Prospective multicenter trial assessing effectiveness, refractive predictability and safety of a new aberration free, bi-aspheric intraocular lens

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ABSTRACT

Purpose: To determine the effectiveness and safety of the Softec HD IOL; and to present refractive outcomes for lenses manufactured at an IOL power tolerance of 0.11 D.

Methods: Three-hundred and ninety adult patients requiring removal of a cataractous lens with implantation of a monofocal IOL in at least one eye were eligible for study participation across eight US investigative sites. Patients were enrolled unilaterally. After routine surgery, subjects were examined for adverse events (AEs), best corrected visual acuity (BCVA) and manifest refraction correction at 12 months postoperatively.

Results: Three-hundred and sixty-six (95%) of patients completed the 12-month postoperative visit. The percent of patients achieving best corrected Snellen acuity 20/40 or better was 98.9%, and 81.1% of patients achieved best corrected Snellen acuity 20/25 or better. Of those patients (80%) implanted with a lens available in 0.25 D increments (manufactured at a tolerance of 0.11 D) 40.9%, 69.8% and 93.8% of patients were within ±0.25 D, ±0.50 D and ±1.0 D of predicted target refraction respectively. Overall incidence of cumulative and persistent IOL Grid AEs was 2.2% with no AE meeting or exceeding the FDA Grid of Historical Controls.

Conclusions: The Softec HD IOL is a safe and effective lens. The high manufacturing tolerance of the lens appears to enhance refractive outcomes.

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1. Introduction

Modern day foldable aspheric intraocular lenses (IOLs) were first introduced to the United States (US) market in 2001 with Advanced Medical Optics’ (Santa Ana, CA) Z9000 IOL. The optic of the modern day aspheric is not uniformly curved, and has at least one surface that flattens toward the periphery. This flattening, or asphericity, differentially refracts off-axis light rays so as to focus them with on-axis, paraxial rays. In emmetropic eyes, the ideal point of focus (paraxial focus) is directly on the retina for all light rays. If light rays fall short of paraxial focus, myopia is assumed and visa versa.

Over the past decade, the benefits of aspheric IOLs have been studied and detailed. Benefits attributed to aspheric IOL technology, specifically superior contrast sensitivity, were first reported in 2002 by Packer and colleagues [1] and have been demonstrated with other aspheric designs [1–3]. Improvements of visual acuity [4,5], reading speed, [6] and driving safety [7] attributed to the aspheric optic have also been reported. However, results are mixed with some studies finding little to no benefit with an aspheric IOL compared to a spherical IOL [8–10]; and some studies indicating decreased depth of focus with asphericity [11,12].

Inconsistent study results may be attributed to a myriad of factors including lens tilt and decentration, the amount of spherical aberration incorporated within the lens, and variability of corneal spherical aberration within subjects [13]. Aspheric IOL designs differ by manufacturer and within a manufacturer, causing some experts to suggest matching patients to specific lenses through pre-operative corneal aberration profiling [14–16]. Regardless, surveys of US and European cataract surgeons indicate that the aspheric lens is preferred to the spherical [17,18].

Lenstec, Inc. (St. Petersburg, FL) produces a bi-aspheric, aberration neutral IOL, the Softec HD, which has been on the market.
Twenty-six surgeons performed study surgeries. Eyes were prepped and anesthetized for the cataract procedure per each surgeon’s standard methodology. Surgeons performed phacoemulsification and made a continuous curvilinear capsulorhexis (CCC) surgeon’s standard methodology. Surgeons performed phacoemulsification and made a continuous curvilinear capsulorhexis (CCC) surgery per his standard technique for pre-surgical biometry (A-scan ultrasound or Zeiss IOL Master) and keratometry (manual or automated IOL Master) measures. Investigators were instructed to utilize the power calculation formula with which they were most comfortable, obtaining the calculation from the IOL Master (Carl Zeiss Meditec, Jena, Germany). An A constant of 118.54 for the SRK/T formula and 118.24 for the Hoffer Q, Holladay 1, or Holladay 2 formulas were recommended by the study sponsor, though not optimized for the IOL Master at this stage. All subjects received the same treatment (Softec HD IOL) in this single-group study.

2.2. Surgical technique

Twenty-six surgeons performed study surgeries. Eyes were prepped and anesthetized for the cataract procedure per each surgeon’s standard methodology. Surgeons performed phacoemulsification and made a continuous curvilinear capsulorhexis (CCC) of up to 5.5 mm. Lenses were loaded in the LENSTEC Softec Injection System with DuoVisc (Alcon Laboratories, Ft. Worth, TX), 2% hydroxypropylmethylcellulose or sodium hyaluronate; and injection system. With DuoVisc (Alcon Laboratories, Ft. Worth, TX), of up to 5.5 mm. Lenses were loaded in the LENSTEC Softec Injection System with DuoVisc (Alcon Laboratories, Ft. Worth, TX), 2% hydroxypropylmethylcellulose or sodium hyaluronate; and injected into the capsular bag with both haptics securely positioned in the bag. Viscoelastic was irrigated and aspirated, and the wound hydrated and sealed. Each surgeon utilized his standard preoperative, intra-operative and postoperative medication regimen.

3. Results

3.1. Patient characteristics

Of the 390 subjects enrolled, 366 (95%) completed the 12-month postoperative visit. The subject population was 58.2% female and 41.8% male, the majority of which were Caucasian (85.6%). The mean age of the population was 70.8 years (range 24.4–90.8 years). Macular degeneration, with clinician predicted BCVA better than 20/40, was present in 3.1% of cases.

3.2. Effectiveness assessment

The primary efficacy endpoint, the percentage of eyes with BCVA 20/40 or better at the 12-month postoperative visit (98.9%), exceeded the FDA Grid of Historical Controls (88.3%) for the “All Eyes” cohort. Similarly the “Best Case” cohort, those patients without pre-existing conditions, exceeded the Grid (98.8% versus 93.6%). Fig. 1 presents Snellen visual acuity by cumulative percentages for the full cohort. The cohort’s mean spherical equivalent (SE) was −0.13 (±0.72) D.

Of the 366 subjects completing the study, 291 (80%) were implanted with an IOL in dioptic range from 18 to 25. In this subgroup of study subjects 99.3% had a BCVA 20/40 or better and 80.0% were 20/25 or better 12 months postoperatively. Mean SE was −0.11 (±0.66) D. The mean predicted target (as determined by the IOL Master) versus achieved manifest refraction spherical equivalent (MRSE) was calculated 1, 3–6 and 12 months postoperative,
Table 1
Target versus achieved refraction in subjects with IOL in range from 18.0 to 25.0 D.

<table>
<thead>
<tr>
<th>Sample size</th>
<th>1 Month postoperative</th>
<th>3–6 Months postoperative</th>
<th>12 Months postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>306</td>
<td>295</td>
<td>291</td>
</tr>
<tr>
<td>Mean target versus achieved refraction (D)</td>
<td>0.04 (0.52 SD)</td>
<td>−0.08 (0.52 SD)</td>
<td>−0.10 (0.52 SD)</td>
</tr>
<tr>
<td>±0.25 D</td>
<td>43.1</td>
<td>40.7</td>
<td>40.9</td>
</tr>
<tr>
<td>±0.50 D</td>
<td>72.2</td>
<td>68.5</td>
<td>69.8</td>
</tr>
<tr>
<td>±0.75 D</td>
<td>87.6</td>
<td>85.1</td>
<td>85.9</td>
</tr>
<tr>
<td>±1.00 D</td>
<td>93.5</td>
<td>94.6</td>
<td>93.8</td>
</tr>
</tbody>
</table>

Table 2
Percentage of adverse events in the Softec HD IOL study group and the FDA grid of historical controls.

<table>
<thead>
<tr>
<th>Softec HD IOL (n = 366)</th>
<th>FDA Grida</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative adverse events through 1 year</td>
<td></td>
</tr>
<tr>
<td>Cystoid macular edema</td>
<td>0.8%b</td>
</tr>
<tr>
<td>Hypopyon</td>
<td>0%</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0%</td>
</tr>
<tr>
<td>Dislocated lens</td>
<td>0%</td>
</tr>
<tr>
<td>Pupillary block</td>
<td>0%</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>0%</td>
</tr>
<tr>
<td>Secondary surgical interventionc</td>
<td>0.8%</td>
</tr>
<tr>
<td>Persistent adverse events at 6 months and/or 1 year</td>
<td></td>
</tr>
<tr>
<td>Corneal stromal edema</td>
<td>0%</td>
</tr>
<tr>
<td>Cystoid macular edema</td>
<td>0.8%b</td>
</tr>
<tr>
<td>Iris</td>
<td>0.3%</td>
</tr>
<tr>
<td>Raised IOP requiring treatment</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

a Grid rate for sample size of 300 subjects.
b Identical cases reported in persistent and cumulative CME rows.
c All unrelated to Softec HD IOL.

3.3. Safety assessment

Overall incidence of cumulative and persistent IOL adverse events (AEs) in the Softec HD IOL study group was 2.2%. No AE met or exceeded the FDA Grid of Historical Controls. Specific adverse events rates and Grid rates can be found in Table 2. The 3 secondary surgical reinterventions (0.8%) were an epiretinal membrane peel with vitrectomy and focal laser, a repositioning of a floppy iris from the corneal wound in the first postoperative week, and a YAG Laser vitreolysis for vitreous wick syndrome. Three patients (0.8%) developed cystoid macular edema (CME) that all resolved prior to the 12-month postoperative visit. The raised IOP requiring treatment was attributable to a triamcinolone acetonide injection given to treat one of the 3 CME patients. Non-Grid adverse events included one subretinal hemorrhage and nine instances of haptic break occurring at surgery.

4. Discussion

The objective of this study was to prove the efficacy, refractive predictability and safety of the Softec HD IOL as established by the FDA Grid of Historical Controls. The Grid was developed to provide a control for safety and performance endpoints. Weighted averages were derived from data collected during eight posterior chamber IOL investigations undertaken between December 1989 and December 1997. The number of patients seen 12 months postoperatively achieving best corrected acuity (BCVA) 20/40 or better (99.9%) exceed the Grid rate (88.3%); and 81.1% of patients achieved BCVA 20/25 or better. Likewise, the Softec HD was found to be safe with an overall AE rate of 2.2%. AEs did not exceed the Grid rate. Haptic break did occur at 3 of the 8 clinical sites. Breaks were found to be related to the improper loading of the lens into the injector. After further training, no further haptic breaks occurred. Surgeons have since reported no haptic break in over 1000 consecutive implants.

The Softec HD effectiveness and safety results compare favorably to the standard aspheric IOLs on the market including the AcrySof IQ SN60WF (Alcon Laboratories, Ft. Worth, TX) and the Tecnis 1-piece ZCB00 (Advanced Medical Optics, Santa Anna, CA). Clinical trial results for the SN60WF parent lens (SB30AL) indicate 99.3% of the overall population and 100% of the best case population achieved a BCVA 20/40 or better [21]. The overall AE rate was 8.0%. The ZCB00 IOL clinical trial (parent lens AAB00) resulted in
99.1% of the best AAB00 population achieving a BCVA of 20/40 or better 4–6 months postoperatively [22]. An overall AE rate of 6.5% was reported.

As a secondary step in the present study, predicted target refraction was compared with postoperative spherical equivalent refraction for the purpose of reporting accuracy related to the 0.11 D manufacturing tolerance of the 18.0–25.0 D IOL series. Current ISO standards call for a manufacturing tolerance of 0.40 D [1]. Results indicated that 40.9% of patients achieved postoperative refraction within ±0.25 D of target at the 12-month postoperative visit. Within ±0.5 D and ±1.0 D of target were 69.8% and 93.8% of patients respectively. Percentage distributions were consistent from 1 month to 12 months postoperatively.

Gale and colleagues [23] performed a study of approximately 4800 eyes that underwent cataract surgery from January 2003 to May 2006. The authors analysed postoperative refractive outcomes in an effort to establish benchmark standards. They concluded that 55% and 85% of patients achieve a refractive outcome within ±0.5 D and ±1.0 D of target respectively. Similar results have been published with Zaidi and colleagues [24] citing 65.7% and 80.0% of patients within ±0.5 D and ±1.0 D of target respectively, and Lundström and colleagues [25] reporting 77.7% of patients within ±1.0 D with a mean predicted versus achieved refraction of 0.71 D. Table 3 reports target versus achieved results for the current study and all studies cited here.

The Gale study demonstrated increased refractive accuracy over time as the facility employed new technology. The authors broke data audits into three cycles based on the introduction of a partial coherence interferometer (IOL Master) and the introduction of two new IOL models. The authors attribute an 11% increase (48.9–60.2%) in patients achieving a refractive outcome within ±0.5 D of target to (1) use of the appropriate biometry formula, (2) routine use of optical biometry, and (3) continuous customisation of A constants.

It has long been common knowledge that several factors affect the ability to achieve accurate refractive results. These variables include (1) accuracy of preoperative measures (biometry and keratometry), (2) surgical technique, (3) the ability to estimate postoperative effective lens position (ELP), and (4) dioptric power accuracy of the implanted IOL [26]. Gale demonstrated that optimising several of the above variables resulted in greater refractive accuracy. Likewise, the results of the current study suggest that stringent manufacturing tolerances, up to approximately four times (0.11 D versus 0.40 D) more stringent than published standards [27], may increase refractive accuracy. This finding is particularly encouraging as refractive accuracy was not a planned outcome variable in the current study. As such, preoperative keratometry and biometry measures were not standardized, a particular biometry formula was not mandated, and customized A constants were not possible. Regarding biometry it may be noted that studies have validated the accuracy of the IOL Master in comparison to A-scan ultrasound [28–30], with IOL Master often preferred for refractive predictability [28,30] and simplicity [28,29]. It is likely that even greater refractive accuracy with a 0.11 D manufacturing tolerance would be obtained in a setting which standardizes these variables.

Benefits and drawbacks attributed to asphericity, such as contrast sensitivity and depth of focus respectively, were not tested as part of the current study. Craig et al. compared contralateral eyes of 37 subjects implanted with the aspheric Softec HD in one eye and the spherical parent IOL, the Softec 1, in the fellow eye [31]. These researchers reported no differences between IOL groups for BCVA or contrast sensitivity, however the study groups were small. Investigators did find statistically significant differences in push-up test range of focus and defocus curve range of focus; these differences favored the Softec HD eye. Reading speed was also assessed with no difference found between lens groups for speed, though statistically significant differences between critical print size (the smallest print size that the patient can read at maximum speed) were found. Again, these differences favored the Softec HD IOL. No between-group differences existed with regard to total higher order aberrations, however the aspheric lens had 20% less spherical aberration than the spherical lens group with a 6 mm pupil diameter.

In conclusion, the Softec HD IOL with an aberration free, bi-aspheric optic, is an effective and safe lens. The manufacturing tolerance of the lens may enhance its attractiveness as patients demand more accurate refractive outcomes.

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**References**


