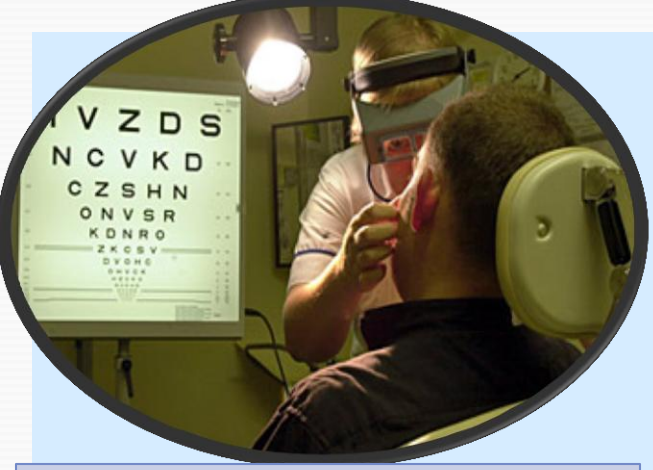
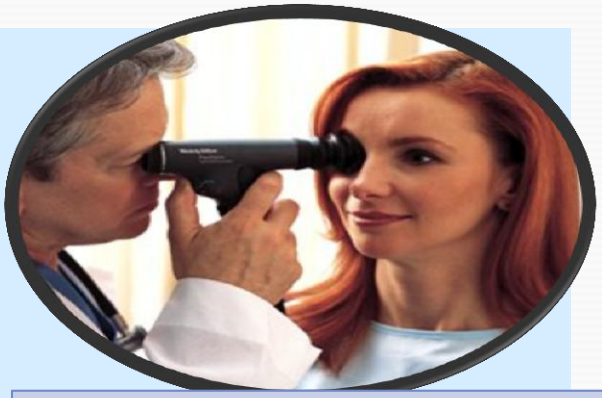
ROLE OF NEWER DIAGNOSTIC TOOLS IN EVALUATION OF GLAUCOMA

CURRENTLY USED DIAGNOSTIC TECHNIQUES IN GLAUCOMA



Refraction- test short/long sighted vision

Tonometry- measure IOP.

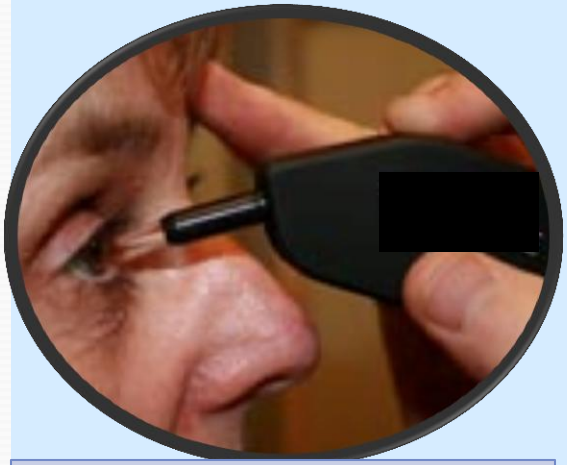


ophthalmoscope- examine interior of eye. (lens, retina, optic nerve)

History

Diagnosis

Slit-lamp examination.



Pachymetry-measure corneal thickness.

gonioscopy-measure irido-corneal angle.

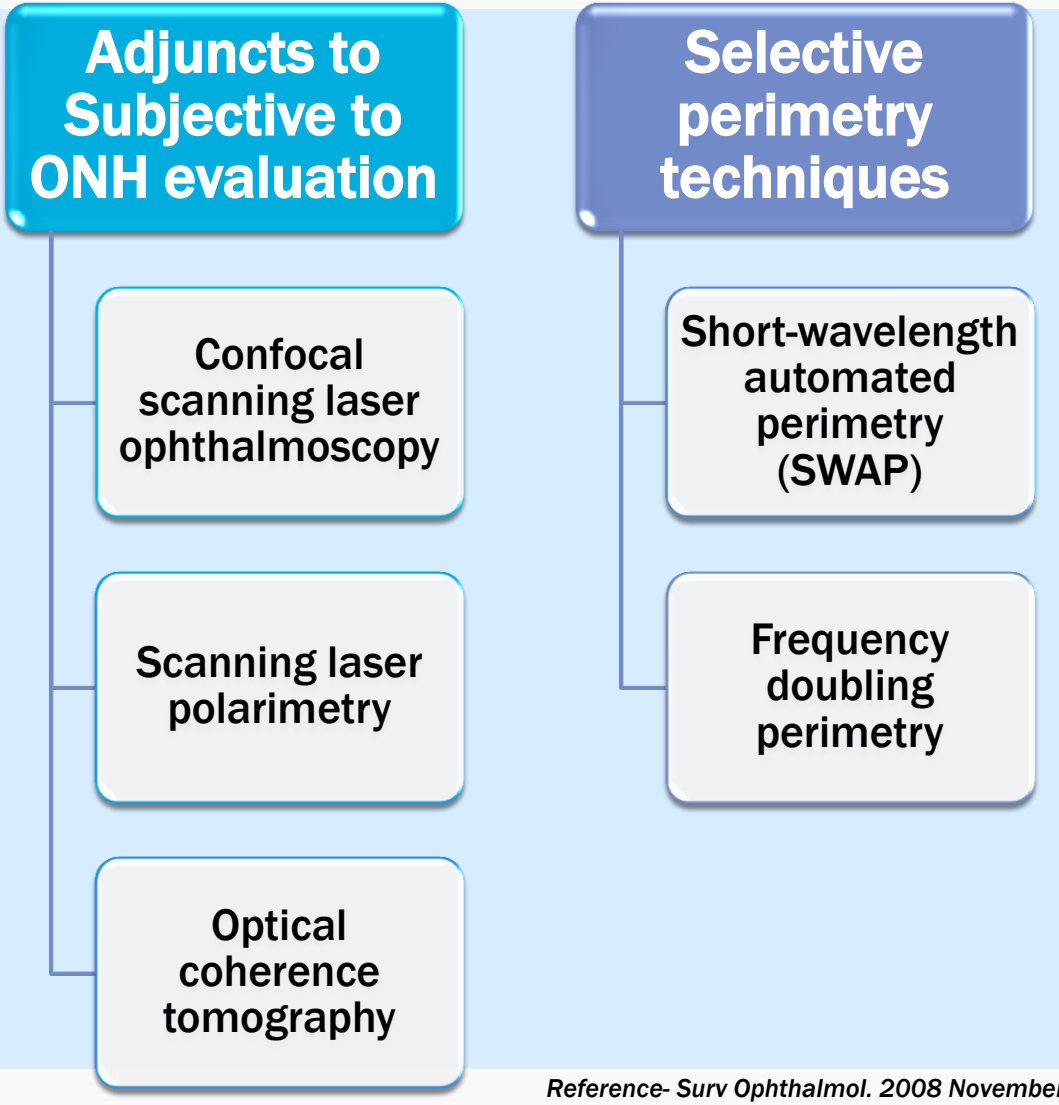
Perimetry-measure extent of vision loss.

NEED FOR NEWER DIAGNOSTIC TECHNIQUES

- Glaucoma detection relies on examination of structural damage to optic nerve & measurements of visual function.
- Clinical examinations are subjective, thus prone to variabilit
- Recent research has focused on objective methods to aid in glaucoma diagnosis
- Newer techniques have been extensively studies as adjuncts to the existing techniques

Reference- Surv Ophthalmol. 2008 November ; 53(SUPPL1): S17–S32.

NEWER TECHNIQUES FOR GLAUCOMA EVALUATION



Reference- Surv Ophthalmol. 2008 November ; 53(SUPPL1): S17–S32.

CONFOCAL SCANNING LASER OPHTHALMOSCOPY (CSLO)

- Available for glaucoma detection since 1992
- **Provides quantitative 3D composite image of ONH & posterior segment**
- Commercially available instrument, HRT
- Uses confocal optics to obtain multiple measures of retinal heights at consecutive focal planes.
- **Provides a topographic map extending from lamina cribosa to the retinal anterior surface.**

HRT- Heidelberg retinal tomography

Reference- Surv Ophthalmol. 2008 November ; 53(SUPPL1): S17–S32.

HRT PARAMETERS & ASSESSMENTS

- Parameters generated by CSLO- rim area, rim volume, cup shape measure, linear cup/disk (C/D) ratio, retinal height variation along the contour line & RNFL thickness

- HRT assessments of the ONH are capable of distinguishing between healthy and glaucomatous eyes, **with a range of sensitivities from 51–97% and a range of specificities from 75–95%**

- Amongst the many HRT parameters associated with glaucoma development **the most predictive values were mean height contour, rim area, and mean cup depth.**

Reference- Surv Ophthalmol. 2008 November ; 53(SUPPL1): S17–S32.

STRENGTHS

- Good image quality through undilated pupils
- Ability to upgrade existing machines with newer software, allowing to build upon long-term databases.
- Superimposing baseline & follow-up images allows for automated detection of ONH changes
- HRT use in ancillary study to OHTS has resulted in a well-characterized data set, beneficial for future investigations of this technique.
- An additional improvement to the HRT version 3.0 software is a larger and ethnicity-specific normative database.

LIMITATIONS

- Some topographic measurements are based on a reference plane constructed from a user-drawn contour line, so that operator input is required for particular analyses.
- Topographic change analysis & GPS don't require a user-drawn contour line.
- In some eyes, IOP can significantly influence HRT measurements

Reference- Surv Ophthalmol. 2008 November ; 53(SUPPL1): S17–S32.
Indian J Ophthalmol. 2011 Jan; 59(Suppl1): S59–S68.

TAKE HOME MESSAGE ON HRT

- Provides localized, objective and quantitative information on the volume, area and depth of retinal height changes
- Uses sophisticated statistical analysis that automatically identifies repeatable change greater than the variability of the superpixels comprising an individual's images.
- Is a promising tool for early glaucoma diagnosis.

Reference- Surv Ophthalmol. 2008 November ; 53(SUPPL1): S17–S32.

SCANNING LASER POLARIMETRY (SLP)

- Non-invasive method to objectively measure the RNFL
- Potential diagnostic tool for detecting damage in early glaucoma.
- Consists of CSLO with a polarized laser beam; when the polarized light passes through the birefringent RNFL,

a measurable phase shift is created, which can be correlated to the RNFL thickness.

- SLP was first commercially available as the GDx Nerve Fiber Analyzer

Reference- Surv Ophthalmol. 2008 November ; 53(SUPPL1): S17–S32.

COMMERCIALLY AVAILABLE SLP INSTRUMENTS

- GDx VCC (variable cornea compensation) and the latest GDx ECC (enhanced corneal compensation) (both from Carl Zeiss Meditec, Dublin, CA, USA).
- GDx has undergone numerous implementations, to provide more reliable & reproducible measurements of RNFL thickness.
- Has good diagnostics accuracy, with reported AUCs values for glaucoma detection ranging from 0.90 to 0.978
- GDx-VCC and RNFL photography correlate with damage in corresponding hemiretinas, the best GDx-VCC parameter had a higher degree of discriminant ability than the best RNFL photographic parameter.

Reference- Surv Ophthalmol. 2008 November ; 53(SUPPL1): S17–S32.

AUC - area-under-the curve

INDICATIONS

- Early and moderate glaucomatous damage identification and follow ups to detect progression
- Advance cases: limited role, but can help when perimetry is not feasible
- Preperimetric glaucoma- helps identifying loss before seen on visual field, useful in ocular hypertensives
- Glaucoma suspects: GDx VCC is an important tool in defining the management strategy of glaucoma suspects
- Also useful in monitoring neurological patients.

LIMITATIONS

- Doesnot measure actual RNFL thickness (inferred value)
- Does not differentiate true biological changes from variability
- Young children database not available
- Requires a wider database from the Indian population
- Limited use in moderate/ advanced glaucoma
- Anterior & posterior segment pathology does affect the accuracy.

LIMITATIONS

- Unreliable values in patients with media opacities, OSDs, peripapillary atrophy, keratorefractive surgery.
- Vitreous opacities, optic nerve crescents, and other nonglaucomatous retinal distortions may induce erroneous RNFL measurements.
- Some GDx-VCC scans are characterized by problematic atypical birefringence patterns (ABPs); enhanced corneal compensation (ECC), was developed to reduce this artifact.
- Newer GDx instruments are not backward compatible with older once, thus RNFL measures acquired with different GDx instruments are not comparable.

ABP- ABPs result from artifact introduced by the device's attempt to compensate for poor noise-to-signal ratio.

TAKE HOME MESSAGE FOR GDX

- RNFL measurements with GDX is highly reproducible in a long term situation
- Useful for longitudinal assessment of RNFL
- Useful adjunct for early diagnosis of glaucoma cases
- Limited use in management of advanced glaucoma cases
- Caution should be exercised when using for longitudinal evaluation of RNFL in eyes with atypical retardation patterns.

OPTICAL COHERENCE TOMOGRAPHY (OCT)

- Uses low-coherence interferometry to perform high-resolution cross-sectional imaging of tissue morphology, providing an optical biopsy.
- Permits direct, real-time visualization of retinal pathology
- Provides quantitative measurements of retinal architecture at higher resolutions than CSLO and SLP.
- The commercially available ophthalmic time domain OCT (Stratus OCT; Carl Zeiss Meditec, Inc., Dublin CA) has ~10-micron axial image resolution.

CLINICAL APPLICATIONS OF OCT

- RNFL analysis- RNFL thickness measurements is graphed in a TSNIT orientation & compared to age matched normative data. Decreased RNFL thickness represents glaucoma.
- ONH analysis- disc margins are objectively identified by using signal from and of RPE. Key parameters include cup to disc ratio and horizontal integrated rim volume
- Macular thickness analysis- thinning of macula may reflect glaucomatous loss
- A recent software upgrade of Stratus OCT (Stratus OCT Version 5.0) has included the Glaucoma Progression Analysis to evaluate the association between average RNFL thickness and age.

ADVANTAGES

- Easy to operate
- Best resolution amongst all
- Rapid image acquisition time
- Images are obtained without undue discomfort to patient (non-contact technique)
- Qualitative & quantitative data can be collected and analysed in an objective & reproducible way
- Only technology capable of imaging the ONH, RNFL and macula
- Can obtain posterior segment images without pupillary dilation.

LIMITATIONS

- Localised NRR/ optic cup changes might be missed by interpolation algorithm
- Depends on the skill of the operator
- Poor image quality in dense media opacities
- Difficult in unco-operative patients
- Expensive instrumentation.
- Automatic demarcation of optic disc borders may be inaccurate in some cases which would confound interpretation of optic disc topography

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Indian J Ophthalmol. 2011 Jan; 59(Suppl1): S59–S68.

TAKE HOME MESSAGE FOR OCT

- Non-invasive, non-contact method of producing high speed & high resolution images.
- Can be used to produce anterior & posterior segment imaging of retina, measure NFL thickness to evaluate glaucoma.
- **Has good sensitivity & specificity for differentiating normal from glaucomatous eyes.**
- A new-generation OCT – frequency-domain OCT (also known as spectral-domain OCT or Fourier domain OCT) – has recently entered the market.
- **It holds great promise for becoming the gold standard of structural imaging of glaucoma, although the published data are still very limited.**

MERITS AND LIMITATIONS OF ONH AND RNFL ANALYZERS AND OPTIC DISC/RNFL PHOTOGRAPHY

Analysis method	Merits	Limitations*
ONH photography	• Evaluated in clinical trials and long clinical experience • Established technique that will not change over time • Excellent for educational purposes • Allows evaluation of details such as presence of disc hemorrhage • Useful as baseline even after cataract surgery	• Subjective interpretation dependent on clinical expertise • Poor agreement among experts in diagnosis and detection of change • Poorly tolerated by patients, usually requiring pupil dilation
RNFL photography	• Early detection of structural changes	• Requires highly trained photographer

*Some limitations to all techniques include the lack of widespread availability to the non-specialist, high price of the devices, and lack of consensus on how to interpret the findings for diagnosis and progression.

Can J Ophthalmol 2009;44(Suppl 1):S1–S93.

MERITS AND LIMITATIONS OF ONH AND RNFL ANALYZERS AND OPTIC DISC/RNFL PHOTOGRAPHY (CONT'D)

Analysis method	Merits	Limitations*
CSLT	• Long track record, stable technology • Diagnostic and progression software available and tested in clinical studies • Easy to acquire images through undilated pupils • Simultaneous evaluation of ONH and RNFL parameters • Easy-to-read printouts and interactive software (useful for progression) • Portable device (HRT 3)	• Relatively low specificity for screening situations • Sometimes influenced by cataract surgery • Progression analysis not yet fully validated in long-term studies • Difficult to detect optic disc hemorrhages • Relatively limited RNFL analysis

*Some limitations to all techniques include the lack of widespread availability to the non-specialist, high price of the devices, and lack of consensus on how to interpret the findings for diagnosis and progression.

Can J Ophthalmol 2009;44(Suppl 1):S1–S93.

MERITS AND LIMITATIONS OF ONH AND RNFL ANALYZERS AND OPTIC DISC/RNFL PHOTOGRAPHY (CONT'D)

Analysis method	Merits	Limitations*
SLP	• Easy to acquire images through undilated pupils • Large normative database • Good specificity in most studies • Easy-to-read printouts	• Evolving technology • Indirect measurement of RNFL • Restricted to RNFL evaluation • Lack of validated progression analysis
OCT	• High axial resolution • Allows evaluation of RNFL and ONH • Large normative database • Easy-to-read printouts	• Sometimes requires pupil dilation • Evolving technology • Lack of validated progression analysis • Nonportable device

*Some limitations to all techniques include the lack of widespread availability to the non-specialist, high price of the devices, and lack of consensus on how to interpret the findings for diagnosis and progression.

Can J Ophthalmol 2009;44(Suppl 1):S1–S93.

SHORT WAVELENGTH AUTOMATED PERIMETRY (SWAP)

- Isolates short-wavelength-sensitive pathway & differs from conventional perimetry for its narrow-band blue-light stimulus & the yellow background illumination.
- Can be installed on HFA perimeters, similar to SAP, uses SITA strategy that reduces the overall test duration
- More sensitive than SAP for detection of early functional deficits
- SWAP defects may occur 3–5 years before abnormalities are seen on Full-threshold SAP, they are predictive of both the onset & location of future SAP defects.
- Traditionally indicated as a test to evaluate visual function in glaucoma suspects, especially younger ones.

LIMITATIONS

- Any diffuse depression of sensitivity on SWAP testing should be interpreted with caution.
- May not be sensitive enough to monitor progression in more advanced cases
- Associated with higher test-retest variability than SAP; SWAP-SITA decreases testing time and inter-test variability
- It is important to explain the appearance of the SWAP target and to give practice before performing the patient's first SWAP examination.
- Results are more heavily influenced by ocular media opacities than SAP, complicating diagnosis in elderly patients.

TAKE HOME MESSAGE

- SWAP is mainly useful in-
  - Glaucoma suspects with a normal white on white perimetry
  - Ocular hypertension
  - Glaucoma subjects with mid visual field loss

- Has limited use in moderate and advanced glaucoma

FREQUENCY DOUBLING PERIMETRY

- Determines the contrast sensitivity for detecting the frequency doubling stimulus.
- Portable & considerably easier to use for both technician & patient
- The exam is faster than SAP & more resistant to blurring effects
- The FDT Matrix (Carl-Zeiss Meditec) is latest commercially version offering a new additional testing program alongwith previous versions of this technology
- High sensitivity & specificity to discriminate glaucomatous patients from normal subjects

FREQUENCY DOUBLING PERIMETRY

- Results predict future onset & location of functional loss assessed by SAP in glaucoma suspects
- FDT Matrix is a promising instrument providing early diagnosis of glaucomatous functional loss, especially helpful for subjects unable to perform SAP
- Advantages are lower test-retest variability compared to SAP 22 & SWAP.
- Disadvantages- unreliable FDT testing results seen in patients with age-related and posterior sub-capsular cataracts

MERITS AND LIMITATIONS OF MANUAL PERIMETRY, SAP, SWAP, AND FDT

Perimetry Type	Advantages	Disadvantages
Manual (i.e., Goldmann)	• Long track record • Easier to do than SAP	• Nonstandardized • Well-trained technician required
SAP	• Quantitative and standardized algorithms • Diagnostic and progression statistics available	• Expensive and nonportable equipment
SWAP	• May detect defects and change earlier than SAP	• More influenced by cataract
FDT	• Sensitive to early changes • Good patient acceptance • Portable — screening tool	• No progression software available

Canadian Ophthalmological Society evidence-based clinical practice guidelines for the management of glaucoma in the adult eye. *Can J Ophthalmol* 2009;44(Suppl 1):S1–S93.

VISUAL FIELD TESTING IN GLAUCOMA

Recommendation

SAP be used as the standard for VF testing for glaucoma diagnosis & monitoring. SITA Standard is recommended as the preferred choice for following patients with glaucoma, while SITA Fast could be considered for screening and diagnosis. Newer psychophysical tests such as SWAP and FDT perimetry technology might be useful in some cases, but their role in glaucoma management has not been fully assessed.

1. Artes PH, et al. *Invest Ophthalmol Vis Sci* 2002;43:2654–9.
2. Artes PH, et al. *Invest Ophthalmol Vis Sci* 2005;46:2451–7.

Canadian Ophthalmological Society evidence-based clinical practice guidelines for the management of glaucoma in the adult eye. *Can J Ophthalmol* 2009;44(Suppl 1):S1–S93.

TO CONCLUDE

- There is no gold standard for presence or progression of glaucoma
- Relative sensitivities & specificities of current structural or functional techniques are uncertain
- Advances in evaluation techniques provide more objective documentation & precision for diagnosis and progression detection
- It is essential that clinicians understand the strengths and limitations of each instrument and interpret the data accordingly.
- Use good quality images in conjunction with a complete clinical examination & assessment of visual function for patient management.