Innovations in Eyecare

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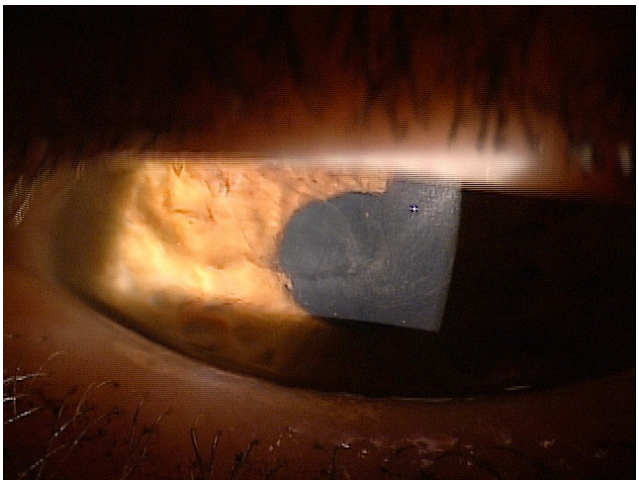
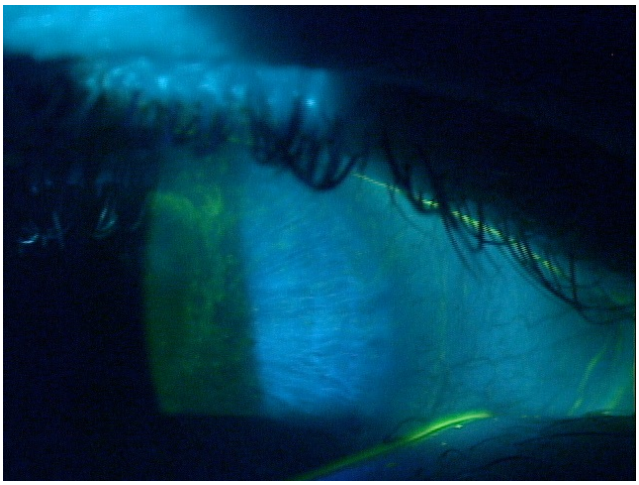
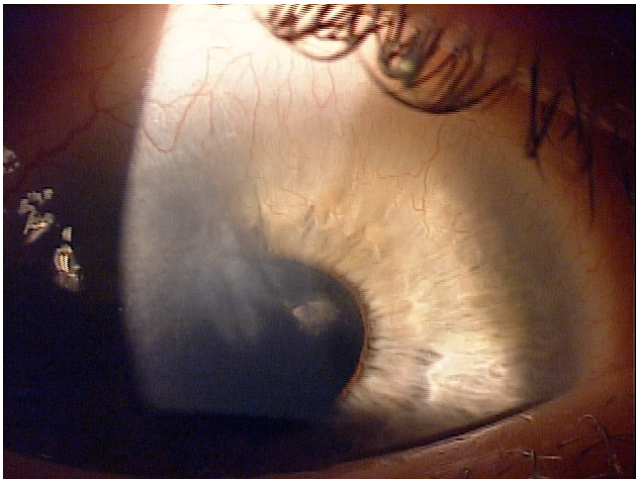




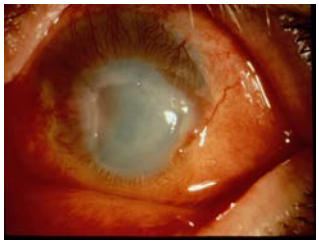


Stem Cell Technologies

Limbal Stem Cell Deficiency

Sequelae

- Persistent epithelial defects
- Corneal scarring and ulceration
- Conjunctivalization of the cornea
- Severe visual loss
- Chronic pain
- Keratoplasty failure

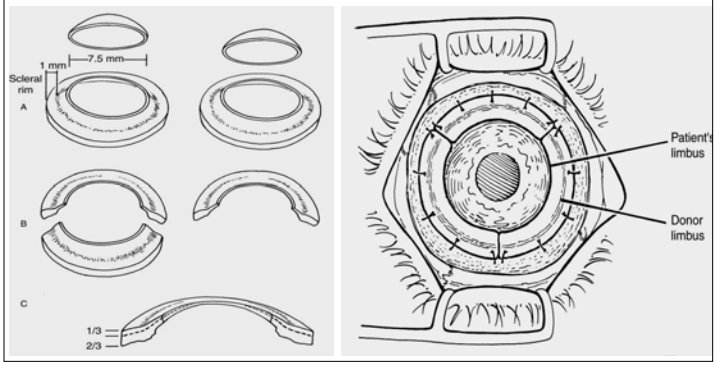


Limbal Stem Cell Transplantation

Procedures	*Donor*
Autograft	
– Conjunctival limbal autograft	*fellow eye*
Allograft	
– Living-related conjunctival limbal allograft	*relative*
– Keratolimbal allograft	*cadaver*

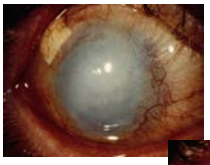
Keratolimbal Allograft

Donor **Recipient**

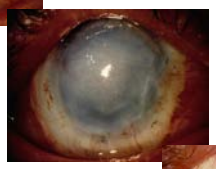


Keratolimbal Allograft

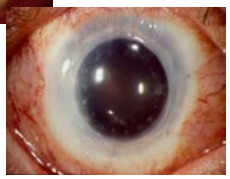
S/P Tube Shunt



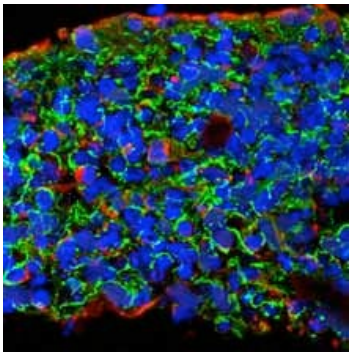
S/P KLAL



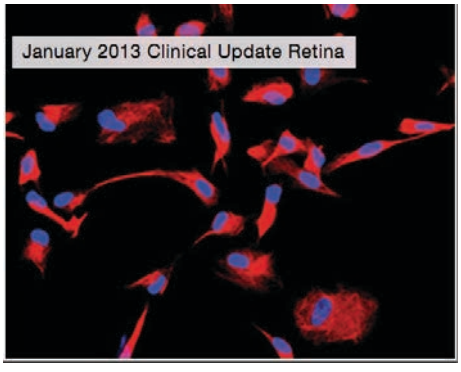
S/P PK
VA 20/30



RPE Tissue regenerated from Stem Cells



RPE Tissue Regenerated from Pluripotent Skin Stem Cells



Cryopreserved formulation of retinal stem cell therapy candidate

- Cryopreserved formulation of ReNeuron Group's human retinal progenitor cell therapeutic candidate
- From RP in phase II to Rod Cone Dystrophy phase II

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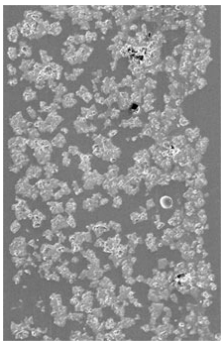
Stem Cell Coated Contact Lenses

- Aniridia patients
- Contact lens overwear?
- Various ocular surface disease issues:
  - Steven's Johnson syndrome
  - Ocular pemphigoid
  - GVH
  - Chemical burns



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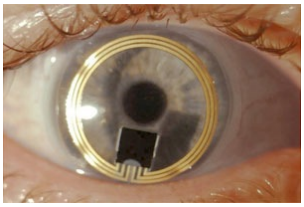
Sensimed Triggerfish lens: Diurnal IOP measurements



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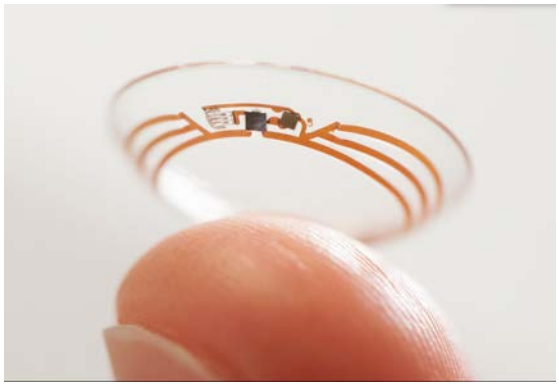
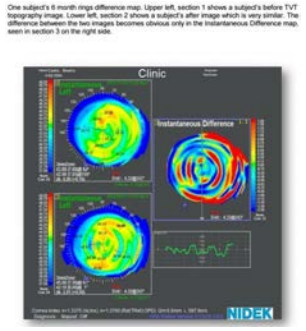
Glucose Monitoring Contact Lens



Corneal Altering Technology

- Contact lens reshaping technology after instillation of drops that can alter the cornea collagen structure
- Approved in Mexico and now working on US FDA approval



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Cryopreserved amniotic membrane

- Class II medical device comprising of CRYOTEK™ amniotic membrane into a thermoplastic ring set
- Combines the functionality of a symblepharon ring with the biologic actions of CRYOTEK™ amniotic membrane to create a unique treatment option for corneal and limbal wound healing

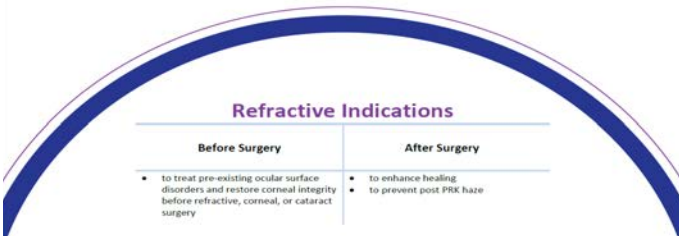
Clinical Evidence

- A safe and effective method to promote healing of the corneal surface with minimal side effects[1]
- Inhibits abnormal angiogenic processes and inflammation, thus promoting scarless healing[1-7]
- Stimulates healthy re-epithelialization of the corneal wound without sutures[1,2,4-6,8]
- Provides pain relief and reduces haze, resulting in improved visual acuity by a mean (SD) of 2.5 (2.6) Snellen lines[2]

1. Pachigolla G, et al. Eye Contact Lens. 2009;35:72-75. 2. Sheha H, et al. Cornea. 2009;28:1118-1123. 3. Gomes JA, et al. Curr Opin Ophthalmol. 2005;16:233-240. 4. Shay E, et al. Cornea. 2010;29:359-361. 5. Kheirkhah A, et al. Arch Ophthalmol. 2008;126:1059-1066. 6. Shammas MC, et al. Am J Ophthalmol. 2010;149:203-213. 7. Shay E, et al. Invest Ophthalmol Vis Sci. 2011;52:2669-2678. 8. Lazarro DR. Eye Contact Lens. 2010;36:60-61.

Ocular Surface Disorders

Diseases with Pre-existing Epithelial Defects to promote wound healing and reduce complications (debridement is optional)	Diseases without Epithelial Defects to prevent further damage and promote regeneration (no debridement/PTK)	Diseases with Unhealthy Epithelium or Basement Membrane to promote regeneration (after debridement/PTK)
• neurotrophic persistent corneal epithelial defect • post-infectious recalcitrant corneal ulcers (e.g. herpetic, vernal, and bacterial) • non-healing epithelial defect after PRK/PTK • acute chemical/thermal burns • acute Stevens-Johnson syndrome/toxic epidermal necrolysis	• dry eye syndrome • superficial (punctate) keratitis • filamentary keratitis • radiation keratitis; whorl pattern indicative of limbal stem cell injury • exposure (Graves) keratopathy	• recurrent corneal erosion, EBMD • Salzmann's nodular degeneration • bullous keratopathy during/following DSEK • haze after PTK • *partial* limbal stem cell deficiency • corneal dystrophy (e.g., Reiss Buckler)



Refractive Indications

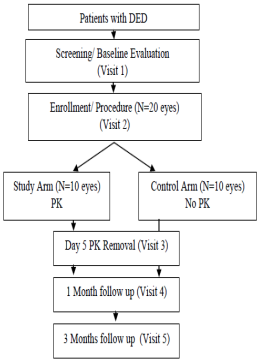
Before Surgery	After Surgery
• to treat pre-existing ocular surface disorders and restore corneal integrity before refractive, corneal, or cataract surgery	• to enhance healing • to prevent post PRK haze

Corneal Nerve Regeneration after Self-Retained Cryopreserved Amniotic Membrane in Dry Eye Disease

Thomas John, MD

- A **prospective, controlled study** to compare self-retained amniotic membrane (PROKERA® Slim, Bio-Tissue, Miami, FL) and conventional treatment in patients with moderate to severe DED (DEWS 2-4).
- Twenty (20) subjects were enrolled and randomized to receive PROKERA Slim (PKS) for 5 days, or conventional treatment.
- Changes in signs and symptoms, corneal topography, corneal sensitivity, and corneal nerve density were evaluated at baseline, month, and 3 months.

1

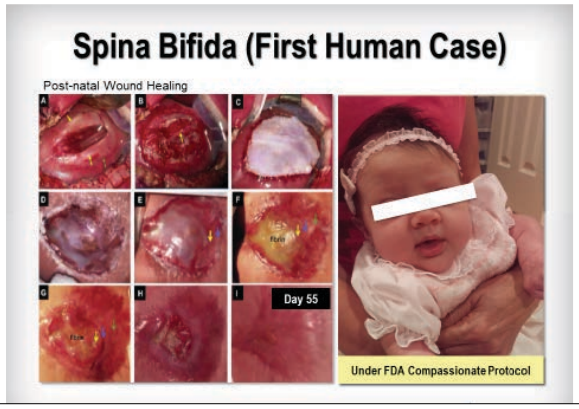


John T, Tighe S, Sheha H. et al (2017). Corneal Nerve Regeneration After Self-Retained Amniotic Membrane in Dry Eye Disease. Journal of Ophthalmology.

Insertion & removal

- Set patient expectations! Inform the patient they may experience some initial stinging and foreign body sensation
- Apply topical anesthesia
- Rinse the PROKERA® a with a sterile solution (saline, BSS etc…)
- Hold the upper eyelid
- Ask the patient to look down
- Insert the PROKERA® into the superior fornix, preferably using your fingers to hold the ring
- Slide the PROKERA® under the lower eyelid

Amniotic Membrane Treatment



One year later…

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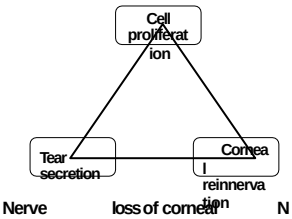
Endogenous nerve growth factor (NGF) and its role in NK:

Neurotrophic keratitis (NK) is a result from impaired trigeminal corneal innervation

- ↓ Lacrimation and blink reflex
- ↓ Epithelial cell vitality, metabolism, mitosis
- ↓ Epithelial trophism and repair
- ↑ Stromal and intracellular edema
- ↓ Microvilli
- ↓ Development of the basal lamina

Endogenous NGF maintains corneal integrity by three mechanisms



Nerve damage → **loss of corneal sensitivity** → **NK**

Mastropasqua et al. (2017) JCell

Active ingredient structurally identical to human nerve growth factor produced in ocular tissues

- Naturally occurring neurotrophin is responsible for differentiation, growth, and maintenance of neurons
- The regenerative potential of nerve growth factor (NGF) was discovered by Nobel-prize winning scientists in the early 1950s
- Cenegermin-bkbj, a novel recombinant human nerve growth factor (rhNGF), is **STRUCTURALLY IDENTICAL** to the NGF protein

Lambiase A, Rama P, Bonini S, Caprioglio G, Aloe L. Topical treatment with nerve growth factor for corneal neurotrophic ulcers. *N Engl J Med* 1998;338:1174-80.

Cenegermin-bkbj: Recombinant human NGF (rhNGF) Proprietary treatment developed by Dompé

~10x more potent than murine NGF based on in vitro studies

Phase I study (74 healthy subjects)

- Favorable safety and tolerability
- No immunogenicity and no significant changes in serum NGF

Safety and pharmacokinetics of escalating doses of human recombinant nerve growth factor eye drops in a double-masked, randomized.Ferrari MP, Mantelli F, Sacchetti M, et al. clinical trial. BioDrugs. 2014;28(3):275e283

Human Nerve Growth Factor

- Approved for the treatment of neurotrophic keratitis in adults and children age 2 and older
- Available for ordering since January 2019
- Developed by Dompé pharmaceuticals, available through specialty pharmacy

Bonini S, Lambiase A, Rama P *et al.* Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. *Ophthalmology* 2018;125:1332-1343.

Efficacy established as early as week 4

Endpoint of complete corneal healing: **0 mm staining in the lesion area and no persistent staining in the rest of the cornea** (last post-baseline observation carried forward; chi-squared test).

1. Bonini S, Lambiase A, Rama P *et al. Ophthalmology* 2018;125:1332-1343.
2. Chao W, JEDC R Det al. Data on file. Healing of persistent epithelial defects or corneal ulcers by recombinant human nerve growth factor eye drops in patients with stage 2 or 3 neurotrophic keratitis. Presented at: Congress of the European Society of Ophthalmology (SOE).10–13 June, 2017, Barcelona, Spain. 2017.

Pool Safety Report

Oxervate is neither systemically absorbed, nor immunogenic

- In Phase I (NGF0112) in healthy patients at doses up to 180 µg/ml , serum concentrations of NGF did not differ from basal levels.
- In Phase I/II (NGF0212/REPARO) in NK patients, NGF serum levels were below the lower level of quantification in almost all patients (detectable serum NGF levels likely reflected known inter- and intra-individual fluctuations independent of study treatment).
- No systemic immunogenicity was detected in any clinical studies. With no (or negligible) systemic exposure, off-target pharmacological activity or toxicity are unlikely.
- The hydrophilic rhNGF solution has a very low residence time in the eye (quickly removed with the tear flow).

1. Bonini S, Lambiase A, Rama P et al. Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. Ophthalmology. 2018;125:1332-1343
2. Mauro P, Ferrari et al. Safety and Pharmacokinetics of Escalating Doses of Human Recombinant Nerve Growth Factor Eye Drops in a Double-Masked, Randomized Clinical Trial. BioDrugs (2014) 28:275–283

Cenegermin-bkbj ophthalmic solution 0.002% Weekly Device Kit

OXERVATE Prescribing Information, 2018.

Cenegermin ophthalmic solution 0.002% Dosing and Administration

Every 2 hours instill 1 drop of OXERVATE™ (cenegermin-bkbj) ophthalmic solution 0.002% in the affected eye(s)

Apply 6 times daily

Continue for 8 weeks

Study Conclusions

Up to 72% of patients achieved complete corneal healing;
*80% of healed patients were recurrence free after 1 year**

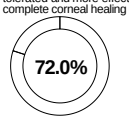
After 8 weeks of treatment, 6 times daily

Study NGF0212

50 clinical trial sites in Europe and the U.S.

(REPARO) (N=52 per group)

European patients with NK in one eye



Vehicle response rate 33.3%

completely healed

In the majority of patients across two clinical studies OXERVATE™ (cenegermin ophthalmic solution 0.002%) was well tolerated and more effective than vehicle in promoting complete corneal healing of moderate or severe NK.

Study NGF0214 (N=24 per group)

U.S. patients with NK in one or both eyes

Vehicle response rate 16.7%

completely healed

Of patients who healed after one 8-week course of treatment…

80%

Remained healed for one year

1. Bonini S, Lambiase A, Rama P et *al. Ophthalmology* 2018;125:1332-1343.
2. Chao W, J. BDC, R. D et *al.* Data on file. Healing of persistent epithelial defects or corneal ulcers by recombinant human nerve growth factor eye drops in patients with stage 2 or 3 neurotrophic keratitis. Presented at: Congress of the European Society of Ophthalmology (SOE) 10–13 June, 2017, Barcelona, Spain. 2017.

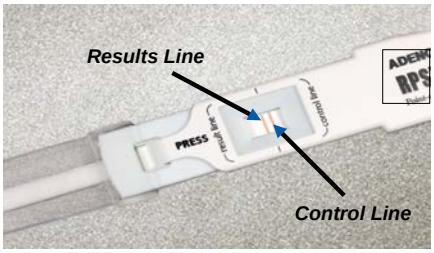
Point-of-Care Diagnostics

Adenovirus

Reading & Interpreting the Results

Positive Results:

The ***Results Line and Control Line*** are **RED** in the result window, indicating that Adenovirus antigen ***is present***.



MMP-9

Reading & Interpreting the Results

Positive Results:

Means MMP-9 greater than 40 units per sample

MMP-9

Reading & Interpreting the Results

Measures the presence of MMP-9 on the ocular surface
5 minute test
Point-of-Care
Measures 40 units and above
Positive or negative
Directs inflammation treatment

Osmolaritv Reader & Pens

Tear Collection

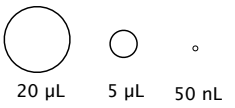
Osmolarity in the Diagnosis of Dry Eye Disease

Clinical Test	PPV
Osmolarity	87%
Schirmers	31%
TBUT	25%
Staining	31%
Meniscus Height	33%

Source: DEWS Report, Ocular Surface April 2007 Vol 5 No 2, & Tomlinson A, et. al., IOVS 47(10) 2006

Precision @ 50 nL

- < 2% coefficient of variation @ 50 nanoliters
  - Glucose ≥ 5.0% CV @ 5 microliters
  - Cholesterol > 4.0% CV @ 20 microliters

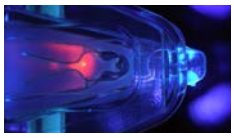


- Safe, simple collection
  - No reports of corneal or conjunctival trauma in 468 eyes [TearLab™ FDA 510(k) submission]
- Winner 2009 MDEA for In Vitro Diagnostics

Source: Kimberly MM et. al., Clinica Chimica Acta 364 (2006), Volles DF et. al. Pharmacotherapy 18:1 (1998).,

Future of Tear Biomarker Analysis:
Next Generation Platform

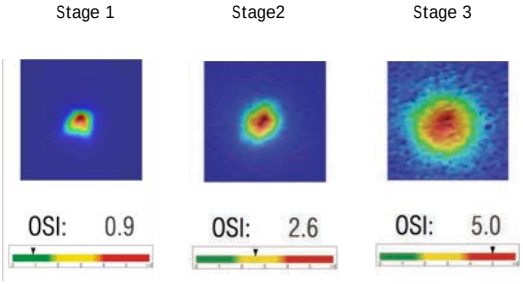
- Quantitative
- Ability to measure
  - Osmolarity
  - Inflammation biomarkers
  - Allergy biomarkers
  - Specific drug related biomarkers
- Rapid testing (< 2 minutes)
- Multiplexed biomarkers
- EHR Integration
- Clinical Application:
  - Normalization using osmolarity
  - Customized chips with designed sensitivity & specificity



Next Generation Platform

- When?
  - 510k submission earlier this year
  - If approved would be Fall of 2019
    - First test will have osmolarity + 1 or 2 additional markers
    - Likely to be focused on inflammation
    - New iterations possible every 6 months

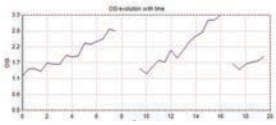
Objectively Diagnosing Cataracts



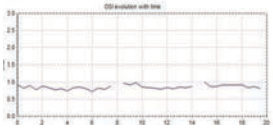
The HD Analyzer™ is the Only Tool that Objectively Measures How Early Cataractous Haze Affects Vision Quality

Non-invasive TFBUT Dry Eye Patients

Tear Film Unstable



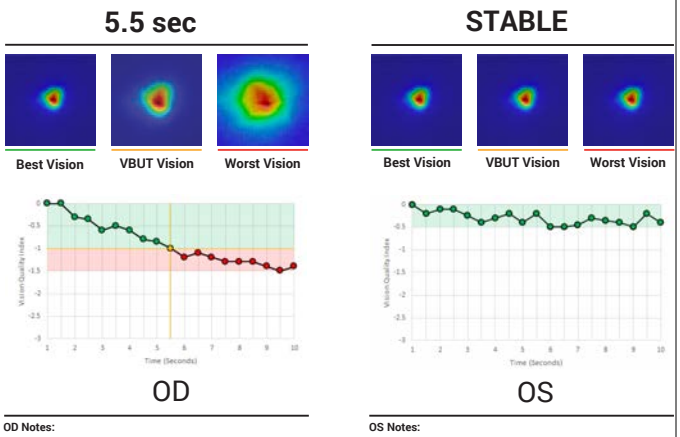
Tear Film Stable



Objectively Measures How the Tear Film Affects Vision Quality

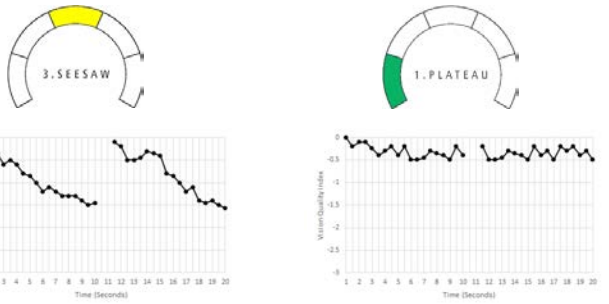
DOB: 11/15/75 11:52 A

Vision Break Up Time



DOB: 11/15/75 11:52 A

Vision Stability Pattern



OD

OD Notes:

OS

OS Notes:

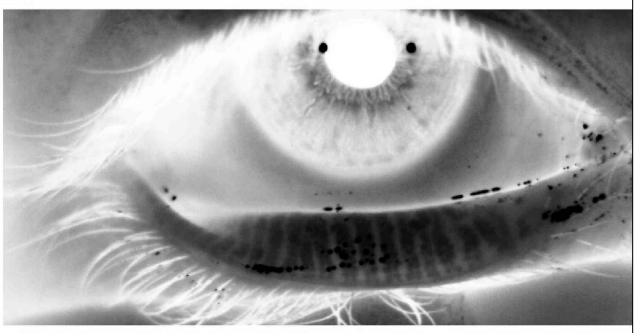
DEMO, PATIENT
1234

OD

Notes:

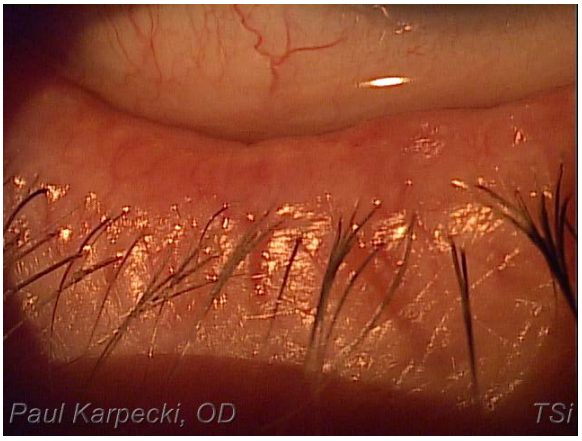
DEMO, PATIENT
1234

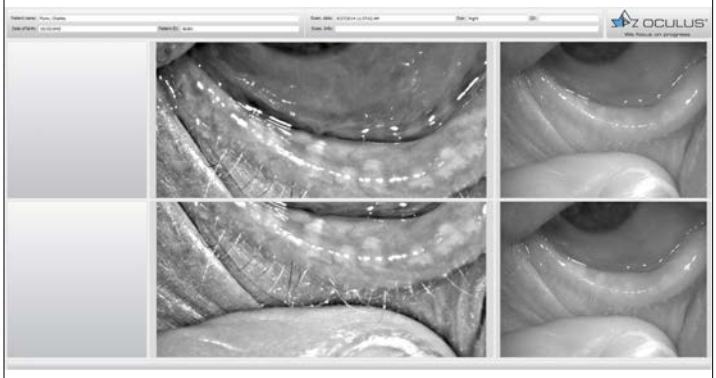
OD

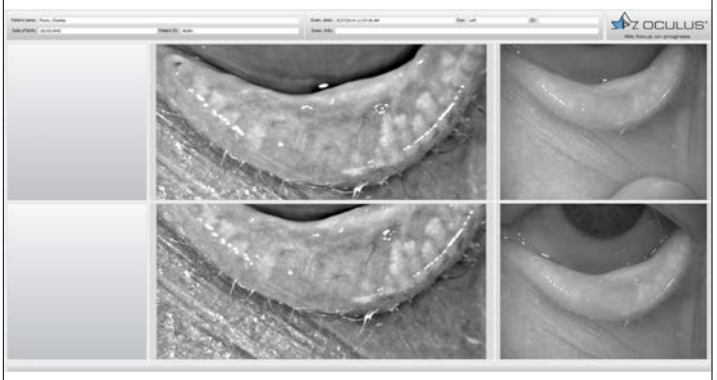


Notes:

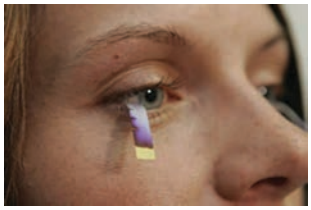
Meibography







Assessment of Tear Film Quantity



Benefit of TMH: Non Invasive and Fast

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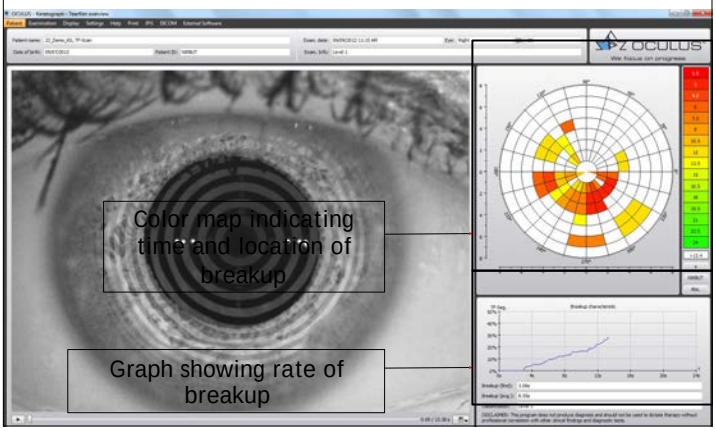
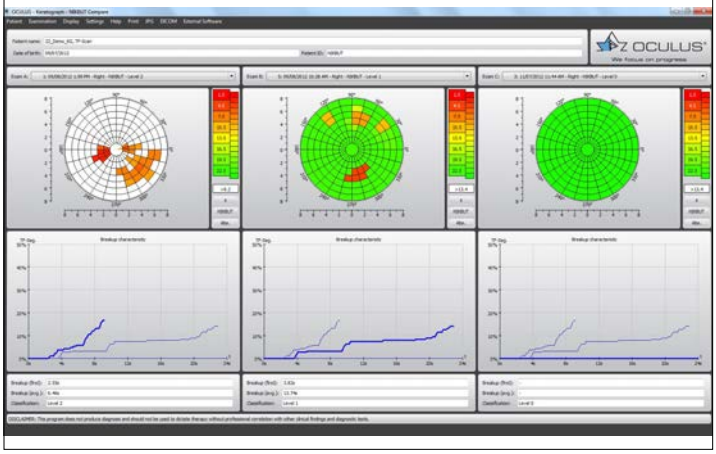
Non Invasive Breakup Time (NIKBUT)

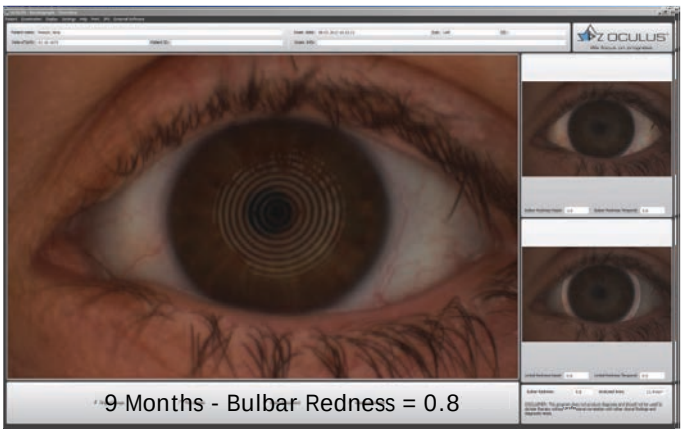


NIKBUT Compare



Automatic Assessment of Bulbar Redness

Case: 43, F, Treated for MGD



Tear Module

The Tear Module for Includes Acquisition and Viewing modes to enhance the dry eye application

MEIB

Meibomian Gland IR photography

Adds adjustable contrast when viewing

BLINK

Blink Detection

Records blinks over a period of time

Calculates average blinks per minute and blink interval

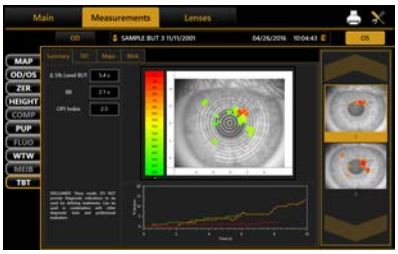
TBT

Tear Film Break up Time

Calculates First Break up and Average Breakup

Allows video playback highlighting the corneal surface

Tear Film Breakup Time



Sector Map

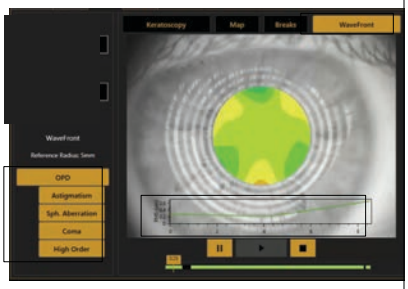
Shows each sector where Breakup was detected for all TBT acquisitions of the selected exam
Sectors color-coded by time when Breakup occurred

Tear Film Breakup Time

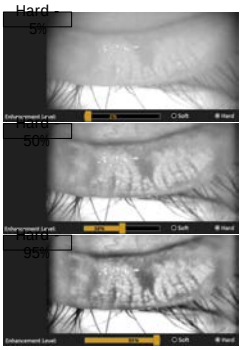
Maps Tab - WaveFront

WaveFront allows you to play back a recording of the selected acquisition with an overlay of Wavefront Aberrometry Maps to show the effect of the tear film breakup on the patients visual quality
The user can choose to overlay any or all of the following

Wavefront Aberrometry maps:
- *OPD (total Wavefront Aberration)*
- *Astigmatism*
- *Spherical Aberration*
- *Coma*
- *High Order*



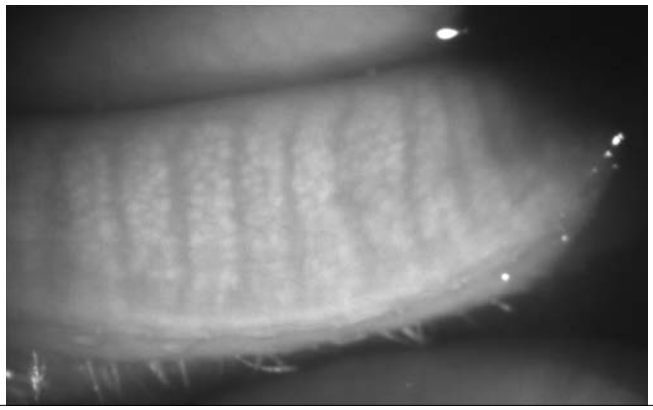
Meibography– Contrast Enhancement

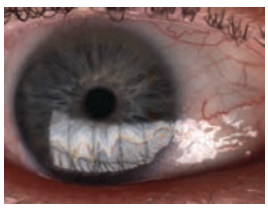


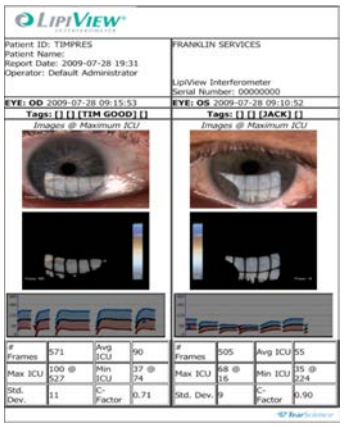
Hard Contrast Enhancement

As the slider percentage is increased the bright areas of the image are made darker relative to the dark areas

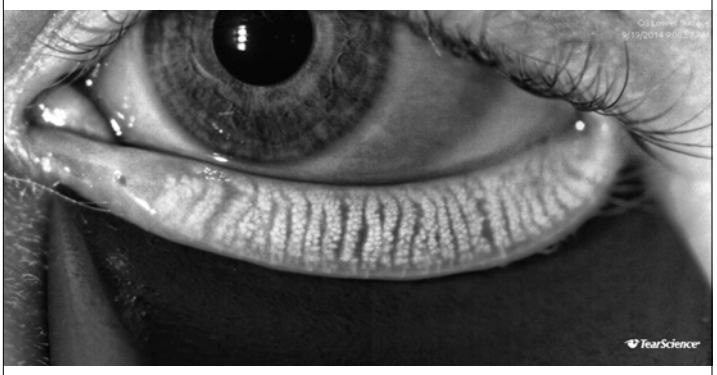
IR Slit Lamp Imaging



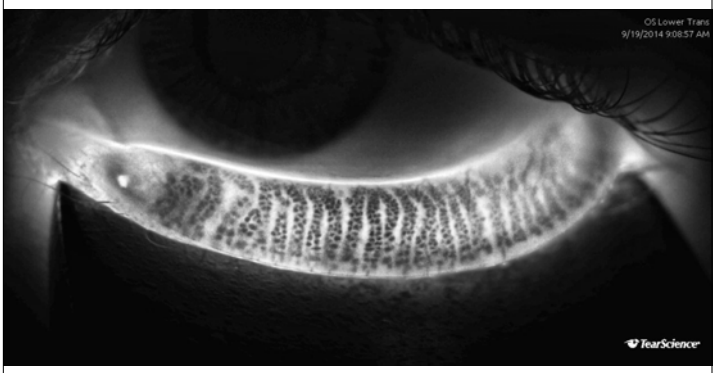




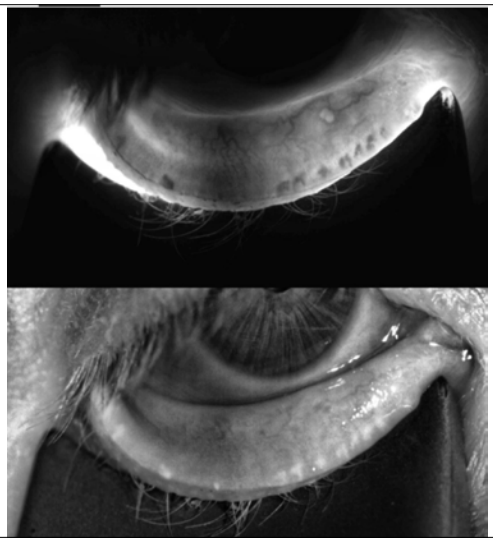
PARTIAL OR INFREQUENT BLINKING



67



68



Thermal Pulsation

FDA-cleared device for Meibomian Gland Dysfunction (MGD), shown to restore gland function.

In-office procedure, taking 12 minutes per eye.

70

22

Core Therapy: Treat obstruction

Novel Approach:

Heat the inner lid surface with simultaneous gland evacuation

Safe, effective, precise, proven:

- Restores Meibomian Gland function
- Applies a combination of heat and pressure directly to the inner eyelid
- FDA-cleared and clinically approved
- Independent proven results in peer-reviewed studies [1,2,3]

1. Finis, D. et al. Ocular Surface 2014 Apr; 12(2); 146-54
2. Greiner, JV. Clin Experiment Ophthalmol. 2013 Aug;41(6):524-30
3. Blackie CA, et al. Treatment for meibomian gland dysfunction and dry eye symptoms with a single-dose vectored thermal pulsation: a review. Current Opinion in Ophthalmology 2015, 26:306–313.

71

21

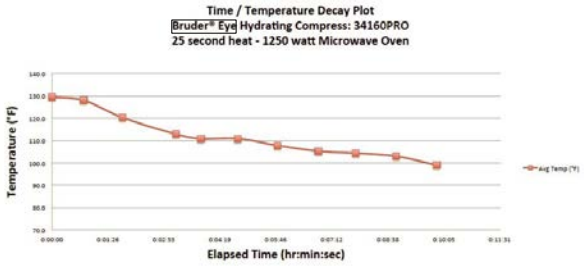
Eye Hydrating Compresses

Moist heat compress
30 angstrom opening pulls in ambient hydration and then release
20-25 seconds in microwave
Brings MG temperature over 104 degrees for ~10 min
Antibacterial via silver ionization
Washable, durable

39

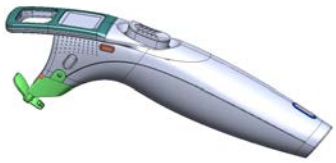
Heat transfer through lid, tarsal plates to MGs a key challenge
Heating target should be 45 degrees C (113 degrees F)
Up to 8 minutes to reach 40 degrees C at inner lid
Secretions melt at 32-45 degrees C (several factors impact range)

Patented Technology

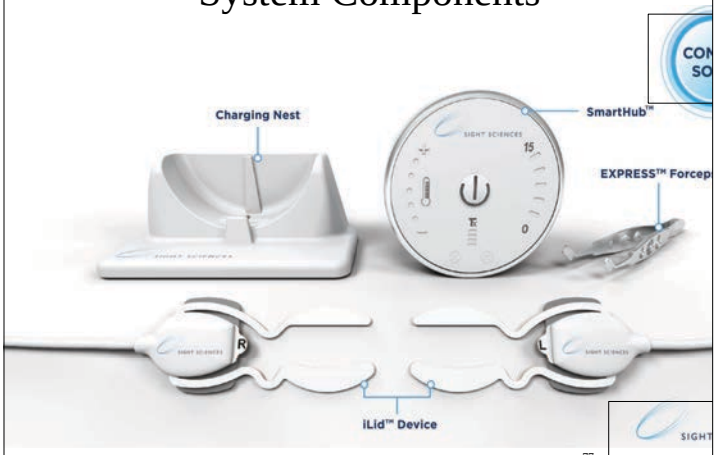


Handheld MG Treatment

IR technology
Back surface heating
Viewing area
Mechanical expression
ionization
Hand-held devices



System Components



The TearCare® System

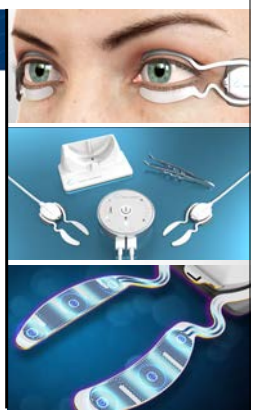
Innovative
The only wearable, open-eye procedure

Non-Invasive
The iLid™ devices are applied to the outer eyelids and conform to their anatomy

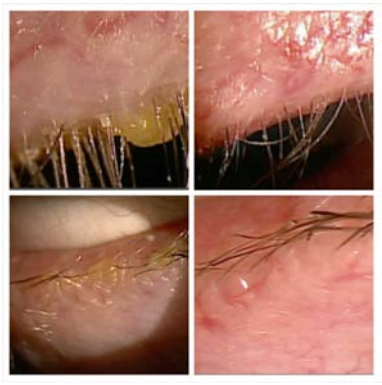
Intelligent
SmartHub™ and iLid™ devices automatically regulate heat delivery

Efficient
Small & convenient for doctor's office with no capital equipment investment needed

Customized
Thermal treatment and clearing the

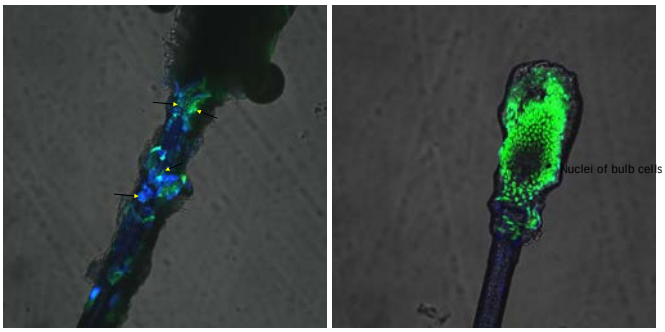


Blepharoexfoliation

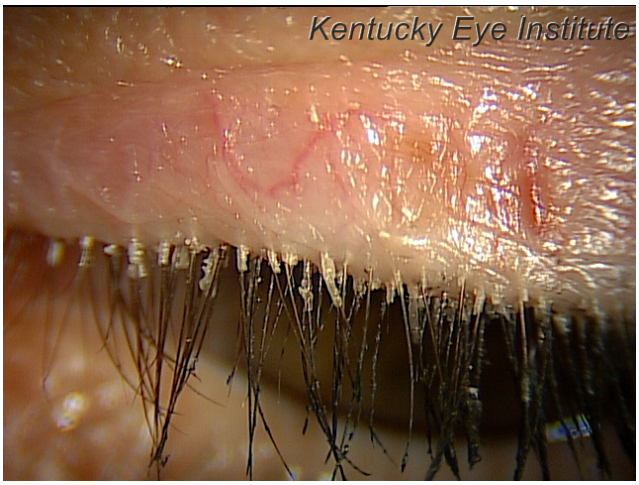


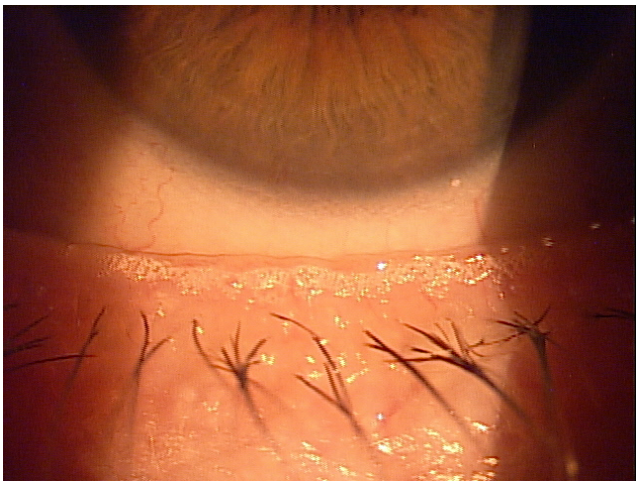
79

Bacterial Biofilm in Lash Follicles



80





IPL

- Intense Pulsed Light Therapy
- Clear association between DED and lid margin inflammatory disease
- Widely accepted as a treatment for dermatological rosacea
- More than 80% of patients with rosacea have MGD
- 20% have ocular signs first

83

IPL

- Theoretical MOA
- Telangiectatic vessels and skin erythema release inflammatory mediators
- IPL targets the abnormal erythematous blood vessels
- Temperature effect on glands?
- Photomodulation affecting cytochrome C or activating fibroblasts and collagen synthesis

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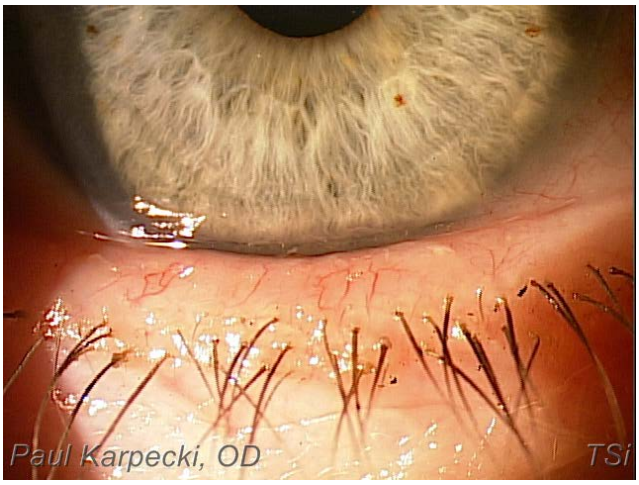
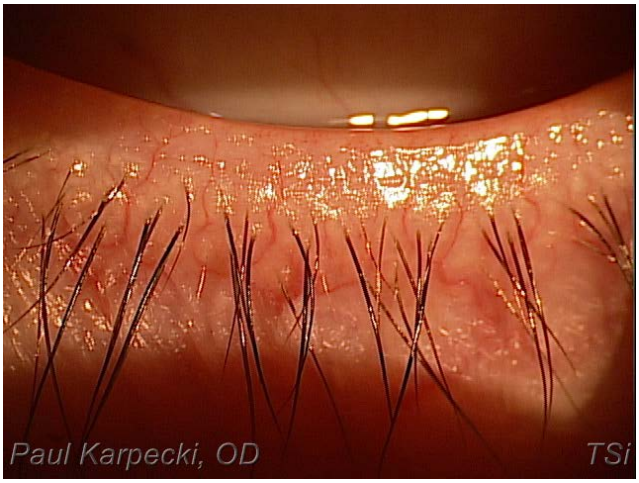
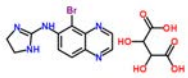




Eye Whitening

Low dose brimonidine (0.025%)
– Eye whitener
– Low dose alpha adrenergic
– 300% whiter eyes than Visine
– Lasts 6-8 hours
– No rebound hyperemia or tachyphylaxis

Product Profile



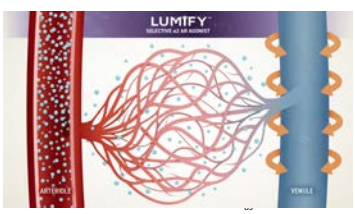
Brimonidine Tartrate

- **Description:** Brimonidine Tartrate (0.025%) drop – OTC NDA. Primary Inactive Ingredients - glycerin, borate buffer system, BAK preservative.
- **Target Indication:** Relief of ocular redness due to minor eye irritations.
- **MOA:** Highly selective α2-AR-specific agonist with minimal action at α1-AR, minimizing the side effects of tachyphylaxis and hyperemia associated with currently marketed, first generation ophthalmic vasoconstrictors (naphazoline, tetrahydrozoline, phenylephrine and oxymetazoline)
- **Dosing:** Topical solution; instill 1-2 drops in the affected eye(s) up to four times daily
- **Current Stage of Development:** Phase III completed; NDA submitted

Mechanism of Action

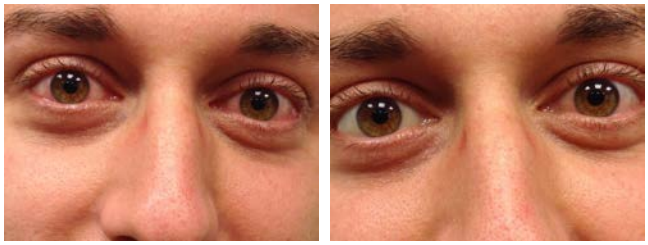
- α1-AR or Mixed α1-/α2- Agonist
  - Generalized arteriolar and venular constriction reduces redness
  - Arterial constriction creates relative ischemia

Selective α2- Agonist
  - Preferential venular constriction reduces redness
  - Normal arterial perfusion allows for reduced potential for ischemia



Phase II – Efficacy in a CAC model

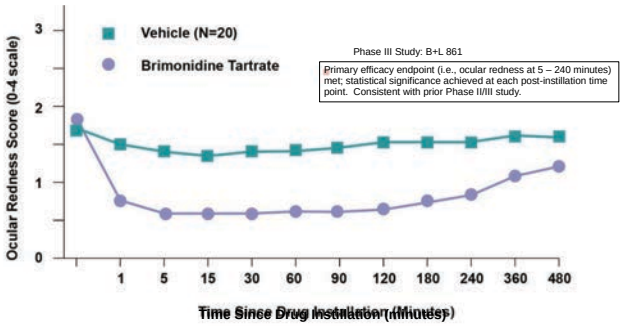
Brimonidine 0.025% in right eye
and oxymetazoline in left eye
(5 minutes post-dose)



Eyes before treatment
(baseline)

Phase III Efficacy – Clinician Redness Score

Significantly greater redness relief beginning 1 minute post-instillation and lasting up to 8 hours, compared to vehicle

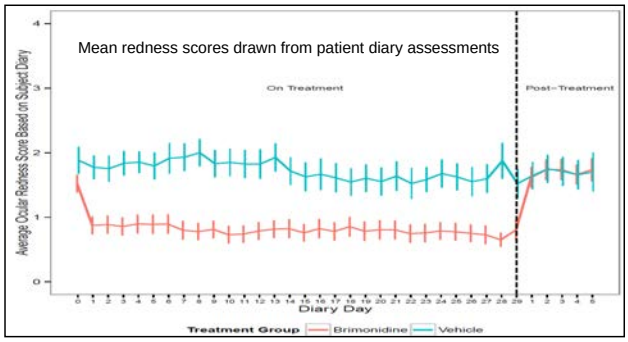


Phase III Study: B+L 861

Primary efficacy endpoint (i.e., ocular redness at 5 – 240 minutes) met; statistical significance achieved at each post-instillation time point. Consistent with prior Phase II/III study.

Phase III Efficacy – Patient Diary Assessments

Sustained efficacy across treatment period without tachyphylaxis
No evidence of rebound after cessation of treatment



Phase III Safety – Adverse Events

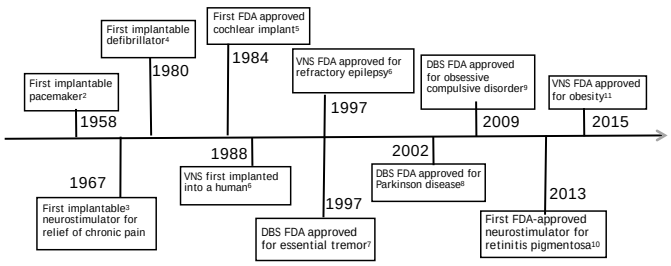
4 subjects reporting at least 1 ocular TEAE, 1 considered related to the study treatment (pain) which was considered mild in severity

Patients Treated with Brimonidine Tartrate (0.025%) N=40	
Adverse Events - Ocular	Events/subjects
All AEs	4 (10%)
TEAEs	4 (10%)
SAEs	0 (0%)
Number of subjects withdrawn due to an AE	0 (0%)

AE = Adverse Event, SAE = Serious Adverse Event; TEAE = Treatment Emergent Adverse Event.
Source: Table 14.3.1.1

NEUROSTIMULATION

PROVEN TECHNOLOGY FOR OVER 30 YEARS[1]



VNS – vagal nerve stimulation.
DBS – deep brain stimulation.

1. Mekhail et al. *Pain Pract*. 2010; 2. Van Hemel and Van der Wall. *Neth Heart J*. 2008; 3. Benabid. INS website. Accessed 2016; 4. Van Welsenes et al. *Neth Heart J*. 2011; 5. NIH website. Accessed 2016; 6. Rielo. Medscape website. Accessed 2016; 7. Karas et al *Neurosurg Focus*. 2013; 8. Gardner. *Soc Stud Sci*. 2013; 9. FDA website. Accessed 2016; 10. FDA website. Accessed 2016; 11. FDA website. Accessed 2016.

CRANIAL NERVE STIMULATION

TARGETING NUMEROUS DISEASE CONDITIONS

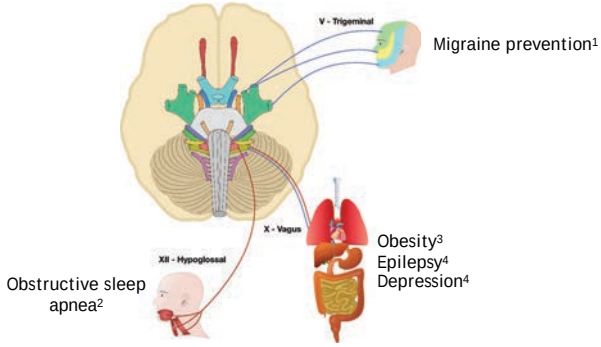


Image adopted from Netters.[5]

1. Zhu and Marmura. *Curr Neurol Neurosci Rep*. 2016; 2. FDA website. Accessed 2016; 3. FDA website. Accessed 2016; 4. FDA website. Accessed 2016.

TRIGEMINAL NERVE (CN V)

BRANCHES AND FUNCTION

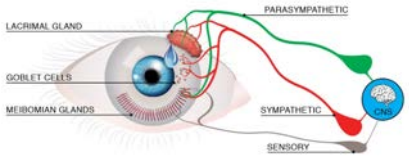
- Largest cranial nerve (CN V) with 3 divisions[1,2]
  - Ophthalmic nerve (V1)
  - Maxillary nerve (V2)
  - Mandibular nerve (V3)
- Ophthalmic nerve (V1) comprises 3 branches[1,3]
  - Lacrimal nerve
  - Nasociliary nerve
  - Frontal nerve
- Ophthalmic nerve innervates the lacrimal functional unit (LFU), including[4-6]:
  - Lacrimal gland
  - Meibomian glands
  - Goblet cells

1. Tewfik. Medscape website. Accessed 2016; 2. Morton et al. In: Morton et al, eds. *The Big Picture: Gross Anatomy.* 2011. Accessed 2016; 3. Waxman. In: Waxman SG. eds. *Clinical Neuroanatomy.* 2013. Accessed 2016. 4. Kossler et al. *Ophthal Plast Reconstr Surg.* 2015; 5. Beuerman et al. In: Pflugfelder et al, eds. *Dry Eye and Ocular Surface Disorders.* 2004; 6. Dartt. *Ocul Surf.* 2004.

LFU REGULATES TEAR PRODUCTION[1-3]

BY COMMUNICATING WITH CENTRAL NERVOUS SYSTEM (CNS)

- LFU maintains a healthy environment for the eye by regulating tear production
  - In response to any external and internal stimuli, LFU communicates with CNS
  - Sensory signals are carried via afferent neurons from LFU to CNS
  - Parasympathetic and sympathetic signals are carried via efferent neurons from CNS to LFU
  - This afferent and efferent signaling and communication occurs via the trigeminal nerve

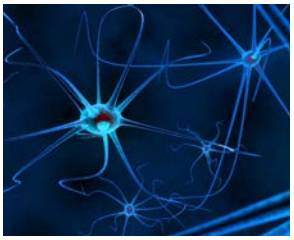


1. Kossler et al. *Ophthal Plast Reconstr Surg.* 2015; 2. Beuerman et al. In: Pflugfelder et al, eds. *Dry Eye and Ocular Surface Disorders.* 2004; 3. Dartt. *Ocul Surf.* 2004.

NEUROSTIMULATION

TARGETING TRIGEMINAL NERVE (CN V)

- The trigeminal nerve is responsible for innervation of the lacrimal functional unit (LFU)[1-4]
- Emulates neural signals essential to increase tear secretion[1-4]
- A drug-free option[5-7]



1. Kossler et al. *Ophthal Plast Reconstr Surg.* 2015; 2. Beuerman et al. In: Pflugfelder et al, eds. *Dry Eye and Ocular Surface Disorders.* 2004; 3. Brinton et al. *J Neural Eng.* 2016; 4. Dartt. *Ocul Surf.* 2004; 5. Jenkins and Tepper. *Headache.* 2011; 6. Danilov and Kublanov. *J Behav Brain Sci.* 2015; 7. Mekhail et al. *Pain Pract.* 2010.

Neuro-stimulation Technology

- Tear stimulant for aqueous deficient dry eye
- Inserted in nasal canal
- Wireless stimuli to create tears

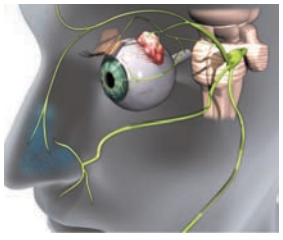
OC-01/OC-02 for the Treatment of Signs and Symptoms of Dry Eye Disease (DED) Administered Via a Nasal Spray

- OC-01 and OC-02 are being developed to directly address loss of tear film homeostasis in DED and are delivered as a nasal spray.
- Drug candidates bind to nicotinic acetylcholine receptors (nAChRs), which are located on the trigeminal nerve accessible within the nasal cavity, to stimulate tear film production.
- Trigeminal parasympathetic pathway is well characterized with nerves that innervate the lacrimal functional unit (LFU) including cornea, conjunctiva, accessory lacrimal glands, meibomian glands, and goblet cells[1,2,3]

1van der Werf, F. R. A. N. S., Baljet, B., Prins, M. A. A. R. T. E. N., & Otto, J. A. (1996). Innervation of the lacrimal gland in the cynomolgous monkey: a retrograde tracing study. Journal of anatomy, 188(Pt 3), 591.
2LeDoux, M. S., Zhou, Q., Murphy, R. B., Greene, M. L., & Ryan, P. (2001). Parasympathetic innervation of the meibomian glands in rats. Investigative ophthalmology & visual science, 42(11), 2434-2441.
3Dartt, D. A., Mccarthy, D. M., Mercer, H. J., Kessler, T. L., Chung, E. H., & Zieske, J. D. (1995). Localization of nerves adjacent to goblet cells in rat conjunctiva. Current eye research, 14(11), 993-1000.

Trigeminal-Parasympathetic Pathway & DED

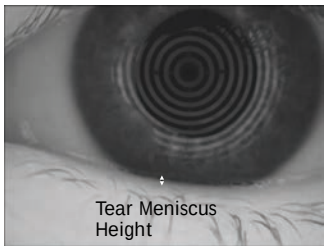
- The parasympathetic nervous system (PNS) controls tear film homeostasis
  - 34% of basal tear production is due to inhaled air through the nasal passage[1]
- Efferent parasympathetic nerves innervate the lacrimal functional unit (LFU) including cornea, conjunctiva, accessory lacrimal glands, meibomian glands, and goblet cells[2,3,4]
- Intervention @ the trigeminal-parasympathetic pathway represents a novel approach to producing complete tear film in patients with Dry Eye Disease (DED)



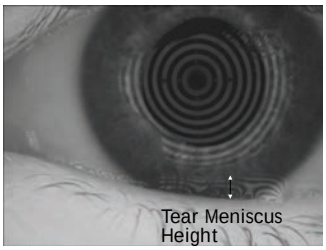
1Gupta A, Heigle T, Pflugfelder SC. Nasolacrimal stimulation of aqueous tear production. Cornea. 1997 Nov;16(6):645-8.
2van der Werf, F. R. A. N. S., Baljet, B., Prins, M. A. A. R. T. E. N., & Otto, J. A. (1996). Innervation of the lacrimal gland in the cynomolgous monkey: a retrograde tracing study. Journal of anatomy, 188(Pt 3), 591.
3LeDoux, M. S., Zhou, Q., Murphy, R. B., Greene, M. L., & Ryan, P. (2001). Parasympathetic innervation of the meibomian glands in rats. Investigative ophthalmology & visual science, 42(11), 2434-2441.
4Dartt, D. A., Mccarthy, D. M., Mercer, H. J., Kessler, T. L., Chung, E. H., & Zieske, J. D. (1995). Localization of nerves adjacent to goblet cells in rat conjunctiva. Current eye research, 14(11), 993-1000.

Before and 15 seconds After Administration of OC-02 Nasal Spray

OC-02 Before Administration

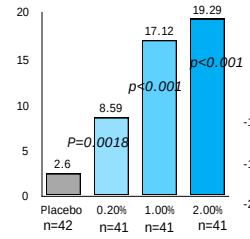


OC-02 15 Seconds After Administration

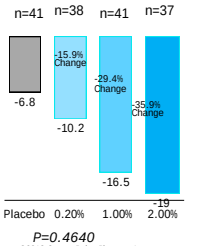


OC-02 Phase 2b Results Demonstrate Significant Improvement in Both Signs and Symptoms of Dry Eye and Clear Dose Response

Mean Change in Schirmer's Score (N=165)



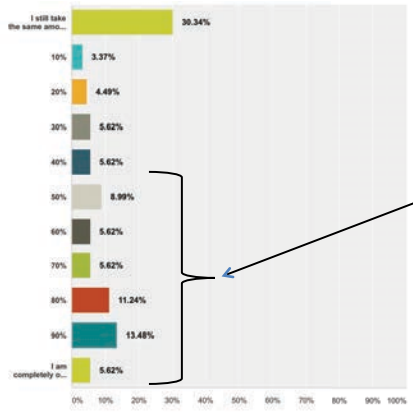
Mean Change in Eye Dryness Score (N=165)



- OC-02 was well-tolerated with no ocular adverse events or drug-related serious adverse events.
- The most common adverse events were typical of nasal sprays and included cough, sneezing, and nose and throat irritation.
- These events were predominantly mild, transient and self-limiting.

EyeGraine: Subgroup of Chronic Daily Headache

- Symptoms
  - Primary Symptoms
    - Frequent Headaches
      - 3+ days per week
    - Neck Pain/Stiffness
  - Secondary Symptoms
    - Dry eyes
    - Fatigue with near work
    - Photophobia, especially at night headlights



70% off of at least some medications at 90 days

52% of patients off of 50% or more of their headache medications

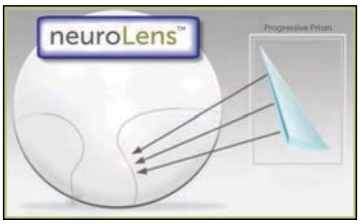
No reported side effects

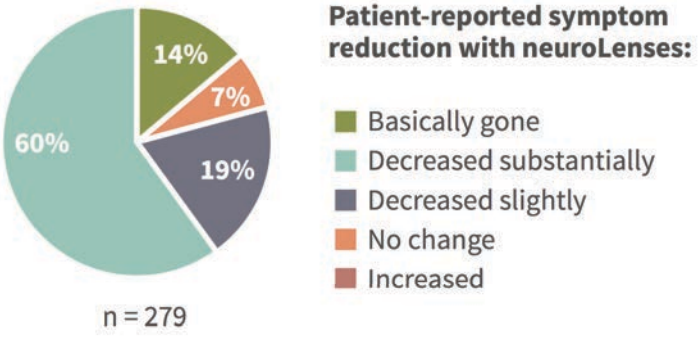
Research confirmed

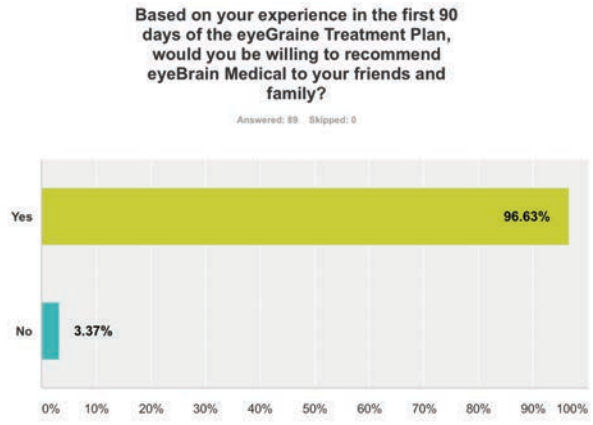
- Pursuits and Saccadic eye movements
  - Sends it proprioceptive signal via the trigeminal nerve
    - Ophthalmic branch
- Trigeminal Nerve (V) :
  - Stimulation of Ophthalmic branch
    - Frontal headaches (sinus headaches)
    - Terminates in lower brain stem (back of head headaches /neck pain)
    - Cornea sensation (Dry Eye)

The Solution (neuroLens)

- Synchronizes binocular vision at all distances, eliminating need for compensating eye movements.
- Progressive prism technology, using measurements from SightSync
- Built into spectacle lenses with patient's Rx





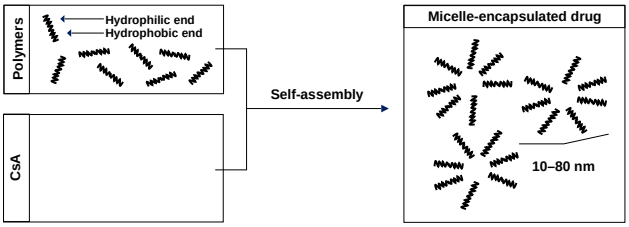


n = 89

Cyclosporine 0.09%

The nanomicelle structures in OTX-101 are formed using polymers which entrap the lipophilic molecule (CsA) within its hydrophobic core, while the hydrophilic (water soluble) domain of the polymers make up the outer shell[5]

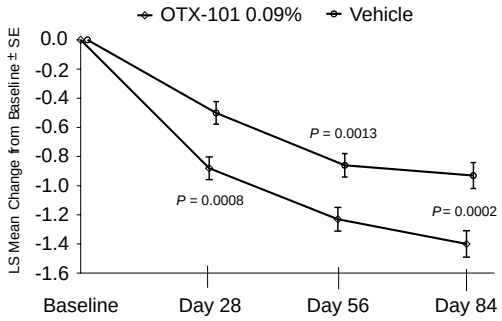
These water-soluble micelles help improve solubility/ocular tissue bioavailability of CsA



CsA, cyclosporine A.

Change from Baseline in CFS in Patients Treated with Active vs Vehicle

Total Score

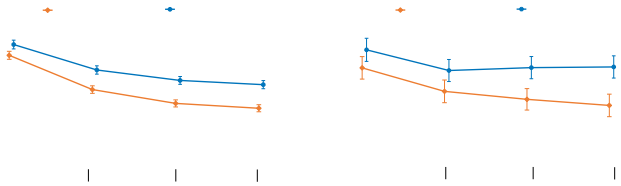


P-values from ANCOVA model of 0.09% vs vehicle.
ANCOVA, analysis of covariance; CFS, corneal fluorescein staining; LS, least squares; SE, standard error.

Correlation between central CFS and VA

Central CFS scores[a]

Snellen VA[a]



On day 84, there was a high correlation between reduced central corneal staining and improved Snellen VA (*P* = 0.0117) in the OTX-101 (0.09%) treatment group[b]

Decreased Snellen VA logMAR scores correlate to improvement in VA.
[a]*P* values for OTX-101 0.09% vs vehicle.
[b]*P*-value from restricted maximum likelihood of mixed-effect model repeat measurement of VA vs CFS.
CFS, corneal fluorescein staining; SE, standard error; VA, visual acuity.

Safety

Summary of Administration Site Treatment-Emergent AEs

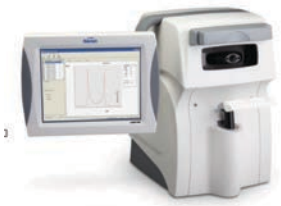
Instillation site TEAE	OTX-101 0.09% (N = 524)	Vehicle (N = 524)
Pain	114 (21.8)	21 (4.0)
Lacrimation	4 (0.8)	0
Pruritus	4 (0.8)	1 (0.2)
Reaction	4 (0.8)	3 (0.6)
Hypersensitivity	1 (0.2)	0
Foreign body sensation	1 (0.2)	0
Warmth	1 (0.2)	0
Discomfort	0	3 (0.6)
Irritation	0	1 (0.2)

Treatment-related AEs were mostly mild

Data presented as n (%) patients.
N is number of patients in the safety population.
AE, adverse event; TEAE, treatment-emergent adverse event.

Corneal hysteresis: One Device, Four Parameters:

Reichert Corneal Response Technology

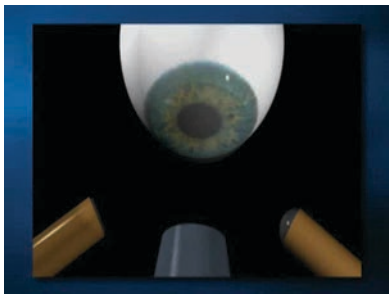


Ocular Response Analyzer

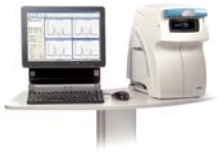
- **IOPG** - Goldmann Correlated IOP
- **IOPCC** - Corneal Compensated IOP
- **CH** - Corneal Hysteresis
- **CRF** - Corneal Resistance Factor

Method of Operation

Measured by rapidly deforming the cornea under a gentle air pulse



Corneal Biomechanics



Ocular Response Analyzer is the only instrument capable of measuring the biomechanical properties of the cornea

CH is independently predictive of glaucoma visual field progression rate
CH is predictive of response to IOP reduction medication
CH facilitates the "corneal compensated" IOP (IOPcc): an IOP measurement that is less influenced by corneal properties than other tonometers, including Goldmann.
This is superior to CCT-based adjustment formulas.

CCT-based IOP adjustment is not advisable
From the OHTS

Data

Published in final edited form as:
Ophthalmology. 2012 March ; 119(3): 437–442. doi:10.1016/j.ophtha.2011.03.018.

Adjusting Intraocular Pressure for Central Corneal Thickness Does Not Improve Prediction Models for Primary Open-Angle Glaucoma

James D. Brandt, M.D.[1], **Mae O. Gordon, PhD**[2,3], **Feng Gao, PhD**[3], **Julia A. Beiser, M.S.**[2], **J. Phillip Miller, A.B.**[3], and **Michael A. Kass, M.D.**[2] **for the Ocular Hypertension Treatment Study Group**

[1] University of California, Davis, Department of Ophthalmology & Vision Science

[2] Washington University School of Medicine, Department of Ophthalmology and Visual Sciences

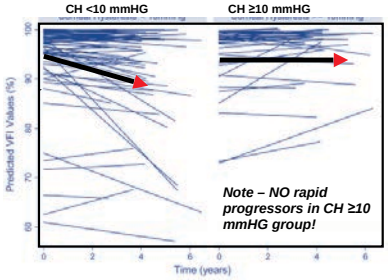
[3] Washington University School of Medicine, Division of Biostatistics

Abstract

Purpose—To determine if the accuracy of the baseline prediction model for the development of primary open-angle glaucoma (POAG) in ocular hypertension patients can be improved by correcting intraocular pressure (IOP) for central corneal thickness (CCT).

Design—Re-analysis of the baseline prediction model for the development of POAG from the Ocular Hypertension Treatment Study (OHTS) substituting IOP adjusted for CCT using 5

Corneal Hysteresis in Glaucoma
Predictive of Progression in Prospective, Longitudinal Study (DIGS)



Time (years)

- Univariate model: each 1 mmHg decrease in CH was associated with a 0.25%/year increase in rate of VFI decline ($P<0.001$)
  - By comparison, each 1 mmHg higher baseline GAT IOP was associated with a 0.11%/year faster rate of VFI loss ($P<0.001$)
- In the multivariate model, CH was >3X more associated with rate of VF progression than CCT (17.4% vs 5.2%)
- The relationship between CH and IOP is complex:
  - For eyes with lower CH, the impact of IOP was significantly larger than in eyes with higher CH levels.

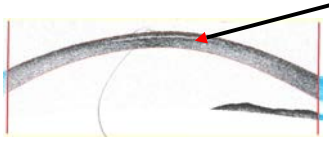
The prospective longitudinal design of this study supports the role of CH as an important factor to be considered in the assessment of risk for glaucoma progression

Medeiros FA et al. *Ophthalmology.* 2013;120:1533-1540.

IOPcc – a superior indicator of IOP
Case 1: IOPcc Ignores Edema!

57 yo post LASIK female

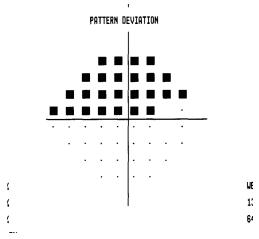
- Complaining of blurry vision and pain in right eye
- GAT: 15 mmHg
- IOPcc: **46 mmHg!!**
- OCT image showed fluid under the flap (edematous)



Patient Diagnosed with Angle Closure Glaucoma

Data Courtesy of William Wiley, MD. Cleveland Clinic

IOPcc – a superior indicator of IOP
Case 2: IOPcc agrees better with status of VF loss



53 yo black male with Glaucoma
- CCT 598/582
- GAT: 15mm Hg
- On IOP medication OU

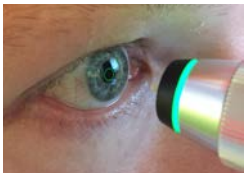
IOPcc Measurements
- IOPg: 15.5 OD / 15.0 OS
- IOPcc: 19.2 OD / 18.9 OS

Note: IOPcc is the opposite direction from a CCT adjustment and is properly associated with the status of glaucoma

Data Courtesy of Nathan Radcliffe, MD
Assistant Professor of Ophthalmology
Weill Cornell Medical College, New York-Presbyterian Hospital
Data Courtesy of William Wiley, MD. Cleveland Clinic

Contact tonometer: Intelligent Positioning Assistant

Green light on the probe base indicates correct vertical alignment



The probe should point perpendicularly to the center of the cornea (the reflection of the light ring is seen symmetrically inside the sphere of the pupil).

Red light on the probe base indicates incorrect vertical alignment of the tonometer.

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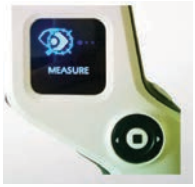
Advanced Navigation Interface

The advanced navigation interface includes 3 buttons and a 128x128 pixel OLED color display for effortless selection and menu browsing.



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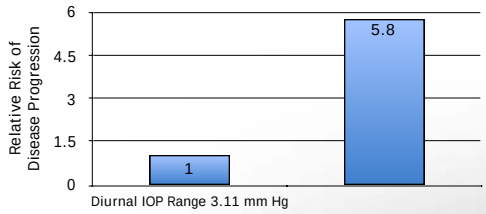
Self-Monitoring Makes a Difference



Arsani S, Zeimer R, Wilensky J, et al. Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma. *J Glaucoma*. 2000;9:134-142.

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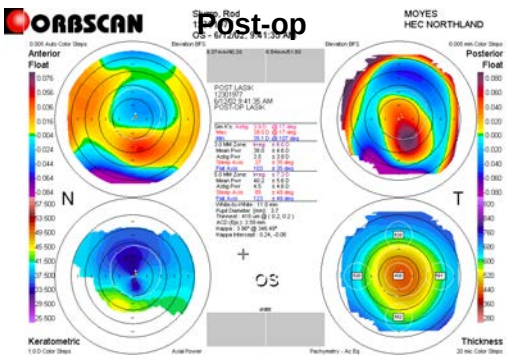
Collagen Cross Linking (CXL)

Ectasia Diagnosis and Management



Corneal Cross-Linking

- First introduced by Theo Seiler MD
- Involves saturating the cornea with riboflavin (Vit B2)
- Expose cornea to UV light (370 nm) for 30 minutes
- Riboflavin absorbs UV light and produces singlet oxygen
- Causes cross-linking of collagen fibers and extracellular matrix proteins
- To protect the endothelium:
  - Soak cornea for 30 minutes prior
  - Originally required debridement of corneal epithelium
  - Ensure riboflavin has penetrated to the AC

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Corneal Cross-Linking

- Riboflavin prevents penetration of uv light
- Older corneas vs. younger corneas and progression of keratoconus
- CXL appears to be the first technology than can halt the progression of ectasia

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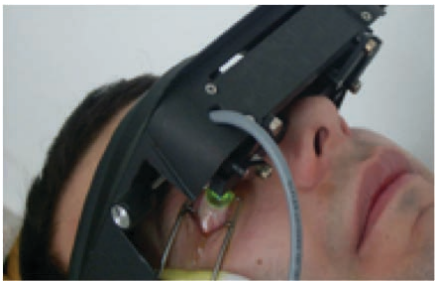
Corneal Cross-Linking



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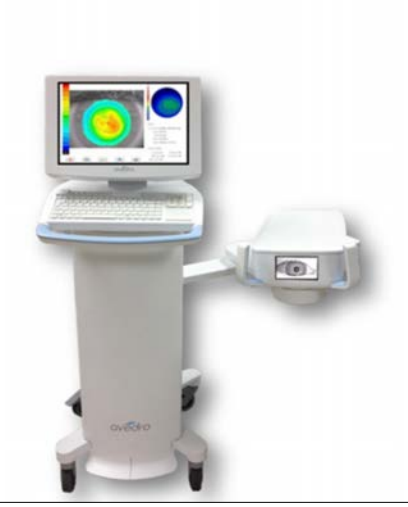

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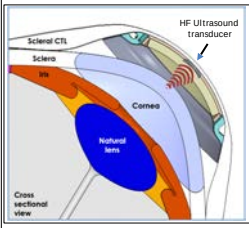
Other potential applications

- Physician sponsored IND for infectious keratitis treatment
  - Ulcers limited to 250 microns
  - May also help with infectious load
- Treatment of corneal edema
  - Cross linking reduces imbibition pressure
  - Internationally it appears to work for 3 mo to 12 mo duration
- Treatment for fluctuating vision post RK

On-Eye Crosslinking: Comfort and Control

Scleral CTL with fiber optic UV delivery

- Eyes open/closed for comfort
- Eliminates motion challenges
- Customized treatment
- Small touchscreen control



Closed-loop ultrasound elastography feedback control

- Accurately measure pre-treatment corneal biomechanics
- CXL induced tissue changes monitored in real time
- UV transparent fluid interface provides acoustic medium and oxygen supply

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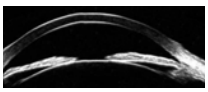
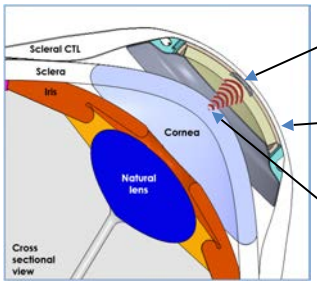
Ultrasonic Dosimetry (Patents Pending)

Accurate dosing of the UV requires monitoring corneal changes during the treatment

- The cornea is an ideal tissue to query with ultrasound
- Only CXLens' on-eye delivery of UV enables real time ultrasonic dosimetry

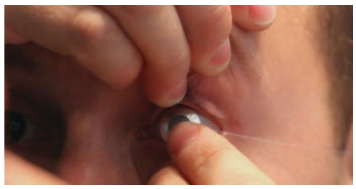




- CXLens® UV delivery system design includes a high frequency (HF) ultrasonic transducer within the optical diffuser
- Positional stability of scleral lens enables precise acoustic measurement of ophthalmic structures
- Doppler capability allows assessment of stiffness of corneal membrane

TECLens Approach to Vision Correction

CXLens® - Crosslinking Lens



CXLens® is single use ultraviolet energy delivery and ultrasound monitoring system built into a scleral contact lens.

Placed directly on the eye, this next generation CCXL technology enables a multitude of superior capabilities and advantages.

CXLens® Non-Surgical Vision Correction

Myopia
Crosslink the center of the cornea to stiffen (and thus flatten) the central region

Hyperopia
Create annular crosslinked region to flatten periphery and steepen center

Astigmatism
Create a custom 'butterfly' pattern to flatten areas that are aspherically too steep

DALK-Deep Anterior Lamellar Keratoplasty

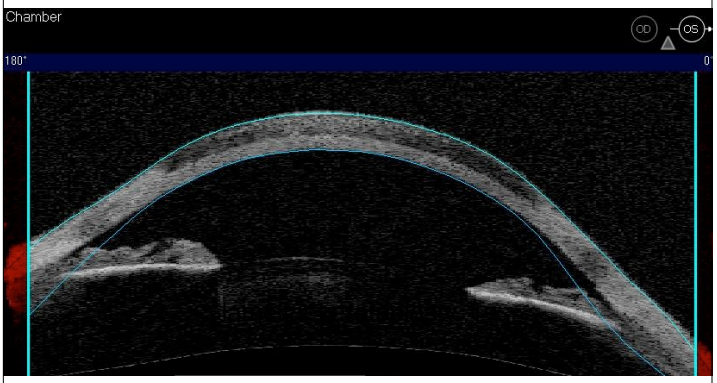


image courtesy of Dr. L. Buratto

Innovations in Eyecare Part II

Paul M. Karpecki, OD, FAAO

Kentucky Eye Institute, Lexington KY
Gaddie Eye Centers, Louisville KY
Retina Associates of KY
UPike KY College of Optometry
Chief Clinical Editor, Review of Optometry
Medical Director, TECP

Presbyopia Correction

- Accommodating IOLs
- Corneal Inlay Technology
- Scleral expansion
- Pharmaceutical agents/ eye drops

Presbyopia Correction

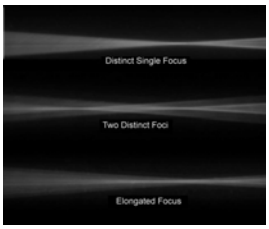
- Accommodating IOLs
- Corneal Inlay Technology
- Scleral expansion
- Pharmaceutical agents/ eye drops

Elongation Of Focus

Monofocal IOL

Multifocal IOL

TECNIS Symfony ® IOL



[1] Data on File. Tecnis Symfony Green Light Bundle Bench Test DOF2014CT0005. Abbott Medical Optics Inc. 2014

Extended Depth Of Focus

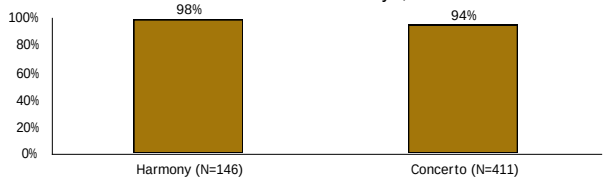
Unique optics, creating a different visual experience

- The proprietary echelette design introduces a novel pattern of light diffraction that elongates the focus of the eye[1]
- The echelette is the relief or profile of the lens (height differential) within each ring
- The height, spacing, and profile of the echelettes to create a diffractive pattern for an elongated focus

1. TECNIS® Symfony® IOL DFU

Patient Satisfaction

Percent of patients who would recommend EDOF IOLs to friends and family1,2



1. DOF2016CT0024 Concerto Study Report, 2. DOF2015OTH0009 Symfony Harmony Observational Study

Scleral Expansion for Presbyopia

- Restarted Clinical trial with redesign of method for creating the tunnels
- Now called the “VisAbility implant system”

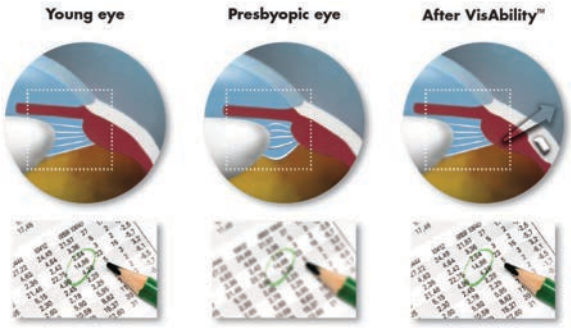
Scleral Expansion Micro-Insert System

Docking Station Incisional System

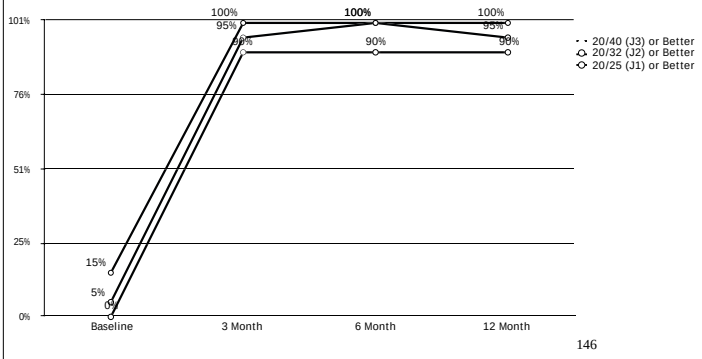
- No marking
- Docking station “locks” with 4-point fixation
- Scleratome “docks” into position

How does it work?

Implants may help the focusing muscles of the eye work better and improve near vision



Uncorrected Near Visual Acuity @ 40cm (Two Sites - Binocular (OU), n=20)



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Topical Treatment for Presbyopia

- Miotic therapies
  - Contains miotics but also proprietary components that allow full 12-14 hours of near and far vision
- Lens restoration
  - Contains drops that selectively target and disrupt the disulfide bonds in the lens
  - Total of 3-4 weeks of treatment and permanent results thus far

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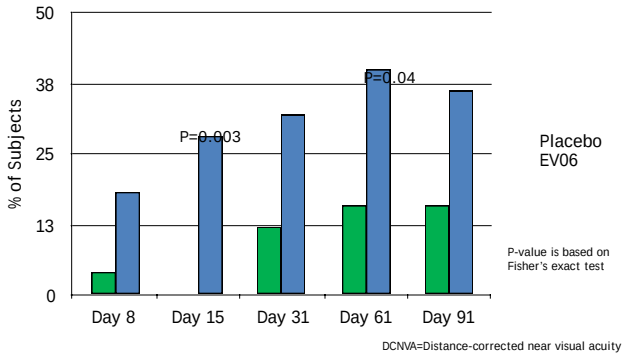
Percent of Subjects with Gain of ≥10 Letters in DCNVA



DCNVA=Distance-corrected near visual acuity

Note: Preliminary analysis based on LOCF in study eye only

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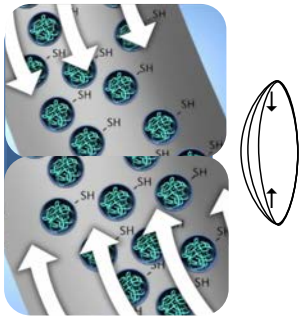
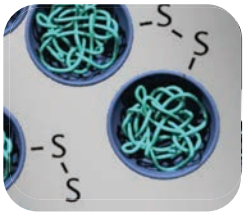
How Is Accommodation Lost?

Young Eye



Cytosol Displacement Centrally = Accommodation

Aging Eye



Oxidation induced disulfide bonds form between crystalline proteins - a Leading Potential Cause

Lens Stiffening = Compromised Accommodation

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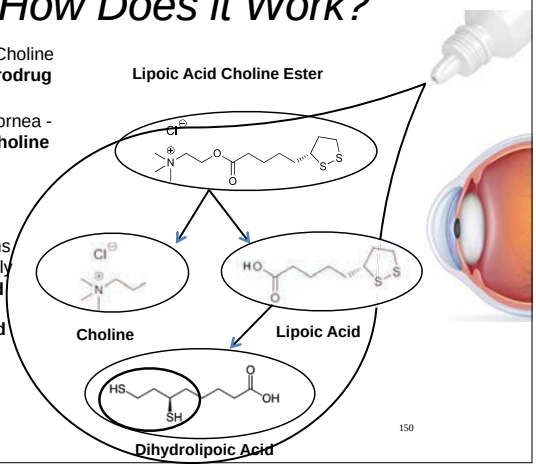
What is EV06?
How Does it Work?

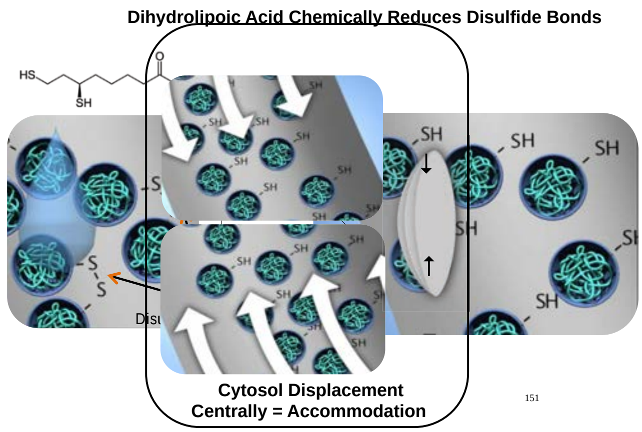
- EV06 (Lipoic Acid Choline Ester, 1.5%) is a **prodrug**
- EV06 penetrates cornea - metabolized into **Choline & Lipoic Acid**, two naturally occurring substances
- Enzymes within lens fiber cells chemically reduce **Lipoic Acid** to active form **Dihydrolipoic Acid**



150

LENS ELASTICITY IS REGAINED

Dihydrolipoic Acid



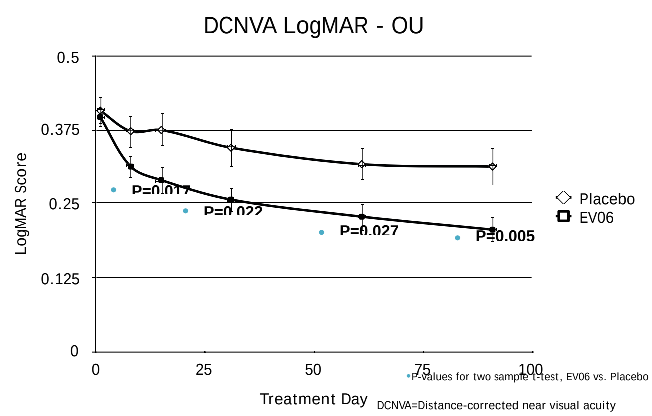
EV06 Safety & Tolerance Results

- No Subjects Discontinued For Adverse Events, Safety Concerns, or Tolerability
- No Sight Related Adverse Events
- Upon Instillation
  - Mean EV06 Comfort Rating 3.0
  - Mean Placebo Comfort Rating 2.7
    - (Scale 0 – 10; "0" = Very Comfortable)
- No Change In Best Corrected Distance Visual Acuity

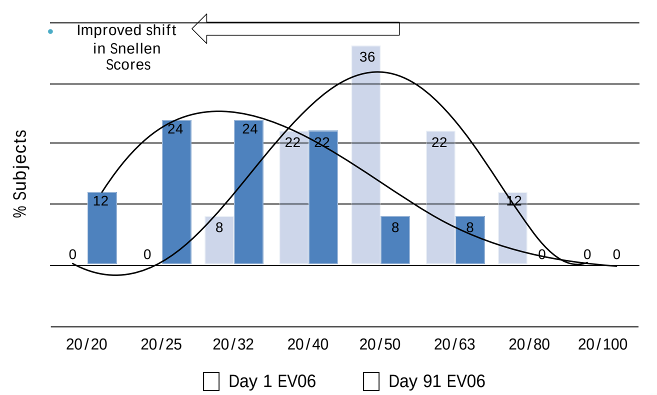
EV06 Efficacy Results

- Achieved both Primary Efficacy Results:
  - Improvement in Distance Corrected Near Vision Acuity (DCNVA) in the Study Eye after treatment, which continued throughout the dosing period
  - Higher proportion of subjects with gain of ≥10 letters in DCNVA in the study eye vs. placebo

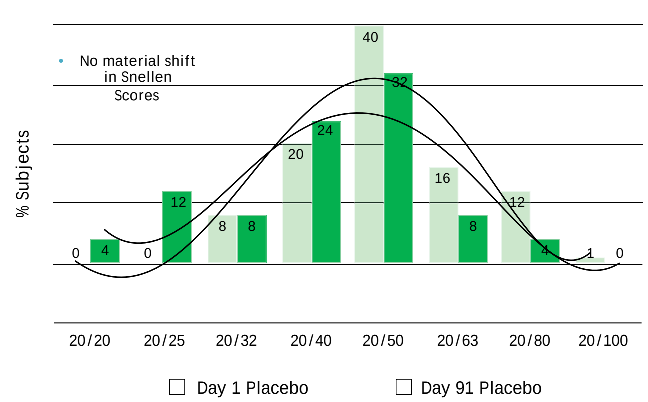
Improvement in Distance Corrected Near Vision Acuity



EV06 DCNVA Snellen score - Day 1 & Day 91



Placebo DCNVA Snellen score - Day 1 & Day 91



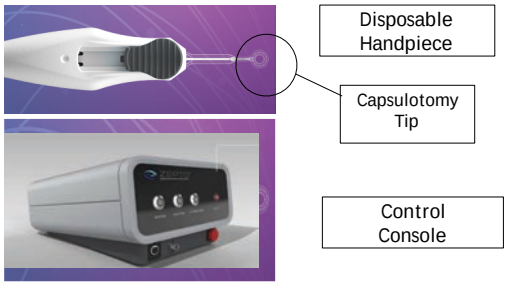
Light Adjustable IOL

- Currently available in Europe
- 6 mm silicone optic and PMMA haptic IOL
- Using a UV laser so as to change the refractive error
- Post operative enhancement, correction, adjustment
- Corrections to .1D accuracy
- Can trial mono vision through UV protection lenses
- Optometry's role in post-operative treatment is a necessity

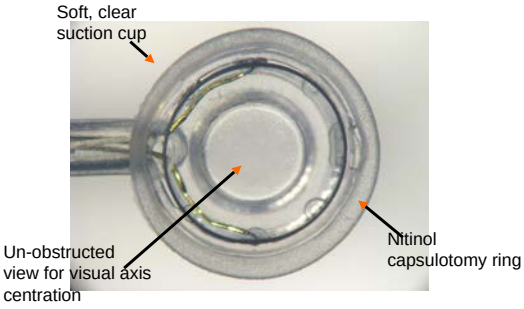
Light Adjustable IOL

- Optometry role
- IOL polymer does not have 'healing' issues
- UV light adjustable corrects consistently every time
- Working on payment system currently but expect post-operative uv light correction as additional

Capsulotomy System Consists of:



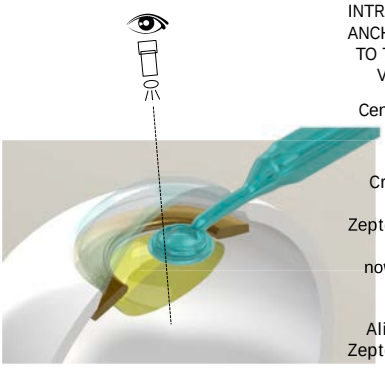
Capsulotomy Tip



Operating Principles

- Suction pulls capsule against capsulotomy ring
- Electrical energy applied to ring for 4 milliseconds
- Phase transition of water molecules

Precision Pulse Capsulotomy



ZEPTO INTRAOPERATIVELY ANCHORS SURGERY TO THE PATIENTS VISUAL AXIS

Center Zepto on P1*

Create capsulotomy

Zepto capsulotomy is now reference marker

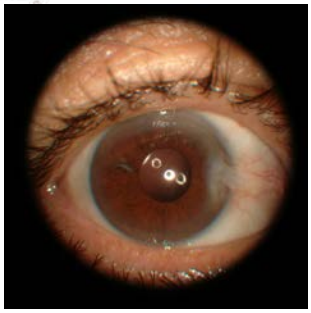
Align IOL with Zepto capsulotomy

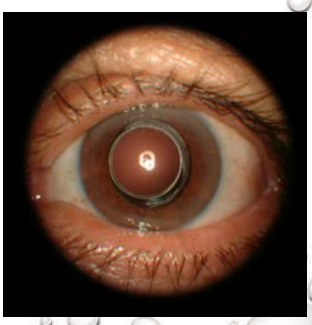
THE BENEFITS OF THE 3D CAPSULE

UNIQUE 3D DESIGN

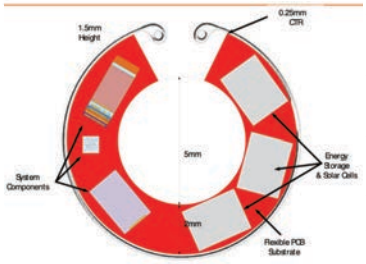
incision (2.2 mm)

18 MONTHS POST IMPLANTATION-NO YAG



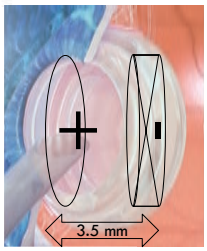


THE WIRELESS PRESSURE SENSOR



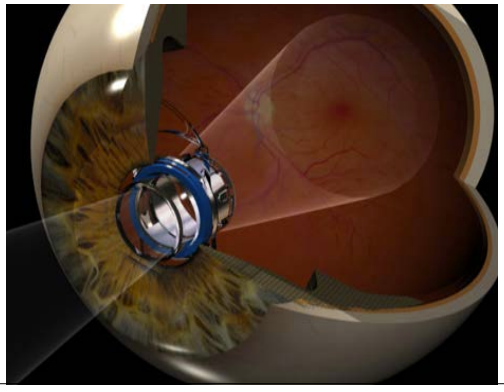
- Designed to fit within the central slot of the prosthetic capsule
- Communicates through tissue up to to a peripheral device
- Measures IOP 4 times/ hour without intervention
- Easily removed if needed
- Central 5mm is an open aperture

LOW VISION INTRAOCULAR TELESCOPE ASSEMBLY

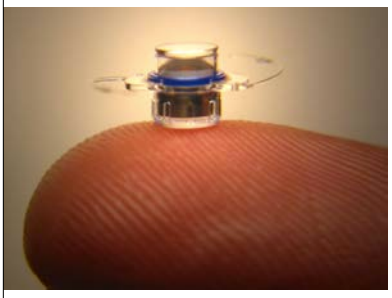


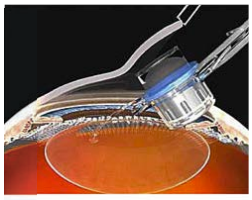
- Not all AMD patients had significant disease at the time of cataract surgery
- A platform for modification of the optical state of the eye has huge benefits
- The assembled parts can be inserted through traditional sub 3mm incisions.
- The telescope can be "tuned" for optimal magnification, field of view and prismatic offset.

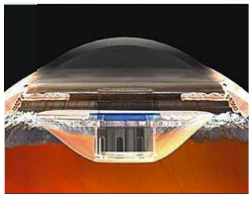
Telescopic IOL for Advanced AMD



Telescopic IOL for Advanced AMD







Implantable Miniature Telescopess

- Renders retinal image ~2.7x larger than natural lens
  - Images seen upon viable perimacular tissue
  - Field of view 20-24 degrees
- 67% achieve >/= 3 lines of improved VA (control = 13% - worse seeing eye for treatment eye)*
- Improved ADL's and Vision-Targeted Psychosocial Domains*

*Hudson H. A team approach helps severely visually impaired AMD patients. *Ophthal Management*. 2012; 52-54.

MIGS

MIGS

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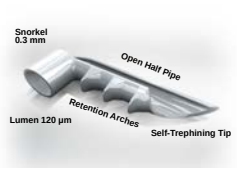
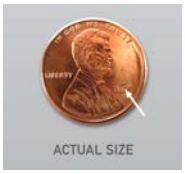
MIGS

Smallest medical device known to be implanted in the human body and weighs just 60 µg





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MIGS

Designed to be used in conjunction with cataract surgery to safely and effectively reduce IOP while facilitating the eye's natural outflow in mild to moderate OAG patients currently on hypotensive medication

- Lowers IOP and may reduce or eliminate medication burden[1]
- Decrease risk of IOP fluctuations associated with non-adherence to prescription medication regimens
- Avoid serious complications associated with end-stage filtration and shunt procedures
- Spare the conjunctiva and safely preserve future treatment options
- Minimizes risks of hypotony and bleb related complications

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Newest MIGS device

- -7.6mmHg reduction in IOP
- Increased IOP reduction at 2 years compared to 1 year
- Likely approval in late 2018

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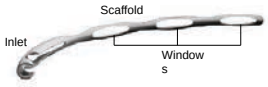
Microstent

VIEW FROM ANTERIOR CHAMBER



VIEW FROM CANAL

- Flexible, biocompatible 8 mm length microstent
- Made out of nitinol (highly biocompatible material used in cardiovascular stents)
- Contoured to match canal curvature
- Three open windows face anterior chamber
- The canal-facing surface is completely open for unobstructed collector channel access

Investigational Device in the US

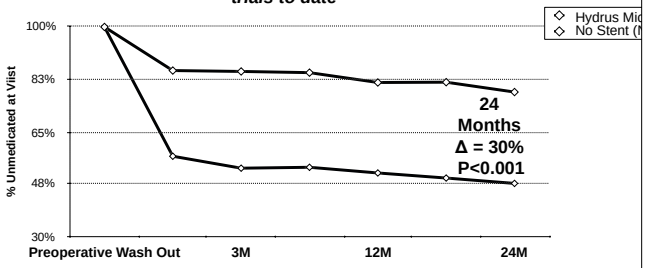
Real-time Confirmation of Accurate Delivery

Visual Confirmation of Proper Placement – No Need for Targeting

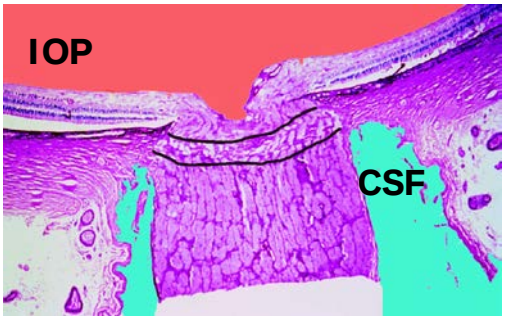
HORIZON: Medication Free

MEDICATION FREE 0-24 MONTHS

Largest treatment effect of all MIGS pivotal trials to date

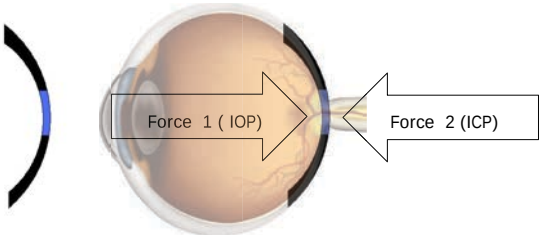


N=369 Hydrus and 187 phaco

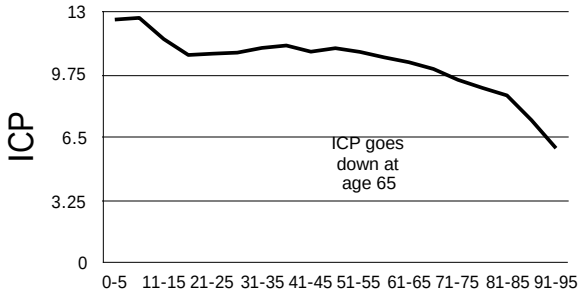


Jonas JB, Berenshtein E, Holbach L.Anatomic relationship between lamina cribrosa, intraocular space, and cerebrospinal fluid space. Invest Ophthalmol Vis Sci. 2003 Dec;44(12):5189-95.

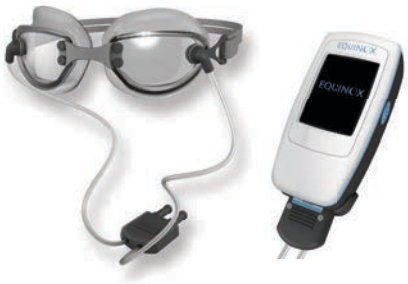
Basic physics

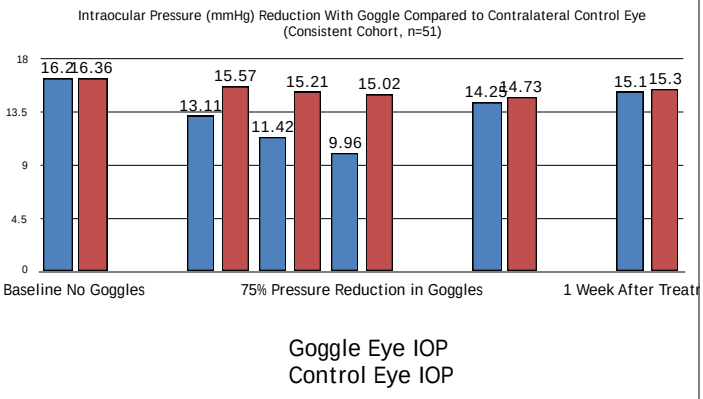


ICP changes with age



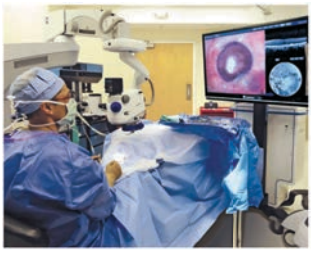
Solution?





Other options for Augmented Reality

- Surgical Systems
- AMD



Providing the whole picture by both maintaining a Wide Field of View and recovering the Central Field

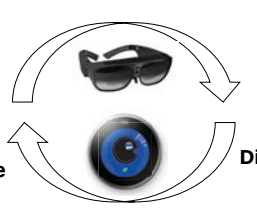
View with AMD (central scotoma)

View with Magnification (this limits the Field of View)

How it Works:

Open Market AR Hardware + Proprietary Software [1]

Image Capture



Display

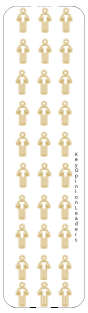
Vision w/AMD

Adaptive Systems [1]

Simulated Natural Vision

1. Patents pending & FTO completed

Technology Validation

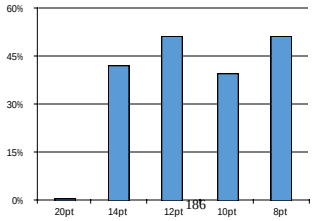


30 Users to Date
73 – 105 Age Range
20/60 – 20/400 Vision
Mostly Dry AMD

Technology validated
improved reading
&
everyday tasks easier

50% Improvement

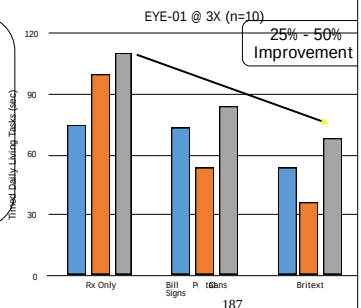
% increase in reading speed



Clinical Trial: Validation of Features

A New Timed Instrumental Activities Of Daily Living (TIADL) Measure For Evaluation Of Rehabilitation Outcomes *(V.L. Gills[1], M.MacKeben[2], D.C. Fletcher[1,2])*

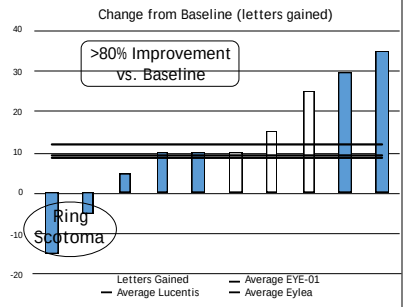
Timed Independent Activities of Daily Living (TIADLs):
- Reading a bill
- Identifying & Reading food cans
- Sign spotting & reading



Clinical Trial: Validation of Features

Quantitative Evaluation of reading ability and visual acuity

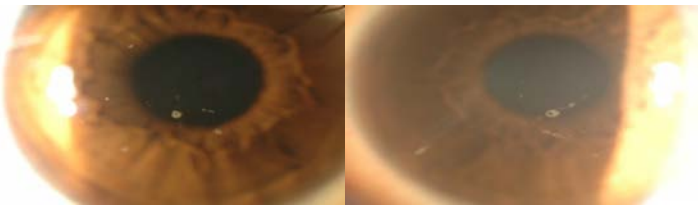
MNRead Reading Assessment:
- Critical print size
- Reading Acuity
- Scotoma pattern dependencies



Gene Therapy & Genomics

- Generic variants causing most ocular diseases are being discovered
- Examples include glaucoma, dry AMD, Fuchs' and all corneal dystrophies
- Early treatment vs. repair
- Prevention of disease progression (e.g. Avellino Labs)
- Ocular anatomy and architecture are uniquely situated for gene based research

Case 1 Slit Lamp Examination

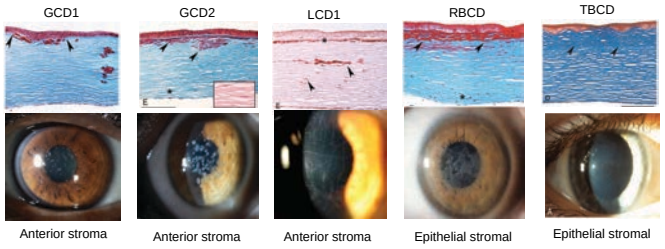


Considerations and DDx

- Corneal scarring from long-standing CL wear?
- EBMD - Cogan's or MDF?
- Appears to be anterior stromal
- A Stromal Dystrophy?

TGFBI Corneal Dystrophies

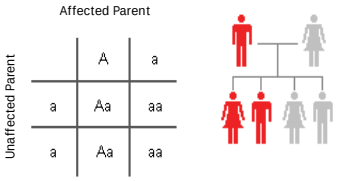
histologic and clinical appearances



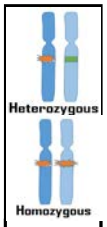
Weiss JS, Møller HU, et al. **IC3D classification of corneal dystrophies--edition 2.** Cornea. 2015 Feb;34(2):117-59.

Autosomal Dominant Inheritance Pattern

If only one parent has a single copy of a dominant allele for a dominant disorder, their children will have a 50% chance of inheriting the disorder.

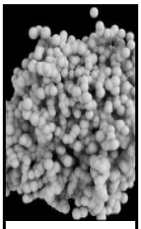


Mechanism of *TGFBI* Induced Corneal Dystrophy

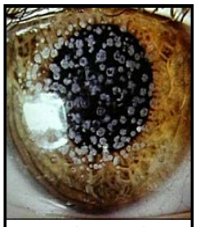


TGFBI Gene Mutation

Damage To Cornea



Excessive Production Of TGFBIp Protein



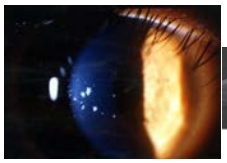
Protein Deposits on Cornea

Post LASIK Exacerbation

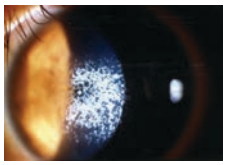
In 2004 , Jun et al published a case in Ophthalmology. A 25 year old female experienced decreased vision five years after LASIK. Genetically confirmed as GCD2

Roo Min Jun, MD, et al.
Opthalmology III.3 (2004):463-468

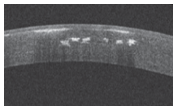
OD - No Surgery, 5 years later



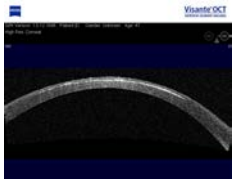
OCT cross section



OCT cross section

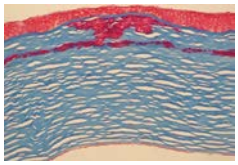


OS – 5 years post LASIK



Right Eye OCT showing protein deposits at the interface of the flap

Histology slide after penetrating keratoplasty from a similar patient with GCD1 accelerated post LASIK



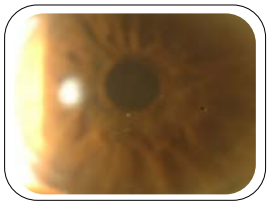
Subtle Phenotype

Daughter - age 21

Patient 'qualified' for LASIK on slit lamp exam, then genetically tested

Mother – age 47

No positive family history reported by patient.



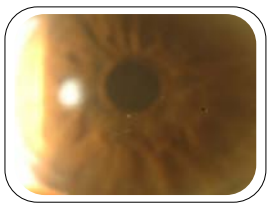
Subtle Phenotype

Daughter - age 21

Patient 'qualified' for LASIK on slit lamp exam, then genetically tested
Tested Positive GCD2

Mother – age 47

No positive family history reported by patient.
Tested Positive GCD2



CLIA Licensed Diagnostic Laboratory

licensed by U.S. Division of Laboratory Services, under the Center for Clinical Standards and Quality

Clinical Trial*:
100% Sensitivity, Specificity

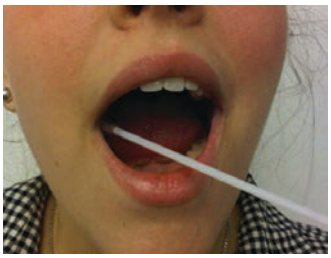
CLIA Testing:
100% Accuracy, Precision

*Clinical Trial
734 corneal dystrophy subjects
136 normal controls

AMD – A Genetic Disease

Macula Risk

A test that identifies AMD patients who will progress to vision loss

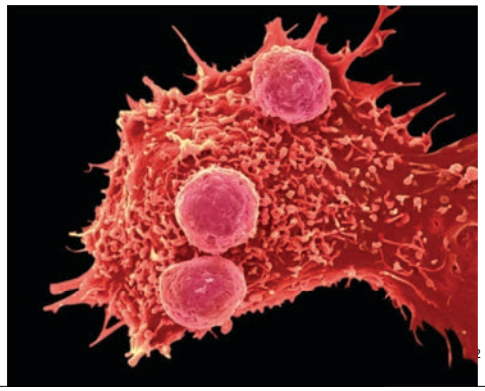


Cheek Swab

Genetic Testing for Ocular Disease

- Akin to "23 and Me"
- Only for ocular conditions ranging from AMD and Stargardt's to Leber's, Fuchs and even glaucoma

CRISPR Gene Editing and an Adenovirus vector



CRISPR can remove the damaged or faulty genes

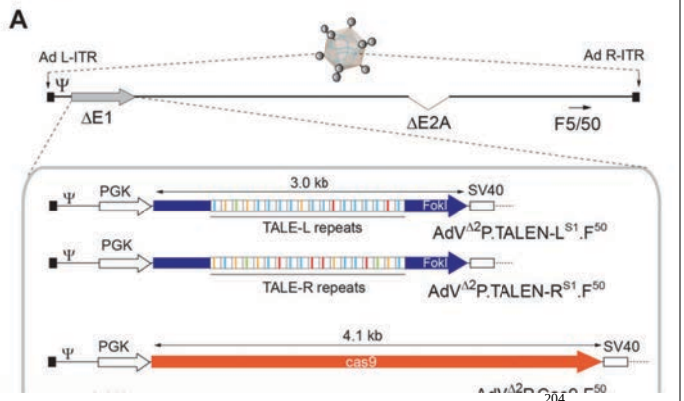
Modified Adenovirus can present the proper genetic code to the body for integration

Article | OPEN

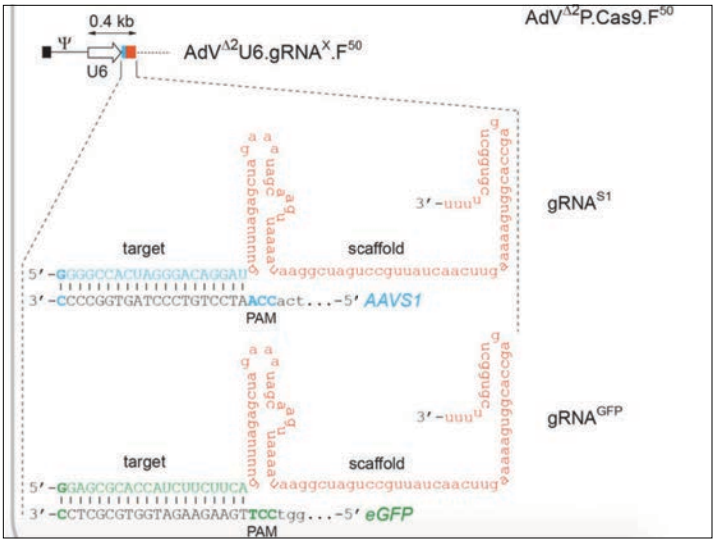
Adenoviral vector delivery of RNA-guided CRISPR/Cas9 nuclease complexes induces targeted mutagenesis in a diverse array of human cells

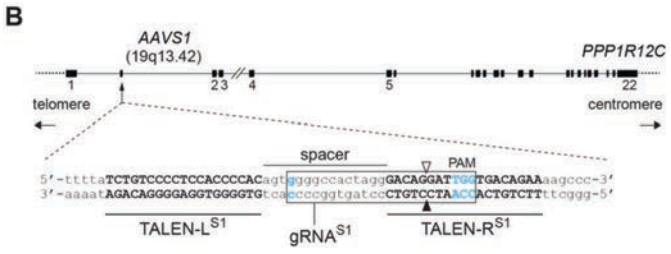
Ignazio Maggio, Maarten Holkers, Jin Liu, Josephine M. Janssen, Xiaoyu Chen & Manuel A. F. V. Gonçalves

From: Adenoviral vector delivery of RNA-guided CRISPR/Cas9 nuclease complexes induces targeted mutagenesis in a diverse array of human cells



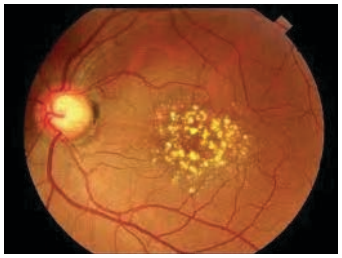
CRISPR followed by injecting the correct code for Leber's Optic Neuropathy currently in clinical trials





AMD Opportunity

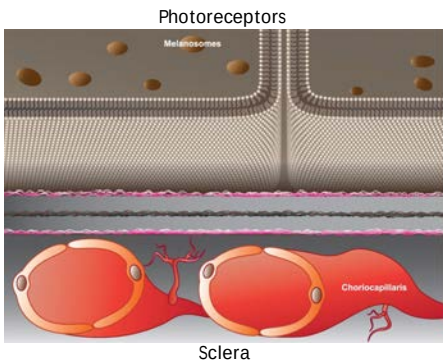
Medical Utility - The AMD Problem



How can the Primary Eye Care Professional identify those at Risk?

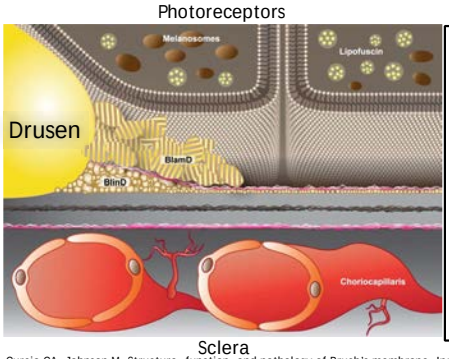
Only 15% to 20% of Early / Intermediate AMD will progress to Advanced disease

Dark Adaptometry



Curcio CA, Johnson M. Structure, function, and pathology of Bruch's membrane. In: Ryan SJ, et al, eds. *Retina, Vol 1, Part 2: Basic Science and Translation to Therapy*. 5th ed. London: Elsevier; 2013:466-481.

Dark Adaptometry



Cholesterol accumulation leads to panmacular deposits (BlinD and BlamD)

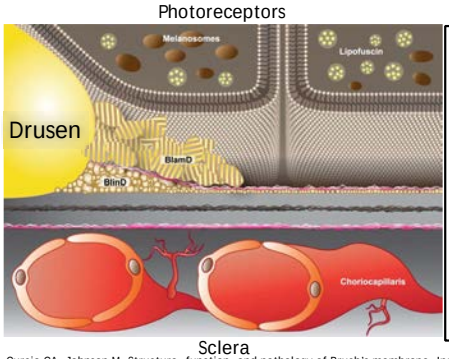
Peaks in these deposits eventually become clinically visible drusen

These extracellular cholesterol deposits affect photoreceptor health by impairing transport, causing inflammation, and predisposing to CNV

In addition, they impair normal transport, including that of vitamin A, across Bruch's membrane

Curcio CA, Johnson M. Structure, function, and pathology of Bruch's membrane. In: Ryan SJ, et al, eds. *Retina, Vol 1, Part 2: Basic Science and Translation to Therapy*. 5th ed. London: Elsevier; 2013:466-481.

Dark Adaptometry



In effect, AMD causes a localized deficiency of vitamin A, and dark adaptation is the best test to measure this change

Curcio CA, Johnson M. Structure, function, and pathology of Bruch's membrane. In: Ryan SJ, et al, eds. *Retina, Vol 1, Part 2: Basic Science and Translation to Therapy*. 5th ed. London: Elsevier; 2013:466-481.

Dark Adaptometry

Dark adaptation is the process of adjusting from day vision to night vision

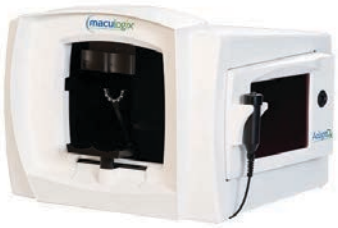
Easy-to-measure aspect of night vision

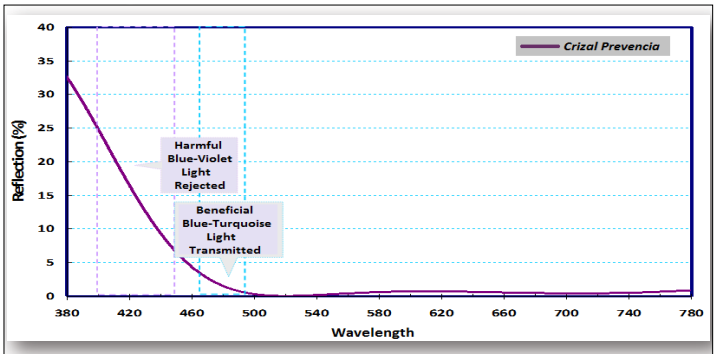
Dark Adaptometry

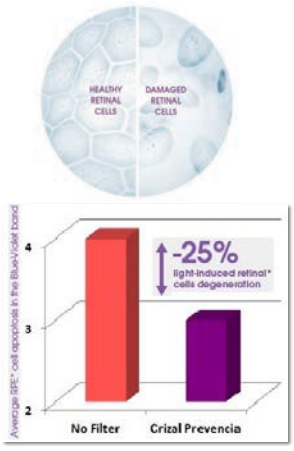
First dark adaptometer for rapid, routine clinical use

Simple, objective tool to measure dark adaptation as earliest functional correlate of macular dystrophies

Two clinical protocols
- ≤6.5-minute rapid test (for quick assessment)
- ≤20-minute extended test (for benchmarking)







A Breakthrough Study in Blue Light- Sleep patterns


Medscape

Blue Light-Blocking Glasses May Help, Study Suggests

Nova Southeastern University College of Optometry

Study Independently conducted

Randomized Controlled Crossover Trial (The gold standard)

24 Subjects wore BluTech after 6:00 PM for 5 days, and then Clear Lenses with Anti-reflective Coating Only* for the following 5 days

Actigraphy watches noninvasively recorded sleep patterns

Melatonin samples collected from saliva after day 5

Mood & neurobehavioral performance assessed with NIH Toolbox Emotion and Cognition Batteries, respectively.

CONCLUSION:
Wearing BluTech Lenses is clinically proven to double your nighttime Melatonin levels, which MAY improve sleep and cognition.

Key Findings:
Wearing BluTech for just 5 days, participants demonstrated:

1. Increase in Melatonin levels by 96% (P=0.036)
2. Less awakening during sleep, reduced sleep onset latency
3. Improved cognition using pattern comparison test (P=0.047)


Retina

Enrichment of Macular Pigment Enhances Contrast Sensitivity in Subjects Free of Retinal Disease: Central Retinal Enrichment Supplementation Trials – Report 1

RESEARCH QUESTION

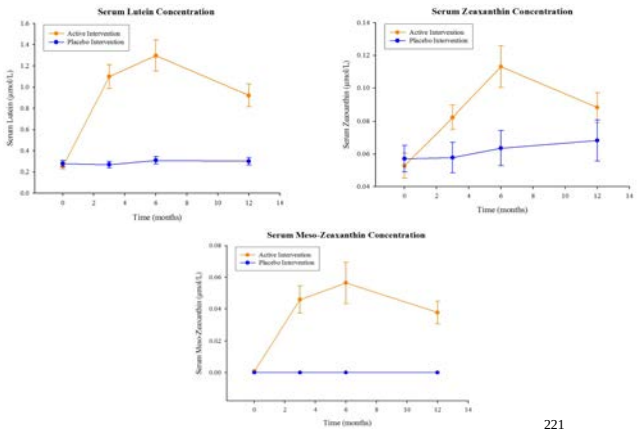
"Does supplementation with all three macular carotenoids in a ratio (mg/day) of **10:10:2 (L:MZ:Z),** for 12 months, enhance visual function in normal subjects (without retinal disease) when compared to placebo?"

Active:
10:10:2 mg/day
(MZ:L:Z)

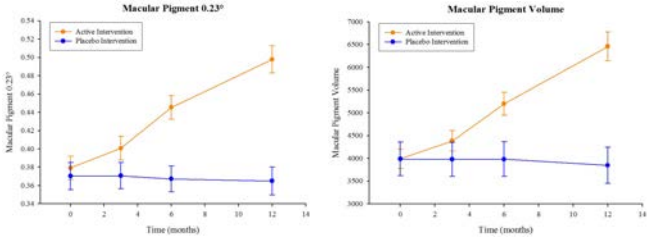
or

PLACEBO
No Active Ingredient

SERUM CAROTENOID RESPONSE



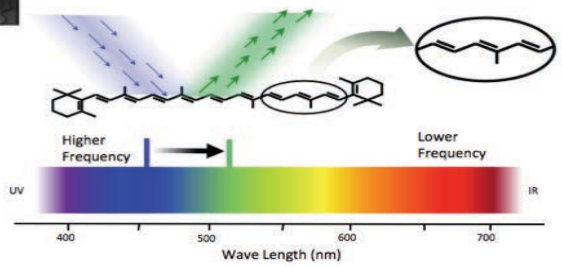
MACULAR PIGMENT RESPONSE



All subjects in active intervention exhibited augmentation of MP;
MP Volume mean ± SD = 2436 (± 1451), range 738 to 6464;
In percentage terms, mean ± SD = 73% (± 62%), range 16% to 337%;

Raman Spectroscopy Sir C. V. Raman, Nobel Prize in Physics,1930

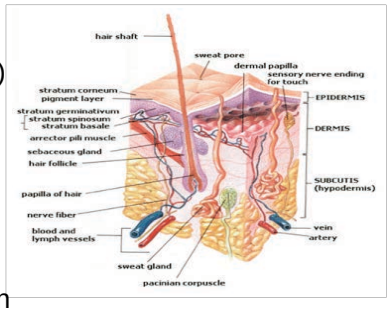
When blue light (at exactly 473 nm) is shined onto carotenoids, the energy of the reflected light is *'shifted'* to green (510 nm) due to a molecular characteristic shared among all carotenoids. This is known as *'Raman shift'*

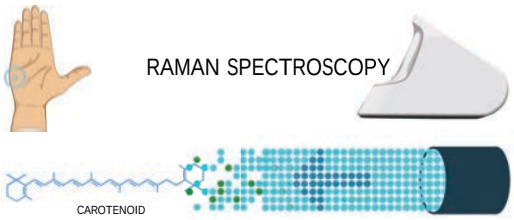


Skin Carotenoids

Measured in stratum corneum (0.1 mm) layer of the skin

α- and β- Carotenes,
Lycopene,
Lutein,
Zeaxanthin,
α-, β-Cryptoxanthin





510 nm PHOTONS

473 nm PHOTONS

Resonance Raman spectroscopic evaluation of skin carotenoids as a biomarker of carotenoid status for human studies

Susan T. Mayne [a,*], Brenda Cartmel [a], Stephanie Scarmo [a,b], Lisa Jahns [c], Igor V. Ermakov [d], Werner Gellermann [d]

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[b] Center for Science in the Public Interest, 1220 L Street, N.W., Suite 300, Washington, DC 20005, USA
[c] USDA/ARS Grand Forks Human Nutrition Research Center, 2420 2nd Avenue North, Grand Forks, ND 58203, USA
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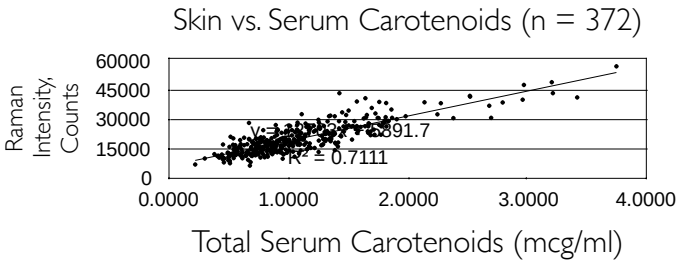
Biomarker

ABSTRACT

Resonance Raman spectroscopy (RRS) is a non-invasive method that has been developed to assess carotenoid status in human tissues including human skin in vivo. Skin carotenoid status has been suggested as a promising biomarker for human studies. This manuscript describes research done relevant to the development of this biomarker, including its reproducibility, validity, feasibility for use in field settings, and factors that affect the biomarker such as diet, smoking, and adiposity. Recent studies have evaluated the response of the biomarker to controlled carotenoid interventions, both supplement-based and dietary [e.g., provision of a high-carotenoid fruit and vegetable (F/V)-enriched diet], demonstrating consistent response to intervention. The totality of evidence supports the use of skin carotenoid status as an objective biomarker of F/V intake, although in the cross-sectional setting, diet explains only some of the variation in this biomarker. However, this limitation is also a strength in that skin carotenoids may effectively serve as an integrated biomarker of health, with higher status reflecting greater F/V intake, lack of smoking, and lack of adiposity. Thus, this biomarker holds promise as both a health biomarker and an objective indicator of F/V intake, supporting its further development and utilization for medical and public health purposes.

*Arch Biochem Biophys. PMC 2014 M

Initial Study: Correlation study of skin carotenoids and serum carotenoid levels ; r = 0.84 (p<0.0001)



ARVO 2016
RESEARCH: A VISION OF HOPE MAY 1 – 5 | SEATTLE

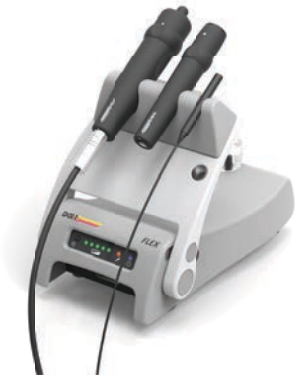
Interrelationships between Macular, Skin, and Serum Carotenoids Tue, May 03

Author Block: *Christopher D. Conrady[1], James E. Bell[1], Brian M. Besch[1], Aruna Gorusupudi[1], Werner Gellermann[1], Kelliann Farnsworth[1], Paul S. Bernstein[1]*
[1] Ophthalmology, University of Utah - Moran Eye Center, Salt Lake City, Utah, United States

Conclusion:

"Skin RRS is a reasonable biomarker of macular carotenoid status that can be readily performed in a wide variety of research, clinical, and non-clinical settings."

Today's UltraSound Technology



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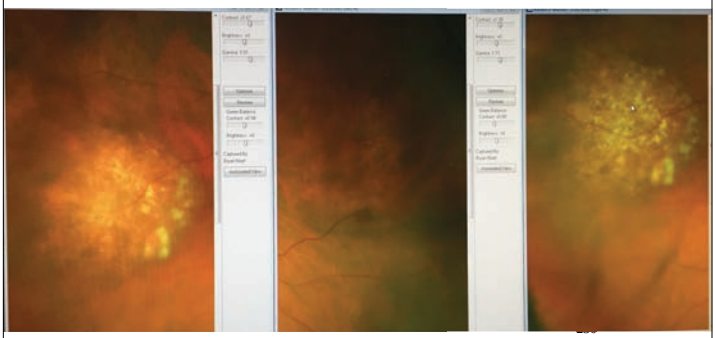
Keys to Determining if a Nevus is a Choroidal Melanoma



Keys to Determining if a Nevus is a Choroidal Melanoma

- Symptoms
  - Flashes
  - Floaters
  - Decreased VA
- Orange pigment (lipofuscin) on the surface of the lesion
- Touching the disc margin area

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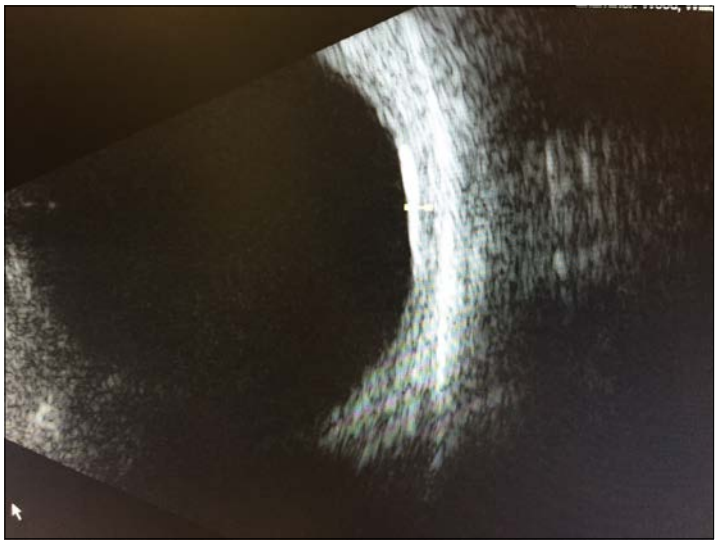
Keys to Determining if a Nevus is a Choroidal Melanoma

- Height over 2mm on **ultrasound**
- Subretinal fluid on or off the lesion
- Increasing basal diameter

232



Common Indications for B-Scan Ultrasound Testing

- Nevi
- PVD
- Potential RD (flashes/floaters/cobwebs)
- Obstructed view to the retina
  - Opaque corneas
  - Dense cataracts
  - Vitreous hemorrhages
  - Hyphema
- Optic nerve head drusen

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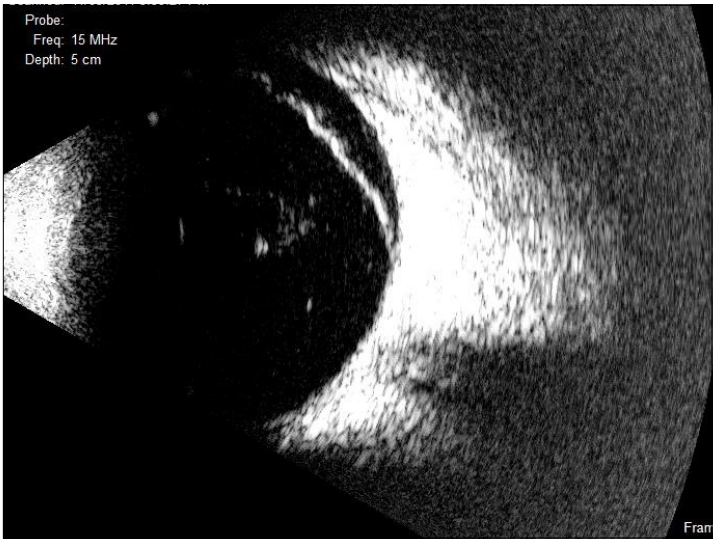
Common Indications for Ultrasound Testing

Exophthalmos
Asteroid hyalosis
Dislocation of lens
Trauma
Hyphema
Intraocular foreign bodies
Any potential intraocular tumor



Common Indications for Ultrasound Testing

Valuable in differentiating:

Choroidal detachments (serous v. hemorrhagic)
RDs (rhegamatogenous v. exudative)
Retinal tear v. retinal detachment v. retinoschisis
ONH drusen from papilledema

Another application: Myopia Control

Patient John Doe
ID# 020419153310
DOB 01 Jan 1960
Gender Male

Dr. Smith
DGH Technology, Inc.
110 Summit DR; Suite B
Exton, PA 19341
Practice Phone

Axial Length Progression

OD Average Measurements (mm) 4 Files

ScanDate	Scan Type	Lens Type	Vitreous Type	Ct.	Rank	ACD	LT	VCD	AXL	Change from Prev	Change from Initial
02/04/2019 10:38:47 AM	C	Norm	Norm	8	3.0	3.63	4.49	15.16	23.29	------	------
02/04/2019 10:42:20 AM	C	Norm	Norm	8	3.0	3.64	4.49	15.20	23.32	0.03	0.03
02/04/2019 10:43:42 AM	C	Norm	Norm	8	3.0	3.63	4.49	15.16	23.28	-0.04	-0.01
02/04/2019 10:45:05 AM	C	Norm	Norm	8	3.0	3.43	4.41	15.24	23.08	-0.20	-0.21

OS Average Measurements (mm) 4 Files

Scan Date	Scan Type	Lens Type	Vitreous Type	Ct.	Rank	ACD	LT	VCD	AXL	Change from Prev	Change from Initial
02/04/2019 10:39:38 AM	C	Cat	Norm	8	3.0	3.50	3.98	15.46	22.94	------	------
02/04/2019 10:42:59 AM	C	Norm	Norm	8	3.0	3.55	4.60	15.25	23.39	0.45	0.45
02/04/2019 10:44:02 AM	C	Norm	Norm	8	3.0	3.55	4.51	15.23	23.30	-0.09	0.36
02/04/2019 10:45:29 AM	C	Norm	Norm	8	3.0	3.57	4.53	15.22	23.32	0.02	0.38

Signature _____

Robotics in Ophthalmic Surgery

Robotics in Surgery

- da Vinci is the first surgical system approved by the U.S. FDA for minimally invasive general surgery in 2000
- Increasingly becoming standard equipment in many operating rooms
- Temple University presented the potential use of the da Vinci robot in transscleral, subretinal injections
- No tremor, reduction in incidence of RPD

Robotics in Perimetry

- Patients were very receptive
- Twenty-two adults, naïve to perimetry, participated in four visual field tests conducted using an Octopus 900 (Haag-Streit AG) controlled with the Open Perimetry Interface to enable automated feedback.
- All participants received an initial introduction to perimetry from a human

Robotics in Perimetry

- All participants received an initial introduction to perimetry from a human operator and then participated with the following feedback conditions:
  - human
  - humanoid robot (NAO Robot, Softbank Robotics, Japan)
  - computer speaker

Robotics in Perimetry

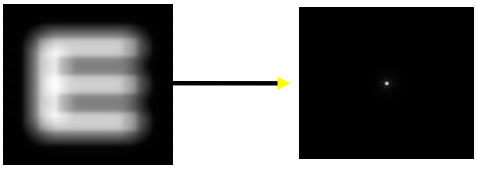
- Post-hoc testing revealed no difference in overall rating of experience between the human and the robot
- But both were preferred to the computer speaker

PSF Refraction Technology

PSF Refraction Technology

PSF Refraction Technology

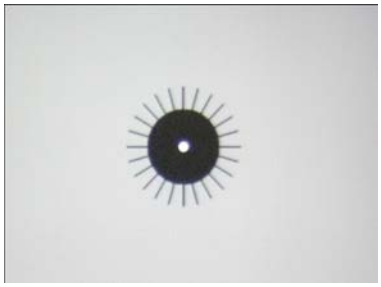
- Based on point spread function (PSF) rather than Snellen recognition

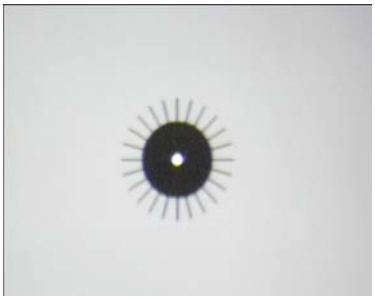


PSF Refraction Technology

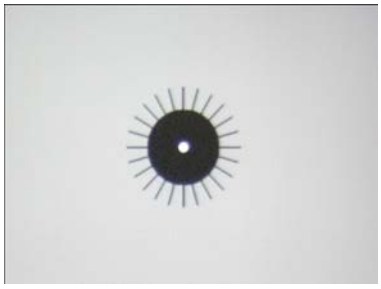
- Subjective focus
- Measures down to 0.05D
- Statistical increase in VA in pilot study
- Spectacles developed to match the technology

PSF Refraction is More Sensitive





PSF Refraction is More Sensitive



Study from SCO

- VASR stands for voice activated subjective refraction
- The scientific evidence showed that it was equally or more accurate to that of an eye doctor's manual reaction in 97% of the cases
- Drs. Christopher Lievens, Christina Newman, Alan Kabat, and a second year optometry student (Jacob Weber)
- The results revealed that there was no statistically significant difference between Vmax VASR and the manual phoropter refractions.

Study from SCO

- 14% of patients had better acuity with the VASR System (> 1 line Snellen compared to the phoropter refraction), 3% of subjects had worse acuity with VASR (>1 line Snellen worse refraction), and 83% had less than 1 line Snellen line difference compared to a faculty physicians traditional refraction.
- The student had only 2 hours of training compared to decades of training from SCO faculty
- The VASR autorefraction system utilizes wavefront aberrometry and the subjective refraction component utilizes proprietary point spread function (PSF) technology
- 20-30 seconds quicker with manual refraction***
- Submitted to IOVS for publication under Kabat A. et al

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Preferred by Patients

- A comparative study of 13 Keratoconus patients (26 eyes), refracting patients first with a standard phoropter, and then using a PSF (point spread function) Refractor
- 69% of patients achieved higher VA with the PSF Refractor
- 31% of patients achieved equal VA with the PSF Refractor
- 0% of patients achieved worse VA with the PSF Refractor

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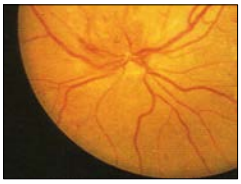
Current NAION study QRK207

A Phase 2/3, Randomized, Double-Masked, Sham-Controlled Trial of QPI-1007 Delivered By Single or Multi-Dose Intravitreal Injection(s) to Subjects With Acute Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)



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Purpose of the study

- Determine the effect of QPI-1007 on visual function in subjects with recent-onset NAION.
- Assess the safety and tolerability of intravitreal injections of QPI-1007 in this population.
- Evaluate the structural changes in the retina following administration of QPI-1007.

Study Design

- This is a double masked, randomized, sham-controlled efficacy and safety study that will enroll approximately 530 subjects with recent-onset NAION.
- Subjects will be randomized into one of 5 groups in a 1:1:1:1:1 ratio, and assigned to receive QPI-1007 and/or a sham procedure. Subjects will have a one in five (20%) chance of receiving sham procedure (no active treatment).
- 5 cohorts: single low dose injection, single high dose injection, multiple low dose injections, multiple high dose injections, and sham injection procedure.
- Total study time involvement is approximately 12 months.

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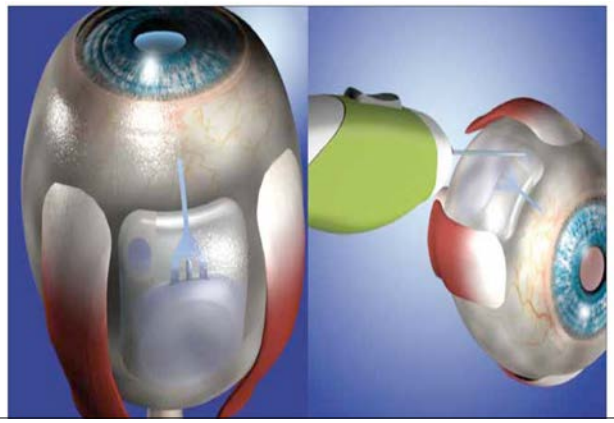
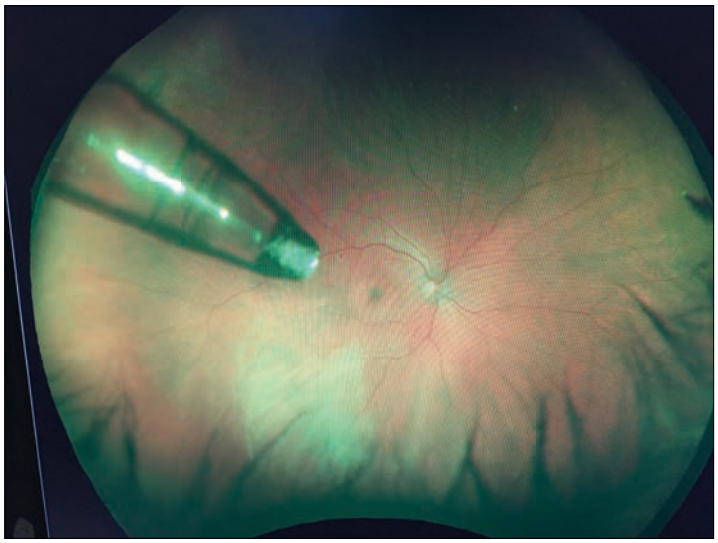
Key Inclusion Criteria

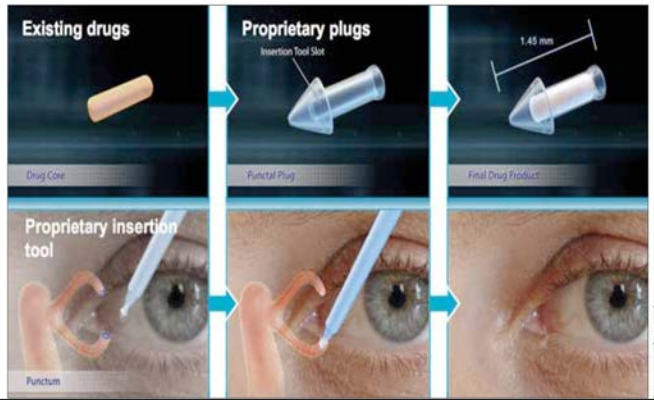
- Males and females 50-80 years old
- Positive diagnosis of first episode of NAION in the study eye with symptom onset within **14 days** prior to planned study drug administration/sham procedure
- Clear ocular media and able to undergo adequate pupil dilation to allow a good fundus examination

Drug Delivery Advances



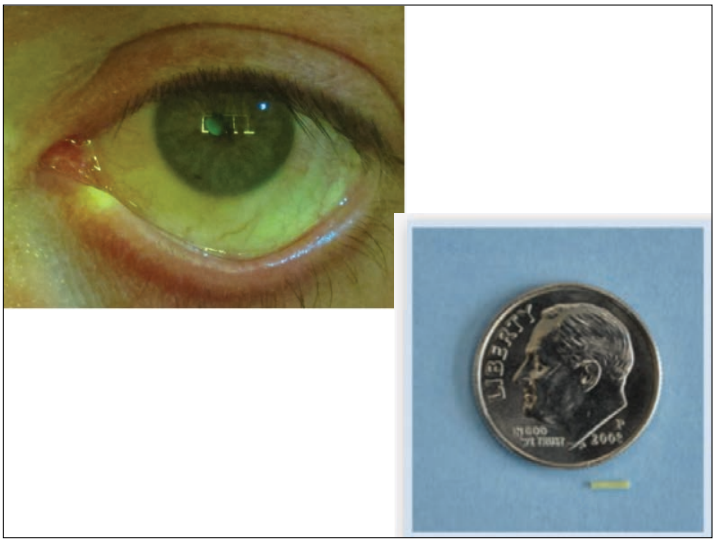


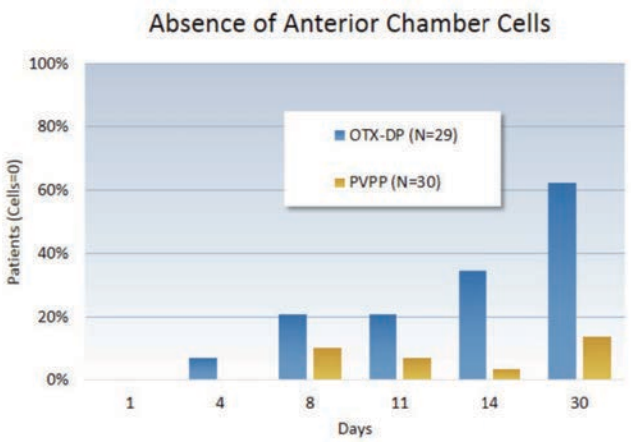
Drug Delivery Advances

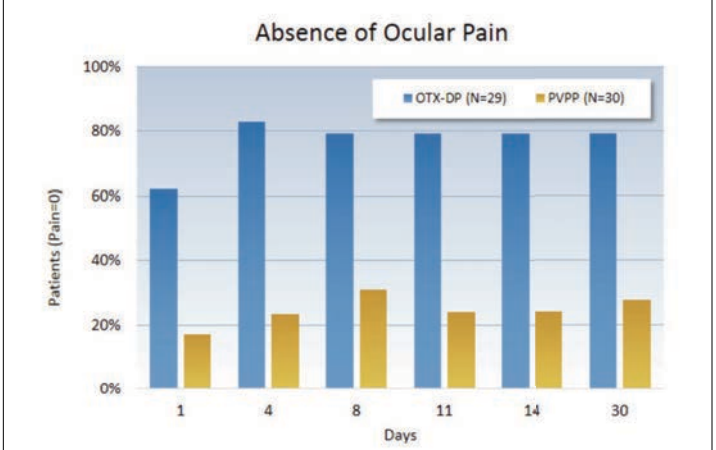


Ocular Therapeutix Drug Deliver

- Dextenza post cataract
- Dextenza for allergic conjunctivitis
- Sustained release Travoprost
- Dry eye therapy via a punctal plug







Punctal Plug Drug Deliver

- Newest technology
- 94% retention rates in clinical study
- Statistical improvement in inflammation and pain following cataract surgery with only an NSAID within the plug

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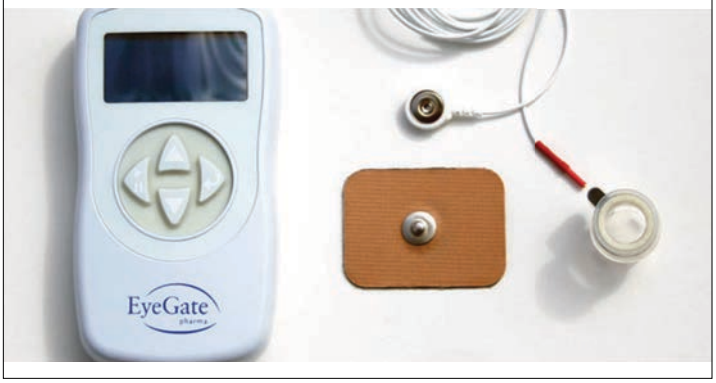
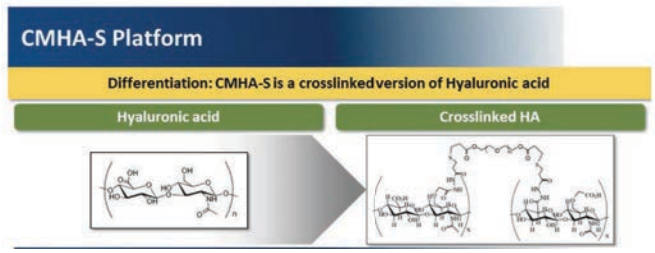
Iontophoresis



Ocular Bandage Lens



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Ocular Bandage Lens

- In a recent PRK clinical trial
- 45 subjects and 3 arms
- OBG vs. BCL vs. Control (AT's and ungs)

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Ocular Bandage Lens

Positive Clinical Trial Results

Completed First Human Clinical Trial in PRK Patients

Re-epithelialization Wound Healing Study*: OBG vs. Standard of Care (Bandage Contact Lens + Artificial Tears)

- ✓ Approximately 55% more patients treated with OBG healed by Day 3
- ✓ As early as Day 1 (24 hr. post-op) average wound size was around 36% smaller and 83.3% smaller by Day 3 with OBG alone

	Number of Subjects Per Arm	Healed Wound on Day 3		Day 1		Day 3	
		Number	Percent	Horizontal*	Vertical*	Horizontal	Vertical
Arm 1 Ocular Bandage Gel	12	10	83.3%	4.1	4.5	0.1	0.2
Arm 2 Ocular Bandage Gel + Bandage Contact Lens	14	9	64.3%	5.3	6.5	0.3	0.3
Arm 3 (Standard of Care) Bandage Contact Lens + Artificial Tears	13	7	53.8%	5.4	6.2	0.6	0.6
Ocular Bandage Gel: % Better than Bandage Contact Lens		54.8%	35.9%	27.4%	83.3%	66.7%	

*Length in mm

SIMPLE DROPS

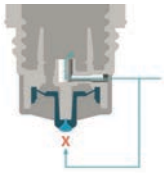
- Offers a preservative-free treatment regimen for your patients
- Provides convenience of multiple medications into one combination drop
- May increase patient compliance by reducing the number of drops taken per day
- May reduce costs to your patients with a low monthly cost

GLAUCOMA FORMULATIONS

PRESERVATIVE-FREE DROPS

All Simple Drops compounded formulations are made preservative-free.

- Products with preservatives may cause adverse reactions such as superficial punctate keratitis, corneal erosion, and conjunctival allergy[4,5]
- Discomfort associated with adverse symptoms can lead to decreased compliance and/or discontinuation of treatment[5]
- Reducing the exposure to preservatives involves reducing the number of drops and/or removing the preservatives completely



4. Inoue, K. Managing adverse effects of glaucoma medications. Clinical Ophthalmology 2014; 8: 903-913.
5. Bagnis, A, Papadia, M, Scotto, R, Traverso, C. Antiglaucoma drugs: The role of preservative-free formulations. Saud of Ophthalmology 2011; 25(4): 389-394.

SIMPLE DROPS COMPOUNDED FORMULATIONS

Topical Offerings	Size
Latanoprost 0.005% PF	7.5mL
Dorzolamide 2% PF	10mL
Dorzolamide 2%/Timolol 0.5%	10mLmL
Timolol 0.5%/Latanoprost 0.005% PF	5mL
Brimonidine 0.15%/Dorzolamide 2% PF	10mL
Timolol 0.5%/Dorzolamide 2%/Latanoprost 0.005% PF	5mL
Timolol 0.5%/Brimonidine 0.15%/Dorzolamide 2% PF	10mL
Timolol 0.5%/Brimonidine 0.15%/Dorzolamide 2%/ Latanoprost 0.005% PF	5mL

MEDICATIONS FOR GLAUCOMA

- **Duo Glaucoma Drop**
  - Latanoprost and timolol
- **Triple Glaucoma Drop**
  - Timolol, bromonidine and dorzolamide
- **Quad Glaucoma Drop**
  - Brimonidine, dorzolamide, latanoprost and timolol

DRY EYE FORMULATIONS

NEW TOTAL TEARS OFFERINGS FOR DRY EYE

Topical Offerings	Size
Klarity-C (Chondroitin sulfate/cyclosporine 0.1% ophthalmic emulsion PF)	5.5mL bottles
Klarity (Chondroitin sulfate ophthalmic solution PF)	10mL bottles

BENEFITS OF CHONDROITIN SULFATE

- Enhances patient comfort associated with surgical trauma, contacts, and dry eye
- Provides as a lubricant to the ocular surface[1]
- Contains Chondroitin Sulfate, known to preserve the cornea
- Shown to have anti-inflammatory effects[1,2]

1. Moon W A, Lee H, Shin K C, et al. Short term effects of topical cyclosporine and viscoelastic on the ocular surfaces in patients with dry eye. Korean Journal of Ophthalmology 2007; 21(4):pgs189-194.
2. Llamas-Moreno J F, Baiza-Duran L M, Saucedo-Rodriguez L R, et al. Efficacy and safety of chondroitin sulfate/xanthan gum versus polyethylene glycol/ propylene glycol/hydroxypropyl guar in patients with dry eye. Clinical Ophthalmology 2013; 7:pgs995-999.

Allergic Conjunctivitis

ZERVIATE

- FDA approval of ZERVIATE (cetirizine ophthalmic solution) 0.24%
- First topical ocular formulation of the antihistamine cetirizine

RTH258 (Injection)

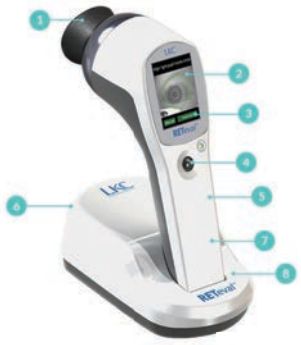
- RTH258 for wet AMD meets endpoints in phase 3 trials
- A single-chain antibody fragment VEGF inhibitor
- Showed long-lasting efficacy dosed every 8 weeks compared with aflibercept
- A majority of the patients were maintained in a 12-week interval through week 48 after the loading phase

Apple-like companies

Hand-held Portable non-mydriatic Full-Field ERG + VEP

1. Soft eye cup for patient comfort
2. IR camera to view eye during testing
3. Immediate test results right on the device
4. Simple joystick control
5. Ergonomic to fit comfortably in hand
6. Small charging base
7. Lithium Ion battery for up to 8 hours* of use
8. Docking station offers USB connectivity

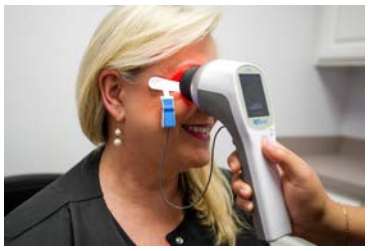
*Approximately 70 patients before recharging, depending on protocol used.



Hand-Held, Full-Field ERG

Quick Facts
- The first, and only FDA cleared, hand-held, mobile, non-mydriatic Full-Field ERG device
- Affordable ERG testing in the palm of your hand
- Easily integrates into your current practice flow
- No dedicated test room or additional staff required

OF RETEVAL IN USE



Hand-Held, Full-Field ERG

Quick Facts
- Complementary to other tests of *function* like visual fields and *cone-isolation contrast sensitivity (ColorDx)*
- Largely unaffected by cataracts
- May be useful for following progression of disease (e.g. diabetes)
- Normative database for easy, color coded interpretation of most protocols

Pupillometry

Pupillographer

Quick Facts

- Objective, quick, portable pupillary light reflex testing (PLR/RAPD)
- Modern, accurate alternative to the century old swinging flashlight test
- Confidently examine your dilated patient knowing a possible RAPD has not been missed

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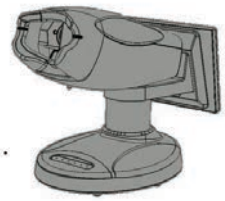
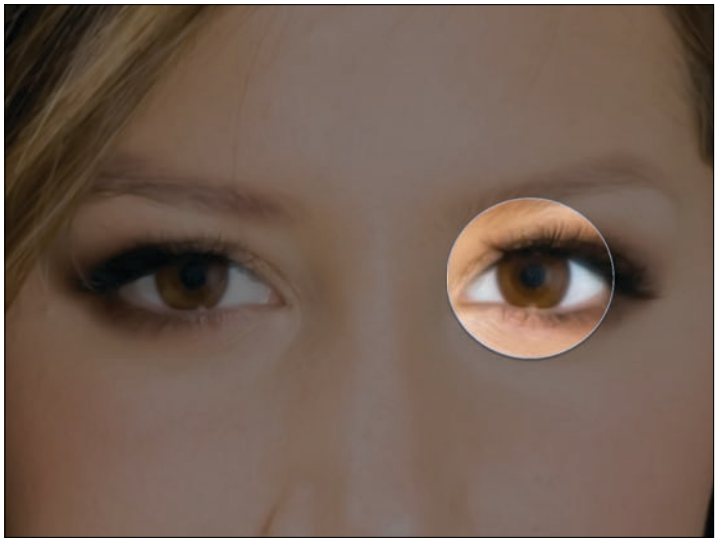
Pupil diagnostics have just been transformed from the dark ages to the 21st Century

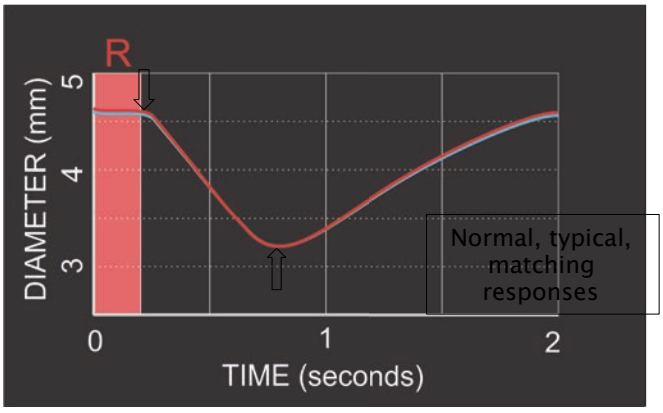


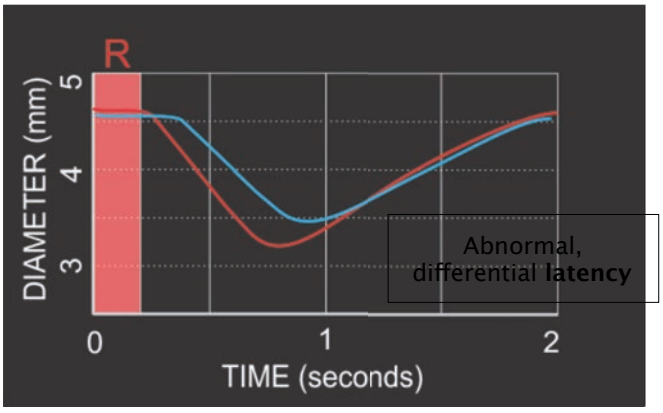


Test: Full Field Stimuli

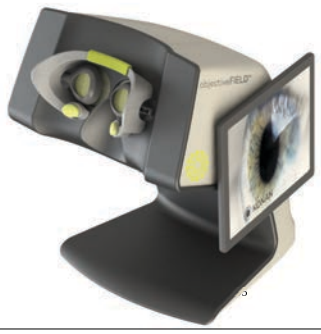
Analog of
Swinging Flashlight

Expanded Stimuli





Objective Visual Field Testing

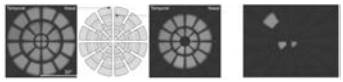


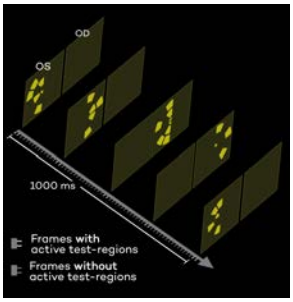
Testing multiple clusters at once!

Statistically independent clusters of visual stimuli are presented concurrently and bilaterally at multiple locations in the subject's visual field.

The resulting set of pupillary responses evoked by each of the visual stimuli provides a map of visual field function across the visual field of one or both eyes.

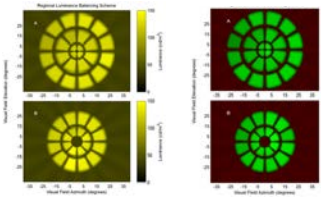
The appearance or non-appearance of stimuli, and their intensity, color and spatial frequency are controlled by statistically independent sequences.



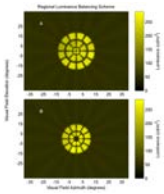


Three Stimulus Methods

- Normative database for each protocol from 179 persons, each tested twice



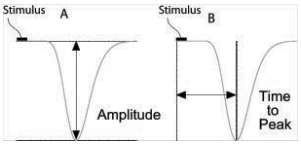
wide field
Glaucoma, Neurological



Macular
AMD, Diabetes

Data obtained

- Pupil responses, down = contraction
- Pupil constriction amplitude = sensitivity; also get response delay (time to peak)

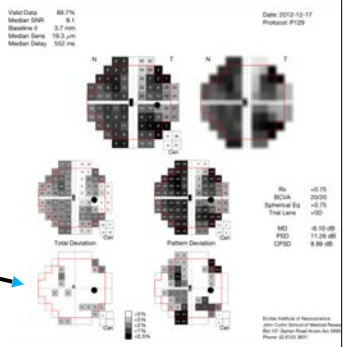


- These two measures are relatively independent and combining them into a composite report can improve the capacity to detect functional abnormalities.
- Analysis are tolerant of up to 15% loss of data due to blinks or loss of fixation.

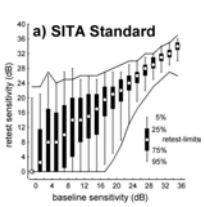
- so 176 sensitivities and 176 delays, and SE for each

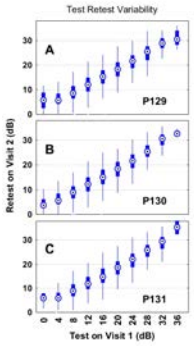
30-2+ Report

- Emulates SAP report
- True 30-2 pattern
- Plus 4 extra central regions
- Red border shows 24-2 pattern



Test-retest variability



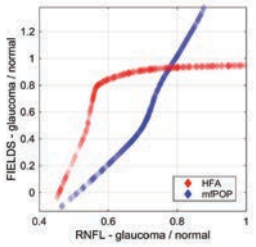


OFA test-retest data:

40 glaucoma patients and 175 controls
Each was tested twice about 2 weeks apart with the three different 6-minutes tests currently on the OFA.

Correlation with RNFL Loss

- The nonlinear relationship between HFA and early RNFL damage is well known[1].
- Abstract Submission WGC 2019
  Structural and Functional testing
  WGCSUB-1214
  Sensitivities of cortically mediated objective perimetry correspond linearly with RNFL loss
  - 25 glaucoma patients and 27 stroke patients
  - Conclusions: The mfPOP method reported cortical losses similar to HFA and Matrix. Taken together the results indicate that cortically mediated mfPOP sensitivities reflect a more linear relationship with RNFL loss.

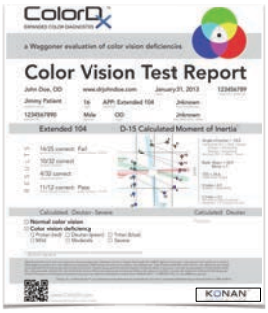


1. IOVS 2007 48: 3662-68

Advanced Color Testing

- Uses cone isolation contrast testing
- Individual Landolt C's that stimulate the 3 cone receptors
- Extremely accurate
- Ideal for early pathology detection such as glaucoma

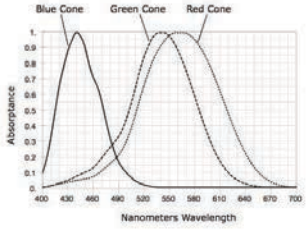
ColorDx™
EXPANDED COLOR VISION DIAGNOSTICS

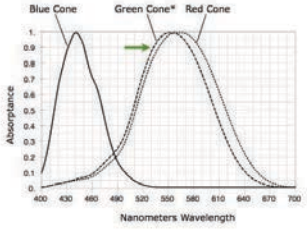


Color Deficiency

- Affects 1 in 200 females
- Affects 1 in 8 males
- 30 Million Americans have some level of color deficiency
- Deuteranopia being most common
- Protanopia occurs more often with acquired disease
- Ishihara misses 100% of protanopia

Color Deficiency

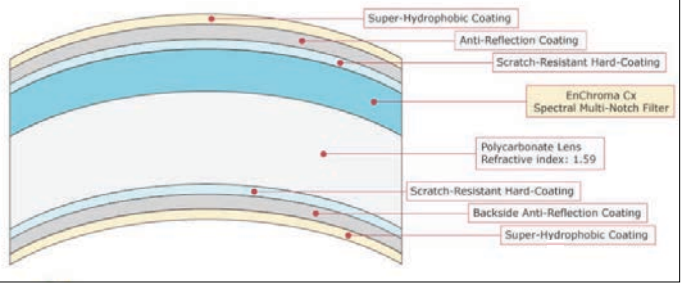


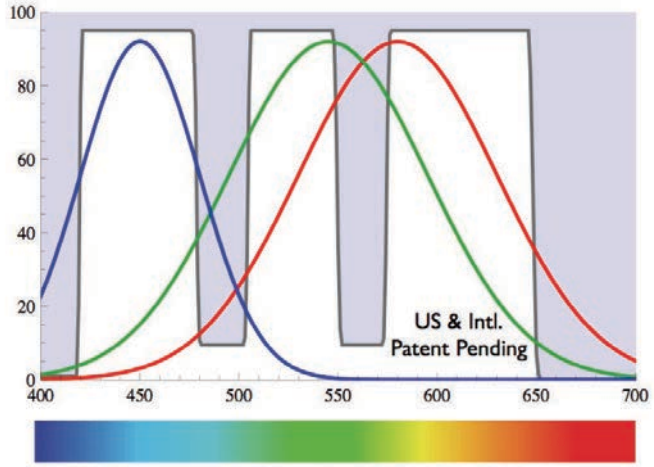


Artificial Intelligence for Color Enhancement

- Clear lenses
- AI helps ensure 'actual' color potential
- Indoor and outdoor lens

Wavelength Blocking Lenses





Wavelength Blocking Lenses

THANK YOU!

Karpecki@Karpecki.com