Retinal nerve fibre layer thickness measurements after successful retinal detachment repair with silicone oil endotamponade

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Received 15 July 2014
Revised 15 October 2014
Accepted 26 November 2014
Published Online First 15 December 2014

ABSTRACT

Aims To measure peripapillary retinal nerve fibre layer thickness (RNFL) by using spectral domain optical coherence tomography (OCT) in patients who underwent successful retinal detachment repair with silicone oil tamponade.

Methods Sixty patients treated with pars plana vitrectomy and silicone oil tamponade for retinal detachment were prospectively enrolled in a study. Peripapillary RNFL thickness was measured with a Cirrus HD-OCT at 7, 30, 90 and 180 days postoperatively, using an Optic Disc Cube 200×200 protocol. The fellow eye of each study patient served as a control. Median peripapillary RNFL thickness in silicone oil filled eyes was compared with control eyes.

Results The median RNFL thickness in the group of vitrectomised eyes was significantly higher compared with control eyes at every visit. The analysis of variance showed that the median thickness in vitrectomised eyes differed between visits (F=4,3023; p=0.006). There was no time-related trend for RNFL thickness in this group. The analysis of variance of RNFL thickness in the fellow, unoperated eyes showed no difference between visits (F=2,3426; p=0.075).

Conclusions In patients with silicone oil tamponade, peripapillary RNFL was significantly thicker in comparison with fellow unoperated eyes over a 6-month period.

Trial registration number NCT 01255306.

INTRODUCTION

Silicone oil has been in use for 50 years in the treatment of complex retinal detachment in spite of numerous reports of associated complications, including cataract, keratopathy, intraocular pressure (IOP) rise and secondary glaucoma.[1–9] Migration of silicone oil into ocular tissues, including the optic nerve, and subsequent induction of inflammatory response mediated by macrophages has been documented by several human and animal studies.[10–13]

A long-term study of silicone oil tamponade in rabbit eyes has shown a significant decrease in myelinated optic nerve fibres after 12 months of tamponade, suggesting a destructive effect of silicone oil.[14]

An objective assessment of retinal nerve fibre layer (RNFL) of silicone oil filled eyes poses a challenge in a clinical setting due to limitations in imaging through silicone oil tamponade.

Optical coherence tomography (OCT) as a non-contact and non-invasive technology is successfully used to image and monitor diseases of the retina and optic nerve. Using the first generation of OCT technology (OCT version A4, 1997, Humphrey Instrument), Mastropasqua *et al*[15] were unable to show good reproducibility of RNFL measurements in silicone oil filled eyes. The latest commercially available OCT platform uses spectral domain technology, greatly improving image acquisition and resolution.

Errera *et al*[16] reported possible emulsified silicone oil deposition within retinal layers using spectral domain (SD)-OCT in eyes that have had silicone oil tamponade.

At this moment we are unaware of any report on measurement of the peripapillary RNFL thickness in silicone oil filled eyes using SD-OCT.

The purpose of this study was to measure peripapillary RNFL thickness by using SD-OCT in patients who underwent successful retinal detachment repair with silicone oil tamponade.

MATERIALS AND METHODS

Participants

We prospectively enrolled 60 patients with primary rhegmatogenous retinal detachment and proliferative vitreoretinopathy up to PVR stage C1 between April 2010 and June 2011 at the University Department of Ophthalmology, University Hospital Center 'Sestre milosrdnice', Zagreb, Croatia. The project was approved by the University Hospital Center, 'Sestre milosrdnice' Ethics Committee.

The study was also registered under ClinicalTrials.gov identifier NCT 01255306. All subjects signed an informed consent form.

To be eligible for the study, patients had to meet the following criteria: primary rhegmatogenous retinal detachment in the affected eye, healthy fellow eye that would serve as a control, no history of previous retinal surgery in either eye, no pre-existent glaucoma.

Standard 23 G pars plana vitrectomy and silicone oil tamponade was performed under subtenon anaesthesia in all patients. The surgical procedure was performed by one of two surgeons (ZV and GB). Retinal detachment was repaired in a standard fashion after vitreous removal and meticulous shaving of the periphery. Retina was reattached either through direct fluid–silicone oil exchange (OXANE1300, Bausch&Lomb, New York, USA), or after reattachment with perfluorocarbon liquid (Okta-line, Bausch&Lomb) followed by silicone oil instillation. All patients received endolaser photocoagulation of the retina in the area of primary retinal break and areas of peripheral pathological

To cite: Zoric Geber M, Bencic G, Vatavuk Z, *et al*. *Br J Ophthalmol* 2015;**99**:853–858.

Table 1 Demographics

Characteristic	Total	p Value
Age (years)	61.11±12.83	NA
Gender (M/F)	30/27 (53/47%)	0.791*
Eye L/R	30/27 (53/47%)	0.791*
Pseudophakic/phakic	20/37 (35/65%)	0.034*
Emetropic	39/57	NA
Hypermetropic	5/57	NA
Myopic (≤6 D)	8/57	NA
Highly myopic (>6 D)	5/57	NA

*χ^2 test.
NA, not applicable.

changes. In all cases, the retina was completely attached at the end of the procedure.

Follow-up examinations were performed at 7, 30, 90 and 180 days postoperatively and included uncorrected and best corrected visual acuity, slit lamp examination, dilated fundus examination, applanation tonometry and gonioscopy. Both the study eye and the contralateral healthy eye were subjected to the same examination regimen. Patients were excluded from the study if more than one half of the anterior chamber was filled with silicone oil or if a silicone oil related cataract developed that prevented the visualisation of the fundus. Also, patients in whom the retina did not completely attach under silicone oil tamponade in the follow-up period were excluded from the study.

RNFL thickness measurement

RNFL thickness measurement was performed with a Cirrus spectral-domain, high-definition OCT (Carl Zeiss Meditec Inc, Dublin, California, USA; software V.3.0). Each silicone oil filled eye and contralateral healthy eye were scanned with Optic Disc Cube 200×200 protocol. This protocol collects a cube of data through a 6 mm square shaped grid by acquiring a series of 200 A scans from 200 linear B scans. Cirrus high-definition OCT uses an algorithm that identifies the centre of the optic nerve head and automatically places a calculation circle of 3.46 mm diameter around it.

Each eye of each patient was previously dilated with 1% tropicamide before scanning and all scans were performed by the same operator. The OCT software calculates the average RNFL thickness for the overall peripapillary area. The signal strength of each scan was reviewed with minimum acceptable signal strength of 5. In cases of signal strength less than 5, the scan was repeated to reduce artefacts that may have influenced the accuracy of measurements.

Table 2 Incidence of elevated intraocular pressure (IOP)

Study group	N	%
Normal IOP	25	43.86
Raised IOP	32	56.14
7 days	15	26.32
30 days	11	19.30
90 days	5	8.77
180 days	1	1.75
Total	57	100.00

Statistical analysis

Descriptive statistics were used to present demographic and clinical characteristics (median and IQR for quantitative continuous variables, frequencies for categorical variables). Categorical data were analysed using the χ^2 test. Median RNFL thickness was calculated for study eyes and fellow eyes. Comparison of RNFL thickness between the study groups was evaluated by Mann–Whitney test.

We used Friedman analysis of variance to compare the differences within the groups (study eyes, fellow eyes) across repeated measurements. In accordance with standard statistical practice, p values less than 0.05 were described as significant. All statistical analyses were performed using the SPSS V.15.0 package (SPSS Inc, Chicago, Illinois, USA).

RESULTS

Out of 60 patients enrolled in the study, three were excluded from final analysis. One patient developed a severe inflammatory reaction in the early postoperative period which subsided following intense local and periocular corticosteroid therapy. Two patients were excluded due to an incomplete set of RNFL measurements. (One patient developed a cataract 3 months following the vitrectomy which precluded further RNFL measurements and the other was lost to follow-up). During the follow-up period no epiretinal membrane formation or other retinal pathology which might have influenced the RNFL measurement was registered in any of the study or control eyes. A total of 57 patients completed all follow-up visits and were statistically analysed. Demographic and clinical characteristics are shown in table 1.

The incidence of raised IOP during the follow-up period was 56.14% (32 out of 57 patients). In 26 patients (81.25%) elevated IOP was recorded within 30 days after silicone oil endotamponade (range 22–36 mm Hg). In all affected patients, the topical and systemic antiglaucoma medications controlled the IOP and was maintained throughout the course of the study.

Table 3 Median peripapillary RNFL thickness values of silicone oil filled eyes and control eyes

	Vitrectomised eyes			Control eyes			
RNFL thickness (μm)	N	Median	IQR	N	Median	IQR	p Value*
7 days	57	98	87.75–105	57	88	81–94	0.0007
30 days	57	94	84–103	57	88	81–96	0.0227
90 days	57	95	82.75–104	57	88	80–95	0.0128
180 days	57	96	83–110.25	57	90	82.25–97	0.0081

*Mann–Whitney U test.
RNFL, retinal nerve fibre layer.

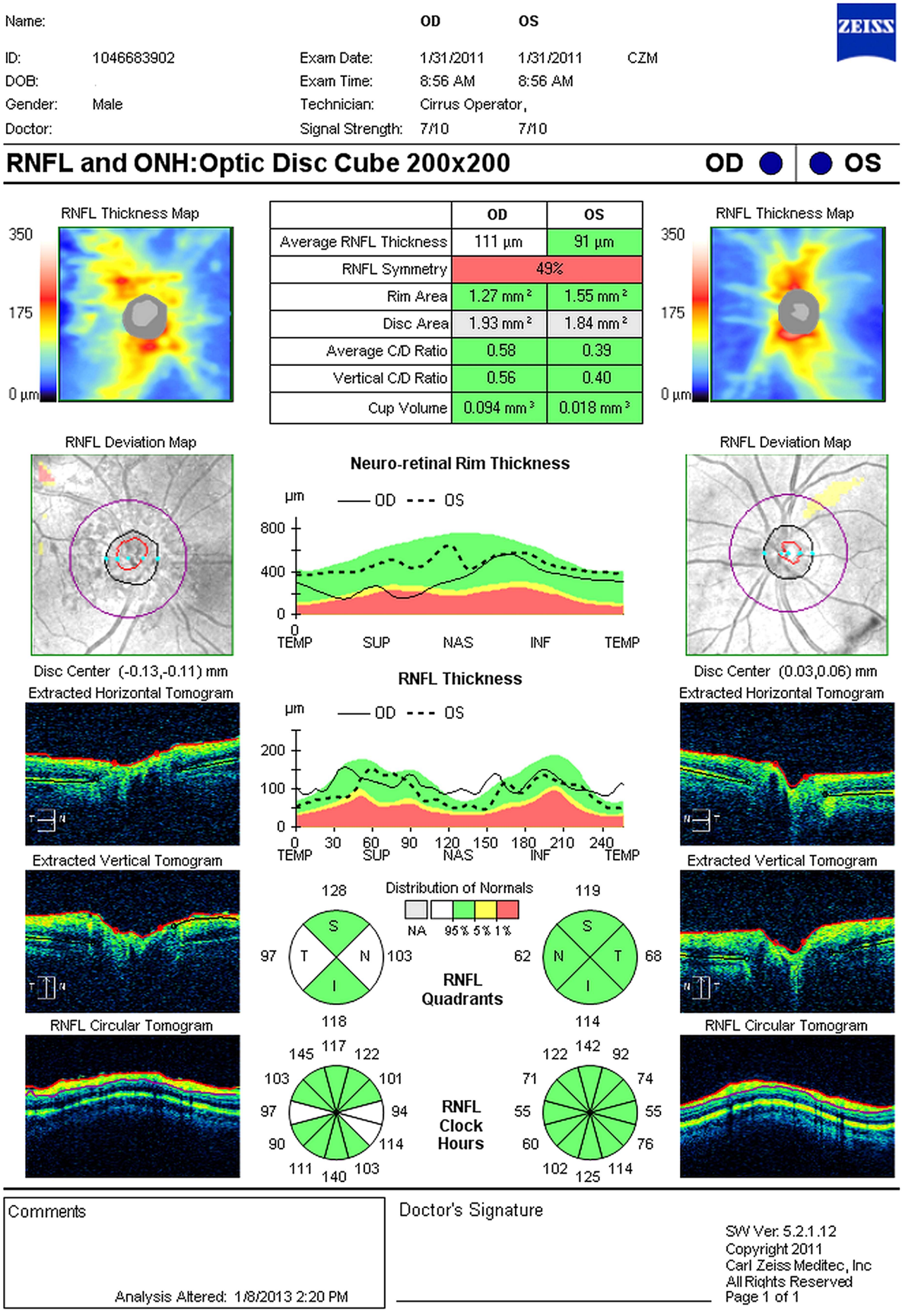

Figure 1 Optic disc cube 200×200 scan showing a marked difference in retinal nerve fibre layer (RNFL) thickness between silicone oil filled eye (OD) and control eye (OS).

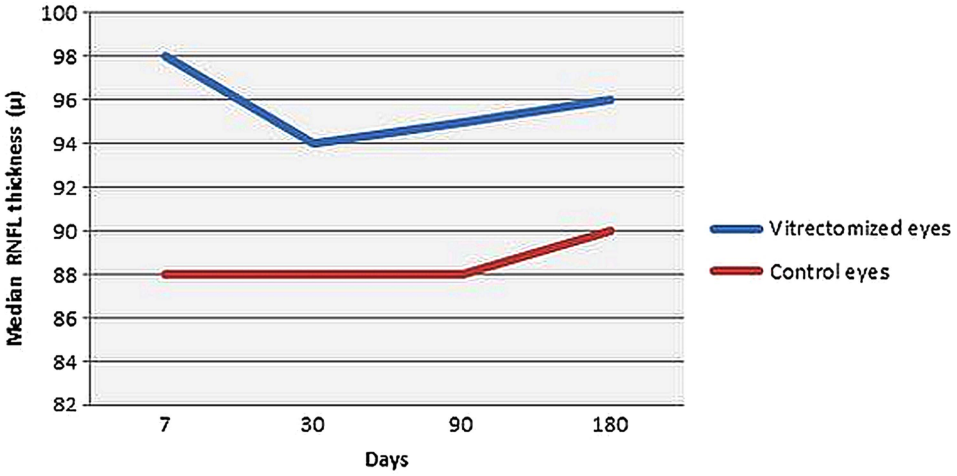

Figure 2 Median retinal nerve fibre layer thickness change in vitrectomised versus control eyes over the course of the study.

The incidence of elevated IOP at each follow-up visit is shown in table 2.

Table 3 shows that the median RNFL thickness in the group of vitrectomised eyes was significantly higher compared with control eyes at every visit. A typical OCT scan of the RNFL and optic nerve clearly demonstrating the difference in RNFL thickness between silicone oil filled eye and control eye is presented in figure 1. The analysis of variance showed that the median thickness in vitrectomised eyes differed between visits ($F=4,3023$; $p=0.006$), as presented in figure 2. We were not able to see a time-related trend for RNFL thickness in this group. The analysis of variance of RNFL thickness in the fellow, unoperated eyes showed no difference between visits ($F=2,3426$; $p=0.075$).

Figure 3 represents the box and whisker plots comparing the distribution of median RNFL thickness in silicone oil filled eyes and fellow, unoperated eyes.

DISCUSSION

The effect of silicone oil on ocular tissues, including RNFL, has been a focus of several histopathological studies, yet in vivo studies on this topic are currently lacking. We are unaware of studies reporting the measurement of the peripapillary RNFL thickness in silicone oil filled eyes using OCT. In our study, peripapillary RNFL of eyes with retinal detachment repaired with silicone oil was significantly thicker compared with fellow unoperated eyes. As shown in figure 2, the median RNFL thickness at day 7 after retinal detachment repair was 98 µm compared

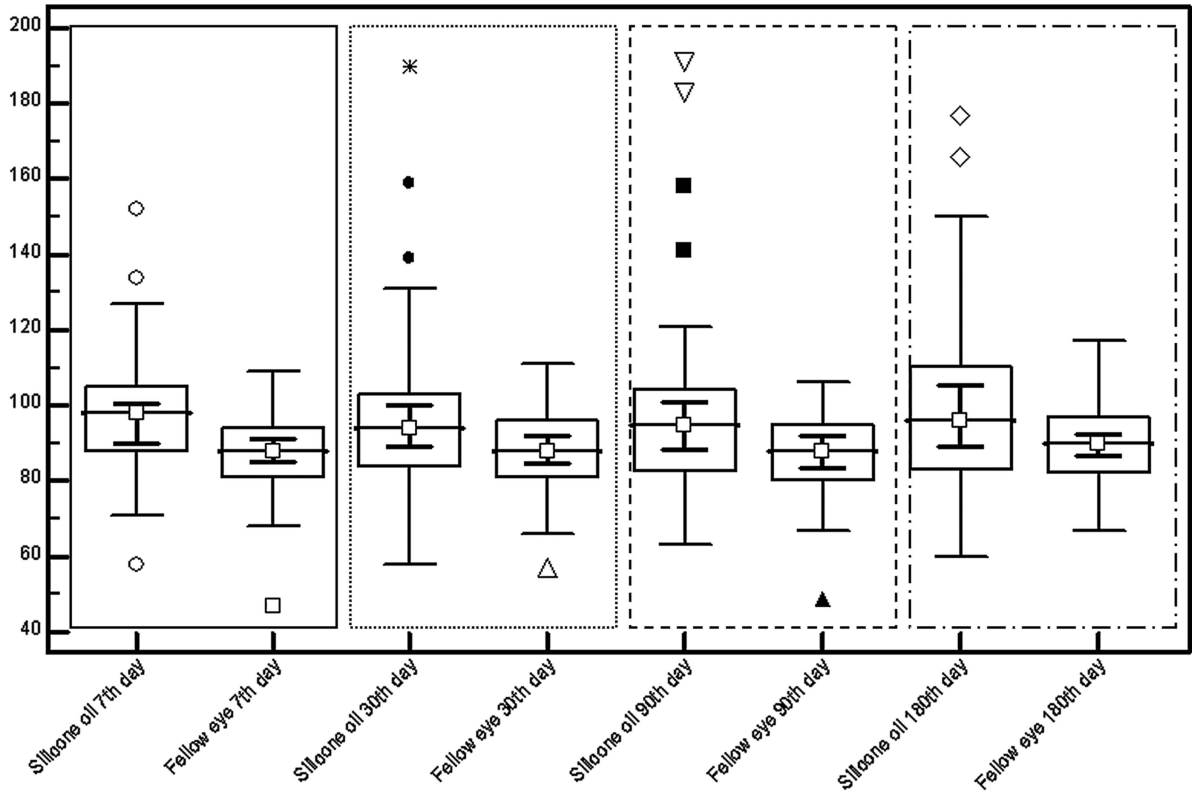

Figure 3 Box and whisker plot of retinal nerve fibre layer thickness in silicone oil filled eyes and fellow eyes over the follow-up period. The central box represents the values from the lower to upper quartile (25th–75th percentile). The middle line represents the median.

with 88 μm in the fellow eyes. This initial thickening may be partly caused by surgical manipulation and early postoperative retinal readjustment. The median RNFL thickness in study eyes decreased after the first follow-up visit. After that early postoperative period, and in spite of clinically fully reattached retina, RNFL still remained significantly thickened over the course of 6 months.

Lee *et al*[17] have described thinning of the peripapillary RNFL after vitrectomy for rhegmatogenous retinal detachment using a third-generation Stratus OCT. To exclude the influence of vitrectomy on the RNFL, they compared the RNFL thickness in the area of undetached retina between affected eyes and control fellow eyes. While we used a less traumatic 23 gauge vitrectomy, Lee *et al* used 20 gauge vitrectomy with either SF6 or C3F8 tamponade in their cohort, with no patient receiving silicone oil tamponade. Interestingly, their results showed no difference in RNFL thickness between affected and fellow eye after 6 months. It was only after 12 and 24 months that the RNFL of the affected eye exhibited significant thinning in comparison with the fellow eye.

Recently, several reports on OCT findings in silicone oil filled eyes have been published. Errera *et al*[16] demonstrated emulsified silicone oil droplets underneath epiretinal membranes and within retinal layers in eyes that have had silicone oil tamponade using spectral domain OCT. Mrejen *et al*[18] have shown in vivo visualisation of silicone oil in the optic nerve and the retina using adaptive optics. Silicone oil particles were imaged at the level of the photoreceptors and at the optic nerve head. We were also able to visualise hypereflective dots in the optic disc on SD-OCT images (figure 4).

Several histopathological studies, performed in animal models and on enucleated eyes, have demonstrated that silicone oil can migrate into various ocular tissues, including the retina and optic nerve as early as 1 month after silicone oil instillation.[10–14] These studies also confirmed the presence of an associated inflammatory cellular infiltration in silicone oil affected tissues.

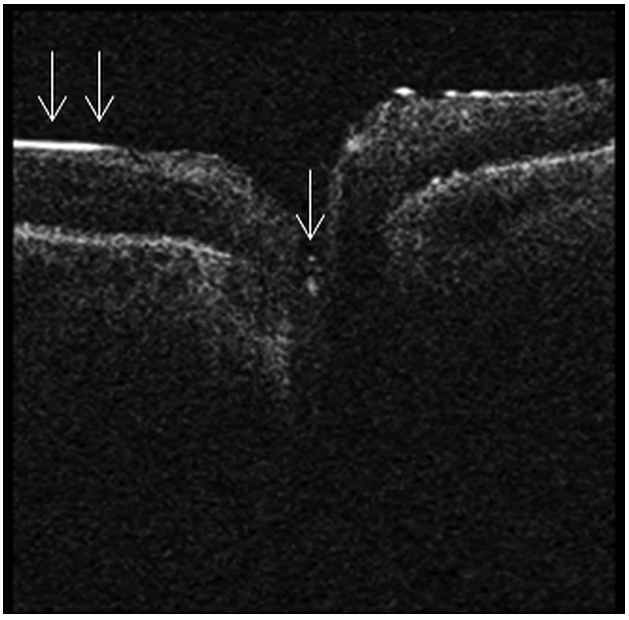

Figure 4 Spectral domain optical coherence tomography showing hyperreflective dots in the optic disc area (arrow) and hyperreflective line representing silicone oil (double arrow).

Wickham *et al*[13] have demonstrated microglobules of silicone oil in the drainage angle, iris, ciliary body, retina, epiretinal membranes and optic nerve. Budde *et al*[19] analysed 74 enucleated eyes with silicone oil, and observed deposition of silicone oil together with an associated inflammatory reaction in the retrolaminar portion of the optic nerve in 14 eyes. Silicone oil vacuoles in some eyes constituted 40% of the cross-sectional area of the optic nerve.

Some authors consider that elevated IOP is the main factor for the shift of silicone oil into optic nerve (Pseudo-Schnabel's cavernous optic nerve degeneration), while others propose that elevated IOP is not sufficient and postulate active mechanism based on a finding of silicone oil in ventricles of the brain.[20 21]

In our study, high IOP was medically controlled in all subjects, therefore we could not assess the effect of intraocular pressure on RNFL thickness under silicone oil tamponade.

The influence of refractive errors, in particular high myopia, on RNFL thickness measurements has been the focus of several studies and they noted a tendency for the decrease in RNFL thickness with increasing axial length.[22] In this study, only five participants were highly myopic, which had a minimal influence on RNFL measurements of the cohort. It is known that reduced transparency of optical media, as opposed to the optical properties of silicone oil, affects the quality of OCT scans.[23] The optical properties of silicone oil have merely an effect on segmentation algorithms of the OCT.[15]

We cannot rule out the possibility that silicone oil has a direct subclinical toxic effect on the retina. This is less likely considering the priority of modern silicone oils compared with earlier oils.[24] There are several limitations in our study. We could not control all the factors that may have had an influence on study findings. The pathological response of retinal detachment itself, as well as the surgical repair, may have been responsible for some of the reported changes. We used a fellow, healthy eye for the control group instead of a separate control group of individuals who underwent vitrectomy with no oil, due to high concordance of OCT values between both eyes of the same individual.[25] Also, this study did not analyse the effect of silicone oil on different retinal layers which could also have contributed to the interpretation of results.

Concerning these findings and the objective limitations of the study we hypothesise that silicone oil and consequent events may have contributed to the RNFL thickening.

In conclusion, this study has shown that peripapillary RNFL exhibits thickening under silicone oil over a 6 month period in vitrectomised eyes. The consequence of this finding and its clinical implications should be evaluated in a larger sample size prospective trial using the latest technological advances.

Contributors MZG set up the study, followed the patients and drafted the manuscript. GB recruited the patients for the trial, operated on them, reviewed results of the trial and drafted the manuscript. ZV recruited the patients for the trial, operated on them, reviewed results of the trial and critically reviewed the manuscript. RI helped set up a study, was involved in reviewing the results and drafted the manuscript. TRF helped set up a study, reviewed the results and critically reviewed the manuscript.

Competing interests None.

Patient consent Obtained.

Ethics approval Local Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Kleinberg TT, Tzekov RT, Stein L, *et al.* Vitreous substitutes: a compressive review. *Surv Ophthalmol* 2011;56:300–23.

2 Abrams GW, Azen SP, McCuen BW II, *et al*. Vitrectomy with silicone oil, or long acting gas in eyes with severe proliferative vitreoretinopathy: results of additional and long term follow up. Silicone Study report 11. *Arch Ophthalmol* 1997;115:335–44.
3 Leaver PK, Grey RH, Garner A. Silicone oil injection in the treatment of massive preretinal retraction. II. Late complications in 93 eyes. *Br J Ophthalmol* 1979;63:361–7.
4 Casswell AG, Gregor ZJ. Silicone oil removal I. The effect on the complications of silicone oil. *Br J Ophthalmol* 1987;71:893–7.
5 Casswell AG, Gregor ZJ. Silicone oil removal II. Operative and postoperative complications. *Br J Ophthalmol* 1987;71:898–902.
6 Silicone Study Group. Silicone Study Report 4. Postoperative intraocular pressure abnormalities in the Silicone Study: results of a randomized clinical trial. *Ophthalmology* 1993;100:1629–35.
7 Al-Jazzaf AM, Netland PA, Charles S. Incidence and management of elevated intraocular pressure after silicone oil injection. *J Glaucoma* 2005;14:40–6.
8 Jonas JB, Knorr HLJ, Rank RM, *et al*. Intraocular pressure and silicone oil tamponade. *J Glaucoma* 2001;10:102–8.
9 Nguyen QH, Lloyd MA, Heuer DK, *et al*. Incidence and management of glaucoma after intravitreal silicone oil injection for complicated retinal detachments. *Ophthalmology* 1992;99:1520–6.
10 Knorr HL, Seltsam A, Holbach L, *et al*. Intraocular oil tamponade. A clinic-pathologic study of enucleated eyes. *Ophthalmologe* 1996;93:130–8.
11 Biswas J, Verma A, Davda MD, *et al*. Intraocular tissue migration of silicone oil after silicon oil tamponade: a histopathological study of enucleated silicone oil-filled eyes. *Indian J Ophthalmol* 2008;56:425–8.
12 Wickham L, Asaria RH, Alexander R, *et al*. Imunopathology of intraocular silicone oil: enucleated eyes. *Br J Ophthalmol* 2007;91:253–7.
13 Wickham L, Asaria RH, Alexander R, *et al*. Imunopathology of intraocular silicone oil: retina and epiretinal membranes. *Br J Ophthalmol* 2007;91:258–62.
14 Papp A, Kiss EB, Tímár O, *et al*. Long-term exposure of the rabbit eye to silicone oil causes optic nerve atrophy. *Brain Research Bull* 2007;74:130–3.
15 Mastropasqua L, Caprineto P, Ciancaglini M, *et al*. Reproducibility of nerve fiber layer thickness measurements using optical coherence tomography in silicon oil-filled eyes. *Ophthalmologica* 2001;215:91–6.
16 Errera MH, Liyanage SE, Elgohary M, *et al*. Using spectral-domain optical coherence tomography imaging to identify the presence of retinal silicone oil emulsification after silicone oil tamponade. *Retina* 2013;33:1567–73.
17 Lee YH, Lee JE, Shin YI, *et al*. Longitudinal changes in retinal nerve fiber layer thickness after vitrectomy for rhegmatogenous retinal detachment. *Invest Ophthalmol Vis Sci* 2012;53:5471–4.
18 Mrejan S, Sato T, Fisher Y, *et al*. Intraretinal and intra-optic nerve head silicone oil vacuoles using adaptive optics. *Ophthalmic Surg Lasers Imaging Retina* 2014;45:71–3.
19 Budde M, Cursiefen C, Holbach LB, *et al*. Silicone oil–associated optic nerve degeneration. *Am J Ophthalmol* 2001;131:392–4.
20 Shields CL, Eagle RC Jr. Pseudo-Schnabel's cavernous degeneration of the optic nerve secondary to intraocular silicone oil. *Arch Ophthalmol* 1989;107:714–7.
21 Eller AW, Friberg TR, Mah F. Migration of the silicone oil into the brain: a complication of intraocular silicone oil for retinal tamponade. *Am J Ophthalmol* 2000;129:685–8.
22 Mohammad Salih PA. Evaluation of peripapillary retinal nerve fiber layer thickness in myopic eyes by spectral-domain optical coherence tomography. *J Glaucoma* 2012;21:41–4.
23 Schuman JS, Pedut-Kloizman T, Hertzmark E. Reproducibility of nerve fiber layer thickness measurements using optical coherence tomography. *Ophthalmology* 1996;103:1889–98.
24 Friberg TR, Verstraeten TC, Wilcox DK. Effects of emulsification, purity, and fluorination of silicone oil on human retinal pigment epithelial cells. *Invest Ophthalmol Vis Sci* 1991;32:2030–4.
25 Caramoy A, Foerster J, Allakhiarova E, *et al*. Spectral-domain optical coherence tomography in subjects over 60 years of age, and its implications for designing clinical trials. *Br J Ophthalmol* 2012;96:1325–30.

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Br J Ophthalmol 2015 99: 853-858 originally published online December 15, 2014
doi: 10.1136/bjophthalmol-2014-305839