Different tamponade effects of intraocular silicone oil and sterilized air after single pars plana vitrectomy for rhegmatogenous retinal detachment

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Abstract

Purpose: To investigate different fundus vasculature and structure changes after single pars plana vitrectomy (PPV) following silicone oil (SO) or sterilized air in macular-off rhegmatogenous retinal detachment (RRD) patients.

Method: 39 eyes (39 patients) with macular-off RRD underwent standard three-port 23-gauge PPV and intraocular SO or gas tamponade. Optical Coherence Tomography (OCT) and angiography were used to evaluate fundus structure and vasculature including retinal layers thicknesses and vessel density (VD) changes throughout observation for 12 weeks. Retinal layers were segmented into: NFL, GCL+IPL, INL, OPL, ONL+IS, OS+RPE and BRM. Fundus vasculature was segmented into superficial and deep capillary plexus (SCP, DCP), and choriocapillaris plexus (CCP).

Result: For fundus vasculature, SO tamponade led to significant decrease in both SCPVD and DCPVD, while only SCPVD was found significantly decreased in gas tamponade eyes. For specific retinal layer, SO led to significant decrease in NFL and INL thicknesses. OPL, ONL+IS and OS+RPE thicknesses had significant increase in both SO tamponade and gas tamponade eyes.

Conclusion: Different intraocular tamponades could have various impacts on retinal vasculature and structure. Compared to sterilized air, silicone oil tamponade could have relatively more negative effects on retinal vasculature and specific retinal layer thickness change.

Introduction

Rhegmatogenous retinal detachment (RRD) is the most common type of retinal detachment. With an annual incidence to be about 10.5 people per 100,000 population[1], RRD is one of the leading causes for permanent vision loss. After years of surgical revolution and progression on retinal repair, fundus surgeons could now achieve amazing reattachment rates for RRD. However, progressive visual loss after successful retinal reattachment could still be a big problem with underlying mechanism unknown. Theoretically, one of the main reasons could be irreversible photoreceptor cell death including various death pathways like apoptosis and necrosis [2]. According to clinical observation, the maintenance of macular structure is related to the postoperative visual outcome [3]. However, patients with no macular abnormalities by means of Optical Coherence Tomography (OCT) could also suffer from progressive visual impairment. A series of reports have indicated unexplained severe visual damage without abnormalities on OCT or fluorescein angiography especially after intraocular silicone oil (SO) use [4–6].

Pars plana vitrectomy (PPV) is one of the most popular and effective surgical options for RRD patients. SO and gas are frequently-used as intraocular tamponade for PPV[7, 8]. Compared to the spontaneously dissolved gas, SO is a kind of biochemically inert polymer which has the advantage of prolonged tamponade. Adequate intraocular tamponade time is essential to retinal reattachment, especially for macular-off RRD. SO was used to be considered well-tolerated and not affecting retinal physiology[9]. However, some researchers have noticed potential harmful effects of silicone oil to retinal structure[10,

11]. Visual abnormality like central scotoma, decreased foveal sensitivity and macular dysfunction have been considered to be related to intraocular SO use[4–6, 12], which led to a new term: Silicone Oil-Related Visual Loss (SORVL).

Detailed fundus imaging and observation are essential to understand the underlying mechanism of SORVL. The application of OCT in RRD patients allowed the detection of microscopic fundus structural abnormalities after retinal repair[13–15]. Negative tamponade effects of SO has been described such as thickness change in specific retinal layers and choroidal thinning[14–16]. However, few studies focused on the investigation of different fundus changes owing to different intravitreal tamponade materials, or included follow-up observations. On the other hand, in most previous researches, the study designs were widely divergent. Different length of postoperative observation time could lead to controversial results[13, 17, 18]. For retinal repair, single PPV, PPV combined with buckling or cataract surgery, different surgical operations and various tamponade choices could all have impact on postoperative fundus changes[12, 13, 17–21]. Moreover, fundus vasculature change after single PPV for RRD has yet to be studied thoroughly.

To eliminate the influence of different surgical options on fundus vasculature and structure, and to investigate different tamponade effects between SO and sterilized air in follow-up observation, in the present study, we performed detailed OCT/OCTA examinations for macular-off patients underwent single PPV following SO or sterilized air tamponade for retinal repair. By mean of fundus change comparison, we intended to figure out whether SO tamponade could lead to more pronounced fundus abnormalities compared to gas tamponade.

Patients And Methods

Patients

This retrospective, single-center study observed 39 patients suffered primary macular-off RRD of the inpatients Department of Ophthalmology, Shanghai General Hospital Affiliated to Shanghai Jiao Tong University, from January 2018 to March 2019. This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Shanghai General Hospital affiliated to Shanghai Jiao Tong University. Exclusion criteria included traumatic or tractional retinal detachment, appearance of choroidal detachment, previous intraocular surgery, proliferative vitreoretinopathy over B level, sign of epi-retinal membrane, macular hole, macular degeneration or other macular disorder, high myopia (axial length≥26 mm), secondary glaucoma, lens turbidity or massive postoperative vitreous hemorrhage, persistent sub-retinal fluid or intra-retinal cystic space.

Surgery

Standard three-port 23-gauge PPV was performed using the Alcon Constellation system (Alcon Laboratories, Inc., Fort Worth, TX, USA). All the procedures were performed by the same surgeon (Dr. Haiyun Liu). Extent of RRD (number of quadrants) and number of retinal tears were recorded before

surgery, and double confirmed during the procedure. Before surgery, adequate doctor-patient communications were carried with each of our patients. The choice for type of tamponade was first discussed during the conversation, based on intraocular pathological condition and patient' s will of undertaking secondary surgery for SO removal, and was finally decided by the surgeon during the operation. After drainage of subretinal fluid during air-fluid exchange, intraocular tamponade of SO or gas was used. 24 patients with intraocular SO tamponade were defined as Silicone Oil (SO) group, and 15 patients with intraocular Gas tamponade were defined as Gas group. Normally, we know that sterilized air could be spontaneously absorbed in 2 weeks. Upon the first postoperative follow-up visit (at 2 weeks), patients of the Gas group actually had no remaining intravitreal air tamponade. But for ease of expression, we denominated the 'Gas/SO group' and 'Gas/SO tamponade' in the present study, based on intravitreal tamponade choices during surgery. No patients underwent combined cataract surgery during the procedure. SO removal was performed around four months after retinal reattachment surgery and no patient appeared recurrent retinal detachment.

Retinal and choroidal vascular layer imaging

OCT and angiogram imaging was acquired using the RTVue XR Avanti device (AngioVue software, version 2017.1.0.155; Optovue Inc., Fremont California, USA). The Angio Retina mode (6 × 6 mm) and the technique including the SSADA method has been previously described[22]. The segmentation of fundus vasculature was automatically produced by the build-in software into: superficial capillary plexus vessel density (SCPVD), deep capillary plexus vessel density (DCPVD), and choriocapillaris plexus vessel density (CCPVD) (Fig. 1). Two experienced doctor and technician (S, Zhang, H, Zhou) independently reviewed the images and occasionally corrected the segmentation lines when necessary before data extraction. Low qualified images were excluded based on one or more of the following criteria: low signal strength index (< 60), presence of blink artifacts, motion or doubling artifacts due to poor fixation, and bad media opacity. For each layer, the VD was calculated separately in foveal (1 mm), parafoveal (1–3 mm) and perifoveal (3–6 mm) areas according to the ETDRS grids.

Retinal and choroidal layer thickness imaging

We got seven sets of retinal layer thickness data with the automatic segmentation by RTVue XR Avanti device for retinal layers thickness analysis (Fig. 2): NFL (nerve fiber layer), GCL + IPL (ganglion cell layer, inner plexiform layer), INL (inner nuclei layer), OPL (outer plexiform layer), ONL + IS (outer nuclei layer, inner segment), OS + RPE (outer segment, retinal pigment epithelium) and BRM (Brunch's membrane). Choroidal thickness was obtained with the automatic built-in software of the SS-OCT device (Topcon FastMap, version 10.13.003.06, Topcon Medical Systems, Fig. 3). All patients underwent three times postoperative examinations (2 weeks, 6 weeks, 12 weeks).

Data analysis

All statistical analyses were performed using Python (version 3.7.3, Python Software Foundation). All values were given as mean ± SD. Measured value of VD and layer thickness were tested using paired t-

test between two adjacent time points to present postoperative fundus change. Values of $p < 0.05$ were considered to be statistically significant.

Results

All 39 patients underwent three times postoperative examinations with excellent completion. Demographics and clinical characteristics of two subgroups were shown in Table 1.The mean age of our patients was 56.85 ± 11.2 years. The mean duration of presumed RD (duration of corresponding visual symptoms) before surgery was 10.97 ± 5.99 days. The mean axial length was 23.84 ± 0.72 mm. No significant difference of mean age, sex, axial length and symptom duration before surgery was found between SO group and Gas group. However, the intraocular pathological conditions of retinal detachment had some minor differences between SO and Gas groups. Although the number of retinal tears had no significant difference between these two groups ($p = 0.453$, Table 1), the SO group had relatively larger extent of retinal detachment than the Gas group ($p = 0.006$, Table 1).

Fundus vasculature

From 2 weeks to 6 weeks, no significant result of fundus vasculature was observed in Gas tamponade eyes. On the other hand, parafoveal CCPVD was found significantly increased in SO tamponade eyes ($p = 0.013$, Table 2).

From 6 weeks to 12 weeks, SCPVD was found significantly decreased in Gas tamponade eyes, especially in perifoveal area (Table 3). However, no significant change of DCPVD was observed. As for SO tamponade eyes, both SCPVD and DCPVD were found significantly decreased (Table 3).

No other significant result of retinal or choroidal vessel density changes was found during observation.

Retinal and choroidal layer thickness

From 2 weeks to 6 weeks, foveal OPL thickness was found significantly increased in SO tamponade eyes ($p = 0.015$, Table 4). OS + RPE and foveal ONL + IS thicknesses were found significantly increased in both Gas tamponade and SO tamponade eyes. BRM thickness was found significant decreased in both Gas tamponade eyes (Table 4).

From 6 weeks to 12 weeks, NFL thickness was found significantly decrease in SO tamponade eyes. Foveal OPL thickness was still found significantly increased in SO tamponade eyes ($p = 0.033$, Table 5). ONL + IS thicknesses were found significantly increased in both gas and SO tamponade eyes (Table 5).

No other significant result of retinal or choroidal layer thickness changes was found during observation.

Discussion

As described before, the present follow-up study had a relatively rigorous design. Evaluation indicators included retinal perfusion system, choroidal capillary plexus, retinal and choroidal layers thicknesses. Before us, study designs of previous researches on fundus observation after RRD surgery divergent widely. Combined operation with cataract surgery [20, 21], either or both scleral buckling and PPV [12, 13, 17–21], various intraocular tamponade choice[12, 15, 17, 21], could all have impact on fundus structure and vasculature. Moreover, few study focused on the observation of different tamponade effects of silicone oil with other intravitreal materials on fundus structure and vasculature changes after retinal reattachment. We performed only single PPV for retinal repair to eliminate potential bias due to surgical option. It is unethical to randomly choose intravitreal SO or sterilized air as tamponade materials during procedure. After adequate communication with each patient, considering of patients' will of undertaking a second operation (SO removal), the decision was made by both the patients and the surgeon. It is understandable that the SO group had relatively larger extent of detachment than the Gas group (Table 1). However, the symptom duration, number of retinal tears had no significant difference between Gas group and SO group. Thus, we believe that the intraocular pathological conditions between two groups were similar and our work could be reliable in observation of different tamponade effects of silicone oil and sterilized air on postoperative fundus changes. The recommended time for SO removal is yet to reach a consensus. Theoretically, the removal of SO is to avoid SO-related complications such as cataract, glaucoma, and keratopathy. As routine practice in our ophthalmic clinical center, RRD patients underwent retinal repair with anatomically well-reattached retina according to OCT follow-up and no sign of obviously progressive PVR for around 3 months are suggested for SO removal. Thus, the duration of observation in the present study was 12 weeks.

Retinal vessel density, choroidal thickness and vessel density change

The retinal and choroidal vasculature changes after PPV for retinal repair have not reached a commitment, which is due to different study designs of previous researches as described above. For retinal perfusion, Wang et al, found significant increase in macular perfusion during observation (12 weeks) after retinal reattachment[21]. However, in their study, the PPV operation was combined with cataract surgery. Phacoemulsification has been demonstrated to increase retinal VD after surgery [23, 24]. Wu et al. found significantly lower SCPVD and DCPVD in macular-off RD following Gas tamponade eyes than the fellow eyes[18]. Although such finding is consistent to our results, we have to realize that the length of their cross sectional observation time was relatively longer than us (3.6 ± 2.4 months, range 2–9 months). In the present study, we found decreased retinal perfusion in both SO tamponade and Gas tamponade eyes from 6 weeks to 12 weeks (Table 3). Of which, only SCPVD was found significant decreased in Gas tamponade eyes, and SO tamponade led to pronounced decrease in both SCPVD and DCPVD (Table 3). Although the macular perfusion system and structure could be influenced after macular detachment. We still postulate that intraocular SO tamponade might lead to poorer postoperative macular perfusion than Gas tamponade, especially in deep capillary plexus vessel density.

For choroidal capillary plexus status, previous studies used choroidal thickness as an evaluation indicator. Akkoyun et al. reported increased subfoveal choroidal thickness 1 week after retinal repair, which they thought represent postoperative inflammatory reaction[25]. Karimi et al reported time-related reduce of subfoveal choroidal thickness in SO tamponade eyes after PPV which may possibly due to tamponade effect of silicone oil[16]. However, choroidal thickness change is not necessarily associated with choroidal vessel change[26, 27]. According to our observation, we failed to find any significant result of choroidal thickness change during observation. We only found significant increase of parafoveal CCPVD in SO tamponade eyes from 2 weeks to 6 weeks ($p = 0.013$, Table 2). We thought that it may be attributed to the relatively greater amount cryopexy and laser photocoagulation during procedure following SO use, which lead to more severe choroidal inflammation after surgery. Compared to choroidal thickness, choroidal vessel density might be a more sensitive method to monitor postoperative choroid status. Future study should verify the choroidal vasculature change in long-term follow-up.

Retinal layer thickness change

In most previous studies on retinal structure change after RRD surgery, the retinal layers were divided in a relatively general way. In the present study, the retinal layers were strictly segmented into seven layers as introduced in the method section. Due to different study design and observation length, the result of postoperative NFL thickness after retinal repair is a little bit controversial. The report of short term increase may be related to postoperative inflammation[15]. NFL thickness may have a decreasing trend in long term follow up[28]. In the present study, the NFL thickness kept steady from 2 weeks to 6 weeks in both SO and Gas tamponade eyes. From 6 weeks to 12 weeks, we found pronounced decrease of NFL thickness in SO tamponade eyes than in Gas tamponade eyes ($p = 0.003$, Table 5). NFL thickness decrease echoed the experimental results of inner retina thickness change and loss of neuronal connections after surgical repair of RRD[29]. Furthermore, previous study has also described the potential toxic effect of SO on ganglion cells[14]. Thus, according to the more significant decrease of NFL thickness in SO tamponade eyes, we may demonstrate that SO tamponade could have more negative impact on ganglion cells compared to Gas tamponade.

We found significant increase of foveal OPL thickness in SO tamponade eyes across the whole observation ($p = 0.015$,Table 4; $p = 0.033$, Table 5). Yasin et al. reported thicker INL and OPL in both SO tamponade and Gas tamponade eyes after successful retinal repair than in fellow eyes[15]. Theoretically, the inflammatory reaction after retinal detachment and reattachment repair may be observed as increase in the volume of OPL thickness. Intermediate filament protein like vimentin and glial fibrillary acidic protein extends throughout the cytoplasm of the Müller cells[30]. Marcel et al. also reported a time related increase of INL-OPL thickness after successful retinal reattachment[17]. In the light of these findings, we suspect the more pronounced increase of OPL thickness may indicate more severe and longer-lasting fundus inflammation due to SO tamponade.

The photoreceptor lied in the ONL + IS and the OS + RPE layer in the present study (Fig. 2). The integrity and thickness of IS/OS could be an important predictor of postoperative VA after RD surgery[31, 32]. We found significant increase of ONL + IS and OS + RPE thickness in both SO tamponade and Gas

tamponade eyes across observation (Table 4&5), which might indicate photoreceptor recovery[33](One can even tell the increase from Fig. 1, A4, B4&C4). Furthermore, we found significant decrease of BRM thickness in Gas tamponade eyes from 2 weeks to 6 weeks (Table 4). Thickness change of Brunch's membrane after retinal repair has not been previously reported.

Recent years, numerous researches has been done for the underneath mechanism of Silicone Oil-Related Visual Loss (SORVL). Some researchers considered such visual abnormalities to be related to SO tamponade effect[34], and several pathophysiologic hypotheses have been proposed. One theory speculated that photo-toxicity may have a role, as oil transmits light more in the blue spectrum than aqueous[35]. SO has also been reported to dissolve fat soluble elements from the retina[36]. The fat soluble macular pigments like lutein and zeaxanthin are thought to protect the macula from photo-oxidative damage[37]. In addition, lost buffering capacity of the vitreous cavity and presence of intraocular SO lead to impaired retinal homeostasis. Potassium, magnesium and cytokines levels were found to be influenced due to SO tamponade, which may cause metabolic exhaustion and degeneration of the Müller cells[38–40].

The present study has certain limitation. Due to clinical practical routine in our ophthalmic center, we only compared different tamponade effects between SO and gas, and the observation time was relatively short. In several previous studies, fellow eyes were used as control[13–15, 18, 21]. However, unaffected eyes with asymptomatic feature could have vascular abnormalities in fundus diseases like retinal vein occlusion and primary open-angle glaucoma[41, 42]. Retinal detachment could also be bilateral in quite a number of patients. Thus, we did not take fellow eyes data as baseline or control to avoid potential bias. The present study put emphasis on observation of various fundus changes due to different intraocular tamponades. We analyzed fundus changes in macular-off RRD patients, the impact of disease influence on postoperative fundus abnormalities should be taken into account.

In conclusion, we observed different intraocular tamponade impacts of silicone oil and gas on fundus vasculature and structure in macular-off rhegmatogenous retinal detachment patients after single pars plana vitrectomy. Silicone oil tamponade had relatively more negative effect on retinal vasculature and specific retinal layer thickness change during observation.

Declarations

Acknowledgement:

We would like to acknowledge all the patients that participated in this study.

Statement of Ethics: This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Shanghai General Hospital affiliated to Shanghai Jiao Tong University. All patients signed informed consent forms.

Disclosure Statement: None of the authors has financial or other conflicts of interest concerning this study.

Data availability: No relative data

Authors' contributions:

Yifan Zhou: write this article, data analysis

Siqi Zhang, Hao Zhou, Min Gao: perform the experiment

Haiyun Liu and Xiaodong Sun: design the experiment

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Tables

Please see the supplementary files section to view the tables.

Figures

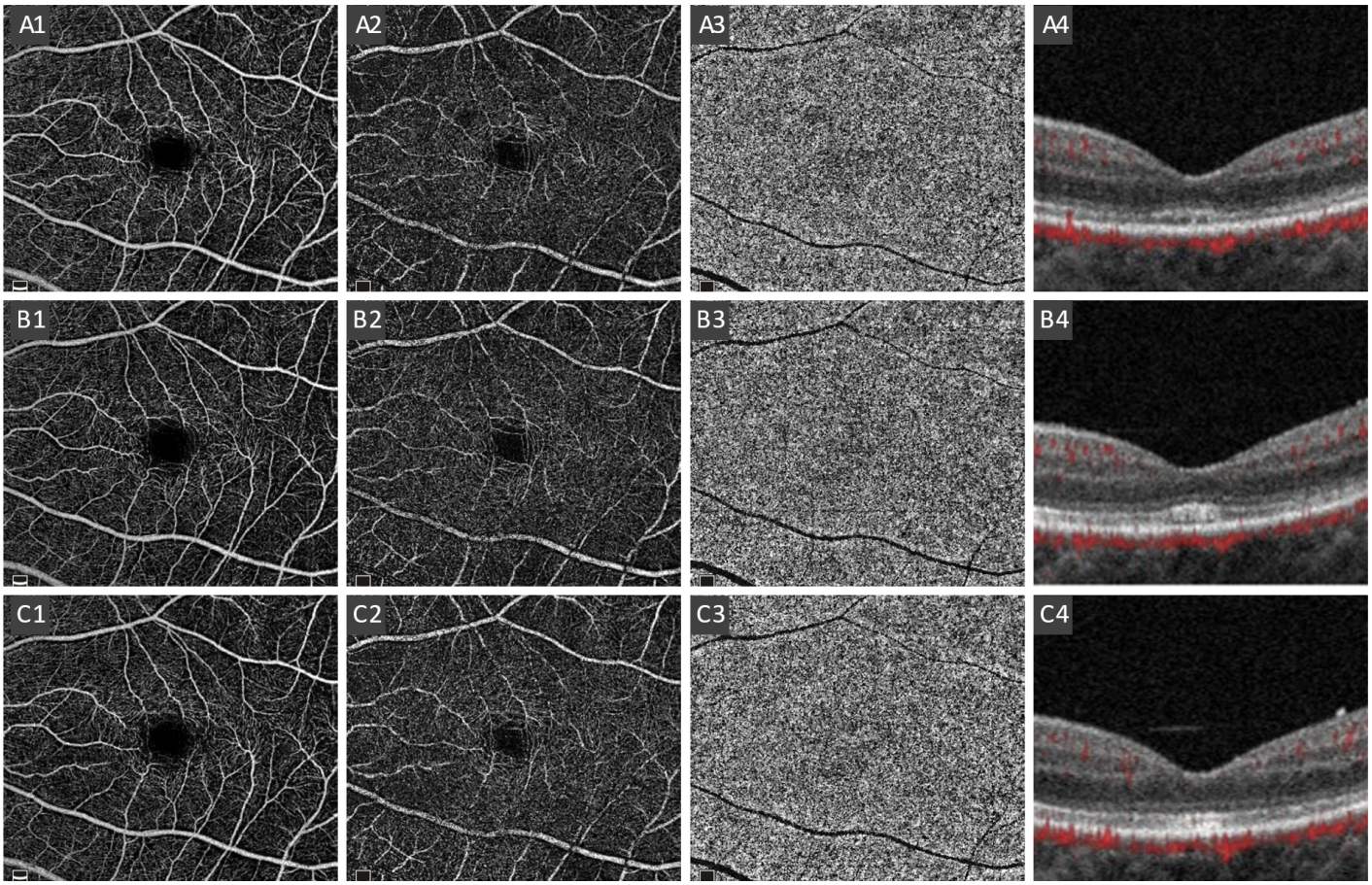

Figure 1

A1-3, B1-3 and C1-3 showed SCPVD, DCPVD and CCPVD change in one RRD eye after successful retinal repair during at three postoperative follow up time points (2 weeks, 6 weeks and 12 weeks) respectively. A4, B4 and C4 showed macular ultrastructure with blood flow signal.

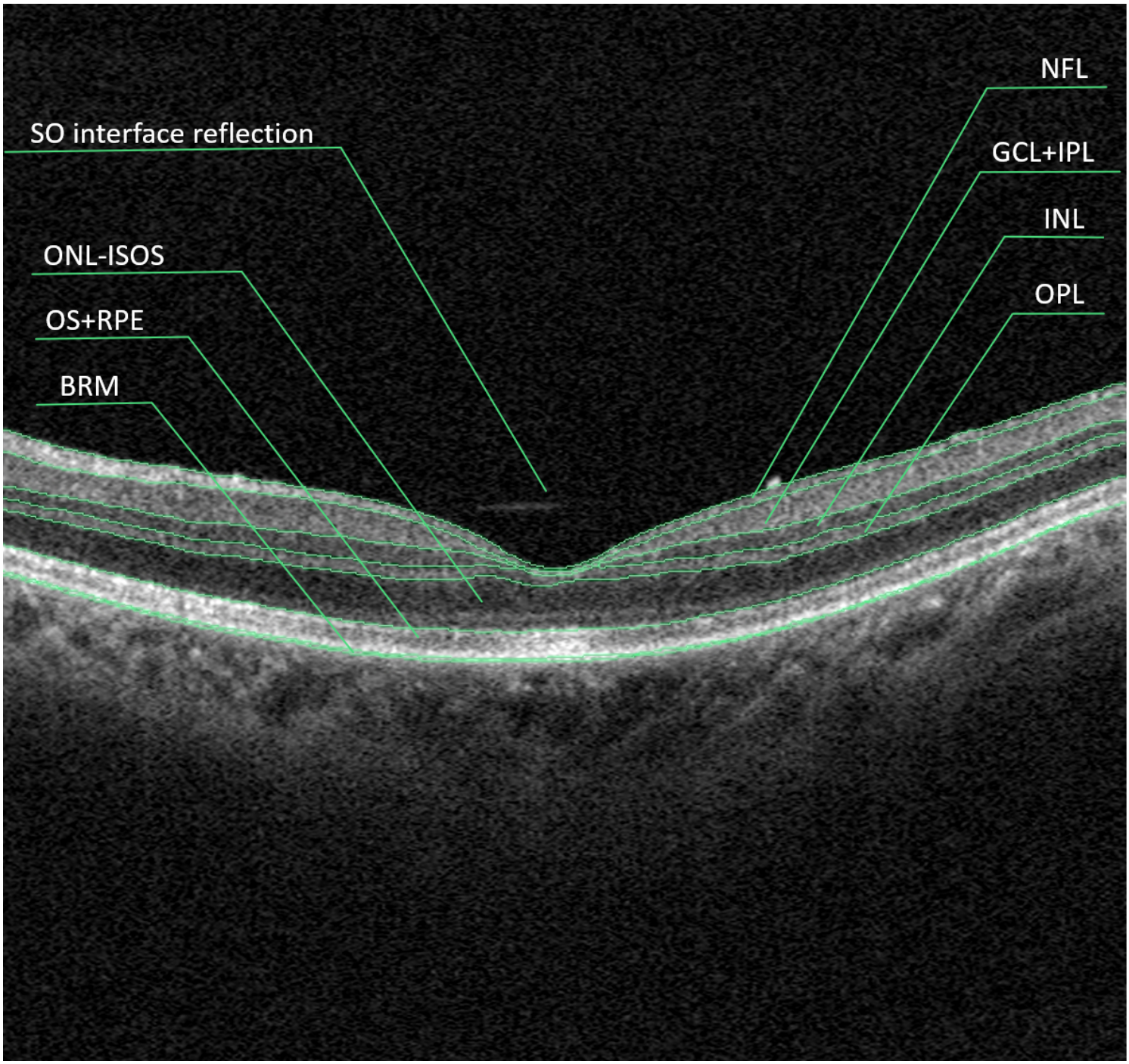

Figure 2

Automatic retinal layer segmentation produced by AngioVue software.

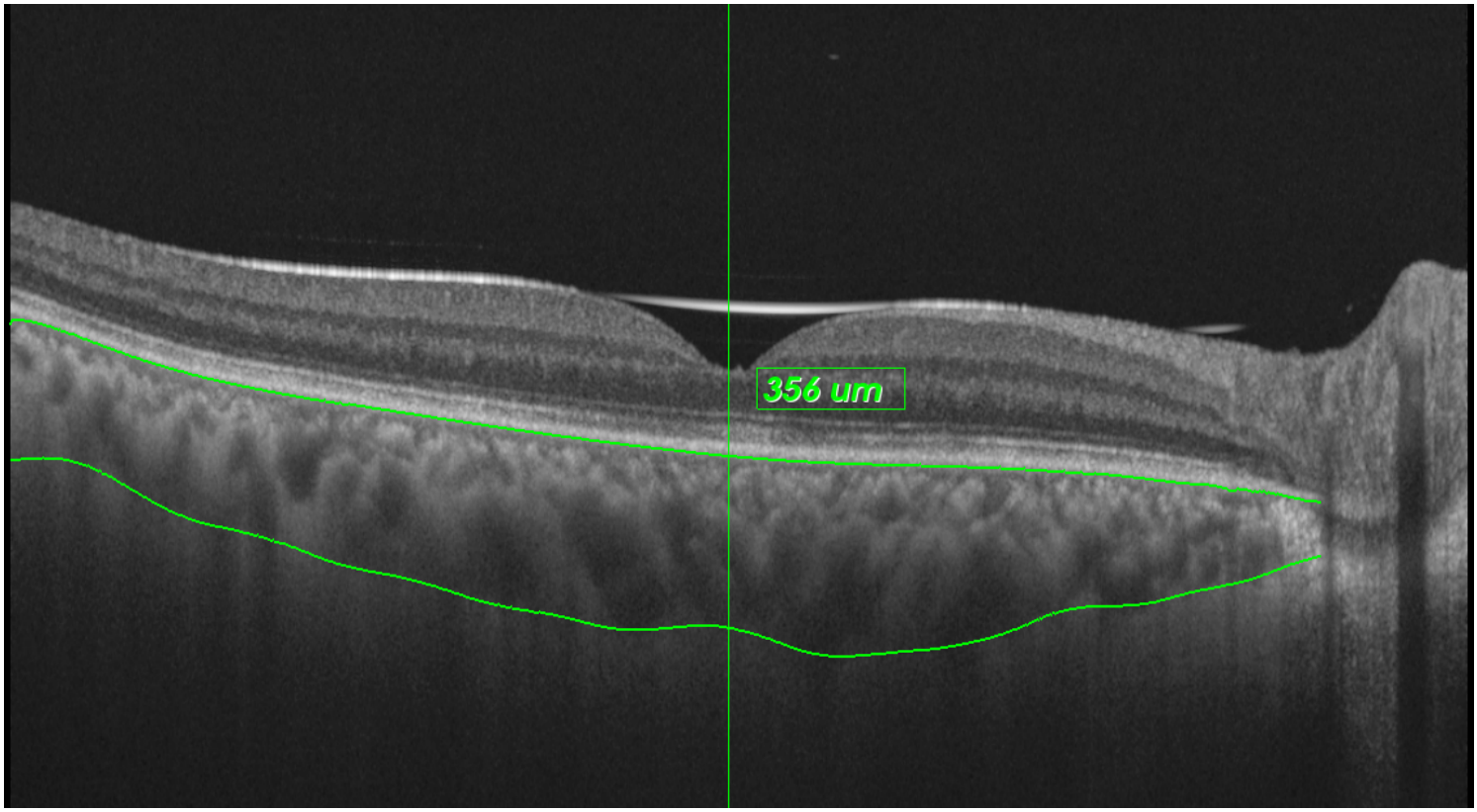

Figure 3

Choroidal imaging and thickness analysis by SS-OCT device.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Newtable2.xlsx
- Newtable5.xlsx
- Newtable3.xlsx
- Newtable1.xlsx
- Newtable4.xlsx