The dynamic structure-function model: A new approach to monitor glaucoma progression

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OMICS International Conferences on Eye Disorders and Treatment
July 15, 2015
Overview

• Glaucoma progression
• A new model to detect and monitor glaucoma progression
Background

• “Glaucoma” stands for a family of disease
• Primary open-angle glaucoma (POAG) is the most common form of the disease
• If left untreated, POAG can lead to blindness
• While there is no cure, treatment can prevent further damage from occurring
• Early detection of POAG is therefore crucial
But is early detection enough?

• Or should efforts also focus on early detection of progression?

• Decisions based on the presence of progression:
  • To treat or not to treat
  • How aggressive to be with the treatment
Age, life expectancy and risk of progression
How do we detect progression?

- Structural changes:
How do we detect progression?

• Functional changes:
How should we detect progression?

• There are several structural and functional tests available
• For each test, there are several different parameters/indices to choose from
• It would be easy if:
  1. All tests/parameters yielded similar findings
  2. If all patients progressed in the same manner
1. Similar findings on all tests

- The correlation between structure and function is relatively weak

2. Progression similar in all patients

- Depending on the patient, change can be detected in structure or function

<table>
<thead>
<tr>
<th></th>
<th>OHTS</th>
<th>EGPS</th>
<th>EMGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure 1st</td>
<td>55%</td>
<td>40%</td>
<td>1%</td>
</tr>
<tr>
<td>Function 1st</td>
<td>35%</td>
<td>60%</td>
<td>86%</td>
</tr>
<tr>
<td>S + F together</td>
<td>10%</td>
<td>0%</td>
<td>13%</td>
</tr>
</tbody>
</table>

Zangwilll, J Curr Glaucoma Prac, 2008
Progression differs in different patients

<table>
<thead>
<tr>
<th></th>
<th>Chauhan</th>
<th>Kamal</th>
<th>Artes</th>
<th>Strouthidis</th>
<th>Girkin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Structure only</strong></td>
<td>40%</td>
<td>29%</td>
<td>17 - 42%</td>
<td>9 - 21%</td>
<td>13 - 32%</td>
</tr>
<tr>
<td><strong>Function only</strong></td>
<td>4%</td>
<td>5%</td>
<td>17 - 42%</td>
<td>15 - 20%</td>
<td>0 - 6%</td>
</tr>
<tr>
<td><strong>S + F</strong></td>
<td>29%</td>
<td>8%</td>
<td>4 - 19%</td>
<td>3 - 12%</td>
<td>15 - 34%</td>
</tr>
<tr>
<td><strong>No progression</strong></td>
<td>27%</td>
<td>59%</td>
<td>58 - 83%</td>
<td>46 - 73%</td>
<td>47 - 53%</td>
</tr>
</tbody>
</table>
A change of perspective...
A change of perspective

• If structure and function provide different information, and
• If progression can be detected by different means in different patients,
• Then using structural and functional data jointly should improve our ability to detect progression
The Dynamic Structure-Function Model

• The dynamic structure-function (DSF) model uses structural and functional data jointly over time to monitor glaucoma progression

• Makes no assumption about the nature of the associations between structure and function (e.g. linear or non-linear)

• Is individualized
Dynamic Structure-Function Model for Glaucoma Progression

- Centroids: current state of the disease
Centroids

![Centroid plot](image)
Dynamic Structure-Function Model for Glaucoma Progression

- **Centroids**: current state of the disease
- **Velocity vectors**: trend of change of the centroids over time
Descriptive velocity vector

![Graph showing sensitivity and rim area]
Descriptive velocity vector

![Graph showing sensitivity and rim area as percentages of normal.](image-url)
Predictive velocity vector
Prediction accuracy of the DSF

• 220 eyes with ocular hypertension or primary open-angle glaucoma from:
  • Diagnostic Innovations in Glaucoma Study
  • African Descent and Glaucoma Evaluation Study

• Each eye had 11 longitudinal visits with pairs of:
  • Rim area (RA) (Heidelberg Retinal Tomograph)
  • Mean sensitivity (MS) (Standard Automated Perimetry)
Methods

- We predicted the 11\textsuperscript{th} pair from:
  - The first 10 pairs

- We predicted the 10\textsuperscript{th} pair from:
  - The first 9 pairs

- We compared the prediction accuracy of the DSF model to that obtained using Ordinary Least Square Linear Regression (OLSLR) using the Wilcoxon signed-rank test
Prediction accuracy of the DSF model

- DSF has better PE than OLSLR in short series
- DSF has similar PE than OLSLR in longer series

Hu et al, IOVS, 2014
Example 1: DSF has better PE in short series

Subject 3 (OD): prediction visit 7

Subject 3 (OD): prediction visit 9

Hu et al, IOVS, 2014
Example 2: DSF has worse PE than OLSLR

Hu et al, IOVS, 2014
Why does the DSF model perform better when short series are used?

• The use of centroids make the DSF model relatively conservative

• This effect increases when:
  • Longer series are used
  • Progression occurs

• Even though the DSF model is conservative, overall, it has better prediction accuracy than OLSLR in short series in progressing eyes
DSF validated in independent dataset

(a) DIGS and ADAGES dataset
(b) OHTS dataset

Bauchle et al, ARVO, 2015
DSF compared to a Bayesian model

(a) DIGS and ADAGES dataset

(b) OHTS dataset

Racette et al, WGC, 2015
Conclusion and future direction

• Detecting glaucoma progression is challenging
• The DSF model shows promising initial results
• Future work will focus on assessing:
  • the sensitivity and specificity of the model (using permutation analysis)
  • The impact of including more than 2 tests/parameters
Collaborators

Iván Marín-Franch, PhD

Rongrong Hu, MD
Financial disclosures:  
None

Funding sources:

DIGS & ADAGES: U10EY14267, EY019869, EY08208, EY11008, and EY13959

OHTS: grants EY09341, EY09307, Horncrest Foundation, awards to the Department of Ophthalmology and Visual Sciences at Washington University, the NIH Vision Core Grant P30 EY02687, Merck Research Laboratories, Pfizer, Inc., White House Station, New Jersey, and unrestricted grants from Research to Prevent Blindness, Inc., New York, NY

Racette Lab: BrightFocus Foundation, IUPUI DRIVE award, Glaucoma Research Foundation, unrestricted award from Research to Prevent Blindness, Indianapolis, IN
Thank you!