Glaucoma Detection using High-speed, High-resolution Fourier Domain Optical Coherence Tomography

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Financial Disclosure

- The author acknowledges no financial interest.
Pathology of Glaucoma

- Loss of retinal ganglion cells (RGCs) and their axons (RNFL)
- Glaucomatous damage to RNFL precedes functional loss by up to 5 years


Circumpapillary Nerve Fiber Layer (cpRNFL)

Optic Nerve Head

Macular Thickness

Looking for Glaucoma in the Macula

- RGCs and RNFL make up about 30-35% of macular thickness, where ganglion cells are most concentrated
  - RGC bodies are 10 to 20 times the diameter of their axons
  - RGC layer is more than one cell layer thick in macula (cell density up to 4-6 cell bodies thick)

Looking for Glaucoma in the Macula

• In glaucoma, loss of RGCs also occur at the posterior pole

• Experimental glaucoma studies showed substantial loss of RGCs in zone surrounding fovea


Using Macular Thickness for Glaucoma

• Reduced macular thickness can be used as a measure of glaucoma

• Visual function correlates with macular thickness

**OCT Circumpapillary vs. Macular Mapping**

- cpRNFL thickness measurements outperform macular thickness in terms of magnitude of association with visual function


**Problem using Macular Thickness for Glaucoma**

- Macular thickness represents *total* retinal thickness
  - Reduced macular thickness in glaucoma mainly due to RGC and RNFL loss
  - So, 65-70% macular thickness unchanged in glaucoma
- Retinal structures other than RGC confound the data so that the macular thickness not as sensitive as cpRNFL thickness measurement
Macular Thickness for Glaucoma

- Crucial to differentiate retinal layers so that only layers affected by glaucoma be measured for glaucoma discrimination

OCT Retinal Layer Segmentation

- Inner retinal complex thickness equal to cpRNFL for glaucoma detection
  - But, only 65% of glaucomatous eyes had good SNR to perform segmentation on Stratus OCT

Tan O, Huang D. et al., ARVO e-abstract, 2005
At first, OCT was slow. Now: A generational leap.

FD-OCT (RTVue) has 65x speed & 2x resolution of TD-OCT (Stratus).

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Macular Segmentation with Optical Coherence Tomography

Hiroshi Isikawa,¹,²  Daniel M. Stein,¹  Gadi Wollstein,¹,²  Siobahn Beaton,¹,²  James G. Fujimoto,³  and Joel S. Schuman¹,²


“...two approaches to minimize these factors [speckle noise and uneven tissue reflectivity]: higher resolution, and improved signal quality (signal-to-noise ratio).”
Simultaneous 2048 pixels at a time

Sequential 1 pixel at a time

Small blood vessels
IS/OS
Choroidal vessels

1024 A-scans in 0.04 sec
Higher speed, higher definition and higher signal.

512 A-scans in 1.28 sec
Motion artifact

Slow OCT undersamples the macula

Spoke pattern misses info between each linear scan (up to 1.6 mm space between spokes)
6 lines, 768 A-scans, 1.9 sec
High speed improves macular mapping

5 mm grid
34 lines
19,496 A-scans
0.78 sec

Purpose

- To evaluate the newly developed Fourier-domain optical coherence tomography in glaucoma detection
Study Design

• **AIGS is a large, multi-center, prospective, longitudinal trial to develop and use advanced imaging technologies to improve the detection and management of glaucoma**
  - David Huang MD PhD (Director)
  - www.AIGStudy.net

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Study Design

• **AIGS cross-sectional cohort**

  • 30 Normal eyes
    - Absence of glaucomatous optic nerve
    - Absence of risk factors for glaucoma
    - Absence of VF defects

  • 31 perimetric Glaucoma eyes
    - Characteristic optic nerve head abnormalities
    - Glaucomatous VF defects
Methods:
Circumpapillary and macular scans

Stratus OCT, Zeiss Meditec
400 A-scan per-second
9-10 micron axial resolution

RTVue FD-OCT, OptoVue
26,000 A-scan per-second
5 micron axial resolution

Methods:

Stratus FMTM 6mm radial

Stratus TD-OCT
9-10 µ axial resolution; 400 axial scans / sec

FMTM vertical scan, center at fovea,
128 a-scan, take 0.3s

RTVue MM7 7mm rectangular

RTVue FD-OCT
5 µ axial resolution; 26,000 axial scans / sec

MM7 vertical scan, center at fovea, 933 a-scan, take 0.035s
Inner Retinal Layers Preferentially Affected by Glaucoma

**Inner Retinal Layer (IRL)**

**Ganglion cells:**
- **Axons** = nerve fiber layer
- **Body** = ganglion cell layer
- **Dendrites** = inner plexiform layer

*Perform Retinal Layer Segmentation on all eyes*

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**Results:**

*Average Thickness reduced in cpRNFL, Retina, IRL in Glaucoma*

<table>
<thead>
<tr>
<th></th>
<th>cpRNFL</th>
<th>Retina</th>
<th>IRL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean ± SD</strong></td>
<td><strong>Mean ± SD</strong></td>
<td><strong>Mean ± SD</strong></td>
<td><strong>Mean ± SD</strong></td>
</tr>
<tr>
<td>Normal TD-OCT</td>
<td>Glaucoma TD-OCT</td>
<td>Normal FD-OCT</td>
<td>Glaucoma FD-OCT</td>
</tr>
<tr>
<td>cpRNFL L</td>
<td>100.3 ± 8.6</td>
<td>76.0 ± 13.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Retina</td>
<td>245.6 ± 12.1</td>
<td>224.5 ± 14.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IRL</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

*mean ± standard deviation, p = p-value*
**Results:**

*Reduced Average IRL Thickness maps in Glaucoma*

Normal | Glaucoma

**Results:**

*Fractional Macular IRL Thickness Loss Map*
### Results:

**FD-OCT Capability for Glaucoma Discrimination**

<table>
<thead>
<tr>
<th></th>
<th>Stratus OCT</th>
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<th>FD-OCT</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>AROC</td>
<td>SE</td>
<td>AROC</td>
<td>SE</td>
</tr>
<tr>
<td>cpRNFL</td>
<td>0.94</td>
<td>0.04</td>
<td>0.90</td>
<td>0.04</td>
</tr>
<tr>
<td>Retina</td>
<td>0.87</td>
<td>0.06</td>
<td>0.90</td>
<td>0.05</td>
</tr>
<tr>
<td>IRL</td>
<td>n/a</td>
<td>n/a</td>
<td>0.96</td>
<td>0.02</td>
</tr>
<tr>
<td>cpRNFL + IRL</td>
<td>n/a</td>
<td>n/a</td>
<td>0.97</td>
<td>0.02</td>
</tr>
</tbody>
</table>

### Discussion

- *Fourier-domain OCT (RTVue)* offers faster speed and higher resolution in-vivo retinal scans compared with Time-domain OCT (Stratus)
Discussion

• **Like** Stratus TD-OCT, the *Fourier-domain OCT* demonstrated the ability to differentiate glaucoma from normal eyes using cpRNFL thickness measurements.

Discussion

• **Unlike** Stratus TD-OCT, *retinal segmentation analysis* with Fourier-domain OCT allowed determination of macular inner retinal layer thickness in all eyes.
  
  • Demonstrated ability to objectively quantify damage to RGCs and RNFL to discriminate between glaucomatous and normal eyes.
Conclusions:

Enhanced Glaucoma Detection using FD-OCT Macular Mapping

Early results from our ongoing prospective study shows that macular IRL thickness provided by Fourier-domain OCT can serve as an additional parameter for detection of glaucoma and may complement the cpRNFL thickness measurement for glaucoma discrimination.

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  - “Advanced Imaging for Glaucoma” www.AIGStudy.net
- Carl Zeiss Meditec, Inc.

MT = Macular Thickness
IRL = Inner Retinal Layer
cpRNFL = circumpapillary RNFL