RESEARCH SUBJECT INFORMATION AND CONSENT FORM

1.1 TITLE:

1.2 A Single-center, Prospective Study Evaluating the Safety and Efficacy of YAG Vitreolysis for Symptomatic Weiss Ring Due to Posterior Vitreous Detachment

1.3 PROTOCOL NO.: YAG-001

SPONSOR: Center for Eye Research and Education, Boston, MA

1.4 INVESTIGATOR: Chirag P. Shah, MD, MPH

PHONE NUMBER: (800) 635-0489

SITE(S): Ophthalmic Consultants of Boston
50 Staniford Street, Suite 600
Boston, MA 02114

VERSION & DATE: Version 1, October 25, 2014

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You are invited to participate in a research study. However, before you give your consent to be a volunteer, we want you to read this consent form and ask as many questions as necessary to be sure that you understand what your participation will involve.

NATURE AND PURPOSE OF THE STUDY

You are being asked to participate in this study because you have symptoms of floaters from a posterior vitreous detachment (PVD). Currently standard of management for floaters is observation, although treatment with a surgery called vitrectomy is sometimes performed. The purpose of this study is to evaluate the safety and efficacy of treating the floater with an in-office YAG (yttrium aluminum garnet) laser procedure. The YAG laser is not approved by the Food and Drug Administration (FDA) to treat floaters but is FDA approved to remove a film that occasionally grows behind a lens implant after cataract surgery (posterior capsulotomy) and to make a small hole in the colored part of the eye to treat glaucoma (iridotomy).All eligible participants will be assigned randomly (like the

flip of a coin) to receive either the YAG laser (67% chance) or a fake (sham) laser (33% chance) procedure. Follow-up visits will occur at one week, one month, three months, and six months after the laser procedure. There will be a total of 5 study visits lasting six months. Only one laser session will be performed at the first study visit.

SUBJECT SELECTION

You are being offered an opportunity to participate in this research study because you are symptomatic with floaters in an eye for at least 6 months that correlates to a floater observed in the eye called a posterior vitreous detachment Weiss ring.

The study will enroll 75 participants at Ophthalmic Consultants of Boston in a 2:1 randomization of YAG laser to fake (sham) laser.

STUDY DURATION

A screening visit is required and will take place on the same day as the start of the research study to determine if you qualify and are willing to participate. If the study doctor decides you are qualified and you agree to participate in this study, you will receive either the YAG laser procedureor sham laserprocedure, followed by check-ups one week, one month, three months, and six months after your procedure. The study duration is a total of 6 months.

STUDY PROCEDURES

Should you decide to participate, you will first sign this Subject Information and Consent Form before any study-related procedures are performed. You will be asked about your medical history, family history, and demographic information. The following is a description of the procedures that will be performed during this study:

Eye Exams

At each visit you will have an eye examination. Your vision will be checked at each study visit. You will receive a numbing eye drop so that the eye pressure can be checked. The fluid pressure in the eye will be checked with a device called applanation tonometry. Your pupils will be dilated with eye drops so that the study doctor can examine your eye (slit lamp/indirect ophthalmoscopy). The study doctor will then use special lenses to look at your retina under high magnification and will gently push on the outside of the eye during exam (scleral depression). These procedures are all part of a standard retina exam by an eye doctor.

At the first and last visits, you will also have a picture of the retina taken by a device called spectral domain optical coherence tomography (SD-OCT),a photograph picture of your retina taken by a machine called Optos,and an ultrasound imaging test (B-scan) of the floaters.

At the first visit, you will have an ultrasound test (A-scan) to determine the axial length of the study eye.

Questionnaires
At the first and last visits, you will complete two questionnaires about your floaters and about how your vision affects your daily life (VFQ-25).

YAG or Sham Laser Procedure
During your first visit, you will receive either a YAG laser or a sham laserprocedure. You will not know which group you will be a part of. The laser procedure will begin with a numbing drop placed into the eye. Then a lens will be placed on the eye to focus the laser. The laser will then be performed. Afterwards, the lens will be removed and the fluid pressure inside the eye will be checked 30 minutes after the procedure using a device called applanation tonometry.

PHYSICIAN AVAILABILITY

A physician will be present at the time of the laser or sham laser procedureand on-call at all other times. In the event of any type of medical emergency, the study doctor will be on call and available, throughout the study.

RISK AND DISCOMFORTS

Likely effects and risk of research on the subjects:

<u>Risks of Laser Treatment</u>
The risks of YAG laser treatment that occur in about 1 in every 100 patients are an increased eye pressure, glaucoma and cataract formation. Risks that occur in about 1 in every 1000 patients are eye inflammation, retinal tear, retinal detachment, retinal edema, and optic nerve injury.. The minor side effects include conjunctival hemorrhage (bleeding outside the eye), eye redness and irritation, headache, or new floaters.

Anesthetic drops and a contact lens will be used as part of the laser procedure. Risks associated with their use include allergic reaction, infection, and corneal abrasion (scratch on the clear front surface of the eye). If any of these problems occur, they will be treated and usually clear up rapidly.

Risks of Intraocular Pressure Test

The instrument used to measure the pressure inside your eye could cause a corneal abrasion (scratch on the clear front surface of your eye). If this occurs, it will be treated and usually clears up rapidly.

BENEFITS

It is understood that participation in this study may not derive any direct medical benefits to you. You may have a good response to treatment; however, it is possible that you may not see an improvement in your condition. Information from your participation in this study may benefit persons with symptomatic floaters from posterior vitreous detachment Weiss ring in the future.

COSTS AND REIMBURSTMENTS

You will not receive payment for your participation in this study.

Research Procedures

The laser procedure, eye exams, and all imaging tests will be provided free of charge through the Center for Eye Research

IN CASE OF INJURY

It is important that you tell your study doctor if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call him or her at the telephone number listed on the first page of this form. You will get medical treatment if you are injured as a result of taking part in this study. Your study doctor will explain the treatment options to you and tell you where you can get treatment.

The study sponsor will pay for the reasonable costs of all diagnostic procedures and medical treatment for illness or injuries that are the result of your participation in the study, if the costs are not covered by your medical insurance. In the case of injury resulting from the study, you do not lose any of your legal rights to seek payment or any other legal rights by signing this form.

PREGNANCY STATEMENT

YAG laserproceduredoes not pose any risk for patients who are pregnant.

TREATMENT ALTERNATIVE

Taking part in this study is voluntary. Your study doctor will keep you informed of other treatment options which may include one of the following options:

- Observation
- Pars plana vitrectomy which is surgical removal of the vitreous in the operating room

Please discuss these and other options with your doctor and the study doctor.

OFFER TO ANSWER ANY QUESTIONS ABOUT THIS STUDY

If you have any questions or problems during this study, or if you think that you may have experienced a research-related injury, you should contact Dr. Chirag Shah at (800) 635-0489.

If you have any questions regarding your rights as a research volunteer, please contact Sterling Institutional Review Board at 888-636-1062 during regular working hours. Sterling Institutional Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study.

USE AND DISCLOSURE OF MEDICAL INFORMATION

As part of this study, Dr. Shah, the Study Doctor, and his team at the research facility will keep records of your participation in this study. These study records will include personal information that you provide including your age, sex, etc., the results of procedures and tests you undergo during the study or had before the study, information about your response to treatments you receive under the study, and other medical information relating to your participation in the study. Under federal law your study records cannot be used or disclosed for research purposes unless you sign this authorization. You may not participate in the study unless you sign this authorization. If you sign this informed consent form, you will be agreeing to the disclosures described below:

a. Your study records and medical records may also be reviewed by Sterling Institutional Review Board which is an ethics committee that reviews the conduct of human research studies.

The research facility and the Sterling Institutional Review Board will review and use your study records only for purposes of this study. They will keep your identity confidential and, except for the disclosures described above, will not disclose your study records to other parties unless disclosure is required by law. Once the research facility discloses information in your study records or medical

records to the Sponsor or its consultants, the information will no longer be protected by federal law. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. However, the investigator will only use your information for purposes of the study and will not disclose your study records to parties unless disclosure is required by law. If reports or articles are written about the study, you will not be identified by name in them. Your study records may be retained at the research facility indefinitely following the completion of the study. You will not have the right to review your records while the research is in progress. However, you will be able to review your records after the research has been completed.

This authorization has no expiration date. However, you have the right to revoke this authorization at any time. You can do this by giving written notice to the study doctor, informing them that you are revoking your authorization to use and disclose medical information. The study doctor's contact information is on page 1 of this document.

If you revoke this authorization to use and disclose your medical information, you will not be permitted to continue your participation in the study after the revocation. If you drop out of the study, you do not have to revoke your authorization to use and disclose your medical information. However, if you drop out of the study and do decide to revoke your authorization to use and disclose your medical information, the information that has already been collected in your study record may continue to be used and disclosed as described above, however, no new information will be obtained or added.

CLOSING STATEMENT

You have read and understood the information which has been stated above and have received satisfactory answers to all of questions which you have asked and you willingly sign this consent form. You will receive a copy of the signed informed consent. You hereby consent to be a participant in this study.

PATIENT'S DECLARATION:

RIGHT TO WITHDRAW OR REMOVAL FROM STUDY

I understand that I am free to withdraw from this study at any time, and I agree to inform the physician immediately if I intend to withdraw. It is understood that my decision to participate in this study or to withdraw from this study will not influence the availability of my future medical care and will involve no penalty or loss of benefits to which I am otherwise entitled.

I agree that the physician in charge of the study can remove me from this study without my consent for any reason, including, but not limited to:
a. His/her judgment that any condition or circumstance that may jeopardize my welfare or the integrity of the study.
b. My failure to follow the instructions of the investigator(s).
c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

SIGNATURES

I have read in a language that I understand well, the above information, 7 pages total. The content and meaning of this information has been explained to me. I hereby voluntarily consent and offer to take part in this study and authorize the use and disclosure of my medical information.

_____	_____	_____
Date	Print Subject Name	Subject Signature

_____	_____	_____
Date	Name of Person conducting the Informed Consent discussion	Signature of Person conducting the Informed Consent discussion

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Clinical Study Protocol

A Single-center, Prospective Study Evaluating the Safety and Efficacy of YAG Vitreolysis versus Sham for Symptomatic Weiss Ring Due to Posterior Vitreous Detachment.

Clinical Phase:	Prospective, Phase II
Protocol #:	YAG-001
Date:	Amendment 1 26 January 2015
Principle Investigator:	Chirag P. Shah, MD, MPH

Clinical Study Protocol Synopsis

TITLE	A Single-center, Prospective Study Evaluating the Safety and Efficacy of YAG Vitreolysis versus Sham for Symptomatic Weiss Ring Due to Posterior Vitreous Detachment.

SITE LOCATION(S)	Ophthalmic Consultants of Boston, 50 Staniford Street, Suite 600, Boston, MA 02114
PRINCIPAL INVESTIGATOR	Chirag P. Shah, MD, MPH

STUDY DURATION	24 months (includes an 18-month enrollment period, and an observation visit at month 6 for each subject)
ESTIMATED STUDY COMPLETION DATE	December 2016
POPULATION	
SAMPLE SIZE:	75 subjects
TARGET POPULATION:	Treatment-naive patients with symptomatic Weiss ring for at least 6 months who accept the risks of laser.

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TREATMENT(S)

Laser

Iridex yttrium aluminum garnet (YAG) laser

Procedure:

Subjects will be randomized in a 2:1 ratio to YAG vitreolysis versus sham YAG. Patients will have intraocular pressure checked by applanation tonometry before and 30 minutes post-procedure. Patients will be dilated with phenylephrine 2.5% and tropicamide 1% and receive proparacaine prior to YAG laser. No post-operative eye drops will be administered. A Karickoff lens with goniosol will be used to perform the YAG vitreolysis. The number of shots will be determined at the discretion of the treating physician. Single shot mode will be used. The maximum energy per pulse will be 7 mJ. The endpoint of treatment is the disruption of the Weiss ring into smaller fragments as well as any other vitreous opacities deemed visually significant by the treating physician. Only one treatment session will be performed.

Sham laser treatment will be applied under the same procedure used for laser treatment but without switching on the laser beam and by imitating depression of the laser pedal.

ENDPOINT(S)

Primary: To determine patients' subjective improvement in floater symptoms based on the floater-specific

	questionnaire.
Secondary:	• Mean change in visual acuity from Baseline as measured by ETDRS vision testing at 6 months • Mean change in baseline in the National Eye Institute Visual Functioning Questionnaire-25 (NEI VFQ-25) near activities subscale • Mean change in baseline in the National Eye Institute Visual Functioning Questionnaire-25 (NEI VFQ-25) distance activities subscale • Qualitative changes on infrared and color photography • Incidence and severity of ocular and systemic adverse events

PROCEDURES AND ASSESSMENTS	At Baseline – • Patients complete questionnaire regarding: duration of floater symptoms prior to presentation, severity of floater symptoms, number of floaters, and activity most inconvenienced by presence of floaters • Medical, ocular history and demographics collected • ETDRS and Snellen best-corrected visual acuity • Optos (Scotland, UK) color photography • Heidelberg Spectralis Optical Coherence Tomography (OCT) and infrared photo (Heidelberg Engineering, Germany) • B scan ultrasound of Weiss ring with caliper measurement of nearest distance between: 1. Weiss ring and retina, 2. Weiss ring and posterior lens capsule (only in phakic eyes) • Slit lamp and indirect ophthalmoscopy with scleral depression of study eye • Applanation tonometry • Visual Functioning Questionnaire-25 (VFQ 25) At week 1, month 1, month 3 • Non-best-corrected Snellen visual acuity • Slit lamp and indirect ophthalmoscopy with scleral depression of study eye • Applanation tonometry At month 6 • ETDRS and Snellen best-corrected visual

	acuity • Optos color photography • Heidelberg Spectralis OCT and infrared photo • Slit lamp and indirect ophthalmoscopy with scleral depression of study eye • Applanation tonometry • Assessment of floater symptoms questionnaire • VFQ 25 questionnaire
Statistical Plan	This study will enroll 75 patients. Sample calculations show that 48 patients are needed to show a symptomatic improvement on a 10-point scale from 6 to 3 with a standard deviation of 3 with an alpha of 0.05 and power of 0.9. Further, 75 patients are needed to show a difference between YAG and sham groups at month 6 reporting partial success (30% improvement) and failure (10% improvement) with a standard deviation of 25%, alpha of 0.05, and power of 0.9.

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2. INTRODUCTION AND RATIONALE

2.1 Introduction

Changes in the vitreous occur throughout life and can often lead to symptomatic floaters. In youth, hyaluronan keeps collagen fibrils separated in the vitreous cavity to maintain transparency. With time, hyaluronan dissociates from collagen, causing crosslinking and aggregation of collagen with subsequent fibrous structures that scatter light [i,ii,iii]. This process of vitreous liquefaction is accelerated in myopia, with posterior vitreous detachment (PVD) developing 10-15 years earlier in myopes than emmetropes[iv]. A PVD is marked by the separation of the posterior cortical vitreous from the internal limiting membrane, due both to vitreous liquefaction and weakening of vitreous retinal adhesion. Clinically, a PVD is often marked by a certain degree of fibroglial tissue, known as a Weiss ring, free floating over the optic nerve. A PVD allows the vitreous body to move with head or eye movement; the Weiss ring and vitreous opacities cast shadows onto the retina, and are perceived as floaters.

Symptomatic floaters significantly and negatively impact quality of life. Wagle and colleagues[v] evaluated the utility value of symptomatic floaters in a population of 266 patients. Patients were willing to trade off an average of 1.1 years out of every 10 years of remaining life to eliminate their symptomatic floaters. They were willing to take an 11% risk of death and 7% risk of blindness. These utility values were comparable to those reported by patients with age-related macular degeneration, diabetic retinopathy, hypertension, mild angina, mild stroke, colon cancer, and asymptomatic human immunodeficiency virus (HIV) infection. These results show that floaters negatively affect patients as much as significant ocular and systemic diseases. Further, there was no difference between acute and chronic floaters, challenging the widely held belief that floaters become less symptomatic with time.

Presently, there are only three possible management options for patients with symptomatic floaters: observation, pars plana vitrectomy (PPV) either with a one-incision Intrector (Insight Instruments) or a standard three-port vitrector, and yttrium aluminum

garnet (YAG) vitreolysis. Koch presented results from a vitrectomy for floaters with an Intrector at the American Academy of Ophthalmology (AAO) meeting in 2013. The surgeon performs a one-step, one-incision, limited core vitrectomy while visualizing through an indirect ophthalmoscope. Of 20 patients, 85% were satisfied after the Intrector procedure. The remaining three dissatisfied patients underwent standard three-port PPV and were then satisfied. There were no reported complications after 2 years of follow-up.

Standard three-port PPV is the most definitive means to remove the vitreous and its symptomatic floaters, but does carry risk. Retinal detachment has been reported in between 2.5% and 10.9% of eyes post-operatively[vi, vii, viii]. Other studies, however, did not report retinal detachment after 25 gauge vitrectomy. [ix, x]

Some ophthalmologists are performing YAG vitreolysis to vitreous floaters in an effort to pulverize the fibroglial tissue. Little has been published on this technique. A rabbit model evaluated the effects of YAG laser on the protein and viscoelastic properties of the vitreous, and also the protective role of vitamin C against laser photodisruption[xi]. Eyes treated with 5 mJ x 100 pulses to the anterior vitreous showed no changes to the vitreous humour. Likewise, rabbits treated with 25 mg/kg body weight of vitamin C for 2 weeks prior to YAG showed no vitreous changes after the procedure. When YAG laser was applied to the mid-vitreous or the posterior vitreous, at doses of 5 mJ x 100 pulses or 10 mg x 50 pulses, there was an increase in protein content, refractive index, and the viscosity of the vitreous humor.

The few cases series in the literature evaluating YAG for vitreous floaters in human subjects report some symptomatic success and a good safety profile. A single center retrospective case series evaluated the safety and efficacy of YAG laser in 39 eyes with symptomatic posterior vitreous detachments[xii]. The symptomatic floater had to be at least 2 mm away from each the posterior lens capsule and retina. The maximum energy used per pulse was 1.2 mJ. Patients were allowed to have subsequent YAG laser sessions with a minimum interval of two months between sessions. The average power per treatment

session was 310.4 mJ (range 163– 875 mJ). The average number of treatment sessions per patient was 1.62 (range 1–6 sessions). At a mean of 26.6 months follow-up (range 15–53 months) there were no post-operative complications. The researchers used a questionnaire to assess patient satisfaction, reporting that 7.7% of patients were subjectively worse, 53.8% were the same, 35.8% received moderate benefit (30–50% improvement), and 2.5% received significant benefit (50–70% improvement). In patients undergoing repeat YAG procedures, subsequent treatments were not associated with any further improvement in symptoms. Of those eyes with some degree of symptomatic improvement, only 6.6% proceeded to PPV compared to 47.8% of eyes that gained no clinical benefit. The researchers conclude YAG vitreolysis for symptomatic floaters is a safe and moderately effective procedure that leads to improvement in about one-third of patients. Given its safety profile, the researchers feel YAG vitreolysis is a worthwhile primary intervention given that it decreases the number of patients undergoing vitrectomy, which can potentially have more complications.

A Polish series of ten eyes reported only two patients after YAG vitreolysis reported persistent clouds in their visual field. The YAG power ranged from 3 mJ to 7 mJ for a single shot; the total energy required ranged from 56 mJ to 216 mJ[xiii].

Another case series of 15 eyes used energy levels of 5 to 7.1 mJ with total energy ranging from 71 to 742 mJ. The authors report improved symptoms in all eyes with no complications after one-year follow-up[xiv].

A study of ten eyes treated with YAG laser for symptomatic floaters utilized a scanning laser ophthalmoscope to identify the position, the size and the motility of the vitreous floaters. The authors found well-suspended floaters responded better YAG vitreolysis compared to ill-suspended vitreous floaters[xv].

3. STUDY OBJECTIVES

This is a randomized, masked, sham-controlled trial evaluating the safety and efficacy of YAG vitreolysis for symptomatic Weiss ring due to posterior vitreous detachment. This

is a single-center trial that will take place at the Ophthalmic Consultants of Boston. Patients will be randomized in a 2:1 ratio to YAG vitreolysis versus sham YAG.

4. STUDY DESIGN

4.1 Study Description and Duration

Patients complete a questionnaire (see Appendix 2) at baseline and month 6 regarding: duration of their symptoms prior to presentation, laterality, severity and number of their floaters, and activity most inconvenienced by the presence of floaters[xvi]. These data, along with age, sex, and lens status, will serve as baseline characteristics.

ETDRS and Snellen best-corrected visual acuity (BCVA) will be checked at baseline and month 6. A B-scan will be performed at baseline to confirm the presence of a PVD and measure the distance of the symptomatic Weiss ring floater from the retina and posterior lens capsule. Spectralis Optical Coherence Tomography (OCT) and infrared photo (Heidelberg Engineering, Germany) will be checked at baseline and month 6. Optos (Scotland, UK) color photography will be checked at baseline and month 6. A slit lamp and indirect ophthalmoscope examination with scleral depression will be performed at baseline, week 1, month 1, month 3, and month 6, along with applanation tonometry.

Patients will be asked to quantify their post-operative improvement as a percentage as well as choose a descriptive analogy[xvii] at month 6. Options will include: (a) Worse: floaters are worse; (b) Failure: floaters are the same; (c) Partial success: some improvement but still floaters of moderate inconvenience; (d) Significant success: significant improvement with only slight inconvenience; (e) Complete success: complete resolution of floaters. The equivalent percentage improvements are worse or failure 0%, partial success 30–50%, significant success 50–70%, and complete success 100%. The percent improvements will be compared between YAG and sham groups.

Patients will also be asked to rate their disturbance by the floaters on a 0-10 scale, with 0 being no symptoms to 10 being debilitating symptoms. Patients must report their disturbance to be at least a 4 out of 10. Patients will complete this question at baseline and at 6 months. Analyses will compare baseline to month 6 results in a paired analysis,

and also between YAG and sham groups at month 6.

Patients complete the Visual Functioning Questionnaire-25 (VFQ-25) at baseline and month 6. These results will be compared between YAG and sham groups in a comparative analysis, and between baseline and month 6 in a paired analysis.

The YAG vitreolysis will be performed using an Ellex laser. The maximum energy per pulse will be 7 mJ[xviii]. Patients will have an intraocular pressure check before and 30 minutes (±5 minutes) after the procedure. Patients will be dilated with phenylephrine 2.5% and tropicamide 1% and receive proparacaine prior to the YAG. There will be no post-operative drops. A Karickoff lens will be used to perform the YAG vitreolysis. The number of shots will be determined at the discretion of the treating physician. The endpoint is disruption of the Weiss ring into smaller fragments, as well as disruption of any other visually significant appearing floaters at the discretion of the treating physician. Only one treatment session is permitted.

Patients will be followed by Snellen non-BCVA, applanation, and clinical examination at 1 week, 1 month, 3 months, and 6 months (ETDRS and Snellen BCVA will be checked at 6 month). All ocular and systemic adverse effects will be recorded. The primary endpoint will be patients' subjective improvement based on the two floater-specific questions. Secondary endpoints include VFQ-25 results, BCVA, qualitative changes on infrared and color photography, and adverse effects.

This study will enroll 75 patients. Sample size calculations show that 48 patients are needed to show a symptomatic improvement on a 10-point scale from 6 to 3 with a standard deviation of 3 with an alpha of 0.05 and power of 0.9. Further, 75 patients are needed to show a difference between YAG and sham groups at month 6 reporting partial success (30% improvement) and failure (10% improvement) with a standard deviation of 25%, alpha of 0.05, and power of 0.9.

An interim analysis will be performed approximately one year after initiation of the study, in early 2016, and submitted for presentation at the American Society of Retina

Specialists annual meeting, Retina Society, and/or the American Academy of Ophthalmology annual meeting.

5. SELECTION, WITHDRAWAL, AND REPLACEMENT OF SUBJECTS

5.1.1 Inclusion Criteria

A subject must meet the following criteria to be eligible for inclusion in the study:

1. Symptoms of floaters that correlate to the presence of a posterior vitreous detachment for at least 6 months
2. Documented posterior vitreous detachment on clinical examination, OCT, and B scan
3. Self-rating of visual disturbance by the floaters must be at least 4 on a 0-10 scale, with 0 being no symptoms to 10 being debilitating symptoms.
4. Symptomatic Weiss ring (PVD) must be at least 3 mm away from the retina and 5 mm from the posterior lens capsule of the crystalline lens, as measured on B-scan. For pseudophakic patients, there is no minimum required distance from the intraocular lens.
5. Able to position for the YAG laser procedure.
6. Accept the risks of YAG laser including but not limited to retinal detachment, intraocular hemorrhage, retinal damage, cataract formation, optic nerve damage, inflammation, and irreversible loss of vision.
7. Willing and able to comply with clinic visits and study-related procedures
8. If the patient has two symptomatic eyes, only one eye can be randomized and included in the study.
9. Provide signed informed consent

5.1.2 Exclusion Criteria

A subject who meets any of the following criteria will be excluded from the study:

1. Snellen best corrected visual acuity worse than 20/50 in the fellow eye

2. History of retinal tear, retinal detachment, or uveitis in the study eye

3. History of diabetic retinopathy, macular edema, retinal vein occlusion, or aphakia in the study eye

4. History of glaucoma or high intraocular pressure defined as having a history of glaucoma surgery or currently taking two or more topical glaucoma medications in the study eye

5. Table 1 Schedule of Events

Study Procedure	**Screening + Baseline**	**Week 1 (± 4 days)**	**Month 1 (± 7 days)**	**Month 3 (± 7 days)**	**Month 6 (± 7 days)**
Visit	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Inclusion/Exclusion	X				
Informed Consent	X				
Medical/OcularHistory	X				
Demographics	X				
VFQ	X				X
Floater Questionnaire	X				X
ETDRS & Snellen BCVA[2]	X				X
Snellen non-BCVA[2]	X	X	X	X	X
Applanation Tonometry[1]	X	X	X	X	X
Ophthalmic Exam: SLE, DFE & Scleral Depression[1]	X	X	X	X	X
SD-OCT with infrared on Heidelberg Spectralis[1]	X				X
Optos photograph[1]	X				X
Group 1 Administer YAG laser[1]	X				
Group 2 Administer sham laser[1]	X				
Adverse Events	X	X	X	X	X
B scan ultrasound[1]	X				

[1]Study eye only

[2]Both eyes at screening; study eye only at subsequent visits

6. Study Visit Descriptions

6.1 Screening + Baseline / Day 0

After the subject has provided informed consent, the following information will be collected:

- Inclusion/exclusion
- Demographics
- Medical history, ocular history and concurrent illnesses

The following procedures and assessments will be conducted:

- Patients complete questionnaire regarding: duration of floater symptoms prior to presentation, severity of floater symptoms, number of floaters, and activity most inconvenienced by presence of floaters
- ETDRS and Snellen best corrected visual acuity (BCVA) testing (both eyes)
- Ophthalmic exam including slit lamp exam (SLE) and depressed dilated fundus exam (DFE) (study eye)
- Spectral-domain optical coherence tomography (SD-OCT) on Spectralis Heidelberg (study eye)
- Optos photograph (study eye)
- B scan ultrasound (study eye)
- Applanation tonometry (study eye)
- VFQ 25
- Laser treatment or sham treatment if eligible (study eye)
- Documentation of laser procedure specifications used

6.2 Week 1, Month 1, 3

- Snellen non-best-corrected visual acuity (study eye)
- Slit lamp and indirect ophthalmoscopy with scleral depression (study eye)
- Applanation tonometry (study eye)
- Adverse effects

6.3 Month 6

- ETDRS and Snellen best-corrected visual acuity (study eye)
- Optos color photography (study eye)
- Heidelberg Spectralis OCT and infrared photo (study eye)
- Slit lamp and indirect ophthalmoscopy with scleral depression (study eye)
- Applanation tonometry (study eye)
- Assessment of floater symptoms questionnaire
- VFQ 25

All attempts should be made to keep subjects on the study schedule.

5. ETHICAL AND REGULATORY CONSIDERATIONS

5.1 Good Clinical Practice Statement

It is the responsibility of the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

5.2 Informed Consent

The principles of informed consent as described in ICH Guidelines for GCP will be followed.

It is the responsibility of the investigator or designee (if acceptable by local regulations) to obtain written informed consent from each patient prior to his/her participation in the study and after the aims, methods, objectives, and potential hazards of the study have been explained to the patient in language that he/she can understand. The Informed Consent Form (ICF) will be signed and dated by the patient and by the investigator or authorized designee who reviewed the ICF with the patient.

Patients who can write but cannot read will have the ICF read to them before signing and dating the ICF.

Patients who can understand but who can neither write nor read will have the ICF read to them in presence of an impartial witness, who will sign and date the ICF to confirm that informed consent was given.

The original ICF will be retained by the investigator as part of the patient's study record, and a copy of the signed ICF will be given to the patient.

If new safety information results in significant changes in the risk/benefit assessment, the ICF will be reviewed and updated appropriately. All study patients will be informed of the new information and provide their written consent if they wish to continue in the study. The original signed revised ICF will be maintained in the patient's study record and a copy will be given to the patient.

5.3 Subject Confidentiality and Data Protection

The investigator will take all appropriate measures to ensure that the anonymity of each study subject will be maintained.

The patient's and investigator's personal data will be treated in compliance with all applicable laws and regulations.

5.4 Institutional Review Board

An appropriately constituted Institutional Review Board (IRB), as described in ICH Guidelines for GCP, will review and approve:

- The protocol, ICF, and any other materials to be provided to the patients (e.g. advertising) before any patient may be enrolled in the study
- Any amendment or modification to the study protocol or ICF before implementation, unless the change is necessary to eliminate an immediate hazard to the patients, in which case the IRB will be informed as soon as possible

Ongoing studies will be reviewed by the IRB/EC on an annual basis or at intervals appropriate to the degree of risk.

In addition, the IRB will be informed of any event likely to affect the safety of patients or the continued conduct of the clinical study.

6. PROTOCOL AMENDMENTS

The investigator will not implement a change in the design or operation of the protocol or ICF without an IRB-approved amendment.

7. STUDY DOCUMENTATION

7.1 Retention of Records

The investigator will retain all essential study documents, including ICFs, source documents, Case Report Forms (CRFs), and drug accountability records for at least 2 years following the completion or discontinuation of the study, or longer if a longer period is required by relevant regulatory authorities. Records will be destroyed in a manner that ensures confidentiality.

APPENDIX 1: YAG LASER PROCEDURE

The following procedures will be implemented to minimize the risk of potential adverse events associated with YAG laser treatment of Weiss ring.

- Verify study eye
- Instill 2 drops of 0.5% proparacaine hydrochloride into the study eye
- Fill Karickoff lens half-way with goniosol

For YAG laser treatment:

- Single shot mode with a maximum pulse energy of 7 mJ per pulse. The treating physician will start at 1 mJ and titrate up until he/she reaches enough power to achieve disruption of the Weiss ring.
- The endpoint of treatment is the disruption of the Weiss ring into smaller fragments as well as any other vitreous opacities deemed visually significant by the treating physician. Only one treatment session will be performed.
- At the end of the treatment: record total energy (in mJ), energy per shot (in mJ), and total number of shots
- Obtain IOP by applanation tonometry 30 minutes (± 5 minutes) after treatment

For sham laser treatment:

- Sham laser treatment will be applied under the same procedure used for laser treatment but without switching on the laser beam and by imitating depression of the laser pedal.

Appendix 2: Floater Questionnaire

Baseline:

1. How long have you had symptomatic floaters?
2. Do you have symptomatic floaters in the right, left, or both eyes?
3. Which eye is more symptomatic? Right or left or both equally symptomatic
4. How many floaters do you have in the more symptomatic eye (or the study eye if both eyes equally affected)?
5. What activity is most inconvenienced by the presence of floaters?
6. Please rate your visual disturbance by the floaters on a 0-10 scale, with 0 being no symptoms to 10 being debilitating symptoms.

Month 6:

1. Please rate your visual disturbance by the floaters on a 0-10 scale, with 0 being no symptoms to 10 being debilitating symptoms.
2. Please quantify your post-operative improvement as a percentage.
3. How would you describe your floaters today compared to right before the laser procedure?
    a. Floaters are worse
    b. Floaters are the same
    c. Some improvement but still floaters of moderate inconvenience
    d. Significant improvement with floaters only of slight inconvenience
    e. Complete resolution of floaters

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