

Literature Review:

Accommodating IOLs



Editor: Ming Wang, MD, PhD, Research Associate Professor of Biomedical Engineering of Vanderbilt University and Director at Wang Vision Institute in Nashville, Tennessee



Reviewer: Y. Ralph Chu, MD, Adjunct Assistant Professor of Ophthalmology at the University of Minnesota Medical School and Medical Director, Chu Vision Institute in Edina, Minnesota

Coeditor: Tracy Swartz, OD, MS
Panel Members: Helen Abdelmalak, OD; Y. Ralph Chu, MD; Arun Gulani, MD; Walid Haddad, MD; Paul Karpecki, OD; and Jay S. Pepose, MD, PhD



Coreviewer: Megan Buliano, OD, Clinical Associate at the Chu Vision Institute in Edina, Minnesota

With the FDA's first approval of an accommodating IOL in November 2003, a significant step toward treating presbyopia was taken. In this brief review, we focus on some of the most recent literature concerning accommodating IOLs and pseudophakic accommodation. The Crystalens Model AT-45 (Eyeonics Inc., Aliso Viejo, CA), the 1CU Akkommodative (HumanOptics AG, Erlangen, Germany), and the dual-optic accommodating IOL (Visiogen Inc., Irvine, CA) will be discussed. The following is a list of the articles reviewed.

1. Findl O, Kiss B, Peternel V, et al. Intraocular lens movement caused by ciliary muscle contraction. *J Cataract Refract Surg.* 2003;29:669-676.
2. Cumming JS, Slade SG, Chayet A; AT-45 Study Group. Clinical evaluation of the Model AT-45 silicone accommodating intraocular lens: results of feasibility and the initial phase of a Food and Drug Administration clinical trial. *Ophthalmology.* 2001;108:2005-2010.
3. Lindstrom RL. Food and Drug Administration study update. One-year results from 671 patients with the 3M multifocal intraocular lens. *Ophthalmology.* 1993;100:91-97.
4. Steinert R, Aker BL, Trentacost DJ, et al. A prospective comparative study of the AMO ARRAY zonal-progressive multifocal silicone intraocular lens and a monofocal intraocular lens. *Ophthalmology.* 1999;106:1243-1255.
5. Langenbacher A, Huber S, Nguyen NX, et al. Measurement of accommodation after implantation of an accommodating posterior chamber intraocular lens. *J Cataract Refract Surg.* 2003;29:677-685.
6. Mastropasqua L, Toto L, Nubile M, et al. Clinical study of the 1CU accommodating intraocular lens. *J Cataract Refract Surg.* 2003;29:1307-1312.
7. McLeod SD, Portney V, Ting A. A dual optic accommodating foldable intraocular lens. *Br J Ophthalmol.* 2003;87:1083-1085.

CRYSTALENS MODEL AT-45

The Crystalens Model AT-45 accommodating IOL was FDA-approved on November 14, 2003. It is used in primary implantation within the capsular bag for the visual correction of aphakia in adult patients who had a cataractous lens removed.

Description

The Crystalens is a modified, hinged, plate-haptic silicone lens with polyimide loops. The lens has a high refractive index of 1.43 with a UV filter. The length of the lens plate is 10.5 mm, with a total IOL length of 11.5 mm. The lens optic is biconvex with a diameter of 4.5 mm.

The IOL offers near and intermediate focal ranges by way of anterior displacement of the lens optic due to fluctuating pressures within the vitreous cavity as the ciliary body contracts.

Study Outcomes

Findl et al¹ studied five different accommodative IOLs, including designs with the ring-haptic, plate-haptic lenses, and three-piece IOLs, and they concluded that a plate-haptic lens has an advantage over a three-piece lens in inducing pseudophakic accommodation. After comparing the results of pharmacologic-induced accommodation with pilocarpine and cyclopentolate, the investigators found that a deep anterior chamber depth with the plate-haptic group resulted in more IOL movement and a greater range of pseudophakic accommodation.

In an FDA study by Cumming et al,² the Crystalens AT-45 was found to provide excellent uncorrected distance, intermediate, and near visual acuities. Distance-corrected near visual acuity with the Crystalens resulted in 97% of patients' reading J3 or better. This result compared favorably to two studies. In Lindstrom's study³ with the Array multifocal IOL (Advanced Medical Optics, Inc., Santa Ana, CA), 48% of patients achieved J3 or better. In a study by Steinert et al⁴ with the 3M multifocal IOL (3M, St. Paul, MN), 37% of patients achieved J3 or better.

1CU AKKOMMODATIVE IOL

The 1CU Akkommodative IOL is based on the focus-shift principle. It has modified haptics that bend within the bag as the lens capsule moves anteriorly. This mechanism occurs in a similar fashion to that of the Crystalens. Langerbucher et al⁵ observed that approximately 1.80 D of accommodation occurs per 1 mm of anterior movement of the lens optic.

Description

The 1CU Akkommodative IOL is a foldable, single-piece IOL with an optic diameter of 5.5 mm and an overall length of 9.8 mm. The lens is composed of hydrophilic acrylic material with a refractive index of 1.46. The IOL has a biconvex, square-edged optic and four flexible haptics that bend when constricted in the capsular bag after ciliary body contraction.

Visual Outcomes

In a study by Mastropasqua et al,⁶ the 1CU Akkommodative IOL provided a statistically significant improvement in distance-corrected near acuity versus a conventional monofocal IOL. In the study group, the dis-

tance-corrected near visual acuity using Jaeger notation was 5.43 ± 0.98 at 7 days, 2.33 ± 0.48 at 1 to 3 months, and 3.66 ± 2.12 at 6 months postoperatively. Distance-corrected near visual acuity with the monofocal IOL measured Jaeger 7.43 ± 0.50 at all follow-ups with no change over time. The decrease in the accommodative amplitude for the 1CU Akkommodative IOL during the first 6 months was attributed to opacification of either the anterior or posterior capsule.

"The use of an accommodating IOL to improve near visual acuity in cataract surgery patients seems promising."

DUAL-OPTIC ACCOMMODATING IOL

The dual-optic accommodating IOL involves a different design than the lenses previously reviewed. This IOL has two lens optics.

Description

The dual-optic accommodating IOL is designed with an anterior converging or high-plus-powered lens and a posterior diverging lens, similar to a Galilean telescope. Pseudophakic accommodation occurs when the zonular tension is released during ciliary body contraction, thereby resulting in a compression of the optic and spring haptic. This results in axial lengthening of the capsular bag when the anterior optic releases forward.

Early Analysis

Ray tracing analysis results produced a significantly greater change in pseudophakic accommodation with the dual-optic accommodating IOL versus a monofocal IOL, according to McLeod et al.⁷ In this study, an anterior lens power of +32.00 D was used with a posterior lens power of -12.00 D and a 0.5-mm distance between the lenses. This model calculated approximately 2.20 D of accommodation with a 1-mm forward displacement of the anterior optic compared to a 19.00-D single-optic IOL, which resulted in 1.20 D of change.

THE BOTTOM LINE

According to study results, the use of an accommodating IOL to improve near visual acuity in cataract surgery patients seems promising. Longer-term studies with larger patient samples are needed. However, new lens developments and modifications will push the field forward and continue to make the pursuit of presbyopia therapy exciting. ■

**Reviewer:**

Y. Ralph Chu, MD, holds no financial interest in any product or company mentioned herein. He may be reached at (952) 835-1235; yrchu@chuvision.com.

Coreviewer:

Megan Buliano, OD, FAAO, holds no financial interest in any product or company mentioned herein. She may be reached at (952) 835-1235; megan.buliano@chuvision.com.

Panel Members:

Helen J. Abdelmalak, OD, is a resident in optometry at the Wang Vision Institute in Nashville, Tennessee. She holds no financial interest in any product or company mentioned herein. Dr. Abdelmalak may be reached at (615) 321-8881; dra@wangvisioninstitute.com.

Jay S. Pepose, MD, PhD, is Professor of Clinical Ophthalmology at Washington University, St. Louis. He holds no financial interest in any product or company mentioned herein. Dr. Pepose may be reached at (636) 728-0111; jpepose@peposevision.com.

Arun Gulani, MD, is Assistant Professor, Department of Ophthalmology; Director of Refractive Surgery; and Chief, Cornea and External Disease for the University of Florida at Jacksonville. He holds no financial interest in any product or company mentioned herein. Dr. Gulani may be reached at (904) 504-0090; arun.gulani@jax.ufl.edu.

Walid Haddad, MD, is a cornea fellow at the Wang Vision Institute in Nashville, Tennessee. He holds no financial interest in any product or company mentioned herein. Dr. Haddad may be reached at (303) 470-8388; md@walidhaddad.com.

Paul Karpecki, OD, FAAO, is Clinical Director of Cornea, Cataract, and Refractive Surgery at the Moyes Eye Institute in Kansas City, Kansas. He holds no financial interest in any product or company mentioned herein. Dr. Karpecki may be reached at (816) 746-9800; pkarpecki@moyeseye.com.

Tracy Swartz, OD, MS, is Educational Director at the Wang Vision Institute in Nashville, Tennessee. She holds no financial interest in any product or company mentioned herein. Dr. Swartz may be reached at (615) 321-8881; drswartz@wangvisioninstitute.com.

Ming Wang MD, PhD, holds no financial interest in any product or company mentioned herein. Dr. Wang may be reached at (615) 321-8881; drwang@wangvisioninstitute.com.

Keming Yu, MD, PhD, is a cornea fellow at the Wang Vision Institute in Nashville, Tennessee. He holds no financial interest in any product or company mentioned herein. Dr. Yu may be reached at (615) 321-8881; yukeming66@hotmail.com.

Sterile**INDICATIONS AND USAGE**

ZYMAR[®] solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

Aerobic Gram-Positive Bacteria:

<i>Corynebacterium propinquum</i> *	<i>Streptococcus mitis</i> *
<i>Staphylococcus aureus</i>	<i>Streptococcus pneumoniae</i>
<i>Staphylococcus epidermidis</i>	

Aerobic Gram-Negative Bacteria:

Haemophilus influenzae

* Efficacy for this organism was studied in fewer than 10 infections.

CONTRAINDICATIONS

ZYMAR[®] solution is contraindicated in patients with a history of hypersensitivity to gatifloxacin, to other quinolones, or to any of the components in this medication.

WARNINGS**NOT FOR INJECTION.**

ZYMAR[®] solution should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

In patients receiving systemic quinolones, including gatifloxacin, serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria, and itching. If an allergic reaction to gatifloxacin occurs, discontinue the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

PRECAUTIONS

General: As with other anti-infectives, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Information for Patients: Avoid contaminating the applicator tip with material from the eye, fingers or other source.

Systemic quinolones, including gatifloxacin, have been associated with hypersensitivity reactions, even following a single dose. Discontinue use immediately and contact your physician at the first sign of a rash or allergic reaction.

Drug Interactions: Specific drug interaction studies have not been conducted with ZYMAR[®] ophthalmic solution. However, the systemic administration of some quinolones has been shown to elevate plasma concentrations of theophylline, interfere with the metabolism of caffeine, and enhance the effects of the oral anticoagulant warfarin and its derivatives, and has been associated with transient elevations in serum creatinine in patients receiving systemic cyclosporine concomitantly.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There was no increase in neoplasms among B6C3F1 mice given gatifloxacin in the diet for 18 months at doses averaging 81 mg/kg/day in males and 90 mg/kg/day in females. These doses are approximately 2000-fold higher than the maximum recommended ophthalmic dose of 0.04 mg/kg/day in a 50 kg human.

There was no increase in neoplasms among Fischer 344 rats given gatifloxacin in the diet for 2 years at doses averaging 47 mg/kg/day in males and 139 mg/kg/day in females (1000 and 3000-fold higher, respectively, than the maximum recommended ophthalmic dose). A statistically significant increase in the incidence of large granular lymphocyte (LGL) leukemia was seen in males treated with a high dose of approximately 2000-fold higher than the maximum recommended ophthalmic dose. Fischer 344 rats have a high spontaneous background rate of LGL leukemia and the incidence in high-dose males only slightly exceeded the historical control range established for this strain.

In genetic toxicity tests, gatifloxacin was positive in 1 of 5 strains used in bacterial reverse mutation assays: Salmonella strain TA102. Gatifloxacin was positive in *in vitro* mammalian cell mutation and chromosome aberration assays. Gatifloxacin was positive in *in vitro* unscheduled DNA synthesis in rat hepatocytes but not human leukocytes. Gatifloxacin was negative in *in vivo* micronucleus tests in mice, cytogenetics test in rats, and DNA repair test in rats. The findings may be due to the inhibitory effects of high concentrations on eukaryotic type II DNA topoisomerase.

There were no adverse effects on fertility or reproduction in rats given gatifloxacin orally at doses up to 200 mg/kg/day (approximately 4500-fold higher than the maximum recommended ophthalmic dose for ZYMAR[®]).

Pregnancy: Teratogenic Effects. Pregnancy Category C:

There were no teratogenic effects observed in rats or rabbits following oral gatifloxacin doses up to 50 mg/kg/day (approximately 1000-fold higher than the maximum recommended ophthalmic dose). However, skeletal/craniofacial malformations or delayed ossification, atrial enlargement, and reduced fetal weight were observed in fetuses from rats given ≥ 150 mg/kg/day (approximately 3000-fold higher than the maximum recommended ophthalmic dose). In a perinatal/postnatal study, increased late post-implantation loss and neonatal/perinatal mortalities were observed at 200 mg/kg/day (approximately 4500 times the maximum recommended ophthalmic dose).

Because there are no adequate and well-controlled studies in pregnant women, ZYMAR[®] solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Gatifloxacin is excreted in the breast milk of rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when gatifloxacin is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in infants below the age of one year have not been established.

Geriatric use: No overall differences in safety or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

Ophthalmic Use: The most frequently reported adverse events in the overall study population were conjunctival irritation, increased lacrimation, keratitis, and papillary conjunctivitis. These events occurred in approximately 5-10% of patients. Other reported reactions occurring in 1-4% of patients were chemosis, conjunctival hemorrhage, dry eye, eye discharge, eye irritation, eye pain, eyelid edema, headache, red eye, reduced visual acuity and taste disturbance.

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