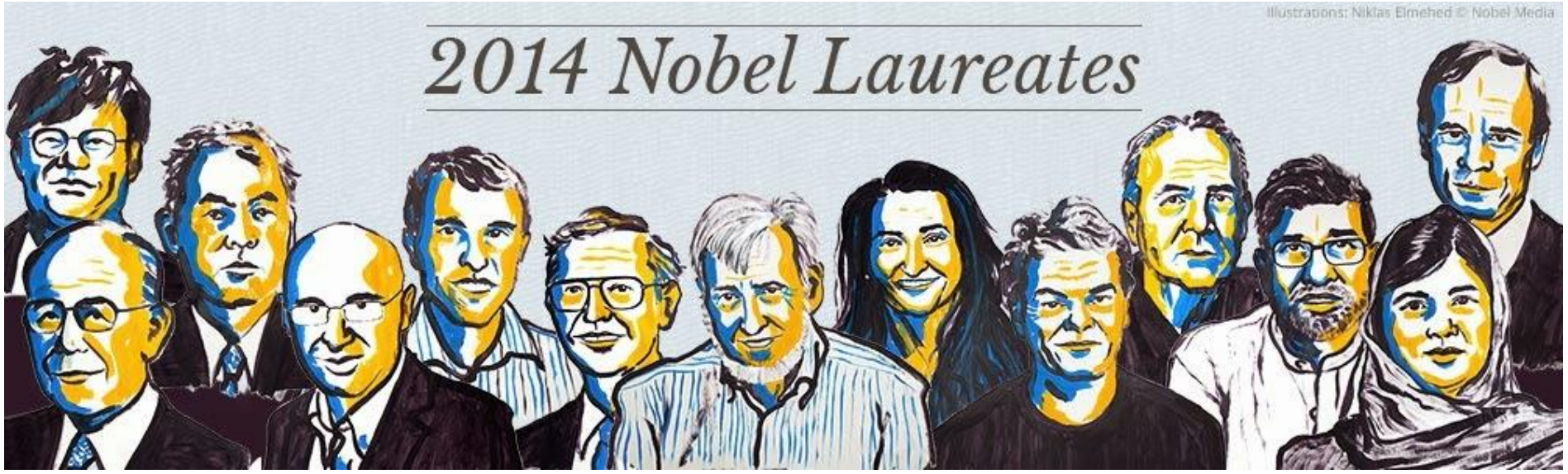
www.light2015.ie

UNESCO

BLIAIN IDIRNÁISIÚNTA AN TSOLAIS 2015



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Imaging Domains

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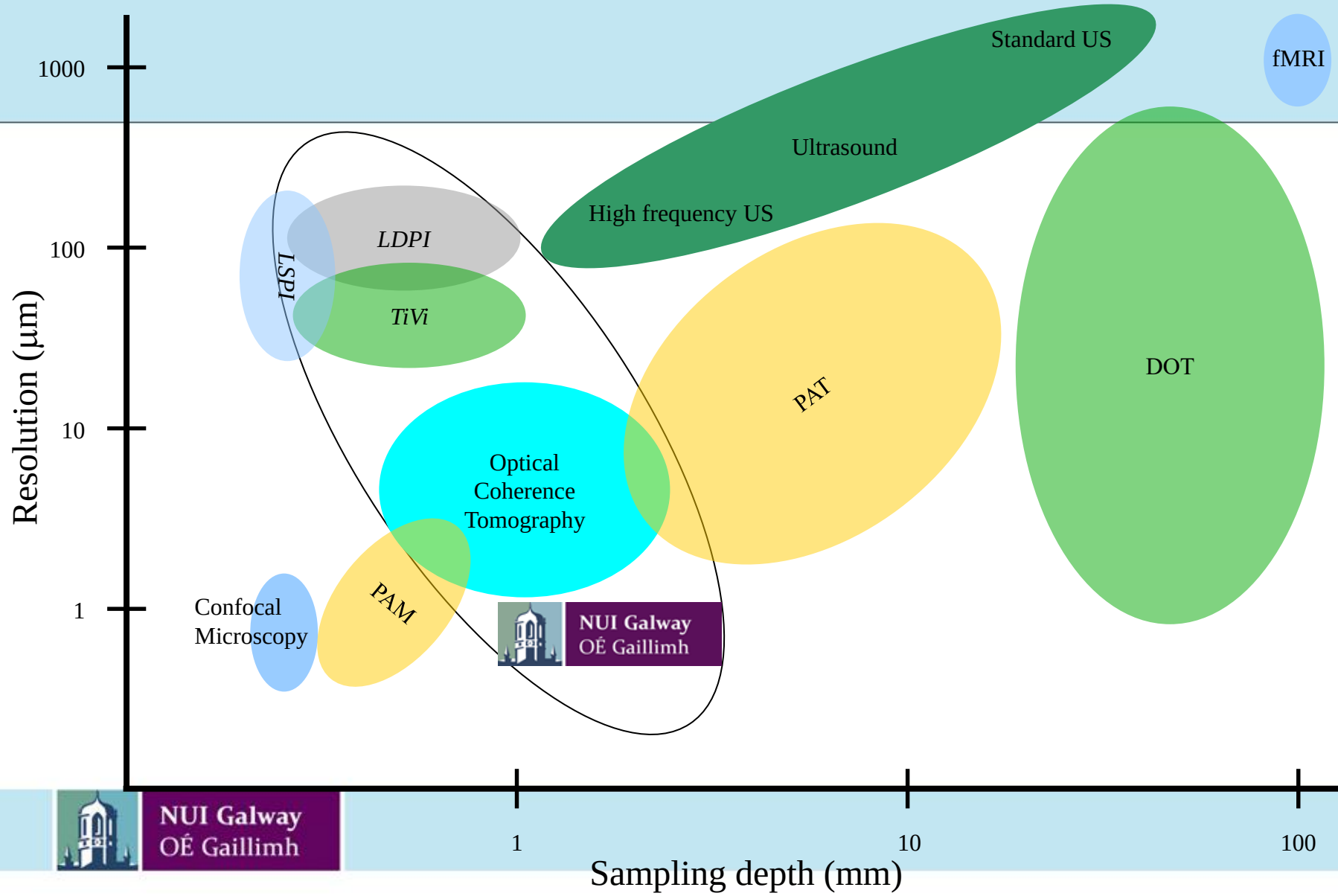

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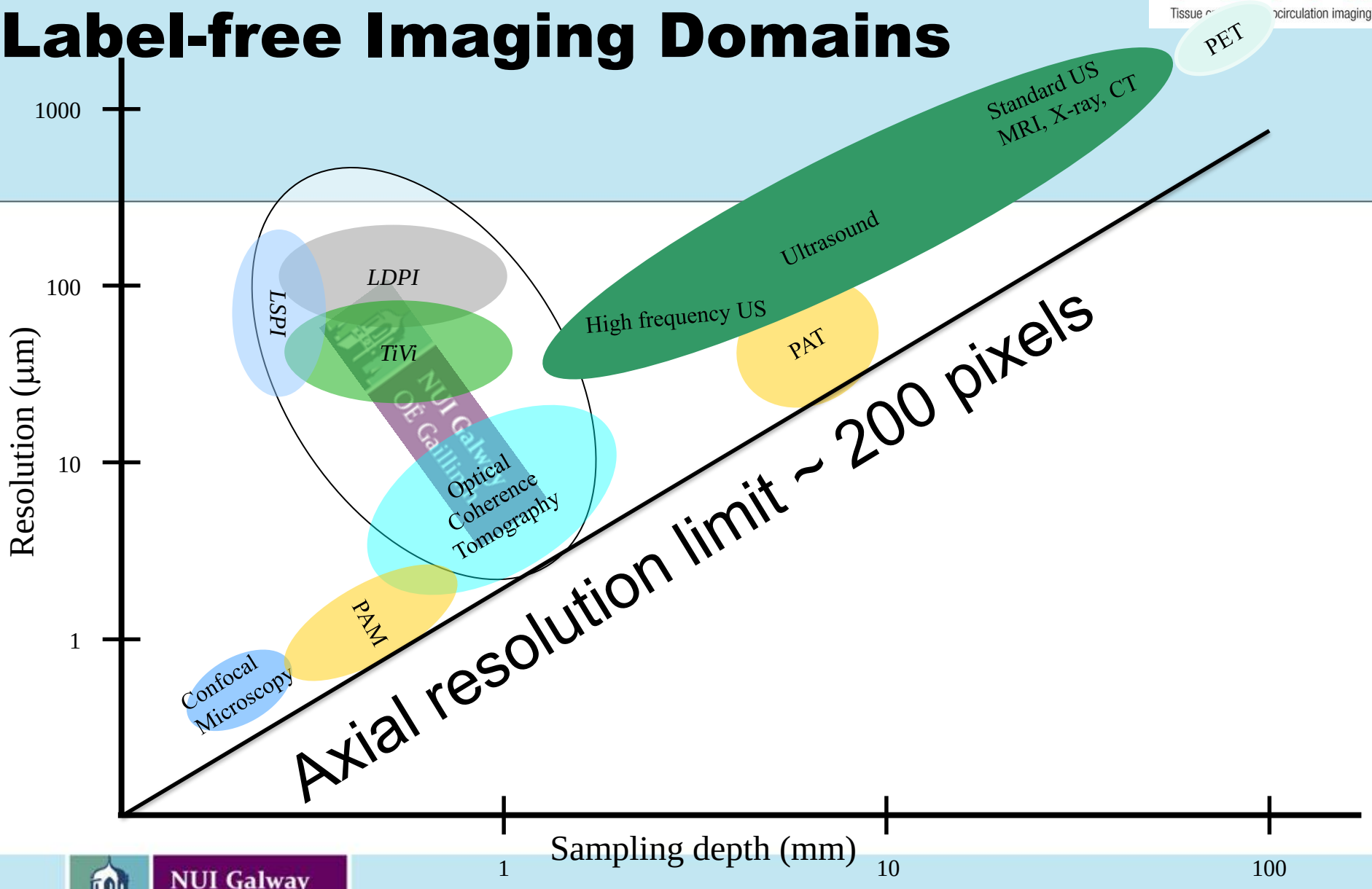
Label-free Imaging Domains



The Royal Swedish Academy of Sciences has decided to award the

2014 NOBEL PRIZE IN CHEMISTRY

to:

Eric Betzig, Stefan W. Hell and William E. Moerner

"for the development of super-resolved fluorescence microscopy"

Mobile platform

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J. Biophotonics 1–4 (2010) / **DOI** 10.1002/jbio.201000050

Journal of
BIOPHOTONICS

LETTER

Cellular phone-based photoplethysmographic imaging

Enock Jonathan and Martin J. Leahy*

Tissue Optics and Microcirculation Imaging (TOMI) Facility, National Biopho
Department of Physics, University of Limerick, Ireland

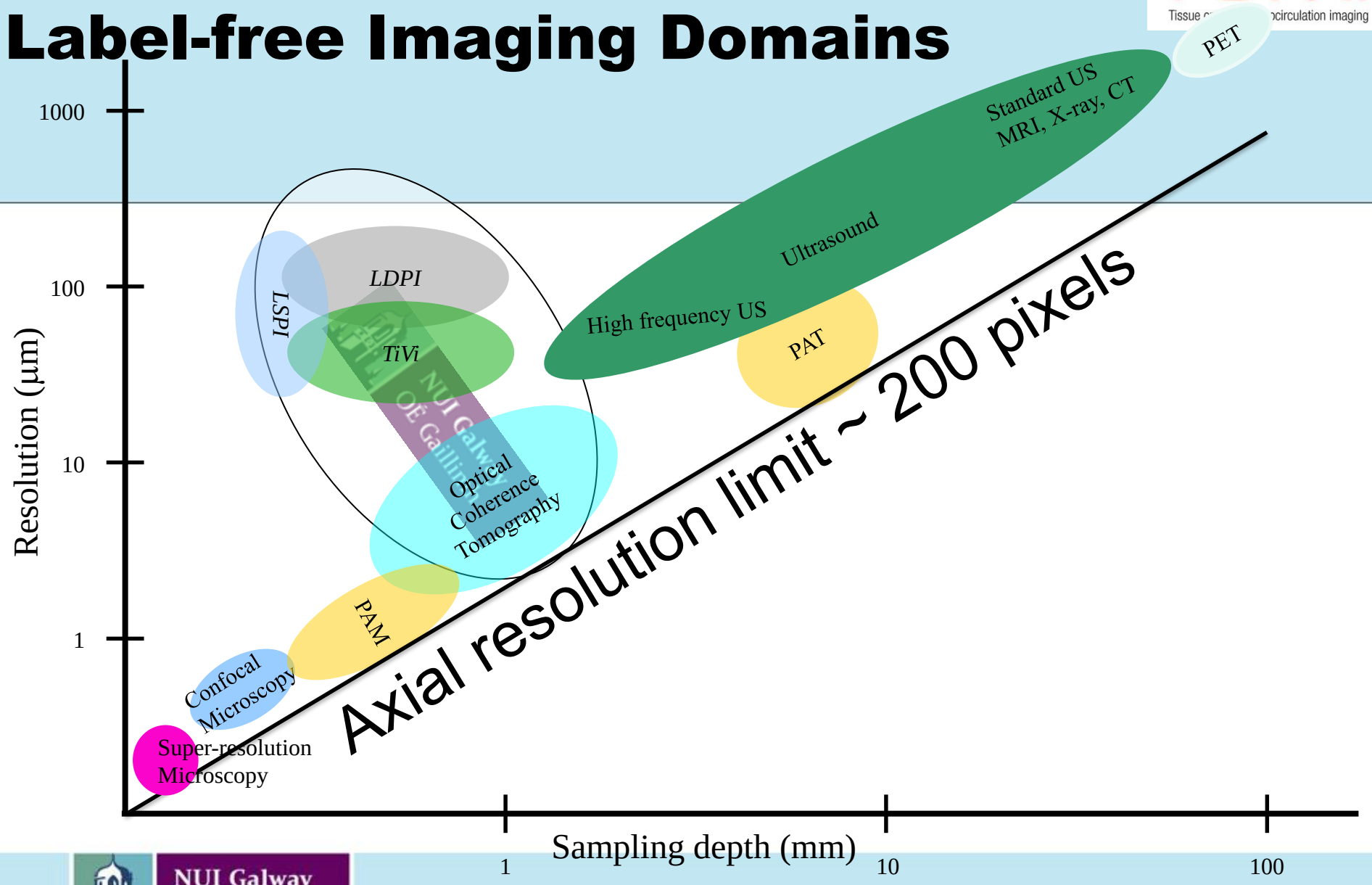
Received 4 April 2010, revised 3 August 2010, accepted 3 August 2010
Published online 6 September 2010

Key words: photoplethysmography, biophotonics, optical imaging, cel

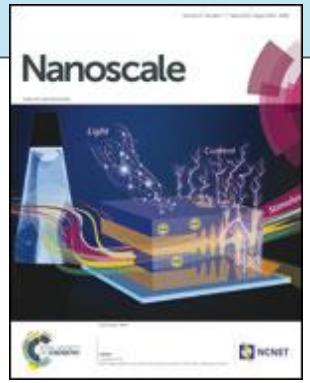
We present study results on visible light reflection photoplethysmographic (PPG) imaging with a mobile cellular phone operated in video imaging mode. PPG signal components around 0.1 Hz attributed to the sympathetic component of the heart rate, 1 Hz as the heart rate and 2 Hz as heart rate high order harmonic were quantified on the index finger of a healthy volunteer. The green channel reported PPG signals throughout the sampled area. The blue and red channel returned plethysmographic information, but the signal strength was highly position specific. Our results obtained with a cellular phone as the data acquisition device are encouraging, especially in the broad context of personal or home-based care and the role of cellular phone technology in medical imaging.

Cellu

Label-free Imaging Domains



Nanostructural sensitivity at depth



Resolution (μm)

1000
100
10
1

atoms (C H N O P S)
molecules (DNA, lipids, proteins, etc)
molecular systems
organelles (mitochondria, nuclei, etc.)
cells
tissue
organ
body

Spectral decoding

Structural Sensitivity (μm)

100
10
1

1 Sampling depth (mm) 10 100

Alexandrov et al. *Nanoscale*, **6**, 3545-3549

Optical Coherence Tomography

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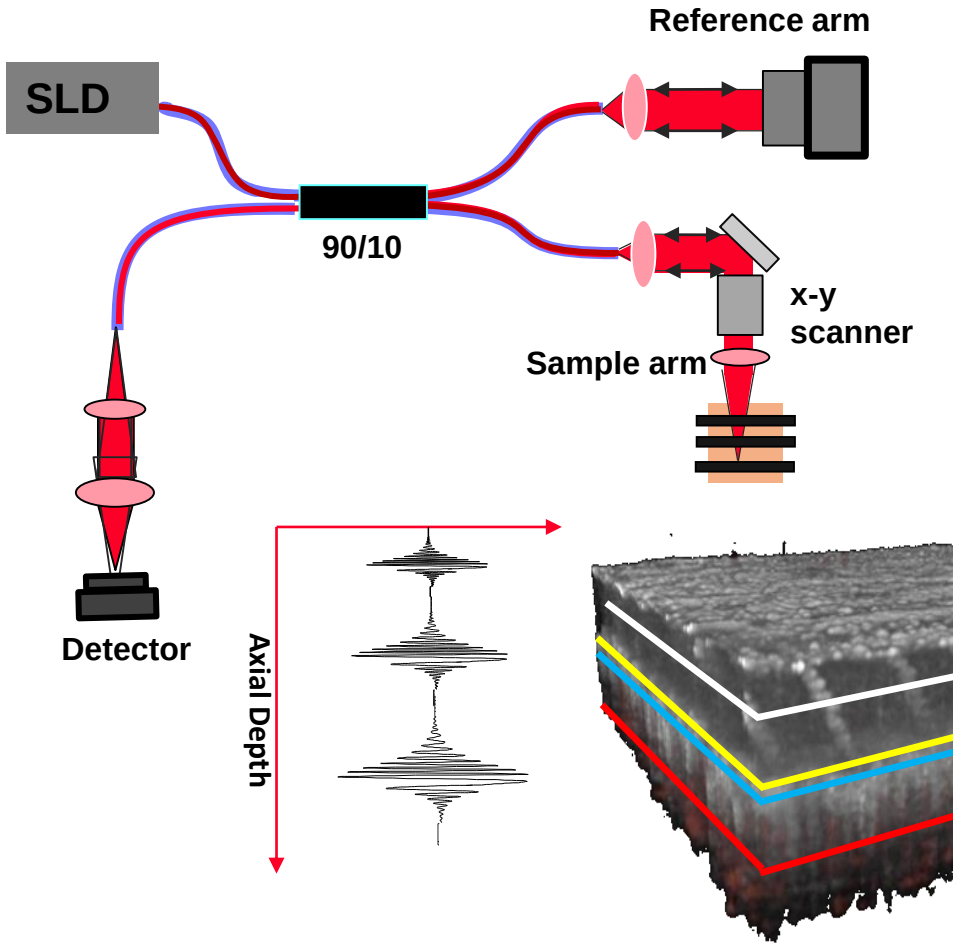
- OCT uses low coherence interferometry to produce a two or three dimensional image of optical scattering from internal tissue microstructures.
- OCT can provide both micro structural and functional information with high resolution and sensitivity
  - High resolution (2-15 μm)
  - 3D imaging in scattering tissue (2-3 mm)
  - Non invasive – “Optical Biopsy”



Commercially available OCT systems

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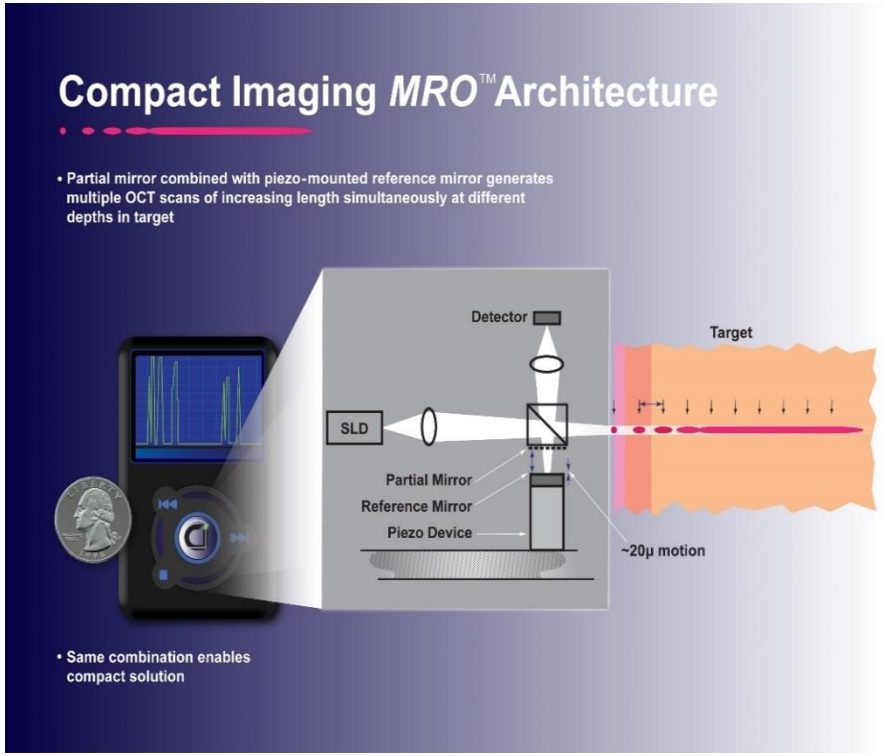
Cirrus HD-OCT

ILUMIEN

Skintell

Conventional clinic-scale OCT instruments, priced from €45,000 to over €120,000, were commercialized early in the last decade for use by ophthalmologists, dermatologist, cardiac surgeons

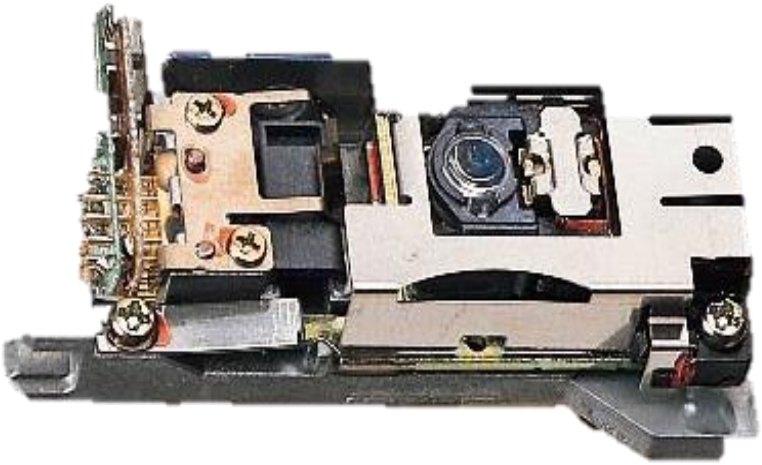
Compact imaging solution with MR-OCT



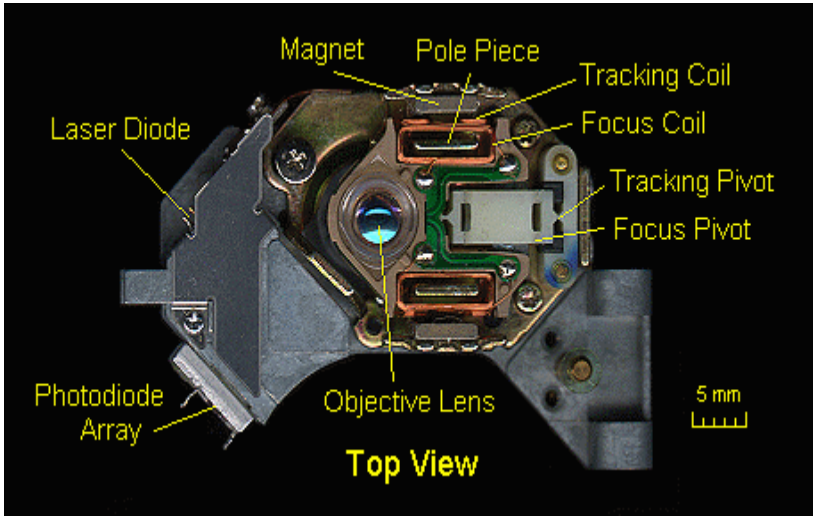
MR-OCT features

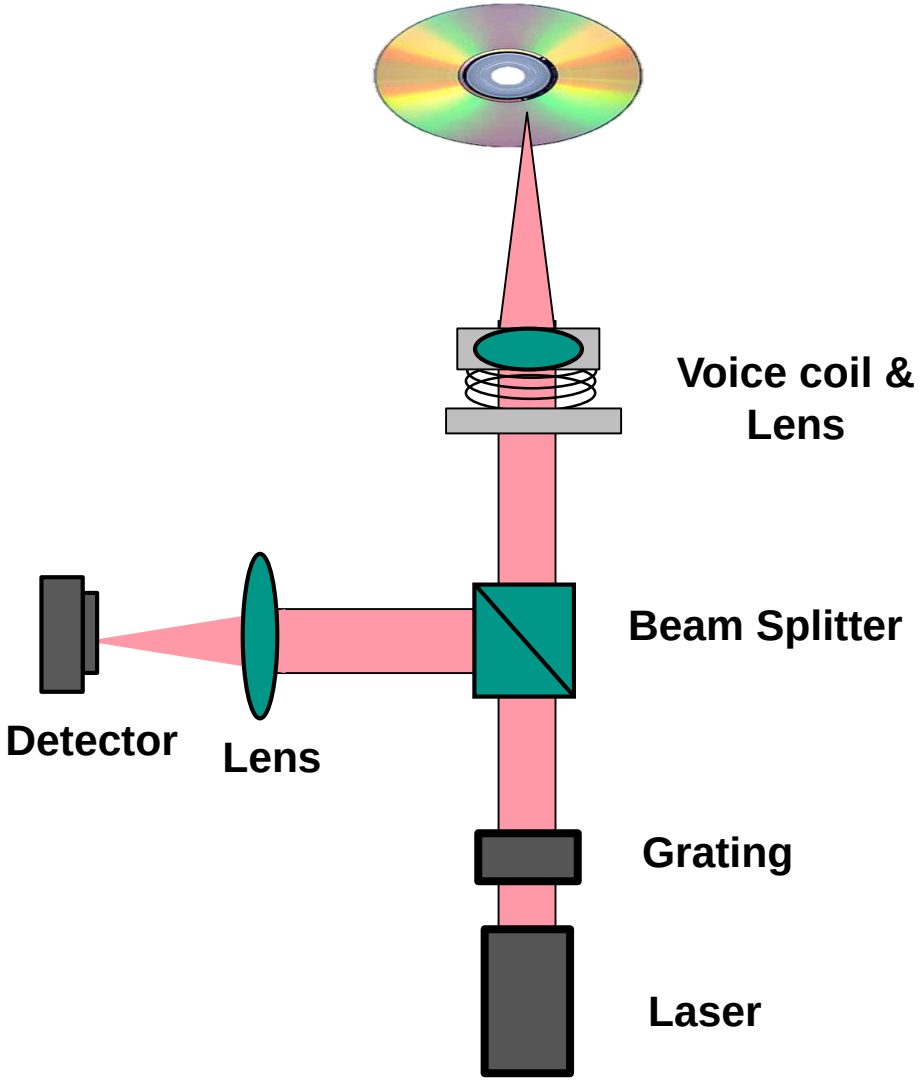
- Small form factor: About the size of a computer DVD read/write head
- Robust, cost-effective design: Virtually solid state, typical of handheld devices
- Low-operating power requirements
- Flexible “free space” optical architecture

CD ROM Pickup Unit



Cost 10$!!!





Replacing CD ROM Pickup Unit with MR-OCT

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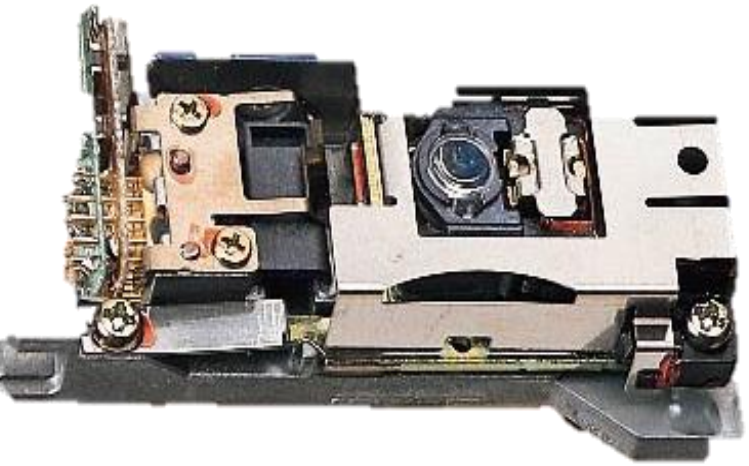
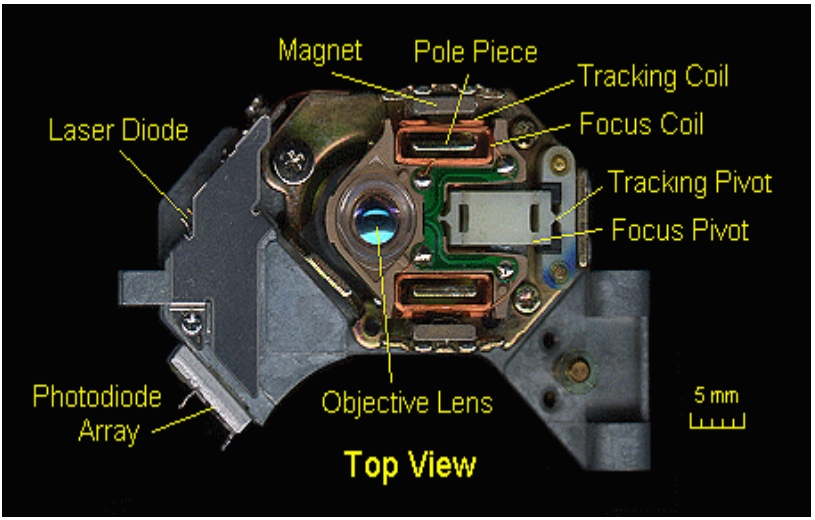
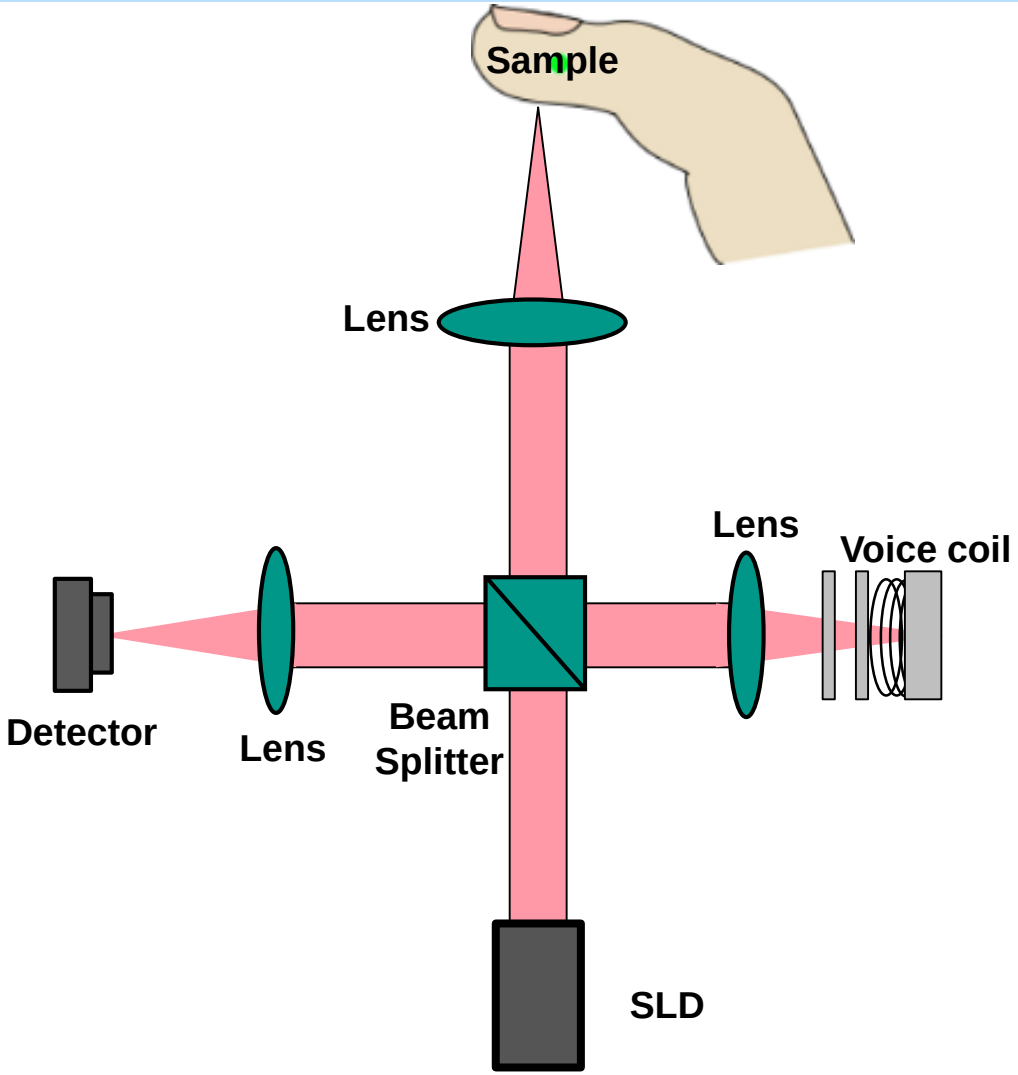
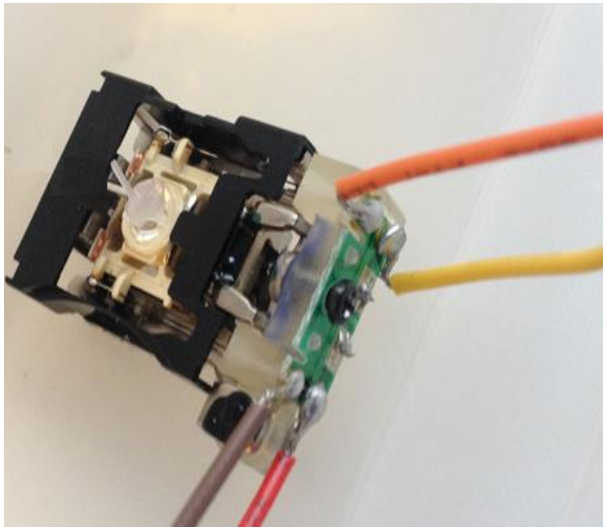


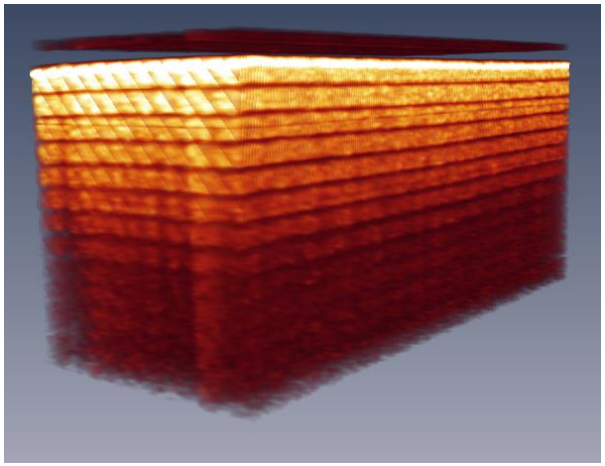
Cost 10$!!!





CD ROM Pickup head actuator





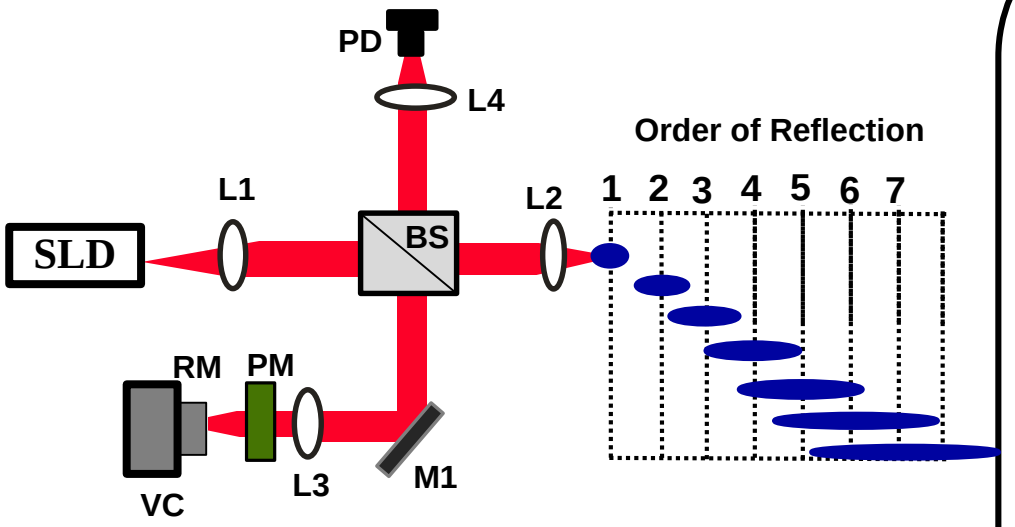
MR-OCT of Scotch tape with VCM

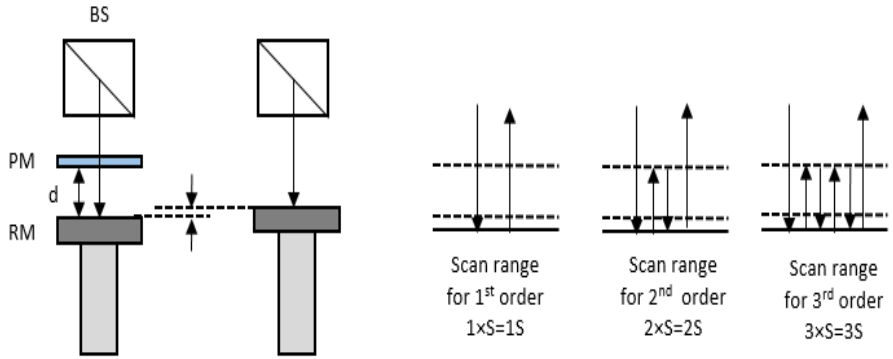
Voice coil motor (VCM) actuator used in CD pick up head to ensure the constant focus on the optical disc

Voice coil features

- Low operational voltage
- Long life
- Light weight
- Inexpensive

Multiple Reference Optical Coherence Tomography (MR-OCT)





- MR-OCT is similar to conventional TD-OCT, except a partial mirror is placed very close to the reference mirror.
- The partial mirror causes the light to be reflected back and forth multiple times between the partial mirror and the reference mirror.
- Each reflection between the partial and reference mirrors is delayed by the round trip time between the two mirrors.

Multiple Reference Optical Coherence Tomography (MR-OCT)

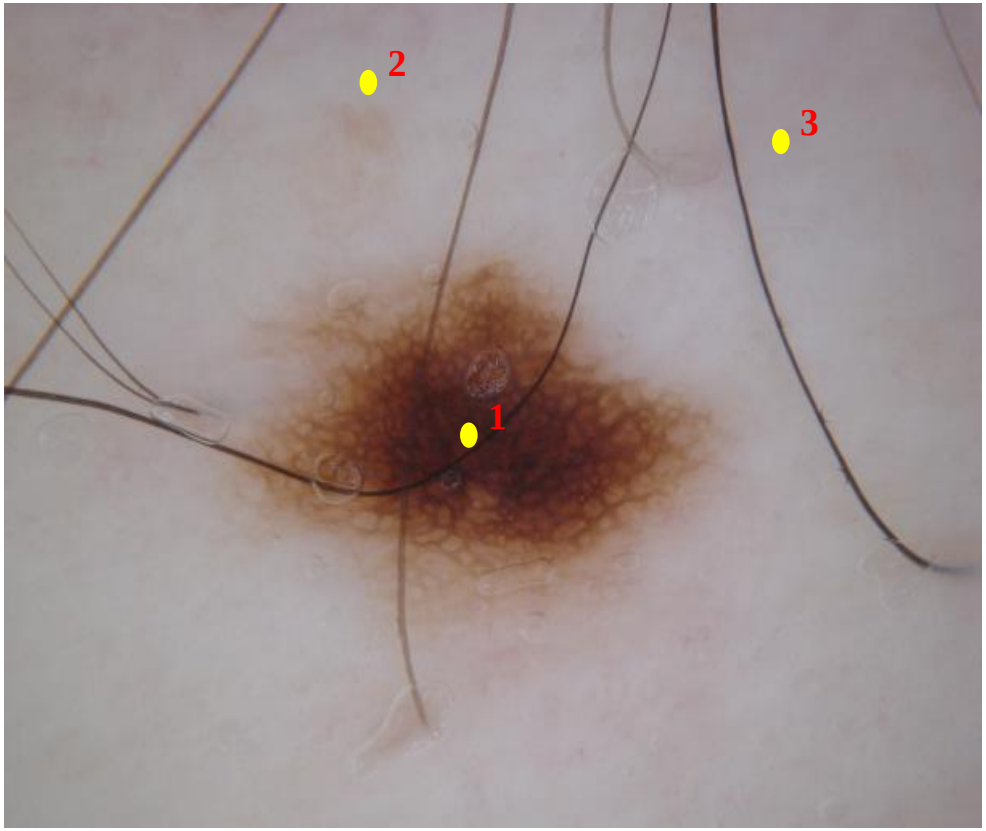
The detected signal at the output of an interferometer can be expressed as:

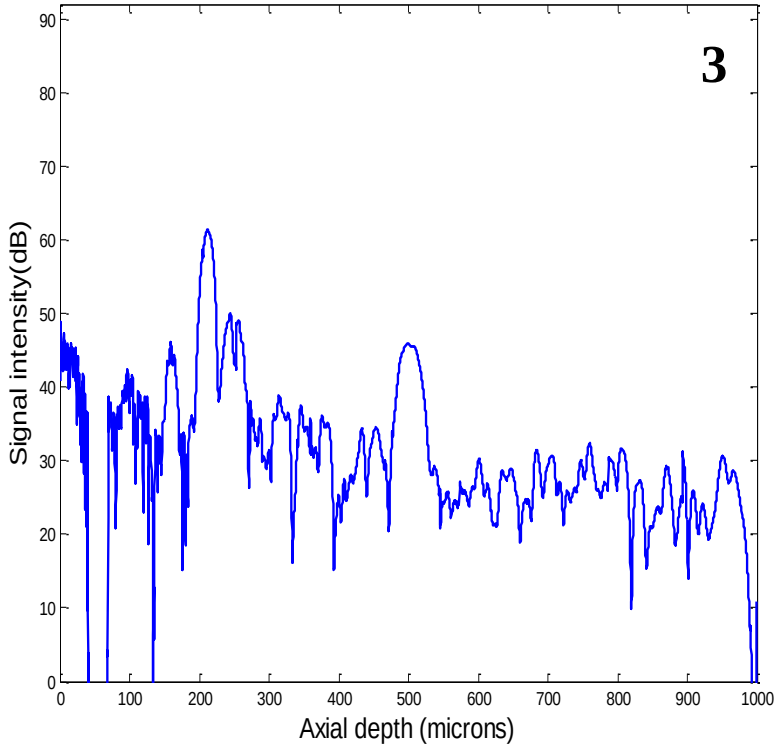
$$I_d = I_{R\times n} + I_S + I_{PM} + 2\sqrt{I_{R\times n} + I_S}\, e^{-4ln2\left(\frac{\Delta l - nd}{l_c}\right)^2} \times cos\left(\frac{4\pi}{\lambda_0}\Delta l - nd\right)$$

$I_{R\times n} = T^2(1-T)^2$ represents the reference arm intensity of orders '*n*'

Systematic increase in the path length (Δl) change corresponds to systematic increase in the beat frequency of the detected interference signals associated with the multiple references.

Co-registering MR-OCT beam with dermascope image





cmOCT of the thumb for a 5x5x3 mm region

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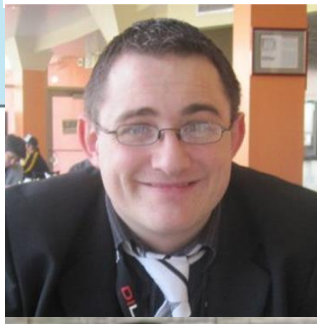
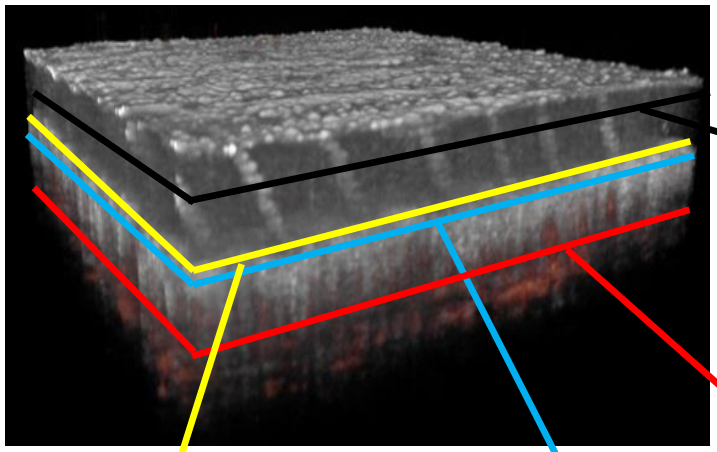
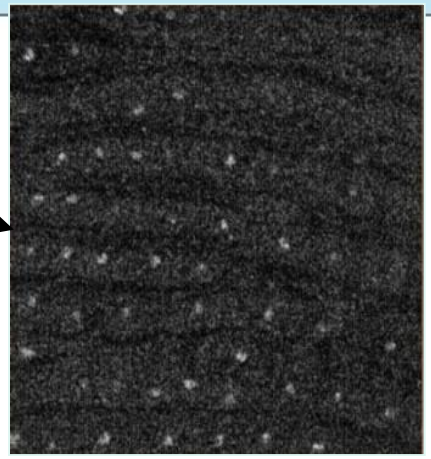
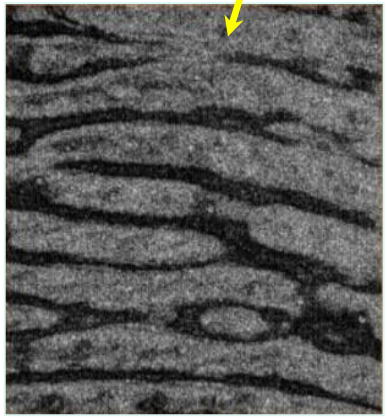


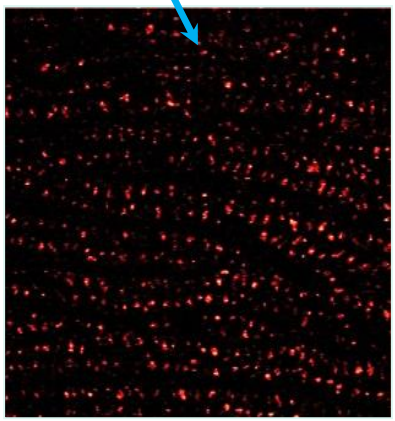




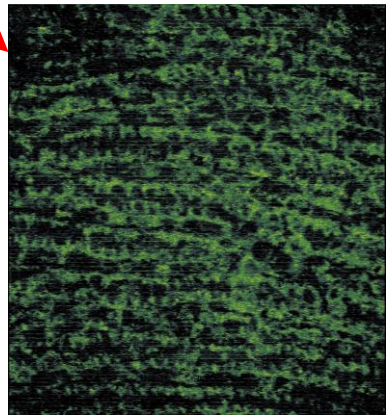
Sweat ducts



Sub-surface Fingerprint



Rising Capillary Loops



Microcirculation Map

AuthenTec

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Zam et al., 2013. J. Biophoton. 6 (9) , 663-667.
McNamara et al., 2014, *J. Biomed. Opt. 18 (12), 126008*

Fingerprint Microcirculation

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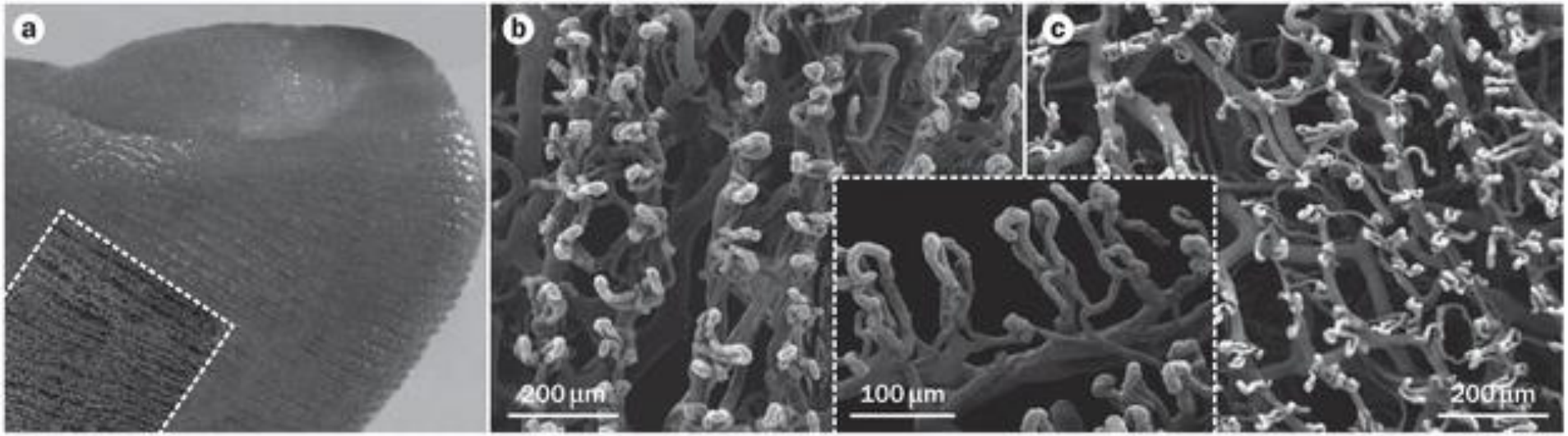
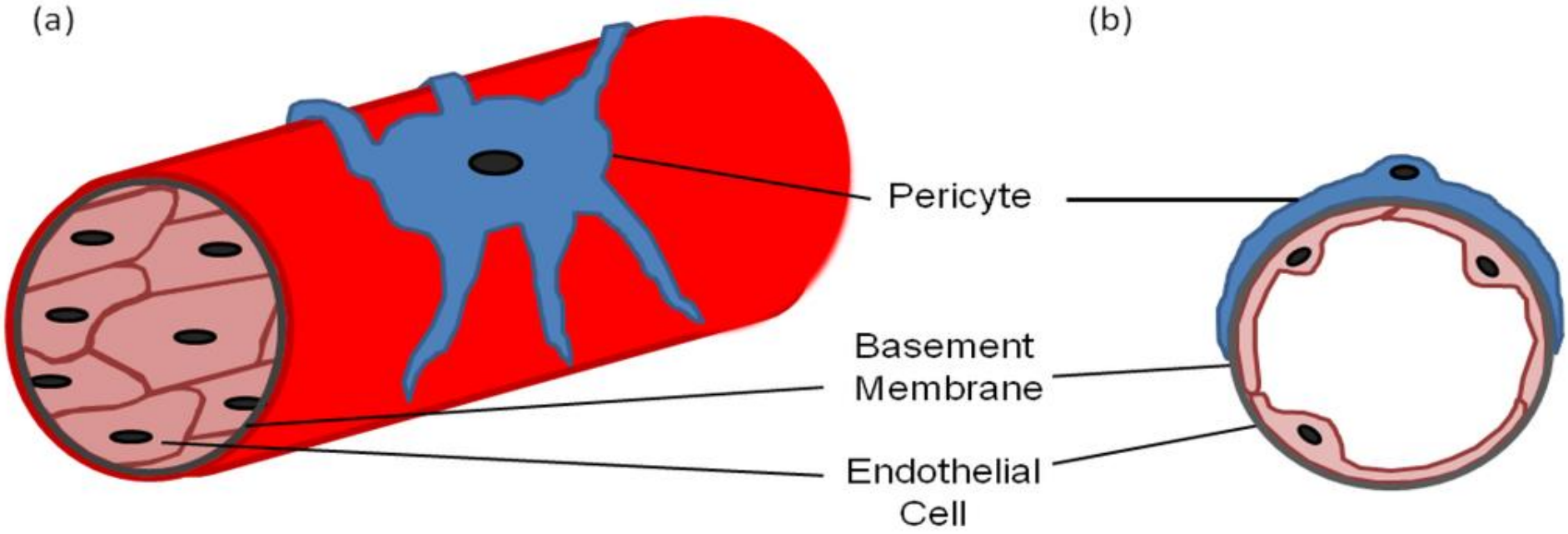


Nature Reviews | Rheumatology

NUI Galway
OÉ Gaillimh

Flavahan, N Nature Reviews Rheumatology, 11, 146–158 (2015)
doi:10.1038/nrrheum.2014.195

Capillaries



Capillaries

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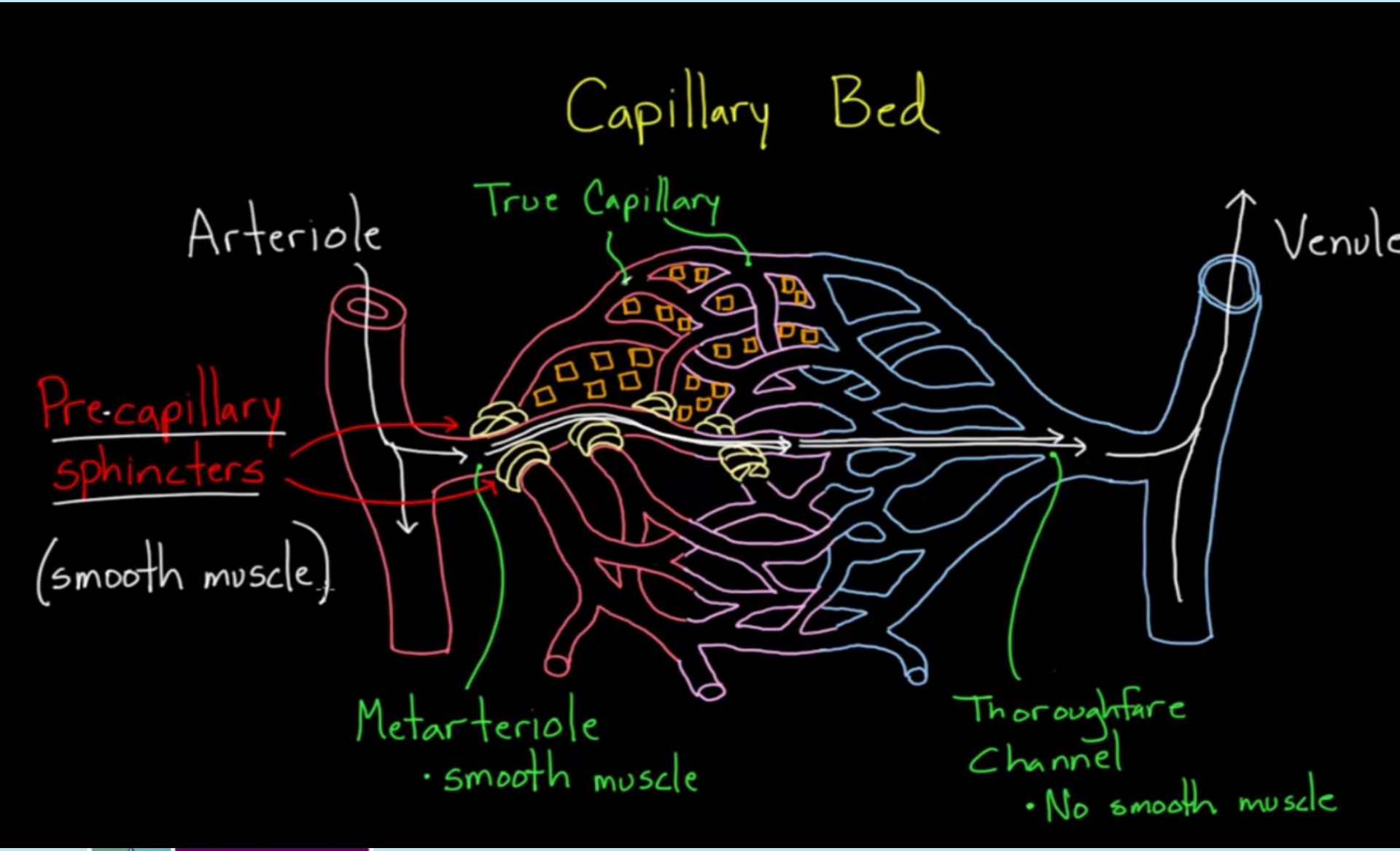

Capillaries

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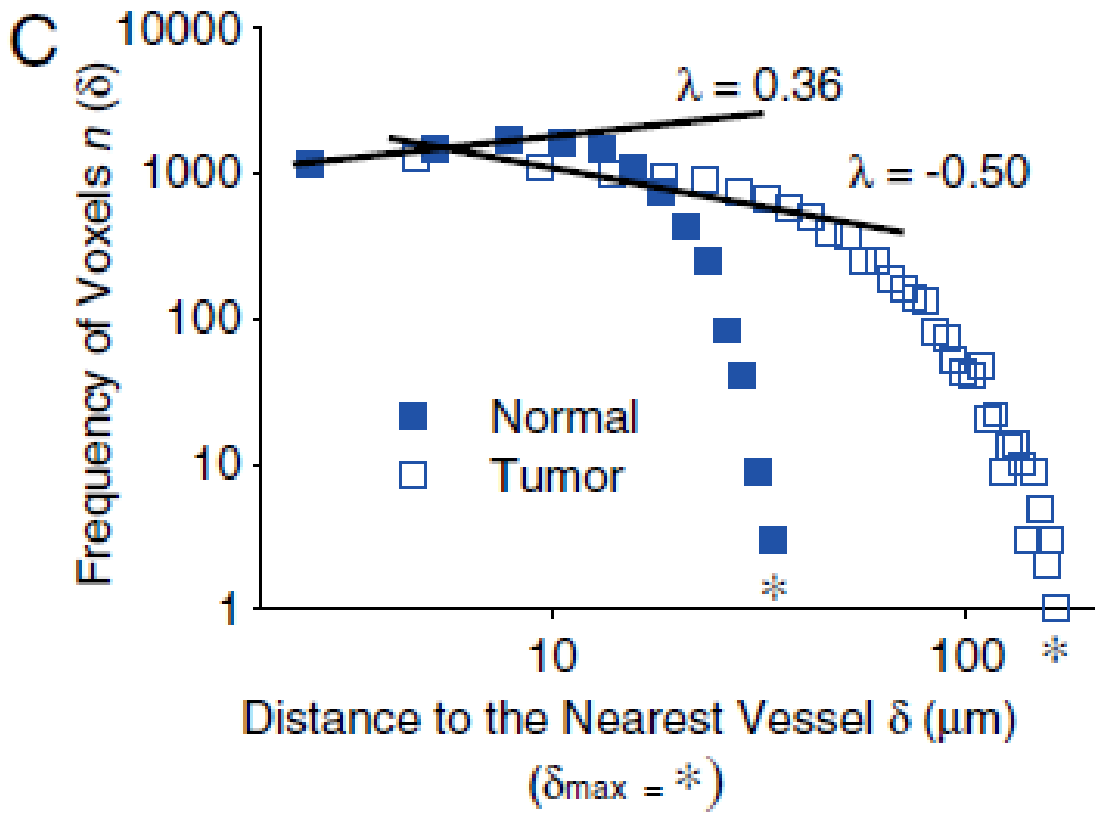
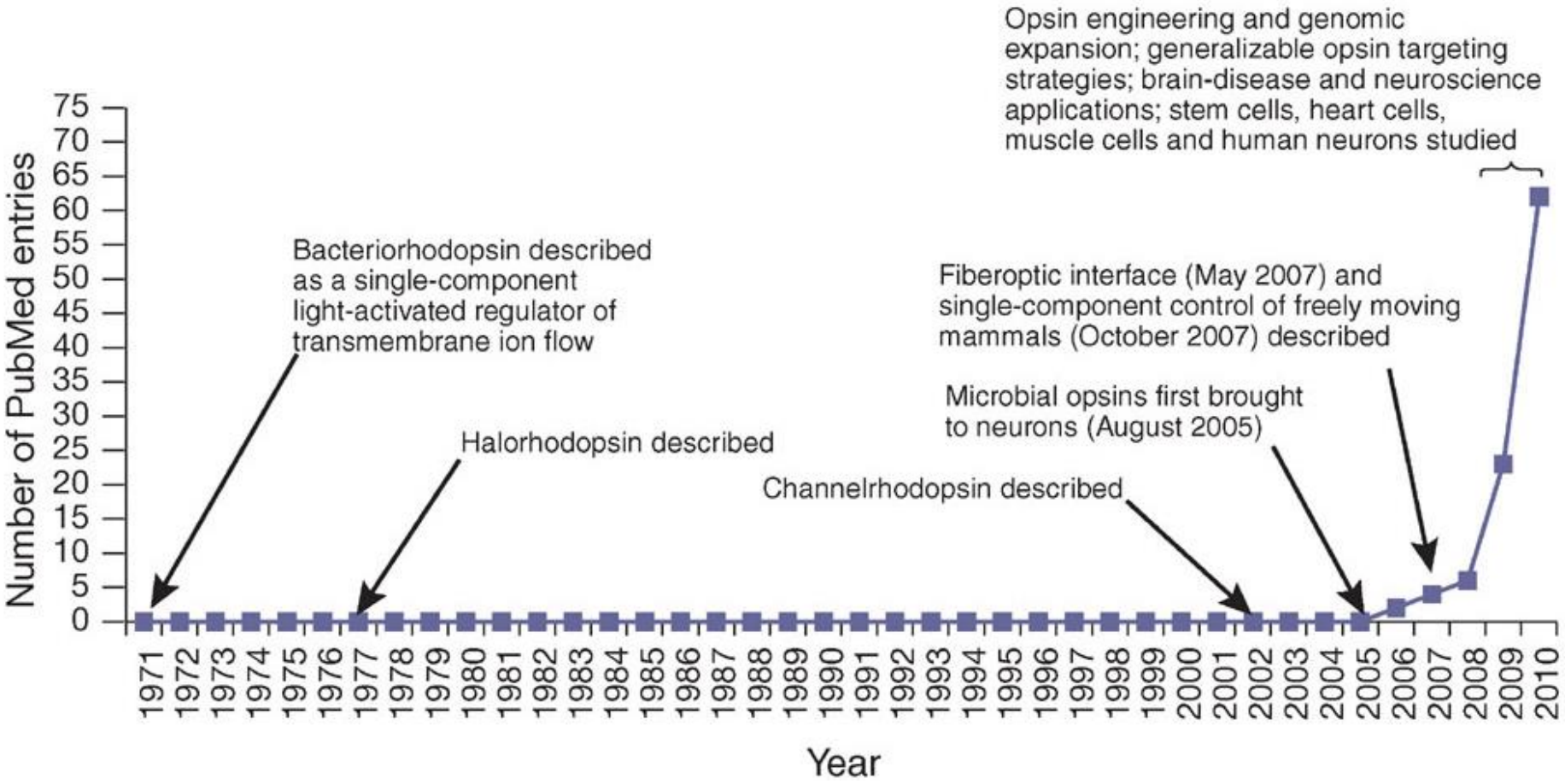
National University of Ireland, Galway

Scaling rules for diffusive drug delivery in tumor and normal tissues



RISE OF OPTOGENETICS



Graphical illustration of 'optogenetics' emerging in the scientific literature.

Karl Deisseroth, Optogenetics, Nature Methods 8, 26–29 (2011) doi:10.1038/nmeth.f.324

How optogenetics works

A light-sensitive protein from algae

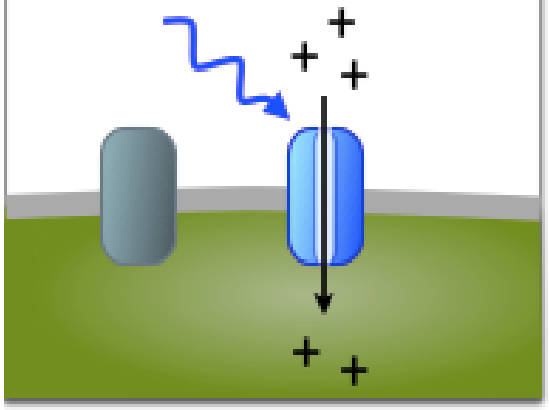
Opsins

Take the gene for this protein...

... and insert the DNA into specific neurons in the brain

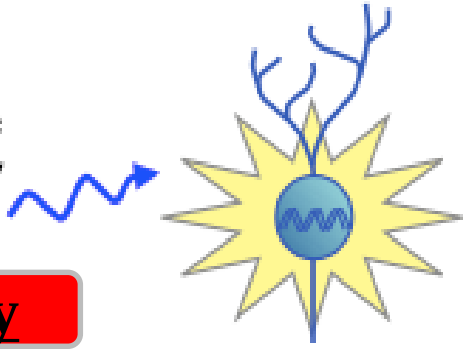
Vector

This protein is an ion channel that opens in response to **blue light**



Neurons communicate by "**firing**." This is an electrical signal created by opening & closing ion channels.

So now you can cause neurons to fire just by flashing **blue light!**



LightDelivery

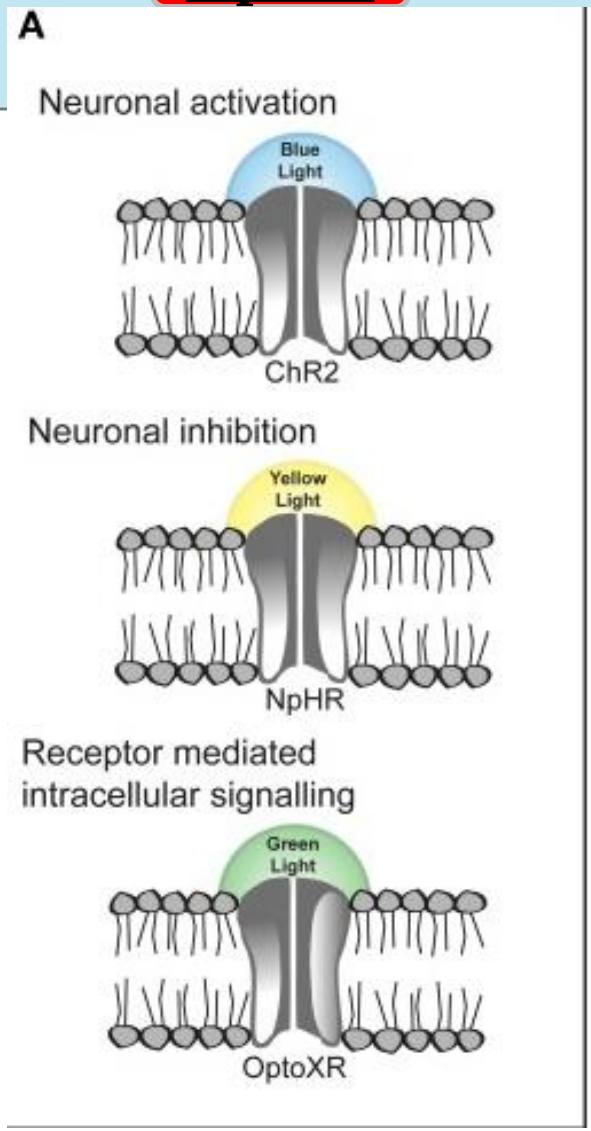
With the right combination of neurons, you can activate an entire brain circuit to control specific behaviors (like movement)

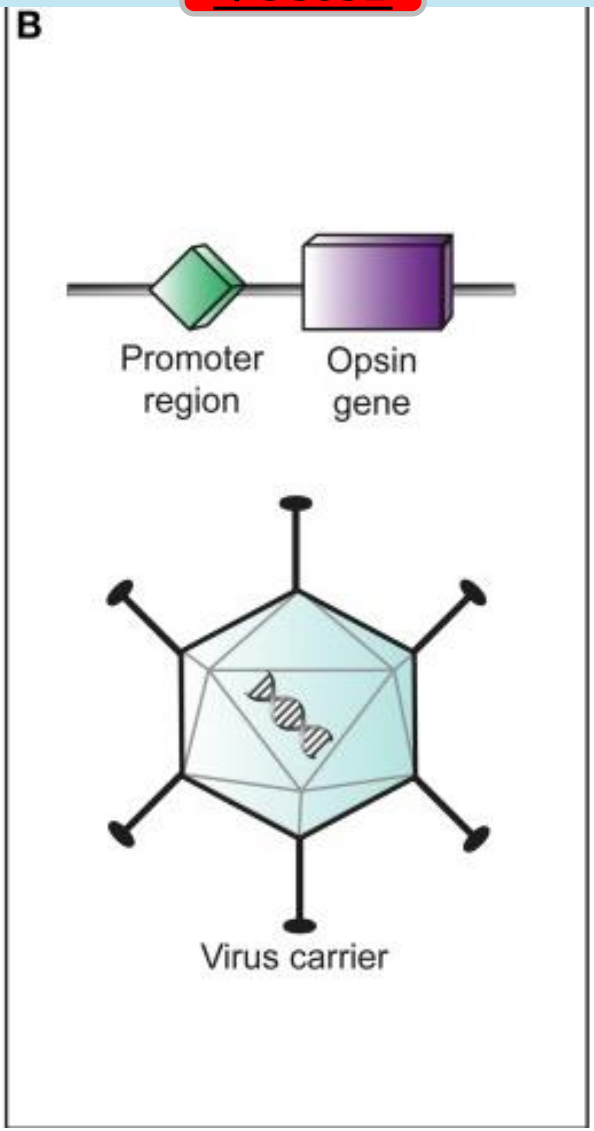
http://www.wiringthebrain.com/2013/09/why-optogenetics-deserves-hype.html

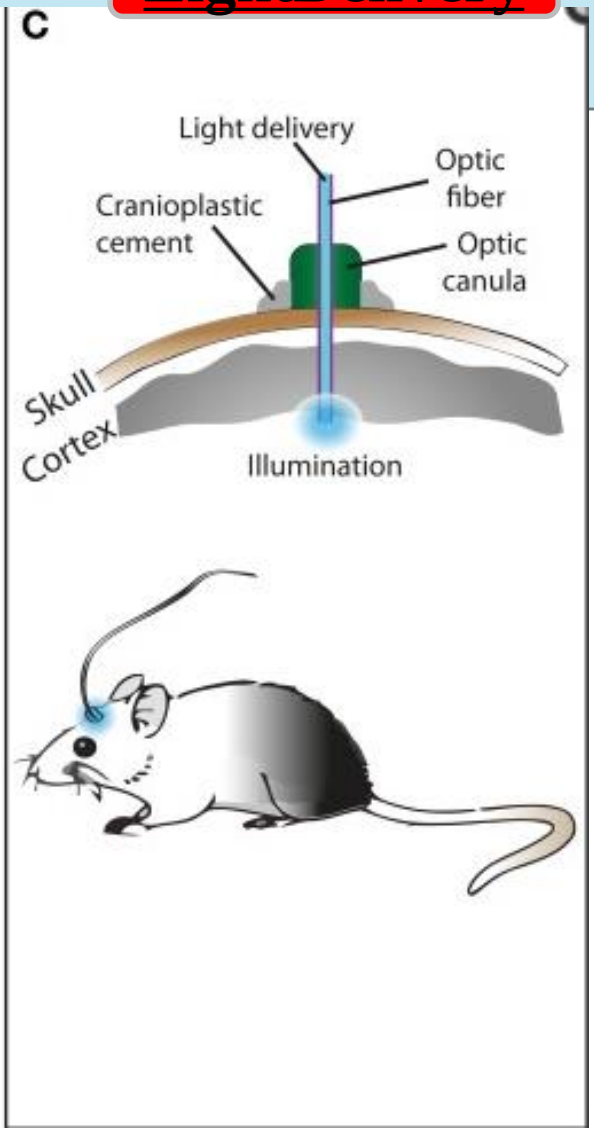
Opsins

Vector

LightDelivery







http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3764402/figure/F1/

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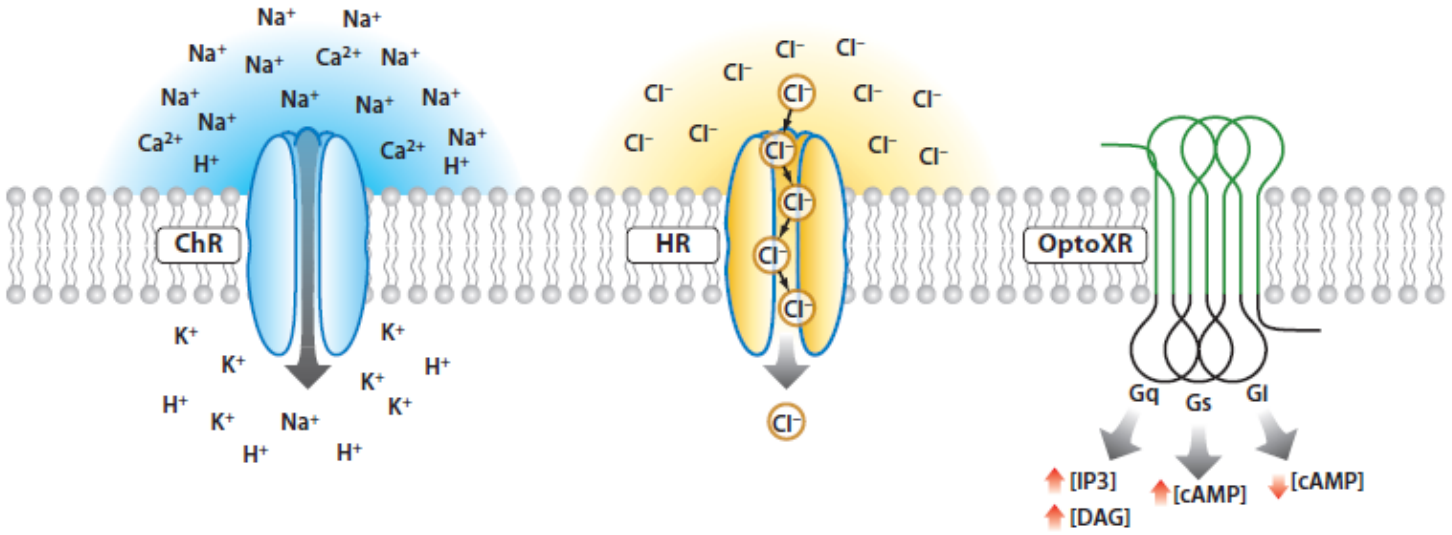


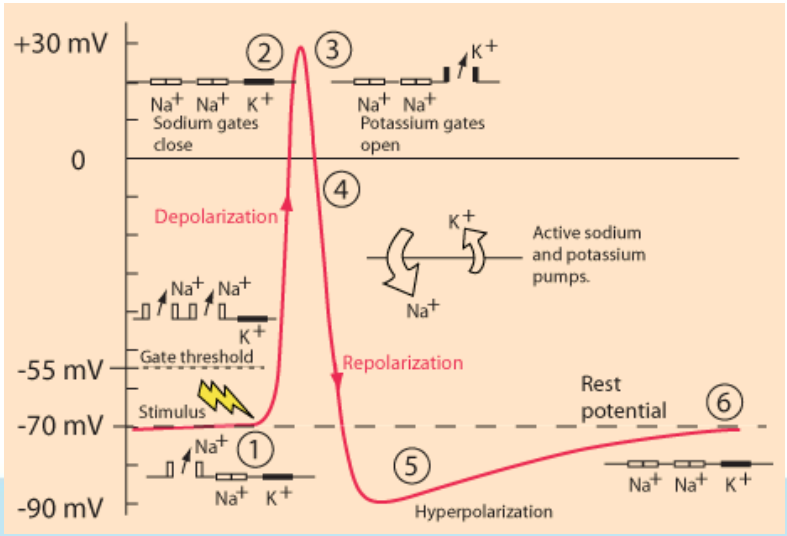
Figure 1

Optogenetic tool families. Channelrhodopsins conduct cations and depolarize neurons upon illumination (*left*). Halorhodopsins conduct chloride ions into the cytoplasm upon yellow light illumination (*center*). OptoXRs are rhodopsin-GPCR (G protein–coupled receptor) chimeras that respond to green (500 nm) light with activation of the biological functions dictated by the intracellular loops used in the hybrid (*right*).

Deisseroth, K. et al. (2011). "The Development and Application of Optogenetics". *Annual Review of Neuroscience"* . 34:389–412

Nernst

$$E = \frac{RT}{zF} \ln \frac{[\text{ion outside cell}]}{[\text{ion inside cell}]}$$



http://hyperphysics.phy-astr.gsu.edu/hbase/biology/actpot.ht

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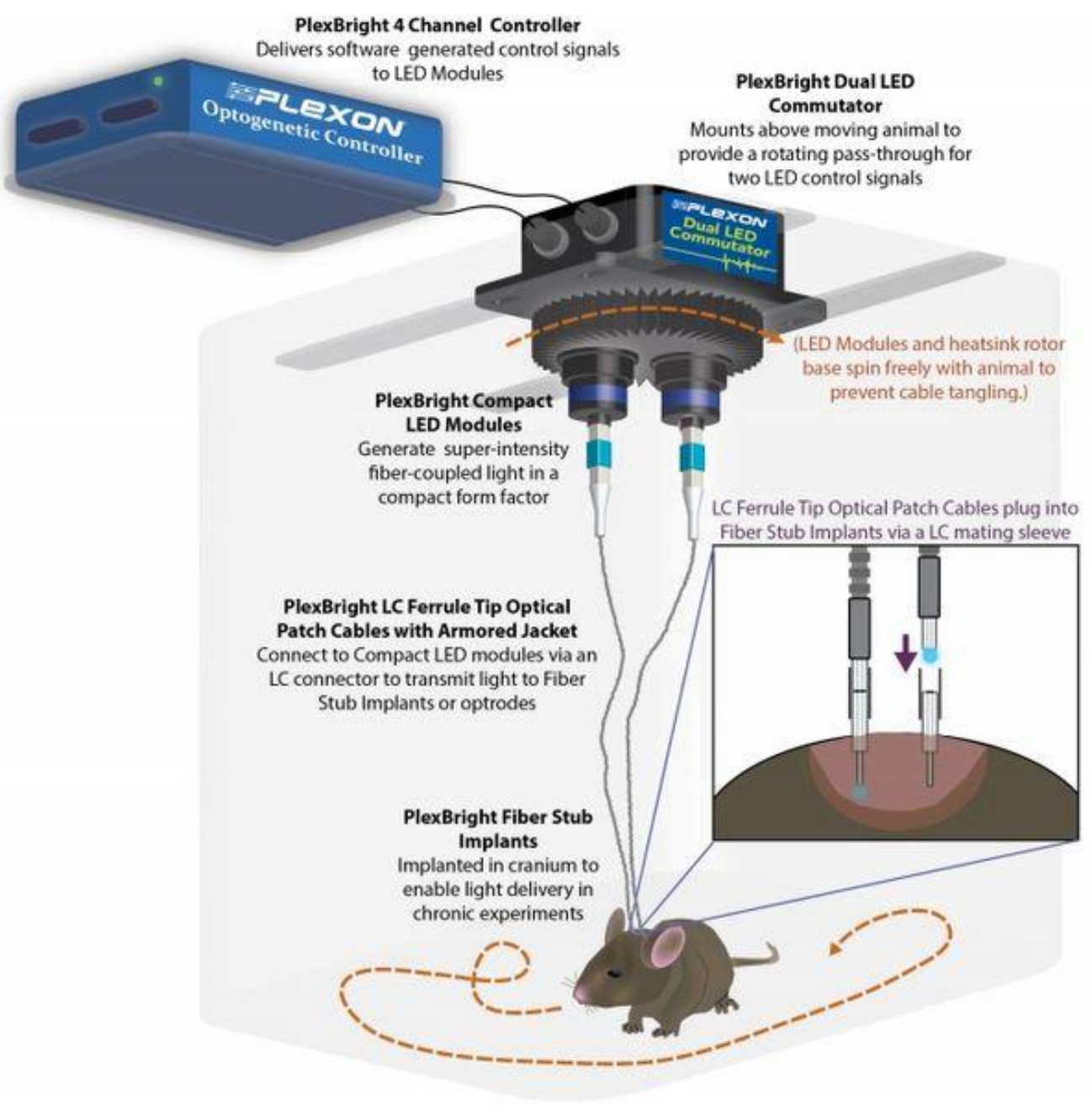

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http://www.openoptogenetics.org/index.php?title=File:Plexon_overview.jpg

Channels through cell membranes

1990, Peter Agre

1998, Roderick MacKinnon

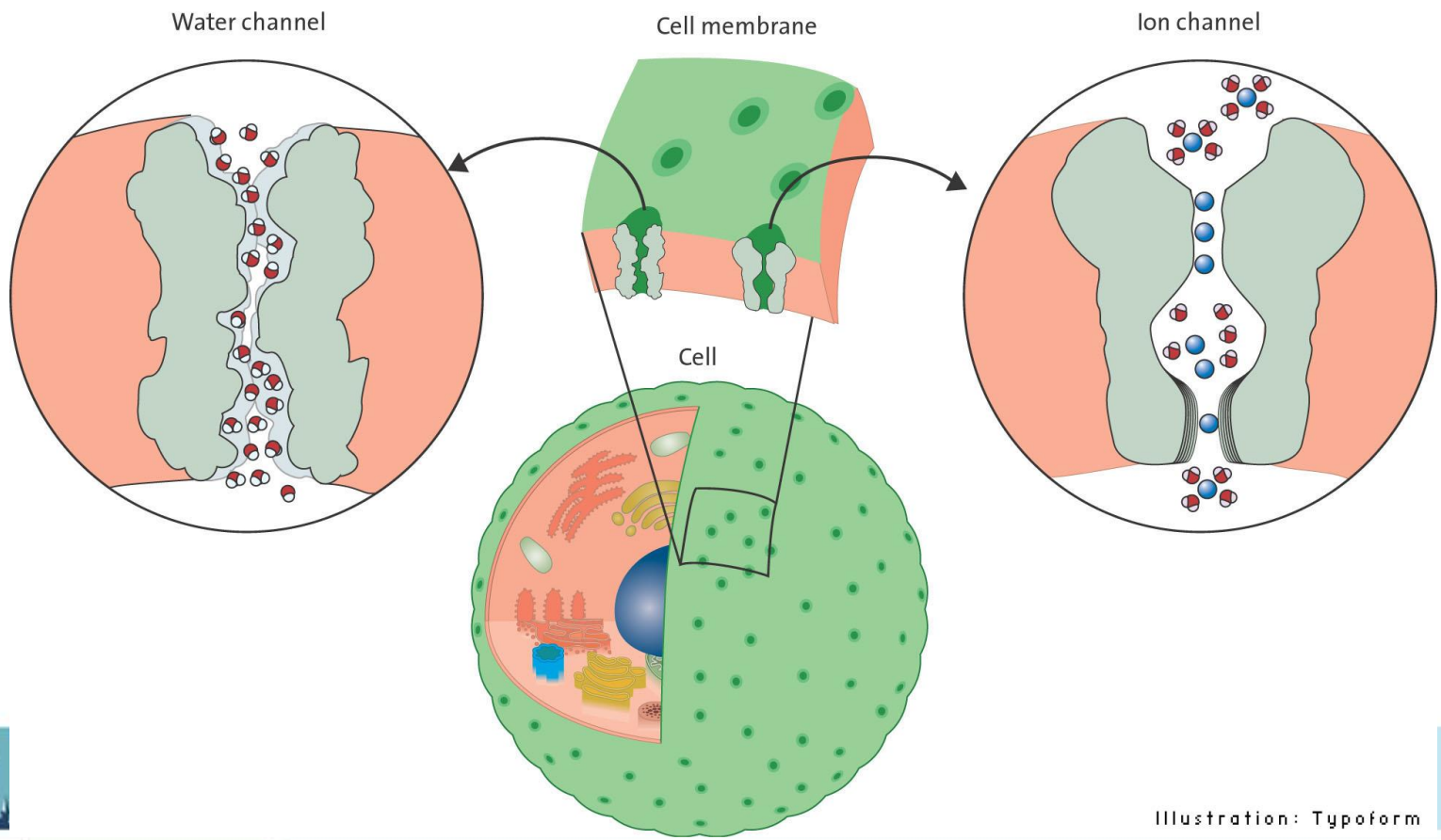
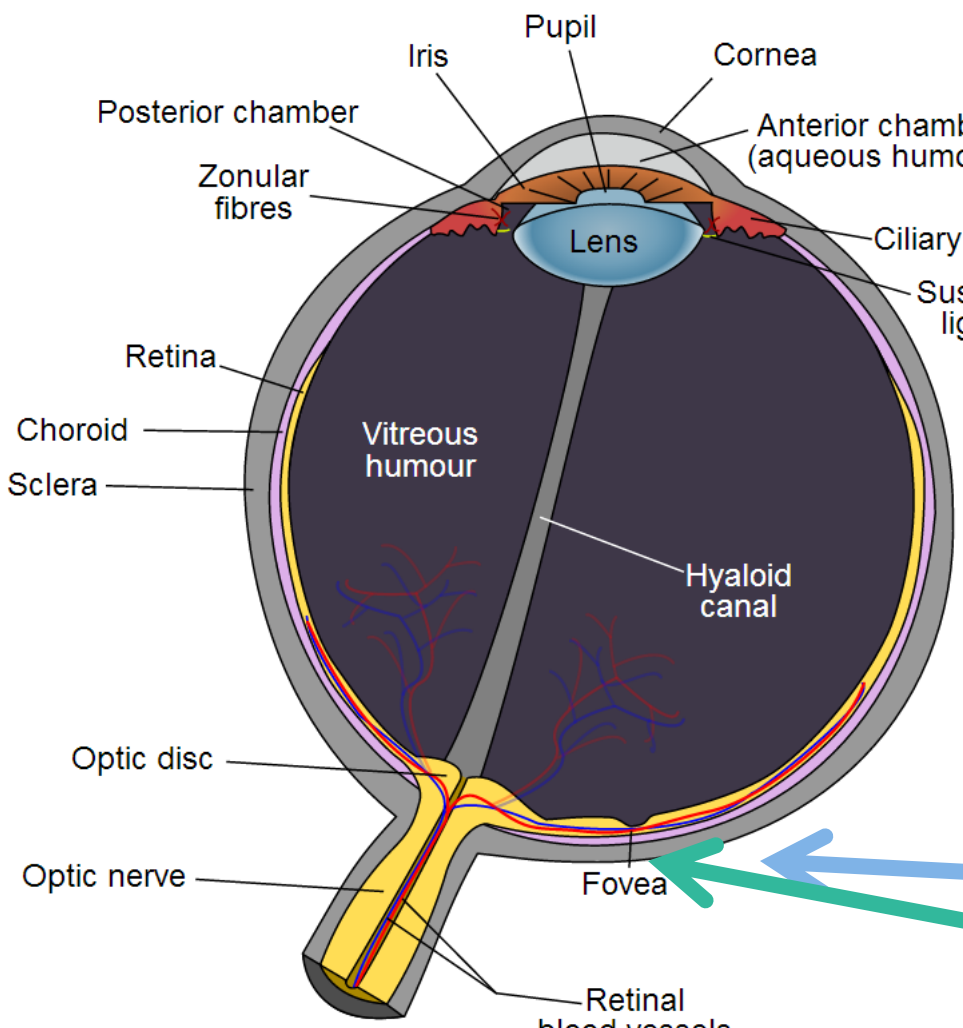
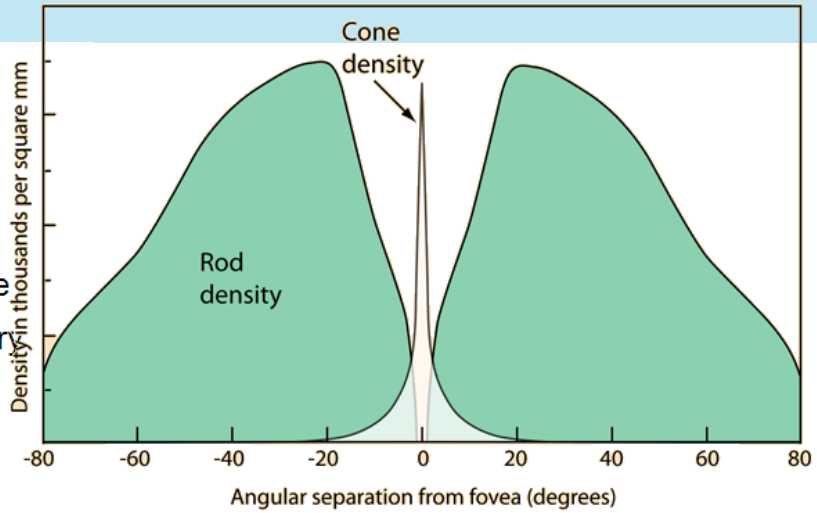
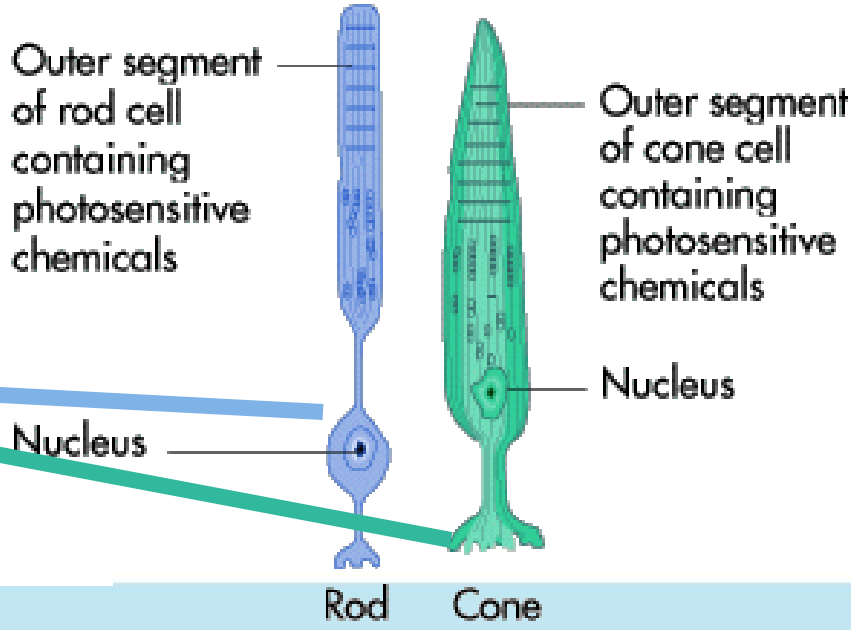


Illustration: Typoform

The Eye

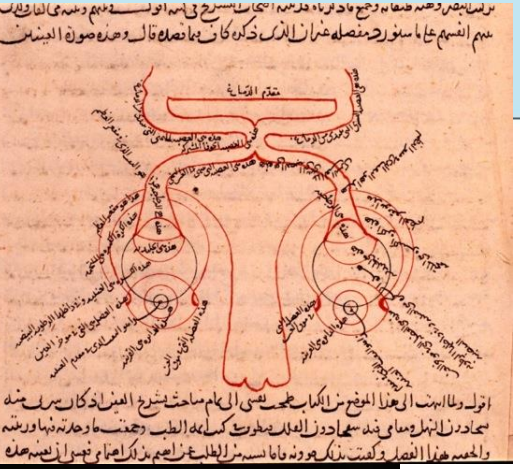

Pupil
Iris
Cornea
Posterior chamber
Anterior chamber
(aqueous humour)
Zonular
fibres
Lens
Ciliary muscle
Suspensory
ligament
Retina
Choroid
Sclera
Vitreous
humour
Hyaloid
canal
Optic disc
Optic nerve
Fovea
Retinal
blood vessels

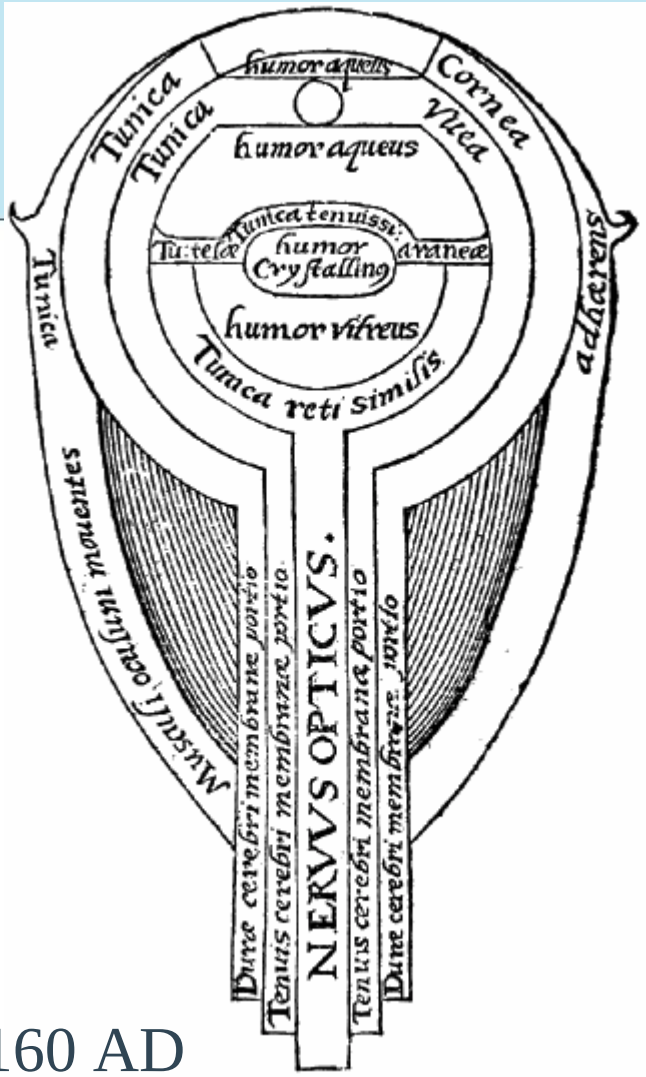

Cone
density
Rod
density
Density in thousands per square mm
-80
-60
-40
-20
0
20
40
60
80
Angular separation from fovea (degrees)


Outer segment
of rod cell
containing
photosensitive
chemicals
Outer segment
of cone cell
containing
photosensitive
chemicals
Nucleus
Nucleus
Rod
Cone

Alhazen's *Thesaurus Opticus, c. 1015 AD*

TOMI
Tissue optics & microcirculation imaging





Based on teachings of Galen c. 160 AD

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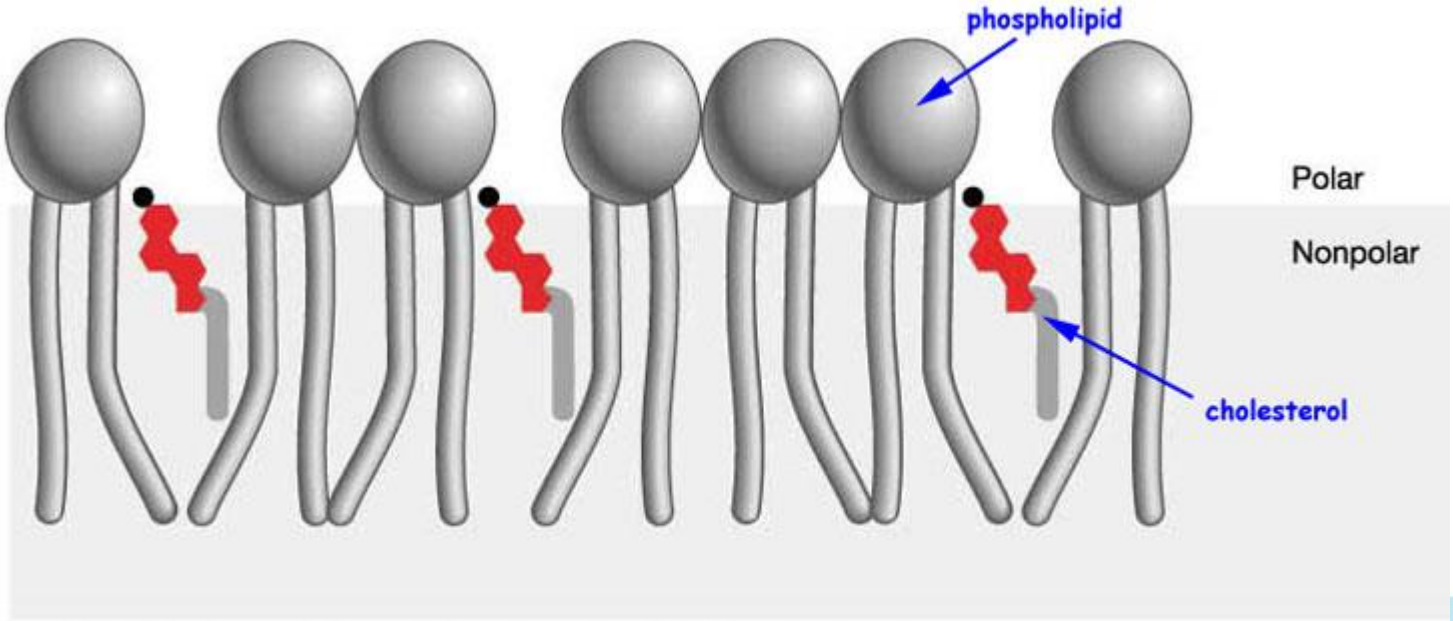
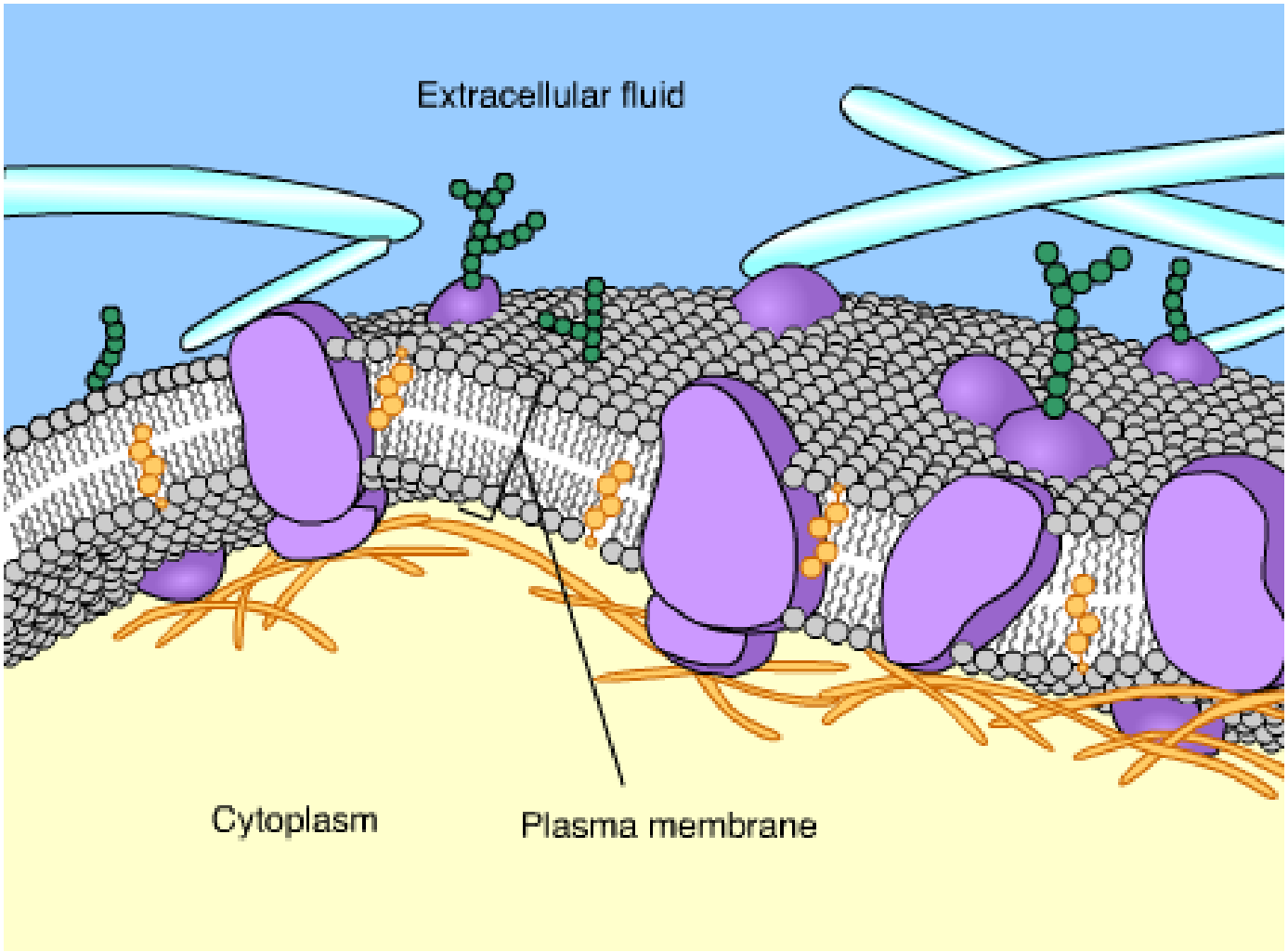
Phospholipid

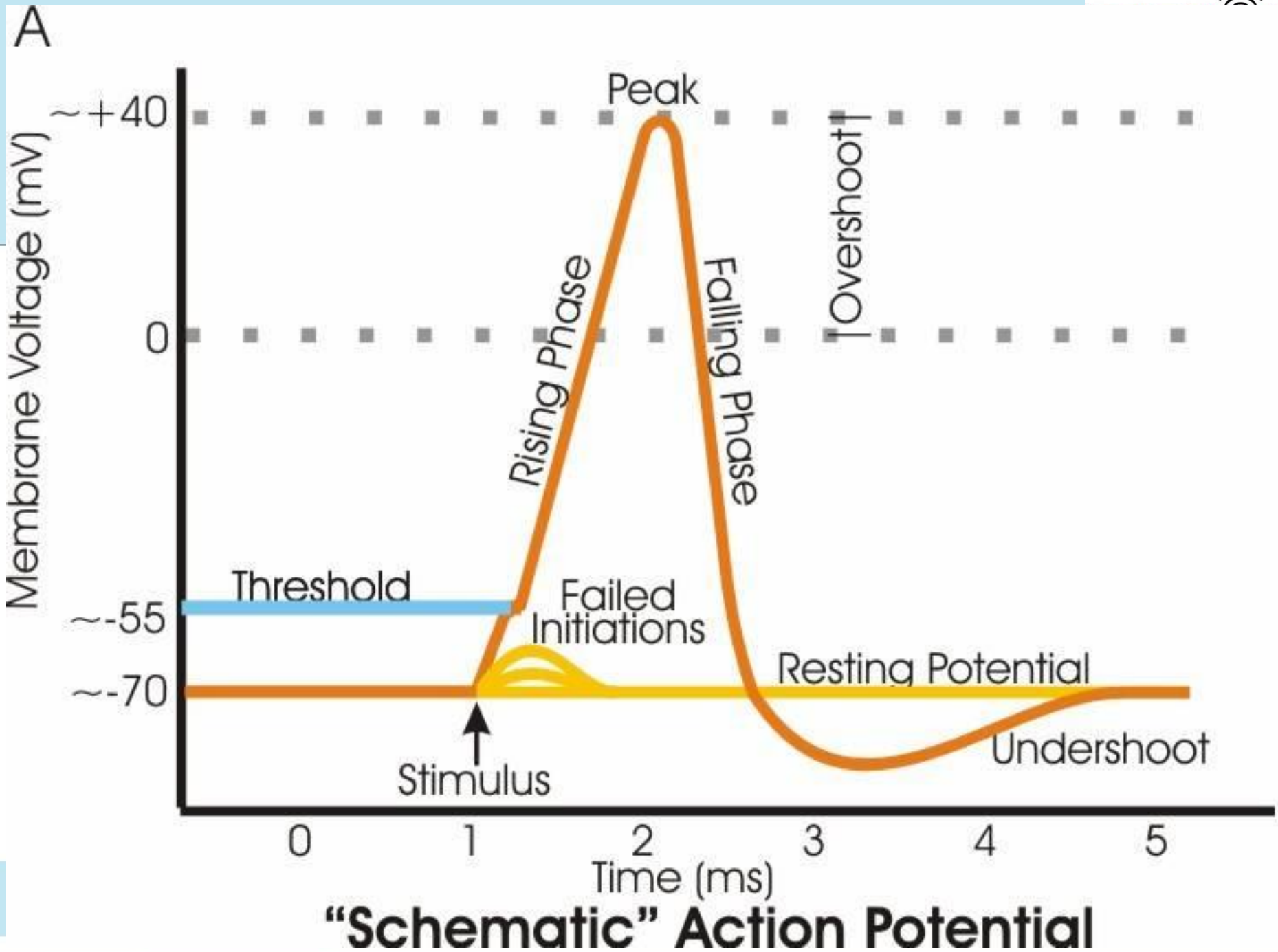
- A molecule that is a constituent of the inner bilayer of biological membranes, having a polar, hydrophilic head and a non-polar, hydrophobic tail.



Relative sizes of phospholipids and cholesterol molecules.
Cholesterol fills the gaps created by unsaturated (kinked) hydrocarbon tails.

Cell Membrane



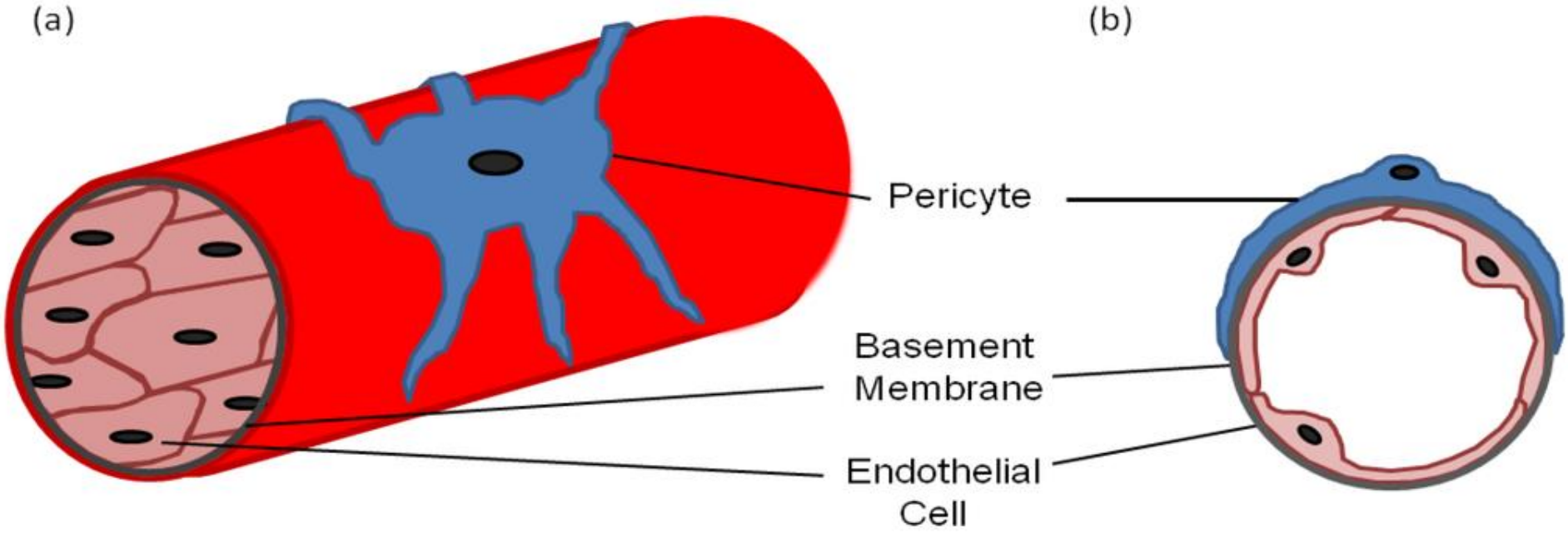


"Schematic" Action Potential

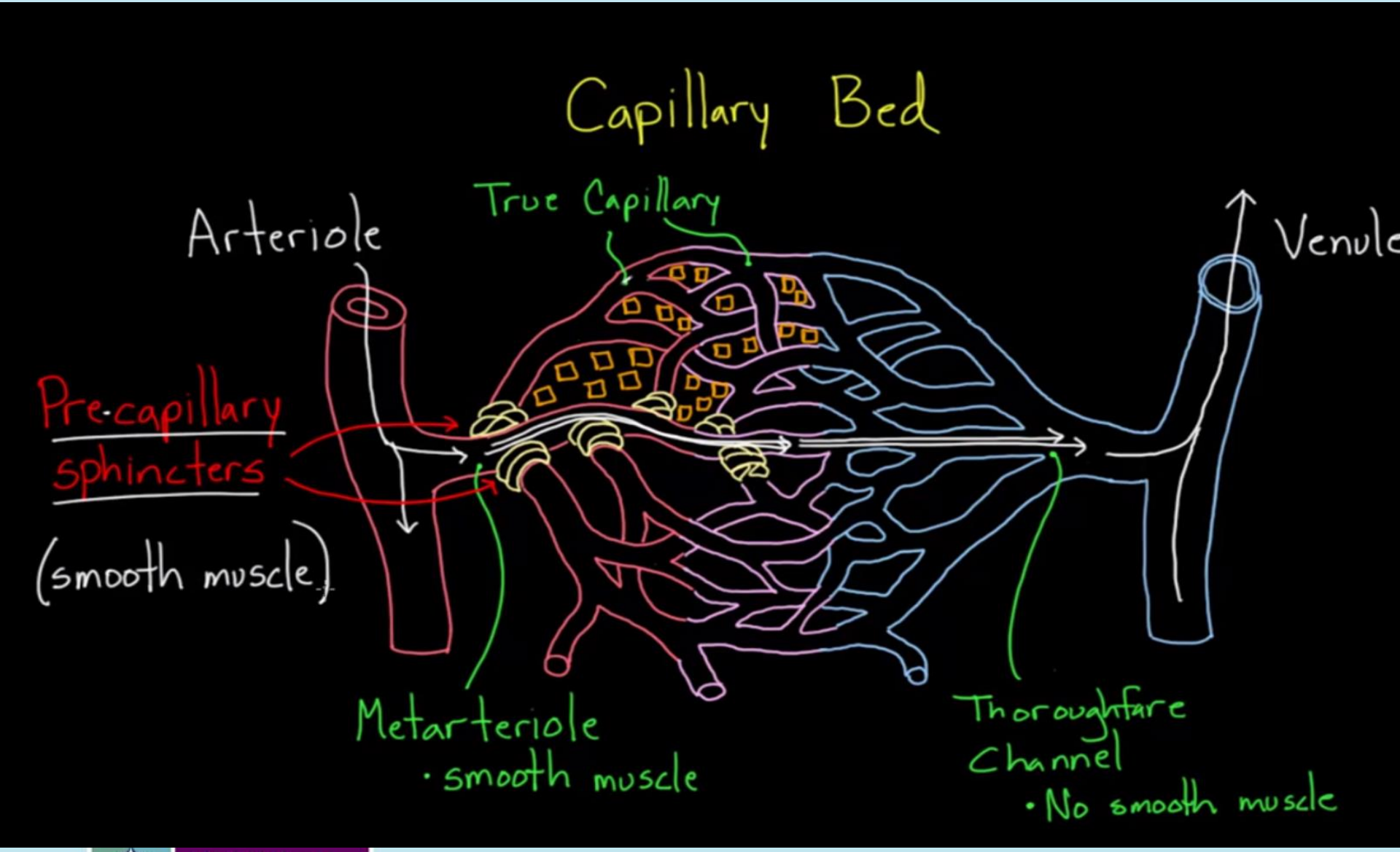
Optogenetics

- The video on optogenetics which I showed today is here:
- http://video.mit.edu/watch/explained-optogenetics-26357/
-
- And a more extensive lecture from Ed Boyden here:
- http://www.youtube.com/watch?v=pP0usNLRV48
-

Capillaries



TOMI
Tissue optics & microcirculation imaging



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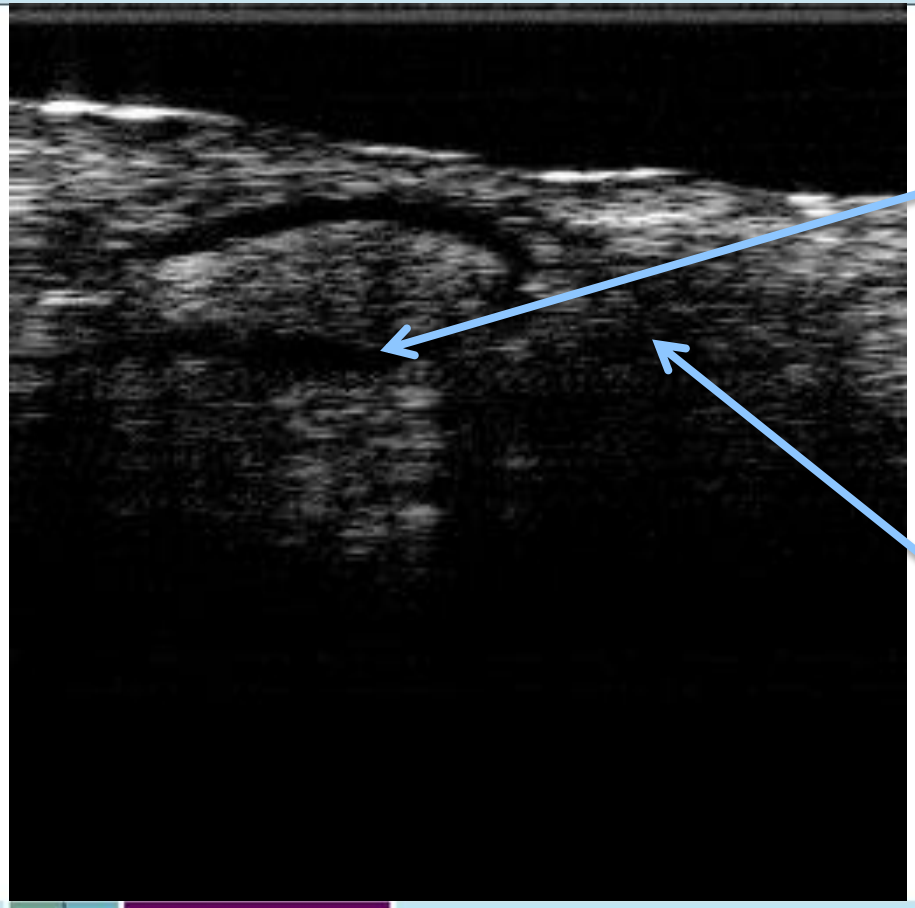
Capillaries

TOMI
Tissue optics & microcirculation imaging

NUI Galway
OÉ Gaillimh

National University of Ireland, Galway

Principle of cmOCT

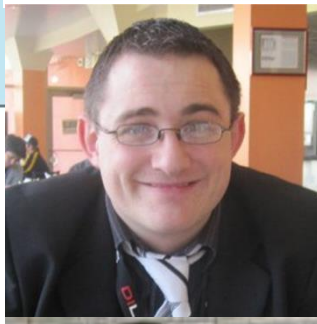


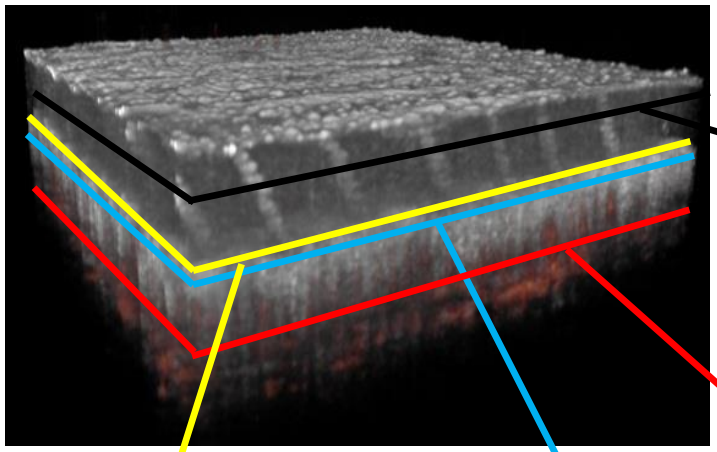
200 µm embedded capillary tube with flowing fluid

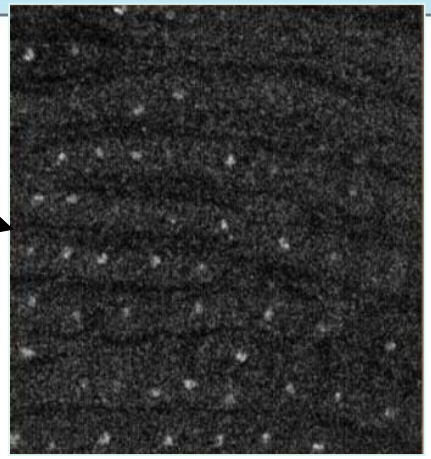
Excised section of Pig Skin

cmOCT of the thumb for a 5x5x3 mm region

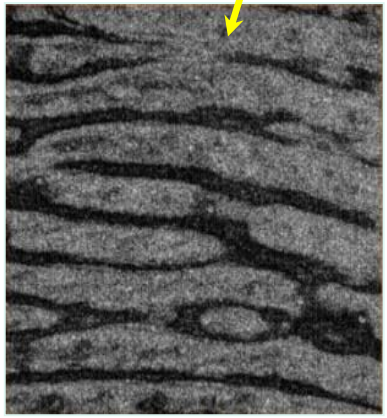
TOMI
Tissue optics & microcirculation imaging



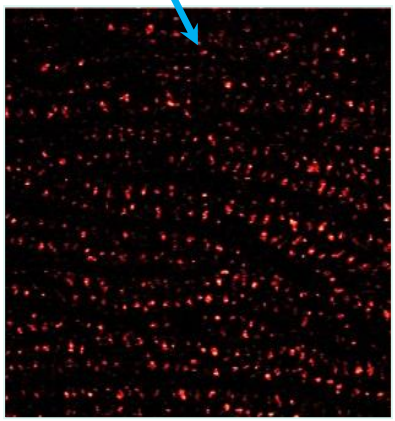




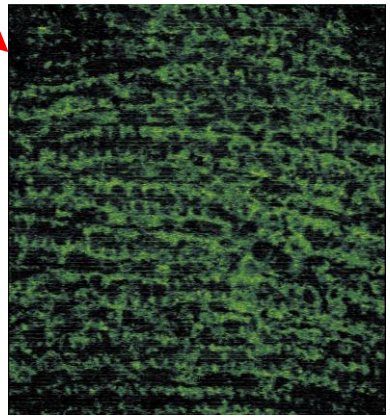
Sweat ducts



Sub-surface Fingerprint



Rising Capillary Loops



Microcirculation Map

AuthenTec

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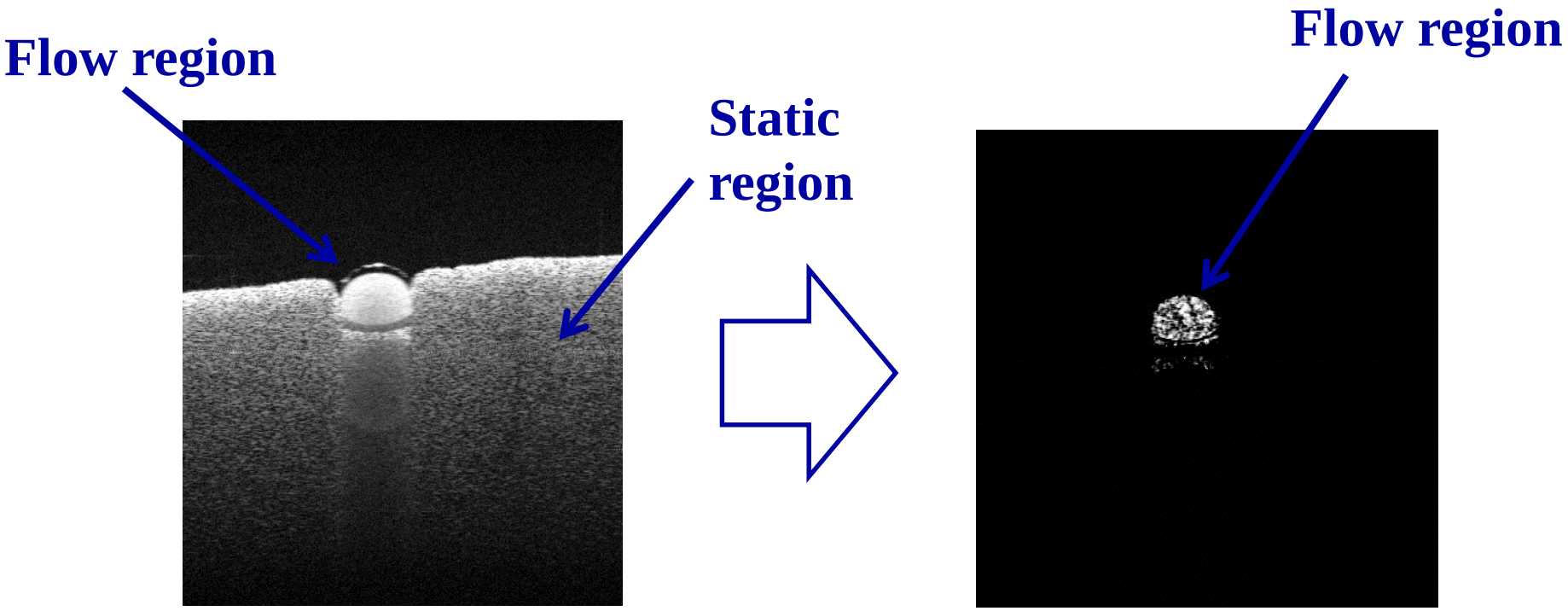
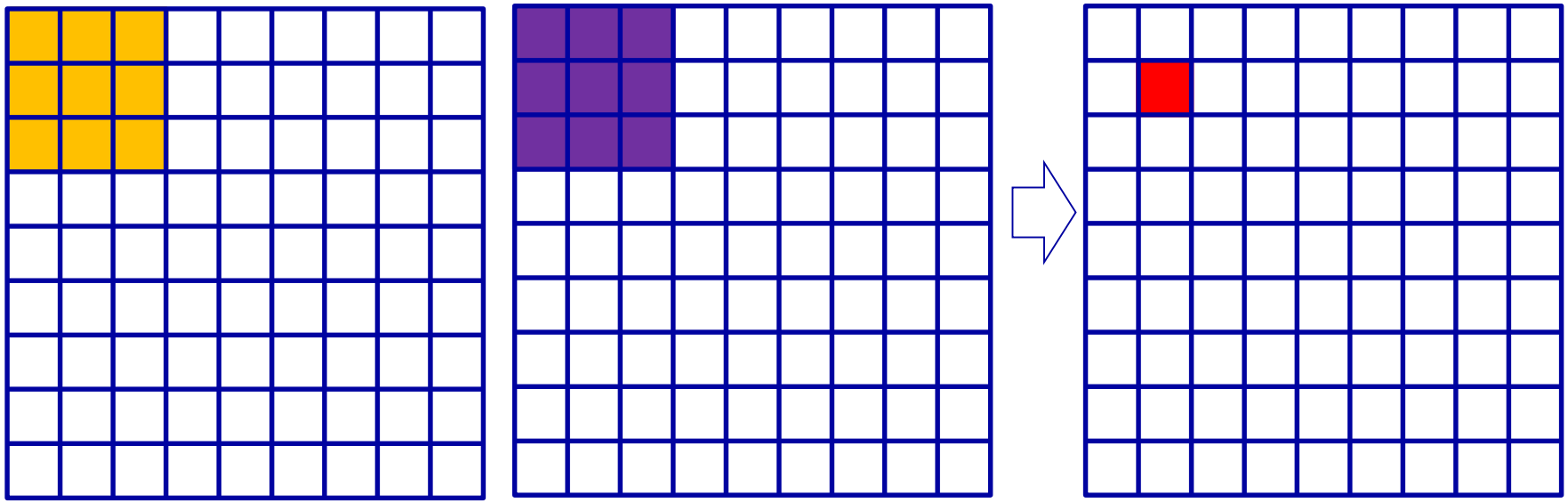
Zam et al., 2013. J. Biophoton. 6 (9) , 663-667.
McNamara et al., 2014, *J. Biomed. Opt. 18 (12), 126008*

Correlation mapping OCT (cmOCT): Principle



Joey Enfield, Enock Jonathan, and Martin Leahy, "In vivo imaging of the microcirculation of the volar forearm using correlation mapping optical coherence tomography (cmOCT)," Biomed. Opt. Express 2, 1184-1193 (2011)

Correlation mapping OCT (cmOCT): Principle

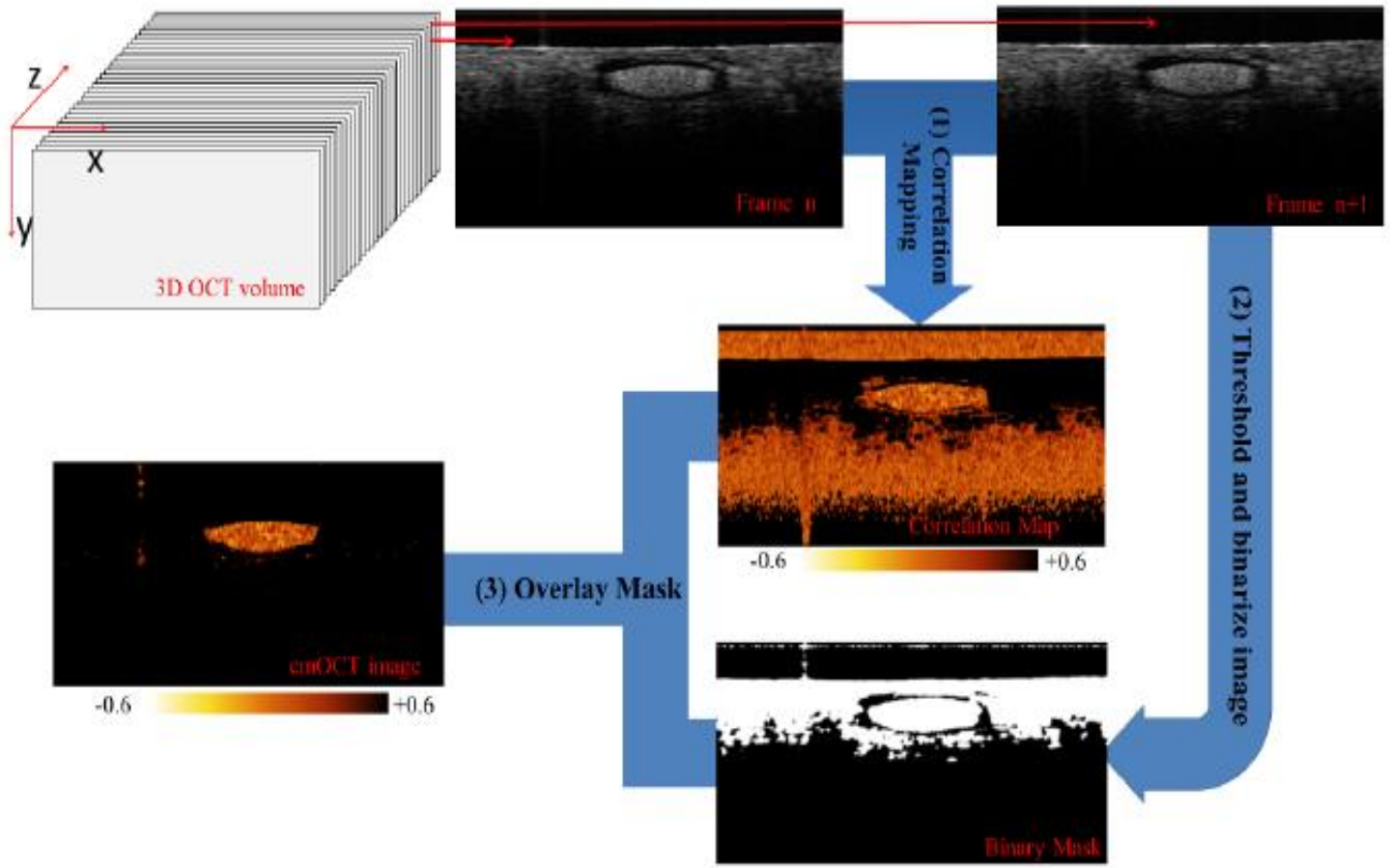


Frame A **Frame B** **Correlation Image**

$$cc(x,z) = \sum_{p=0}^{M} \sum_{q=0}^{N} \frac{\left[I_A(x+p,z+q) - \bar{I}_A(x,z)\right]\left[I_B(x+p,z+q) - \bar{I}_B(x,z)\right]}{\sqrt{\left[I_A(x+p,z+q) - \bar{I}_A(x,z)^2\right]\left[I_B(x+p,z+q) - \bar{I}_B(x,z)^2\right]}}$$

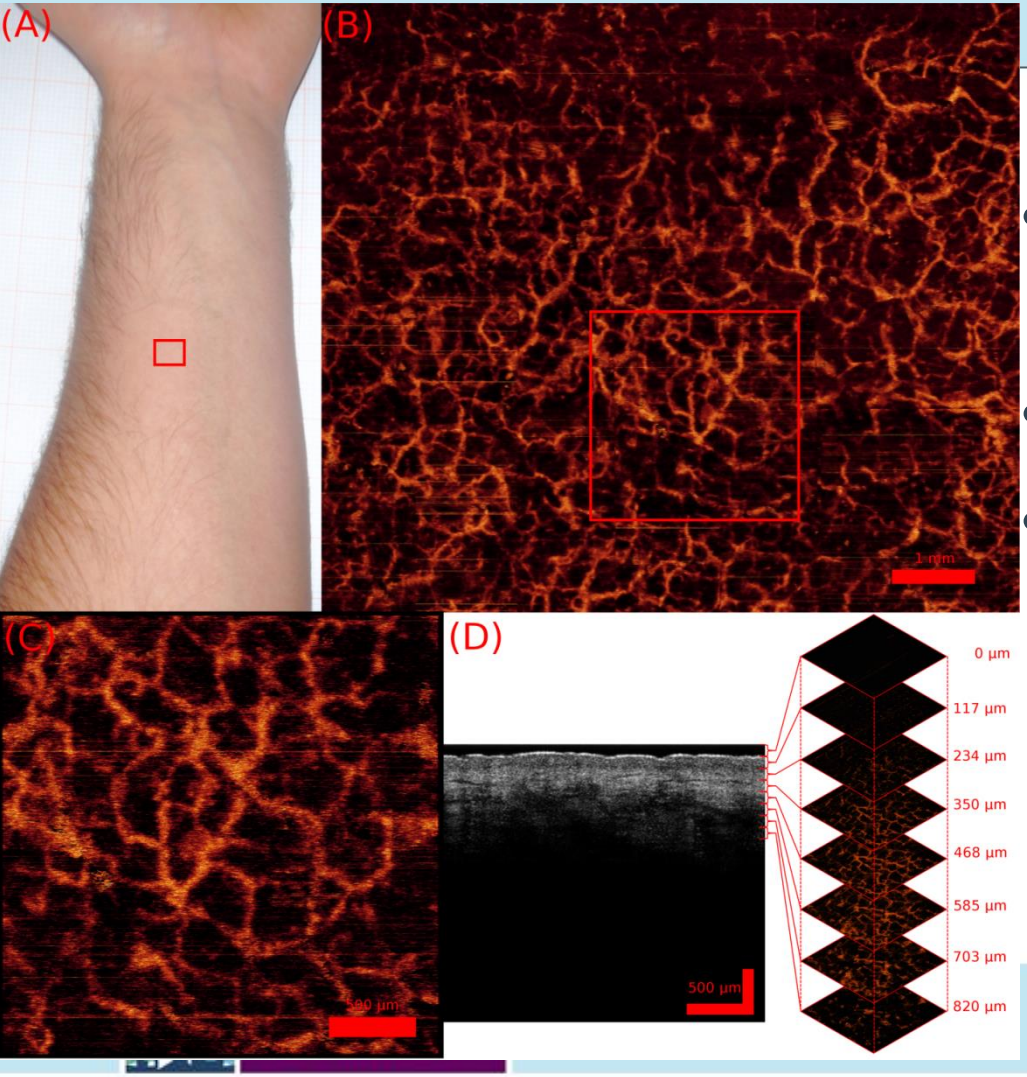
Where M, N are the grid size

Correlation mapping OCT (cmOCT): Principle



Joey Enfield, Enock Jonathan, and Martin Leahy, "In vivo imaging of the microcirculation of the volar forearm using correlation mapping optical coherence tomography (cmOCT)," Biomed. Opt. Express 2, 1184-1193 (2011)

cmOCT



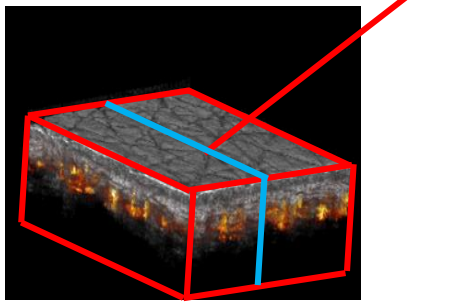
- Correlation mapping OCT
- 8 sequential frames
- 2-D correlation map average correlation value for a square grid measuring 7x7

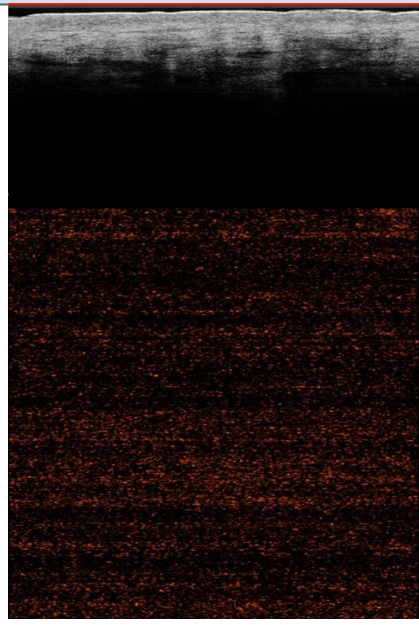
Jonathan et al. 2011 J. Biophotonics 4 (5)

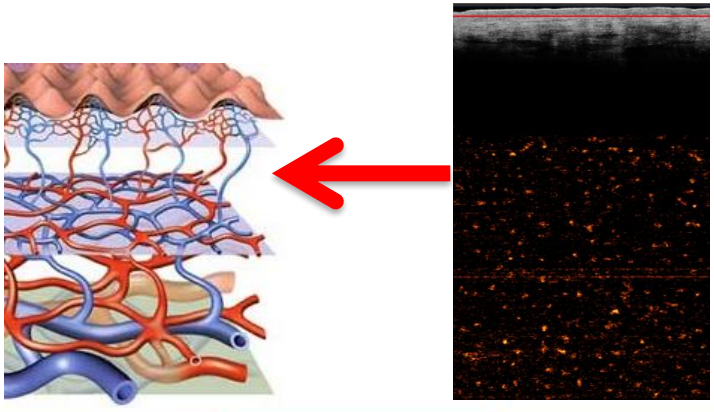
Enfield, J. 2011 Biomedical Optics Express 2 (5) 1184-1193.

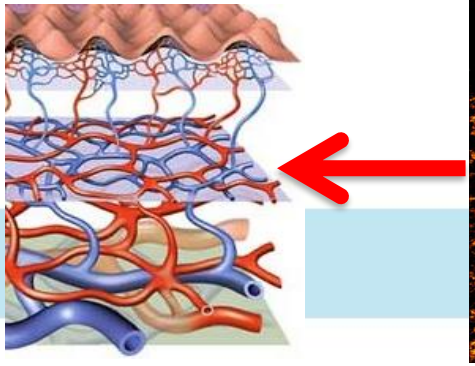
In-vivo Human Results

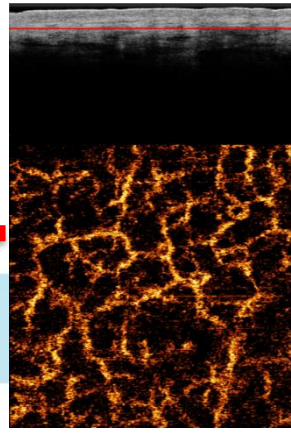
- To determine location depth slices can be examined



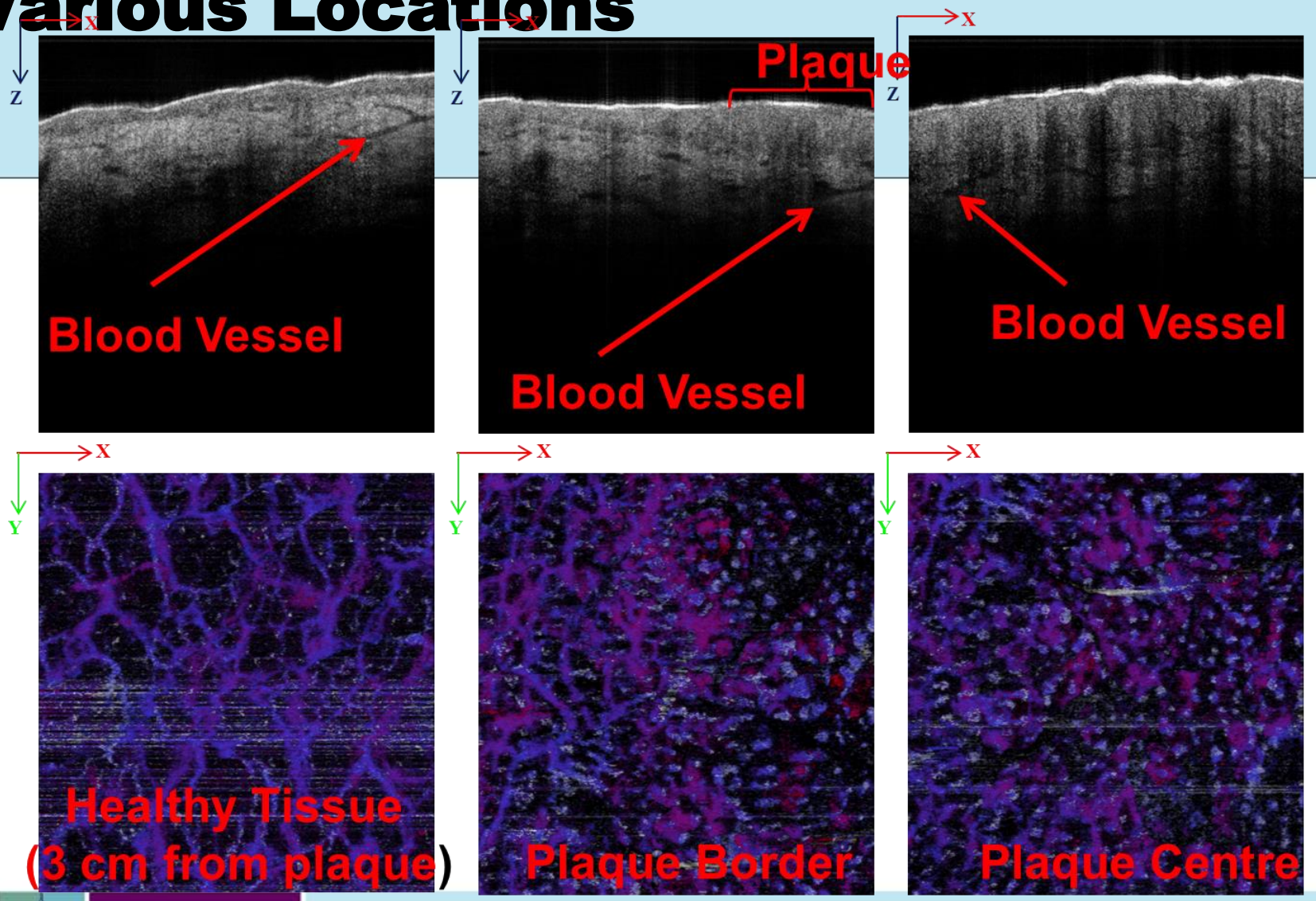








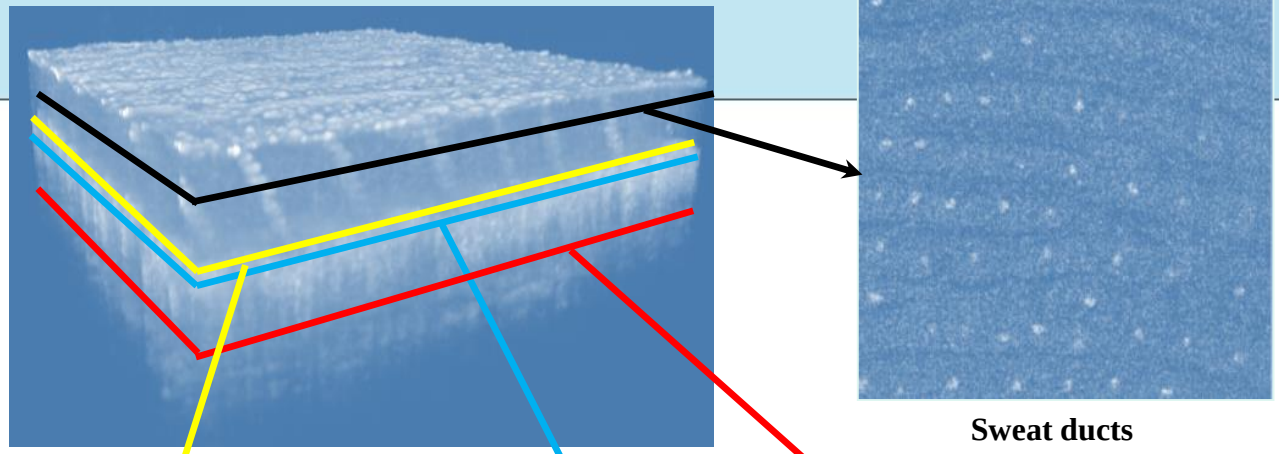
cmOCT of Patient's Forearm at Various Locations



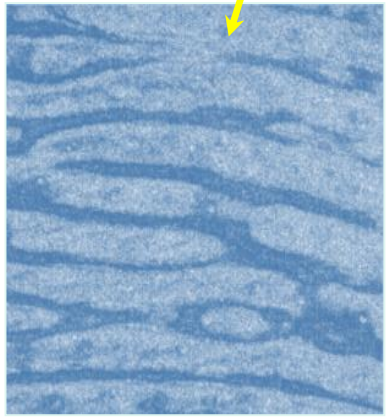
All figures are 3x3 mm

Zafar et al. May 2013 (accepted) Skin Research and Technology.

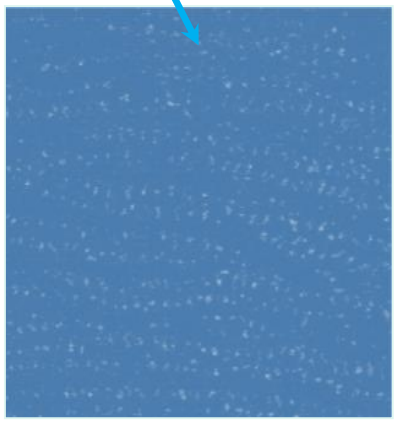
Results: cmOCT of the thumb for a 5x5x3 mm region



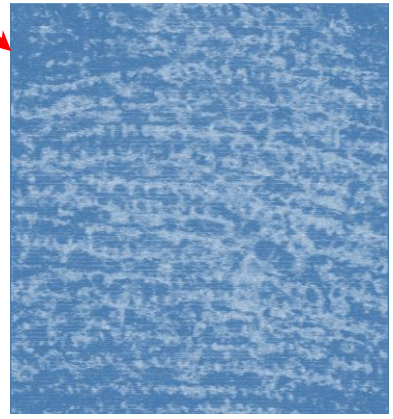
Sweat ducts



Sub-surface Fingerprint



Rising Capillary Loops



Microcirculation Map

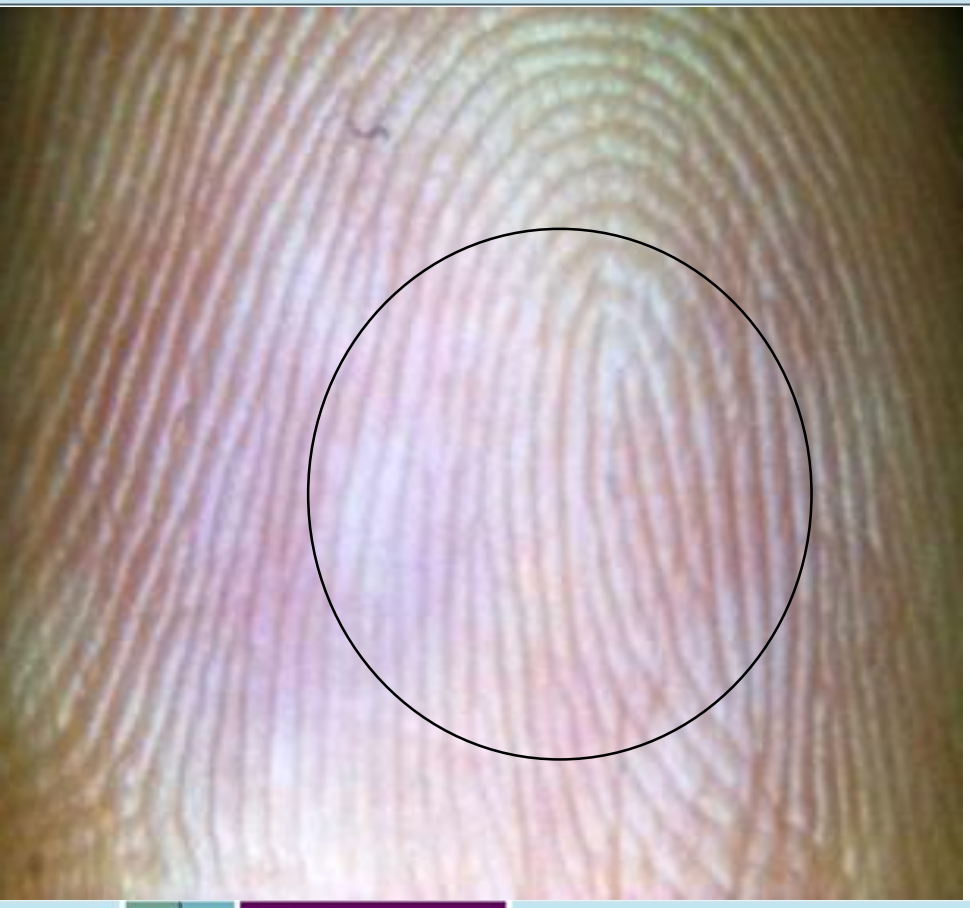
Zam et al., 2013. J. Biophoton. **6** (9) , 663-667.
McNamara et al., 2014, *J. Biomed. Opt.* **18** *(12), 126008*

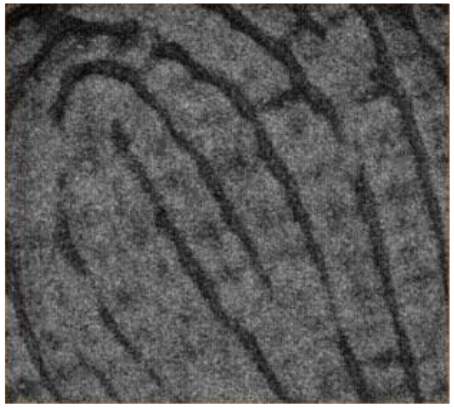
Secure biometric access to smartphones

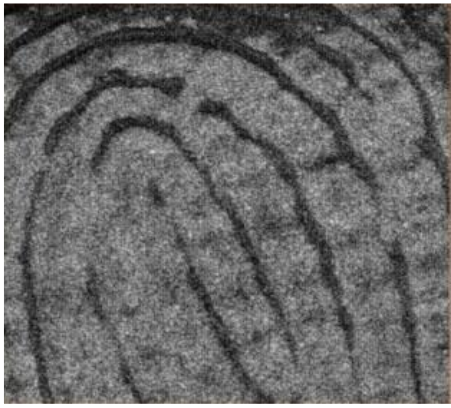
http://www.digitaltrends.com/mobile/can-apple-hand-over-your-fingerprint-to-the-nsa/

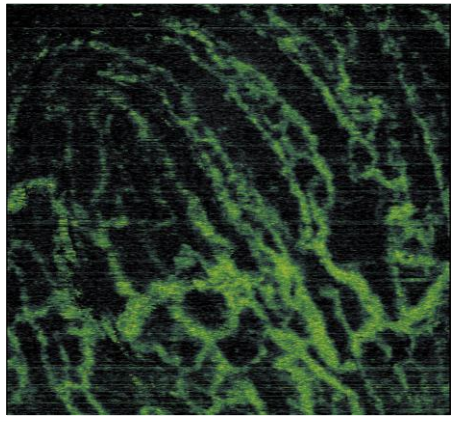
Middle finger

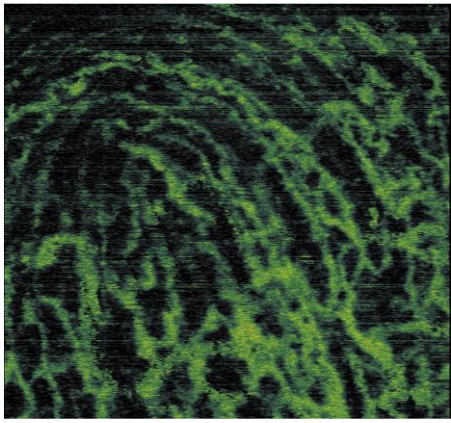
Day 1 Day 30











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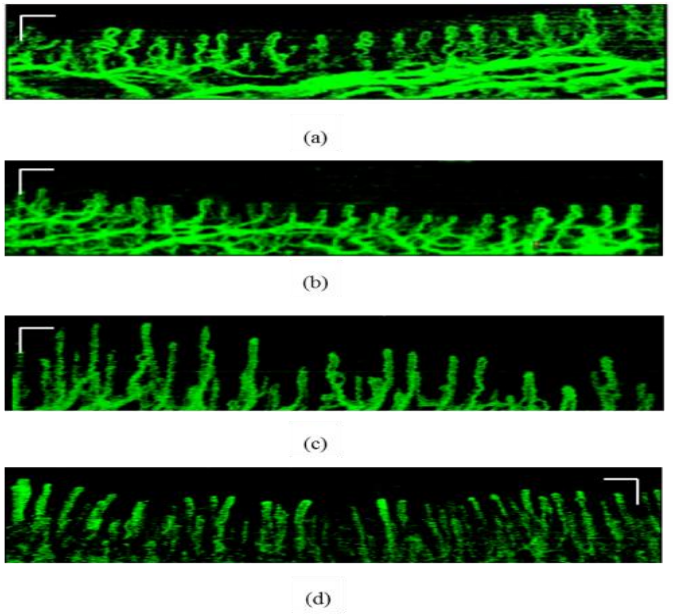
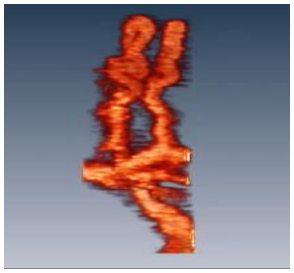
Nailfold Capillaroscopy

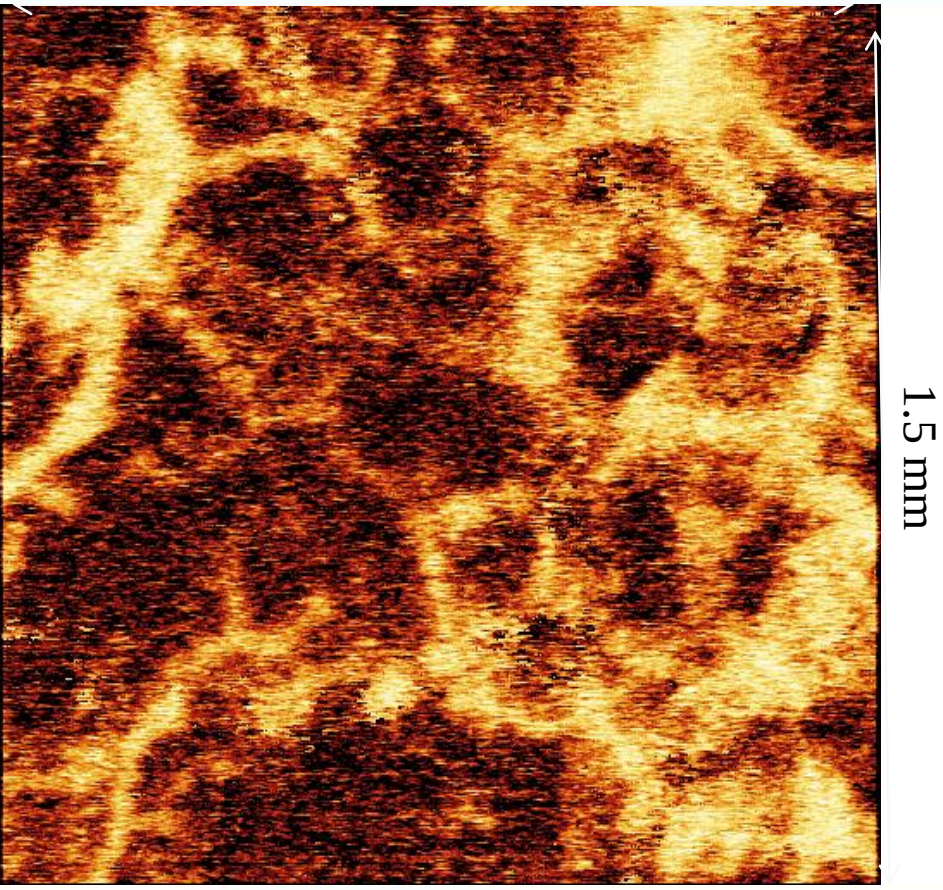


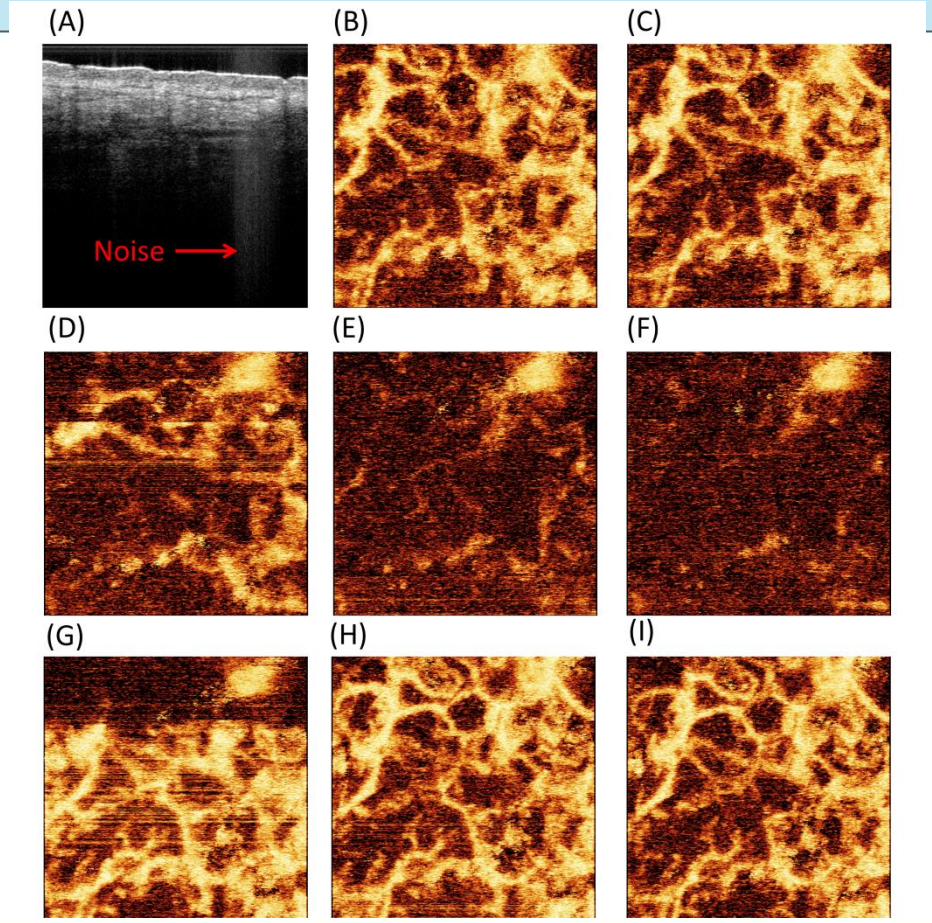


Age, Gender, Race:
(a) 24, male, Caucasian
(b) 34, male, Caucasian,
(c) 20, female, Caucasian
(d) 32, male, Indian

By carefully combining the composite projection images (X=2.9 mm, Y =0.75 mm) of the nailfold curvature, the overall plexus morphology and variability could be estimated in each participant. Similarities between participants (a) & (b) and participants (c) & (d) were apparent. Participants (a) & (b) had average capillary lengths = 200-300 μm, capillary densities = 8.27 & 9.31 per mm with some twisted loops. Participants (c) & (d) had average capillary lengths = 400-500 μm, densities = 11.9 & 9.31 per mm with no twisted loops.

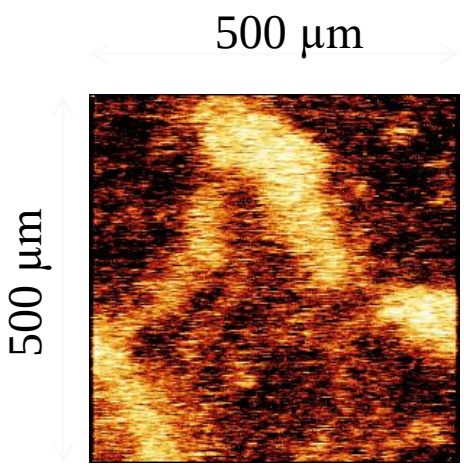
Human Reactive hyperaemia

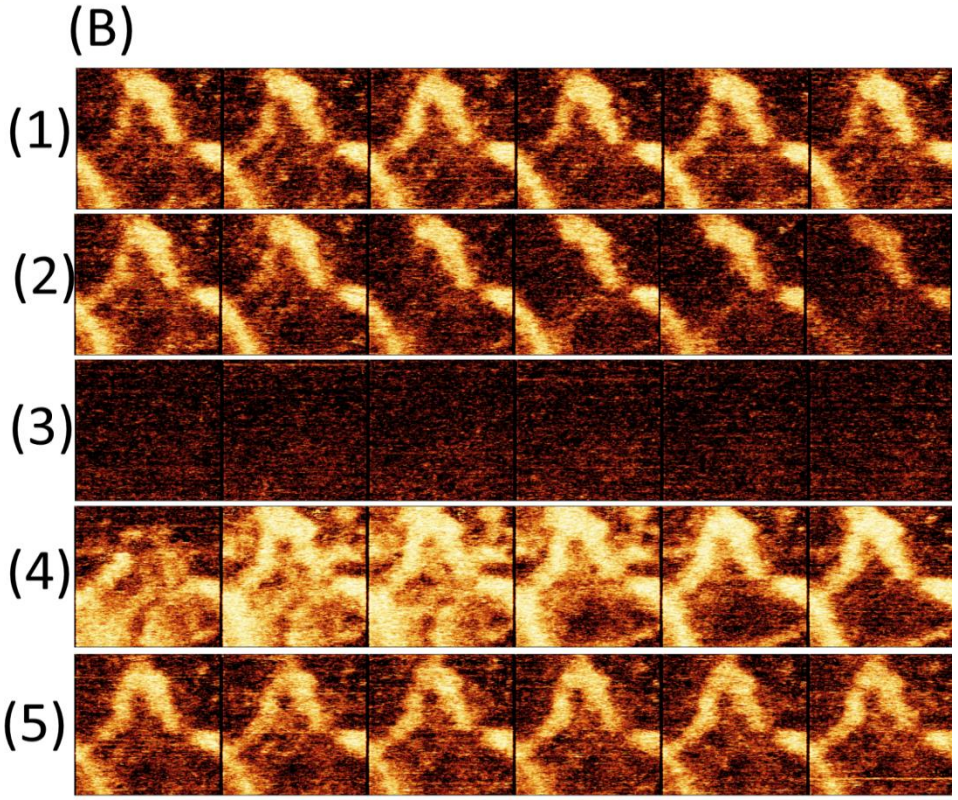




Human Reactive hyperaemia

- To improve this a 256x256 region can be acquired in 5 s.
- The scanning area is reduced to 500x500 μm so a small region of microcirculation is imaged.





Depth Resolved RH

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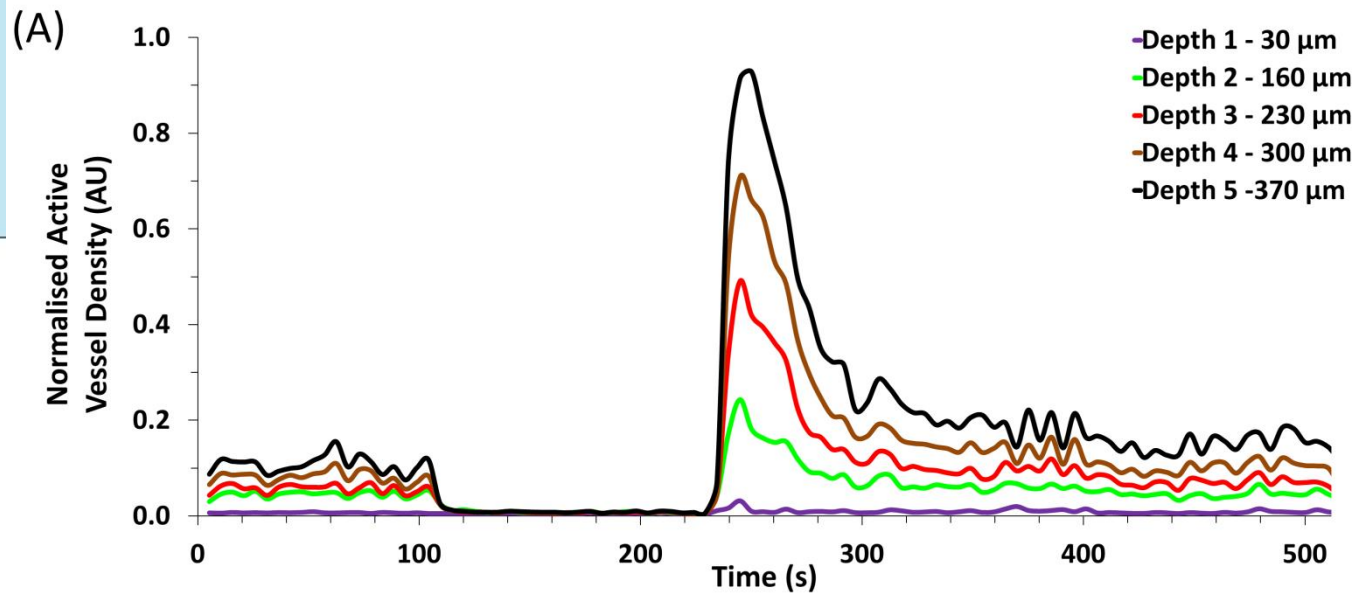
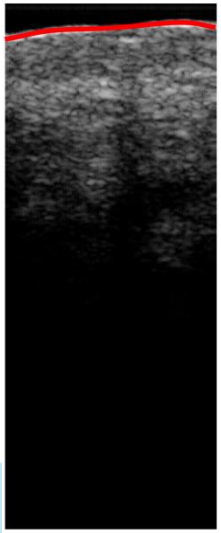
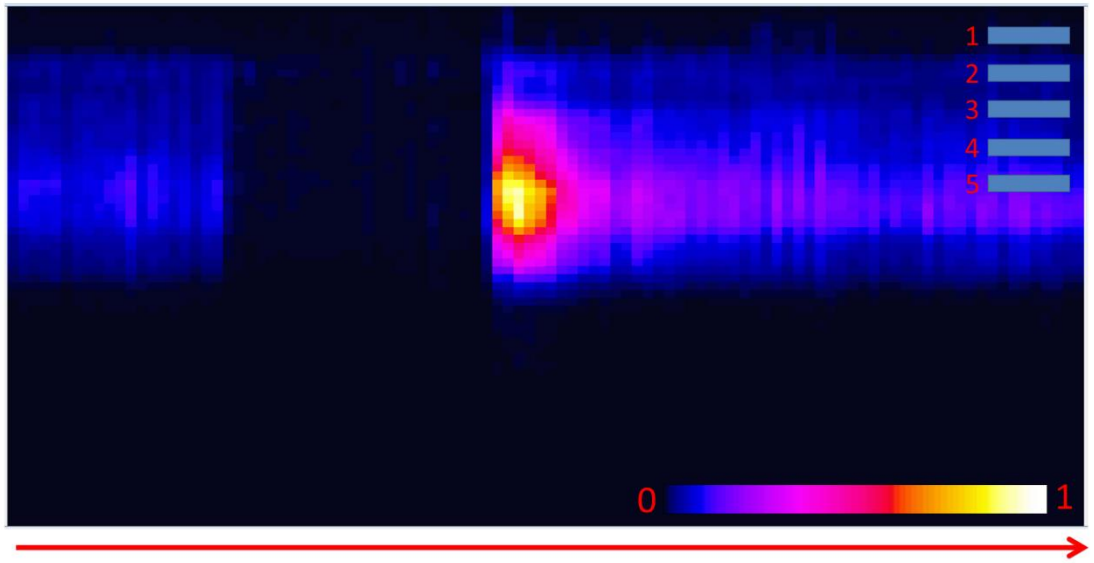
Tissue optics & microcirculation imaging







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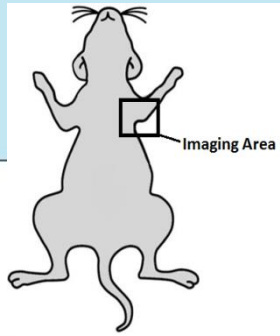
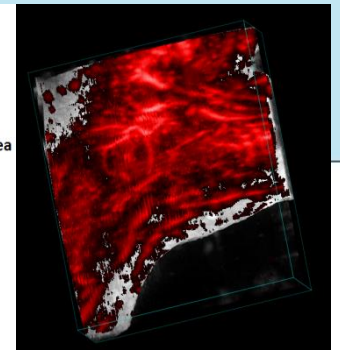
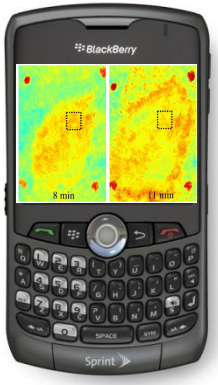
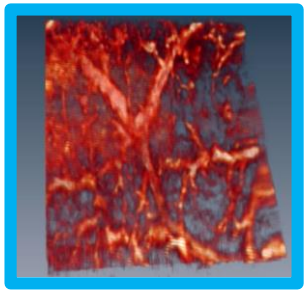
Microcirculation Imaging Techniques – TOMI lab

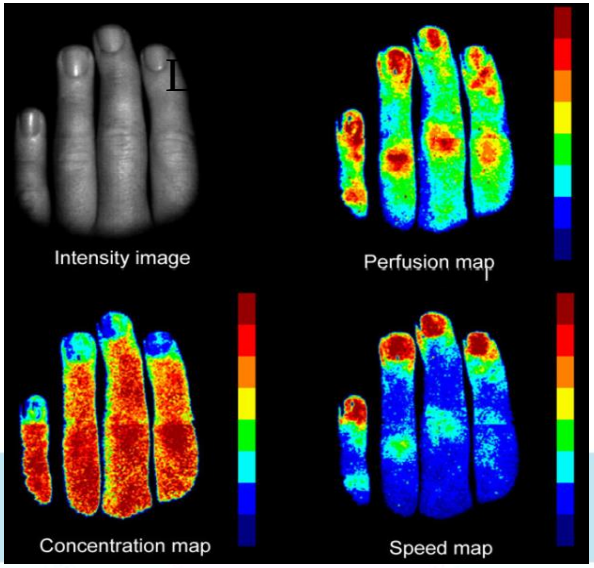
- Laser Doppler perfusion imaging (LDPI)
- Laser speckle contrast imaging (LSCI)
- Tissue viability imaging (TiVi)
- Photoacoustic tomography (PAT)
- Optical coherence tomography (OCT)

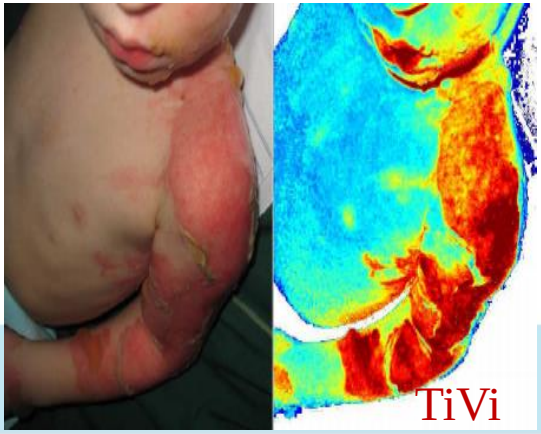


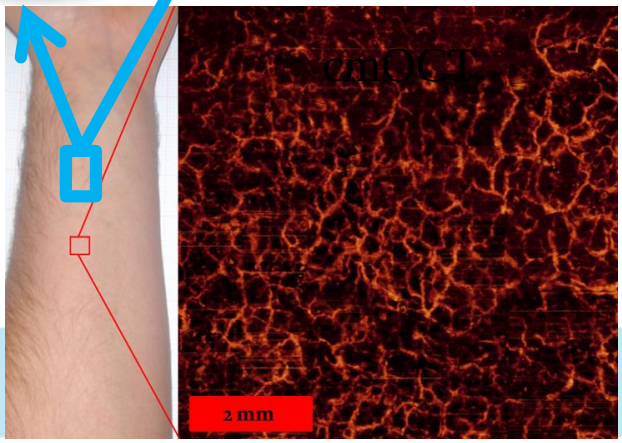








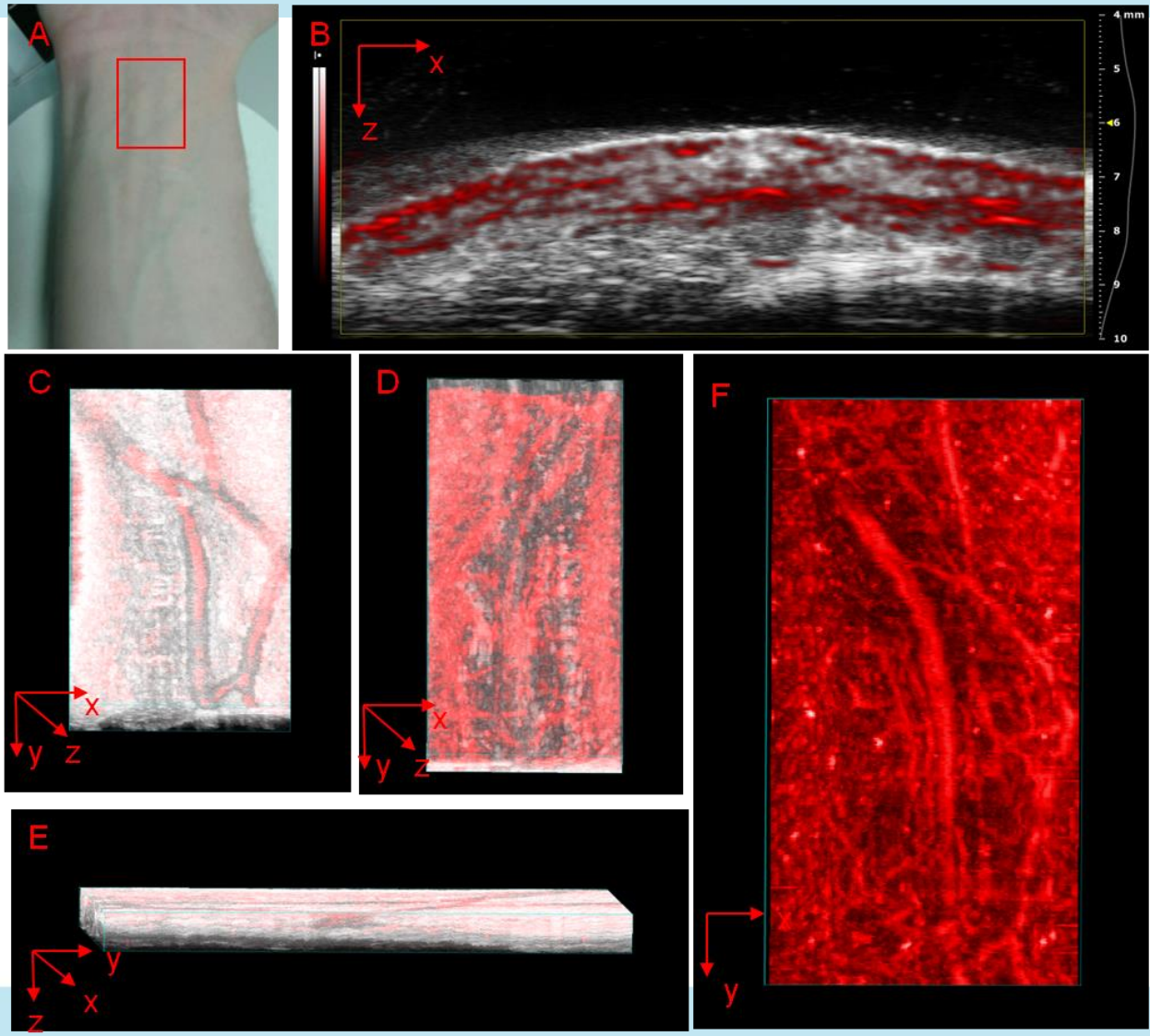




In vivo imaging of human forearm using 40 MHz transducer

TOMI
Tissue optics & microcirculation imaging

- In vivo PA and high frequency ultrasound images of the human forearm for a 30.5 (length) x 14.1 (width) x 10 (depth) region using 40 MHz probe at 860 nm.



NUI Galway
OÉ Gaillimh

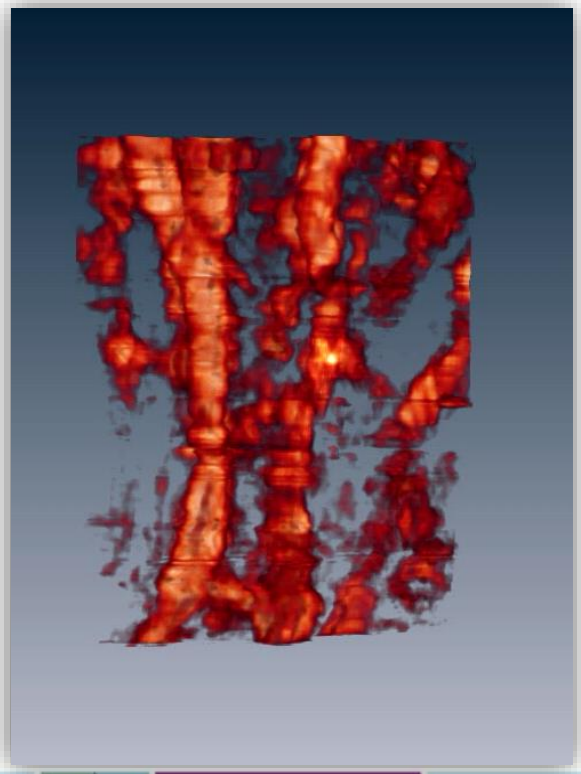
submitted to Journal of Investigative Dermatology, May 2014.

Comparison of 15, 21 & 40 MHz transducers

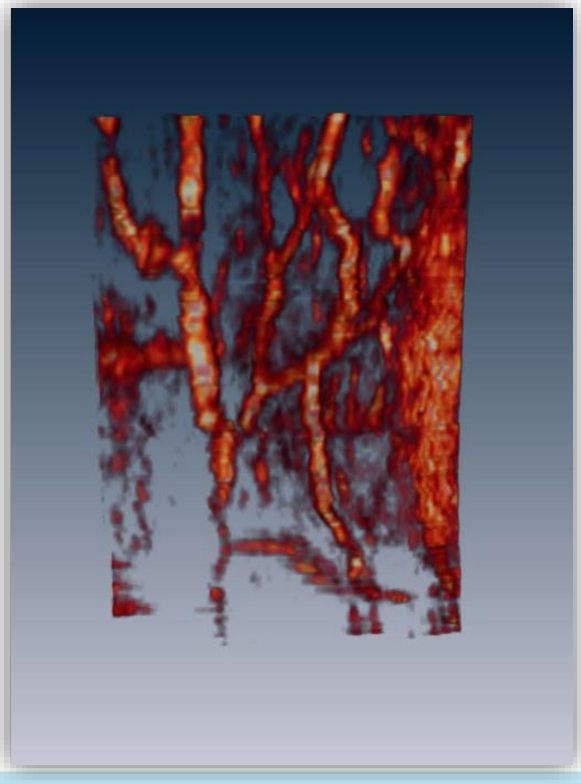
TOMI
Tissue optics & microcirculation imaging

• Comparison of *in vivo* images of the human forearm acquired at the same location using 15 MHz, 21 MHz and 40 MHz transducer probes at 1064 nm.

15 MHz (rendered)
30.5 mm x 23 mm (l x w).



21 MHz (rendered)
30.5 mm x 23 mm (l x w).



40 MHz (rendered)
30.5 mm x 14 mm (l x w).

NUI Galway
OÉ Gaillimh

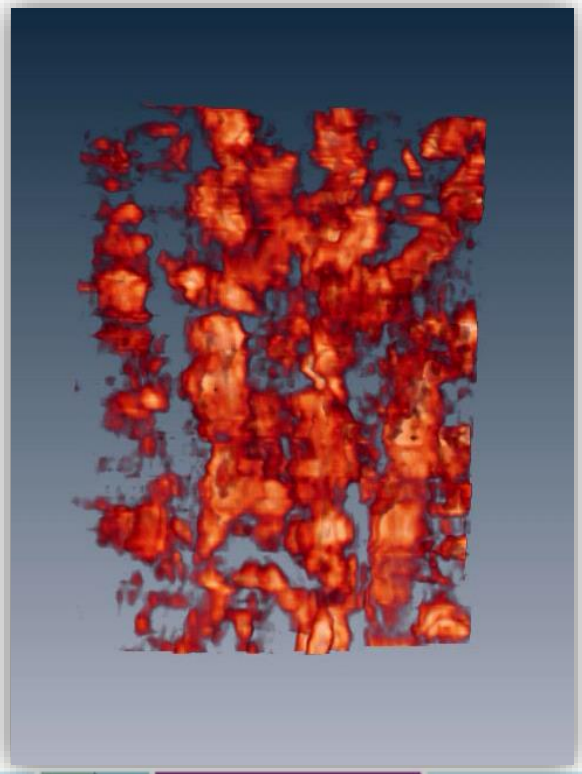
Leahy et al., submitted to Journal of Investigative Dermatology, May 2014.

Comparison of 15, 21 & 40 MHz transducers

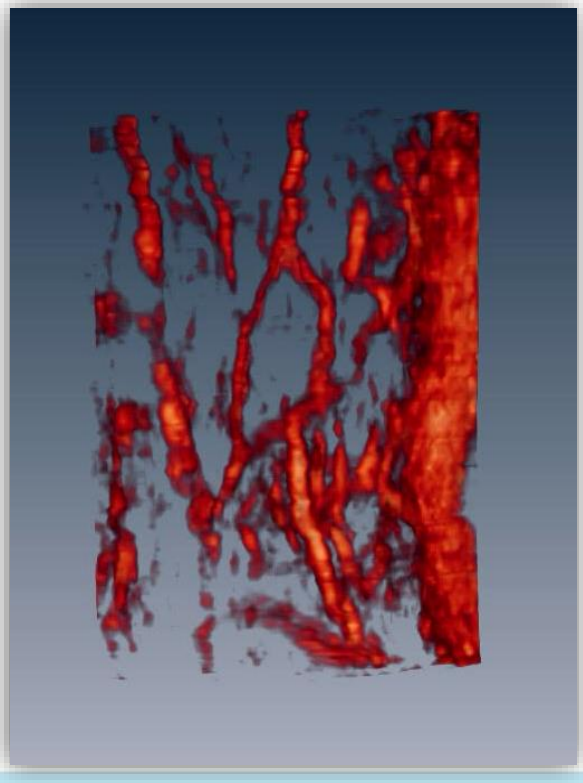
TOMI
Tissue optics & microcirculation imaging

- Comparison of *in vivo* images of the human forearm acquired at the same location using 15 MHz, 21 MHz and 40 MHz transducer probes at 800 nm.

15 MHz (rendered)
30.5 mm x 23 mm (l x w).



21 MHz (rendered)
30.5 mm x 23 mm (l x w).

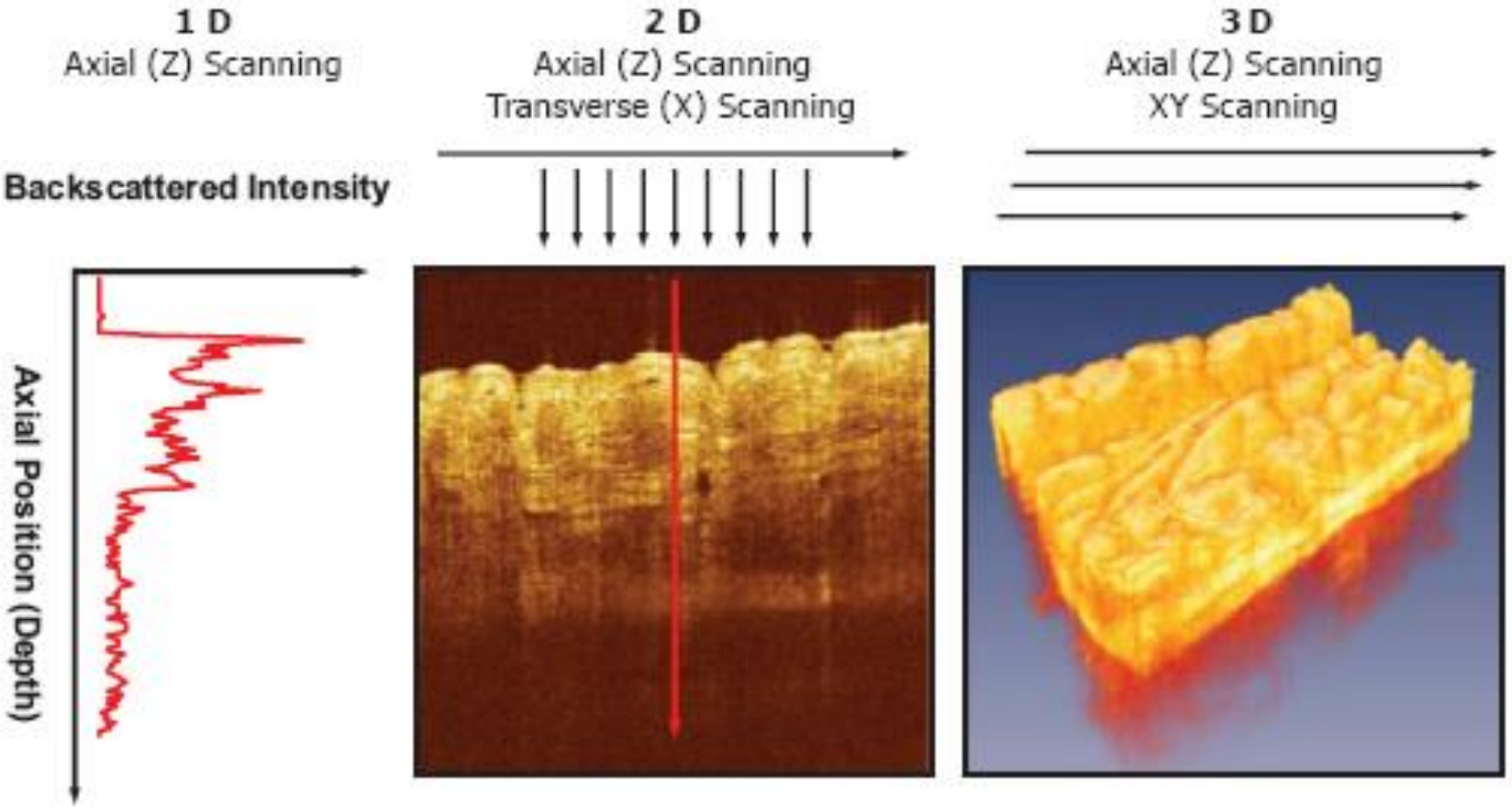


40 MHz (rendered)
30.5 mm x 14 mm (l x w).

NUI Galway
OÉ Gaillimh

submitted to Journal of Investigative Dermatology, May 2014.

OCT: optical analogue of pulsed-wave ultrasound

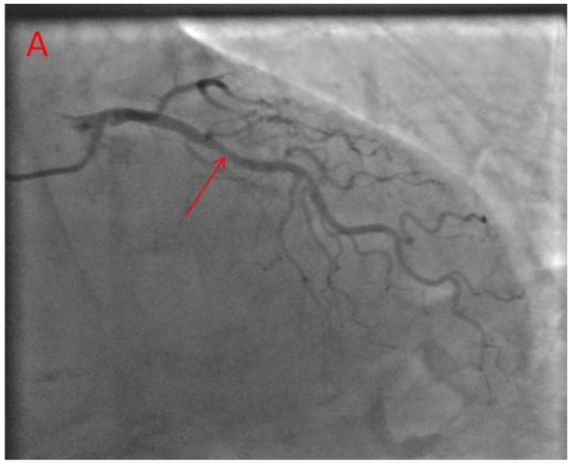


J. Fujimoto, 2008

Materials & Methods

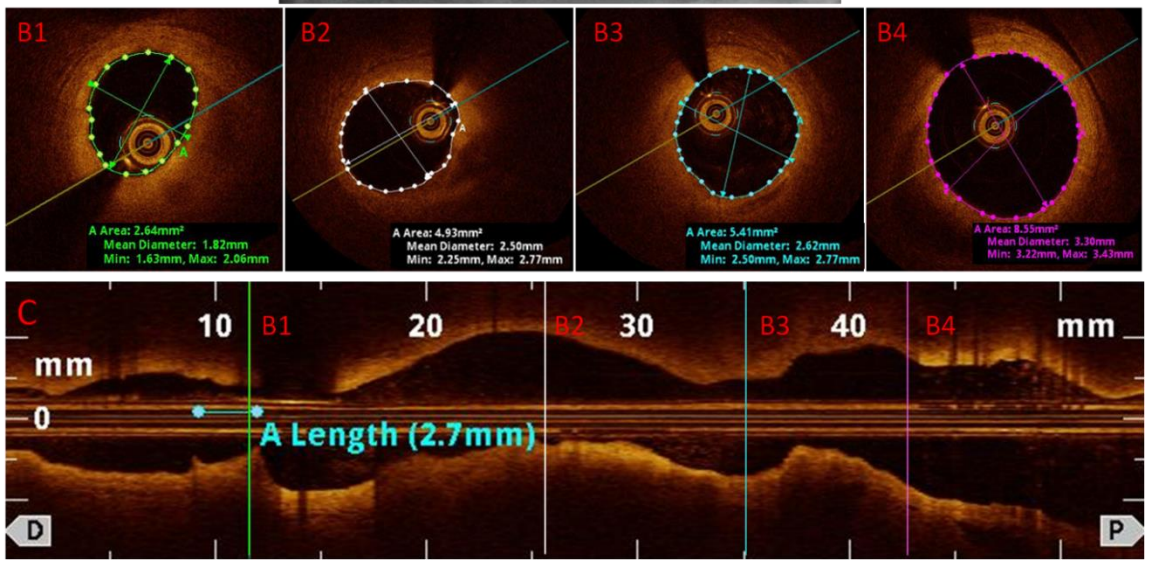
TOMI
Tissue optics & microcirculation imaging

- The minimal lumen area (MLA) and minimal lumen diameter (MLD) were measured at the cross section with the smallest lumen area using FD-OCT.



NinePoint_4.mp4

- Reference lumen area (RLA) was measured at reference cross section with the largest lumen within 10 mm proximal or distal to MLA and before any side branch.



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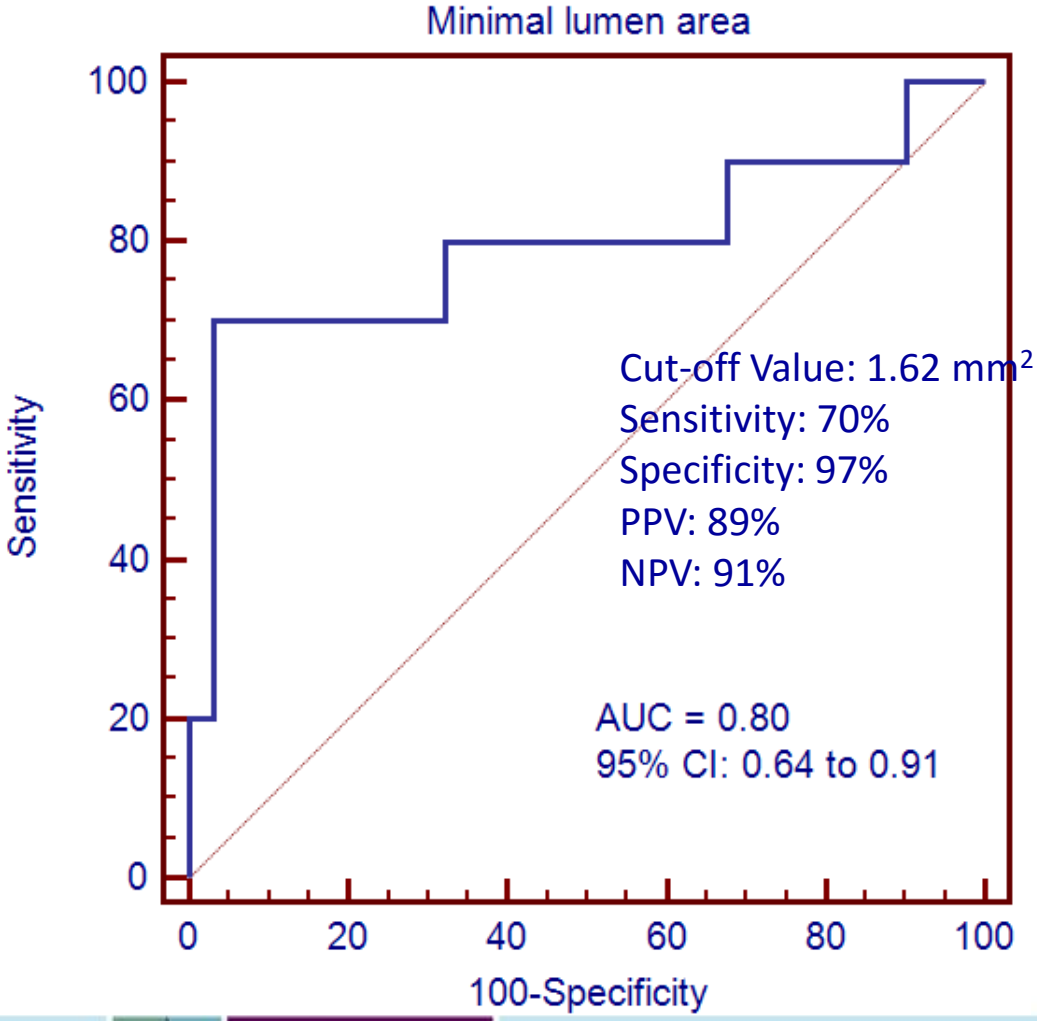
Results

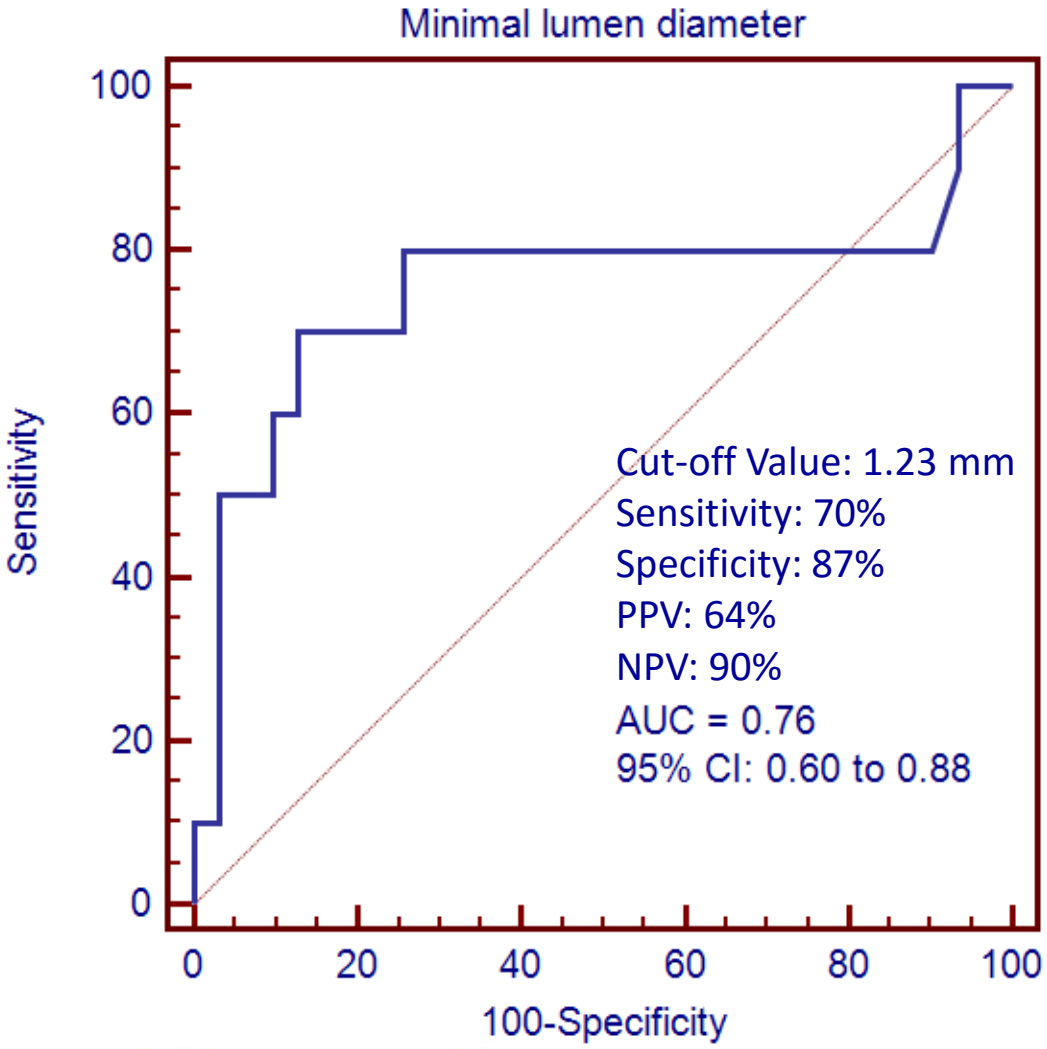


• In the overall group, the diagnostic efficiency of MLA in identifying significant stenosis was moderate (area under the curve (AUC)= 0.80).

Zafar et al., Journal of Cardiology, 64(1), 2014.

Results

TOMI
Tissue optics & microcirculation imaging



- In the overall group, the diagnostic efficiency of MLD in identifying significant stenosis was moderate (area under the curve (AUC)= 0.76).

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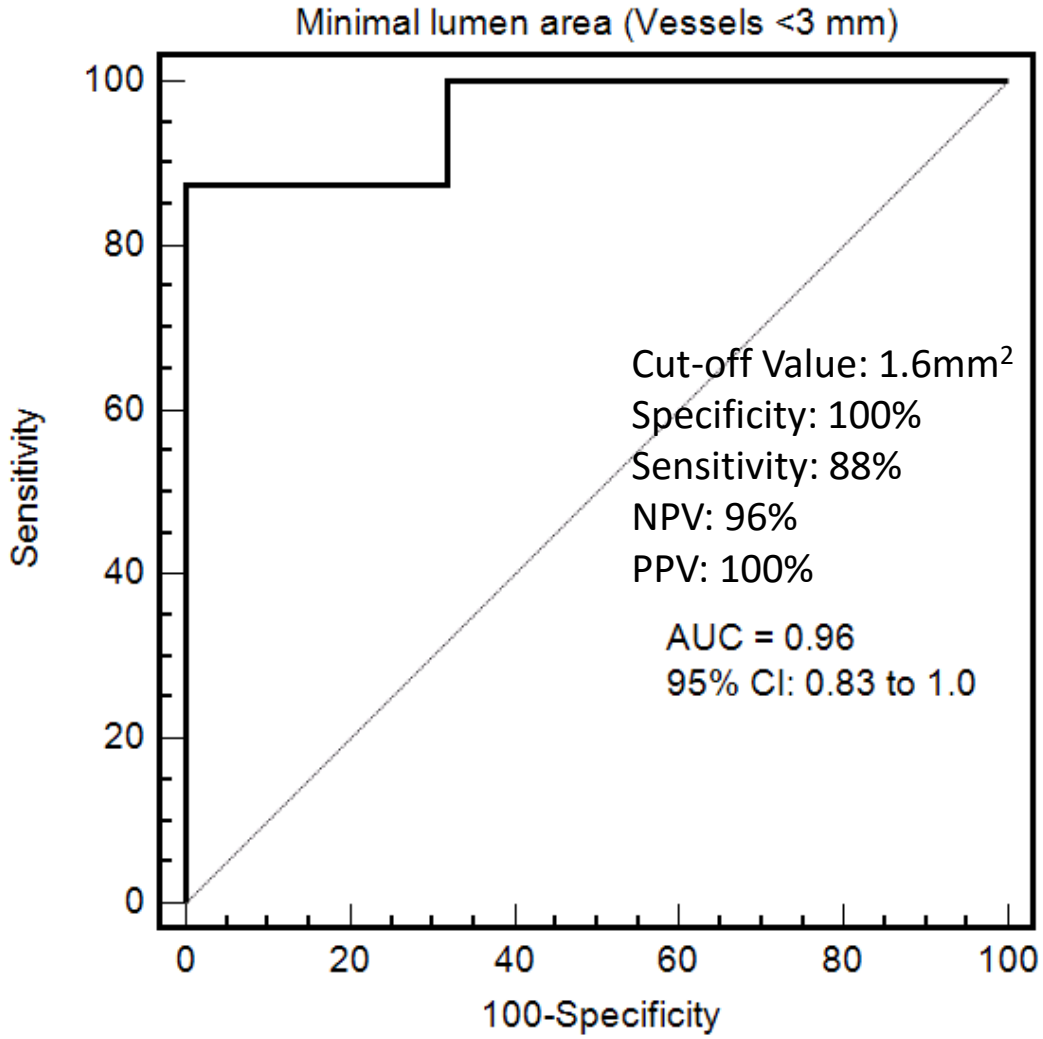
Zafar et al., Journal of Cardiology, 64(1), 2014.

Results

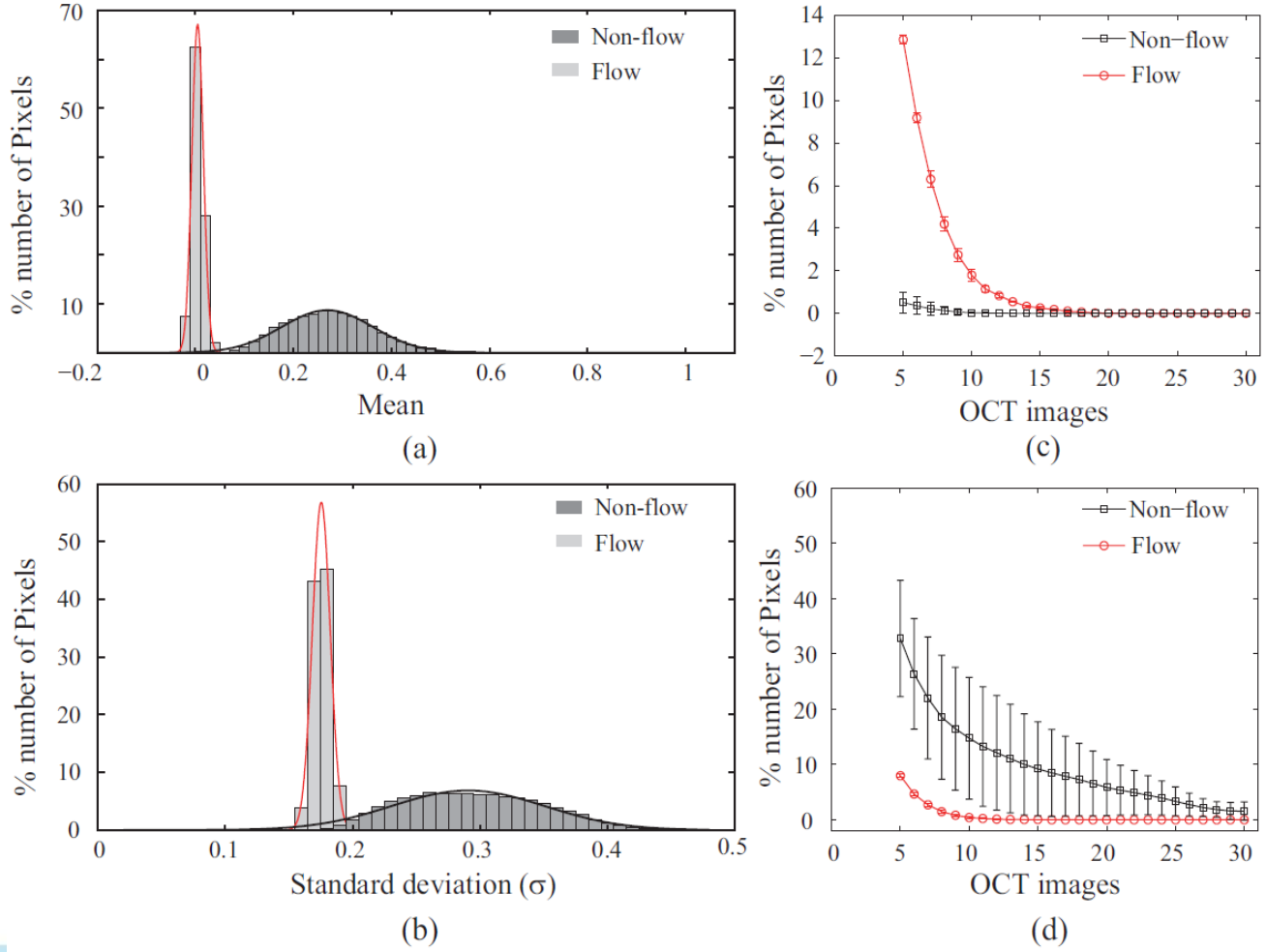


- The diagnostic efficiency of MLA in identifying significant stenosis in vessels having reference diameter < 3 mm was high (AUC= 0.96).

Zafar et al., Journal of Cardiology, 64(1), 2014.

Intracoronary microcirculation

every-frame CC mapping approach and determination of threshold value for corresponding mean and SD maps.



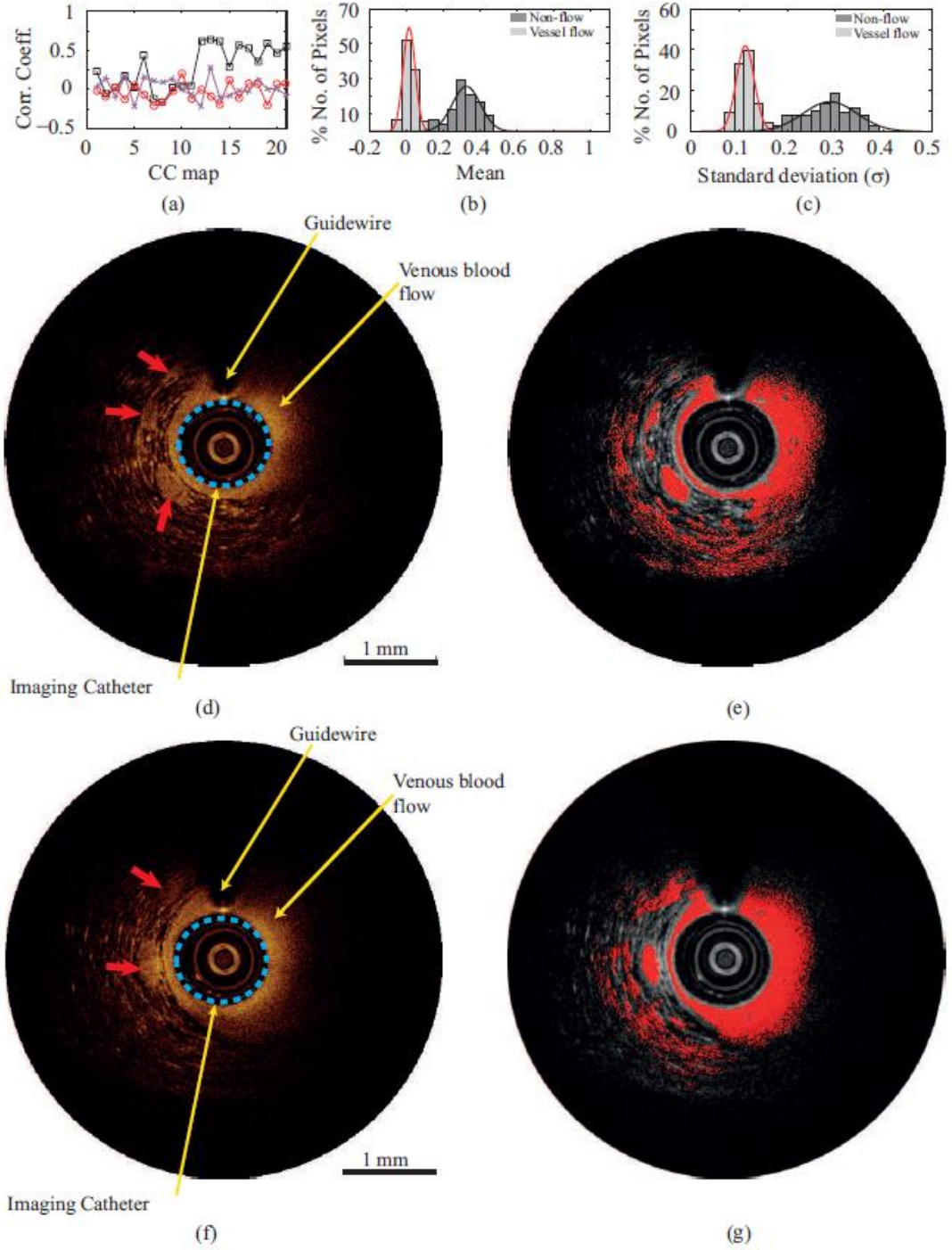
(a-b) histogram plot of mean and SD from CC maps for N = 31 images. Minimal overlap between flow and non-flow distribution in (a).

Joseph et al. Biomedical Optics Express 2015, **6**, 3, 668
http://dx.doi.org/10.1364/BOE.6.000668

Intracoronary microcirculation

Human Coronary Sinus using the every frame CC mapping method.

(d and f) Cross-sectional OCT images obtained with zero pullback. Bold red arrows indicate the vessels. (e and g) Flow maps corresponding to (d) and (f) superimposed onto the respective OCT images. Flow regions are marked red.



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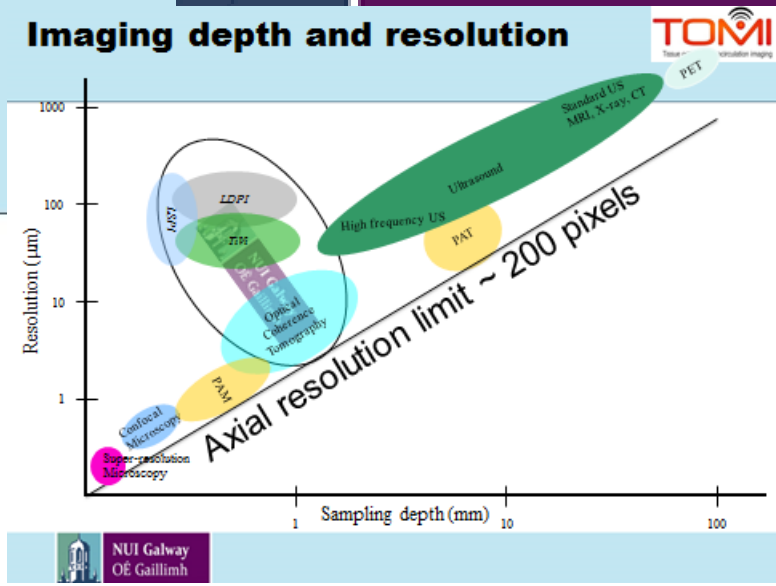
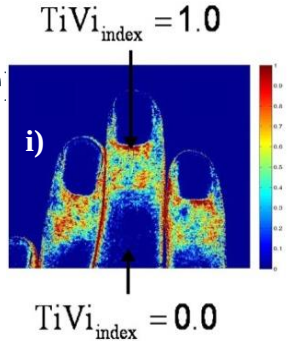
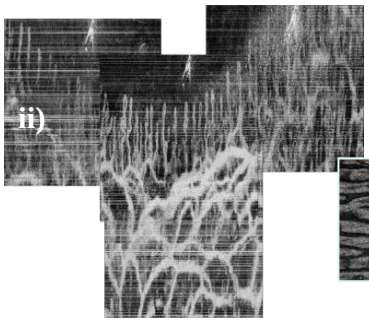
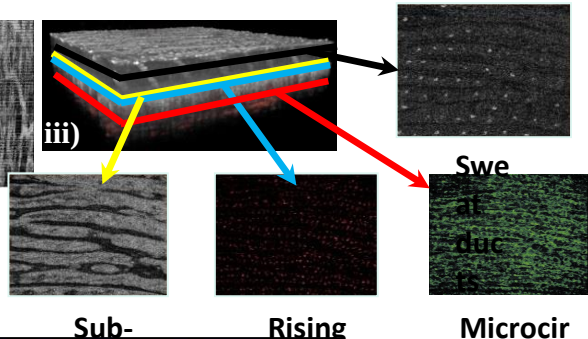
Summary

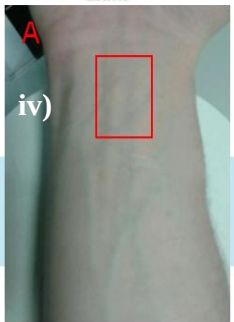
- In vivo / Ex vivo
- Scattering or non-scattering tissue?
- Depth versus resolution
- Speed – frames per second – motion?
- Functional – flow, oxyge molecular sensitivity
- Sub-resolution content/activity
- Fit for purpose

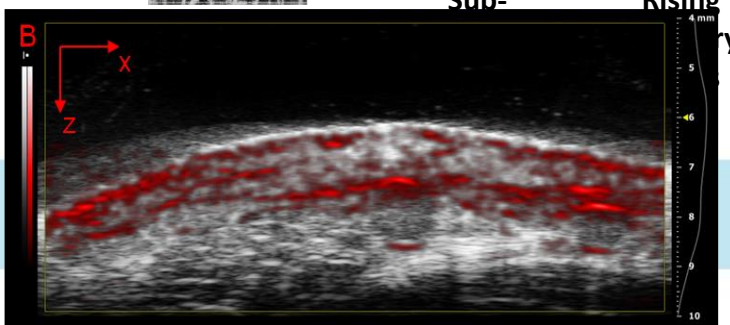


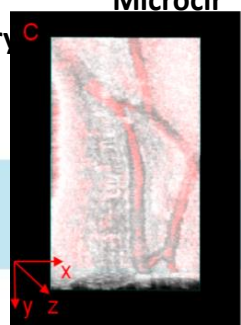












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NBIPI: Tissue Optics and Microcirculation Imaging Facility

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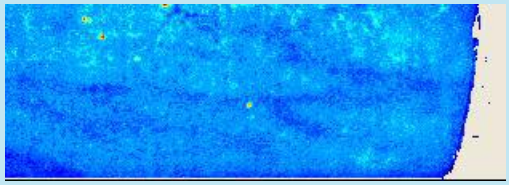
Tissue optics & microcirculation imaging



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Wheelsbridge AB

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'ELITEAM'- ESTABLISHMENT OF THE ELI INSTITUTE AT THE UNIVERSITY OF SZEGED: FOUNDATION OF INTERDISCIPLINARY RESEARCH IN THE FIELD OF LASERS AND THEIR APPLICATIONS

THANK YOU FOR YOUR ATTENTION!

TÁMOP-4.2.2.D-15/1/KONV-2015-0024 project

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