OCT angiography of ONH blood flow in glaucoma

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Financial Interests:
Dr. D. Huang has a significant financial interest in Optovue, a company that may have a commercial interest in the results of this research and technology. This potential individual conflict of interest has been reviewed and managed by OHSU.
Optovue, Inc.: stock options, patent royalty, grants, speaker honorarium & travel support
Carl Zeiss Meditec, Inc.: patent royalty

Ultrahigh-Speed Swept-Source OCT

Developed by MIT Optic & Quantum Electronic Group (Fujimoto) and OHSU Center for Ophthalmic Optics and Lasers (Huang)

Performance features:
• 100,000 axial scans/sec
• 1050 nm tunable laser (deep penetration)
• 5.3 µm axial resolution in tissue

Experimental System - Not FDA-approved

Potsaid B, et al., Optics Express 2010; 18:20029
OCT captures tissue function as well as structure

<table>
<thead>
<tr>
<th>Signal</th>
<th>Information</th>
<th>En Face</th>
<th>Cross Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflectance</td>
<td>Anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doppler shift</td>
<td>Total retinal blood</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>flow (global</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>circulation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decorrelation</td>
<td>Angiography</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(local circulation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OCT ANGIOGRAPHY

Split-Spectrum Amplitude Decorrelation Angiography (SSADA) with Ultrahigh-Speed OCT

David Huang, MD, PhD  www.COOLab.net
Aim: Quantitative Angiography of the Optic Nerve Head, Retina, Choroid

- Non-invasive
- No exogenous contrast needed
- Quantitative
- Not sensitive to incidence angle variation
- Accurate over a wide range of reflected signal strength
- Reproducible
- Able to detect early glaucoma from normal

David Huang, MD, PhD www.COOLLab.net

OCT amplitude-decorrelation angiography uses intrinsic contrast – no dye injection!

Problem: 8 frames at one position do not provide sufficient angiography quality
Solution: Split-Spectrum Amplitude Decorrelation (SSADA) Algorithm

8 frames at one position now provides good angiography quality

Intentional lowering of OCT resolution to optimize flow detection

More channels of flow information
Less axial motion noise

Orbital pulsation $$\rightarrow$$ Z motion
Blood flow $$\rightarrow$$ X, Y motion
More sensitive to noise than flow

Yali Jia, PhD, David Huang, MD, PhD www.COOLLab.net
**SSADA** improves signal to noise ratio of flow detection


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**En face Projection Angiogram**

Yali Jia, PhD, David Huang, MD, PhD [www.AIGStudy.net](http://www.AIGStudy.net)
Comparison of Angiography Algorithms

More continuous microvascular network

More continuous microvascular network

Less Noise

Less Noise

>2x SNR

>2x SNR

Full-Spectrum Amplitude Decorrelation

Split-Spectrum Amplitude Decorrelation

Split-Spectrum Amplitude Decorrelation


Retinal/ONH and choroidal circulation can be separately projected

Retinal/ONH and choroidal circulation can be separately projected

Yali Jia, PhD,
David Huang, MD, PhD
www.AIGStudy.net

Fast axis
(200 axial scans)

Retina

ONH

Lamina Cribrosa

Choroid

Maximum Decorrelation Projection

Retina

ONH

Choroid
Motion error can be removed with 3D registration of x-fast and y-fast scans

3D OCT angiography of central macula

SSADA algorithm used

3x3x3 mm OCT 3D angiography acquired in a 3-second scan
3D OCT angiography of optic nerve head


OCT Angiography of the Optic Nerve Head – Layer by Layer

Quantitative angiography: measurement areas

Flow Index was reduced in ONH, but not macula or peripapillary retina/choroid

<table>
<thead>
<tr>
<th>Area</th>
<th>Normal (N=6)</th>
<th>Glaucoma + Suspect (N=6)</th>
<th>P-value (Wilcoxon)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONH – Whole Disc</td>
<td>0.159 ± 0.020</td>
<td>0.108 ± 0.013</td>
<td>0.008</td>
</tr>
<tr>
<td>ONH – Temporal Ellipse</td>
<td>0.151 ± 0.014</td>
<td>0.072 ± 0.022</td>
<td>0.005</td>
</tr>
<tr>
<td>Peripapillary Retina</td>
<td>0.141 ± 0.023</td>
<td>0.122 ± 0.024</td>
<td>0.191</td>
</tr>
<tr>
<td>Peripapillary Choroid</td>
<td>0.226 ± 0.016</td>
<td>0.168 ± 0.071</td>
<td>0.105</td>
</tr>
<tr>
<td>Macular Retina</td>
<td>0.120 ± 0.017</td>
<td>0.112 ± 0.039</td>
<td>0.819</td>
</tr>
<tr>
<td>Macular Choroid</td>
<td>0.213 ± 0.019</td>
<td>0.189 ± 0.025</td>
<td>0.173</td>
</tr>
</tbody>
</table>

Flow index (dimensionless)
Pilot Study Subject Characteristics

- **Normal**
  - 20 eyes of 20 subjects
  - Age: 50 ± 9 years (mean ± SD)

- **Glaucoma**
  - 10 eyes of 10 subjects
  - 6 perimetric glaucoma, 3 pre-perimetric glaucoma, 1 suspect (ocular hypertension)
  - Age: 66 ± 10 years

Repeatability & Reproducibility

<table>
<thead>
<tr>
<th>ONH Region</th>
<th>Scan Set</th>
<th>Intra-Visit Repeatability (n = 3)</th>
<th>Inter-Visit Reproducibility (n = 3)</th>
<th>Inter-Subject Variability (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Disc</td>
<td>2(1X), 2(1Y)</td>
<td>1.2%</td>
<td>9.1%</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>2(1X1Y)</td>
<td>1.2%</td>
<td>8.7%</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>1(2X2Y)</td>
<td>1.1%</td>
<td>6.6%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Temporal Ellipse</td>
<td>2(1X), 2(1Y)</td>
<td>1.7%</td>
<td>9.5%</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>2(1X1Y)</td>
<td>1.9%</td>
<td>11.6%</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>1(2X2Y)</td>
<td>1.8%</td>
<td>8.5%</td>
<td>7.4%</td>
</tr>
</tbody>
</table>

Less variable than OCT NFL measurement!
Glaucoma reduced ONH flow index

Glaucoma caused a -19% drop in whole disc and -24% drop in temporal ellipse

OCT Angiography Showing Reduced ONH Blood Flow in Pre-Perimetric Glaucoma

Normal (OS)

Preperimetric Glaucoma (OS)

Disc flow index = 0.159

Disc flow index = 0.125
**ONH flow index vs. visual field**

![Graph showing the relationship between ONH flow index and visual field (VF) with different markers for Glaucoma and Suspect groups.](image)

<table>
<thead>
<tr>
<th>VF</th>
<th>MD</th>
<th>PSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Disc</td>
<td>0.60</td>
<td>-0.81</td>
</tr>
<tr>
<td>Temporal Ellipse</td>
<td>0.64</td>
<td>-0.80</td>
</tr>
</tbody>
</table>

**Difference between normal and glaucoma not due to age, c/d ratio or rim area**

![Graphs showing the difference in ONH flow index between normal, glaucoma, and suspect groups across age, c/d area ratio, and cSLO rim area.](image)
Conclusions

• ONH microcirculation is reduced in glaucoma
• Pre-perimetric changes can be detected by quantitative OCT angiography
• Whole disc flow index can be measured with 6.6 % reproducibility and 1.2 % repeatability
• OCT angiography with the SSADA algorithm may be a useful new tool in the evaluation of glaucoma

OCT Angiography (SSADA) v. Fluorescein/ICG Angiography

OCT Advantages
• 3 dimensional
  – Easily separates disc, retinal, and choroidal circulations
  – Sections & projections along any plane
• Quantitative
  – Flow index
• No injection
  – No vomiting or anaphylactic reaction

OCT Disadvantages
• Small field (3 mm)
  – Field will increase with higher speed
• No visualization of leakage and stain
  – But can visualize fluid space and thickening
Applications of OCT Angiography & Doppler OCT

- Diabetic Retinopathy:
  - Assess capillary dropout & macular ischemia
  - Visualize Neovascularization in 3D
  - Evaluate global reduction in blood flow
- Age-related Macular Degeneration
  - Assess choroidal ischemia
  - See flow in choroidal neovascular membrane
- Glaucoma
  - Evaluate global reduction in blood flow
  - Evaluate reduced disc perfusion
- Inherited Retinal Diseases
  - Evaluate macular ganglion cell function
- Diagnosis, prognosis, tracking, assessing treatment effectiveness

David Huang, MD, PhD  www.AIGStudy.net
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www.COOLLab.net