Optical Coherence Tomography (OCT): Multi-Modal Imaging & Enhanced Analysis

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Disclosure Statement: Nothing to Disclose

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OCT Angiography (OCT-A)
• Non-invasive imaging
  • Assessment of blood flow
  • Three-dimensional reconstruction
### Angiography: OCT-A vs. FA or ICG

<table>
<thead>
<tr>
<th>OCT-A</th>
<th>FA or ICG</th>
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</table>
| • Non-Invasive  
• Dye-less  
• Three-dimension  
• Acquisition time ~6 seconds  
• Smaller acquisition area ranging from 2mm² to 12mm² | • Invasive intravenous dye administration  
• Dye-based  
• Fluorescein  
• Indocyanine Green  
• Acquisition time ~10 minutes  
• Wider field of view |
• Multiple B-scans of specified retina
  • Reflected signal of non-mobile tissue will be stationary, constant and unchanged
  • Moving erythrocytes within vasculature results in time-dependent backscattering of OCT signal resulting in difference over course of repeated B-scans
OCT-A Artifacts

- **Projection artifact**
  - Reflected light demonstrates decorrelation similar to blood flow
  - Artifactual images of blood vessel projected onto a deeper tissue layer

- **Ghosting**
  - Larger retinal vessels creates a shadowing artifact of deep outer retina

- **Attenuation Artifact / Masking / Shadowing**
  - Structures or opacities may resulting in an insufficient imaging signal
  - Attenuated signal to underlying structure creates an attenuation artifact (OCT-A shows poor/no blood flow despite presence of flow)

- **Motion artifact – Decorrelation of signal**
  - **White**
    - Decorrelation of signal over entire B-scan due to axial movement of the retina and choroid
    - Bulk movement
      - Patient movement (Breathing, cardiac cycle)
      - Fixation loss
      - Micro-saccade
  - **Black**
    - Loss of OCT signal to retina
    - Blink
Projection Artifact

B SCAN – Time 0

B SCAN – Time 1

INCIDENT LIGHT
REFLECTED LIGHT
INCIDENT LIGHT
REFLECTED LIGHT
INCIDENT LIGHT
REFLECTED LIGHT
INCIDENT LIGHT
REFLECTED LIGHT

BLOOD FLOW

RPE
<table>
<thead>
<tr>
<th>Vasculature Segmentation</th>
<th>Retinal Layer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial Capillary Plexus</td>
<td>Nerve Fiber Layer (NFL)</td>
</tr>
<tr>
<td></td>
<td>Ganglion Cell Layer (GCL)</td>
</tr>
<tr>
<td>Deep Capillary Plexus</td>
<td>Inner Plexiform Layer (IPL)</td>
</tr>
<tr>
<td></td>
<td>Inner Nuclear Layer (INL)</td>
</tr>
<tr>
<td>Avascular Zone</td>
<td>Outer Retina</td>
</tr>
<tr>
<td>Choriocapillaris</td>
<td></td>
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<tr>
<td>Choroid</td>
<td>Sattler’s Layer</td>
</tr>
<tr>
<td></td>
<td>Medium-sized</td>
</tr>
<tr>
<td></td>
<td>Haller’s Layer</td>
</tr>
<tr>
<td></td>
<td>Large-sized</td>
</tr>
</tbody>
</table>
## Diabetic Retinopathy

<table>
<thead>
<tr>
<th>OCT-A Imaging</th>
<th>OCT-A Not Visualized</th>
</tr>
</thead>
</table>
| - Microaneurysm (MA)  
  - Superficial capillary layer  
  - Deep retinal capillary layer  
  - Neovascularization  
  - Projection into vitreous  
  - Not obscured by leakage as in FA/ICG  
  - Retinal non-perfusion  
  - Reduced capillary density | - Microaneurysm (MA)  
  - Only ~50% of MA visualized  
  - ~50% of MA not visualized due to slow or no flow  
  - Diabetic Macular Edema (DME)  
  - OCT-A does not visualize leakage  
  - DME optimally visualized in structural OCT |
Retinal Occlusive Diseases

Vein Occlusion
- Microvascular occlusion in deep vascular plexus
- Deep vascular plexus affected more than superficial vascular plexus
- Enlarged foveal avascular zone
- Neovascularization above ILM
- Capillary nonperfusion

Artery Occlusion
- Nonperfusion in superficial vascular plexus
- Nonperfusion in deep vascular plexus
Non-Neovascular Age-Related Macular Degeneration

- Nascent geographic atrophy
  - Progression of non-neovascular age-related macular degeneration
  - Thinning RPE (Near large drusen)
  - OCT
    - Increased light transmission
    - RPE thinning overlying drusen
    - Loss of overlying ONL
  - OCT-A
    - Loss of choriocapillaris flow under drusen

- Complete loss of RPE & Outer Retina (CRORA)
  - OCT
    - Geographic atrophy
  - OCT-A
    - Choriocapillaris loss (slow flow)
    - Anterior shifting of larger choroidal vessels
Neovascular Age-Related Macular Degeneration

Choroidal Neovascular Membrane (CNVM)

<table>
<thead>
<tr>
<th>CNVM Type</th>
<th>Location</th>
<th>OCT-A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sub-RPE</td>
<td>• Vessel network between RPE &amp; Bruch’s membrane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Trunk vessels under RPE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Vessels under fibrovascular PED</td>
</tr>
<tr>
<td>2</td>
<td>Overlying RPE (Between RPE &amp; Retina)</td>
<td>• Vessel network in the avascular outer retina</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Truck vessels</td>
</tr>
<tr>
<td>3</td>
<td>Intra-Retinal</td>
<td>• Retinal Angiomatous Proliferation (RAP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• High flow vessels from middle to deep retina</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Anastomose with deep retinal capillary plexus</td>
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Choroidal Visualization
Choroidal Visualization

- Traditional Spectral Domain OCT (SD-OCT)
  - ~800nm light wavelength
    - Scattered by photoreceptors
    - Absorbed by RPE
  - Weak signal resulting in suboptimal visualization of choriocapillaris and choroid

Enhanced Depth Imaging (EDI-OCT)
- Spaide et al. (2008) moved objective lens closer to eye, inverted image and increased signal depth
- Moves objective lens of SD-OCT closer to eye
  - Light backscattered from choroid is closer to zero-delay line, increases signal depth and enhances choroidal image to the choroidal-scleral junction

Swept Source (SS-OCT)
- SD-OCT 70,000-85,000 A-scans per second
- SS-OCT 100,000 A-scans per second
- 1050nm light wavelength with deeper choroidal penetration to the choroidal-scleral junction
  - 1050nm light wavelength results in less scattering reflection by the RPE and deeper penetrance
Choroid

- Choroidal thickness greatest sub-foveal
- Sub-foveal choroidal thickness in normal eyes
  - Mean thickness: 287μm SD±76μm‡
  - Range: 262μm - 354μm‡
  - Parafoveal superior and inferior choroid in the macula region thinner than sub-foveal choroid
  - Parafoveal nasal and temporal choroid thinner than sub-foveal choroid
  - Nasal choroid thinnest, especially approaching optic nerve
- Choroidal thickness decreases with age
  - Estimated to thin 15.6μm with each decade of life
  - In individuals ≥60 years of age
    - Choroidal thins ~4-5μm per year
    - Sub-foveal choroidal thickness ~197μm

Central Serous Chorio-Retinopathy (CSCR)

- Thickened choroid
  - Increased choroidal vascular permeability – Choroidal hyperpermeability
  - Hydrostatic pressure changes
- Thinning of inner choroidal layer
<table>
<thead>
<tr>
<th>Age-Related Macular Degeneration</th>
<th>Normal Eye (Age-Matched)</th>
<th>Non-Neovascular AMD</th>
<th>Neovascular AMD</th>
</tr>
</thead>
</table>
|                                 | • Sub-foveal choroidal thickness 272μm | • Sub-foveal choroidal thickness 213μm  
• Thinner choroid associated with progression | • Sub-foveal choroidal thickness 195μm  
• EDI-OCT or SS-OCT may visualize neovascularization of the back surface of RPE in PED |
Polypoidal Choroidal Vasculopathy (PCV)

- Increased sub-foveal choroidal thickness ranging (80μm - 210μm)
- Increased choroidal thickness may be associated with
  - Increased diameter of choroidal vessel lumen
  - Choroidal vessel dilation
- Decreased choroidal thickness following photodynamic therapy (PDT)
Increased Choroidal Thickness

- Central serous chorio-retinopathy
- Polypoidal choroidal vasculopathy

Decreased Choroidal Thickness

- Macular degeneration
- Myopia
- Diabetic retinopathy
- Retinitis pigmentosa
Sclerochoroidal Calcification

- Uncommon
- Clinical presentation
  - Yellow-white sub-retinal lesions
  - Typically in the superior temporal mid-peripheral fundus
  - Elevated lesion with overlying RPE atrophy
- EDI-OCT or SS-OCT
  - Calcified mass in sclera
  - Displaces choroid inward with choroidal compression
Choroidal Lesions

**Choroidal Nevus**
- Intact choroid vascular spaces
- Nevus hyper-reflectivity

**Choroidal Melanoma**
- Loss of choroid vascular spaces
- Choriocapillaris compression
- Shaggy photoreceptors
- Intra- and sub-retinal fluid

**Choroidal Metastasis**
- Loss of choroid vascular spaces
- Possible choriocapillaris compression
- Shaggy photoreceptors
- Intra- and sub-retinal fluid
Fundus Auto-Fluorescence (FAF)
Fundus Auto-Fluorescence (FAF)

- FAF utilizes short-medium wavelength of light to detect lipofuscin accumulation
- Lipofuscin → Byproduct of phagocytized outer segment of photoreceptors
- Lipofuscin accumulates in RPE
- Lipofuscin represents a biomarker of
  - Normal aging
  - Chronic retinal disease
- Lipofuscin deposition in RPE may precede clinical / visual manifestations
• Normal ocular fundus
  • Normal RPE function
  • Mildly hyperfluorescent due to normal levels of lipofuscin in RPE cells
• ONH
  • Absence of RPE
  • Absence of lipofuscin
  • Hypofluorescent
• Retinal vasculature
  • Hypofluorescent
  • Signal absorption by blood
• Fovea
  • Hypofluorescent
  • Signal absorption by high density of macular luteal pigment
### FAF Abnormal

<table>
<thead>
<tr>
<th>Hypofluorescent (Dark)</th>
<th>Hyperfluorescent (Bright)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- RPE atrophy</td>
<td>- Increased Lipofuscin</td>
</tr>
<tr>
<td>- Retinal hemorrhages</td>
<td>- Best</td>
</tr>
<tr>
<td>- Exudation</td>
<td>- Stargardt</td>
</tr>
<tr>
<td>- Pigmentation</td>
<td>- Old hemorrhages</td>
</tr>
<tr>
<td>- Hard drusen</td>
<td>- Soft drusen</td>
</tr>
</tbody>
</table>
Hydroxychloroquine (Plaquenil®)

American Academy of Ophthalmology Guidelines

2002
- Dilated fundus exam
- Automated VF 10-2
- Color vision
- Optional:
  - mfERG
  - FA

2011
- Dilated fundus exam
- Automated VF 10-2
- 1 of the following:
  - SD-OCT
  - mfERG
  - FAF

2016
- Considers risk of toxicity
- Baseline
- At 5 years
- Annual screening:
  - Automated VF 10-2
  - SD-OCT
- Additional screening:
  - mfERG
  - FAF
- Geographic atrophy → Atrophic AMD
  - Atrophic retina has absence of RPE and lipofuscin
  - Atrophic area demonstrates hypo-fluorescence (decreased intensity) with high contrast to surrounding non-atrophic retina
Fundus Autofluorescence

- Geographic atrophy in non-neovascular AMD
  - Hypofluorescent (Dark)
  - Hyperfluorescent junctional zone (Bright banded surround)
    - Compromised RPE (prior to cell death)
    - Impaired RPE not supportive of photoreceptor outer segment
    - Junctional zone indicative of geographic atrophy progression
- Fundus Autofluorescence in Age-Related Macular Degeneration (FAM) Study
  - Clinical fundus appearance may NOT correlate with FAF imaging
  - FAF may be indicative of disease progression not clinically visible
Fundus Autofluorescence (FAF)

- Non-Invasive Retinal Imaging Modality
- Utilizes naturally occurring fluorophores to produce brightness map of retina

- **Infers Functional Status**
  - Images Lipofuscin and Melanin
  - Biomarker for cellular aging and oxidative cell damage
  - Gain health knowledge of photoreceptor-RPE complex
Fundus Autofluorescence Image

- Hyperfluorescence
  - Excess Accumulation of Lipofuscin = increased oxidative stress
- Hypofluorescence
  - Loss of RPE and overlying photoreceptors = Metabolic INactivity
CSLO Imaging FAF

**PROS**
- Optics reduce light detection to single plan
  - Eliminates interference from media
- Averages 9-16 images
  - High Contrast
  - High Resolution
- More reliable quantification of macular pigment density
- Multi-mode imaging capability*

**CONS**
- Image averaging can negatively impact quality
  - Poor fixation/eye mvmt
- Conflicts with FA
Clinical Implications for OCT FAF

- Macular Pathology
  - Exudative AMD
  - Non-Exudative AMD
  - Vitelliform Dystrophies
  - Central Serous Chorioretinopathy

- Drug Toxicity/Maculopathy
  - Tamoxifen
  - Hydroxychloroquine

- Retinal Dystrophy/Degeneration
  - Retinitis Pigmentosa

- Retinal Inflammatory Conditions
  - White-Dot Syndromes

- Ocular Malignancy
  - Choroidal Melanoma

- Optic Nerve Pathology
  - Optic Disc Drusen
  - Glaucoma
Ganglion Cell Analysis (GCA)
Retinal Labeled Layers (Image zoomed to ~15°)

 GCC

 Blood Vessels

 Temporal Nerve Fiber Layer

 Choroid

 Nerve Fiber Layer
 Ganglion Cell Layer
 Inner Plexiform Layer
 Inner Nuclear Layer
 Outer Plexiform Layer
 Outer Nuclear Layer

 External Limiting Membrane
 Inner Photoreceptor Segm.
 Inner / Outer Photoreceptor Segm.
 Outer Photoreceptor Segm.
 RPE Interdigitation
 RPE / Bruch’s Membrane Complex
GCC:
Background

Ganglion Cell & Perimetry
- **50%** of rNFL may be lost before perimetric defects present
- 20% loss of ganglion cells = 5 dB VF loss
- 40% loss = 10 dB VF loss
- **10% or fewer axons may remain in cases with Severe VF loss**

Ganglion Cell Allocation
- 50% of all retinal ganglion cells confined to macular region
GCA Comparison

**RTVue**
- RTVue (Optovue) GCC analysis
  - Macular analysis segments the GCC from the remaining retinal layers.
  - Measures GCC thickness
    - 7 mm² area
    - centered 1 mm temporal to the fovea
  - Provides a color coded GCC thickness map
  - Normative Database
    - Age 18-84
    - Ethnically Diverse
    - Applies to:
      - rNFL
      - GCA
      - Macular Thickness Scans

**Cirrus OCT**
Annulus measured within the macular region
- Centered on Fovea
- Corresponds to thickest concentration of GCL
Analysis:
- Sectoral thickness measurements
- Deviation Map
- Thickness Map
*Normative Database*

**Spectralis OCT**
Measures total retinal macular thickness
- 25-30 degree volume scan
- Centered over fovea
Analysis
- Hemispheric asymmetry
- Mean thickness
- Color coded thickness map
- Asymmetry Analysis
- OD/OS
Clinical Applications -- GCC

- Optic Nerve Disease
  - Glaucoma
  - Optic Neuropathies

- Retinal Vasculopathies
  - Currently being researched
  - Diabetic change
  - Hypertensive change

- Retinal Dystrophies
  - Rod/Cone
  - RP