# Advanced Technologies in Diabetes and Glaucoma?

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## Competing interests

- Research Support
  - Heidelberg Engineering, Zeiss , Ziemer Ophthalmology, Reichert
- Principal Investigator
  - Optovue Ivue Normative database study
- Principal Investigator
  - Zeiss, GDx- PRO Normative database study

## Ophthalmic technolgy

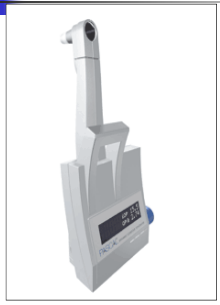
## Alternate to Goldmann tonometry

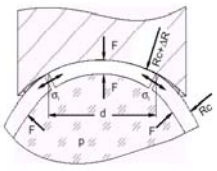
- Central corneal thickness
- Corneal curvature
- Age related changes to cornea
- IOP effects on cornea
- Biomechanical properties
  - Rigidity
  - Hydration
  - Elasticity

Whitacre, M. M. and Stein, R. (1993) Sources of error with use of Goldmann-type tonometers, Surv Ophthalmol, 38, 1-30

## Pascal -Dynamic Contour Tonometer

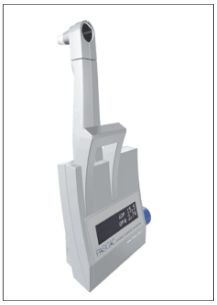
## Dynamic contour tonometer





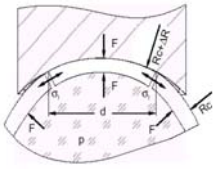
## Dynamic contour tonometer (cont 2)

- Minimal corneal deformation, allowing transducer to measure IOP directly
- Digital output
- Continuous recording of IOP waveform



## Dynamic contour tonometer (cont 3)

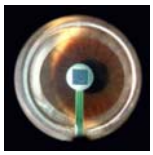
- The corneal biomechanical contribution to IOP measurement is largely removed when the cornea takes up the shape of the tip.
- Tip radius of curva
- Pressure sensor is





## The PASCAL SensorTip:

- Contour-matched concave tip surface
- Built-in pressure sensor
- Transparent tip permits view of cornea interface for centering and control.



## PASCAL SensorCaps

- SensorCap protects the patient
- SensorCap protects the tip

## Ocular pulse amplitude (OPA)

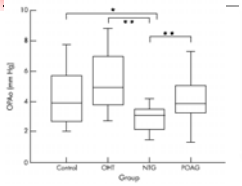



**Table 2** Group comparisons by two sample Wilcoxon tests

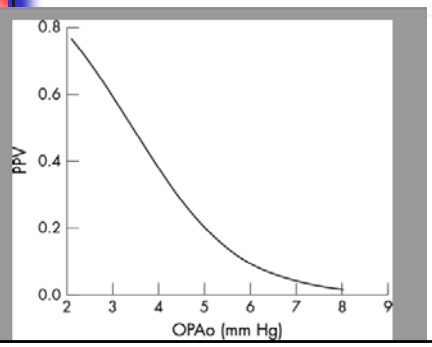
| | OPA | Pachymetry (CCT) |
|---|---|---|
| POAG/NTG | p<0.01* | p=0.43 |
| POAG/OHT | p=0.09 | p=0.03* |
| POAG/control | p=0.99 | p=0.57 |
| NTG/OHT | p<0.01* | p=0.01* |
| NTG/control | p<0.01* | p=0.68 |
| OHT/control | p=0.09 | p<0.01* |

*Indicates local statistical significance.

O Schwenn, R Troost, A Vogel, F Grus, S Beck, N Pfeiffer

*Br J Ophthalmol* 2002;86:981–984

## OPA and NTG

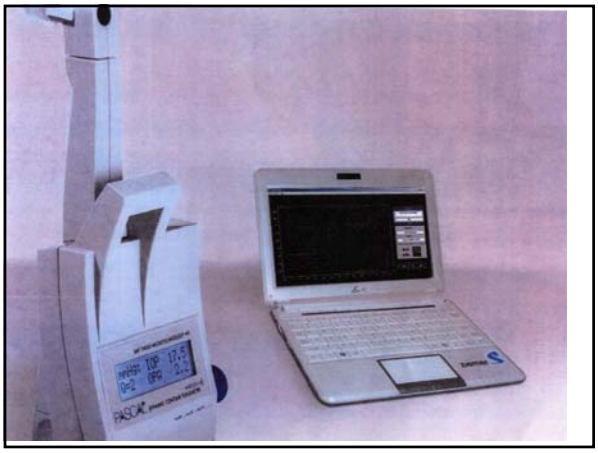


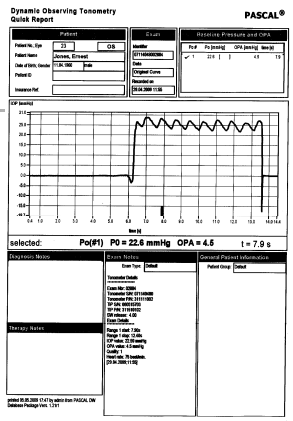

## Ocular Pulse Amplitude in Normal Tension and Primary Open Angle Glaucoma

*Ingeborg Stalmans, MD, PhD,* Alon Harris, PhD,† Veerle Vanbellinghen, BSc,* Thierry Zeyen, MD, PhD,* and Brent Siesky, PhD†*

**Conclusions:** OPA is reduced in normal tension and POAG patients compared with healthy controls. OPA is influenced by IOP, but not by corneal thickness.

(*J Glaucoma* 2008;17:403–407)

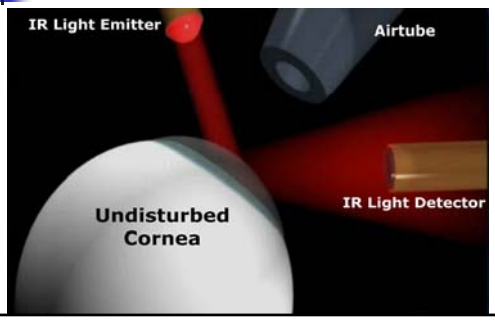




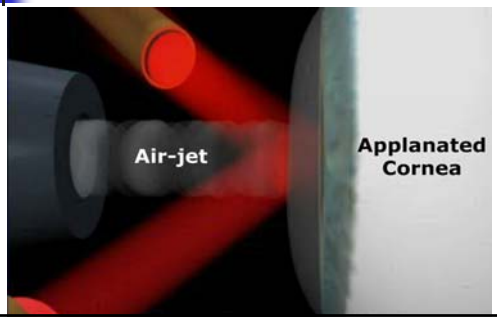

## Ocular Response Analyzer

- **IOPG** - Goldmann Correlated IOP
- **IOPCC** - Corneal Compensated IOP
- **CH** - Corneal Hysteresis
- **CRF** - Corneal Resistance Factor
- **CCT** - Central Corneal Thickness

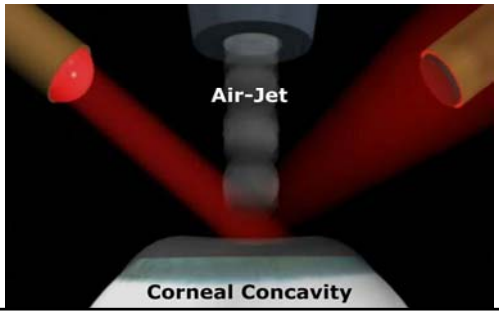
## Applanation Detection



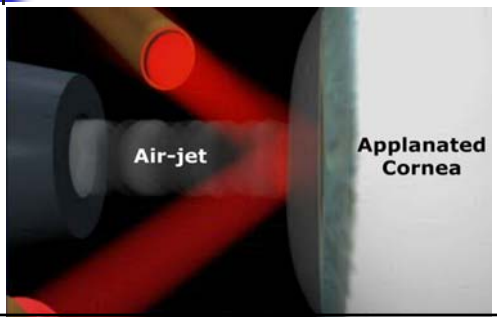
## Applanation Detection II



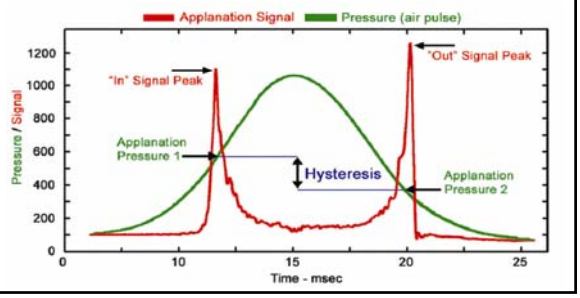

## Applanation Detection III




## Applanation Detection IV



## Applanation Signal Plot




## Corneal hysteresis

- Lower in glaucoma patients
- Correlated with lamina cribrosa compliance

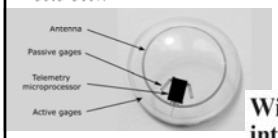
## Intraocular pressure telemetry

## Need of IOP telemetry

- 24-hour IOP measurement not easy
- Uncertain cases of NTG, progression, high risk for progression
- Need to evaluate clinical efficacy of drugs
- New drugs and modalities testing
- May be more accurate than clinical measurements
- Continuous monitoring will help identify spikes in IOP both short and long term

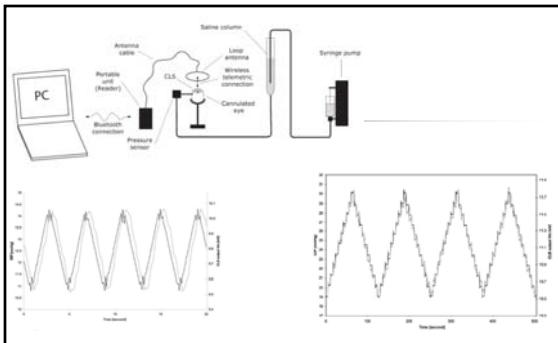
## Temporary devices contact lenses

Leonardi M, Leuenberger P, Bertrand D, et al. First steps toward noninvasive intraocular pressure monitoring with a sensing contact lens. *Invest Ophthalmol Vis Sci*. 2004;45: 3113–3117.




**Wireless contact lens sensor for intraocular pressure monitoring: assessment on enucleated pig eyes**

Matteo Leonardi,[1] Elie M. Pitchon,[1,2] Arnaud Bertsch,[1] Philippe Renaud[1] and André Mermoud[2]




3-mmHg changes mean 12.5 mmHg

1-mm Hg changes 20-30 mmHg

## Temporary devices

**Advantages**

- Non invasive
- not permanent
- can be used on ad-hoc basis

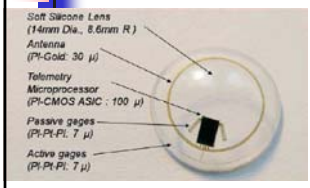
**Disadvantages**

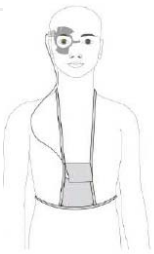
- Eye movement may have greater effect when compared to permanent devices
- Surface tension, light exposure, temperature
- Reproducibility

SENSIMED

innovation in medical micro-technology

## Triggerfish



| Central Corneal Radius (Flat Meridian) | 7.0–7.65 mm 48–44 D | | 7.65–8.4 mm 44–40 D | |
|---|---|---|---|---|
| Corneo-scleral Profile | Fluent | Marked | Fluent | Marked |
| Base Curve | 8.4 (STEEP) | 8.7 (MEDIUM) | 8.7 (MEDIUM) | 9.0 (FLAT) |

Cost 500 Euro. Not available for sale in USA

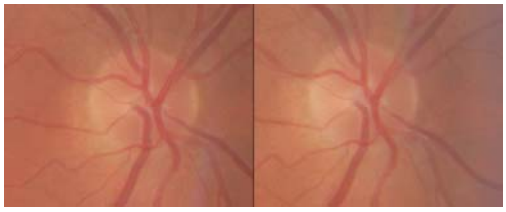
## IMAGING DEVICES

## Imaging devices- Journey

- Have come a long way
- From devices for research
- To clinically useful and available technology

## Gold standard

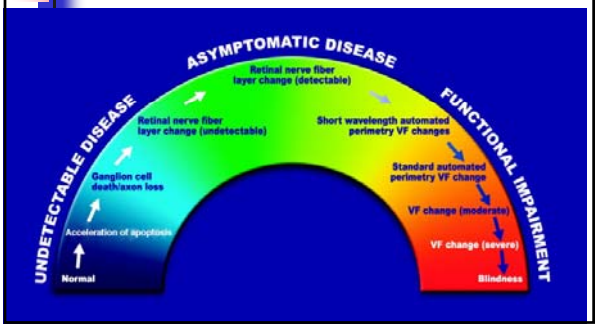
- Simultaneous stereo photography!
  - Problems?



## When to use imaging technology?

- Role in glaucoma diagnosis is growing
- Documents structure of optic disc or RNFL
- How does statistical significance relate to clinical significance?? Unknown

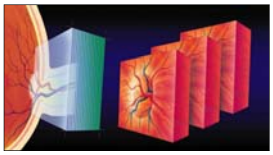
## AJO 2004 Weinreb et al



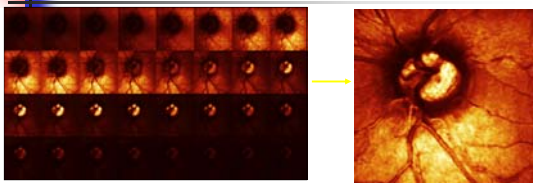

## Heidelberg Retina Tomograph

- First
- Relatively unchanged
- Confocal scanning laser ophthalmoscopy

## SLO video

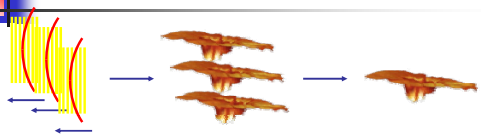
## Local Surface Height Measurements



Up to 64 Series of the individual optical section images are combined to create a single 3-D topographical image

Final image has 384 x 384 = 147,456 local surface height measurements (pixels)

## Compute Mean Image Topography

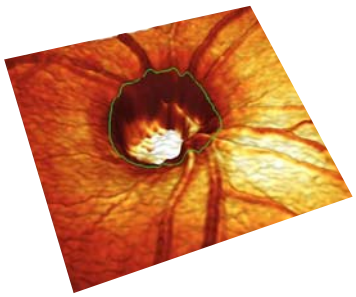


3 sets of raw image series

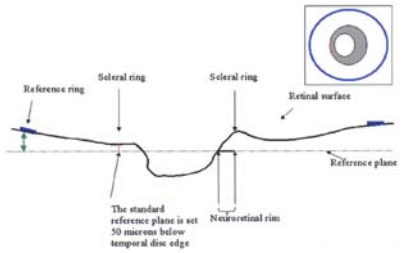
3 topographical images (3-D image)

1 mean topographical image

## 3D Topographic Image of the ONH and RNFL

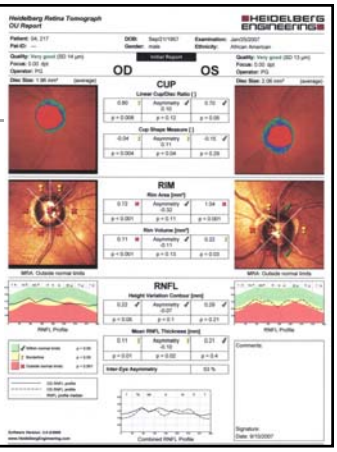


## Reference plane of HRT




RJ Watkins, L Panchaal, J Uddin, **P Gunvant**: Vertical cup-to-disc ratio - Agreement between direct ophthalmoscopic estimation, fundus biomicroscopic estimation and scanning laser ophthalmoscopic measurement. ***Optometry and Vision Science***, 2003: 80: 454-459.

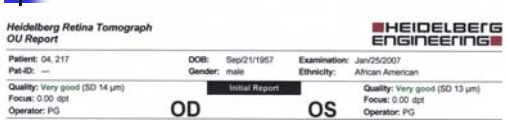
## HRT-3




## HRT-3 OU printout

- 4 sections
  - Patient demographics and quality checks
  - Optic disc cup
  - Neuroretinal rim
  - Retinal nerve fiber layer (RNFL)

## Patient demographics




## Probability Indices

- p > 0.05- 95% of normality
- p < 0.05 > 0.001 borderline
- p <0.001

- Within Normal Limits
- Borderline
- Outside Normal Limits

## Detecting Glaucoma with the HRT 3

Cup Analysis →

Rim Analysis →

RNFL Analysis →


**All Analyses are adjusted for age and optic disc size and utilize large ethnic specific databases**

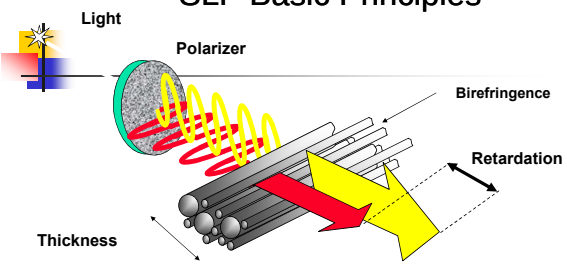
## Optic disc size

Patient Information
- Ethnicity for database
- Optic Disc Size

**small** **< 1.6 mm²**
**average** **1.6 - 2.5 mm²**
**large** **> 2.5 mm²**

## GDx-Variable Corneal Compensator

## SLP Basic Principles




The amount of retardation from the RNFL is directly proportional to the RNFL thickness[1].
Retardation =Birefringince* thickness

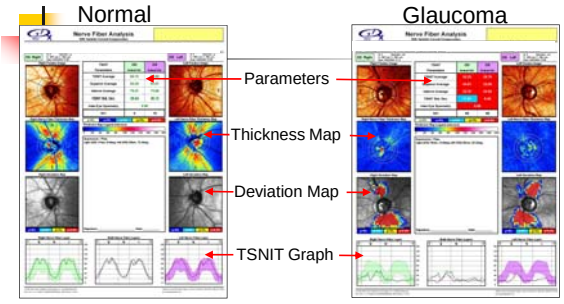
[1] Weinreb et al. *Arch Ophthalmology* 1990; 108: 557-560.

- Variable Corneal Compensation eliminates the effect of Corneal Polarization
- Extremely user friendly
- Minimal user experience required

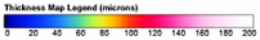
## GDx-VCC Measurement technique

- Obtain individual corneal compensation
- Then measure parapapillary retardation
  - Why?
  - Total Birefringence = Cornea + Lens + RNFL

## GDx-VCC Printout

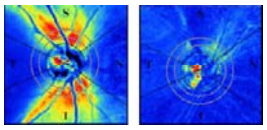


## Thickness map

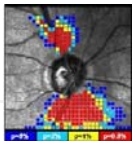



- Thin Blue
- Thick: Yellow, orange & red

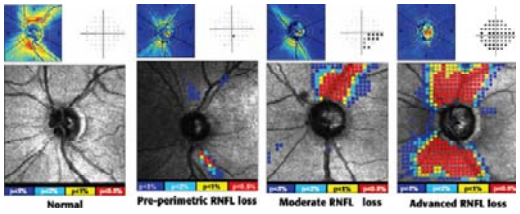
- Pink and white: Present only in uncompensated scans!!!



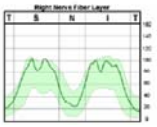
## Deviation Map



- 128x128 pixels= 20x20 degrees
- 32x32 square grid each square is 4x4 pixels (super pixel)

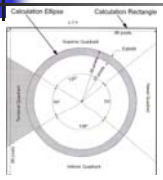



## TSNIT Map and Table of parameters



| TSNIT Parameters | OD Actual Val. | OS Actual Val. |
|---|---|---|
| TSNIT Average | 64.13 | 63.62 |
| Superior Average | 83.24 | 81.61 |
| Inferior Average | 79.37 | 73.95 |
| TSNIT Std. Dev. | 29.54 | 26.13 |
| Inter-Eye Symmetry | 0.96 | |
| NFI | 4 | 10 |

## Interpretation of output



**Understanding parameters**

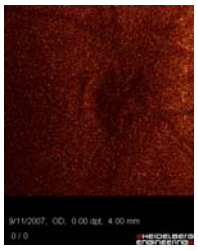
**TSNIT average**: Average of thickness values in circle.
**Superior average**: Average of all pixels in superior 120 degree of calculation circle
**Inferior average**: Average of all pixels in inferior 120 degrees of calculation circle

**NFI: Nerve fiber indicator**
<30 low likelihood of glaucoma
30-50 glaucoma suspect
>50 high likelihood of glaucoma

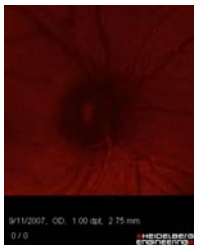
## Some artifacts in imaging

The artifacts that I am mentioning affect all imaging devices.

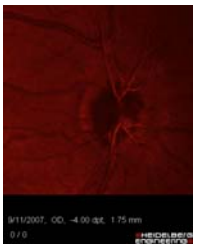
## Some artifacts in imaging -1



## Some artifacts in imaging -2

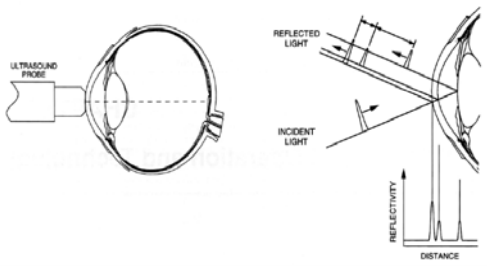


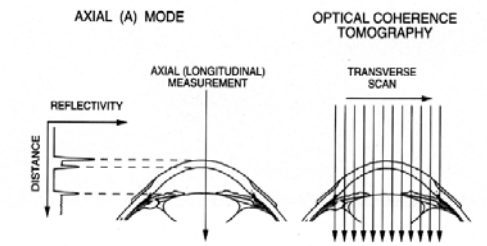
## Some artifacts in imaging-3 Defocus



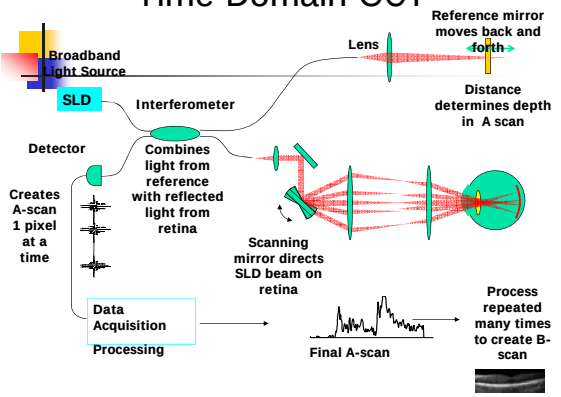
## Optical Coherence Tomography

## OCT-Principles

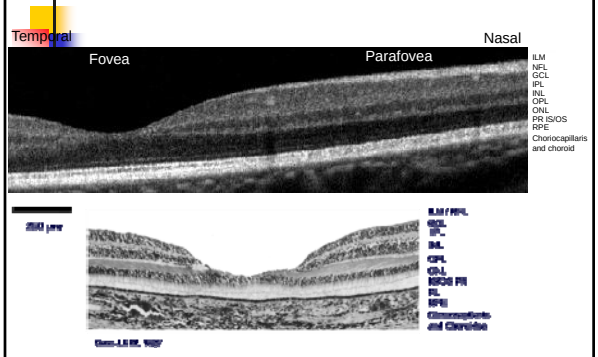



## Time Domain OCT

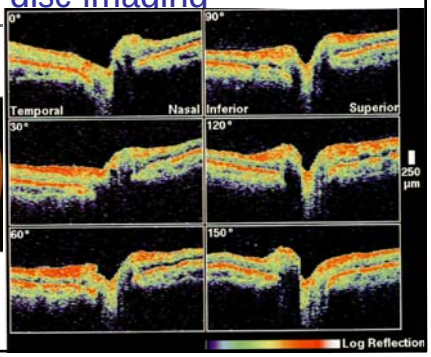


## Retinal Layers with OCT

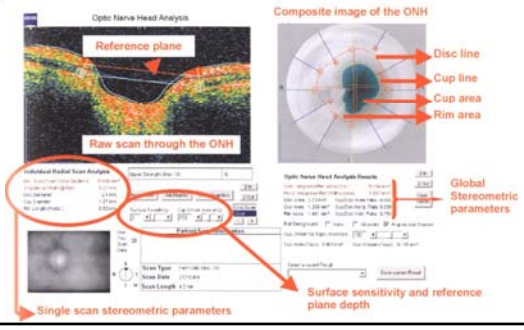



## Optic disc imaging

Six radial scans



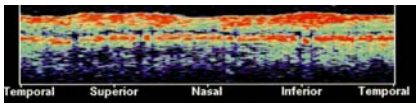

## Optic nerve head analysis



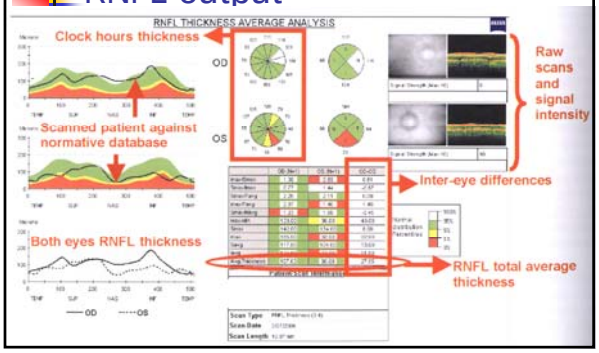
## RNFL measurements

RNFL-3.4: Takes 512 A-scans at a diameter of 3.4 mm

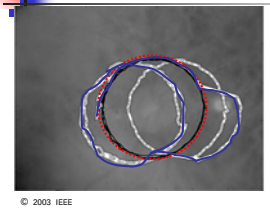
Fast RNFL3.4 : Takes 256 A-scans at a diameter of 3.4 mm




## RNFL output




## Stratus OCT Does Not Stop Eye Movement

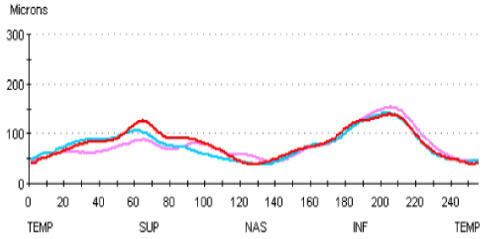


© 2003 IEEE

"Tracking the Optic Nervehead in OCT Video..." Koozekanani, et al, 2003

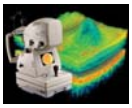
- While Time Domain OCT scans, the eye keeps moving
- The black line is the camera's perspective
- The white line is the actual scan path

## Image registration issues

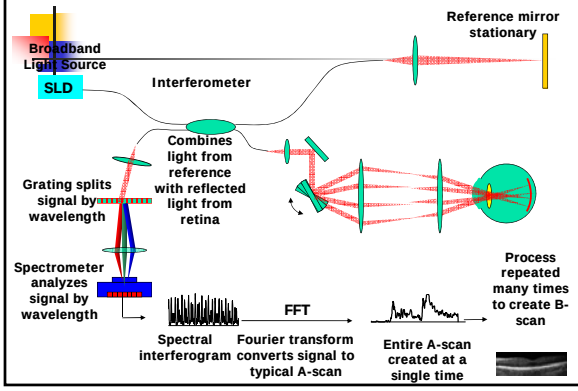



## Fourier Domain OCT's




## Fourier Domain OCT

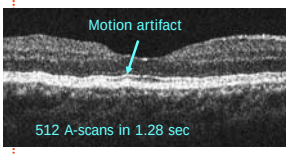


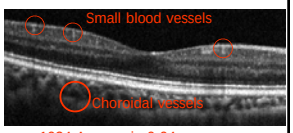
## Time Domain OCT

- Sequential
- 1 pixel at a time
- 1024 pixels per A-scan
- 400 A scans per second
- 512 A-scans in 1.28 sec
- Slower than eye movements

## Fourier Domain OCT

- Simultaneous
- Entire A-scan at once
- 2048 pixels per A scan
- 26 to 40 K A scans per second
- 1024 A-scans in 0.04 sec
- Faster than eye movements



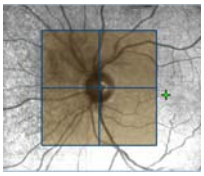




1024 A-scans in 0.04 sec

Slide courtesy of Dr. David Huang, USC

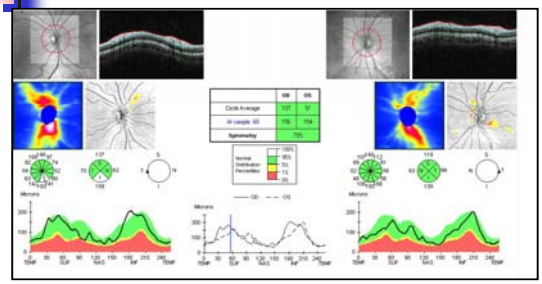
## Glaucoma – RNFL Thickness Analysis

- Optic Disc scan
  - Cube scan with 6mm x 6mm area



## Glaucoma – RNFL Thickness Analysis

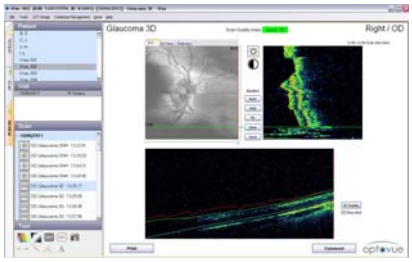
An OU analysis example (1)



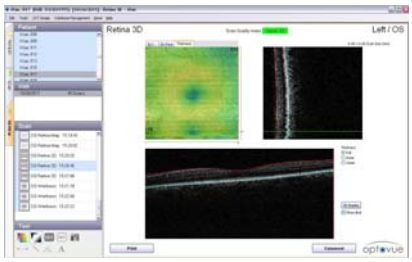
## Eye movement and Fourier domain OCT

## Eye Motion – X direction

Notice large horizontal shift through ONH.

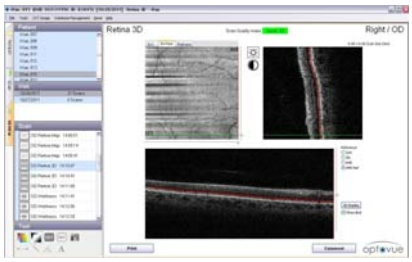


## Eye Motion – Y direction



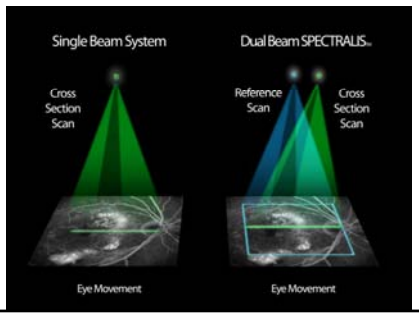

Note appearance of 2 foveas in thickness map and foveal depression in B-scan #118. Subject looked down and back so fovea was scanned twice.

## Eye Motion – Z direction

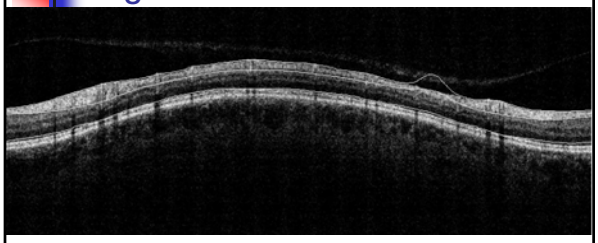



Ripple appearance in enface, SLO or thickness view

## SPECTRALIS® with TruTrack™ Follows the Eye



## Segmentation failure

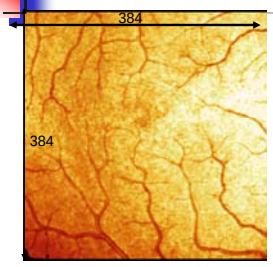


## Retina Module Premium Edition

HRT3

Glaucoma, Retina, Cornea

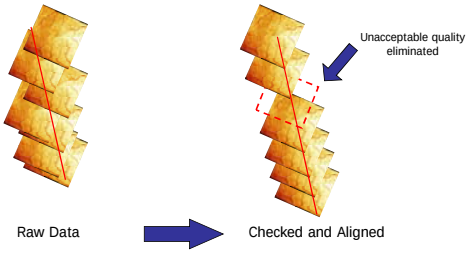
## HRT Single Scan Construction



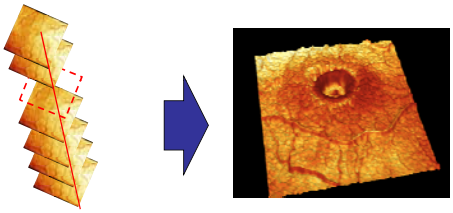

- 24-millisecond scan time
- Reduces artifacts from eye movements
- 147,456 data points captured
- Field of view: 15° × 15°

## HRT Alignment and Validation of Images

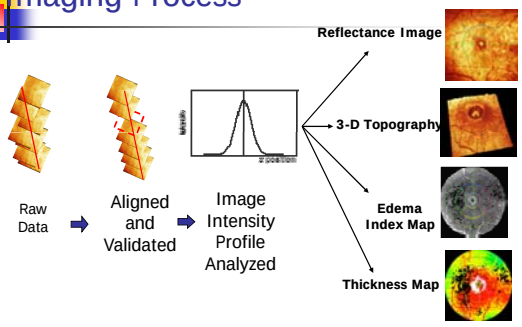
TruTrack™ Image Alignment Technology




## HRT 3-D Composite Image




## Summary of the TruTrack™ Imaging Process

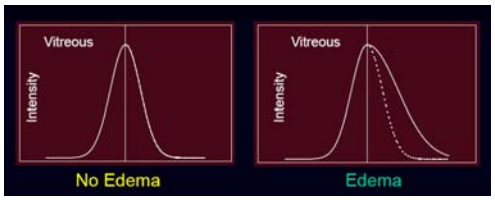


## Edema Index

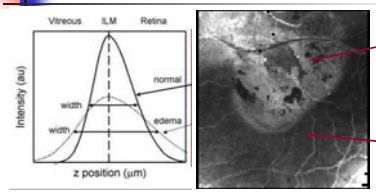
- Edema Index measures fluid accumulation in the retina
- Based on light scattering effects typically due to fluid
- Possible to detect early fluid accumulation prior to clinically significant thickening because of light scattering properties of fluid within the retina

## Confocal Intensity Profile

- If fluid is present, the amount of light scatter within the retina increases, widening the confocal intensity profile




## Edema Index Map



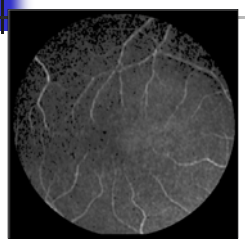



Light Areas
- More scatter
- More fluid

Dark Areas
- Less scatter
- Less fluid

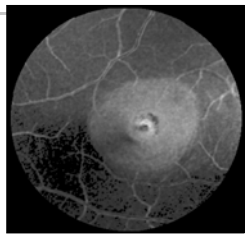
- Blood Vessels are light because of fluid
- White cloudy appearance indicates presence of excess fluid

## Edema Index Maps Interpretation



No Edema

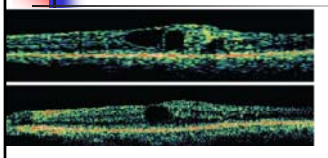
Even gray appearance

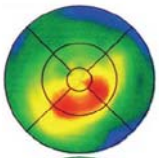


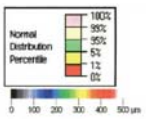
Edematous Eye

Large white cloudy areas

## OPTICAL COHERENCE TOMOGRAPHY AND DIABETES





## FLUORESCEIN ANGIOGRAPHY

## Fluorescein Angiography Background:

- Reaches ocular circulation by binding to serum albumin
- Fluorescence= when molecule absorbs light of 1 wavelength and then re-emits it at a higher wavelength thus lower energy
- Camera has 2 filters: Blue to excite, Yellow-Green to capture images

## IVFA and diabetes

- Diabetic retinopathy: determine extent of non-perfusion, IRMA vs neovasc
- Confirm neovascularization at disc
- Macular edema
- Neovascularization of iris vs normal blood vessels

## NPDR: Red Free

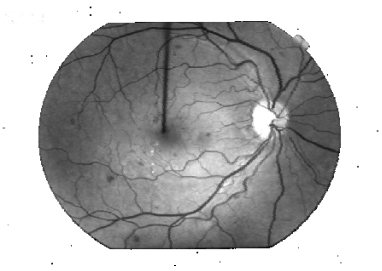


Image courtesy Dr. Jen Sandersen

## NPDR: Early Phase

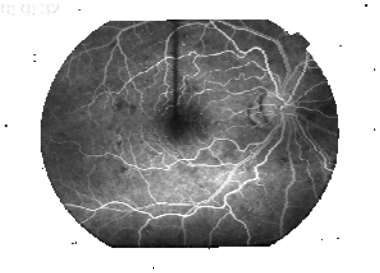


Image courtesy Dr. Jen Sandersen

## NPDR: Mid phase (or is it PDR?)

Image courtesy Dr. Jen Sandersen

## NPDR: Late phase

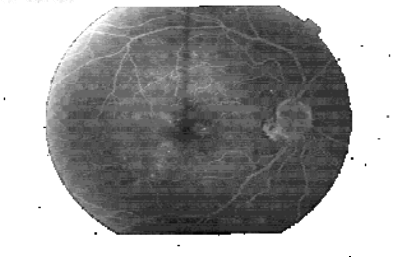


Image courtesy Dr. Jen Sandersen

## Proliferative Diabetic Retinopathy: NVE in Mid phase

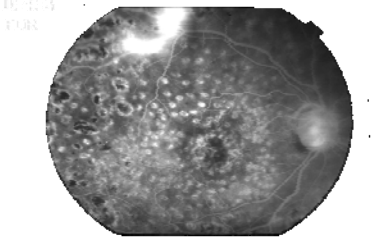


Image courtesy Dr. Jen Sandersen

## PDR: NVD in late phase

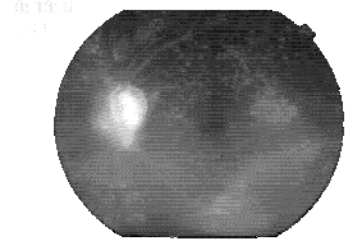
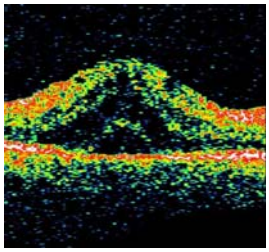


Image courtesy Dr. Jen Sandersen

## CME



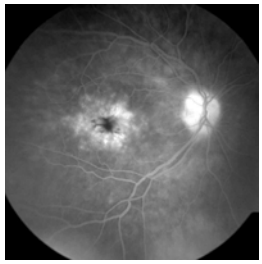


Image courtesy Dr. Jen Sandersen

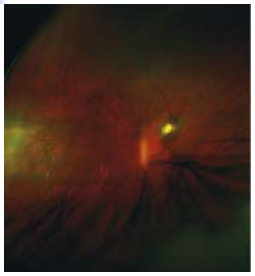
## Fundus Photography

- Invaluable
- Cheap
- Great for follow-up
- 30-50 degrees

## Indocyanine green angiography

- 98% protein bound
- Does not extravasate from choriocapillaris
- Excitation and emission wavelengths near-infrared
  - Allows penetration to deeper structures
  - Through overlying hemorrhages
- Suitable for choroid evaluations

## Optos Optamap



- Confocal scanning laser ophthalmoscope
- 180-200 degree field of view
- Possible benefit to diabetic retinal screening

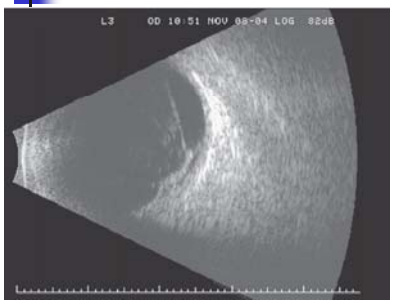
**Nonmydriatic screening for diabetic retinopathy by ultra-widefield scanning laser ophthalmoscopy (Optomap)**

Aljoscha S. Neubauer · Marcus Kernt · Christos Haritoglou · Siegfried G. Priglinger · Anselm Kampik · Michael W. Ulbig

Graefes Arch Clin Exp Ophthalmol (2008) 246:229–235

- CSME and Optos
- Sensitivity (average 91%) and specificity (average 81%) in identifying individuals with CSME

## Ultrasonography




Retinal detachment