Practical applications of vitreous imaging for the treatment of vitreous opacities with YAG vitreolysis

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Abstract
Purpose To demonstrate the methodology and efficacy of using scanning laser ophthalmoscopy (SLO) and dynamic optical coherence tomography (OCT) to identify and treat symptomatic vitreous floaters using yttrium–aluminum garnet laser vitreolysis (YLV).
Methods This is a case series highlighted from a cross sectional retrospective study conducted at the Vitreous Retina Macula Specialists of Toronto. Forty eyes from thirty-five patients were treated with YLV between November 2018 and December 2020 for symptomatic floaters and imaged with SLO and dynamic OCT. Patients were re-treated with YLV if they reported ongoing significant vision symptoms during follow-up which correlated to visible opacities on exam and or imaging. Three cases will be highlighted to present the practical applications of SLO and dynamic OCT imaging for YLV treatment.

Results Forty treated eyes were enrolled in this study, with twenty-six eyes (65%) requiring at least one repeat YLV treatment following the first treatment due to ongoing symptomatic floaters. Following the first YLV, there was a significant improvement in overall mean best corrected visual acuity compared to before treatment (0.11 ± 0.20 LogMAR units vs. 0.14 ± 0.20 LogMAR units, p = 0.02 (paired t test)). Case 1 demonstrates a dense, solitary vitreous opacity that has been localized with dynamic OCT imaging to track its movements and retinal shadowing with the patient’s eye movements. Case 2 shows the utility of adjusting the fixation target to monitor the movement of vitreous opacities in real-time. Case 3 exhibits an association between decreased symptom burden and vitreous opacity density after YLV.

Conclusion Image-guided YLV facilitates the localization and confirmation of vitreous opacities. SLO and dynamic OCT of the vitreous can provide a real-time evaluation of floater size, movement, and morphology, to help clinicians target treatment and monitoring of symptomatic floaters.

Keywords Floaters · YAG laser · Vitreolysis · Scanning laser ophthalmoscopy · Dynamic OCT · OCT
Introduction

Vitreous opacities, or “floaters” as they are commonly described, are a common ocular finding that may cause visual discomfort as they act as the cast shadows on the retina. While most patients are able to adapt to these focal dark spots or lines, some patients experience significant distress from symptoms such as decreased visual acuity, reduced contrast sensitivity, scotomas, and intraocular glare [1–4]. These symptoms have been shown to substantially diminish a patient’s perception of quality of life [5].

The majority of vitreous opacities are primary vitreous opacities, which develop from materials within the vitreous body [6]. As the human eye ages, the vitreous body liquifies due to the dissociation of hyaluronan from collagen, resulting in the formation of lacunae pockets that are devoid of collagen, and walls of collagen fibrils that have been displaced [6]. These collagen fibril bundles cross-link and aggregate, becoming thickened and irregular, and cause visual phenomena by scattering photons and interfering with the transmission of light to the retina [6]. A posterior vitreous detachment (PVD) may result in a sudden onset of symptomatic primary vitreous opacities as the separation of the vitreous from the retina and movement of the vitreous body results in shadows from the Weiss ring and vitreous opacities being cast on to the retina [3]. Secondary vitreous opacities arise from materials that are exogenous to the vitreous body, such as blood, proteins, amyloid, or neoplastic cells [6].

At present, the therapeutic mainstays for symptomatic vitreous opacities are typically conducted with vitrectomy or yttrium aluminum garnet (YAG) laser vitreolysis. Although vitrectomy has been shown to be effective for removing opacities, with previous studies reporting a 84–100% rate of patient satisfaction [7], it is an invasive surgical procedure with potential risks and complications. The most common complications following “floatectomy” as reported in the literature include cataract formation (22.5–60%), retinal tear (0–16.4%), retinal detachment (2.5–10.9%), and cystoid macular edema (1.3–5.5%) [8–10]. Furthermore, there have been no published randomized clinical trials that have directly compared YLV to pars plana vitrectomy for vitreous opacity management [11]. YAG laser vitreolysis (YLV) has recently emerged as an alternative method for treating vitreous opacities by vaporizing vitreous opacities at high temperatures, thus disintegrating the aggregate collagen fibrils and causing them to displace out of the visual axis [12].

Methods

This retrospective cross-sectional study was conducted at the Vitreous Retina Macula Specialists of Toronto. This investigation was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants on intake. As this was a retrospective study and all patient data were collected as part of routine diagnosis and treatment, then anonymized for analysis, research ethics committee approval was not obtained. Patients were selected based on a history of persistent disturbance from vitreous opacities that are impacting quality of life and activities of daily living. If the patients reported active photopsias or flashes, they were not treated until the symptoms resolved. Other exclusion criteria included secondary vitreous opacities as described previously, active ocular inflammation, and active vitreous and retinal pathologies such as vitreous hemorrhage, asteroid hyalosis posterior uveitis, retinal tears, and retinal detachment. In total, 40 eyes from 35 patients with symptomatic primary vitreous opacities were treated with YAG laser vitreolysis from November 2018 to December 2020. All patients underwent ultra-widefield retinal imaging (Optos California, Dunfermline, United Kingdom) before and after vitreolysis (Fig. 1). Best corrected visual acuity (BCVA) was measured during initial consultation between one week to one month before the YAG laser vitreolysis was performed. Vitreous opacities were identified using
ultra-widefield scanning laser ophthalmoscopy (SLO) imaging (Optos California, Dunfermline, United Kingdom) to confirm the impact of visual impairment caused by shadowing over retinal tissue. To co-localize the positions of multiple vitreous opacities with respect to the retina and to each other, SLO OCT imaging was combined with structural B-scans and vitreous en-face OCT (Zeiss Plex Elite 9000; Oberkochen, Germany). Dynamic OCT (Zeiss Plex Elite 9000; Oberkochen, Germany) was also performed to detect the real-time movement of the vitreous opacities in vivo and their resultant shadowing over the macula.

Patients were dilated with three sets of tropicamide 1% and phenylephrine 2.5% 15 min before the procedure. A Volk Singh Mid-Vitreous lens (Volk; Mentor, United States) was applied to the eye with a Genteal Hypermellose (0.3%) gel (tropicamide and phenylephrine) coupling agent (Alcon, Geneva, Switzerland). The position and location of each vitreous opacity was confirmed with pre-operative imaging prior to initiating treatment. Using the Ultra-Q Reflex laser (Ellex Medical, Adelaide, Australia) an initial power setting of 10 mJ/spot was used for laser photoablation of the vitreous opacities. The power level was titrated up by 5 mJ increments until gas bubbles were seen, along with vitreous opacity destruction. The laser was applied with refocusing between vitreous opacity spots until the opacity was destroyed or a cumulative total power of 1.5 J was reached. If there were residual vitreous opacities remaining after the maximum total power was reached, the patient was brought back for a staged procedure at their next follow-up visit. After each vitreolysis session, the patients were brought back for follow-up at an average of 1 month after treatment. At each follow-up appointment, BCVA was measured, and a repeat YAG laser vitreolysis was performed if the patient was still symptomatic and vitreous opacities were detected with slit lamp microscopy and swept-source OCT vitreous imaging.

Paired t-tests were used to compare LogMAR BCVA values between baseline and after each treatment. Histograms were constructed to verify that the data were normally distributed. Data presented are mean ± SEM. Statistical significance was defined as $P < 0.05$. Analysis was conducted using IBM SPSS version 20 and Microsoft Excel.

Results

A total of 40 eyes from 35 patients underwent YAG laser vitreolysis for this study. The mean age of patients enrolled in this study was 59.2 (SD ± 9.3, range 30–73), and fifteen patients were female (42.9%). Twenty-six eyes (65.0%) required at least one repeat YLV treatment following the first treatment due to ongoing symptomatic floaters, with 14 eyes (35.0%) requiring a third YLV procedure.

Overall, 31 patients (88.6%) reported resolution of their visual disturbance after their final YLV treatment. Four patients elected to proceed with elective pars plana vitrectomy surgery for residual symptomatic vitreous opacities. One patient (2.9%) did develop a cataract following treatment, and underwent subsequent cataract surgery, which was uncomplicated and yielded a good visual outcome. No patients developed a retinal tear or retinal detachment. Patients were followed for a mean 129 ± 118 days after their first YLV treatment (range 13–482 days).

Figure 2 represents the mean LogMAR BCVA values measured for patients prior to YAG laser vitreolysis compared to one month after the first treatment, one month after the second treatment, and one month after the third treatment. Overall, there was a significant improvement in BCVA ($p = 0.02$, paired t-test) after the first YLV (0.11 ± 0.20 LogMAR...
units) compared to BCVA measurements before treatment (0.14 ± 0.20 LogMAR units). Patient who underwent a second treatment did not experience a significant change in visual acuity compared to the initial pre-treatment assessment or after the first treatment session. After the third treatment, LogMAR BCVA values trended lower (0.07 ± 0.09 LogMAR units) compared to the pre-treatment ($p=0.08$), post-first treatment ($p=0.17$) and post-second treatment ($p=0.65$) but the results were not statistically significant.

Lastly, subgroup analysis was performed including only patients whose visual acuity at baseline was worse than 20/20. Compared to baseline LogMAR BCVA (0.26 ± 0.05), there was a significant improvement in visual acuity after both the first (0.14 ± 0.03, $p=0.006$) and second YLV treatments (0.11 ± 0.03, $p=0.009$) (Fig. 3). Furthermore, there was a significant improvement in visual acuity between the first and second YLV treatments ($p=0.026$).

Case 1

A 63-year-old male presented with a history of a symptomatic floater in the left eye. Using dynamic OCT, the patient’s floater was detected as a dense, solitary opacity inferotemporal to the optic disc (Video 1). Using real-time imaging, we were able to track the movement of this vitreous opacity while the patient performed horizontal duction movements, and observe its shadow being cast on the patient’s macula. By describing the shape and movements of the opacity to the patient and reviewing the dynamic OCT video with the patient, we could confirm that this was indeed the opacity that was causing their visual disturbance. Therefore, a targeted YLV was performed, by confirming the position of the opacity with both slit lamp microscopy and SLO imaging and adjusting the B-scan focus depth to localize the depth of the floater.

Four months after YLV, the vitreous opacity is again captured with dynamic OCT, this time appearing more diffusely distributed within the vitreous compared to before treatment (Video 1). The patient reported an improvement in their floater symptoms.
Case 2

A 66-year-old female was referred for symptomatic floaters in the left eye. These floaters were characterized to have the structure of a dense, broken Weiss ring on SLO, which appears faintly hyperreflective on the real-time OCT vitreous B-scan (Video 2). Upon follow-up assessment four months after YLV, the posterior vitreous face appears fully detached from the retina on dynamic OCT imaging. The gain has been increased to better highlight the posterior vitreous interface and vitreous opacities (Video 3). As the patient is asked to perform horizontal duction movements, the movement of dense amorphous vitreous opacities can be seen casting a shadow on the retina on the real-time OCT B-scan (Video 3). Using SLO imaging to characterize the morphology of the remnant vitreous opacities and dynamic OCT to verify effects of shadowing on the macula, we were able to confirm the patient’s reports of ongoing floater symptoms and provide diagnostic-guided repeat YLV treatment.

One month after repeat YLV treatment in the left eye, and four months after initial YVL, the patient still reported ongoing floater symptoms. The initially ring-shaped vitreous opacity appeared more diffuse and amorphous on SLO imaging, however still causing significant shadowing on the macula. The patient would subsequently undergo a total of three repeat YLV treatments for the left eye: three, four, and six months after their initial treatment. Unfortunately, the patient still reported bothersome floaters, which were confirmed with SLO imaging that identified dense amorphous vitreous opacities.

Case 3

A 65-year-old female was treated with YLV for symptomatic floaters in the right eye. Initial pre-treatment SLO imaging identified a dense focal vitreous opacity inferior to the optic disc. The motility, range, and shadow effect of this opacity was explored by adjusting the fixation target on the imaging device to monitor the movement of the vitreous opacity in real time as the patient adjusted their eye positions (Video 4). The patient underwent YLV, with subsequent follow-up one month later revealing decreased symptom burden and a more diffuse and web-like vitreous opacity with SLO imaging.

Discussion

The use of YAG laser for the treatment of vitreous opacities was first reported in the 1980s [15]. Since its initial inception, YLV has become more widely adopted as patients have become increasingly aware and interested in the procedure for management of their visual debilitations [16]. Despite this, the procedure remains controversial due to a lack of high-quality evidence on treatment efficacy, and potential adverse events.

Several previous studies have shown variable rates of patient satisfaction and relatively low rates of complications following YLV. In the only published randomized clinical trial on YVL, Shah and Heier reported that 53% of patients described significant or complete resolution of symptoms in the YAG-treated group compared to 0% in the control sham laser group [3]. Other studies have demonstrated variable rates of YLV success, including Delaney et al. [14] with 38% of eyes experiencing moderate symptom improvement, Souza et al. [17] publishing a 46.1% rate of floater symptom amelioration, and Luo et al. [1] with 75% of patients reporting “significant success”. As for complication rates, one study reported a 0.8% adverse event rate out of nearly 1300 patients who were treated with YLV, including 7 cases of intraocular pressure spikes, 2 cases of lens damage, and 1 case of retinal hemorrhage[16].

Qualitative and quantitative measurement of vitreous opacities has been attempted by several groups in the past with varying degrees of success. Souza et al. [17] used a 5-level qualitative scale to grade color fundus photographs before and after YLV. The criteria used in their grading system was not published, and unfortunately such qualitative grading scales are typically subject to interpreter discretion and intergrader variability. Sun et al. [12] obtained infrared fundus images using the Heidelberg Retina Angiograph 2 system to generate a high-quality composite of ten averaged images, and used ImageJ to evaluate the area of the floaters and their shadows cast. Overall, their study showed a significant decrease in median shadow area from 1.41 to 0.12 cm² after YLV (p=0.001), with 64% of eyes achieving significant and complete resolution of vitreous floaters [12]. Shaimova et al. [8] measured the area of false nonperfusion on OCT angiography with RTVue xR Avanti to determine the size of the artifactual shadow.
cast by vitreous opacities. This information is useful for evaluating patient symptomatology as the umbra and penumbra casted by vitreous opacities on the retina have been mathematically investigated to cause entoptic phenomena of “cloud” or “smoke”[18]. While these two methodologies can provide numerical values for vitreous opacity size and shadow area, which can be beneficial for research purposes, such measurements and calculations are cumbersome and time consuming to perform, and likely less practical in a clinical setting. Furthermore, these three studies all describe retinal/vitreous imaging analysis using still images, which does not recapitulate the real-world dynamics of mobile vitreous opacities.

Ultrasound characterization allows visualization of vitreous opacities in real-time by detecting the disparity in acoustic impedance between the dense floaters with high echogenicity and the vitreous body with low echogenicity [19]. Clinical analysis of ultrasound B-scan imaging for vitreous opacities is primarily qualitative [20], although a few studies have evaluated the applications of quantitative ultrasonography. Garcia et al. [21] quantified vitreous echodensity by measuring acoustic scattering in B-scans in arbitrary unit (AU) measurements; with higher AUs indicating higher levels of energy scatter. While this method is useful for characterizing the overall vitreous density, it does not provide information on the localization of vitreous opacities, or their impact on retinal shadowing and patient symptomatology. Mamou et al. [19] analyzed quantitative ultrasound imaging by defining regions of interest within B-scans and algorithmically determining three parameters: energy, mean amplitude of acoustic values, and percentage of vitreous filled by echodensities. These parameters provide a more detailed assessment of vitreous structure and floater severity and allow for quantitative comparison between patients and across treatments.

En face SLO OCT imaging can provide information on the morphology of vitreous opacities and highlight structural details such as individual vitreous fibrils to facilitate comparisons between pre- and post-YLV treatment (Fig. 4). Dynamic OCT captures the movement of the patient’s vitreous in real time, allowing for the localization of vitreous opacities and their shadows as the patient fixates on a target or is asked to perform eye movements [22]. Both the depth (Fig. 5) and gain (Fig. 6) of the OCT B-scan
can be manipulated to reveal vitreous opacities that may have been missed on the standard OCT B-scan. These imaging modalities are also helpful to screen and select for patient characteristics that are more amenable for successful YLV, including a single floater, clear vitreous, floater > 2 mm from the retina, floater > 5 mm from the crystalline lens, and no peripheral pathology [23]. As previous studies have demonstrated an increased risk of retinal damage when laser pulses of 4–8 mJ were directed 2–4 mm from the retina, and when higher energy settings of 4–15 mJ resulted in complications such as crystalline lens damage, retinal hemorrhages, and retinal tears/detachment [23], it is especially important to evaluate the vitreous anatomy in order to identify which patients might be at higher risk of adverse events if treated with YLV, and when an appropriate endpoint would be to stop performing repeat YLV procedures for non-resolving floaters.

This study was limited by its retrospective nature, and lack of quantifiable outcome measurements aside from BCVA. While SLO and dynamic OCT imaging provide valuable information for clinicians to evaluate vitreous opacities, they cannot provide an objective quantification of the anatomic characteristics of these opacities, nor the degree of visual debilitation that they cause for the patient. Furthermore, there is currently no universally accepted grading scale for assessing vitreous opacities, which limits the applicability of these imaging techniques for statistical analysis in research studies and quantitative treatment guidelines.

**Conclusion**

YLV is a promising treatment modality for symptomatic vitreous opacities due to being less invasive, lower cost, and relatively safe compared to pars plana vitrectomy [1]. Dynamic OCT and SLO imaging offer a multi-modal approach to identify and characterize vitreous opacities in real time to correlate floater morphology with patient-reported symptom burden and provide guidance for treatment localization. Additionally, these novel applications of vitreous imaging modalities may be beneficial for monitoring response to YLV treatment, and titrating treatment endpoints.

Standardizing YLV treatment with imaging-guided floater localization may improve the consistency of the therapy and reduce the variability of treatment outcomes that have been described in several previous studies [6, 7]. Further prospective comparison studies between symptomatic floater treatments modalities are required to provide strong evidence for clinicians to manage this very common condition with potentially significant impacts on visual quality.

**Author contributions** All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Shangjun Jiang, John Golding, and Netan Choudhry. The first draft of the manuscript was written by Shangjun Jiang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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**Declarations**
Conflict of interest  The authors have no relevant financial or non-financial interests to disclose.

Ethical approval  This is an observational study. Western Institutional Review Board has confirmed that no ethical approval is required.

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