What's New in Glaucoma

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What's New in Glaucoma

What's New in Instrumentation

SWAP: Short Wavelength Automated Perimetry

- Goal is to test only the blue cone system.
- Bright yellow background (100 cd/m^2) desensitizes red and green cones.
- Dark blue (440 nm) Size V spot stimulates blue cones.

Visual Field Alternatives

Matrix Perimeter

- Based on FDT
- Glaucoma management

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

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%

FDT as Predictor of VF Loss

- Location of the FDT and SAP defects corresponded in 14 of 17 patients
- FDT defects in 59% of the converters occurred as much as 4 years before SAP
  - Mean: 21 months

However…..

- Only 59% of SAP defects were previously identified by abnl. FDT

- 24% had SAP defects BEFORE FDT
- 18% of converters NEVER developed FDT defect
- 24% of normal SAP's showed abnl. FDT but never developed abnl. SAP
  - False positives?

Glaucoma Progression Analysis

Applying GPA To Your Practice

GPA Follow-Up Printout Overview
Single Field Analysis with GPA Results

- Original single field analysis will be printed if GPA has not been set up
- Once GPA is set up for a patient, progression is automatically identified at each visit

Finding Progression
Sorting Out Variability
CCT Assessment

- Should become standard
- Equipment widely available
- Consider potential effect of LASIK on IOP findings

Heidelberg IOPac

- Portable, battery op.
- Stores up to 1000 pats.
- USB and infrared interface
- Down load to PC and printer
- Detachable probe
  - Easily replaced if necessary

Convenient and Durable

- Made for a busy practice
- Pocket-sized
- Only 7 ounces
- Specially-designed resting position protects the probe

IOPac™ Advanced with Glaucoma Risk Assessment Calculator

- Only pachymeter with a Glaucoma Risk Calculator

- 6 risk factors established in the Ocular Hypertension Treatment Study (OHTS) used to estimate the degree of glaucoma risk[1]

Glaucoma and refractive screening

- Generate reliable CCT correction of IOP

Assess refractive surgery candidates using the 9-zone refractive map

Central Corneal Thickness
in the Ocular Hypertension Treatment Study (OHTS)

- "The implication that IOP can be "corrected with an arithmetic, linear "correction factor" of some mmHg/ µm clearly represents an oversimplification of what is undoubtedly a complex and nonlinear relationship between corneal thickness and "true" IOP."
  - James D. Brandt, M.D.

"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"

Goldmann's Tonometer 1954

- Assumed CCT to be fairly constant
  - 500 microns

PASCAL at work:

- Slit lamp mounted
- Technique similar to GAT but…
- Constant pressure
- Do need proparacaine
- No fluorescein
- Self-calibrating
- Battery operated

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

Pascal DCT

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

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

DCT vs. GAT

- Intra-observer variability
  - GAT 1.1mm
  - DCT 0.65mm
- Inter-observer variability
  - GAT 1.28mm
  - DCT 0.44mm

IOP Measurements Using DCT After LASIK

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

David

- 46yo WM followed as glaucoma suspect
- Visual Fields Normal OU

Goldmann v. DCT

- CCT R 479 µm L 485 µm
- July 22
  - TA R 18 L 21
  - DCT R 24.9 L 26.0
- March 5
  - TA R 15 L 16
  - DCT R 18.5 L 21.9
  - TP R 14.8 L 17.4

Justin

- 31yo WM referred as glaucoma suspect
- C/D 0.9 OU
- VF Normal OU

Justin

- CCT R 564 L 570
- 11/30/04 1/25/05
- Goldmann R 12 L 12 R 11 L 11
- Pascal DCT R 20 L 19 R 19 L 21

Heidelberg HRT 3

- OHTS Ancillary Study Results
- Glaucoma Probability Score
- Enhanced Glaucoma Analysis
- Enhanced Progression Software
- Portable Design
- More operator friendly

What's *not* new in the HRT3

- Same CSLO technology
- Proven Moorfields Regression Analysis
- Integrated progression analysis
- Ability to use past data

Three-Dimensional Imaging

- Series of optical section images at different locations
- Layer-by-layer three-dimensional image
- Laser scanning tomography

GPS-Glaucoma Probability Score

- New automated analysis that combines 3-D modeling of the entire topographical image with an advanced neural network classification technique

3-D Model: Normal vs Glaucoma

- The 3-D model undergoes specific patterns of change as a result of glaucomatous damage

GPS: Clear and Simple

- Provides similar results as Moorfields
- Fast assessment
- Global and sectoral indicators
- No operator drawing or intervention needed

The CSLO Ancillary Study to the OHTS

- 439 OHTS patients
- Imaged annually with HRT
- HRT correlated with vertical and horizontal C/D ratios by stereo photog.

The Confocal SLO Ancillary Study to the OHTS

- Purpose: to evaluate effectiveness of CSLO in detecting the presence and progression of glaucomatous optic disc damage and to determine whether disc topographic measurements are an accurate predictor of VF loss

Disc measurements associated with development of POAG

- Larger CD ratio, mean height contour
- Mean cup depth, cup volume
- Reference plane ht., rim to disc area
- Smaller rim area and volume
- ONL classification
- Predictive value
  - 14% (HRT classification and MRA overall)
  - 40% (MRA temporal superior)

How Predictive is the HRT?

- 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 .

OCT GDx Developments

- Progression Analysis software
  - Soon to come

Russell

- 38yo WM G suspect
- 20/20 OU
- IOP 26 OU
- Ant seg normal
- FH dad has glaucoma
- Discs VF as seen

Russell Plan?

- IOP: 26 OU
- Age: 38 yo
- Race: white
- Family history: +

Russell

- CCT: R 498 L 500
- Risk Analysis
- IOP 26 = High risk
- C/D 0.2 =Low risk
- CCT 500= High risk
- IOP/CCT Risk=36%
- CD/CCT Risk=15%

Contrast Sensitivity in
Refractive Surgery

- "Contrast sensitivity is likely a more sensitive indicator of visual function than visual acuity in refractive surgery. The Vector Vision System unmasks aberrations from the transition zone of ablated and unablated cornea in PRK…"

CS and Glaucoma

- Detect CS loss before perimetry in many cases.
- Documented improvements in CS following initiation of treatment.

Experimental Glaucoma

- 47 monkeys with laser treatment to one eye to inhibit outflow facility and increase IOP.
- Tested for CS and white on white perimetry.

Visual Function Recovery?

- Conducted a study to determine whether improvements occurred in central vision as measured by contrast sensitivity following the reduction of IOP in previously untreated glaucoma patients.

Pomerance and Evans
IOVS August 1994

- 16 Newly Diagnosed and Previously Untreated Glaucoma Patients
  - Tested at baseline
  - Tested again after treatment with beta-blocker

- 25 Healthy volunteers.

- Tested and retested over same time period.

Recovery of Vision

- Significant depression of CS before treatment.
- Significant improvement at all spatial frequencies ($p < 0.0001$).
- No correlation between IOP change and vision improvement.

CS and Glaucoma
Reduction of IOP

- Documented improvements in CS following initiation of treatment.
- Recent (IOVS 01/05) 3 year study of unilateral glaucoma with surgical reduction of IOP.
  - 12 patients
  - Elevated IOP in one eye (mean 38.4 $\pm$ 4.5 mmHg)
  - Pathologic cupping
  - Normal white-on-white perimetry

Improvement of Spatial Contrast Sensitivity Threshold After Surgical Reduction of IOP in Unilateral High-Tension Glaucoma

- Purpose: To measure the effect of a surgical reduction of IOP on the contrast sensitivity in eyes showing a high IOP but ***no glaucomatous visual field defect...***

Methods

- 10 consecutive subjects with untreated IOP >/= 30m Hg in one eye and </= 18 in the other
- + increased cupping but normal VF in both eyes
- VA 20/20 OU.
- All patients underwent primary trabeculectomy .
- Contrast sensitivity measured at preop (3x to eliminate learning curve effects) and post-op visits
- Investigators were masked
- CSV-1000 by Vector Vision used to measure CS

Results

- Preop. CS was worse in eyes with high IOP compared to those with normal IOP.
- Improvement of CS was noted at 3, 6, and 12 cyc/deg in *each surgical eye* at the end of follow-up.

- Improvement seen at first postop. visit- 2 months
- *Approached the values found in the fellow untreated eyes*

- No change was found in the untreated normal eyes

Results (cont.)

- The improvement correlated directly with the amount of decreased IOP obtained by surgery
- Increased CS was NOT paralleled by changes in BCVA and corneal thickness
- CCT was WNL in treated and normal untreated eyes

Conclusion

- Eyes with no VF defects but with IOP >/= 30mmHG, show a decreased spatial contrast sensitivity
- Reduction of IOP is paralleled by an improvement of spatial contrast sensitivity

Mechanism of improvement?

- Mechanism for the improvement is unknown
- Better axonal flow across the optic nerve?
- Reverse the damage before ganglion cell death?

Possible Applications

- Earlier detection of functional damage
  - Before visual field loss
  - ***Preceding ganglion cell death and NFL thinning??***
- Measurement of *functional improvement* due to lowering of IOP
  - Rapid
  - Beyond just a measure of IOP lowering
- Guide to determining a target IOP
- Verification of compliance

What's New in Treatment

TRAVOPROST BAK FREE Solution and TRAVOPROST Solution

Study Design:

- Double masked, randomized, parallel group, multi-center
- 3 month study
- Dosed once daily in PM
- IOP measured: 8 AM, 10 AM, 4 PM at weeks: 2, 6, 12
- N= 346 randomized to travoprost 0.004%
- N= 344 randomized to travoprost 0.004% BAK-free

Study Results

- Across all 9 study visits, mean IOP reduction range: 7.3 – 8.5 mm Hg travoprost 0.004% BAK-free
  7.4 – 8.4 mm Hg travoprost 0.004%
- Statistical equivalence was also demonstrated for the comparison of mean IOP changes
- 6.4% of patients treated with travoprost BAK-free, and 9.0% treated with original travoprost experienced an adverse event due to hyperemia

IOP-Lowering Conclusions

- IOP-lowering of TRAVOPROST BAK FREE Solution is equal to original TRAVOPROST Soulution[1]
- The IOP-lowering endurance of TRAVOPROST BAK FREE Solution, beyond 24 hours, is equal to original TRAVOPROST Solution through 60 hours[2]

An Alternative Preservative

- Ionic buffer system
- Boric acid
- Propylene glycol
- Sorbitol
- Zinc chloride

Is a Non-BAK –Preserved Drop Used in a Chronic Fashion Safe?

Pre-Clinical Toxicity Comparisons:
TRAVOPROST BAK FREE Solution to Latanoprost Solution*

- *In vitro* toxicity study of human corneal epithelial cells
- *In vivo* confocal examination of rabbit cornea

In Vitro Toxicity Study
Human Corneal Epithelial Cells

- Cultured human corneal epithelial cells (HCE)
  - exposed to 100 µl of undiluted travoprost 0.004% without BAK or latanoprost 0.005% and other media
  - assayed after 25 minutes
- Quantified the effects of each media on HCE by count of resultant live and dead cells
- Conclusion: Travoprost 0.004% without BAK is significantly less toxic than latanoprost 0.005%

In Vivo Toxicity Study
Confocal Examination of Rabbit Cornea

- Baseline *in vivo* confocal microscopy measurements taken
- Ten days later, the eye was exposed for 3 minutes to either TRAVATAN® Z Solution or XALATAN*
- Immediately following exposure, the eye was re-examined for any changes in epithelial cell dropout, morphology, or thickness
- Conclusions:
  - TRAVATAN® Z Solution does not cause corneal epithelial toxicity
  - XALATAN* induces superficial cell loss, presumably due to exposure to the relatively high concentration of BAK (0.02%)

Confocal Examination: Rabbit Cornea
Epithelial Surface Cell Area Loss
Confocal Images: Rabbit Cornea
Three Minute Continuous Exposure

Istalol® Highlights

- Once a Day beta-blocker enhanced with potassium sorbate[1]
  - Efficacious
  - No Gel-induced Blur[1]
  - Convenient QD dosing schedule

- Ideal 2nd drug to add to PG therapy
  - Lower pressure is desired
  - Minimize diurnal fluctuations

- Ideal drug to switch to when patients using PGs complain of
  - Chronic hyperemia
  - Iris and eyelid discoloration
  - Long lashes
  - Cost

- Optimally timed when used in the morning[2]

Istalol®
(timolol maleate ophthalmic solution) 0.5%

- Indicated for:
  - the treatment of elevated intraocular pressure (IOP) in patients with ocular hypertension and primary open angle glaucoma

- Contraindicated:
  - in patients with bronchial asthma; a history of bronchial asthma; severe chronic obstructive pulmonary disease; sinus bradycardia, second- or third-degree atrioventricular block; overt cardiac failure; cardiogenic shock; or hypersensitivity to any component of this product.

- Most commonly reported adverse experiences:
  - Burning and stinging upon instillation (38%). Additional events reported less frequently (4-10%) included blurred vision, cataract, conjunctival injection, headache, hypertension, infection, itching, and decreased visual acuity.