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Combination of a monofocal and one type of extended depth-of-focus (zonal refractive) intraocular lens (COMEDI) in bilateral cataract surgery protocol: a monocentric, randomised, parallel group trial in cataract surgery

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ABSTRACT

Introduction Modern intraocular lens (IOL) designs for cataract treatment can be broadly classified into three focal range categories; monofocal, extended depth-of-focus (EDOF) and multifocal IOLs.

Monofocal IOLs allow spectacle independence for one focus, typically distance. In contrast, EDOF IOLs provide a greater range of vision, extending spectacle independence to intermediate distance, while multifocal IOLs enable spectacle independence at all distances with the drawback of positive dysphotopsias and reduced contrast perception. EDOF lenses are an attractive compromise with fewer dysphotopic side effects than multifocals. The purpose of this study is to assess whether implanting an EDOF IOL in the second eye of a patient who received a monofocal IOL in the first eye can improve spectacle independence while maintaining the same optical quality as bilateral monofocal IOL implantation.

Methods and analysis This study compares combined monofocal and EDOF IOL implantation versus bilateral monofocal IOL implantation in terms of clinical and patient-reported outcomes in a monocentric, randomised, patient-masked and assessor-masked, parallel group trial in 88 bilateral cataract patients. The primary outcome measure is binocular photopic distance corrected intermediate visual acuity. The secondary outcome measures include (un)corrected distance and near visual acuity, reading speed at intermediate distance, quality of visual function assessments, patient-reported spectacle independence, contrast sensitivity, aberrometry, stereopsis and straylight measurement at the 3-month follow-up.

Ethics and dissemination The protocol was approved by the ethical committee of the University Hospital of Brussels (BUN 23219_EDOF).

Trial registration number NCT06002399

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Bilateral extended depth-of-focus (EDOF) intraocular lens (IOL) implantation offers an attractive compromise providing a greater range of spectacle independence than monofocals with fewer dysphotopic side effects than multifocals.

WHAT THIS STUDY ADDS

⇒ This prospective study aims to assemble a substantial and well-balanced cohort of patients to investigate the monofocal-EDOF IOL combination, considering eye dominance.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study will allow surgeons to counsel the patient who was previously implanted with a monofocal IOL in one eye, to what extent an EDOF IOL in the second eye will affect spectacle independence and optical quality.

INTRODUCTION

Cataract extraction is the most frequent performed surgical procedure of all medical specialties with an estimated 20 million cases per year worldwide.[1] The investigation to enhance optical quality and increase spectacle independence has led to remarkable innovations within the domain of intraocular lens (IOL) technology in the last decade.

The first optical solution was the monofocal IOL, which has long been the golden standard for cataract surgery and refractive lens exchange due to its reliability in providing clear distance vision. It has a single focal point, which allows patients to enjoy spectacle independence, usually set for far distance. Nevertheless, this lens design still requires glasses for near and intermediate tasks. To overcome this burden, multifocal IOLs were designed in the late 1980s to increase spectacle independence at all distances.[2] The most successful of these lenses are based on various optical principles (diffraction,

refraction) designed to split incoming light into different focus points but do not provide a true simulacrum of accommodation. As a result, they are associated with unpleasant visual phenomena known as positive dysphotopsias as well as reduced contrast perception.[2] In some cases, patients may be so disturbed by these photopsias that they may request the lens to be removed.[3]

More recently, a new category of lenses known as extended depth-of-focus (EDOF) IOLs has reached the market purporting a compromise between monofocal and multifocal IOLs. The EDOF IOL is engineered to extend the range of vision by manipulating the way light passes through the lens. Similar to its multifocal predecessors, it employs various optical principles, such as diffractive or extended focal length designs, to enhance uncorrected intermediate vision though with a marked reduction in the undesired optical issues associated with multifocal IOLs.[4]

Traditionally, it has been recommended to implant the same IOL design in both eyes.[5 6] Combining two different IOL technologies in one patient, however, known as 'blended vision' or 'mix and match,' leverages the brain's ability to adapt to different visual inputs from each eye.[7–20] This synergetic approach is often used in the combination of an EDOF IOL in the dominant eye and a multifocal IOL in the non-dominant eye. This strategic pairing aims to provide patients with the best of both worlds—sharp distance vision and improved intermediate and near vision, while minimising visual disturbances and aberrations derived only from the non-dominant eye. Less is known, however, about the combination of a monofocal IOL with an EDOF IOL. Since EDOF IOLs hardly affect optical quality for distance vision,[21] it is maybe not important to choose the dominant eye for its implantation in the EDOF-mono mix and match strategy.

Certain patients who have received a monofocal IOL implant in one eye may express disappointment with their uncorrected intermediate and near vision and may seek ways to reduce their reliance on spectacles for these focal ranges. One solution is to consider implanting a monofocal IOL targeted specifically for intermediate or near vision in the second eye, a practice referred to as 'monovision'. Nevertheless, it is important to note that this method is not satisfactory for all patients and a preoperative trial with contact lenses is often required.

The optimal blending of IOL designs is not yet known and despite the frequency of cataract surgery, there is scant evidence on monofocal-EDOF IOL combination. The pilot study of Shemez *et al*[22] reported only 23 patients in the monofocal-EDOF IOL combination group without investigating the effect of eye dominance and postoperative objective optical quality outcome parameters such as stereopsis, aberrometry and straylight measurement. Therefore, the aim of this study is to investigate the visual performance and patient satisfaction following the combined implantation of a monofocal and EDOF IOL, compared with standard bilateral monofocal IOL implantation. This prospective study will be the first to gather a large and well-balanced cohort of patients, to shed the light on monofocal-EDOF IOL combination taking into account eye dominance.

This study fits in the needs of the fast-changing field of cataract and refractive surgery, where personalised solutions are tailored to meet the distinctive visual requirements and preferences of each patient.

METHODS AND ANALYSIS

Objective

This study compares combined monofocal and EDOF IOL implantation (combi-group) versus bilateral monofocal IOL implantation (mono-group) in terms of clinical and patient-reported outcomes on quality of vision in a monocentric, randomised, double-masked, parallel group trial in 88 immediate sequential or delayed sequential bilateral cataract patients. Monofocal IOL implantation will be performed with the Lentis L-313 or Lentis Tplus LS-313 (toric) and EDOF implantation will be performed with the Lentis Comfort LS-313 MF15 and Lentis Comfort toric LS-313 MF15 (Teleon Surgical B.V., Spankeren, Netherlands).

The primary outcome measure will be the binocular photopic distance corrected intermediate visual acuity (DCIVA) at 66 cm. The secondary outcome measures include comparisons of binocular-corrected and uncorrected distance (4 m) and near visual acuity (40 cm), binocular reading speed at intermediate distance, quality of life assessments (NEI VFQ-25 questionnaire (online supplemental appendix A)), patient-reported spectacle independence (PRSIQ (online supplemental appendix B)), overall patient satisfaction (additional follow-up questionnaire in Likert scale with five questions with each five answers ranging from not at all satisfied to very satisfied (online supplemental appendix C)), binocular mesopic and photopic contrast sensitivity, stereopsis, aberrometry and straylight measurements at the 3-month follow-up appointment. The effect on quality of vision of EDOF IOL implantation in either the dominant or the non-dominant eye will be assessed. Adverse events will be reported and compared 3 months postoperatively.

The trial will be conducted in a compliance with the approved protocol, the Declaration of Helsinki (2008), the principles of Good Clinical Practice (GCP), as laid down by the Commission Directive 2005/28/EC, the standards for IOLs set by the International Organization for Standardization (ISO) 11979-7:2014[23] and the Belgian law of 7 May 2004 regarding experiments on the human person and any relevant amendments.

Trial design

The trial is designed as a parallel, randomised, patient and assessor masked trial with 1:1 allocation between the mono-group and the combi-group. Once a patient is assessed for eligibility, provides informed consent, and is enrolled, pseudo-anonymised data will be collected and managed using the primary source documents and

the study software REDCap (Research Electronic Data Capture tools hosted at Vrije Universiteit Brussel).

Patient and public involvement statement

This study protocol was designed without patient or public involvement. Patients were not engaged in discussions regarding the study's design or the interpretation of its findings. Furthermore, patients were not involved in the process of writing or editing this paper.

Recruitment

Patients diagnosed with bilateral cataract and scheduled to undergo bilateral phacoemulsification cataract extraction, at the Ophthalmology Department of the University Hospital of Brussels, will be screened consecutively. After a thorough discussion on the surgery and IOL options with the principal investigator or coinvestigator, the patient is provided with specific information on the trial and a study information brochure. Participant information sheets with information for informed consent are given to the patient as well to read at home. Completion of informed consent forms and subsequent enrolment in the study take place after the first visit. All investigatory teams have GCP2 certification.

Inclusion criteria

This study will include bilateral cataract patients aged between 50 and 90 years without concomitant ocular comorbidities as detailed in the exclusion criteria. We chose the age ranges of 50–90 years for two reasons, the first is that it represents the vast majority of patients undergoing cataract surgery in our department. The second issue was that younger patients with cataract often still retain some accommodation, which will be lost after cataract surgery. In our experience, this has an impact on their expectations and satisfaction regarding postoperative intermediate vision. To avoid the possible influence of loss of accommodation, we chose the lower age limit of 50 years. Additionally, eligible participants must demonstrate the ability to read and comprehend the study information, provide informed consent and complete the quality of vision questionnaire. Finally, patients must also express a willingness and have the capability to attend the 1-week, 1-month and 3-month follow-up appointments.

Exclusion criteria

The exclusion criteria are (1) any prior form of refractive surgery; (2) prior ocular surgery in the preceding 6 months to inclusion; (3) corneal opacities; (4) retinopathy; (5) optic neuropathy; (6) glaucoma; (7) uveitis; (8) amblyopia; (9) preoperative corneal astigmatism greater than three diopters (D); (10) expected postoperative refractive astigmatism higher than 0.5D; (11) irregular corneal astigmatism higher than 0.5 µm at 4 mm on topography, since they may impact both primary and secondary outcomes.

Randomisation and masking

Once the inclusion data are entered by a member of the study personnel (PI or study nurse) into the trial software, randomisation will take place. The randomisation will be performed with an equal 1:1 allocation to all following parameters: (1) the mono-group or combi-group; (2) scheduling of dominant or non-dominant eye first; (3) implantation of EDOF IOL in dominant or non-dominant eye in case of combi-group allocation.

Throughout the trial, participants will remain masked to the IOL type until the final trial visit when they will receive their implant cards. The surgeons will not be masked; however, assessments of all outcomes susceptible to influence (including corrected distance visual acuity (CDVA), UCVA, refraction and questionnaire) will be conducted by assessors who are unaware of the intervention details. The treating surgeon is explicitly not permitted to perform these postoperative examinations. All electronic patient records refer to the intervention in terms of IOL with spherical and cylindrical power without mentioning the IOL type, so that patients cannot be inadvertently unmasked. The IOL type will still be recorded with an identification label that will be scanned into the patient's electronic file, but this may not be accessed by the masked assessors.

Interventions

The study calendar is provided in table 1 and the planned patient participation pathway in figure 1 (online supplemental appendix E). All patients will be evaluated 1 month (preoperative day −41 to −1) prior to surgery, within the first week (postoperative day 1 to 8), 1 month (postoperative day 21 to 35) and 3 months (postoperative day 70 to 100) after surgery, but all results which will be reported will refer to the 3-month follow-up visit. In case of delayed sequential eye surgery, the timing of examinations is expressed as days preoperatively to the first eye surgery and days postoperatively to the second eye having undergone surgery.

Preoperative examinations

Monocular and binocular visual acuity will be recorded both uncorrected and distance corrected in photopic conditions (10 cd/m^2) for distance (4 m) using the Early Treatment Diabetic Retinopathy Study (ETDRS) vision chart. The results will be expressed and analysed in LogMAR units. Refraction will be measured in standard format, where the spherical and cylindrical corrections are given, together with the axis of the cylinder.

All patients will undergo optical biometry (IOLMaster 700, Carl Zeiss Meditec AG, Jena, Germany), corneal topographic mapping with measurement of corneal spherical aberrations (Pentacam HR, Oculus Incorporation, Wetzlar, Germany), retinal imaging by optical coherence tomography (SPECTRALIS, Heidelberg Engineering, Heidelberg, Germany), ocular dominance (Miles or motor dominance test at 3 m)[24] and stereopsis testing (TNO test for stereoscopic vision). Preoperative calculation of the implanted IOL will be performed using the Barrett Universal II Formula aiming for the closest to plano target for monofocal IOLs, while for EDOF

Table 1 Study calendar showing the trial procedures

Examination		Light condition	Monocular/binocular	−1 m	1 w	1 m	3 m
IOP			Monocular	*	*	*	X
Slit lamp examination			Monocular	*	*	*	X
Dilated fundus examination			Monocular	*	*If toric IOL	*	
Optical biometry			Monocular	*			
Scheimpflug-based topography with measurement of corneal spherical aberrations			Monocular	*			
Macular OCT			Monocular	*			
Aberrometry			Monocular				X
Ocular dominance			Binocular	X			
Stereopsis			Binocular	X			X
Visual acuity	UDVA (4 m)	Photopic	Monocular	*	*	*	X
			Binocular	*		*	X
	CDVA (4 m)	Photopic	Monocular	*	*	*	X
			Binocular	*		*	X
	UIVA (66 cm)	Photopic	Monocular				X
			Binocular				X
	DCIVA (66 cm)	Photopic	Monocular				X
			Binocular				X
	UNVA (40 cm)	Photopic	Monocular			*	X
			Binocular			*	X
	DCNVA (40 cm)	Photopic	Monocular			*	X
			Binocular			*	X
Defocus curve distance corrected (from −3D to −1D in 0.50D steps and from −1D to +1D in 0.25D steps)		Photopic	Binocular				X
Reading speed at intermediate distance (66 cm) at 2.5, 2.0, 1.6, 1.25 and 1.0 m print sizes		Photopic	Binocular				X
Contrast sensitivity		Photopic without glare	Binocular				X
		Mesopic with and without glare	Binocular				X
Straylight			Monocular				X
NEI VFQ-25 questionnaire							X
Patient Reported Spectacle Independence Questionnaire (PRSIQ)							X
Patient Satisfaction Questionnaire in Likert scale							X

*Refers to standard of care and is not considered a study specific examination; X refers to study-specific examinations.
Time window ranges: −1 m = preoperative day −41 to −1; 1 w = 1–8 days postoperative; 1 m = 21–35 days postoperative; 3 m = 70–100 days postoperative.
CDVA, corrected distance visual acuity; D, Diopter; DCIVA, distance-corrected intermediate visual acuity; DCNVA, distance-corrected near visual acuity; IOL, intraocular lens; IOP, intraocular pressure; m, month; NEI VFQ-25, National Eye Institute Visual Function Questionnaire–25; OCT, optical coherence tomography; UDVA, uncorrected distance visual acuity; UIVA, uncorrected intermediate visual acuity; UNVA, uncorrected near visual acuity; w, week.

IOLs a target between 0 and +0.25D in dominant eyes and a target between 0 and −0.25D in non-dominant eyes will be selected. A toric IOL will be calculated starting from 0.50D corneal astigmatism both for monofocal and EDOF IOLs with an objective to achieve a postoperative residual astigmatism at spectacle plane of less than 0.50D.

Surgical interventions

Surgery can be conducted using either local or general anaesthesia, depending on what is most suitable and the preferences of both the patient and the surgeon. Patients have the option to decide between two approaches: bilateral immediate sequential surgery (as is becoming increasingly common in Europe)[25] or delayed sequential surgery (up to a maximum of 14 days between procedures).

Essential surgical information, such as the intervention dates and corneal incision location, will be meticulously documented in the electronic case report form (eCRF). Additionally, any deviations from the predefined surgical protocols will also be diligently recorded in the eCRF.

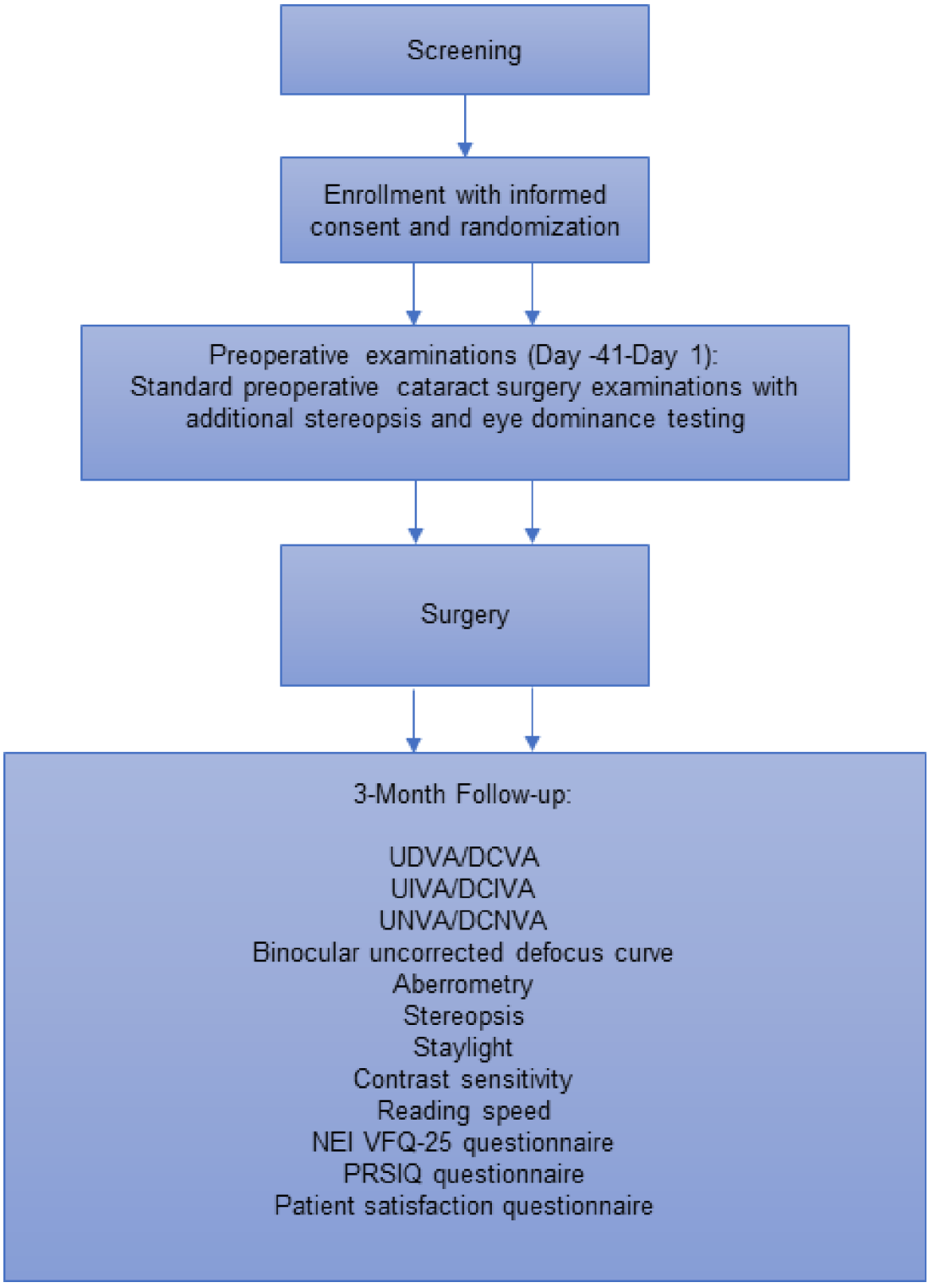

Figure 1 Planned patient participation pathway. All abbreviations are listed in table 1.

Standard sutureless phacoemulsification surgery will be performed by two experienced surgeons, namely SND and KTM, with a 2.2 mm main clear corneal incision on the steepest axis. Pharmacological mydriasis will be induced using an ophthalmic insert containing 0.25 mg tropicamide and 5.38 mg phenylephrine (Mydriasert, Laboratoires Théa). A manual continuous curvilinear capsulorhexis will be performed of up to 5.5 mm. The inferior segment of the non-toric EDOF IOL will be implanted inferonasally if angle kappa or alpha is higher than 0.3 mm on aberrometry to make sure the visual axis runs through the upper far segment of the IOL.

Intraocular lens

All IOLs that will be implanted in this study are 1-piece, biconvex aspheric posterior surface, square edge, acrylic

hydrophilic lenses with hydrophobic surface properties (Hydrosmart technology) and UV filter. They have plate haptics with an overall length of 11 mm and an optic size of 6 mm. Monofocal IOL implantation will be performed with the Lentis L-313 or Lentis Tplus LS-313 (Teleon Surgical B.V., Spankeren, Netherlands), the latter in the case of need for toric IOL implantation. EDOF IOL implantation will be performed with the Lentis Comfort LS-313 MF15 and Lentis Comfort toric LS-313 MF15 (Teleon Surgical B.V., Spankeren, Netherlands). Both are zonal refractive, rotational asymmetric EDOF IOLs with an addition of 1.5D in a sector-shaped near vision anterior segment. All ANSI criteria for an EDOF IOL are fulfilled by the LENTIS Comfort defocus graphs (ANSI Z80.35–2018).[26] Moreover, all criteria outlined in the American Academy of Ophthalmology Task Force Consensus Statement for Extended Depth of Focus Intraocular Lenses are fully met by the Lentis Comfort IOL.[27] Finally, the Lentis Comfort IOL is aligned with the inclusive approach for classification of EDOF IOLs as outlined by Megiddo-Barnir *et al*.[28]

Postoperative care and follow-up

The immediate follow-up appointments for clinical examinations are, as per standard of care in our institution, within the first week and the first month after surgery. A teleconsultation is performed the first day after surgery.

All patients will receive a uniform postoperative medication regimen. This consists of a combination of topical tobramycin 0.3% and dexamethasone 0.1%, administered four times a day for a duration of 1 week. Following this initial period, the dosage will be gradually reduced by one drop per week. Additionally, non-steroidal anti-inflammatory indomethacin 0.1% eye drops will be prescribed, to be used three times a day starting from 2 days prior to surgery for a period of 4 weeks, with the aim of preventing macular oedema. In the event of a drop intolerance or allergy to the study protocol, substitutions can be made. However, such substitutions should be justified and reported into the eCRF.

Primary outcome

The primary outcome measure of this study is the comparison of binocular photopic (10 cd/m^2) DCIVA at 66 cm between both groups, measured on a Radner chart expressed in LogMAR units, at 3 months following cataract extraction of the second eye.

Secondary outcomes

All secondary outcome measures will be evaluated at 3 months postoperatively. Measurements in photopic condition will always be performed with 10 cd/m^2 and in mesopic condition with 1.3 cd/m^2.

Monocular and binocular UDVA and CDVA will be measured at 4 m using the corresponding ETDRS charts under photopic conditions and 100% contrast (ESV-3000 ETDRS System, Vectorvision). To acquire the defocus curve, binocular vision will be tested under photopic conditions and 100% contrast at 4 m using an iPad ETDRS chart (Multifocal Lens Analyzer V.3.0.8, Qvision Academy, Spain). Both eyes will be uncorrected for distance acuity and additional lenses will be added over the range of +1.00D to −1.00D in 0.25D steps and −1.00 to −3.00 D in 0.50 D steps while recording visual acuity for each step. In order to avoid memory effects, presenting letter sequences will be randomised and patient's eyes will be occluded between each lens appearance, so that the subject will not be aware of which lens has been inserted and whether the letter on the chart has been changed or not.[29] Intermediate and near visual acuity will be measured both monocular and binocular, respectively, at 66 cm and 40 cm using ETDRS near acuity charts (Radner reading charts in Dutch, English and French, Precision Vision) with 100% contrast and photopic condition.

Binocular reading speed at intermediate distance (66 cm) will be assessed at 2.5 m, 2.0 mr, 1.6 m, 1.25 m and 1.0 m print sizes with the MNRead application on a tablet device under photopic condition.

Objective quality of vision will be measured with following exams: contrast sensitivity, straylight and aberrometry. Contrast sensitivity will be measured without glare in photopic and mesopic condition and with glare in mesopic condition (log10 units, MTF cut-off, with ClinicCSF application V.2.0.1 of Qvision Academy, Spain). The value where the patient cannot see any patch will be selected. After adaptation to the dark, mesopic testing will be performed first, followed by photopic. Straylight (Strehl ratio and log units calculated with C-Quant (Oculus GmbH, Wetzlar, Germany)) and aberrometry (the root mean square of tilt, coma, trefoil, spherical aberration, HOAs, and total aberration will be measured monocularly at 4 mm pupil, performed with the i-Trace device (Tracey Technologies, Texas)).

Subjective patient satisfaction will be measured with the visual performance NEI VFQ-25 and PRSIQ questionnaires, which will be administered on a tablet device or paper and linked after completion into the study eCRFs.

Stereopsis will be assessed in seconds of arc (TNO test for stereoscopic vision).

The effect on all previously mentioned outcome parameters of EDOF IOL implantation in either the dominant or the non-dominant eye will be assessed, however, this study is not powered to measure this effect.

Adverse events will be reported and compared.

Safety and adverse events

Phacoemulsification with intraocular lens implantation is a common clinical procedure, but it comes not without potential complications. These complications encompass posterior capsular rupture (adverse event (AE) in 1%–4%), suprachoroidal haemorrhage (serious adverse event (SAE) in 0.04%), cystoid macular oedema (AE in 2%), infectious endophthalmitis (SAE in 0.07%), zonular dehiscence (AE in 0.46%) and corneal endothelial decompensation (SAE more common in pre-existing

endothelial disease) and retinal detachment (SAE in 0.9% in 4 years after surgery)[30]

Throughout the trial, we will diligently document any surgery-related adverse events (including duration and severity) in each group in the eCRF and explore their potential causes. Patients who encounter adverse events during the treatment and follow-up phases will receive appropriate interventions.

In the case of SAEs, we will promptly report them to the Ethical Committee. Participants affected by SAEs will be withdrawn from the study to ensure their well-being and safety. It is important to note that if a participant withdraws consent for further data processing, this will not prevent the reporting of SAEs. We will transparently explain this aspect to all participants involved in the study.

Dissatisfied patients after surgery will be seen again to record their comments. Possible reinterventions will be offered to the patients on the basis of standard of care and no treatment option will be withheld. Possible reinterventions include refractive laser touch up, nd:YAG capsulotomy and in extreme cases, IOL exchange. All additional interventions will also be captured in the trial study software. In the event of exchange of the EDOF IOL with a monofocal IOL, we will describe this as an adverse event as well as a reintervention. The patient will remain in the study for the trial duration and all subsequent data will still be captured to include the outcomes of these cases.

Sample size

The primary objective of this study is to determine whether the combination of a monofocal and EDOF IOL presents an advantage over bilateral monofocal IOL implantation in the daily life of patients undergoing cataract surgery while conserving equal optical quality. Therefore, at 3 months, we will measure and record the difference in binocular photopic DCIVA between both groups in logMAR units using a Radner chart. According to Rosser *et al*, a difference of 0.1 logMAR or one line is considered clinically relevant.[31] Therefore, we have powered the study to detect a difference of 0.12 logMAR being just more than one line.

A maximum of 44 patients in each group are required to detect the superiority of binocular photopic DCIVA in the monofocal-EDOF IOL group of 0.12logMAR (SD 0.18logMAR),[32] implying an effect size of 0.66, with a power of 0.8 and allowing for a 0.05 type I error. This is obtained with an O'Brien Flemming stopping rule for one two-sided interim analysis after 30 patients with a 0.5 power, representing the minimum number of patients per group. These totals take into account an assumed loss of 10% due to drop-out to reach 27 and 39.

Statistical analysis

A linear mixed model will determine whether there is a difference in binocular photopic DCIVA between both groups in logMAR, accounting for the correlations implied due to clustered observations as each patient is measured for both eyes. This model also allows for bringing in an interaction with the eye dominance as predictor as well as baseline measurements. A log-transformation of the outcome may be required to deal with some skewness as was observed in earlier studies, to normalise residuals.

In this exploratory data analysis, the variable selection is performed in a stepwise forward–backward procedure using the AIC, in order to build a model with only relevant predictors. The AIC helps avoid overfitting, with data being too limited in size to perform a full cross-validation that requires setting aside a test set. All nominal/ordinal predictors with more than two levels that are retained in the model will be further evaluated using contrasts, applying Holm correction for multiple comparisons.

Statistical analysis will be performed by the in-house consultancy centre SQUARE, Vrije Universiteit Brussel, Laarbeeklaan 103, 1090 Jette, Belgium.

Baseline measurements, primary and secondary outcome variables are summarised in the study calendar provided in table 1.

ETHICS AND DISSEMINATION

Ethics

The protocol conforms to both the principles of GCP and Declaration of Helsinki. Final ethical approval was obtained by the ethics board of the University Hospital of Brussels (BUN 23219_EDOF study) and the trial has been registered on ClinicalTrials.gov (NCT06002399). Any amendments to the protocol will be reviewed by the ethical board and communicated to the participants.

Participant information brochures will be provided to all potential participants (online supplemental appendix D). Written informed consent will be obtained from all participants before they are enrolled in the study. Participants will be reminded of their rights to withdrawal from the study without there being negative consequences on the care they will receive.

Participants' anonymity and confidentiality will be maintained during the study, in accordance with the requirements of the Belgian and European Privacy legislation (https://www.dataprotectionauthority.be/legislation-and-standards. The primary source documents involve all original documents, surveys, records and images as well as the eCRFs pertaining to the study. The elements of the eCRF that are source documents are the quality of vision VFQ-25, PRSIQ and patient satisfaction questionnaire responses as these data are directly entered. The PI will be responsible for the pseudonymisation of the data at point of entry. REDCap clinical trial software will be used for building and managing a secure study database. After the study, relevant documents will be stored securely at the Ophthalmology Department of University Hospital Brussels for 10 years for specific scientific research purposes.

Dissemination policy

Trial findings will be distributed to all potential beneficiaries of the research including patients and their general physicians alongside advisory bodies. This will be done by means of papers in open access medical journals as well as presentations at national and international medical congresses. Trial results will also be disseminated to the trial participants in a one-page summary written in lay language. Additional data will be available upon reasonable request after completion of the trial.

Trial status

The first participant has been recruited in November 2023. The estimated completion date is September 2025.

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Competing interests The authors have no financial interest in any of the interventions or products associated with this trial.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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