NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of YAG laser vitreolysis for symptomatic vitreous floaters

Floaters are small dark shapes that float across your vision. They can look like spots, rings, squiggly lines or cobwebs, and can sometimes affect sight. They are usually caused by changes in the jelly-like substance (vitreous) inside the eye. In this procedure, a special type of laser (YAG) fires short pulses of energy into the floaters, to break them up (vitreolysis). It is done as an outpatient procedure. The aim is to reduce disturbance to sight caused by vitreous floaters.

Contents

Abbreviations

Word or phrase	Abbreviation
Best-corrected visual acuity	BCVA
Comatic aberration	CA
Confidence interval	CI
Early Treatment Diabetic Retinopathy Study	ETDRS
High-order aberration	HOA
Intraocular pressure	IOP
Interquartile range	IQR
Modulation transfer function	MTF
National Eye Institute Visual Function Questionnaire	NEI VFQ
Posterior vitreous detachment	PVD
Spherical aberration	SA
Standard deviation	SD
Strehl ratio	SR
State-Trait Anxiety Inventory	STAI
Vitreous floaters symptoms questionnaire	VFSQ

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in December 2021 and updated in June 2022.

Procedure name

- YAG laser vitreolysis for symptomatic vitreous floaters

Professional societies

- British and Eire Association of Vitreoretinal Surgeons

- Royal College of Ophthalmologists.

Description of the procedure

Indications and current treatment

Vitreous floaters are microscopic clumps of collagen fibres in the vitreous that cast shadows on the retina, appearing as floaters. The most common cause of vitreous floaters is posterior vitreous detachment (PVD), when the posterior hyaloid face separates from the retina.

Vitreous floaters can be primary or secondary. Primary vitreous floaters originate from the vitreous body. Secondary floaters originate from outside the vitreous body, generally from proteins, amyloid or cells.

Vitreous floaters usually do not threaten vision and can be managed conservatively. When they do affect vision, treatment options include vitrectomy and vitreolysis with YAG laser.

What the procedure involves

This procedure aims to improve vision and reduce symptoms by removing or reducing the size of floaters.

The pupil is dilated and anaesthetic eye drops are administered. A specialised contact lens is placed on the cornea. Coaxial illumination is used. A laser microscope focuses on the front surface of the floater and creates short bursts of energy (nanosecond pulses). The laser energy usually starts at a low level, and is increased until it is high enough to break up the floater. The laser is stopped once all visually significant floaters are treated.

YAG laser vitreolysis is done as an outpatient procedure. Depending on the characteristics and numbers of floaters, more than 1 session may be needed.

Outcome measures

Contrast sensitivity is the ability to detect subtle differences in shading and patterns. It can be measured using the Pelli-Robson chart by finding the lowest contrast letters a person can read correctly. The chart uses a single large letter size (6/18 optotype), with contrast varying across groups of letters. A Pelli-Robson score of 2.0 indicates normal contrast sensitivity of 100%. Scores less than 2.0 signify poorer contrast sensitivity. Pelli-Robson contrast sensitivity score

of less than 1.5 is consistent with visual impairment and a score of less than 1.0 represents visual disability.

Visual acuity refers to a person's ability to see small details and reflects the clarity or sharpness of vision. Visual acuity is often measured according to the size of letters viewed on a Snellen chart, or the size of other symbols, such as the Landolt C or the E Chart. 'Normal' distance visual acuity is often quantified using the Snellen chart, at 6/6 (metre) or 20/20 (feet). This means the person can read at 6 metres (or 20 feet) what someone with normal vision can read at 6 metres. A vision of 6/12 means the person can see at 6 metres what someone with normal vision can see at 12 metres, so representing worse vision. A visual acuity of 6/6 can also be expressed as 1.00 decimal and is equivalent to 0.0 logMAR (with higher logMAR values representing worse vision). The Early Treatment Diabetic Retinopathy Study (ETDRS) letter score is another means of testing visual acuity, in which 85 letters approximates 6/6 Snellen, with lower letter scores representing worse vision.

The National Eye Institute Visual Function Questionnaire (NEI VFQ) measures visual functioning in 11 domains: general vision, ocular pain, near activities, distance activities, vision-specific social functioning, vision-specific mental health, vision-specific role difficulties, vision-specific dependency, driving, colour vision, and peripheral vision. It has different versions, such as 25-item and 39-item versions. Each domain is scored from 0 to 100 points, with higher scores representing better functioning.

The State-Trait Anxiety Inventory (STAI) is a psychological inventory based on a 4-point Likert scale (from 0 to 3 points) and consists of 40 questions. The STAI measures 2 types of anxiety – state anxiety (anxiety about an event) and trait anxiety (anxiety level as a personal characteristic). Higher total scores indicate greater anxiety levels.

Efficacy summary

Visual disturbance

In a randomised controlled trial of 21 people (21 eyes) with symptomatic vitreous opacities who had YAG laser vitreolysis or sham YAG laser vitreolysis, based on a 10-point scale (with 0 indicating no symptoms and 10 indicating debilitating symptoms), the mean visual disturbance score statistically significantly reduced from 6.9 (SD 1.6) at baseline to 2.2 (SD 2.2) at 6-month follow up ($p<0.001$) in the YAG laser vitreolysis group, and from 7.5 (SD 1.8) to 5.4 (SD 2.8) ($p=0.009$) in the sham group. The difference between the 2 groups was -3.2 points ($p=0.011$) at 6 months (Ludwig 2021).

In a randomised controlled trial of 52 people (52 eyes) with symptomatic Weiss ring floaters who had YAG laser vitreolysis or sham YAG laser vitreolysis, the mean 10-point visual disturbance score decreased from 6.4 (SD 1.6) at baseline to 3.3 (SD 2.5) at 6-month follow up in the YAG laser vitreolysis group and from 6.4 (SD 1.9) to 6.3 (SD 1.5) in the sham group. The difference between the 2 groups was -3.0 points ($p<0.001$) over 6 months (Shah 2017).

In a case series of 34 people (34 eyes) with symptomatic Weiss ring floaters, there was a statistically significant reduction of 3.1 points ($p<0.001$) at a mean follow up of 2.3 years compared with baseline value (Shah 2020).

In a case series of 32 people (32 eyes) with symptomatic vitreous floaters, there was a statistically significant reduction of 2.5 points at 6 months after YAG laser vitreolysis compared with baseline value ($z=-3.97$; $p<0.001$; $r=0.84$; Souza 2020).

Visual acuity

In the randomised controlled trial of 21 people (21 eyes), the mean best-corrected visual acuity (BCVA) improved from 0.17 (SD 0.1) logMAR at baseline to 0.12 (SD 0.1) logMAR ($p=0.326$) at 6-month follow up in the YAG laser vitreolysis group, and from 0.18 (SD 0.1) logMAR to 0.11 (SD 0.1) logMAR ($p=0.359$) in the sham group. The difference between the 2 groups was -0.06 logMAR ($p=0.833$) at 6 months (Ludwig 2021).

In the randomised controlled trial of 52 people (52 eyes), there was no statistically significant change in ETDRS BCVA between baseline and 6 months in both groups (all $p>0.05$). The mean BCVA changed by -0.2 letters in the YAG laser vitreolysis group and by -0.6 letters in the sham group (difference 0.4; 95% CI -6.5 to 5.3; $p=0.94$; Shah 2017)

In the case series of 34 people (34 eyes), the change in ETDRS BCVA was 0.53 letters (95% CI -1.3 to 2.3; $p=0.57$) at a mean follow up of 2.3 years compared with baseline value (Shah 2020).

In the case series of 34 people (34 eyes), Snellen fraction visual acuity changed from 0.74 (SD 0.29) at baseline to 0.76 (SD 0.32) at 10 days after the second session ($p=0.65$) and visual acuity with pinhole was 0.82 (SD 0.26) and 0.82 (SD 0.28) respectively ($p=0.31$; Garcia 2021).

In the case series of 32 people (32 eyes), there was no change in ETDRS BCVA during the 6-month follow-up period (exact data were not reported; Souza 2020).

Contrast sensitivity

In the randomised controlled trial of 21 people (21 eyes), there was no statistically significant change in Pelli-Robson contrast sensitivity between baseline and 6 months in the YAG laser vitreolysis group (baseline, 3.0% [SD 1.8%]; 6 months, 2.2% [SD 1.6%]; p=0.223) and the sham group (baseline, 2.6% [SD 1.1%]; 6 months, 2.0% [SD 1.2%]; p=0.305). The difference between the 2 groups was 0.2% (p=0.848) at 6 months (Ludwig 2021).

In the case series of 34 people (34 eyes), there was a statistically significant improvement in Pelli-Robson contrast sensitivity at 10 days after the second sessions compared with baseline value (baseline, 1.43 [SD 0.23]; final, 1.59 [SD 0.19]; p<0.001; Garcia 2021).

Floater symptoms and presence

Subjective assessment

In the randomised controlled trial of 52 people (52 eyes), based on a 5-level scale (worse, less than 0%; same, 0%; partial success, 30% to 50%; significant success, 50% to 70%; and complete success, 100%), 53% (19/36) of people in the YAG laser group reported their symptoms as significantly or completely better compared with 0% in the sham group at 6-month follow up. The difference between the 2 groups was statistically significant at 6 months (difference, 53%; 95% CI 36% to 69%; p<0.001; Shah 2017)

In the case series of 34 people, based on a 5-level scale, 50% of people stated that their floaters were significantly or completely better at a mean follow up of 2.3 years compared with 41% at 6 months (p=0.47; Shah 2020).

In a case series of 51 people (51 eyes) with symptomatic floaters, based on a 5-level scale, 71% (36/51) of people reported their symptoms as significant or complete improvement at 6-month follow up. The difference between PVD and non-PVD groups was not statistically significant at 6 months (73% compared with 69%, p=0.344; Lin 2021).

In the randomised controlled trial of 21 people (21 eyes), on a 4-level scale (same or worse, 0%; limited success, 30% to 50%; significant success, 50% to 70%; complete success, 100%), the proportion of people who reported significant or complete improvement was 77% in the YAG laser vitreolysis group and 25% in the control group at 6-month follow up (Ludwig 2021).

In a case series of 50 people (55 eyes) with symptomatic vitreous floaters, the proportion of eyes that had significant or complete success was 56% (31/55) at

6-month follow-up (Sun 2019). When considering the floater severity, the proportion of eyes that had significant or complete success was 71% (12/17) of eyes with preoperative mild floaters, 57% (12/21) of eyes with preoperative moderate floaters, and 41% (7/17) of eyes with preoperative severe floaters at 6-month follow up. The difference between groups was statistically significant (p=0.007; Sun 2019).

Objective evaluation

In the randomised controlled trial of 21 people (21 eyes), a masked evaluator graded the fundus photographs on a 4-level scale and found that improvement was greater in the YAG laser vitreolysis group (significant improvement, 53%; limited and complete improvement, 47%; exact data for each improvement was not reported separately) than the sham group (limited improvement, 63%; no improvement 37%) at 6-month follow up (Ludwig 2021).

In the case series of 50 people (55 eyes), based on a 4-level qualitative scale, the infrared fundus images showed that 64% (35/55) of eyes had significant or complete success at 6 months after YAG laser vitreolysis. When considering the floater severity, the proportion of eyes that had significant or complete success was 82% (14/17) of eyes with preoperative mild floaters, 67% (14/21) of eyes with preoperative moderate floaters, and 41% (7/17) of eyes with preoperative severe floaters at 6-month follow up. The difference between groups was statistically significant (p=0.038; Sun 2019).

In the randomised controlled trial of 52 people (52 eyes), a masked grader rated the fundus photographs on a 5-level scale and reported that 94% (34/36) of people in the YAG group had significantly improved or completely resolved floaters compared with 0% in the sham group at 6-month follow up. The difference between groups was statistically significant (difference, 94%; 95% CI 87% to 102%; p<0.001; Shah 2017).

In the case series of 34 people (34 eyes), a masked reviewer evaluated the fundus photographs on a 5-level scale and found that 94% of people were significantly or completely better at a mean follow up of 2.3 years compared with baseline (Shah 2020).

In the case series of 32 people (32 eyes), a masked grader reviewed the colour fundus photographs and reported that complete vitreous opacity improvement was observed in 56% of people (18/32), partial improvement in 38% (12/32), and no change in 6% (2/32) at 6-month follow up (Souza 2020).

Visual-related quality of life

Visual Function Questionnaire (VFQ)

In the randomised controlled trial of 21 people (21 eyes), the NEI VFQ-25 scores for general vision and mental health were statistically significantly higher in the YAG laser vitreolysis group than the sham group at 6-month follow up (general vision, 75.8 compared with 59.2, p=0.037; mental health, 84.3 compared with 70.3, p=0.048; Ludwig 2021).

In the randomised controlled trial of 52 people (52 eyes), the NEI VFQ-25 scores for general vision, peripheral vision, role difficulties and dependency were statistically significantly better in the YAG group than the sham group at 6-month follow up (general vision: 69.4 compared with 53.1; difference 16.3; 95% CI 0.9 to 31.7; p=0.04; peripheral vision: 94.4 compared with 82.8; difference 11.6; 95% CI 0.8 to 22.4; p=0.04; role difficulties: 93.1 compared with 75.8; difference 17.3; 95% CI 8.0 to 26.6; p<0.001; and dependency: 98.8 compared with 93.2; difference 5.6; 95% CI 0.4 to 10.8; p=0.03; Shah 2017).

In the case series of 34 people (34 eyes), when comparing with baseline values, there were statistically significant improvements in near vision activities (baseline, 78.7; final, 85.8; difference, 7.1; 95% CI 1.6 to 12.6; p=0.016), distance vision (baseline, 84.6; final, 89.0; difference, 4.4; 95% CI 0.3 to 8.5; p=0.042), mental health (baseline, 71.7; final, 85.7; difference, 14.0; 95% CI 9.1 to 18.8; p<0.001), and role difficulties (baseline, 81.3; final, 93.4; difference, 12.1; 95% CI 5.6 to 18.7; p<0.001) at a mean follow up of 2.3 years (Shah 2020).

In the case series of 50 people (55 eyes), the mean overall NEI VFQ-25 score statistically significantly increased from 71.44 (SD 12.77) at baseline to 88.54 (SD 12.74) at 6 months after YAG laser vitreolysis (t=11.82, p=0.001; Sun 2019).

In the case series of 34 people (34 eyes), the median VFQ-25 score statistically significantly increased from 73.05 (interquartile range [IQR] 19.25) before YAG laser vitreolysis to 93.76 (IQR 8.73) at 10 days after the second session (p<0.01). The median VFQ-39 score also statistically significantly improved from 74.60 (IQR 19.01) to 95.01 (IQR 6.50; p<0.001). Subgroup analysis showed that there were statistically significant differences in the median changes of NEI VFQ-25 and NEI VFQ-39 scores between people with myopia and people without myopia (VFQ-25: 20.06 compared with 15.07, p<0.05; VFQ-39: 22.27 compared with 16.15, p<0.01; Garcia 2021).

In the case series of 32 people (32 eyes) there were statistically significant improvements in the near visual function (z=−2.97; p=0.003; r=0.633) and visual

disturbance rate (z=−3.97; p<0.001; r=0.84) at 6 months compared with baseline after YAG laser vitreolysis (Souza 2020).

State-Trait Anxiety Inventory (STAI)

In the case series of 34 people (34 eyes), the median STAI score statistically significantly improved from 38 (IQR 11; p<0.001) before YAG laser vitreolysis to 18 (IQR 19) at 10 days after the second session (Garcia 2021).

Vitreous floaters symptoms questionnaire (VFSQ)

In the case series of 51 people (51 eyes), the composite score, distance activities, near activities, social functioning, peripheral vision and mental health statistically significantly improved after YAG laser vitreolysis (all p<0.05) but not driving (p=0.162). Comparison of the changes in VFSQ-13 between the PVD group and the non-PVD group showed no statistically significant difference in all domains (distance activities, 9.38 [SD 14.97] compared with 10.80 [SD 12.53]; near activities, 3.33 [SD 10.61] compared with 10.23 [SD 16.65]; driving, 1.25 [SD 15.12] compared with 2.27 [SD 7.36]; peripheral vision, 5.00 [SD 10.26] compared with 9.09 [SD 19.74]; social functioning, 7.50 [SD 14.28] compared with 3.41 [SD 8.78]; mental health, 7.08 [SD 13.32] compared with 8.71 [SD 15.53]; composite score, 5.59 [SD 9.16] compared with 7.42 [SD 9.65]; all p>0.05; Lin 2021).

Patient satisfaction

In the case series of 34 people (34 eyes), 76% (26/34) of people were quite or very satisfied with YAG laser vitreolysis, 12% (4/34) were moderately satisfied and 12% (4/34) were dissatisfied (Garcia 2021).

Safety summary

Retinal tear and detachment

Retinal tear was reported in 3 people who had YAG laser vitreolysis in the case series of 34 people (34 eyes; Shah 2020). These events were evident at 1.4 years to 2.8 years.

Retinal tear was reported in 1 person and retinal detachment in 2 people in a review of 16 complications voluntarily reported to the American Society of Retina Specialists Research and Safety in Therapeutics Committee during a 6-month period (Hahn 2017).

Retinal haemorrhage

Mild retinal haemorrhage was reported in 1 person (1 eye) in the case series of 50 people (55 eyes). The person had previous severe floaters and PVD, and was then given glucocorticoid, ocular nerve nutrient and vitamin C for 2 weeks. This event subsequently resolved (Sun 2019).

Laser injury-related transient posterior pole retinal haemorrhage was described in 2 people in the review of 16 complications. Of these events, 1 person remained asymptomatic, while the other person had a transient scotoma that lasted a few weeks and corresponded to the area of subretinal haemorrhage with nearby retinal whitening (Hahn 2017).

Intraocular pressure (IOP), ocular hypertension and secondary glaucoma

The mean IOP increased from 14.1 mmHg (SD 3.6) at baseline to 14.5 mmHg (SD 3.0; p=0.841) at 6-month follow up in the YAG laser vitreolysis group, and decreased from 15.9 mmHg (SD 1.7) to 15.3 mmHg (SD 1.7; p=0.992) in the sham group in the randomised controlled trial of 21 people (21 eyes). There was no statistically significant difference between the 2 groups at baseline or 6 months (all p>0.05; Ludwig 2021).

No statistically significant change in IOP was found at a mean follow up of 2.3 years from baseline (difference, -0.09 mmHg; 95% CI -1.2 to 1.0; p=0.88) in the case series of 34 people (34 eyes). In the same study, bilateral ocular hypertension was observed in 1 person at 0.6 years after 1 session of unilateral YAG laser vitreolysis (Shah 2020).

The mean IOP changed from 15.71 mmHg (SD 2.4) at baseline to 15.34 mmHg (SD 3.27) at 6 months after YAG laser vitreolysis (p=0.23) in the case series of 50 people (55 eyes; Sun 2019).

Temporary ocular hypertension developed in 2 people in the case series of 34 people (34 eyes). The IOP was controlled to normal IOP levels with ocular hypotensive medications (Garcia 2021).

Prolonged elevation of the IOP was described in 5 people in the review of 16 complications. Of these 5 cases, 3 resulted in secondary glaucoma, and trabeculectomy was needed in 2 of these cases (Hahn 2017).

Worsening of vision and symptoms

Temporary blurred vision during the first hour after YAG laser vitreolysis was reported in 5 people in the randomised controlled trial of 21 people (21 eyes). These cases spontaneously resolved on the first day (Ludwig 2021).

Worse visual quality was reported in 3 people in the case series of 51 people (51 eyes). These people complained of more tiny asteroid floaters or floater remnants (Lin 2021).

Worsening of floaters was described in 3 people during a mean follow up of 2.3 years in the case series of 34 people (34 eyes). Of the 3 people, 1 person had a pars plana vitrectomy and the symptoms were 100% improved at 1.5 years after surgery, without any complications (Shah 2020).

Worsening of symptoms was reported in 1 person (1 eye) in the case series of 50 people (55 eyes; Sun 2019).

An increased number of symptomatic floaters was seen in 1 person in the review of 16 complications (Hahn 2017).

Other complications

Anterior and intermediate uveitis was reported in 1 person at 0.9 years after a single laser session in the case series of 34 people (34 eyes; Shah 2020).

Focal cataract was described in 5 people (5 eyes) in the review of 16 complications. Of these events, 3 focal cataracts were within the visual axis and 2 had associated posterior capsule rupture (Hahn 2017).

One posterior chamber intraocular lens was pitted peripherally with the YAG laser in the randomised controlled trial of 52 people (52 eyes). This happened when anterior floaters were treated, although this finding was not visually significant (Shah 2017).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events that they have heard about) and about theoretical adverse events (events that they think might possibly occur, even if they have never happened).

For this procedure, professional experts listed the following additional anecdotal or theoretical adverse events: induced inflammation, retinal contusion, retinal damage and lens damage.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to YAG laser vitreolysis for symptomatic vitreous floaters. The following databases were searched, covering the period from their start to 7 June 2022: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with symptomatic vitreous floaters.
Intervention/test	YAG laser vitreolysis.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 255 people (approximately 260 eyes) from 2 randomised controlled trials (Ludwig 2021; Shah 2017), 5 case series (Shah

2020; Lin 2021; Sun 2019; Garcia 2021; Souza 2020) and a review of complications (Hahn 2017).

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on YAG laser vitreolysis for symptomatic vitreous floaters

Study 1 Ludwig GD (2021)

Study details

Study type	**Randomised controlled trial**
Country	Brazil (single centre)
Recruitment period	2018 to 2019
Study population and number	n=21 (21 eyes; YAG laser vitreolysis, n=13; control, n=8) Patients with symptomatic vitreous opacities
Age and sex	Mean 62 years (range 48 to 83 years); 76% (16/21) female
Patient selection criteria	Inclusion criteria: symptomatic vitreous opacities because of PVD, including Weiss rings, symptoms for at least 6 months, posterior vitreous detachment reported in clinical examination and ocular ultrasound (B-scan), vitreous opacity located at least 5 mm from the lens, if phakic and 3 mm from the retina, and a visual discomfort of at least 4 on a scale of 0 to 10 points, with 0 being asymptomatic and 10 indicating impairing symptoms. Exclusion criteria: visual acuity worse than 0.4 logMAR in the fellow eye, history of retinal detachment, retinal tear, uveitis, glaucoma using 2 or more drugs, previous macular oedema and aphakia, or other associated diseases that may compromise data analysis.
Technique	YAG laser vitreolysis: the pupil of the studied eye was dilated with 1% tropicamide and 2.5% phenylephrine. Proparacaine was administered and a Volk Singh Mid vitreous lens was positioned with gosiosol before administration of the YAG laser. Vitreolysis was done using the Visulas YAG III (Zeiss) device. A maximum energy per pulse of 7.2 mJ was used. The energy was initially fixed at 4 mJ and slowly increased to a level at which the performing physician observed photodisruption of the opacity and formation of gas bubbles. Only 1 laser treatment session was done to avoid any unmasking by the patient and the subsequent evaluator. Control: matching treatment was done. The same lens was positioned; however, a paper filter was placed on the surface to prevent the laser energy from passing through the lens. The YAG laser energy was at its lowest setting of 0.1 mJ. For both groups, no eye drops were administered after the procedure.
Follow up	6 months
Conflict of interest/source of funding	None

Analysis

Follow-up issues: All patients were followed for 6 months, except for 3 patients of the control group that were lost to follow up because of their dissatisfaction with the results. These 3 patients were excluded from the study. Patients were assessed at 30 minutes after the end of the laser session, and then 1 week, 1 month, 3 months and 6 months.

Study design issues: This prospective double-blind randomised clinical trial (RBR-2jq3v) compared the effects of vitreolysis with Nd:YAG laser for the treatment of vitreous opacities with a placebo procedure, analysing the symptoms reported by patients and signs observed by researchers. Primary outcomes were visual disturbance on a 10-point scale, changes in a 4-level symptom severity scale, contrast sensitivity measured with the Pelli-Robson chart and the NEI VFQ-25. Secondary results included objective change in vitreous opacities, BCVA, variation in IOP and adverse events.

Randomisation was done using a random number for each patient, 1 for intervention and 2 for placebo. Only 1 eye had the intervention (the eye to which the patient referred the most complaints) and the fellow eye was observed. All procedures were done by the same physician. Intention-to-treat analysis was not used.

A masked evaluator rated the fundus photography for the presence of floaters using the 4-level scale used by patients to report their postoperative symptoms compared with the baseline. The following percentages were used to quantify the level of improvement: 0% or worse; limited success, 30% to 50%; pronounced success, 50% to 70%; and total success, 100%.

Study population issues: At baseline, there were no statistically significant differences in age, sex, most symptomatic eye (left versus right), lens status (phakic versus pseudophakic), duration of symptoms and visual disturbance scale.

Key efficacy findings

Number of patients analysed: 21 (21 eyes)

Procedural data

Variable	YAG laser vitreolysis (n=13)		Control (n=8)		P value
	Mean	SD	Mean	SD	
Laser shots	144.7	46.1	92.0	24.4	0.008
Energy per pulse, mJ	6.1	1.4	0.2	0.1	<0.001
Total energy, J	0.8	0.4	0.1	-	<0.001

BCVA and contrast sensitivity measurements, mean±SD

Variable	YAG laser vitreolysis (n=13)			Control (n=8)			Difference between intervention and control	
	Initial	6 months	P value	Initial	6 months	P value	Difference (6 months)	P value
BCVA, logMAR	0.17±0.1	0.12±0.1	0.326	0.18±0.1	0.11±0.1	0.359	-0.06	0.833
Contrast sensitivity	3.0%±1.8%	2.2%±1.6%	0.223	2.6%±1.1%	2.0%±1.2%	0.305	0.2%	0.848
Visual disturbance	6.9±1.6	2.2±2.2	<0.001	7.5±1.8	5.4±2.8	0.09	-3.2	0.011

IOP comparison between groups

IOP	YAG laser vitreolysis (n=13)		Control (n=8)		P value
	Mean	SD	Mean	SD	
Pre-procedure	14.1	3.6	15.9	1.7	0.206
Immediate post	14.9	4.0	15.5	1.5	0.704
1 week	14.2	2.9	15.8	1.2	0.179
1 month	14.3	2.9	15.3	1.4	0.407
3 months	14.5	3.5	15.0	1.3	0.728
6 months	14.5	3.0	15.3	1.7	0.505

Intervention: IOP at pre-procedure compared with 6 months postprocedure, p=0.841
Control: IOP at pre-procedure compared with 6 months postprocedure, p=0.992

Subjective assessment of floaters 6 months after procedure:

- YAG laser vitreolysis group:
  - Pronounced improvement: 46.2%
  - Complete improvement: 30.8%
  - Limited improvement: 23%
- Control group:
  - Pronounced improvement: 25%
  - Limited improvement: 50%
  - No improvement: 25%

Objective grading of floaters 6 months after procedure (the masked evaluator rated the fundus photography):

- YAG laser vitreolysis group:
    - Pronounced improvement: 53.3%
    - Limited and complete improvement: 46.7% (exact data for each improvement were not reported separately)
- Control group:
    - Limited improvement: 62.5%
    - No improvement: 37.5%

NEI-VFQ 25: The YAG laser vitreolysis group reported a statistically significantly improvement in general vision (75.8 compared with 59.2; p=0.037) and mental health was observed compared with the sixth month values of the YAG laser vitreolysis group and the control group (84.3 compared with 70.3, p=0.048).

Key safety findings

No retinal detachment, retinal tear, uveitis, cystoid macular oedema, macular holes or other significant adverse effects were identified.

YAG laser vitreolysis:

- Temporary blurred vision during the first hour after the procedure, n=5. These cases spontaneously resolved on the first day.

Study 2 Shah CP (2017)

Study details

Study type	**Randomised controlled trial**
Country	US (single centre)
Recruitment period	2015 to 2016
Study population and number	n=52 (52 eyes; YAG laser vitreolysis, n=36; control, n=16) Patients with symptomatic Weiss ring floaters
Age and sex	YAG laser vitreolysis: mean 61.4 years Control: mean 61.1 years Both groups: 67% (35/52) female
Patient selection criteria	Inclusion criteria: symptomatic Weiss ring floater secondary to PVD; floater symptom duration of at least 6 months; PVD documented on clinical examination, optical coherence tomography, and B-scan (all performed by the same examiner; if complete PVD was not visible for all 3 modalities, the patient was excluded); a self-rated visual disturbance of at least 4 on a 0- to 10-point scale, with 0 indicating no symptoms and 10 indicating debilitating symptoms; symptomatic Weiss ring (PVD) located at least 3 mm from the retina and 5 mm from the posterior lens capsule of the crystalline lens, as measured on B-scan to maximise safety (patients with pseudophakia had no minimum required distance from the intraocular lens); ability to undergo YAG laser procedure; and acceptance of associated risks. Exclusion criteria: Snellen BCVA worse than 20/50 in the non-study eye; history of retinal tear, retinal detachment, uveitis, diabetic retinopathy, macular oedema, retinal vein occlusion, or aphakia in the study eye; and history of glaucoma or high IOP, defined as a history of glaucoma surgery or currently taking 2 or more topical glaucoma medications in the study eye.
Technique	YAG laser vitreolysis: YAG vitreolysis was done using the Ultra Q Reflex laser (Ellex Medical). After IOP was measured, the pupil of the studied eye was dilated with phenylephrine, 2.5%, and tropicamide, 1%. Proparacaine eye drops were administered, and an Ocular Karickhoff 21 mm Vitreous Lens with goniosol was applied before YAG laser administration. In all patients, laser application ceased after vaporization of the Weiss ring and all other visually significant floaters. Patients received only 1 laser treatment session to prevent unmasking of controls. Control: they were fitted with a sham lens that had a lens filter glued to the surface to prevent YAG energy from passing through the lens. The YAG laser energy was at its lowest setting of 0.3 mJ.
Follow up	6 months
Conflict of interest/source of funding	Obtained funding: all authors. Conflict of interest: none.

Analysis

IP overview: YAG laser vitreolysis for symptomatic vitreous floaters

Follow-up issues: Patients were clinically assessed at 30 minutes postoperatively and then at week 1, month 1, month 3 and month 6.

Study design issues: This single-centre, masked, sham-controlled randomised clinical trial (NCT02897583) evaluated YAG laser vitreolysis compared with sham vitreolysis for symptomatic Weiss ring floaters from PVD. Primary 6-month outcomes were subjective change in symptoms measured from 0% to 100% using a 10-point visual disturbance score, a 5-level scale, and the NEI VFQ-25. Secondary outcomes included objective change assessed by masked grading of colour fundus photography and ETDRS BCVA.

In all patients, 1 eye (the eye with the most patient-determined floater-related symptoms) was treated, and the other eye was observed. Patients were assigned to YAG and sham groups in a 2:1 ratio to maximise the number of treated patients and obtain more robust efficacy and safety data for YAG vitreolysis.

A priori sample calculations assumed a modest improvement in symptoms of 30% in the YAG group compared with 10% in the sham group, yielding a sample of 75 patients with an SD of 25%, α of .05, and power of 0.9. A planned interim analysis showed a statistically significant difference among the 13 patients who had completed the study. Thus, the decision was made to schedule no further screening visits beyond those already scheduled, resulting in 52 enrolled patients. This RCT was adequately powered.

One author did all the treatments. Another author graded the masked wide-angle photographs for the presence of floaters by using the 5-level scale used by patients to self-report their postoperative symptoms compared with baseline. The following percentages were used to quantify the level of improvement: worse, less than 0%; same, 0%; partial success, 30% to 50%; significant success, 50% to 70%; and complete success, 100%.

Study population issues: The mean duration of symptomatic floaters was 6.7 years (range, 0.5 to 63.0 years; median, 2.0 years) in the YAG group and 5.0 years (range, 0.5 to 30.0 years; median, 3 years) in the sham group.

Other issues: No adverse events judged to be of clinical relevance occurred after YAG laser vitreolysis in this small prospective study, which was underpowered to identify less common potential complications. This study included a small sample with a short follow-up period. The current study focused on comparing YAG vitreolysis with sham but not with vitrectomy. The study also allowed just 1 treatment session per patient to prevent unmasking. However, this strategy might not reflect real-world treatment, in which patients might be treated with additional YAG vitreolysis sessions for persistent floaters after initial treatment. Results from this study cannot be generalised to all patients with symptomatic floaters because only those with Weiss rings arising from PVD were treated.

Key efficacy findings

Number of patients analysed: 52 (52 eyes)

YAG laser vitreolysis (n=36):

- Initial energy per pulse: 3 mJ
- maximum energy per pulse: 7 mJ

The 36 eyes treated with YAG laser vitreolysis received a mean of 218 laser shots with a mean power of 1316 mJ.

Improvement in self-reported floater-related visual disturbance:

- YAG group, 54%; control, 9%; difference, 45%, 95% CI 25% to 64%, p<0.001

There was no appreciable learning curve effect with YAG vitreolysis; the first 10 patients reported similar improvements as the last 10 patients (54% compared with 55%; p=0.93).

10-point visual disturbance scores

Variable	YAG group (n=36)		Sham group (n=16)		Difference between YAG and sham groups at 6 months, p value
	Baseline	6 months	Baseline	6 months	
Mean±SD (95% CI)	6.4±1.6 (5.9 to 6.9)	3.3±2.5 (2.5 to 4.0)	6.4±1.9 (5.5 to 7.3)	6.3±1.5 (5.4 to 7.1)	-3.0 (-4.3 to -1.7), p<0.001
Median (range)	7.0 (4.0 to 10.0)	3.0 (0 to 7.0)	6.0 (4.0 to 10.0)	7.0 (3.0 to 8.0)	Not applicable
First quartile	5.0	1.0	5.0	5.8	Not applicable
Second quartile	7.0	3.0	6.0	7.0	Not applicable
Third quartile	7.3	5.0	8.0	7.0	Not applicable

Subjective assessment of floaters on a 5-level qualitative scale: 53% of patients (19/36) in the YAG group reported their symptoms as significantly or completely better compared with 0% in the sham group at 6 months after treatment (difference, 53%; 95% CI 36% to 69%; p<0.001).

Objective change in masked grader photographs on a 5-level qualitative scale: 94% of patients (34/36) in the YAG group had significantly improved or completely resolved floaters compared with 0% in the sham group at 6 months after treatment (difference, 94%; 95% CI 87% to 102%; p<0.001). This objective 95% improvement was significantly greater than the subjective patient-reported improvement of 53% (p<0.001).

NEI-VFQ-25 scores

Variable	YAG group (n=36)			Sham (n=16)			Difference between YAG and sham groups at 6 months	
	Baseline	6 months	P value	Baseline	6 months	P value	Difference (95% CI)	P value
General vision	72.9	69.4	0.20	60.9	53.1	0.02	16.3 (0.9 to 31.7)	0.04
Ocular pain	86.5	92.0	0.07	90.6	94.5	0.14	-2.5 (-10.8 to 5.0)	0.51
Near vision	80.9	86.8	0.2	75.8	80.5	0.23	6.3 (-4.0 to 16.7)	0.22

Variable	YAG group (n=36)			Sham (n=16)			Difference between YAG and sham groups at 6 months	
	Baseline	6 months	P value	Baseline	6 months	P value	Difference (95% CI)	P value
Far vision	80.6	90.0	<0.001	82.3	83.3	0.70	6.7 (-1.4 to 14.8)	0.10
Colour vision	96.5	99.3	0.10	95.3	95.3	>0.99	4.0 (-10 to 9.0)	0.11
Peripheral vision	88.9	94.4	0.04	89.1	82.8	0.48	11.6 (0.8 to 22.4)	0.04
General health	72.2	69.4	0.32	71.9	64.1	0.02	5.4 (-8.8 to 19.6)	0.45
Mental health	70.5	83.7	0.001	65.6	75.8	0.005	7.9 (-2.2 to 18.0)	0.12
Role difficulties	81.6	93.1	0.002	74.2	75.8	0.68	17.3 (8.0 to 26.6)	<0.001
Dependency	94.2	98.8	0.04	94.3	93.2	0.61	5.6 (0.4 to 10.8)	0.03
Driving	75.5	79.4	0.29	79.2	76.6	0.73	2.8 (-14.5 to 20.2)	0.74

Visual acuity letter scores (approximate Snellen equivalents)

Variable	Visual acuity				Difference between YAG and sham groups at 6 months
	YAG group (n=36) at baseline	Sham group (n=16) at baseline	YAG group (n=36) at 6 months	Sham group (n=16) at 6 months	
Mean±SD (95% CI)	81.7±10.3 (78.4 to 85.1) (20/25, 20/32 to 20/20)	81.9±8.1 (78.0 to 85.9) (20/25, 20/32 to 20/20)	81.6±7.7 (79.0 to 84.2) (20/25, 20/25 to 2020)	81.4±7.8 (77.2 to 85.5) (20/25, 20/32 to 20/20)	0.18 (-4.47 to 4.83), p=0.94
Median (range)	84 (31 to 95) (20/20, 20/250 to 20/12.5)	83.5 (58 to 95) (20/20, 20/63 to 20/12.5)	83.5 (50 to 90) (20/20, 20/100 to 20/16), p=0.84	84 (66 to 92) (20/20, 20/50 to 20/16), p=0.71	Not applicable
First quartile	78 (20/25)	80.5 (20/25)	79 (20/25)	77 (20/32)	Not applicable
Second quartile	84 (20/20)	83.5 (20/20)	83.5 (20/20)	84 (20/20)	Not applicable
Third quartile	88 (20/16)	86.25 (20/16)	85.25 (20/20)	86.25 (20/20)	Not applicable

The BCVA changed by -0.2 letters in the YAG group and by -0.6 in the sham group (difference, 0.4; 95% CI -6.5 to 5.3; p=0.94).

Key safety findings

No retinal tears, retinal detachments, elevated intraocular pressure, or other significant adverse events occurred in the YAG group by postoperative month 6.

YAG laser vitreolysis: one posterior chamber intraocular lens was pitted peripherally with the YAG laser when anterior floaters were treated, although this finding was not visually significant.

Sham group: a single retinal tear through lattice degeneration happened in a patient.

Study 3 Shah CP (2020)

Study details

Study type	**Case series (prospective)**
Country	US (single centre)
Recruitment period	2015 to 2016
Study population and number	n=34 (34 eyes) Patients with symptomatic Weiss ring floaters
Age and sex	Not reported
Patient selection criteria	Inclusion criteria as described in Shah (2017)
Technique	YAG laser vitreolysis as described in Shah (2017)
Follow up	Mean 2.3 years (range 1.1 to 3.0 years)
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: This study reported long-term complications and efficacy in patients enrolled in the randomised clinical trial (Shah 2017). Patients had the option of enrolling in an extension study if they received sham laser and wished to receive YAG vitreolysis treatment, or if they received YAG vitreolysis and had residual floaters that the treating surgeon felt could be treated. Therefore, patients in the previous sham group could access 1 or 2 YAG vitreolysis treatment sessions and patients in the previous YAG group could have a second or third treatment session.

All 52 patients were contacted and of these, 35 returned for this long-term observational visit. The primary outcome measures included subjective percentage of improvement (from 0% to 100%), 10-point visual disturbance score, 5-level qualitative scale and NEI VFQ-25. Secondary outcomes included objective change based on masked grading of colour wide-angle fundus photography, ETDRS BCVA, and adverse events.

Study population issues: Of the 35 patients, 27 patients were originally in the YAG vitreolysis arm and 8 patients were originally in the sham arm; 24 were phakic and 11 pseudophakic. In this cohort of 35 patients, 23 patients had a single YAG session, 11 had 2 sessions, and 1 patient had 3 sessions. One pseudophakic patient had worsening floaters and was treated with a pars plana vitrectomy. This patient was excluded in the analysis of the long-term follow-up cohort

Other issues: There were several weaknesses to this long-term follow-up study. There were no standardised guidelines dictating when additional YAG vitreolysis should be performed. There was no control arm followed to the final follow-up of this observational study, precluding the ability to calculate the inherent rate of symptomatic variation and adverse events over time in this population. Only Weiss ring floaters were included in this study; the results are unlikely transferrable to other floater types. Two important metrics, contrast sensitivity and reading speed, were not assessed during this study. Only 35 of the 52 patients enrolled in the

initial randomised controlled trial voluntarily returned for the present long-term follow-up vision, allowing for the possibility of selection bias.

Key efficacy findings

Number of patients analysed: 34 (34 eyes)

Improvement in symptoms on a 5-level scale: At final follow up, 50% (17/34) of patients stated that their floaters were significantly or completely better, compared to 41.2% of this same cohort at 6 months (p=0.47).

Subjective percentage of improvement (from 0% to 100%): There was a 59.4% improvement in symptoms compared with baseline (range, 0% to 100%; median, 80%; 95% CI 47.6% to 71.3%).

Among the 26 patients originally randomised to the YAG vitreolysis arm, floater symptoms improved non-significantly by 9.6% at the final visit compared with 6 months (range, –30 to 100; median, 1; p=0.10, 95% CI –1.4 to 20.6). Three of these patients reported diminishment of treatment effect (–30% to –15%) at final visit.

Improvement in visual disturbance (10-point scale): The improvement in the visual disturbance score compared with baseline was –3.1 (range, –10 to 2; median, –2; 95% CI –4.1 to –2.1; p<0.001).

Additional YAG laser treatments: 9 patients in the original YAG laser group had additional treatment sessions (8 patients had a second treatment session and 1 had 2 additional sessions). Of these 9 patients, there was an additional nonsignificant 17.8% improvement in symptoms at final visit compared to month 6 (range, –30 to 100; median, 10; 95% CI –2.3 to 37.9; p=0.17).

NEI VFQ-25 scores

Parameters	Baseline	Final follow up	Difference	Range	Median	95% CI	P value
Near vision activities	78.7	85.8	7.4	-25 to 50	0	1.6 to 12.6	0.016
Distance vision	84.6	89.0	4.4	-16.7 to 41.7	0	0.3 to 8.5	0.042
Mental health	71.7	85.7	14.0	-6.3 to 56.3	12.5	9.1 to 18.8	<0.001
Role difficulties	81.3	93.4	12.1	-12.5 to 75	12.5	5.6 to 18.7	<0.001

No improvements in other parameters compared with baseline.

ETDRS BCVA: difference from baseline, 0.53; 95% CI -1.3 to 2.3; p=0.57

IOP: difference from baseline, -0.09; range, -7 to 7; median, 0; 95% CI -1.2 to 1.0; p=0.88

Objective grading of floaters between baseline and final follow up:

- Worse: n=1
- Unchanged: n=1
- Significantly improved: n=7

- Completely resolved: n=25

Key safety findings

Retinal tears at 1.4 to 2.8 years: n=3

The first had a retinal tear with a cuff of fluid and a demarcation line that developed sometime between 1.4 and 2.8 years after YAG; it was observed. All of these tears were asymptomatic and detected on examination.

The second had a horseshoe tear developing between month 6 and 2.07 years that was laser demarcated. She reported new floaters within the last year of her final follow-up visit.

The third had several small pseudophakic breaks noted at the time of vitrectomy (which was done 1.4 years after YAG vitreolysis, with no tears evident during his 6-month exam) that were lasered intraoperatively. He had worsening of floaters after 1 YAG vitreolysis session at 6 months, subjectively and objectively. He was 100% improved (complete resolution on the 5-level scale) 1.5 years after vitrectomy without any postoperative complications.

Worsening of floaters: n=3

Uveitis: n=1

This male patient was diagnosed with anterior and intermediate vitritis 0.9 years after a single session of YAG vitreolysis. His workup was negative, and he responded to topical Durezol (Alcon Laboratories, Fort Worth, TX) under the management of a uveitis specialist.

Bilateral ocular hypertension: n=1

This patient was diagnosed with bilateral ocular hypertension 0.6 years after 1 session of unilateral YAG vitreolysis.

Study 4 Lin TZ (2021)

Study details

Study type	**Case series (prospective)**
Country	China (single centre)
Recruitment period	2020
Study population and number	n=51 (51 eyes) Patients with symptomatic floaters
Age and sex	Mean 56.80 years (SD 10.82); 73% (37/51) female
Patient selection criteria	Inclusion criteria: primary symptomatic floaters found on pupil-dilated vitreous and fundus examination; at least 3 months' duration of floater symptoms; floaters located at least 3 mm and 5 mm from the retina and posterior lens capsule of the crystalline lens, respectively, as assessed using a B-scan ultrasound or reference to lens thickness on oblique illumination by slit lamp in order to improve safety; ability to undertake YAG laser procedure; acceptance of related risks. Exclusion criteria: patients with peripheral retinal breaks/lattice degeneration, or a history of glaucoma, severe cataract, vitreous haemorrhage, retinal holes or macular disease.
Technique	Following the measurement of IOP, the pupils were dilated with 0.5% tropicamide and 0.5% phenylephrine. One drop of 0.4% benoxinate hydrochloride was also administered, and a Volk Singh Mid vitreous lens was placed on the eye with gel (Dikeluo® Ofloxacin Eye Ointment, Shenyang Sinqi Pharmaceutical Co., Ltd., China). YAG laser vitreolysis was done using the Ultra Q Reflex laser (Ellex Medical Lasers Ltd., Adelaide, Australia) with a maximum energy per pulse of 9 mJ. Initially, the energy was set at 5 mJ and gradually increased to an appropriate level when the creation of gas bubbles could be observed.
Follow up	6 months
Conflict of interest/source of funding	Conflict of interest: none Funding: This study, including the journal's Rapid Service Fees, was supported in part by the National Science Foundation of Liaoning Province, China (2020-MS-360). The funding organisation had no role in the design or conduct of the research.

Analysis

Follow-up issues: Patients were followed up at 1, 3 and 6 months after the procedure.

Study design issues: This study evaluated and compared the subjective and objective efficacy of YAG laser vitreolysis for 2 types of primary symptomatic floaters (complete PVD type and non-PVD type) by comparing changes in questionnaire scores and objective visual quality measures before and after treatment. The main measures of objective visual quality were as follows: the Strehl ratio (SR), internal spherical aberration (SA), internal comatic aberration (CA), internal high order aberration (HOA) and area ratio of modulation transfer function (MTFa). All values were obtained at the 4-mm zone of pupil. The main subjective measures included

VSFQ-13 and improvement in vitreous floaters using a 5-level scale. VFSQ-13 assessed symptoms related to vitreous floaters based on 6 parts of visual quality (distance activities, near activities, driving, social functioning, peripheral vision, and mental health) to determine whether the floaters were bothersome. The equivalent percentage of improvement was used: (1) worse: less than 0%; (2) the same: 0 to 30%; (3) partial success: 30% to 50%; (4) significant success: more than 50%; (5) complete success: 100%.

All procedures were done by an experienced retinal specialist (first author). During the 6-month follow-up period, all patients had YAG laser vitreolysis only once. After 6 months, rescue therapy with repeated YAG laser vitreolysis was possible, but the results were excluded from statistical analysis.

Study population issues: Of the 51 eyes with floaters, 29 (57%) were non-PVD type, and the rest were PVD type. At baseline, there were no statistically significantly differences between groups in age, gender, LogMAR BCVA, IOP, spherical equivalent, power of YAG laser and number of shots.

Other issues: There were several limitations in the study, including its small sample size, open design and short follow-up period as well as being a single-centre study and having no control group. Risk factors correlated with the poor outcomes of laser vitreolysis was not analysed because of the small sample.

Key efficacy findings

Number of patients analysed: 51 (51 eyes)

Mean laser shots: 221.22±117.15

Mean energy of laser: 7.09±1.25 mJ per pulse

Number of shots between PVD and non-PVD groups: 246.47±98.07 compared with 202.06±128.69, p=0.094

Subjective efficiency of a 5-level qualitative scale after treatment

	Worse	Same	Somewhat better	Significantly better	Complete resolution
Non-PVD	0%	17%	14%	14%	55%
PVD	14%	14%	0%	18%	55%
Total	6%	16%	8%	16%	55%

Between non-PVD and PVD groups, there was no statistically significant difference in the proportion of patients who reported their symptoms as significant or complete improvement after treatment (69% compared with 73%, p=0.344).

Seventeen of 29 (58.62%) eyes with non-PVD floaters and 18 of 22 (81.82%) eyes of PVD type could be noticed on SLO images (p=0.020). Except for the eyes with invisible floaters on SLO images, the significant or complete resolution of floater measurement in the PVD group and non-PVD group were both 100%.

Objective visual quality measures before and after treatment in all eyes

Variables	Preoperation	Postoperation	P value
SR	0.03±0.02	0.04±0.05	0.090
Internal SA	0.05±0.05	0.04±0.04	0.031
Internal CA	0.08±0.08	0.05±0.03	0.071
Internal HOA	0.23±0.22	0.16±0.07	0.044
MTF area ratio, %	26.19±14.73	29.19±17.98	0.013

Change of VFSQ-13 scores and objective visual quality measures after YAG laser vitreolysis in 2 groups

VFSQ-13	Non-PVD (n=29)	PVD (n=22)	P value
Distance activities	10.80±12.53	9.38±14.97	0.370
Near activities	10.23±16.65	3.33±10.61	0.061
Driving	2.27±7.36	1.25±15.12	0.389
Peripheral vision	9.09±19.74	5.00±10.26	0.206
Social functioning	3.41±8.78	7.50±14.28	0.133
Mental health	8.71±15.53	7.08±13.32	0.359
Composite score	7.42±9.65	5.59±9.16	0.267
Objective visual quality			
SR	0.01±0.40	0.01±0.02	0.226
Internal SA	-0.01±0.02	-0.02±0.04	0.242
Internal CA	-0.01±0.03	-0.03±0.11	0.247
Internal HOA	-0.04±0.12	-0.10±0.27	0.222
MTF area ratio, %	4.12±8.52	2.02±4.91	0.212

In the analysis of VFSQ-13, the composite score, distance activities, near activities, social functioning, peripheral vision, and mental health had all improved statistically significantly after YAG laser vitreolysis (all $p<0.05$) but not driving ($p=0.162$).

There were five eyes with high myopia (all SE≤-10.00D), 4 eyes in the PVD group and 1 eye in the non-PVD group. Three patients were satisfied with the treatment (50% to 100% improvement). Two patients in the PVD group complained of no change in floaters after treatment.

Key safety findings

No complications associated with YAG laser vitreolysis.

Worse visual quality, n=3 based on the questionnaire scores. These 3 patients complained of more tiny asteroid floaters or floater remnants.

Study 5 Sun XL (2019)

Study details

Study type	**Case series (retrospective)**
Country	China (single centre)
Recruitment period	2015 to 2017
Study population and number	n=50 (55 eyes) Patients with symptomatic vitreous floaters
Age and sex	Mean 60.34 years (SD 9.76); 50% (25/50) female
Patient selection criteria	Inclusion criteria: patients who had a diagnosis of vitreous floaters with B-ultrasound and slit-lamp microscope and had Nd:YAG laser vitreolysis; resorted to Nd:YAG vitreolysis treatment for symptomatic floaters because of life disturbance; had no systemic severe diseases and symptomatic progression of floaters within the past 2 months before recruitment. Exclusion criteria: floater(s) located within 2 mm of the retina or the crystalline lens; vitreous haemorrhage and other severe vitreous pathologic floaters; a history of intravitreal injections or intraocular surgery; complicated with vitreous proliferation, uveitis, fundus lesion, and other severe ocular diseases; risk of retinal detachment; and lost to follow-up.
Technique	Nd:YAG (Ultra Q Reflex-YAG, Ellex Medical, Australia) vitreolysis treatment: the studied eye was dilated with tropicamide eye drops preoperatively. The energy was initially set at 2.5 to 3.5 mJ and titrated to an appropriate level until plasma formation with the creation of gas bubbles. A maximum energy per pulse of 5.5 mJ was used. The number of laser shots given per patient was at the surgeon's discretion, but no more than 500 accumulative pulses within 20 min in all cases. Laser administration was ceased after vaporization of the Weiss ring and all other visually significant floaters. If there were more residual floaters, another laser treatment was performed after 1 week.
Follow up	6 months
Conflict of interest/source of funding	None

Analysis

Study design issues: This study described the treatment efficacy of Nd:YAG on vitreous floaters by evaluating the changes of floater area in fundus infrared imaging. Subjective evaluation included NEI VFQ-25 and symptom improvement on a 4-level scale: failure, floaters were the same or worse (0% to 30%); partial success, some improvement but still floaters of moderate inconvenience (31% to 70%); significant success, significant improvement with only slight inconvenience (71% to 99%); complete success, complete resolution of floaters (100%). Objective evaluation covered IOP, visual acuity, and floater areas calculated using Image J software. YAG vitreolysis was done by the same physician.

Study population issues: At baseline, patients reported intolerable floaters for 14.6±6.2 months before resorting to YAG laser treatments. Of 50 patients, 28 (56%) reported that reading activities were mostly affected by floaters, 20 (40%) for driving and one half of the patients complained the bothersome floaters all the time. Symptomatic severity of the bothersome floaters was evaluated based on the life inconvenience of patients and the IR imaging. Seventeen (30.91%) eyes were considered as severe, 21 (38.18%) were moderate, and the remaining 17 (30.91%) eyes were mild. Physically aging (n=15), PVD (n=21), and high myopia (n=13) were significant causes of floaters. The preoperative intraocular pressure was 15.71 ± 2.4 mmHg, and all study eyes had normal IOP.

Key efficacy findings

Number of patients analysed: 50 (55 eyes)

Mean laser shots for 55 eyes: n=209

Mean total energy delivered to each eye: 708 mJ (range 188 to 1,002 mJ)

Mean working time for each eye: 12.3 minutes (range 10.3 to 16.5 minutes)

1 session: n=38 eyes

2 sessions: n=17 eyes

Mean IOP: 15.71±2.4 mmHg at baseline compared with 15.34±3.27 mmHg at 6 months after treatment, p=0.23

There was also no significant change in the visual acuity in the follow-up (exact data not reported).

Mean NEI VFQ-25 score: 71.44±12.77 at baseline compared with 88.54±12.74 at 6 months (t=11.82, p=0.001)

Subjective visual symptom improvement:

- Failure: n=4 eyes, with 1 reporting worse symptoms and 3 reporting few improvements
- Partial success: n=20 eyes
- Significant success: n=23 eyes
- Complete resolution: n=8 eyes

Follow-up self-reported improvement by patients

Preoperative severity	Failure	Partial success	Significant success	Complete success
Mild (n=17)	1	3	6	6
Moderate (n=21)	0	5	10	2
Severe (n=17)	3	12	7	0
Sum	4	20	23	8

Between the 3 groups categorised by the preoperative floater severity: p=0.007.

Follow-up improvement evaluating by floater shadow areas in fundus IR images

Preoperative severity	Failure	Partial success	Significant success	Complete success
Mild (n=17)	1	2	7	7
Moderate (n=21)	1	6	11	3
Severe (n=17)	1	9	7	0
Sum	3	17	25	10

Between the 3 groups categorised by the preoperative floater severity: p=0.038.

Fundus IR imaging quantification of floater shadow areas:

Median shadow areas of floaters: 1.41 cm^2 (range 0.29 to 12.85) at baseline compared with 0.12 cm^2 (range 0 to 2.77) after treatment (t=5.849, p=0.001).

Association between VFQ-25 scores and floater areas: the shadow areas of floaters were negatively correlated with VFQ-25 scores before (r=−0.73, p=0.001) and after (r=−0.72, p=0.001) operations. In addition, there was no significant difference in the objective and subjective clinical efficacy (p=0.877).

Key safety findings

There were no significant YAG-related intraoperative complications, such as retinal detachment, fundus haemorrhage, and other pathological changes.

Mild retina haemorrhage: n=1 eye. The patient had previous severe floaters and PVD. The patient was given glucocorticoid, ocular nerve nutrient, and vitamin C for 2 weeks and had subsequently resolution. The authors considered that the inadequate distance of the focus from the retina and inappropriate delivery of energy might be the potential causes of retinal injury.

Study 6 Garcia BG (2021)

Study details

Study type	**Case series (prospective)**
Country	Spain (single centre)
Recruitment period	Not reported
Study population and number	n=34 (34 eyes) Patients with symptomatic vitreous floaters
Age and sex	Mean 57.06 years (SD 15.33); 44% (15/34) female
Patient selection criteria	Inclusion criteria: patients were over the age of 18, had phakic or pseudophakic eyes and had attended the clinic with the main complaint of symptomatic floaters, had a transparent lens or an intraocular lens without posterior capsular opacity. Exclusion criteria: acute PVD cases, patients with amblyopia or ocular pathology.
Technique	Laser vitreolysis with the Nd: YAG Ultra-Q Reflex device
Follow up	10 days after the second session
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were followed up at day 1 and week 1 after the first session of laser treatment. After 1 month, every patient had a second session. They were then followed up at days 1 and 10.

Study design issues: This pre and post-test study assessed the quality of life in patients treated with Nd:YAG laser for symptomatic floaters. Health-related quality of life of the patients was measured before and after the intervention with VFQ-25 and VFQ-39. Anxiety level was measured with STAI. Visual acuity, contrast sensitivity, and safety parameters were also considered. All patients were treated by the same medical team using the same treatment and post-treatment protocol.

Study population issues: At baseline, the percentage of frequent drivers was 67.6% and 88.2% used electronic devices daily. The mean duration of symptoms was 2.5 years (SD 3.67), with patients having had more than 2 previous consultations for vitreous floaters.

Key efficacy findings

Number of patients analysed: 34 (34 eyes)

Before and after data for VFQ and STAI

Outcome	Baseline		Posttreatment		P value
	Median	IQR	Median	IQR	
VFQ-25	73.05	19.25	93.76	8.73	<0.01
VFQ-39	74.60	19.01	95.01	6.50	<0.001
STAI	38	11	18	19	<0.001

The analyses of the items of the NEI VFQ-25 questionnaire showed that there were statistically significant differences in the subscales for general vision, near activities, distance activities, driving, ocular pain, mental health, role difficulties, dependency, and social functioning, with $p \leqslant 0.05$. The only subscale that did not achieve the statistical significance was the peripheral vision subscale (exact data for each subscale were not reported).

Subgroup analysis – comparison between different age groups (18 to 40 years, 41 to 64 years, and 65 years or above):

- NEI VFQ-25: p=0.62
- NEI VFQ-39: p=0.071
- STAI: p=0.53
- Perceived satisfaction with the treatment: p=0.45

Subgroup analysis – comparison between patients with PVD and patients without PVD

- NEI VFQ-25: p=0.91
- NEI VFQ-39: p=0.24
- STAI: p=0.15
- Perceived satisfaction with the treatment: p=0.31

Change from baseline data for myopic and non-myopic patients

Outcome	Myopic: n=20		Non-myopic: n=14		P value
	Median	IQR	Median	IQR	
VFQ-25	20.06	12.55	15.07	12.91	<0.05
VFQ-39	22.27	12.89	16.15	11.52	<0.01
STAI	-22	18.50	-9	20.75	>0.05
Satisfaction	4	2	4.5	1	>0.05

Snellen visual acuity (mean±SD): 0.74±0.29 at baseline compared with 0.76±0.32 after treatment (p=0.65)

Visual acuity with pinhole (mean±SD): 0.82±0.26 at baseline compared with 0.82±0.28 after treatment (p=0.31)

Contrast sensitivity (mean±SD): 1.43±0.23 at baseline compared with 1.59±0.19 after treatment (p<0.001)

Key safety findings

Temporary ocular hypertension: n=2. These cases were controlled to normal IOP levels with ocular hypotensive medications. The authors stated that this could be because of a dysfunction in the trabecular meshwork in older patients.

Study 7 Souza CE (2020)

Study details

Study type	**Case series (prospective)**
Country	Brazil (2 centres)
Recruitment period	2017 to 2018
Study population and number	n=32 (32 eyes) patients with symptomatic vitreous floaters
Age and sex	Mean 59.4 years (range 32 to 82 years): 61% (19/31) female
Patient selection criteria	Inclusion criteria: symptomatic floaters because of PVD, skill to undergo YAG laser vitreolysis, compliance of related risks, duration of floater symptoms of 6 months and beyond without evidence of regression, PVD presented on both clinical examination and colour fundus photographs. Exclusion criteria: BCVA worse than 20/70, history of glaucoma, retinal vein occlusion, diabetic retinopathy, retinal tear, retinal detachment, macular oedema and uveitis.
Technique	The eyes were pre-operatively dilated with phenylephrine 2.5% and tropicamide 1%. Immediately before the YAG laser treatment, proparacaine was given, and a Volk Singh MidVitreous lens with goniosol was applied to the eye. The laser instrument used was the LIGHTLas YAG laser (LightMed, San Clemente, CA, USA). The YAG laser was initially set at its lowest energy of 0.5 mJ. Only one pulse per burst was performed and all participants had only 1 laser session. Post-operative topical medications were not prescribed. Laser vitreolysis was not done if the vitreous floaters were located within 2 mm of the retina or the crystalline lens.
Follow up	6 months
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were assessed at 1-week, 2-week, 1-month, and 6-month follow ups.

Study design issues: This double-centre, interventional and prospective study evaluated the efficacy and safety of YAG laser vitreolysis in patients with symptomatic vitreous floaters, using the colour fundus imaging objective assessment and the subjective information from NEI VFQ-25. The colour fundus photographs were graded for the presence of floaters using a 5-level scale: worse (less than 0%), same (0%), partial improvement (30% to 50%), significant improvement (50% to 70%), and complete improvement (100%).

The primary outcomes were objective and subjective changes measured by masked grading of colour fundus photographs and self-reported percentage of vitreous floaters improvement, and the near and distance activities subscale of the NEI VFQ-25. Secondary outcomes included ETDRS BCVA and adverse events. All laser treatments were done by the same surgeon (first author).

Study population issues: Patients had prepapillary (single membranous ring-shaped opacities or Weiss ring) and/or central (discrete and fibrous opacities floating freely around the centre of the vitreous cavity) vitreous opacities.

Other issues: This study included a small sample which was underpowered to identify less common potential complications.

Key efficacy findings

Number of patients analysed: 32 (32 eyes)

Mean laser shots: n=366

Mean power per session: 366.7 mJ (range 102 to 528 mJ)

Colour fundus photograph outcomes:

- Complete vitreous opacity improvement: 56.2% (n=18)
- Partial improvement: 37.5% (n=12)
- No change in vitreous opacities: 6.3% (n=2)

NEI VFQ-25 before and after the procedure:

- Near visual function: z=-2.97, p=0.003, r=0.633
- Distance visual function: p=1.00

Patients stated that their floaters symptoms ameliorated in 46.1% following the YAG vitreolysis.

Visual disturbance rate improvement showed a statistically significant reduction of 2.5 after the treatment ($z=-3.97$; $p< 0.001$; $r=0.84$).

ETDRS BCVA: no change during the 6-month follow-up period (exact data were not reported).

Key safety findings

Increased intraocular pressure, intraocular lens dislocation, retinal tear, retinal detachment or recurrence of symptomatic vitreous floaters were not observed in the patients during the follow-up period. In addition, none of the patients showed significant visual decline or reappearance of vitreous floaters.

Study 8 Hahn P (2017)

Study details

Study type	**Review**
Country	US (multiple centres)
Recruitment period	2016 to 2017
Study population and number	n=15 (16 complications) Patients with complications following laser vitreolysis for symptomatic floaters
Age and sex	Not reported
Patient selection criteria	Not reported
Technique	YAG Laser vitreolysis
Follow up	Not reported
Conflict of interest/source of funding	None

Analysis

Study design issues: This retrospective assessment analysed cases of complications following laser vitreolysis as voluntarily reported to the American Society of Retina Specialists Research and Safety in Therapeutics Committee, an independent task force formed to monitor device-related and drug-related safety events, during a 6-month period.

Study population issues: Of the 15 patients, 14 patients were treated with laser vitreolysis by a comprehensive ophthalmologist and 1 patient by a retina specialist. In 14 patients, a single complication was reported, whereas in 1 patient, both glaucoma and a retinal tear were reported.

Other issues: The authors stated that this collection of reported complications, although robust, was likely underreported and not comprehensive. This type of analysis could not estimate complication rates or their relative frequencies. Nearly all reported complications were submitted by physicians other than the treating clinician, suggesting underreporting in one's own patients.

Key efficacy findings

Number of patients analysed: 15 (16 complications)

Key safety findings

Focal cataracts: n=5; of these, 3 focal cataracts were within the visual axis and 2 had associated posterior capsule rupture. Subsequent cataract extraction was done in 2 of these cases, while further details were not

available for the third. A fourth cataract was reported in the posterior cortex peripherally and was observed. The remaining case did not include details beyond the presence of cataract.

Prolonged elevation of the IOP: n=5; of these, 3 resulted in secondary glaucoma, and trabeculectomy was needed in 2 of these cases.

Retinal detachment: n=2

Retinal tear: n=1

Laser injury-related transient posterior pole retinal haemorrhage: n=2; of these, 1 patient remained asymptomatic, while the other patient had a transient scotoma that lasted a few weeks and corresponded to the area of subretinal haemorrhage with nearby retinal whitening.

An increased number of symptomatic floaters: n=1

Validity and generalisability of the studies

- Studies were conducted in Brazil (n=3), US (n=2), China (n=2) and Spain (n=1). No data were collected in the UK.
- There was some patient overlap between 2 studies (Shah 2017, 2020). However, the total sample of 255 patients was derived from removing duplications.
- Of the 8 studies, 7 studies described follow-up periods, with most studies (n=5) reporting 6-month outcomes.
- There was variation in patient inclusion criteria (such as types of floaters) and procedure technique (such as laser energy delivered, number of sessions, and durations between sessions) between studies. Most studies required patients to have symptoms for at least 6 months.
- When reported, in most patients 1 eye was treated and a single session was done.
- Two randomised controlled trials were included, with 1 trial being adequately powered and of good methodological quality.
- Both randomised controlled trials compared YAG laser vitreolysis with sham YAG laser vitreolysis. There might be a placebo effect on some subjective improvement in the sham group by the stimulated procedure.
- There were different devices used for this procedure. It was unclear whether all these devices were licensed for vitreolysis.
- Floaters can reduce with time, although most studies required that floaters had been present for at least 6 months, so resolution might be less likely by that stage. Nonetheless, the lack of a control group in some studies makes it difficult to distinguish a treatment effect from natural history.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

There is currently no NICE guidance related to this procedure.

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

Three professional expert questionnaires for YAG laser vitreolysis for symptomatic vitreous floaters were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Company engagement

A structured information request was sent to 2 companies who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

Ongoing trials:

- YAG laser vitreolysis for floaters (NCT03970148); single group assignment; Croatia; estimated enrollment, n=100; estimated study completion date, December 2020 (no study results published).

References

1. Ludwig GD, Gemelli H, Nunes GM et al. (2021) Efficacy and safety of Nd:YAG laser vitreolysis for symptomatic vitreous floaters: a randomized controlled trial. European journal of ophthalmology 31(3): 909-14
2. Shah CP and Heier JS (2017) YAG laser vitreolysis vs sham YAG vitreolysis for symptomatic vitreous floaters: a randomized clinical trial. JAMA ophthalmology 135(9): 918-23
3. Shah CP and Heier JS (2020) Long-term follow-up of efficacy and safety of YAG vitreolysis for symptomatic Weiss ring floaters. Ophthalmic surgery, lasers & imaging retina 51(2): 85-8
4. Lin TZ, Li TT, Zhang XM et al. (2021) The Efficacy and Safety of YAG Laser Vitreolysis for Symptomatic Vitreous Floaters of Complete PVD or Non-PVD. Ophthalmology and Therapy. https://doi.org/10.1007/s40123-021-00422-6
5. Sun XL, Tian JY, Wang JY et al. (2019) Nd:YAG laser vitreolysis for symptomatic vitreous floaters: application of infrared fundus photography in assessing the treatment efficacy. Journal of Ophthalmology. https://doi.org/10.1155/2019/8956952
6. Garcia BG, Orduna Magan C, Alvarez-Peregrina C et al. (2021) Nd:YAG laser vitreolysis and health-related quality of life in patients with symptomatic vitreous floaters. European Journal of Ophthalmology
7. Souza CE, Lima LH, Nascimento H et al. (2020) Objective assessment of YAG laser vitreolysis in patients with symptomatic vitreous floaters. International Journal of Retina and Vitreous, 6:1
8. Hahn P, Schneider EW, Tabandeh H et al. (2017) Reported complications following laser vitreolysis. JAMA Ophthalmology, 135 (9); 973-6

Literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	08/06/2022	1946 to June 07, 2022
MEDLINE In-Process (Ovid)	08/06/2022	1946 to June 07, 2022
MEDLINE Epubs ahead of print (Ovid)	08/06/2022	June 07, 2022
EMBASE (Ovid)	08/06/2022	1974 to 2022 June 07
EMBASE Conference (Ovid)	08/06/2022	1974 to 2022 June 07
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	08/06/2022	Issue 5 of 12, May 2022
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	08/06/2022	Issue 5 of 12, May 2022
International HTA database (INAHTA)	08/06/2022	n/a

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Literature search strategy

Number	Search term
1	Eye diseases/ or Vision Disorders/
2	Vitreous Body/
3	1 and 2
4	(vitre* adj4 (opacit* or degenerat* or disorder* or disease* or disab* or impair* or abnormal* or disturb*)).tw.
5	(floater* or musca* volitan*).tw.
6	Vitreous Detachment/
7	(vitre* detach* or PVD).tw.
8	(Weiss* ring* or Martegiani* ring*).tw.
9	or/3-8
10	Laser Therapy/ or Lasers, Solid-State/ or Lasers/
11	(YAG* or Neodymium-YAG* or Nd:YAG* or Nd-YAG* or yttrium alumin?um garnet).tw.
12	(laser* adj4 (therap* or surg* or treatment* or procedur* or operat* or cut* or non-thermal* or pulse* or solid-state* or q-switched or ablat* or photoablat* or knife or knives or scalpel*)).tw.
13	(vapori* or vapouri*).tw.
14	Vitreolysis.tw.
15	or/10-14
16	Tango Reflex*.tw.
17	Ultra Q Reflex*.tw.
18	16 or 17
19	9 and 15
20	18 or 19
21	animals/ not humans/
22	20 not 21

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Broadhead GK, Hong T and Chang AA (2020) To treat or not to treat: management options for symptomatic vitreous floaters. Asia-Pacific journal of ophthalmology (Philadelphia, Pa.) 9(2): 96-103	Review	Treatment seems to be more effective with the use of vitrectomy to remove floaters as compared with YAG vitreolysis, although currently there are no prospective trials comparing and assessing these treatments. When indicated, vitrectomy for floaters is an effective means of treating what may be a visually distressing phenomenon, although patients should be fully counselled regarding possible surgical complications.	Review article
Cowan LA, Khine KT, Chopra V et al. (2015) Refractory open-angle glaucoma after neodymium-yttrium-aluminum-garnet laser lysis of vitreous floaters. American journal of ophthalmology 159(1): 138-43	Case series n=3	Secondary open-angle glaucoma is a complication of Nd:YAG vitreolysis for symptomatic floaters that may present with an increase in intraocular pressure immediately, or many months after the surgery. Furthermore, this complication may be permanent and require chronic medical therapy or glaucoma surgery.	Small sample
Delaney YM, Oyinloye A and Benjamin L (2002)	Non-randomised	The results showed Nd:YAG vitreolysis to be a safe but only moderately effective	Limited efficacy data were reported.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Nd:YAG vitreolysis and pars plana vitrectomy: surgical treatment for vitreous floaters. Eye (London, England) 16(1): 21-6	comparative study n=31	primary treatment conferring clinical benefit in one third of patients. Pars plana vitrectomy, while offering superior results, should be reserved for patients who remain markedly symptomatic following vitreolysis, until future studies further clarify its role in the treatment of patients with floaters and posterior vitreous detachment.	Studies with larger samples or better design are included.
Frankhauser F, Kwasniewska S and van der Zypen E (1985) Vitreolysis with the Q-Switched laser. Archives of ophthalmology, 103(8): 1166-71	Case series 10 eyes treated for floaters for thickened posterior hyaloid membranes	Since laser vitreolysis is able to solve a number of clinical problems, obviating the need for vitrectomy, the former procedure should receive increasing attention for the treatment of pathologic problem in the vitreous cavity.	Small sample
Huang KH, Weng TH, Chen YJ et al. (2018) Iatrogenic posterior lens capsule rupture and subsequent complications due to Nd:YAG laser vitreolysis for vitreous floaters: a case report. Ophthalmic surgery, lasers & imaging retina 49(11): e214-e7	Case report n=1	Nd:YAG laser vitreolysis has the potential to cause disastrous complications, even though it could be an option for treating visually significant vitreous strands and floaters. Nevertheless, these side effects should be kept in mind, and the procedure should be performed with great caution, particularly in young and phakic patient groups.	Single case report
Hosseini H, Mehryar M and Farvardin M (2008) Triamcinolone-	Case report n=1	This study described the application of triamcinolone-assisted neodymium: YAG laser vitreolysis. This	Small sample

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
assisted neodymium: YAG laser vitreolysis. Ophthalmic surgery, lasers & imaging: the official journal of the International Society for Imaging in the Eye 39(3): 234-6		approach could be a useful addition to the application of laser use in similar cases. Adding this step could facilitate the procedure and increase the success rate. However, significant complications can occur within this procedure and caution must be exercised not to generalise too widely on the base of this case.	
Katsanos A, Tsaldari N, Gorgoli K et al. (2020) Safety and efficacy of YAG laser vitreolysis for the treatment of vitreous floaters: an overview. Advances in therapy 37(4): 1319-27	Review	The currently available evidence offers some indications that YAG laser vitreolysis may be a viable option for the symptomatic relief of selected patients with bothersome complaints due to vitreous opacities. In particular cases with chronic Weiss rings may represent a patient group that will likely benefit the most from this procedure. On the other hand, notwithstanding how annoying the symptoms can be, the safety profile of this treatment seems far from optimal considering that the presence of vitreous floaters is not a vision-threatening condition.	Review article
Koo EH, Haddock LJ, Bhardwaj N et al. (2017) Cataracts induced by neodymium-yttrium-aluminium-garnet laser lysis of vitreous floaters. The British journal	Case series n=2	Secondary cataract formation accompanied by loss of integrity of the posterior capsule is a potential complication of Nd:YAG laser vitreolysis for symptomatic floaters.	Small sample

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
of ophthalmology 101(6): 709-11			
Lim JI (2017) YAG laser vitreolysis-is it as clear as it seems? JAMA ophthalmology 135(9): 924-5	Review	Authors concluded that opacities close to the lens and underlying vital structures should not be treated with YAG laser because of the risk of damage to the lens and retina. In addition, thick membranes that require higher energies or eyes with vitreous haze, which could scatter laser energies, and perhaps very mobile opacities should also be excluded. Larger studies are needed to determine the true incidence of retinal tears, retinal pigment epithelium damage, and long-term effects from vaporising the vitreous.	Review article
Little HL and Jack RL (1986) Q-switched neodymium: YAG laser surgery of the vitreous. Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie 224(3): 240-6	Case series n=56 (59 eyes) Vitreous opacities, n=25 eyes	Vitreous results for Nd: YAG vitreous surgery are less dramatic than those obtained in posterior capsulotomies. This difference in visual results is explained by the presence of associated retinal pathology in eyes with vitreous pathology. The best results with treatment occurred in diabetic eyes having flat retinas with vitreous haemorrhage, with or without attachments of the posterior hyaloid to disc fronds. Eight of 18 such eyes had objective and subjective visual improvement.	Different indications were included and the sample for vitreous floaters was small.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Liu XD, Wang Q and Zhao J (2020) Acute retinal detachment after Nd:YAG treatment for vitreous floaters and postertior capsule opacification: a case report. BMC ophthalmology 20(1): 157	Case report n=1	As myopic patients are at risk of developing retinal detachment; Nd:YAG vitreolysis and capsulotomy should be performed with caution. The laser energy should be as low as possible and careful focus is necessary to reduce interference to the retina.	Small sample
Luo JH, An XJ and Kuang Y (2018) Efficacy and safety of yttrium-aluminium garnet (YAG) laser vitreolysis for vitreous floaters. The Journal of international medical research 46(11): 4465-71	Case series n=30	The results showed that YAG laser vitreolysis was a well-tolerated and effective treatment for vitreous floaters. Randomised, controlled trials involving large numbers of participants monitored over an extended follow up period are required to confirm these results.	Studies with larger samples or better design are included.
Milston R, Madigan MC and Sebag, J (2016) Vitreous floaters: Etiology, diagnostics, and management. Survey of ophthalmology 61(2): 211-27	Review	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	Review article

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
		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.	
Nguyen JH, Nguyen-Cuu J, Yu F et al (2019) Real-world assessment of vitreous structure and visual function after Nd:YAG laser vitreolysis. Ophthalmology, 126(11): 1517-26	Non-randomised comparative study (retrospective) n=132 (38 with floaters that were treated by Nd:YAG, 35 without floaters, and 59 with untreated floaters)	As a group, patients previously treated with Nd:YAG for bothersome vitreous floaters had less dense vitreous, but similar visual function as untreated controls with vitreous floaters. Since some treated eyes had less dense vitreous and better visual function than untreated controls.	Limited data relating the efficacy of the procedure were reported.
Noristani R, Schultz T and Dick HB (2016) Cataract formation after YAG laser vitreolysis: importance of femtosecond laser anterior capsulotomies in perforated posterior capsules. European journal of	Case report n=1	YAG laser vitreolysis presents a new and promising therapeutic approach for floaters. However, the complications are unknown. Authors describe the induction of cataract as a major complication.	Small sample

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
ophthalmology 26(6): e149-e151			
Ruiz-Moreno JM (1998) Retinal detachment after vitreolysis with the Nd:YAG laser. Lasers and Light in Ophthalmology 8(4): 231-3	Case series n=10	Based on the results, authors did not think that vitreolysis by photodisruption with the Nd:YAG laser should be used for the treatment of vitreous floaters in pseudophakic patients, due to the high risk of causing serious complications, such as retinal detachment.	Small sample
Ryan EH (2021) Current treatment strategies for symptomatic vitreous opacities. Current opinion in ophthalmology 32(3): 198-202	Review	Patients with severe, persistent symptomatic vitreous opacities are highly motivated to seek relief of their symptoms. Pars plana vitrectomy appears to be far more effective than does YAG laser vitreolysis. Given the lack of readily available objective measurements of the density of vitreous opacities, a thorough history, good clinical examination, and excellent judgment is critical to creating a good outcome. Extra caution regarding recommending surgery should be exercised when the patient is phakic and or has not yet had a vitreous detachment.	Review article
Sendrowski DP and Bronstein MA (2010) Current treatment for vitreous floaters. Optometry (St.	Review	In terms of ‘‘off-label’’ treatment, laser and surgical options for vitreous floaters have not been adequately defined. The primary purpose of ‘‘off-label’’ laser and surgical options are the alleviation of symptoms	Review article

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Louis, Mo.) 81(3): 157-61		associated with vitreous floaters. A secondary benefit may be the reduction of the patient's mental stress created by the floaters. Alternately, the primary risks of ''off-label'' use of laser and surgical options are the unwanted ocular complications of retinal tears, vitreoretinal haemorrhages, endophthalmitis, and retinal detachments. Currently, there are no clinical studies that provide adequate information about the ocular benefits or complications associated with such treatment options. Although patient symptomology from vitreous floaters can be reduced or in some cases alleviated by laser or surgical intervention, the patient benefit may not offset the potential risk from the procedure. The decision for treatment of symptomatic vitreous floaters should be done on a case-by-case basis. Patient annoyance, stress, and anxiety created by the vitreous floaters is an important factor in that decision-making process.	
Shah CP and Fine HF (2018) Management of floaters. Ophthalmic Surgery Lasers and	Review	For those still bothered by a discrete floater after 6 months of observation, author will consider referring for YAG vitreolysis. Among those with more diffuse	Review article

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Imaging Retina 49(6): 388-91		floaters or for those who have failed YAG vitreolysis, author will have several ongoing discussions about vitrectomy surgery, consciously focusing on the risks, and will proceed for the right patient, all the while hoping to do no harm.	
Shields RA, Cheng OT, Ruby AJ. et al. (2021) Retinal complications after yttrium-aluminum-garnet laser vitreolysis for vitreous floaters. Ophthalmic Surgery Lasers and Imaging Retina 52(11): 610-3	Case series n=2	The first patient developed a vitreous haemorrhage and subsequent branch retinal vein occlusion from laser damage to a major retinal venule. The second patient developed a temporal scotoma from a full-thickness retinal break in the posterior pole requiring laser retinopexy, As evidenced by the two cases presented here, extreme care must be taken during YAG laser vitreolysis in titrating the laser's power and selecting the distance of focus from the lens, retina, or both.	Small sample
Singh IP (2020) Modern vitreolysis-YAG laser treatment now a real solution for the treatment of symptomatic floaters. Survey of ophthalmology 65(5): 581-8	Review	The new illumination design, coupled with the modified laser energy delivery system, may represent an alternative option to vitrectomy in management of clinically significant floaters in carefully selected patients; however, randomised, controlled clinical trials with large cohorts and long-term follow-up are necessary to optimally assess the efficacy and safety of laser vitreolysis.	Review article

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Singh IP (2018) Novel OCT application and optimized YAG laser Enable visualisation and treatment of mid- to posterior vitreous floaters. Ophthalmic surgery, lasers & imaging retina 49(10): 806-11	Case series n=2	The results suggest that, with proper equipment, training and technique, laser vitreolysis may be an effective and safe treatment for mid- to posterior vitreous floaters. Prospective, randomised clinical trials are in progress and needed to confirm these findings.	Small sample
Stonecipher KG (2016) Laser vitreolysis for floaters: this safe and effective procedure is well within the scope of any ophthalmologist. Cataract & Refractive Surgery, 48-50	Review	Laser vitreolysis has become a positive addition to clinical practice. The treatment is safe, effective and painless with a very low complication rate. The bottom line is that the procedure has enabled scores of patients to achieve functional improvements in their vision and greatly improved their quality of life the process.	Review article
Su D, Shah CP and Hsu J (2020) Laser vitreolysis for symptomatic floaters is not yet ready for widespread adoption. Survey of ophthalmology 65(5): 589-91	Review	Treatment with laser vitreolysis, the use of an Nd:YAG laser to vaporise the collagenous vitreous opacities appears to be used more frequently; however, data regarding long-term safety and effectiveness are lacking. Laser vitreolysis of symptomatic floaters should not be routinely performed without additional studies documenting its safety and long-term efficacy.	Review article

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Sun IT, Lee TH and Chen CH (2017) Rapid cataract progression after Nd:YAG vitreolysis for vitreous floaters: a case report and literature review. Case Reports in Ophthalmology 8(2): 321-325	Case report and literature review n=1	Although Nd:YAG vitreolysis has been reported as an effective and less invasive treatment for symptomatic vitreous floaters, it should be used carefully, especially in phakic eyes. Crystalline lens injuries and rapid cataract progression may occur following Nd:YAG vitreolysis. While dealing with this type of complicated cataract, we should be aware of the possibility of posterior lens capsule rupture during surgery and the need for combined vitrectomy. Further prospective studies are necessary to evaluate the efficacy and safety of Nd:YAG vitreolysis.	Small sample
Tassignon MJ, Stempels N and Brihaye M. (1989) Indications for Q-switched Nd-YAG laser in vitreous pathology. Lasers and Light in Ophthalmology 2(3): 163-72	Case series n=71 eyes vitreous floaters, n=3 eyes	Nd: YAG laser treatment should be considered as the first choice in important vitreous floaters. This treatment has several advantages over vitrectomy.	Small sample
Thompson JT (2018) Much ado about nothing (or something): what is the role of vitrectomy and Yttrium-Aluminum-Garnet laser for vitreous floaters? Ophthalmology Retina 2(9): 879-80	Review	The appropriate use of vitrectomy and YAG laser vitreolysis for symptomatic vitreous floaters remains uncertain. Contrast sensitivity testing using the Freiberg vision test may provide further quantitative evidence of visual impairment. This information can assist in making a	Review article

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		decision about whether to recommend vitrectomy or YAG vitreolysis for symptomatic vitreous floaters. Randomised studies with long-term follow-up are needed to define the optimal treatment and to refine the indications for treating symptomatic vitreous floaters.	
Tsai WF, Chen YC and Su CY (1993) Treatment of vitreous floaters with neodymium YAG laser. The British journal of ophthalmology 77(8): 485-8	Case series n=15	Although authors confined the indications for treatment to very strict criteria, by accumulating samples and experience, Nd-YAG laser may prove to be a safe and ideal method for treatment of all persistent vitreous floaters in the future.	Small sample
Van der Veken A, Van de velde F, Smeets B et al. (1997) Nd:YAG laser posterior hyaloidotomy for the treatment of a premacular vitreous floater. Bull Soc Belge Ophtalmol, 265: 39-43	Case report n=1	The finding suggests that a fragment of the neurosensory retina became detached together with the internal limiting membrane in the process of the vitreous collapse.	Single case report
Vandorselaer T, Van De Velde F an; Tassignon MJ (2001) Eligibility criteria for Nd-YAG laser treatment of highly symptomatic vitreous floaters. Bulletin de la Societe belge	Case series n=9	Vitreous floaters are frequently found in daily practice and may occasionally cause important visual and psychological impairment. The Nd-YAG laser is currently the most innocuous and least invasive technique for treating highly symptomatic floaters.	Small sample

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d'ophtalmologie: 15-9		Vitreolysis is successful in case of well-suspended condensations. Ill-suspended floaters are associated with a low success rate. If 1 or 2 laser sessions are unsuccessful, vitrectomy remains the only alternative.	