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LIGHT-ADJUSTABLE INTRAOCULAR LENSES

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Although progress in preoperative biometry and operating techniques for implantation of IOLs has led to postoperative refractions that, on average, are close to the usually emmetropic target values, individual variability in the achieved equivalent sphere can be large, and significant amounts of astigmatism are often either introduced or remain uncorrected, even when toric IOLs are used. These residual errors in refraction arise from such factors as imprecise biometry, the effects of the incision, variations in wound healing, and variability in the position of the IOL. These residual errors make a further refractive correction, such as spectacles, contact lenses, or corneal refractive surgery, necessary if good visual acuity is to be achieved.

The problem is even more serious when bifocal, multifocal, or other aspheric IOLs are implanted, as failure to achieve the target refraction means that the effectiveness of these corrections in providing clear vision over a range of distances (from distance to near) may be compromised. Evidently, even though the depth of focus (DOF) may be usefully enlarged with such lenses, one end of the DOF must correspond to distance vision to be fully effective in practice. Displacement of the postoperative refraction in the

hyperopic direction means that the range of object vergence covered by the DOF is shifted in that direction and near vision is compromised; alternatively, a shift in the myopic direction will give poor distance vision (Figure 20-1). Similarly, monovision demands not only that one eye should be in focus for distance and the other for near but also that the dioptric difference between the 2 postoperative ocular refractions should not be too large (see Chapter 16). Failure to achieve the target refraction in each eye will therefore not only compromise either or both distance and near vision but may lead to symptoms of discomfort and a loss of stereopsis due to an excessive level of anisometropia or an absence of effective monovision (because both eyes have similar refraction).

How large are these postoperative errors? Surveys suggest that with single-vision IOLs and current techniques, most patients are within 2.00 D of the intended postoperative refraction.¹⁻⁴ Murphy et al, for example, found that 72% of 1700 cataract cases had postoperative refractions within 1.00 D of the target, and 94% were within 2.00 D.³ However, only 6% of eyes attained uncorrected visual acuities of 6/12 or better (0.3 logMAR, decimal 0.5), although a higher proportion of patients with satisfactory

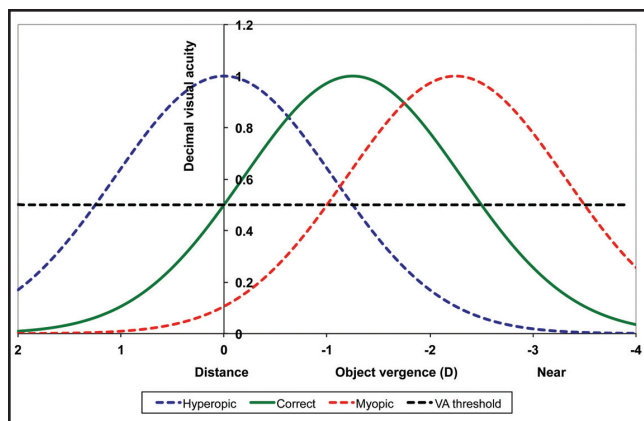


Figure 20-1. Schematic illustration of the effect of failure to achieve the target refraction with a hypothetical aspheric IOL designed to provide enhanced depth of focus (DOF) for distance and near vision. The DOF, defined as the range of object vergence within which the decimal visual acuity exceeds 0.5 (6/12 equivalent, 0.3 logMAR), is 2.50 D. A slightly myopic target refraction of -1.25 D makes optimal use of the available DOF and gives reasonable distance, intermediate, and near vision (full green line). A failure to achieve this target refraction compromises near (blue) or distance (red) vision, although the DOF remains unchanged.

uncorrected postoperative acuity have been found in other studies.⁵ It would obviously be desirable to adopt a cataract surgery technique in which it was possible to alter the postoperative power of the implanted IOL over a range of at least ± 2.00 D in sphere and cylinder to correct these residual refractive errors and provide optimal vision without the need for a spectacle or other correction. Following earlier attempts to develop an IOL with power that could be altered after the lens had been implanted but were limited to changes in spherical power, in 2003, Schwartz described the light-adjustable IOL (marketed by Calhoun Vision, Pasadena, CA) in which both spherical and astigmatic powers can be adjusted together with, in principle, the higher-order aberrations.⁶⁻⁸

THE BASIC LIGHT-ADJUSTABLE LENS

The light-adjustable lens (LAL) consists of a moulded, flexible, silicone polymer matrix, containing a photoreactive silicone macromer, a benzoin-based photoinitiator, and UV absorbers. An additional UV-absorbent layer is applied to the back of the lens. Irradiation of the LAL with UV light (365 nm) causes photopolymerization of the macromer molecules. These then form silicone polymers, which create an

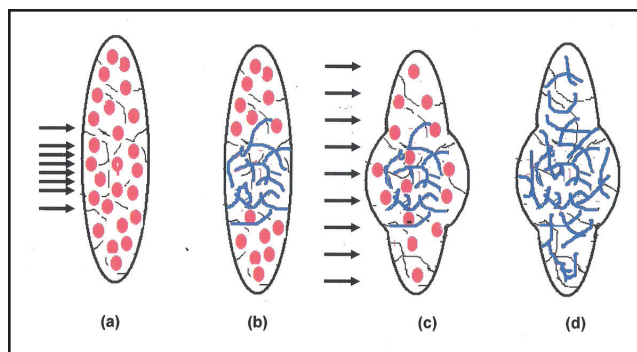


Figure 20-2. Basic LAL procedure for increasing the power of the LAL in cases where the postoperative eye has been left hyperopic. (A) Initially, the macromer molecules (red) are uniformly distributed throughout the lens. (B) A central exposure to an appropriate UV irradiation profile (black arrows) polymerizes some of the macromers (blue). (C) After 24 hours, the macromers have migrated to re-establish a uniform but lower concentration throughout the lens. This causes the central region of the lens to increase its curvature. (D) A final uniform UV exposure then “locks in” this increased curvature by polymerizing all of the remaining macromers.

interpenetrating network within the silicone matrix. The silicone polymers accumulate in the region of the lens that has been irradiated, their concentration being proportional to the exposure received (irradiance \times time). In practice, the incident UV flux is varied in a controlled way across the surface of the lens. If, for example, the lens periphery receives more irradiation, the resultant concentration of polymers is higher in this region. As a result, after the UV exposure, the concentration of unpolymerized macromers in the lens periphery is lower because it has been depleted by the polymerization process. In contrast, because the lens center received a lower irradiation, the concentration of macromers in this region remains relatively high. Thus, an unstable diffusion gradient is created and, over a period of 12 to 15 hours, some of the unchanged macromers diffuse along the gradient from the center to the periphery of the lens to progressively reduce the gradient and eventually re-establish a uniform macromer concentration throughout the silicone matrix. As a consequence of this movement of the macromers into the lens periphery, this region of the lens swells and flattens the surfaces of the lens, reducing its power. Thus, any residual myopia can be corrected. Had the center of the lens been irradiated more than its periphery, polymerization would have been highest in this region with migration of macromers toward the central region. The resultant central swelling would steepen the lens surfaces and increase the lens power, thus correcting any residual hyperopia (Figure 20-2).

Rather than using a rotationally symmetric pattern of irradiation to change the spherical power, a pattern that varies along (or perpendicular to, depending on the cylinder notation used) the axis of astigmatism can be applied to give a cylindrical correction, and the spatial pattern of irradiation used is analogous to those used in excimer laser corneal refractive surgery (Figure 20-3). Exposures required for refractive changes of approximately 1.00 D are of the order of 1 J/cm^2 , the patient's eye typically being exposed to the UV at an irradiance level of approximately 12 mW/cm^2 for approximately 40 to 120 seconds.⁹

After the desired final refractive outcome has been achieved, the whole lens can be exposed to a spatially uniform distribution of UV to polymerize all of the remaining macromers. This “locks in” the power of the lens, which is then unaffected by exposure from ambient UV, such as sunlight. The UV-absorbing layer (thickness $50 \mu\text{m}$) on the rear surface of the lens is intended to protect the retina from possible UV light damage during the irradiation process.

PRACTICAL PROCEDURE

The procedure for implantation of the LAL is similar to that for other 3-piece, folding IOLs with poly(methyl methacrylate) haptics. Power is selected from the available range of +10.00 to +30.00 D following appropriate biometry and calculation using a formula provided by the manufacturer, with the aim being to achieve the target refraction. Under topical anesthesia, anterior capsulotomy and phacoemulsification are performed, and foldable lens insertion forceps are used to implant the LAL in the capsular bag. The operated eye is patched overnight. A period of 7 to 21 days is then allowed for healing and refractive stabilization. During this period, the patient wears UV-absorbing spectacles to prevent premature polymerization in the lenses by UV from ambient light sources, such as the sun. At the end of this period, the refraction is reassessed, and any necessary adjustments in spherical or cylindrical power within the range of ± 0.25 to ± 2.00 D are made by the application of an appropriate spatial distribution of UV light using suitable nomograms.¹⁰ The irradiation is applied using a digital light-delivery device, consisting of a UV source (a mercury arc lamp filtered to produce light of spectral bandwidth $365 \pm 4 \text{ nm}$), projection optics, and control interface installed on a standard slit lamp. The projection system includes a digital mirror device,

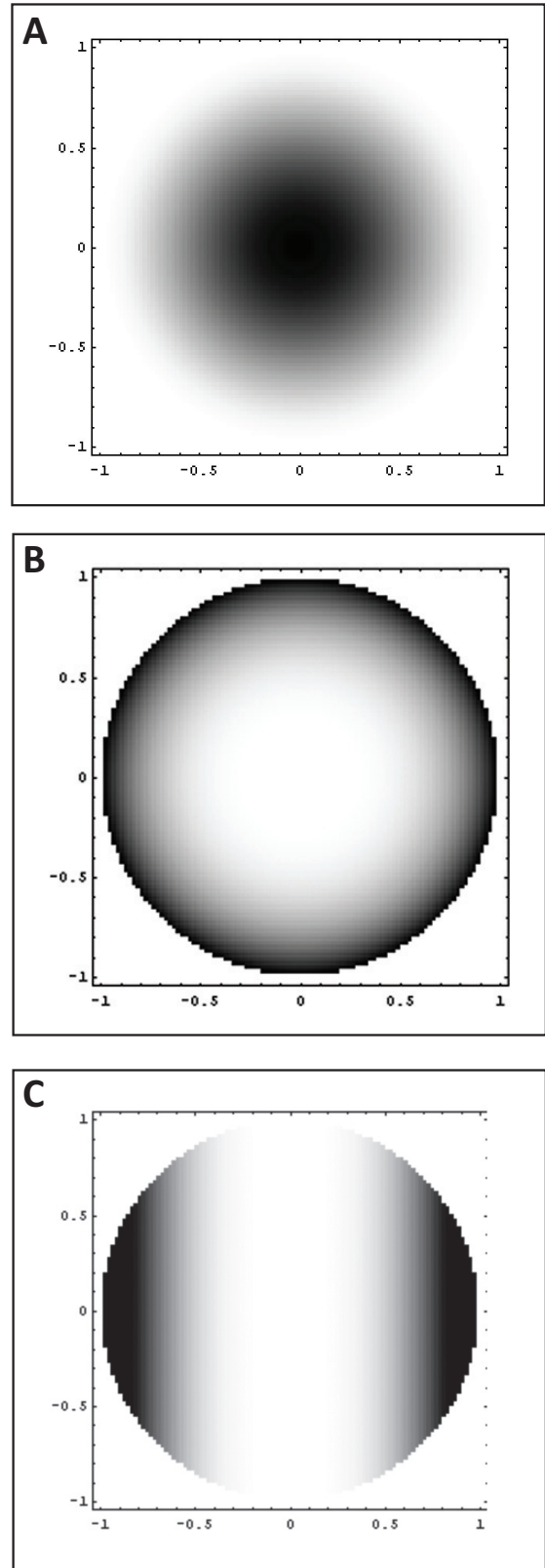


Figure 20-3. Basic irradiation patterns (A) decrease in lens power (eye initially myopic), (B) increase in lens power (eye initially hyperopic), and (C) astigmatism. Dark areas represent low irradiance, and light areas represent high irradiance.

which forms a pixelated micromechanical spatial light modulator.¹⁰ This can be programmed to deliver not only spatial irradiation patterns to correct spherocylindrical errors but also, in principle, spherical or other higher-order aberrations. The patient is fully dilated and is positioned on the chin and headrest of the light-delivery device. A fixation point is provided to maintain eye stability during the UV exposure. As discussed previously, a further refraction is performed 1 to 2 days after irradiation to assess the correction achieved. Depending on the result, the LAL is either immediately locked, or a further adjustment in power is made. If the latter is required, it is followed by further refractive assessment the next day, and, if the result is satisfactory, the LAL is locked in. Although in the majority of cases only a single adjustment is required, occasionally 2 or 3 adjustments may be necessary before the lens is locked in.¹¹

PROPERTIES OF CURRENT LIGHT-ADJUSTABLE LENSES AND SAFETY CONSIDERATIONS

Biocompatibility and Other Properties of the Lens Material

Biocompatibility and other properties of the lens material were extensively investigated early in the lens development.^{6,10,12} Cytotoxicity, hydrolytic stability, photostability, mechanical properties, and resistance to Nd:YAG laser exposure were all studied and proved to be satisfactory. Mechanical properties of the Calhoun LALs are similar to those of conventional, commercially available, silicone IOLs.

Optical Performance of Lenses

Manufacturing tolerances, modulation transfer, and resolution were all within acceptable limits.¹³ The adjustment procedure produces consistent, reproducible, and stable power changes.^{9,10,14}

Safety of Ultraviolet Exposures in the Adjustment Process

The human cornea is usually considered to absorb UV light below approximately 300 nm, with the peak of the action spectrum for photokeratitis occurring

around 270 nm. At 365 nm, the total corneal transmittance to the plane of the lens is approximately 75% due to reflection, scattering, and absorption losses. Thus, although most of the UV light is transmitted, a small fraction of light is absorbed and could potentially cause damage to the cornea. Taking into account the thresholds for corneal and retinal damage from monkey and other studies, Schwartz⁶ suggested that the upper limit for 365-nm exposure at the cornea should be approximately 27 J/cm² and that no more than 2 J/cm² should reach the retina in any 24-hour period.

The expected lack of damage to the corneal endothelium with exposures of approximately 30 J/cm² has subsequently been supported by laboratory studies on cats.¹⁵ More importantly, in a specular microscope study of 10 patients who had undergone LAL implantation, Lichtinger et al¹⁶ found that any loss in endothelial cell density was comparable to that found in patients who had been implanted with conventional IOLs after a similar phacoemulsification procedure.

The concentrations of the UV-absorber and photoinitiator in the lens are such as to be expected to provide both effective photoinitiation and protection of the retina from any adverse effects of transmitted UV.⁶ This prediction has been confirmed by studies on rabbit eyes implanted with the LAL, where doses of up to 235 J/cm² (5 times the normal expected maximum exposure used in clinical practice to adjust the LALs) failed to cause any histopathologically detectable corneal, anterior segment, or retinal damage.¹⁷

CLINICAL RESULTS

Only a few small-scale pilot studies have so far been published, all with limited numbers of patients and periods of follow-up. Chayet et al¹⁸⁻²⁰ have demonstrated successful correction of 1.50 D postoperative myopia or hyperopia and 2.00 D astigmatism, and the results remained stable during 9 months of follow-up. Figure 20-4 shows the improvements in uncorrected distance visual acuity achieved as a result of lens adjustment in their initially myopic and hyperopic groups, and demonstrates the improvement in uncorrected visual acuity that can be achieved when initial postoperative errors are in the ± 2.00 -D range. Other studies^{21,22} have shown that postoperative residual errors in sphere and cylinder can be reduced to within ± 0.25 D in the majority of cases.

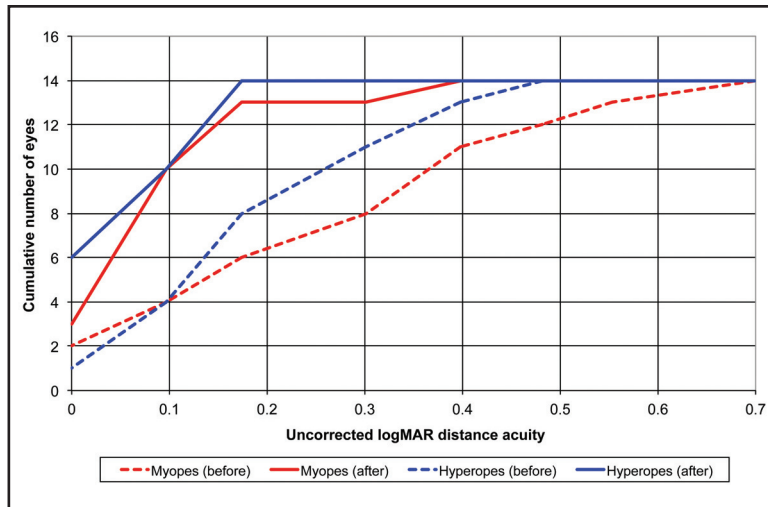


Figure 20-4. Improvements in uncorrected distance decimal visual acuity achieved following lens power adjustment in groups of 14 eyes in 2 studies by Chayet et al.^{18,19} The dashed curves show the cumulative frequency distributions immediately after implantation of light-adjustable IOLs; the full curves represent after adjustment of lens power. Note that the initial refractions were deliberately intended to be ametropic. (Based on data compiled from Chayet A, Sandstedt C, Chang S, et al. Correction of myopia after cataract surgery with a light-adjustable lens. *Ophthalmology*. 2009;116(8):1432-1435 and Chayet A, Sandstedt CAS, Chang SH, Rhee P, Tsuchiyama B, Schwartz D. Correction of residual hyperopia after cataract surgery using the light adjustable intraocular lens technology. *Am J Ophthalmol*. 2009;147(3):392-397.)

In considering these results, it must be remembered that the repeatability of refractive measurements is only approximately ± 0.30 D.^{22,23} Thus, in general, the above results for refractive correction suggest that the refractive outcomes are both stable and very close to the target refractions. On the other hand, a variety of exclusion criteria were applied when selecting patients for the pilot studies so that the results may not fully represent normal clinical populations of cataract patients.

One issue still to be fully resolved is the possibility of differences in the transmittance of individual corneas at 365 nm and the effect that this might have on the adjustment procedure.¹⁰ Note, however, that should the correction undershoot or overshoot, it would still be possible to reduce the error to a clinically insignificant level by a second adjustment. A further concern is the necessity to be able to fully dilate the pupil (to >7 mm) to ensure that the lock-in exposure covers the entire 6-mm diameter of the current lenses. Schwartz et al¹⁰ considered possible ways to overcome this difficulty.

Overall, the clinical results with the current single-vision LALs are very promising. The results of larger-scale studies with longer follow-up should soon be available.

POSSIBLE FUTURE DEVELOPMENTS

Although discussion so far has focused on the adjustment of spherocylindrical corrections, it was envisaged from the outset of the development of the LAL that it would theoretically be possible to introduce or correct higher-order aberrations (eg, spherical

aberration) or to modify the lens so that it acted as a bifocal or multifocal or had any desired aspheric or diffractive configuration.⁶⁻⁸ All that is required is to generate an appropriate apodization of the UV beam by suitably programming the digital mirror device in the light-delivery system. This possibility has been explored by Sandstedt et al⁹ in a series of in vitro experiments and with LALs implanted in rabbits. It was demonstrated that it is possible to modify the originally single-vision LAL to form a center-near bifocal, with the power and diameter of the near portion being selected by the operator, or a bifocal with an annular addition zone. Of particular interest is that, in spite of the dependence on diffusion effects to generate the power changes, the boundaries of the bifocal or other segments created in vitro appear to be sharply defined so that abrupt discontinuities in the power profile of the LAL can be achieved. Other LALs were successfully modified, both in vitro and when implanted in rabbits, to create aspheric designs of presbyopic addition by effectively modifying the spherical aberration of the lenses. Finally, the possibility of correcting or introducing other higher-order aberrations was demonstrated by generating additional Zernike fourth-order tetrafoil aberration in a rabbit eye.

Despite the success of these studies, it does not appear that similar trials have been conducted on human eyes. Doubts have been raised as to whether human patients are capable of maintaining fixation for the 1 to 2 minutes required in the lens-adjustment procedure. This might affect the fidelity with which the intended power adjustment is produced. However, it is claimed that this is not a problem, and incorporation of an eye tracker is a possible solution.⁹ It would

obviously be straightforward to combine a wave aberrometer with the LAL light delivery device, so that the wavefront measurement formed the basis of the computations for the exposure pattern needed to achieve the desired levels of Zernike second-order spherocylindrical correction and higher-order aberration.¹⁴ Full customization for the characteristics and needs of the individual patient would therefore be possible.

With regard to customization, one attractive possibility with presbyopic corrections created using light-adjustable IOLs is that patients would have the opportunity to evaluate the effectiveness of the lens in relation to their individual needs before the corrections were locked in. If the patient were to consider that the initial result was unsatisfactory, a further adjustment could be made (eg, to restore bifocal lenses to single-vision form and monovision).⁶

At present, readjustments in the lens form and power can be done only before the lenses are locked in, after approximately 2 weeks. If the lenses are not locked, further polymerization of the remaining macromers will occur; the combination of sunlight and the normal small photopic pupil will eventually mean that this occurs primarily in the central region of the lens, thus increasing its power and making the eye more myopic (although exposures of up to 2 hours to mid-day levels of sunlight do not produce significant optical changes). Schwartz et al⁶ and others^{7,8} have speculated that it will eventually be possible to develop a lens material that does not require corrections to be locked in. If this could be achieved, any changes in refraction with age could be corrected every year or two as necessary. Longer life expectancy combined with the trend to perform cataract surgery at earlier ages²⁴ makes this a very attractive possibility. It may be, however, that this goal will prove to be a difficult one. For example, increasing the exposure required to adjust the lens would make the LAL less sensitive to sunlight but would increase radiation safety hazards.

A further speculation is that it may be possible to use LAL materials in attempts to restore active accommodation to the presbyope.^{7,8} As with single-vision IOLs, failure to achieve the targeted “unaccommodated” refraction may occur with any design of A-IOLs. Incorporating an anterior LAL element would allow appropriate power adjustments to be made so that optimal use was made of any active accommodation achieved. A more remote possibility is that of refilling the capsular bag or inserting a flexible lens with mechanical characteristics matching those of the

youthful crystalline. However, one of the many problems is that the refilled bag must render the patient emmetropic when the eye is unaccommodated. If a light-adjustable material were to be used, the power could again be altered after implantation to achieve the desired refractive result.

It is clear that this technology has not only proven effective in clinical pilot studies but is also opening up a number of intriguing avenues for possible future development. The LAL does not appear to demand any novel surgical skills, nor are costs excessive. Customization to the needs of the individual patient is easy to achieve. It must be remembered, however, that, at its present stage of development, although the LAL technology effectively guarantees that the target refraction can be achieved, the ultimate optical and visual performance conferred on the presbyope is no better than that achievable with optimized conventional lenses, whatever the modality used (bifocal, multifocal, aspheric, monovision, etc), because the optical constraints are similar.

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