Optical Coherence Tomography & Advanced Fundus Imaging

Gillian J McLellan
BVMS PhD DECVO DACVO DVOphthal
MRCVS

May 2016
Objectives

• Overview of:
  Confocal laser scanning ophthalmoscopy (cLSO)
  Optical coherence tomography (OCT)

• Theoretical Basis

• Practical Considerations
  Clinical applications
  (Research applications)
Overview

Advanced Fundus Imaging Techniques

• Non-invasive
  Potential for longitudinal evaluation

• Non-contact
  Don’t distort tissues

• Optical
  Safe (ish)

• High resolution
  “In vivo histology”
Important things to know:

• Value of multi-modal imaging approach (complementary information)
Limitations

• Not every structure is clear
• Optical clarity can be compromised by disease
  – Understand limitations of optical technologies
  – still a place for other e.g. *ultrasound* technologies
Relationship between spatial resolution and penetration depth when comparing imaging techniques

From: Smith & Chauhan
Prog Ret Eye Res 2015
Volume 44, 1–14
• Most commercial systems enable acquisition of en-face color or monochromatic fundus images

• Value of multi-modal imaging approach
  – one size does NOT fit all
Tissue-Light Interaction

Biomedical Optics
- Effect of photons on tissue
- Effect of tissue on photons
  - Absorption
  - Reflection
  - Scattering
  - Fluorescence

cLSO - Theory

- Laser projected, and light detected, as narrow beam (pinholes)

From: Girkin C
Advantages of confocal

- Allows imaging at low light intensities
- Greatly enhances contrast
- Can position illumination beam to minimize effect of opacities in ocular media
- Can be used in animals with small pupils / small eyes
cLSO use: multi-modal imaging

- Heidelberg Retinal Tomograph (HRT)
  - Used to study ONH topography in humans

- Retinal Nerve Fiber Analyzer
  - GDx / Scanning Laser Polarimeter

http://www.heidelbergengineering.com/products/hrt-glaucoma-module/
cLSO wavelength

• Light used is monochromatic
  “pseudo-color mapping” by instrument software

• Vary wavelength to:
  – Alter depth of imaging
  – Excite fluorescence (intrinsic fluorescence or dyes)
  (vary barrier filters)
Fundus Autofluorescence

• Blue laser optimally excites lipofuscin autofluorescence
• Barrier filter short wavelength cutoff at 520nm
• Intrinsic fluorescence and increased back scatter from tapetum
  — Reduces image quality
  — BUT still of value in tapetal species
Auto-fluorescence

- RPE Lipofuscin

Vitamin E Deficient Cocker Spaniel
INTRODUCTION - OCT

- Optical coherence tomography widely used in clinical ophthalmology in humans.
- OCT data recognized as an end-point in major clinical trials in macular diseases.
- Value in glaucoma diagnosis/monitoring of disease progression not yet established.
  - ONH cupping / Retinal Nerve Fiber Layer Thickness.
OCT - Theory

• “Low coherence interferometry”?! 
• Evaluates the interference pattern of back-scattered light from tissues.
• Generates multiple single-line “A-scans”
• Together these A-scans provide a cross-sectional image
• Either
  – Evaluates “time of flight” relative to a reference arm traversing known distances (time domain) 
    OR
  – Collects all light wavelengths simultaneously – each wavelength represents a different tissue depth (spectral domain)
OCT - Theory

Time Domain vs Spectral Domain

**Time Domain OCT**
- “Stratus”
- Slow acquisition (400/sec)
- Lower axial resolution
  - 10-15 microns
- Greater movement artifact
- Inaccuracies may relate to improper scan placement
- First generation OCT has been reported in dogs and cats

**Spectral Domain OCT**
- “Cirrus”, Spectralis, Optovue....
- Fast acquisition (24K->70K/sec)
- Higher axial resolution
  - 3-6 microns
- Less movement artifact
- Easier to determine precise location of scan
- Produces 3D data sets
- Also known as Fourier domain OCT
SD-OCT - 3D data sets

Images acquired with Cirrus OCT (Carl Zeiss)
OCT SIGNAL FROM TISSUE LAYERS

Combination of:
Its reflectivity AND the absorption & scattering properties of the overlying layers

**STRONG REFLECTIONS:**
Boundaries between materials of different Refractive Index
“Horizontal” alignment – e.g. corneal collagen lamellae, ILM, RNFL, RPE/Choroid, plexiform layers

**ATTENUATION:** Blood, pigment
“in vivo histology”
Anatomic correlates??

Outer retina lines – human macula

- External limiting membrane
- IS/OS junction
- COST line (cone outer segment tips)
- RPE
From: Optical Coherence Tomography as a Diagnostic Tool for Retinal Pathologies in Avian Ophthalmology

The Association for Research in Vision and Ophthalmology Copyright © 2016. All rights reserved.
OCT - Reproducibility

- Central to use of OCT in longitudinal studies
- Understand nature of artifacts that affect both qualitative and quantitative data
- Impact of age & disease processes
- Scan location
- Impact of software algorithms on data derived
Disease progression or resolution
Are you looking at the same place?

Sept 8

Sept 16

Sept 23

Jan 8
PCG cat, Siamese, 4.2 yrs, IOP=18 mmHg

Normal cat, Siamese, 3.7 yrs, IOP=16 mmHg
Success in OCT & cLSO depends on:

• Globe Immobilization, alignment, dilation
• Clear Ocular Media
• Corneal Hydration vs ocular surface desiccation
OCT - Practicalities

• Combining with other procedures?
• May affect ERG (Laser!)
• How will other procedures affect corneal integrity?
• Ensure IOP controlled if possible
Species-specific considerations

• Each species presents its own challenges!
“a hand-held scanner – a clear benefit for surgeons working with a supine six-ton elephant.”
(E. Buckland, Bioptigen)
Dogs
Optic nerve color coded thickness maps
Rabbits

• Positioning
• Unique ONH anatomy
• Lack of vascular landmarks for longitudinal studies
• Defies most automated segmentation algorithms
Rodents

- Small size!
- Very short focal length
  - Corrective lens
  - Rodent-specific attachment

Pigs

- ONH shape (poor circle fit)
- Prominent retinal blood vessels
Review of OCT limitations – scan quality

• EVALUATE DURING SCAN SESSION
• Signal strength correlates with thickness parameters (humans, cats, NHPs)
• Quality “measures” vary between instruments
  – Intensity level of signal / uniformity
  – Assess quality of signal / image “while you scan”!
Impact of Ocular disease

• Generally negative impact on scan quality:
  – Myopia, globe enlargement, axial length, high IOP
    • Shown to increase artifacts, reduce RNFL thickness and alter sectoral distribution of thickness values
  – Opacities in ocular media (corneal disease, cataract, uveitis, glaucoma related...)
  – Corneal drying
    • (KCS, exposure during scan)
Limitations of segmentation algorithms

• Proprietary software constantly changing
• Research specific algorithms
  computer assisted grading
  retinal layer boundary detection
• Labor intensive / costly to develop own methods
• Not consistent between instruments
OCT: SEGMENTATION ERRORS

• Segmentation
  – What layers are recognized and delineated?
  – Varies between manufacturers / instruments

• Segmentation Errors
  – Misidentification of outer retinal layers common
  – Inner retinal misidentification less common
Segmentation Errors – sources?

- Increase with decreasing scan quality
- Proprietary software designed for human eyes
- Increase in subalbinotic or albinotic animals?
- Off center scan angle
Limitations of Manual Measurements

- Subjective
- Labor intensive
- Inter-observer variability
- (single consistent observer?)
- Methods require validation
Multimodal Imaging benefits

Adaptive Optics (...it’s complicated)

Adaptive optics scanning laser ophthalmoscopy
Roorda, A et al, 2002 / Vol. 10, No. 9 / OPTICS EXPRESS

Carroll Lab, Medical College of Wisconsin
AO in the veterinary literature

Summary

- Recent advances in ocular imaging will:
  - Enhance understanding of pathogenesis
  - Enhance our ability to make accurate diagnoses
  - Enhance our ability to monitor progression

...mean that we can throw away our ophthalmoscopes?
Important things to appreciate:

• Value of multi-modal imaging approach
• Limitations of technology
• Image quality is paramount
• Your own limitations!
  — Technical expertise
  — Time
  — Computational ability
  — Budget!!
Carp(e) diem