

Current Trends in Presbyopia and Dysfunctional Lens Syndrome: From Drops to Glasses to Contacts to Surgical Procedures

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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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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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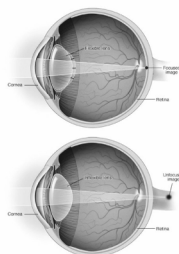
Presbyopia and Accommodation

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



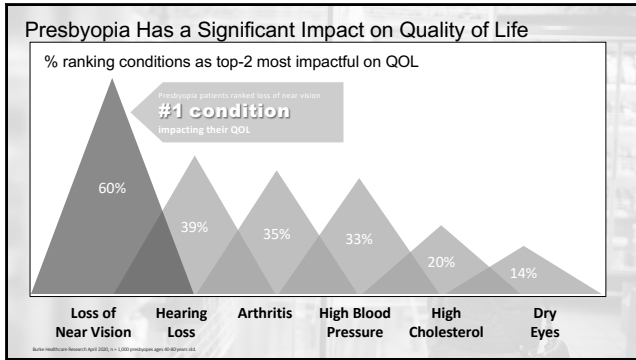
1. Gnanapavan, M., et al. Age-Related Maculopathy. 2014;20(10):1407-1412. 2. Gnanapavan, M. and Davies, L.N. Progress in Retinal and Eye Research. 2013;38:1234-1245. 3. McDermott, P.J., et al. Archives of Ophthalmology. 2005;123(11):1577-1581.

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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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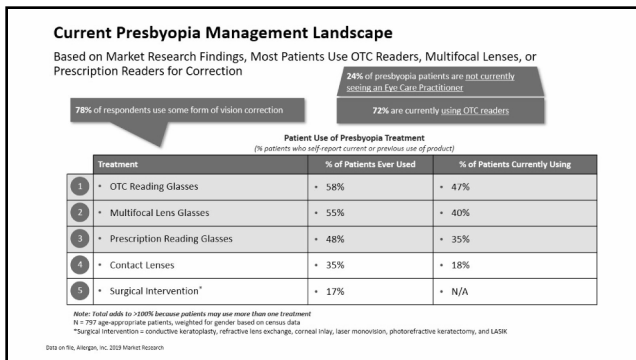


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Current Presbyopia Options to Increase QOL Have Drawbacks

	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

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What Opportunities Exist for Presbyopia?

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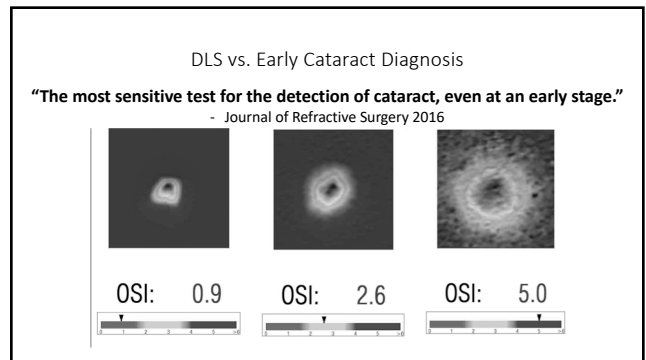
Dysfunctional Lens Syndrome: Where Does Presbyopia Fit In?

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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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."



AutoMedicare Research April 2015, n = 1,000 participants

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Presbyopia – An Untapped Frontier?

THE QUALITY OF THE IMAGE CAPTURED 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

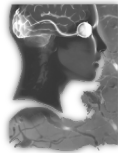


Perceptual Learning uses visual stimulation tasks to improve the image processing function in the visual cortex, thereby compensating for the eyes' function.

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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

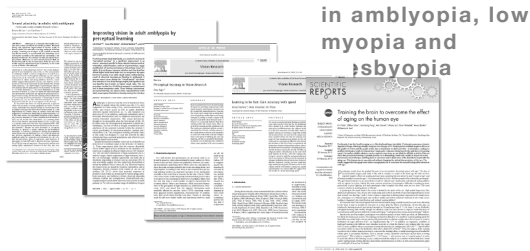
Prof. Gilbert, Rockefeller U., topical review:

- 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:



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Neuroplasticity Breakthroughs In Vision



AMBLYOPIA

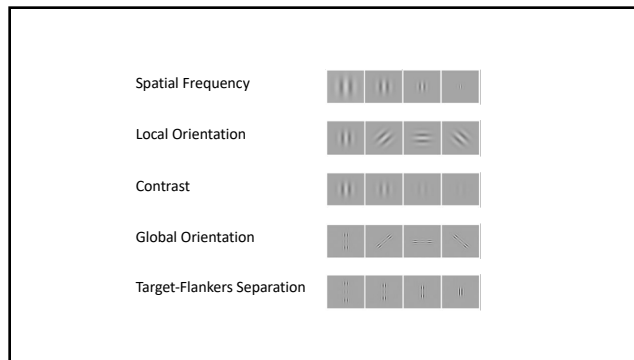
- Studied in the leading laboratories and clinics, including UC Berkeley Eye Clinic, McGill U, Montreal & Tel Aviv U.
- Proven effective in numerous studies over 10 years
- FDA-approved treatment for adult amblyopia (Prof. Polat).
- Acknowledged as "a treatment for amblyopia that works better than patching"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



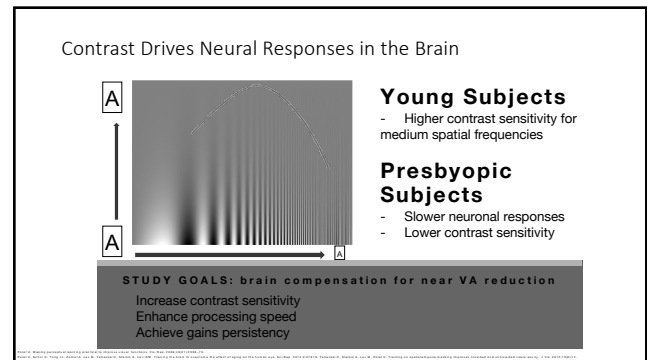
PRESBYOPIA

- 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

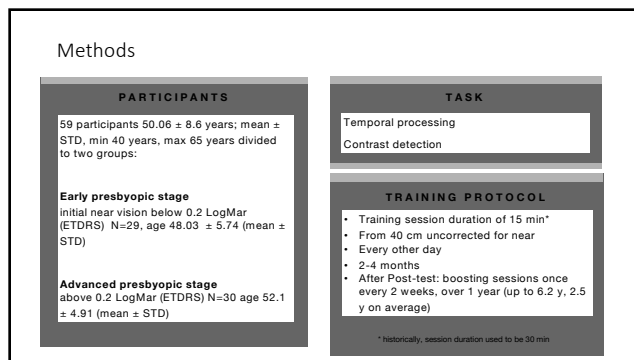
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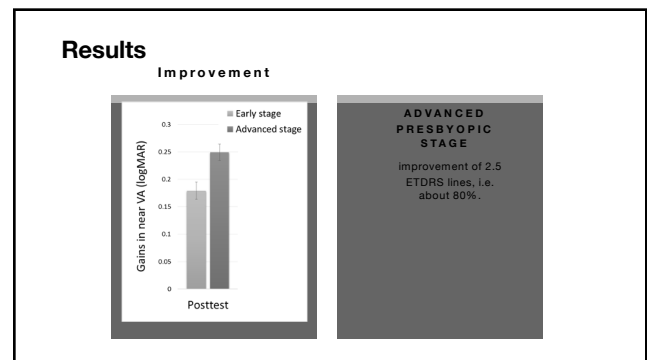
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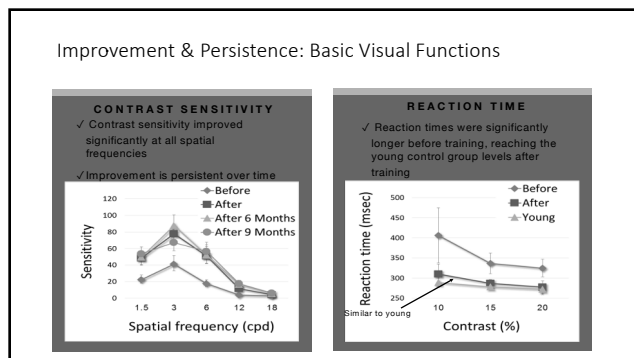
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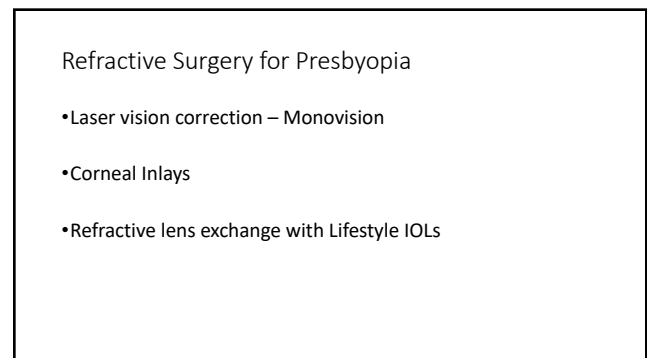
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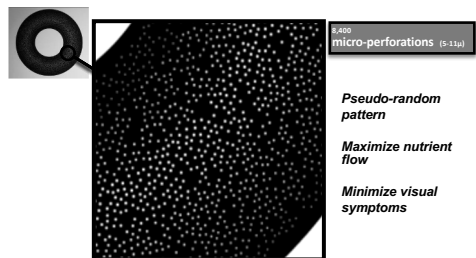


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Inlay Design

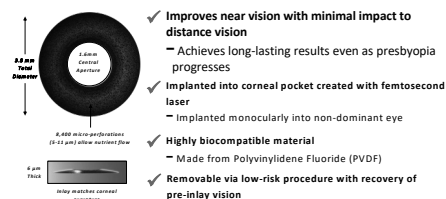


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KAMRA® Inlay

First US approved corneal inlay; commercially available in 50 countries

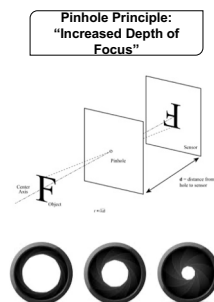
Effective, Reliable and Safe Presbyopia Solution



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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



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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

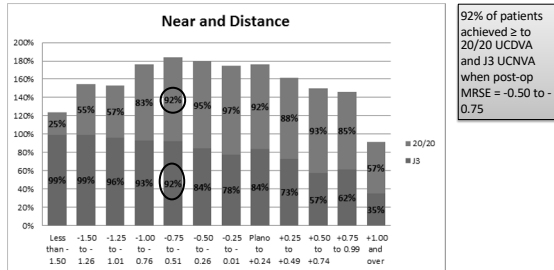
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Post-op Exam

- 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



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Presbyopia-correcting IOL Technologies:
Where are we now?

- Multifocals (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

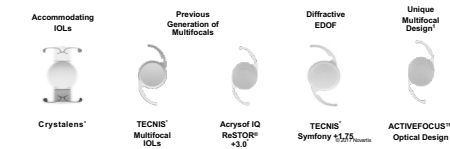
1. Plano Outcome
2. Proactive Tx of Ocular Surface Disease
3. Pre Op Counseling – Setting Realistic Expectations
4. Properly Screen Candidates
5. Pick the Right IOL

- Other:
6. Pick the Right Surgeon
 7. Posterior Capsular Opacification
 8. Poor IOL Centration

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ATIOLs Provide The Opportunity to
Treat More Than Just the Cataract

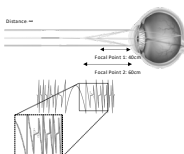
What are your patient's post-op visual goals?



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PANOPTIX TRIFOCAL IOL

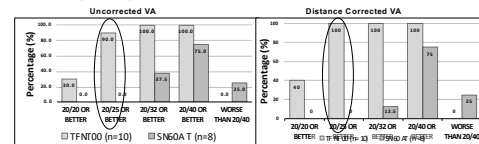
- SUPERPOSITION OF FOCAL POINTS
- LIGHT REDIRECTION - 120 cm intermediate focal point redirected to distance
- 3 FOCI – Trifocal with 40cm, 60 cm and distance
- 88% LIGHT UTILIZATION - at 3.0 mm pupil
- LIGHT ALLOCATION - 50% of available light to distance, 25% to intermediate and 25% to near



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

Proportion of patients that achieved a certain binocular VA at all tested distances



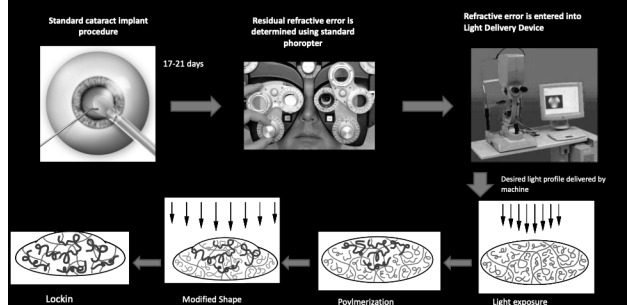
Light Adjustable Lens (LAL)

- FDA Approved 11/17 for pts with pre-existing astigmatism of $\geq 0.75D$ 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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Prediction to Prescription



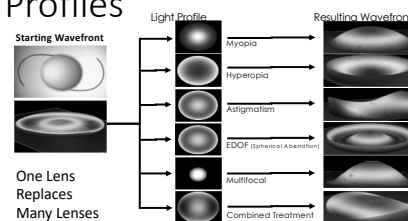
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FDA Clinical Results

- 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:**
 - Usual target: 0.75D-1.00D anisometropia
 - W/ average 0.5D SD., hard to hit target
 - If miss first eye, acuity degradation/ binocular fusion
- **RxLAL will dramatically increase binocular accuracy**
 - Standard deviation reduced to 0.2D.
 - 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. 2012/2016 ADOCS Survey 2. Average of all EDs 3. Device Data/PCA 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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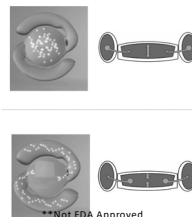
Accommodating IOL – LensGen Juvene



- 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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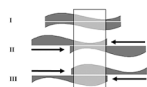
Accommodating IOL – Alcon FluidVision Lens



- 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



- 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

**Not FDA Approved

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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??

Visual Quality	Vivity IOL		Trifocal IOL		Multifocal IOL	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Contrast Sensitivity	15.1%	11.1%	15.1%	11.1%	15.1%	11.1%
Visual Acuity	12.1%	11.1%	12.1%	11.1%	12.1%	11.1%
Visual Quality	12.1%	11.1%	12.1%	11.1%	12.1%	11.1%
Visual Quality	12.1%	11.1%	12.1%	11.1%	12.1%	11.1%
Visual Quality	12.1%	11.1%	12.1%	11.1%	12.1%	11.1%
Visual Quality	12.1%	11.1%	12.1%	11.1%	12.1%	11.1%
Visual Quality	12.1%	11.1%	12.1%	11.1%	12.1%	11.1%



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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

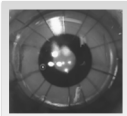
- IOL Material
 - Single-piece hydrophobic acrylic
- Mask
 - PVDF & nano-particles of carbon
 - 1.36mm aperture
 - 3.23mm total diameter
 - 3200 microperforations
 - 5 microns thick



**Not FDA Approved

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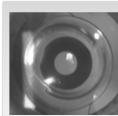
Presbyopia Correction No Longer Only for the Perfect Cornea!



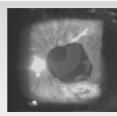
Post-RK
David Kent, MD



Post-LASIK
Sathish Srinivasan, MD



Keratoconus
Omid Kermani, MD



Iris Transmembranes
Burkhard Dick, MD

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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



Baxter Healthcare Research April 2020, n = 1,000 participants ages 40-60 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
Alcon's (Ocular Therapeutics)	Stimulating muscarinic receptor	Contracture of ciliary muscles, increases production of aqueous humor, increases accommodation ¹
CSF-1 (Draxis)	Pilocarpine	Miotic
CSF-1 (Novartis Pharmaceuticals Corporation)	Pilocarpine	Miotic
AGN 190584 (Allergan)	Pilocarpine	Miotic
Acadstream™ (Kedalion)	Pilocarpine	Miotic
Novartis and Pharmacia Corporation, Inc. (Novartis)	Pilocarpine, Acetylcholine Esterase Inhibitor	Contracture of ciliary muscles, increases production of aqueous humor, increases accommodation ²
True Vision Treatment™ Contact Lenses and Eye Drops Kit (Vella Health)	Hyaluronidase and collagenase	Alters cornea ³
VP1-001 (Viewpoint Therapeutics)	Stabilizing alpha-crystallin molecule	Target's protein misfolding to restore native, functional shape ⁴

► Miotic drops increase depth of field by inducing a pinhole effect

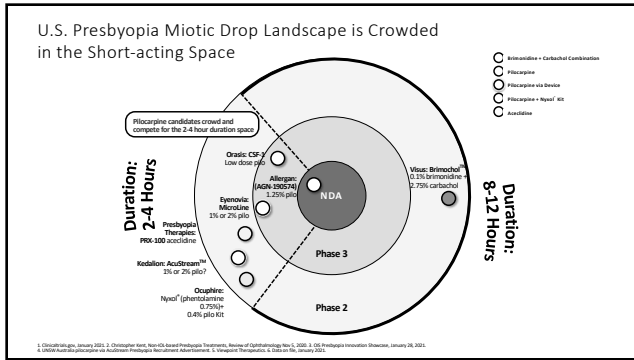
– Low risk, highly effective and easily reversible compared to surgical alternatives

– 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

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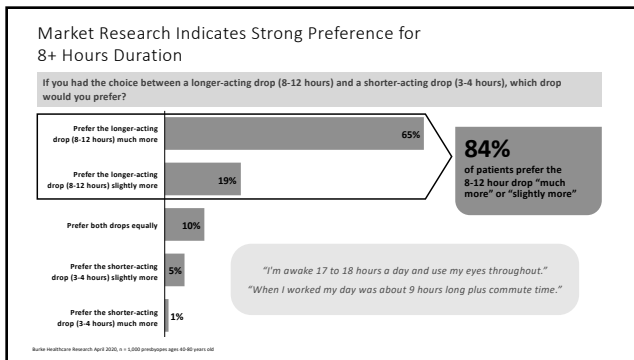
Which Patients May Be the Best Candidates for Miotic Drops?

- 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

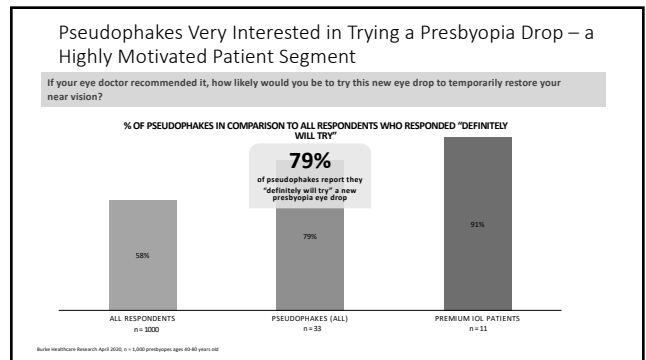
Contraindications

- High myopes
- Past history of retinal tears

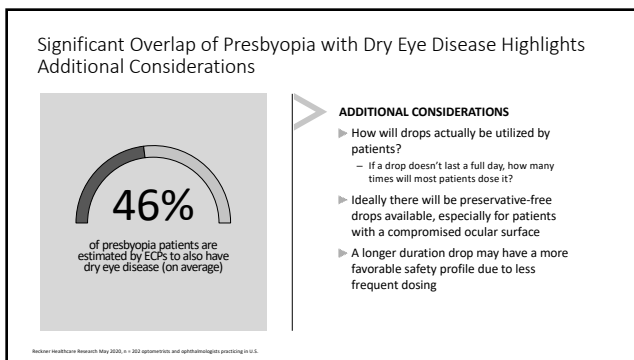
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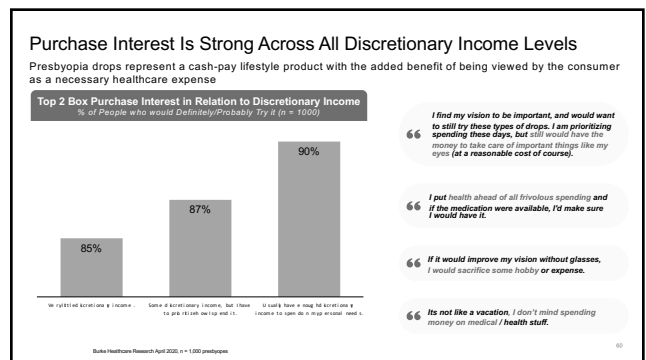
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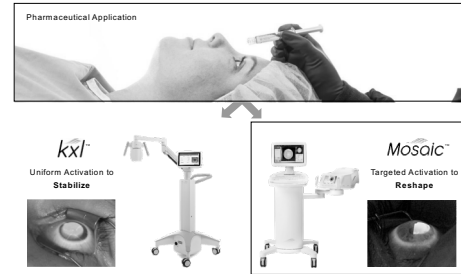
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What Do We Know about the Topical Presbyopia Market?

- 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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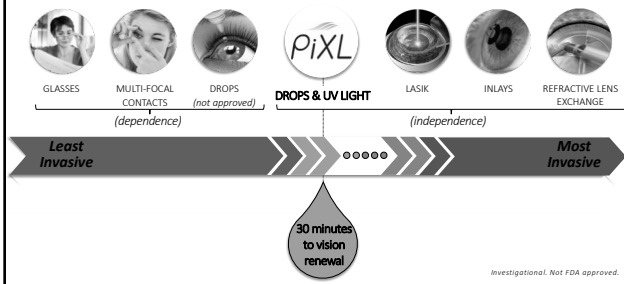
Avedro's Approach: Non-invasively Stabilizing and Reshaping the Cornea *Corneal Remodeling Technology*



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

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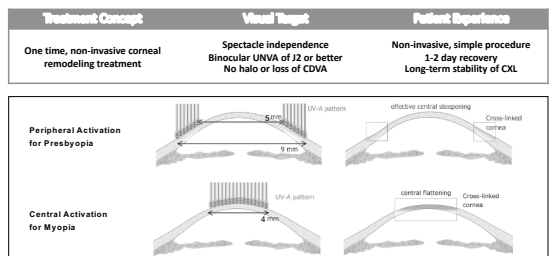
Corneal remodeling for non-invasive reshaping the cornea without ablation or incision



Investigational. Not FDA approved.

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PiXL for Vision Improvement *Non-invasive corneal remodeling*

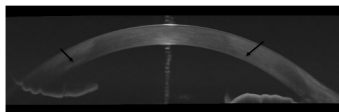


Investigational. Not FDA approved.

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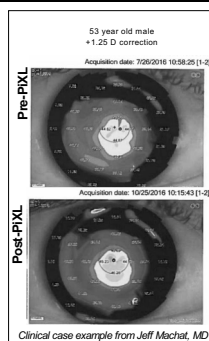
PiXL for Presbyopia *Spatially targeted, epithelium-on, accelerated cross-linking*

More than 200 eyes treated internationally with PiXL to date



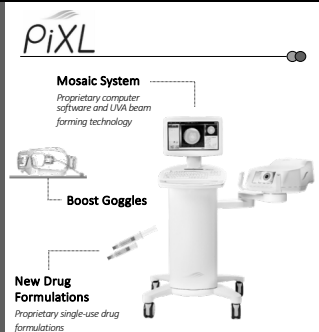
- Midperipheral cross-linking, no UVA applied to central cornea
- Image above: High resolution OCT image showing mid peripheral corneal stromal demarcation line after epi-ON PiXL with oxygen

Investigational. Not FDA approved.



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- A potential non-invasive solution for presbyopia
- Filling a gap in refractive treatment options
- Drops, UV light and O₂
- 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

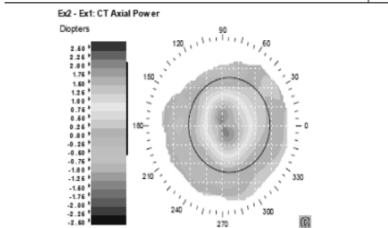


Investigational. Not FDA approved.

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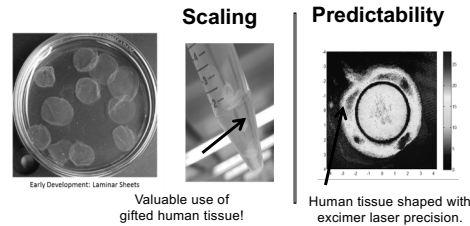
Allogenic Corneal Inlay (Allotex) PEARL: PrEsbyopic Allogenic Refractive Lenticule

- Increasing central corneal power to improve near vision



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Excimer laser shaped corneal inlays



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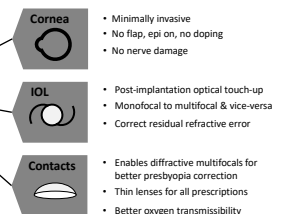
The LIRIC Platform: Laser Induced Refractive Index Change for Refractive Error Correction

LIRIC: a disruptive technology

Poised to revolutionize:

- refractive surgery
- cataract surgery
- contact lenses

A revolutionary way to
refine the optics of the eye



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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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