Recent advances in optical coherence tomography (OCT) and OCT angiography for biomedical applications

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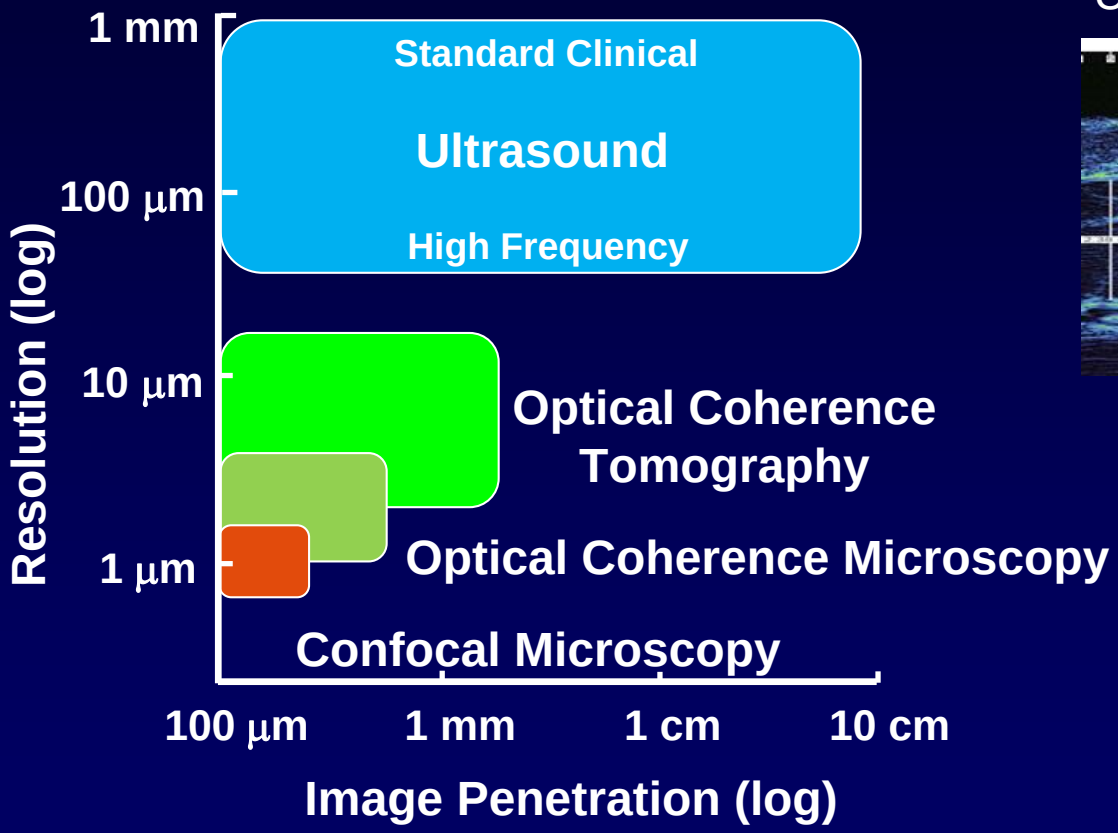
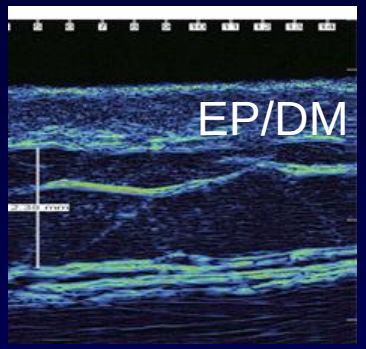
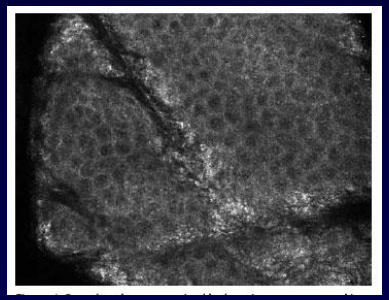
Subsurface Imaging Techniques

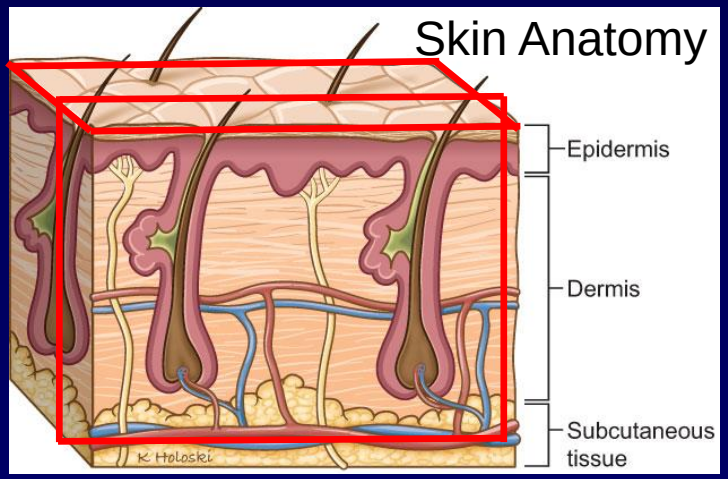


Ultrasound



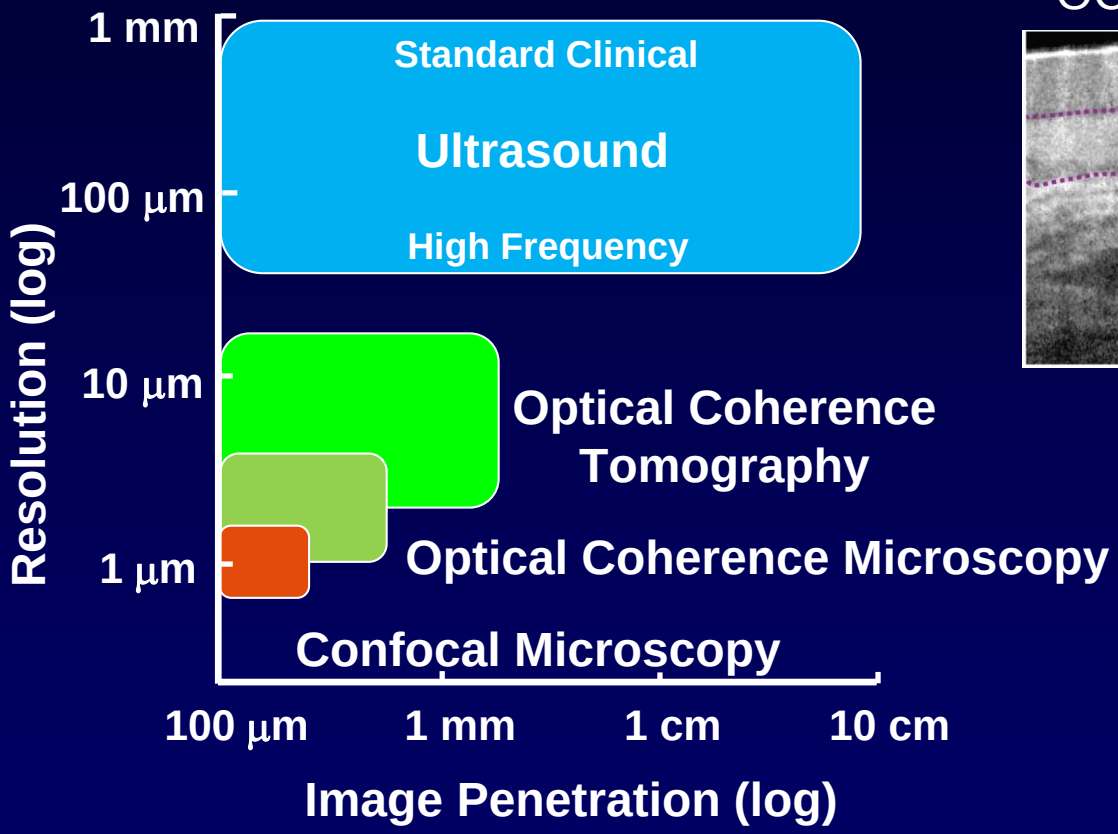
Confocal Microscopy



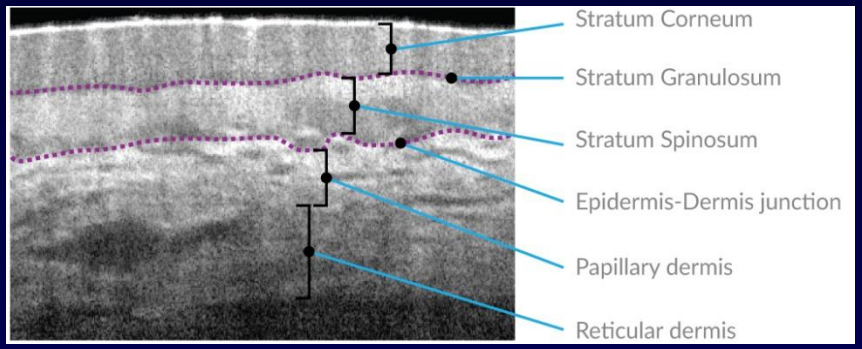


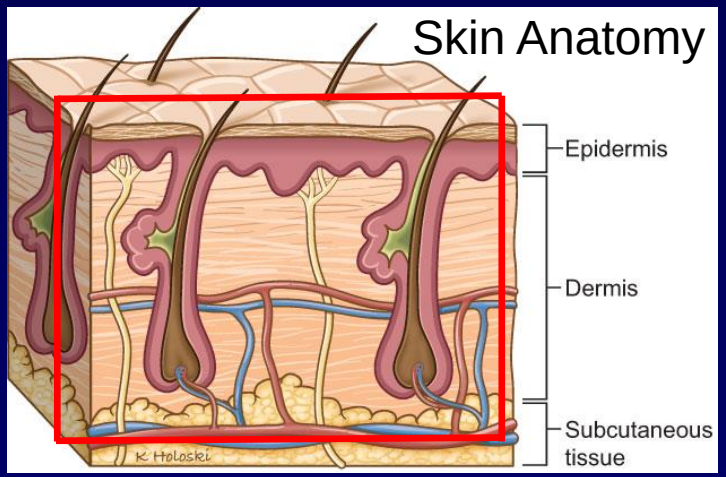
http://www.scielo.br/scielo.php?pid=S0365-05962009000600009&script=sci_arttext&tlng=en
https://www.researchgate.net/figure/Normal-skin-Ultrasound-imaging-has-been-routinely-used-by-dermatologists-in-our

Subsurface Imaging Techniques



OCT

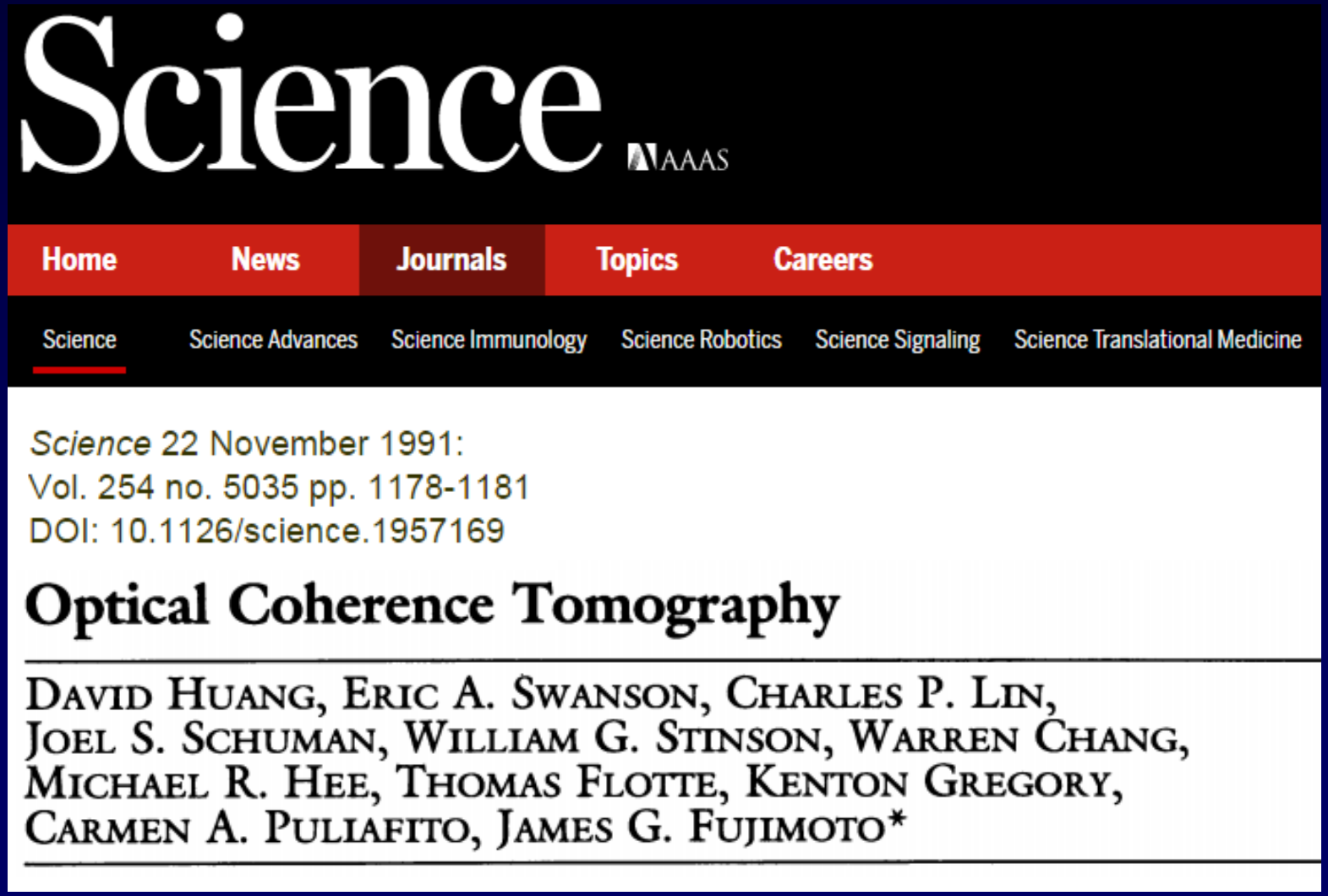




https://vivosight.com/researcher/vivosight-scanner/

Optical Coherence Tomography (OCT)

- **How it begins….**



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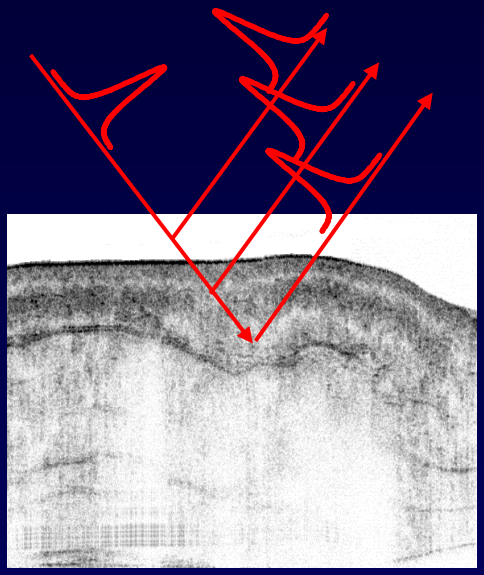
Science 22 November 1991:
Vol. 254 no. 5035 pp. 1178-1181
DOI: 10.1126/science.1957169

Optical Coherence Tomography

DAVID HUANG, ERIC A. SWANSON, CHARLES P. LIN, JOEL S. SCHUMAN, WILLIAM G. STINSON, WARREN CHANG, MICHAEL R. HEE, THOMAS FLOTTE, KENTON GREGORY, CARMEN A. PULIAFITO, JAMES G. FUJIMOTO*

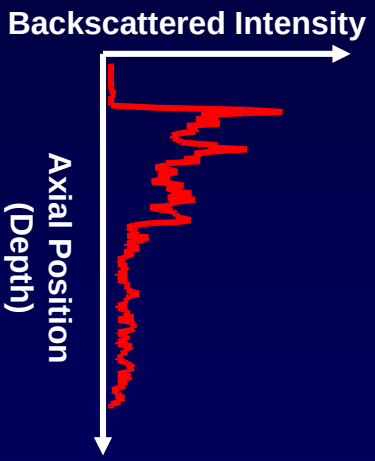
Huang, *et al.*, Science (1991).

Optical coherence tomography (OCT) – I

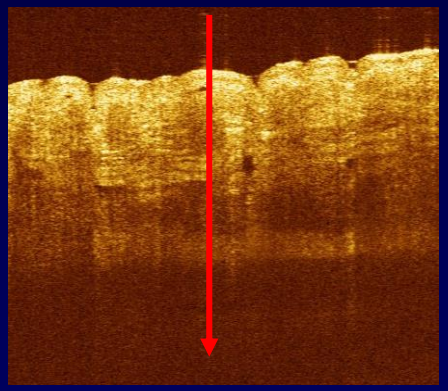


Specimen

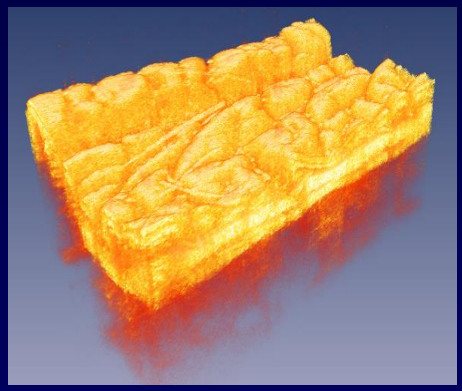
1 D
Axial (Z) Scanning



2 D
Axial (Z) Scanning
Transverse (X) Scanning



3D
Axial (Z) Scanning
XY Scanning

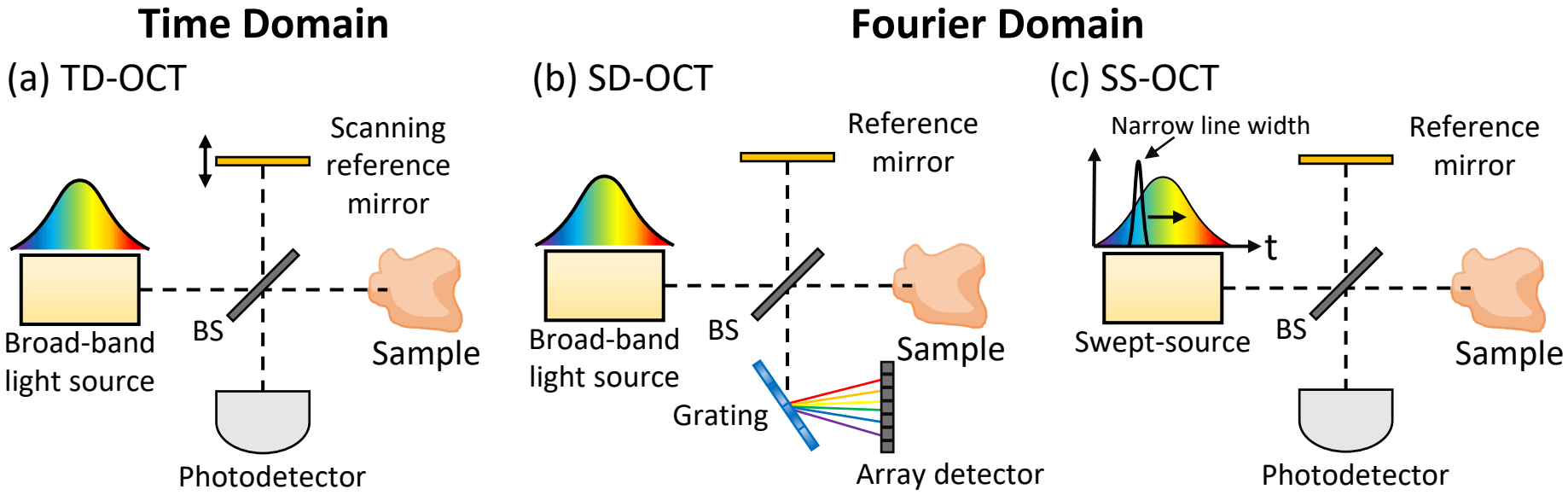


- Imaging speed – real time
- Imaging depth – mm
- Depth-resolved
- Spatial resolution – μm

Huang, *et al.,* Science (1991).

Optical coherence tomography (OCT) – II

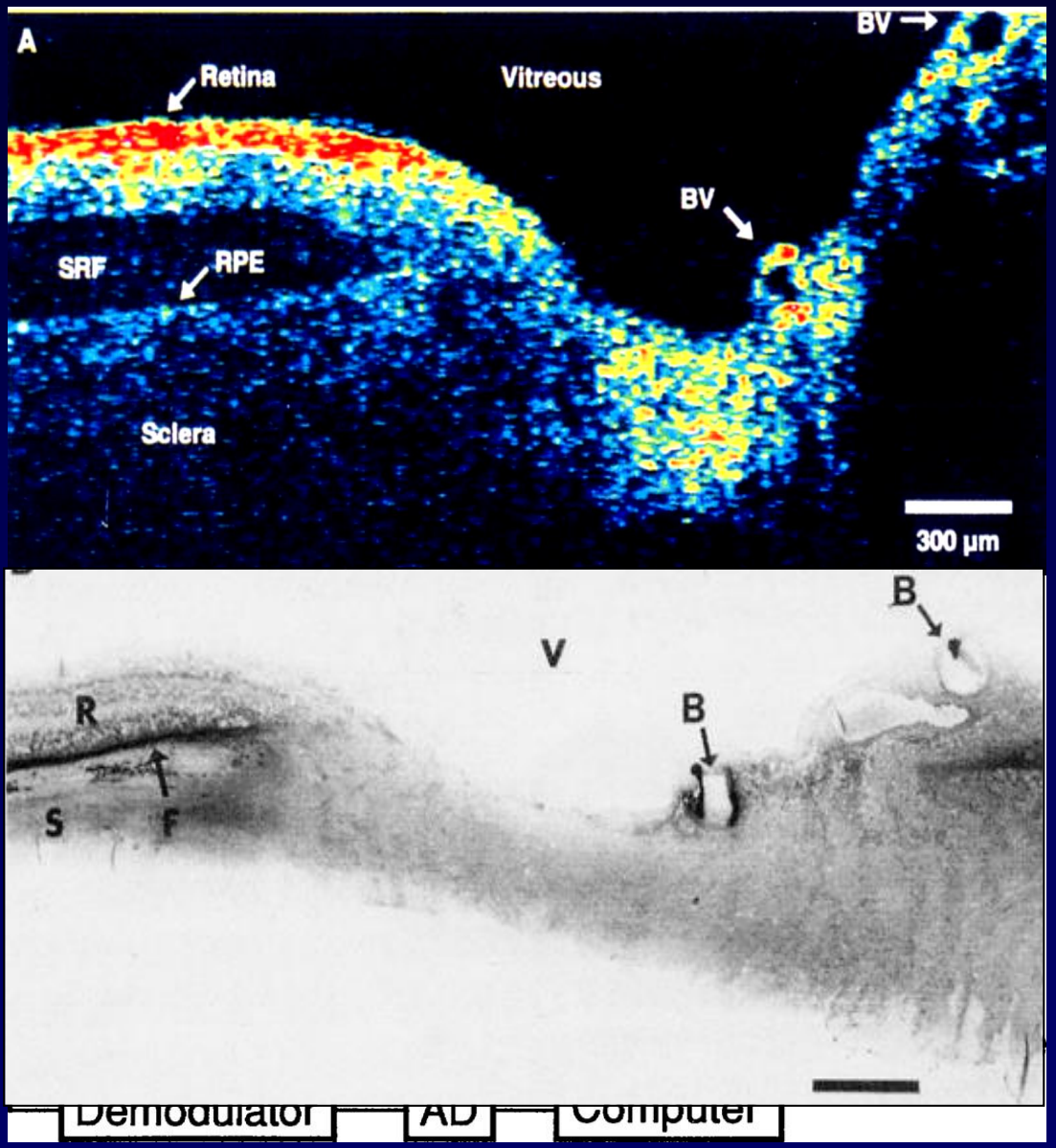
- Time-domain OCT[1]
- Fourier-domain OCT[2-6]
  - Spectral-domain OCT (SD-OCT)[2,4,5]
  - Swept-source OCT (SS-OCT)[3,6]



1. Huang, *et al.,* Science (1991).
2. Fercher *et al.,* Opt. Comm (1995)
3. Chinn *et al.*, OL (1997)
4. Leitgeb *et al.*, OE (2003)
5. De Boer *et al.*, OL (2003)
6. Choma *et al.*, OE (2003)

OCT Retinal Imaging (1991)

D. Huang, E. Swanson, et al, Science vol. 254, pp. 1178 (1991)



Early Research Prototype OCT (ca 1994)

Running at 40 A-scans per second

More than 5000 patients imaged at the New England Eye Center

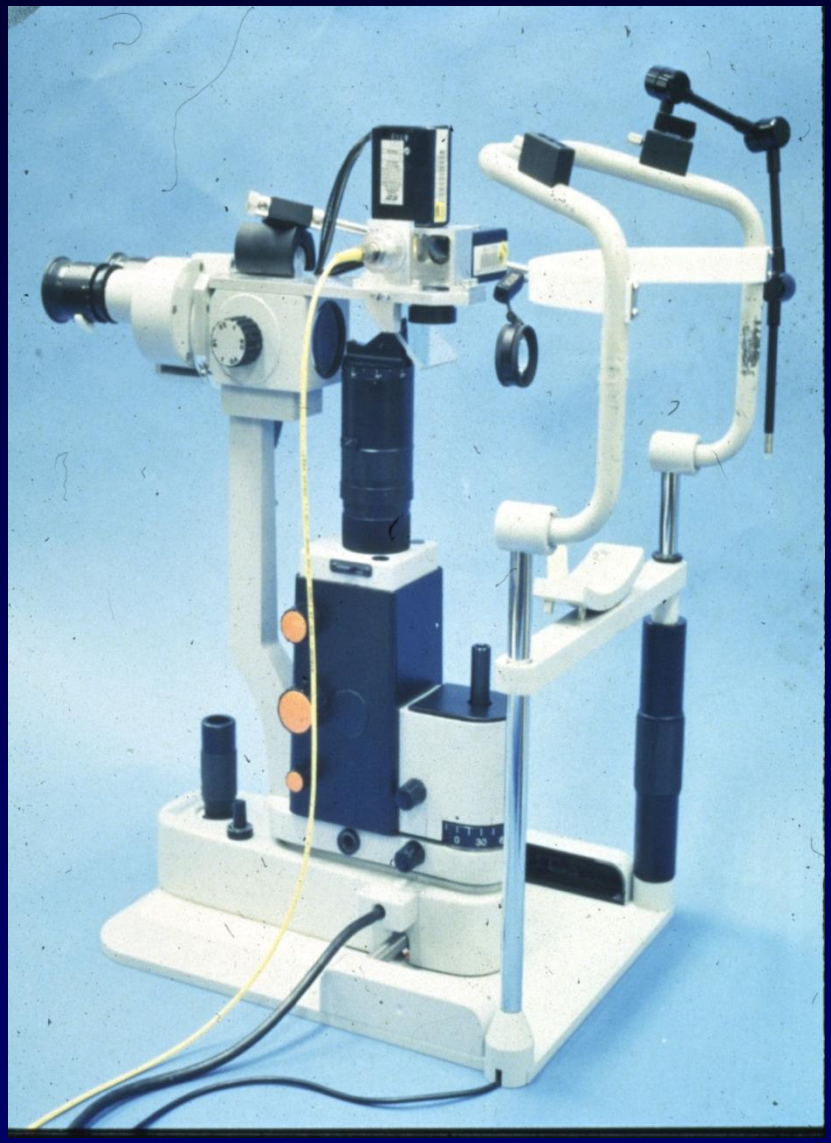
First OCT studies of

- Glaucoma
- Diabetic retinopathy
- Macular degeneration

Carmen Puliafito, MD

Joel Schuman, MD

Courtesy of Eric Swanson



Commercial Development of Ophthalmic OCT

Academia | Start-up | Multiple Generations of Products | Maturity

1980ies Basic research

1991 patent application

1995 early prototype

1996 OCT1 (lab tool)

1997 OCT1

2000 OCT2 (modified)

2002 Stratus OCT

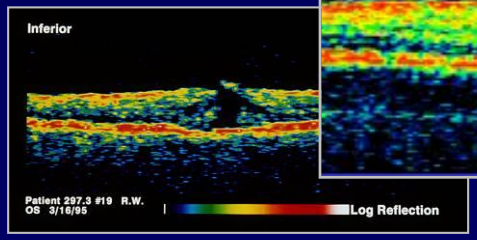
2007 Cirrus HD-OCT

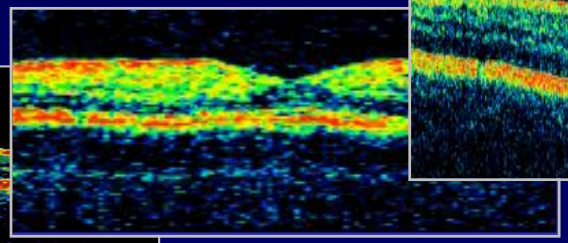
7+ other companies launch OCT systems

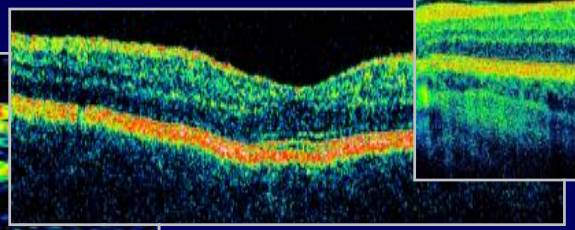
1st generation

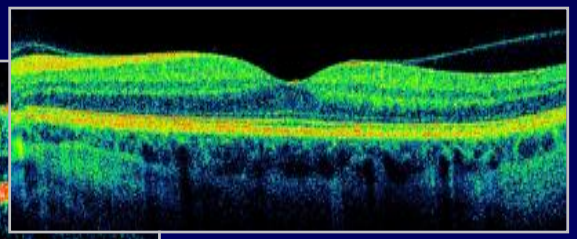
2nd gen.

3rd gen.



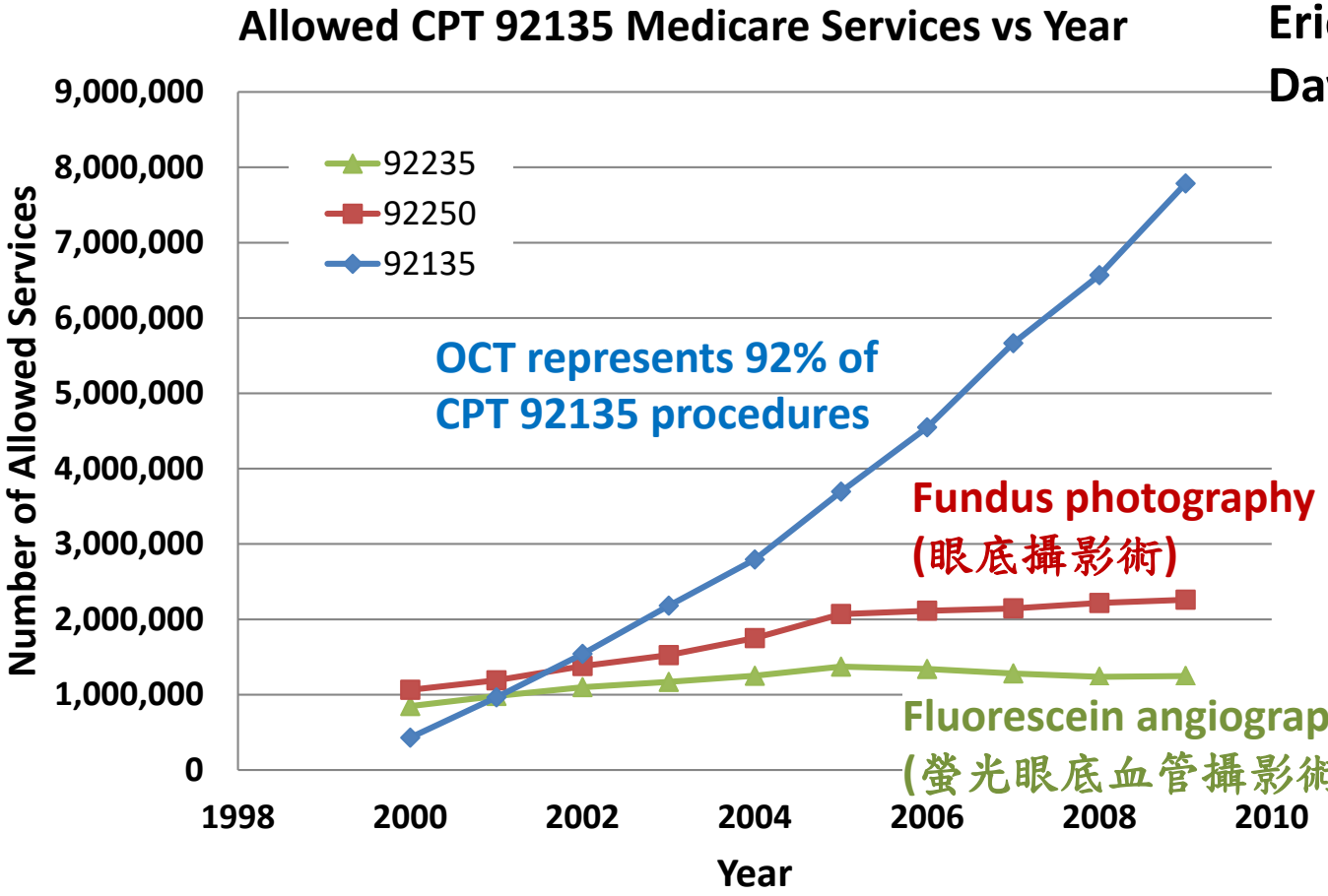


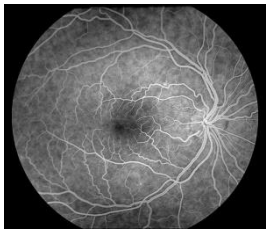




Since the first demonstration of OCT for ophthalmic OCT applications, there has been tremendous improvement on the performance of the OCT for retinal imaging.

OCT procedures surpassed the sum of other ophthalmic imaging procedures





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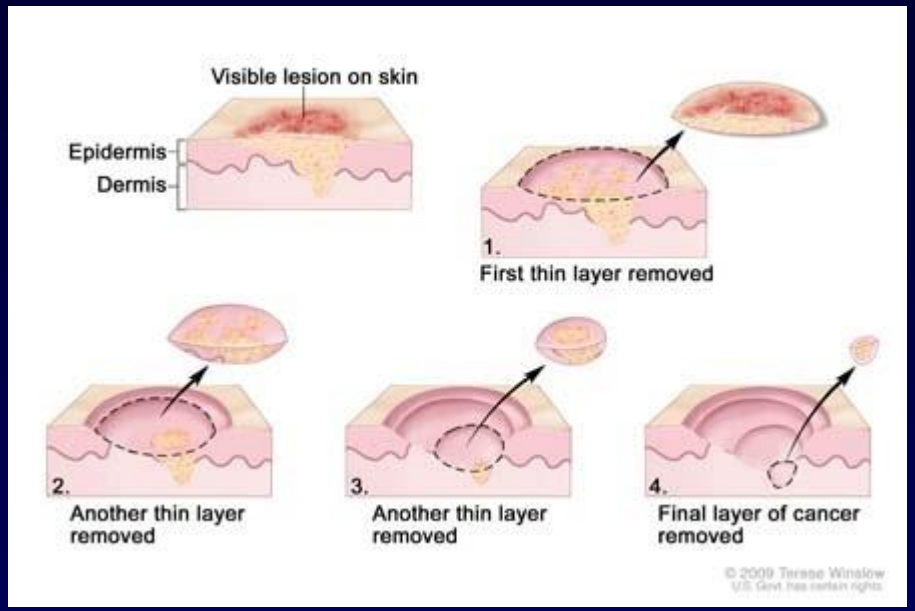
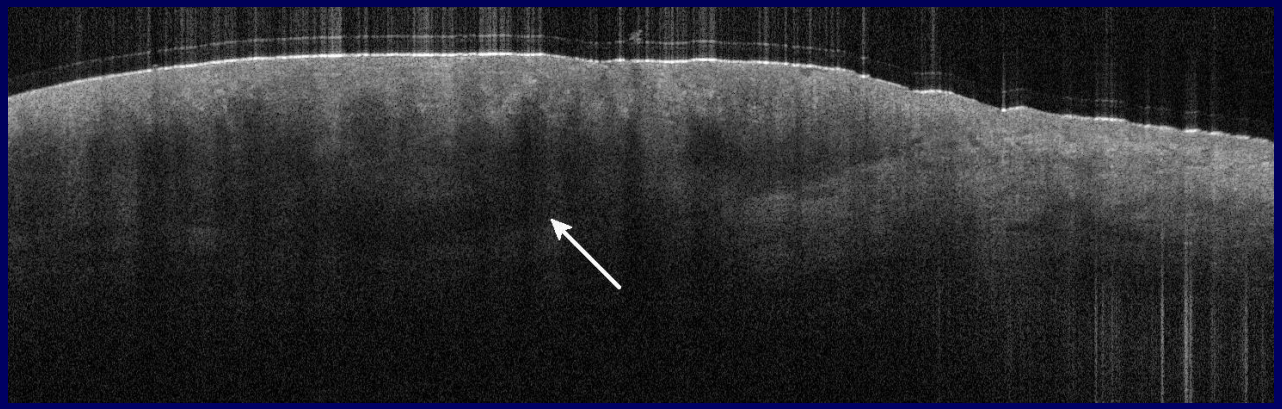
Existing Commercial Ophthalmic OCT Products

All based on the SD-OCT platform (i.e. spectrometer) - <100kHz axial (depth) scan rate.

(a) Cirrus-HD OCT 5000 from Zeiss; (b) Optovue Inc. RTVue and Handheld iVue OCT systems for ophthalmology; (c) Topcon 3DOCT-2000 for ophthalmology; (d) Heidelberg Engineering Spectralis OCT for ophthalmology; and (e) Nidek RS-3000 Advance for Ophthalmology.

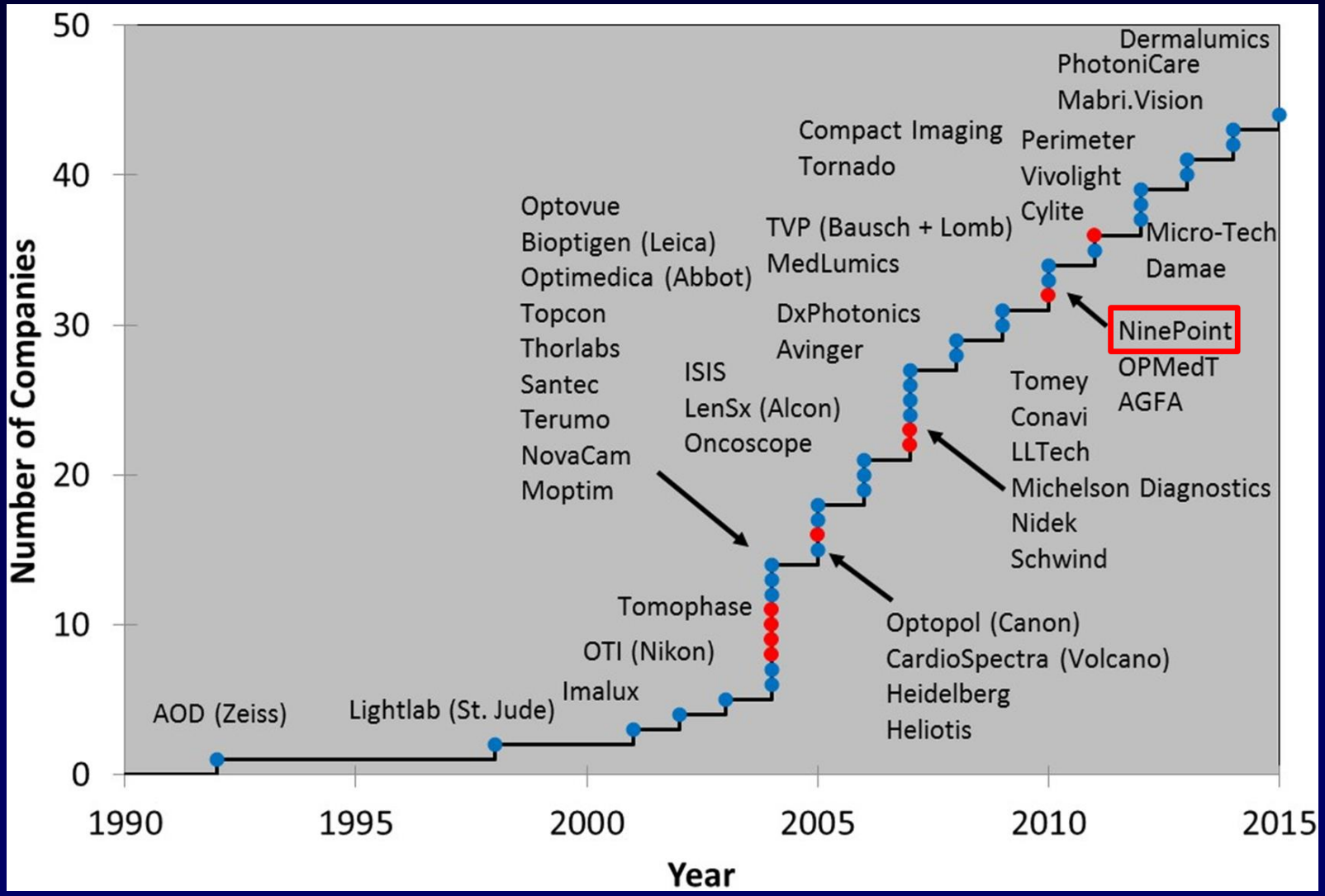
OCT in Dermatology





J Welzel, “Optical coherence tomography in dermatology: a review”, Skin Res. Technol. Vol7., Iss.1, pp1-9, (2001)

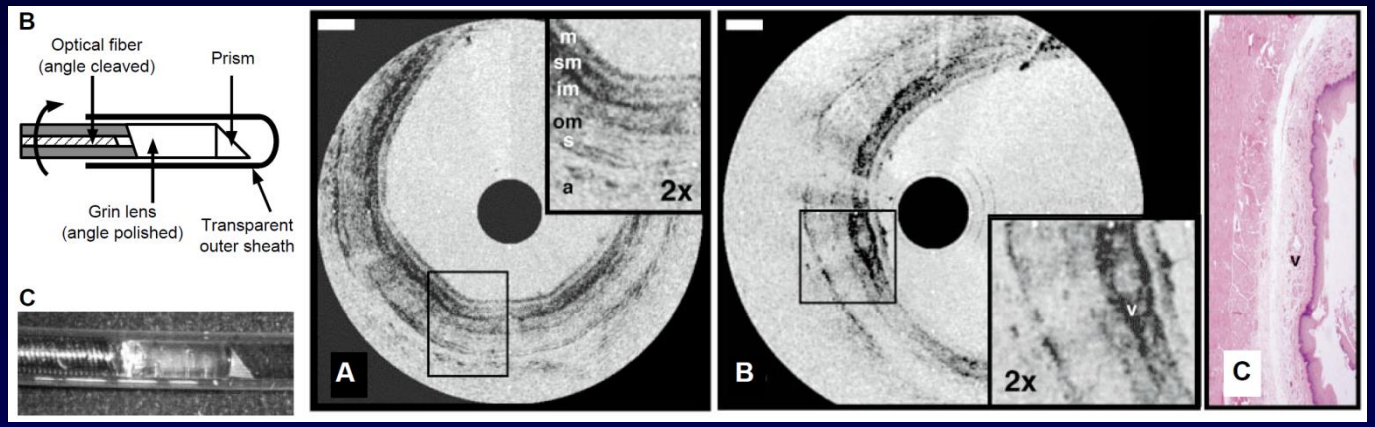
Companies Developing OCT Systems



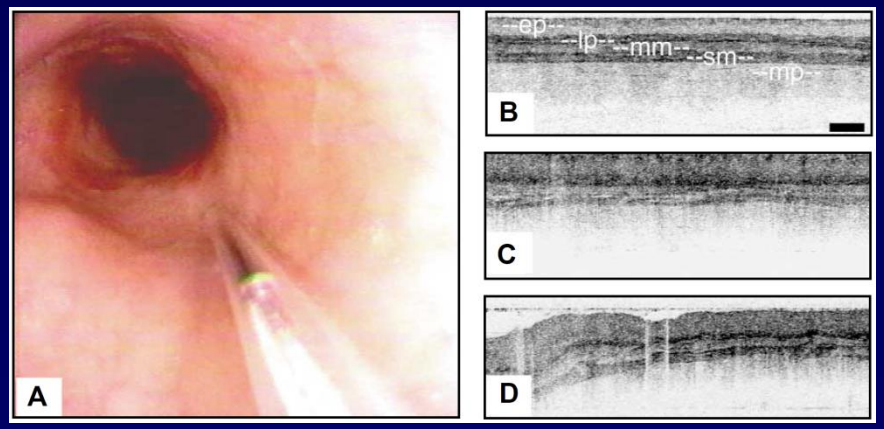
http://iovs.arvojournals.org/data/Journals/IOVS/935468/i1552-5783-57-9-OCT1-f15.png

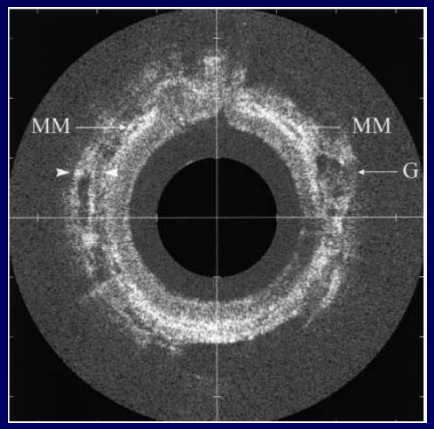
Endoscopic OCT

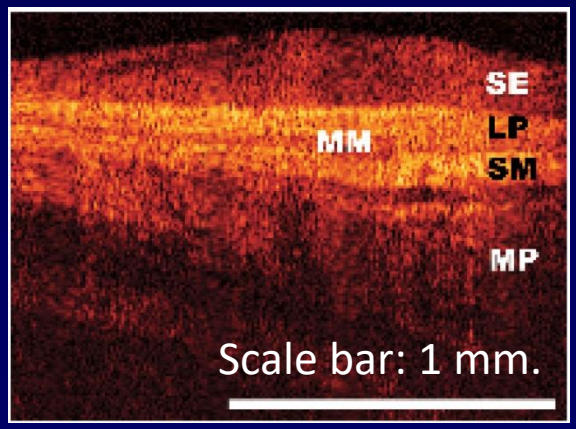
- **First demonstrated in rabbit esophagus *in vivo* in 1997[1].**



- **Subsequently, *in vivo* OCT imaging of the human GI tract was demonstrated by multiple groups in parallel in 2000[2-4].**

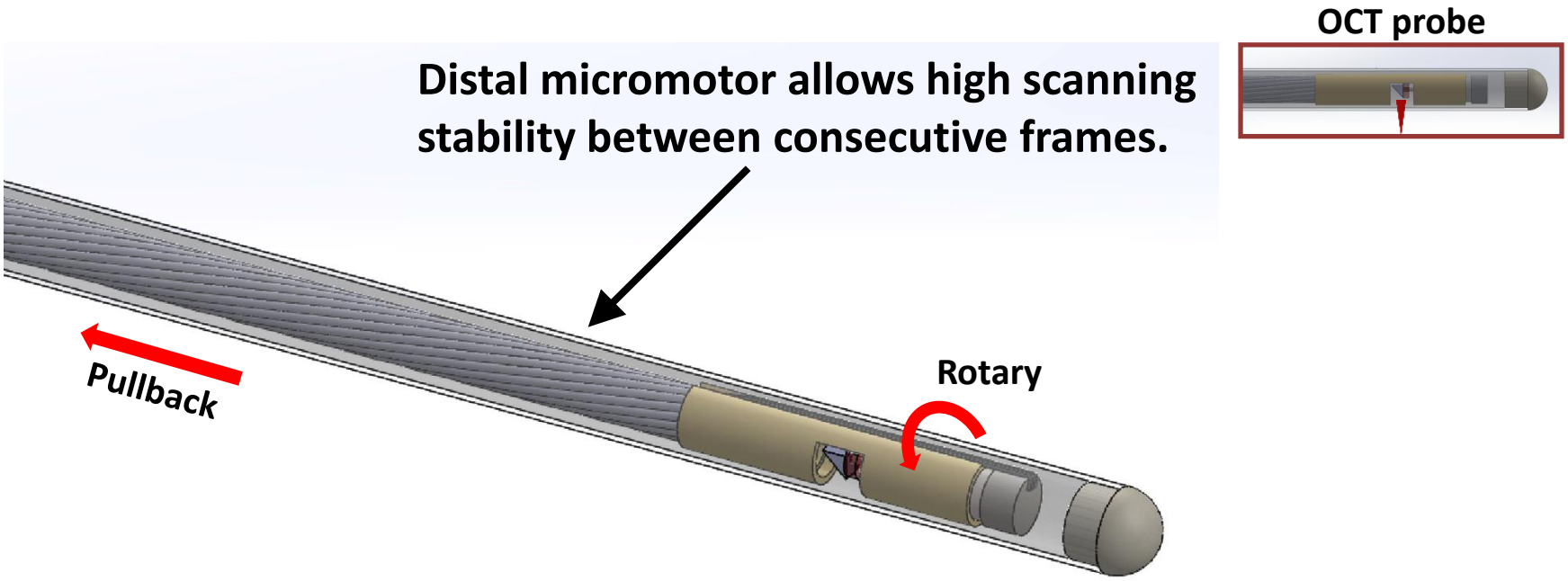






1. Tearney, *et al.,* Science (1997).
2. Bouma, *et al.,* GIE (2000).
3. Sivak, *et al.,* GIE (2000).
4. Jackle, *et al.,* Endoscopy (2000)

Ultrahigh Speed Endoscopic OCT System



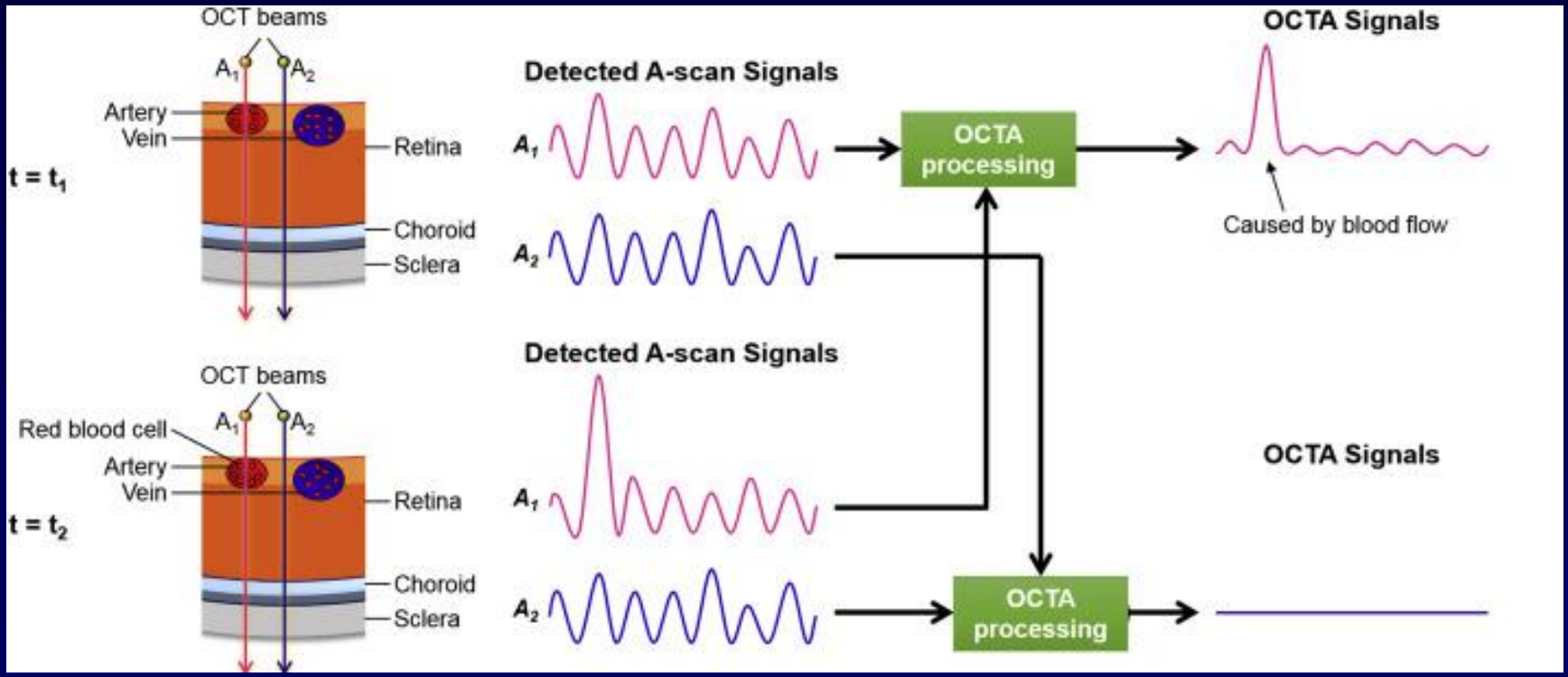
The rotational speed of the micromotor in the rendering is slowed down significantly for the purpose of illustration.

- 600,000 depth scans per second
- 400 frames/images per second
- 2.4 mm depth range (in tissue)
- ~8 µm axial/20 µm transverse resolution*
- ~101 dB detection sensitivity
- 3.4 mm diameter micromotor probe
- 10 x 16 mm^2 field of view
- 8 second acquisition time
- Real time display for imaging guidance
- >10x faster than commercial system

*full width at half maximum (FHWM)

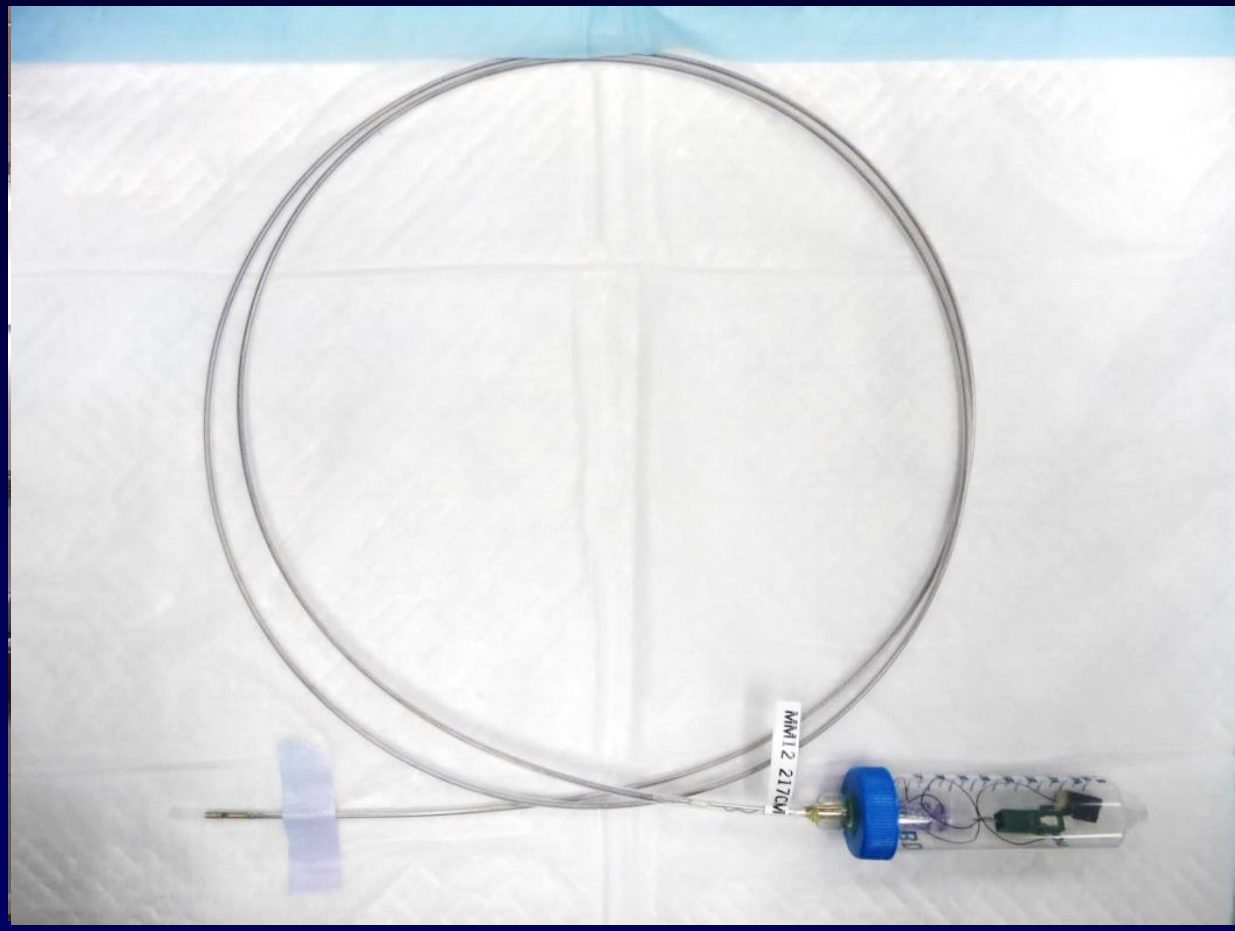
Endoscopic OCT Angiography (OCTA)

- **Endoscopic OCTA was performed by calculating the intensity decorrelation (D) between consecutive OCT images, resulting from the moving erythrocytes in the microvascular network[1].**

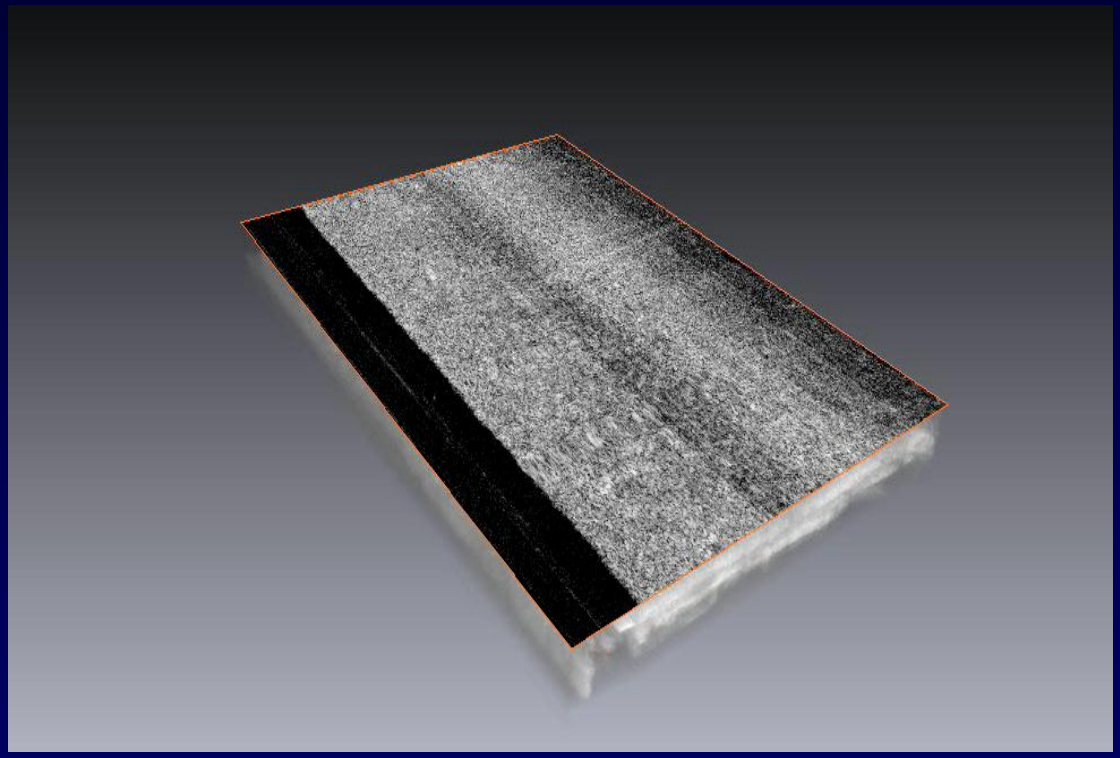


1. Kashani, *et al.,* Prog. Retin. Eye. Res. (2017).

Clinical Endoscopic OCT Imaging



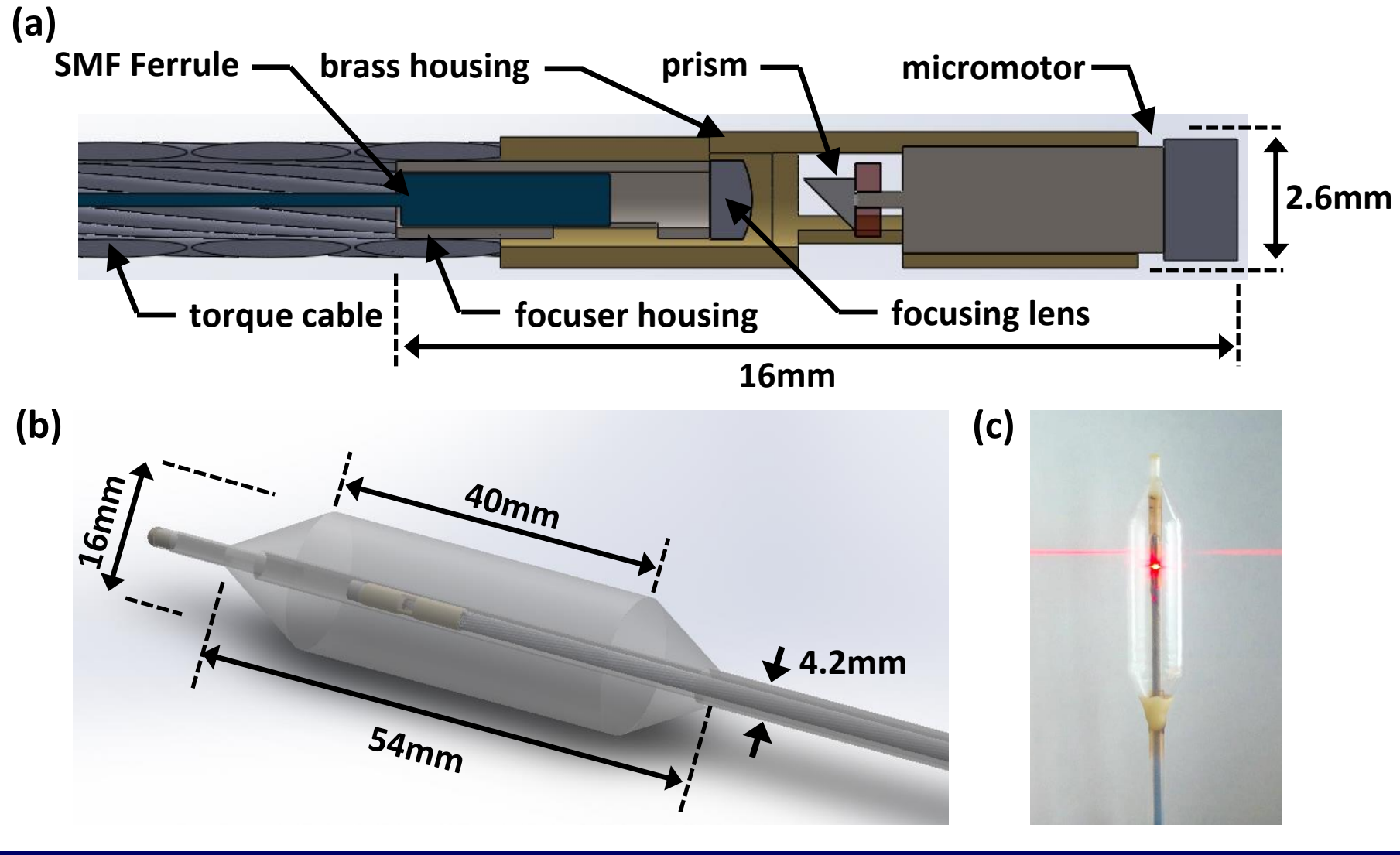
Endoscopic OCTA



Endoscopic OCTA of normal human esophagus

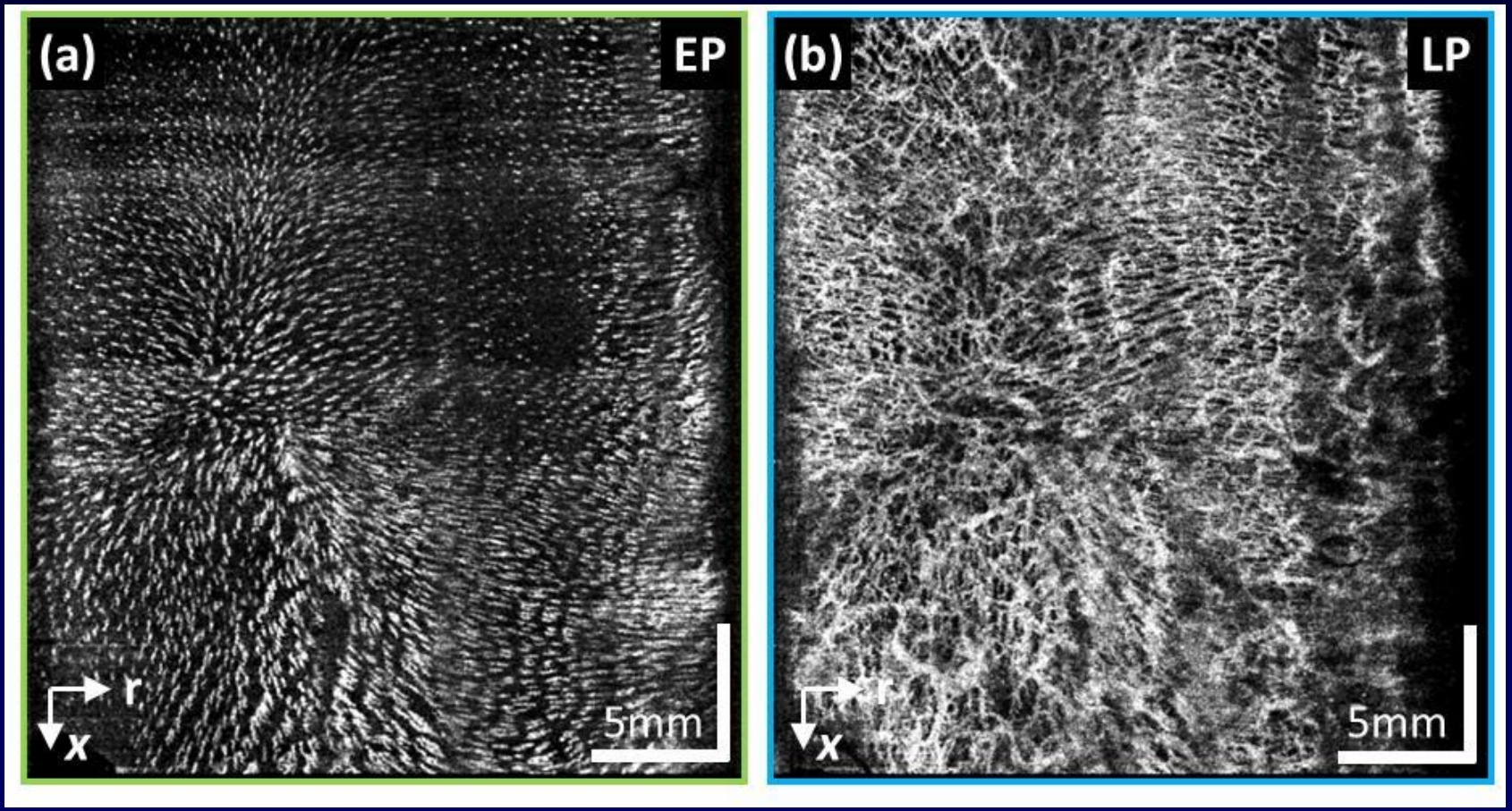
Tsai, *et al.,* Gastroenterology (2014).

Micromotor Balloon Imaging Catheter



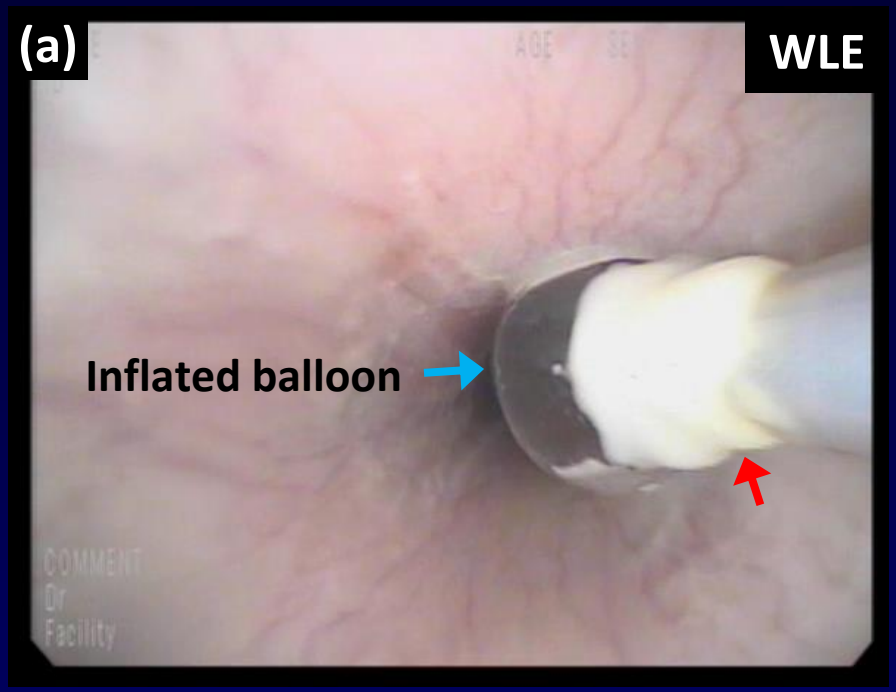
Lee, *et al*., Biomed. Opt. Express (2016).

OCTA Imaging of the Human Buccal Mucosa



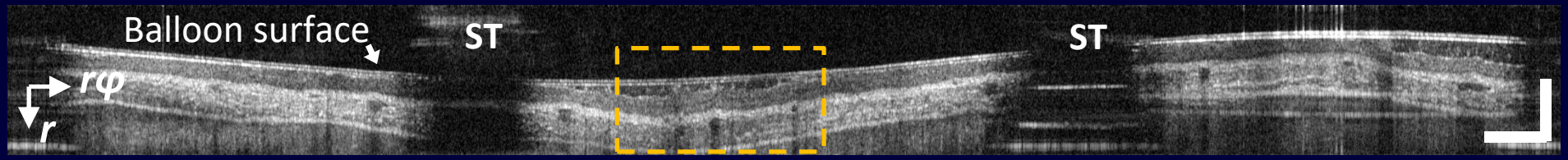
*unpublished data.

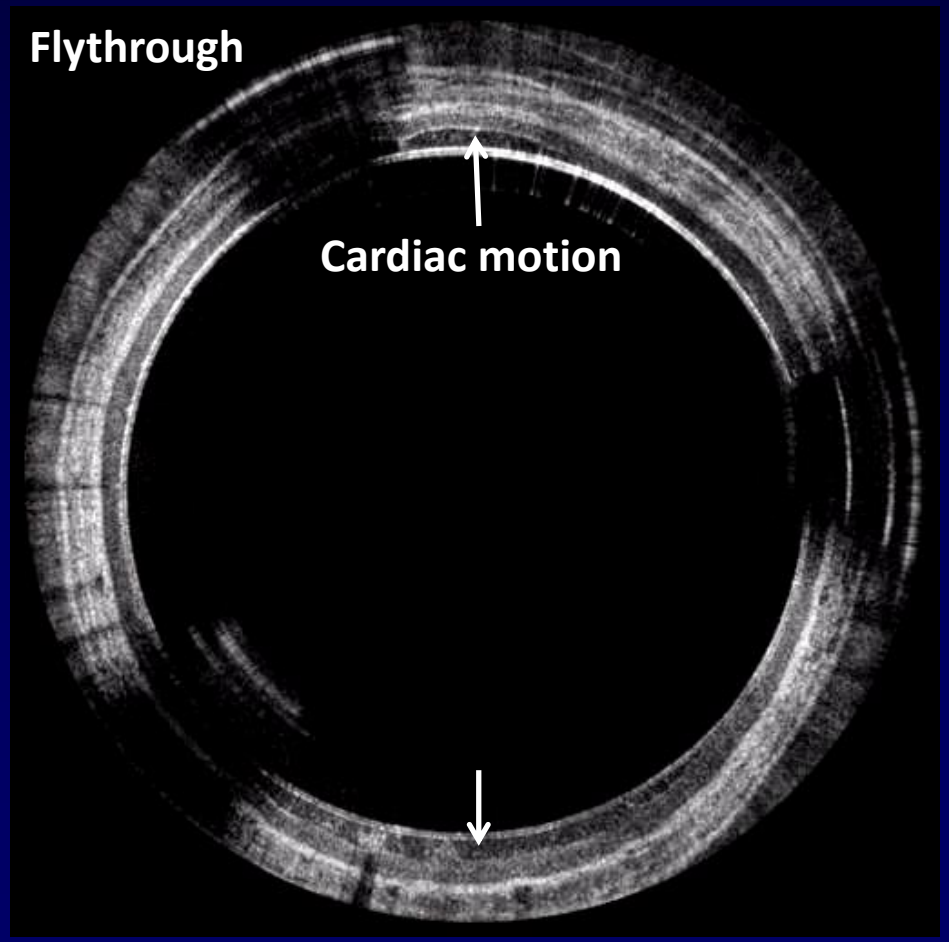
Animal Imaging Procedures

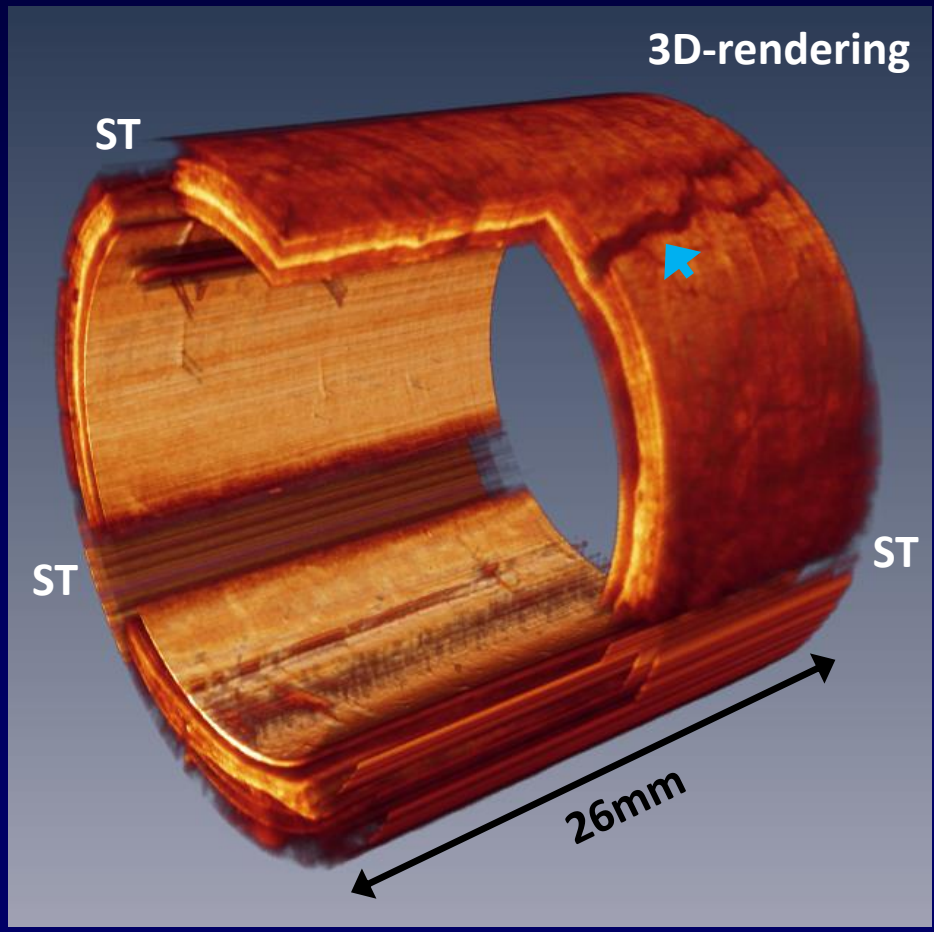


- Sedation: intramuscular injection of 5 mg/kg telazol and 2 mg/kg xylazine.
- A 16.7 mm ID overtube was placed using a dual channel endoscope to facilitate the introduction of the micromotor balloon catheter.

OCT images of the Swine Esophagus

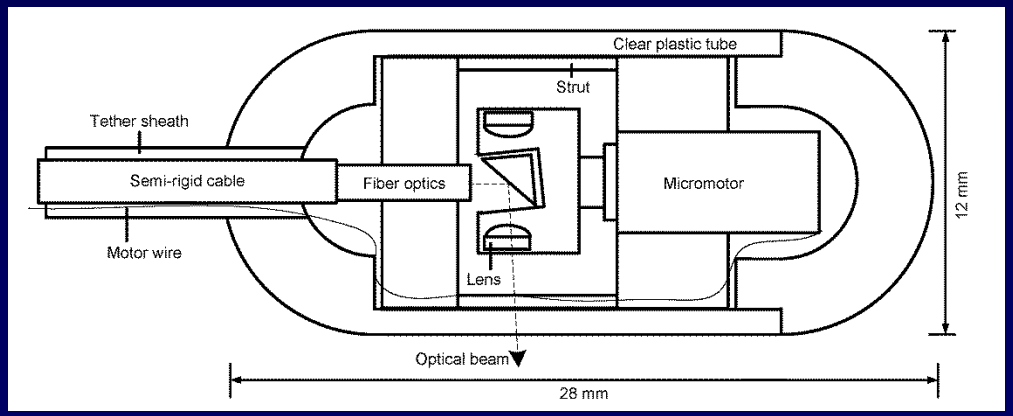






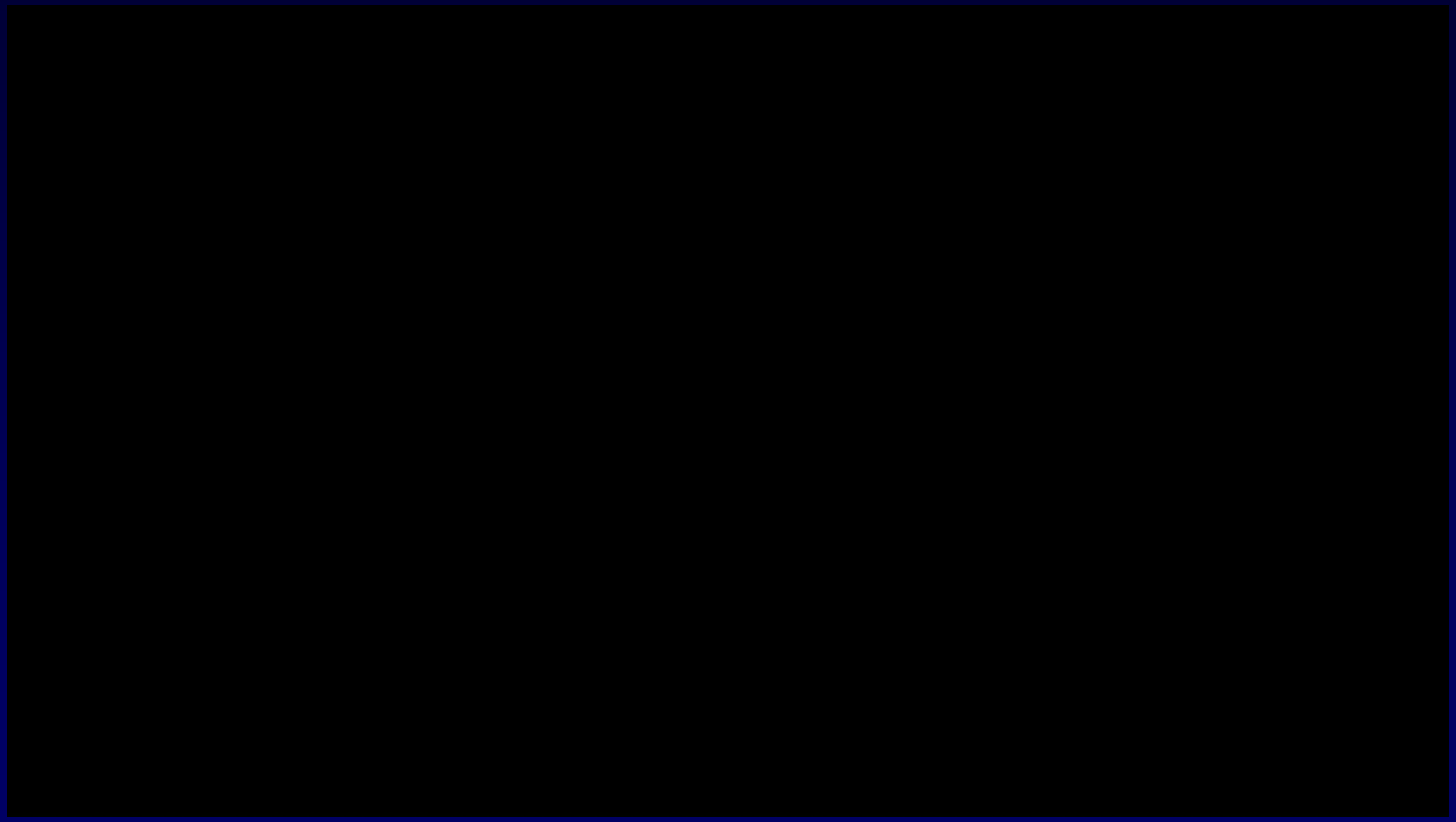
En face OCT Capsule with Micromotor

- **Ultrahigh speed OCT can deliver volumetric imaging up to 20x faster than commercial endoscopic OCT**
- **Tethered capsule can image circumference and extremely long length (>20 cm) of esophagus**
- **Semi-rigid tether enables introduction into esophagus of sedated patients, independent of endoscope**



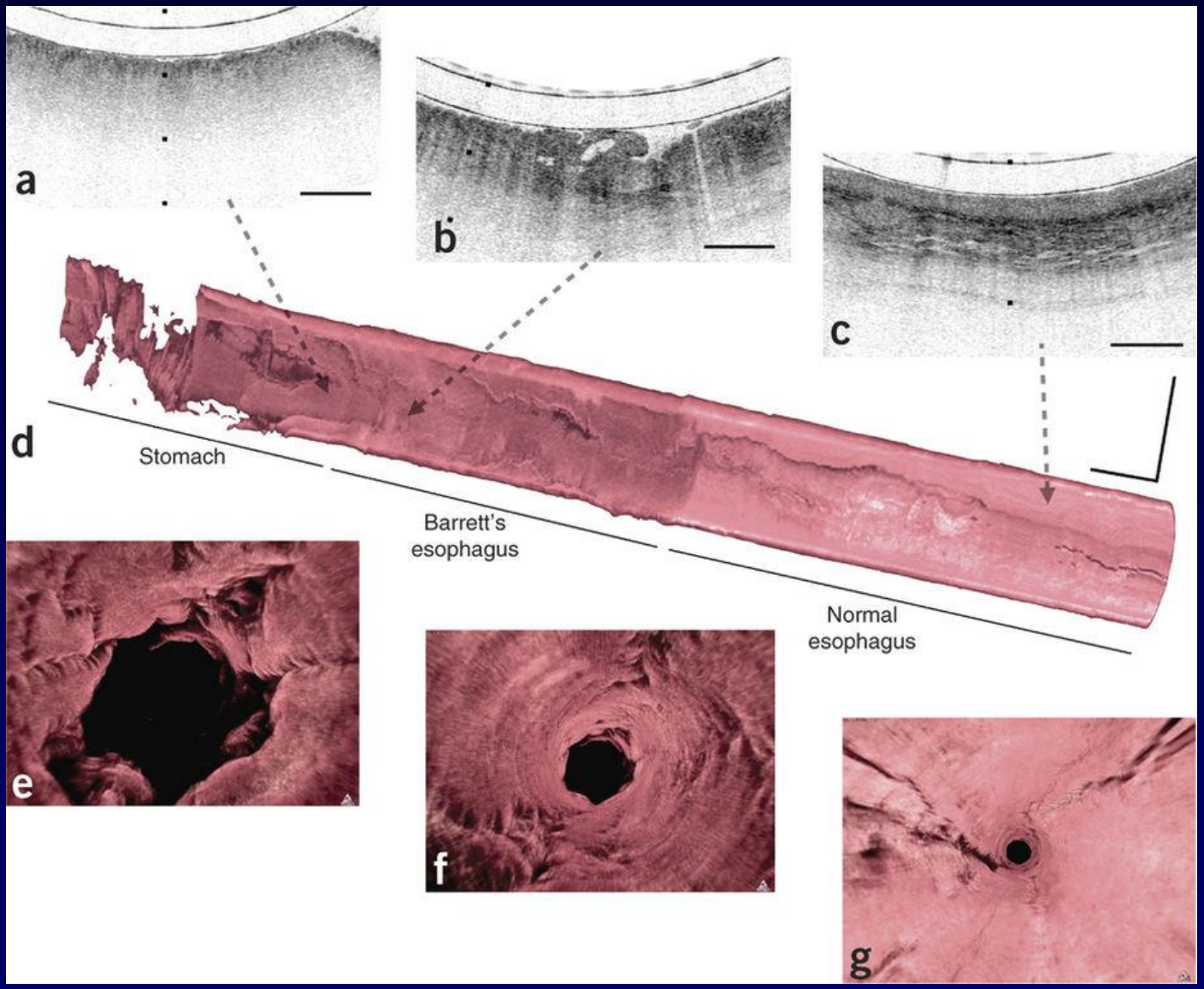
K. Liang, *et al*., Am J Gastroenterology (2016).

Tethered Capsule Imaging Procedure



Gora, *et al*., Gastroenterology, vol. 145, pp. 723 (2013).

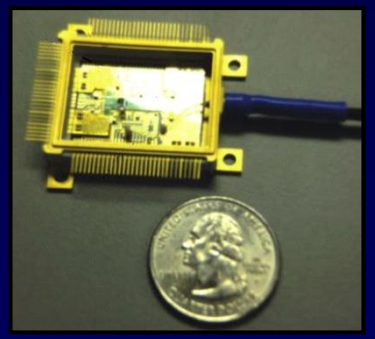
Tethered Capsule Imaging



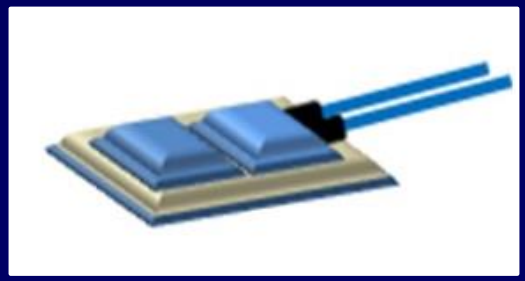
Gora, *et al*., Nat Medicine, **19**, 238-240 (2013)

Photonic Integrated Circuit (PIC)

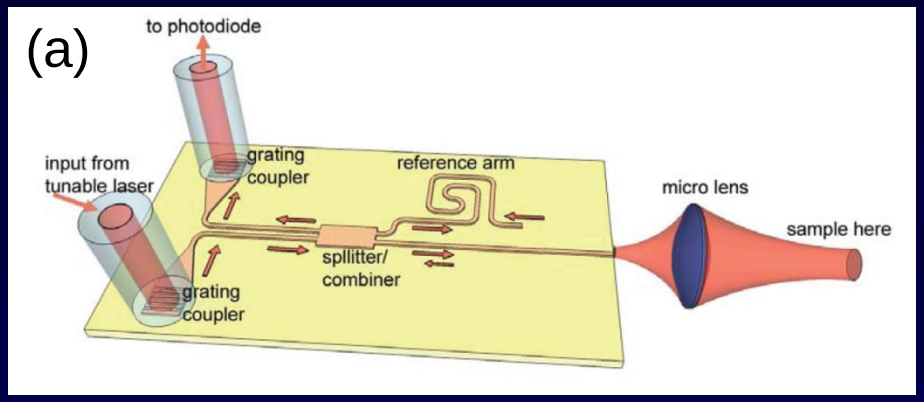
- PICs are revolutionizing fiber optic telecommunications
  - ~$100M's in R&D investment
  - ~$5B's market
  - High performance: Very low loss, wide bandwidth, high-speed
  - Manufacturable with high yields and high volumes
  - Compact: PICs with 100's to 1000's of optical elements
  - Small incremental cost to add additional electro-optical functions
- Integrated optics will offer tremendous promise for the future of OCT

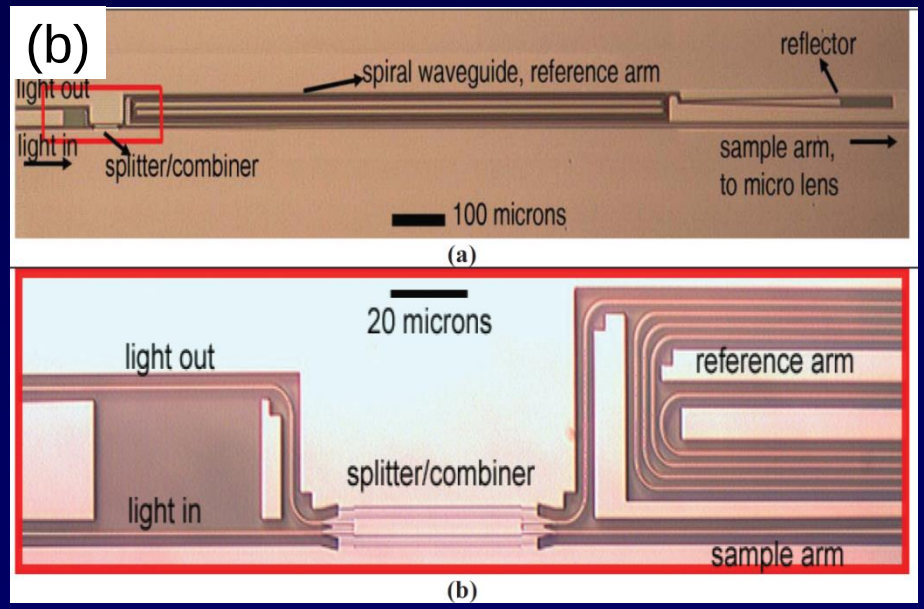


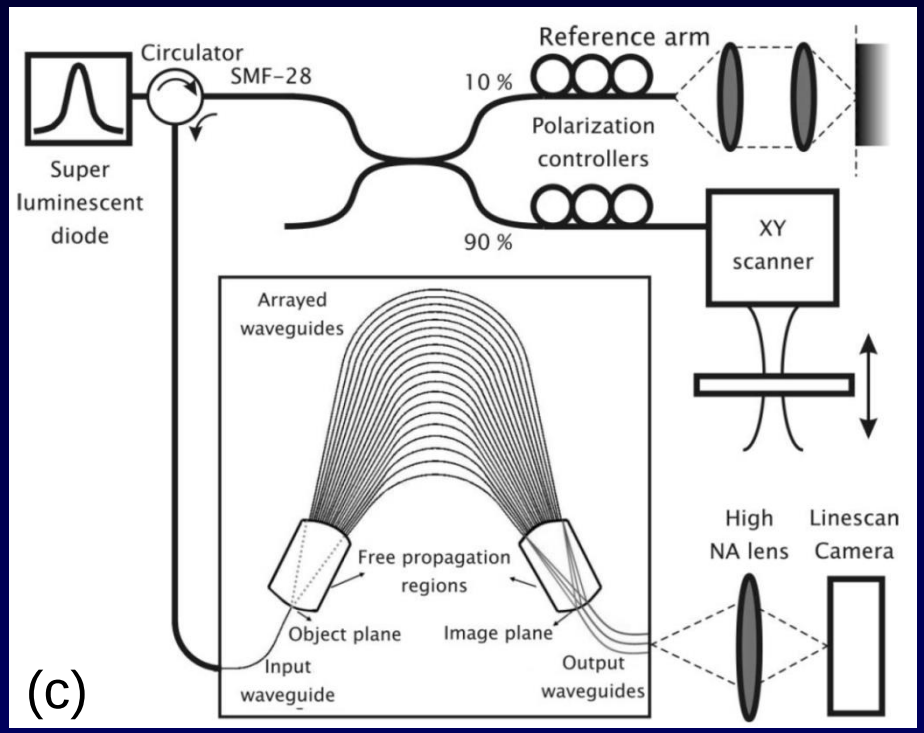
Future OCT System

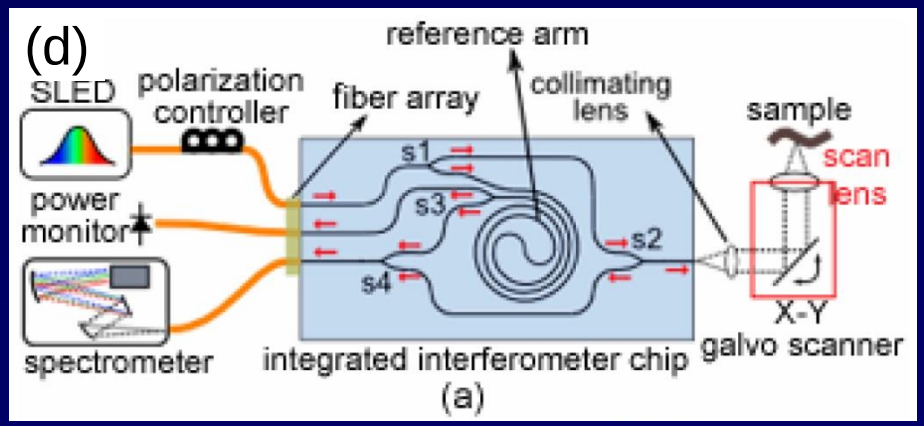


Silicon Photonics Integrated OCT System



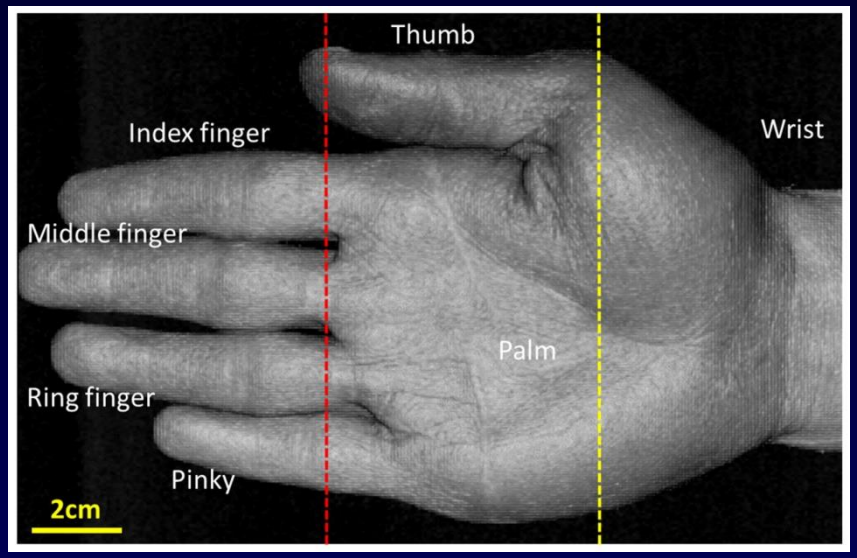


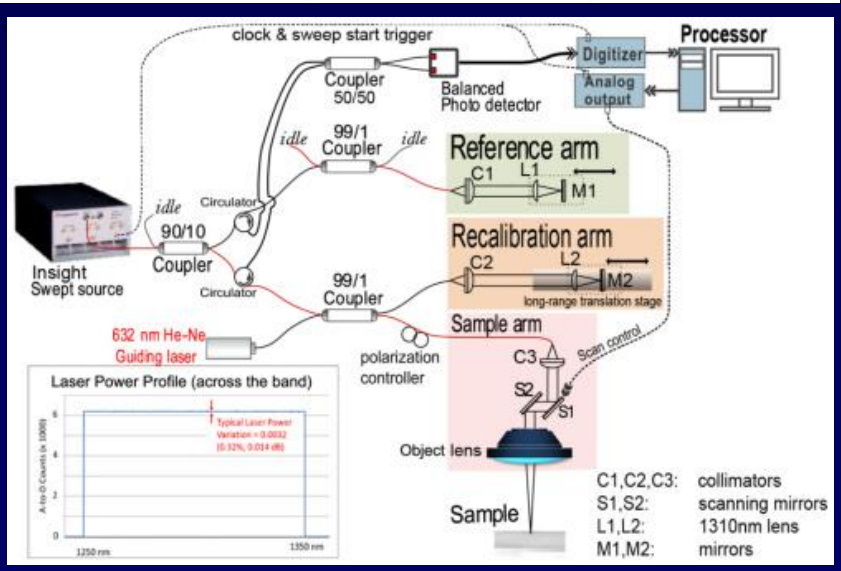


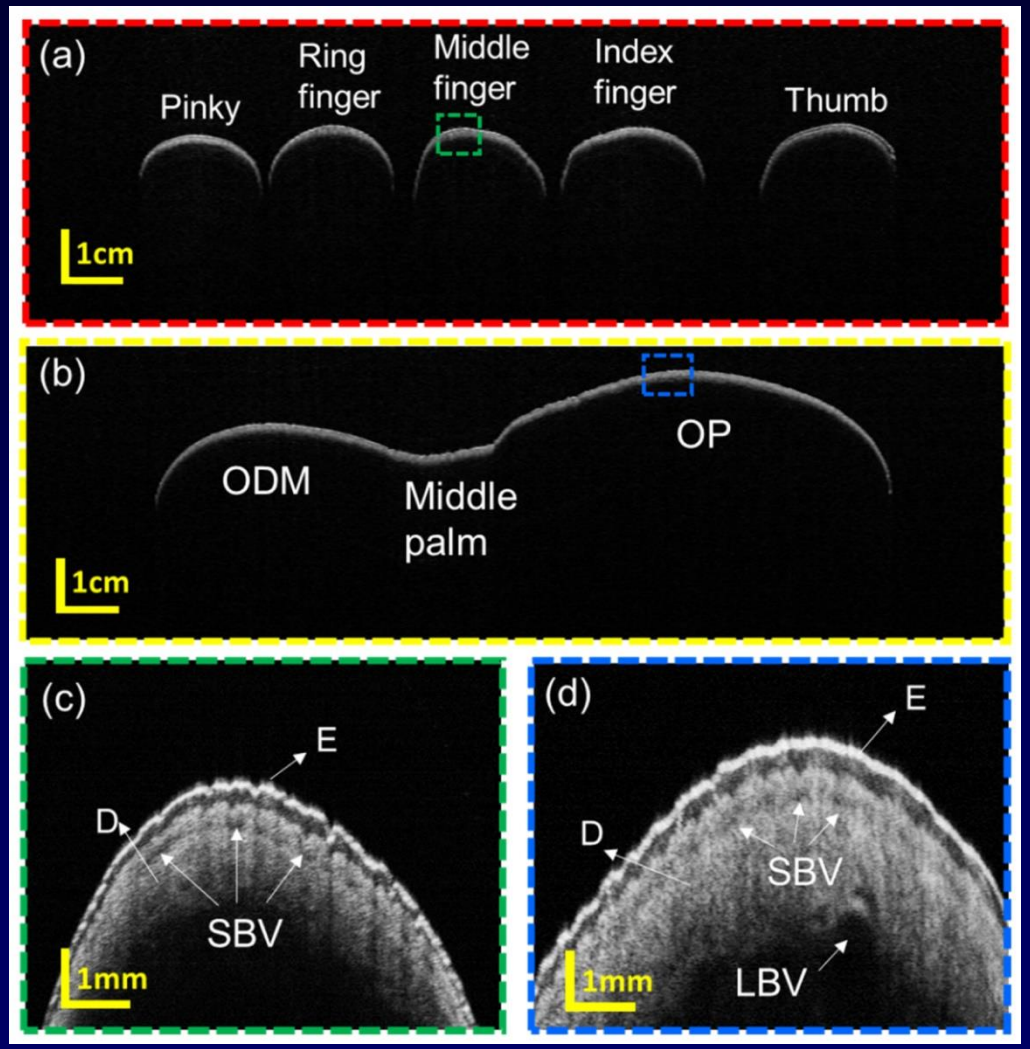


(a, b) Yurtsever et al., SPIE Proceeding (2010)
(c) Nguyen, et al., Opt Lett (2011)
(d) Yurtsever et al., Biomed Opt Express (2014)

Long range OCT

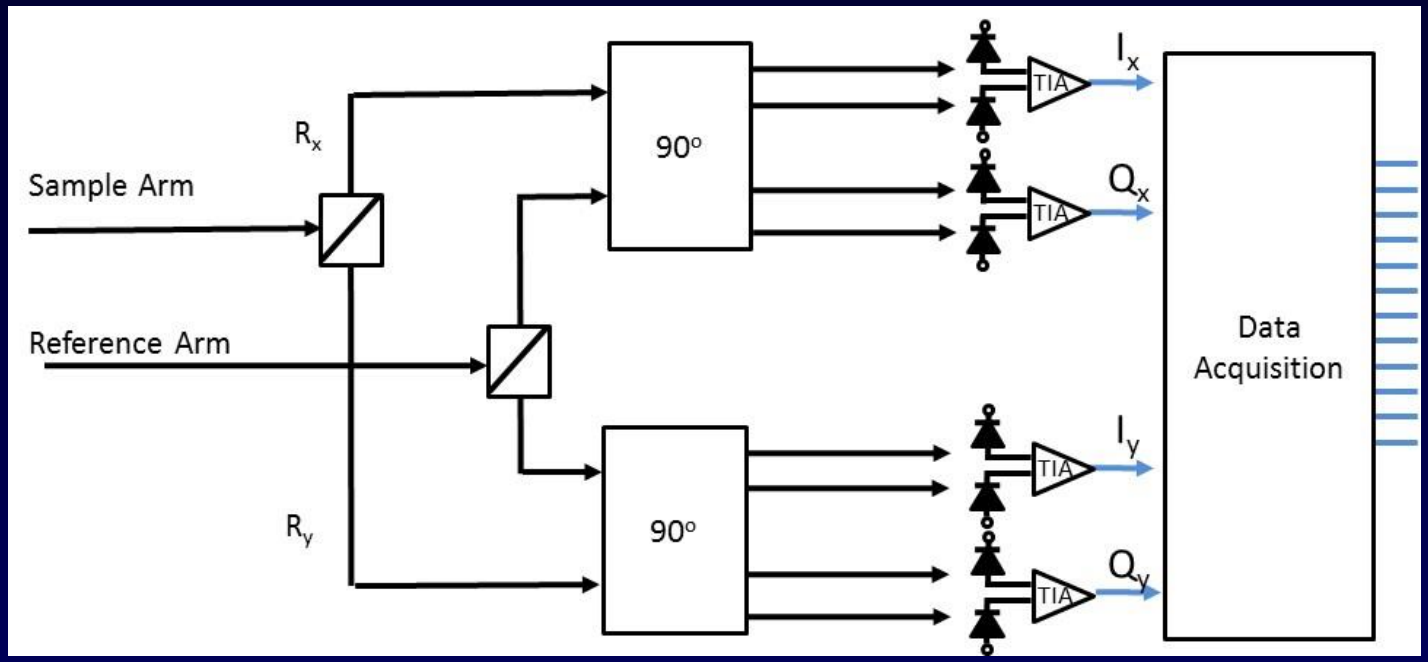




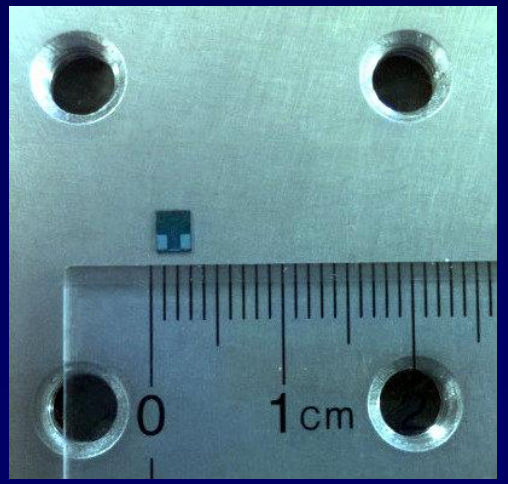


Song, *et al*., Biomed. Opt. Express (2016).

Coherent Receiver Integrated OCT System



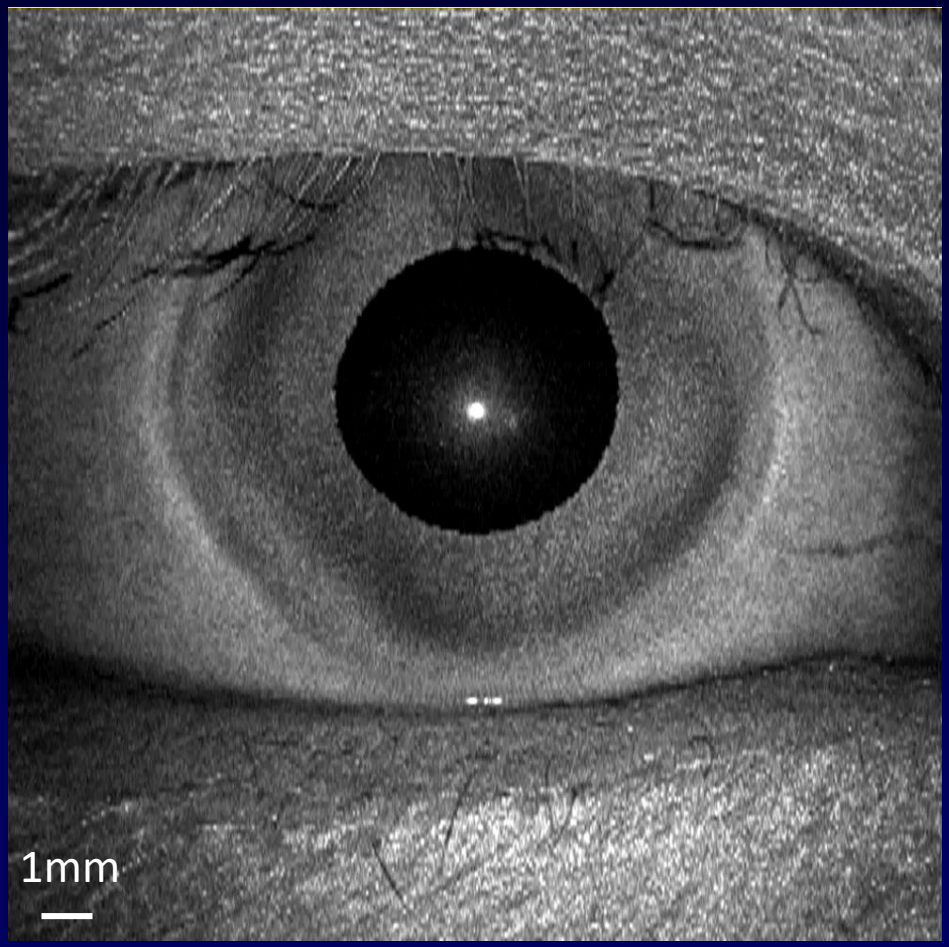
- Dual polarization, dual balanced, in phase and quadrature (IQ) detection
- >70 nm optical bandwidth at 1550 nm
- Low loss (~ 4 dB)
- > 25 GHz electrical bandwidth
- 3 mm x 4 mm die size

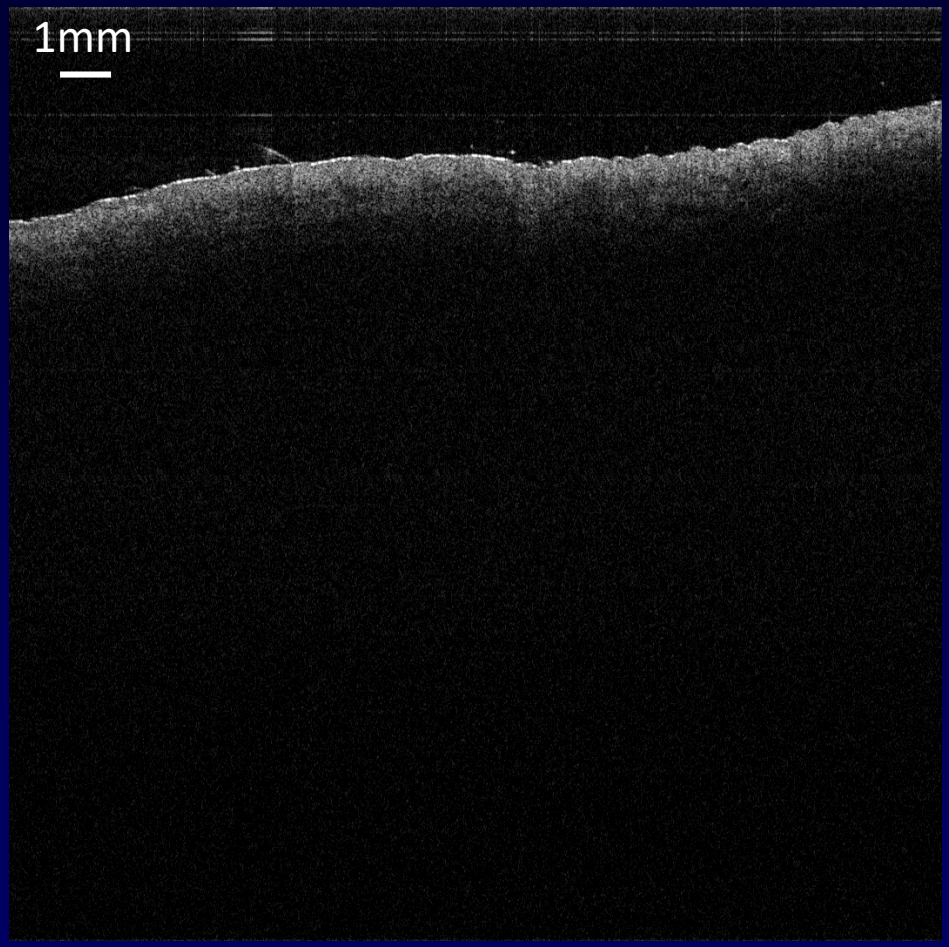


Wang , Lee, *et al.,* Biomed Opt Express (2014)

Collaboration with Acacia Communication

Anterior Eye Imaging using VCSEL and Integrated Receiver @1310nm





- Scan pattern: 2000 x 200 A-scans/volume
- Acquisition time: 2 s
- Scan field: 18 × 18 mm^2

*unpublished data

OCT Imaging at ~1 Cubic Meter Volume

Wang *et al.*, Optica (2017)

OCT Imaging at ~1 Cubic Meter Volume

DC

50cm

- Scan pattern: 1000x1000 A-scans/volume
- Scan volume (~200cm depth, ~100cm horizontal, ~100cm vertical)
- Edge of chess board to back of mannequin ~80cm

Meter Range OCT for 3D Documentation

10cm

先進生醫光電影像實驗室

Advanced Biomedical Optical Imaging Laboratory

李翔傑助理教授 (Hsiang-Chieh Lee)

hclee2@ntu.edu.tw

Graduate Institute of Photonics and Optoelectronics

Department of Electrical Engineering

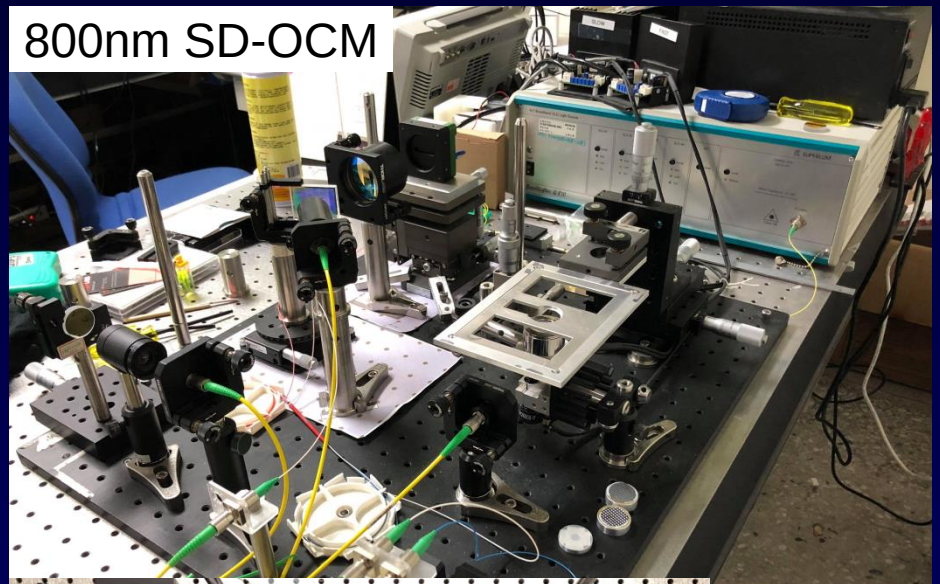
Molecular Imaging Center

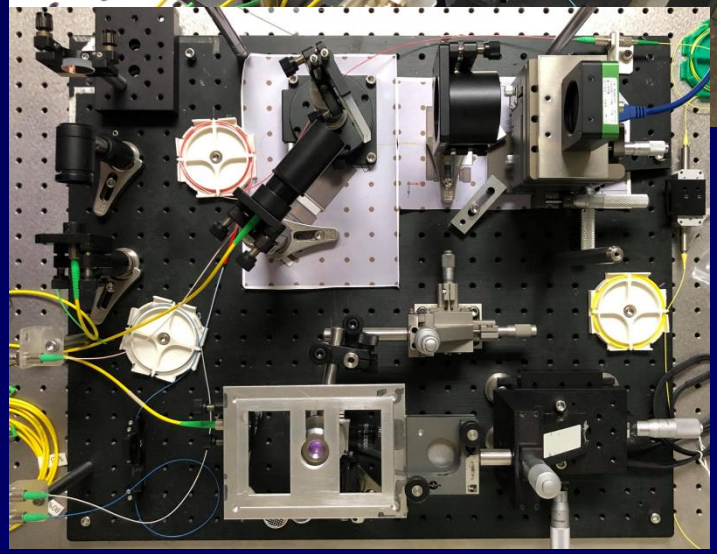
National Taiwan University

Advanced Biomedical Optical Imaging Lab

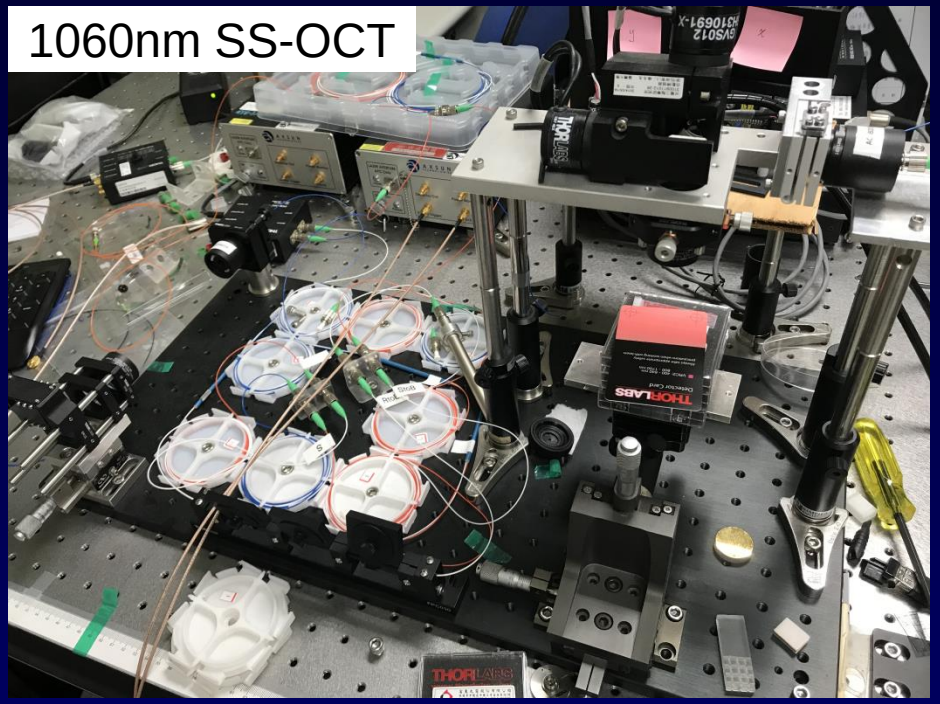
- **MIC Room 114:**

800nm SD-OCM





1060nm SS-OCT



800nm SD-OCM (~100kHz Ascans/sec)

- **customized spectrometer with a USB 3.0 line-scan camera (e2V) and off shelf optics**
- **Inverted microscope (sample arm)**

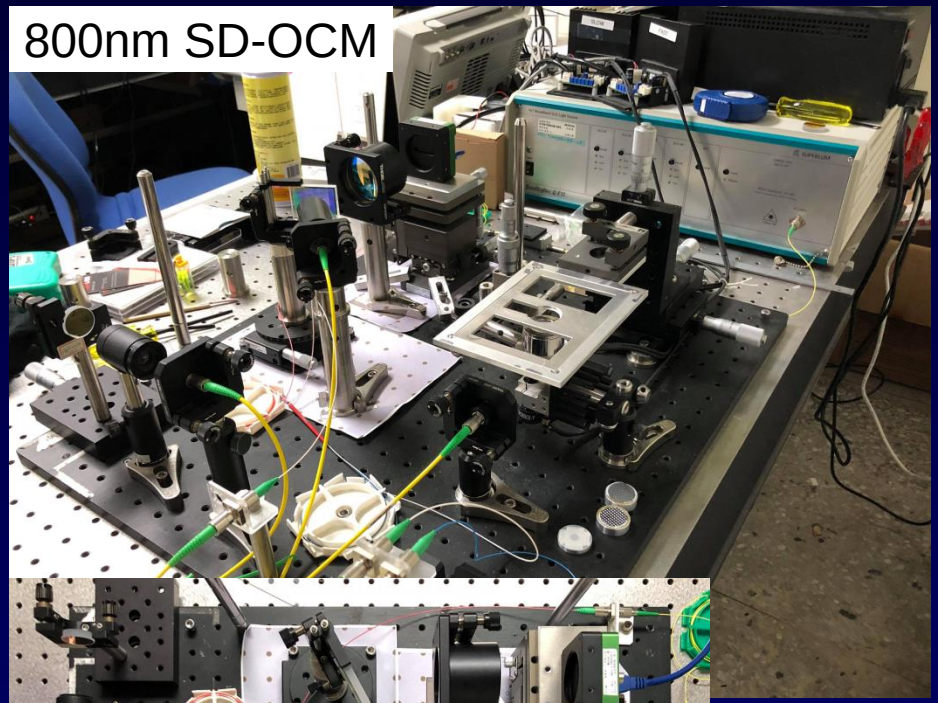
1060 SS-OCT (100 or 200kHz Ascans/sec)

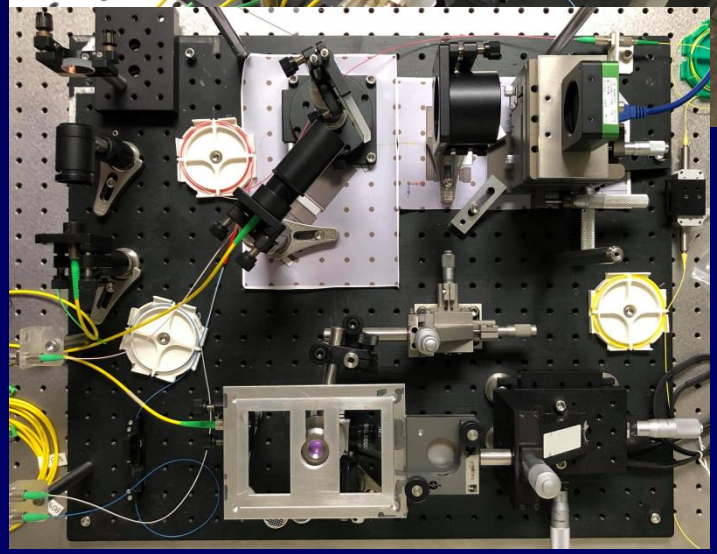
- **suitable for human/animal study**

Advanced Biomedical Optical Imaging Lab

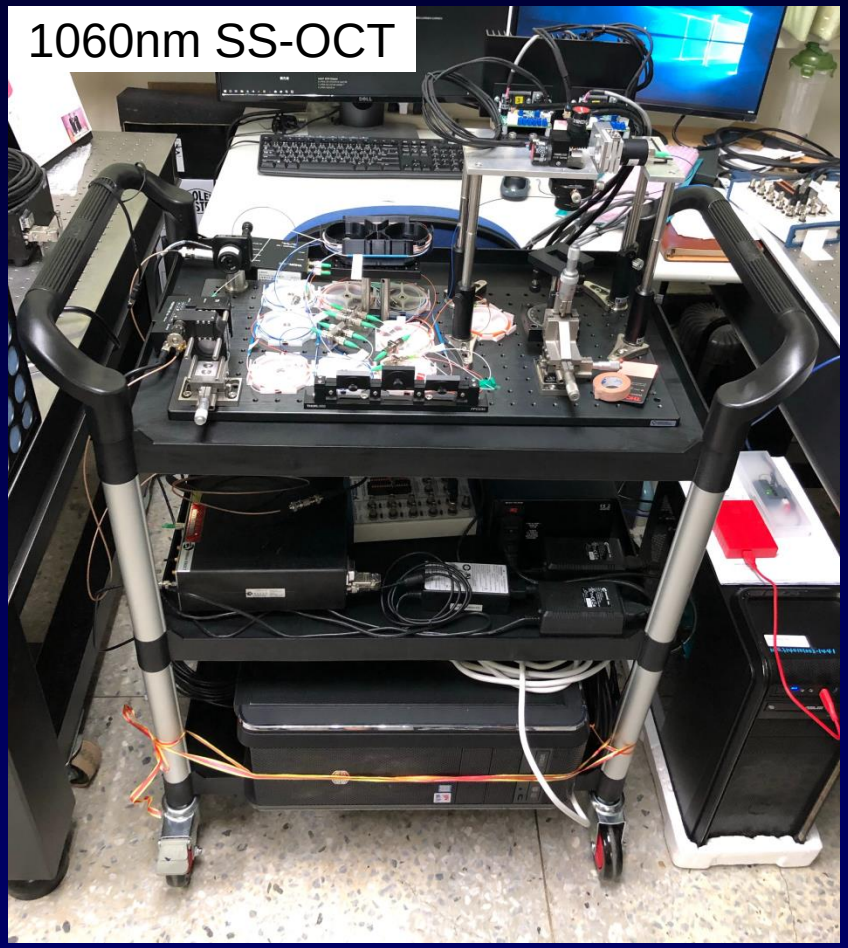
- **MIC Room 114:**

800nm SD-OCM





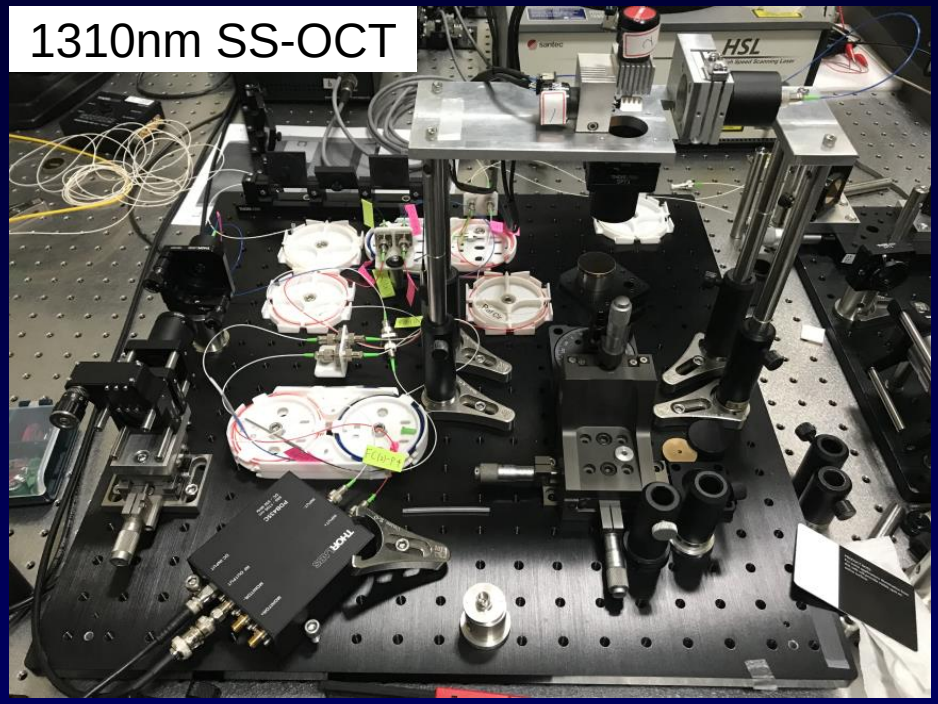
1060nm SS-OCT



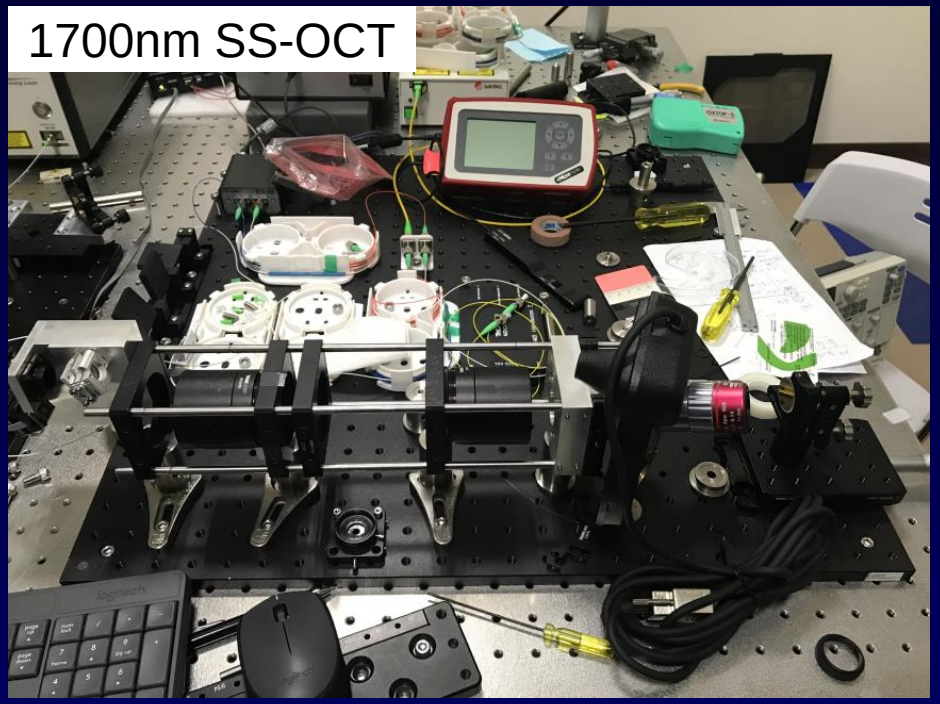
Advanced Biomedical Optical Imaging Lab

- **MIC Room 109:**

1310nm SS-OCT



1700nm SS-OCT



1310nm SS-OCT (20 or 100kHz Ascans/sec)

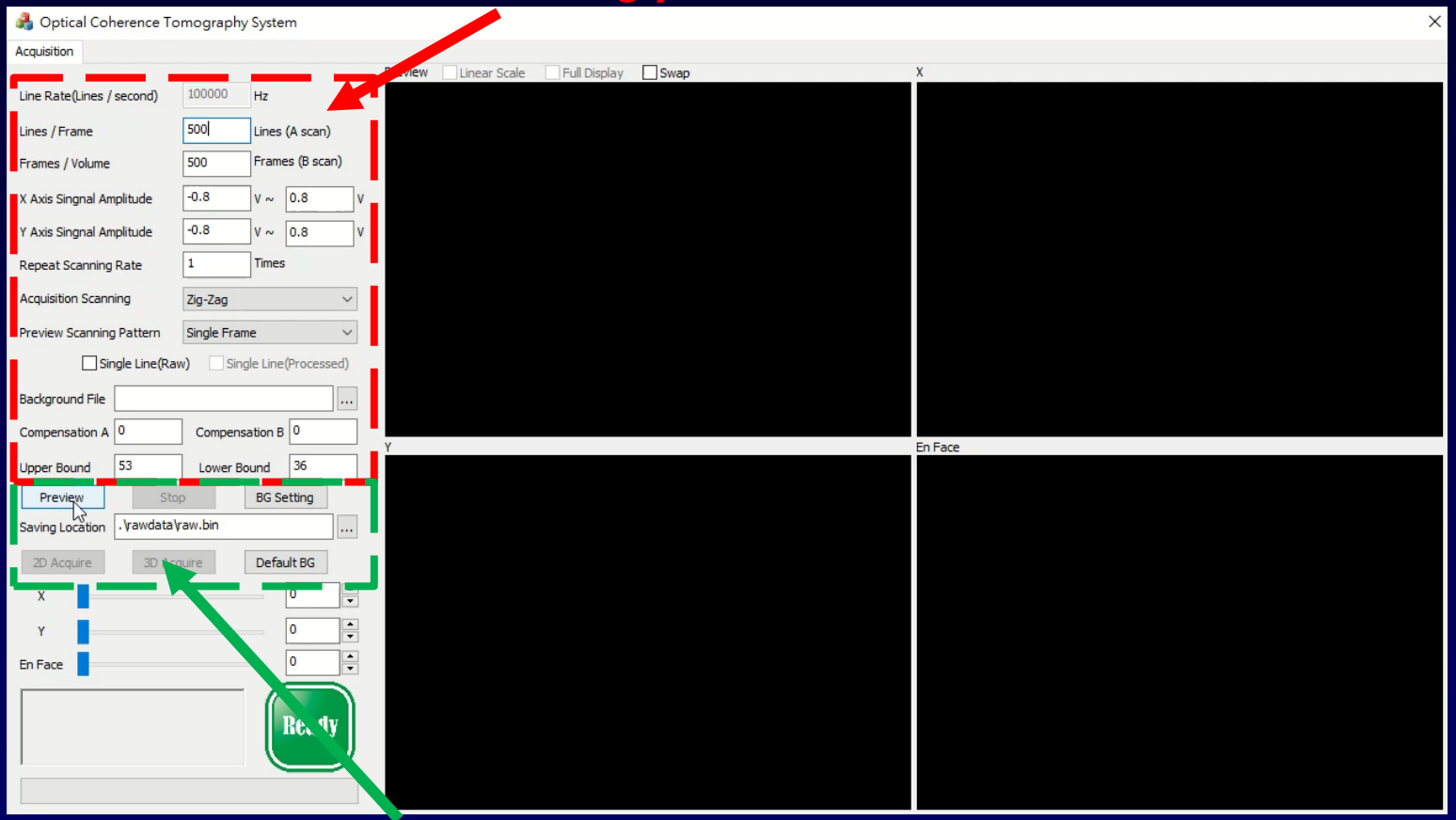
- **suitable for human/animal study**
- **platform for future catheter based OCT system development**

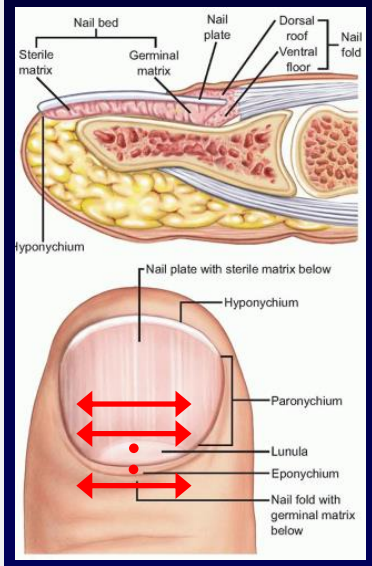
1700nm SS-OCT (90kHz Ascans/sec)

- **4f fiber optic scanning confocal microscope**
- **increased imaging depth due to decreased tissue scattering**

Customized Graphic User Interface (GUI)

Parameter setting panel

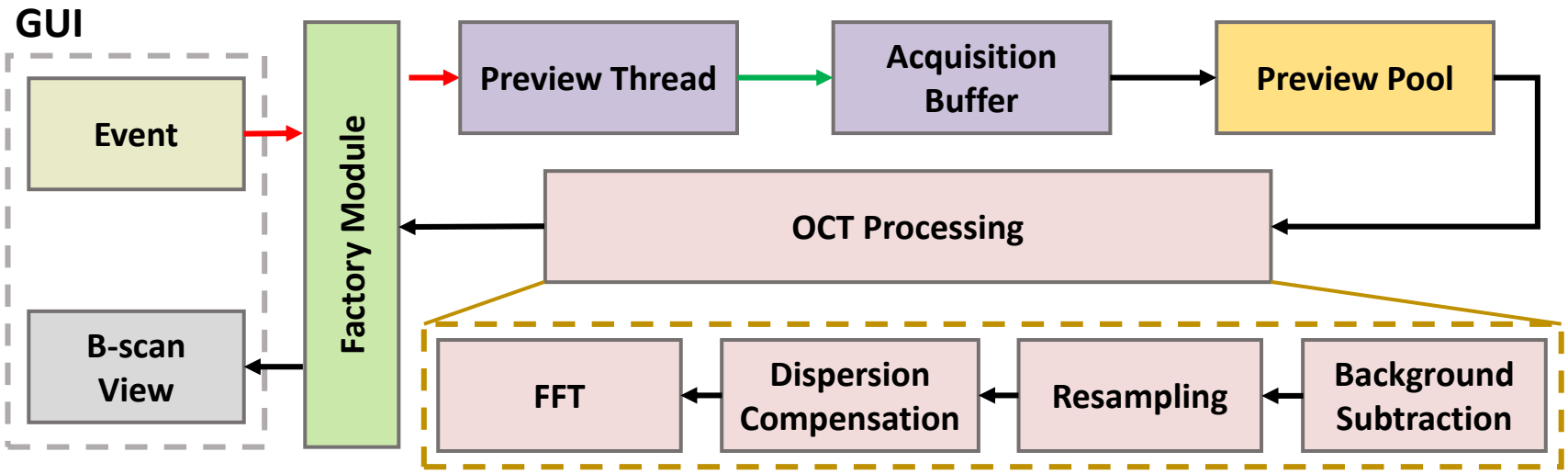




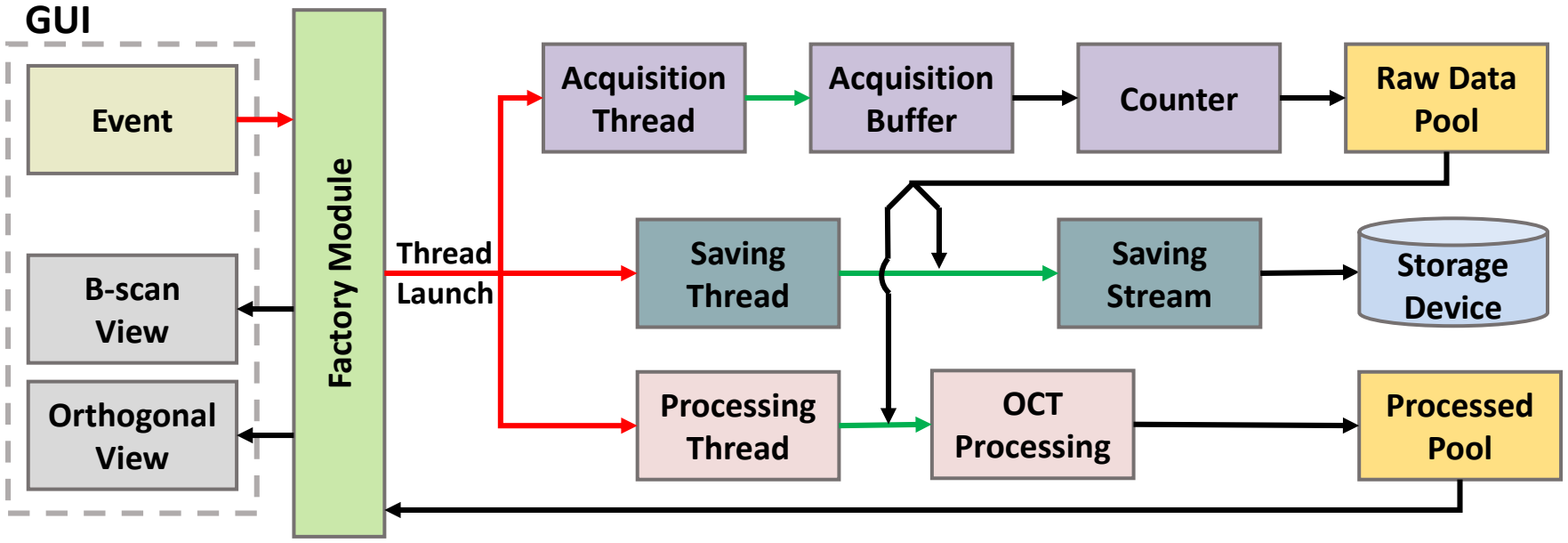
Event button panel

Test system: 1 μm OCT with an A-scan rate of 100 kHz.
Software Engine: C++ plus MFC for graphic user interface (GUI) (multithreading config.)

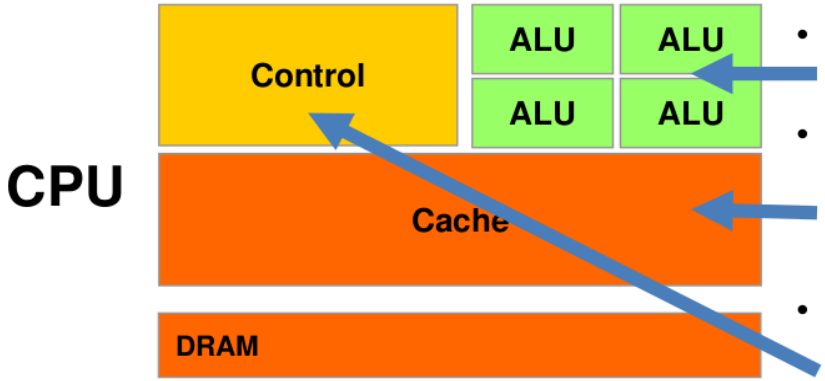
Preview Mode



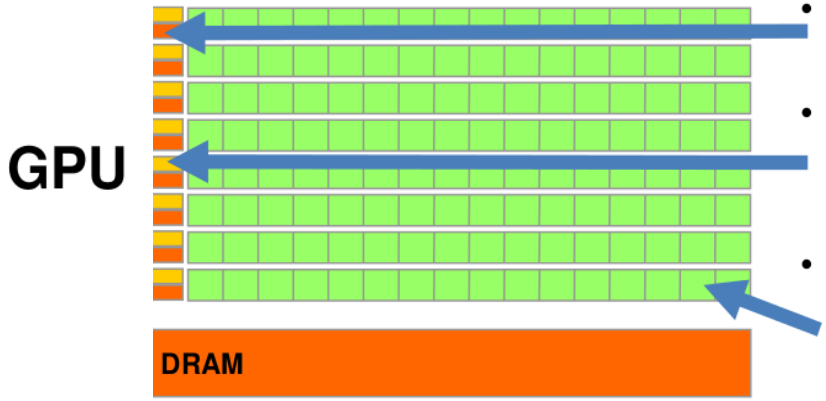
Acquisition Mode



CPU vs. GPU



- Powerful ALU
  - Reduced operation latency
- Large caches
  - Convert long latency memory accesses to short latency cache accesses
- Sophisticated control
  - Branch prediction for reduced branch latency
  - Data forwarding for reduced data latency

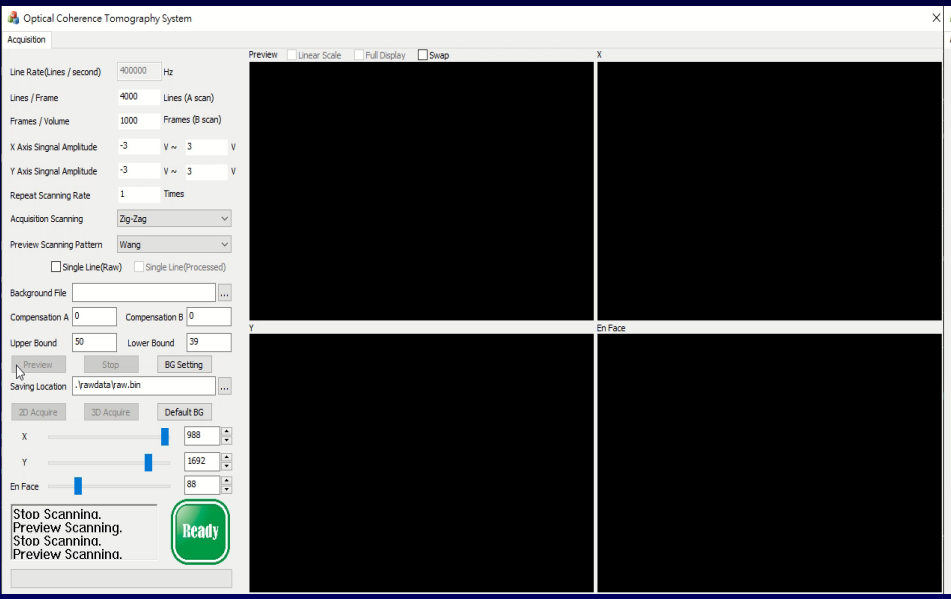


- Small caches
  - To boost memory throughput
- Simple control
  - No branch prediction
  - No data forwarding
- Energy efficient ALUs
  - Many, long latency but heavily pipelined for high throughput
- Require massive number of threads to tolerate latencies

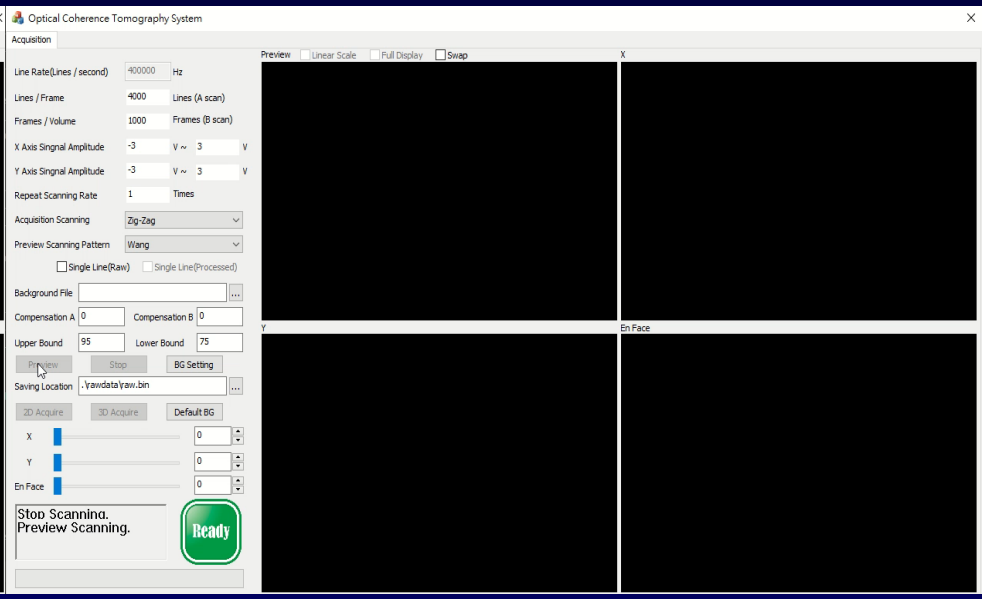
https://www.cnblogs.com/biglucky/p/4223565.html

Framework Ⅰ – ATS-GPU: preview

400 kHz light source (Thorlabs, SL134000-SP1)



OCT images processed by CPU with multithreading

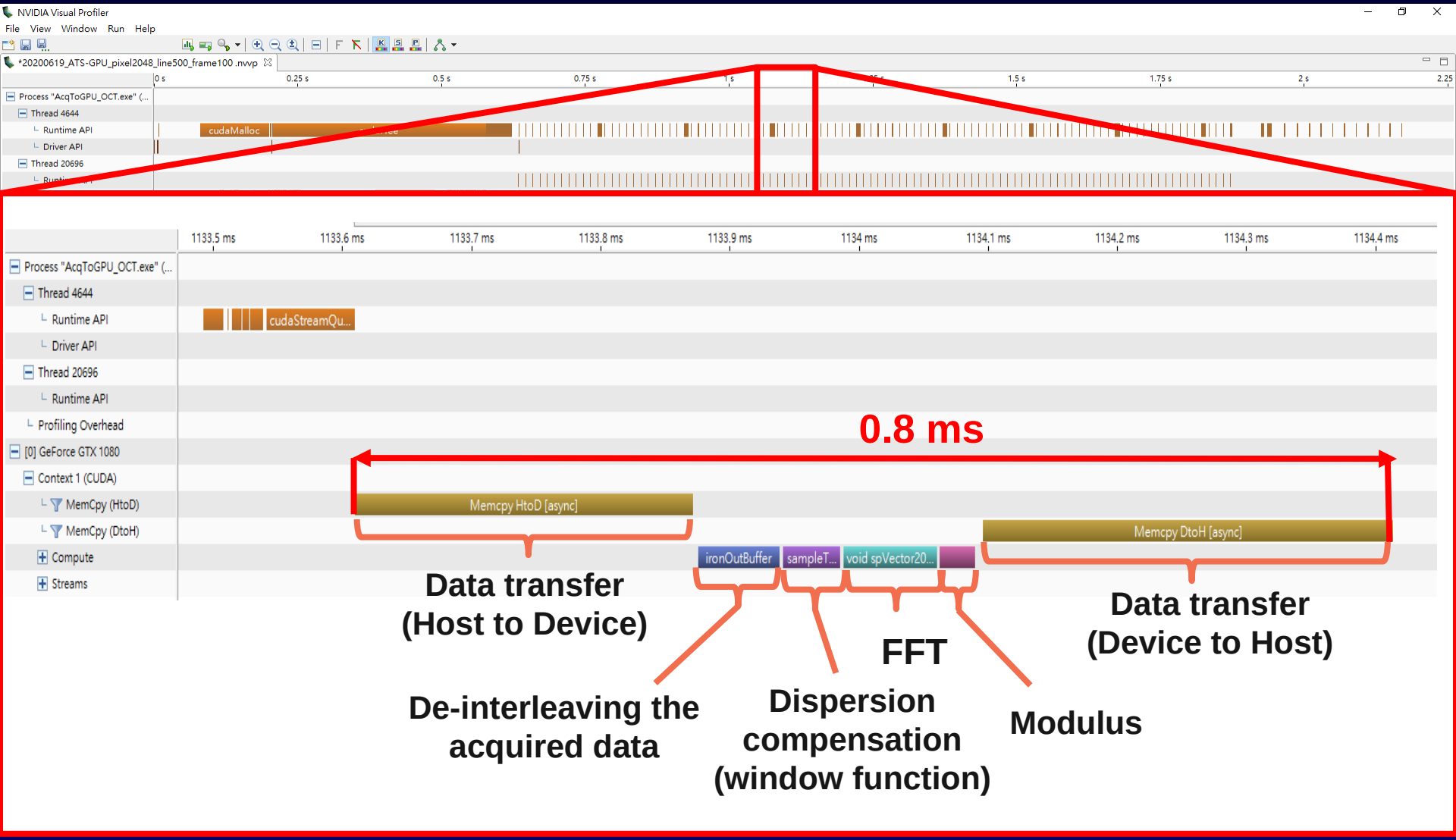


OCT images processed by AlazarTech GPU

Moving a tweezer on the tooth specimen

1024 pixels/A-scan, 4000 A-scans/B-scan, 1000 B-scans/C-scan

Framework Ⅰ – ATS-GPU



Early Detection of Oral Cancer Lesions with Optical Imaging Technology

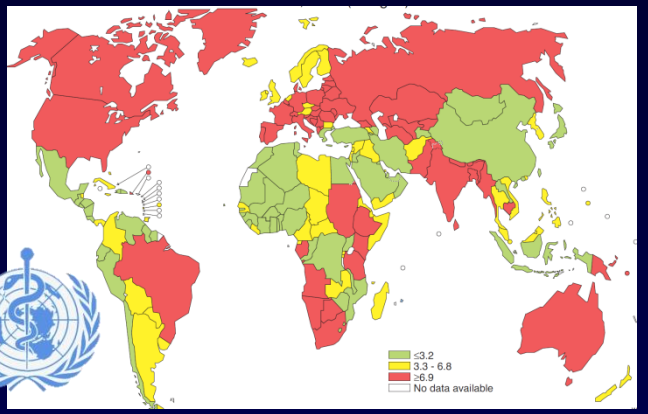
Unmet Clinical Need – Oral Cancer

Carcinogenetic substances

~3000 deaths*

~7000 new cases*

*2017 data



~300,000 new cases annually†

† Incidence & Prevalence of Oral Cancer" Oral Cancer Foundation (2015)

¶ adapted from https://teachmeobgyn.com/gynaecology/cervix/cervical-cancer/

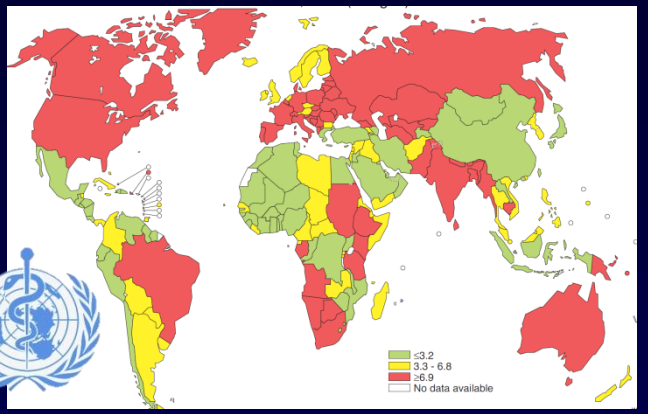
Unmet Clinical Need – Oral Cancer

Carcinogenetic substances

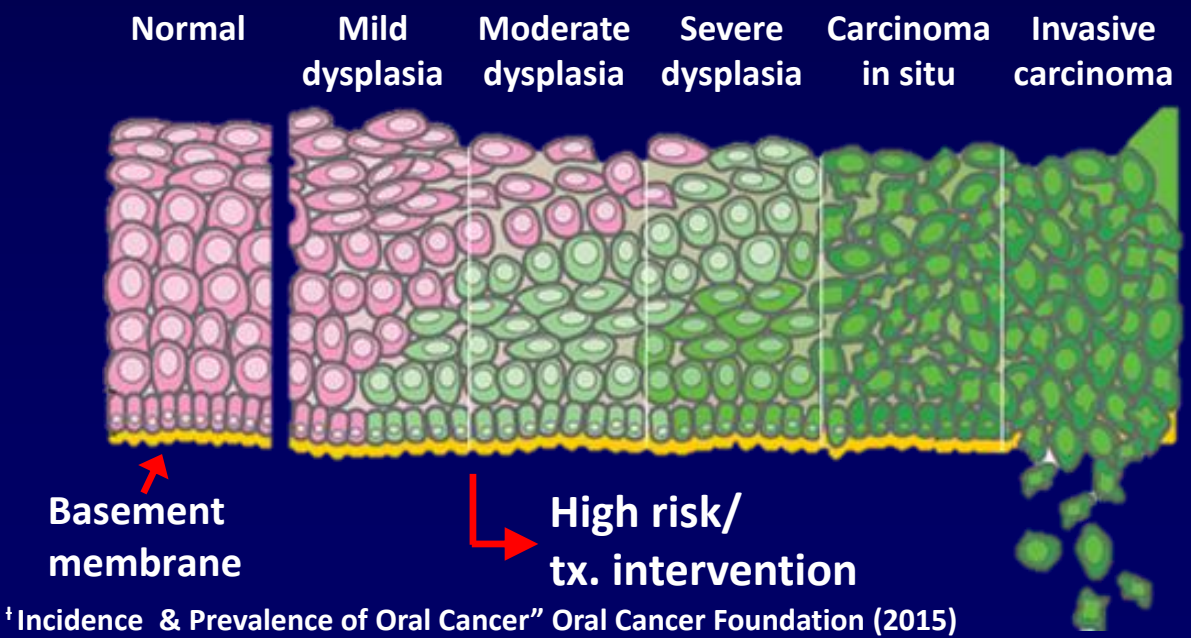
~3000 deaths*

~7000 new cases*

*2017 data



~300,000 new cases annually†



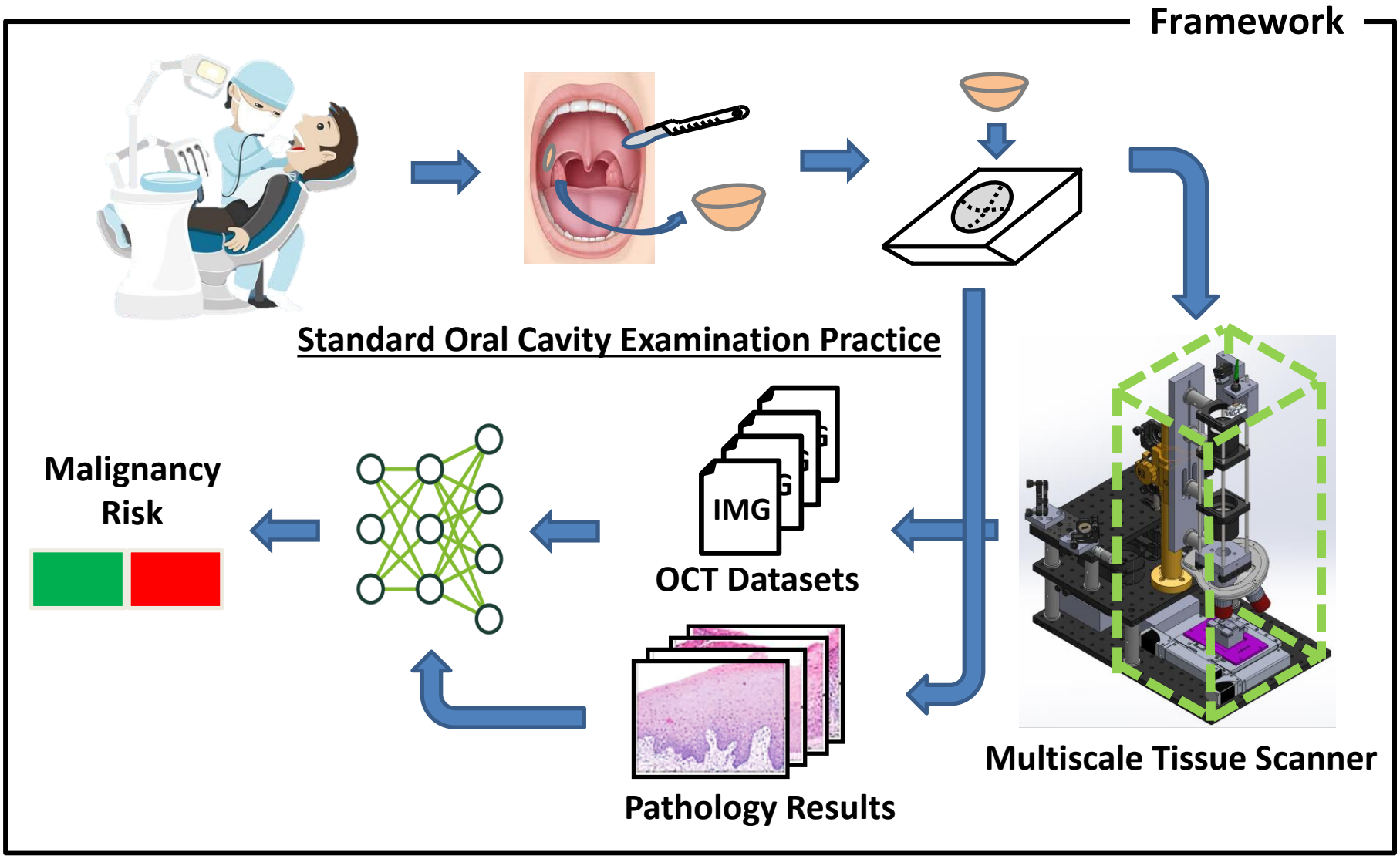
Neoplastic progression of oral cancer¶

Stage	5-yr survival rate
I	79.9%
II	71.0%
III	56.5%
IV	35.6%
2012-2016 MOHW (Taiwan) Data	

† Incidence & Prevalence of Oral Cancer" Oral Cancer Foundation (2015)

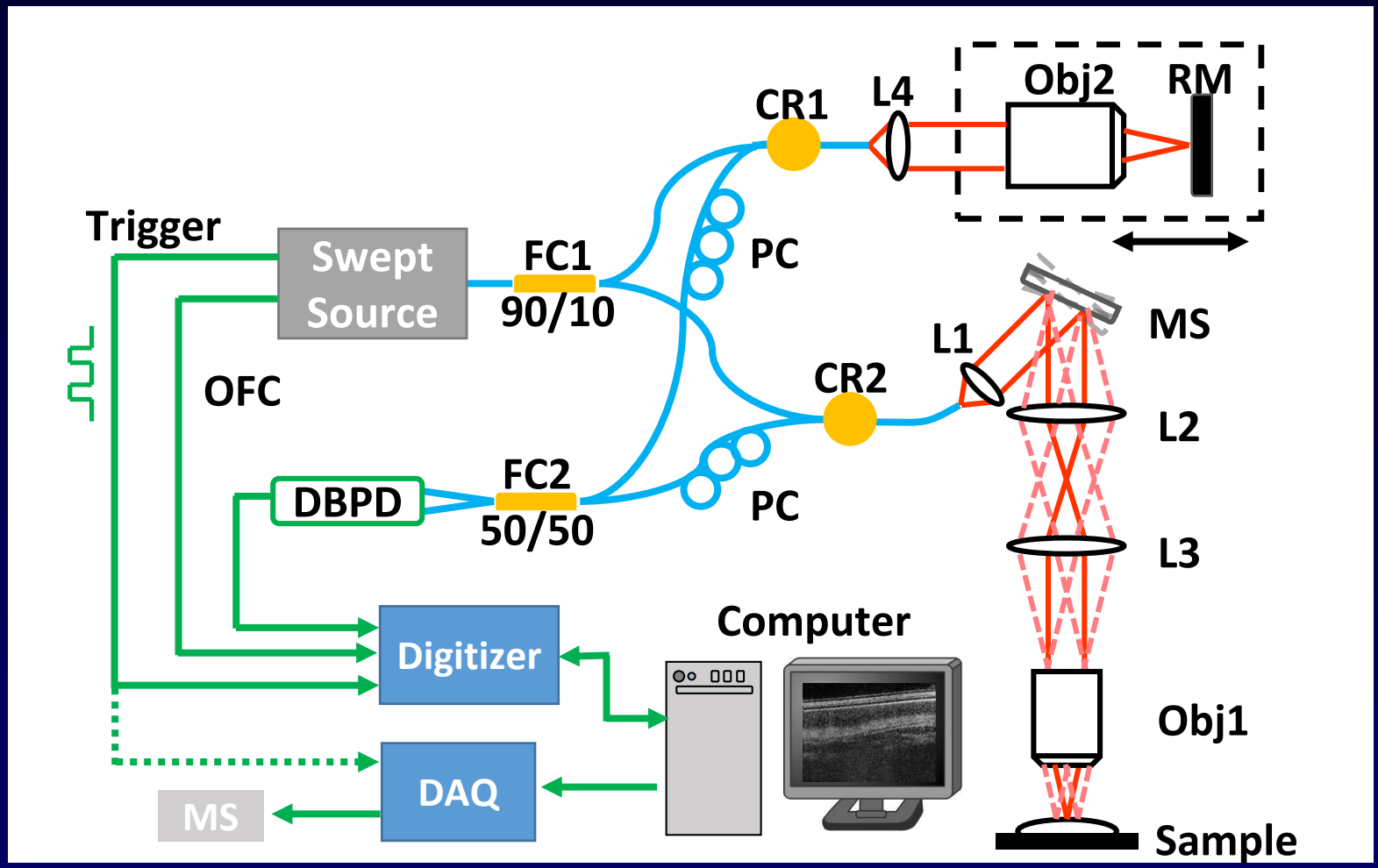
¶ adapted from https://teachmeobgyn.com/gynaecology/cervix/cervical-cancer/

Early Detection of Oral Cancer



¶ adapted from https://www.123rf.com/stock-photo/dentist_cartoon.html?sti=o8hsfwc1qmwlmqv16l|

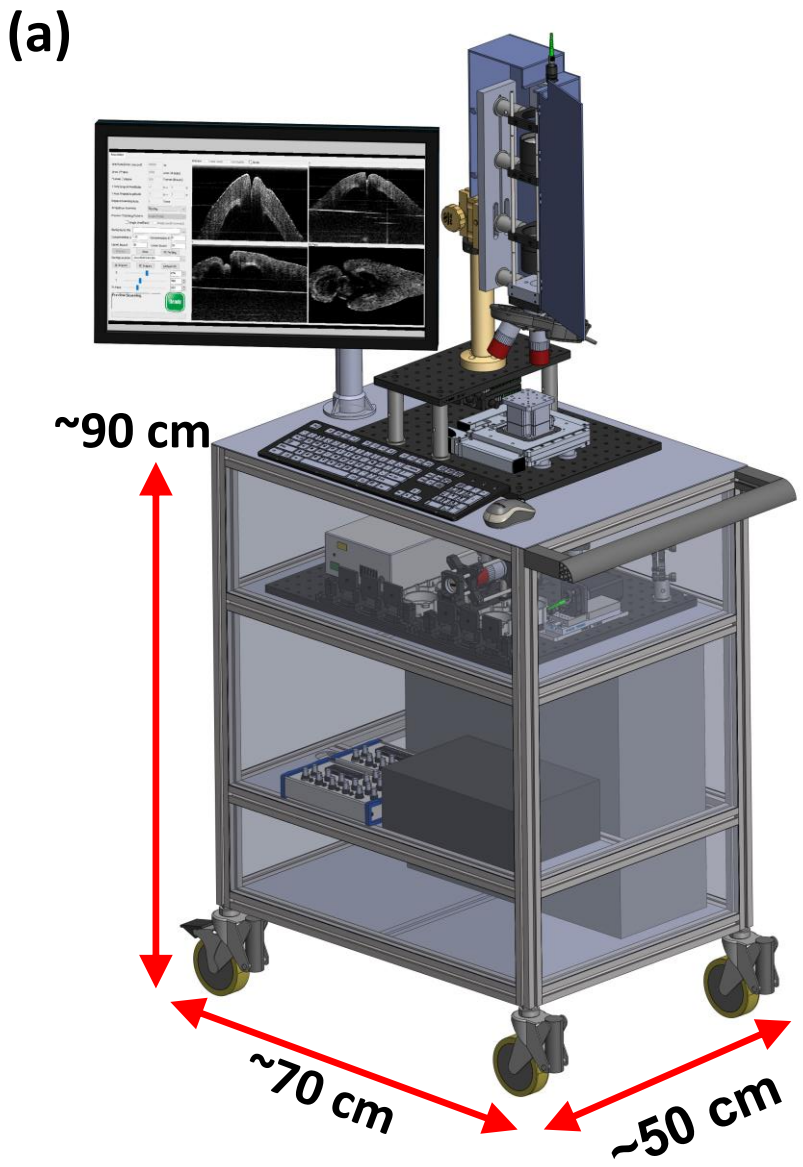
Multiscale Tissue Scanner – I



– Light source (Santec):
- Central wavelength: 1690 nm
- A-scan rate: 90 kHz
- Axial resolution: 7.2 μm

– MEMS scanner
– 3D motorized stage

Multiscale Tissue Scanner – I



Multiscale Tissue Scanner – II

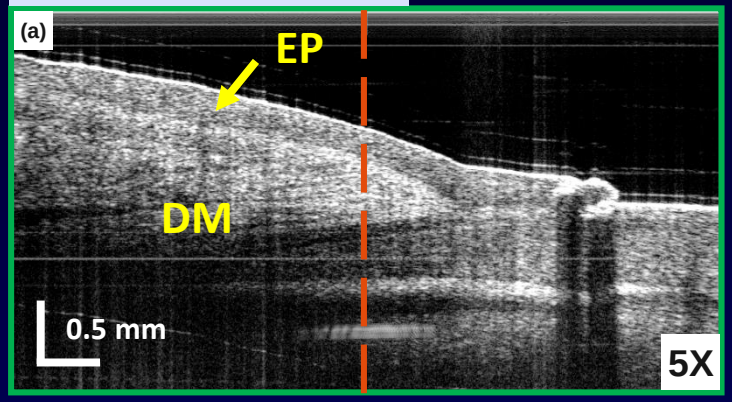
System Operating Video

Custom developed graphic user interface (GUI)

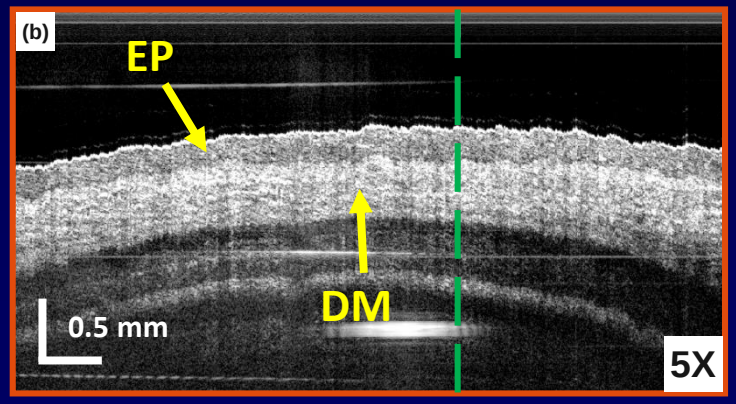
Preliminary Results – Human Finger

Finger nail junction

Cross-section

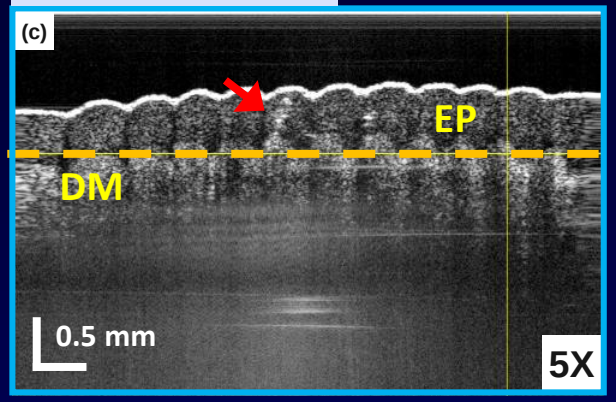


Reconstructed cross-section

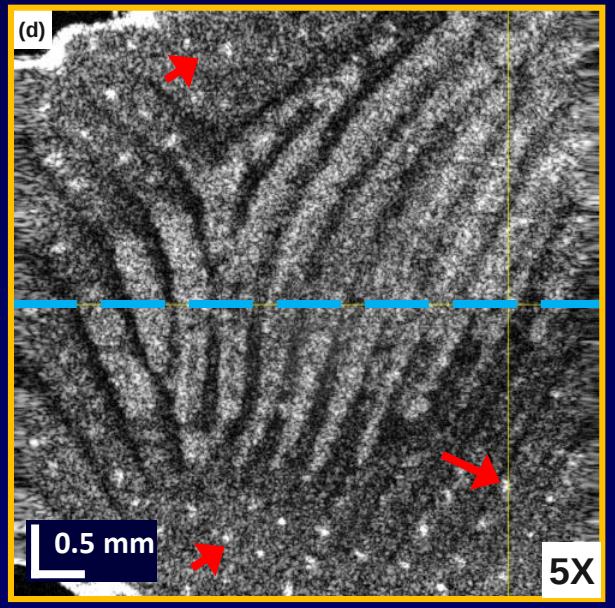


Ventral surface

Cross-section



Reconstructed *en-face*



Red arrows: sweat duct

EP: epidermis
DM: dermis
FOV: 5.5 mm X 5.5 mm

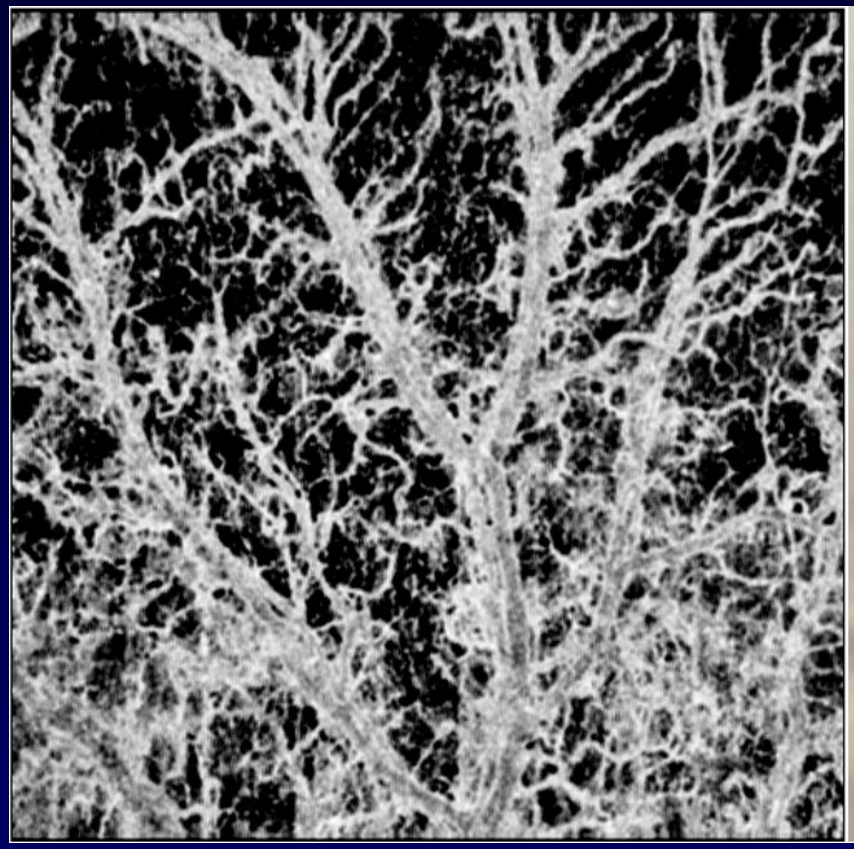
(a), (b) Cross-sectional image and reconstructed cross-sectional image of the finger nail junction, respectively

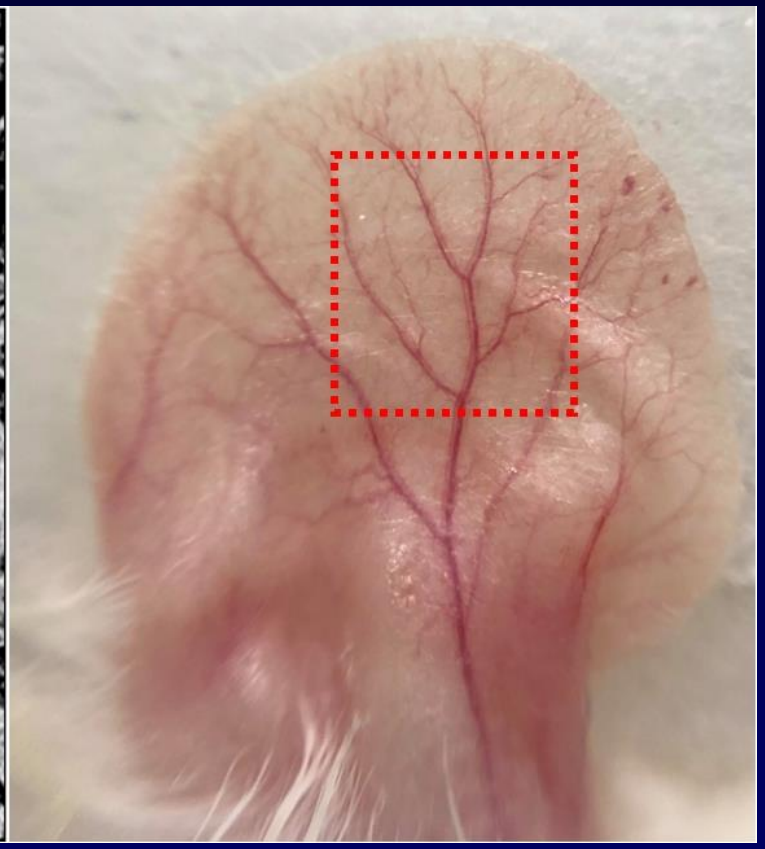
(c), (d) Cross-sectional image and reconstructed *en-face* image of the ventral surface of finger, respectively

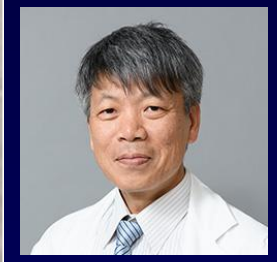
✓ The junction between epidermis and dermis, and the sweat ducts can be seen clearly in our long wavelength OCT system.

Quantitative Microvascular Imaging with Optical Coherence Tomography Technology

OCT Angiography of the Mouse Ear Skin



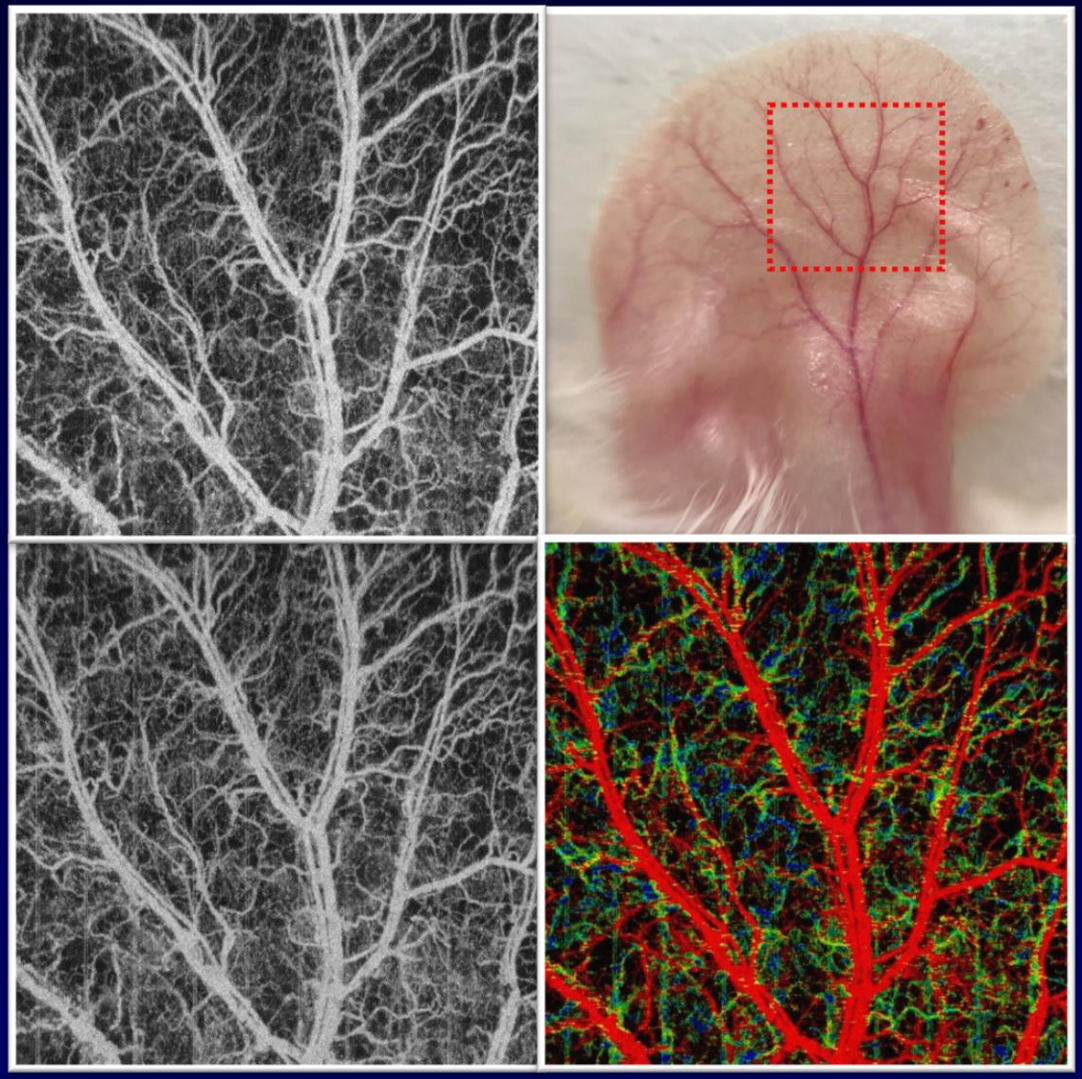




B-scan Frame rate : 80 Hz

Imaging field of view: 4.08 x 4.08 mm^2

OCT Angiography of the Mouse Ear Skin



High speed

Low speed

Imaging field of view: 5.1 x 5.1 mm^2

OCT Imaging of the Guinea Pig Cochlea

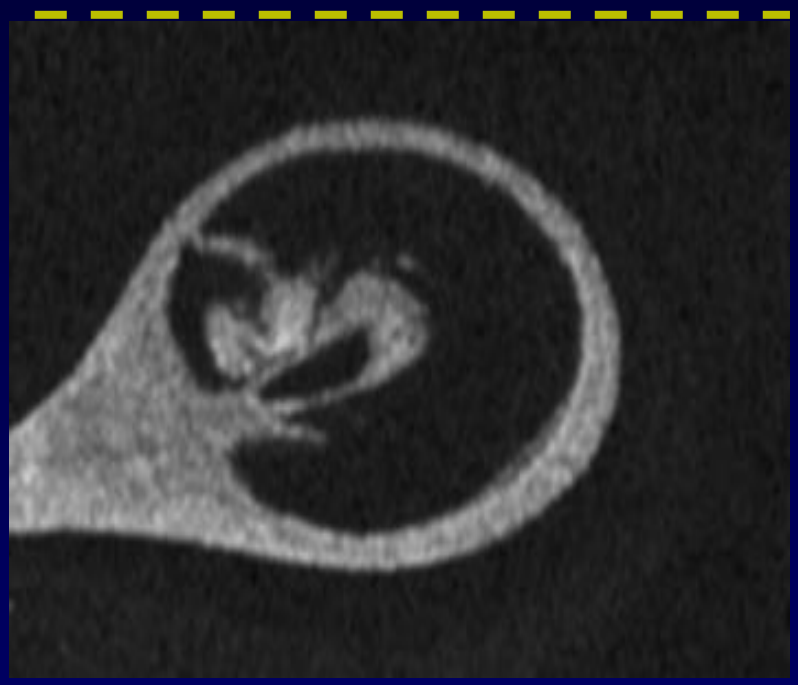
Hearing loss and deafness

- Congenital causes and acquired causes
  - birth asphyxia
  - chronic ear infections
  - the use of particular drugs
- sensorineural hearing loss (SNHL)
  - exposure to excessive noise
  - not completely recoverable
- Internal ear
  - vestibular system
  - cochlea

Ref.[1]

[1] Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014".

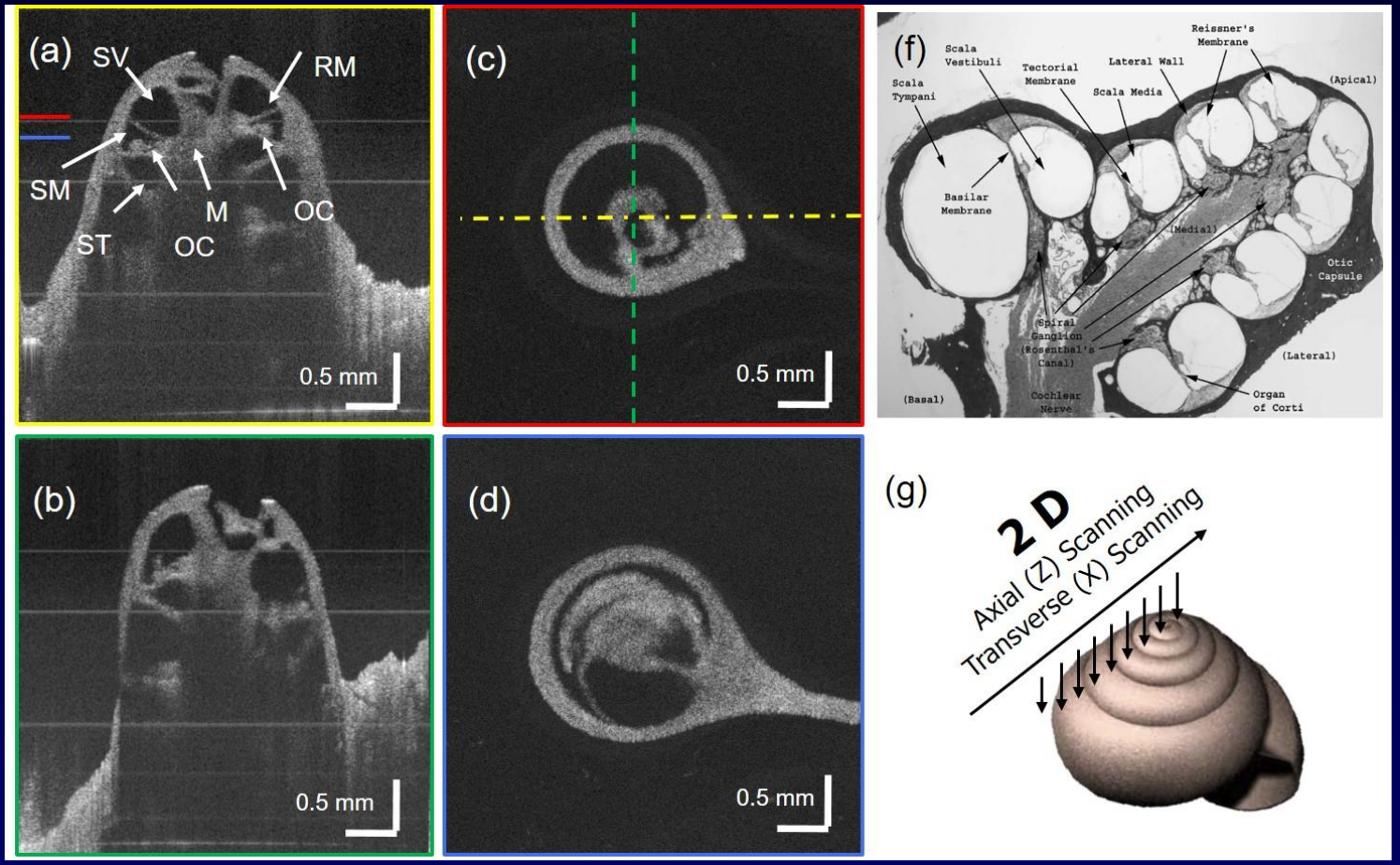
OCT imaging of guinea pig cochlea



(a) En-face image

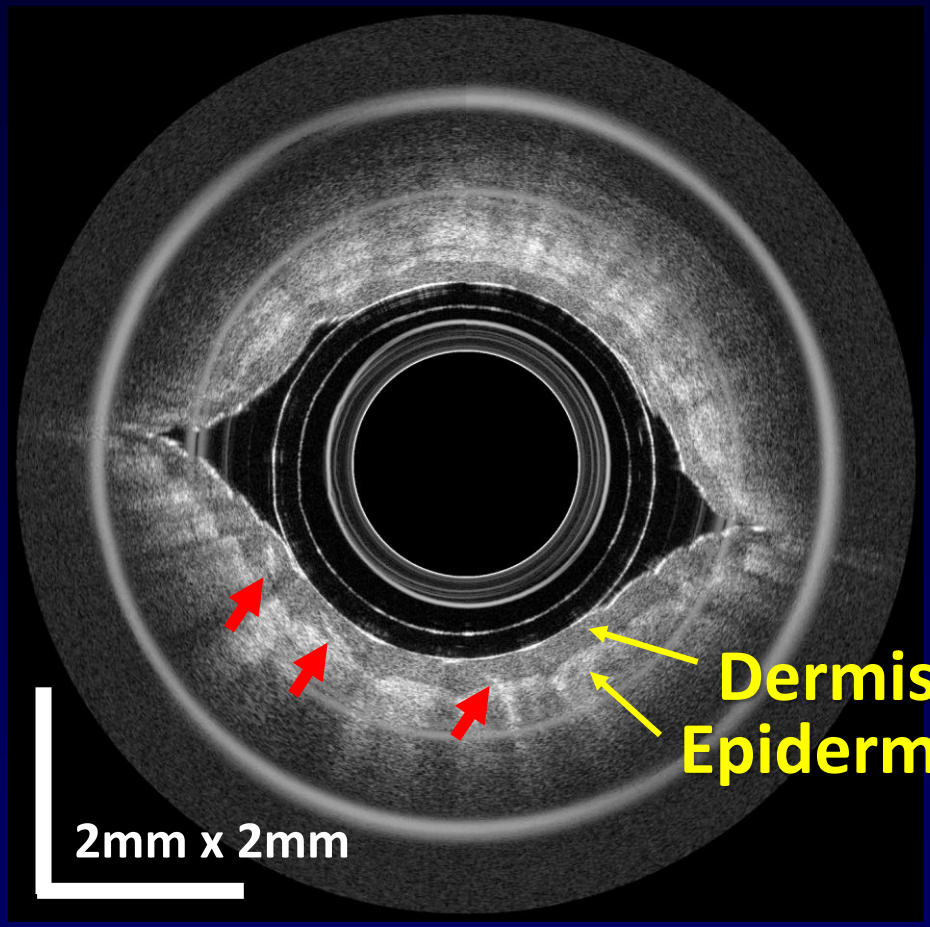
(b) Cross sectional image

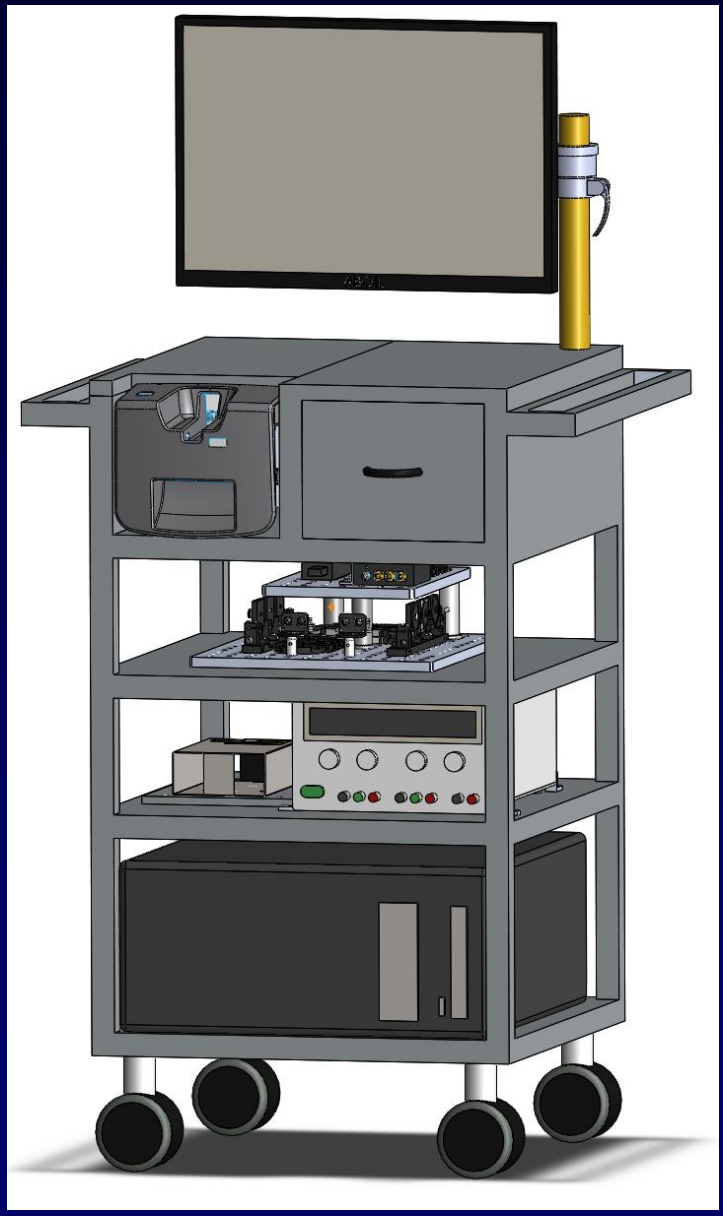
OCT imaging of guinea pig cochlea



(a)~(d) OCT images for the guinea cochlea, and (g) the scanning direction for each B scan image.

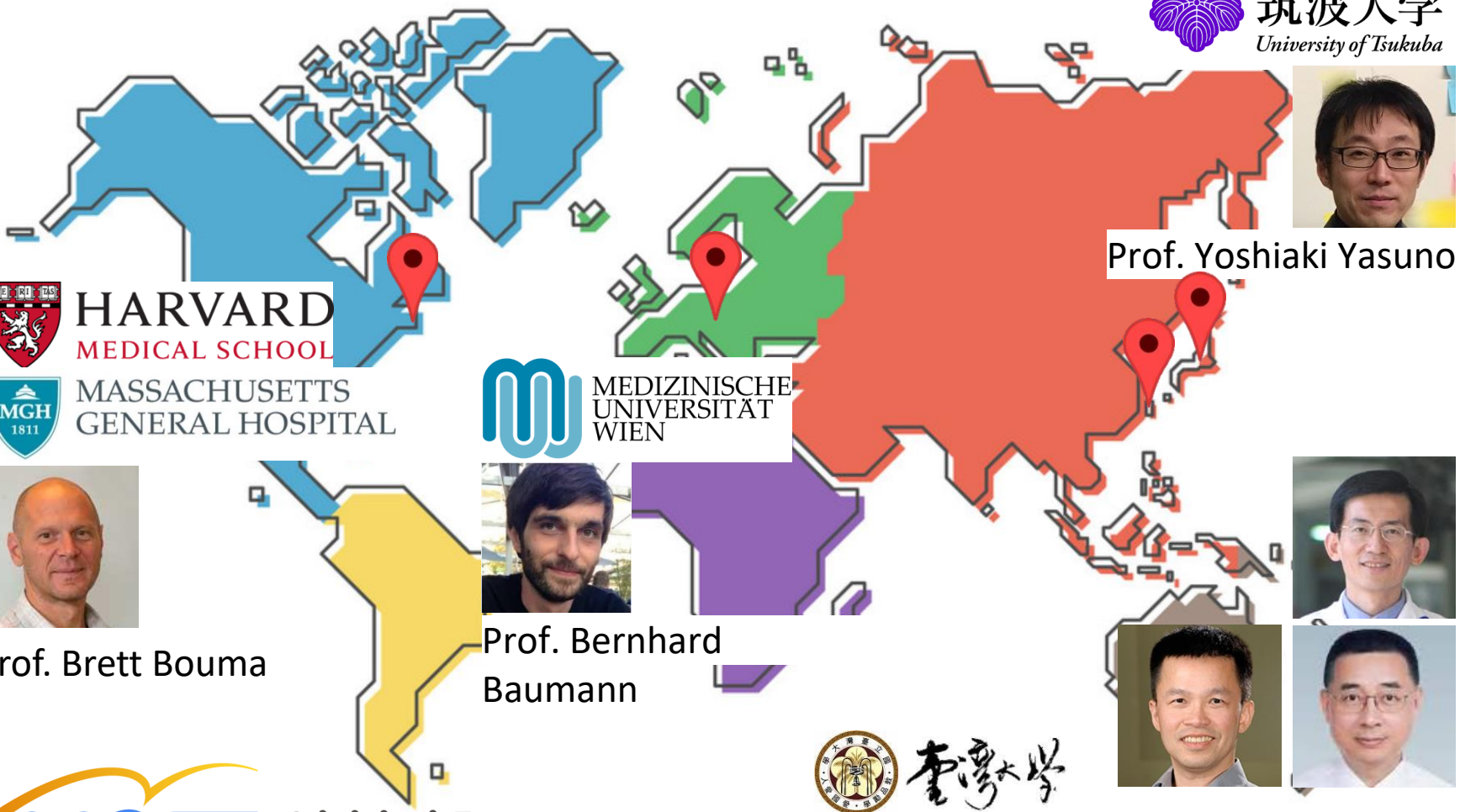
Catheter-based OCT System – Preliminary Results



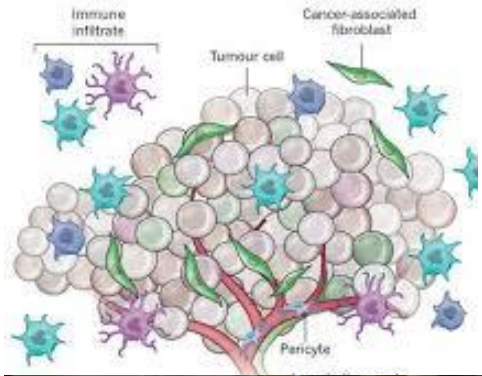


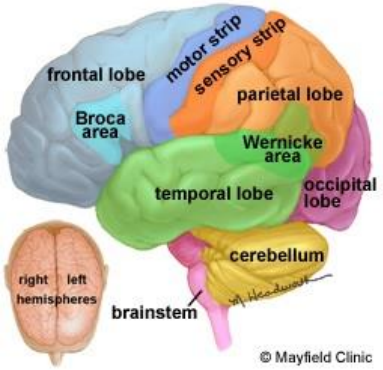
- 1.3 µm, 100kHz Santec
- 10 fps (10,000 A-scans/B-scan)

International Collaboration

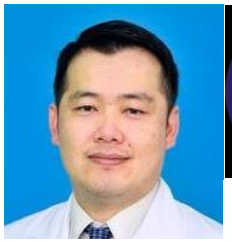


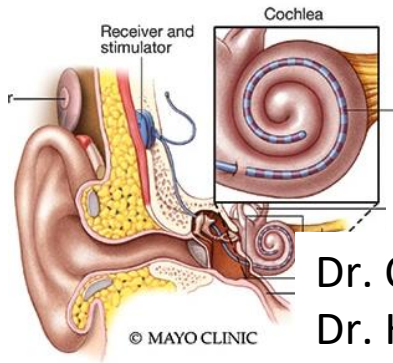
Domestic Collaboration





Dr. Ming-Kai Pan





人工電子耳

Dr. Chih-Hung Wang

Dr. Hsin-Chien Chen

Thanks for your attention.

If you want to go fast, go alone.
If you want go far, go together.

~African Proverb~