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Accuracy of intraocular lens power calculation for cataract surgery after deep anterior lamellar keratoplasty

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ABSTRACT

Background: The purpose of this study was to assess the accuracy of intraocular lens power (IOL) formulas for cataract surgery after deep anterior lamellar keratoplasty (DALK).

Methods: This retrospective study included eyes which had previously undergone DALK and underwent standard phacoemulsification with monofocal IOL implantation between January 2012 and January 2021 at Ospedali Privati Forlì "Villa Igea" (Forlì, Italy). The predicted spherical equivalent (SE) was calculated using the Barrett Universal II, Emmetropia Verifying Optical (EVO), Haigis, Hoffer Q, Hoffer QST, Holladay 1, Holladay II, Kane and SRK/T formulas. Prediction error (PE) was calculated as the actual postoperative SE refraction minus the SE predicted refraction.

Results: 82 eyes of 82 patients were included. The mean PE was negative using all formulas. Friedman test revealed a statistically significant difference of the median absolute PE (MedAE) among the different IOL formulas (P = 0.005). On the basis of the MedAE, the fomulas were ranked as follows: SRK/T (0.805 D), Kane (0.810 D), EVO (0.845 D), Hoffer QST (0.847 D), Barrett (0.895 D), Holladay 1 (0.915 D), Haigis (1.010 D) and Hoffer Q (1.070 D) formulas.

Conclusions: All formulas had a tendency towards a myopic refractive surprise in post-DALK eyes. Although the SRK/T, Kane, EVO and Hoffer QST formulas were more accurate, predictability of refractive outcomes was lower than in virgin eyes.

Keywords: cataract surgery; intraocular lens power; keratoplasty; deep anterior lamellar keratoplasty.

Deep anterior lamellar keratoplasty (DALK) has the advantages of avoiding the complications associated with open-sky surgery and eliminating the risk of endothelial rejection.[1,2] While simultaneous DALK and cataract surgery is technically feasible,[3] sequential cataract surgery allows the use of keratometry readings following DALK for the intraocular lens (IOL) power calculation.[4]

However, the postoperative refraction in eyes that have previously undergone keratoplasty can be unpredictable. DALK can alter the posterior to anterior corneal curvature radii ratio. Consequently, the keratometric refractive index, which is currently employed by IOL formulas, becomes invalid, and an error is introduced in the estimation of corneal power.[5,6] Moreover, changes in the anterior chamber anatomy may lead to incorrect prediction of effective lens position.[7]

Currently, data on selection of IOLs for cataract surgery after DALK are limited.[8,9] Thus, in an effort to improve the refractive outcomes, we compared the accuracy of IOL calculation formulas for prediction of refractive outcomes following cataract surgery in post-DALK eyes.

PATIENS AND METHODS

This was a retrospective review of 82 consecutive cases of phacoemulsification with implantation of monofocal IOL in eyes that had previously undergone DALK. All surgeries were performed between January 2012 and January 2021 at Ospedali Privati Forlì “Villa Igea” (Forlì, Italy). Patients with Snellen correct distance visual acuity (CDVA) < 20/40 at 1 month after cataract surgery were excluded from the analysis. The study adhered to the tenets of the Declaration of Helsinki and was prospectively approved by the local Ethics Committee (Comitato Etico, Ospedali Privati Forlì).

Surgical technique

DALK was performed as per our previously described technique.[10] Briefly, from the base of the deep partial-thickness trephination, 450-550 um in depth and 9mm in diameter, a probe was inserted and replaced with a cannula to attempt pneumatic dissection. Following partial anterior keratectomy, the central 6-mm optical zone was bared.[11] In cases of failed big-bubble formation, visco-bubble and manual layer-by-layer dissection was sequentially attempted, as necessary. A 9-mm anterior lamellar graft was prepared by means of microkeratome dissection using a 400-um head, punched to a diameter of 9 mm and sutured using double running 10-0 nylon sutures. The first suture was removed within three months from surgery, whereas the second was removed within one year.[10] All cataract surgeries were performed at least 3 months after complete suture removal. Anaesthesia and akinesia were obtained by means of peribulbar injection of 10 mL of 0.75% ropivacaine solution. Standard phacoemulsification with IOL implantation was performed through a 2.4-mm scleral tunnel incision (Stellaris PC, Bausch & Lomb, Rochester, NY). In all cases, a monofocal IOL was implanted within the capsular bag. A single 8-0 Vicryl suture was used to close the scleral incision. Betamethasone 0.2% and chloramphenicol 0.5% eye drops were administered every 2 hours for the first week after cataract surgery and gradually tapered off over 1 month.

Intraocular lens power calculation

Axial length was measured using optical low-coherence reflectometry (Lenstar, Haag-Streit AG, Koeniz, Switzerland). Anterior segment optical coherence tomography (OCT) (Casia; Tomey, Tokyo, Japan) was used to measure anterior keratometry readings.

As recommended by Savini et al., lens constant optimisation was not performed because different IOL models were employed.[12] Instead, the lens constants from the IOLCON website[13] were used for all IOL models. The predicted spherical equivalent (SE) was calculated using the following formulas: Barrett Universal II,[14] Emmetropia Verifying Optical (EVO),[15] Haigis,[16] Hoffer Q,[17] Hoffer QST,[18] Holladay 1,[19] Holladay II,[20] Kane[21] and SRK/T.[22] Prediction error (PE) was calculated as the actual postoperative SE refraction minus the SE predicted refraction.[23] A negative PE indicated a more myopic refraction than predicted by the formula. The mean PE, its standard deviation (SD), the median absolute error (MedAE) and the mean absolute error (MAE) were calculated, as well as the percentage of eyes with a PE within ±0.25 D, ±0.50 D, ±0.75 D and ±1.00 D.[24]

Statistical analysis

Statistical analysis was conducted using R (version 4.0.0) and RStudio (version 1.2.5042) software. The normality of data distribution was assessed by means of the Kolmogorov-Smirnov test. Due to the non-normal distribution of data, the Friedman test was performed to compare the MedAE. Post-hoc pairwise comparisons were performed with the Wilcoxon signed-rank test. The Cochran's Q test was used to assess statistically significant differences in the percentage of eyes with a PE within ± 1.00 D. A P value < 0.05 was considered statistically significant.

RESULTS

The study included 82 eyes of 82 patients who underwent cataract surgery with monofocal IOL implantation after DALK. Demographic and baseline clinical characteristics are summarised in Table 1. Indications for keratoplasty were corneal ectasia in 48 eyes (58.5%), bacterial keratitis in 12 eyes (14.6%), herpetic keratitis in 9 eyes (11.0%), post-traumatic leucoma in 4 eyes (4.9%), granular corneal dystrophy in 3 eyes (3.7%), interstitial keratitis in 3 eyes (3.7%), corneal scarring secondary to ocular rosacea in 2 eyes (2.4%), and lattice corneal dystrophy in 1 eye (1.2%).

Table 1. Demographical and clinical characteristics of the patient cohort.

Characteristic	Value
Age (years)	52.9 ± 13.5
Sex (m/f)	51/31
Axial length (mm)	25.05 ± 2.00
Anterior chamber depth (mm)	3.61 ± 0.63
Keratometry (steep) (D)	42.42 ± 2.12
Keratometry (flat) (D)	46.36 ± 2.37
Lens thickness (mm)	4.19 ± 0.44

The mean time between DALK and cataract surgery was 21.8 ± 13.7 months (range 15-72 months). The Hoya iSert 250 was implanted in 44 eyes (53.7%), Bausch & Lomb MX60 in 28 eyes (34.1%), AJL LLASHP60 in 9 eyes (11.0%) and Zeiss CT LUCIA 611P in 1 eye (1.2%). Using the SRK/T formula, the mean predicted SE refraction was -0.43 ± 1.08 D. One month postoperatively, mean refractive SE was -0.90 ± 1.17 D, while mean refractive astigmatism was 2.80 ± 1.49 D.

Table 2 shows the refractive PE calculated for each formula. The mean PE was negative using all formulas, indicating a myopic refractive surprise. The lowest MedAE was obtained by the SRK/T formula, followed by the Kane, EVO, Hoffer QST, Barrett, Holladay 1, Haigis and Hoffer Q formulas. The Friedman test revealed a statistically significant difference of the MedAE among the different IOL formulas (P = 0.005). Pairwise comparison revealed a significant difference of the Hoffer QST and EVO formulas compared with the Barrett and Haigis, and a significant difference of the SRK/T compared with the Haigis (Table 3).

Table 2. Refractive outcomes for all eyes sorted by median absolute error.

	Mean PE	MedAE	MAE	PE SD
SRK/T	-0.49	0.805	1.06	1.29
Kane	-0.47	0.810	1.10	1.34
EVO	-0.48	0.845	1.07	1.32
Hoffer QST	-0.49	0.847	1.05	1.30
Barrett	-0.50	0.895	1.12	1.34
Holladay 1	-0.23	0.915	1.07	1.35
Haigis	-0.45	1.010	1.21	1.46
Hoffer Q	-0.19	1.070	1.11	1.39

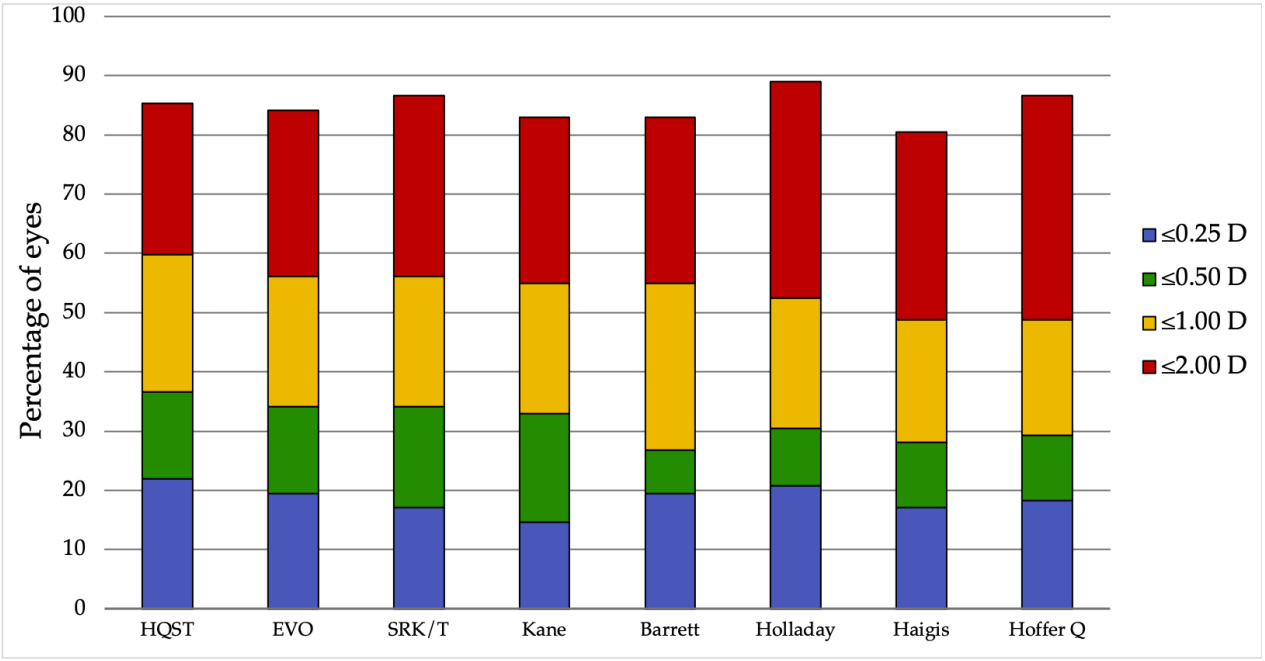
PE: prediction error; SD: standard deviation; MAE: median absolute error; MedAE: median absolute error.

Table 3. Matrix of the *P* values for the pairwise comparisons of the median absolute errors.

	SRK/T	Kane	EVO	Hoffer QST	Barrett	Holladay 1	Haigis	Hoffer Q
SRK/T	1							
Kane	0.595	1						
EVO	0.810	0.056	1					
Hoffer QST	0.771	0.110	0.474	1				
Barrett	0.298	0.701	0.022	0.009	1			
Holladay 1	0.527	0.989	0.500	0.982	0.548	1		
Haigis	0.004	0.001	<0.001	<0.001	0.003	0.024	1	
Hoffer Q	0.334	0.551	0.254	0.217	0.908	0.196	0.042	1

Figure 1 depicts the percentage of eyes with prediction errors within ± 0.25 D, ± 0.50 D, ± 1.00 D, and ± 2.00 D for each of the formulas. The highest percentage of eyes within ±1.00 D were obtained with the Hoffer QST (59.8%), EVO (56.1%) and SRK/T (56.1%). However, Cochran's Q test failed to identify a significant difference among formulas (*P* = 0.117).

Figure 1. Stacked histograms comparing the percentage of eyes within ± 0.25 D, ± 0.50 D, ± 1.00 D and ± 2.00 D of predicted spherical equivalent refraction.



DISCUSSION

Cataract surgery is an effective procedure for improving vision in eyes that have previously undergone DALK.[8,9] However, accurate IOL power calculation is crucial to ensure good refractive outcomes, thus representing an important aspect of the post-keratoplasty visual rehabilitation.

The current study evaluated the accuracy of third- and fourth-generation formulas in 82 eyes that had previously undergone DALK. Final refraction was within ±1.00 D of the refractive target in 50% to 62% of eyes. These results compare favourably with those of combined keratoplasty and cataract surgery,[25] thus supporting sequential cataract surgery following DALK to minimise postoperative refractive error.

Nevertheless, the prediction error derived from all formulas was significantly less accurate compared to those observed in virgin eyes, wherein more than 90% of eyes can be expected to be within ±1.00 D.[26,27] Many factors might contribute to the lower accuracy of IOL calculation after DALK including the inaccurate estimation of both corneal power and effective lens position. Interestingly, all formulas had a tendency towards a myopic refractive surprise. This may result from the alteration of the keratometric index with underestimation of the corneal power and consequent overestimation of the IOL power. Although optimisation of IOL constants might theoretically eliminate this systematic error, a large number of cases would be required to substantially improve refractive outcomes. Nevertheless, our results suggest that the use of anterior segment OCT keratometric readings following complete suture removal can allow relatively accurate IOL power calculation.

Of the 8 formulas evaluated in the study, the lowest variance of the prediction error was obtained using the SRK/T, Kane, EVO and Hoffer QST. The Hoffer QST, EVO and

SRK/T also resulted in the highest percentage of eyes within ±1.00 D (59.8%, 56.1% and 56.1%, respectively). Since neither the Kane, EVO nor the Hoffer QST formulas have been published, it is not possible to discuss the reasons for their good performance. On the other hand, the SRK/T formula is known to have a nonphysiologic behaviour with a tendency to result in hyperopic prediction error as the average keratometry decreases.[28,29] This might counterbalance the bias in predicted refraction occurring after DALK.

Currently, there is limited data published in literature regarding IOL power calculation in post-keratoplasty eyes. In a previous study by Tourabaly et al. based on 33 eyes which had undergone DALK, the highest refractive accuracy was obtained using the Hoffer Q formula.[9] However, only three third-generation formulas were analysed. Moreover, the PEs rather than the absolute errors were compared, and this does not provide evidence of the accuracy of IOL formulas.[30]

This series only included cases of cataract surgery with monofocal IOL implantation. In post-keratoplasty eyes, however, postoperative astigmatism is one of the leading causes of suboptimal vision despite the presence of a clear graft.[31,32] While sequential cataract surgery with toric IOL implantation following DALK can be useful to reduce refractive astigmatism and improve visual outcomes,[33,34] monofocal IOL still remains the most reasonable option for eye with irregular or low astigmatism.

This study has limitations including its retrospective design and inclusion of multiple IOL models, which did not allow IOL constant optimisation. Moreover, sample size subgroup analysis based on axial length, time interval between keratoplasty and cataract surgery or other variables was not performed due to the relatively small sample size. Further research is needed to improve the results of IOL power selection following DALK. Finally, since this study specifically evaluated the accuracy of IOL formulas following 9mm DALK

using our standard technique,[10,35,36] our results may not be generalized to patients who had previously undergone DALK using other techniques.

In conclusion, third-generation and fourth-generation formulas yielded a myopic prediction error in post-DALK eyes. Although the SRK/T, Kane, EVO and Hoffer QST formulas were more accurate, predictability of refractive outcomes was substantially lower compared to that observed in virgin eyes.

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References

1. Reinhart WJ, Musch DC, Jacobs DS, Lee WB, Kaufman SC, Shtein RM. Deep anterior lamellar keratoplasty as an alternative to penetrating keratoplasty a report by the american academy of ophthalmology. *Ophthalmology* 2011; **118**: 209-18.
2. Busin M, Scorcia V, Leon P, Nahum Y. Outcomes of Air Injection Within 2 mm Inside a Deep Trephination for Deep Anterior Lamellar Keratoplasty in Eyes With Keratoconus. *Am J Ophthalmol* **2016**; 164:6-13.
3. Zaki AA, Elalfy MS, Said DG, Dua HS. Deep anterior lamellar keratoplasty--triple procedure: a useful clinical application of the pre-Descemet's layer (Dua's layer). *Eye (Lond)* 2015; **29**:323-6
4. Shimmura S, Ohashi Y, Shiroma H, Shimazaki J, Tsubota K. Corneal opacity and cataract: triple procedure versus secondary approach. *Cornea* 2003; **22**: 234-8.
5. Savini G, Hoffer KJ. Intraocular lens power calculation in eyes with previous corneal refractive surgery. *Eye Vis (Lond)* 2018; **5**: 18.
6. Diener R, Treder M, Lauermann JL, Eter N, Alnawaiseh M. Assessing the validity of corneal power estimation using conventional keratometry for intraocular lens power calculation in eyes with Fuch's dystrophy undergoing Descemet membrane endothelial keratoplasty. *Graefes Arch Clin Exp Ophthalmol* 2021; **259**: 1061-1070.
7. Koch DD. The Enigmatic Cornea and Intraocular Lens Calculations: The LXXIII Edward Jackson Memorial Lecture. *Am J Ophthalmol* 2016; **171**: xv-xxx.
8. Den S, Shimmura S, Shimazaki J. Cataract surgery after deep anterior lamellar keratoplasty and penetrating keratoplasty in age- and disease-matched eyes. *J Cataract Refract Surg* 2018; **44**: 496-503.

9. Tourabaly M, Knoeri J, Georgeon C, Borderie M, Bouheraoua N, Borderie V. Long-Term Results and Refractive Error After Cataract Surgery With a Scleral Incision in Eyes With Deep Anterior Lamellar Keratoplasty. *Cornea* 2021; **40**: 1466-73.
10. Busin M, Leon P, Nahum Y, Scorcia V. Large (9 mm) deep anterior lamellar keratoplasty with clearance of a 6-mm optical zone optimizes outcomes of keratoconus surgery. *Ophthalmology* 2017; **124**: 1072–80.
11. Scorcia V, Lucisano A, Pietropaolo R, Corona VS, Scorcia G, Busin M. Red reflex-guided big-bubble deep anterior lamellar keratoplasty: a simple technique to judge dissectioin depth. *Cornea* 2015; **9:** 1035-8.
12. Savini G, Abbate R, Hoffer KJ, et al. Intraocular lens power calculation in eyes with keratoconus. *J Cataract Refract Surg* 2019; **45**: 576e581.
13. https://iolcon.org. Accessed June 2021.
14. https://calc.apacrs.org/barrett_universal2105. Accessed June 2021.
15. https://www.evoiolcalculator.com. Accessed June 2021.
16. Haigis W, Lege B, Miller N, et al. Comparison of immersion ultrasound biometry and partial coherence interferometry for intraocular lens calculation according to Haigis. *Graefes Arch Clin Exp Ophthalmol* 2000; **238**: 765-73.
17. Hoffer KJ. The Hoffer Q formula: a comparison of theoretic and regression formulas. *J Cataract Refract Surg* 1993; **19**: 700-12.
18. https://www.hofferqst.com. accessed June 2021.
19. Holladay JT, Prager TC, Chandler TY, Musgrove KH, Lewis JW, Ruiz RS. A three-part system for refining intraocular lens power calculations. J Cataract Refract Surg 1988; **14**:17-24.

20. Holladay JT. Holladay IOL Consultant Software & Surgical Outcomes Assessment. 1005.2015 ed. Bellaire, RX: Holladay Consulting, 2015
21. https://www.iolformula.com. Accessed June 2021.
22. Retzlaff JA, Sanders DR, Kraff MC. Development of the SRK/T intraocular lens implant power calculation formula. *J Cataract Refract Surg* 1990; **16**: 333-40. Erratum in: *J Cataract Refract Surg* 1990; **16**: 528.
23. Holladay JT, Wilcox RR, Koch DD, Wang L. Review and recommendations for univariate statistical analysis of spherical equivalent prediction error for IOL power calculations. *J Cataract Refract Surg* 2021; **47**: 65-77.
24. Hoffer KJ, Savini G. Update on Intraocular Lens Power Calculation Study Protocols: The Better Way to Design and Report Clinical Trials. *Ophthalmology* 2020:S0161-6420(20)30638-2.
25. Flowers CW, McLeod SD, McDonnell PJ, Irvine JA, Smith RE. Evaluation of intraocular lens power calculation formulas in the triple procedure. *J Cataract Refract Surg* 1996; **22**: 116-22.
26. Kane JX, Van Heerden A, Atik A, Petsoglou C. Intraocular lens power formula accuracy: Comparison of 7 formulas. *J Cataract Refract Surg* 2016; **42**: 1490-1500.
27. Melles RB, Holladay JT, Chang WJ. Accuracy of Intraocular Lens Calculation Formulas. *Ophthalmology* 2018; **125**: 169-178.
28. Sheard RM, Smith GT, Cooke DL. Improving the prediction accuracy of the SRK/T formula: The T2 formula. *J Cataract Refract Surg* 2010; **36**: 1829e1834.
29. Eom Y, Kang SY, Song JS, Kim HM. Use of corneal power-specific constants to improve the accuracy of the SRK/T formula. *Ophthalmology* 2013; **120**: 477-481.

30. Hoffer KJ, Aramberri J, Haigis W, et al. Protocols for studies of intraocular lens formula accuracy. Am J Ophthalmol. 2015 Sep;160(3):403-405.e1.
31. Elkadim M, Myerscough J, Bovone C, Busin M. Astigmatism Orientation After Deep Anterior Lamellar Keratoplasty for Keratoconus and Its Correlation With Preoperative Peripheral Corneal Astigmatism. *Cornea* 2020; **39**: 192-195.
32. Feizi S, Zare M. Current approaches for management of postpenetrating keratoplasty astigmatism. *J Ophthalmol* 2011; 2011: 708736.
33. Lockington D, Wang EF, Patel DV, Moore SP, McGhee CN. Effectiveness of cataract phacoemulsification with toric intraocular lenses in addressing astigmatism after keratoplasty. *J Cataract Refract Surg* 2014; **40**: 2044-2049.
34. Pellegrini M, Furiosi L, Yu AC, et al. Outcomes of cataract surgery with toric intraocular lens implantation after keratoplasty. *J Cataract Refract Surg* 2021. doi: 10.1097/j.jcrs.0000000000000730. Epub ahead of print.
35. Myerscough J, Roberts H, Yu AC, et al. Five-year Outcomes of Converted Mushroom Keratoplasty from Intended Deep Anterior Lamellar Keratoplasty (DALK) Mandate 9-mm Diameter DALK as the Optimal Approach to Keratoconus. *Am J Ophthalmol* 2020; **220**: 9-18.
36. Busin M, Mönks T, al-Nawaiseh I. Different suturing techniques variously affect the regularity of postkeratoplasty astigmatism. *Ophthalmology* 1998; **105**: 1200-1205.