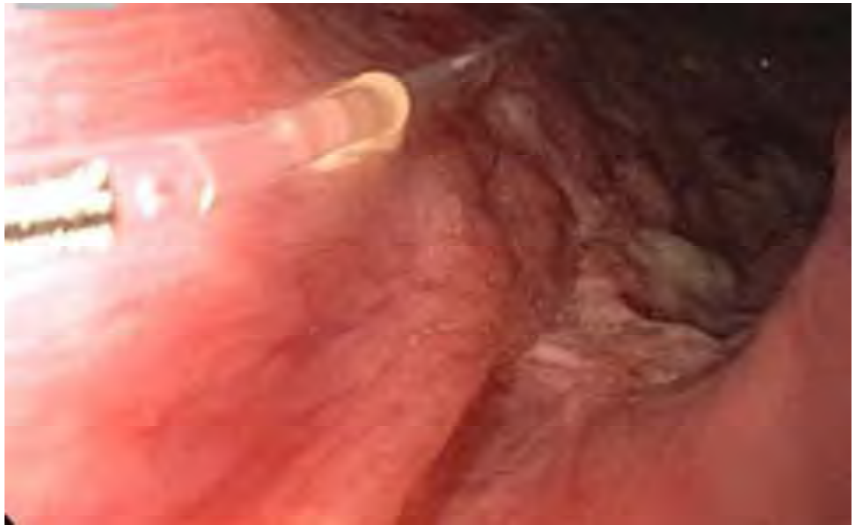
University of Cyprus
Biomedical Imaging and Applied Optics

Optical Coherence Tomography

Optical Biopsy

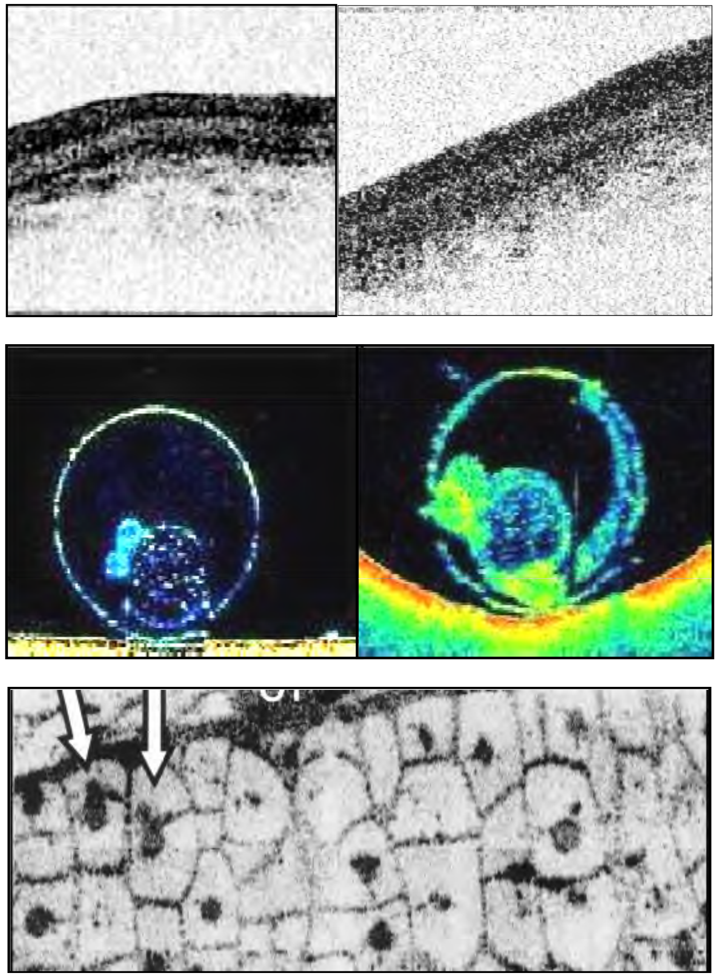
Definition

- The *in situ* imaging of tissue microstructure with a resolution approaching that of histology, but without the need for tissue excision and processing

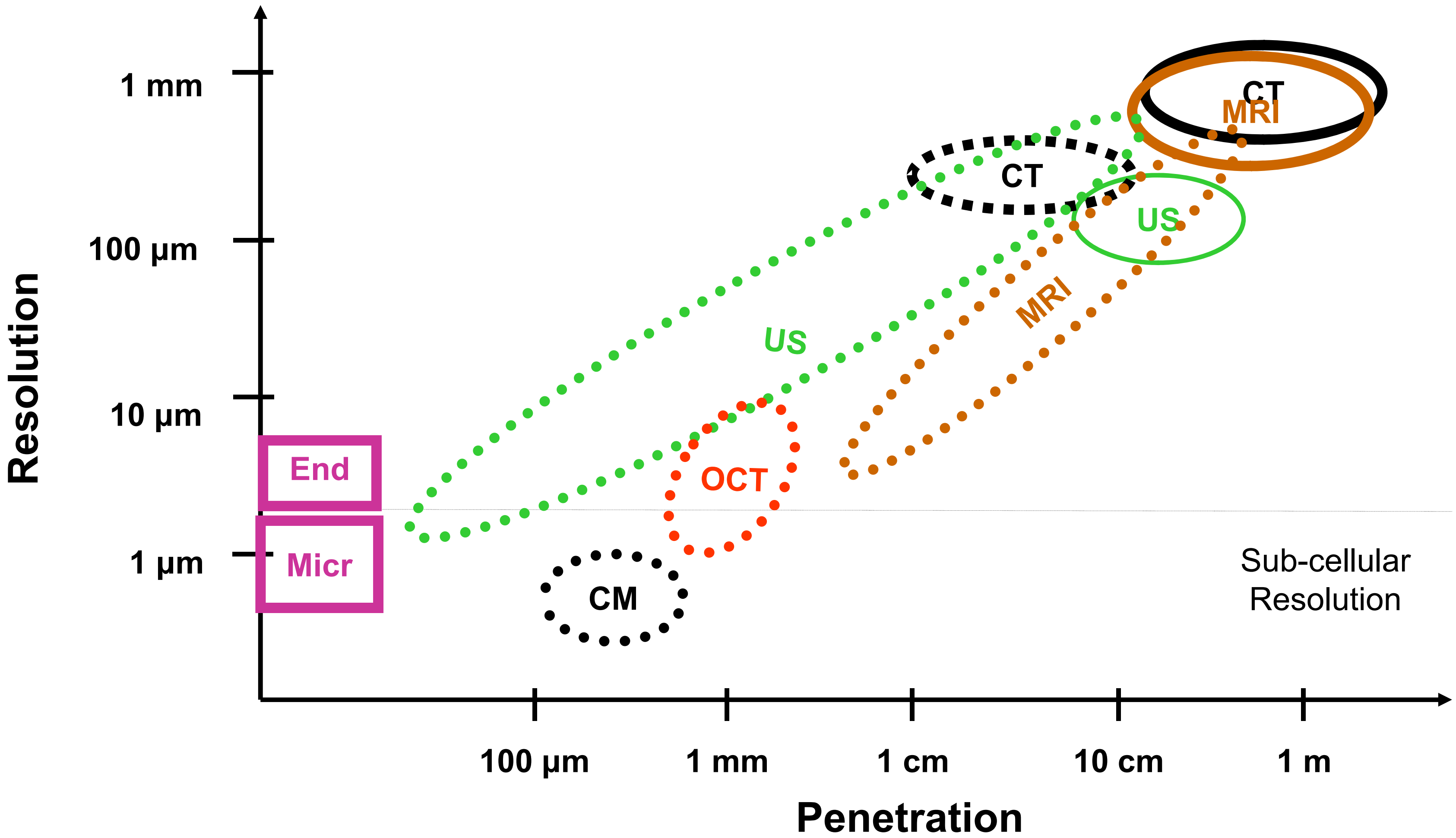


Optical Coherence Tomography

- **Analogous to ultrasound, except that it measures intensity of back-reflected light**
- **Technologically different than ultrasound**
  - Can achieve resolutions in the order of 1-10 μm at depths of 2-3 mm
  - Contrast provided by index of refraction mismatch in tissue
  - Interferometric depth localization

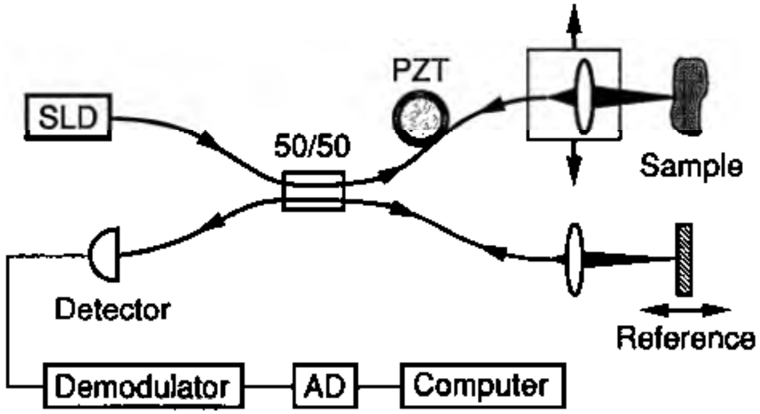


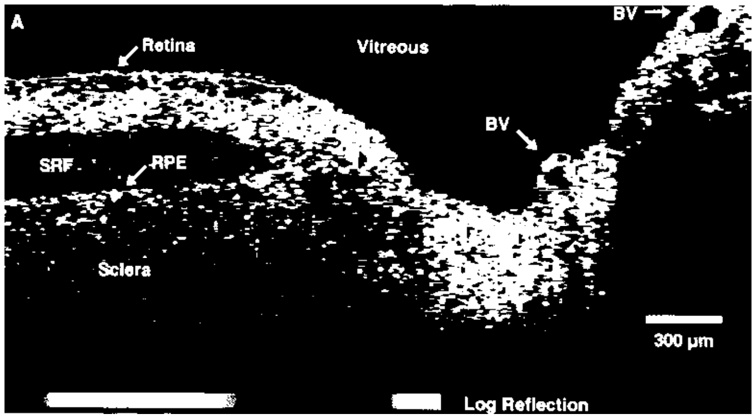
Optical Coherence Tomography



History

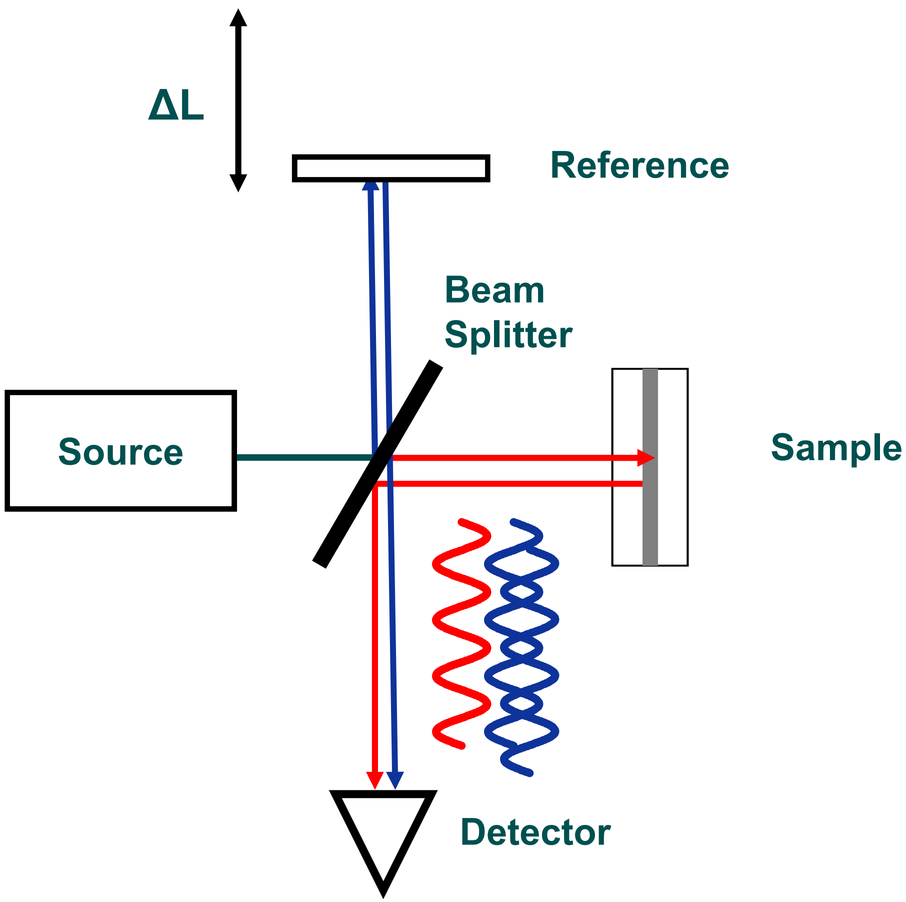
- **Michelson Interferometer**
  - End of 19^{th} century
- **Optical Coherence Domain Reflectrometry (OCDR)**
  - Optical testing of electronics (Youngquist 1987)
  - Fault location in waveguides (1987)
  - Eye length measurement (Frecher 1988)
- **Optical Coherence Tomography (OCT)**
  - First applied to transparent tissues in ophthalmology (Fujimoto 1991)
  - Subsequent development of technology resulted in application in scattering tissues



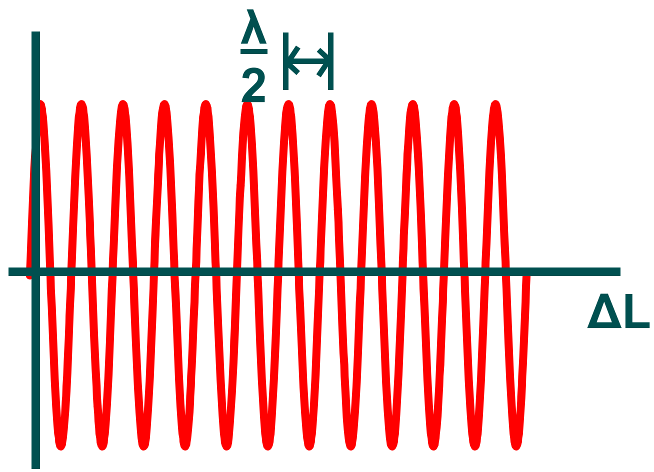


(Huang et al, Science, 254, 1178-1181, 1991)

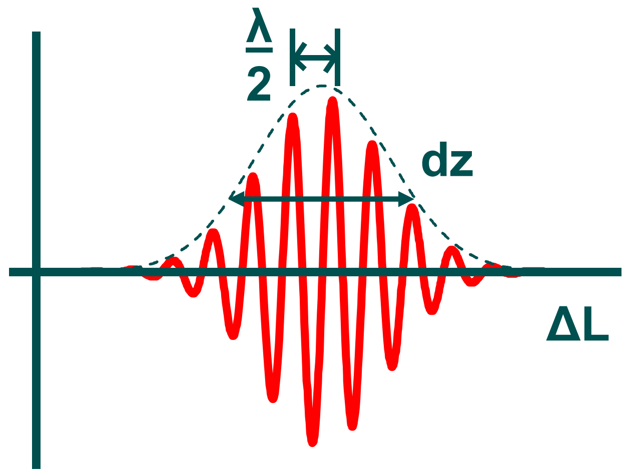
OCT Principles



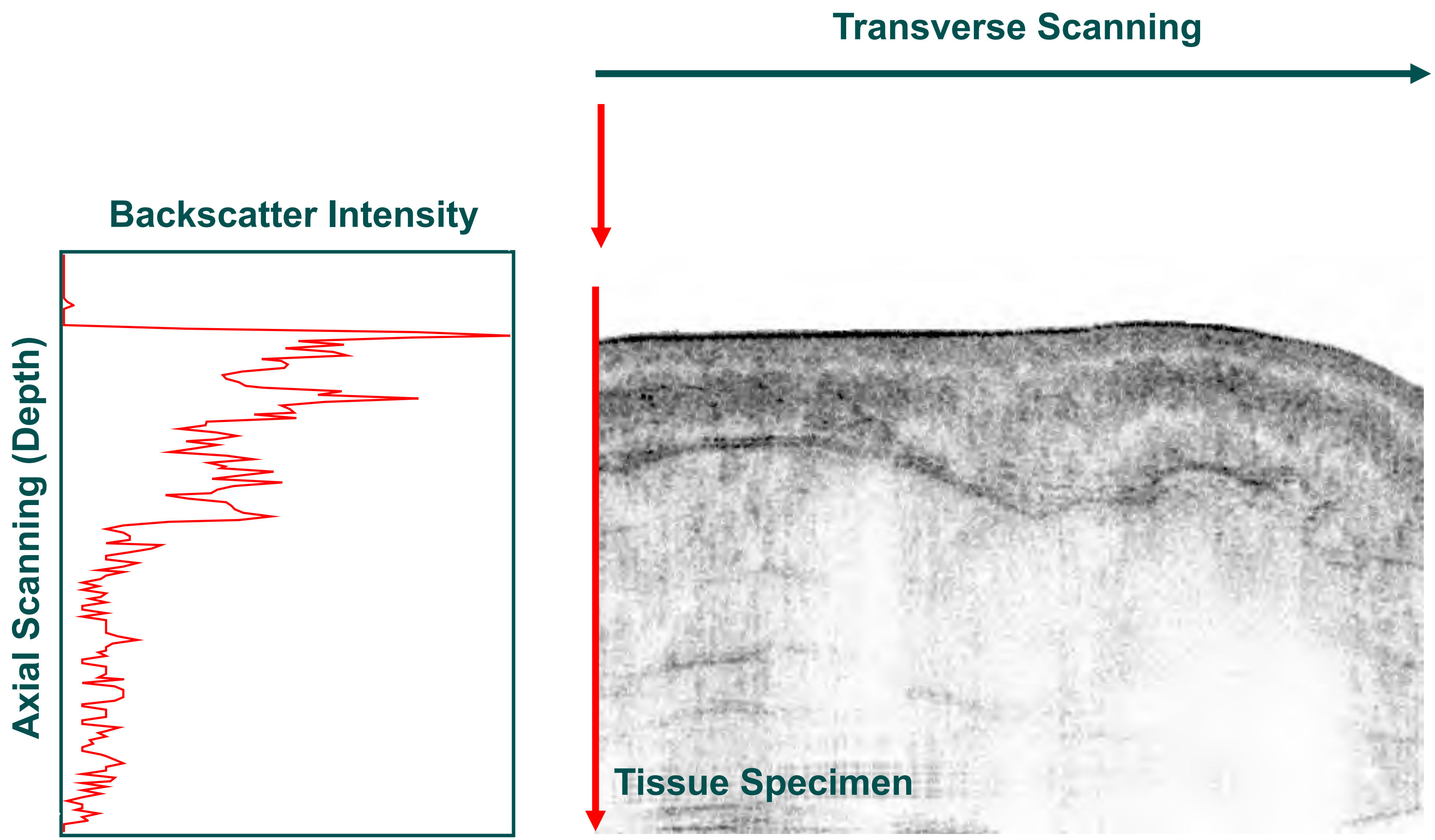
Coherent Laser Source



Low coherence Source



OCT Principles



OCT Principles

- **Monochromatic source**

$$E_s(t-\frac{L_s}{c}) \qquad E_r(t-\frac{L_r}{c})$$

- **Intensity at the detector**

$$I_d(\tau)=I_s+I_r+2\,\mathrm{Re}\left\{\left\langle E_s^*(t)E_r(t+\tau)\right\rangle\right\}$$

$$\boxed{I_d(\tau)=I_s+I_r+2\sqrt{I_sI_r}\,\left|V_{tc}(\tau)\right|\cos(2\pi f_0\tau)} \qquad V_{tc}(t)=A(t)e^{i2\pi f_0\tau}$$

- **Broad spectrum (low coherence) source**

$$S_{xx}(f)=\int_{-\infty}^{\infty} r_{xx}(\tau)e^{-j2\pi f\tau}\,d\tau \qquad r_{xx}(\tau)=\mathrm{E}\left[x(t)x^*(t-\tau)\right]$$

$$V_{tc}(\tau)=\Im\{S(k)\}=\int_{0}^{\infty} S(f)\exp(-j2\pi f\tau)df$$

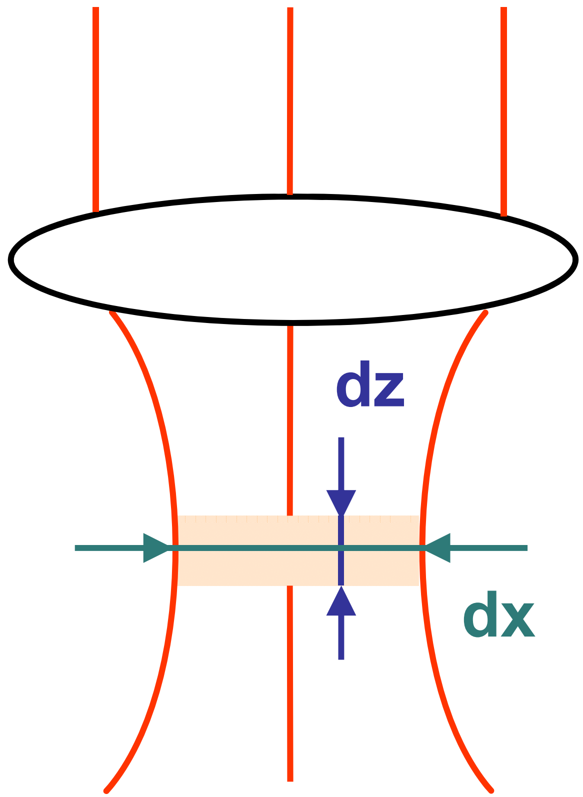
$$\boxed{I_d(\Delta L)=I_s+I_r+2\sqrt{I_sI_r}\,\left|\Im\{S(k)\}\right|\cos(k_0\Delta L)}$$

OCT Principles

- **Axial resolution**

$$dz = \frac{2\ln(2)}{\pi}\frac{\lambda_o^2}{\Delta\lambda}$$

- Choice of source (λ and Δλ) affects axial resolution (dz) but also the penetration (μs)

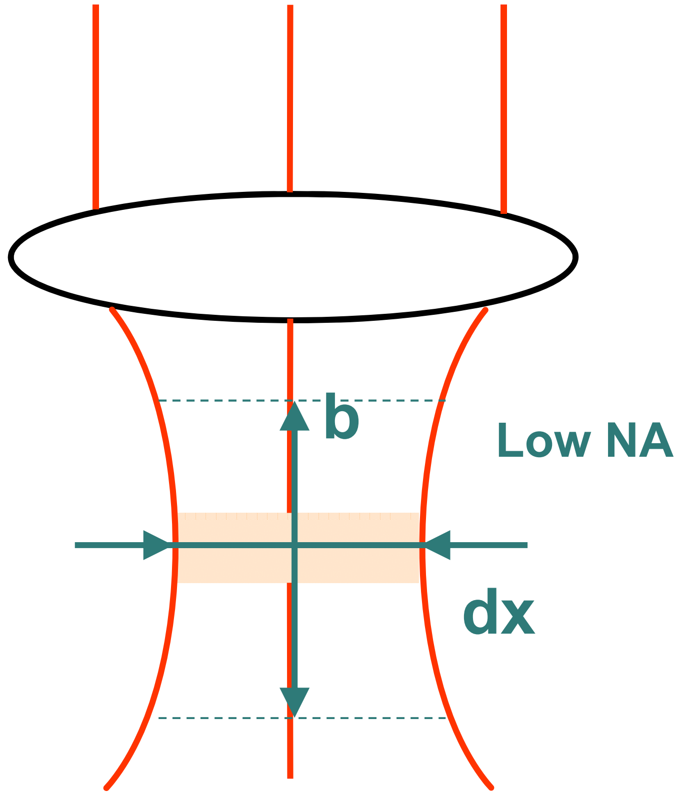


OCT Principles

- **Transverse resolution**

$$dx = \frac{4\lambda}{\pi}\left(\frac{f}{d}\right)$$

- Choice of focusing optics (NA=d/f) affects transverse resolution (dx) and depth of focus (b)



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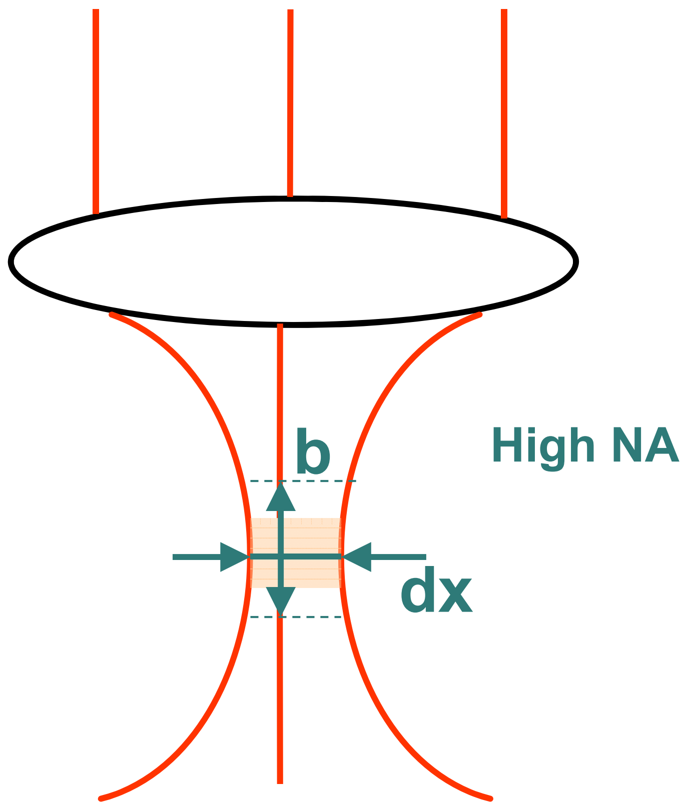
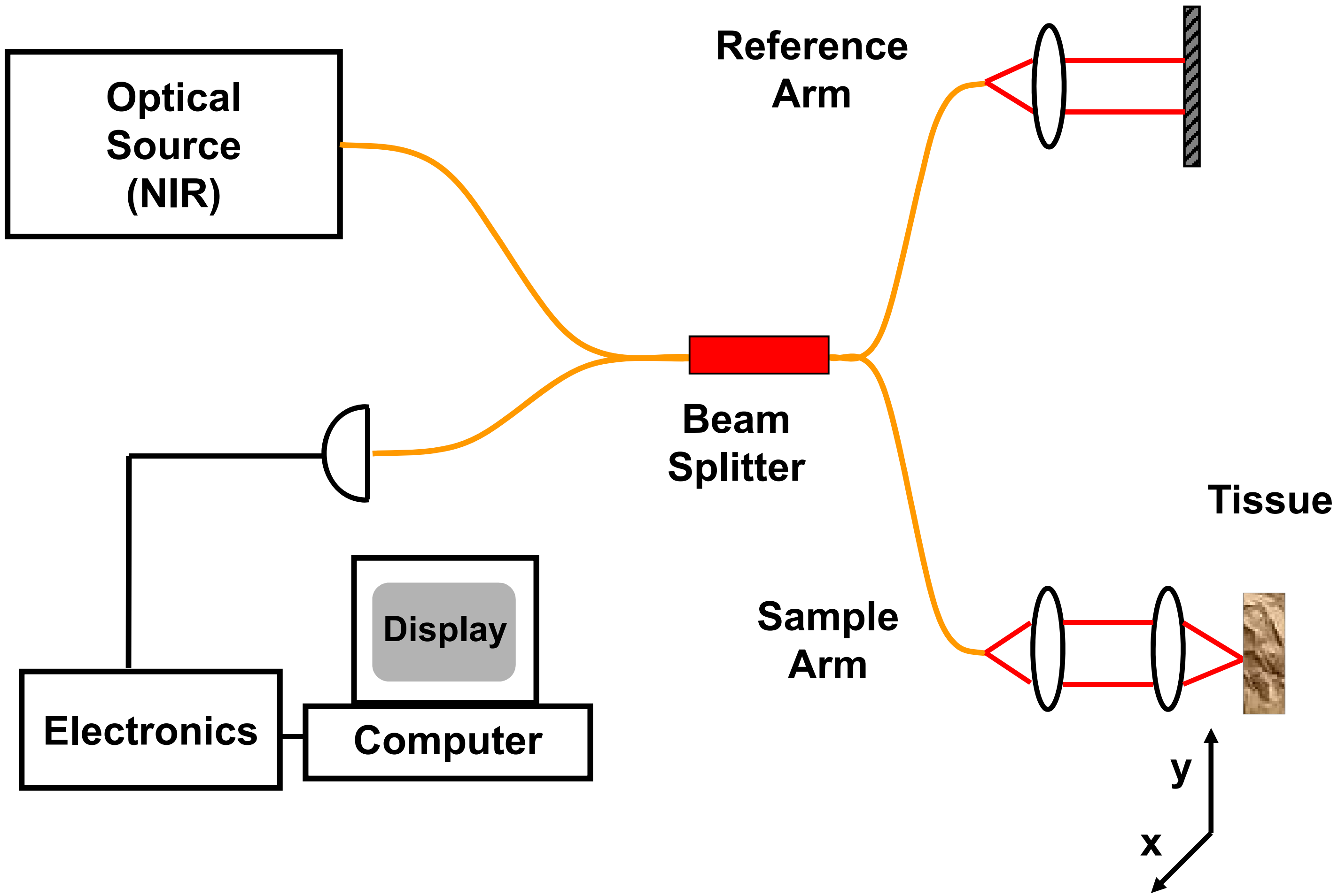
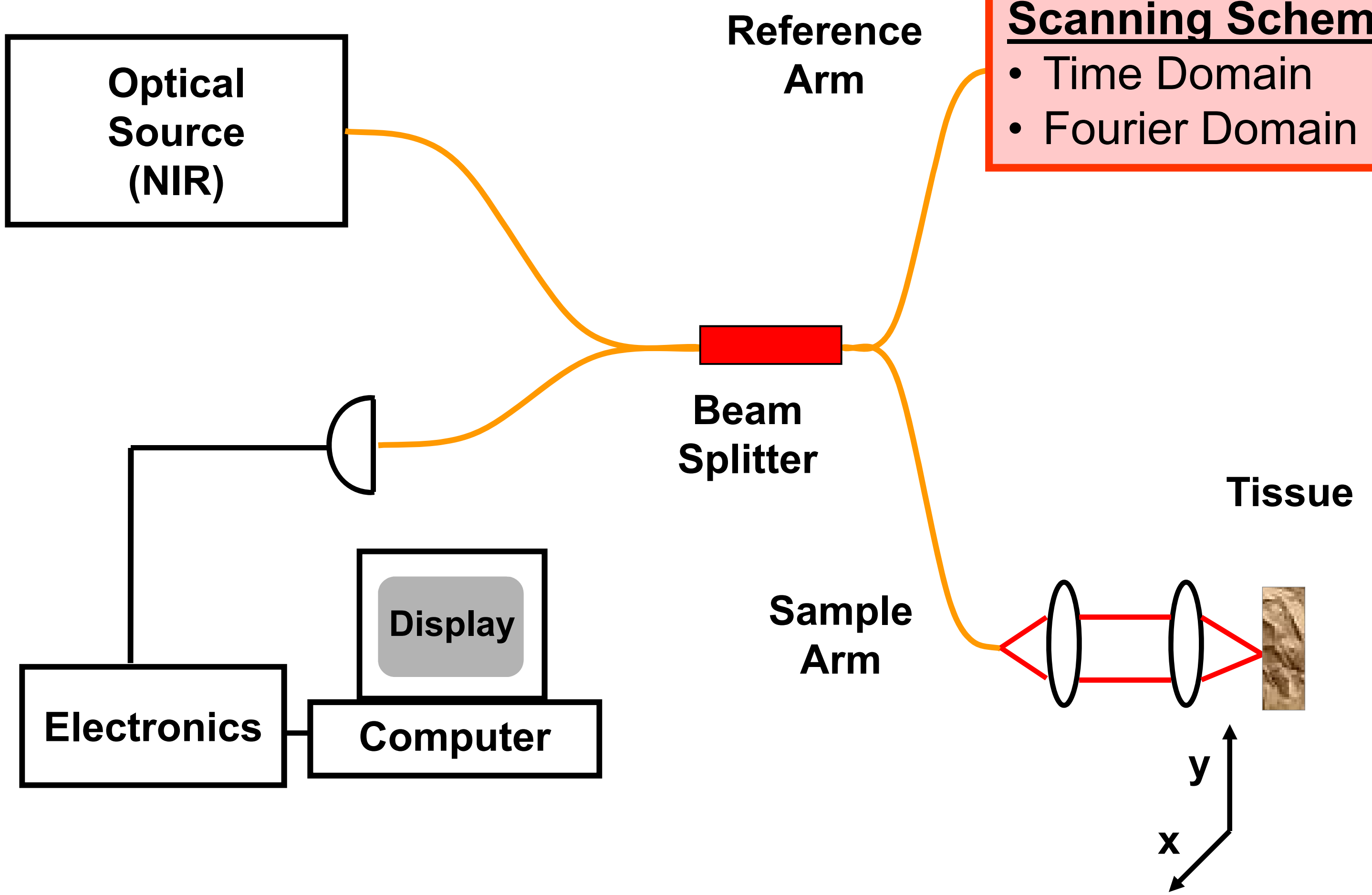


OCT Principles



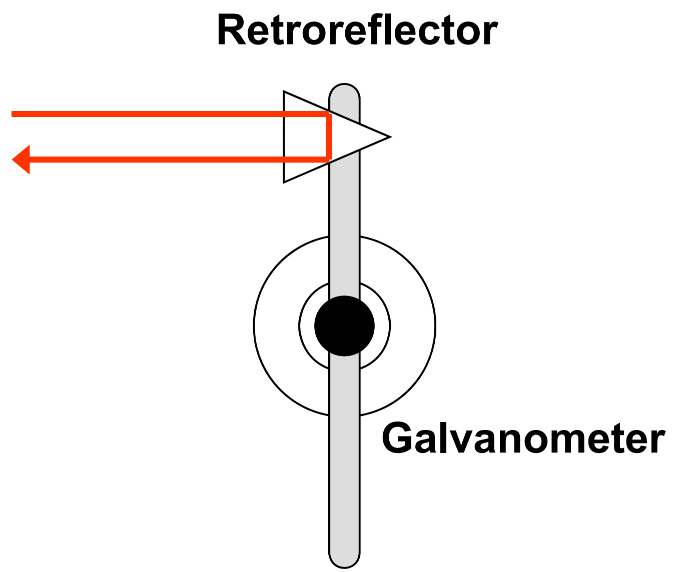
OCT System Design

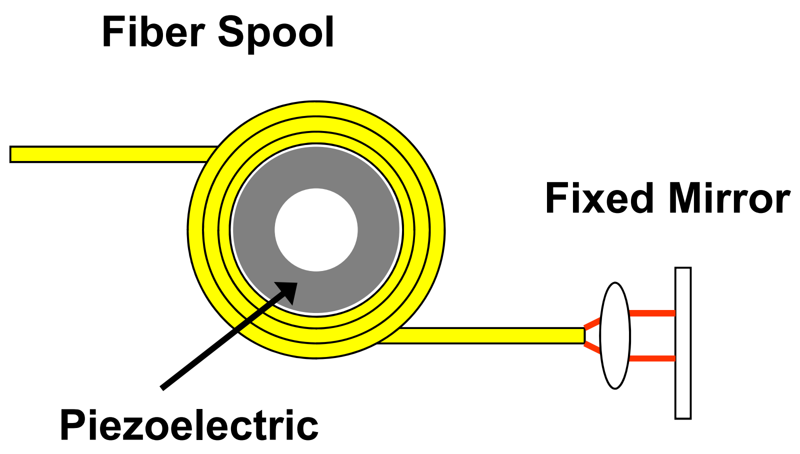


Scanning Schemes
- Time Domain
- Fourier Domain

Time-Domain OCT

- **Axial scanning by modifying the reference arm length in time**
  - Galvanometric mirror scanning
    - < 100 A-Scans/sec
    - Simplest option but also the most slow
  - Piezoelectric fiber stretching
    - < 400 A-Scans/sec
    - Faster but introduces variable dispersion which degrades resolution
  - Helical Rotating Mirror
    - <4 000 A-Scans/sec
    - Very expensive to manufacture
    - Proprietary





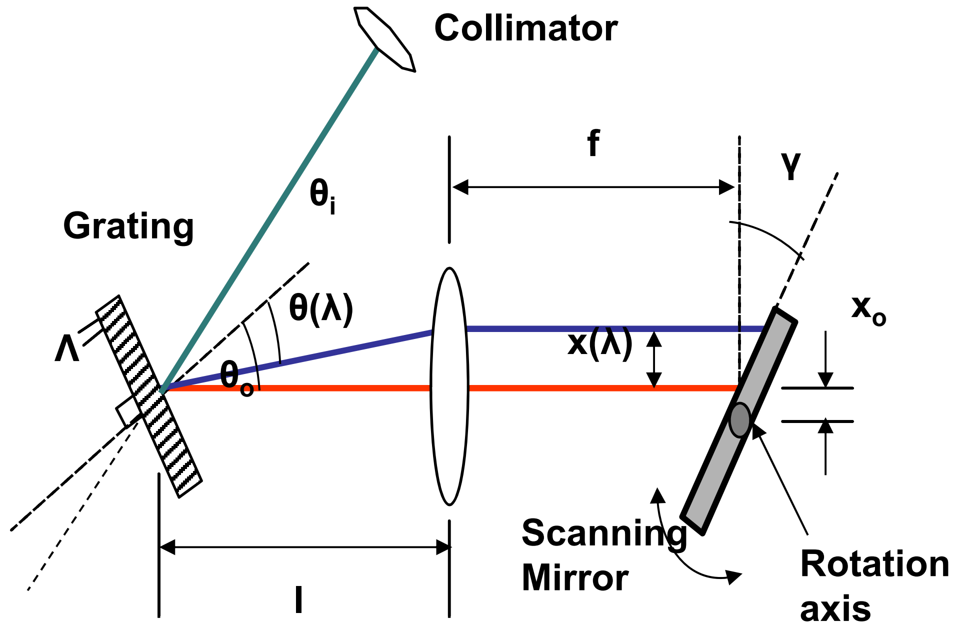
Time-Domain OCT

- Optical phase delay line
  - The technique was originally developed for femtosecond pulse measurements
    - based on Fourier-transform pulse shaping techniques.
  - Relies on the basic property of the Fourier transform

$$x(t-t_0) \xleftrightarrow{\Im} X(\omega)\exp\{-j\omega t_0\}$$

  - phase ramp in the Fourier domain corresponds to a group delay in the time domain.

  - 2-4 000 A-Scans/sec
  - More complicated but faster

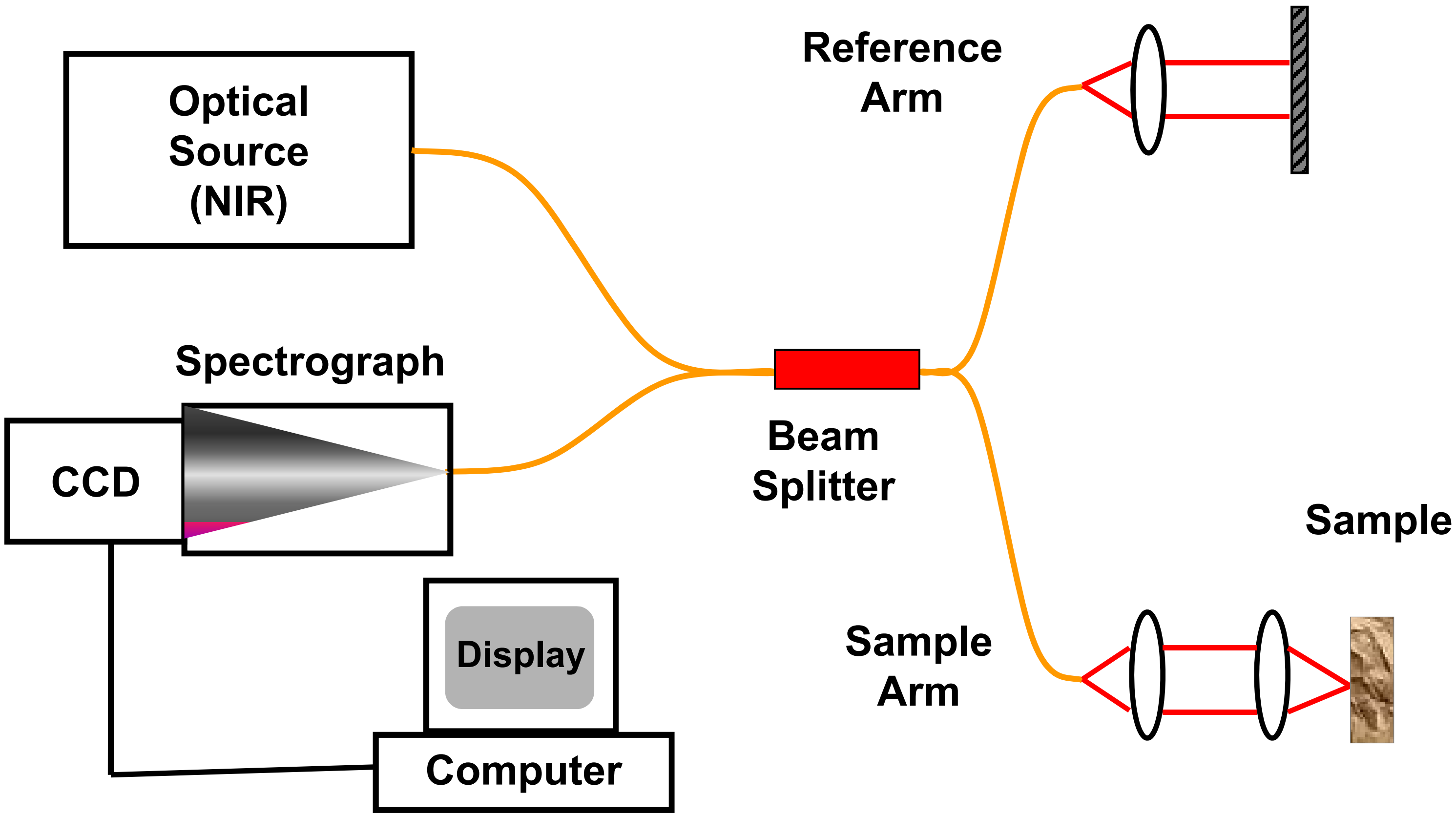


Fourier-Domain OCT

- **Detect the spectrum and take the Fourier Transform to retrieve the A-Scan**
- **Detecting individual wavelengths while keeping the reference arm fixed**
  - Spectrograph
  - Swept source
- **Advantages**
  - 20 000 – 200 000 A-Scans/sec
  - Improved SNR
- **Disadvantages**
  - More expensive hardware
  - More demanding post-processing

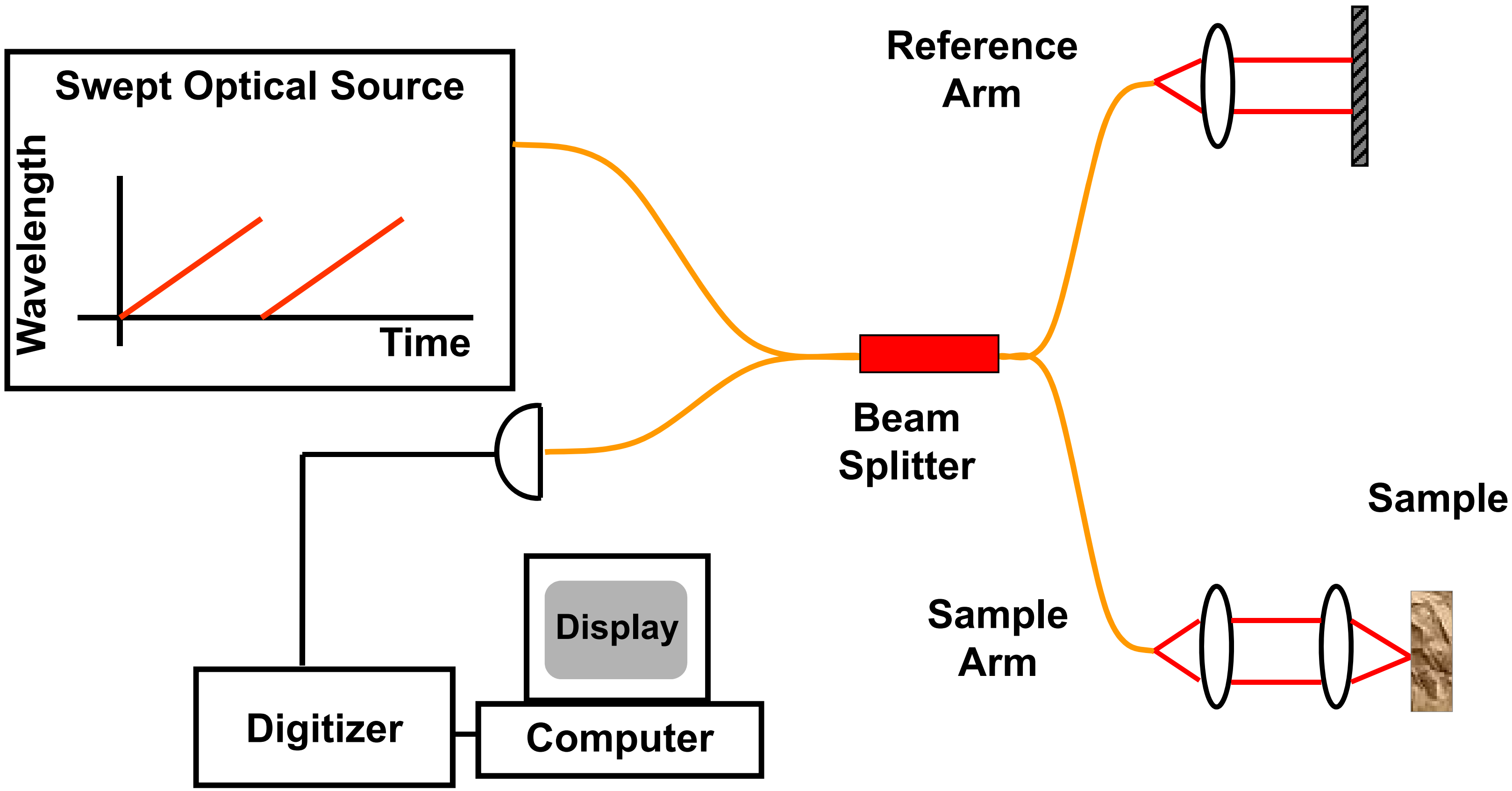
Fourier-Domain OCT

- Spectral FD-OCT

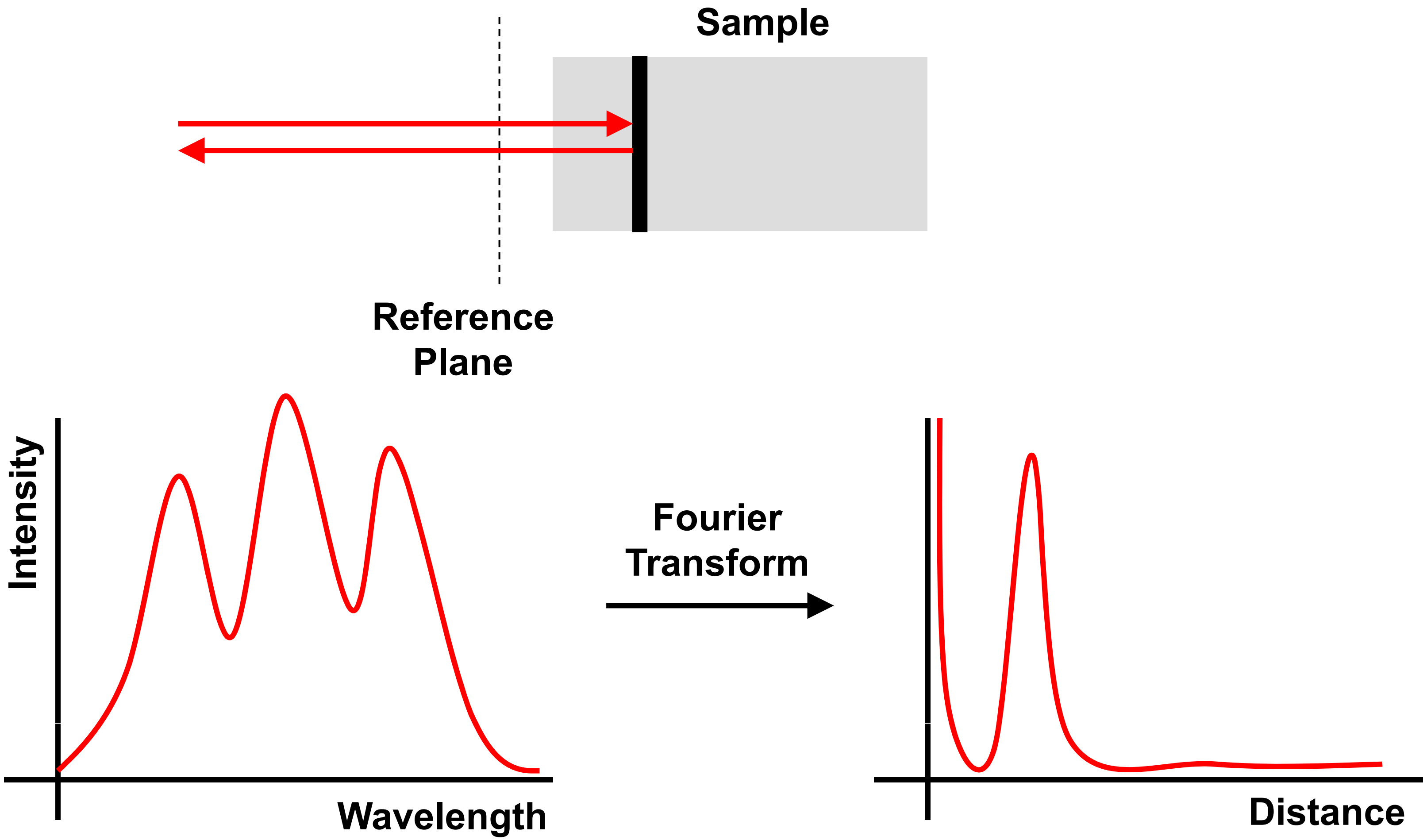


Fourier-Domain OCT

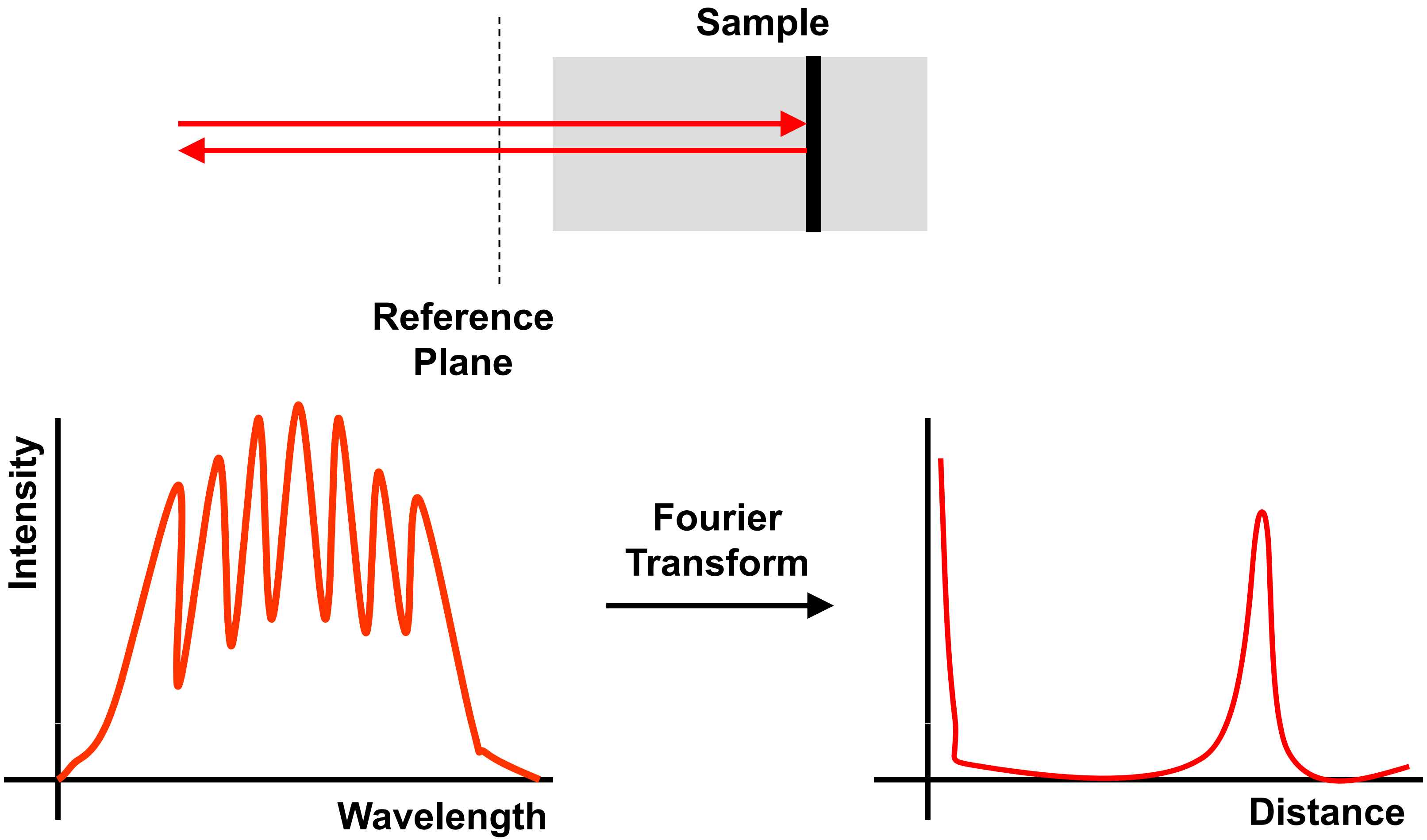
- Swept Source OCT



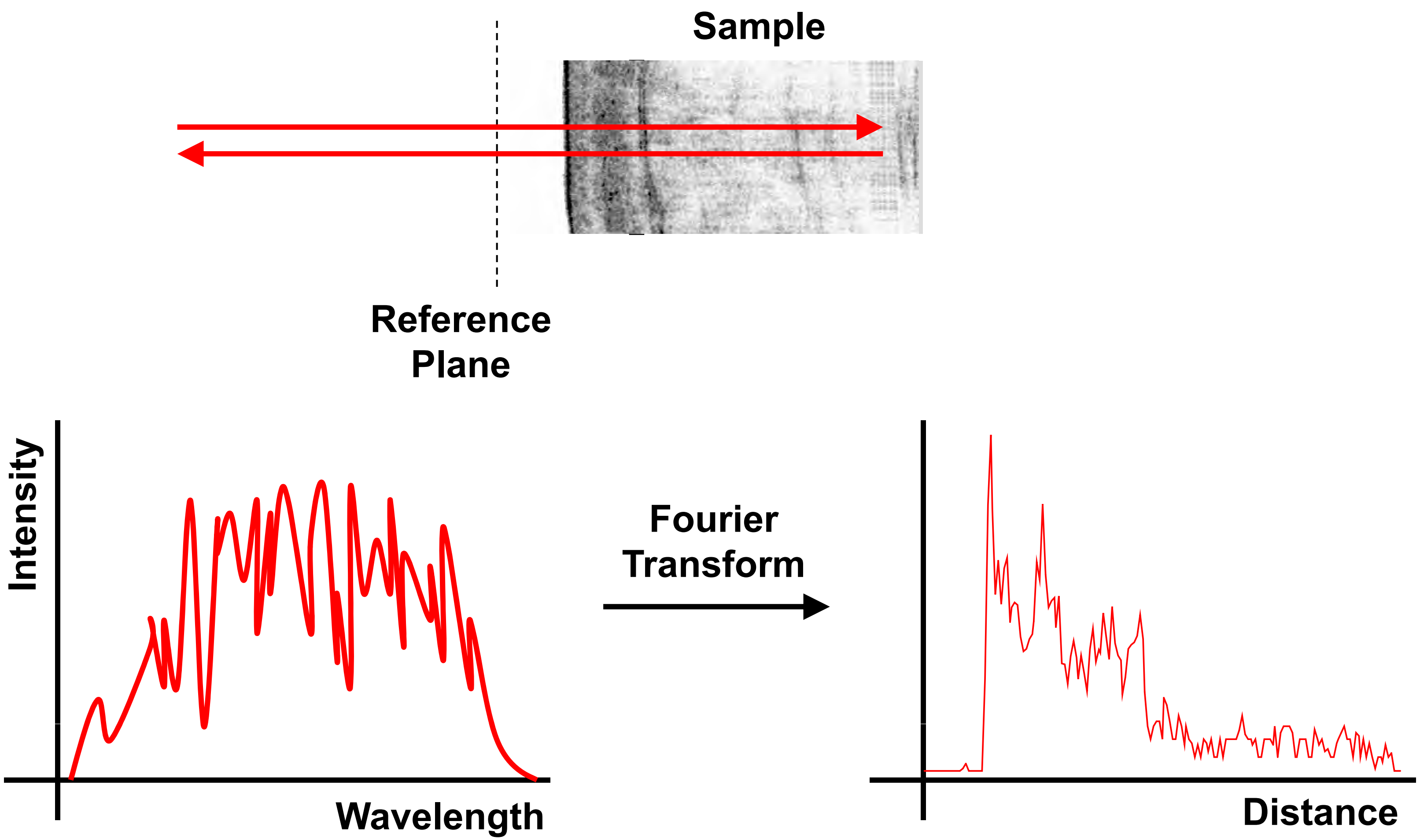
Fourier-Domain OCT



Fourier-Domain OCT



Fourier-Domain OCT



Fourier-Domain OCT

$$I(k) = S(k)\left| a_R \exp(j2kr) + \int_0^{\infty} a(z)\exp(j2k(r + n(z).z)dz \right|^2$$

k:	wavenumber k=2π/λ
r:	path length in the reference arm
r +z:	path length in the object arm
z:	path length in the object arm, measured from the reference plane
z_0:	offset distance between reference plane and object surface
n:	refractive index (n = 1 for $z < z_0$ and varying depending on the sample for longitudinal positions in the object $z > z_0$)
a_R:	reflection coefficient of the reference
a(z):	backscattering coefficient of the object signal, a(z) is zero for $z < z_0$
S(k):	spectral intensity distribution of the light source

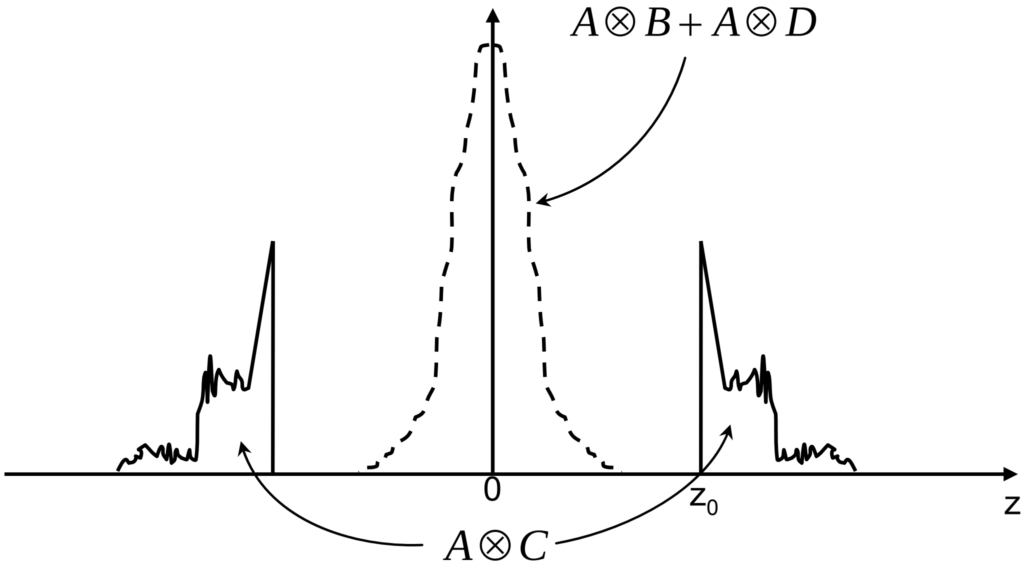
$$I(k) = S(k)\left(1 + \int_{-\infty}^{\infty} \hat{a}(z) e^{-jknz \overbrace{(2)}^{time\ \ scale}} dz + \frac{1}{4}\int_{-\infty}^{\infty} AC[\hat{a}(z)] \mathrm{e}^{-jknz \overbrace{(2)}^{time\ \ scale}} dz \right)$$

$$I(k) = S(k)\left(1 + \frac{1}{2}\Im_z\left\{\hat{a}(z)\right\} + \frac{1}{8}\Im_z\left\{AC\left[\hat{a}(z)\right]\right\} \right)$$

Fourier-Domain OCT

$$F^{-1}\{I(k)\} = F^{-1}\{S(k)\} \otimes \left(\left[\delta(z)\right] + \frac{1}{2}\hat{a}(z) + \frac{1}{8} AC\left[\hat{a}(z)\right] \right)$$

$$= \quad A \quad \otimes \left(\quad B \quad + \quad C \quad + \quad D \quad \right)$$



Period of cosine fringes

$$dk = \frac{\pi}{n z_{\max}}$$

Maximum resolvable depth

$$Z_{\max} = \frac{\lambda_0^{\ 2}}{4n(d\lambda)}$$

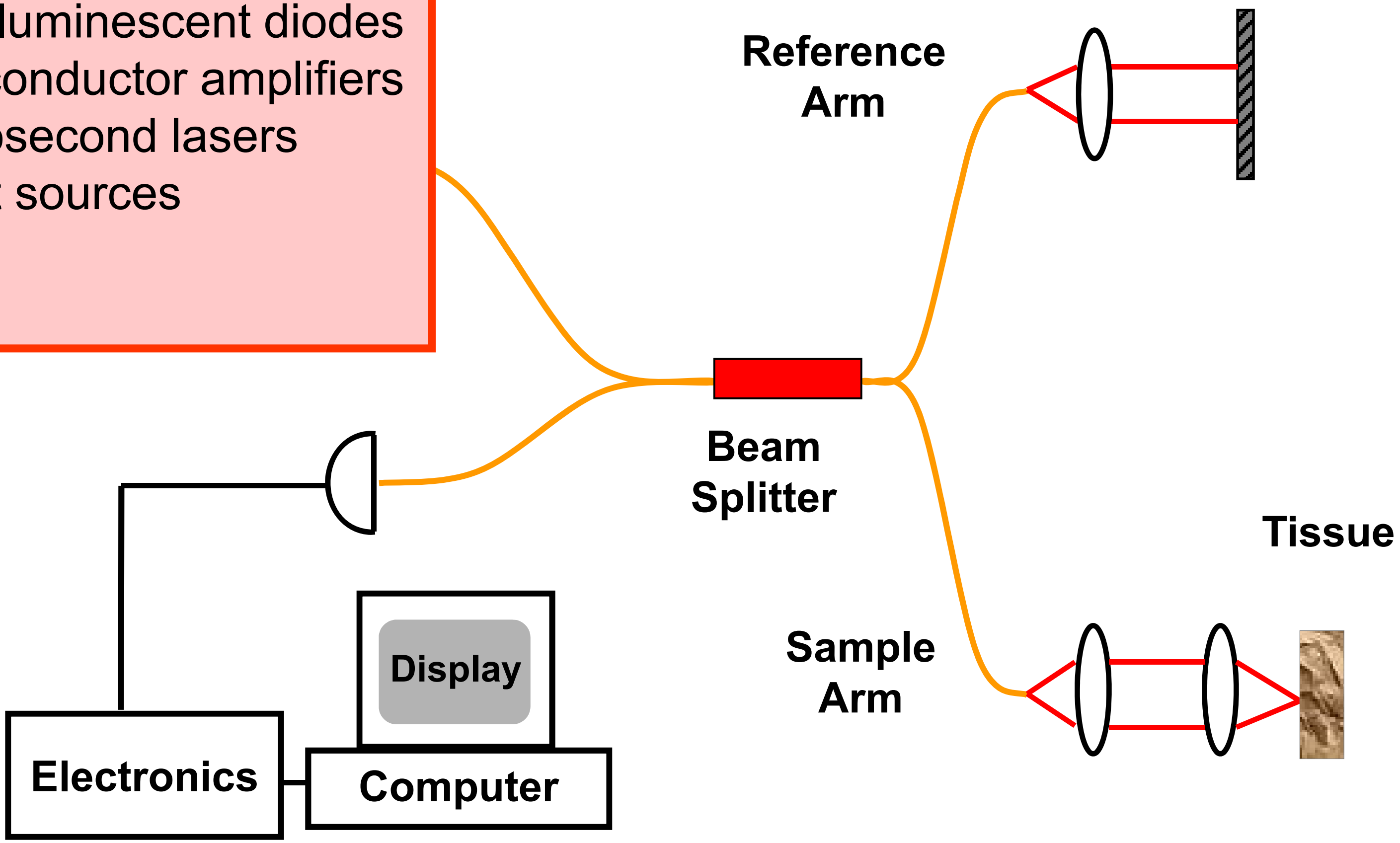
.$d\lambda$ = wavelength sampling interval (defined by the detector separation of a linear detector array)

Sensitivity Gain

$$S_{FD}^{shot} = 2\frac{\Delta\lambda_{FWHM}}{d\lambda} S_{TD}^{shot} \approx 2\frac{Z_{RD}}{dz} S_{TD}^{shot}$$

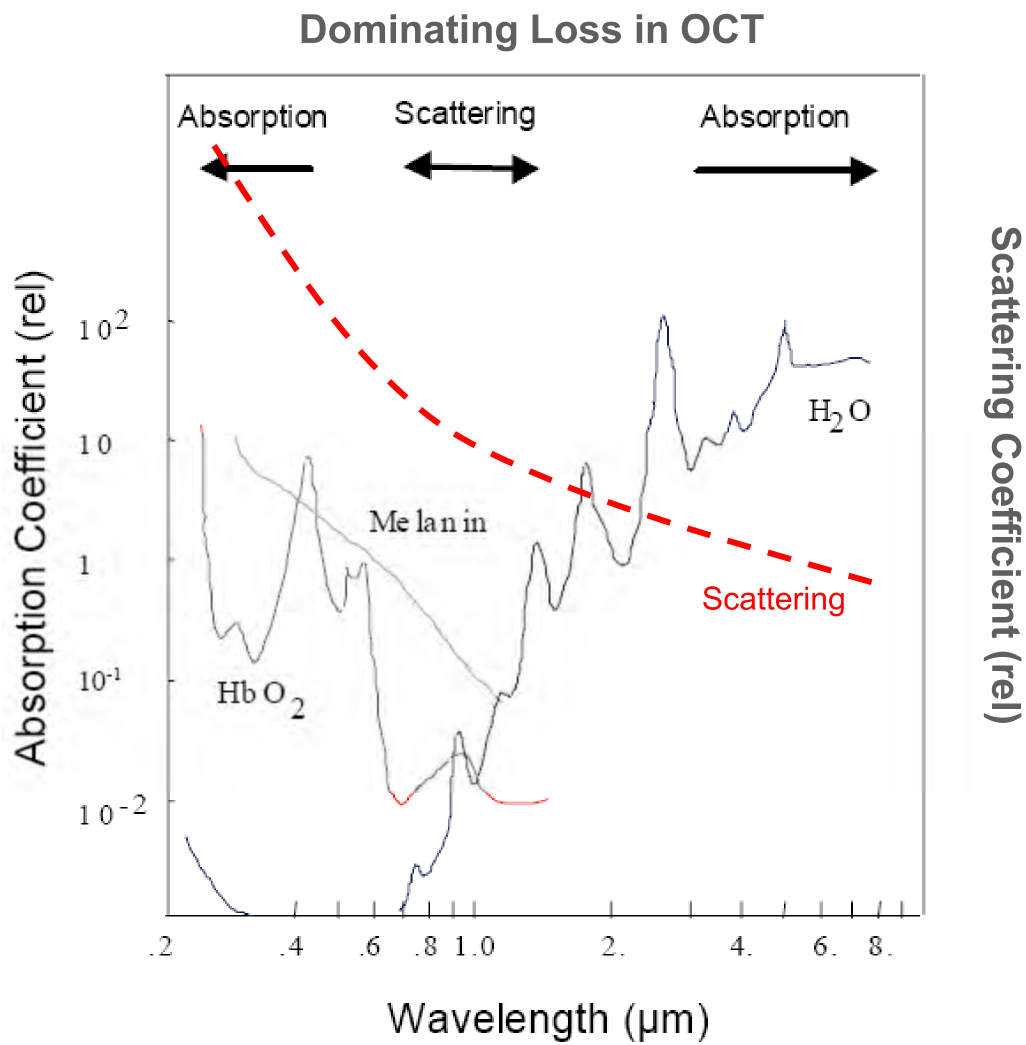
OCT System Design

Light sources
- Superluminescent diodes
- Semiconductor amplifiers
- Femtosecond lasers
- Swept sources
- …



Light Sources For OCT

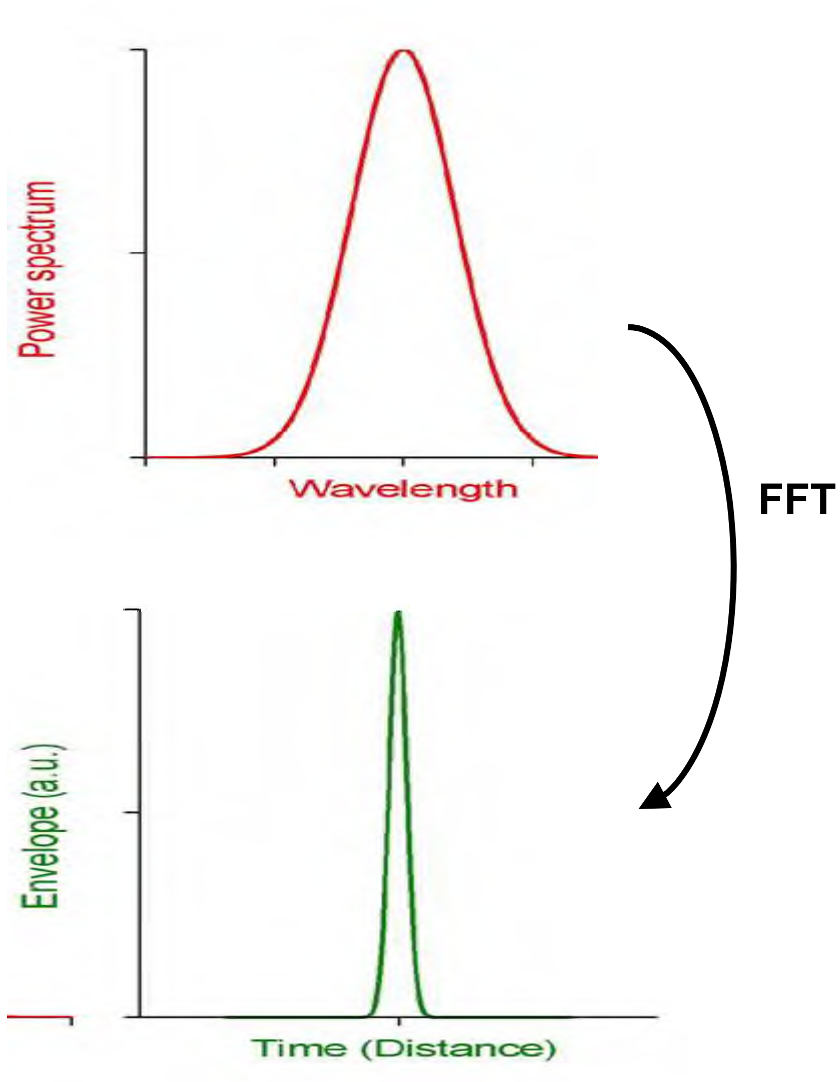
- **Choosing the light source**
  - Four primary considerations
    - wavelength,
    - bandwidth,
    - power (in a single-transverse-mode),
    - stability (portability, ease-of-use, etc)



Light Sources For OCT

- **Light source spectrum**
  - Basic property
    - the temporal coherence envelope function $G(\tau)$ is related to the power spectral function $S(\nu)$ through
      $G(\tau) = FT\{S(\nu)\}$
      - Wiener-Kinchine theorem
    - broadband source ⇔ high axial resolution

$$dz = \frac{2\ln(2)}{\pi}\frac{\lambda_o^2}{\Delta\lambda}$$



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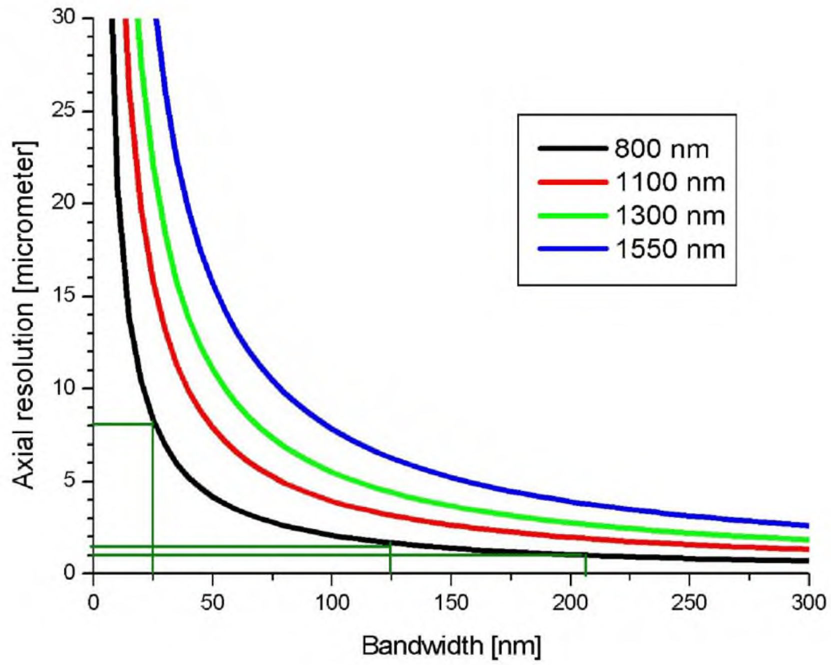
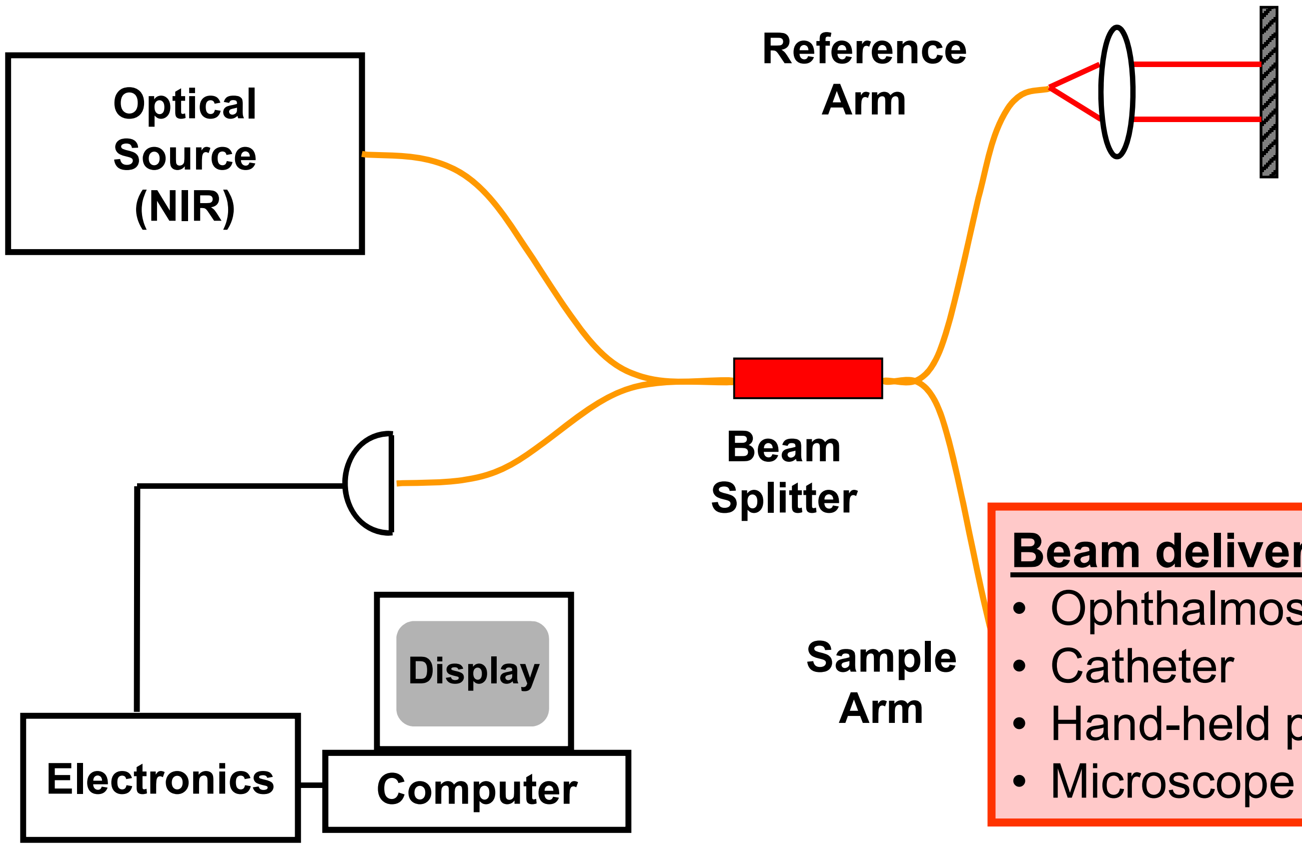


Light Sources For OCT

- **Continuous sources**
  - SLD/LED/superfluorescent fibers,
  - center wavelength;
    - 800 nm (SLD), 1300 nm (SLD, LED), 1550 nm, (LED, fiber),
    - power: 1 to 10 mW (c.w.) is sufficient,
  - coherence length;
    - 10 to 15 μm (typically),
- **Pulsed lasers**
  - mode-locked Ti:Al2O3 (800 nm),
  - 3 micron axial resolution (or less).
- **Scanning sources**
  - tune narrow-width wavelength over entire spectrum,
  - resolution similar to other sources,
  - Fourier Domain OCT
  - advantage that fast scanning is feasible.

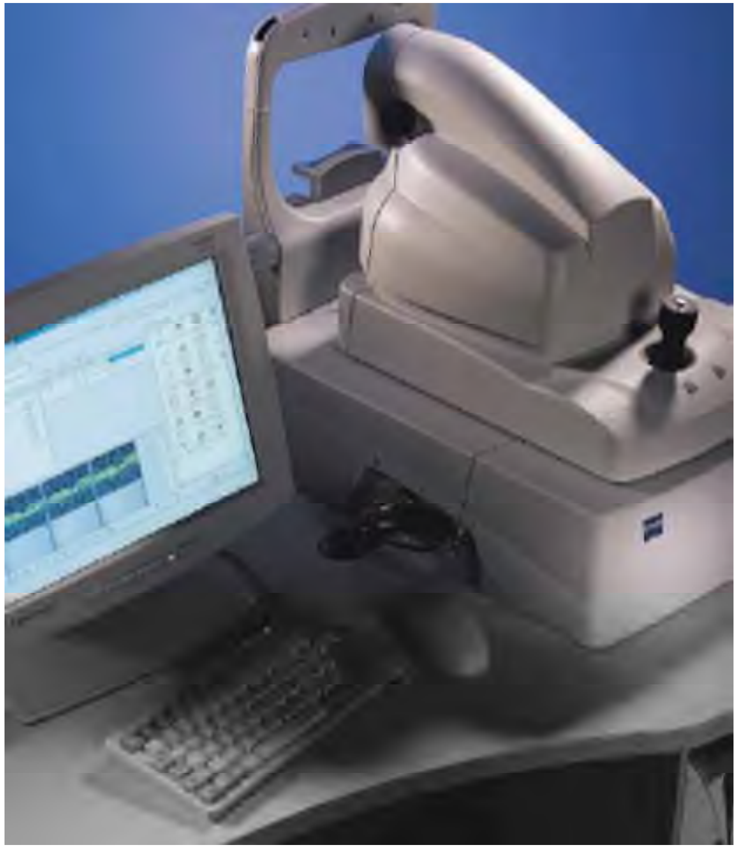
OCT System Design



Beam delivery and probes
- Ophthalmoscope
- Catheter
- Hand-held probe
- Microscope

Imaging Devices

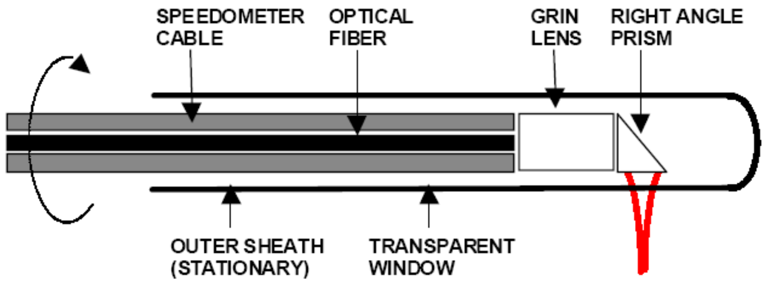
- **Application dependent**
- **Ophthalmoscope**
  - Most widely used OCT instrument
  - Time-domain systems:
    - Zeiss Meditec
  - Fourier-domain systems
    - Zeiss Meditec
    - Heidleberg Engineering
    - Optovue
    - Topcon
  - Some combine OCT with scanning laser ophthalmoscopy

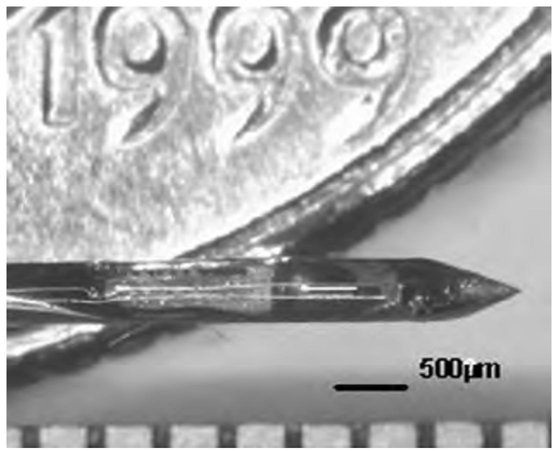


Stratus™ HD-OCT system from Carl Zeiss Meditec

Imaging Devices

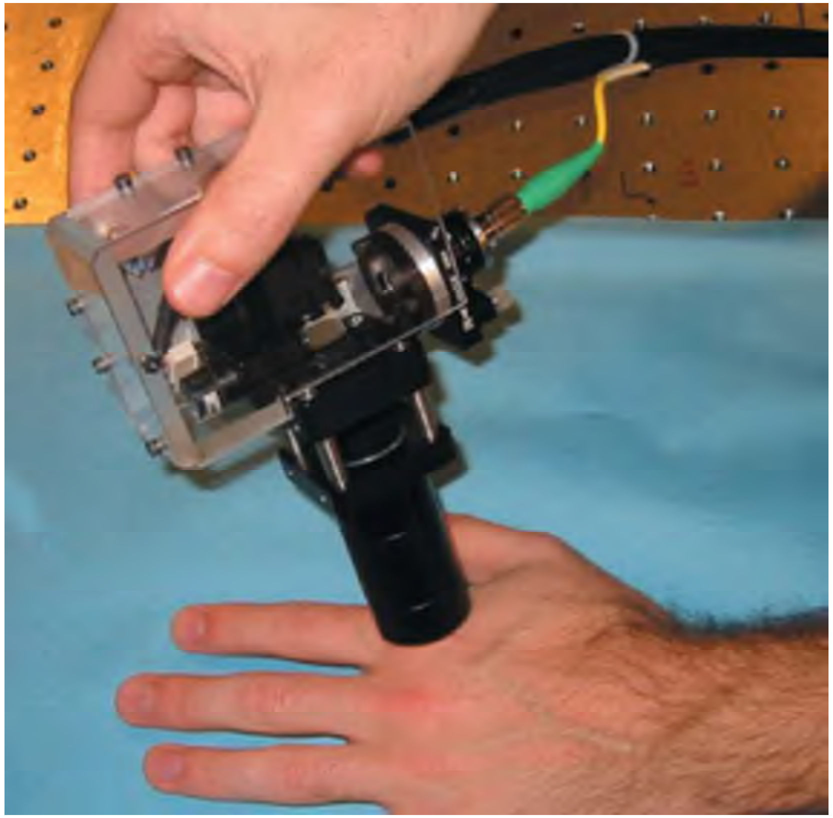
- **Catheters**
  - Diameter < 1 mm
    - Even as small as a needle
  - Scanning Schemes
    - Push-Pull
    - Rotational
    - Helical (volumetric)
  - Availability
    - LightLab, Inc., Helios balloon catheter
    - Custom catheters



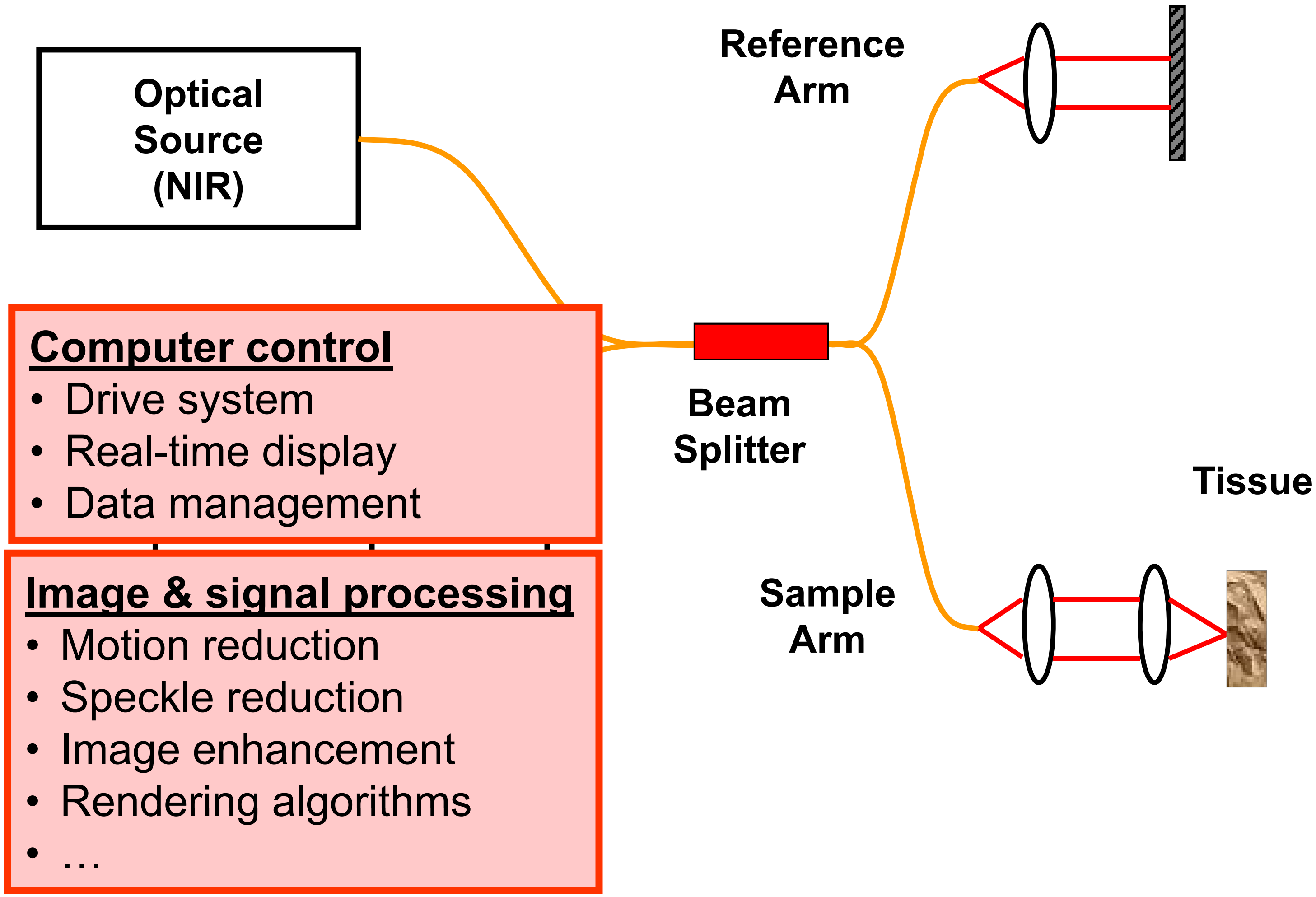


Imaging Devices

- **Handheld Probes and Microscopes**
  - Usually employ orthogonal galvanometrically scanned mirrors
  - Dermatologic, biological and research applications
  - Availability
    - Thorlabs
    - Bioptigen
    - Custom



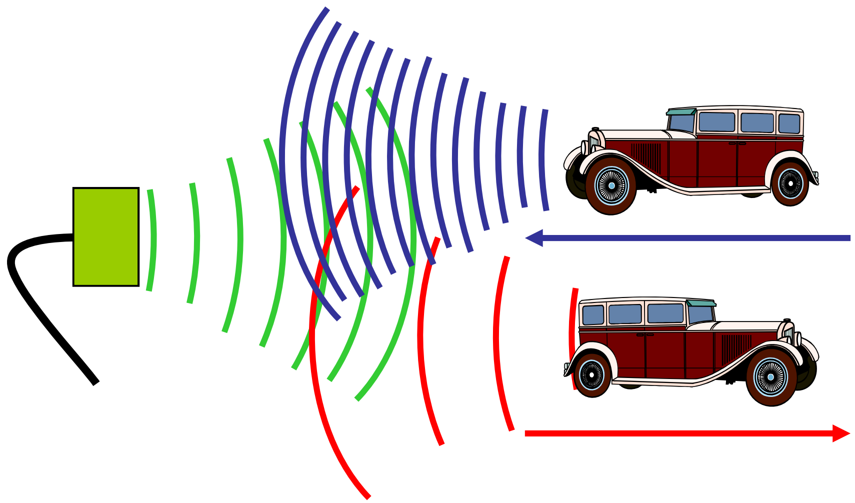
OCT System Design



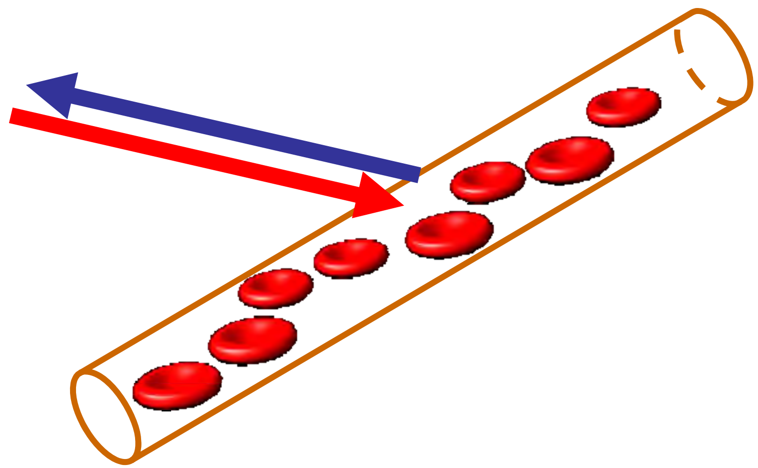
Functional OCT

- **Doppler OCT**
  - Motion of scatterers imparts a frequency shift in the OCT signal

$$f_d = \frac{2v_{ref}}{\lambda_0} \pm \frac{2v_{sc}}{\lambda_0}$$



  - Detection
    - Frequency analysis of OCT interferogram, or
    - Phase sensitive imaging
  - Can detect micro-flows



Functional OCT

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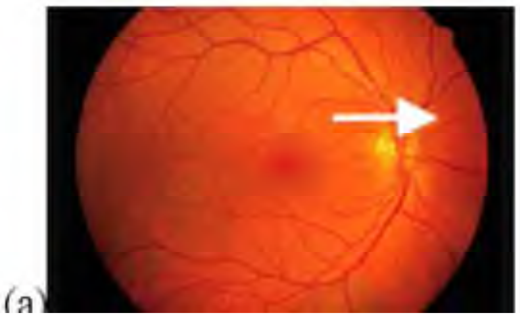
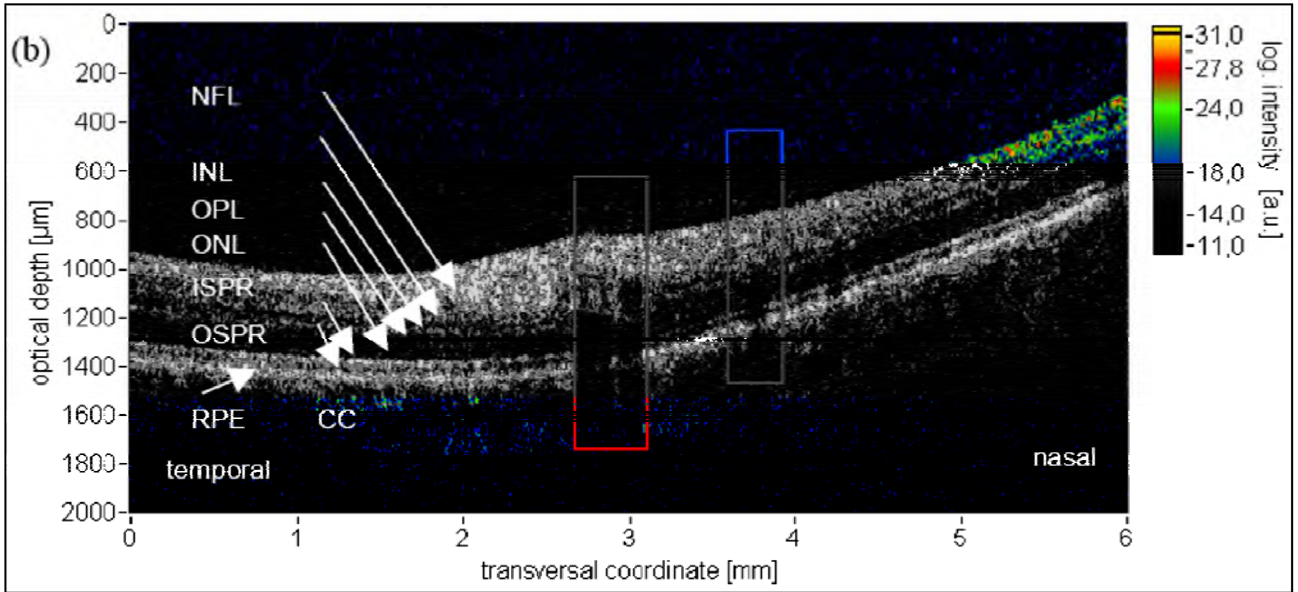
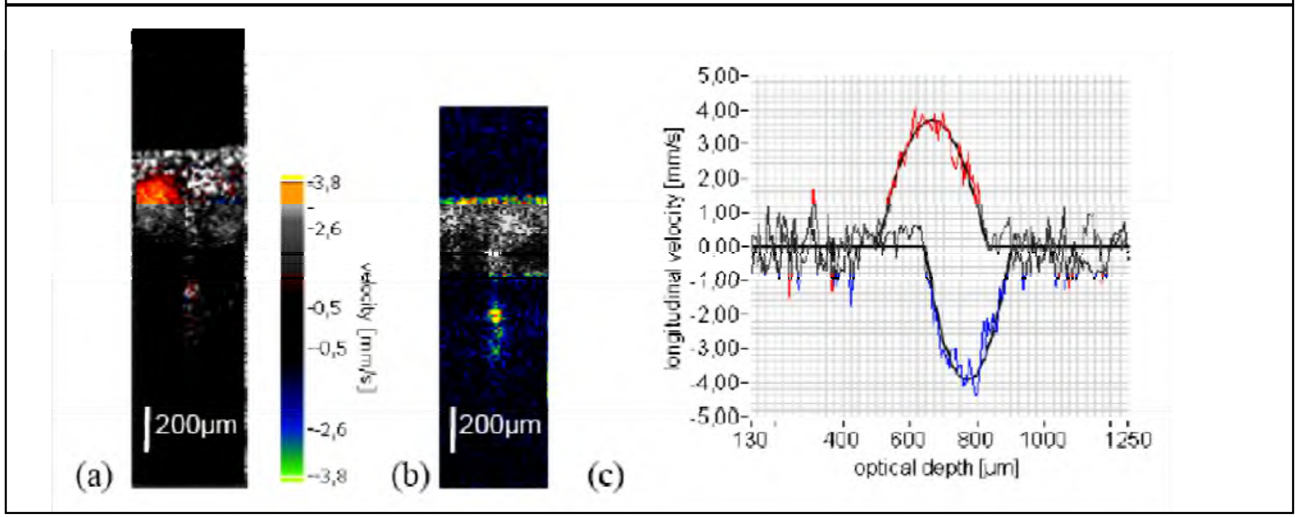


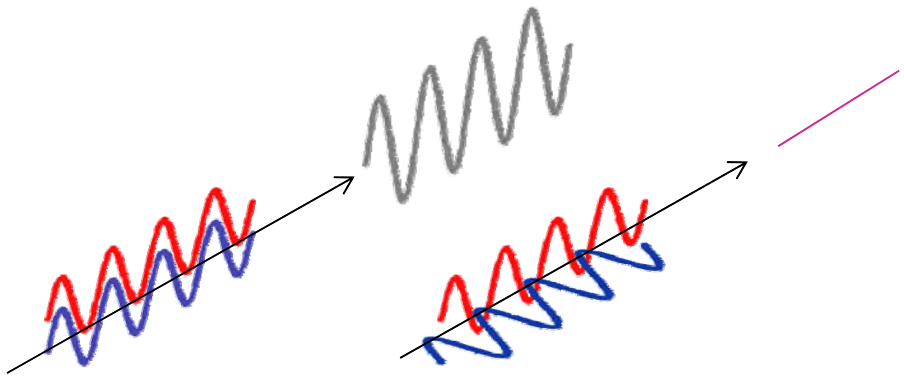


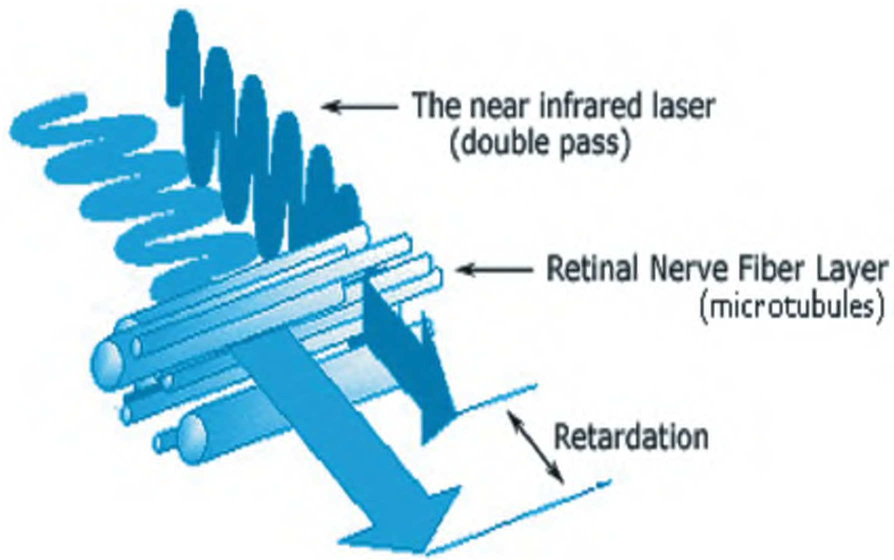


Retinal blood vessel flow Letigeb et al, Opt. Express 11, 3116-3121 (2003)

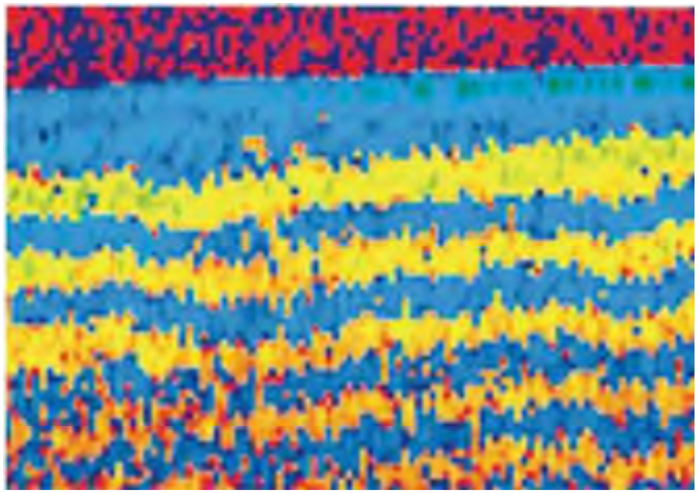
Functional OCT

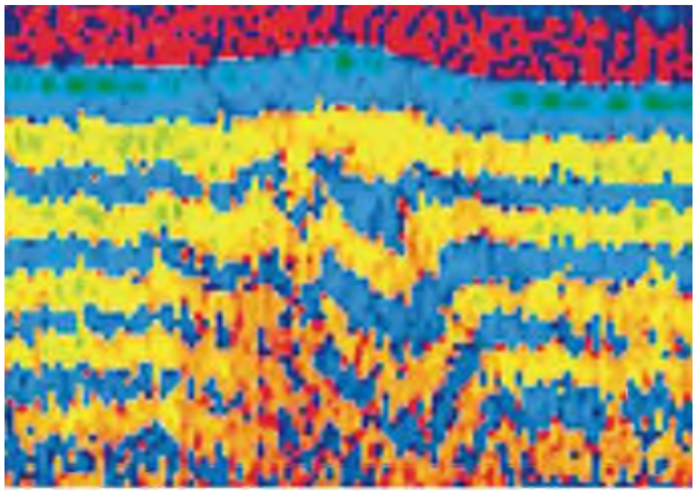
- **Constructive interference**
  - Phase matched
  - Polarization matched
- **Birefringence**
  - One polarization retarded more than other
- **Polarization Sensitive OCT**
  - Interference can be detected separately for orthogonal polarizations
  - Depth-resolved Stokes parameters can be calculated
  - Useful for birefringent materials
    - i.e. collagen layers

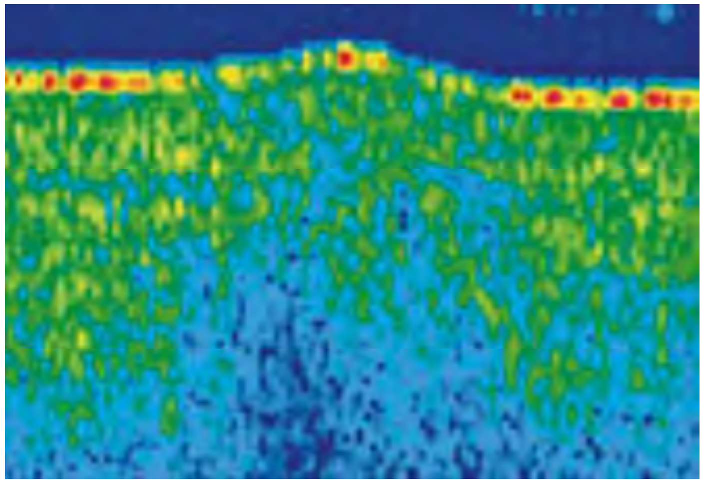




Functional OCT





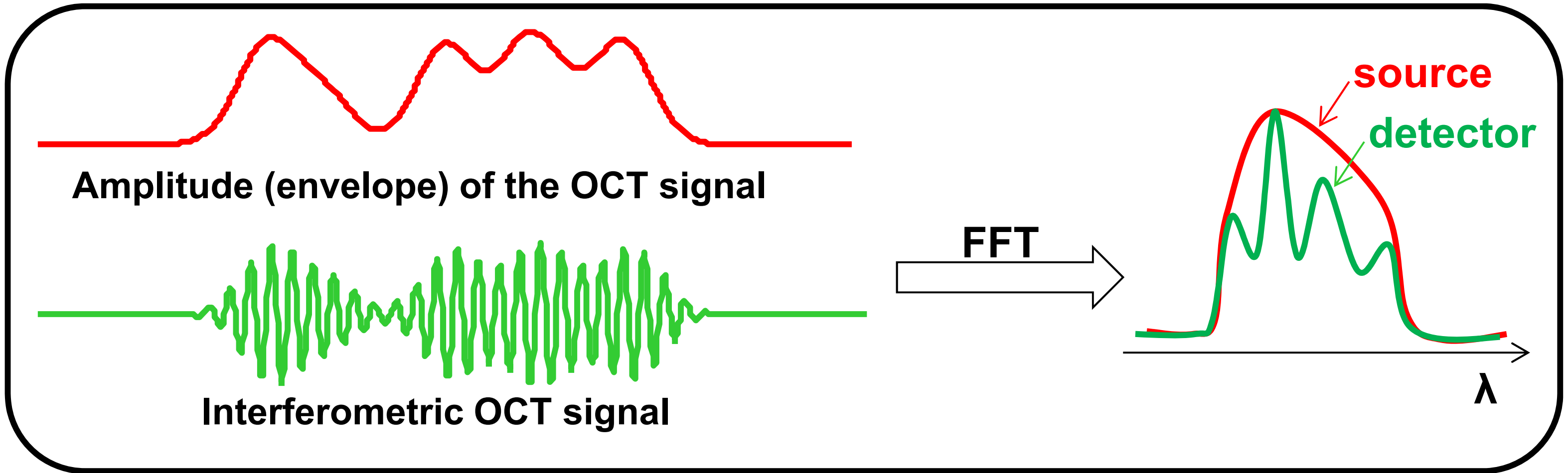


Birefringence of bovine muscle before, during and after laser exposure

deBoer et al, Opt. Lett. 22, 1439-1441 (1997)

Functional OCT

- Spectroscopic OCT



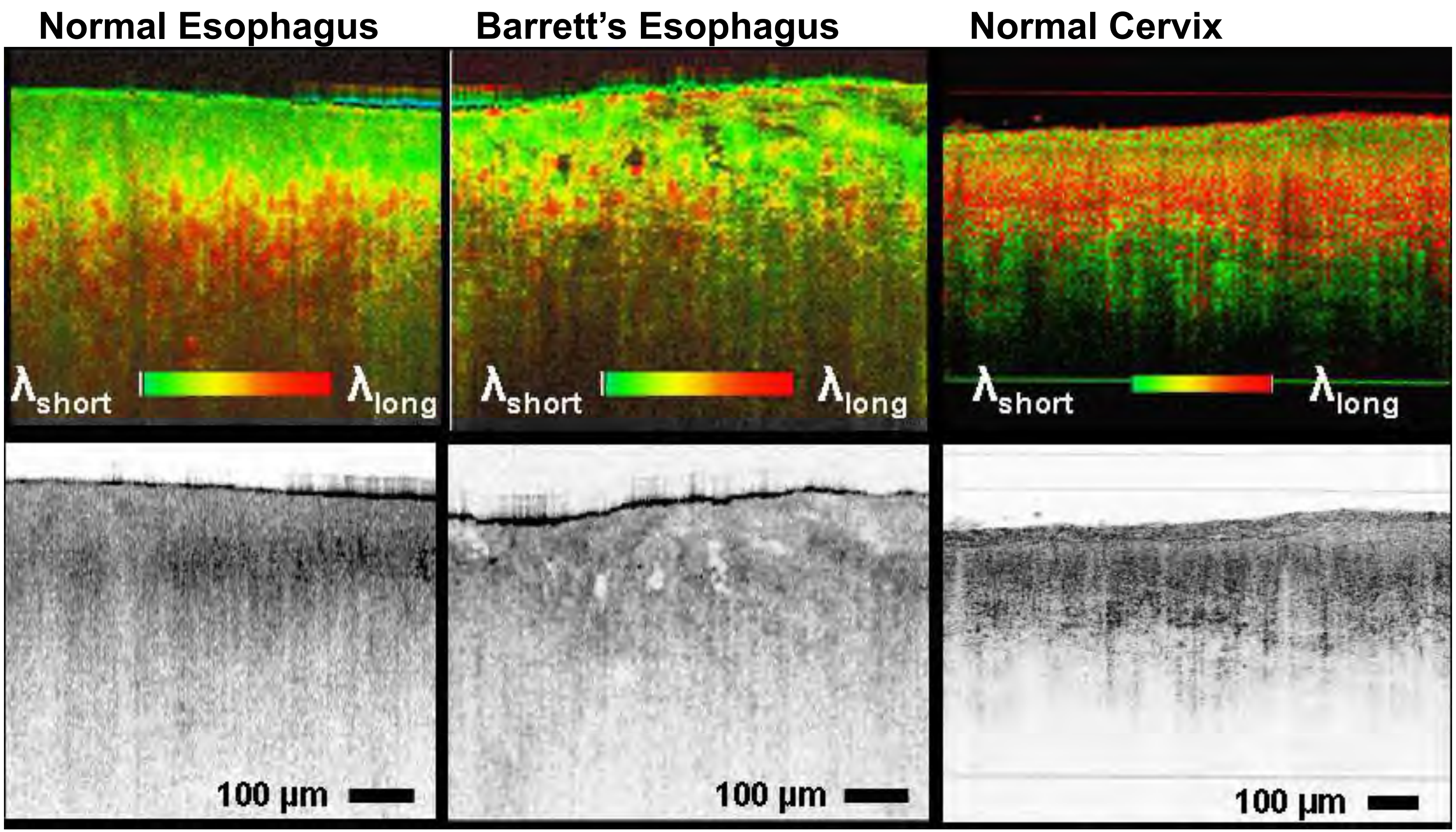
Standard OCT
Demodulation - Envelope

⇒Reflectivity / Scattering

Spectroscopic OCT
Interferometric Signal →Spectral differences (centroid, skewness, shape)

⇒ Spectrally dependent scattering
⇒ Absorption

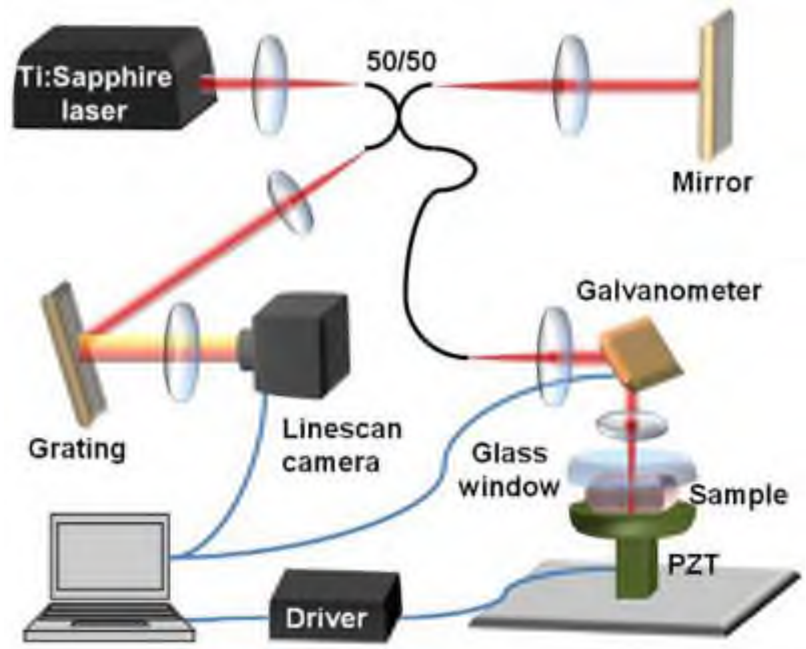
Functional OCT

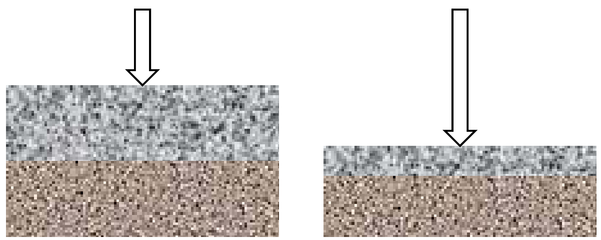


- Longer wavelengths penetrate deeper
- Areas of wavelength-dependent backscattering are visible

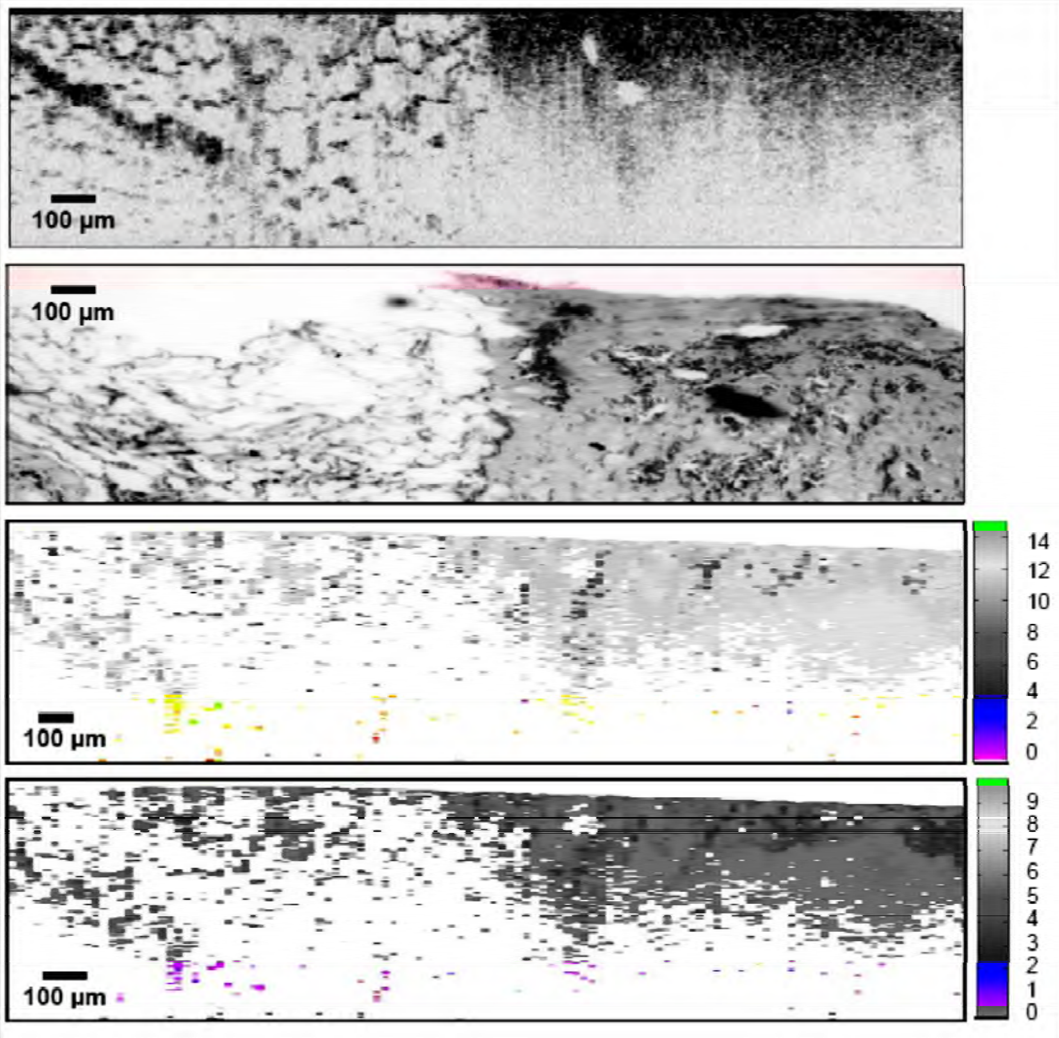
Functional OCT

- **Mechanical Properties of Tissue**
  - Displacement and strain maps from changing forces
- **OCT Elastography**
  - Elasticity measurements can be made from slight mechanical deformations of tissue
  - Correlation of successive images
    - Phase-resolved imaging
  - Depth-resolved, high resolution





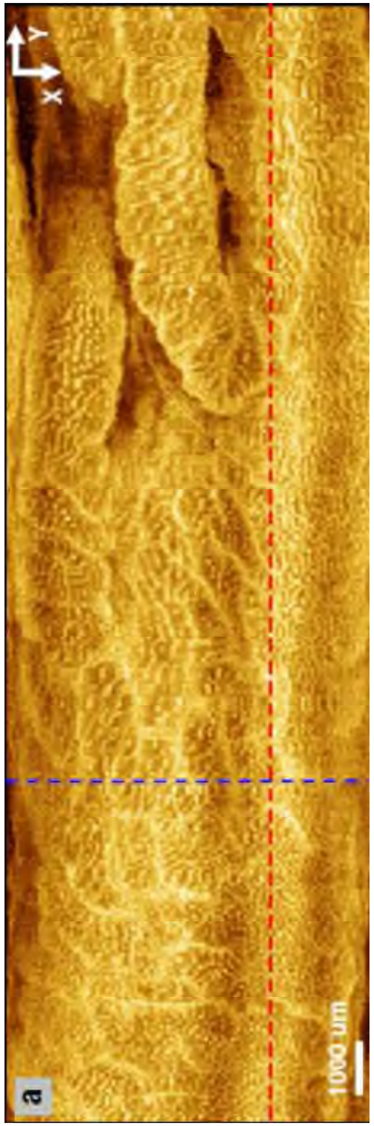
Functional OCT



<u>OCE of breast tissue</u> Liang et al, Optics Express, 16:11052-11065, 2008

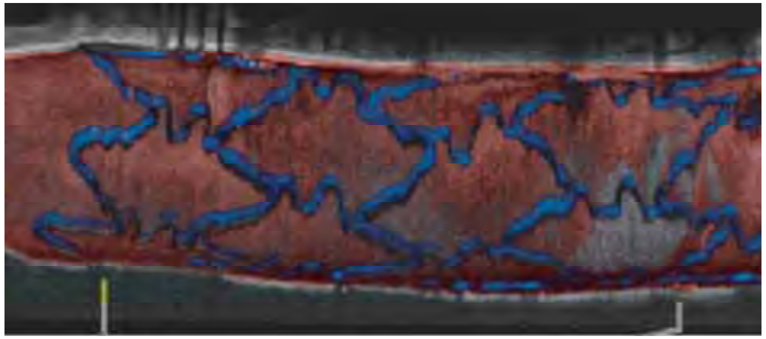
Software and Algorithm Issues in OCT

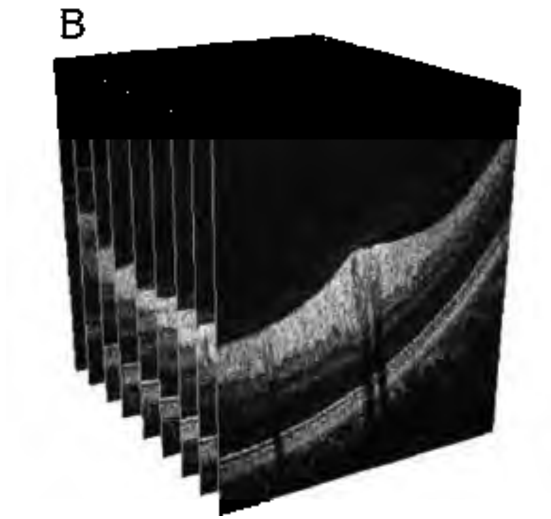
- **OCT is now a high-data-rate streaming technology**
  - Example: to cover 7x20 mm of area in the esophagus requires
    - 1400 AScans x 1000 pix/Ascan x 14 bit = 78.4T bits
    - Sampled at 20 MS/s = 280 Mbit/s
- **Requires very demanding post processing**
  - For real-time display: 20 000 times per second
    - FFT
    - Filter
    - Scale
    - Color code

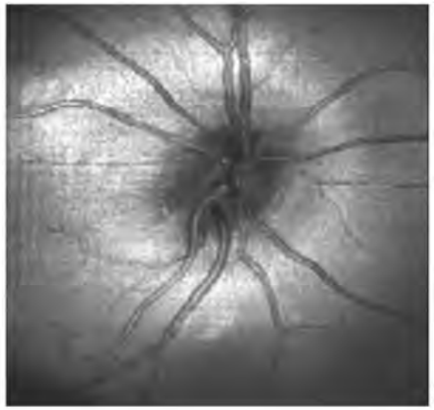


Software and Algorithm Issues in OCT

- **Issues still unresolved**
  - Optimal filtering
  - Exponential decay correction
  - Segmentation
  - Display
  - Visualization

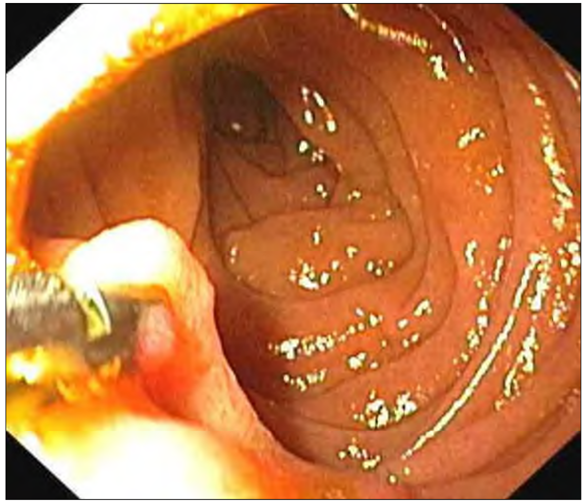


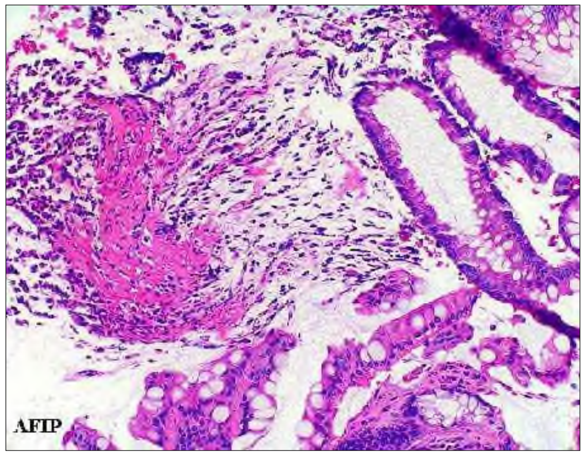




Applications

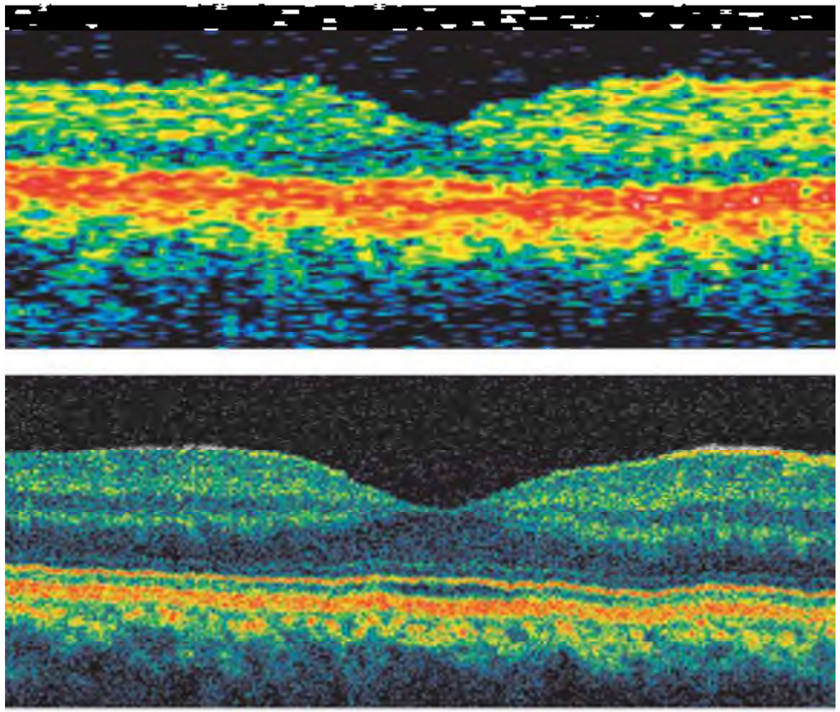
- **OCT can play a role in early diagnosis of disease and improve patient prognosis**
- **High resolution imaging :**
  - Screening for disease where biopsy is impossible, difficult or hazardous
  - Guiding biopsies to improve sensitivity and specificity and reduce the number required
  - Non-invasive monitoring of response to therapy
- **Recent developments**
  - Increased speed (up to 200 fps)
  - Improved resolution (1-5 μm)
  - Compact and reliable systems





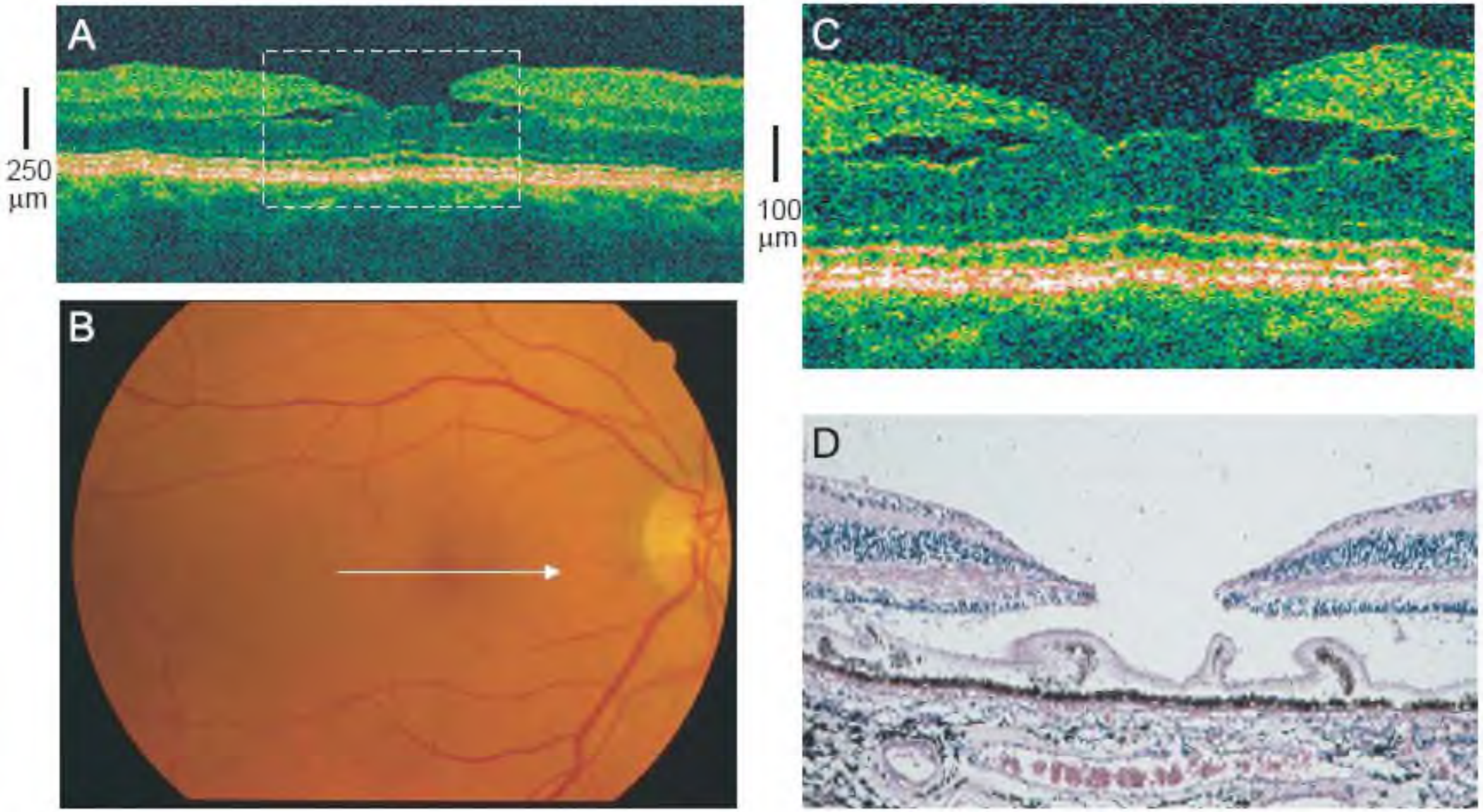
Ophthalmology

- **Diagnosis and management of ocular disorders**
  - Age-related macular degeneration
  - Diabetic macular edema
  - Macular hole
  - Epiretinal membrane
  - Glaucoma
- **Latest developments**
  - Combining OCT with fundus photography and scanning laser ophthalmoscopy
  - 3D visualization of tissue morphology
  - Ultra-high speed, ultra-high resolution OCT with adaptive optics and pancorrection



Standard (10 μm) and UHR (2 μm) OCT of the retina
Drexler, Fujimoto, Progress in Retinal and Eye Research 27 (2008) 45–88

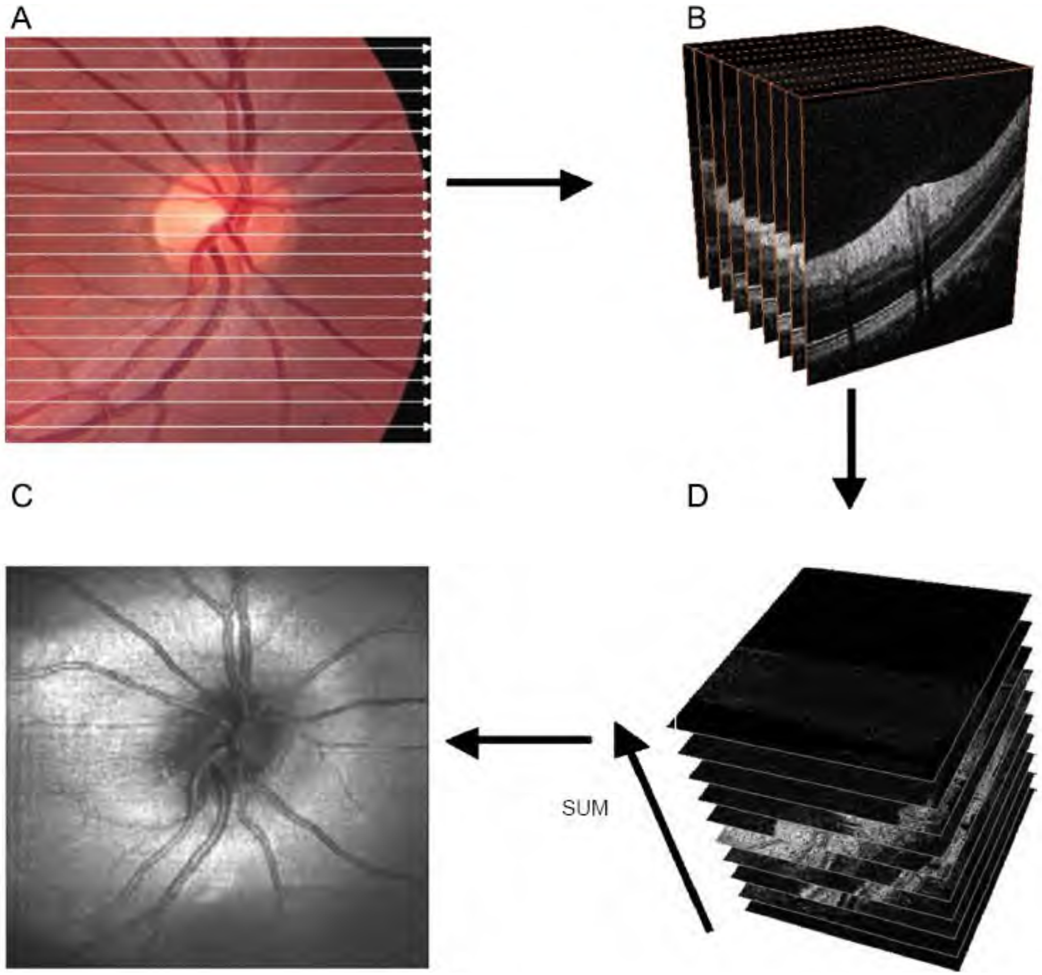
Ophthalmology



Macular Hole

Drexler, Fujimoto, Progress in Retinal and Eye Research 27 (2008) 45–88

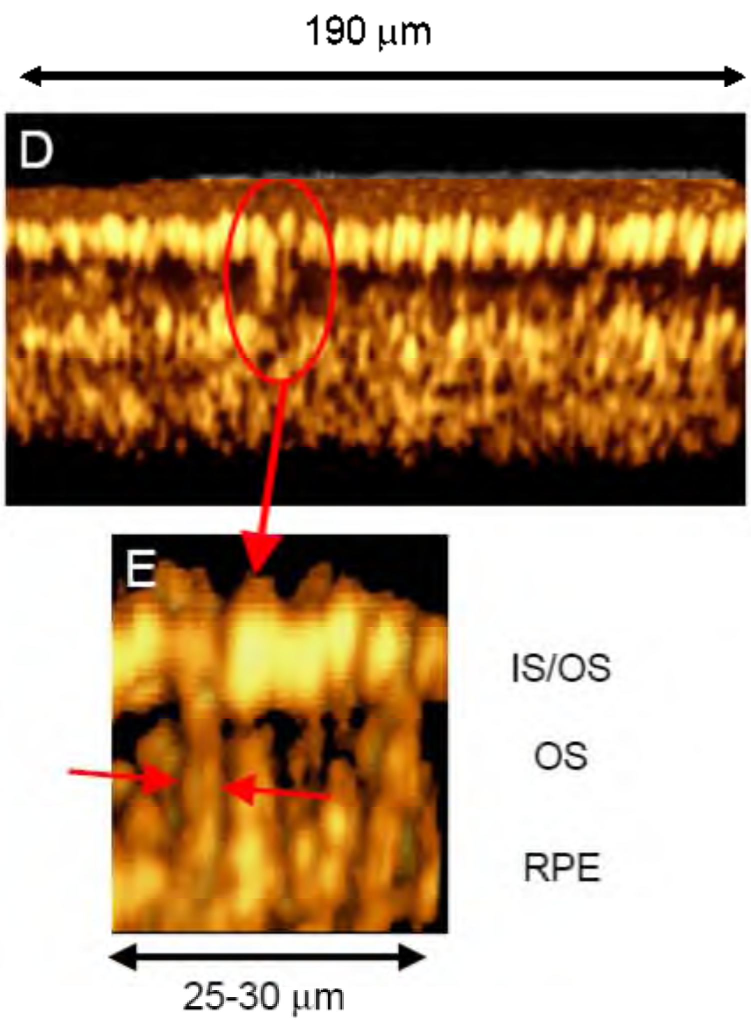
Ophthalmology



<u>3D UHR Imaging of the retina with OCT fundus view</u>

Drexler, Fujimoto, Progress in Retinal and Eye Research 27 (2008) 45–88

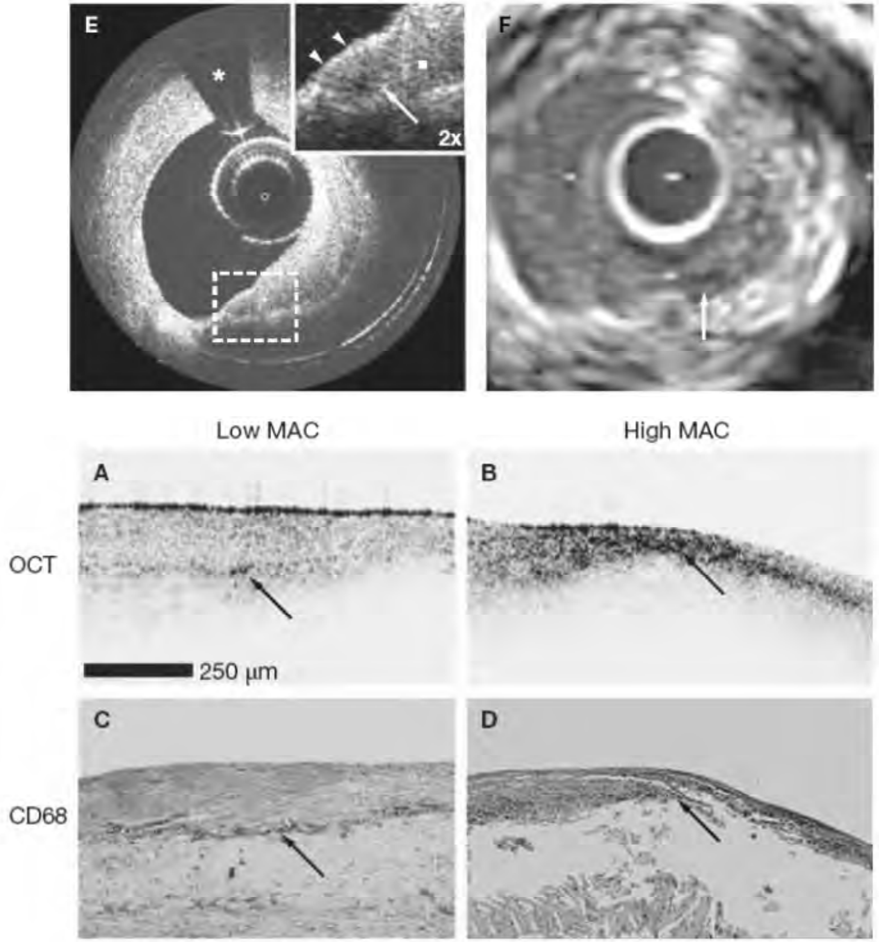
Ophthalmology



Imaging of individual photoreceptors
Drexler, Fujimoto, Progress in Retinal and Eye Research 27 (2008) 45–88

Cardiology

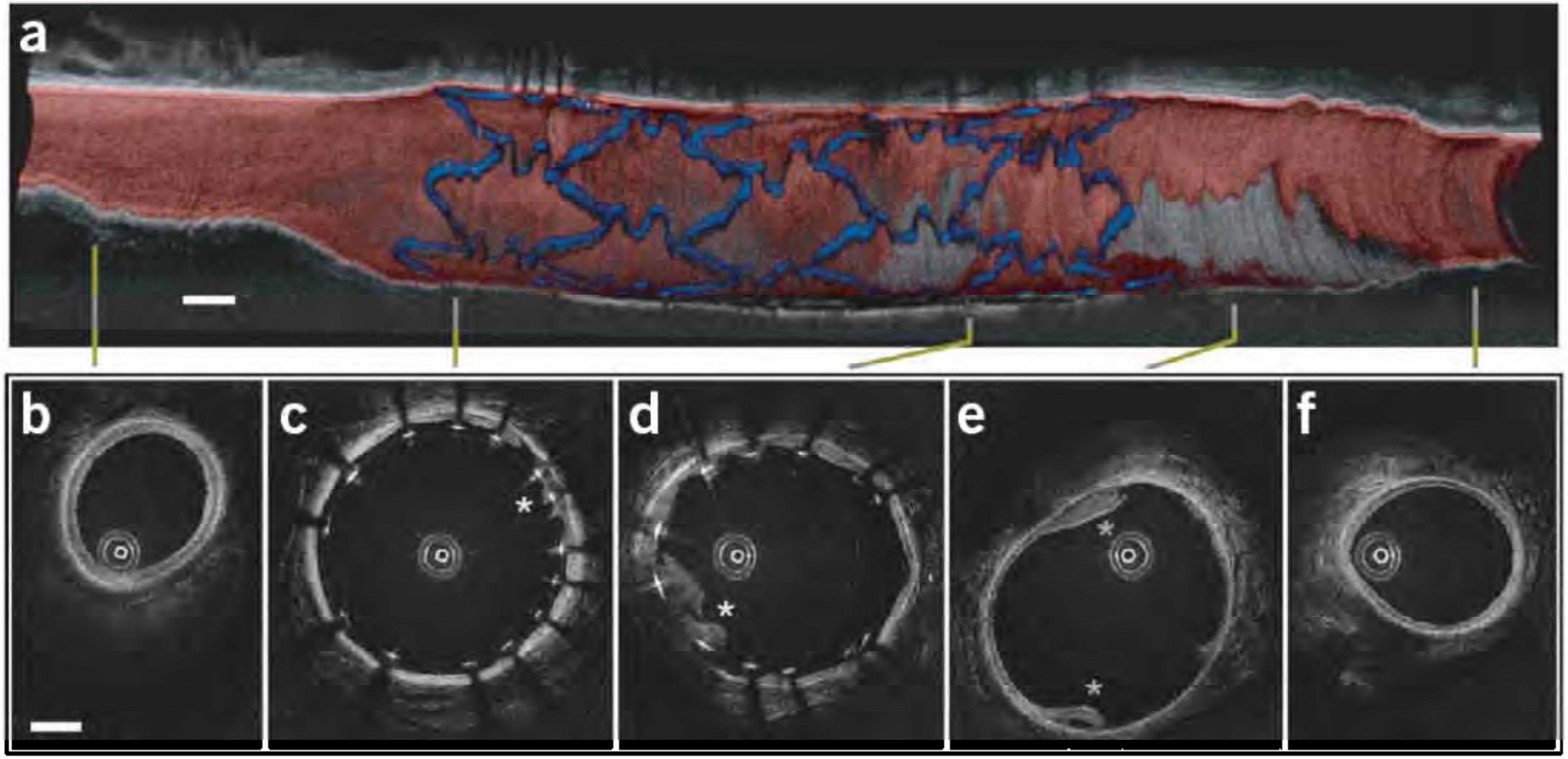
- **Visualization of the vessel wall at the microscopic level**
  - High resolution imaging of coronary architecture
  - Precise characterization of plaque architecture
  - Quantification of macrophages within the plaque
- **Identification of the most common type of vulnerable plaque, the thin-cap fibroatheroma**
- **Monitoring stent deployment**



<u>Lipid rich plaque (OCT and IVUS) and Macrophage content</u>

Low et al, Nature Clinical Practice, 3, 145-162, 2006

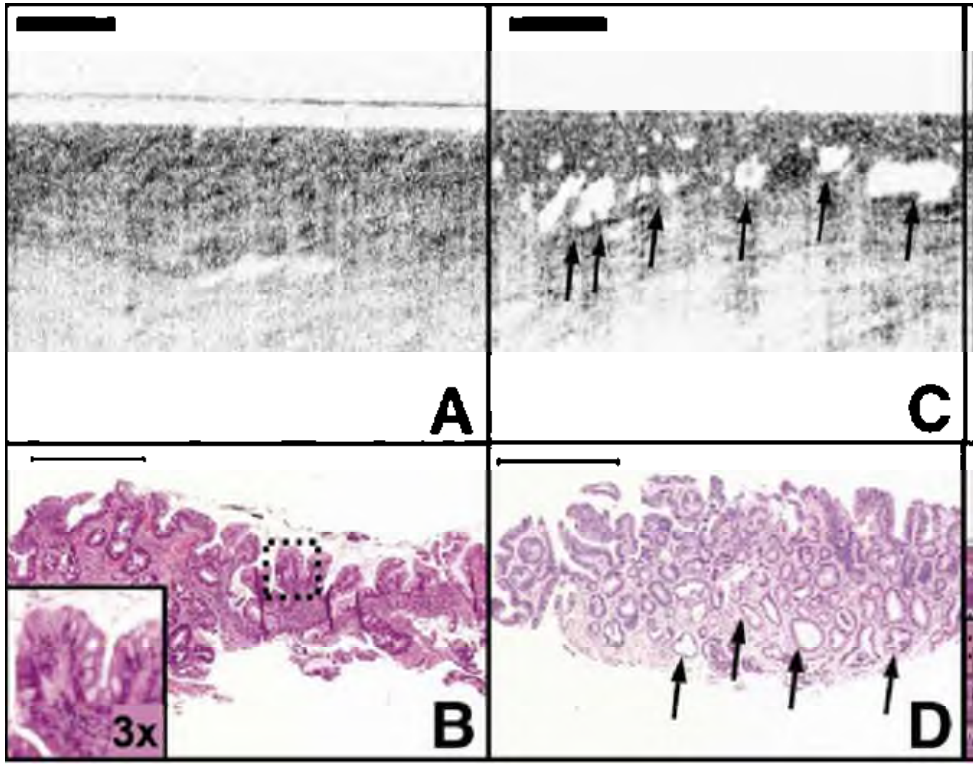
Cardiology



Stented Coronary Artery
Yun, et al, Nature Medicine, 12, 1429-31, 2006

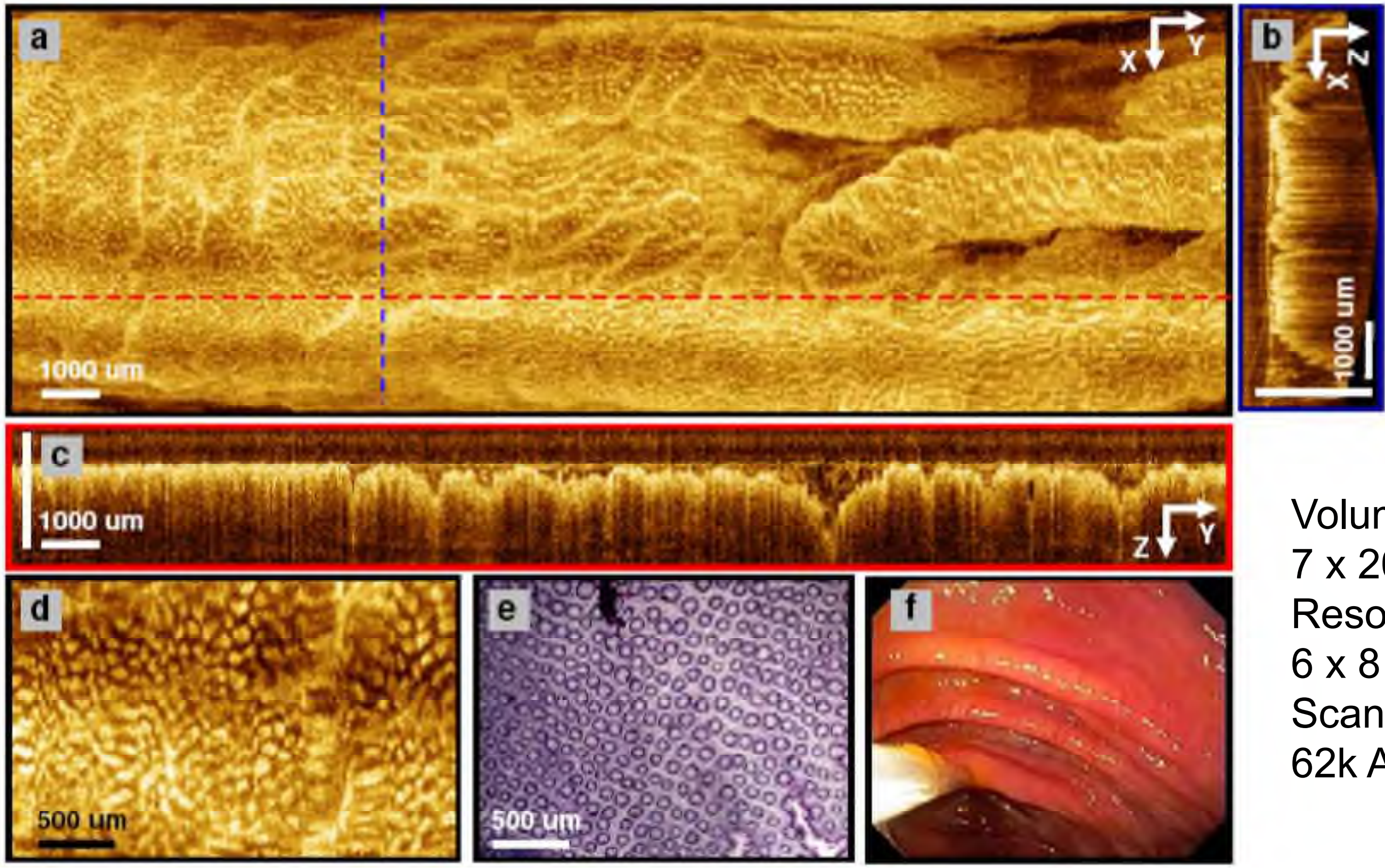
Gastroenterology

- **Especially relevant application for OCT**
  - High incidence
  - Clinical benefits of early detection
  - Need for pre- and post-treatment assessment
- **OCT applied to the GI**
  - Early detection of cancer in Barrett's esophagus patients
  - Study of inflammatory bowel diseases in the colon
- **Major goal = guidance of excisional biopsy**
- **High resolution and high speed now allow whole organ surveying**



<u>Barett;s without and with HGD</u>
Image Size: 2.5 mm, Resolution: 10 x 20 μm
Evans et al, Clin Gastro Hepatol, 4, 38-43, 2006

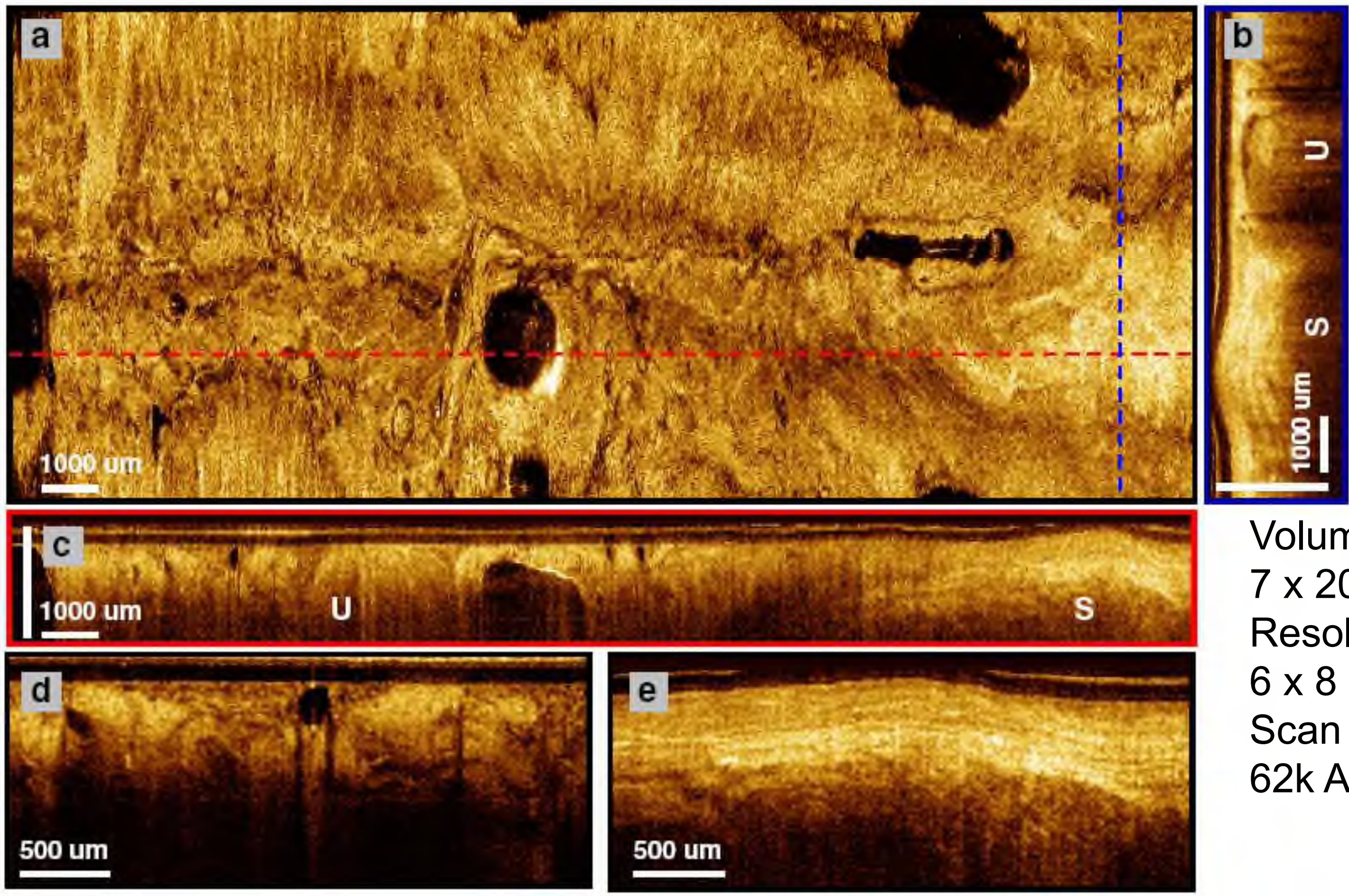
Gastroenterology



Volume:
7 x 20 x 1.6 mm
Resolution:
6 x 8 µm)
Scan Speed:
62k A-Scans/sec

<u>Normal Colon</u>
Adler, et al, Optics Express, 17(2), 784-796, 2009.

Gastroenterology



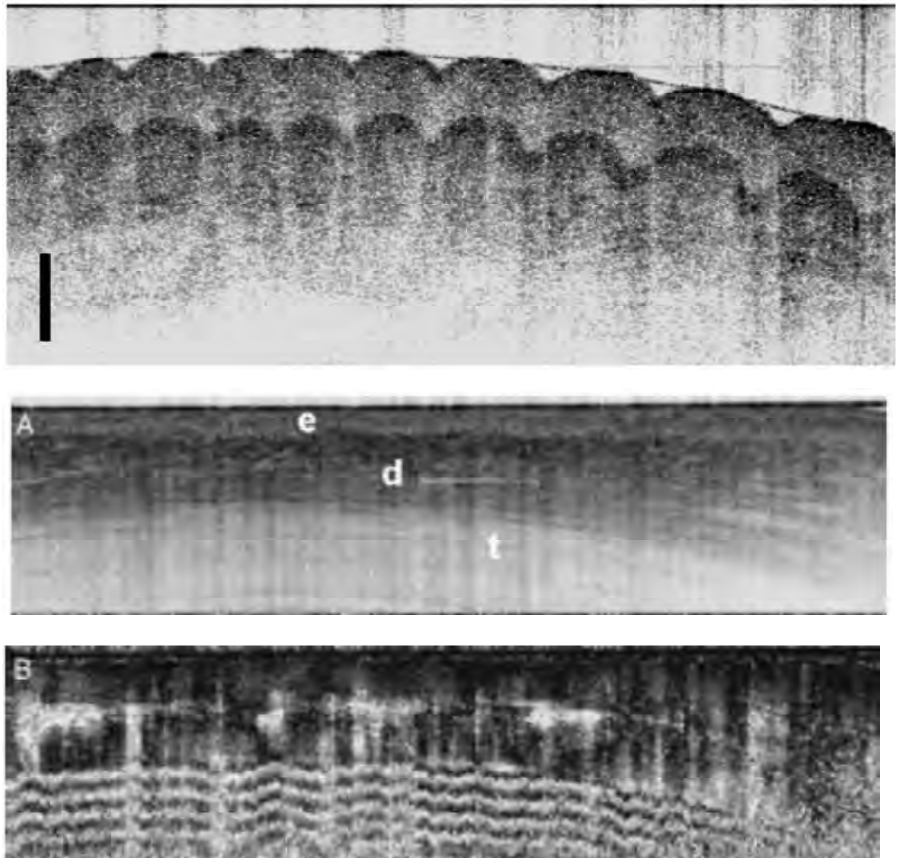
Volume:
7 x 20 x 1.6 mm
Resolution:
6 x 8 μm)
Scan Speed:
62k A-Scans/sec

Ulcerative Colitis

Adler, et al, Optics Express, 17(2), 784-796, 2009.

Dermatology

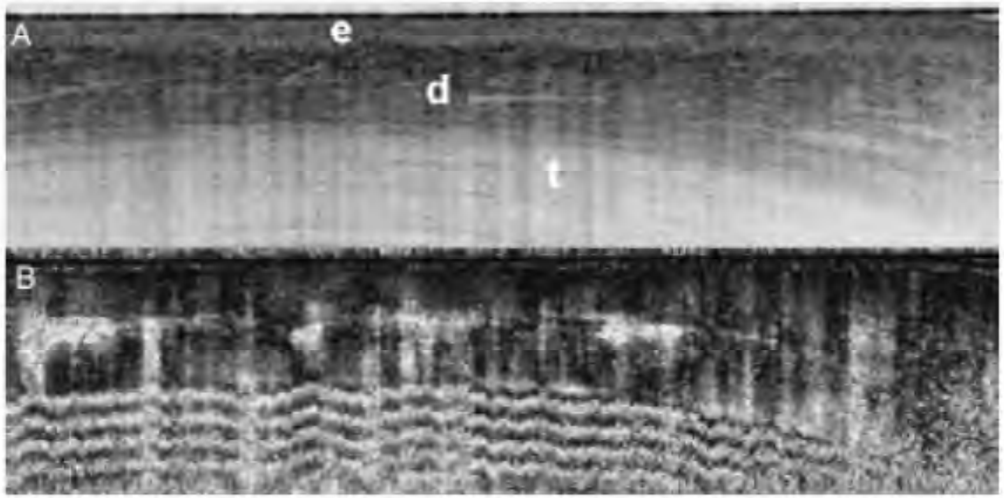
- **OCT can image**
  - The stratum corneum of glabrous skin (palmoplantar)
  - The epidermis and the upper dermis
  - Skin appendages and blood vessels
- **Uses**
  - Useful in non-invasive monitoring of cutaneous inflammation, hyperkeratotic conditions and photoadaptive processes
  - May be of great value, in particular in cosmetics and the pharmaceutical industry
  - Could potentially allow the differentiation between benign and malignant tissues. Beyond a high resolution morphology in OCT images, tissue
- **Additional parameters**
  - Scattering coefficient
  - Refractive index.
  - OCT spectroscopy
  - Tissue birefringence
  - OCT elastography
  - OCT Doppler flow
- **Significant new insights in skin physiology and pathology**

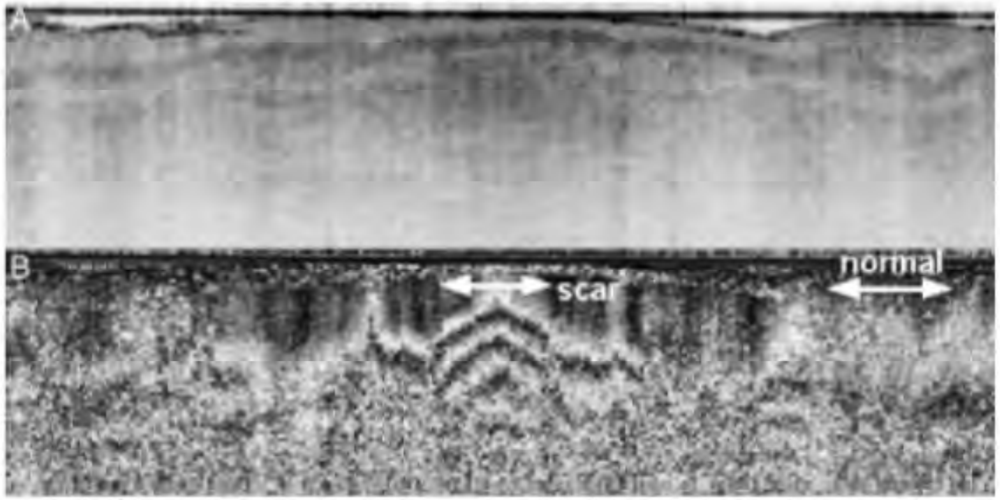


<u>Normal finger skin (standard OCT and birefringes)</u>

Pierce, et al, J Invest Dermatol 123:458 –463, 2004

Dermatology

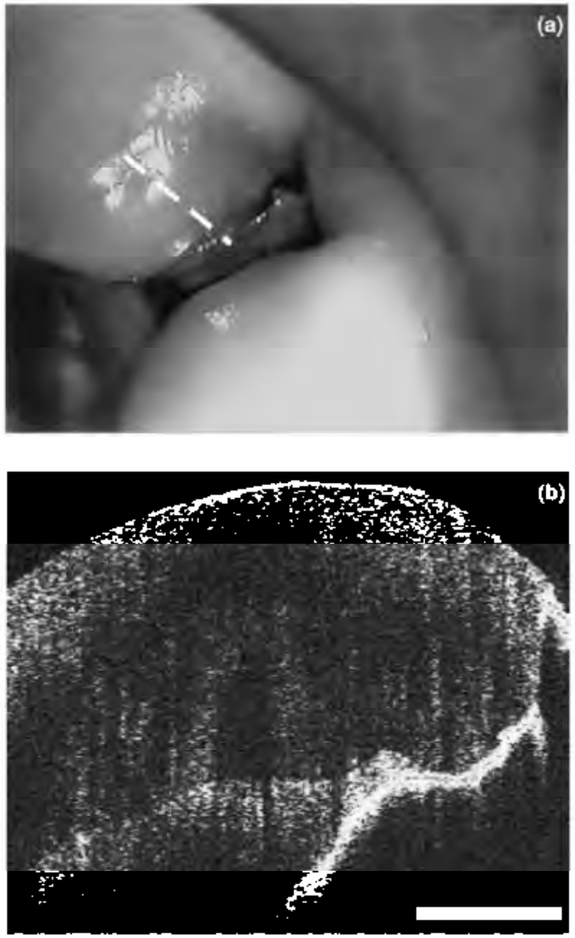




<u>Normal and scar finger skin (standard OCT and birefringes)</u>
Pierce, et al, J Invest Dermatol 123:458 –463, 2004

Dentistry

- **Potential applications in dentistry**
  - Detection of hidden dentinal caries
  - Quantitative monitoring of de- and remineralisation of demineralised lesions
  - Visualisation of interproximal surfaces of premolars and molars
  - Investigation of the effectiveness of restorative fillings
  - Early detection of soft tissue diseases.

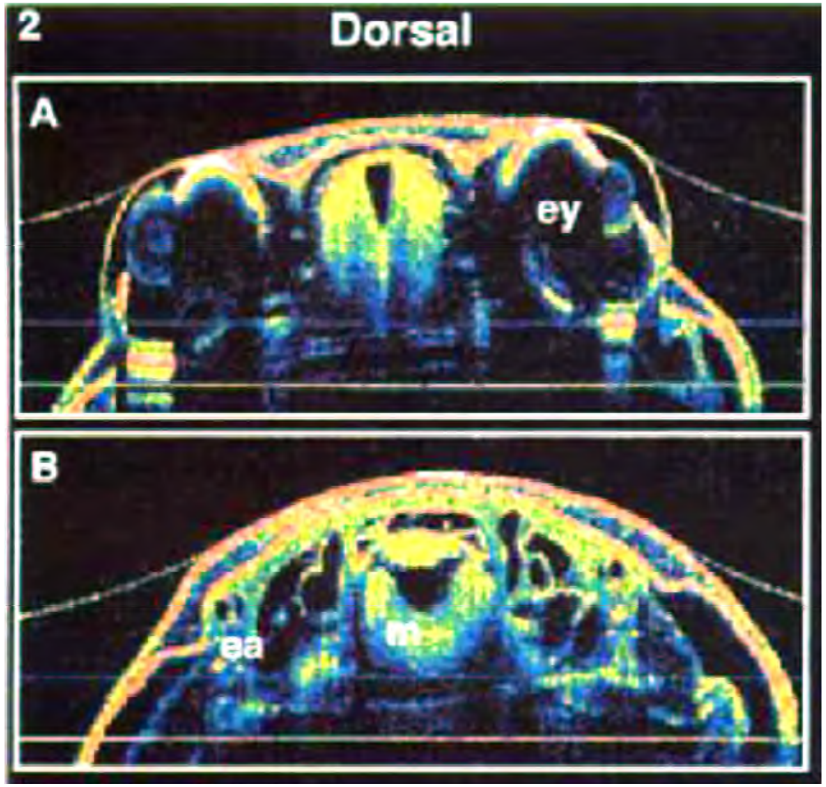


Molar restoration

Brandemburg, et al, Optics Communications 227 (2003) 203–211

Developmental Biology

- **Imaging embryonic morphology**
  - Advancement in the filed of genetics: genes identified, function studied
  - New animal models to study gene expression or lack of expression (knockout animals)
  - Study of developmental and embryologic changes require termination
  - High resolution imaging for developmental biology has the potential for non-invasive:
    - Image embryonic microstructure and phenotypic expression
    - Image function and response to medications
    - Guide interventions and fetal manipulation
    - Monitor response to therapy

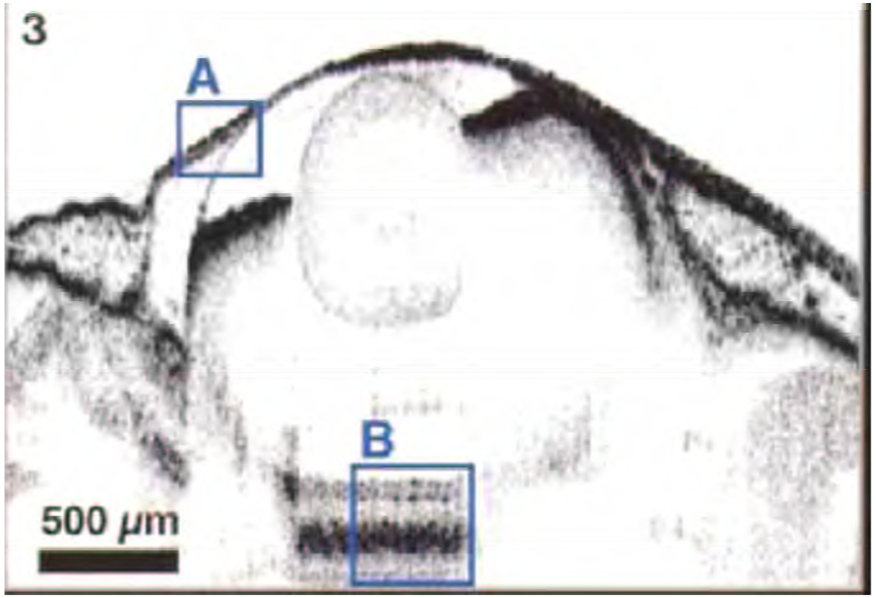


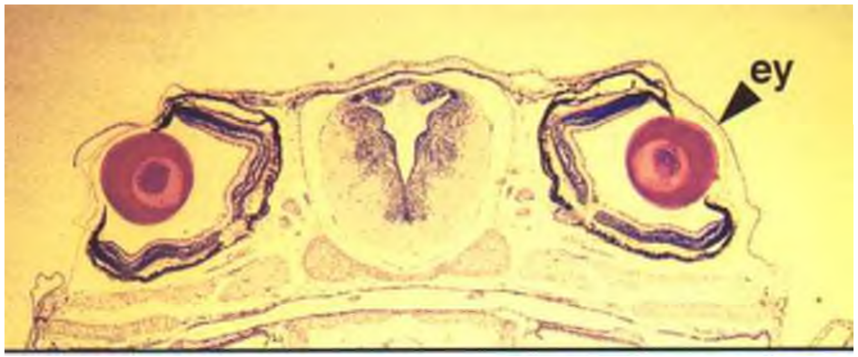
Xenopus Laevis morphology

Boppart, et al, DEVELOPMENTAL BIOLOGY 177, 54–63 (1996)

Developmental Biology

- Anterior eye: cornea, lens, and iris.
- Corneal thickness ~ 10 µm
- Posterior eye: ganglion cell layer, retinal neuroblasts, and choroid



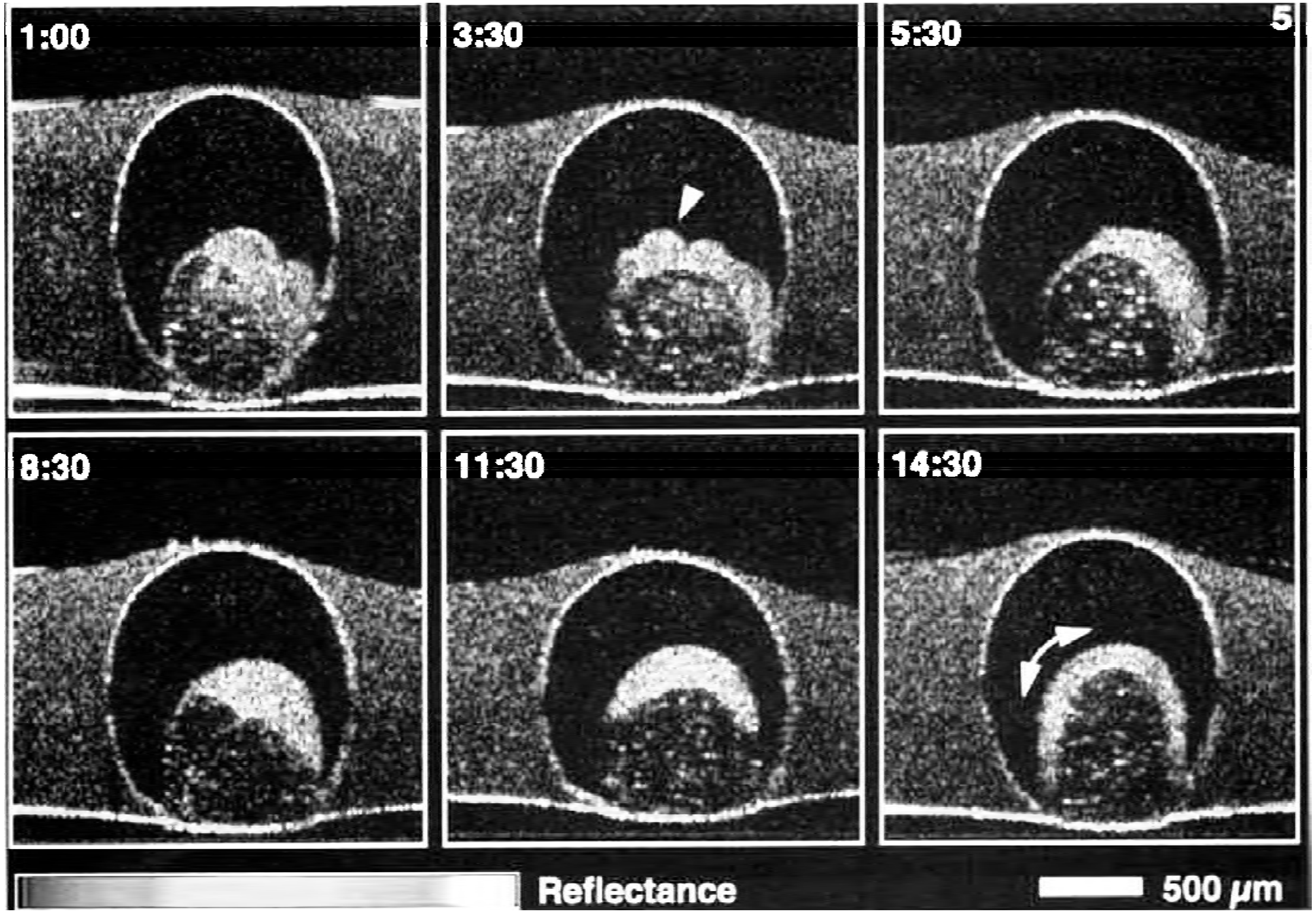


Xenopus Laevis morphology

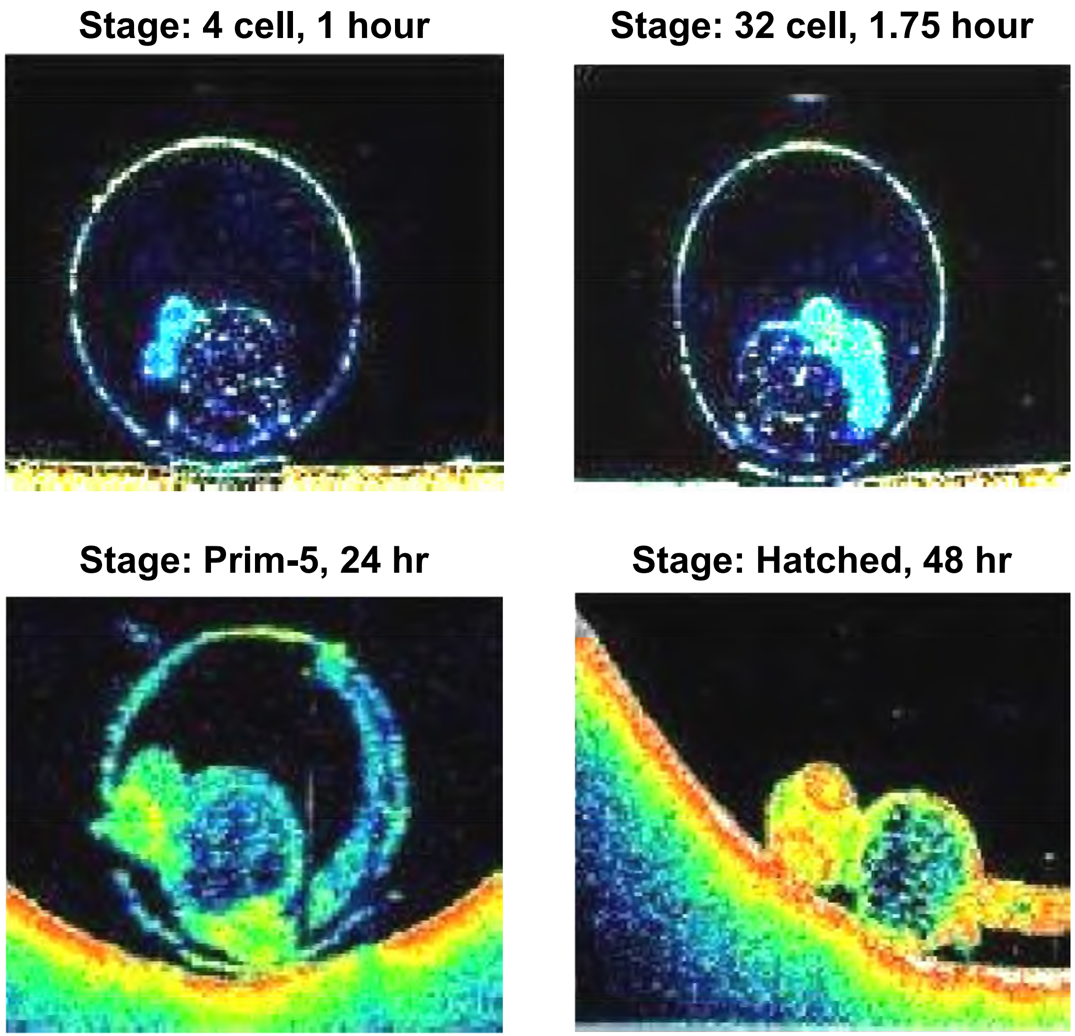
Boppart, et al, DEVELOPMENTAL BIOLOGY 177, 54–63 (1996)

Developmental Biology

Developing Embryo

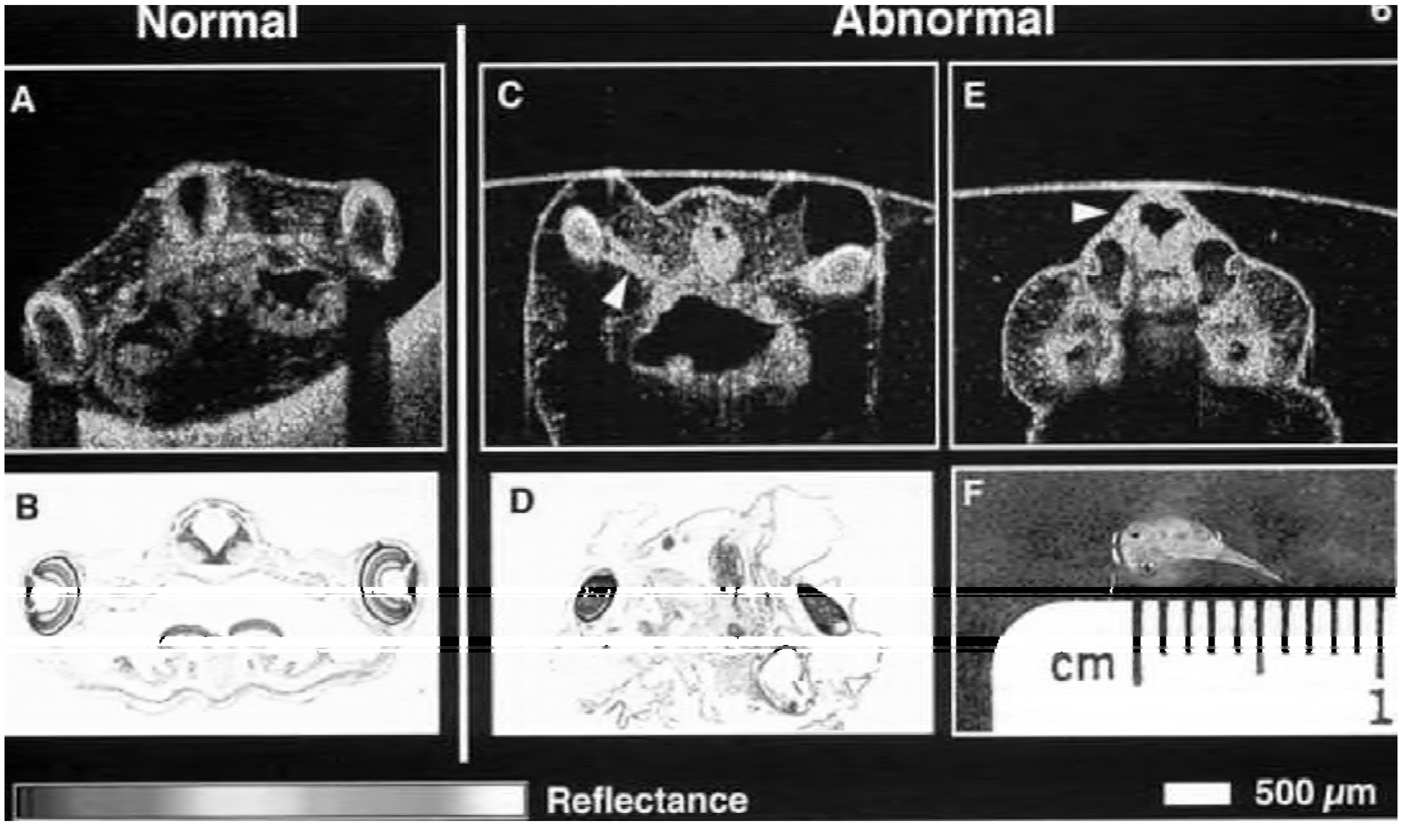


Developmental Biology



<u>Developing Zebra fish embryo</u>
Boppart, et al, DEVELOPMENTAL BIOLOGY 177, 54–63 (1996)

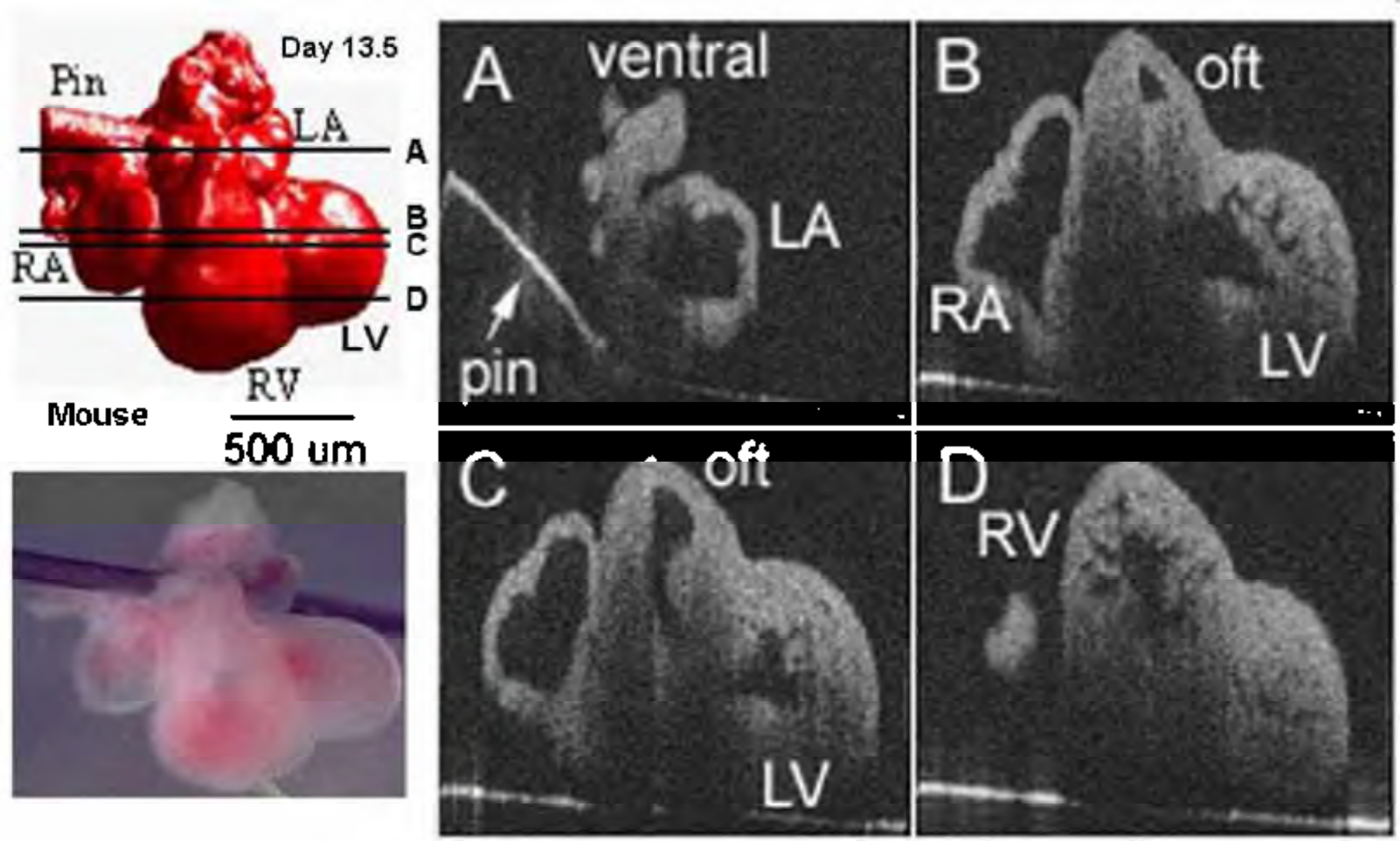
Developmental Biology



Abnormalities in Xenopus Laevis morphology

Boppart, et al, DEVELOPMENTAL BIOLOGY 177, 54–63 (1996)

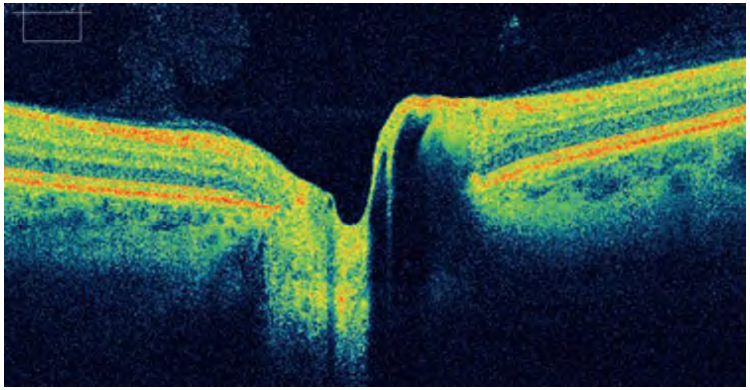
Developmental Biology



<u>4D imaging of mouse embryonic heart</u>
Jenkins, et al, Optics Express, 14, 736-748, (2006)

Commercial OCT Systems

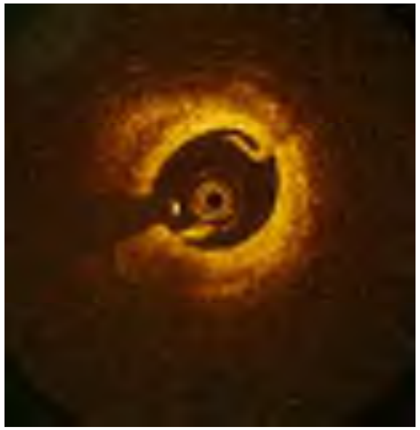
- **First commercial OCT devices**
  - Humphrey Systems (now a part Carl Zeiss Meditec, Inc.)
  - retinal imaging
  - released in 1996
  - FDA approval in 2002.
  - Stratus OCT™ systems selling more than 6000 units
  - Cirrus™ HD-OCT system

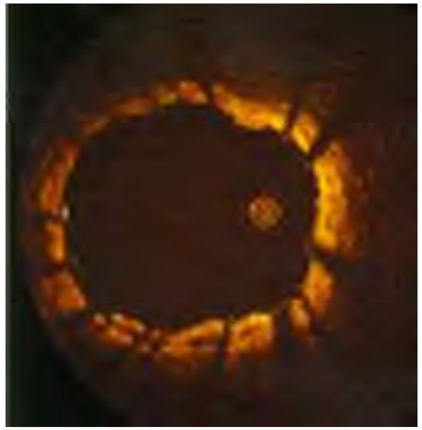


Commercial OCT Systems

- **Many more devices available now**
  - LightLab Imaging
  - Imalux Corporation,
  - ISIS Optronics GmbH
  - OCT Medical Imaging, Inc
  - Michelson Diagnostics, Ltd
  - Novacam Technologies, Inc
  - Lantis Laser Inc
  - OptoVue, Inc
  - Topcon Corporation
  - Optol Technology
  - Heidelberg Engineering
  - Opthalmic Technologies, Inc

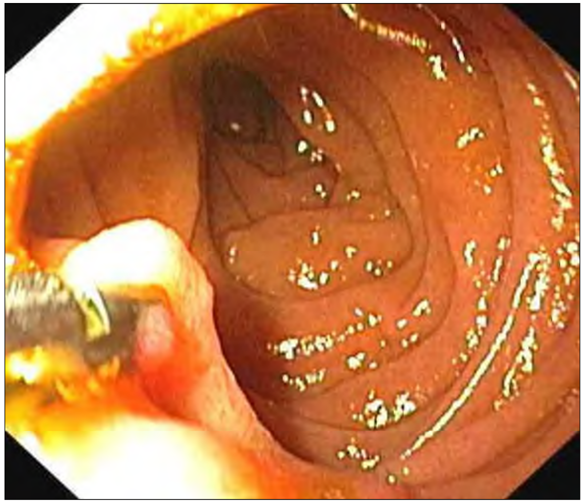
  - Thorlabs, Inc
  - Bioptigen, Inc
- **Individual OCT components**
  - Femtolasers Produktions
  - Nippon Telegraph and Telephone Corporation
  - Thorlabs, Inc
  - MenloSystems GmbH

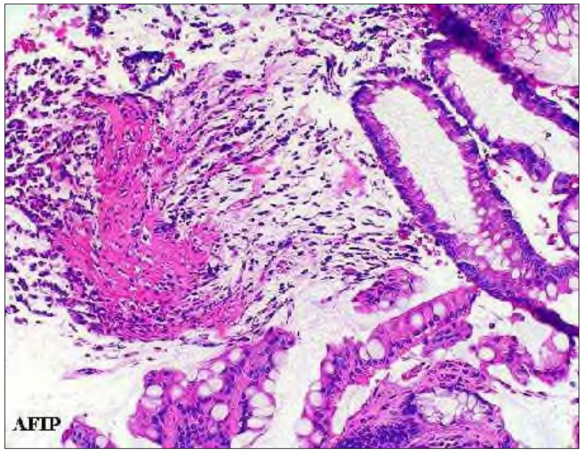




Can we “see” more?

- **Resolution limit**
  - 1-10 μm
  - Especially limited in the lateral direction
- **Many cancerous/pre-cancerous changes in the μm range**
  - Cell proliferation: 5 μm spacing change
  - Nucleus variations: ~2-4 μm diameter change
  - Sub-cellular and Sub-nuclear variations: < 1 μm change

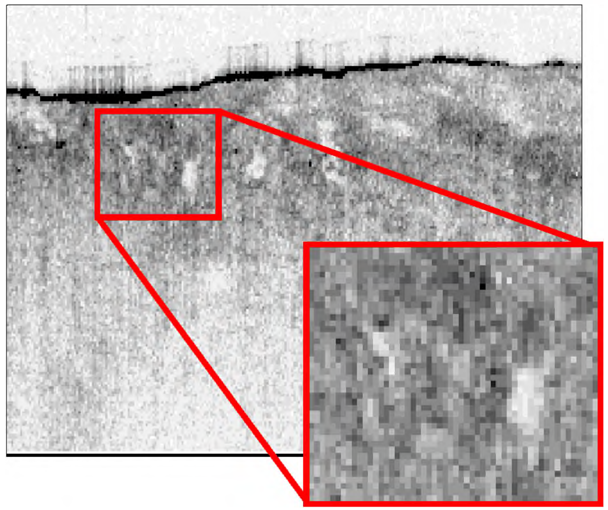




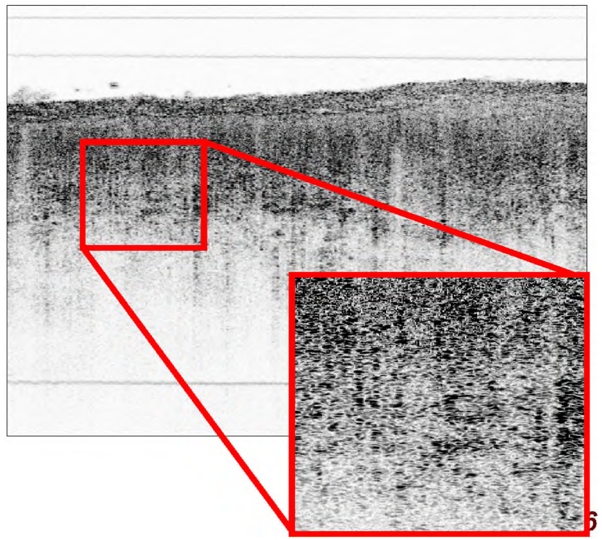
Speckle Analysis

- **Uresolvable features**
  - Coherent technology → speckle
  - Mostly treated as noise
- **Speckle**
  - Contains information regarding the
    - Size
    - Concentration
    - Spacing
    - Periodicity
    - Etc
    - size and distribution of scatterers
  - Diagnostically useful information
  - Statistical and spectral properties

Barett's Esophagus

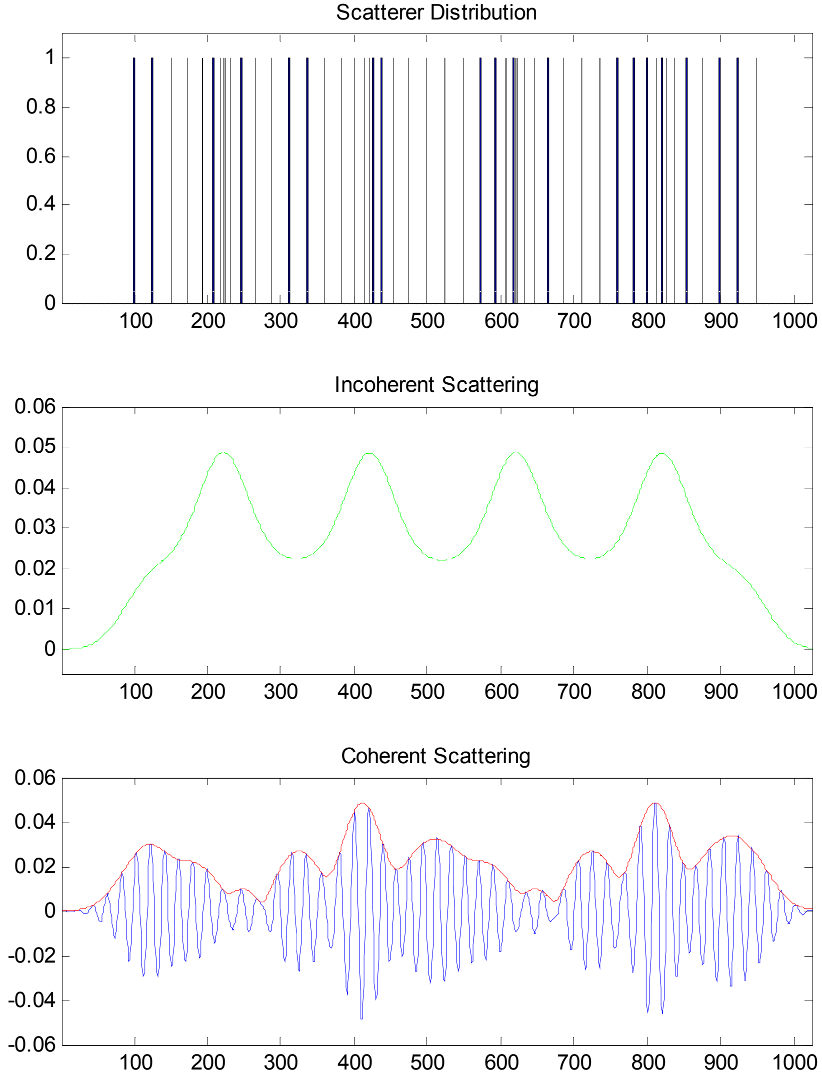


Dysplastic Cervix



Speckle

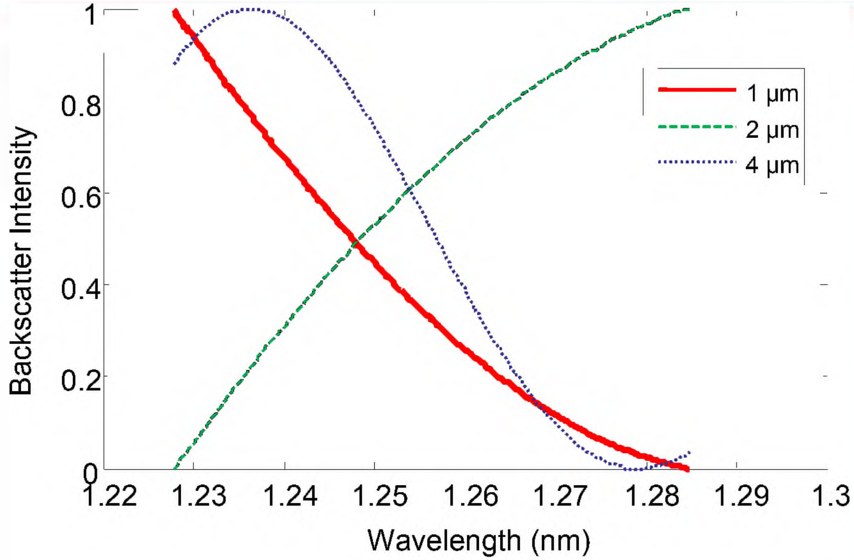
- **Signal scattered from a distribution of scatterers**
- **Incoherent Scattering**
  - Intensity summed
- **Coherent scattering**
  - Field summed
  - Resulting intensity profile may not resemble scatterer distribution
  - Speckle
- **Unresolvable Signal**
  - Contains information regarding the number and distribution of scatterers
  - Diagnostically useful information
  - Statistical and spectral properties

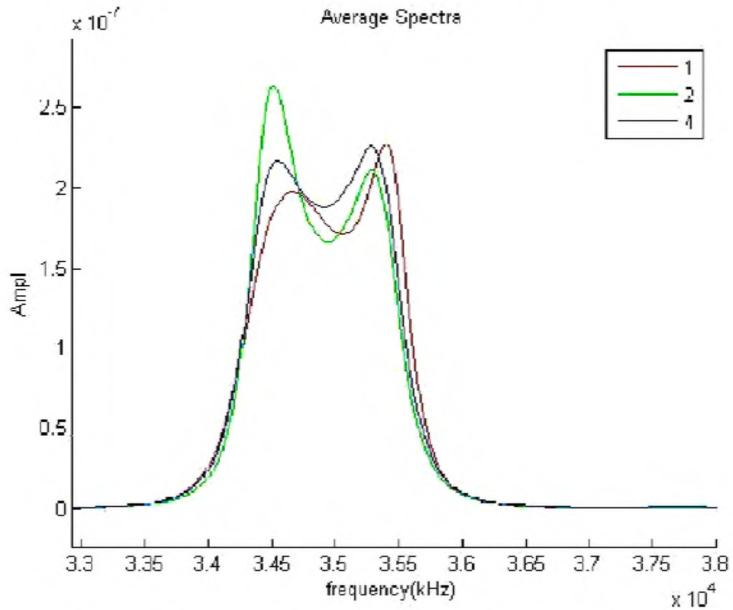


Speckle Analysis

- **Speckle properties reflected in the spectral content**
  - Optical spectrum of OCT
  - S(⌉) = FFT{s(t)}

- **Spectral properties of backreflected signal depend on**
  - Source spectrum
  - Effect of scatterers
    - Size → Spectral dependence of back-scattered light (similar to LSS)





Speckle Analysis

- **Solid Tissue Phantoms**
  - Polystyrene sphere solutions in a gel of acrylamide.
  - Diameter 1μm, 2μm and 4μm
  - $[C]_{1\mu m}$=50 spheres, $[C]_{2\mu m}$=5 spheres and $[C]_{4\mu m}$=2 spheres
- **Data acquired with TD OCT**
  - Imaging Volume: 17μm x 17μm x 15μm
  - Collect images
  - Digitized at 6x carrier frequency
  - Processed off-line

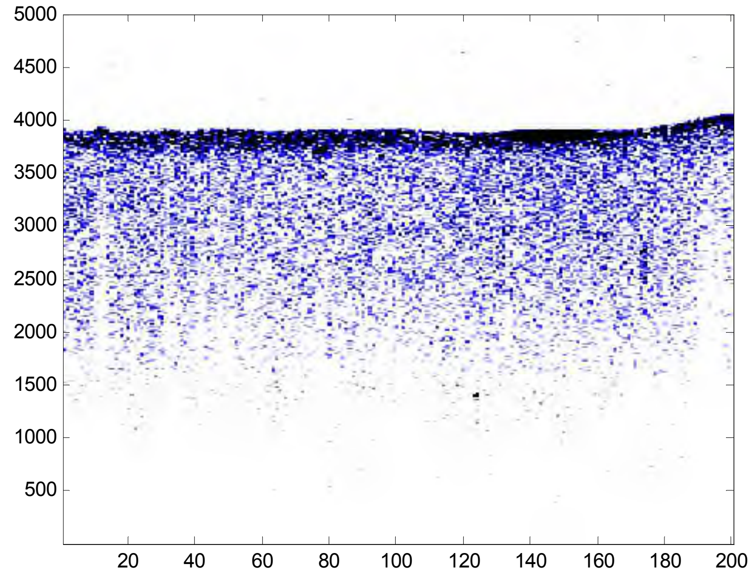


Image acquired from a phantom of 1μm and [C]=50

Speckle Analysis

- **Pre-processing**
  - Normalization to RMS value of 1
- **Spectral estimation**
  - Autoregressive Power Spectral Estimation
  - Effect of distribution and/or concentration
    - Can be reduced by averaging of spatially adjacent scans
    - Spectra only affected by size
- **Classification**
- **K-Means clustering**
- **Scatterer size estimation**

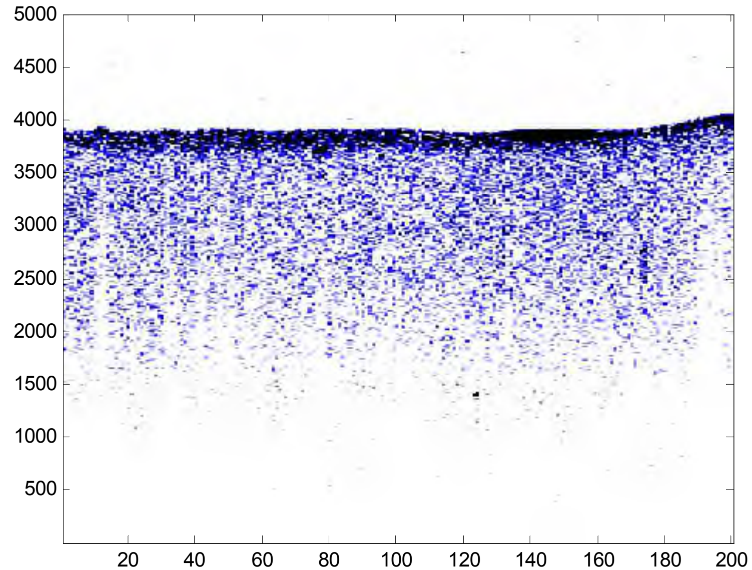
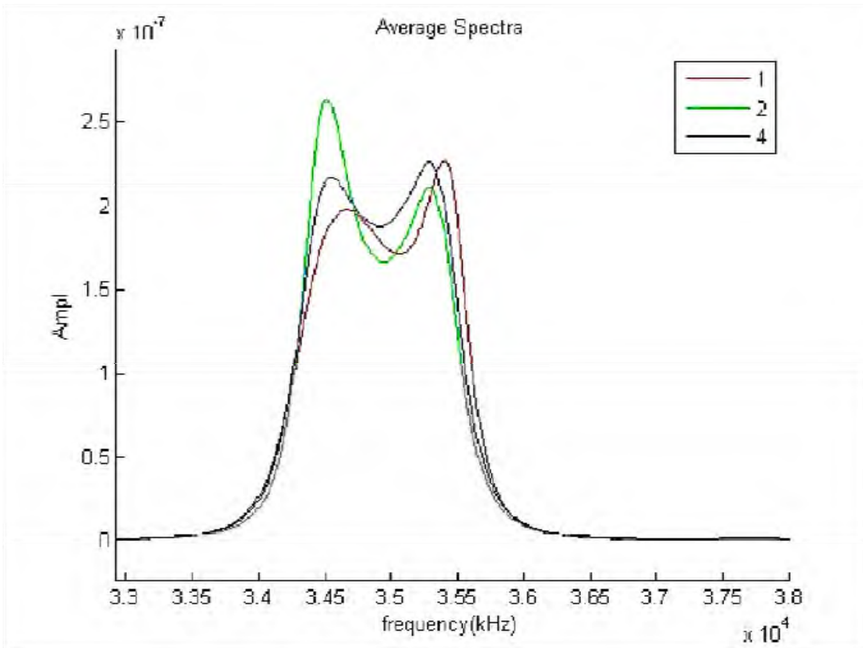


Image acquired from a phantom of 1μm and [C]=50

Speckle Analysis

- **Autoregressive Power Spectral Estimation**
  - Faster convergence from shorter signals
- **Burg's method**
  - Minimizing (least squares) the forward and backward prediction errors
  - Number of coefficients: 100
  - Size of window: 3001 (axial) x 25 (transverse) pixels
- **Principal Component Analysis (PCA)**
  - Reduction of the number of variables (35)
  - New orthogonal basis with no redundant information



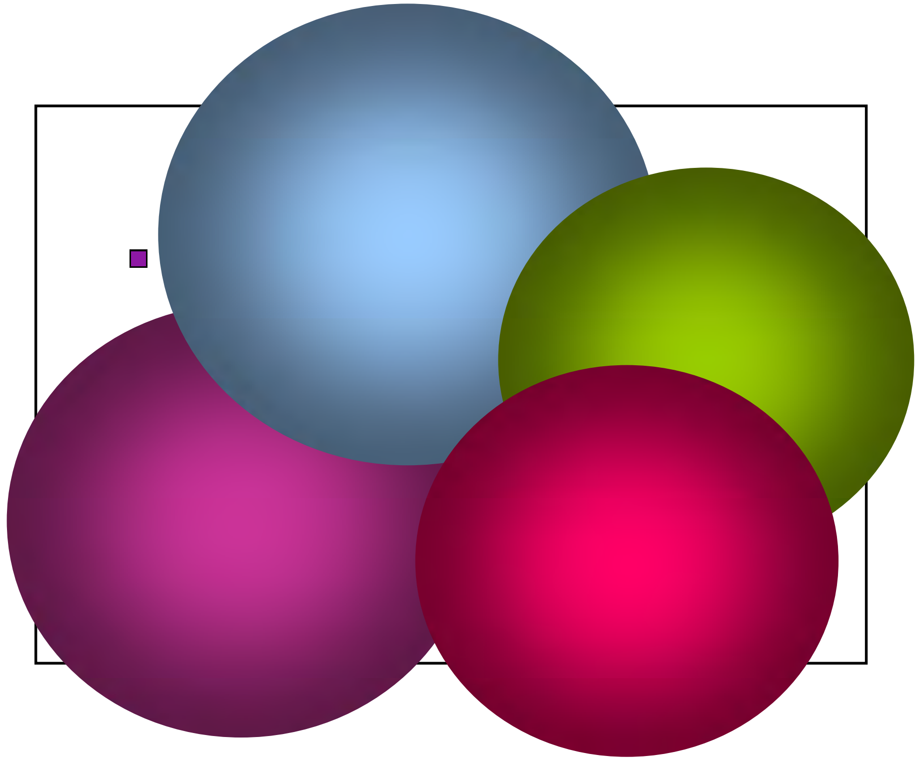
Speckle Analysis

- **Classification**
  - Multivariate Analysis of Variance (MANOVA)
    - New linear combinations of variables
    - Maximum separation between categories
  - Discriminant based classification

- **Scatterer Size Estimation**
  - Principal Component Analysis (PCA)
  - Solution to set of linear equations

$$\widetilde{P_{xx}}\,\widetilde{A} = \widetilde{d}$$

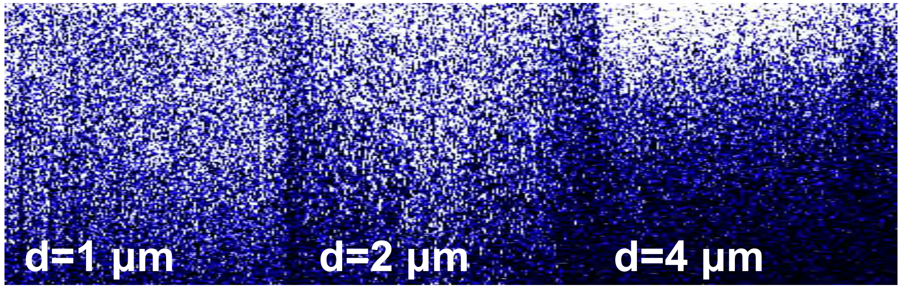
$$\widetilde{A} = \widetilde{P}_{xx}^{-1}\,\widetilde{d}_{training}$$



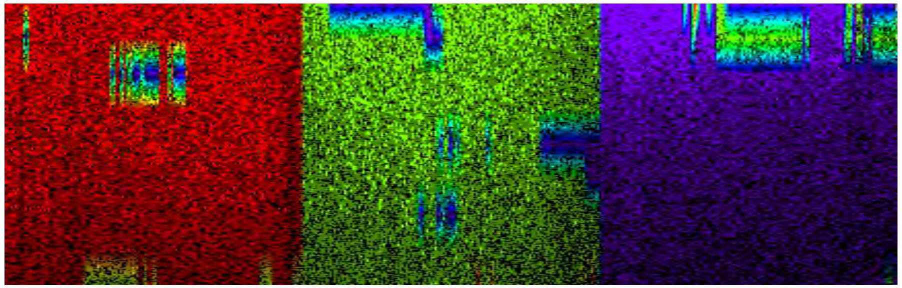
Speckle Analysis

- **Information can be extracted from spectrum**
  - Classification of images based on scatterer size
    - Sensitivity and specificity: 85-99 %
  - Scatterer size estimation from solutions of linear equations
    - Mean error: 16.5%
  - Require a priori information and training

Intensity Image of Microspheres Embedded in Acrylamide



Classification Results Overlayed on Intensity Image



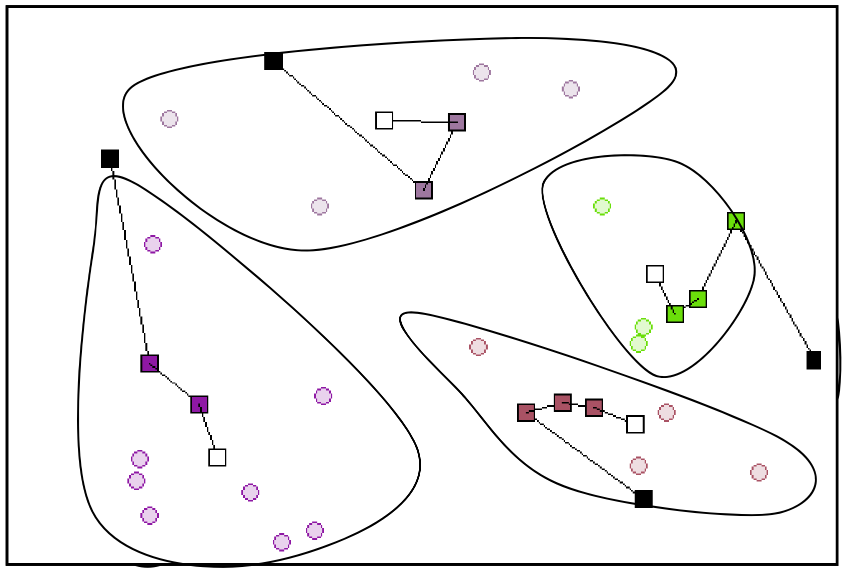
1 x 3 mm (17 x 20 µm)

Speckle Analysis

- **K-Means clustering**
- **Divide the data into a predefined number of clusters (groups)**
  - Minimize the distance from the centroid of each group
  - Assumes each object's attributes are coordinates in multidimensional space
  - Iteratively finds centroids and reassigning the clusters to minimize:

$$V = \sum_{i=1}^{k} \sum_{x_j \in S_i} \left| x_j - \mu_i \right|^2$$

  - Advantage: No a-priori information required

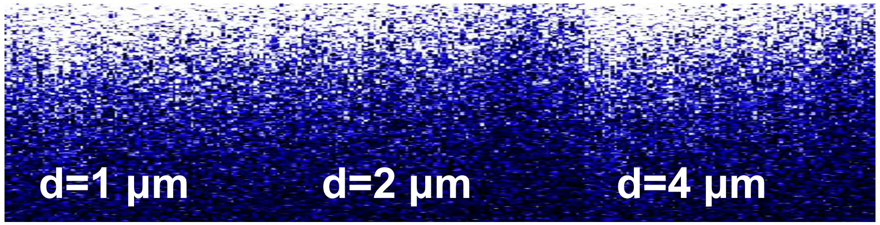


Speckle Analysis

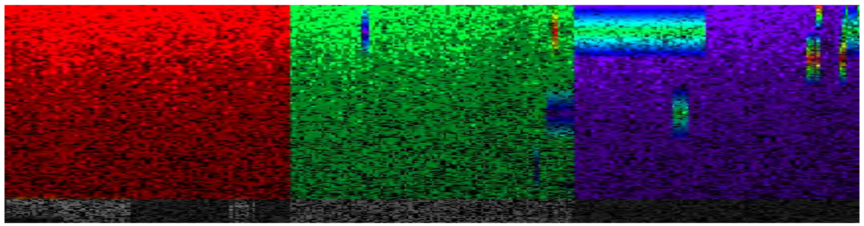
- Clustering areas of same intensity but different size scatterers

Scatterer Diam.	1 μm	2 μm	4 μm
Sensitivity	95.11	97.11	92.56
Specificity	99.44	99.44	99.44

Intensity image of microspheres



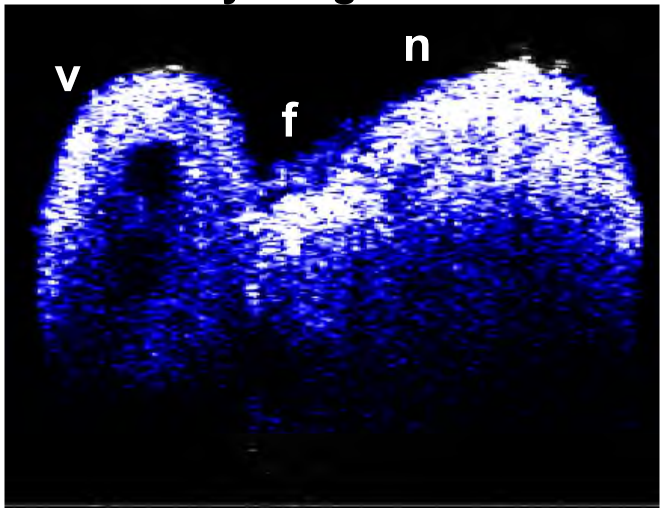
Clustering results of microspheres



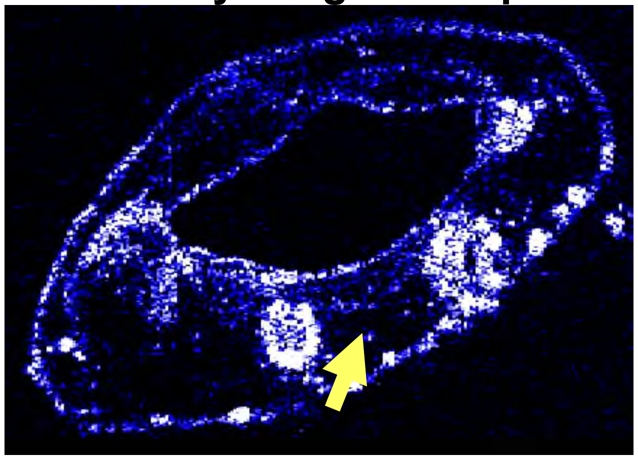
1 x 3 mm (15 x 30 μm)

Speckle Analysis

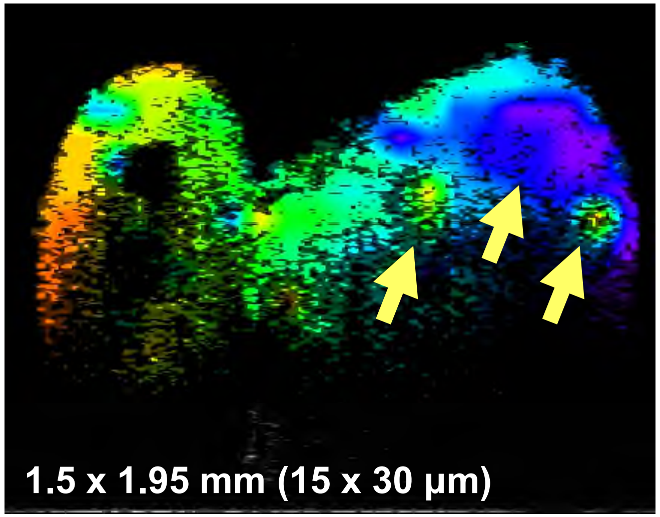
Intensity image of nerve



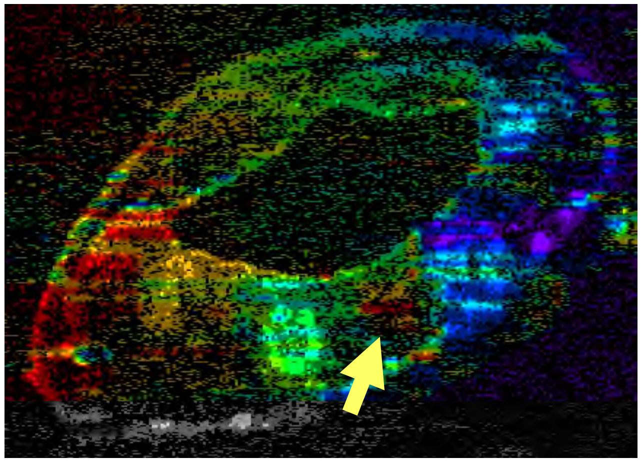
Intensity image of tadpole



Clustering image of nerve



Clustering image of tadpole



1.5 x 1.95 mm (15 x 30 μm)

Conclusions

- **OCT has shown great promise as a diagnostic tool**
- **UHR and ultra high speed systems can provide real time, dynamic and diagnostically relevant information**
- **There is still a lot to be done to confirm benefit to the patients**
  - Perform clinical studies
  - Form standards and consensus
  - Prove benefit to patients