What's the Latest in Presbyopia?

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Today's Agenda

- Discuss presbyopia market and need
- Discuss current options
  - Glasses
  - Contact lenses
  - Laser vision correction
  - Refractive lens exchange
  - Refractive cataract surgery
- Discussion future innovations in presbyopia
  - Topical drop therapy
  - Future refractive surgical options

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THE MISSING EMMETROPE

How to bring non-vision-corrected individuals into your practice for primary eye care services.

BY WALTER G. WHITLEY, OD, MBA, FAAO

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2.0 B

People with Presbyopia around the globe in 2019 – growing to

2.3 B

by 2023

PRESBYOPIA Worldwide

Presbyopes	2019	2024
US	128.7 M	136.5 M
OUS	1.93 Billion	2.17 Billion

~ 1.8 million new presbyopes a year in U.S.

Source: 2019 Market Scope Estimates

Contributing Factors:

- **Aging population**
- **Longer life expectancies**
- **Longer Working Careers**
- **Near Vision needs**
- **Growing Middle Class in emerging markets**

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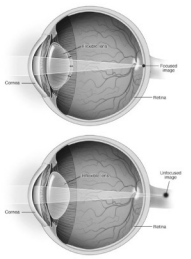
Presbyopia and Accommodation

Presbyopia…simply "The Aging Eye"[1,2]

- Having difficulty reading small print / needing to increase font size
- Needing to hold reading material at arm's length to focus properly
- Needing brighter lighting when reading or doing close-up work
- Suffering from eye-strain & fatigue when doing close-up work



To understand presbyopia, accommodation needs to be understood[1,3]

- The automatic adjustment of the eye for focusing at different distances
- Changes in relative thickness / convexity of the crystalline lens (power)
- The aging lens hardens & loses its ability to change shape (pre-cataract)
- Loss of accommodation is presbyopia

1. Goertz AD, et al. *Acta Ophthalmologica*. 2014;92(6):497-500. 2. Wolffsohn, JS and Davies LN. *Progress in Retinal and Eye Research*. 2019;68:124-143. 3. McDonnell PJ, et al. *Archives of Ophthalmology*. 2003;121(11):1577-1581.

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Presbyopes Today

- Busy, active, height of demands of career and family, limited time
- Concerned about health, self-improvement, self-education
- Access to many information sources
- Highly reliant on near and intermediate distance
- Expectation for excellent vision from best technology
- Have seen parents go through bifocals, then trifocals, then cataract surgery

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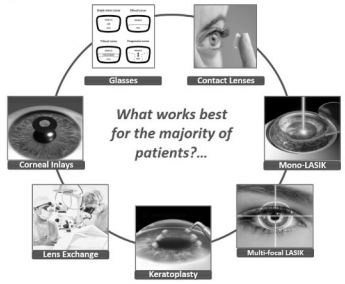
Multiple Presbyopia Correction Modalities



Wolffsohn, JS and Davies LN. *Progress in Retinal and Eye Research*. 2019;68:124-143.

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Current Presbyopia Management Landscape

Based on Market Research Findings, Most Patients Use OTC Readers, Multifocal Lenses, or Prescription Readers for Correction

78% of respondents use some form of vision correction

24% of presbyopia patients are not currently seeing an Eye Care Practitioner

72% are currently using OTC readers

Patient Use of Presbyopia Treatment
(% patients who self-report current or previous use of product)

	Treatment	% of Patients Ever Used	% of Patients Currently Using
1	OTC Reading Glasses	58%	47%
2	Multifocal Lens Glasses	55%	40%
3	Prescription Reading Glasses	48%	35%
4	Contact Lenses	35%	18%
5	Surgical Intervention*	17%	N/A

Note: Total adds to >100% because patients may use more than one treatment
N = 797 age-appropriate patients, weighted for gender based on census data
*Surgical intervention = conductive keratoplasty, refractive lens exchange, corneal inlay, laser monovision, photorefractive keratectomy, and LASIK

Data on file, Allergan, Inc. 2019 Market Research

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Current Presbyopia Options to Increase QOL Have Drawbacks

Current Options	Drawbacks
Glasses	Negatively impacts self confidence. Inconvenient, fogging
Contact Lenses	Inconvenience, CL-related dry eye, compliance issues, adjustment to monovision and lack of depth perception, adaptation to multifocal
Multifocal IOLs	Glare/halos, not usually an option for early presbyopes
Refractive Lens Exchange (RLE)	Especially for early presbyopes, the cost and risk of surgery may not outweigh benefits
Corneal Inlay	Expensive, complications, adjustment to monovision, reduced distance vision
Monovision Laser Vision Correction	Hyperopic treatments less predictable, irreversible, dry eye, adjustment to monovision, loss of binocularity and depth perception

Burke Healthcare Research April 2020, n = 1,000 presbyopes ages 40-60 years old.

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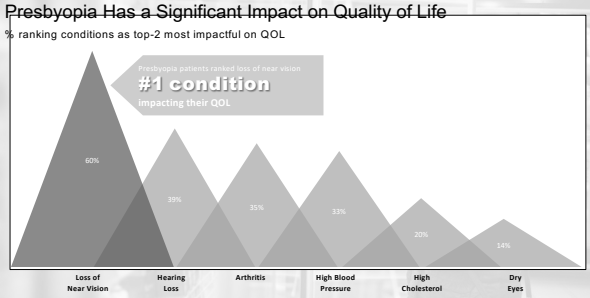
Presbyopia Has a Significant Impact on Quality of Life

% ranking conditions as top-2 most impactful on QOL



Burke Healthcare Research April 2020, n = 1,000 presbyopes ages 40-60 years old.

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Dysfunctional Lens Syndrome: Where Does Presbyopia Fit In?

- Characterizes a spectrum of changes that occur with age, including presbyopia, opacification, loss of image quality, and higher-order aberrations

Stage 1	Stage 2	Stage 3
42-50 years old	>50 years of age	>65
Lens start to stiffen	Loss of accommodation	Full cataract
Loss of near va	Light scatter	Poor visual quality
Develop HOA	Decrease contrast and night va	Nucleus yellows and va degrades

Treatment Options????

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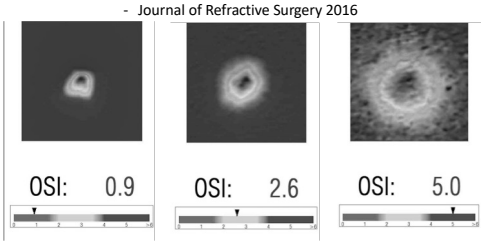
DLS vs. Early Cataract Diagnosis

"The most sensitive test for the detection of cataract, even at an early stage."

- Journal of Refractive Surgery 2016



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Life Without Glasses Evokes Freedom, Youthfulness & Self Confidence

"It would also offer me the freedom to enjoy myself without limitations."

"I would have more options for how I want to look for the day."

"I would feel free again, and more spontaneous."

"Feeling more attractive, improving my self image."

"Being able to feel young again, not needing reading glasses."

"It would be nice not to carry glasses and not look old in doing so."

"Freedom from glasses that are often scratched, smudged and bent."

Burke Healthcare Research April 2020, n = 1,000 presbyopes

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Presbyopia – An Untapped Frontier?

THE QUALITY OF THE IMAGE CAPTURE BY THE EYES

Current methods used to treat near vision loss focus on correcting the quality of images captured by the eyes – most often using glasses.

THE IMAGE PROCESSING ABILITIES OF THE BRAIN

Perceptual Learning uses visual stimulation tasks to improve the image processing function in the visual cortex, thereby compensating for the eyes' function.

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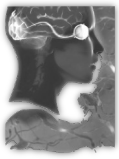
What Is Neuroplasticity?

- ***Neuroplasticity*** is defined as a change in neural pathways and synapses due to changes in experience, environment, neural processes, or changes resulting from bodily injury.
- Its role is widely recognized in development, learning, memory, and rehabilitation.
- The visual cortex retains the capacity for perception-dependent neuroplasticity following **perceptual learning** of both the physical structure (anatomy) and the functional organization (physiology) throughout life.



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Perceptual learning as a treatment approach

Prof. Gilbert, Rockefeller U., topical review:

- Adult **neuroplasticity** constitutes the mechanism of perceptual learning in normal visual experience and in recovery of function after CNS damage.
- It can be seen at multiple stages in the visual pathway, including the primary visual cortex.
- The manifestation of the functional changes associated with perceptual learning involve both long term modification of cortical circuits during the course of learning, and short term dynamics in the functional properties of cortical neurons.

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Perceptual Learning has been Extensively Researched and Published:

Found effective in amblyopia, low myopia and presbyopia

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Neuroplasticity Breakthroughs In Vision

AMBLYOPIA

- Studied in the leading laboratories and clinics, including UC Berkeley Eye Clinic, McGill U. Montreal & Tel Aviv U.
- Proven effective in numerous studies over 10 years
- FDA-approved treatment for adult amblyopia (*Prof. Polat*).
- Acknowledged as "a treatment for amblyopia that works better than patching" (*Prof. Levi, U.C. Berkeley, Optometry*)

PRESBYOPIA

- Studied in the leading laboratories and clinics, including UC Berkeley Eye Clinic
- Proven effective - studies over 7 years
- A treatment for uncorrected presbyopia (*Prof. Polat, Tel Aviv U. & Prof. Levi, U.C. Berkeley, Optometry*)
- Tested on Israeli Defense Force pilots with presbyopia

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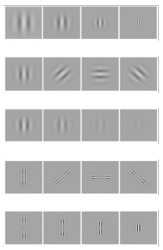
Spatial Frequency

Local Orientation

Contrast

Global Orientation

Target-Flankers Separation



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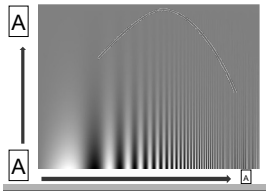
Contrast Drives Neural Responses in the Brain



Young Subjects

- Higher contrast sensitivity for medium spatial frequencies

Presbyopic Subjects

- Slower neuronal responses
- Lower contrast sensitivity

STUDY GOALS: brain compensation for near VA reduction

Increase contrast sensitivity
Enhance processing speed
Achieve gains persistency

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Methods

PARTICIPANTS

59 participants 50.06 ± 8.6 years; mean ± STD, min 40 years, max 65 years divided to two groups:

Early presbyopic stage
initial near vision below 0.2 LogMar (ETDRS) N=29, age 48.03 ± 5.74 (mean ± STD)

Advanced presbyopic stage
above 0.2 LogMar (ETDRS) N=30 age 52.1 ± 4.91 (mean ± STD)

TASK

Temporal processing
Contrast detection

TRAINING PROTOCOL

- Training session duration of 15 min*
- From 40 cm uncorrected for near
- Every other day
- 2-4 months
- After Post-test: boosting sessions once every 2 weeks, over 1 year (up to 6.2 y, 2.5 y on average)

* historically, session duration used to be 30 min

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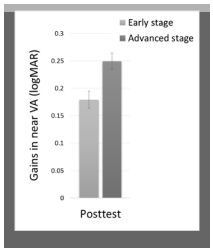
Results

Improvement



ADVANCED PRESBYOPIC STAGE

improvement of 2.5 ETDRS lines, i.e. about 80%.

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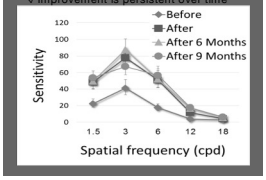
Improvement & Persistence: Basic Visual Functions

CONTRAST SENSITIVITY

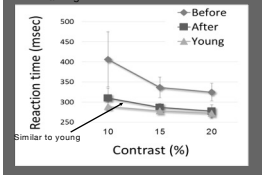
✓ Contrast sensitivity improved significantly at all spatial frequencies

✓ Improvement is persistent over time



REACTION TIME

✓ Reaction times were significantly longer before training, reaching the young control group levels after training



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Refractive Surgery for Presbyopia

- Laser vision correction – Monovision
- Corneal Inlays
- Refractive lens exchange with Lifestyle IOLs

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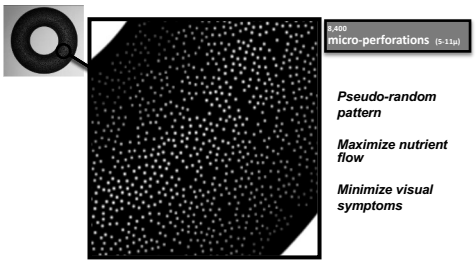
Inlay Design



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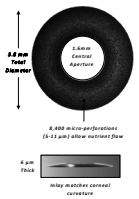
KAMRA® Inlay

First US approved corneal inlay; commercially available in 50 countries

Effective, Reliable and Safe Presbyopia Solution



- ✓ **Improves near vision with minimal impact to distance vision**
  - Achieves long-lasting results even as presbyopia progresses
- ✓ **Implanted into corneal pocket created with femtosecond laser**
  - Implanted monocularly into non-dominant eye
- ✓ **Highly biocompatible material**
  - Made from Polyvinylidene Fluoride (PVDF)
- ✓ **Removable via low-risk procedure with recovery of pre-inlay vision**

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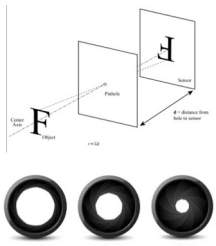
How It Works

- The inlay works like an aperture in a camera (opening)
- This small opening allows only focused images in the eye
- Only focused light rays to reach the retina
- Same principle used in camera lenses to increase depth-of-focus

Pinhole Principle: "Increased Depth of Focus"



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Indications for Use

- Patient who is between 45 and 60 years old
- Cycloplegic refraction between +0.50 D and
- -0.75 D with less than or equal to 0.75 D of
- refractive cylinder
- Patient does not require glasses or contact lenses for clear distance vision
- Patient requires near correction of +1.00 D to +2.50 D of reading add

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Corneal Inlay Patient- Exclusion Criteria

- Any ocular or systemic disease that is a contraindication for corneal refractive procedures including:
  - Keratoconus
  - Uncontrolled and/or severe dry eye
  - Cataracts
  - Macular degeneration
  - Corneal dystrophy or degeneration
  - Amblyopia or Strabismus
- Patients with unrealistic expectations
- Patients with psychological conditions

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Post-op Exam

- Minimum follow-up:
  - 1 day
  - 1 week
  - 1, 3, 6 months
  - 1 year
- Patients should be ***seen more frequently*** if abnormal post-op findings are observed

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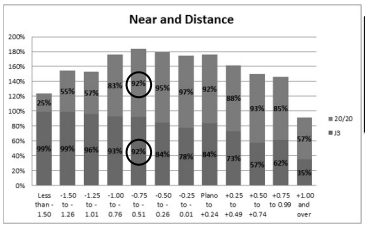
Effectiveness of Post-op MRSE



92% of patients achieved ≥ to 20/20 UCDVA and J3 UCNVA when post-op MRSE = -0.50 to -0.75

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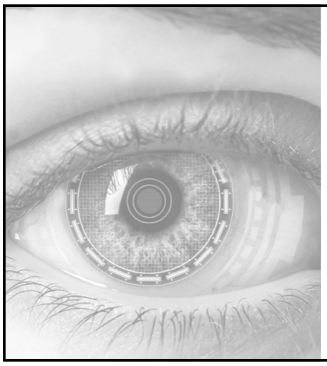

Presbyopia-correcting IOL Technologies are Booming!

- Mulifocals (10 IOLs)
- Trifocals (3 IOLs)
- EDOF (2)
- Accommodating (3 IOLs)
- Small Aperture IOL
- Light adjustable lens (RxSight)
- Refractive Indexing IOL (Perfect Lens)

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Premium IOLs: 5 Pearls ("P's") for Success

1. **P**lano Outcome
2. **P**roactive Tx of Ocular Surface Disease
3. **P**re Op Counseling – Setting Realistic Expectations
4. **P**roperly Screen Candidates
5. **P**ick the Right IOL

Other: 6. **P**ick the Right Surgeon
7. **P**osterior Capsular Opacification
8. **P**oor IOL Centration

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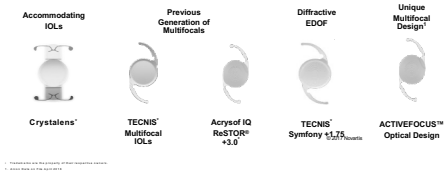
ATIOLs Provide The Opportunity to Treat More Than Just the Cataract

What are your patient's post-op visual goals?



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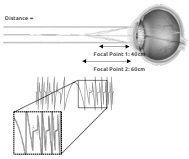
PANOPTIX TRIFOCAL IOL

- **SUPERPOSITION OF FOCAL POINTS**
- **LIGHT REDIRECTION** - 120 cm intermediate focal point redirected to distance
- **3 FOCI** – Trifocal with 40cm, 60 cm and distance
- **88% LIGHT UTILIZATION** - at 3.0 mm pupil
- **LIGHT ALLOCATION** - 50% of available light to distance, 25% to intermediate and 25% to near



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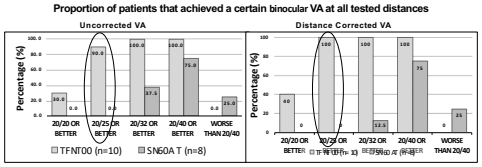
Composite Binocular VA at all three distances (distance, intermediate and near) at 6 month



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Light Adjustable Lens (LAL)

- FDA Approved 11/17 for pts with pre-existing astigmatism of ≥0.75D undergoing cat sx
  - Spherical and cylindrical errors up to 2D
- First and only lens designed to be ***adjusted*** after implantation by UV light
- 3 piece IOL design
- 6.0mm biconvex optic; 13.0mm overall length
- UV absorbing back layer: 50-100 µm

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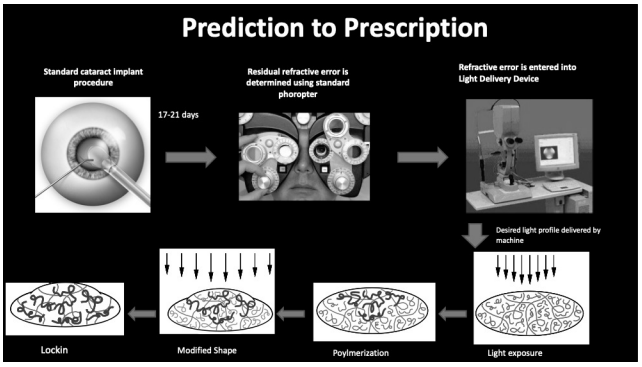

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FDA Clinical Results

- 91.8% within 0.50 D of target manifest refraction spherical equivalent
- Results showed that 100% of study eyes had a best corrected visual acuity of 20/40 or better at the 6 month po visit.

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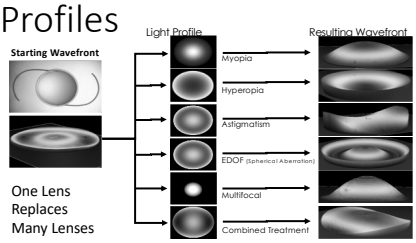
Flexible Treatment Profiles



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RxLAL Will Expand Monovision Use

- **Monovision used 3-4x more than PC-IOLs**[1]
  - Usual target: 0.75D-1.00D anisometropia
  - W/ average 0.5D SD[2], hard to hit target
  - If miss first eye, acuity degradation/ binocular fusion
- **RxLAL will dramatically increases binocular accuracy**
  - Standard deviation reduced to 0.2D[3]
  - Patient ability to test-drive/adjust final outcome
  - LASIK-like outcomes
- **Creates new premium channel opportunity**

IOL Type	Refractive Error (Standard Deviation)
Non-Adjustable	0.5D
RxLAL	0.2D

1. 2015/2016 ASCRS Survey 2. Average over all IOLs 3. Osama Data FDA Study

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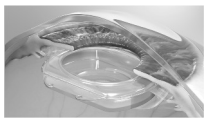
What's Coming Next in IOL Technology?

- Modular IOL Systems
- Accommodating
- Multifocal / trifocal
- Extended Depth of Focus



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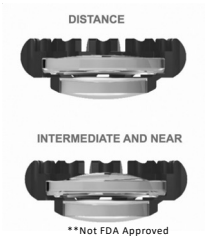
Accommodating IOL – LensGen Juvene



**Not FDA Approved

- Modular, curvature-changing, fluid-optic IOL
- Two-part IOL - Base and Modular
- Advantages
  - Doesn't split light
  - Up to 3D of continuous range vision
  - No change in ELP
  - No PCO up to 4 years
- Astigmatism?? Drug Delivery?? Exchangeable 2nd implant??

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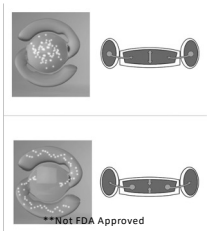
Accommodating IOL – Alcon FluidVision Lens



**Not FDA Approved

- Entire lens is hollow and filled with liquid silicone
- Fluid changes changes in optic
- Avg. accommodation range 2D
- Dr. Nichamin ESCRS 2018
  - 29 eyes
  - Distance 20/20
  - Intermediate 20/20-20/25
  - Near 20/22-20/27

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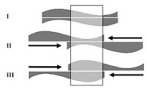
Accommodative IOL – Akkolens Lumina



**Not FDA Approved

- Two piece sulcus IOL
  - Fixed and variable
  - Hydrophilic acrylate
- Shifting optics
  - Can provide 3-4 D focal range when shifted
- Dr. Alio -59 eyes of 43 pts
  - Accommodative range of 3.1D

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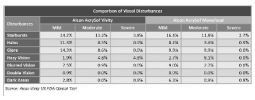
EDOF - Vivity IOL

- Non-diffractive IOL
- Novel X-Wave shaping technology creates an extended focal range by stretching and shifting the wavefront
- Low incidence of visual disturbances
- Possible for AMD?? Glaucoma??



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J&J Vision – Tecnis Eyhance

- First lens[1] in the monofocal IOL category in Europe to deliver improved intermediate vision and 20/20* distance vision
- TECNIS Eyhance IOL offers the same well-established low incidence of halo, glare, or starburst as TECNIS® 1-piece IOLs

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J&J Vision – Tecnis Synergy

- Gives broad range of continuous vision covering from distance to 33 cm
- Eliminates the visual gaps present in trifocal and other multifocal technology
- Continues to deliver superior performance in low-light conditions
- Violet-filtering technology demonstrates reduction in halo intensity for tasks like night driving

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Trifocal IOL - PhysIOL

- Aspheric diffractive trifocal
- 2 diffractive structures that give +3.5D add for N and +1.75D for intermediate
- Less glare and halos
- Designed to reduce the loss of light energy resulting from any diffractive system
- Diffractive anterior surface entirely convoluted
- Height of the diffractive step varied
- Distributes light to near, intermediate and distant foci adjusted according to the pupil aperture

**Not FDA Approved

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"Pinhole" IOL Design

- IOL Material
  - Single-piece hydrophobic acrylic
- Mask
  - PVDF & nano-particles of carbon
  - 1.36mm aperture
  - 3.23mm total diameter
  - 3200 microperforations
  - 5 microns thick

**Not FDA Approved

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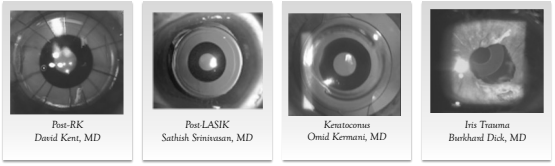
Presbyopia Correction No Longer Only for the Perfect Cornea!



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FUTURE INNOVATIONS FOR PRESBYOPIA

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Patients Looking for Efficacy, Durability and Favourable Side Effect Profile

Thinking about the features of this potential new eye drop medication, which features are most appealing to you?

- **Efficacy** – restore functional near vision as well as current solution (glasses/contacts)
- **Duration** – lasting throughout a work day (minimum)
- **Side Effect Profile & Tolerability –** minimal brow ache/headache, minimal burning/stinging
- **Cosmesis** – eyes should be white and quiet

EFFECTIVE	…as reading glasses	94%
LONG-LASTING	… at least 8 hours	96%
COMFORTABLE	…mild/minimal side effects	83%

Burke Healthcare Research April 2020, n = 1,000 presbyopes ages 40-80 years old

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Pharmacologic Treatments for Presbyopia Are Coming, With Miotic Drops Occupying the Majority of Development

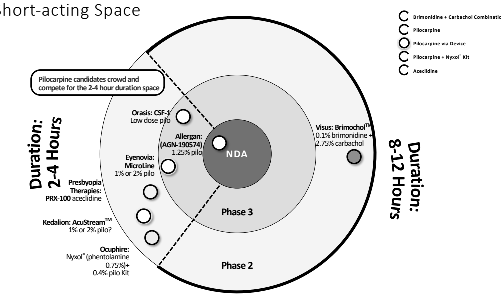
Topical Drops in Development	Active Ingredient(s)	Mechanism of Action
Brimochol™ (Visus Therapeutics)	Carbachol + brimonidine tartrate	Carbachol: Miotic Brimonidine tartrate: Prevents pupil dilation, inhibits contraction of ciliary muscle, increases bioavailability of carbachol[1,2], prevents redness[3]
CSF-1 (Orasis)	Pilocarpine	Miotic
PRX-100/Liquid Vision (Presbyopia Therapies)	Aceclidine	Miotic
AGN 190584 (Allergan)	Pilocarpine	Miotic
MicroLine (Eyenovia)	Pilocarpine	Miotic
AcuStream™ (Kedalion)	Pilocarpine	Miotic
Nyxol® and Pilocarpine Combination Kit (Ocuphire)	Phentolamine mesylate and pilocarpine	Miotic (both pilocarpine and phentolamine mesylate products) Vasodilates small muscles (phentolamine mesylate product)[6]
True Vision Treatment® Contact lenses and Eye Drops Kit (Yolia Health)	Hyaluronidase and collagenase	Alters cornea[7]
UNR844 (Novartis)	Lipoic acid choline ester	Lens-softening agent
VP1-001 (Viewpoint Therapeutics)	Stabilizing alpha-crystallin molecule	Target's protein misfolding to restore native, functional shape[8]

- Miotic drops increase depth of field by inducing a pinhole effect
  - Low risk, highly effective and easily reversible compared to surgical alternatives
  - Miotic drops aren't without side effects - headache, brow ache, IOP fluctuations, myopic shift and hyperemia[4,5]
  - Single-agent cholinergic miotics likely to have more of an issue with these side effects than combination drops
- Lens softening topical agents intend to increase ability to accommodate with usage over time

1. Suzuki et al. Ocular and Systemic Pharmacokinetics of Brimonidine and Timolol After Topical Administration in Rabbits: Comparison Between Fixed-Combination and Single Drugs. *Ophthalmol Ther* (2020) 9:115–125; 2. Allergan patent application (Pub. No.: US 2018 / 0078500 A1). 3. LUMIFY Product Insert www.fda.gov accessed 9/24/2020. 4. Becker-Shaffer's Diagnosis and Therapy of the Glaucomas (Eighth Edition), 2009. 5. Korczyn et al. Effect of Pilocarpine on Intraocular Pressure in Normal Humans. *Ophthalmic Res.* 14:182-187 (1982). 6. Pepose. Phentolamine Mesylate Ophthalmic Solution Provides Long Lasting Pupil Modulation And Improves Visual Acuity. ARVO 2020 Abstract: #3364450 7. Yolia Health. 8. Viewpoint Therapeutics, February 2021

57

U.S. Presbyopia Miotic Drop Landscape is Crowded in the Short-acting Space



1. Clinicaltrials.gov, January 2021. 2. Christopher Kent, Non-IOL-based Presbyopia Treatments, Review of Ophthalmology Nov 5, 2020. 3. OIS Presbyopia Innovation Showcase, January 28, 2021. 4. UNSW Australia pilocarpine via AcuStream Presbyopia Recruitment Advertisement. 5. Viewpoint Therapeutics. 6. Data on file, January 2021.

58

Which Patients May Be the Best Candidates for Miotic Drops?

- Emmetropes
  - Least comfortable with vision correction surgery
- Post-LASIK emmetropes
  - Have already made significant investment to be glasses-free
  - If LASIK was performed prior to wavefront-guided procedures and aspheric optical zones, pupil constricting drops may also help to address higher order aberrations, glare and halo
- Hyperopes
  - Will improve vision at distance and near
- Pseudophakes
  - Monofocal IOL patients may opt to use drops instead of readers
  - Premium IOL patients may want additional near vision than their IOL provided

Contraindications

- High myopes
- Past history of retinal tears

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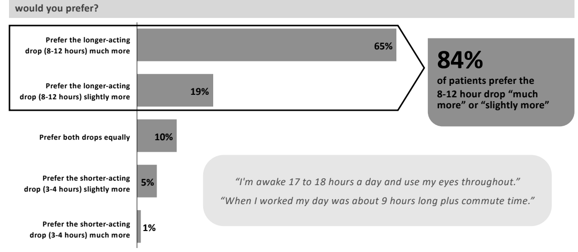
Market Research Indicates Strong Preference for 8+ Hours Duration

If you had the choice between a longer-acting drop (8-12 hours) and a shorter-acting drop (3-4 hours), which drop would you prefer?



"I'm awake 17 to 18 hours a day and use my eyes throughout."

"When I worked my day was about 9 hours long plus commute time."

Burke Healthcare Research April 2020, n = 1,000 presbyopes ages 40-80 years old

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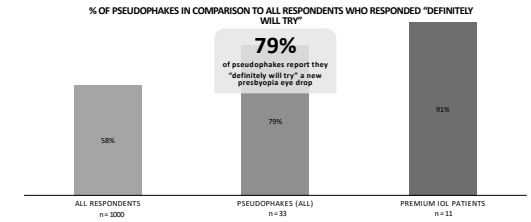
Pseudophakes Very Interested in Trying a Presbyopia Drop – a Highly Motivated Patient Segment

If your eye doctor recommended it, how likely would you be to try this new eye drop to temporarily restore your near vision?



Burke Healthcare Research April 2020, n = 1,000 presbyopes ages 40-80 years old

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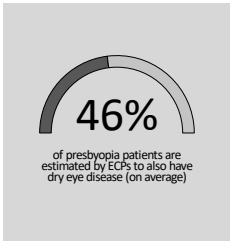
Significant Overlap of Presbyopia with Dry Eye Disease Highlights Additional Considerations



ADDITIONAL CONSIDERATIONS

- How will drops actually be utilized by patients?
  - If a drop doesn't last a full day, how many times will most patients dose it?
- Ideally there will be preservative-free drops available, especially for patients with a compromised ocular surface
- A longer duration drop may have a more favorable safety profile due to less frequent dosing

Reckner Healthcare Research May 2020, n = 202 optometrists and ophthalmologists practicing in U.S.

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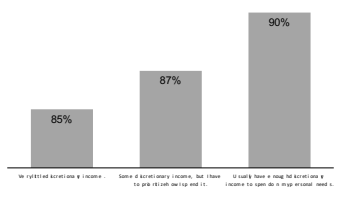
Purchase Interest Is Strong Across All Discretionary Income Levels

Presbyopia drops represent a cash-pay lifestyle product with the added benefit of being viewed by the consumer as a necessary healthcare expense

Top 2 Box Purchase Interest in Relation to Discretionary Income
% of People who would Definitely/Probably Try it (n = 1000)



> ***I find my vision to be important, and would want to still try these types of drops. I am prioritizing spending these days, but*** *still would have the money to take care of important things like my eyes* ***(at a reasonable cost of course).***

> ***I put*** *health ahead of all frivolous spending* ***and if the medication were available, I'd make sure I would have it.***

> ***If it would improve my vision without glasses,*** *I would sacrifice some hobby* ***or expense.***

> ***Its not like a vacation,*** *I don't mind spending money on medical* ***/ health stuff.***

Burke Healthcare Research April 2020, n = 1,000 presbyopes

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What Do We Know about the Topical Presbyopia Market?

- The unmet need for a topical drop to improve near vision is significant
- Duration of action is important to patients and will likely lead to less frequent dosing
- Side effect profiles will vary based on active ingredient concentrations and differing MOAs
- Tolerability will be an important consideration – does it burn and sting?
- Cosmesis will factor in patients' receptivity to drops – will patients accept hyperemia to achieve NVA improvement?
- Exercise caution with patients who have compromised ocular surface, especially for drops with short duration of action

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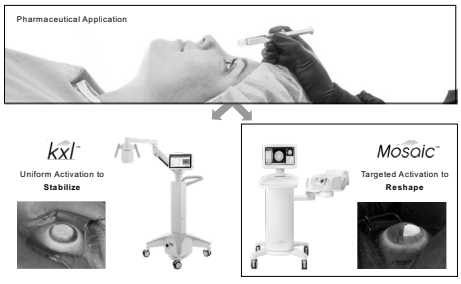
Avedro's Approach: Non-invasively Stabilizing and Reshaping the Cornea

Corneal Remodeling Technology



The Mosaic System, Boost Goggles, and transepithelial drug formulations are not sold in the United States

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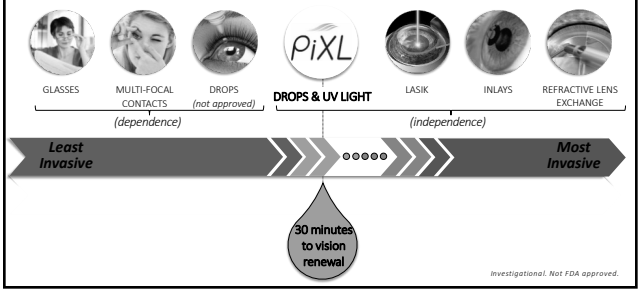
Corneal remodeling for non-invasive reshaping the cornea without ablation or incision



Investigational. Not FDA approved.

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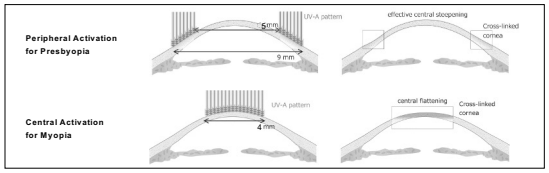
PiXL for Vision Improvement
Non-invasive corneal remodeling

Treatment Concept	Visual Target	Patient Experience
One time, non-invasive corneal remodeling treatment	Spectacle independence Binocular UNVA of J2 or better No halo or loss of CDVA	Non-invasive, simple procedure 1-2 day recovery Long-term stability of CXL

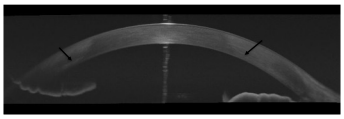


Investigational. Not FDA approved.

67

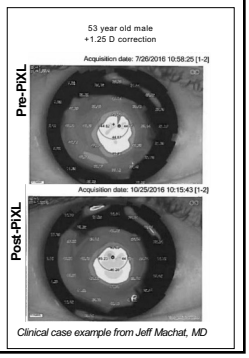
PiXL for Presbyopia
Spatially targeted, epithelium-on, accelerated cross-linking

More than 200 eyes treated internationally with PiXL to date



- Midperipheral cross-linking, no UVA applied to central cornea
- Image above: High resolution OCT image showing mid peripheral corneal stromal demarcation line after epi-ON PiXL with oxygen

Investigational. Not FDA approved.



Clinical case example from Jeff Machat, MD

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- A potential non-invasive solution for presbyopia
- Filling a gap in refractive treatment options
- Drops, UV light and O_2
- Targeted corneal reshaping with long-term durability of cross-linking
- Likely advantageous for post operative cornea adjustability
- Early clinical results are promising
- **Multicenter Phase II Study in 2019**

PiXL

Mosaic System
Proprietary computer software and UVA beam forming technology

Boost Goggles

New Drug Formulations
Proprietary single-use drug formulations

Investigational. Not FDA approved.

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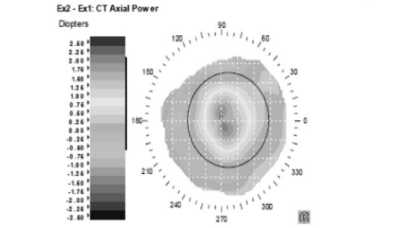
Allogenic Corneal Inlay (Allotex)
PEARL: PrEsbyopic Allogenic Refractive Lenticule

- Increasing central corneal power to improve near vision



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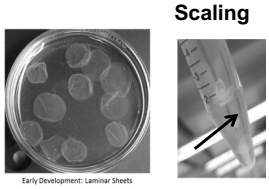
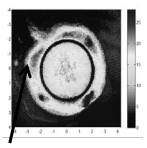
Excimer laser shaped corneal inlays

Scaling



Valuable use of gifted human tissue!

Predictability



Human tissue shaped with excimer laser precision.

www.allotex.com

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European Multicenter Study:
Interim data analysis (20 eyes)

	Preoperative	Post-op (last visit)
UCNVA of 20/40 or better (monocular)	0%	95%
Near Vision (binocular)	Gain: +17 letters (mean)	
Intermediate Vision (binocular)	Unchanged: +2 letters (mean)	
Distance Vision (binocular)	Unchanged: -2 letters (mean)	

*** last visit was 1 or 3 months after surgery

c/o Aylin Kylic, MD

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The LIRIC Platform: Laser Induced Refractive Index Change for Refractive Error Correction

LIRIC: *a disruptive technology*

Poised to revolutionize:
- **refractive surgery**
- **cataract surgery**
- **contact lenses**

A revolutionary way to refine the optics of the eye

Cornea
- Minimally invasive
- No flap, epi on, no doping
- No nerve damage

IOL
- Post-implantation optical touch-up
- Monofocal to multifocal & vice-versa
- Correct residual refractive error

Contacts
- Enables diffractive multifocals for better presbyopia correction
- Thin lenses for all prescriptions
- Better oxygen transmissibility

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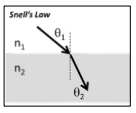
The LIRIC Platform

Low-Pulse Energy Femtosecond Laser

- **Refractive Index Modification**
  - Refractive error correction[1,2,3]
  - Presbyopia correction[4,5]

Refractive Index Bends Light



Air	1.00
Water	1.33
Cornea	1.39
Contact Lens	1.42
Glass	1.50

1. Gandara-Montano et al., Optical Materials Express, 2017
2. Gandara-Montano et al., Optical Materials Express, 2018
3. Zheleznyak et al., ARVO 2018
4. Zheleznyak et al., ARVO 2019
5. Butler et al., ARVO 2019

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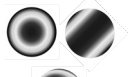
The LIRIC Platform

Low-Pulse Energy Femtosecond Laser

- **Refractive Index Modification**
  - Refractive error correction[1,2,3]
  - Presbyopia correction[4,5]

Sph & Cyl



Custom HOAs

Presbyopia

1. Gandara-Montano et al., Optical Materials Express, 2017
2. Gandara-Montano et al., Optical Materials Express, 2018
3. Zheleznyak et al., ARVO 2018
4. Zheleznyak et al., ARVO 2019
5. Butler et al., ARVO 2019

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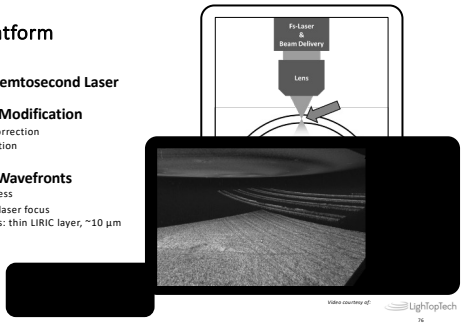
The LIRIC Platform

Low-Pulse Energy Femtosecond Laser

- **Refractive Index Modification**
  - Refractive error correction
  - Presbyopia correction
- **High Resolution Wavefronts**
  - Multiphoton process
  - Scanning µm-size laser focus
  - Repeat treatments: thin LIRIC layer, ~10 µm



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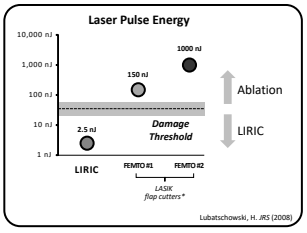
The LIRIC Platform

Low-Pulse Energy Femtosecond Laser

- **Refractive Index Modification**
  - Refractive error correction
  - Presbyopia correction
- **High Resolution Wavefronts**
  - Multiphoton process
  - Scanning µm-size laser focus
- **Below damage threshold**
  - No ablation
  - No tissue cutting
  - No flap required
  - Epi-on, no doping required

Laser Pulse Energy



Lubatschowski, H. *JRS* (2008)

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Cornea: *Overcoming the limitations of laser refractive surgery*

Cornea

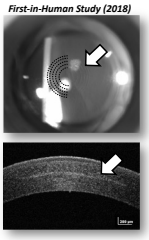
Minimally invasive surgery
- No incision, no flap, no dopants (Zheleznyak et al., ARVO 2019)
- Less keratocyte cell death (Wozniak et al., Exp Eye Res 2018)

Potentially less dry eye
- No corneal nerve damage (Wozniak et al., ARVO 2019)

Maintain tissue integrity
- Tissue sparing, no ablation

High optical quality
- High precision wavefront induction

First-in-Human Study (2018)



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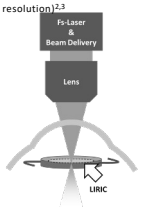
IOL:
Overcoming the limitations of cataract surgery

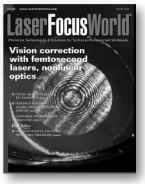
IOL

Residual Refractive Error
- Standard cataract surgery: ±0.5 D sphere, >1 D astigmatism in 45% of patients[1]
- LIRIC customized correction (0.05 D resolution)[2,3]

Monofocal to Multifocal

Multifocal to Monofocal





1. Behndig et al., JCRS 2012
2. Gandara-Montano et al., OMEX 2018
3. Pepose et al., AAO 2017

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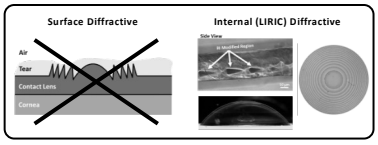
Contact Lens:
Overcoming limitations of traditional contacts

Contacts

Superior Presbyopia Correction
- Internal diffractive multifocals superior to refractive multifocals



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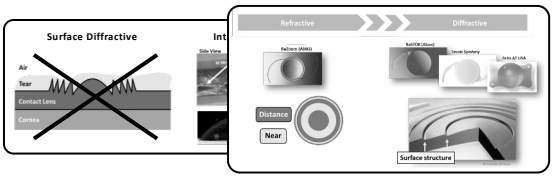
Contact Lens:
Overcoming limitations of traditional contacts

Contacts

Superior Presbyopia Correction
- Internal diffractive multifocals superior to refractive multifocals
- Similar evolution to multifocal IOLs (e.g. refractive to diffractive)



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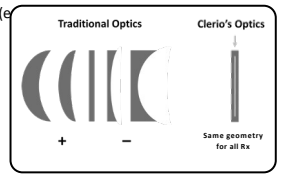
Contact Lens:
Overcoming limitations of traditional contacts

Contacts

Superior Presbyopia Correction
- Internal diffractive multifocals superior to refractive multifocals
- Similar evolution to multifocal IOLs (e

Higher Oxygen Transmissibility
- Thin lenses for all Rx



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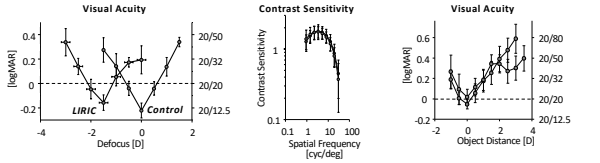
Demonstrated High Visual Performance

Myopia Correction
-1.5 D sphere in hydrogel phase plates

Presbyopia Correction
+2.5D diffractive bifocal in a contact lens



Zheleznyak et al., ARVO 2018
Butler et al., ARVO 2019

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Conclusions

- Numerous technologies are available today
- Education is key!!
- Stay on the cutting edge of science and technology!

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Wwhitley@cvphealth.com

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