THE RETINA CLINIC
LONDON

Prof. Paulo Eduardo Stanga
Consultant Ophthalmologist & Vitreoretinal Surgeon/Director

Patient Information Sheet

EFFECT OF YAG LASER VITREOLYSIS ON VITREOUS STRUCTURE AND VISUAL FUNCTION IN PATIENTS WITH VISION DEGRADING MYODESOPSIA SECONDARY TO MYOPIC VITREOPATHY OR POSTERIOR VITREOUS DETACHMENT

Chief Investigator
and U.K Local Principal Investigator: Professor Paulo Eduardo Stanga
The Retina Clinic London
140 Harley Street
London W1G 7LB, U.K.

Telephone Number: +44 (0) 20 4548 5310 (Clinic)

+44 07787100482 (Prof. Stanga Mobile Phone)

U.S.A Collaborators: J. Sebag, MD (Ultrasound Image Frame Selection)

Institute for Vitreous Macula Retina

7677 Centre Ave, Suite 400

Huntington Beach CA 92647, U.S.A.

Jonathan Mamou, PhD (Ultrasound Images Analyst and Study Statistician)

Weill Cornell Medicine, Department of Radiology

416 E 55th St., B1, New York 10022, U.S.A.

Ronald Silverman, PhD, Ronald Silverman Lab,

Columbia University Irving Medical Centre, 635 West

165 St, Research Annex, Room 711, New York, NY

10032, U.S.A.

You are being invited to take part in this research study taking place in London, U.K. at The Retina Clinic London with Prof. Stanga leading the study and being responsible for your diagnosis, investigations and treatment.

A site in California, U.S.A will carry out a parallel study, using a similar protocol to the one designed and used by Prof. Stanga. The U.S.A. site is led by Dr. Jerry Sebag.

Dr. Mamou (New York, U.S.A.), Dr. Silverman (New York, U.S.A) and Dr. Sebag will contribute to the analysis and interpretation of all ultrasonogram results. Therefore, your anonymised ultrasound results will be sent to them for analysis and interpretation.

The U.K. and the U.S.A. sites and studies are associated in terms of using similar protocols and the same statistician for the analysis and interpretation of ultrasound results, and benefitting from the same funding source.

You have vitreous opacities (floaters) and are choosing to have Neodymium-doped yttrium-aluminium-garnet (Nd:YAG) vitreolysis laser therapy as treatment.

You should understand the purpose of the study, and the risks and benefits of participating in order to make an informed decision of if you want to take part in this study.

This Patient Information Sheet explains:

- Why we are doing this study
- What is required from you in this study
- Any potential benefits of participating in this study
- Any risks and discomforts that may occur if you participate in this study
- How your personal and medical information obtained during the study will be used and shared

Your Principal Investigator (PI) will explain this study to you. You do not have to participate in this study. Your participation in this study is voluntary and your personal decision.

You must take your time to make your decision about participating in this study. You may also want to discuss the information in this Patient Information Sheet with your family, friends, or any other doctors who take care of you. You can ask your study investigator if you have any questions.

Choosing not to participate in this study will not affect your care or relationship with your doctor or the clinic.

Please note that exactly the same treatment is available outside this clinical study, on a self-funding basis. Please ask your study investigator or the team for further details, if

interested.

Why are you being asked to participate in this study?

The purpose of this study is to measure how your vision, the structure of your vitreous and your quality-of-life changes after the YAG laser vitreolysis (YVL) treatment of the opacities in the gel (vitreous), commonly referred to as floaters, that fills your eye and to identify the best candidates for YVL treatment of vitreous floaters.

Floaters can cause disturbances in your vision, intermittently blocking your vision and be very annoying, to the point of leading to symptoms of depression in some patients.

You are being offered participation in this study to have YVL to treat your vitreous floaters.

The purpose of this study is not to assess how to carry out the YVL of vitreous floaters, as the treatment will be performed in the same way as it is currently performed by Prof. Stanga outside this clinical trial and on a self-funded basis.

Please note that other treatment options are available, including full and limited vitrectomy surgery. Please ask your study investigator or the team for further details, if interested.

How many people will take part in this study?

50 patients will take part in this study in London. Another 50 patients will take part in the U.S.A. parallel study.

What will happen during this research study?

If you decide to participate in this study, you will be asked to sign this consent form. You will also receive a copy of the completed form for you to keep. Your study investigator and the research team will collect your medical and ophthalmologic history including age, sex, vision, previous eye conditions, previous eye treatments and other past medical history which may seem relevant to the study investigator such as systemic diseases.

The research team will also administer a series of test to provide a way for the floaters to be analysed in how they affect your socially, psychologically and functionally. The same set of tests will be repeated at the following time points after the final treatment is performed: 3 months, 6 months and 12 months. None of these tests are invasive or experimental. All tests are standard for evaluating vision and the eye. You will have the following tests completed to ensure you are eligible to participate in this study:

1. Visual Function testing using the ETDRS logMAR eye charts to measure your best corrected vision and your vision at low luminance.
2. Reading function assessment using the hand-held MNREAD chart.
3. National Eye Institute Visual Function Questionnaire (NEI VFQ-25) to assess more general aspects of vision.
4. Vitreous Floaters Functional Questionnaire (VFFQ) to capture the full essence of how vitreous floaters in particular can impact the quality of life (Sebag 2018c, and Nguyen-Cuu et al 2017).

5. High-Definition Analyser (HDA): this is an eye scan to test the Objective Scatter Index (OSI)
6. Light Distortion Analyser (LDA): this is an eye scan to test the distortion of light (LDI, Light Disturbance Index)
7. C-Quant: this is a straylight meter for quantification of light scattering in the eye
8. Contrast Sensitivity Function test using the Freiburg Acuity Contrast Test (FrACT) to measure your ability to see gradations of contrast from black through to grey and white.
9. Ultrasonography to image the vitreous opacities (floaters) in your eye and to establish the axial length of your eye using sound waves.
10. Electroretinography (ERG) to assess retinal electrical activity with a non-invasive test.
11. Optos ultra widefield multiwavelength and autofluorescence imaging of the retina.
12. Widefield swept-source optical coherence tomography (WF SS-OCT) scan centered on the fovea to evaluate the retinal structure.
13. Microperimetry to test the sensitivity of the central visual field.
14. Biomicroscopy (Slit lamp) and Indirect Ophthalmoscopy with 360-degree scleral indentation for detection of pre-existing or induced retinal tears or lesions.

You may receive up to 5 treatment sessions. The number of required sessions will be determined by the study investigator during the study. These sessions will be between 2 and 6 weeks apart. Prior to each laser treatment, the study investigator will perform a comprehensive eye examination and review your medications and any medical event/diagnosis since your last visit.

Table 1 - Study Participant Visit Schedule

Visit	Screening	Treatment[1]	Month 3 (±7 days)	Month 6 (±7 days)	Month 12 (±7 days)
Assessments					
Patient Information Sheet and eligibility criteria review	X				
Current/ongoing medication review	X	X	X	X	X
Comprehensive eye examination	X	X	X	X	X
Visual function and reading testing	X		X	X	X
Questionnaires	X		X	X	X
Ultrasonography	X		X	X	X

Electroretinography	X		X	X	X
Eye imaging	X		X	X	X
Microperimetry	X		X	X	X
Nd:YAG laser treatment		X			
Symptom monitoring	X	X	X	X	X

1. You may receive up to 5 treatment sessions. Each treatment session will be 2-6 weeks apart. This indicates the assessments performed at each Treatment visit.

How long will I be in the study?

You will be asked to repeat testing after your final laser treatment at the following time points: 3 months, 6 months, and 12 months. In some instances, follow-up visits will continue annually. This frequency is standard-of-care and similar to as you would experience if you were not in this study.

Do I have to participate, and can I stop being in the study?

You do not have to participate in this study as participation is entirely voluntary. If you do decide to take part, you will need to sign and date the consent page of this form to indicate that you have decided to take part.

You can change your mind and decide to stop at any time. Tell your study investigator if you are thinking about stopping or decide to stop. He will tell you how to stop safely. This decision will not affect your future care or relationship with your physician or with your medical care.

The study investigator may stop you from taking part in this study at any time if it is in your best interest.

Confidentiality

All data and participant information for the study will be recorded on Case Report Forms according to protocol, GDPR laws, and kept for analysis by the research team. Patient information may be recorded on Nextech EMR which is The Retina Clinic London's Electronic Medical Records system for diary management purposes, and for storing copies of Case Report Forms. This software and all its records are located onsite within The Retina Clinic London's server. The server is backed-up daily and protected by a firewall.

Only The Retina Clinic London employees, investigators, and study team members will have access.

How will we use information about you?

We may need to use information from [you] [from your medical records] [your GP] for this research project.

To maintain confidentiality, any samples and associated clinical data that are sent to collaborators will not have any patient identifiers, but only de-identified coding. The codes linking specimens/data to patient identifiers will not be shared with collaborating sites. The associated clinical data will consist of [age], [sex], [clinical pathology], [visual acuity], [contrast sensitivity function], [questionnaire scores], and [ultrasound imaging].

We will keep all information about you safe and secure.

Some of your information will be sent to the United States of America where external collaborating sites are located. They must follow our rules about keeping your information safe. As mentioned, these sites will only receive anonymised data with pseudonymised patient information. The sites will have no access at all to information linking patient data and the pseudonymised data.

External Collaborators will only be used for the processing and analysis of testing results, pre-YVL and post-YVL treatment.

External collaborators are listed below:

J. Sebag, MD (Ultrasound Image Frame Selection), Institute for Vitreous Macula Retina, 7677 Centre Ave, Suite 400, Huntington Beach CA 92647, U.S.A.

Jonathan Mamou, PhD (Ultrasound Images Analyst and Study Statistician), Weill Cornell Medicine, Department of Radiology, 416 E 55th St., B1, New York 10022, U.S.A.

Ronald Silverman, PhD, Ronald Silverman Lab, Columbia University Irving Medical Centre, 635 West 165 St, Research Annex, Room 711, New York, NY 10032, U.S.A.

External collaborators will be advised to consult their IRB or Ethics Committee for any required approval prior to sharing specimens and data.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Are there possible risks related to participating in this study?

There are no significant potential adverse effects as a result of study testing as all the tests (including the imaging) are non-invasive (Stanga P.E., Valentin-Bravo F.J., Reinstein U., Stanga S.E.F., Marshall J., Archer T.J., Reinstein D.Z., New terminology and methodology for the assessment of the vitreous, its floaters and opacities, and their effect on vision: Standardised and Kinetic Anatomical & Functional Testing of VFO (Vitreous Floaters and Opacities) (SK VFO Test). Ophthalmic Surgery, Lasers and Imaging Retina, (2023). In Press.).

The testing cumulatively will take between 3-4 hours. The eyedrops used as part of the testing such as 1% tropicamide (Bausch and Lomb, Vaughan, Ontario, Canada L4K 4B4) and 2.5 % phenylephrine (Bausch and Lomb, Vaughan, Ontario, Canada L4K 4B4) are widely used in ophthalmic care and screening to dilate pupils, are generally well tolerated with low risks of allergic reactions or side effects, and generally last approximately 4-6 hours. The main though very rare side effect of the

eyedrops is the potential risk of raised pressure in the eye, however population studies have estimated the odds of this risk at an extremely low level of 1 in 18,000 cases. Each participant will have a thorough examination by an ophthalmologist prior to instillation of any dilating eyedrops to determine their risk of raised pressure.

The YAG laser procedure carries risks. As part of the procedure, a lens is to be applied to the eye which may very rarely cause disruption to the eye surface and temporary irritation of the eye surface. A standard gel of artificial tears is applied to the lens to minimise this risk, and the incidence of eye surface irritation from contact lenses used for diagnostic and treatment purposes in standard care is less than 1% and hence very low.

By nature of the YAG laser, there are potential risks of injury to the lens or retina as a result of lasering too close to the lens or retina, such as cataract, retinal haemorrhages, retinal tears or retinal detachments. To minimise this risk, we have selectively targeted patients who have their vitreous opacities within pre-defined safety limits (3mm in front of the retina, 6mm behind the lens) and have further included laser offsets as part of the protocol laser procedure, which will be followed in all treatments and re-treatments, to minimise the risk of collateral damage. We do not expect this risk of collateral damage to be higher than 1%. The risk of injury to your eye during the study is the same as if you were funding the treatment yourself outside of the study.

What happens if I am injured because I took part in this study?

If you are injured or become ill as a result of taking part in this study, you should contact your study doctor. All of the necessary medical facilities are available for treatment, as is reasonably possible. In the event you suffer a research related injury, the costs will be billed to yourself, the same as if you were funding the treatment yourself outside of the study. The Retina Clinic London will not pay for the treatment of any injury or complication due to the medical condition(s) you already possess. You will be charged for those expenses, if any. The Retina Clinic London will not provide any other kind of compensation such as compensation for lost wages, disability, or discomfort. You do not give up any of your legal rights by signing and dating this consent form and taking part in this study.

Will I benefit from taking part in this study?

Study subjects may benefit from receiving treatment for vision degrading myodesopsia with resolution/improvement of floater symptoms, free of charge, rather than funding the same treatment yourself outside of the study.

The results of this study may show quality-of-life improvement and improved visual function after YVL for floaters, thus making the procedure more widely accepted as a viable treatment option for this problem.

If I do not take part in this study, what other alternatives or choices do I have?

You do not have to participate in this study to receive care for your eye condition. Instead, you may choose to undergo vitrectomy (surgical excision of the gel in the centre of the eye), YAG laser treatment outside of the study as a self-paying patient, or choose to have no treatment at all.

Who will see the medical information about me that is collected during the study?

We will follow the appropriate UK Government laws that say we must keep your study records private and confidential. We will protect your privacy by giving each patient a unique code. A separate file maintaining the link between the code and identity will be created.

However, we cannot guarantee total privacy and confidentiality. Your personal information may be given out as required by law. Certain people may need to see your study records, and these people must also keep the records confidential. The people who may also see your information are:

- Staff members supporting the conduct of this study at The London Retina Clinic, London
- Staff supporting the conduct of the study at Institute for Vitreous Macula Retina in Huntington Beach, CA.
- Staff supporting the conduct of the study at Weill Cornell Medical, Department of Radiology
- Staff supporting the conduct of the study at Columbia Irving Medical Centre, Ronald Silverman Lab

What are the costs of taking part in this study?

There is no cost to participate. The diagnostic testing as described above will be paid for by the study. Additional testing unrelated to this study protocol will be charged directly to the participant.

Will I be paid for participating in this study?

No, you will not be paid for your participation in this study.

Does the study staff receive payment for doing this study?

The research study staff is not paid directly for participation in this study.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time.

No matter what decision you make, there will be no penalty and you will not lose any of your health care benefits. Leaving the study will not affect your medical care.

We will tell you about new information or changes in the study that may affect your health or your decision to continue in the study.

By signing this form, you do not lose any of your legal rights to seek payment in case of injury resulting from this study.

Who can answer my questions about the study?

If you have any questions about your rights while participating in this study, or if you have any concerns regarding the conduct of this study or if you wish to complain about any aspects of this study, you may contact Prof. Stanga directly on his mobile under +44 7787 100482., on his email under p.stanga@theretinacliniclondon.com or in writing to The Retina Clinic London, attn. Prof Paulo Stanga, 140 Harley Street, London W1G 7LB, United Kingdom. If you are not happy with the response received or would like to complain to another party, the Sponsor's representative can be emailed on florencia@theretinacliniclondon.com.