Review of “Intraoperative aberrometry vs. standard calculation methods for bilateral toric IOL implantation with a wavefront aberrometer” by Susie Drake, MD, Robert Hyde, MD, Shilpa Gulati, MD, Alex Pleet, MD, Mei Zhou, MD, Kai Kang, MD, and Siya Hsu, MD, Illinois Eye and Ear Infirmary, University of Illinois at Chicago

Cataract surgery is the most commonly performed surgery worldwide, with a predicted 32 million total cataract operations performed in the world by 2020 by the World Health Organization. An aging population and a developing technological society have created demands for efficient strategies for precise surgical outcomes. Many people in the baby boomer generation have had prior refractive surgery, so more precise IOL power calculations and toric IOL alignment are essential to obtain excellent post-refractive visual acuity.

Traditional methods of IOL power calculations rely on either ultrasonic or non-contact optical methods to measure axial length and central corneal power. Immersion A-scan or B-scan ultrasonography remains the gold standard for measuring axial length and may achieve a resolution of 0.10 to 0.12 mm. Central corneal power is calculated via manual or automated keratometry. Although these traditional methods of biometry and IOL power calculations are generally accurate for cataract surgery using monofocal IOLs in eyes with average axial lengths, all current formulas have inherent flaws when the axial length is on the extremes of the normal range. Patients with prior refractive surgery also tend to demand a perfect postoperative visual outcome, but these methods may underestimate IOL power and potentially lead to hyperopic surprise and dissatisfied patients. Misalignment of toric IOLs can also lead to postoperative problems. The commonly implemented 3-step ink marker procedure for toric IOL orientation can result in an average error of 5 degrees, which may lead to reduction in astigmatic correction and hyperopic spherical surprise.

Intraoperative aphakic autorefractive wavefront analysis using wavefront analysis and manifest refraction have been applied to cataract surgery to improve estimation of post-surgical refractive error. Wavefront analysis can be used to detect irregular astigmatism and higher-order aberration and thus can guide IOL selection to optimize postoperative visual outcome. The OptiWave Refractive Analysis (ORA) intraoperative wavefront aberrometer (Alcon, Fort Worth, Texas) is the first intraoperative aberrometry system on the market for use during cataract surgery. ORA uniquely uses Talbot-Moiré interferometry, a technology in which the optical wavefront from the device passes through a pair of gratings; its diffraction produces a fringe pattern and the analysis results in an estimation of IOL power. Given its efficiency and small size, this technology can be used intraoperatively at the operating microscope.

Various clinical studies have looked at the utility of the ORA system in cataract surgery. Donnenfeld and colleagues found that most successful readings were achieved in aphakia with viscoelastic in limbal relaxing incisions and toric IOLs found that eyes with wavefront aberrometer-assisted surgery had significantly better uncorrected visual acuity and lower mean astigmatism compared to controls. Others have reported that in patients with prior histories of laser keratorefractive surgery, 85.7% achieved a final refractive goal of +/-0.50 D of the target refraction compared to 68.6% using standard calculation methods. More recently, studies with larger numbers of eyes revealed some deficiencies in the intraoperative aberrometry system. For example, Huelle and colleagues performed a clinical trial investigating the quality and reproducibility of aberrometry-based intraoperative refraction during cataract surgery. This group investigated 74 eyes and found that most successful readings were achieved in aphakia with viscoelastic and worse outcomes were found in pseudophakia with viscoelastic. They concluded that more efforts are required to improve the precision of measurement before this strategy can be used to guide cataract surgery. Fram and colleagues further compared the accuracy of established methods (Haigis-L and Masket) and newer methods, including intraoperative aberrometry (ORA) and a Fourier-domain OCT-based IOL formula (Optovue, Fremont, California) for IOL power calculations.
determination after cataract surgery in patients with past LASIK surgery. They found that there was no statistically significant difference among these methods, with mean absolute error of 0.37 D for the Haigis-L formula, 0.34 D for ORA, and 0.39 D for Optovue. In “Intraoperative aberrometry vs. standard preoperative biometry and a toric IOL calculator for bilateral toric IOL implantation with a femtosecond laser: One-month clinical study results,” Woodcock et al report the astigmatic outcomes in subjects with bilateral cataracts undergoing toric IOL implantation with intraoperative aberrometry measurements in 1 eye, and standard power calculation and a toric IOL calculator with inked axis marking in the contralateral eye. This prospective, multicenter, randomized, observer-masked, contralateral cohort study enrolled 130 patients (260 eyes) with bilateral cataracts scheduled for femtosecond laser-assisted cataract extraction combined with implantation of an AcrySof IQ aspheric toric IOL (Alcon) at 12 sites in the United States. Inclusion criteria consisted of age ≥22 years with bilateral cataracts requiring the above mentioned procedures, clear ocular media other than cataract, and potential postoperative visual acuity of ≥0.2 logMAR (20/32). Exclusion criteria consisted of: prior limbal relaxing or arcuate incisions, complications during surgery unrelated to the investigational device, lens/zonular instability, corneal diseases, ambylopa or degenerative retinal diseases.

For each patient, the eye with a more visually significant cataract was first randomized to a test or control group, and the contralateral eye was assigned to the opposite group. Procedures for test eyes were based on intraoperative aberrometry measurements, while procedures for control eyes were based on standard preoperative biometry assessments, conventional IOL power formulas, the AcrySof IQ toric IOL calculator and ink marking for positioning. Intraoperative aberrometry measurements were obtained from the test group using the ORA system with VeriEye. The AcrySof IQ toric IOL calculator was used as a guide for cylinder power selection and lens positioning, and standard IOL formulas were used to calculate the spherical power component of the lens. Surgeries were staggered by 1 week for each patient, and postoperative exams were performed on day 1 and week 1 for both eyes, and month 1 after surgery on the second eye. Postoperative logMAR vision and refraction were evaluated in a masked fashion by a technician or optometrist. The primary effectiveness parameter was the proportion of eyes with postoperative refractive astigmatism ≤0.50 D at 1 month, while secondary endpoints included: the proportions of eyes at 1 month with refractive astigmatism ≤0.25 D, ≤0.75 D, and ≤1.0 D; the proportion of eyes meeting manifest refraction spherical equivalent absolute prediction errors of ≤0.25 D, ≤0.50 D, ≤0.75 D, and ≤1.00 D relative to predicted postoperative spherical equivalent at 1 month; postoperative uncorrected distance visual acuity (UDVA); and postoperative best corrected distance visual acuity (BDVA).

Of the 260 enrolled eyes, 248 eyes were randomized and 242 eyes completed the study. The proportion of eyes at 1 month with postoperative refractive astigmatism ≤0.50 D was higher in the test than in the control group (89.2% vs. 76.6%, P=0.006). McNemar’s test evaluating paired outcomes in individual subjects showed that 71.2% achieved postoperative refractive astigmatism ≤0.50 D in both eyes; 18.0% achieved ≤0.50 D in the test but not in the control eye; 5.4% achieved ≤0.50 D in the control but not in the test eye; and 5.4% failed to achieve ≤0.50 D in both eyes. Furthermore, the proportions of eyes with postoperative refractive astigmatism ≤0.25 D, ≤0.75 D, and ≤1.0 D were higher in the test than in the control group, and mean postoperative astigmatism was lower in the test than in the control group (0.29±0.28 D vs. 0.36±0.35 D, P=0.041). While statistically insignificant, the mean absolute value of the prediction error was slightly lower in the test than in the control group. Mean postoperative UDVA and BDVA were also similar in the test and control groups.

The main strengths of this study are that it improves upon prior evaluations of intraoperative aberrometry with a larger subject population, is a clinically useful comparison to conventional methods, and is a randomized, multicenter, prospective, observer-masked design. Inclusion criteria were well defined, and attrition rate was low. While intraoperative aphakic refractive astigmatism was not measured in the control group, both test and control group eyes demonstrated similar profiles of preoperative astigmatism. The contralateral cohort structure allowed this study to control for intraoperative surgical variables that have been proposed to contribute to unreliable toric IOL power and placement calculations.

The primary outcome highlighted by the study is that there was a larger fraction of astigmatic eyes with ≤0.50 D of postoperative refractive astigmatism following cataract surgery with the intraoperative aberrometer compared to the AcrySof IQ toric IOL calculator. Although the fraction of eyes with this outcome was higher in the test group than in the control group, the difference (~12%) was rather modest. Likewise, the difference in the mean postoperative astigmatism between the test and the control groups, while statistically significant, was rather small (0.29±0.28 D vs. 0.36±0.35 D). While individual preferences and lifestyle concerns certainly must be accounted for when choosing a surgical approach for a given patient, one might question whether a difference of ~0.07 D would be of much clinical significance in choosing between these 2 methods in a general population.

While the authors analyzed the proportion of eyes with ≤0.25 D, ≤0.50 D, ≤0.75 D, and ≤1.0 D postoperative refractive astigmatism in the test and control cohorts, the proportion was only statistically significantly higher in the ≤0.50 D group. Importantly, while the authors point out that a previous report considered a postoperative refraction of 1.0 D as the cutoff point for subjects to elect excimer enhancement, the authors in this current study failed to show a significant difference in the proportion of eyes with that refractive outcome. Additionally, there is no mention of the location of the surgical incisions used in this study, a factor which could potentially account for 0.25 to 0.50 D of astigmatic change. The nature of this study makes it impossible to blind the surgeons to the study groups, which may add performance bias to the study. Variability in surgeon technique with preoperative markings, compounded
by the multicenter study design, could also account for the differences in outcomes.

Interestingly, although one of the motivations for this study was the questionable precision of alignment with standard toric IOL markers, the authors did not include an analysis that addressed whether alignment was responsible for the differences in postoperative astigmatism between the 2 groups. Instead, they reported differences in postop cylinder power. Because intraoperative aberrometry reportedly accounts for the anterior and posterior curvature of the cornea, while the preoperative measurements in the control cohort used standard biometric techniques—which make assumptions about the posterior corneal curvature—further analysis is warranted. For example, it is unclear whether the better postoperative astigmatism in the test cohort was due to the intraoperative measurement in an aphakic eye (influenced by surgical factors such as corneal incision, wound edema, etc.) or whether the total corneal power was simply more accurately calculated. The authors’ passing reference to an earlier study that demonstrated a significant difference in astigmatism measurements obtained with the Pentacam (Oculus, Arlington, Washington) and those obtained with several automated keratometers is revealing. It would have been helpful if the current study had compared the postoperative astigmatism in eyes in the test cohort with another cohort that had undergone preoperative IOL measurements with an imaging system that directly measures the anterior and posterior corneal curvatures.

While the reduction in postoperative astigmatism between test and control groups was small but statistically significant, there was no difference in uncorrected postoperative visual acuity. Median uncorrected visual acuity (Snellen equivalent) was 20/21 in the test cohort and 20/22 in the control. Although the authors suggest a trend toward improvement in the uncorrected visual acuity in the test group and there was a somewhat larger number of test group eyes that experienced 20/20 vision or better, the authors made no claim whether these results were statistically significant.

A number of technical points related to the use of the ORA system are missing from this study. First, while the authors state that there were no safety concerns in the study, there is no data comparing adverse intraoperative events or postoperative complications. There is no discussion of the surgical obstacles introduced by the use of the ORA system as well: instrumentation employed, duration of operation, instrumentation cost, or challenges faced by the surgeon in employing the device. There is likewise no mention of the amount of time required by the surgeon to learn and effectively use the device to achieve reliable results.

Finally, as the authors themselves point out, primary outcomes were examined only at postoperative month 1, so it is unclear whether the differences in outcomes will be stable over longer time points. Certainly the stability of the postoperative outcome would be of high concern in choosing a new system that offered marginally more beneficial outcomes. It would also be interesting to know how generalizable this approach would be to post-refractive or ectatic corneas; a similar study would be clinically useful in this patient population because their apheric measurements with intraoperative aberrometry may depart most from measurement by conventional methods.

As our instrumentation and surgical technique for cataract surgery continue to improve, patient expectations for optimal refractive outcomes after cataract surgery continue to grow. Toric IOLs allow for correction of astigmatic error at the time of cataract surgery; however, Woodcock et al have illustrated areas of imprecision in our current use of toric IOLs. This imprecision is in both the preoperative measurement of toric IOL power and in the standard eye marking techniques for proper toric IOL alignment. Intraoperative wavefront aberrometry with the third generation ORA system provides 1 method to improve the precision of toric IOL selection. It remains to be seen whether this new system offers significant benefit to the patient in terms of spectacle independence or visual quality of life measures. These advantages will need to be balanced with the cost of the device and increased intraoperative time.

References
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**Intraoperative aberrometry vs. standard preoperative biometry and a toric IOL calculator for bilateral toric IOL implantation with a femtosecond laser: One-month clinical study results**

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**Purpose:** To compare astigmatic outcomes in subjects with bilateral cataracts undergoing toric intraocular lens (IOL) implantation with intraoperative aberrometry measurements in one eye, and standard power calculation and a toric IOL calculator with inked axis marking in the contralateral eye.

**Setting:** Twelve sites in the U.S.

**Design:** Prospective, multicenter, randomized, observer-masked, contralateral cohort study.

**Methods:** The eye with more visually significant cataract was randomized to intraoperative aberrometry measurements or standard preoperative biometry and use of a toric calculator, with the contralateral eye automatically assigned to the other group. The primary effectiveness outcome was the proportion of eyes with postoperative refractive astigmatism ≤0.50 D at one month.

**Results:** Of the 130 subjects (260 eyes) enrolled, 124 (248 eyes) were randomized and 121 (242 eyes) completed the trial. The percentage of eyes with astigmatism ≤0.50 D at 1 month was higher in the intraoperative aberrometry than in the standard group (89.2% vs. 76.6%, P=0.006). Mean postoperative refractive astigmatism was lower in the intraoperative aberrometry group (0.29±0.28 D vs. 0.36±0.35 D, P=0.041). Secondary effectiveness endpoints, including manifest refraction spherical equivalent prediction error, uncorrected distance visual acuity, and best corrected distance visual acuity, were similar. No safety outcomes were related to the intraoperative aberrometry system.

**Conclusions:** Use of the intraoperative aberrometry system increased the proportion of eyes with postoperative refractive astigmatism ≤0.50 D and reduced mean postoperative refractive astigmatism at 1 month compared with standard methods. Other efficacy outcomes were similar. There were no safety concerns using the intraoperative aberrometry system.