Rapid Fire 2: glaucoma management
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Eye Recommend (DM)

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So, you’ve diagnosed, staged, and initiated treatment for glaucoma ... now what?

1. Establishing solid baseline data
2. Staging disease severity
3. Establishing a target IOP
4. Initiating treatment
5. **Detecting disease progression**
6. **Altering treatment**

Detecting progression

From a review of 400,000+ AVFs from 75,000+ patients

- most **reduce** over time, but few (<15%) become **blind** (MD< -22dB)\(^2,3\)
- the likelihood of **improve** (MD< -14dB) is linked to baseline VF loss (MD< -6dB), rate of change (≥ -1.5dB/year), and life expectancy\(^4\)
- VF assessment is variable: many patients "**improve" over time

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### Risk factors for progression

Progression is more likely in the presence of risk factors including:

**Non-modifiable:**
- older patient age at baseline
- severe or rapidly progressing disease at baseline
- initial VF loss that is central or involves both hemifields
- exfoliation (in OAG) and disc hemorrhages (in NTG)
- thin CCT (≤555µm) and/or low CH (≤10mmHg)

**Modifiable (other than elevated IOP):**
- IOP fluctuations, particularly at low IOPs
- compromised/fluctuating ocular perfusion pressure

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Detecting progression
Detecting progression through statistical analyses

Trend-based analysis \(^1\)-\(^4\)

- identifies change over time in both structure and function
  - “clinically significant change”
- allows rate of change to be quantified and extrapolated
- requires more tests, and is less sensitive to diffuse loss

\[ \text{Rate of Progression: } -0.7 \pm 0.2\% / \text{year (95\% confidence)} \]


Which is better, one (OCT) or two (AVF)?

In “early” (pre-perimetric) glaucoma, VF progression becomes clinically detectable at an average RNFL thickness of \(~75\mu m\) \(^1,2\)

\[ \text{MD at RNFL thickness of } 75\mu m = -0.7 \pm 0.2\% / \text{year} \]

However, -3dB MD equates to a 50% loss of retinal ganglion cells \(^3\)

- the logarithmic scale of AVF analysis masks early loss \(^4\)

OCT is also less variable, facilitating earlier detection of change \(^5\)

Which is better, one (OCT) or two (AVF)?

In advanced glaucoma (MD ≥ -12dB), both RNFL and GCIPL reach a measurement floor at ~50μm (glial/vascular/non-neural tissue)\(^1,2\)

![Graphs showing RNFL and GCIPL over Field Loss (dB) and Probability (percent)](image)

However, GCIPL tends to reach its floor later, and a larger area remains above that floor, allowing ongoing progression analysis\(^3\)

VF loss remains detectable, albeit with significant variability\(^4\)


Which is better, one (OCT) or two (AVF)?

Early (including pre-perimetric) glaucoma:
- clinical exam and OCT (RNFL ≥ GCIPL > ONH)
- obtain baseline 24-2 and 10-2 for future reference

Moderate glaucoma:
- clinical exam and OCT (RNFL ≥ GCIPL > ONH)
- AVF (24-2, and 10-2 guided by GCIPL abnormalities)

Advanced glaucoma:
- 10-2 > 24-2 AVF (or 24-2 with stimulus size V)
- clinical exam and OCT (GCIPL > ONH ≥ RNFL)

Utilize all the tools at your disposal:
progression is detected by only one method >90% of the time\(^1,2\)

Leverage OCT in early disease and AVF in advanced disease\(^3\)


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6/12/19
Detecting structural progression

**Clinical examination: review of ONH/RNFL photos**

- **pros:** “backward compatible”; reveals DH and NRR pallor
- **cons:** qualitative; subjective; requires expertise

There can be significant inter-individual (but less intra-individual) variability in estimating both disc margin and rim margin.

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Detecting structural progression

The most common ONH changes noted on clinical exam are **rim thinning** (4x faster) and/or **inferior-temporal excavation**.

Detecting structural progression

**Optical coherence tomography: Guided Progression Analysis**

**Event-based analysis:**
- highlights change from baseline in both RNFL and GCIPL thickness that exceeds normal variability
  - change on one occasion: possible loss
  - change on two or more successive occasions: likely loss


**Trend-based analysis:**
- plots thickness over time to quantify rate of change in:
  - average, superior, and inferior RNFL thickness
  - average C/D ratio
  - average, superior, and inferior GCIPL thickness

Detecting structural progression

Retinal nerve fiber layer (RNFL) thickness
- widening of an existing (inferior-temporal) RNFL defect
- repeatable inter-visit change in average RNFLT ≥5μm
- a rate of average RNFL thinning ≥2 to 3μm/year

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Smaller changes are more significant in advanced disease
Allow for age-related thickness loss of up to 0.5μm/year

Detecting structural progression

**Retinal nerve fiber layer (RNFL) thickness**

- widening of an existing (inferior-temporal) RNFL defect
- inter-visit change in average RNFLT ≥5μm
- a rate of average RNFL thinning ≥2 to 3μm/year

In suspects who go on to develop VF loss (manifest disease), the rate of RNFL loss is ~2µm/year, 4x the normal age-related loss.\(^1\)


**Macular (ganglion cell/inner plexiform layer: GCIPL) thickness**

- widening of an existing (inferior-temporal) GCIPL defect\(^1\)
- inter-visit change in average GCIPLT ≥4μm\(^2\)
- a rate of average GCIPL thinning ≥1 to 1.5μm/year\(^3\)

The advantage of GCIPL in advanced glaucoma


Case examples:
patient DF
Patient DF

History
• 55 year-old Caucasian woman
• good general health (hormone replacement therapy)
• unremarkable family history
• ocular hypertension (IOPs occasionally in low 20s)

July 2012
• moderate myopia (-4.00) with good BCVA (6/6)
• normal binocularity, pupil reactions, and confrontation VFs
• normal anterior segment structures
• IOPs 16/19
• CCTs 541/539
Retinal nerve fiber layer (RNFL) thickness

Patient DF

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
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<tbody>
<tr>
<td>Average RNFL Thickness</td>
<td>91 μm</td>
<td>97 μm</td>
</tr>
<tr>
<td>RNFL Symmetry</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>Rim Area</td>
<td>1.12 mm²</td>
<td>0.99 mm²</td>
</tr>
<tr>
<td>Disc Area</td>
<td>1.36 mm²</td>
<td>1.46 mm²</td>
</tr>
<tr>
<td>Average C/D Ratio</td>
<td>0.41</td>
<td>0.56</td>
</tr>
<tr>
<td>Vertical C/D Ratio</td>
<td>0.38</td>
<td>0.58</td>
</tr>
<tr>
<td>Cup Volume</td>
<td>0.055 mm³</td>
<td>0.125 mm³</td>
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</tbody>
</table>

Don't rely solely on global summary parameters: qualitatively assess the scan for accuracy or artifacts, and scrutinize the deviation and thickness maps for focal defects.

### Patient DF

**July 2012**
- treatment initiated with latanoprost HS
- IOP ≤14 and AVF stable for 5 years

**October 2017**
- suggestion of event-based change on 24-2 O.S.
- concurrent irritation O.D. (both CL- and PGA-related?)
  - discontinued PGA O.D. only: IOP increased to 22
    - treated IOP O.S. also now above target at 16

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**February 2018**
- trialed Lumigan RC
  - better comfort O.D. and IOP decreased to 16/13

**July 2018**
- structural GPA: possible progression on both RNFL and GCIPL analyses
Patient DF

November 2018

- IOP 14/15 on Lumigan RC
- clinical exam shows expanding superior RNFL defect with small DH, and large inferior DH O.S.
- structural GPA: **likely** progression on both RNFL and GCIPL analyses
Progressive RNFL loss: clinical exam and *en face* imaging

Patient DF

RNFL GPA: July 2012 through November 2018

GCIPL GPA: July 2012 through November 2018
Patient DF

February 2019
- AVF shows expanding inferior arcuate defect O.S.
- functional change commensurate with structural loss
- IOP 20/13 on Lumigan RC
- sporadic use O.D. due to recurrent irritation
- switched to DuoTrav HS
- discontinued after 1 week due to stinging/burning

March 2019
- switched to Lumigan RC HS and Timoptic XE QD (morning)
- adherent and tolerant
- follow-up late March (13/12) and early May (12/12)
Patient DF

Lessons learned

Objective imaging complements the clinical exam\(^1\)

> "... a thorough clinical examination combined with a healthy dose of common sense is superior to imaging technology ..."

Diagnose real disease, not red disease
- at the same time, recognize that green is not always good

Don’t rely solely on summary parameters
- scrutinize thickness and deviation maps for focal defects

Disease progression is not necessarily linear
- stay vigilant and be ready to respond

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Case examples:
patient JK
Patient JK

History
• 70 year-old Caucasian man
• good general health (rabeprazole for acid reflux)
• family history significant for glaucoma (3 siblings)
• longstanding bilateral parapapillary atrophy

January 2009
• emmetropic with good BCVA (6/6)
• normal binocularity, pupil reactions, and confrontation VFs
• normal anterior segment structures
• IOPs 18/18
• CCTs 468/484
Patient JK

July 2013
• IOPs 20/20: treatment initiated with latanoprost HS

Patient JK

August 2013
• IOPs remained 20/19 on latanoprost
  • switched to travoprost HS
  • IOPs dropped to 14/16
Patient JK

February 2014

- IOPs increased to 18/19 on travoprost

Patient JK

December 2014

- assumed care: IOPs still elevated at 19/19 on travoprost
Patient JK

December 2014
• switched to DuoTrav HS: IOPs dropped to 11/11

Patient JK: macular structure/function correlation
Patient JK

December 2014 through June 2019

- IOPs ~11 (highest 14/13; 11/11 (June 2019)) on DuoTrav HS
- 10-2 appears stable since late 2014 baseline

Patient JK

Guided Progression Analysis (GPA) is not (yet) available for the 10-2, making statistical determination of progression difficult...
Patient JK

... however, structural GPA is now available for GCIPL scans

<table>
<thead>
<tr>
<th>Baseline 1</th>
<th>Baseline 2</th>
<th>Exam 3</th>
<th>Exam 4</th>
<th>Exam 5</th>
<th>Exam 6</th>
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GCIPL GPA: stable July 2013 through March 2019

Lessons learned

**Aggressive** IOP reduction is necessary in advanced disease
- an IOP consistently ≤12 appears to have stabilized both structural and functional status

In advanced disease, macular analyses become more helpful
- at or near the RNFL floor of ~50μm, consider complementary GCIPL and 10-2 AVF analyses

Leverage statistical progression analyses
- GPA is available for structural and functional tests
  - both RNFL and GCIPL scans
  - however, only 24-2, not (yet) 10-2 analyses