Visual and refractive outcomes and glistenings occurrence following implantation of two monofocal, aspheric, hydrophobic acrylic intraocular lenses: Clareon® (Alcon Laboratories Inc.) and Tecnis PCB00® (Johnson & Johnson Inc.).

Nick Stanojcic[1,2], David O'Brart[1,2], Christopher Hull[3], Vijay Wagh[1], Elodie Azan[1], Mani Bhogal[1], Scott Robbie[1], Ji-Peng Olivia Li[2.]

1. Department of Ophthalmology, Guy's and St Thomas' NHS Foundation Trust, Lambeth Palace Road, London SE1 7EH.
2. King's College London
3. City, University of London, School of Health Sciences, Centre for Applied Vision Research, Northampton Square, London, EC1V 0HB

Running head: An RCT comparing Clareon and Tecnis PCB00 intraocular lenses

Financial/Proprietary Interests: Professor O'Brart holds non-commercial research grants from Alcon Laboratories, Inc., Rayner Ltd and Avedro Inc.

Key Words: Cataracts, Intraocular lenses, Glistenings

Funding: Study was supported by independent research grant from Alcon (IIT #34114517)

Corresponding author: Professor David O'Brart, Department of Ophthalmology, Guy's and St Thomas' NHS Foundation Trust, Lambeth Palace Road, London SE1 7EH. email: david.obrart@gstt.nhs.uk

Abstract

Purpose: To compare the Clareon® (Alcon Laboratories, Inc.) intraocular lens to theTecnis PCB00® (Johnson & Johnson Inc.) in terms of visual performance, refractive outcomes, glistenings occurrence and quality of life outcomes.

Setting: Guy's and St Thomas' NHS Foundation Trust, London, England.

Design: Single-center, single-masked, prospective, randomized, controlled trial.

Methods: 139 patients with bilateral cataracts were randomized to receive Clareon® or Tecnis PCB00® IOLs. Visual acuity, refraction, central corneal thickness (CCT), endothelial cell loss, contrast sensitivity and mesopic gap acuity, evaluation of glistenings and rates of peri- and postoperative complications were recorded. Quality-of-life outcomes were measured with the EuroQOL 5-dimension questionnaire (EQ-5D) and patient-reported outcome measures questionnaire (Cat-PROM5). Optimised A-constants were available for PCB00®, but not for Clareon ®.

Results: 71 patients (140 eyes) received Clareon® and 68 patients (134 eyes) received PCB00® IOLs. Data were analysed for the first implanted eye. At 12 months, mean uncorrected distance visual acuity (logarithm of minimum angle of resolution [logMAR]) was 0.02+/-0.10 and 0.01+/-0.08 (mean+/-standard deviation [SD]; P=0.49; 95% Confidence Interval [CI] -0.02, 0.04) in Clareon® and PCB00® IOL groups respectively. Corrected visual acuity was -0.02+/-0.09 and -0.03+/-0.06 respectively (P=0.45; 95%CI -0.02, 0.04). Increase in CCT was 14+/-19 and 16+/-28 micrometers, respectively (P=0.63; 95%CI -10.16, 6.16). Mean absolute refraction spherical equivalent (SE) error from target refraction was 0.41+/-0.28 for Clareon and 0.25+/-0.2 for PCB00 (P=0.002; 95%CI 0.08, 0.24) groups. Glistenings were minimal (median grade 0), with no difference in grades between groups (P=0.2. PROMS improved post-operatively and were similar in both groups.

Conclusions: There were no differences in visual outcomes between Clareon® and PCB00® IOLs. Glistenings were rarely observed in either IOL with no difference in grades. There was no difference in peri- or post-op complications. Surgeon optimization of the A-constant for new Clareon® IOL lenses is recommended.

Introduction

Any Intraocular lens (IOL) needs to meet fundamental standards, including biocompatibility with no induction of inflammation/tissue reaction, excellent optical properties and no degradation of shape or optical clarity with time. Whilst infrequent, degradations of IOL materials causing visual impairment and necessitating lens explantation have been reported.[1]

Glistenings, which are small, water-filled vacuoles 1-30 micrometers in diameter, are one type of material degradation of IOLs.[2-4] First reported in the mid-1980s,[5] they occur in all IOL materials, including poly (methyl methacrylate) (PMMA), silicone and hydrophobic acrylic IOLs,[6-9] but are more commonly associated with hydrophobic acrylic lenses, [6, 9-10] with an incidence of almost 100% in some older models,[11] especially with increasing time.[12] The majority of clinical studies investigating glistenings show no influence on visual outcomes.[13-19] However, there are rare single case reports of the need for IOL explantation as a result of their occurrence.[20-23] For these reasons, IOL manufacturers have striven to improve industrial processes to reduce glistenings as well as develop 'glistenings free' hydrophobic acrylic polymers.

The Clareon® (Alcon Laboratories, Inc.) IOL is a single-piece, aspheric monofocal IOL made from a new hydrophobic acrylic polymer (Clareon CNA0T0, which has a higher water content (1.5%) than other hydrophobic acrylic materials. In laboratory studies this lens has been shown to produce low levels of surface haze, roughness and light scatter, minimal glistenings and little axial displacement when compared to other hydrophobic acrylic IOLs.[24-26] Whilst these results are encouraging, there are no published clinical studies at this time. The aim of this randomized controlled trial was to evaluate visual performance, refractive outcomes, patient satisfaction and glistenings occurrence at 12 months following implantation of the Clareon® IOL compared to the Tecnis PCB00® (Johnson & Johnson Inc.), which has a low rate of reported glistenings.[27] Glistenings were quantified subjectively using our standardized 8-point ordinal scale [19]. In addition to standard visual acuity testing, we employed an array of computerized vision tests, to measure mesopic acuity, functional contrast sensitivity and forward light scatter, (Advance Vision and Optometric Tests [AVOT], City Occupational Ltd, London, UK).[28, 29] Patient reported outcome measures (PROM) and utility values were derived from quality of life (QoL) questionnaires, namely EQ-5D-3L and Cat-PROM. [30-31]

Patients and Methods

The study was a prospective, single-centre (Guy's and St Thomas' Hospital NHS Foundation Trust (GSTT), London, United Kingdom) randomized controlled trial (RCT) (Clinicaltrials.gov registration number NCT02825693), approved by West-Midlands Solihull Research Ethics Committee (reference 17/WM/0414), which adhered to the tenets of the Declaration of Helsinki.

Patients were recruited from the cataract service at GSTT, between February and July 2018. Informed consent was obtained by members of the trial team (DPSO, NS, VKW, EA, SR, MB) as per the trial protocol. Inclusion and exclusion criteria are listed in table 1. Patients were randomized to receive either Clareon® or PCB00® IOLs (each receiving the same lens in both eyes) using a shuffled, closed envelope system selected by a masked observer unrelated to the study. All treatments were delivered by the National Health Service, free at the point of care. If a patient failed to attend a follow-up visit, they were contacted and offered another appointment. If they failed to attend this, they were considered lost to follow-up.

Cataract Surgery

To maintain surgical consistency, femtosecond laser (FL) assisted cataract surgery (FLACS) was performed in all eyes using the LenSx platform (Alcon Laboratories, Inc.). The FL was used to undertake capsulotomy, lens fragmentation and astigmatic keratotomies. Strict criteria for suitability for FLACS was followed so that no recruited patients would be excluded from the trial (table 1). Astigmatic keratotomies were performed on patients with corneal astigmatism greater than 0.8 diopters (D) based on corneal topography. All operations were performed under a local anaesthetic (LA) unless clinically indicated otherwise. All outcomes' analysis was undertaken only on the first operated eye, except for PROMS data which was collected on bilateral cases. No other additional procedures were planned, other than the FL astigmatic keratotomies. Phacoemulsification was performed in all eyes using an active-fluidics torsional phacoemulsification system (Centurion, Alcon Laboratories, Inc.). The IOL used for in-the-bag placement was randomized to either Clareon® (Alcon Laboratories, Inc.) or Tecnis® PCB00 (Johnson & Johnson Inc.). Operations were performed by six surgeons who had completed at least 30 FLACS procedures (NS, EA, DPSO, VW, MB, SR) before study commencement.

Characteristics of the Clareon® or PCB00® IOLs

Both Clareon® and PCB00® incorporate an aspheric anterior surface [32] and are made from hydrophobic acrylic polymers developed to minimize the glistenings formation. The lenses have several similar characteristics, but are composed of differing acrylic polymers, with the Clareon® IOL employing a blue light filtering chromophore (table 2).

Data Collection

Outcomes reported in this study are shown in table 3. Data collection occurred preoperatively, on the day of surgery and at 1, 6 and 12-months postoperatively (table 3). Visual acuity and other assessments (corneal topography, specular microscopy, etc.) were conducted by trained technicians, masked to the participants' treatment arm. Participants were masked to their treatment arm but because of the nature of the intervention, neither the surgeon nor the surgical team could be masked. Visual acuities (uncorrected distance visual

acuity (UDVA), corrected distance visual acuity (CDVA)) were measured with a standard Early Treatment Diabetic Retinopathy Study (ETDRS) backlit chart at 4 meters (m) (Precision Vision, Illinois, USA). Participants' refractive errors were measured using an auto-refractor (RK-510A, Nidek Co. Ltd.) and checked subjectively by a single investigator (NS). Biometry was performed using partial coherence interferometry (IOL Master 500, Carl Zeiss Meditec AG). Corneal topography and Central Corneal Thickness (CCT) were determined using a Scheimpflug device (Pentacam HD, Oculus Optikgeräte GmbH). Macular spectral-domain optical coherence tomography (OCT) was performed with a modular ophthalmic imaging platform (Spectralis, Heidelberg Engineering GmbH) at 1 month and then as per clinical need. The endothelial cell count (ECC) was measured with a specular microscope (EM-3000, Tomey GmbH [Europe], Germany) preoperatively and then at 1 month. Visual comorbidities and risk factors for complications of cataract surgery were recorded prospectively. The risks for posterior capsule rupture were calculated for patients using a composite risk calculation system.[33]

Advanced Vision and Optometric Tests (AVOT)

Advanced Vision and Optometric Tests (AVOT, City Occupational Ltd, London, UK, (http://www.city.ac.uk/avot)) were performed under background mesopic conditions (ambient illuminance on the display surface <0.3 lux, a background display screen luminance of 1Cd m^{-2}). The following specific tests were used:
i) Gap acuity using a Landolt ring for positive (target lighter than the background) and negative contrast (a darker target on a lighter background) at a viewing distance of 3m.
ii) Functional contrast sensitivity (FCS) using a Landolt ring (as for gap acuity) with a 3' gap for both positive (target lighter than the background) and negative contrast (a darker target on a lighter background) at a viewing distance of 3m. A gap size of 3' (Landolt ring size 15') was employed to avoid eyestrain and to minimize the effects of micro-fluctuations of accommodation.[34]
iii) Forward light scatter utilizing a flicker cancellation method[35-36] with a single ring of fixed size designed to produce specified luminance levels in the plane of the pupil from a viewing distance of 70cm. Both 'low threshold' and 'high threshold' were evaluated, with the software calculating the straylight parameter and integrated straylight parameter.

Digital Imaging and Objective Quantification of Glistenings

The methodology used for grading glistenings has been published previously.[19] Following pupillary mydriasis, with tropicamide 1% and phenylephrine 2.5%, central vertical slit images of 10.0 millimeters (mm) by 2.0mm at an angle of 40 degrees and 16x objective magnification of the IOLs were taken with a 5MP digital camera (Topcon DC-4, Topcon, Tokyo, Japan) mounted on an SL (Topcon SL-701, Topcon). We used strictly controlled ambient and display screen equipment illumination as per the published protocol (ISO of 800, a shutter speed of 1/30 second, sharpness of '+32' (default), denoising of '0' (default), contrast 'of 50' (default) and 'auto-brightness' setting at "off"), with the ambient illuminance on not exceeding 0.3lux [20].

The best of five colour digital images from each study eye was selected on the basis of its image clarity for analysis and was processed by fitting the pupil, identifying its centre and over-laying a 3.0mm by 1.0mm grid divided into 1.0mm^2 areas. Three ophthalmologists (NS, JO and DPSO) assessed and graded the images independently within the 3 defined 1.0mm^2 grid squares by counting the number of glistenings they could identify, while disregarding artifacts such as anterior or posterior surface particulates such as pigment, IOL scratches and scuff marks, posterior capsule irregularities and vitreous floaters. To reduce assessor bias, image strips were randomized and presented to the graders for evaluation in PowerPoint (Microsoft Corporation, WA, USA) by a fellow researcher not involved in grading (CH).

Grades of glistenings density were assigned to each 1.0mm^2 area according to an 8–point ordinal scale based on increments of 10 glistenings per mm^2 from zero (grade 0) to more than 60 (grade 7). In addition to our system [19], glistening density was also graded, by the three independent graders, using the previously published Miyata grading scale.[37]

Patient Reported Outcomes and Quality of Life Questionnaires

PROMs were assessed with the Cat-PROM5 tool consisting of 5 questions that provide a Rasch calibrated psychometrically robust measure, specifically designed for cataract surgery, in which a higher score indicates greater visual disability.[30-31] Quality of life outcomes were assessed using the EuroQOL EQ-5D questionnaire, consisting of 2 components: 5 questions about 5 dimensions of health-related quality of life (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), which were scored as 1, 2, or 3 (1 meaning no problems and 3 meaning extreme problems). The 5 responses were then weighted and combined to create a summary index with values 0 to 1, where 1 indicates no problems. The visual analogue scale was a continuous scale anchored by best imaginable and worst imaginable health, with values ranging from 0 to 100 (where 100 indicates best possible health). The EQ-5D was chosen because it is well recognized by public bodies (such as the National Institute for Health and Care Excellence in the UK) for comparative health economic analyses [38].

Statistical Analysis

Results were analysed as per intention to treat. Continuous data were reported using means +/- SDs if the data appeared Gaussian. Binary data were reported as frequencies and percentages and evaluated with the Fisher exact test. Student t tests were used for parametric data with non-parametric equivalent tests used when data failed the parametric test assumptions. All statistical tests were 2-sided with a significance level of 5% (α=0.05). Intraoperative or postoperative adverse events were defined as any event that involved unintentional trauma to an ocular structure, requiring additional treatment or having a negative effect on participants' eyesight. The EQ-5D index scores were calculated using the visual analogue score method calibrated for the UK.

The Rasch-calibrated Cat-PROM5 scores (logits) were calculated from the questionnaire responses in accordance with the developer's instructions [30-31]. The UDVA at 12 months was designated as the primary outcome with peri-operative and postoperative complications, incidence and density of glistenings, refraction, corneal thickness and the results of AVOT tests (mesopic gap acuity at positive and negative contrast, functional contrast sensitivity at positive and negative contrast, and forward light scatter expressed through the straylight and integrated straylight parameter) all as secondary outcome measures.

Results

Subjects and Patient Demographics

One hundred and forty-five patients were recruited. Five withdrew before the surgery date and 140 continued with the trial.

Seventy-one patients (142 eyes) were randomized to the Clareon® arm with 140 eyes treated. Two patients decided against second eye surgery: one had unilateral surgery and withdrew after 1-month; the other decided against second eye surgery but continued with first-eye follow-ups until study end. Therefore 69 patients were available for analysis at 6 months. One patient (both eyes) missed their 12-month follow up, so that 68 Patients were available for analysis at 12-months.

Sixty-eight patients (136 eyes) were randomized to the PCB00® group. Of these, 134 eyes (68 patients) were treated, with 1 having only one eye treated and withdrawing after 1-month, 1 not having second-eye surgery but attending follow-ups until study end and 1 withdrawing after 6-months. One patient had bilateral surgery but due to health problems, missed 1- and 6-month follow-up but attended for 12-month follow up. Therefore at 6 months, 67 patients attended for follow up and at 12 months 66 patients attended. Two patients did not receive the PCB00 IOL as intended due to surgical complications but received the Alcon MA60AC sulcus IOL. They were considered in the visual outcomes' results analysis and for glistenings analysis at 12-months on "an intention-to-treat" basis.

The patient demographics and full baseline data are shown in table 4, with no significant differences between the two treatment arms.

Surgical Procedures and Peri-operative Events

All surgeries except 4 second-eye procedures (2 per group) were undertaken under LA. One patient (PCB00® group) had to have surgery in two stages due to feeling 'dizzy' after FL procedure and surgery was completed the following day under general anaesthetic. All patients were able to receive the FL treatment successfully as planned. Perioperative events and complications are shown in table 5, with no differences between treatment arms.

Post-operative results

Post-operative visual, refractive, EEC, CCT and PROMS results are shown in table 6. There were no differences in UDVA at 12 months, change in CCT at 12 months, ECC loss at 1-month, residual refractive cylinder at 12 months and changes in PROM indices [CatPROM scores, EQ5-3D index scores and visual analogue scale (VAS)] at 12 months. Mean absolute refraction spherical equivalent (SE) error from target refraction at 12 months was 0.41+/-0.28 for Clareon and 0.25+/-0.2 for PCB00 (P=0.002; 95%CI 0.08, 0.24) groups, with consequently mean manifest refraction SE error greater (P<0.001) and SE refraction within +/- 0.50 D reduced in the Clareon® group at 12 months (P<0.012) (table 6, figures 1 and 2).

Rates of post-operative adverse events are documented in table 7. There were no differences in rates of posterior capsular opacification (PCO), YAG capsulotomies, negative dysphotopsias or cystoid macular oedema (CMO) between treatment groups (table 7).

Advance Vision and Optometric Tests (AVOT)

There were no differences between the groups in terms of mesopic gap acuity at either positive or negative contrast, functional contrast sensitivity at either positive of negative contrast or the forward light scatter as expressed with either the straylight parameter or the integrated straylight parameter (table 8). In general, the raw data were skewed, and so non-parametric tests were used, and median and quartile values are reported (table 8).

Glistenings

There was no statistically significant difference in the median glistenings grades for all graders between the Clareon® and PCB00® lenses (P=0.2; Mann-Whitney test) when we used the grading scale previously described by our group.[19] The median grade for the two IOL groups was 0 (<1 glistening/mm^2). Four Clareon® IOLs developed grade 1 glistenings (between 1-10 glistenings per mm^2) whereas only 1 PCB00® IOL was similarly affected.[19] In two of these 4 Clareon® IOLs we found small surface scratch marks from the injector plunger (Monarch, Alcon Laboratories, Inc.). In no cases were median glistening grades >10mm^2 seen in any IOL in either group.

All Miyata grades were zero for both groups.

Discussion

This is the first study to investigate the performance of the Clareon® IOL using an RCT. At 12 months, visual results were excellent, in terms of LogMar UCVA

and CDVA, contrast sensitivity and forward scatter, with no differences compared to the PCB00® IOL (tables 6 and 8; figures 1 and 2). There was, however, a significant difference between IOLs in mean manifest refraction SE error, mean absolute SE refractive error from target refraction at 12 months (table 6). The proportion of patients with SE refraction within +/-0.50 D was significantly higher in the PCB00® lens group (table 6, figures 1 and 2). We believe this is due to the use of the non-optimized, A-constant for the new Clareon® IOL (119.1) compared to the Tecnis® IOL which has been in the market longer and has well established optimized and surgeon-personalized A-constants which were applied during this study. This difference in methodology appears to have resulted in the slight hyperopic overcorrection found. Given the similarity of the pre-operative characteristics of the IOLs investigated (table 2), the standardization of surgeries and post-operative assessments in this trial and the very similar variances of the refractive results between the two IOL groups at 12 months (table 6), we believe that a simple adjustment/surgeon optimization of the A-constant would result in similar (non-statistically significant) refractive outcomes and optimize refractive outcomes for the Clareon® lens.

The Clareon® IOL is manufactured using a new hydrophobic acrylic material (Clareon CNA0T0), developed to provide greater resistance to glistenings formation and improve lens clarity characteristics post-surgery. This study has demonstrated that there were typically no detectable glistenings at 12 months, with a median grade of 0 (<1 glistening per mm^2) for the Clareon IOL as well as the PCB00®. However, some of the IOLs in our study had a small number of glistenings. Although there are no strict criteria to state how many glistenings are allowed for any particular IOL to be labeled “glistenings-free”, historically experts in the field have used the cut off to be up to 50 glistenings per mm^2, probably based on a historical grading scale.[37] It is of note that none of the IOLs in either treatment arm of our study had more than 10 glistenings mm^2 (Grade 2 on the St Thomas’ scale).[19] Interestingly, in 2 of the only 4 Clareon® IOLs in which we detected grade 1 glistenings, we found minimal scratch marks from the injector plunger on the IOL surface, which may have been a contributing factor. We expect that such scratches would not have occurred if we had used the ‘AutonoMe’ (Alcon Laboratories, Inc.) platform for IOL delivery. Further studies may clarify if automated IOL delivery systems could reduce scratches and perhaps the occurrence of associated glistenings.

The relatively high water content of the Clareon CNA0T0 material (1.5%) [24] may explain why it is can be classified as “glistenings-free” [37] as the amount of fluid in hydrophobic acrylic materials has previously been shown to be negatively correlated with the occurrence of glistenings.[42] It is important to note that one limitation of this study is the 12-month follow up; a longer follow up is needed when examining the development of glistenings, ideally over 10 years. Cataract surgery is being undertaken in increasingly younger patients. Indeed, in the case of refractive lens exchange, this is often at the onset of presbyopia and this taken together with increasing life expectancy, means that modern IOLs need to maintain optical clarity for several decades. At present, long-term data regarding IOL material clarity for periods greater than 10 years is lacking. Even minimal amounts of IOL material degradations, such as glistenings, noted

in the early/medium post-operative period should be taken seriously and further longer-term follow-up research is required.

One difference between the IOLs in this study is that Clareon® contains a blue light-filtering chromophore and the PCB00® does not. There has been controversy concerning the use of blue light filters in IOLs. At present there is no strong evidence from clinical studies to either confirm or dismiss any theoretical benefits of blue-light filtering IOLs for macular protection.[39] Blue-light filtering IOLs have previously been found to have little effect on visual acuity or on contrast vision. [40, 41]. It is of note that in this study, where we undertook both positive and negative contrast acuity testing under mesopic conditions, we found no differences between IOL groups (table 8).

In terms of postoperative adverse events, all levels of PCO (including small peripheral non-visually significant PCO) were recorded on slit-lamp examination by one observer (NS) and was confirmed by the consensus of two graders (DO'B, NS) who carefully analysed digital images of these patients. At 12 months, both groups showed a low rate of Nd:Yag laser posterior capsulotomy with no differences between treatment arms (table 7). However, it would be interesting to see how the PCO develops over a longer follow-up time.

Both Clareon® and PCB00® are described broadly as 'square-edge-design' IOLs. Recent research has shown that edges of such IOLs vary but are smoother than designs from 10 years ago.[43] Of 9 hydrophobic acrylic IOLs in one study, Clareon® had the lowest edge thickness at 167.2 microns [43] while another found that the IOL designs with optic edge curvature and full functional optics, such as Clareon®, demonstrated the lowest level of glare-type photic phenomena.[44] The Clareon® IOL features a full 6.0 mm optic and a modified edge profile where the center point of the edge radius lies posterior to the optical plane, designed to reduce dysphototopsia. The Tecnis PCB00® employs optic bodies that incorporate additional peripheral non-imaging components, thus reducing the functional optic diameter. In laboratory testing with non-sequential ray-tracing evaluations, the Clareon® IOL has been shown to produce the main image beam without any secondary glare components whereas the Tecnis ZCB00® (an IOL very similar to the PCB00®) has shown secondary glare components.[44] In this study, we had only one patient in each group with negative dysphotopsias that resolved at 12 months follow up, probably due to neuroadaptation (table 7).

As expected, all PROMS improved very significantly in both groups post operatively. All the indices remained stable and were not significantly different between the groups from 6 months to 12 months (table 6).

In summary, we found no significant difference in visual outcomes between Clareon® and PCB00® lenses. Glistenings were rarely observed in both IOLs, with no difference in median grades on two grading systems. There was no significant difference in peri- or post-operative complications. PROMs improved to a similar degree in both groups. As with any new lens, Clareon® requires optimization/surgeon personalization of the manufacturer-proposed A-constant to improve predicted refractive outcomes.

WHAT WAS KNOWN

- Hydrophobic acrylic IOLs, especially with AcrySof material, have been found to have a propensity to develop glistenings following implantation.
- Previous studies differ in their grading/evaluation of IOL glistenings in vivo and few studies have found association between glistenings and visual function
- New IOL designs with new materials, of which Clareon® is one, have been developed for greater clarity and resistance to glistenings formation.

WHAT THIS PAPER ADDS

- In this trial, both Clareon® and PCB00® IOL rarely develop glistenings with up to 12-month follow-up and when they do occur it is at very low levels.
- Visual and quality of life outcomes with Clareon® and PCB00® IOL are comparable.
- The new Clareon® IOL may require optimization/surgeon personalization of the manufacturer-proposed A-constant to improve predicted refractive outcomes.

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Table 1. Inclusion and exclusion criteria for enrolment in the trial	
Inclusion criteria	Exclusion criteria
1) Bilateral cataracts requiring surgical intervention 2) Good visual potential in both eyes 3) Age18-100 years 4) Ability to understand informed consent and the objectives of the trial 5) Not pregnant, not breast feeding 6) No previous eye surgery 7) Corneal astigmatism less than 1.5D in both eyes	Any patient with co-existing ocular condition that might reduce visual acuity and hence confound the results such as: 1) age-related macular degeneration 2) glaucoma 3) previous retinal vascular disorders 4) previous retinal detachment or tear 5) any neuro-ophthalmological condition 6) any inherited retinal disorder or pathology 7) previous strabismus surgery or record of amblyopia 8) previous TIA, CVA or other vaso-occlusive disease 9) already enrolled in another study 10) Exclusion criteria related to clinical contraindications for FLACS, such as: 1. Significant corneal opacities 2. Small pupils following pharmacological dilation 3. Patients unable to lie sufficiently flat to be positioned underneath the laser machine

Table 2. Characteristics of the two intraocular lenses under investigation.		
Lens Type	Clareon	PCB00
Optic diameter (mm)	6	6 (functional diameter 4.9)
Overall length (mm)	13	13
Material	Hydrophobic acrylic	Hydrophobic acrylic
Design	Biconvex Anterior aspheric surface; Modified square (anterior) precision edge curvature	Biconvex Anterior aspheric surface; Square optic edge: Protec® Frosted, continuous 360 Posterior square edge
Haptics	Stableforce®	'C' style offset from optic
Refractive index	1.55	1.47
Filters	UV and blue light	UV

Table 3. Schedule for data collection in this study				
	Pre-op	1 months	6 months	12 months
Patient information and informed consent	X			
Visual acuity testing, refraction, slit lamp biomicroscopy, tonometry, Pentacam® scanning	X	X	X	X
AVOT tests		X	X	X
Dilation of pupils (g.tropicamide 1% and g.phenylephrine 2.5%)	X	X	X	X
Intraocular lens photographs		X	X	X
Dilated fundal examination	X	X	X	X
Biometry	X		X	
OCT macula	X	X		
Endothelial cell count	X	X		
EQ5D3L and catPROM5 questionnaires	X	X	X	X
Adverse Event Collection		x	x	x

Table 4. Baseline Characteristics of the two treatment groups. (All measured values mean ± SD unless stated otherwise).			
	Clareon N=71	**PCB00 N=68**	**P value (95% CI)**
Gender (male/female)	19/52	26/42	n/a
Right eye/left eye	38/33	42/26	n/a
Mean age (range)	68.9 +/- 10.2 (47, 90)	68.4 +/- 9.3 (37, 81)	0.76 (-2.78, 3.78)
Mean pre-op CDVA (LogMAR)	0.43 +/- 0.45	0.41 +/- 0.36	0.77 (-0.12, 0.16)
Mean SE refractive error (D)	0.02 +/- 1.7	-0.25 +/- 0.88	0.25 (-0.19, 0.73)
Mean AL (mm)	23.54 +/- 0.75	23.78 +/- 0.88	0.09 (-0.51, 0.03)
Mean ACD (mm)	3.27 +/- 0.36	3.3 +/- 0.35	0.62 (-0.15, 0.09)
Mean target refraction (D)	-0.11 +/- 0.13	-0.09 +/- 0.12	0.35 (-0.06, 0.02)
Mean IOP (mmHg)	12 +/- 4	13 +/- 4.4	0.16 (-2.41, 0.41)
Mean CCT (microns)	527 +/- 35	533 +/- 36	0.32 (-17.91, 5.91)
Mean ECD (cells/mm2)	2540 +/- 297	2473 +/- 297	0.19 (-32.65, 166.65)
Mean predicted odds ratio of PCR for all treated eyes [33]	1.75 +/- 1.99 (n=140)	1.70 +/- 1.01 (n=134)	0.8 (-0.33, 0.43)
Mean CAT-PROM5 calibrated score	0.95 +/- 2.31	0.96 +/- 2.18	0.98 (-0.76, 0.74)
Mean EQ-5D-3L index score	80.69 +/- 15.85	81.90 +/- 15.40	0.65 (-6.46, 4.04)
Mean EQ-5D visual analogue scale score	0.917 +/- 0.106	0.900 +/- 0.120	0.38 (-0.02, 0.06)

Table 5. Peri-operative events			
	Number of events		P value
	Clareon	PCB00	
Iris trauma/prolapse	1	1	1
Retained cortical matter	1	1	1
Angle trauma	0	1	0.49
Stuck haptics	0	1	0.49
Mal-positioned haptics	0	1	0.49
Posterior capsule rupture	0	1	0.49

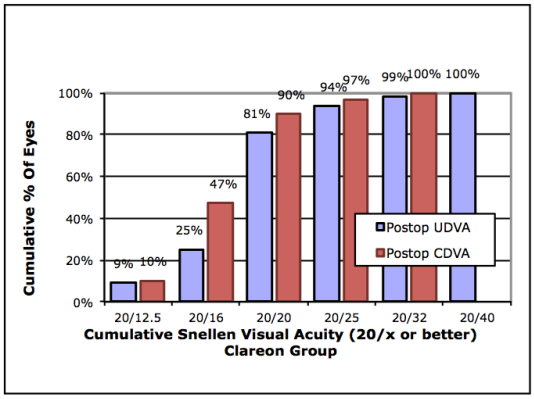
*Fisher's exact test

Table 6. Post-operative results (first-treated eyes)			
	Clareon N=68	PCB00 N=66	P value (95% CI)
Mean UDVA (LogMAR)	0.02 +/- 0.1	0.01 +/- 0.08	0.49 (-0.02, 0.04)
Mean change in CCT (pre-op vs 12 month)	14 +/- 19	16 +/- 28	0.63(-10.16, 6.16)
Mean ECC difference (pre-op vs 1 month) (cells/mm^2)	-243 +/- 351	-359 +/- 340	0.054(-234.14, 2.14)
Mean phacoemulsification energy	8.4 +/- 6.3	10.2 +/- 10.1	0.22 (-4.67, 1.07)
Mean manifest refraction SE error (D) 12 months	0.23 +/- 0.40	0.02 +/- 0.3	**0.001 (0.01, 0.33)**
Mean absolute SE refractive error from target refraction (D) 12 months	0.41 +/- 0.28	0.25 +/- 0.20	**0.002 (0.08, 0.24)**
Residual refractive cylinder (D) 12 month	-0.9+/-0.53	-0.74 +/- 0.47	0.062(-0.33, 0.01)
SE refraction within +/- 0.50 D* 12 months	78% (53/68)	94% (62/66)	**0.012**
SE refraction within +/- 1.00 D* 12 months	99% (67/68)	100% (66/66)	1.0
Mean change in CAT-PROM calibrated score (pre-op vs 6 months)	-8.16 +/- 3.02	-7.67 +/- 3.27	0.35 (-1.56, 0.56)
Mean change in CAT-PROM calibrated score (pre-op vs 12 months)	-7.41 +/- 3.03	-7.56 +/- 2.76	0.761(-0.82, 1.12)
Mean Change in EQ-5D-3L index score (pre-op vs 6 months)	0.03 +/- 0.12	0.06 +/- 0.15	0.194(-0.08, 0.02)
Mean Change in EQ-5D-3L index score (pre-op vs 12m months)	-0.02 +/- 0.12	-0.02 +/- 0.15	1 (-0.05, 0.05)
Mean change in EQ-5D visual analogue scale (pre-op vs 6 months)	11.29 +/- 18.5	10.12 +/- 16.86	0.7 (-4.78, 7.12)
Mean change in EQ-5D visual analogue scale (pre-op vs 12 months)	6.82 +/- 16.76	5.89 +/- 15.22	0.73 (-4.45, 6.31)

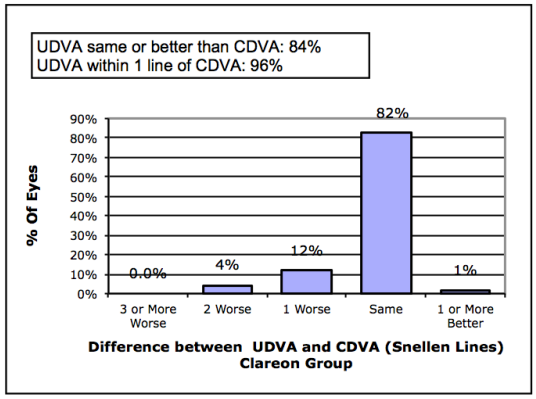
*Fisher's exact test

Table 7. Post-operative adverse events			
	Number of events (%)		P value
	Clareon N=68	PCB00 N=66	
Posterior capsular opacification (PCO)	6 (7)	9 (6)	0.82
PCO requiring Nd:YAG capsulotomy	2 (1.5)	2(1.5)	1
Negative dysphotopsias at 6 months	2 (1.5)	2 (1.5)	1
Negative dysphotopsias at 12 months	0	0	1
Cystoid macular oedema (includes asymptomatic with 0.0 UDVA)	6 (4.3)	11(8.3)	0.2
Chronic CMO	1 (0.7%)	0	0.49

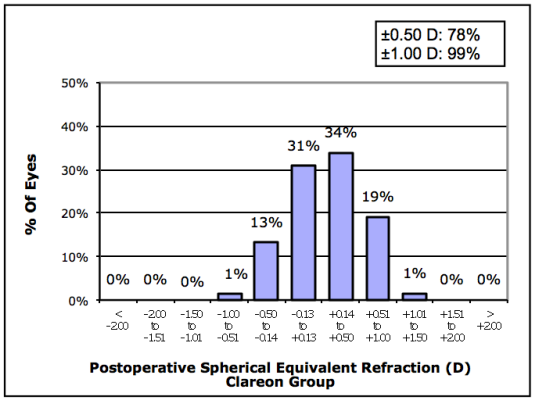
Table 8. Advance Vision and Optometric Test results (AVOT)			
Vision test	Clareon N=68 Median value (lower quartile, upper quartile)	PCB00 N=66 Median value (lower quartile, upper quartile)	P-value
Mesopic gap acuity (positive contrast, minutes of arc)	3.47 (2.34, 4.90)	3.09 (2.35, 4.39)	0.139
Mesopic gap acuity (negative contrast, minutes of arc)	3.08 (2.08, 5.43)	2.61 (2.07, 4.42)	0.280
Mesopic Functional CS (positive contrast; contrast threshold%)	90.16(64.26, 175.91)	84.29(57.62,121.79)	0.159
Mesopic Functional CS (negative contrast; contrast threshold %)	88.05 (50.62, 99.47)	86.56 (48.03, 98.66)	0.454
Straylight parameter	17.97 (16.53, 21.03)	19.33 (17.58, 21.19)	0.159
Integrated straylight parameter	8.79 (8.09, 10.28)	9.46 (8.60, 10.37)	0.157



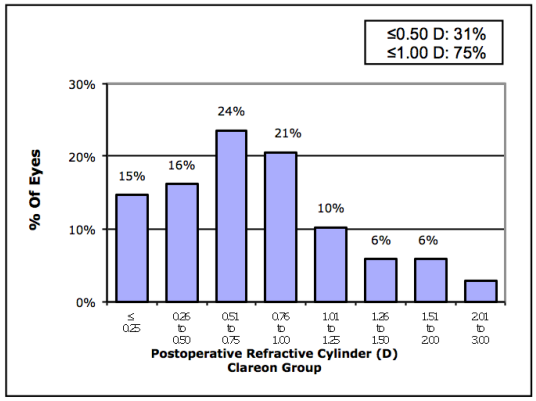
Uncorrected Distance Visual Acuity



Uncorrected Distance Visual Acuity vs. Corrected Distance Visual Acuity

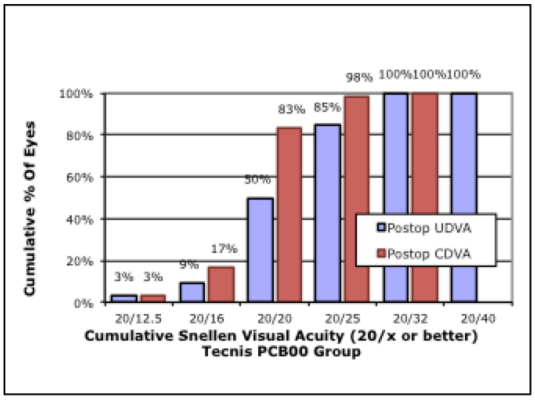


Spherical Equivalent Refractive Accuracy

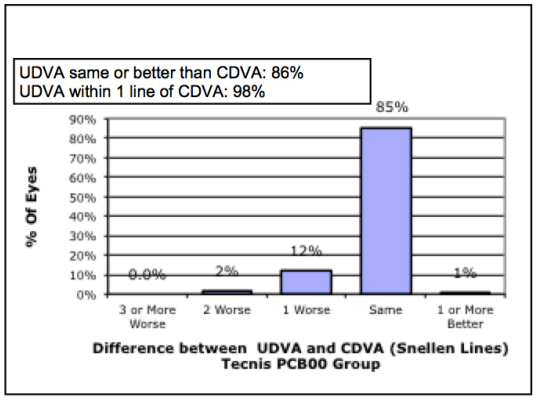


Refractive Cylinder

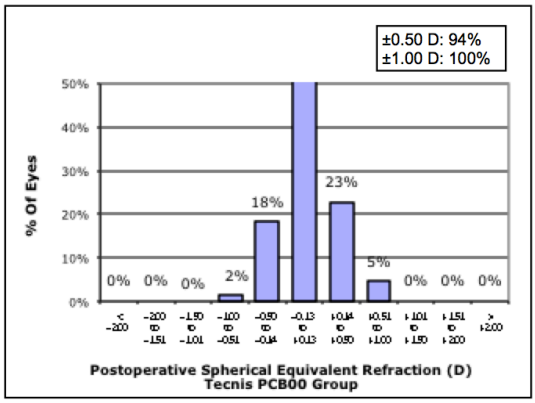
Fig 1. Visual and refractive outcomes at 12 months - Clareon group (n=68).



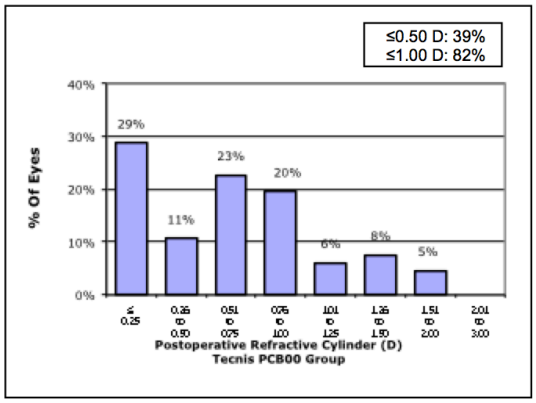
Uncorrected Distance Visual Acuity



Uncorrected Distance Visual Acuity vs. Corrected Distance Visual Acuity



Spherical Equivalent Refractive Accuracy



Refractive Cylinder

Fig 2. Visual and refractive outcomes at 12 months - PCB00 group (n=66).