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CORRESPONDENCE

Sir,

Methodological remarks concerning the recent meta-analysis on the effect of intravitral bevacizumab in central serous chorioretinopathy

We read with great interest the recent meta-analysis by Chung *et al*,[1] which reached important conclusions about the effect of intravitral bevacizumab in central serous chorioretinopathy; nevertheless, some methodological issues need to be addressed concerning this meta-analysis.[1]

Specifically, the authors state that 'The mean difference and SD at the 6-month follow-up were calculated from the data in the included studies.' This seems an intriguing statement that should be further clarified by the authors to substantiate the validity of the meta-analysis and guarantee the reproducibility of their results. The included studies presented mean ± SD at baseline and at the 6-month time point; the SD of the difference (with the latter representing a new measure) was not provided by the included articles.

Given that the variance of a an A–B difference inherently necessitates knowledge about the covariance (A, B), any attempt to estimate the SD of the difference would imply assumptions about the covariance; the latter is not negligible and seems of corollary importance in light of the longitudinal nature of the baseline—6-month comparison. Therefore, the authors should disclose their assumptions regarding the calculation of covariance and provide the relevant formulas with the corresponding statistical references supporting their approach; critical discussion of any limitations potentially stemming from such assumptions would be of interest.

An alternative way would be contact with the authors of each study, asking them to calculate *de novo* the difference and provide the meta-analysts with the exact SD data. Nevertheless, Chung *et al* did not provide any statement disclosing contact with the authors of individual studies.

In conclusion, thorough clarification of the methods used by Chung *et al*[1] seems desirable, so as to further solidify the validity of their approach. Reliable calculation of variance often represents a challenging notion in the field of meta-analysis.

Conflict of interest

The authors declare no conflict of interest.

Reference

1 Chung YR, Seo EJ, Lew HM, Lee KH. Lack of positive effect of intravitreal bevacizumab in central serous chorioretinopathy: meta-analysis and review. *Eye* 2013; **27**: 1339–1346.

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Sir,

Reply to 'Lack of positive effect of intravitreal bevacizumab in central serous chorioretinopathy: meta-analysis and review'

We appreciate the interest of Sergentanis and Chatziralli in our published manuscript, 'Lack of positive effect of intravitreal bevacizumab in central serous chorioretinopathy: meta-analysis and review.'[1] They have addressed methodological issues concerning meta-analysis because the SD of difference was not provided in the manuscript.

We absolutely agree that it would have been more meaningful meta-analysis if we contacted the authors of each study, asking them to calculate *de novo* the difference as Sergentanis and Chatziralli have rightly pointed out. Alternatively, Hedges *g* formula for pooled SD was used to estimate difference SD. And then, paired SD was calculated, as follows, pooled SD × sqrt(2 × 1 − *r*)).

Although our meta-analysis failed to verify the positive effect of IVB in CSC, the outcome of this treatment is still unknown owing to many limitations, such as small sample sizes, clinical heterogeneity, and methodology. Therefore, further investigation including more studies with larger scales and better methodologies will help to clarify the uncertain relationship between CSC and IVB.

Reference

1 Chung YR, Seo EJ, Lew HM, Lee KH. Lack of positive effect of intravitreal bevacizumab in central serous chorioretinopathy: meta-analysis and review. *Eye* 2013; **27**: 1339–1346.

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Sir,

Opaque intraocular lens implantation

We read with interest the recent correspondence by Yusuf *et al*[1] describing the factors influencing black intraocular lens (IOL) selection for intractable diplopia.

We present retrospective data on our experience with opaque IOLs over a span of 11 years (2003–2014) at our tertiary strabismus and vitreoretinal referral centre in Scotland. Our findings are summarised in Table 1.

Five of our six patients were phakic, and underwent routine phacoemulsification surgery, with insertion of a custom-made Ophtec 0.0D black polycarbonate Ani II ('no hole') IOL into the capsular bag. This lens takes ~12–14 weeks to manufacture, and technical specifications are shown in Figure 1. Its 9-mm optic diameter allows implantation in the capsular bag, and limits side illumination in scotopic conditions. However, as

Table 1 Patient characteristics

Case	Age (years)	Gender	Diagnosis resulting in intractable diplopia	Previous treatment	Approximate duration of occlusive therapy until IOL surgery (months)	Preoperative lens status	Surgical procedure	Date of surgery	IOL implant	Visual acuity (VA)		Postoperative sequelae	Follow-up (months)
										Preoperative	Postoperative		
1	38	Male	Traumatic retinal detachment	Squint surgery, OCL, occlusive glasses	10	Phakic	Right phaco-aspiration, IOL into capsular bag (LA)	July 2007	Ophtec Black Ani II no hole (9.0 mm optic; overall length 13.75 mm)	Hand movements	Light perception	Mild postoperative uveitis	9
2	45	Female	Traumatic retinal detachment; decompensation of phoria	Prism, OCL, pilocarpine	30	Phakic	Left phaco-aspiration, IOL into capsular bag (GA)	December 2008	Ophtec Black Ani II no hole	6/9	Light perception	Secondary exotropia – requiring squint surgery	9
3	41	Male	Severe anisomyopia and amblyopia	Squint surgery x2, OCL, patch	12	Phakic	Left phaco-aspiration, IOL into capsular bag (GA)	October 2009	Ophtec Black Ani II no hole	6/60	'0' (Final VA 6/60 with clear IOL)	Removal of black IOL, secondary lens implant. Monocular diplopia	28
4	45	Female	Intracranial haemorrhage with acquired nystagmus and diplopia	Botulinum Toxin A, patching	7	Phakic	Right phaco-aspiration, IOL into capsular bag (LA)	September 2011	Ophtec Black Ani II no hole	6/60	No light perception	Worsening of convergent squint—listed for squint surgery	Patient demise at 23 months
5	49	Female	Retinal detachment, full-thickness macular hole	OCL	9	Pseudo phakic	Left Secondary IOL implant into sulcus (LA)	December 2012	Morcher 85F (6.00 mm optic; overall length 12 mm)	6/120	Light perception	Side illumination	1
6	56	Male	Microvascular third nerve palsy, Diabetes (no eye disease)	OCL, patching	22	Phakic	Right phaco, IOL into capsular bag (LA)	July 2013	Ophtec Black Ani II no hole	6/12	Light perception	Mild postoperative uveitis	2

Abbreviations: GA, general anaesthetic; IOL, intraocular lens; LA, local anaesthetic; OCL, occlusive contact lenses.

it is not foldable, implantation requires a proportionately larger corneal incision, which could potentially prolong postoperative recovery and increase the risk of future infection and globe rupture.

Whilst we have not formally tested for its near-infrared (NIR) properties, other opaque polycarbonate IOLs in use, such as Ophtec 'pupil occluder' iris claw IOLs, have been shown to be NIR-blocking, thereby providing total light occlusion and minimising the risk of treatment failure.[1,2] Clinically, all five patients had good resolution of intractable diplopia, albeit with variable light perception. The absolute occlusion with consequent symptomatic reduction of field resulted in explantation of the opaque IOL in one patient. This highlights the importance of considering loss of visual field with complete occlusion, and subsequent poor adaptation to monocular vision.

One patient had known Type II diabetes mellitus. Implantation of opaque IOLs in diabetics may be considered a relative contraindication,[3] and has not previously been described in the literature to our knowledge. Systemic conditions like diabetes tend to cause bilateral symmetrical ocular pathology.[4] In the authors' opinion, regular fundus surveillance of the fellow eye provides a reasonable proxy that predicts development of diabetic eye disease in the occluded eye. However, we concur that higher risk patients may benefit from longer-term follow-up with posterior segment imaging including optical coherence tomography, for example, those with choroidal naevi, suspicious discs, or lattice degeneration.

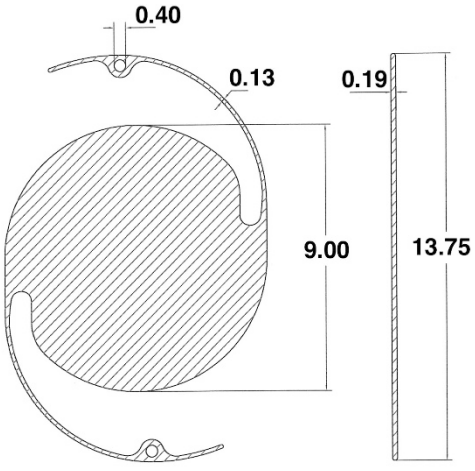

Figure 1 Custom-made Ophtec Ani II 0.0 Dpt. Black. Polycarbonate, nonfoldable, posterior chamber IOL (incision >9 mm). Reformatted image, reproduced with permission from Ophtec BV.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We are grateful to Ophtec BV for granting permission to reproduce a reformatted technical drawing of the custom-made Ophtec 0.0D black polycarbonate Ani II ('no hole') intraocular lens. We are also grateful to Dr John Ellis for his contribution to the work.

Disclaimer

Patient details are anonymised.

References

1 Yusuf IH, Fung THM, Patel CK. Primary black intraocular lens selection. *Eye* 2014; **28**: 1380–1382.
2 Yusuf IH, Peirson SN, Patel CK. Inability to perform posterior segment monitoring by scanning laser ophthalmoscopy or optical coherence tomography with some occlusive intraocular lenses in clinical use. *J Cataract Refract Surg* 2012; **38**(3): 513–518.
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Presentation: Part of this work was previously presented as a poster in the Autumn 2014 meeting of the Scottish Ophthalmological Club, and will be presented in poster format at the 2015 Annual Congress of the Royal College of Ophthalmologists.

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Sir,
Response to 'Opaque intraocular lens implantation'

We thank Professor MacEwen and coauthors[1] for responding to our letter describing the factors influencing primary black intraocular lens (IOL) selection.[2] They present the first study describing the clinical outcomes following primary implantation of a large (>7 mm optic) black IOL within the capsular bag. The Ophtec Black Ani II IOL (Ophtec BV, Groningen, The Netherlands) is a novel device produced from a material that is identical to the Artisan 201 iris-claw IOL, which has been proven to be occlusive to near infra-red (NIR) light.[3] This series adds to the growing experience with black IOL implantation, and several observations warrant further comment.

The mechanism of light perception following black IOL implantation is a curious phenomenon and its identification is critical to minimize the risk of treatment failure.[4,5] High rates of postoperative satisfaction are reported in patients with NIR-transmitting black IOLs,[6] despite near universal postoperative light perception.[5] We have suggested previously that trans-optical NIR light transmission across NIR-transmitting black IOLs may underlie intractable ghosting and treatment failure.[4,5] Such symptoms are extinguished by secondary NIR-blocking Ophtec black iris-claw IOL implantation.[4,7] Postoperative light perception in this series suggests para-optical light leakage despite a 9 mm occlusive optic, exceeding the scotopic pupil diameter. It is unlikely that formed, foveal images would result as a consequence: perceptions of 'ghosting' following Ophtec Ani II Black IOL implantation are unlikely.

Numerous black IOLs are available for clinical use, each with specific dimensions and properties that must be tailored to lens status/pupil size and the risk of retinal or optic nerve disease in each individual patient.[2] We have recently described ultra-widefield imaging in a patient with a NIR-transmitting black IOL using the Heidelberg Spectralis Scanning Laser Ophthalmoscope (Heidelberg Engineering, Heidelberg, Germany). This novel discovery may drive primary implantation of NIR-transmitting black IOLs to achieve a balance of efficacy and safety – permitting detection of retinal and optic nerve pathology across the life of the implant.

All black IOLs are likely to alleviate symptoms in patients with intractable diplopia and represent valid treatment modalities. However, it is essential that both patient and surgeon are informed of the risks of treatment failure and the possibility of ultra-widefield retinal imaging when a primary black IOL is selected.

Conflict of interest

The authors declare no conflict of interest.

References

1 Gong JWL, O'Colmain U, MacEwen CJ. Opaque intraocular lens implantation. *Eye (Lond)* 2015; **29**: 978–980.
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