Major review

Vitreous floaters: Etiology, diagnostics, and management

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\textbf{A B S T R A C T}

Vitreous is a hydrated extracellular matrix comprised primarily of water, collagens, and hyaluronan organized into a homogeneously transparent gel. Gel liquefaction results from molecular alterations with dissociation of collagen from hyaluronan and aggregation of collagen fibrils forming fibers that cause light scattering and hence symptomatic floaters, especially in myopia. With aging, gel liquefaction and weakened vitreoretinal adhesion result in posterior vitreous detachment, the most common cause of primary symptomatic floaters arising from the dense collagen matrix of the posterior vitreous cortex. Recent studies indicate that symptomatic floaters are not only more prevalent, but also have a negative impact on the quality of life that is greater than previously appreciated. We review the literature concerning management of symptomatic vitreous floaters, currently either with observation, vitrectomy, or Nd:YAG laser. Published evidence is consistent with a low-risk profile and excellent success rate for floater vitrectomy, particularly with sutureless small gauge instruments and a limited core vitrectomy without PVD induction. Nd:YAG laser treatment of floaters, reported less commonly, claims resolution of floaters ranging between 0% and 100%; however, both peer-reviewed literature and assertions on web-based nonpeer-reviewed laser vitreolysis sites remain to be substantiated, and at present only vitrectomy has proven value. Prospective studies using objective, quantitative outcome measures are required to assess the relative efficacy and safety of these two procedures as well as new therapies such as pharmacologic vitreolysis.
1. Introduction

The vitreous body is an extracellular matrix that is highly hydrated and relatively acellular except in the periphery where hyalocytes reside in the vitreous cortex. Vitreous consists of 98% water and macromolecules, the most important being collagens and hyaluronan, organized in an exquisitely clear gel (Fig. 1).64 Floaters arise from molecular changes within the vitreous body and at the vitreoretinal interface that occur throughout life and ultimately attain sufficient prominence to alter vitreous structure. Structural changes within the vitreous body can result from inflammation, vitreoretinal dystrophies,27 myopic27 and diabetic vitreopathy,28 but most commonly stem from aging.93 In addition to altering the internal structure of the vitreous body, aging also weakens vitreoretinal adhesion.

The strength of attachment of the vitreous body to the retina depends on the topographic location. The strongest zone of vitreous attachment is at the vitreous base where there is a relatively higher concentration of collagen and lower concentration of hyaluronan, resulting in a more condensed and solid vitreous consistency.90 The densely packed basal collagen fibrils align perpendicular to the retina and insert through discontinuities in the inner limiting membrane (ILM) to anchor on Müllerian glia and astroglia, forming an unbreakable adhesion.26,102 In other regions of the vitreoretinal interface, collagen fibrils are orientated parallel to the ILM. Although the mechanism of attachment here is not completely understood, it is thought to result from interface macromolecules including laminin, fibronectin, and chondroitin as well as heparin sulphate proteoglycans, forming a glue-like adhesion.32,38,43,65 The presence of different types of collagen may also contribute to this attachment.53 Vitreoretinal adhesion has been found to be stronger over areas where the ILM is thinner, including the margin of the optic disk (where the ILM of Elschnig may be supported by few astrocytes)15 over retinal blood vessels, and in a 500 to 1500 µm disk-shaped zone surrounding the fovea.25,26 The strength of vitreoretinal adhesion may also relate to the thickness of the posterior vitreous cortex, in particular over retinal blood vessels and at the macula where there is a thinner vitreous cortex related to the rarefaction of the collagen fibrils.32,70

At birth, the human vitreous body is a colloidal gel; however, with aging, liquefaction occurs within the vitreous body that can subsequently coalesce into pockets, called lacunae or cisterns. Recent swept source optical coherence tomography (OCT) imaging of posterior vitreous structure in young individuals has confirmed the presence of the bursa premaculares originally described by Worst that is unrelated to aging, although cisterns are believed to result from aging. Vitreous gel liquefaction likely results from dissociation of hyaluronan from its association with collagen, allowing cross-linking and aggregation of collagen fibrils (Fig. 2) into macroscopic fibers that scatter incident light (Fig. 3).70,75,93 Lacunae, on the other hand, are regions devoid of collagen fibrils, owing either to aggregation and displacement of collagen to the periphery of the lacuna, or possibly enzymatic destruction of collagen, transforming the gel vitreous to a liquid consistency,89 facilitating collapse. Lacunae (Fig. 4) increase vitreous heterogeneity, scatter light (especially at gel-liquid interfaces) and can disturb vision, if severe. Vitreous gel liquefaction increases with age, being first evident at the age of 4 years.24,45,93

Posterior vitreous detachment (PVD) occurs as a separation of the posterior vitreous cortex from the ILM of the retina, that begins posteriorly and progresses up to the posterior border of the vitreous base. Johnson15 describes perifoveal PVD as a slow insidious process until vitreopapillary separation. PVD is a common age-related process caused by a combination of vitreous liquefaction and vitreoretinal dehiscence allowing liquid vitreous to enter through a cortical defect into the retrocortical (preretinal) space,124 triggering a so-called rhegmatogenous PVD. PVD is more common with increasing age and in postmortem studies is reported at an incidence of 63% by the eighth decade.24,93,106 There is also purported to be a higher incidence of PVD in older women, which may relate to differences in biochemical composition of vitreous from hormonal changes at menopause.12,24,93 Risk factors for earlier PVD include myopia and collagen disorders such as Marfan and Stickler syndrome.81 PVD at younger ages not only induces the phenomenon of floaters, but also, due to firm vitreoretinal adhesion to an irregular posterior vitreous base, results in retinal tears and rhegmatogenous retinal detachment.77,83

2. Etiology of vitreous floaters

Floaters, previously called myodesopsia (Greek) and muscae volitantes (Latin), are visual phenomena caused by vitreous...
opacities that produce linear gray shadows with focal dark spots or nodules. Related to inertia of the vitreous body and intravitreal currents, floaters move with eye and head movements. The vitreous body and its internal structures move with characteristic damping because of viscous drag. Floaters are more visible when viewed against a bright background such as a sunny sky because the dark shadows created by the vitreous opacities appear accentuated. Floaters can arise from changes in structures endogenous to the vitreous body, as well as from exogenous sources (amyloid, asteroid bodies,

Fig. 2 — Ultrastructure of human vitreous. Transmission electron microscopy of human vitreous shows collagen fibrils organized in a bundle of parallel fibrous structures. The upper image (inset) shows typical collagen striations seen with higher magnification. The lower image shows a bundle of collagen fibrils in cross-section. (From Sebag J, Niemeyer M, Koss M: Anomalous PVD and vitreoschisis. In: Vitreous—in Health and Disease [J. Sebag, ed.] New York: Springer; 2014. pg 246.)
macrophages of Whipple disease, blood (called synchysis scintillans, when chronic), lymphocytes, opercula, medulloe-pithelioma, endophytic retinoblastoma, dexamethasone and other implants, foreign bodies, parasites).23

2.1. Primary vitreous floaters

Primary vitreous floaters are defined as those arising from structures that are endogenous to the vitreous body. Packed bundles of collagen fibrils (Fig. 2) form visible fibers78 that first appear in the central vitreous where they have a linear configuration.75 They become more numerous, thickened and irregular with increasing age (Fig. 3) and are common at young ages with axial myopia.27 With advancing age, the vitreous body liquefies and forms lacunae (Fig. 4), the walls of which interfere with photon transmission to the retina, contributing to the sensation of floaters. Primary vitreous floaters cause disruption and scattering of light and are appreciated as mobile dark lines and spots or nodules within the visual field. Some linear floaters have a translucent “glass noodle” appearance, others are described as “spider web-like.” The origin(s) of these different appearances is not known, although it is conceivable that the translucent tubular structures are remnants of the embryonic hyaloid vasculature, whereas the dark linear opacities are collagen aggregates. Vitreoretinal disorders such as Stickler syndrome and Wagner disease may be responsible for increase and variation in primary vitreous floaters.20 The clinical manifestations of these conditions are variable depending on the specific genotype. For example, collagen gene mutations may determine a more

Fig. 3 — Human vitreous structure. Dark-field slit microscopy of human vitreous structure demonstrates the transition from a clear vitreous in youth (top panel) to prominent fibers in the adult (middle panel), to thickened and tortuous fibers in old age (bottom panel). (Reprinted from Sebag J, Silverman RH, Coleman DJ: To see the invisible—the quest of imaging vitreous. In: Vitreous—in Health and Disease [J. Sebag, ed.] New York: Springer; 2014. pg 197.)
“membranous” appearance in Stickler type 1 (COL2A1) as opposed to fibrils and “beading” described in Stickler type 2 (COL11A1). Stickler type 1 will also exhibit a folded membrane present behind the lens.

Floaters are most noticeable when situated in the visual axis. With increasing size and number, floaters can be considerably symptomatic. PVD causes the sudden onset of primary floaters as a result of the collapse of the vitreous body and separation at the vitreoretinal interface with anterior displacement of the posterior vitreous cortex (Fig. 5). This structure scatters incident photons because of the high density of collagen fibrils (Fig. 5A). A notable type of floater resulting from PVD is a Weiss ring, the remnant of vitreopapillary attachment and peripapillary glial tissue at the optic disk, outlining the area of Martegiani and often including the septum interpapillo-maculare. A Weiss ring can be visualized by ophthalmoscopy or biomicroscopy as an annular structure adjacent and anterior to the optic disk (Fig. 6). This ring can cast a prominent shadow onto the retina, which patients often describe as circular or semicircular in appearance, particularly when it is only a few millimeters anterior to the macula.

2.2. Secondary vitreous floaters

Secondary floaters are opacities in the vitreous body whose origin is exogenous to the vitreous body, generally consisting of proteins, amyloid, or cells. The most common cause of secondary vitreous floaters is preretinal or vitreous hemorrhage, which induces the sudden onset of floaters and hazy vision.

- Vitreous hemorrhage can be related to an acute PVD with traction on retinal blood vessels, retinal tears involving retinal blood vessels, ischemic conditions leading to retinal or optic disk neovascularization, retino-vascular abnormalities, trauma, neoplasms, and to some rare abnormalities which include vitreoretinal dystrophies, that is, x-linked chisis, familial exudative vitreoretinopathy, Stickler syndrome. Retinal detachments can be associated with vitreous hemorrhage as well as the release of retinal pigment epithelial cells into the vitreous body, producing symptomatic floaters in addition to the curtain effect of the detached retina.

- Avulsed retinal tissue (operculum) may also induce the symptom of a floater following anomalous PVD with a retinal break but no retinal detachment. Vitrectomy to repair a retinal detachment removes these floaters and opercula as an important beneficial side effect, and can thus...
be considered one of the first surgical procedures to remove floaters (H. Schubert, MD—personal communication, 2015).

- Asteroid hyalosis is a benign accumulation of calcium pyrophosphate spheres within the vitreous body that usually causes minimal disturbance of vision.\textsuperscript{14,40}
- Inflammatory conditions (infectious or noninfectious), or malignant neoplasms, such as lymphoma, lead to increased vitreous cells, with the potential to cause symptomatic vitreous floaters if sufficiently numerous.\textsuperscript{14}
- Secondary vitreous floaters may also occur following intraocular injections. After vitreoretinal surgery, there can be remnant perfluorocarbon or silicone oil bubbles. Intravitreal injections for anti-vascular endothelial growth factor treatment may contain air bubbles that usually resorb in days, but the injected agents themselves may complex with vitreous macromolecules and alter vitreous structure.

3. Clinical diagnostics

3.1. Presentation and characterization of vitreous floaters

Floaters arising from intravitreal structural changes, typically related to myopic vitreopathy,\textsuperscript{27} tend to be chronic and progressive, whereas floaters arising from PVD\textsuperscript{93} are acute in onset. As reported by patients, these floaters range in appearance from small dots with linear patterns, to “spider web-like” objects that float across the visual field with head or eye movement. Primary vitreous floaters are increasingly recognized to be more prevalent than previously thought. A recent electronic survey of 603 self-reporting participants, found that 76% of participants reported seeing floaters, and 33% reported vision impairment because of their floaters.\textsuperscript{103} In this group, myopes were 3.5 times more likely and hyperopes were 4.4 times more likely to report seeing floaters, and 33% reported vision impairment because of their floaters.\textsuperscript{103} In this study, myopes were 3.5 times more likely and hyperopes were 4.4 times more likely to report moderate-to-severe floaters compared to emmetropes. Although interpretations from this study are limited, related to self-reporting and the younger demographic of smartphone users (<5% of subjects in this study were older than 50 years of age), it does challenge the perception that floaters are uncommon. The generally accepted notion that patients will either adapt to floaters or that floaters will resolve over time is also defied by a study of utility values in 266 patients with floaters where duration of symptoms did not influence the findings, suggesting that many do not successfully adapt to their symptoms.\textsuperscript{103} There is furthermore no data to support the concept that primary floaters will become less symptomatic as a result of inferior displacement of vitreous structures below the visual axis, although this is often mentioned anecdotally.
3.2. Imaging vitreous floaters (ultrasound, spectral domain OCT, scanning laser ophthalmoscopy, dynamic light scattering)

Although physical examination with slit lamp biomicroscopy can be used to visualize central and posterior vitreous structure, it is difficult to image the entire vitreous body. Further, ophthalmoscopy, both direct and indirect, cannot adequately evaluate fine vitreous structure.

Ultrasound can be used to image opacities within the entire vitreous body based on their echodensity as well as impedance differences at gel-liquid interfaces (Figs. 6B, 6C, 7). Conventional diagnostic B-scan ultrasound systems typically assess differences in the sound wave impedance at interfaces of tissues with different densities, such as the retina and vitreous, but can also be used to detect interfaces between liquefied and gel vitreous (Fig. 4), as well as detect echoes from vitreous collagen aggregates. Oksala used ultrasonography to detect echoes from gel-liquid interfaces in 444 healthy patients and found that the vitreous body was acoustically homogeneous in all individuals under the age of 20 years. Gel-liquid interface echoes were detected in 5% of individuals aged 21–40 years, 19% of those aged 41–50, 63% aged 51–60, and in 80% of individuals older than 60 years of age. Not all these interfaces, however, result in symptomatic floaters. Indeed, it is probable that only central vitreous opacities are likely to be symptomatic. This has been confirmed by Mamou and colleagues who found that the vitreous echodensities in the premacular region had the highest correlation with diminished contrast sensitivity (CS) and dissatisfaction with vision as quantified by the National Eye Institute validated Visual Function Questionnaire (NEI VFQ; see the following paragraphs).

Ultrasonography is routinely used to diagnosis PVD, since the dense collagen matrix of the posterior vitreous cortex is adequately imaged with conventional B-scan ultrasound once it separates from the retina (Figs. 6C, 7). Thus, in the typical evaluation of patients complaining of floaters, ultrasound is usually only used to establish the diagnosis of PVD and rule-out retinal detachment, although ultrasonography provides real-time imaging of internal and peripheral vitreous structure. There are recent advances, however, expanding the role of ultrasonography in the evaluation of patients with floaters. Quantitative ultrasonography of vitreous, developed to generate an objective, reproducible, and quantitative index of vitreous echodensity, provides a useful measure of floater severity. Such a clinical metric can furnish clinicians with a quantitative assessment of severity based on vitreous structure, and theoretically offers a useful adjunct to functional assessments of vision (see the following). Recent studies have indeed demonstrated a positive correlation between quantitative ultrasonography, contrast sensitivity (CS), and quality of life as quantified by the NEI VFQ. Such objective metrics for measuring vitreous structure and floater-induced visual disability as well as assessing quality of life, provide a rational way to gauge clinical severity and select patients for therapy. These indices can also be used as quantitative outcome measures to evaluate the effects of vitrectomy, neodymium-doped yttrium aluminium garnet (Nd:YAG) laser, or pharmacologic vitreolysis. Future developments of superior ultrasound technology such as pulse-encoded imaging with an annular array probe will likely provide even better techniques with which to characterize vitreous structure clinically and to evaluate the response to various treatments.

OCT allows detailed imaging of both the transverse and coronal (en face) aspects of the vitreoretinal interface. Recent imaging studies have combined spectral domain OCT with scanning laser ophthalmoscopy to better evaluate the vitreomacular interface in various disease states including vitreous floaters (see the following paragraph); however, to date, OCT can only image floaters when the vitreous opacities are within a few millimeters of the retina, and therefore, it is not an effective technique to identify all vitreous opacities that are responsible for symptoms. Although it is unlikely that the

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Fig. 7 — Ultrasonography of vitreous floaters. A: Vitreous floaters are seen as focal echodensities on B-scan ultrasonography in this 30-year-old man with high (−6.75 D) myopia and myopic vitreopathy. B: After separation away from the retina during posterior vitreous detachment (PVD), the posterior vitreous cortex can be imaged by ultrasound. This 48-year-old woman has high myopia (−8.50 D) and PVD. Visual acuity was 20/30, but contrast sensitivity (CS) was reduced to 3.99 %. Weber by both internal vitreous opacities resulting from myopic vitreopathy, as well as the dense posterior vitreous cortex (see Fig. 5A) located anterior to the retina after PVD. The patient underwent limited vitrectomy. At one month post-op VA = 20/30 and CS = 1.82 %Weber; at 3 months, VA = 20/30 and CS = 1.9 %Weber; at 6 months VA = 20/30 and CS = 1.93 %Weber. The patient is very happy with her vision.
peripheral vitreous is responsible for clinically significant floaters, the central and anterior vitreous may be important but are currently not adequately visualized by OCT. When vitreous opacities are located posteriorly, a “floater scotoma” can at times be observed as shadowing on the OCT image of the retina created by the vitreous opacities (see the following paragraph).69 There are cases of prefoveal focal vitreous opacities that cause bothersome floaters that are better on imaged by OCT than ultrasonography.

Scanning laser ophthalmoscopy can provide useful evaluation and documentation of vitreous opacities. As shown in Fig. 8, both the umbra and penumbra cast by vitreous opacities can be visualized. It might be useful to perform image analysis of such scanning laser ophthalmoscopy photos with the aim of quantifying the umbra and penumbra effects as a way of indexing floater size and density. Such quantitative measures of vitreous structure could then be used as an index of clinical severity, as has previously been done with ultrasonography (see the previous paragraphs).51

Dynamic light scattering uses a laser-based nanodetector system for noninvasive in vivo visualization of particles from 3 nanometers to 3 microns in size within the ocular media including the cornea, lens, aqueous, and vitreous.1 Dynamic light scattering can thus be used to detect morphometric changes in the constituent molecules of ocular media; for example, the aggregation of lens crystallins in cataract formation16 and vitreous collagens as seen in myopic vitreopathy,27 aging,75,93 and diabetic vitreopathy.28,79 This technique has also been used to evaluate the effects on vitreous macromolecules following pharmacologic vitreolysis with ocriplasmin, hyaluronidase, and collagenase.71

**Fig. 8** – SLO imaging of vitreous opacities. Note the densely dark areas that represent the umbra and the surrounding (and larger) gray areas that represent the penumbra cast by the vitreous opacities. This is particularly well visualized in the lower portion of the photo. SLO, scanning laser ophthalmoscopy.

### 4. Floaters and vision

The personality profile of a patient complaining of floaters tends to be that of a detail-oriented person who seeks perfection, at least in their vision, at times in a nearly obsessive manner. Studies have shown that motivation is what distinguishes floater patients who “doctor shop” from those who do not.95 What is unclear, however, is what motivates these patients, and there are concerns that at least in some cases the patient’s problem may be more psychologic than ophthalmic. Indeed, there is one report claiming that symptoms of floaters may be outward manifestations of secret fears or failure to adjust to life events.22

Most patients, however, do not fit this profile and are simply seeking a better quality of life. The finding that contrast sensitivity (CS) is diminished and straylight increases (see the following sections) in eyes with bothersome floaters supports the legitimacy of floater patient unhappiness with vision.36,51,76 Nonetheless, there is often considerable difficulty in distinguishing between patients who are truly unhappy because of their floaters and those who are unhappy for other reasons, but fixate on their floaters. Clearly, the former have a higher likelihood of being aided by a treatment of their floaters than the latter. The challenge to clinicians is, as always, to select cases that are appropriate for treatment. In the past, this was largely done on the basis of subjective complaints and assessments of a patient’s personality. Then, as now, it is advisable for the clinician to meet a patient more than once, at times on several occasions, to determine appropriate candidacy for therapy. Fortunately, objective clinical measures are now available to determine the severity of floaters both on structural (quantitative ultrasonography) and well as functional (CS and straylight measures) criteria. These have made decision-making a more scientific and rational process.

#### 4.1. Quality of life assessments

Recent studies indicate that floaters can have a significantly negative impact on the quality of life.101,108 Using a utility value analysis approach to establish the effects of vitreous floaters on the quality of life, these studies found that for younger patients (<55 years of age) this negative effect is so severe that they are willing to accept a 7% risk of blindness to be rid of floaters101 and that persistent floaters can significantly reduce patients’ self-perception of quality of life.108 Interestingly, a strongly positive correlation was detected between quality of life assessment by NEI VFQ testing and quantitative ultrasonography,51 lending objective support to patient complaints. Furthermore, studies using the NEI VFQ to quantify the effects of floaters on vision found that there was a statistically significant improvement in both VFQ and CS following vitrectomy.36,51 Other studies used nonstandardized self-administered questionnaires but also detected improvement following vitrectomy.18,53

#### 4.2. Light scattering and straylight

Straylight or disability glare refers to a perceived spreading of light around a bright light source. In 2009, Van den Berg and
colleagues published an excellent review of this phenomenon.\textsuperscript{57} Light scattering by opacities within the optical media (cornea, aqueous, lens, posterior capsule, and vitreous) can present as visual symptoms including hazy vision, difficulty driving at night, and decreased facial recognition. Physio-
physical and optical measurement techniques have been developed to generate measures of straylight effects.\textsuperscript{5,6,7} A common technique is the use of a compensation comparison measurement, which compares unwanted scattered light that reduces retinal contrast and light required to form retinal images. Optical measurements typically have been limited to measuring the central region of the point spread function, which is problematic owing to its susceptibility to artifacts.\textsuperscript{4} Newer techniques have been able to expand to include a wider range and therefore minimize these artifacts.\textsuperscript{51} Vitreous floater-induced light scattering can increase the visual effects associated with straylight, and a statistically significant improvement in straylight measurements was found following vitrectomy for floaters.\textsuperscript{56}

### 4.3. Contrast sensitivity (CS)

CS measurements can be used to complement visual acuity testing, which measures 100% contrast only within the central few degrees of the visual field. Clinically, chart-based methods, such as the Pelli-Robson chart and the Mars Letter Contrast Sensitivity Test have been used for assessing the effects of ocular media opacities on CS. This includes, for example, patients with posterior capsule opacification following cataract surgery,\textsuperscript{89} pterygia encroaching on the central cornea and thus the visual axis,\textsuperscript{50} following refractive surgery procedures such as LASIK and more recently, small-incision lenticule extraction.\textsuperscript{30,60} Computer-based CS testing has been applied to assess patients following various forms of refractive surgery. The computer-based Freiburg Acuity Contrast Test provides similar results to the Pelli-Robson Chart and is not significantly affected by differences in visual acuity.\textsuperscript{51} A recent review of the effects of multi-focus intracocular lenses on CS considered findings from six studies (follow-up ranging from 2 months to 1 year) that all showed degradation of CS, in some studies described as visual acuity at different contrast levels or differences between high and lower contrast acuity.\textsuperscript{57}

Sadun and Sebag recently hypothesized that floaters affect vision and in turn negatively impact quality of life, by reducing CS.\textsuperscript{56,76} They theorized that light scattered from the irregular uneven surfaces of primary vitreous floaters creates a large penumbra that degrades CS (Fig. 9). In contradistinction, the asteroid bodies of asteroid hyalosis are spherical with a smooth surface (Fig. 10A), likely causing less light scattering and casting a smaller penumbra, thus not affecting CS and vision as much as floaters with an uneven surface (Fig. 10B). In addition to a slower accumulation of vitreous opacities over time, this could explain why patients with asteroid hyalosis rarely complain of floaters or visual disturbances and do not seek therapy. The exception would be PVD in a patient who has asteroid hyalosis with sudden aggregation of asteroid bodies and introduction of light scattering by the dense collagen matrix of the posterior vitreous cortex, rapidly degrading vision.

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**Fig. 9** — Combined SD-OCT/SLO imaging of vitreous floaters (FL). A central umbra (U) with surrounding penumbra is seen on transverse OCT imaging (color photo above) and on SLO imaging (grayscale photo below). SD-OCT, spectral domain optical coherence tomography; SLO, scanning laser ophthalmoscopy. (Reprinted from Huang L, Yee KMP, Wa CA, Nguyen J, Sadun AA, Sebag J: Vitreous floaters and vision: current concepts and management paradigms. In: Vitreous—in Health & Disease [J. Sebag, ed.] Springer, New York, 2014, pg 778.)

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The postulate that vitreous floaters degrade CS was tested using the computer-based Freiburg Acuity Contrast Test method.\textsuperscript{5,6} In 2014 investigators reported preliminary results of 16 floater patients,\textsuperscript{76} and a subsequent study of 38 floater patients,\textsuperscript{36} where there were significant (in excess of 60%) reductions in the CS of patients with floaters compared to age-matched controls (P < 0.01). Furthermore, CS in each floater patient was found to normalize following limited vitrectomy.\textsuperscript{72,76} Quality of life, as assessed by NEI VFQ measures, was positively correlated with the degree of vitreous opacification\textsuperscript{51} and also improved following limited vitrectomy (see the following sections).\textsuperscript{36,76}

### 5. Treatment of floaters: evidence for safety and efficacy

Once diagnosed, patients complaining of floaters are usually managed conservatively with reassurance and the suggestion that over time they will adapt to the visual symptoms, or that the floaters will settle inferior to the visual axis. In discussing treatment options, a careful and thorough history should be taken, including family history of retinal detachment, prematurity, feeding problems, arthritis, and midline defects. Funduscopic examination should rule-out vitreous base infiltrates and pars planitis. OCT imaging should be performed to examine for macular edema and premacular membranes with macular pucker. A thorough examination may also include fluorescein angiography to detect occult areas of nonperfusion. In myopes, the palate and hearing could be checked. If posterior capsule opacification, retinal
detachment, macular pucker, and cystoid macular edema are found in addition to floaters, informed consent should emphasize the potentially limited benefit of therapeutic intervention. This workup should be detailed as patients typically present with relatively good visual acuity, and there are potential risks to treatment as a result of endophthalmitis, rhegmatogenous retinal detachment, cystoid macular edema, and macular pucker. These must be clearly identified in a balanced, unpressured explanation of risks and benefits. For patients with clinically significant and persistent floaters that remain highly symptomatic and impact on quality of life, our review of the literature indicates that interventional options are increasingly being considered. These fall into 2 categories: floatectomy by vitrectomy, particularly sutureless small gauge limited vitrectomy; and floaterrhexis, by Nd:YAG laser vitreolysis, or in the future by pharmacologic vitreolysis. Vitrectomy is definitive in that offending vitreous opacities are permanently removed. In contrast, Nd:YAG laser breaks large floaters into smaller ones, whereas pharmacologic vitreolysis can theoretically dissolve floaters, but this remains to be proven.

5.1. **Vitrectomy for floaters**

Symptomatic floaters can be surgically removed with vitrectomy, and numerous studies have evaluated the success of vitrectomy for treating vitreous floaters versus the potential risks. (Table 1) To date, 630 cases have been reported, with information regarding various sized instruments and different degrees of invasiveness. What all vitrectomies have in common is the removal of both collagen and hyaluronan, which is in contradistinction to Nd:YAG laser treatments. Although initial studies used 20G instrumentation, current approaches typically use 25G vitrectomy instruments. It is not known whether 27G vitrectomy instruments offer any advantage over 25G. Three-port entry with operating microscope visualization and endoillumination is the most commonly used approach, although Koch in Frankfurt, Germany uses a single-port approach with indirect ophthalmoscopy.

Current surgical techniques are sutureless because highly shelved small gauge sclerotomies are self-sealing, obviating the need for sutures. Aspiration settings and cut rates are the same as typically used for vitrectomy, that is, between 400 and 600 aspiration and 1800 to 2500 cuts per minute. The amount of vitreous removed varies from extensive with surgical induction of PVD at some centers, to limited without PVD induction and with preservation of 3 to 4 mm of retrolental vitreous. The preservation of retrolental vitreous is thought by some to mitigate cataract formation post-op, and there are some data to support this contention (see the following sections). The amount of vitreous removed determines how much balanced salt solution is infused, varying from more than 10–15 mL in extensive vitrectomies to around 5 mL for limited vitrectomies, although no actual measurements have been performed in any reported studies. Future surgical techniques might involve robotic surgery as a way to further enhance control over how much and which parts of the vitreous body are removed.

5.1.1. **Efficacy**

The success rate of vitrectomy for floaters is usually reported to be high. Although visual acuity is not severely affected by
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>% retinal break</th>
<th>% retinal detachment</th>
<th>Other complications</th>
<th>PVD induction (%)</th>
<th>Gauge used</th>
<th>Evaluation and success</th>
<th>Follow-up period (months)</th>
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<td>6</td>
<td>0</td>
<td>0</td>
<td>None reported</td>
<td>0</td>
<td>Not given</td>
<td>NEI VFQ 39 plus additional floater specific questions: 100% were very satisfied with procedure</td>
<td>Range: 8–44</td>
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<td>Schulz-Key et al, 2011</td>
<td>73</td>
<td>1.3</td>
<td>6.8</td>
<td>60% cataract in phakic patients</td>
<td>37.3</td>
<td>20 gauge</td>
<td>Nonstandardized questionnaire: 88% satisfied with results of operation</td>
<td>Mean, 37 (range: 5–108)</td>
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<td>de Nie et al, 2013</td>
<td>110</td>
<td>10.0</td>
<td>10.9</td>
<td>33.6% cataract (phakic patients); 5.5% cystoid macular edema; 3.6% macular pucker; 0.9% glaucoma; 0.9% macular hole</td>
<td>51.8% 20 gauge; 48.2% 23 gauge</td>
<td></td>
<td>Questionnaire based on NEI VFQ-25: 85% patients were satisfied or very satisfied with results from vitrectomy</td>
<td>Mean, 26.4 (range: 4–136)</td>
</tr>
<tr>
<td>Delaney et al, 2002</td>
<td>15</td>
<td>6.7</td>
<td>6.7</td>
<td>6.6% asteroid hyalosis; 6.6% cataract (all patients—number of phakic patients unknown)</td>
<td>0</td>
<td>Not given</td>
<td>Nonstandardized questionnaire: full resolution of symptoms in 93.3%</td>
<td>Mean, 31.5 (range: 6–108)</td>
</tr>
<tr>
<td>Mossa et al, 2002</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>20% cystoid macular edema; 40% cataract (phakic patients)</td>
<td>33.3% gauge not given</td>
<td>Not specified</td>
<td>Reported resolution of floaters</td>
<td>6</td>
</tr>
<tr>
<td>Hoerauf et al, 2003</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>50% cataract; 5.2% hypotony; 7.8% ocular hypertension; 1.72% macular pucker; 0.9% choroidal hemorrhage</td>
<td>25.9</td>
<td></td>
<td>Nonstandardized questionnaire: 100% subjectively happy with procedure</td>
<td>Median 13</td>
</tr>
<tr>
<td>Tan et al, 2011</td>
<td>116</td>
<td>16.4</td>
<td>16.4% retinal breaks (30% with PVD induction)</td>
<td>37.5% hypotony; 12.5% ocular hypertension</td>
<td>Not specified</td>
<td>25</td>
<td>Visual acuity: mean logMAR improved from 0.20 to 0.13</td>
<td>12</td>
</tr>
<tr>
<td>Martinez-Sands et al, 2009</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0.6% cystoid macular edema; 1.12% vitreous hemorrhage</td>
<td>7.1</td>
<td>25</td>
<td>Modified 9 item Questionnaire—100% subjectively happy; 37.5% improved VA by one or more lines</td>
<td>Mean, 18 months (range: 12–28)</td>
</tr>
<tr>
<td>Mason et al, 2014</td>
<td>168</td>
<td>7.1</td>
<td>0</td>
<td></td>
<td>0</td>
<td>25</td>
<td>Normalized contrast sensitivity in each case and NEI VFQ improvement</td>
<td>Range 3–9</td>
</tr>
<tr>
<td>Sebag et al, 2014</td>
<td>76</td>
<td>0</td>
<td>0</td>
<td></td>
<td>25</td>
<td>25</td>
<td>Normalized contrast sensitivity in each case and NEI VFQ improvement</td>
<td>Mean, 17.5 (range: 3–51)</td>
</tr>
<tr>
<td>Huang et al, 2014</td>
<td>98</td>
<td>0</td>
<td>0</td>
<td>23.5% cataract (phakic patients); 1.67% macular pucker</td>
<td>25</td>
<td>25</td>
<td>No statistically significant improvement in VA. Straylight values improved in 97% of cases</td>
<td>Not given</td>
</tr>
<tr>
<td>Mura et al, 2011</td>
<td>39</td>
<td>Not given</td>
<td>Not given</td>
<td></td>
<td>Not given</td>
<td>25</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

logMAR, logarithm of minimum angle of resolution; NEI VFQ, National Eye Institute Visual Function Questionnaire; PVD, posterior vitreous detachment; VA, visual acuity.
vitreous floaters, several studies did report a small improvement in acuity ranging from 26% to 50% of participants in cases that were not confounded by additional procedures of cataract removal. Other measures of vision improvement included CS and straylight values. Another measure of success is symptomatic improvement following surgery, often assessed using a questionnaire. These questionnaires posed questions relating to ease of daily activities, including reading, using computers, watching television, and driving as well as overall satisfaction with the results of the procedure. Studies have used a combination of standardized and nonstandardized questionnaires. Across the various studies, survey results showed the percentage satisfied ranged from 85% to 100% of participants; however, the subjective basis of this testing makes it vulnerable to a placebo effect, found by many studies to be a significant factor in patients undergoing Nd:YAG laser treatments for floaters (see the following sections).

5.1.2. Safety
A range of complications is reported among different studies. Peri-operative complications include intraoperative and postoperative retinal tears, retinal detachment, choroidal hemorrhage, and proliferative vitreoretinopathy. The most common complication, however, is the development of cataracts.

5.1.2.1. Retinal breaks and detachments. The reported incidence of retinal breaks varied between 0% and 16.4%, with the larger sample sizes tending to exhibit higher percentages of retinal breaks and detachments. The more serious complication of a retinal detachment following vitrectomy has an incidence between 0% and 10.9%. More cases of retinal detachment are reported in those studies with longer follow-up periods, often occurring relatively late in these follow-up periods. Thus, it is possible that the short-term studies did not consider a long enough follow-up to record a valid complication rate, or conversely that the long-term studies may have other confounding circumstances such as age, natural history of the disease, or subsequent cataract surgery. It is therefore unclear at what point in time a postoperative retinal detachment should no longer be considered a complication of floater vitrectomy.

The induction of PVD during surgery may be an important factor in the development of retinal breaks. In the studies examined, patients who had not already developed a PVD naturally would often have a PVD induced during the vitrectomy. The risk of iatrogenic tears associated with vitrectomy may increase with PVD induction during surgery. Although one study found a nearly 3-fold higher incidence of retinal tears following PVD induction (30.5% vs. 11.6%; P = 0.019), this association was not always present. Smaller gauge instrumentation appear to reduce the risk of postoperative retinal tears, retinal detachment, choroidal hemorrhage, and proliferative vitreoretinopathy. The most common complication, however, is the development of cataracts.

5.1.2.2. Intraocular pressure problems. Changes in intraocular pressure are a complication of vitrectomy that can lead to either hypotony or ocular hypertension. Hypotony is uncommon, even when using small gauge instruments and sutureless technique, but can be prevented using air tamponade at the time of vitrectomy. Acute postoperative ocular hypertension is rare, but can be treated with intraocular pressure-lowering medications and generally resolves within 3 weeks of the surgery. Chronic glaucoma has been described in patients after vitrectomy, potentially occurring many years later. Introduction of oxygen and toxicity to the trabecular meshwork during the vitrectomy has been hypothesized as a cause, with increased risk following lens removal. Other possible contributing mechanisms include surgical inflammation and debris, increased susceptibility of the optic disk postvitreous removal and an altered biochemical environment. Thus, detection of this potential complication needs long-term follow-up; however, glaucoma has not been consistently shown among all studies. Longer term monitoring of IOP and optic disk morphology may be of value until this risk is further elucidated and potentially minimized with refined vitrectomy procedures. To date, however, IOP problems have not been encountered to any appreciable degree following vitrectomy for floaters.

5.1.2.3. Cataracts. Cataracts following vitrectomy in phakic patients are common, occurring in approximately 53% to 76% of cases, depending on the vitreoretinal pathology that necessitated vitrectomy and systemic conditions such as diabetes. These studies have shown that cataracts will develop within 2 years following the procedure in patients over 50 years of age. The use of a gas bubble increases the incidence of cataract following a vitrectomy. One study did report a lower incidence of cataract formation; however, it was unclear how many of these patients were aphakic in the vitrectomy treatment group. A recent study found that cataract surgery was required in only 23% of cases following floater vitrectomy, with a mean age of 64 years. No patients aged younger than 53 years required cataract surgery. The authors suggested that this was the result of lower intravitreal oxygen tension related to not inducing PVD at floater vitrectomy surgery, and protection of the lens provided by endogenous antioxidants in the anterior vitreous that was left intact during vitrectomy surgery. These findings were confirmed in a more recent study that followed patients for 2 years.
comparing the incidence of cataract surgery following extensive vitrectomy to limited vitrectomy for floaters. The incidence after limited vitrectomy was half of that following extensive vitrectomy. Targeted floatectomy may thus preserve a relatively hypoxic environment and further reduce the incidence of cataracts.

5.1.2.4. Endophthalmitis. Endophthalmitis is a potential serious complication of any intraocular surgery, including vitrectomy. Cases of endophthalmitis often have a poor visual outcome. The reported risk has decreased over time, with more recent reports ranging from 0.018% to 0.04% for post-vitrectomy cases. Of the floater vitrectomy studies available, 3 cases of endophthalmitis were reported, consistent with its low incidence.

5.2. Nd:YAG laser vitreolysis

Nd:YAG lasers are most commonly used for treating posterior capsule opacification following cataract surgery and opacified anterior vitreous membranes, as well as for performing peripheral iridotomy; however, Nd:YAG lasers have also been used to severe collagenous vitreous strands, transvitreal sheets or bands and most recently to break up vitreous opacities. This is generally performed by focusing the laser onto vitreous opacities visible at the slit lamp. Typically, only opacities relatively far from the retina are treated (see the following), thus these may represent a subset of floaters that might be appropriate to treat with Nd:YAG laser, although it is not known whether these opacities induce enough floaters to be clinically significant. Unlike vitrectomy, the procedure is closed eye obviating the risk of endophthalmitis and possibly not increasing the risk of cataract, although if vitreous physiology is altered, there may cataractogenic effects via increased oxygen levels and altered antioxidant activity. As the Nd:YAG laser is focused on collagenous vitreous opacities, the hyaluronan component may be minimally affected by the laser energy.

The mechanism of laser vitreolysis may be lysis of fibers and rhexis of aggregates, followed by displacement out of the visual axis because nothing is removed from the vitreous in this closed-eye procedure. Nd:YAG laser vitreolysis thus may be considered an alternative technique that can be offered to treat symptomatic vitreous floaters; however, Nd:YAG laser vitreolysis is not currently offered by the overwhelming majority of ophthalmologists as a treatment for symptomatic floaters and, to date, there are only 91 cases of Nd:YAG laser vitreolysis of floaters in the literature (Table 2), compared to 630 floater vitrectomy cases (Table 1). However, as a result of marketing and promotion efforts by one laser manufacturer, the use of this treatment may be expanding.

5.2.1. Efficacy

There have been several published studies claiming efficacy of Nd:YAG laser vitreolysis for floaters (Table 2), but few case reports are available. These studies are highly variable in design and treatment protocols, with all having relatively small sample sizes. Assessment of the outcome and success of the procedure was generally subjective, with none using standardized questionnaires, and the majority relying on self-
reporting of whether there was resolution of floater symptoms. Most importantly, no objective outcome measures of vision or vitreous structure were used in any Nd:YAG laser vitreolysis studies.

Using the patient’s subjective claim of the resolution of floaters as an outcome measure, the success rates claimed by existing publications are highly variable, ranging from 0% to 100%. Vandorselaer and colleagues suggested that the likelihood of success of the treatment relates to the type of floater with regards to its suspension characteristics. They claimed significantly higher success rates in the treatment of floaters that were suspended by vitreous strands, as opposed to those located loosely within the vitreous body; however, no objective measures or imaging studies were performed to support this contention.

Although not specified in several of the studies, it appears that Nd:YAG laser for treating floaters is not necessarily a simple procedure, often requiring several sessions of treatment. The reported number of required sessions ranged between 1 and 6. There was also variability in the laser energy used and distance from the retina of opacities treated, although it is not clear how the distance from the retina was measured and whether any reproducible objective method was used. Delaney and colleagues used 2 mm as a threshold distance with only 1.2 mJ per pulse. In contrast, Tsai and colleagues used energy pulses ranging from 5 to 10 mJ but kept a minimum distance of 4 mm from the retina. Little and Jack used energy pulses ranging from 4 to 15 mJ in their study, and maintained a distance of 3 mm from the retina. This greater energy requirement may have been used in other parts of the study such as cutting vitreous bands in the posterior chamber rather than disrupting vitreous opacities. Such heterogeneity in the study groups diminishes the value of the reported findings.

In addition to the aforementioned published studies, there are nonpeer-reviewed reports available online relating to the “success” of laser treatments for floaters. One website reported 200 patients within a single practice treated with laser vitreolysis because there are theoretical considerations as to vitreous hemorrhage or uveitis, are at times highly symptomatic and can significantly impact on vision and quality of life. The current treatment options available for vitreous floaters are vitrectomy and Nd:YAG laser. Vitrectomy has a low-risk profile with an excellent success rate, as determined by objective measures of vision and standardized quantification of patient satisfaction. On the other hand, Nd:YAG laser for floaters remains an off-label procedure that is not commonly reported in the peer-reviewed literature. The response rate to laser is highly variable and, while the reported complications are minimal, rigorous study protocols have also been cases of a permanent increase in IOP reported following Nd:YAG laser vitreolysis for floaters, leading to open-angle glaucoma.

5.3. Pharmacologic vitreolysis

Nonsurgical therapy of vitreoretinal disorders has been under development for nearly 2 decades. To date, 7 agents have been studied, and 5 clinical studies have either failed (hyaluronidase as Vitrase) or been stopped (collagenase, natokinase, urea, chondroitinase). Although purified dispase is still being tested, clinical trials of ocriplasmin have shown safety and efficacy for symptomatic vitreomacular adhesion or vitreomacular traction. Ocriplasmin is therefore approved by the US Food and Drug Administration for the treatment of symptomatic vitreomacular adhesion by the European Union European Medicines Agency for treating vitreomacular traction, including macular holes. Although there are theoretical concerns about untoward effects on zonules and the photoreceptors, this has not been realized in over a thousand clinical trial cases and an even greater number of patients who have received treatment in practice during the past few years. Theoretically, a pharmacologic approach to dissolve or otherwise alter the size, shape, or surface characteristics of clinically significant floaters is attractive; however, to date no studies have been undertaken. The target depends on the nature of the agent. It would seem most appropriate to develop an agent that dissolves or at least breaks down collagen, the most optically offensive molecule in the vitreous body, especially when cross-linked and aggregated. Such studies should carefully monitor the effects of pharmacologic vitreolysis because there are theoretical considerations as well as some clinical evidence, that this treatment might well induce floaters, rather than dissolve them. Indeed, in large multicenter clinical trials the incidence of floaters in patients treated with ocriplasmin was twice as high as in controls.

6. Conclusions

Primary vitreous floaters that result from myopia or age-related vitreous degeneration, and secondary floaters, usually from vitreous hemorrhage or uveitis, are at times highly symptomatic and can significantly impact on vision and quality of life. The current treatment options available for vitreous floaters are vitrectomy and Nd:YAG laser. Vitrectomy has a low-risk profile with an excellent success rate, as determined by objective measures of vision and standardized quantification of patient satisfaction. On the other hand, Nd:YAG laser for floaters remains an off-label procedure that is not commonly reported in the peer-reviewed literature. The response rate to laser is highly variable and, while the reported complications are minimal, rigorous study protocols
have not been used. The advantages of Nd:YAG laser is that the eye remains closed and that vitreous components are torn and severed, but not removed. Centrally-suspended, single floaters might be candidates for laser lysis or displacement, but this remains to be demonstrated.

Management of floaters should be individualized, prepared by good history taking, and well-documented by imaging, allowing for more targeted, limited, and focal intervention. Vitrectomy techniques could be refined by removing only floaters without infusion or using a robot-guided small gauge 1- or 2-port high-speed vitrectomy that only removes floaters, filters out the collagen and reinfuses the autologous anoxic hyaluronan, thus possibly mitigating cataract, although other effects may be induced. Further prospective studies using objective, quantitative, standardized outcome measures already used for the assessment of vitrectomy are required for evidence-based conclusions regarding the relative efficacy and safety of Nd:YAG laser treatments. Ultimately, the future will most likely see vitrectomy made simpler or replaced by pharmacologic vitreolysis as a less invasive treatment for patients with floaters.29,42,71–73

7. Method of literature search

A MEDLINE database search was performed using the keywords “vitreous,” “floaters,” “treatment,” “vitrectomy,” and “laser.” The GOOGLE search engine was also searched with combinations of the previously mentioned terms. The reference lists of identified trials were hand searched. There were no language or date restrictions in these searches. Non-English articles were assessed using the available English abstracts. This search produced 19 studies, all retrospective case series with the exception of 2 prospective cohort studies. Eleven studies (published between 2000 and 2014) examined the potential of vitrectomy as a treatment for floaters; 6 published studies (between 1985 and 1998) examined Nd:YAG laser as a treatment for floaters, and one study examined both vitrectomy and laser (published 2002). Additional non-peer-reviewed data reporting on the use and outcomes of Nd:YAG laser for the treatment of floaters were found with a GOOGLE search using combinations of the previously mentioned search terms. The electronic databases were last searched in May 2015.

8. Disclosures

Rebecca Milston and Michele C. Madigan report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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REFERENCES


