Optic Nerve Head and Retinal Nerve Fiber Layer in Glaucoma

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Pathogenetic Concept of Glaucoma

• What we call "glaucoma" is actually not known since there are several possible driving forces which present as change of the optic nerve.

• Glaucomatous optic neuropathy implies
  • Loss of neural tissue (RNFL and Ganglion Cell)
  • Activation of glial cells
  • Tissue remodeling
  • Change of blood flow - an unstable ocular perfusion, either due to IOP fluctuation or a disturbed autoregulation (due to primary vascular dysregulation syndrome) leading to a mild reperfusion injury

Tissue Change Shows At Retinal Surface

Loss of ganglion cells or nerve fiber tissue within the retinal layers will show as shape change at the retinal surface
Optic Disc Change is the Primary Indicator

- OHTS reports 55% of subjects reached endpoint (POAG) based on changes in the optic disc only
- A further 10% of subjects had concurrent optic disc and visual fields changes
- Only 35% of glaucoma was found by visual field changes

Glaucous Disc Classifications

1. Focal
2. Myopic
3. Senile sclerotic
4. Concentric
5. Advanced

Kass et al., Arch Ophthalmol. 2002;120:701-703

Frequency of Glaucoma Disc Types

- Focal Glaucoma: 18%
- Myopic Glaucoma: 7%
- Senile Sclerotic Glaucoma: 16%
- Concentric Cup Enlargement: 26%
- Normal Appearing Optic Disc: 17%
- Non-classifiable Optic Disc: 16%

Identification

Identification of structural, contour and color changes is best done stereoscopically by two methods:

1. Indirect fundus lens (78 or 90)
2. Direct fundus lens (Goldmann)
Identification

- The direct ophthalmoscope can be used.
- Select a spot size with smaller diameter than the optic disc
- The incorporated grid may help in estimating the cup/disc and the rim/disc ratio

Qualitative evaluation

- Contour of the neuroretinal rim
- Optic disc hemorrhages
- Parapapillary atrophy
- Bared circumlinear vessels
- Appearance of retinal nerve fiber layer
Quantitative evaluation

- Optic disc size (vertical disc diameter)
- Cup/disc ratio (vertical)
- Rim/disc ratio
- Retinal nerve fiber layer height (RNFLH)

Neuroretinal Rim

- The contour of the rim depends on the shape of optic disc canal
- The disc is usually vertically oval
- Black subjects have larger discs
- In normal discs with small cups ISNT rule
- Optic cup is usually horizontally oval, rounded in large discs or vertically oval
- Cupping tends to be symmetrical OU
Patterns of rim loss

Optic disc haemorrhages
Parapapillary atrophy

The ISNT rule
Bared circumlinear vessel

Retinal nerve fibre layer

- The RNFL appearance is best assessed with a red-free (green) photograph.
- Clinically, the RNFL can be assessed with the red-free light or a short, narrow beam.
Optic disc size

Vertical disc diameter
Different disc sizes

Ophthalmoscopic Evaluation of the Optic Nerve Head

Size and shape of the optic disc .1
Size, shape, (and pallor) of the neuroretinal rim (2) .2
Size of the optic cup in relation to the area of the disc .3
Configuration and depth of the optic cup .4
Ratios of cup-to-disc diameter and cup-to-disc area .5
Position of the exit of the central retinal vessel trunk on the lamina cribrosa .6
Presence and location of splinter-shaped hemorrhages (2) .7
Occurrence, size, configuration, and location of parapapillary chorioretinal atrophy .8
Diffuse and/or focal decrease of the diameter of the retinal arterioles .9
Visibility of the retinal nerve fiber layer (RNFL) .10

“5Rs” Assessment of the Optic Disc in Glaucoma

1. Observe the scleral Ring to identify the limits of the optic disc and its size

2. Identify the size of the Rim
“5Rs” Assessment of the Optic Disc in Glaucoma

1. Observe the scleral Ring to identify the limits of the optic disc and its size
2. Identify the size of the Rim
3. Examine the Retinal nerve fiber layer
4. Examine the Region of parapapillary atrophy
“5Rs” Assessment of the Optic Disc in Glaucoma

1. Observe the scleral Ring to identify the limits of the optic disc and its size
2. Identify the size of the Rim
3. Examine the Retinal nerve fiber layer
4. Examine the Region of parapapillary atrophy
5. Look for Retinal and optic disc hemorrhages

Early Pathological Changes in the Optic Nerve

- Generalized loss of neuroretinal rim (cup enlargement)
- Focal loss of neuroretinal rim (cup enlargement)
- Thinning and translucency of neuroretinal rim
- Loss of nerve fibers
- Baring of vessels (due to thinning nerve fibers)
- Cup/disc ratio asymmetry
- Superficial splinter hemorrhage
Standard automated perimetry and stereoscopic disc photographs

• Rim area correlated with the overall retinal sensitivity
• Rim area correlated with MD and CLV
• CDR correlated with root mean square of retinal sensitivity

Methods

4. Perimetry

Using Octopus 301 automated, static perimeter using central 30° testing with TOP strategy
Methods

5. Imaging of the RNFL
Using the Topcon TRC.50 IX retinal Fundus camera attached to Topcon Image net computer system

Parameters of Optic Disc Examination

- Cup changes:
  - CDR, RDR, max, min, vert/horiz.
- Rim Changes:
  - Thinning, transparency, asymmetry, erosion, notching and pallor
- Peri-papillary changes:
  - RNFL drop-out, peri-papillary halo and atrophy
- Vascular changes:
  - Nasal displacement, venous congestion, occlusion, shunts, splinter hemorrhages
Indefinite Correlation - Case 1

- Pigmentary glaucoma in a young myopic male
- Headache and colored halos on physical exercises
- Optic disc shows large oval cup with symmetrical rim
- Field shows early NFB defect

Indefinite Correlation - Case 2

- A 34 yr male on anti-glaucoma treatment for 3 yrs
- Optic disc shows large cup with symmetrical rims
- Field shows shallow, paracentral defects
Non-glaucomatous field defects in glaucoma suspects

- Glaucoma patients are not immune from other types of field defects.
- 59 year-old lady diagnosed as glaucoma and received treatment for years.
- One eye became HM, and the other eye showed early cataract, field testing never done.
- Visual field revealed temporal hemianopic defect
- MRI revealed pituitary macroadenoma.
Normal Optic Disc and Visual Field
IOP >24 mm Hg - 6.4% Blind in 20 Years
Abnormal Optic Disc and Normal Visual Field
IOP >22 mm Hg - 51% Blind in 20 Years

Only One Hemifield Defect
76% Blind in 20 Years
Both Hemifields Affected
84% Blind in 20 Years

Ocular Hypertensives

- **OHTS**: (24-32 mm Hg)
  - 20% IOP reduction resulted in 54% reduction of the progression rate compared with the untreated group (4.4% vs 9.5%)
Early Glaucoma

- **EMGT:** IOP reduction of 25%
  - 45% of patients progress
- **CIGTS:** IOP reduction from 35% to 48%
  - Target IOP
  - No progression

Moderate Glaucoma

- IOP < 17 mm Hg
  - No progression
Advanced Glaucoma

- **AGIS:** Mean IOP of 12.3 mm Hg and IOP always <18 mm Hg
  - No progression

Normal Tension Glaucoma

- **CNTGS:** IOP reduction of 30%
  - 3 times less progression (from 60% to 20%)
Standard automated perimetry with digitalized disc photography

- Rodenstock analyzer and octopus perimetry by Caprioli
- CDR and rim area correlated best with MD and less with CLV

Standard automated perimetry with RNFL photographs

- RNFL defects precedes the visual field defects by 6 ys
- RNFL defects was found with normal 30-2 program but abnormal 10-2 program
- Correlation between RNFL scores and MD
- Correlation between Localized RNFL defects and CLV
Early POAG C/D 0.5 & minimum R/D 0.1.

Marked lower RNFL slitting and a starting wedge defect.

Early upper nerve bundle defects with a cluster of 3 non-edge locations each significant at p< 5%.

C/D 0.8 & minimum R/D 0.14.

An upper temporal starting wedge, lower temporal slitting with upper and lower nasal diffuse loss of RNFL.

An upper and lower incomplete arcuate defects with a para-central nasal scotoma and an early nasal step.
A solitary para-central defect with early glaucomatous nerve bundle defect.

A lower temporal starting wedge defect and upper marked slitting.

C/D 0.7 a minimum R/D 0.13.

C/D 0.6 & minimum R/D 0.11.

A lower temporal wedge defect and upper slitting of the RNFL.

Superior arcuate defect with dense nasal step, split fixation and a dense para-central scotoma. MD is 7.5 ,LV is 28.2 and there are 11 points of P<0.5.
Advanced POAG C/D 0.9 & minimum R/D 0.00 with marked para papillary atrophy.

Marked diffuse loss of the RNFL.

Severe glaucomatous damage in the form of para-central locations of moderate to severe reduction in sensitivity, dense lower arcuate scotoma and a temporal wedge. MD is 15.1, LV is 57 and there are 30 points of P< 0.5%.

Corroboration of structural change
Structure and function 2011

Corroboration of glaucomatous progression through the use of more than one test may provide more effective and more rapid detection of glaucomatous progression than repeated confirmation of change using a single modality.

Examples of corroborative change include structure-function (e.g. a structural change of the optic nerve and a spatially consistent functional change), function-function (standard achromatic change confirmed by electrophysiologic change or frequency doubling perimetry) or structure-structure (optic disc topographic change confirmed by retinal nerve fiber layer change).
Current methods for measuring structural progression

- Optic nerve head stereophotography
- Retinal nerve fibre layer photography
- Computerised imaging techniques
  - GDx (scanning laser polarimetry)
  - HRT (confocal scanning laser ophthalmoscopy, Heidelberg retinal tomography)
  - OCT (optical coherence tomography)
    - Time domain
    - Spectral domain
    - Adaptive optics
  - Other (retinal thickness analyser)

Structural assessments for measuring progression

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Variable</th>
<th>Other instrument outputs</th>
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<td>Stereophotography</td>
<td>• Cup/disc ratio</td>
<td>• Software for DIP and variable quantification</td>
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<tr>
<td></td>
<td>• Rim area</td>
<td></td>
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<tr>
<td></td>
<td>• Peripapillary atrophy, notch, vessel bending, etc.</td>
<td></td>
</tr>
<tr>
<td>RNFL photography</td>
<td>• RNFL defects</td>
<td>• Software for DIP and variable quantification</td>
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<tr>
<td></td>
<td>• Width, area</td>
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<tr>
<td>Imaging</td>
<td></td>
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<tr>
<td>GDx (polarimetry)</td>
<td>• RNFL retardation of polarised light</td>
<td>• Image area change quantification</td>
</tr>
<tr>
<td></td>
<td>(linearly related to RNFL thickness)</td>
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<tr>
<td>HRT (confocal ONH tomography)</td>
<td>• Neuroretinal rim area</td>
<td>• Cup shape measure</td>
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<tr>
<td></td>
<td>• Retinal height</td>
<td>• Image area change (superpixel-wise) quantification</td>
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<tr>
<td></td>
<td></td>
<td>• RNFL thickness</td>
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<tr>
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<td></td>
<td></td>
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DIP, digital image processing; HRT, Heidelberg retinal tomography; OCT, optical coherence tomography; ONH, optic nerve head; RNFL, retinal nerve fibre layer.
Stereophotography

- Two optic-disc images are captured from two different angles and combined to give a perception of 3D.
- Images are then compared with baseline over time.
- Mainly qualitative changes in neuroretinal rim and cup.
- New/enlarged previous RNFL defects.
- Highly dependent on image quality.
- Used as an endpoint in OHTS to define glaucoma conversion (masked trained readers).
Stereophotography: Baseline

Stereophotography: Follow-up
Stereophotography: Baseline

Stereophotography: Follow-up
OCT™ & GDxVCC™

Clinical Interpretation of Deviation Map

Deviation Map
Reveals deviation from the range of normal, as well as the location and magnitude of the deviations. Deviations are color-coded relative to the range of normal values. (p-values)
TSNIT graph
(Temporal – Superior – Nasal – Inferior – Temporal)
Displays the thickness values along the Calculation Circle

- Normal values are within the shaded area (normative database)
- Abnormal values fall below shaded area

Standard automated perimetry with Heidelberg retinal tomogram HRT

- Lester found corr bet MD and CPSD with cup shape and rim area
- MD and CPSD were correlated with other parameters tested by HRT
HRT III: baseline measurement

- **Assessed structure**
  - Prelaminar optic nerve head
  - Retinal nerve fibre layer thickness
- **Single analysis printout**

HRT III: multiple measurements over time (rim area)

**Quality**
- Image alignment (automatic)

**Variable evaluation**
- Rim area global/sectorial stereometric analysis
- Reference: Baseline

**Change**
- **Event**: Confirmed tick sign icon change
- **Trend (rim area)**: Increase/decrease

**Progression**
- **Event**: Tick sign icon change from green to yellow or red
- **Trend of confirmed decrease**
Standard automated perimetry with OCT

- A study done in collaboration with Alex university and German university and found strong correlation between nerve fiber thickness by OCT and both MD and PSD.

High Resolution OCT
OU Normal

1. Thickness at superior hump in a healthy eye is 111.30 – 157.90,
2. OU symmetry is expected in a healthy patient
3. Quadrant averages
   Mean values for healthy eyes.
   T 89.9 (15.6)
   S 134.6 (23.3)
   N 91.9 (28.9)
   I 138.1 (23.2)
OU Glaucoma

Assessed structure
- Retinal Nerve Fibre Layer (RNFL)
  - Rim thickness
  - Disc cube 200 x 200

Quality
- Signal-to-noise ratio (signal strength)

Variable
- RNFL thickness (µm)
- Rim thickness (µm)
- Rim area (mm²)
  - Global
  - Sectorial
    - Normative database for comparison

OCT SD Cirrus
(baseline measurement)
Example: sectorial progression with OCT Cirrus v6.0

Case Examples

• Progression events detected while glaucoma suspect still in or near the normal range for OCT & Fields.

• Apparent stability in a glaucoma suspect.

• Patient accepts of treatment achieved when progression event occurs.

• Quantification of progression helps clarify treatment decision in elderly patient.
**Case 1: 2009 / 2010 59 YO Male Glaucoma Suspect with Narrow Angles.**

- Normal fields & OCTs
- 2009/2010
- 2010

Case courtesy of Profs Schumann & Wollstein, UPITT

**Case 1: Follow-up testing in 2013 shows continued visual field stability OS but distinct OCT progression.**

Case courtesy of Profs Schumann & Wollstein, UPITT
Case 1: By 2013 findings also were outside normal limits.

June 2013

Dec 2013

Case 1 Question: Which findings are more compelling?

A- Comparison to Normal?
B- Change over time?
C- Neither alone?

Case courtesy of Profs Schumann & Wollstein, UPCI.
Case #2: 40 YO Suspect, with glaucoma family history; Baseline IOP 17, Normal stable fields, Normal OCT

2008

Case 2: 2008 OCT is within normal limits. 2014 equivocal

2008

2014

Case courtesy of Prof. Chris Leung, Hong Kong
Analysis of change over time reveals a different picture.

Case #2: Question: Are you satisfied with the patient's current therapy?
A-Yes  B-No  C-Maybe

Case courtesy of Prof. Chris Leung, Hong Kong
Case #3  32 YO Male presents with high IOPs in 2009

- Prior to treatment, IOPs 28 and 35.
- On therapy, IOPs 16 and 17
- Pigment dispersion but no transillumination or pigment on corneal endothelium.
- Maybe the superior rim is a bit thin OD.

Case #3: Stable, normal fields throughout follow-up

Case courtesy of Prof. Ravi Thomas, Brisbane Australia
Case #3: August 2014 OCT findings are equivocal

- Asymmetrical RNFL thickness
  - OD: 86 microns
  - OS: 97 microns
- Slight thinning OD superior quadrant goes with disc photo.
- Equivocal disc analysis.

Case courtesy of Prof. Ravi Thomas, Brisbane Australia

Case #3: Credible RNFLT change from baseline OU

Case courtesy of Prof. Ravi Thomas, Brisbane Australia
Case #3: Credible RNFLT change from baseline OU

Case #3: 37 YO Male, Pigment Dispersion, IOPs 16 & 17 under Tx, Normal Stable Fields.
Can you see any change?

- 2009
- 2014

Case courtesy of Prof. Ravi Thomas, Brisbane Australia
Case #3: **Question:** Are you now satisfied with this patient’s current therapy?

A - Yes,   
B - No,    
C - maybe

Case courtesy of Prof. Ravi Thomas, Brisbane Australia

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Case #4: **25 Year Old Female Glaucoma Suspect**

- Referred in June 2012 because of cup asymmetry.
- Family history of glaucoma
- Mild myopia, normal visual acuity
- IOPs OD 17 and OS 20
- CCT (US) 598 595
- Vertical diameter of the ONH 1.80 and 1.80
- Not being treated.

Case courtesy of Prof. Alain Bron, Dijon
Case #4: Most recent (2014) fields are normal.

- Average RNFL thicknesses
  - OD = 84 microns
  - OS = 91 microns

Case courtesy of Prof. Alain Bron, Dijon
Case #4: Stable OCT for 10 months, June 2012 – April 2013.

Case 4 Question: Do you think this patient should be on therapy?  
A-Yes,   B-No,   C-maybe,   D-not yet

Case courtesy of Prof. Alain Bron, Dijon
**Case 4 Question:** How soon do you want to see her again?

A-6months  B-12 Months  C-18 Months  D-24 Months

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**Case #5: 46 year old woman referred for suspicious discs in 2008**

- IOP 16 - 18 OU
- CCT 480
- Possible maternal glaucoma
Case #5: 2008 fields were normal.

Case 5: 2008 OCT scans echo the clinical disc exam and suggest RNFL thinning OU.
In 2008, the patient refused treatment.

2008

Case #5: Follow-up visit in 2011: Change from baseline in fields

- In 2011, 3 years later right field remains normal; left shows

- “Possible Progression. “
Case #5: Follow-up visit in 2011: Change from baseline OU in OCT

Case courtesy of Prof. Ravi Thomas, Brisbane Australia

Case #5: Follow-up visit in 2011: Change from baseline in photos.

2009

2011

Case courtesy of Prof. Ravi Thomas, Brisbane Australia
Case #5: 2011 analyses compared to normal limits also have become strongly suggestive of disease.

Case #5: Right Eye Findings since 2011

Case #5: OS Findings since 2011

Case courtesy of Prof. Ravi Thomas, Brisbane Australia
Case #5  Question: Are you satisfied with this patient’s current therapy?
   A-Yes,    B-No,    C-maybe

Case #6: 83 YO male Glaucoma Suspect

- Pressures 23 – 26 OU

- Healthy stable discs
Case #6: Fields are stable, and mostly normal

Case courtesy of Prof. Ravi Thomas, Brisbane Australia

Case #6  Right Eye’s OCT is changing. “Likely Loss”

Case courtesy of Prof. Ravi Thomas, Brisbane Australia
Case #6  Right Eye’s OCT is changing. “ Likely Loss”

Question, Case #6: 83 YO male Glaucoma Suspect

• Does this patient have glaucoma?

A. Yes

B. No

C. Maybe
Question, Case #6: 83 YO male Glaucoma Suspect

• Would you treat this patient?

A. Yes
B. No
C. Maybe

Case courtesy of Prof. Ravi Thomas, Brisbane Australia

Agreement between methods in glaucoma diagnosis

Case study
• Glaucoma detected in right eye
• Agreement across 3 methods
SWAP perimetry with OCT

- 30 patients with POAG, Ocular hypertension and normal controls are currently studied comparing the nerve fiber thickness by OCT with the field parameters by SWAP perimetry.

SWAP perimetry with RNFL photographs

- RNFL defects correlated with MD by Polo et al.
- RNFL defects correlated with CLV by Drance.
SWAP perimetry with Scanning laser ophthalmoscopy HRT

- All disc parameters and RNFL thickness correlate with SWAP better than standard automated perimetry

Topographic correlation

- The optic disc is divided into sectors and the visual field is divided into many sectors
- Many studies proved topographic correlation
b  HRT data compared with normative data

a  Damaged Rim Sectors

b  Optical Disk

c  Visual Field Defective Zones