New Innovations in Laser-Based Retinal Imaging

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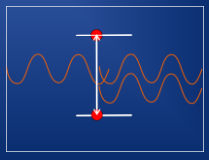
Disclosures

- Topcon, DORC, Bayer, multiple patents

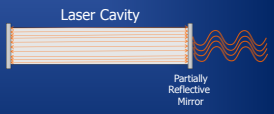
Laser

- Electrons pumped to higher energy state
- Stimulated by photon to go to lower state
- Emission of coherent photon

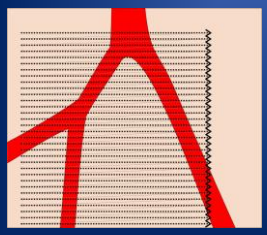


Laser

- Amplification of light through stimulated emission



Scanning Laser Ophthalmoscope



- Scanning systems have many advantages in microscopy
- Confocal imaging
- Rejection of scattered light from out of focus tissue planes

Fundus Illumination Techniques

- Flood Illumination

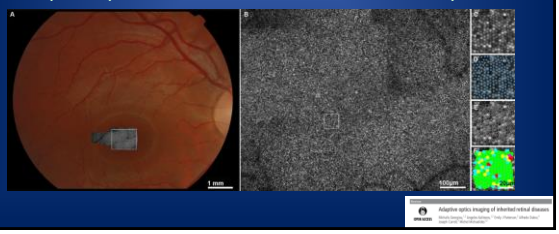
  - No spatial selection
  - Scattering not rejected

- Confocal System

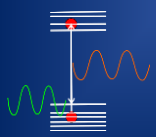
  - Spatial selection
  - Scattered light rejected

Adaptive Optics SLO

- Adaptive optics can overcome aberrations in the eye



Fluorescence Imaging

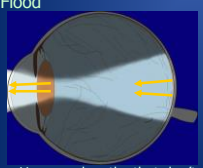


- Fluorescent dyes
  - Fluorescein
  - Indocyanine green
- Autofluorescence
  - No added fluorophores
- Learn information about health and physiology

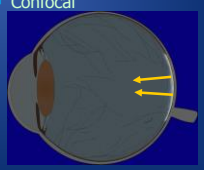
Autofluorescence Imaging

Lens Highly Autofluorescent

- Flood



- Confocal



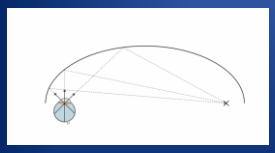
  - Use wavelengths that don't stimulate lens autofluorescence

Field of View

- Scanning Laser Ophthalmoscope
  - Various lens systems can provide 50 or more degrees of field
- System based on ellipsoidal mirror
  - 200 degrees in horizontal axis*

* Not measured the same way

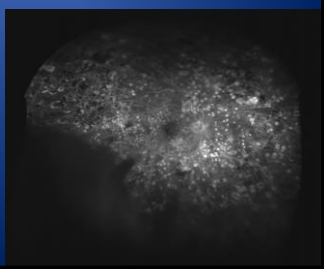
Ellipsoidal Mirror



- Oval shape with 2 foci
- Ray going through one focus will go through the second focus

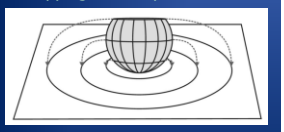
Ultrawide-Field Imaging

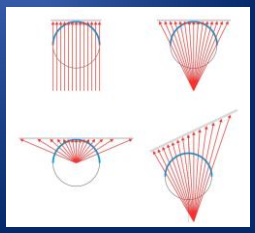
- Artifacts from lashes, nose
- Horizontal field of view larger than vertical
- Prone to significant distortions



Distortions

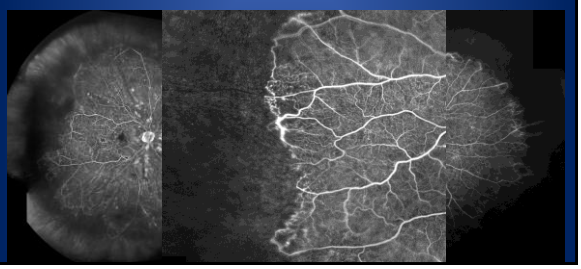
- Mapping of the Eye





PERIPHERAL AREAS OF NONPERFUSION IN TREATED CENTRAL RETINAL VEIN OCCLUSION AS IMAGED BY WIDE-FIELD FLUORESCEIN ANGIOGRAPHY

Ora to Ora Imaging

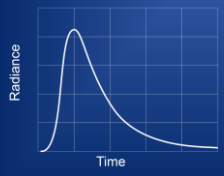


Fluorescence

- Energy added to create excited state
- Excited state can release energy
  - Emission of a photon ⟵
  - Thermal relaxation
  - Donating energy to another molecule (Forster resonance energy transfer *FRET*)

Fluorescence

After instantaneous excitation



- Exponential decay

$$I(t) = I_0 e^{-t/\tau}$$

I(t) – intensity at time t, based on initial intensity, time t, and τ is the "lifetime"

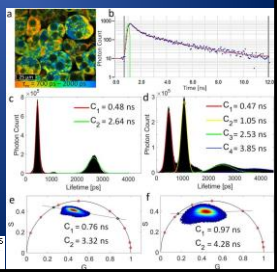
Fluorescence Lifetime Imaging

- Time domain
- Frequency domain


Biophysical Journal: Biophysical Letters

The Phasor Approach to Fluorescence Lifetime Imaging Analysis

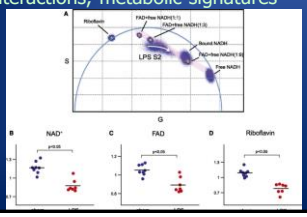
Michelle A. Digman,* Valeria R. Caiolfa,[†‡] Moreno Zamai,[†‡] and Enrico Gratton*



SCIENTIFIC REPORTS

FLI

- Possible to quantify molecular species, molecular interactions, metabolic signatures



Fluorescence Lifetime Imaging Ophthalmoscopy FLIO

- Picosecond pulsed diode laser
- Time correlated single photon measurements

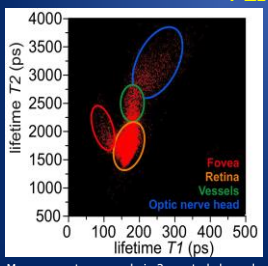
FLIO

- The eye limits our imaging parameters
- Even though there are hundreds or thousands of potential fluorophores, each with a different wavelength and relaxation time…

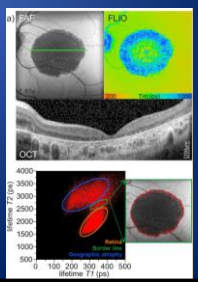

Progress in Retinal and Eye Research

Fluorescence lifetime imaging ophthalmoscopy

FLIO



Measurements are made in 2 spectral channels

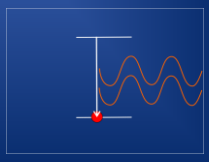


FLIO

- Pretty images
- Hard to know what they mean
  - Lots of molecules contribute to the signal – which ones?
  - What depth?

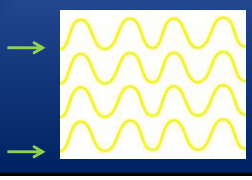
Laser-Based Ranging

- Lasers can produce coherent light output



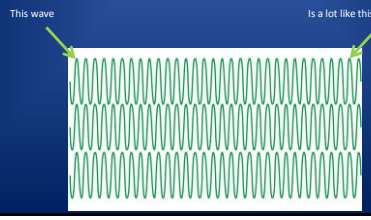
Coherence

- Spatial coherence – correlation between different light waves

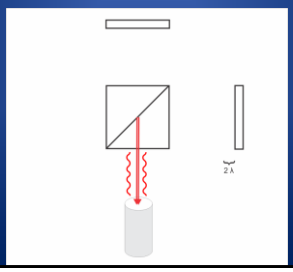


Coherence

- Temporal coherence – correlation of light waves over time

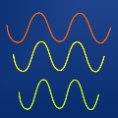


Michelson Interferometer

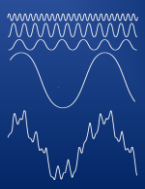


We Want to Image Structures in the Eye

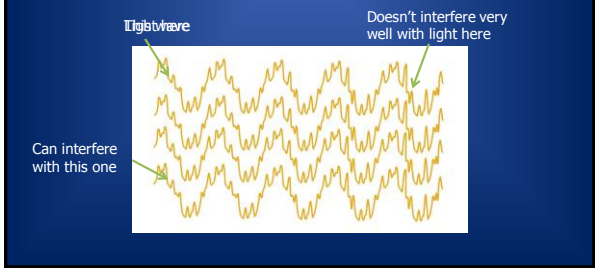
- Tricky solution
- Short coherence length light



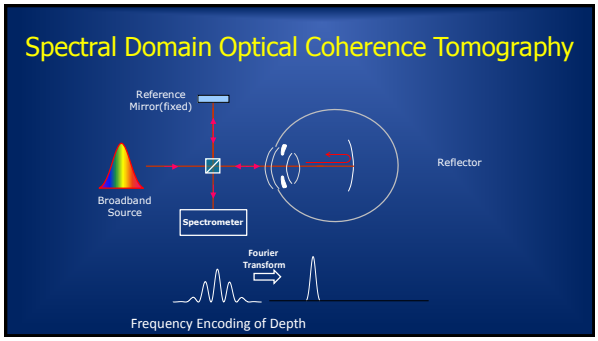
- Summation of periodic functions



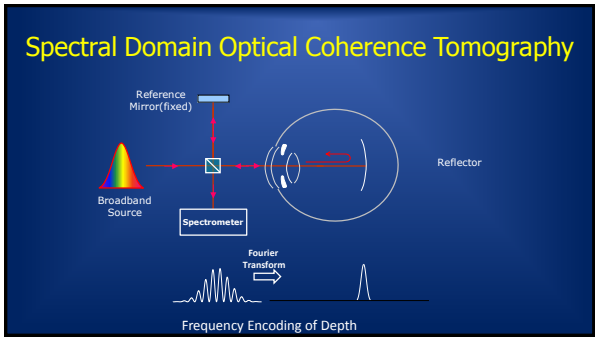
Short Coherence Length Light



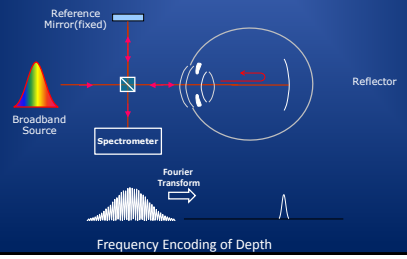
Spectral Domain Optical Coherence Tomography



Spectral Domain Optical Coherence Tomography



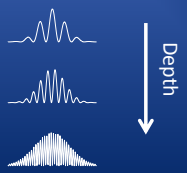
Spectral Domain Optical Coherence Tomography



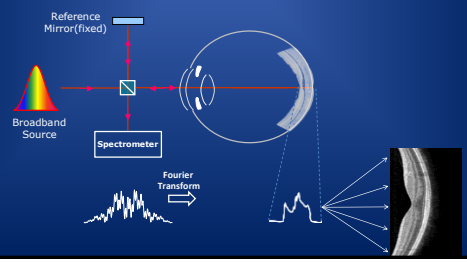
Frequency Encoding of Depth

Spectral Domain OCT

Interference Fringes



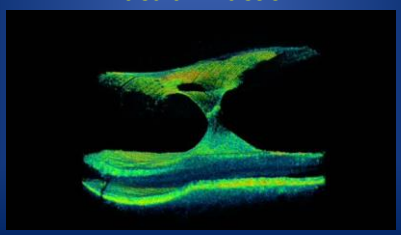
Spectral Domain OCT

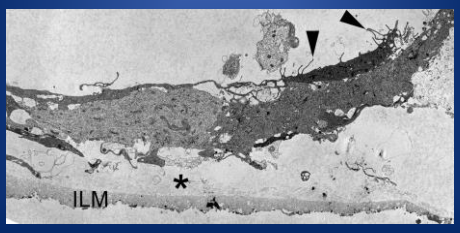


Spectral Domain Optical Coherence Tomography

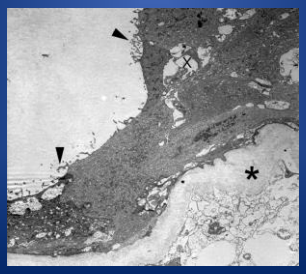
- Much higher speed than earlier time domain methods
- Improved bandwidth of light sources
- B-scan images
- Volume rendering of volume data

Posterior Vitreous Reflectivity in Vitreous Macular Traction



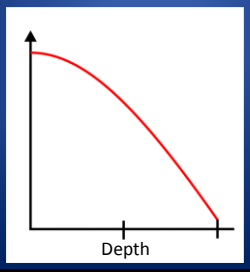


Hans Grossniklaus, MD



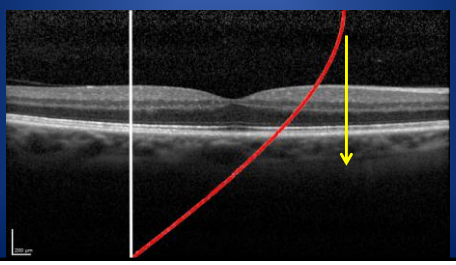
Sensitivity Fall-off with Depth

Spectral Domain

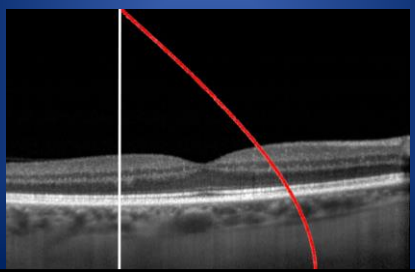


Sensitivity

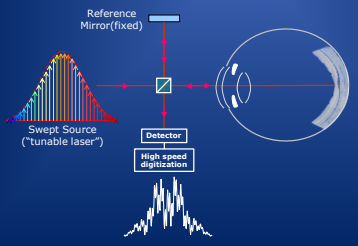
Ordinary SD-OCT



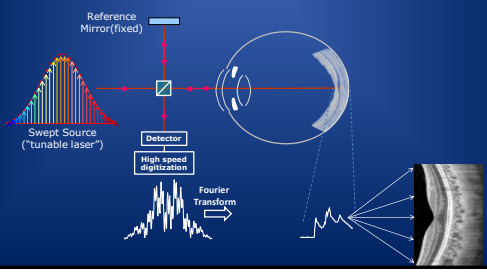
Enhanced Depth Imaging

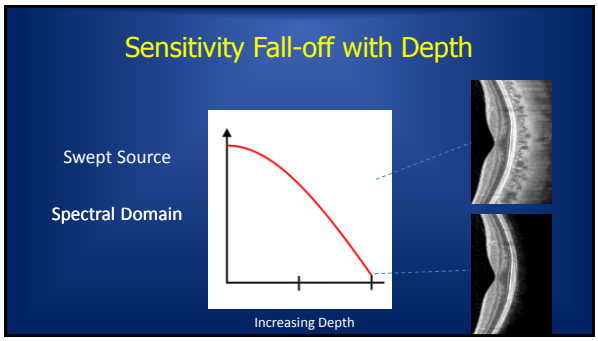


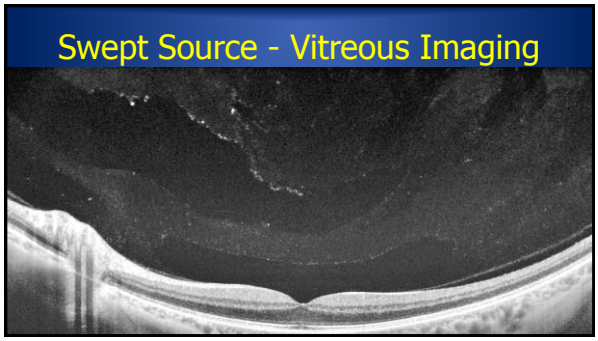
Swept Source OCT

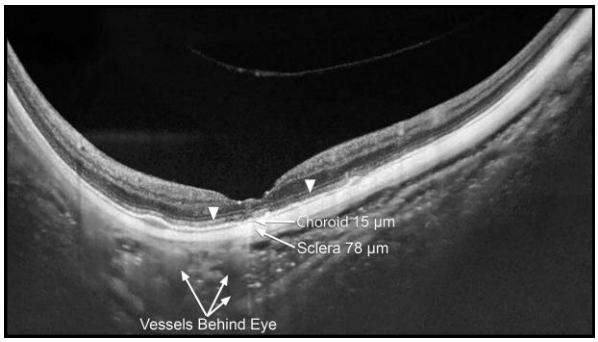


Swept Source OCT

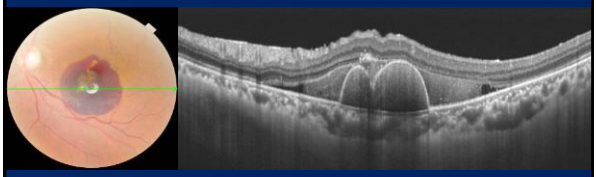



Sensitivity Fall-off with Depth
Swept Source
Spectral Domain
Increasing Depth


Swept Source - Vitreous Imaging

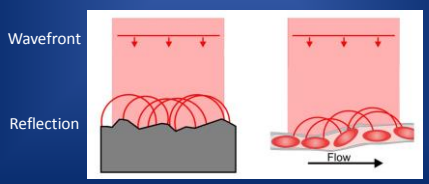

Choroid 15 µm
Sclera 78 µm
Vessels Behind Eye

Swept-Source OCT

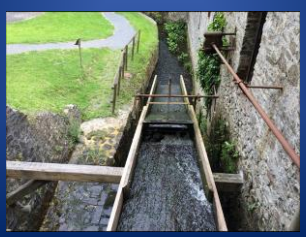


1050nm light and less roll-off in sensitivity

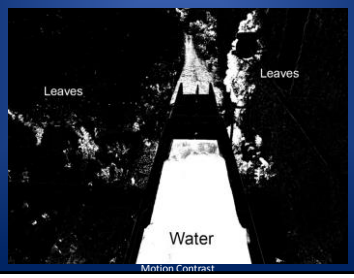
Reflection and Motion



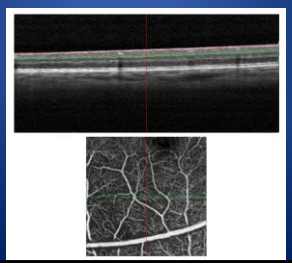
iPhone Pictures



Variance Image

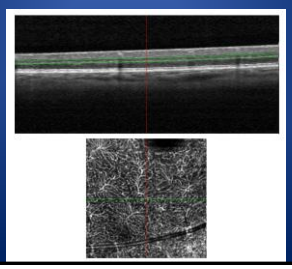


Optical Coherence Tomography Angiography



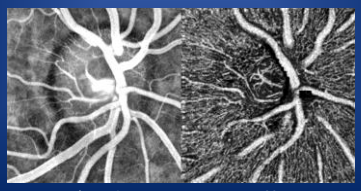
Superficial Vascular Plexus

Layer Selectivity



Deep Vascular Plexus

Radial Peripapillary Capillary Network

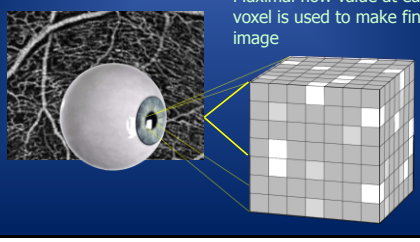


Fluorescein Angiography

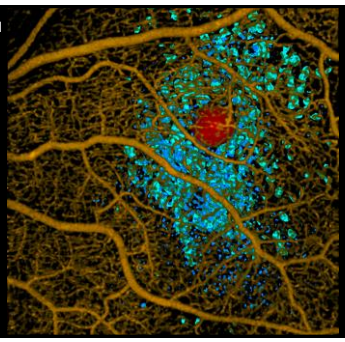
OCT Angiography

OCT Angiography

- Maximal flow value at each voxel is used to make final image



Volume rendered structural and angiographic OCT



Challenges for OCT

- Imaging the choriocapillaris
- Increasing scan speed
- Quantifying blood flow

Brief Overview

- Scanning laser ophthalmoscope
- Ultrawide field SLO
- Autofluorescence
- Fluorescence lifetime imaging
- Optical coherence tomography
- Optical coherence tomography angiography
- Methods of presenting data