Intraoperative Aberrometry

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Sean Ianchulev

Over the last decade, the growing adoption of presbyopia-correcting IOLs has created a growing need for high-precision cataract surgical outcomes driving an unprecedented clinical interest and research in IOL power calculation and biometry. In fact, the number of IOL power estimation studies increased dramatically over the last decade: from an average of 3 per year from 2010 through 2014 to an average of more than 17 per year from 2018 through 2020, with at least 36 formulas and biometric methodologies identified in 2010–2020. [1].

Precision has continued to increase as a result of these innovative approaches, and we see more than 70–75% of eyes within 0.5D of target refractive outcomes [2]. Thanks to advancements in IOL calculators, postoperative mean absolute prediction errors (MAEs) have continued to improve—a further 25% decrease in less than 10 years from 0.4 to 0.3 MAE between 2008 and 2018. [3, 4] On the instrumentation front, biometric precision has accounted for a significant part of that progress as newer technologies seem to have closed the precision gaps in keratometry and axial length measurement variability. Today, instruments such as the IOLMaster and Lenstar allow more accurate IOL power calculations to be performed with a high level of biometric resolution of less than 20 microns [5].

Nevertheless, challenges remain. Effective lens position (ELP) estimation remains a significant source of formulaic predictive uncertainty, despite the fact that newer formulas have been developed and older ones have been optimized with the goal of improving the accuracy of IOL power calculations. Conventional intraocular lens power formulas generally fall into several categories: vergence (Hoffer Q, Holladay 1 and 2, and SRK/T), artificial intelligence (RBF AI), ray tracing (Olsen), or a combination approach (Kane). All of these biometry methods are accurate in normal and long axial length eyes but less so in short axial length eyes, mainly because errors in axial length measurement or ELP estimation are magnified by the higher dioptric power of the IOL. While Hoffer Q and Haigis seem to perform better in that category, there is still a significant need for a more precise estimation. In addition, all of the conventional predictive models have shortcomings when it comes to eyes that have had prior refractive surgery where the postoperative refractive errors are larger than what the conventional models predict in normal eyes.

Despite significant differences across the various IOL formulas, they mostly share the same basic principle deriving from Fyodorov's original equation—they are based on preoperative anatomic parameters, such as axial length and

S. Ianchulev (✉)
Department of Ophthalmology, New York Eye and Ear of Mount Sinai, New York, NY, USA

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corneal curvature, which they use to derive an optical variable—IOL power. The improved second-, third-, and fourth-generation formulas have pushed the predictive efficacy of the preoperative methodology higher, but most of the formulas now operate on the plateau part of their efficacy curve. As surgeons and patients continue to reach for the emmetropic nirvana and postoperative spectacle independence, new approaches and technologies are needed, which can inflect the efficacy curve or put us on a different one altogether.

Intraoperative Refractive Biometry: Aphakic Method

One novel approach that dramatically departs from conventional preoperative methodologies was first introduced by Ianchulev et al. in 2003. Intraoperative refractive biometry was one of the first technologies to deliver automated, on-demand surgical biometry in the operating room more than a decade before intraoperative OCT, imaging, and sensing technologies started to enter the surgical paradigm. In its first embodiment and original implementation, intraoperative refractive biometry used a near-infrared autorefractor to obtain an "optical biopsy" of the eye after the extraction of the cataractous lens. During this unique transiently aphakic state, the surgeon can measure the aphakic spherical equivalent of the eye. Assuming minimal distortion of ocular optics during surgery (as is typical of today's minimally invasive phaco techniques) and high accuracy of auto-refracting devices, the aphakic spherical equivalent informs us about the optical deficit of the aphakic eye at the vertex distance of measurement. Converting and correlating this to the power at the intraocular plane of the final lens position are the basis of the original Ianchulev formulaic method of estimating the emmetropic IOL power biometrically in the OR. The Ianchulev formula was empirically derived as a correlation between the aphakic spherical equivalent and the emmetropic IOL power. It added further validation to earlier theoretical constructs based on Bennett-Rabbetts 1 schematic eye variants, which demonstrate that the expected ratio between the aphakic spherical equivalent and the final emmetropic power is in the range of 1.75–2.01.

This new aphakic methodology positioned the science of IOL power estimation on a new curve of innovation, which was not limited to preoperative assessments but introduced a biometric methodology to the intraoperative surgical paradigm. Because of its purely refractive approach, which is less dependent on anatomic corneal curvature and axial length (which are inherently factored in optically into the aphakic autorefraction), one would expect less confounding by the effect of prior refractive surgery. In fact, preoperative anatomic measurement could be eliminated altogether in this purely aphakic refractive paradigm where diagnostic optical biometry is done "on the table" at the point of cataract surgery. In addition, any optical effect of the surgical incision on the cornea could also be captured in this intraoperative setting.

While the portable intraoperative autorefractor was initially used for this aphakic method, applying the technique intraoperatively was not trivial. Initial clinical experience has shown that in order to achieve the full potential of this method, control over and experience with a number of variables are important. A reliable autorefractor such as the portable Retinomax (Nikon Optical, NJ, USA) or the Nidek AR-20 device (Nidek, Co. Ltd., Japan) should be used because many autorefractors were not optimized to the refractive range of the aphakic setting. Vertex distance, visual axis centration, and parallax are important, as are post-phaco corneal status, intraocular pressure (over/under-filled AC), and type of viscoelastic used for chamber maintenance (Fig. 45.1).

Early clinical work by Ianchulev, Leccisotti, and Wong demonstrated the clinical utility of intraoperative refractive biometry for IOL power estimation. The first formula for intraoperative autorefraction was derived in 2003 and later reported by Ianchulev et al. in a series of 38 eyes, six of which were post-prior LASIK patients. [6] The range of the axial length was 21.4–25.2 mm with a range of IOL power implanted from 12.0

to 28.5 D. Autorefraction vertex distance was 13.1, and A constant of the IOL used was 118.40. A strong linear correlation was found in a series of 38 eyes across a wide range of emmetropic IOL powers (Fig. 45.2).

Using linear regression, the following empiric formula was derived based on a strong "linear fit" between aphakic spherical equivalent and emmetropic IOL:

$$\text{Ianchulev formula}: P = 2.01 \times \text{ASE}$$

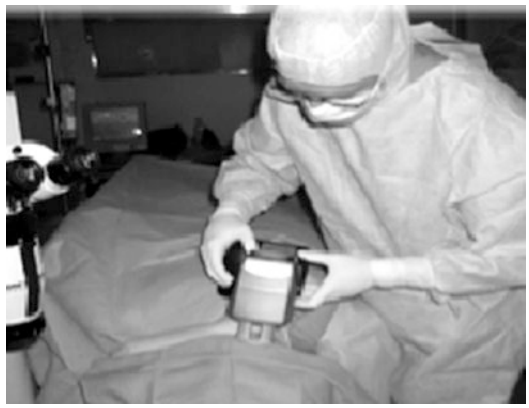

Fig. 45.1 An intraoperative refractometry after cataract removal and prior to IOL implantation: a portable autorefractor used during cataract surgery

where P = emmetropic IOL power, *ASE* aphakic spherical equivalent.

In the published series, more than 93% of the variability of the final emmetropic power is accounted for by the linear relationship with aphakic spherical equivalent—in standard eyes, the conventional formulas and the optical refractive model showed equivalent predictive efficacy with a correlation coefficient of 0.96. In addition, 83% of the LASIK eyes and 100% of the normal eyes were within ±1 D of the final IOL power when aphakic autorefraction was used, compared with 67% of LASIK eyes and 100% of the normal eyes using the conventional method.

Several other studies provided additional validation of the original technique and formula described by Ianchulev et al. In a prospective, non-comparative consecutive case series of 82 myopic eyes with a mean preoperative spherical equivalent of −12.80 D [range − 3 D to −27 D], Leccisotti et al. derived a modification of Ianchulev's formula for the myopic population: [7].

$$\text{Leccisotti formula}: P = 1.3 \times \text{ASE} + 1.45$$

where P = emmetropic IOL power and *ASE* aphakic spherical equivalent.

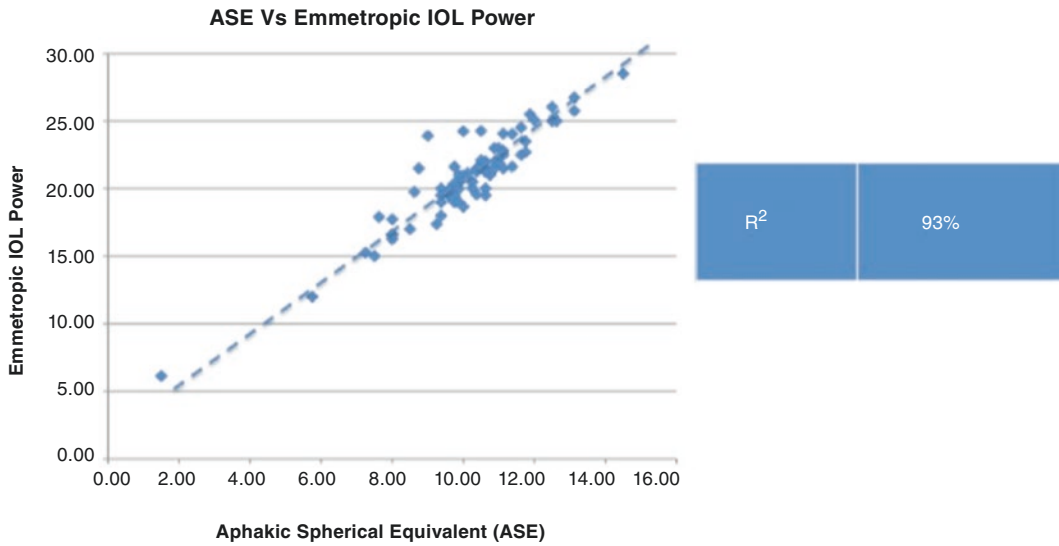

Fig. 45.2 Linear regression of the original Ianchulev et al. series between emmetropic IOL power and aphakic spherical equivalent (ASE)

A more definitive study by Wong et al. compared the Ianchulev formula with and without a Leccisotti modification in a series of 182 eyes and demonstrated that while the Ianchulev formula holds across the wide spectrum of IOL powers, the Leccisotti modification performs slightly better in myopic eyes (AL >25) [8]. In addition, another set of intraoperative aphakic refractive formulas was derived from this series as follows:

$$\text{For AL} < 25.5\,\text{mm}: P = 1.97 \times \text{SE}$$

$$\text{For AXL} \geq 25.5\,\text{mm}: P = 0.015 \times \text{SE2} + 1.5 \times \text{SE} + 1.5$$

where P = emmetropic IOL power and *ASE* aphakic spherical equivalent.

Ultimately, the original methodology by Ianchulev et al. demonstrated that one can develop a purely refractive intraoperative paradigm for IOL calculation, which helps solve important aspects of IOL estimation in post-Lasik eyes. It can also be applicable to the standard cataract case where refractive biometry can refine and verify the final IOL calculation. With the development of new integrated equipment that streamlines automated refraction at the point of surgery, significantly higher accuracy can be achieved from measurement standardization, better centration of autorefraction, and incorporation of additional intraoperative parameters in optical analysis such as keratometry. Intraoperative refractive biometry for IOL calculation may ultimately represent another important tangential point along the expanding interface between cataract and refractive surgery.

While these early efforts with intraoperative aphakic biometry set the stage for subsequent progress and introduced a new technological curve of development for IOL power estimation, there were challenges with the intraoperative refractive technique. Similar to conventional methods, it did not address the perennial problem of effective lens position (ELP). It was dependent on suboptimal biometric instrumentation (autorefractors), which was not specifically designed for the aphakic range nor the intraoperative setting. While simple and effective as a one-step purely refractive measurement, which eliminated the need for preoperative assessments, there was more to be desired for standardization and improved efficacy.

Intraoperative Aberrometry

The original clinical efforts on intraoperative aphakic autorefraction in early 2000 were bolstered by better refractive technology specifically designed for the intraoperative setting. Using wavefront analysis to characterize the entire optical system of the eye, both lower and higher order aberrations, was a natural evolution for high-precision refractive biometry. Previously, in optimizing treatment algorithms for laser keratorefractive surgery, wavefront analysis was introduced to the cataract surgical paradigm as a guidance system for intraocular lens power selection and astigmatic correction with LRIs and toric IOLs.

Technologies

The Hartmann-Shack interferometer system was the most common wavefront aberrometry technology in clinical use. Mechanistically, it works by projecting a ray of infrared light onto the retina and analyzing its reflection as it travels back through the pupil, after being focused by an array of lenslets [9]. The array of spot images is captured by a video sensor, and these spot images are computationally compared to their presumed locations in an aberration-free system while in the process generating a wavefront aberration map.

While a number of Hartmann-Shack systems were in clinical use (LADARWave, WaveScan, and Zywave) for laser refractive surgery, these systems were not suited for intraoperative use in cataract surgery. They needed to be adapted in order to attach to the surgical microscope and further optimized for aphakic measurements.

Figs. 45.3 ORA system™ (Alcon): (**a**) Aberrometer adjusted to the operating microscope. (**b**) Centration and alignment screen. (**c**) User interface

The ORA (formerly Orange) intraoperative wavefront aberrometer, manufactured by WaveTec (Alcon), is the first intraoperative aberrometry system designed for use during cataract surgery (Fig. 45.3). ORA may also be one of the first automated biometry systems for intraoperative diagnostic use in ophthalmology. In addition, it incorporated one of the first cloud-based surgical data collection tools with the help of WaveTec AnalyzOR, which accumulates data from all ORA users. The global surgical dataset of outcomes allowed for software updates, formula optimizations, and surgeon factor adjustments—in a continuous effort to increase the system's predictive accuracy.

The ORA uses a Talbot-Moiré interferometry [10]. In Talbot-Moiré technology, the device processes the optical wavefront through a pair of gratings set a particular distance and angle apart. The grating pair diffracts the transiting wavefront and that diffraction produces a fringe pattern whereby a subsequent analysis of the fringe pattern aberrations produces a refractive value. The Talbot-Moiré interferometry is different from the Hartman Schack device—it has increased speed and is small enough to be coupled with the surgical microscope for intraoperative use. The ORA device was optimized for both aphakic and pseudophakic biometry so that it can guide and inform IOL power selection, toric IOL power and axis, and both length and axis of limbal relaxing incisions [11].

Intraoperative aberrometry with the ORA is technically seamless and well integrated into the cataract surgical flow process. The aberrometer is attached to the surgical microscope and is small enough that it does not interfere with the surgeon's view (Fig. 45.4).

Fig. 45.4 ORA system

Measurement

While it takes less than thirty seconds to obtain a refractive measurement, there are essential steps to ensure precise results (Figs. 45.5, 45.6, 45.7, and 45.8). For testing the aphakic refraction, it is important to have a sealed incision and avoid overhydration. The central cornea needs to be kept clear and free of distortion. IOP should be at physiologic levels, ideally between 18 and 30 mmHg. Minimize any external pressure and interferences from the speculum and drapes. An important question is whether to have the anterior chamber filled with BSS or viscoelastic and whether the type of viscoelastic and its specific refractive index affect the predictive accuracy of

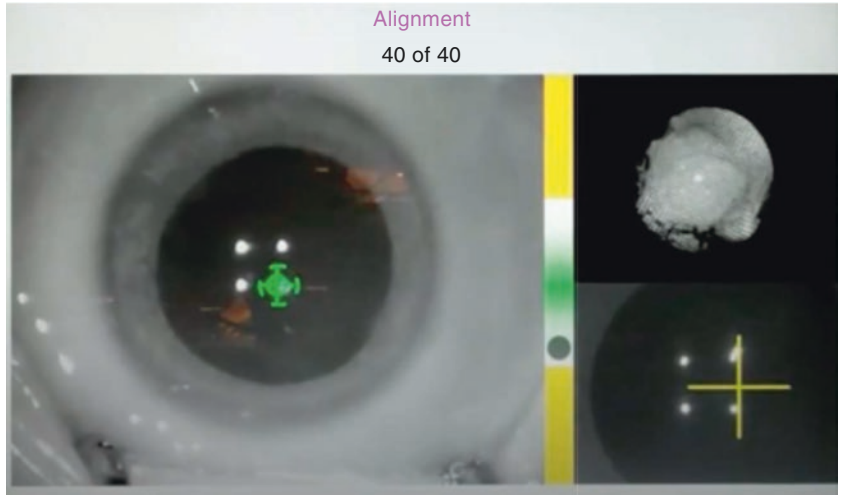

Fig. 45.5 Centration screen

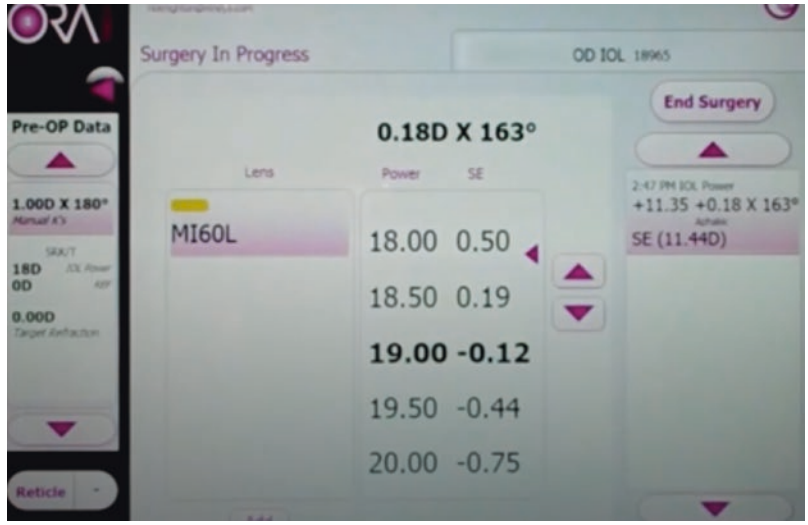

Fig. 45.6 Measurement and IOL power calculation

intraoperative aberrometry. That question was answered in a study of 120 eyes, which investigated the correlation between predicted power error (based on an index of refraction disparity between balanced salt solution (BSS) and ophthalmic viscosurgical device (OVD)) and actual aphakic power error. The IOL power determination was lower with OVD filling the chamber—mostly a result of the differences in the index of refraction between BSS and the OVDs used. The results for DisCoVisc and Amvisc Plus suggested an IOL power approximately 0.50 D lower than readings taken with BSS, while the difference for the other agents was less than 0.25 D. In addition, the MAE outcomes were lower with BSS than with OVD, with the exception of Amvisc, for which the results were identical. The differences were statistically significant with DisCoVisc ($P < 0.001$) and Amvisc Plus.

Another aspect of clinical investigation is whether the type of speculum/blepharostat used may impact the biometry. A controlled prospective study examined several speculum configurations and their refractive impact [12]. It concluded that the speculum with the least impact on the IA reading is the open-blade threaded blepharostat.

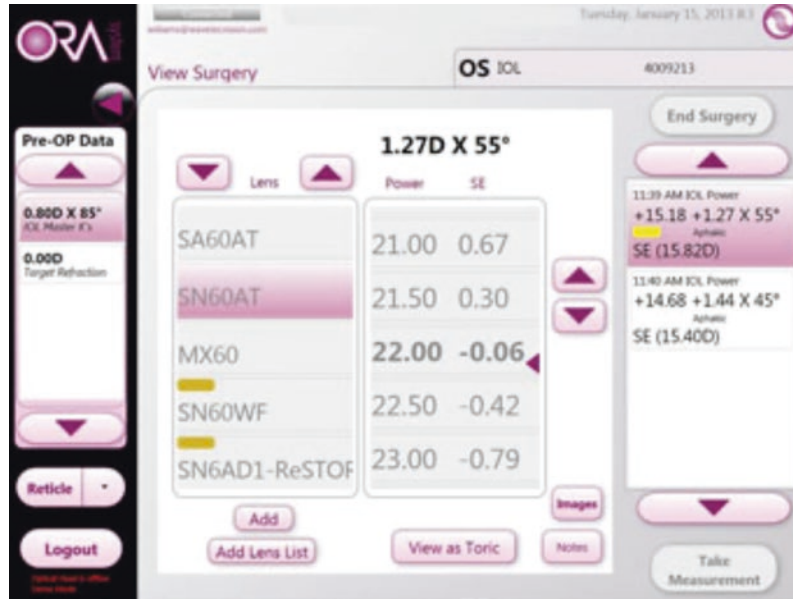

Fig. 45.7 In vivo calculation of residual astigmatism

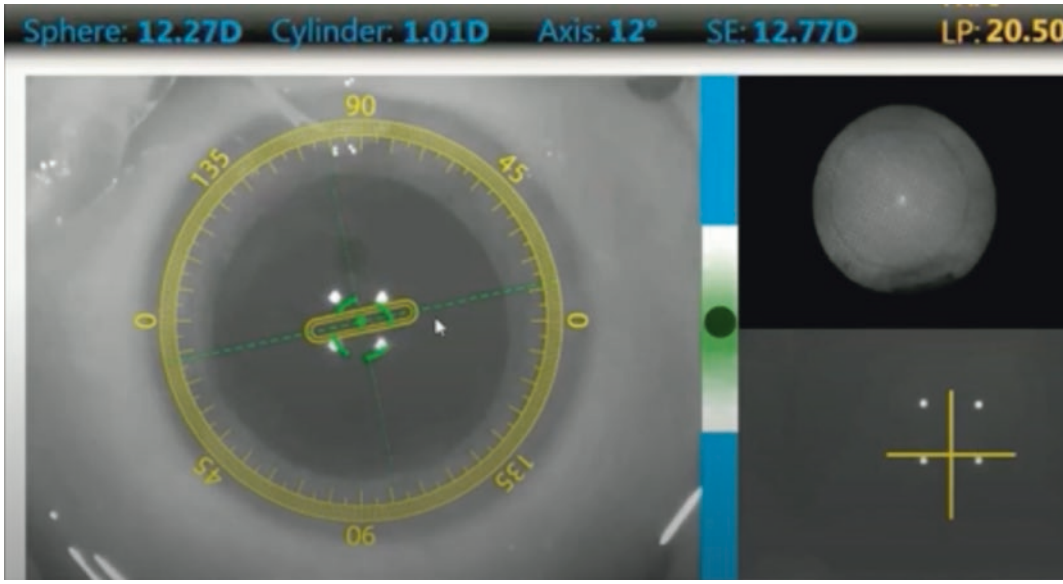

Fig. 45.8 IOL alignment during surgery

Intraoperative Aberrometry for IOL Power Calculation

The first-generation ORange device demonstrated only moderate utility—the correlation between the pseudophakic wavefront refraction from the first-generation ORange device with the 1 week postoperative autorefraction in 32 eyes showed a modest Pearson correlation coefficient of $r = +0.56$, $P < 0.001$ [13].

Over time as the technology and its predictive algorithms improved, so did its clinical utility. With increased adoption and clinical use, the number of studies has shown a dramatic increase

Fig. 45.9 Clinical studies about intraoperative aberrometry: 2004–2020

as well, with close to 90 studies to date, most of which in the last couple of years. There is a race to the emmetropic nirvana as physicians increase their use of premium IOLs and try to deliver superior outcomes (Fig. 45.9).

One of the main applications of intraoperative aberrometry is to calculate and refine IOL power. The other is for astigmatism management. While intraoperative aberrometry ushered in a new on-demand, on-the-table intraoperative paradigm for high-precision biometry and guided IOL implantation, the last decade has also seen parallel improvements of conventional preoperative biometry, driven by higher-fidelity biometric instrumentation for AL and keratometry and by incremental gains in predictive accuracy of our formulaic calculators. Let us examine the latest clinical evidence on intraoperative aberrometry and how it compares to the preoperative paradigm.

Normal Eyes

In virgin eyes, intraoperative aberrometry demonstrates high predictive efficacy. Cionni et al. reported one of the largest milestone studies on intraoperative aberrometry with 24,375 subjects and 32,189 eyes in 2018 [4]. This study used real-world retrospective de-identified data from the ORA cloud analytical aggregator across multiple surgeons. Because the database comprised real-world data from a variety of surgical centers, the preoperative formulas used by surgeons were not standardized or necessarily optimized. Interoperative aberrometry (IA) using the ORA System and preoperative biometry were performed for all cases. The key endpoints were IOL power prediction error with IA vs. preoperative calculation and percentage of cases with prediction error $\leq$ 0.50D. When examining all 32,189 IOL implants, mean and median absolute prediction errors were significantly lower with IA (ORATM System) vs. preoperative calculation ($P < 0.001$). This was also observed for the subset of eyes in which the power of the implanted IOL differed from the preoperatively calculated IOL power ($P < 0.0001$). Absolute prediction error $\leq$ 0.50 D was achieved significantly more frequently with IA: 81.9% vs. 75.9% of eyes, $P < 0.0001$, for all IOLs and 81.3% vs. 68.8%, $P < 0.0001$, for the subset of eyes in which the power of the implanted IOL differed from the preoperatively calculated IOL power. Given the large dataset, many additional findings and analyses were informative. Mean and median absolute prediction errors for non-toric and toric IOLs were consistent with the full dataset. For non-toric IOLs, the absolute prediction error with IA was $\leq$0.50D in 82.4% of eyes (vs. 76.8% with the preoperative calculation). For toric IOLs, the absolute prediction error with IA was $\leq$0.50D in 80.8% of eyes (vs. 74.3% with the preoperative calculation). In 8850 (26.7%) of eyes overall, the IOL power recommended by IA differed from the preoperatively planned IOL, and the surgeon implanted the IA-recommended IOL power.

Smaller clinical reports provide further support to the clinical utility of ORA with most of them demonstrating superior fidelity and predictive accuracy of the intraoperative biometric approach.

A further study by Zhang et al. [14] in 295 eyes reported similar benefits. This is a nonrandom-

ized, consecutive retrospective study to compare the outcomes of IA using the ORATM System versus optical biometry alone for IOL power calculation in eyes undergoing cataract surgery with monofocal IOLs. Subjects fell into four subgroups: (1) pre-ORA group: 61 eyes (20.7%) had cataract surgery with IOLMaster measurements, but without IA using the ORATM System; (2) BOTH group: 107 eyes (36.3%) had the same IOL power recommendation from IOLMaster and IA; (3) ORATM group: For 95 eyes (32.2%), the final IOL power implanted was chosen from ORA recommendations rather than IOLMaster. (4) IOLMaster group: For 26 eyes (8.8%), the final IOL power implanted was based on surgeon's best choice from IOLMaster measurements rather than IA. The percentage of eyes within an error range less than ±0.5D of *target refraction* was 65.3%, 80.4%, 73.1%, and 63.9% for ORA, BOTH, IOLMaster, and pre-ORA groups, respectively. The percentage of eyes within an error range less than ±0.5D of *predicted refraction* was 66.3%, 79.4%, and 69.2% for ORA, BOTH, and IOLMaster groups, respectively. Absolute error was significantly reduced in eyes where IA and IOLMaster recommended the same IOL power based on preoperative target refraction compared with IOL selection based on IA (ORATM System) or IOLMaster alone. Overall, IA using the ORA System provided postoperative refractive results comparable to conventional biometry for monofocal IOL selection.

Not every study showed superior efficacy of intraoperative aberrometry. Davison et al. [15] reported on a single clinic, 112 subjects with a retrospective chart review using the ORATM System in determining the IOL sphere power in eyes with no previous ocular surgery. IOL power calculation results from IA with the ORATM System, and the preoperative calculation was similar in nearly half of the cases (47%, 73/155). For toric and multifocal IOLs, there was a statistically significant bias toward lower-powered lenses with IA with the ORATM System ($P < 0.01$). There were only three instances in which preoperative and IA (ORATM System) calculations differed by 1.5 D; in all instances, an adjustment of the preoperative lens power by 0.5 D toward the IA calculation showed a positive effect. In 35% (22/63) of cases in which IOL power differed by at least 0.5 D between IA with the ORATM System and preoperative calculation, the surgeon chose (for nonspecific reasons) the non-optimal method.

Long Eyes

A study by Hill et al. [16] in 51 consecutive eyes aimed to compare the accuracy of IA and the Hill-radial basis function (RBF) formula with other formulas based on preoperative biometry in predicting residual refractive error. Cataract surgery was performed in eyes with axial myopia (axial length [AL] >25 mm) using standard preoperative measurements, IA and Hill-RBF formula for IOL power calculation. IA with the ORATM System was better than all formulas based on preoperative biometry and as effective as the AL-optimized Holladay 1 formula in predicting residual refractive error and reducing hyperopic outcomes.

- The proportion of patients within ±0.5 D of the predicted error was 74.5%, 62.8%, 82.4%, 79.1%, 73.9%, 76.7%, and 80.4% for SRK/T, Holladay 1, AL-optimized Holladay 1, Holladay 2, Barrett Universal II, and Hill-RBF formulas and IA groups, respectively ($P = 0.09$).
- There was a statistically significant difference between AL-optimized Holladay 1 and IA.
- The groups differed significantly with respect to hyperopic outcomes ($P < 0.007$), occurring in 70.6%, 76.5%, 49.0%, 74.4%, 76.1%, 74.4%, and 45.1% of eyes in the SRK/T, Holladay 1, AL-optimized Holladay 1, Holladay 2, Barrett Universal II, Hill-RBF formulas, and IA groups, respectively. The difference was not statistically significant between AL-optimized Holladay 1 and IA.

These data also suggest that patients with axial myopia can benefit from the use of IA.

Short Eyes

As we mentioned earlier, conventional preoperative formulas were less efficacious in the setting of short eyes, with the Hoffer Q offering the highest predictive efficacy for that subgroup. What is the utility of intraoperative aberrometry in this setting? In a single-center retrospective consecutive case series, Sudhakar et al. compared the accuracy of preoperative biometry-based formulas to intraoperative aberrometry (IA) using the ORA System, with respect to predicting refractive outcomes after cataract surgery in 51 short eyes. [17] Cataract surgery with monofocal, multifocal, and/or toric IOL implantation in short eyes, where standard preoperative measurements and IA were performed. Key outcomes of interest were the difference between predicted and actual postoperative spherical equivalent (SE) (numerical error) and the proportion of eyes within ±0.5 D and ± 1.0 D of their target SE refraction.

- Without optimizing the formulas for the study population (i.e., not using n lens constants and surgeon factors that were specifically optimized for short eyes), the mean numerical errors (MNEs) associated with Hoffer Q, Holladay 2, Haigis, Barrett Universal II, Hill-RBF, and IA (ORATM System) were − 0.08 (95% confidence interval [CI], −0.30 to 0.13), −0.14 (95% CI, −0.35 to 0.07), +0.26 (95% CI, 0.05 to 0.47), +0.11 (95% CI, −0.10 to 0.32), +0.07 (95% CI, −0.14 to 0.28), and + 0.00 (95% CI, −0.21 to 0.21), respectively ($P < 0.001$). The proportion of eyes within ±0.5 diopter (D) of the predicted SE with Hoffer Q, Holladay 2, Haigis, Barrett Universal II, Hill-RBF, and IA (ORATM System) were 49.0%, 43.1%, 52.9%, 52.9%, 60.8%, and 58.8%, respectively ($P = 0.06$). A Bonferroni analysis showed that Hoffer Q, Holladay 2, and IA (ORATM System) had the lowest MNEs and were not significantly different from one another; there was no statistically significant difference with regard to the proportion of eyes within ±0.5 D and ± 1.0 D of the target SE.
- Optimizing for the study population (in those patients receiving one of the monofocal IOLs) changed the performance of many of the formulas with regard to the proportion of eyes within ±0.5 D and ± 1.0 D of the target SE; however, these differences were small and not significant. IA using the ORATM System remained one of the best-performing methods, but its performance was not statistically different from the other methods. When a formula and IA predictions differed by 0.5 D or more, IA's ability to recommend a more emmetropic outcome was no better than chance (50%). For example, when there were disagreements greater than 0.5 D, the Barrett Universal II would have outperformed IA 13.7% of the time, and IA would have outperformed Barrett Universal II 13.6% of the time.

Eyes with Previous Corneal Refractive Surgery

Similar to the clinical setting with short eyes, this is where conventional biometry plateaus in its efficacy. There have been a plethora of formulas and calculators designed specifically for this with adjustments and fudge factors trying to improve our ability to estimate the emmetropic IOL power after prior refractive surgery, and this ends up being one of the most taxing aspects of preparing the patient and the surgeon for the cataract surgery, particularly with premium cases where the expectations are so high.

One of the larger studies on this was reported by Ianchulev et al. in 2014 [18]. It is a retrospective consecutive case series from 66 surgeons and 246 eyes, which was designed to evaluate intraoperative aberrometry using the ORA System for IOL power calculation. Cataract surgery after prior myopic LASIK or photorefractive keratectomy, where standard preoperative measurements and IA using ORA were performed. Key outcomes of interest were the median absolute error of prediction and percentage of eyes within ±0.50 diopters D and ± 1.00 D of refractive prediction error. With IA, 67% of eyes were within ±0.5 D,

85% were within ±0.75 D, and 94% were within ±1.0 D of the predicted outcome. This was significantly more accurate than the other preoperative methods: prediction with IA was almost 45% more accurate than the surgeon's best choice (46% within ±0.5 D) and 34% more than the Shammas method, which came in second (50% within 0.5 D. These outcomes were consistent across all endpoints for 0.75 D and 1.0 D postoperative refractive thresholds. In 246 eyes (215 first eyes and 31 second eyes), IA achieved the greatest predictive accuracy, with a median absolute error of 0.35 D (95% confidence interval, 0.35–0.43 D; $P < 0.0001$) and mean absolute error of 0.42 D. All other methods demonstrated at least a 45% higher error than IA, which in the case of surgeon best choice was 70% higher at 0.60 D (95% confidence interval, 0.58–0.73 D).

Another study by Fram et al. [19] is a retrospective consecutive case series (two surgeons) designed to evaluate intraoperative aberrometry using the ORA system and compare it to preoperative IOL power calculation in 59 eyes with prior LASIK surgery. Patients with historical data ($n = 20$ eyes) were compared using the Masket regression formula, Haigis-L, IA, and Optovue. In the groups with historical data, 35–70% of eyes were within ±0.25 D, 60–85% were within ±0.50 D, 80–95% were within ±0.75 D, and 90–95% were within ±1.00 D of targeted refractive IOL power prediction error. The MedAE was 0.21 D for the Masket regression formula, 0.22 D for the Haigis-L formula, 0.25 D for IA, and 0.39 for Optovue. The MAE was 0.28 D for the Masket regression formula, 0.31 D for the Haigis-L formula, 0.37 D for IA, and 0.44 D for Optovue. There was no statistically significant difference among the methods.

Patients without historical data ($n = 39$ eyes) were compared using Haigis-L, IA (ORA System), and Optovue. In the group without historical data, 49% of eyes were within ±0.25 D, 69–74% were within ±0.50 D, 87–97% were within ±0.75 D, and 92–97% were within ±1.00 D of targeted refractive IOL power prediction error. The MedAE was 0.26 D for Haigis-L, 0.29 D for IA (ORATM System), and 0.28 D for Optovue. The MAE was 0.37 D for Haigis-L, 0.34 D for IA (ORATM System), and 0.39 D for Optovue. There was no statistically significant difference among the methods. Overall, IA aberrometry and Fourier-domain OCT-based formula showed promising results when compared with established methods. The findings of improved benefit with IA and Fourier-domain OCT-based IOL formula were particularly meaningful in patients for whom prior data are not available.

Not all clinical evaluations showed positive results of IA in the post-refractive setting. There are a number of smaller studies that did not report convincing benefits of IA. Some used the first-generation technology, ORange, which lacked in predictive accuracy [20]. Furthermore, in the setting of prior RK, biometric challenges continue to overwhelm both conventional formulas and intraoperative aberrometry. Fortunately, in these modern times, there are not many patients left with RK, but a case report by Zhang et al. [21] illustrates the difficulties in that population. After cataract surgery and IOL power calculations using IA (ORA System), a patient with a history of RK showed hyperopic refraction. This was the experience of the author as well when we used IA in our practice in subjects with RK. The corneal distortion is so pronounced in these patients that small decentration from the visual axis can dramatically change the refractive result.

Intraoperative Aberrometry for Astigmatism Correction

Of recent, cataract surgery has become a growing platform for the simultaneous management of astigmatism using LRIs or toric IOLs, intraoperative guidance with the wavefront aberrometry system could not have been a more timely development. On-the-table instantaneous biometric guidance for toric IOLs in particular has been an essential ancillary tool given that small misalignments of the toric IOL can negate its efficacy and ability to correct the astigmatic axis. For every degree of misalignment, about 3% of the lens cylinder power is lost [22]. It is not impossible to end up with misalignments greater than 20°-30° where the effect of the toric correction will be

null. Also, the astigmatic axis and power can change based on the intraoperative surgical approach due to the effect of the corneal incision. It certainly seems advantageous to evaluate and confirm the refractive parameters of the eye with respect to astigmatic after eliminating the refractive interference of the cataractous lens and factoring in the intraoperative effect of the corneal incision. The ORA features a large dynamic range of −5 to +20 D, using Talbot moiré interferometry to determine the refractive state of the eye. Because of this, ORA can measure phakic, aphakic, and pseudophakic refraction of the eye, both cylinder and sphere. The aberrometer calculates and confirms IOL power after cataract removal and IOL implantation and determines the magnitude and axis of astigmatism after cataract removal and limbal relaxing incisions. It provides continuous, real-time refractive feedback for astigmatic correction when the surgeon is rotating toric IOLs, titrating limbal relaxing incisions or peripheral corneal relaxing incisions, and performing arcuate incisions with a femtosecond laser.

Another consideration with regard to astigmatism correction is posterior astigmatism. ORA can play an important role by uncovering the impact of the posterior cornea following lens removal. Dr. Koch confirmed that the posterior cornea can have, on average, 0.3 D of astigmatism. This can be significant particularly for multifocal patients, who are extremely sensitive to small degrees of astigmatism.

Regular Astigmatism

Multiple studies provide growing evidence and clinical validation for the advantages of intraoperative aberrometry for astigmatic correction. By far, the largest series comes from the Ora aggregate clinical database. Cionni et al. reported one of the largest milestone studies on intraoperative aberrometry with 24,375 subjects and 32,189 eyes in 2018 [4]. This study used real-world retrospective de-identified data from the ORA cloud analytical aggregator across multiple surgeons. While the study did not specifically address toric axis alignment, it provides important assurance that patients with toric IOL implantation demonstrate similar high fidelity of refractive correction as non-toric IOLs. Mean and median absolute prediction errors for non-toric and toric IOLs were consistent with the full dataset. For non-toric IOLs, the absolute prediction error with IA was ≤0.50D in 82.4% of eyes (vs. 76.8% with the preoperative calculation). For toric IOLs, the absolute prediction error with IA was ≤0.50D in 80.8% of eyes (vs. 74.3% with the preoperative calculation).

Several studies are informative with respect to the use of intraoperative aberrometry in the setting of LRIs. Packer et al. [23] conducted a retrospective, case-control chart review to assess whether the use of intraoperative aberrometry reduces the frequency of postoperative laser enhancements compared with cases in which aberrometry was not used in 67 eyes of 48 subjects. Mean postoperative follow-up was 3 months in the IA group and 6 months in the control group. Overall, laser enhancements were performed in seven eyes of five patients, for a rate of 10.4%. The excimer laser enhancement rate was 3.3% (one patient) in the IA group and 16.2% (six patients) in the control group. The odds ratio of a laser enhancement without intraoperative aberrometry was 5.71 ($P = 0.21$) although statistical significance was not reached in this small sample size.

With respect to toric IOL application of intraoperative aberrometry, a large retrospective review investigated factors associated with residual refractive astigmatism after toric IOL implantation in more than 3000 cases [24]. Higher measured surgically induced astigmatism (calculated as the vector difference between the preoperative and postoperative keratometry) was most associated with higher levels of reported residual astigmatism. While there were no differences in the residual refractive astigmatism values associated with use or non-use of a femtosecond laser system, the use of intraoperative aberrometry was associated with significantly lower refractive cylinder values (approximately 0.20 D, $P < 0.01$); the odds ratio indicates a 29% higher likelihood of needing a new IOL rather than being able to

successfully rotate the current IOL. Overall, higher levels of residual refractive astigmatism when present after cataract surgery were most associated with large measured differences in preoperative to postoperative keratometry and intraoperative guidance by aberrometry was associated with lower levels of residual refractive astigmatism.

Another study by Waisbren et al. compared intraoperative aberrometry versus conventional methods and took another look at the toric setting. [25] This is a retrospective case series from two surgeons designed to compare intraoperative refractive biometry to conventional methods for intraocular lens (IOL) power calculation in patients receiving toric IOLs with a sample size of 104 eyes. Patients in the intraoperative aberrometry cohort achieved a statistically significant lower MAE (0.25 ± 0.22) compared to those in the conventional calculations cohort (0.34 ± 0.29) ($P = 0.05$). In the IA group, 45/52 (87%) of eyes were within 0.5 D of the targeted refraction, compared to 41/52 (79%) in the conventional preoperative calculation group ($P = 0.437$). With the help of IA, surgeons were able to reduce astigmatism to <1 D in 45/52 (87%) of patients compared to only 36/52 (69%) of patients who underwent conventional planning ($P = 0.059$). In the IA (ORA System) group, 14/52 (27%) had no postoperative residual astigmatism vs. 18/52 (35%) of the conventional group. Absolute error was significantly improved in patients using IA, while other variables tested, such as proximity to the targeted axis, were also improved but did not achieve statistical significance.

Similar findings are evident from the study reported by Woodcock et al. [26]. This is a multicenter prospective cohort study comparing astigmatic outcomes in patients having toric IOL implantation with intraoperative aberrometry measurements in one eye and standard power calculation in the contralateral eye. The study enrolled 248 eyes of 124 patients. The percentage of eyes with astigmatism of 0.50 D or less at 1 month was higher in the IA group than in the standard group (89.2% versus 76.6%) ($P = 0.006$). The number of patients (14 [53.8%]) falling outside the intended astigmatic target (<0.50 D) was lower in the IA group than in the standard group. The proportions of eyes with postoperative refractive astigmatism of 0.25 D or less, 0.75 D or less, and 1.00 D or less were also higher in the IA group. Similarly, mean postoperative astigmatism was lower in the IA group than in the standard group (0.29 ± 0.28 D versus 0.36 ± 0.35 D; $P = 0.041$). Overall, compared with standard methods, the use of IA increased the proportion of eyes with postoperative refractive astigmatism of 0.50 D or less and reduced the mean postoperative refractive astigmatism at 1 month.

The number of patients falling outside the intended astigmatic target was reduced by more than half in the IA cohort when compared with the group in which the toric calculator was used.

Salomon et al. conducted a toric study, which further informs of the high efficacy of intraoperative guidance for astigmatic correction during IOL implantation [27]. It is a prospective randomized case series to compare refractive outcomes of intraoperative computer-assisted registration and intraoperative aberrometry (IA) using the ORA system for the reduction in cylinder during toric IOL placement in 104 eyes. Toric IOL implantation after phacoemulsification was assisted by intraoperative computer-assisted registration in one group and intraoperative aberrometry in a separate group (contralateral eye). The mean postoperative remaining refractive astigmatism was below 0.5D: −0.29 ± 0.22 D and − 0.46 ± 0.25D with intraoperative computer-assisted registration and IA, respectively. In the computer-assisted registration group, more than 25% of the cases had no postoperative astigmatism, compared with 8% of cases in the IA group. Overall, 92.2% of cases in the computer-assisted registration group had remaining refractive astigmatism of 0.50 D or less, compared with 76.5% in the IA group. The median absolute error in predicting cylindrical correction by IOL was similar for both guidance systems: 0.35 D in the intraoperative computer-assisted registration group and 0.39 D in the IA group, irrespective of the axis ($P = 0.91$). While it appears that the computer-assisted registration group may have a slightly better corrective impact for the astigmatic aberration, it is validating to see such a high

degree of precision for intraoperative surgical guidance systems. Another more recent study by Salomon et al. [28] appears to indicate that further advancements in digital alignment technologies may provide outcomes that are as good or even better than those seen with intraoperative aberrometry.

Astigmatism After Corneal Refractive Surgery

This seems to be a clinical setting in the sweet spot for intraoperative aberrometry. A study by Yesilirmak et al. [29] informs to this exact population. It is a retrospective case review of intraoperative aberrometry for toric IOL power selection in eyes with a history of refractive surgery and significant residual astigmatism following refractive surgery—fifteen eyes; 12 eyes had a history of myopic LASIK and three of hyperopic LASIK. Mean residual astigmatic prediction using IA was 0.64 ± 0.61 D, and the mean postoperative manifest astigmatism was 0.74 ± 0.63 D. Twenty-seven percent of the eyes had 0.25 D or less of astigmatism postoperatively, 47% had 0.50 D or less, 60% had 0.75 D or less, and 73% had 1.00 D. Mean IA prediction error was 0.43 ± 0.33 D, compared to a mean prediction error of 0.77 ± 0.56 D for the calculated preoperative lens choice using the IOLMaster (P = 0.03) and 0.61 ± 0.34 D using the online ASCRS calculator (P = 0.08). 80% of the treated eyes ended up with a spherical equivalent of 0.75 D or less, whereas only 53% of them would have achieved this if the calculated preoperative lens per IOLMaster had been implanted instead.

Conclusion

Intraoperative aberrometry was a timely answer to a major clinical need at the turn of the century when millions of post-LASIK patients were entering the cataract age and the general population started to demand high-fidelity refractive outcomes more suitable to their active lifestyle. Intraoperative aberrometry broke off from the 50-year-old Fyodorov paradigm of preoperative IOL power estimation, inflected the conventional biometry curve of preoperative formulas away from its deepening plateau, and ushered ophthalmic surgery into the new age of intraoperative guidance and biometry as the first such technology to enter the operating room. It was also one of the first cloud-based analytics platforms for any ophthalmic diagnostic and imaging technology, which used aggregate population data to improve software, algorithms, and, ultimately, patient outcomes.

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