• Clinical Research •

Evaluating newer generation intraocular lens calculation formulas in manual versus femtosecond laser-assisted cataract surgery

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Abstract

● **AIM:** To determine the refractive accuracy of the Haigis, Barrett Universal II (Barrett), and Hill-radial basis function 2.0 (Hill-RBF) intraocular lens (IOL) power calculations formulas in eyes undergoing manual cataract surgery (MCS) and refractive femtosecond laser-assisted cataract surgery (ReLACS).

● **METHODS:** This was a REB-approved, retrospective interventional comparative case series of 158 eyes of 158 patients who had preoperative biometry completed using the IOL Master 700 and underwent implantation of a Tecnis IOL following uncomplicated cataract surgery using either MCS or ReLACS. Target spherical equivalence (SE) was predicted using the Haigis, Barrett, and Hill-RBF formulas. An older generation formula (Hoffer Q) was included in the analysis. Mean refractive error (ME) was calculated one month postoperatively. The lens factors of all formulas were retrospectively optimized to set the ME to 0 for each formula across all eyes. The median absolute errors (MedAE) and the proportion of eyes achieving an absolute error (AE) within 0.5 diopters (D) were compared between the two formulas among MCS and ReLACS eyes, respectively.

● **RESULTS:** Of the 158 eyes studied, 64 eyes underwent MCS and 94 eyes underwent ReLACS. Among MCS eyes, the MedAE did not differ between the formulas (P=0.59), however among ReLACS eyes, Barrett and Hill-RBF were more accurate (P=0.001). Barrett and Hill-RBF were both more likely to yield AE<0.5 D among both groups (P<0.001).

● **CONCLUSION:** The Barrett and Hill-RBF formula lead to greater refractive accuracy and likelihood of refractive success when compare to Haigis in eyes undergoing ReLACS.

● **KEYWORDS:** phacoemulsification; cataract; femtosecond laser; intraocular lens

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INTRODUCTION

The predictability of refractive outcomes following uncomplicated cataract surgery has steadily improved over the years, and this is largely attributable to more accurate intraocular lens (IOL) power calculation formulas[1-2]. Although more recent formulas generally outperform those of previous generations, there is considerable debate regarding the selection of the most accurate formula[3-4]. Among the more popular IOL formulas, the Haigis[5], and newer generation Barrett Universal II (Barrett)[6] and Hill-Radial Basis Function (Hill-RBF)[7] formulas have shown superiority to other formulas[8-11]. These formulas are felt to perform relatively consistently across the range of axial lengths (AL)[2]. And their use of multiple-variable vergence models has drawn the attention of cataract surgeons[12].

Although some authors advocate for the use of different formulas for varied ocular parameters[2]. It is important to also consider the modality of cataract surgery being employed. Namely, there has been increasing integration of the femtosecond laser into phacoemulsification surgery given its ability to assist with many critical steps of the procedure[13].

From a refractive standpoint, it has been suggested that the use of refractive femtosecond laser-assisted cataract surgery (ReLACS) may optimize the circularity and centration of the anterior capsulotomy[14] and ultimately the effective lens position when compared to conventional manual cataract surgery (MCS)[15]. The impact of these potential differences on the performance of modern IOL formulas has not been elucidated.

Given this void in the literature, this study was designed to evaluate and compare the performance of the Haigis, Barrett, and Hill-RBF 2.0 IOL formulas within a single IOL platform across eyes treated *via* ReLACS and MCS. This would further add to the literature on comparing the performance of each formula, but more importantly, would provide guidance on whether surgeons should select a particular formula based on the modality of cataract surgery.

SUBJECTS AND METHODS

Ethical Approval This retrospective interventional comparative case series was approved by the Research Ethics Board of the William Osler Health System and was conducted in accordance with the tenets of the Declaration of Helsinki. Electronic medical records were reviewed at a private cataract surgery center (Vaughan, Ontario, Canada) between June 30th, 2017 to August 30th, 2018 to identify patients who: 1) had uncomplicated phacoemulsification surgery with implantation of a Tecnis intraocular lens (AMO Tecnis ZCB00, Johnson & Johnson Vision, Santa Ana, CA, USA); 2) had preoperative biometric testing completed using the IOL Master 700 (Zeiss, Oberkochen, Germany); 3) had a lens thickness (LT) of at least 2.5 mm; 4) had cylinder less than 4.0 D; and 5) AL standard deviation (SD) of 15 μm or less, representing a good reliability index. Only one eye per patient was used, and the better of two eyes included with postoperative best corrected visual acuity (BCVA) of at least 20/40 or better[16]. Exclusion criteria included any history of refractive surgery or corneal disease, postoperative refractive error greater than 2.0 D, and postoperative BCVA worse than 20/40.

Preoperative Examination Preoperative demographic variables of interest included age, gender, and laterality of the included eye. Baseline biometric data obtained from the IOL Master 700 included AL, anterior chamber depth (ACD), keratometry values, LT and horizontal white to white diameter (WTW). In an effort to increase the internal validity of the study, the older generation Hoffer Q formula[17] was included in this analysis to serve as a reference point against which the newer generation formulas would be compared. The postoperative refraction for a Tecnis IOL was predicted using the IOL Master 700 for the Haigis, Barrett, and Hoffer Q formulas. Hill-RBF (version 2.0) calculations were performed using the online web-based calculator[7].

Surgical Technique Standard techniques were employed for cataract extraction using either MCS or ReLACS. MCS was completed using a 2.5 mm main clear corneal incision and the WhiteStar Signature Phacoemulsification System (Advanced Medical Optics, Santa, Ana, CA, USA) for cataract extraction. For eyes undergoing ReLACS, the Catalys Precision Laser System with Liquid Optics Interface (Abbott Medical Optics, Santa Ana, CA) was used to create the 2.5 mm main corneal incision, a 1.2 mm side port incision, a 5.0 mm diameter anterior capsulotomy and for lens fragmentation with grid softening. The eyes then proceeded with standard phacoemulsification surgery as described for the MCS group. All eyes were prescribed topical bromfenac one drop daily, topical besifloxacin one drop three times daily, and loteprednol gel applied three times daily for a total of 30d following the procedure.

Postoperative Examination Manifest refraction was measured at the one-month postoperative visit. The postoperative refractive error was calculated by subtracting the predicted spherical equivalence from the measured spherical equivalence. This calculation was computed for all formulas. The mean errors of all formulas were adjusted to zero by retrospectively optimizing the lens factor. For the Haigis formula, an optimized a0 lens constant of 1.712 was computed using 0.4 and 0.1 as the a1 and a2 constants, respectively[5]. For the Barrett formula, the optimized lens factor was computed to be 2.15. For the Hill-RBF and Hoffer Q formulas, the optimized lens constants were 119.5 and 5.85, respectively. Following optimization, the mean absolute error (AE) and median absolute error (MedAE) were computed.

Outcome Measures The primary outcome was to compare the one-month MedAE between the formulas among MCS and ReLACS eyes. Secondary outcomes included the proportion of eyes achieving an AE within 0.5 D, and the correlation between AE and AL among MCS and ReLACS eyes.

Statistical Analysis Categorical parameters were reported as proportions with differences compared using the Fisher exact test. Continuous variables were reported as mean±standard deviation (SD) with differences compared using the *t* test. Differences in MedAE were compared using the Friedman test. Post-hoc analyses were completed using the Wilcoxon signed-rank test, with multiple comparisons corrected for using the Bonferroni method. Pearson correlational analysis was completed to compute correlation coefficients. Statistical analysis was performed using SPSS (IBM Corp, Armonk, New York; software version 22).

RESULTS

A total of 158 eyes met the inclusion criteria with 64 eyes in the MCS group and 94 eyes in the ReLACS group. Demographic and preoperative characteristics of both groups

Table 1 Baseline characteristics of eyes that underwent ReLACS and MCS

Items	MCS (*n*=64)	ReLACS (*n*=94)	*P*
Age at surgery (y)	73.0±8.0 (48-85)	68.5±9.2 (47-89)	0.002
Female	45.3%	57.4%	0.15
Right eye treated	50%	47.9%	0.87
AL (mm)	23.5±0.9 (21.8-26.4)	23.7±1.3 (21.9-29.1)	0.24
ACD (mm)	3.1±0.3 (2.3-3.9)	3.1±0.4 (2.4-4.3)	0.21
Mean keratometry (D)	44.2±1.7 (38.8-48.2)	43.9±1.7 (38.9-47.3)	0.23
Cylinder (D)	0.79±0.5 (0-2.1)	0.87±0.7 (0-3.5)	0.45
LT (mm)	4.7±0.4 (3.9-5.5)	4.5±0.4 (2.9-5.3)	0.02
WTW (mm)	11.9±0.4 (11-12.9)	11.8±1.1 (11.9-13.2)	0.62
IOL power (D)	21.2±2.8 (10.5-26.5)	21.0±3.6 (8.0-27.0)	0.66

ReLACS: Refractive femtosecond laser-assisted cataract surgery; MCS: Manual cataract surgery; AL: Axial length; ACD: Anterior chamber depth; LT: Lens thickness; WTW: Horizontal white to white diameter; IOL: Intraocular lens. Data are mean±standard deviation unless otherwise indicated. Ranges are indicated within parentheses.

Table 2 One-month refractive outcomes of the intraocular lens formulas within MCS and ReLACS eyes

Items	Haigis	Barrett	Hill-RBF	Hoffer Q	*P*
MedAE (D)					
All eyes	0.27 (0.12-0.50)	0.21 (0.11-0.38)	0.25 (0.11-0.39)	0.25 (0.10-0.46)	0.005
MCS	0.23 (0.08-0.49)	0.21 (0.10-0.38)	0.26 (0.11-0.40)	0.20 (0.10-0.46)	0.59
ReLACS	0.27 (0.12-0.52)	0.21 (0.11-0.38)[a]	0.23 (0.11-0.40)	0.28 (0.11-0.49)	0.001
AE<0.5 D					
All eyes	119/158 (75%)	137/158 (87%)	135/158 (85%)	122/158 (77%)	<0.001[b]
MCS	49/64 (77%)	57/64 (89%)	57/64 (89%)	52/64 (81%)	<0.001[b]
ReLACS	70/94 (74%)	81/94 (86%)	79/94 (84%)	70/94 (74%)	<0.001[b]

MedAE reported as median and IQR. MCS: Manual cataract surgery; ReLACS: Refractive femtosecond laser-assisted cataract surgery; MedAE: Median absolute error. [a]In ReLACS eyes, post-hoc analysis revealed Barrett to have significantly less MedAE compared to Haigis and Hoffer Q, but similar MedAE when compared to Hill-RBF. [b]Across all eyes and within both groups, the Barrett and Hill-RBF had significantly greater proportions of eyes with AE<0.5 D, when compared to Haigis and Hoffer Q.

are illustrated in Table 1. Patients in the ReLACS group were younger (*P*=0.002) and had slightly thinner lenses (*P*=0.02) when compared to the MCS group. There were no differences between the groups when comparing AL, mean keratometry, cylinder, ACD, WTW, IOL power, and distributions of gender and laterality (all *P*>0.05).

Table 2 outlines the refractive outcomes at one-month postoperative within the MCS and ReLACS groups. Across all eyes, the Friedman test confirmed that there were statistically significant differences in the accuracy of the formulas (*P*=0.005). Post-hoc analysis revealed that the MedAE was significantly less when using the Barrett formula [MedAE=0.21 D, interquartile range (IQR): 0.11-0.38 D] compared to Haigis (MedAE=0.27 D, IQR: 0.12-0.50 D, *P*=0.005) and the Hoffer Q formula (MedAE=0.25 D, IQR: 0.10-0.46 D, *P*<0.001). The MedAE of the Hill-RBF formula (MedAE=0.25 D, IQR: 0.11-0.39) was similar to the Barrett formula (*P*=1.0).

When comparing the MedAE among ReLACS eyes, the Friedman test confirmed that there were statistically significant differences in the accuracy of the formulas (*P*=0.001). Post-hoc analyses revealed that the Barrett formula (MedAE=0.21 D, IQR: 0.11-0.38 D) was more accurate than the Haigis formula (MedAE=0.27 D, IQR: 0.12-0.52 D, *P*=0.006) and the Hoffer Q formula (MedAE=0.28 D, IQR: 0.11-0.49 D, *P*<0.001). The distribution of the Hill-RBF formula (MedAE=0.23 D, IQR: 0.11-0.40 D, *P*=1.0) was similar to that of the Barrett formula among ReLACS eyes.

Among MCS eyes, the Friedman test confirmed that there were no statistically significant differences in the accuracy of the formulas (*P*=0.59). The MedAE (IQR) of the Haigis, Barrett, Hill-RBF and Hoffer Q formulas were 0.23 D (0.08-0.49 D), 0.21 D (0.10-0.38 D), 0.26 D (0.11-0.40 D) and 0.20 D (0.10-0.46 D), respectively.

Across all eyes, the Barrett (87% of eyes) and Hill-RBF (85%) formulas were more likely to result in AE less than 0.5 D when compared to Haigis (75%) and Hoffer Q (77%, *P*<0.001). Among ReLACS eyes, Barrett (86%) and Hill-RBF (84%) were similarly more likely to achieve AE less than 0.5 D when compared to Haigis (74%) and Hoffer Q (74%, $P<0.001$). This trend was also observed among MCS eyes ($P<0.001$), with 89%, 89%, 77% and 81% of eyes achieving AE less than 0.5 D using the Barrett, Hill-RBF, Haigis and Hoffer Q formulas, respectively.

Among ReLACS eyes, Pearson correlational analysis did not reveal a significant association between AL and AE when using the Barrett (r=0.076, P=0.47), Haigis (r=0.037, P=0.72), Hoffer Q (r=0.16, P=0.14) or Hill-RBF (r=-0.027, P=0.80) formulas. Among MCS, there was no significant correlation between AL and AE when using the Hoffer Q (r=-0.16, P=0.20) or the Haigis formula (r=-0.143, P=0.26). However, AL and AE were significantly correlated among MCS eyes when using the Barrett (r=-0.25, P=0.04) and Hill-RBF (r=-0.25, P=0.04) formulas.

DISCUSSION

To our knowledge, this study is among the first to evaluate the performance of the Haigis, Barrett, and Hill-RBF formulas among eyes treated *via* ReLACS and MCS. Among MCS eyes, there was no significant difference in MedAE between the formulas, however among ReLACS eyes, there was a pronounced benefit of pursuing the newer generation Barrett and Hill-RBF formulas. Interestingly, our results suggest that AL was associated with the magnitude of AE when these newer generation formulas are used in MCS eyes, however AL did not influence AE among ReLACS eyes. Across all eyes, and especially in ReLACS eyes, the Hoffer Q was suboptimal when compared to the newer generation formulas.

Recently, Whang *et al*[18] compared refractive outcomes between eyes treated *via* femtosecond laser-assisted and conventional cataract surgery using the Barrett and Haigis formulas. Their results indicated superior refractive outcomes among eyes treated using the femtosecond laser-assisted approach[18]. However, their study's analysis was not designed to detect performance differences between formulas, and rather focused on cataract surgery modality as a modulator of refractive accuracy. Our study, therefore, complements their results and found that the Barrett formula was more accurate and was associated with a greater likelihood of refractive success across all eyes, and in eyes undergoing ReLACS. Therefore, these results suggest that surgeons may benefit from using the Barrett formula over Haigis for their ReLACS cases. However, for MCS cases, both formulas are likely to perform comparably.

Although not statistically significant, our results did indicate a trend towards smaller MedAE achieved using the Barrett when compared to the Hill-RBF. The Hill-RBF is an artificial intelligence-based formula that uses pattern recognition and an algorithmic process to predict the optimal IOL power given the AL, ACD and corneal power based on a pre-existing database of patients. In their study of 127 eyes, Wan *et al*[19] did not detect differences in MedAE when comparing the Barrett and Hill-RBF formulas. Similarly, Roberts *et al*[8] found both the Hill-RBF and the Barrett formulas to reduce refractive error in short and long eyes, in their cohort of 400 patients, however they did detect fewer refractive surprises when using the Barrett formula. Kane *et al*[4] found Barrett to be superior in the reduction of absolute error when compared to Hill-RBF in a large cohort of 3122 patients. The apparent superiority Barrett when compared to Hill-RBF may be attributable to its use of multiple parameters to calculate a better estimation of the effective lens position.

ACD, LT, and WTW were included as parameter inputs into the Barrett formula calculation, as they may contribute to a better estimation of lens position and thus more accurate results[6]. The Haigis formula, however, did not use LT or WTW as parameter inputs. These differences may explain the more accurate results obtained by Barrett in the present study. A previous Meta-analysis has shown that when created by ReLACS, capsulotomies were more likely to be of the intended diameter, more horizontally centred, and more circular (depending on the measure of circularity used)[14]. Therefore, the benefit of the Barrett formula among ReLACS eyes may reflect some degree of synergy between the increased accuracy of the estimated lens position by Barrett and the theoretically more predictable and centred capsulorrhexis offered by ReLACS.

The superiority of Barrett to other formulas, including Haigis, has been demonstrated by a number of studies. In their consecutive series of 18 501 cases, Melles *et al*[2] found that the Barrett provided a more accurate prediction of postoperative refraction when compared to Haigis and performed well across a range of ALs. Across all eyes in their series, the MedAE for the Barrett and Haigis formulas were 0.25 and 0.28 D, respectively, which were similar to the results of our study[2]. Similarly, Kane *et al*[4] found Barrett to be superior to Haigis when comparing refractive accuracy in their series of 3241 patients, especially in eyes with AL greater than 22.0 mm.

Given that IOL formulas tend to be less accurate among eyes of very short or long ALs, the present study aimed to evaluate the performance of formulas across the full range of ALs of the included participants. A recent Meta-analysis found that the Barrett and Haigis formulas performed comparably in long eyes[11]. In short eyes, studies did not detect a significant difference in refractive performance between the two formulas[1,4,9]. Our results indicated that AL was not significantly associated with AE in the ReLACS groups when using the Barrett or Hill-RBF, however AL was negatively correlated with AE among MCS eyes when using the Barrett and Hill-RBF formulas. In other words, shorter eyes were more likely to have greater AE among MCS eyes, and this further supports the potential benefit of pursuing ReLACS together with a newer generation formula.

The retrospective design of this study was one of the limitations of this study, as the authors were not able to prospectively match the baseline characteristics of the MCS and ReLACS groups. The sample size was relatively small and not equal between the groups, which warrants investigations in future larger cohorts and of other modern IOL formulas to provide further clarity regarding the ideal choice of IOL formula for ReLACS and MCS, respectively. The strengths of this study include its use of a consistent IOL design with lens constant optimization to allow for sound statistical testing, and an adequate follow up period of one month for all patients, at which time postoperative refraction is typically known to have stabilized.

In conclusion, our study supports the superiority of the newer generation Barrett and Hill-RBF formulas to Haigis overall in patients undergoing phacoemulsification with implantation of a Tecnis IOL. Surgeons employing ReLACS may have increased refractive accuracy especially when using the Barrett or Hill-RBF formulas, as there is a strong opportunity to predict and implement an accurate effective lens position. Further studies are warranted to investigate whether one of these newer generation formulas outperforms the other.

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