



Recent developments in intraocular lens power calculation methods – update 2020

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Contributions: (I) Conception and design: G Savini; (II) Administrative support: G Savini; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: For many decades only a few formulas have been available to calculate the intraocular lens (IOL) power for patients undergoing cataract surgery: the Haigis, Hoffer Q, Holladay 1 and 2 and SRK/T. In recent years, several new formulas for IOL power calculation have been introduced with the aim of improving the accuracy of refraction prediction in eyes undergoing cataract surgery. These include the Barrett Universal II, the Emmetropia Verifying Optical (EVO), the Kane, the Næser 2, the Olsen, the Panacea, the Pearl DGS, the Radial Basis Function (RBF), the T2 and the VRF formulas. Although most of them are unpublished so that their structure is unknown, we give an overview of each formula and report the results of the studies that have compared them. Their performance in short and long eyes is provided and a special focus is given on the issue of segmented axial length, which is a promising method to obtain more accurate outcomes in short and long eyes. Here, the group refractive index originally developed for the IOLMaster may not represent the best method to convert the optical path length into a physical distance. The issue of posterior and total corneal astigmatism (TCA) is discussed in relation to toric IOLs; the latest formulas for toric IOLs and their results are also reported.

Keywords: Lenses; intraocular; biometry; cataract

Submitted Mar 07, 2020. Accepted for publication Jul 24, 2020.

doi: 10.21037/atm-20-2290

View this article at: <http://dx.doi.org/10.21037/atm-20-2290>

Over the past four decades, cataract surgeons had mainly used a few well-known formulas to calculate the intraocular lens (IOL) power in unoperated eyes: the Haigis (1), Hoffer Q (2), Holladay 1 (3), Holladay 2 (unpublished) and SRK/T (4) formulas and they have been used on millions of eyes. Notwithstanding the rapid technological evolution of optical biometry, which saw the introduction of a number of new devices (5-10), little advancement has been observed for IOL formulas, until about 10 years ago, when several new formulas for unoperated eyes have been developed, particularly in the last 5 years (11-13). These formulas were designed to improve the accuracy of refractive predictions, which are still far from being perfect, even in normal unoperated eyes. The effort of researchers has led to the

publication of some landmark papers with thousands of eyes, whose measurements have been used to compare the refractive accuracy of such formulas.

At the same time, new formulas for toric IOLs have been developed. The purpose of this review is to give an update on the best methods to calculate the IOL power in unoperated eyes with and without astigmatism.

New formulas

- ❖ Barrett Universal II formula (BUII): actually, this is not a totally new formula, but the evolution of the Barrett Universal I, which was published by Graham Barrett, MD, in 1987 as a thick-lens paraxial formula

(14,15). The BUII is essentially based on the same concept, although the author subsequently introduced several modifications over the years. These included using data to predict the radius of the globe as alluded to in the original article rather than an empirical method. Later on, lens thickness (LT) and corneal diameter (CD) were added. The name changed into BUII in 2013. The formula is unpublished, so that little is known about its structure. Although Koch *et al.* listed it among vergence formulas (16), the BUII is based on ray tracing (Graham Barrett, personal communication, 2019). It is available for free at https://calc.apacrs.org/barrett_universal2105/ (accessed on February 16th 2020) and uses axial length (AL), keratometry (K), anterior chamber depth (ACD, measured from epithelium to lens) to predict the IOL position; LT and CD can be entered optionally. In several studies it was ranked among the most accurate formulas.

- ❖ Emmetropia Verifying Optical (EVO) Formula: this is a thick-lens formula (unpublished) developed by Tun Kuan Yeo, MD, of Singapore. Version 2.0 is available for free at www.evoiolcalculator.com (accessed on February 16th 2020) and uses AL, K, and ACD as the predictors (LT and central corneal thickness (CCT) are optional). Version 1.0 has been tested by a few studies, which reported its high accuracy.
- ❖ Kane Formula: this is another unpublished formula, which was developed by Jack X Kane, MD. According to its author, it is based on theoretical optics and contains some elements of artificial intelligence, but its structure is largely unknown. The formula is available for free at www.iolformula.com (accessed on February 16th 2020) and uses AL, K, ACD, and gender to predict the IOL position, with LT and CCT being optional factors. An increasing number of studies have reported excellent outcomes with this formula.
- ❖ Ladas Super Formula: this method was originally developed by John G Ladas, MD, *et al.* as a combination of the Hoffer Q, Holladay 1, Holladay 2 (with Wang-Koch adjustment for AL adjustment) and SRK/T formulas (12,17). Based on a three-dimensional model, this method was developed to choose the best formula for each eye. In 2019, the formula was revised using the postoperative data of more than 4,000 eyes and is now based on artificial intelligence (Ladas Super Formula AI), available at www.iolcalc.com (accessed on July 11th, 2020).
- ❖ Næser 2 formula: this is a thick-lens formula developed by Kristian Næser, MD. The original Næser 1 formula was based on the manufacturer's cutting-card for the IOL anterior and posterior curvature (18). The Næser 2 uses calculated data for the architecture of the IOL. AL measurements are optimized so that the refractive outcomes are equally good in short, medium and long eyes. The results reported by the author were as good as those obtained with the BUII formula (19).
- ❖ Olsen Formula: this formula has undergone several refinements over the years. It was first described as early as 1987 (20) and was then refined in subsequent years (21,22), until the most recent version, which is based on ray-tracing and the C constant concept (23). The latter estimates the IOL position solely on the preoperative measurements of ACD and LT. The formula can be downloaded at www.phacooptics.net (accessed on February 16th 2020). Interestingly, the PhacoOptics software offers two options to predict the position of the IOL: by default, four predictors are used for this purpose (AL, K, ACD and LT), as in the earlier versions of this formula; however, AL and K can be omitted from the prediction, so that the C constant approach is adopted. For this reason, two versions of the Olsen formula are described in the literature: the former is the 4-factor version, also known as Olsen_{standalone}, the latter, based on the C constant, is the 2-factor version and is the one installed on optical biometers. The refractive accuracy has been reported to be high for both.
- ❖ Panacea: this (unpublished) formula was developed by David Flickier, MD, and is available for free at www.panaceaiolandtoriccalculator.com (accessed on February 16th 2020). It is the only formula enabling surgeons to enter the corneal asphericity (Q-value) and the ratio between the anterior and posterior corneal curvature, which should improve the refractive accuracy. The results have not yet been published in large studies.
- ❖ Pearl DGS: this formula has been developed by a team of French ophthalmologists (G. Debellemanière, D. Gatinel, and A. Saad, and hence its name), who relied on artificial intelligence. It is available for free at www.iolsolver.com (accessed on February 16th 2020). The formula is unpublished so that nothing is known of its structure. Since it was introduced in 2019, no study has yet reported its outcomes.

- ❖ RBF Calculator (Radial Basis Function): launched in 2016, this was the first IOL power calculation method based purely on artificial intelligence. It is available for free at www.rbfcaculator.com (accessed on February 16th 2020) and is installed on the Lenstar (Haag-Streit, Switzerland). Version 2.0 is based on more than 12,000 eyes and, opposite of the original version, can calculate IOL power for a target different than zero. Required inputs are AL, K and ACD (LT, CCT and CD are optional). Several papers have shown that it leads to good outcomes, although it has not been ranked as the best in any study.
- ❖ T2 Formula: this a modification of the original SRK/T, described by Richard M. Sheard, MD, *et al.* in 2010 (11). The main purpose of the authors was to correct a non-physiological behavior of the corneal height prediction (so-called “cusp phenomenon”) (24). It has been shown to be more accurate than the SRK/T.
- ❖ VRF formula: this vergence formula, developed by Oleksiy Voytsekhivskyy, MD, is one of the few published ones (25). The IOL position is predicted from AL, K, ACD and CD. Compared to standard vergence formulas, the results reported by the author are good, but it still needs to be validated against other modern formulas.

Formulas comparisons

Several studies recently compared the above-described formulas as well as older formulas. They reported similar outcomes, as in most cases the best formulas were the BUII and Olsen, followed by the Haigis. When newer formulas were analyzed, some of these (e.g., Kane and EVO) provided equally excellent outcomes.

In 2016, Kane *et al.* compared the results of different formulas in 3,241 eyes measured with the IOLMaster 500 (Carl Zeiss Meditec, Germany) (26). Since this biometer was not able to measure LT, the Olsen formula could not be investigated. Kane’s study was one of the first to demonstrate that the BUII was more accurate than traditional formulas, including the Haigis and Holladay 2. It displayed a lower mean absolute error (MAE) and median absolute error (MedAE) as well as a higher percentage of eyes with a prediction error (PE) lower than ± 0.50 diopters (D). Such advantage was evident in medium, medium-long and long eyes, but not in short eyes. It is interesting to note that the results were good, but not excellent, notwithstanding constant optimization and use of just one

IOL model. The BUII achieved, in fact, only 72.3% of eyes with a PE within ± 0.50 D, a percentage lower than the corresponding value reported by other studies. This may be due to the inclusion of data from patients operated on by different surgeons and refracted by different examiners.

Just a few months earlier, Cooke and Cooke reported similar outcomes in 1,079 eyes, with the advantage of having measurements from both IOLMaster and Lenstar, so that the Olsen formula could be included (27). The BUII ranked first with the IOLMaster and second with Lenstar, whereas the Olsen_{standalone} formula ranked first with the Lenstar and achieved the highest percentage of eyes with a PE within ± 0.50 D (83.7%). The Haigis formula was the third best. This was the first paper to report better results with the Olsen formula available on PhacoOptics software compared to the Olsen formula pre-installed on the Lenstar.

In 2017, Kane *et al.* further contributed to our knowledge by comparing the BUII to three new formulas in 3,211 eyes: the FullMonte method, the Ladas Super Formula and the RBF (27). They found that none of the newer formulas gave more accurate results over the BUII; they also underperformed traditional formulas, such as the Holladay 1 and SRK/T. The BUII ranked first in two additional papers with small sample size and multifocal IOLs (28,29).

In 2018, Melles *et al.* published their study with the largest database, using 13,301 eyes with the Acrysof SN60WF (Alcon Laboratories, Inc., TX, USA) and 5,200 eyes with the Acrysof SA60AT being analyzed (30). Their findings closely mirror those previously reported (28,31), as the BUII and Olsen formulas ranked first and second, followed by the Haigis formula. In addition to the refractive outcomes, this paper reported some interesting relationships, such as the dependence of the SRK/T on K, the dependence of the Hoffer Q on ACD and the lack of correlation between the PE of the BUII, Haigis and Olsen and AL. However, it did not include newer formulas and for this reason an update was published in 2019 (32). Here the most accurate outcomes were achieved by the Kane, BUII, Olsen and EVO 1.0 formulas, which all achieved at least 80% of eyes with a PE within ± 0.50 D; the RBF was less accurate than the best formulas, but still better than traditional vergence formulas.

In 2020, Darcy *et al.* reported the analysis of 10,930 eyes implanted with 4 different IOL models (33). Preoperative biometry was performed by means of partial coherence interferometry (PCI), so that LT was not available. They found that the Kane was the most accurate formula; they also reported that RBF 2.0 improved over the 1.0 (it

ranked second) and that the Holladay 2 formula with AL adjustment improved over the original Holladay 2 formula. Overall, the percentage of eyes with a PE within ± 0.50 D was still relatively low (between 70% and 72%) (also true for the best performing formulas).

In 2020 another important study was published. Savini *et al.* reported the results of 15 formulas in a smaller sample ($n=150$) of eyes, all with the same IOL model (Acrysof SN60WF) (8). Preoperative biometry was performed with an optical biometer based on swept-source optical coherence tomography (OA-2000, Tomey, Japan). They confirmed the high accuracy of the BUII, EVO 1.0, Holladay with AL adjustment, Kane, RBF 2.0 and Olsen_{standalone} formulas, which achieved at least 88% of eyes with a PE within ± 0.50 D. They also reported good outcomes for the older formulas (Haigis, Hoffer Q, Holladay 1 and SRK/T), which had between 85.33% and 84.67% of eyes with a PE within ± 0.50 D. Finally, they highlighted that today it is possible to have high percentages ($>55\%$) of eyes with a PE within ± 0.25 D and this should become one of the main outcomes to be reported in future studies. These results are similar to those reported by the same group with different optical biometers, the Aladdin (Topcon EU, Italy) and the Galilei G6 (Ziemer, Switzerland) (34,35).

Subgroup analysis: short and long eyes

The refractive accuracy of IOL power calculation in short eyes (AL <22 mm) is still lower than in medium length eyes. Since 1993, it has been well accepted that the Hoffer Q formula performed best in eyes shorter than 22 mm, but recently no formula has been shown to be superior compared to the others. Shrivastava *et al.* did not find statistically significant differences in 50 eyes among the BUII, Haigis, Hoffer Q, Holladay 2 and RBF 1.0 (36). Similar outcomes were reported by Göcke *et al.*, when comparing the same formulas plus the Olsen formulas in 86 eyes (37), as well as by Kane *et al.* in the subgroup of short eyes from their 2016 paper (31). Unfortunately, Melles did not statistically analyze formulas accuracy for short eyes (30). Overall, these studies show that the percentage of short eyes with a PE within ± 0.50 D is lower, i.e., between 50% and 70% of eyes according to the different studies. Caution therefore is required when selecting the IOL power in these eyes and it might be wise to use formulas that take preoperative ACD into account when dealing with eyes that have a shallow (<2.40 mm) ACD (38). This suggestion is valid also in eyes with medium AL and ACD of 3.00 mm or

less or ACD of 3.5 mm or more (39).

The situation is better in long eyes (AL >26 mm), where modern formulas led to remarkable improvements over the past. Formulas whose accuracy is not influenced by AL should be preferred. The SRK/T is still a valid option on condition that specifically optimized constants are used (40). Published papers reported the good performance of the BUII (26,30,31,33,41,42), Kane (32,33), Olsen (26,33,42), and RBF 2.0 (33,41) formulas. The Haigis formula is accurate for long eyes (31), but it does not seem the best option when the AL is >30 mm, as better outcomes have been achieved in these eyes with the BUII and Olsen formulas (41). Overall, around 75% of eyes may be expected to have a PE within ± 0.50 D with the best formulas (42).

Axial length adjustments

The issue of AL adjustment was discussed in 2009 by Fam and Lim (43), who proposed a transformation of the AL and K measurements of the IOLMaster to improve the refractive outcomes in eyes with extreme AL. Subsequently, it gained wide popularity thanks to Wang *et al.* with the so-called Wang/Koch formula (16). In order to reduce the risk of postoperative hyperopia in eyes with AL >25.0 mm and achieve a zero mean PE, they generated some regression formulas to optimize the AL (measured by PCI with the IOLMaster) for the Haigis, Hoffer Q, Holladay 1 and SRK/T formulas. These equations shortened the measured AL. The reason why AL should be shortened in long eyes was explained by the authors: when optical biometry was developed, the optical path length measured by PCI had to be converted into a geometrical distance matching the AL measured by immersion ultrasound biometry (which was the gold standard at that time) (1). Since PCI cannot measure LT, it was not possible to use the specific refractive index of each intraocular dioptric medium and a “group refractive index” was used. This represents an average refractive index, which works correctly in eyes with medium AL, but is not accurate in long eyes, where a higher percentage of vitreous is present. As a consequence, the group refractive index overestimates AL. Subsequent studies have shown that the original Wang/Koch AL adjustment not only avoids postoperative hyperopia, but induces, on average, a myopic outcome (30,41). The authors therefore modified the original formula and made it less aggressive in the reduction of AL (44). A subsequent paper confirmed that the modified Wang/Koch formula induces less myopia (41). The modified Wang/Koch formula should be applied to the

Holladay 1 formula in eyes longer than 26.5 mm and to the SRK/T formula in eyes longer than 27.0 mm (it should not be applied to the Haigis formula). The optimized constants available on the User Group for Laser Interference Biometry (ULIB) website should be used for all IOLs but the Acrysof MA60MA, for which the manufacturer's constant should be used.

However, based on a database of more than 18,000 eyes, they further refined the AL adjustment separately for the Holladay 1 and Holladay 2 formulas. These adjustments rely on nonlinear regression analysis and should be applied to eyes longer than 24.0 mm (45). They are available on the Holladay Consultant software as "Holladay adjustment" and represent the main innovation of the Holladay 2 formula, recently tested by different studies (8,33).

Other authors questioned the validity of traditional AL measurements by optical biometry and investigated the so-called "sum-of-segments AL", which is obtained by adding the length of each segment (CCT, ACD, LT and vitreous). Cooke and Cooke were able to generate the sum-of-segment AL from Lenstar measurements and compare it to the AL shown on the printout, which is obtained with the group refractive index (46). They found that in both short and long eyes the sum-of-segments AL improved the accuracy of Hoffer Q, Holladay 1, Holladay 2 and SRK/T formulas but worsened the performance of the BUII and Olsen formulas. Similar outcomes have been reported by Wang *et al.* using segmented AL rather than AL calculated with a single group refractive index (47). Since sum-of-segments AL is not available on most optical biometers (the only exception is the Argos by MOVU, Japan), an easy way to approximate it would be beneficial. Therefore, the same authors developed the Cooke-modified AL (CMAL), a regression formula which improves the PE of the Hoffer Q, Holladay 1, Holladay 2 and SRK/T formulas (48).

Calculation of toric IOLs

For more than 10 years the attention of researchers has been drawn by posterior corneal astigmatism (PCA). In 2009, Ho *et al.* were the first to compare keratometric astigmatism (KA) and total corneal astigmatism (TCA) (49). Using a rotating Scheimpflug camera (Pentacam, Oculus), they found that 10.3% of the candidates for toric IOLs had either a KA magnitude that differed by >0.50 D from the TCA magnitude or a KA angle that differed by $>10^\circ$ from the TCA angle. In 2011, Koch *et al.* used a dual

Scheimpflug analyzer (Galilei, Ziemer) to observe that PCA shows, in more than 85% of the eyes, a vertically aligned steeper meridian. Given the negative power of the posterior corneal surface, which causes it to behave with regard to refractive astigmatism exactly opposite to the anterior corneal surface, the steeper the curvature of a given posterior corneal meridian, the more negative the power. Therefore, the steep vertical meridian in the posterior surface produces an against-the-rule (ATR) refractive astigmatism (50,51). As a consequence, according to vector analysis KA leads to an estimation error of TCA of 0.22 D @180°, on average. Similar outcomes were subsequently reported by other authors, who confirmed that on average KA overestimates TCA in eyes with WTR astigmatism and underestimates it in eyes with ATR astigmatism (52-54). Not surprisingly, when comparing KA to TCA, the latter was found to predict more accurately the postoperative refractive astigmatism in eyes receiving toric and non-toric IOLs (55,56). Without a doubt, the ideal situation would be that we could determine with a direct measurement the PCA and calculate the TCA in this way. However, this has proven to be a formidable challenge for today's technology. Currently notwithstanding improvements in corneal imaging (Scheimpflug tomographers, anterior segment optical coherence tomographers), there is not really a gold standard for the direct determination of the PCA in a given eye, and in fact, it has been demonstrated that using measured TCA is less accurate than using predicted TCA (57-62).

The first method used to predict TCA was the Baylor toric IOL nomogram, published in 2013, which took into account the mean values of PCA that they found (ATR astigmatism) and aimed to leave eyes after the toric IOL implantation with small amounts of WTR refractive astigmatism. It was required to manually perform the calculation following the guidelines indicated in some tables (63). Shortly after the Barrett Toric Calculator was released. This calculator applies a mathematical algorithm, also based fundamentally on the ATR refractive effect of PCA, to indirectly deduce posterior corneal radii, and is linked to the Barrett Universal II formula. By entering patient data, power is automatically obtained for both the spherical equivalent and the toricity of the IOL. This is available for free on the website of the APACRS (https://calc.apacrs.org/toric_calculator20/Toric%20Calculator.aspx, accessed on February 26th, 2020). Other methods were then developed by Abulafia *et al.* (64), Savini and Næser (58),

Goggin *et al.* (65), and Holladay *et al.* (66), as well as by some IOL manufacturers (67). Other recently introduced toric calculators are those developed by Kane (<https://www.iolformula.com>, accessed on July 11th, 2020) and on the website of the EVO formula (www.evoiolcalculator.com, accessed on July 11th, 2020). The Abulafia-Koch calculator is used to calculate the toricity of the IOL manufactured by Physioll (<https://www.physiolltoric.eu/physiolltoric>, accessed on February 26th, 2020); the Næser/Savini toric calculator is available for free at <https://www.soiweb.com/toric-calculator> (accessed on February 26th, 2020); the Holladay toric calculator is available for free at <https://www.hic-soap.com/calc/preop> (accessed on February 27th, 2020). Overall, these methods are considered today the gold standards to calculate toric IOLs. Their higher accuracy with respect to measured TCA may depend on the fact that direct determinations are still not accurate enough and in addition, prediction can take other factors into account (not only PCA): one of these may be IOL tilting, which has been shown to induce ATR refractive astigmatism (68).

On average, the mean error in the prediction of refractive astigmatism (also known as “error in refractive astigmatism” or “centroid error in predicted residual astigmatism”) is close to zero, because estimating methods perform an optimization of corneal astigmatism to reach this goal. However, since when obtaining the vectorial mean value of the astigmatisms, those with different directions tend to cancel each other, these almost perfect values must be analyzed with caution. Indeed, a clinically relevant standard deviation can be observed in all studies, so that the percentage of eyes within ± 0.50 D of the predicted refractive astigmatism is still relatively low and ranges between 55% and 78% (57-59,69). Further studies and new technological developments are required to improve the direct evaluation of TCA, and therefore the calculation of the power of toric intraocular lenses.

Intraoperative aberrometry

Intraoperative aberrometry is a relatively new technology used to calculate both the sphere and cylinder of the IOL to be implanted. The most common system is the Optiwave Refractive Analysis (ORA, Alcon), which is attached to the microscope and can measure aphakic and pseudophakic refraction during cataract surgery. Usually, the refraction is taken after cataract removal, when the capsular bag is filled with a viscoelastic. In unoperated eyes, studies have shown

that the refractive outcomes of IOL power calculation are similar to those of optical biometry (70,71).

Acknowledgments

Funding: This work was supported by the Italian Ministry of Health and Fondazione Roma.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Dr. Andrzej Grzybowski) for the series “Recent developments in cataract surgery” published in *Annals of Translational Medicine*. The article was sent for external peer review organized by the Guest Editor and the editorial office.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/atm-20-2290>). The series “Recent developments in cataract surgery” was commissioned by the editorial office without any funding or sponsorship. GS reports grants from Italian Ministry of Health, grants from Fondazione Roma, during the conduct of the study; personal fees from Alcon, personal fees from CSO, personal fees from Oculus, personal fees from Zeiss, outside the submitted work. KJH reports personal fees from Carl Zeiss Meditec, personal fees from Haag-Streit, personal fees from Oculus, personal fees from Ziemer, personal fees from Topcon EU/Visia Imaging, personal fees from Tomey, personal fees from Movu, personal fees from Heidelberg Engineering, outside the submitted work. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Savini G, Taroni L, Hoffer KJ. Recent developments in intraocular lens power calculation methods—update 2020. *Ann Transl Med* 2020;8(22):1553. doi: 10.21037/atm-20-2290