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

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Overview

- Glaucoma progression
- A new model to detect and monitor glaucoma progression

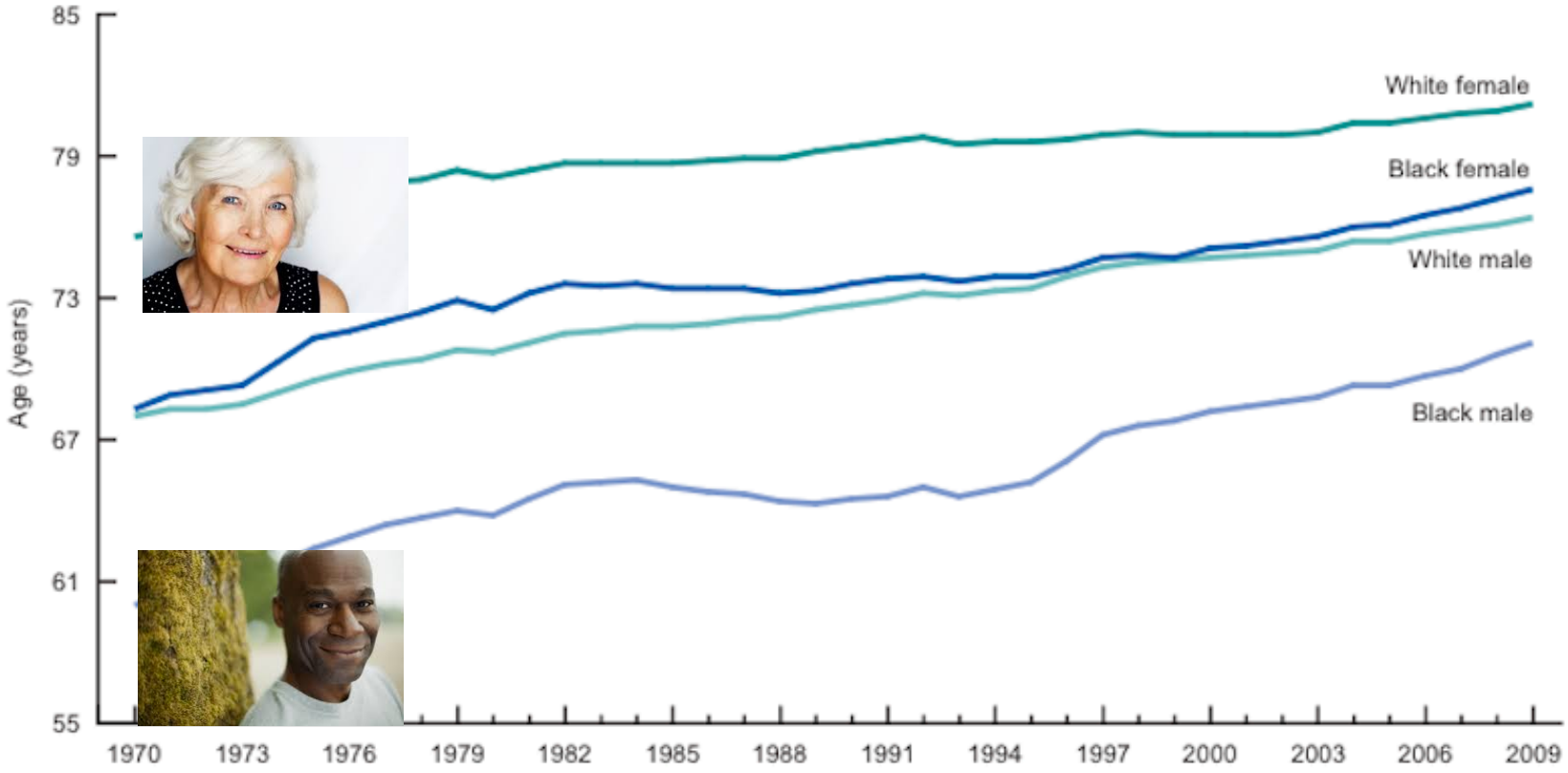
Background

- "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?

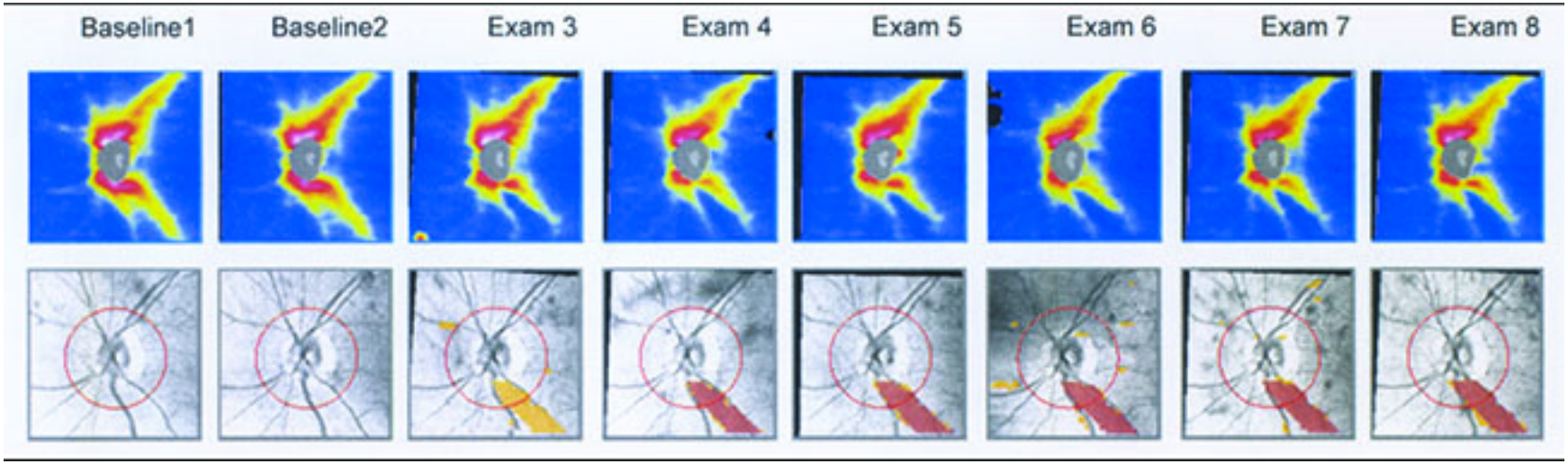
- Or should efforts also focus on early detection of progression?
- Decisions based on the presence of progression:
  - To treat or not to treat
  - How aggressive to be with the treatment

Age, life expectancy and risk of progression



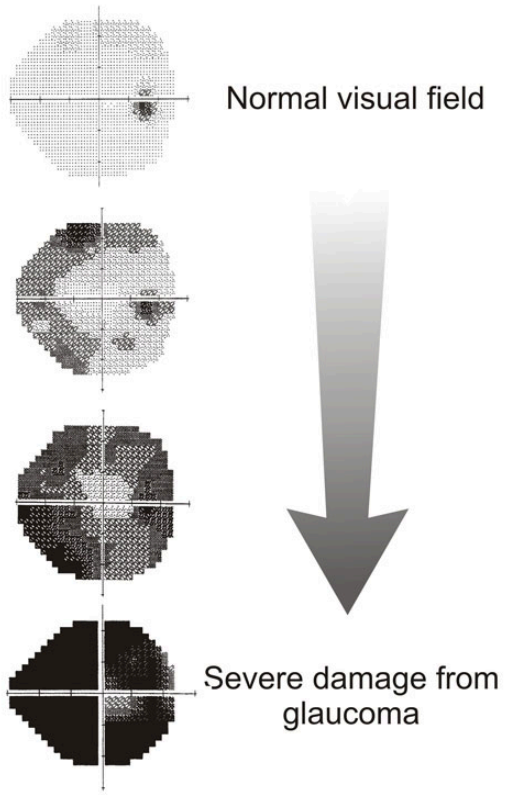
How do we detect progression?

- Structural changes:



How do we detect progression?

- Functional changes:

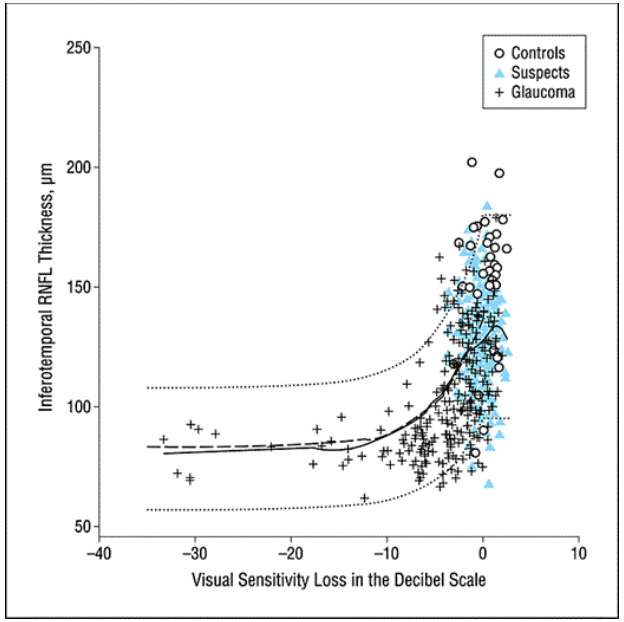


How should we detect progression?

- 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



Rao et al, Ophthalmology, 2011

2. Progression similar in all patients

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

	OHTS	EGPS	EMGT
Structure 1st	55%	40%	1%
Function 1st	35%	60%	86%
S + F together	10%	0%	13%

Zangwilll, J Curr Glaucoma Prac, 2008

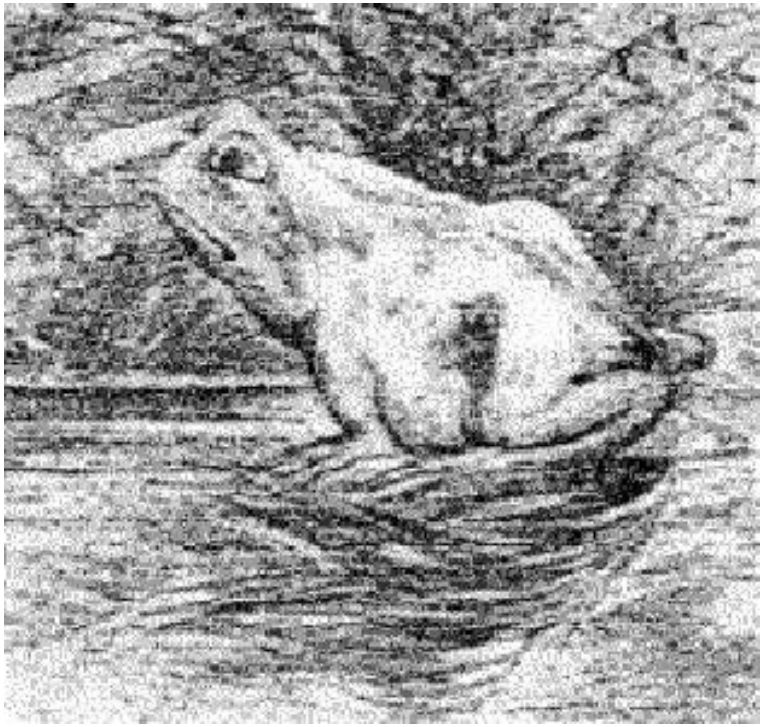
Progression differs in different patients

	Chauhan	Kamal	Artes	Strouthidis	Girkin
Structure only	40%	29%	17 - 42%	9 - 21%	13 - 32%
Function only	4%	5%	17 - 42%	15 - 20%	0 - 6%
S + F	29%	8%	4 - 19%	3 - 12%	15 –34%
No progression	27%	59%	58 - 83%	46 - 73%	47 - 53%

Zangwilll, J Curr Glaucoma Prac, 2008

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

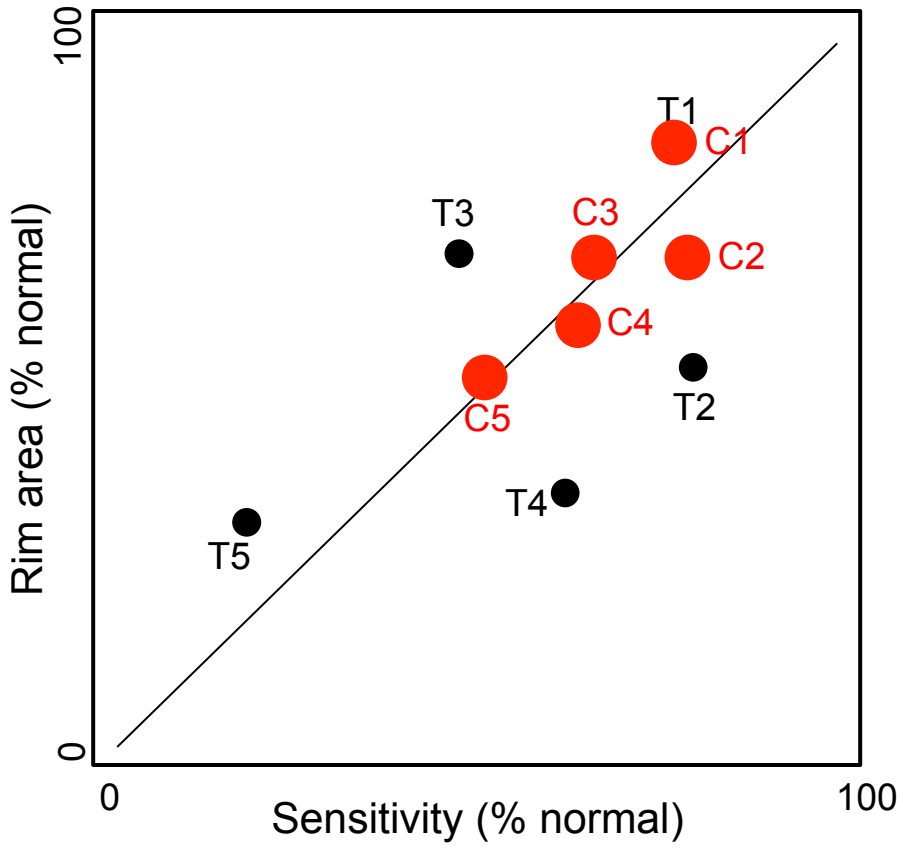
The Dynamic Structure-Function Model

- 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

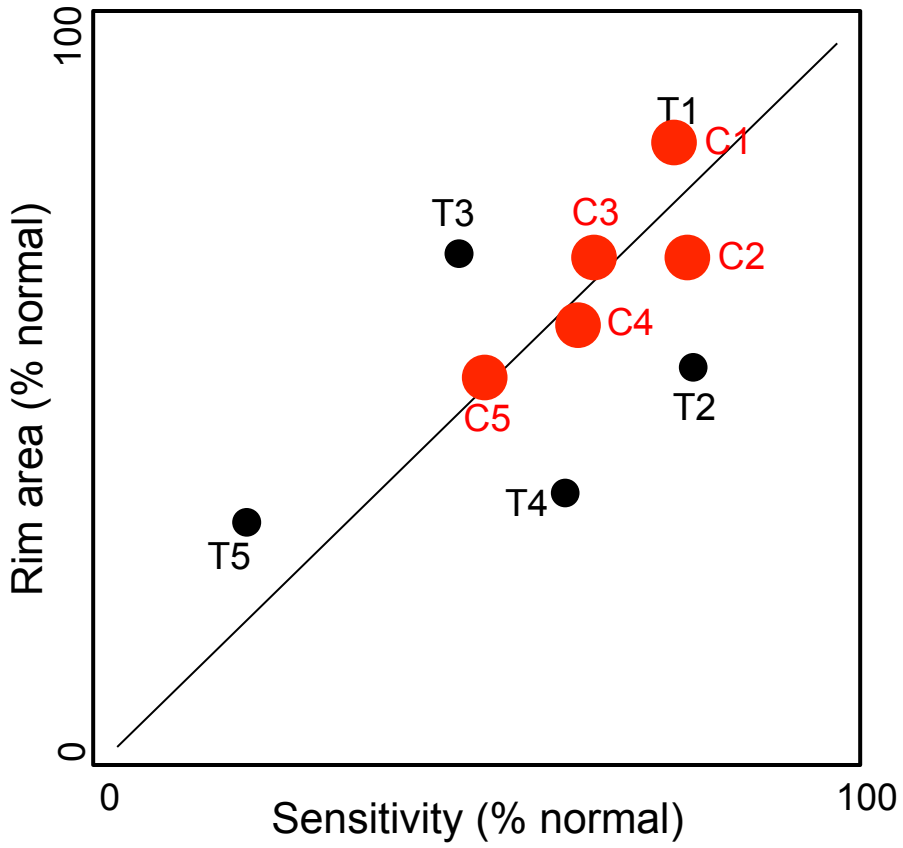
Centroids


100
0
Rim area (% normal)
0
100
Sensitivity (% normal)
T1
C1
T3
C3
C2
C4
C5
T2
T4
T5

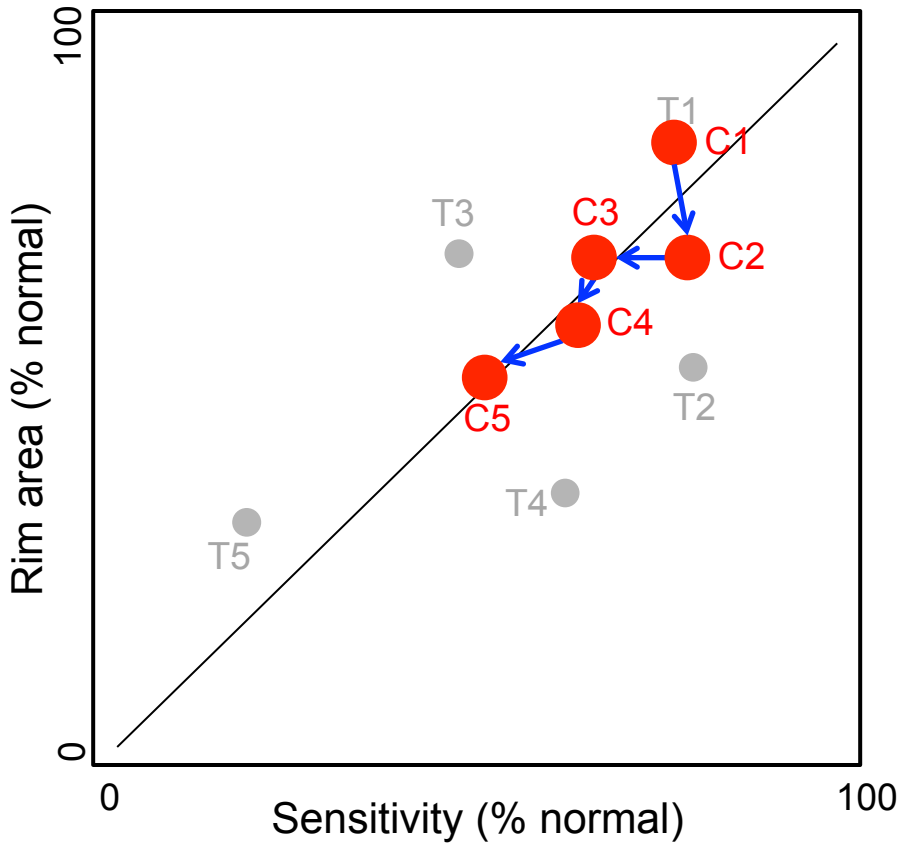
Dynamic Structure-Function Model for Glaucoma Progression

- Centroids: current state of the disease
- Velocity vectors: trend of change of the centroids over time

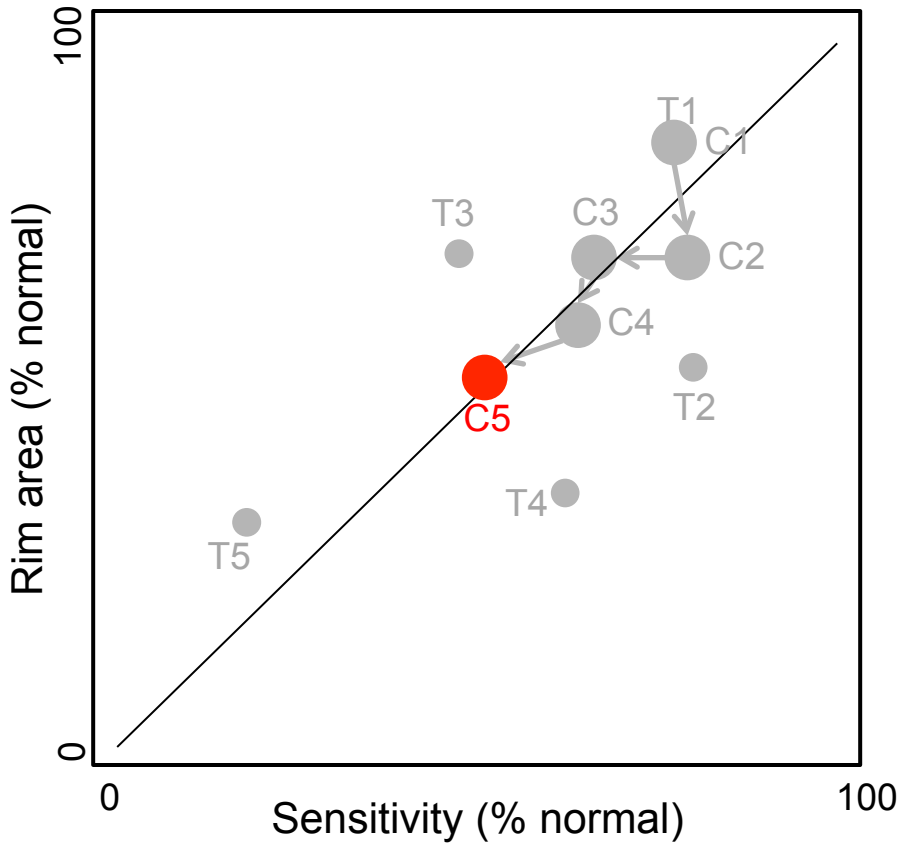
Descriptive velocity vector



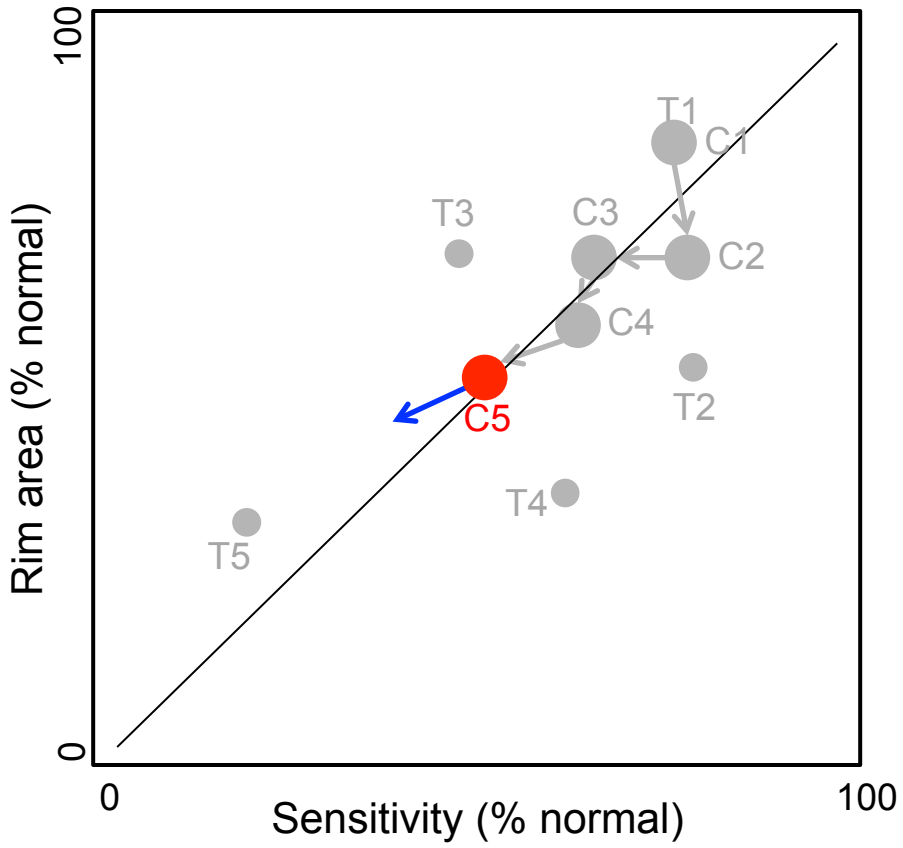
Descriptive velocity vector



Descriptive velocity vector



Predictive velocity vector



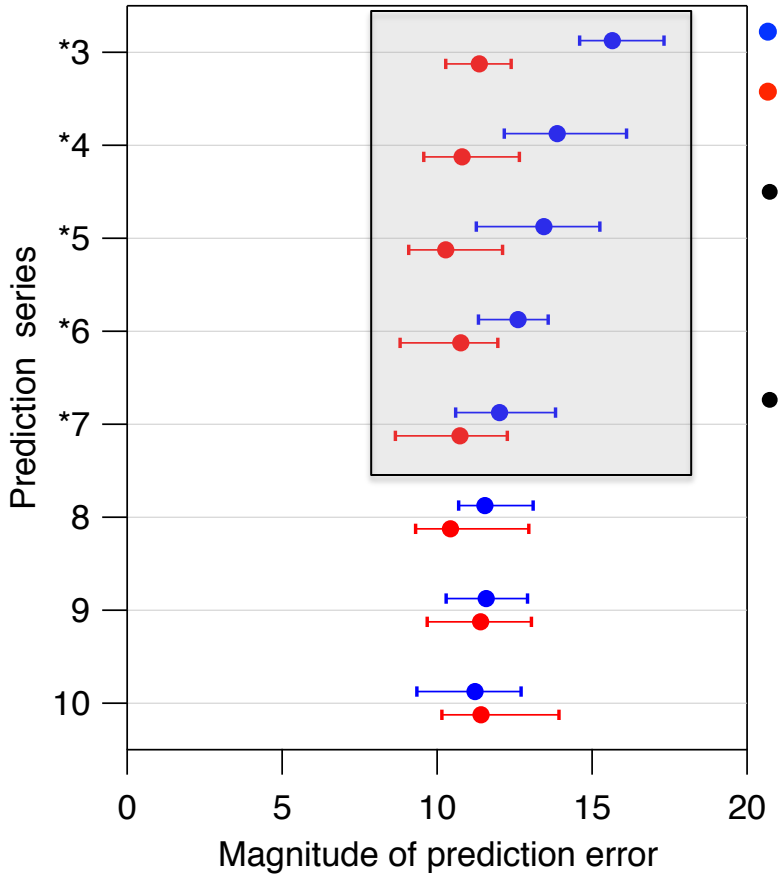
Prediction accuracy of the DSF

- 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 11th pair from:
  - The first 10 pairs
- We predicted the 10th 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

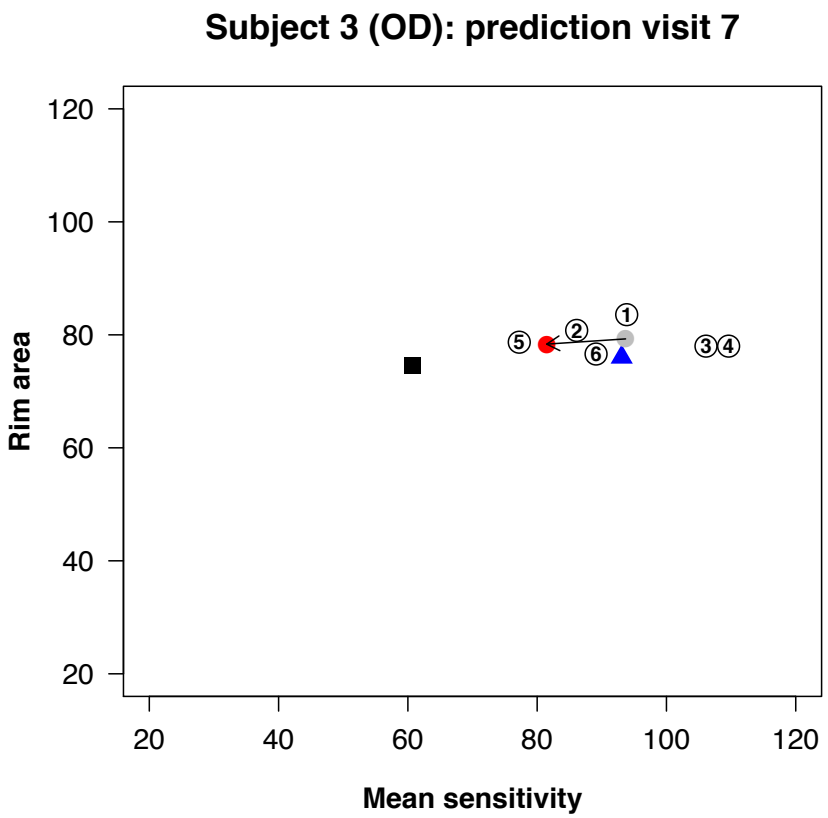


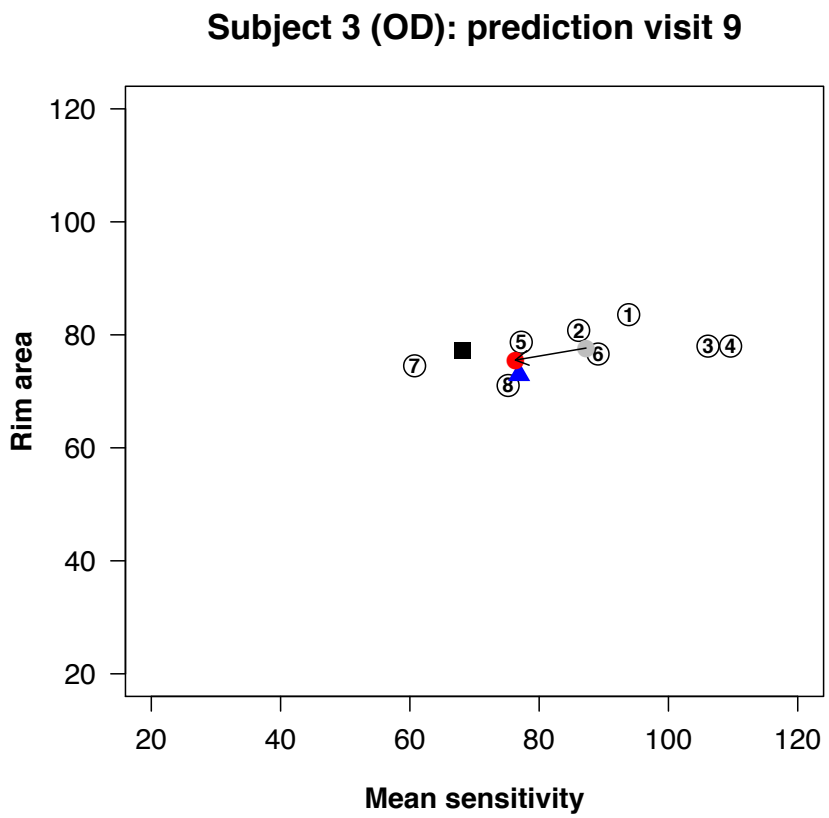
- Linear Regression
- DSF model

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

Hu et al, IOVS, 2014

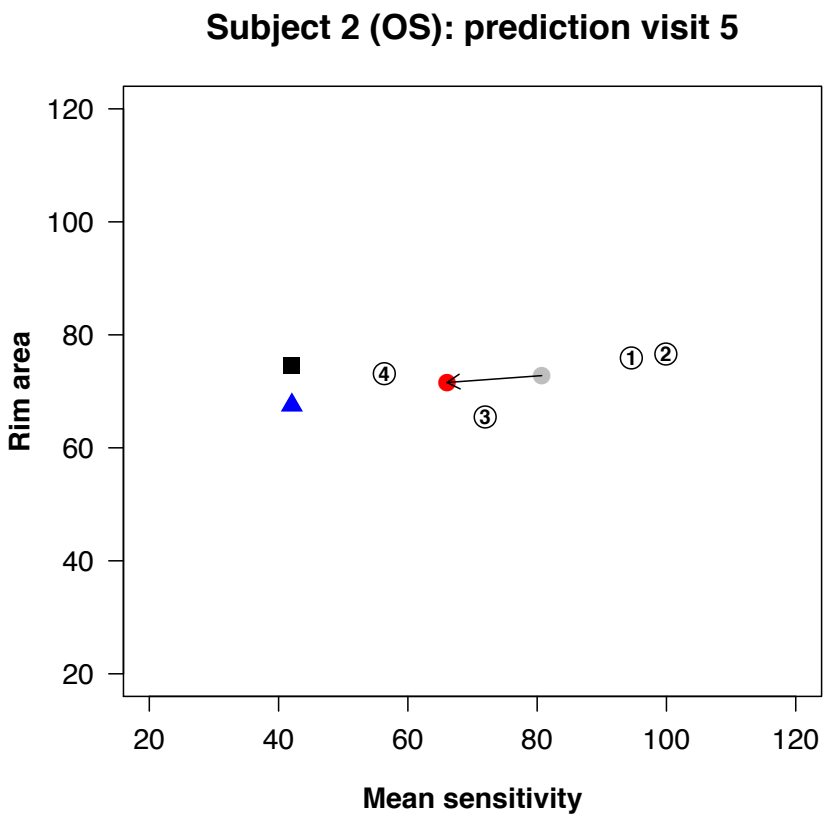
Example 1: DSF has better PE in short series

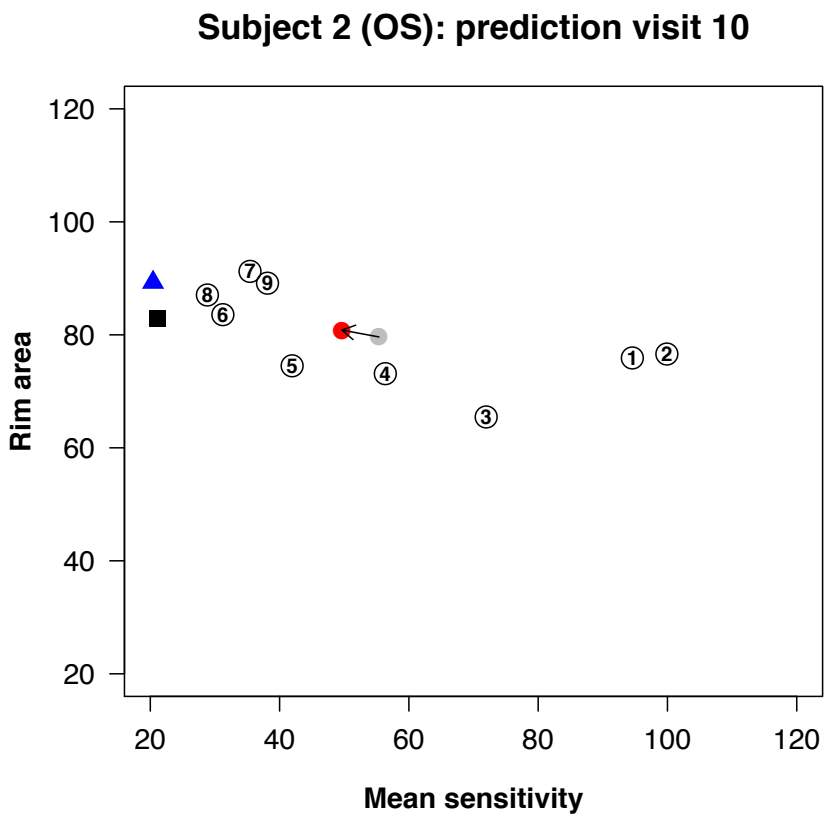




Hu et al, IOVS, 2014

Example 2: DSF has worse PE than OLSLR



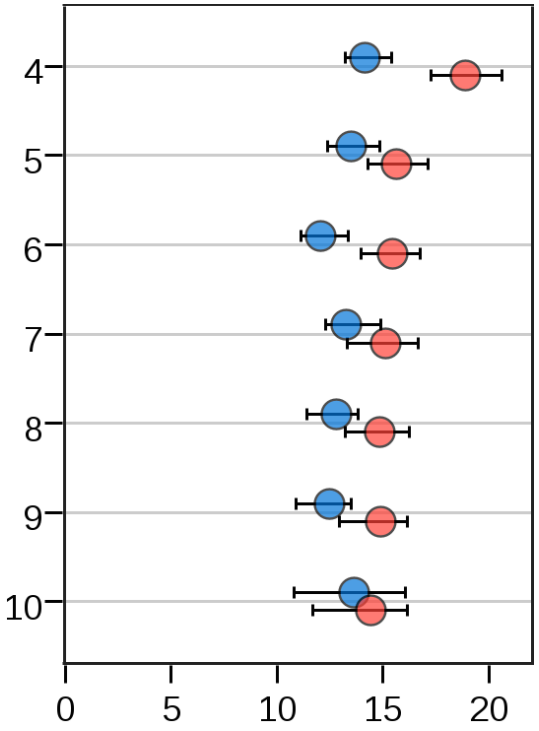


Hu et al, IOVS, 2014

Why does the DSF model perform better when short series are used?

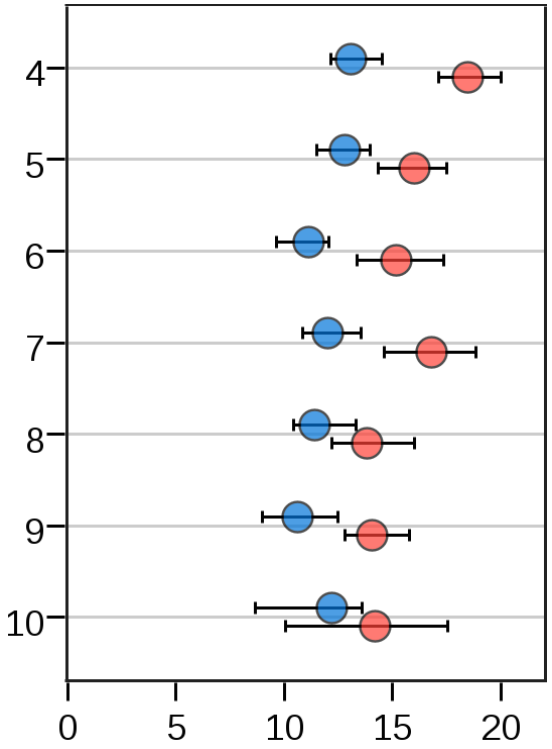
- The use of centroids make the DSF model relatively conservative
- This effect increases when:
  - Longer series are used
  - Progression occurs
- Even though the DSF model is conservative, overall, it has better prediction accuracy than OLSLR in short series in progressing eyes

DSF validated in independent dataset



Bauchle et al, ARVO, 2015

DSF compared to a Bayesian model



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

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Thank you!