Contact Lens Technology: Suspended contact lens

➢ Recent advances in material, engineering knowledge, and manufacturing techniques allow for suspension of soft lenses
➢ Uses the anatomy of the upper lid as inspiration for a unique design feature that allows for suspension
➢ This feature along with other characteristics of the design allow for translational eye movement behind a rotationally stable lens
➢ From co-inventor Dr. Joe Barr: “The lens is designed to work like a translating gas permeable lens”
➢ A patented idea: 2 patents granted and 3 pending
  ➢ Granted: USPTO #10,598,957
  ➢ Granted: USPTO #10,191,302

Lid Stabilized Lens Design

• Lid attached
• Rotationally stable
• 3+ mm of translation
• Comfortable lens design with multiple successful hours of wear

The MOA allows for Translational eye movement behind a rotationally stable lens

New lens standard parameters

➢ Distance Power
  • -12.00 to +6.00
➢ Add Power
  • Full range of add powers (+0.75 to +2.50)
➢ Astigmatism/Cylinder Powers
  • -0.25 to -2.50 DC
  • Axis 1 to 180°
➢ Easy to Fit
  • 2 base curve radii fit 98% of subjects in clinical trials (n=166)
  • No seg-height adjustment

Innovations in EyeCare

Paul M. Karpecki, OD, FAAO

Medical Director, KEPLR Vision
Kentucky Eye Institute, Lexington KY
UPike KY College of Optometry
Chief Clinical Editor, Review of Optometry

Financial Disclosures:

- AI Optics
- Aerie Pharmaceuticals
- Akorn
- Akon Labs
- Aledea
- Allergan/Abbvie
- Allysya Pharmaceuticals
- Alcon Labs
- Alcon Labs
- Aldeyra
- Akorn
- Iomea
- Johnson & Johnson Vision
- Kala Pharmaceuticals
- KEPLR Vision
- Konan Medical
- Lactisceinces
- LenTech
- Lombard/Marco
- Maculogix
- Mallinckrodt
- Miretch
- Neurolabs
- Nivaliq
- Novartis
- Oasis Medical
- Oculis
- OcuMedic
- Ocuphile
- Omega Ophthalmics
- Orasis
- Osmotica
- Oyster Point
- Quark Pharmaceuticals
- RegenerEyes
- Reicher
- Rendia
- RxSight
- Science Based Health
- Sensis Pharma
- Sight Sciences
- Silk Technologies
- Sun Pharmaceuticals
- Surface Biopharma
- Tarsus Medical
- TearClear
- TearLab
- TecLens
- Visant Medical
- Visionix
- Vital Tears
Diurnal IOP measurements

Corneal Hysteresis
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 adjustments are invalid

SCATTER in the data makes accurate mathematical “adjustment” of IOP impossible for individuals!

Corneal Hysteresis in Glaucoma

Predictive of Progression in Prospective, Longitudinal Study (Digs)

- Univariate model: each 1 mmHg decrease in CH was associated with a 0.25%/year increase in rate of VF decline (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.

Note – NO rapid progressors in CH ≥10 mmHg group!

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.
Corneal Hysteresis in Glaucoma

**Purpose:** To investigate the role of \( CH \) as a risk factor for development of glaucoma in a prospective longitudinal study.

**Results:** Fifty four (19\%) of the 287 eyes developed repeatable visual field defects during a 4 year follow-up.

\( CH \) was independently predictive of conversion to glaucoma even when adjusted for age, IOP, and CCT.

Each 1mmHg lower CH was associated with an increase of 21\% in the risk of developing glaucoma during follow up.

**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.

**Self-Monitoring Makes a Difference**

![Graph showing relative risk of disease progression vs. diurnal IOP range](image)

**What’s the first piece of equipment I need to purchase to create a dry eye clinic?**

**Slit Lamp Imaging System**

---

Blepharoexfoliation

Bacterial Biofilm in Lash Follicles

Kentucky Eye Institute

Blepharitis is a Large Unserved Market in Ophthalmology
Demodex is an Underlying Cause of Blepharitis and MGD

2 Species of Mites Contribute to Blepharitis
- Demodex folliculorum: eyelash follicles
- Demodex brevis: meibomian glands in eyelids

Demodex implicated in 45% of Blepharitis Cases
- Meta-analyses of 11 studies and 4,741 pts

Easily and Rapidly Diagnosed at Slit Lamp
- Cytotopic dandruff, or "oil spots" are pathognomonic for Demodex

---

Importance of Eyelid Debridement in MGD/EDED

---

TP-03 is a Novel Drug to Treat Demodex Blepharitis by Eradicating Mites and Collarettes

- **Product Form**: Multi-dose eye drop solution bottle, preserved
- **Indication for Use**: Treatment of Demodex Blepharitis
- **MOA**: Paralysis and death of Demodex mites
- **Diagnosis**: Collarettes on slit lamp examination
- **Dosing**: BID for 8 weeks
- **Efficacy**: Collarette cure, mite eradication, other secondary endpoints
- **Safety**: Very clean to date (mild transient stinging in < 10% of patients)

---

Mercury Study: TP-03 Works by Killing Mites

Ex vivo mites extracted from the lashes of blepharitis patients:

Cure of Collarettes with BID use of TP-03

Baseline Day 28

---

Jupiter Phase 2b Study: High Collarette Cure Rate and Mite Eradication Rate

FDA-requested primary and secondary endpoints

Collarette Cure Rate

<table>
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<tr>
<th></th>
<th>Day 14</th>
<th>Day 21</th>
<th>Day 28</th>
<th>Day 40</th>
<th>Day 50</th>
<th>Day 60</th>
<th>Day 90</th>
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<tr>
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Mite Eradication Rate

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Importance of Eyelid Debridement in MGD/EDED
First Keratolytic drug

• About to begin phase III trials
• Apply two times per week to lower eyelids
• Maintains effects of debridement or could replace debridement
• Critical to MGD & EDED

What are keratolytics?
Agents that soften and shed the skin epithelium or horny outer layer of skin through the process of breaking down keratin

AZR-MD-001 (selenium sulfide)
Triple MOA for the treatment of MGD
A potent keratolytic, with a unique MoA compared to traditional keratolytic agents, such as urea, AHA and BHA

Keratostatic
Slows down both the rate of keratinocyte proliferation and keratin production!

Keratolytic
Softens keratin plug by breaking down disulfide bonds, alleviating hyperkeratinization that leads to blockage of Meibomian glands1

Lipogenesis
Stimulates lipogenesis to increase the quantity of lipids produced by the Meibomian glands2

AZR-MD-001 TRIPLE MOA
Decrease meibomian gland hyperkeratinization of ducts and orifices, loosen meibomian gland blockages, and increase secretion of meibomian gland lipids

LIPOGENESIS
AZR-MD-001 INDUCES LIPOGENESIS AND THUS INCREASES LIPID PRODUCTION IN OIL SECRETING GLANDS

Lipid production was significantly increased by 282% with 0.01 μM SeS2 and by 348% with 0.1 μM SeS2 (P < 0.05) in a biological model to evaluate the lipogenic effect of selenium sulfide

Effect of SeS2 on lipid production
2-h incubation in 3D Human Sebocytes

* Arrows point to lipid staining
IPL and LLLT

- Intense Pulsed Light Therapy/Low Level 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

TREATMENT: Demodex

IT CONSISTS OF A PHASE 1 (WITH A SPECIFIC BLUE LIGHT MASK) AND A PHASE 2 (WITH THE STANDARD SUPPLIED RED LIGHT MASK)

PHASE 1 - BLUE MASK
Blue light stimulates porphyrins and creates an anti-bacterial action.

PHASE 2 - RED MASK
Red light stimulates ATP by increasing and improving cellular activity, it reduces inflammation and oedema and works on Meibomian glands.

IPL and LLLT

- Telangiectatic vessels and skin erythema release inflammatory mediators
- IPL targets the abnormal erythematous blood vessels
- Affects mitochondrial activity
- Temperature effect on glands?
- Photomodulation affecting cytochrome C or activating fibroblasts and collagen synthesis
What if you could keep preservatives in the bottle and off the eye?

Drug BAK Perception: BAK plays a role in IOP reduction

Based on clinical data from nine published studies - Timolol, Dorzolamide/Timolol, Bimatoprost/Timolol, Tafluprost, Travaprost, Latanoprost and Bimatoprost

Efficacy of preservative free product equals the efficacy of BAK-containing products

Is BAK required for IOP Reduction? - NO

Perception: BAK plays a role in IOP reduction

Based on clinical data from nine published studies - Timolol, Dorzolamide/Timolol, Bimatoprost/Timolol, Tafluprost, Travaprost, Latanoprost and Bimatoprost

Efficacy of preservative free product equals the efficacy of BAK-containing products

TearClear Glaucoma Drugs:
On target delivery of intended dose through 30-day use (Monotherapy and Combination Drugs)

TC002: Meets Label claim; BAK Not detected

TC003: Meets Label claim; BAK Not detected

TC004: Meets Label claim; BAK Not detected

TC005: Meets Label claim; BAK Not detected

TearClear Timolol OUS Pilot Study

Figure 1. Mean trough intraocular pressure (IOP) at each assessment day

Mean values of 6 Bottles

Customized Materials for Important Indications

Pipeline

• Glaucoma
  • Beta blockers, prostaglandins, carbonic anhydrase inhibitors, alpha agonists
• Dry Eye
• Allergic Conjunctivitis
• Presbyopia/Myopia
• Post-Op

Respondents Preferred the 8 uL eyedropper When Asked About Ease of Use, Drug Volume, and User Experience

Adults with presbyopia were asked what medication method they would prefer. Over three quarters of respondents (76%) ranked the it over the traditional eyedropper. 17 respondents gave it a perfect score of 50. In total, over a third (35%) of respondents scored the dispenser a 40 or higher on the -50 to 50 scale.
CRANIAL NERVE STIMULATION
TARGETING NUMEROUS DISEASE CONDITIONS

TRIGEMINAL NERVE (CN V)
BRANCHES AND FUNCTION

1st Neurostimulations Technology

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

DISCONTINUED

TAKEAWAYS FROM TRIALS

• Array of positive endpoints reflects broad mechanism of action of neuromodulation
• Effective for aqueous tear deficiency and meibomian gland disease
• Acute, sub acute, and chronic benefits to the ocular surface
• Outstanding safety profile
• High value product for dry eye
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.

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.
- Efferent parasympathetic nerves innervate the lacrimal functional unit (LFU) including cornea, conjunctiva, accessory lacrimal glands, meibomian glands, and goblet cells.
- Intervention @ the trigeminal-parasympathetic pathway represents a novel approach to producing complete tear film in patients with Dry Eye Disease (DED)

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

OC-02 Before Administration

OC-02 15 Seconds After Administration

Tear Meniscus Height

Mean Change in Schirmer's Score

Placebo: 0.20%
Change: 2.00%
N=42

OC-02: 0.20%
Change: 17.12%
N=41

p=0.002

Mean Change in Eye Dryness Score

Placebo: 0.20%
Change: 2.6
N=41

OC-02: 0.20%
Change: 19.29%
N=41

p<0.001

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

- 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.

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Trigeminal Dysphoria: 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

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: Contoured Prism

- 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

Patient-reported symptom reduction with neuroLenses:

- 60% Basically gone
- 19% Decreased substantially
- 14% Decreased slightly
- 7% No change
- 1% Increased

n = 279

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

n = 89
Punctal Occlusion

- May wait on punctal occlusion if have:
  - Allergies
  - Severe MGD
  - Significant blepharitis
  - Inflammatory dry eye?
- Treat those conditions first then plug
- Ideal FIRST treatment option for:
  - Neurotrophic keratopathy
  - Post-LASIK dry eye
  - Lagophthalmos
Drug Delivery Advances

Punctal Plug Drug Deliver

- Post cataract
- Allergic conjunctivitis
- Glaucoma Sustained release Travoprost
- Dry eye therapy

Phase III Punctal Plug Drug Deliver

- Evolute
- 94% retention rates in clinical study
- Statistical improvement in inflammation and pain following cataract surgery with only an NSAID within the plug
Collagen Cross Linking (CXL)

- 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

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
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

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 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 CXL 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

Drug Therapy for keratoconus

- IVMED-80
- Phase IIb trials were positive with >1.8D improvement
- Entering phase III clinical studies
- MOA: Upregulates lysyl oxidase (LOX) and induces corneal crosslinking pharmacologically
Presbyopia Correction

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

Topical Treatment for Presbyopia

- Pupil Modulating Therapies
  - Contains miotics but also proprietary components that allow full 12-14 hours of near and far vision
- Lens Softening
  - 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

How Is Accommodation Lost?

Why Does Presbyopia Happen?

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

Note: Preliminary analysis based on LOCF in study eye only
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

![Chemical structures](image)

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 DCNVA](image)

Ev06 DCNVA Snellen score - Day 1 & Day 91

- Improved shift in Snellen Scores
**Cataract Surgery Outcomes**

**Challenge to consistently achieve great results**
- 2016 toric meta-analysis: ~65% of eyes achieve 20/25 or better
- Limited by ability to predict the post-operative eye

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* Monthly, S. Sources of error in intraocular lens power calculation. *JSEI* 2009: 365-76

**Future presbyopia drops: miotics**

- Orasis Pupil Modulation Eye Drop Solution
  - Demonstrated efficacy, safety, and comfort in Phase 2b Studies
  - Empowering patients with unparalleled comfort and control of their near vision
  - Exceptional near visual acuity
  - No reduction of distance vision
  - High safety and tolerability profile
  - Improved comfort

**Phase 2b Study Design**

- Parallel-group study (active, vehicle)
- Primary endpoint: 3-line improvement in near visual acuity
- Secondary endpoints: 2-line improvement (near), impact on distance and night vision, various safety and tolerability endpoints

**Phase 2b demonstrated Efficacy, Safety & Comfort**

- Proportion of subjects achieving a 3-line improvement vs. baseline (*)
- Proportion of subjects achieving a 2-line improvement vs. baseline (*)

**Post-Op is the New Pre-Op!**

The RxLAL is the world’s first adjustable intraocular lens that allows office-based optimization of vision after lens implantation and healing

- Delivers world’s best clinical outcomes for cataract patients
- Overcomes limitations of both pre-operative and intra-operative prediction processes
- Premium channel driver
- Private pay
A Better Way to Deliver Premium Cataract Surgery

How It Works

The RxSight LDD consists of the following components:
- Anterior segment biomicroscope
- Patient Chin and headrest
- Computer system for planning and performing light treatments
- Ultraviolet (UV) light projection system

Light Delivery Device (LDD)

OPTIC BODY
- Photo-reactive UV absorbing Silicone
- Biconvex
- Anterior surface – rounded edge
- Posterior surface – squared edge
- 6mm diameter

HAPTICS
- Blue core polymethylmethacrylate (PMMA) Monofilament
- Modified ‘C’
- Haptic angle – 10°
- 13mm - RxLAL Total Diameter

At the end of surgery RxLAL Patients are provided with UV Protective glasses to help protect the RxLAL from sources of UV light

- The patient may discontinue wear of the UV protective glasses 24 hours after the final light treatment has been completed
- Exposure to UV light, such as sunlight, can cause uncontrolled changes to the RxLAL

UV Protective Glasses

Pre-Operative Prediction Post-Operative Adjustment

Standard Cataract Implant Procedure
- Low Stress Cataract Surgery
  - Not dependent on prediction of SIA, ELP, Individual Healing, Surgical Technique, Sophisticated Equipment
- Interactive Post-Op Process
  - Refraction optimized with patient after healing is complete and ocular media clear
- Office Based Refractive Treatment on IOL
  - Unparalleled flexibility and accuracy
  - Bifurcated cataract and refractive procedure

Residual Refractive Error is Determined Using Standard Phoropter

Interactive Post-Op Process
- Refraction optimized with patient after healing is complete and ocular media clear
- Office Based Refractive Treatment on IOL
  - Unparalleled flexibility and accuracy
  - Bifurcated cataract and refractive procedure

Refractive Error is Entered into Light Delivery Device

Office Based Refractive Treatment on IOL
- Unparalleled flexibility and accuracy
- Bifurcated cataract and refractive procedure

RxLAL

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- Exposure to UV light, such as sunlight, can cause uncontrolled changes to the RxLAL
**US FDA Study Results**

- RxLAL eyes achieved UCVA of **20/20 or better** at 6 months postoperatively at approximately **2x the rate** of patients receiving a monofocal lens.

- **91.8%** of RxLAL eyes achieved result within **0.50 D** of target MRSE (similar to LASIK results).

- **Superior Quality of Vision** at all measures compared to control lens:
  - Including BCVA, Vision Rating, Driving Difficulty, Dim Light Conditions, Glare, Halos, and all measures of Contrast Sensitivity.

**THE BENEFITS OF THE 3D CAPSULE**

- Unique 3D design allows:
  - No fibrosis around the lens position.
  - Gemini capsule fills the 3D space of a natural lens.
  - No issues with position of the lens, the x, y, and most importantly the z axis. (the most common source of error).
  - Capsule volume stays intact, allowing for future lens implantations.
  - Gemini offers valuable ‘real estate’ for drug delivery and bio sensors.
  - Maximizes the large size of the implant (200 cubic mms) without compromising the small size of the 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

- 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*


### iStent

- iStent® is 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
- 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
Current MIGS Mechanisms to Enhance Conventional Outflow

From Tissue Disruption to Canal Restoration

The Hydrus Microstent

- 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

HORIZON Clinical Trial

4-Year Results

HORIZON 3 – 5 Year Follow up

- HORIZON is unique: only MIGS study with 5 year continuous follow-up
- 83% follow-up at 4 years
- Primary endpoint assessment was based on washed out IOP... wash out was discontinued after 24 months for practical reasons
- Long term effectiveness based on:
  - Medication free
  - Failure rates (progression to surgery)
  - Safety findings (vision, ECD, and adverse events)

Medication Free

Durable effect through 4 Years

% Patients Remaining Medication Free After Preop Wash Out

Key Finding: Reduced Risk of Reoperation

Incisional Glaucoma Surgery:
- Trabeculectomy,
- Tube shunt,
- Cilioablative procedure

More than half of these patients were mild at baseline (VF MD -4 DB or better)
**Corneal Endothelial Cell Counts**

<table>
<thead>
<tr>
<th>Year to Year Mean Central ECL</th>
<th>Count – cells/mm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop-3M 3-12M</td>
<td></td>
</tr>
<tr>
<td>1-24M</td>
<td></td>
</tr>
<tr>
<td>24-36M</td>
<td></td>
</tr>
<tr>
<td>36-48M</td>
<td></td>
</tr>
<tr>
<td>48-60M</td>
<td></td>
</tr>
</tbody>
</table>

-1000 to -750 cells/mm²

-11% vs. 13% ECL post op vs. baseline (75 cells/mm²)

Error bars are 95% Confidence Intervals

<1% difference between groups from years 1 through 5

Rhee DJ. 4 Year Findings from the HORIZON Trial AGS 2020, Washington DC

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**ICP changes with age**

ICP goes down at age 65

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**Solution?**

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**Intraocular Pressure (mmHg) Reduction With Goggles Compared to Contralateral Control Eye**

(Consistent Cohort, n=51)

Baseline No Goggles: 16.36
50% Pressure Reduction in Goggles: 15.02

---

**Bimatoprost SR**

- A biodegradable bimatoprost sustained-release implant (Bimatoprost SR) addresses the problem of nonadherence in glaucoma.
- The implant is placed intracamerally and was designed to deliver a slow release of bimatoprost for IOP lowering over a period of 4–6 months.
- Bimatoprost SR is administered using a prefilled, single-use applicator system.

![Bimatoprost SR](image)

**Diurnal IOP after single Bimatoprost SR treatment**

![Graph showing IOP changes over time](image)

---

**Other options for Augmented Reality**

- Surgical Systems
- AMD

![Augmented Reality](image)

**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)
- Eyedaptic effectively recovers the visual field!

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**How it Works:**

**Open Market AR Hardware + Proprietary Software**

- Image Capture
- Adaptive Systems
- Simulated Natural Vision

![How it Works Diagram](image)

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**Technology Validation**

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

![Technology Validation Graph](image)
A New Timed Instrumental Activities Of Daily Living (TIADL) Measure For Evaluation Of Rehabilitation Outcomes (V.L. Gills¹, M.Mackeben², D.C. Fletcher¹,²)

Clinical Trial: Validation of Features

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

Augmented reality VF

Virtual Reality Platform (VRP) that is cloud enabled to monitor the eye function
- Enhanced version for eyecare professionals
- Simplified model for Home

VRP

VRP has three main components:
- Cloud (Analytics, Storage, Insights)
- WebApp (For Eyecare Providers: Data Management, Reporting)
- Headset (For Patients: Testing, Education)

Validation Study

Scientific Validation

HFA

VRP
Scientific Validation

Correlation and Agreement with HFA

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

Why a Genetic Test for Keratoconus?

Don’t we already know the etiology?

Observable and actionable:
- Relies on patient memory
- May not be accurate or relevant

There is no one gene responsible for the development of keratoconus but there is a strong genetic component or link within each group.¹

Global Keratoconus Risk 2019

Millions of patients are at risk based on corneal curvature alone

309,000,000
Patients with >46D corneal curvature or >2D cylinder
90%
Live in Asia-Pacific Countries
60% in India and China

1,700,000
Between ages 15-30 yrs old

Identifying At Risk Patients

Patients with higher than normal risk for triggering or natural progression of disease

- Patients with >47D cc and/or >2D astigmatism
- Contact Lens and Ortho-K Candidates
- Refractive Surgery Candidates
- Family History of Keratoconus

Using Genetic Testing to Identify Patients at Risk

Extraction → Sequencing → Referencing and Variant Risk Scores → Patient Report

TGFBI Corneal Dystrophies

Histologic and clinical appearances

GCD1 GCD2 LCD1 RBCD TBCD

Anterior stroma Anterior stroma Anterior stroma Epithelial stromal Epithelial stromal

Mechanism of TGFBI Induced Corneal Dystrophy

Heterozygous TGFBI Gene Mutation
Damage To Cornea
Excessive Production Of TGFBIp Protein
Protein Deposits on Cornea

Exacerbation after LASIK is cited in the literature

In 2002, the first case report of exacerbation of GCD2 after LASIK was published in Cornea by E.K. Kim and colleagues.
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

In 2008, a team led by Min Joon published a case in Ophthalmology III.3 (2008):463-468

Genetic Capability Pipeline

Continuous addition of detection capabilities will make the genetic eye test.

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

CRISPR followed by injecting the correct code for Leber’s Optic Neuropathy

LHON
Medical Utility - The AMD Problem

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

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

Dark Adaptometry

Cholesterol accumulation leads to panmacular deposits (Blind and Blamed)
Peaks in these deposits eventually become clinically visible drusen
These extracellular cholesterol deposits affect photoreceptor health by impairing transport, promoting inflammation, and predisposing to CNV
Dark Adaptometry

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


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

- CPT Code 92284 for dark adaptation
- $60.03 average national reimbursement
- Monocular testing qualifies for full reimbursement without use of modifier codes
- Co-billable with OCT, imaging and/or visual field
- Multiple ICD-10 codes

A Breakthrough Study in Blue Light Lenses

- 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 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)

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)
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%;

Skin Carotenoids

- Measured in stratum corneum (0.1 mm) layer of the skin
  - α- and β-Carotenes,
  - Lycopene,
  - Lutein,
  - Zeaxanthin,
  - α-, β-Cryptoxanthin

*Arch Biochem Biophys. PMC 2014 Nov 15.
**Initial Study:** Correlation study of skin carotenoids and serum carotenoid levels; \( r = 0.84 \) (\( p < 0.0001 \))

Skin vs. Serum Carotenoids (\( n = 372 \))

- **Raman Intensity, Counts**
  - 0
  - 15000
  - 30000
  - 45000
  - 60000

- **Total Serum Carotenoids (mcg/ml)**
  - 0.0000
  - 1.0000
  - 2.0000
  - 3.0000
  - 4.0000

**y = 12703x + 5891.7**

**\( R^2 = 0.7111 \)**

---

**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.”
Preferential hyper acuity perimetry delivers accurate, highly sensitive, specific disease detection.

Artificial distortion progressively makes the elevation smaller.

When the distortion caused by CNV is larger than the Artificial Distortion, the patient will preferentially pick this spot of the pathological distortion.

More patients who used it maintained good vision:

<table>
<thead>
<tr>
<th></th>
<th>ITT</th>
<th>PP1</th>
<th>PP2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Care</td>
<td>N=18</td>
<td>N=40</td>
<td>N=32</td>
</tr>
<tr>
<td>N=40</td>
<td>87%</td>
<td>91%</td>
<td>94%</td>
</tr>
<tr>
<td>≥20/40</td>
<td>91%</td>
<td>20/40</td>
<td>94%</td>
</tr>
<tr>
<td>P=0.003</td>
<td>50% INCREASE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

94% of patients maintained 20/40 at time of CNV diagnosis. Absolute Visual Acuity at time of nAMD diagnosis is critical to Visual Acuity Outcomes at year 1.

Drug Delivery Advances:

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Indication</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVM-022</td>
<td>wAMD</td>
<td>Gene therapy</td>
</tr>
<tr>
<td>AKST4290</td>
<td>wAMD</td>
<td>Inhibit the negative biological chronikins that increase with age</td>
</tr>
<tr>
<td>AXT107</td>
<td>wAMD</td>
<td>A peptide derived from the non-collagenous domain of collagen IV, which inhibits VEGF and activates Tie2</td>
</tr>
<tr>
<td>GB-102</td>
<td>wAMD</td>
<td>Small molecule aimed at reducing intravitreal injections to 2x per year in patients with wet AMD currently managed with anti-VEGF.</td>
</tr>
<tr>
<td>GB-103</td>
<td>wAMD</td>
<td>Formulated to allow sunitinib over a longer duration that may enable once yearly dosing instead of twice yearly dosing.</td>
</tr>
<tr>
<td>Zimura</td>
<td>wAMD</td>
<td>Inhibit the complement protein C5 preventing inflammation formation</td>
</tr>
<tr>
<td>ONS-5010</td>
<td>wAMD</td>
<td>Anti-VEGF</td>
</tr>
<tr>
<td>RGX-314</td>
<td>wAMD</td>
<td>One-time subretinal treatment for wAMD that includes the NAV AAV8 vector containing a gene encoding for a monosantional antibody fragment. The expressed protein is designed to neutralize VEGF activity.</td>
</tr>
<tr>
<td>MicroPump</td>
<td>wAMD, chronic DME or glaucoma</td>
<td>Small, refillable via injection, implantable ocular drug pump. The pump can be programmed to dispense precise nanoliter-sized doses or medication</td>
</tr>
<tr>
<td>AR-13503</td>
<td>wAMD, DME</td>
<td>Prokinease inhibitor implant</td>
</tr>
</tbody>
</table>
Elamipretide | DAMD | A peptide compound that penetrates cell membranes, and targets the inner mitochondrial membrane where it binds reversibly to cardiolipin thus normalizing mitochondrial structure and function

Diabetic retinopathy | Using stem cell components to harness the patient’s immune system to drive the resolution of the inflammatory process and initiates tissue remodeling leading to the stabilization and recovery of retinal neurovascular tissue

Risuteganib | OME | Integrin peptide

AXT107 | OME | A peptide derived from the non-collagenous domain of collagen IV, which inhibits VEGF and activates Tie2

OCS-01 | OME | Dexamethasone cyclodextrin nanoparticle drops, Glucocorticoid receptor agonists; Immunosuppressants

THR-149 | OME | PKal Inhibitor

DNS-010 | OME & BRVO | Anti-VEGF

THR-687 | OH | Pan-HGID integrin antagonist

THR-317 | OH, OME, MacTel | anti-PIGF

Complement 3 & 5 Directed Pharmaceuticals

- New drug in phase III FDA trials for geographic atrophy
- Moderate to early stage disease showing the potential for reversal

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

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

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

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

What is it…

- EyeKinetics is an objective machine vision alternative to the SFM for assessing APDs
- Objectively assess pupils in less than 1 minute; an order of magnitude more detailed than the finest human observer
- It includes a scotopic / photopic pupil measurement + PD
- Fast color vision screener in the works

Pupil reflex / SFM facts

- The only reasonably accurate method of quantifying an APD requires neutral density filters (0.3, 0.6, 0.9, 1.2, 1.8)
- 0.3 is when we become suspect
- Glaucoma (asymmetric) is the most common cause of APDs
- At least 50% of open angle glaucoma is normal tension
- Most clinicians would agree that an APD of 0.6 or less would be extremely difficult if not impossible to see without magnification (MA-SFM)
- In one paper, only 2 healthy controls had an APD >0.3
- IMO the most important misconception is that clinically significant APDs are big enough to be seen with the SFM

Test: Full Field Stimuli

Analog of Swinging Flashlight

Expanded Stimuli
Key Clinical Papers

- There is evidence that very subtle APDs (above 0.3) are present in the vast majority of glaucoma subjects.
- Studies have shown that automated objective pupillography identified more than twice as many RAPDs than the SFM.
- Clinically detected asymmetry in disc damage was missed 49% of the time with the SFM compared to 21% with automated objective pupillography.
- When using automated objective pupillography, the pupillary light reflex is strongly correlated with VF functional testing and measurements of RNFL thickness.


Objective VF Analyser

Three Stimulus Methods

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

Data obtained

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

- 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

Binocular Report

Asymmetry Report

Asymmetry Report

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
Artificial Intelligence for Color Enhancement

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

THANK YOU!

Karpecki@Karpecki.com