New Ideas in Glaucoma Management

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Excellence in Optometric Education
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Glaucoma Evolution

POAG

Diagnostics

Therapeutics

Future Considerations
Glaucoma Evaluation is Transforming

- In the past, detection & management relied on functional assessment
  - Visual fields (white-on-white)
    - Insensitive for detecting early POAG
    - High degree of variability
- Recently, structural change over time longitudinal studies have validated the role of structural imaging
  - Are structural defects with normal functional tests false positives or POAG?
Glaucoma Evaluation is Transforming

- Glaucoma considered a NOCTURNAL disease
- IOP increases starting at bedtime and stay high all night
- Concept of “flattening the curve” of IOP
- New emphasis on sleep apnea link to POAG
  - Blood flow issues
  - Sleep lab studies
- Ocular blood flow
  - Systemic medications worsen blood flow to head
  - CMS temporary code for measuring ocular blood flow
Gonioscopy
92020

- Bilateral
- Requires documentation
  - describe visible angle structures
- No limitations to diagnostic groups in most states
- Fee $25.71-
Digital Gonioscopy 92020

- SL-OCT (Heidelberg)
  - Integrated Slit lamp & digital gonioscopy system
  - Haag-Streit BD 900 slit lamp, OCT scanning unit
  - High resolution grey scale or false color reports
  - Fast, easy, non-contact OCT at any position
  - Stores data
  - Measures angle, angle opening distance, angle recess area, trabecular iris contact length, trabecular iris space area
  - Measures pachymetry and biometry
Limitations of Manual Gonioscopy

- Patient discomfort – full globe contact
- Time consuming
- Subjective
- Requires considerable skill and experience

Statement of Assoc. of International Glaucoma Societies (AIGS)
3rd Global Consensus Meeting, May 2006
Pachymetry
76514

- Bilateral
- Measurement of central corneal thickness (CCT) proven by Ocular Hypertension Treatment Study (OHTS) to be standard of care in diagnosis and management of glaucoma, glaucoma suspect and ocular hypertension
- Also billable for keratoconus, corneal transplants, cataracts with corneal dystrophies, guttata, edema
- Requires Interpretation & Report
- Fee $11.92
Pachymetry

- Risk of POAG conversion in OCHTN is 11% (OHTS) in 5 years
- Risk is greater if CCT is THIN
  - 36%
  - Thin is <555um
- Thin corneas are an independent risk factor in OCHTN
- Thin corneas have not yet been found to be an independent risk factor for POAG
CCT Assessment

- Has become standard
- Equipment widely available
  - DGH was used in OHTS
  - Low cost
- Consider potential effect of LASIK on IOP findings
- Also billable for non-glaucoma ICD-9 codes
  - Corneal edema, keratoconus
Pachymetry

- IOP correction by correlation to corneal thickness is NOT POSSIBLE!
  - A linear relationship does not exist!
  - Careful examination of regression analysis (scatter graph of IOP relative to CCT) demonstrates huge bandwidth

- Adjusting IOP by CCT instills a degree of accuracy into an inaccurate measurement

- It is possible to adjust the IOP in the WRONG direction

- Barbados study of black patients shows no correlation of CCT/IOP

- “Trying to be more precise than this is not supported by the data and may be harmful to patient care” Jamie Brandt, MD Dir Glauc Src, UCD / OHTS investigator
Neuroprotectants

- Memantine (Nameda) – blocks Na, K channels, retards apoptosis
- Brimonididine (?)
- BDNF – inhibits programmed cell death
- Erythropoietin- EPO
- Future is neuroprotection to improve environment and
  - neurodegeneration with stem cells
  - Immunobiology with T cell based vaccination
Serial Tonometry
92100

- Bilateral
- Requires Interpretation & Report
  - Example: Angle closure glaucoma
  - multiple measurements over time
- Fee $55.91-
PASCAL at work:

- Slit lamp mounted
- Technique similar to GAT but…
- Constant light pressure
- No fluorescein
- Self-calibrating
- Battery operated
Pascal DCT

- Measures
  - Ocular Pulse Amplitude
  - (OPA)
  - IOP
  - Quality (Q)
  - Heart Pulse (H)

- Stores data
The PASCAL SensorTip

- Contour-matched concave tip surface (7mm)
  - Accurate for corneal radius 5.5-9.2mm and CCT 300-700
- Built-in pressure sensor (1.2mm)
- Transparent tip permits view of cornea interface for centering and control
2010 New CPT & ICD Codes

- Category III Codes
  - 0198T Measure of ocular blood flow
    - by repetitive IOP sampling,
    - with interpretation & report
Comparison of DCT With the GAT

- Univ. Of Zurich
- 228 eyes measure with DCT and GAT
- Compared IOP measurements
- Looked at effects of:
  - CCT
  - Corneal curvature
  - Astigmatism
  - AC Depth
  - Axial length
- Intra-observer and Inter-observer variability
DCT vs. GAT

- DCT median difference: DCT +1.7mm higher than GAT
- GAT: Affected by CCT, curvature, astigmatism, AC depth and axial length
- DCT: NO EFFECT with any parameters
IOP Measurements Using DCT After LASIK

“Corneal ablation of 90.0 +/- 49.18 microns reduced IOP as measured by GAT by 3.0 +/- mm. .. no significant change in IOP was recorded by DCT (-0.2 MM)”

“Assuming that CCT can be used as a correction factor for GAT is a misinterpretation of the results of OHTS… that couldn’t be further from the truth. Adjusting IOP based on CCT is attempting to instill a degree of precision into a flawed measurement. You may actually correct in the wrong direction. The issues related to the most accurate tonometry need to include the material properties of the cornea”

James Brandt, MD
Director Glaucoma Services
UC Davis
IOP Measurements By DCT After LASIK

- “Corneal ablation of 90.0 +/- 49.18u reduced IOP as measured by GAT by 3.0mm...no significant change in IOP was recorded by DCT (-0.2MM)”
- Clinically validated by manometric studies of true intracameral pressure
- LASIK case volume in US is 7,401,400
  - GAT DOES NOT WORK!

Case of “I Have A Peculiar Nerve”

- 45yowm CC: “OD wants R/O Papilledema”, Indistinct optic discs, IOP 20-25 range, pach 637
- PH: Hodgkin’s disease, R hip replacement, 3 vessel CABG, HTN, Hyperlipidemia
- FH: + POAG paternal aunt
- Meds: Darvocet, Amitryptilline, nitrate, isosorbide, norvasc, toprol, plavix, lipitor, ASA
- VA 20/20 OU PERRL-APD
- IOP: 26/23 Pach: 639
- SLE: N1 OU Fundus: As shown
What is the diagnosis?

1. Normal optic nerves
2. Papilledema
3. Optic nerve drusen
4. Ocular histoplasmosis
5. Choroidal nevus
What tests are indicated?

1. VF / Pach / SCODI / Stereo disc photos
2. MRI
3. MRI / VF
4. Histoplasmosis titres
5. IVFA / VF
Case of “I Have A Peculiar Nerve”

- 45yowm CC: “OD wants R/O Papilledema”,
- DCT OD: 24.9 / OPA 4.4 / Q3
- DCT OS: 23.1 / OPA 3.8 / Q3
- SLE: Nl OU Fundus : As prev
- VF OD: Superior and inferior nasal defects
- VF OS: minor changes
- SCODI: Confirms disc elevation limited to disc itself
Corneal Compensated IOP (IOPcc)

- 7CR Autotonometer – Reichert
- Pressure significantly less affected by the cornea than other instruments
  - Hysteresis is a risk factor for glaucoma
- Incorporates bidirectional applanation technology used in ORA, to quantify biomechanical properties of cornea
- Non contact (air puff) simultaneously provides a Goldmann-correlated (IOPg) and IOPcc
- Helpful in patients with cornea disease and glaucoma
i-Care Tonometer

- Hand held, portable
- NO ANESTHESIA
- Disposable probe
- Accurate
- Power – AA batteries
- Measurement in 0.1 sec
  - Measures motion of cornea
- Digital display
- Memory – last 10 results
i-Care Tonometer

- Applications
  - Eye MDs
  - ODs
  - General practitioners
  - Pharmacy
    - Screenings
  - Veterinarians
  - Consumers
    - Self screenings
Icare® tonometer

- Accuracy ±1.2 mmHg (≤ 20 mmHg) compared to GAT
- Requires no calibration
NEW Icare® PRO

- Professional expertise for glaucoma diagnostics and clinical follow-up
- Rechargeable batteries and docking station with integrated charger & data transmission
Icare® Tonovet

- Useful tool for measuring intraocular pressure on animal patients (dog/cat, horse)
- Painless => creates no anxiety in the animal
- Measurement barely noticed by the animal

- Veterinary ophthalmologists
- Other veterinary medical personnel
Visual Field 9208x

- Bilateral
- Requires Interpretation
  - separate report form
  - narrative in body of medical record, on date of service
- Fee $43.88- (-81)  $57.37+ (-82)  $65.92- (-83)
Oculus Easy Field Perimeter

- Screening AND Threshold fields
- Color LCD-Display
- Fixation monitoring
  - CCD camera
- Stores up to 40,000 exams
- Built-in printer
FDT Perimetry Abnormalities as Predictors of Glaucomatous VF Loss

- 105 eyes of 105 glaucoma suspects
  - IOP 23mm+ or disc damage on photos
  - SAP VF normal

- Baseline FDT obtained

- Mean follow-up 41 months

Medeiros FA, et al AJO 137:863-871, 2004
FDT as Predictor of VF Loss

- 16% (17 pats.) converted on SAP VF

- In pats. with abnl. FDT at baseline:
  - Probability of developing abnl. SAP: 30%

- Pats. With NL FDT at baseline:
  - Probability of developing abnl. SAP: 4%
Other Important VF Studies

- Paczka (2001) - found FDT better overall performance in detecting damage than RNFL photographs

- Kondo (1998), Wu (2001) - In patients with SAP VFDs restricted to 1 hemifield, FDT has shown to be able to detect functional losses in the other hemifield

Other Important VF Studies

- Kim (2007/AAO) – when SAP is normal, some patients with VFD detected by FDT showed decreased NFL thickness (OCT)
  - Provide evidence that coincident FDT & OCT abnormalities may be an early sign of glaucoma
Visual Field Testing for Specific Functions

- Short wavelength autoperimetry (SWAP)
  - Bistratified ganglion cell (9%) short-wavelength cones
- Frequency doubling technology (FDT)
  - Magnocellular ganglion cells
- Motion automated perimetry (MAP)
  - Magnocellular ganglion cells (3%)
- High pass resolution perimetry (HPRP)
  - Parvocellular ganglion cells
OptoUS Perimeter

- Fast speed
- Ergonomic design patient friendly
- SAP
- Blue yellow testing in 3 min/eye
- Critical fusion testing
- One min screen
- Three min full threshold
- LAN network
- Recently acquired by Optos
Octopus 301 Perimeter

- Motorized auto eye tracking
- 100% fixation control
- Blazing fast speed
- Ergonomic design patient friendly
- Blue yellow testing in 3 min/eye
- Critical fusion testing
- One min screen
- Three min full threshold
- PeriTrend Analysis
- LAN ethernet
- 800.787.5426
- www.haag-streit.com
Current Perimeters are Highly Variable

- After **one** abnormal visual field test:
  - 86% of patients test within normal limits on next exam

- After **two** consecutive abnormal test results:
  - 66% of patients test within normal limits on next exam

![Graph showing % Patients Returning to "Normal"

<table>
<thead>
<tr>
<th>Number of Consecutive VF Tests</th>
<th>% Patients Returning to &quot;Normal&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>86%</td>
</tr>
<tr>
<td>2</td>
<td>66%</td>
</tr>
</tbody>
</table>

Heidelberg Edge Perimeter

- New “Flicker Defined Form” Stimulus
- Overcomes limitations in Frequency Doubling Technology
- True targeting of M-cell visual pathway
- Less test-retest variability
- Direct link to HRT optic disc assessment
Flicker Defined Form (FDF) Targets M-cells

- The magnocellular (M-cell) pathway is one of the three main neural pathways from the retina to the primary visual cortex.
- M-cells may be the first to sustain damage in glaucoma\(^2,3\).
- There are fewer M-cells so selective testing can find defect to all cells earlier\(^4\).
- FDF selectively targets the M-cells which are sensitive to high frequency and high contrast stimuli.

5. Glovinsky et al. Retinal ganglion cell loss is size dependent in experimental glaucoma. IOVS. 1991;32:484-491
6. Kerrigan-Baumrind et al. The number of ganglion cells in glaucoma eyes… IOVS. 2000;41:741-748
How is Flicker Defined Form (FDF) Different?

- Frequency Doubling Technology is not as selective at stimulating the M-cell pathway as previously thought.\(^5\)

- Standard Automated Perimetry stimulates all retinal cells (broadband stimulus)

- FDF is more selective and targets the M-cell pathway

- FDF studies show less test-retest variability

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HEP: The New Perimeter for Glaucoma Management

- New FDF stimulus for early signs of glaucoma
- Less test-retest variability for improved diagnosis
- Structure-Function Map for combined assessment
- Network-ready
- Test types
  - Contrast sensitivity
  - Letter tests
  - Driving test
New Functional Testing

- Pattern ERG (PERG) – improves with decreased IOP
- Multifocal VEP – higher flicker VEP
- Isolated Check VEP
  - Tests central vision
  - Bright Check Pattern (M-cells)
  - Dark Check Pattern (off pathway cells)
- Pupil perimetry (True Field Analyzer)
  - Computer measures pupil (involuntary) diameter in response to retinal visual stimulation
Researchers view Glaucoma as a disease of the brain
  - Neurodegenerative disease

Glaucoma shares common features with AD, Parkinson’s and Lou Gehrig’s diseases

Offers potential for new treatments that promote nerve health, neurotrophic factors which can help at multiple places in the visual pathway
  - Neuroprotection – Ciliary neurotrophic factor (CNTF)
  - Neuroregeneration – increase axon regrowth
  - Neuroenhancement – improve support between dying RGC and surrounding cells in brain and retina
Visual Evoked Potential

- Nova-DN VEP Vision Testing System (Diopsys)
  - Not new technology, but clinically useful and affordable is
    - Improves sensitivity & specificity in glaucoma diagnosis
  - Short duration transient VEOP (SD-tVEP) to record electrical responses of the entire visual system
  - Objective test, 4-6 minutes
  - Low contrast testing – health of magnocellular pathways
  - High contrast testing – health of parvocellular pathways
  - Serial tracking of disease progression
  - Useful in MS, TBI, Stroke and other CNS disorders
Visual Evoked Potential - Coding

- Nova-DN VEP Vision Testing System (Diopsys)
- CPT: 95930
  - Bilateral
  - No CCI bundling edits in office setting
- ICD – includes many optic nerve and retina disorders, visual disturbances (amblyopia, SVD, night blindness, sudden vision loss, et al), neurological (aphasia, MS, Lyme, TBI, intracranial diseases, conversion, gait abn, coordination, etc)
- Fee: $133.19 (range $60-$180 commercial)
Closing Statements

- Advances in perimetry are continuing
  - Faster third generation algorithms reduce test time by 50%

- Customization for specific needs
  - Early detection / established glaucoma / screening

- Early VF loss is often selective, with specific types of axons disturbed
  - SWAP allows early recognition, HPRP follows progression

- SAP perimetry will continue to be preferred for established glaucoma with VFDs
  - Considerably improved methods of computer-assisted interpretations of serial VFs

- Screening methods will sacrifice sensitivity for specificity and ease of use to detect the half of glaucoma patients who have undiagnosed disease
  - Deployed in non-professional environments
Fundus Photography
92250

- Bilateral
- Not Bundled
- Stereo disc photography
- Requires Interpretation
- Fee $73.67+
Unilateral

Applies to glaucoma and retinal evaluations
- Retinal Thickness Analyzer (RTA)
- Heidelberg Retinal Topography (HRT3, Spectralis)
- Zeiss Optical Coherence Tomography (GDX, Stratus/Cirrus OCT)
  - Optovue (RTVue, iVue)

Requires Interpretation & report

Fee $42.42
Scanning Computerized Ophthalmic Diagnostic Imaging
92133

- Unilateral or bilateral
- Applies to glaucoma or optic nerve evaluations
  - Heidelberg / Heidelberg Retinal Topography (HRT, Spectralis)
  - Carl Zeiss / Optical Coherence Tomography (GDX, Stratus, Cirrus)
  - Optovue / (RTVue, iVue)
  - Marco / Retinal Thickness Analyzer (RTA)
- Requires Interpretation & report
- Fee $42.24
Scanning Computerized Ophthalmic Diagnostic Imaging - 92133

- 360.30-360.34 Hypotony and flat chamber
- 354.22 Glaucomatocyclitic crises
- 365.00-365.04 Glaucoma suspect, OCHTN
- 365.10-365.15 Open angle glaucoma
- 365.20-365.24 Primary angle closure glaucoma
- 365.31-365.32 Steroid induced glaucoma
- 365.41-365.44 Glauc w chamber anomalies
- 365.51 Phakolytic glaucoma
- 365.52 Pseudoexfoliation glaucoma
- 365.59 Glaucoma assoc w lens disorders
Scanning Computerized Ophthalmic Diagnostic Imaging - 92133

- 365.60-365.65 Glaucoma assoc w ocular trauma
- 368.40-368.45 Visual field defects
- 376.00-376.9 Acute inflammations of the orbit
- 377.00-377.03 Papilledemases
- 377.04 Foster-Kennedy
- 377.10 Optic atrophy
- 377.14-377.16 Glaucomatous atrophy
- 377.21 Drusen
- 377.22 Crater like holes of optic disc
- 377.23 Coloboma of optic disc
Scanning Computerized Ophthalmic Diagnostic Imaging - 92133

- 377.24 Pseudopapilledema
- 377.41-377.49 Ischemic optic neuropathies
- 377.51-377.54 Disorders of optic chiasm assoc w pit neoplasms or inflammatory disorders
- 377.61-377.63 Disorders of other visual pathways assoc w neoplasms or inflammations
- 743.20-743.22 Buphthalmos
- 743.57-743.58 Cong anomalies of optic disc & vasc anomalies
GDx VCC

- Image acquisition in less than 1 second
- Uses internal fixation device
- Compact, table-top design
- Portable
- Easiest to use
- Comfortable, objective test for patients
- Easy interpretation
SLP - Strengths

- Provides insight into patient’s RNFL condition
- Screening Mode option (helps identify which patients need full glaucoma workup)
- Compact and portable
- No dilation required
SLP - Weaknesses

- Considerable challenges with artifacts. One study saw atypical birefringence in 51% of glaucomatous eyes.
- Still working on eliminating influence of anterior segment components.
- Long term validity due to continuous platform changes.
Top 5 Stereometric Parameters

- Rim Area
- Rim Volume
- Cup Shape Measure
- Height Variation Contour
- Mean RNFL Thickness
DIAGNOSE: CUP, RIM & RNFL

- Optic disc size measure and “small”, “average” and “large”
- Parameters adjusted for disc size
- Largest normative database
- Ethnic-selectable
- OU asymmetry
- RNFL normative data
- Quality Indicator
- Conclusion:
  Complete Assessment
Monitor Change Over Time

- Baseline compared to follow-up images
  - Absolute change calculated

- Progression Change Probability Analysis
  - Pixel by pixel comparison
  - Independent of reference plane
  - No contour line is needed

- Progression Trend Report
  - Normalized stereometric parameters graphically displayed
How Predictive is the HRT?

- Moorfields Regression Analysis – measures rim area & adjusts for disc size

- **40%** of patients flagged at baseline as “outside of normal limits” by Moorfields Temporal Superior sector analysis developed glaucoma.

- **26%** of patients flagged at baseline as “outside normal limits” by Moorfields Global analysis developed glaucoma.

- **90%** of those with normal HRTs did not develop glaucomatous damage over the next 5 years
What if we could take the world’s leading glaucoma experts and use their combined knowledge to help you diagnose your patients?

The Glaucoma Probability Score takes the first step in this direction by applying machine learning to glaucoma diagnostics.
"Find a bug in a program, and fix it, and the program will work today. Show the program how to find and fix a bug, and the program will work forever."

- Oliver G. Selfridge, in *AI's Greatest Trends and Controversies*
Glaucoma Probability Score

- A new approach to optic disc analysis
- 6 years in development
- Applies the latest in artificial intelligence to glaucoma diagnostics – “Relevance Vector Machine”
- Produces an understandable indicator - probability of disease
- Eliminates the need for contour lines or reference planes
GPS How It Works

- Uses same HRT scan as in the past
- Performs 3-dimensional shape analysis
- Relevance Vector Machine is “trained” to look for glaucoma
- Measures 5 key parameters
- 3 parameters represent cup shape and 2 represent RNFL
GPS: Clear and Simple

- Provides similar sensitivity and specificity as Moorfields
- Fast assessment
- Overall, global and sector indicators
- No operator drawing or intervention needed
Case of the “Ocular migraine?”

- Age: 43yowm CC: “Flashes of light”
- HPI: 20mins / OU / once / 3L soda/Day / -HA, nausea, vomiting / overweight
- Meds: synthroid, Allergy: none
- BVA: OU 20/20  Pupils: PERRL-APD  EOM: full
  EXT: NL, CA auscultation Nl
- Pach: 528/532  SLE: N1 OU  IOP 24/24,17/17
- VF: normal  Optic N: OD 0.80 OS 0.65
- OcHx: Mother & brother susp ONH & Nl VF
CSLO – Strengths & Weaknesses

- **Strengths:**
  - Non-dilated patients
  - Registration of data and measurement of area of retina
  - Measures the complete area – no interpolation
  - Can identify early Glaucoma
  - Can identify edema (can differentiate between thickenings with and without edema)
  - Data is gathered in triplicate – so quality of scan can be quantified
CSLO – Strengths & Weaknesses

- **Weaknesses**
  - **Glaucoma:**
    - Drawing of the contour line,
    - End point Glaucoma…. Not useful
  - **Retina:**
    - New application – beginning to get acceptance
    - Can not identify retinal layers
    - 15 degree image
Support Literature

- Heidelberg Engineering website: www.heidelbergengeineering.com
  - Complete list of published articles on all products
  - Abstracts of published articles
  - Condensed summary of the supporting literature for main topics of interest
  - Downloadable tutorials for all HE products
Optical Coherence Tomography OCT

Optical: Light-based

Coherence: property of light waves in which the oscillations maintain a fixed relationship to each other

Tomography: Cross-sectional imagery
How OCT works

- Similar to ultrasound but uses light instead of sound to image tissue
- Beam of light is directed into tissue and reflections coming from different layers of the tissue are received by a detector
Optical “Ultrasound”

- Basically, the OCT identifies layers of tissue that reflects more than others.
- The computer than analyzes these and designates tissue levels based on the sequence of the reflections
Glaucoma – RNFL Thickness Analysis

- Center of disc is automatically identified for precise registration and repeatability
- RNFL thickness display is of a 1.73mm radius circle around the disc
- TSNIT graph is compared to normative database of about 300 patients
Precise Registration

- Real Time Registration between OCT and LSO Fundus
- Visit-to-visit Registration using the LSO overlay from previous visit
- Optic Disc Registration automatically centers the RNFL TSNIT circle around the disc
Optic Nerve Head Analysis

- The Cirrus™ HD-OCT Optic Nerve Head Analysis software provides automated identification of the optic disc/cup boundaries, rim while accounting for tilted discs, disruptions to RPE and other pathology.
Optic Nerve Head Calculations

In tilted discs, when the nerve exit is oblique, the disc is viewed at an angle by the clinician, foreshortening the image. Therefore areas visualized in the ophthalmoscope examination, photographs, or other images will be reduced.

Measuring the area in the same plane as the optic disc addresses this foreshortening and better ties the results to the anatomy.
Enhanced 3D Visualization

More powerful visualization, including:

• Lighting intensity and direction
• Multiple movie recording modes
• Embedded segmentation surfaces
• Morphology isolation using pixel intensity windows
SD OCT - Strengths

- Unparalleled visualization of the retina
- Registration possible for longitudinal analysis
- Some technologies have married this technology with other imaging technologies (i.e. FA, ICG combined with SD OCT)
SD OCT - Weaknesses

- New technology needs to be presented in a useful clinical package
- Cost
<table>
<thead>
<tr>
<th>Glaucoma Analysis with the RTVue: Nerve Head Map</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nerve Head Map (NHM)</strong></td>
</tr>
<tr>
<td>• Data Captured: 9,510 A scans (pixels)</td>
</tr>
<tr>
<td>• Time: 370 msec</td>
</tr>
<tr>
<td>• Area covered: 4 mm diameter circle</td>
</tr>
<tr>
<td>Provides</td>
</tr>
<tr>
<td>• Cup Area</td>
</tr>
<tr>
<td>• Rim Area</td>
</tr>
<tr>
<td>• RNFL Map</td>
</tr>
<tr>
<td>TSNIT graph</td>
</tr>
<tr>
<td><strong>Ganglion Cell Map (MM7)</strong></td>
</tr>
<tr>
<td>• Data Captured: 14,810 A scans (pixels)</td>
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<tr>
<td>• Time: 570 msec</td>
</tr>
<tr>
<td>• Area covered: 7 x 7 mm</td>
</tr>
<tr>
<td>Provides</td>
</tr>
<tr>
<td>• Ganglion cell complex assessment in macula</td>
</tr>
<tr>
<td>• Inner retina thickness is:</td>
</tr>
<tr>
<td>• NFL</td>
</tr>
<tr>
<td>• Ganglion cell body</td>
</tr>
<tr>
<td>• Dendrites</td>
</tr>
<tr>
<td><strong>3-D Optic Disc</strong></td>
</tr>
<tr>
<td>• Time: 2 seconds</td>
</tr>
<tr>
<td>• Data Captured: 51,712 A scans (pixels)</td>
</tr>
<tr>
<td>• Area covered: 4 x 4 X 2 mm</td>
</tr>
<tr>
<td>Provides</td>
</tr>
<tr>
<td>• 3 D map</td>
</tr>
<tr>
<td>• Comprehensive assessment</td>
</tr>
</tbody>
</table>
The ganglion cell complex (ILM – IPL)

Inner retinal layers provide complete Ganglion cell assessment:

• Nerve fiber layer (g-cell axons)
• Ganglion cell layer (g-cell body)
• Inner plexiform layer (g-cell dendrites)

Images courtesy of Dr. Ou Tan, USC
Spectral-Domain OCT
- 26,000 A-scans/sec
- 5 micron resolution

Scans
- Retina – 6x6mm thickness map, 5 line raster over-sampled & averaged, and Cross Line
- Glaucoma – ONH scan (w/o Optic Disk metrics)
- Cornea – 6x6mm Pachymetry Map with averaged horizontal line scan, and Angle scan
- Follow-up scans with Change Analysis
Ophthalmic Genetics

- Researchers have identified genes for OAG
  - TIGR/Myocilin = juvenile OAG
  - OPTN (optineurin) = Primary OAG (NTG)
    - Optineurin may provide neuroprotection to optic N
  - CYP1B1 = Congenital glaucoma

- Genetic testing will allow clinicians to determine if Pt is predisposed to or affected with specific type of glaucoma, even before symptoms appear

- OcuGene (InSite Vision/Alimed) – simple, in office test, 99% accurate detection of TIGR (trabecular meshwork inducible glucocorticoid response gene)
  - Positives may be treated more aggressively, earlier
Low Tension Glaucoma

- Compromised ocular blood flow
- 50% have a cause / find it / fix it
  - Past hx transfusions, bleed, hypovolemic
  - Medications: B-blockers, digoxin, digitalis
  - MRI: orbits & brain
  - R/O all cardiovascular causes of LTG
    - CBC/anemias, CA doppler, TEE, sleep studies, coagulaopathies (PTT), overly fit (low BP)

- Treatment
  - Decrease IOP, avoid B blockers, start with PG, bromonidene, CAIs last resort
  - Ginko biloba 60mg/D: inc fluidity without affecting platelet aggregation
Characteristics of Glaucoma in Japanese Americans

- Pekmeezi M ArchOphthal 2009;127(2):167
- 1732 patients in Japanese-American clinic over a ten year period
  - 112 with glaucoma, 17% HTG, 70% NTG
- Proportion of patients with NTG was 4-fold higher than those with HTG
Anti-Glaucoma Agents

- **Non-Selective B-Adrenergic Antagonists**
  - Timolol (Timoptic 0.25%, 0.50%, XE, Ista Pharmaceuticals)
  - Levobunolol (Betagan 0.25%, 0.50%)
  - Metipranolol (Optipranolol 0.3%)

- **Selective B-Adrenergic Antagonists**
  - Betaxolol (Betoptic-S 0.25%, 0.50%)
  - Levobetaxolol (Betaxon)
  - Carteolol (Ocupress 1.0%)
Anti-Glaucoma Agents

- Prostaglandin Analogue
  - Latanoprost (Xalatan 0.005%) generic 3/2011
  - Bimatoprost (Lumigan 0.03%, Lumigan 0.01%*)
  - Travaprost (Travatan Z 0.004%) – No BAK
  - Tafluprost (Zioptan PF)
Latanoprost 0.005%

- Topical prostaglandin
- Indications: open angle glaucoma or ocular hypertension
- Side effects – hyperemia of conjunctiva, iris pigmentation/color change, lid erythema, eyelash growth
- Dosage: once daily at bedtime
- Advantages: monotherapy/compliance, favorable SE profile, longest track record, generic March 2011
- Available as Xalatan
Bimatoprost 0.03% & 0.01%**

- Topical prostaglandin
- Indications: open angle glaucoma or ocular hypertension
- Side effects – hyperemia of conjunctiva, iris pigmentation/color change, lid erythema, eyelash growth
- Dosage: once daily at bedtime
- Advantages: monotherapy/compliance, favorable SE profile with lower concentration but equal IOP lowering
  - Switch when having SE with other PGs or as first line PG
- Available as **Lumigan, Lumigan 0.01%**
Tafluprost 0.0015%

- Topical prostaglandin, first preservative-free preparation
- Indications: open angle glaucoma or ocular hypertension
- Supplied: 10 PF ampules per pouch, 3 pouches/box
- Side effects – same as other PGA
- Dosage: once daily at bedtime
- Storage: refrigeration necessary until pouch is opened, then once opened room temperature is fine
- Available as Zioptan / Merck
Anti-Glaucoma Therapy

- **Adrenergic Agonists**
  - Dipivefrin (Propine 0.1%)
  - Epinephrine (Epinal, Eppy-N, Epifrin, Glaucon)
  - Apraclonidine (Iopidine 0.5%, 1.0%)
  - Brimonidine (Alphagan 0.2%, Alphagan P-0.1%, 0.15%) / Timolol (Combigan)
    - 41% less ocular allergy with Alphagan P vs Alphagan over 12 months
    - Only ophthalmic glaucoma drug without BAK

- **Cholinergic**
  - Pilocarpine (Pilocar 0.50% - 8.0%, Pilogel 4%)
  - Carbachol (Carbachol 0.75%, 1.5%, 2.25%, 3%)
  - Echothiophate Iodide (0.03%, 0.06%, 0.125%, 0.25%)
Antiglaucoma - CAI

- **Topical**
  - Dorzolamide (Trusopt)
  - **Dorzolamide-Timolol (Cosopt)**
  - Brinzolamide (Azopt)

- **Oral**
  - Acetazolamide (Diamox)
  - Methazolamide (Neptazane, MZM)
  - Dichlorphenamidine (Darinide)
Ranibizumab / Lucentis

- for injection
- Dose – 0.5mg/monthly
- Administration – 27g needle intravitreal injection
- Indication – neovascular “wet’’ macular degeneration
- Contraindications – ocular infection
- Warnings – risk of endophthalmitis, increased IOP
- Dose – may decrease to q3m after 4 monthly injections
  - Less effective
- Studies – ANCHOR, SAILOR, PIER, MARINA, FOCUS
Bevacizumab / Avastin

- for injection, twice the half life of Lucentis, fraction cost for AMD
- Effect – Anti VEGF for CA of lung and colorectal CA
- Dose – 0.5mg/monthly
- Administration – 27g needle intravitreal injection
- Indication – neovascular “wet’ macular degeneration
- Contraindications – ocular infection
- Warnings – risk of endophthalmitis, increased IOP
- Dose – may decrease to q3m after 4 monthly injections
  - Less effective
Avastin for EVERYTHING Systemic

- Colorectal CA
- Metastatic breast CA
- Metastatic renal CA
- Lung CA
- Exploring uses in
  - prostate,
  - pancreatic,
  - liver and others
Avastin for EVERYTHING ocular

- AMD
- PDR
- PDR with vitreous hemorrhage
- DME
- Vein occlusions
- ROP
- Choroidal melanoma
- NVG
- The future is topical eyedrops, oral formulations
Surgical Glaucoma Therapy

- Argon Laser Trabeculoplasty (ALT, LTP)
- Selective Laser Trabeculoplasty (SLT)
  - Q switched Nd:YAG selectively targets pigmented trabecular cells (increasing activity?)
  - Increases immune system by increasing monocytes & macrophages in TM
  - Selective because it does not cause appreciable damage to TM
  - 50 confluent applications to 180 degrees @0.06mJ
    - No blanching or bubble phase needed
  - Addresses greatest roadblock = compliance with medical therapy
Angle Laser Surgery

- Wise – 1970
- Mechanism – not known but shrinkage of trabecular ring with widening of spaces and decreased resistance to outflow is probable
- Particularly effective (90% controlled after one year)
  - Psuedo-exfoliation (PXF)
  - Pigment dispersion syndrome (PDS)
  - POAG
- Slowly and constantly loses effect
  - 55% at 5 years
  - 30% at 10 years
- Low complications with spike in IOP 30% (post-op)
Surgical Glaucoma Therapy

- Argon Laser Trabeculoplasty (ALT, LTP)
  - Q switched Nd:YAG selectively targets pigmented trabecular cells (increasing activity?)
  - Increases immune system by increasing monocytes & macrophages in TM
  - Causes appreciable damage to TM
  - 85 confluent applications to 180 degrees @0.06mJ
    - Blanching or bubble phase needed to assure proper treatment
  - Addresses greatest roadblock = compliance with medical therapy
  - Usually performed over 180 degrees of TM
    - Can be repeated to the other 180 degrees later if needed
Surgical Glaucoma Therapy

- Selective Laser Trabeculoplasty (SLT)
  - Q switched Nd:YAG selectively targets pigmented trabecular cells (increasing activity?)
  - Selective because it does not cause appreciable damage to TM
  - 50 confluent applications to 180 degrees @0.06mJ using 400u spot size (large) applied for 3 nano-seconds
    - No blanching or bubble phase needed
  - Results – 4.6mmHg decreased IOP at 8 months
  - Addresses greatest roadblock = compliance with medical therapy
SLT Selecta II laser

- Highly absorbed by melanin
- Selectively targets pigment cells
  - preserves surrounding tissue
- Average IOP decrease with SLT
  - 28mmHg to 18mmHg at 12 months
Laser Surgery Before Medical Therapy?

- Glaucoma Laser Trial (GLT)
  - Multicenter/randomized study of safety and efficacy of laser first for newly diagnosed glaucoma
  - IOP better controlled at 2 years and 7 years
    - Less deterioration of cupping
    - Less deterioration of visual field
  - Limitations
    - Temporary effect
    - Better topical drugs with low side effects
Laser Cycloablation

- Historic methods of ciliary body destruction
  - Cyclocryopexy, etc
  - Many complications including cataract, pain, phthsis
  - Simple and in-office procedures

- Ab interno

- Ab externo
  - Non-contact or contact Nd:YAG
  - Non-contact or contact Nd:Diode
Trabectome (NeoMedix)

- One use disposable device
- Bipolar electro-surgical pulse 550KHz/0.1w incr
- Simultaneous irrigation & aspiration
- Ablation of TM and unroofing of schlemm’s canal and juxtacanalicular tissue
- Average IOP decreases from 24mm to 15mm @60m
- Topical Rxs decrease from 3 to 1 @60m
- Advantage – easy, outpatient, option to delay trabeculectomy, less side effects
Trabeculectomy Filtering Surgery

- Conjunctival flap fornix-based
- Half thickness scleral dissection of flap
- Full thickness fistula into anterior chamber and removal of TM
- Replace scleral flap
- Loosely suture corners of flap
  - Can be cut with blades or laser later to release more fluid
  - Used to avoid post-op flat chambers and reformations
- Inject anti-metabolite
- Close conjunctiva
Trabeculectomy Complications

- Over filtration and post op flat chambers
  - Need for reformations
- Infection of bleb
- Cataract formation
- Filter failure with young, fast healers or ocular inflammatory diseases
- Alteration of tear film
- Droopy lids or visible expanding blebs
- Conjunctival dependent
- Long term failure/repeat surgery
Trabeculectomy Complications

- Shallow or flat chambers
- Choroidal detachments
- Hypotony maculopathy
- Hyphema
- Bleb leak
- Bleb infection
- Inadequate fistula and bleb failure
- Cataracts
ExPress Mini-Glaucoma Implant (Optonol Ltd)

- Less time consuming than larger tubes
  - Allows for more extensive surgery later if needed
- Placed under scleral flap
- Conjunctival dependent
- Creates posterior low diffuse bleb within 1-2 days
- Device is 400um wide x 3mm long stainless steel device
- Avoids trabeculectomy failure
Glaucoma Tube Implants

- Developed for patients with high risk of failure from standard surgery
- Design – silicone rubber tubing and ridged plastic or silicone rubber explant
  - Materials do not allow fibroblast to adhere to device
  - Equatorial placement of explant
    - Anterior edge of explant is 8-10mm posterior to corneoscleral junction
  - Tube into anterior chamber by 2mm
  - Superior temporal position is preferred
  - Patching material required to adequately cover implant
    - Sclera, dura, pericardium
Glaucoma Tube Implants

- Drain – allows flow of aqueous from anterior chamber through tube into implant
  - Passive diffusion into surrounding peri-ocular tissues
  - Uptake by lymphatic system and venous capillaries

Available Implants

- Non-valved
  - Molteno
  - Baerveldt
- Valved
  - Ahmed
  - Krupin
- Single plate and double plate designs
Indications

- Failure of conventional therapies
  - Topical
  - Laser
  - Trabeculectomy with or without MMC
- Conjunctival diseases, pemphigoid, chemical injuries, severe dry eyes, trauma related glaucoma with scleral thinning, uveitic glaucoma, congenital glaucoma,
- Neovascular diseases – Neovascular glaucoma, diabetic retinopathy, retinal vascular occlusions.
Glaucoma Tube Implants

- Special intra-operative and post-operative considerations
  - Temporary ligature of drain tube of non-valved implants
    - 2-4 weeks
    - Allows capsule to develop
    - Resistence to flow is established
    - Best completed with absorbable external suture or prolene suture placed into tube
      - Removed via small conjunctival incision in office

- Complications
  - Corneal endothelial issues in vicinity of tube, hypotony, obstruction of tube with fibrin, vitreous, blood, epithelial ingrowth
Baerveldt Implants (Abbott Medical Optics)

- 3 models
- Larger surface area plate than single quadrant devices
  - Single quad insertion
  - Decreased bleb height
- Smooth polished pliable silicone plate
- 4 fenestrations to promote fibrous adhesions
  - Reduces bleb height
  - Open drainage tube
  - Fixation sutures holes
Human Allograft Tissue

- Biocompatible for leaking blebs or exposed implants
- Gamma sterilized
- 2.5 year shelf life
- Nominal thickness 0.5mm
- Freeze dried or hydrated
- Available as sclera, pericardium
Ahmed Implant (New World Medical Inc)

- One way valve design
  - Prevents post op hypotony
- Immediate IOP reduction
- Single stage procedure
- Eliminates “rip chord” sutures, occluding sutures, or tube ligature sutures
Molteno Impants (Molteno Ophthalm Ltd)

- Single or double plates devices
- Double plate devices allow for greater aqueous drainage
- Silicone
- Low profile
- Larger, thinner devices
Cataract Surgery in Glaucoma Patients

- Combined surgery indications
  - Glaucoma treatment failing with topicals
  - Significant disc changes and visual field damage
  - Transient elevations of IOP associated with surgery or topical steroids may cause further damage
  - Cataract surgeons should spare conjunctiva superiorly for future placement of filters or implants
  - Benefit of definitive surgical solution to both problems with one operation
Surgical Glaucoma Therapy

- Trabeculectomy

- Trabeculectomy with surgical adjuncts
  - 5 FU (lower risk eyes)
  - Mitomycin-C (MMC) – higher risk eyes

- Indications
  - Maximum tolerated medical therapy
  - Progression of disease
  - Unable to instill medications
  - Secondary glaucomas (Neovascular glaucoma)

- Consideration
  - Age, HTN, DM, Anticoagulants, Preop IOP, previous vitrectomy
  - Degree of visual impairment,
  - Lens status
  - Comorbidities
Surgical Glaucoma Therapy

- **Future directions**
  - Newer antifibrinolytics
    - CAT-12, a monoclonal antibody to TGF-B2
  - Photodynamic therapy
  - Novel drug delivery systems
    - Collagen implants, bioerodible polymers, liposomes & microspheres
  - Glaucoma drainage implants instead of filtering surgery
    - Shunts aqueous from AC tube through an episcleral plate
  - Ocular genetics
    - Discover genes, gene therapy, primary prevention of glaucoma may become a reality
Surgical Glaucoma Therapy

- Future directions
  - Glaucoma drainage implants instead of filtering surgery
    - Shunts aqueous from AC tube through an episcleral plate
  - Miniature Tube Shunt
    - Ex-Press Mini Glaucoma Implant – Optonol LTD
  - Biocompatible 24 karat gold implant
    - SOLX Gold Shunt – SOLX
  - Device for surgical lowering of IOP (before trabeculectomy)
    - Trabectome – NeoMedix, INC
Glaucoma Pipeline

- Extracellular Matrix metalloproteinases
- Oral neuroprotectants - Memantine (Nameda)
- Sustained release formulations
  - Punctal plugs
  - Weekly preparations
- Home IOP monitors
Neuroprotection in Glaucoma

- Tsai Curr Eye Res 2005
- EPO (erythropoietin) found to have protective effect on RGCs
  - Currently approved and well understood for anemias, post chemo-therapy, and renal diseases
- Others under study include brimonidine, memantine, BDNF
- Future will be neuroprotection to improve environment and neuroregeneration with stem cells
Vitrectomy Causes Cataract & Glaucoma

- Chang, S AJO 2006

- Vitrectomy well known to result in cataract within 2 years
  - O2 now discovered to be responsible
  - After cataract and vitrectomy angle oxygen changed from 12mmHg to 32mmHg

- Study found increased IOP in operated eye compared to fellow eyes
  - 68% of OAG developed in operated eye
  - Presence of natural lens at time of vitrectomy associated with 28 month delay in OAG
Efficacy & Safety of Once Daily vs Once Weekly Latanoprost Treatment

- Kurtz, S JOcPharmTherap Vol20 No4 2004
- 20 patients with ocular hypertension and early glaucoma were treated with once daily vs once weekly latanoprost
- IOP tested after 2^{nd}, 4^{th}, 6^{th}, 9^{th} day and for 3 months on same schedule
  - Mean baseline IOP same for both groups (24)
  - Average IOP for both groups was 17mmHg
    - Difference between groups post treatment was insignificant
- Once weekly latanoprost treatment was as effective and bore fewer minor side effects
Nanosensor IOL

- Fraunhofer Institute in Germany
  - Microelectric Circuits and Systems IMS
- Implant sensor for continuous IOP monitoring
- Integrated a 2.5 by 2.6 millimeter sensor in an IOL
- The top and bottom of the sensor are electrodes
  - The top electrode is flexible, bottom of the sensor is rigid
  - When the intraocular pressure increases, the top electrode is pushed in, reducing the distance between the top and bottom of the sensor and thus increasing the capacitance
- Implant sends the pressure data to a reader that is fitted into the frame of a pair of spectacles
- An antenna in the spectacle frame supplies the sensor with the required energy via an electromagnetic field
- Currently undergoing clinical trials
- Could come available in two to three years time
Nanosensors IOP

- MIT Technology Review
- A pressure sensor to measure glaucoma IOP
- Tiny microchip implanted subretinal
- The sensor is designed to measure IOP
  - wirelessly transmit the data to computer
- One of the major obstacles in creating this type of device is designing a tiny but highly functional chip that uses very little power
  - Sensor runs on nanowatts rather than on microwatts
- The researchers began testing the implant in animals last December
Thank you

McGreal Educational Institute

Missouri Eye Associates