

STUDY PROTOCOL (Version 3, Aug 06, 2019)

Title: Retinal displacement after pneumatic retinopexy versus vitrectomy for the management of primary retinal detachment.

Principal Investigators:

Dr. Rajeev Muni

Dr. Carolina Francisconi

Co-investigators:

Dr. Alan Berger

Dr. Filiberto Altomare

Dr. David Wong

Dr. Louis Giavedoni

Dr. David Chow

Study coordinator:

Philip To

Backup coordinator:

Setting: Ophthalmology department, St Michael's Hospital, Toronto:

1. St Michael's Hospital Eye Clinic, 8th Floor, 61 Queen St East, Toronto M5C 2T2

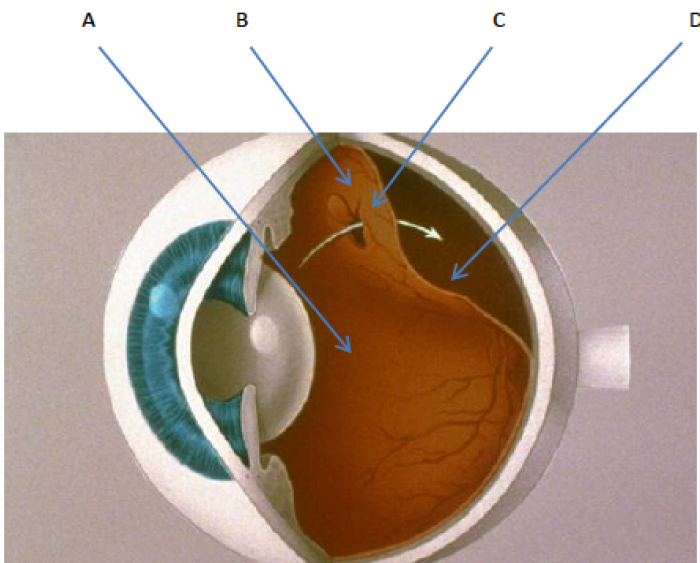
2. Eye treatment room, 8th Floor, Cardinal Carter wing, St Michael's Hospital, Toronto M5B 1W8

I. Background

Retinal detachment

Rhegmatogenous retinal detachment (RRD) is an acute, sight threatening condition, with an incidence of approximately 10 per 100,000 people.¹ During normal ageing, the transparent vitreous gel (see figure 1:A), which fills the eye, liquefies and shrinks, and eventually detaches in 80% of the eyes. When detachment of the gel occurs, a tear in the retina may form (see figure 1:B). Liquefied gel may now enter under the retina via the retinal tear (see figure 1:C), resulting in detachment of the retina (see figure 1:D). Once retinal detachment occurs, sight loss usually develops within several hours to days.

Figure 1: Retinal detachment



Factors that predispose an individual to developing retinal detachment are myopia (near sightedness), advancing age, trauma, and certain hereditary conditions.²

Without surgical intervention by a vitreoretinal surgeon, retinal detachment almost invariably results in permanent sight loss in the affected eye. There is an increased risk of delayed visual rehabilitation the longer the wait for surgery is.³ Both of the treatments under investigation are widely used and accepted by vitreoretinal surgeons⁴

Interventions for retinal detachment Pneumatic retinopexy (PnR) has been employed to repair retinal detachments since the late 1980s and is a minor surgical intervention, carried out in a treatment room. The initial success rate (i.e. the proportion of patients in whom the retina becomes attached after one treatment) is quoted as approximately 70%.⁵⁻⁷ PnR is carried out under topical or local anaesthetic (a freezing injection under the conjunctiva, the superficial skin on the eye). The procedure involves injection of a small gas bubble into the eyeball via a fine needle. This step takes a maximum of 15 minutes. Two gases can be injected into the eye: perfluoropropane (C₃F₈), which lasts 6 weeks, and sulfahexafluoride (SF₆), which lasts about 2 weeks. Both are non-toxic, equally effective, have been validated for this use, and are widely used amongst retina surgeons in the world. After injection of the gas bubble, the patient is required to maintain a strict 'head posture' (for example, head tilt to left) for up to 10 days. The purpose of this 'head posture' is to align the gas bubble (which floats within the eye) to the retinal tear. The buoyant force of the gas bubble, as well as its surface tension, act to reattach the detached retina over several days. The gas bubble spontaneously dissipates after 2-6 weeks, depending on the gas selected. Additionally, laser treatment or cryotherapy is carried out either before or 1-2 days after injection of the gas bubble, to secure the retinal tear. Without this second step, the retina would re-detach once the gas bubble dissipates. Both laser and cryotherapy are widely

accepted methods of securing the tears in the retina and both are considered equally safe and effective. In patients where the retina does not reattach with PnR alone, vitrectomy surgery (PPV) or repeat PnR is needed (see below).⁸ However, the minority of patients who go on to need repeat treatment encounter similar final anatomical success rates and will experience the same gain in vision as those patients who underwent PPV in the first place.^{9,11}

Vitrectomy surgery (PPV) involves ‘keyhole’ surgery to the eyeball, via three tiny (23/25 gauge) incisions to the sclera. This procedure is carried out in the operating room, under regional anaesthetic (a freezing injection to the retro-bulbar space, the space behind the eyeball, where nerves which sense pain and control eye movement are situated) plus sedation (medication to reduce patient anxiety). During PPV, the vitreous gel is removed from the eye using a fine metal instrument called a ‘vitrector’. The vitreous gel is removed to allow space for a larger gas bubble than is possible in PnR, and also to relieve any vitreous traction which may otherwise impair reattachment of the retina. A large gas bubble (same gases as mentioned for PnR) is injected (to reattach the retina, as in PnR), and laser or cryotherapy is applied around the retinal tear to secure it (as in PnR). After treatment, a patient may be required to maintain a ‘head posture’ (for example, head tilt to left) for up to one week. The purpose of this ‘head posture’ is to support the area of the retinal tear optimally, by ‘floating’ the gas bubble up against it. As the gas bubble is larger in PPV, the head posturing requirements are less strict. The gas bubble reabsorbs after 2-6 weeks, depending on the gas selected. The surgery takes 1-1.5 hours. The success rate (i.e. the proportion of patients in whom the retina becomes attached after one treatment) is reported as being as high as 90% in the scientific literature.^{7,12,13}

Both of the treatments may be associated with complications such as bleeding, infection, increased intraocular pressure or cataract. The risk of a sight threatening complication such as a severe intraocular infection or hemorrhage is less than 1:1000 (for both procedures). The risk of cataract development (clouding of the lens, requiring cataract extraction surgery) is less than 10% for PnR^{11,14} and at least 70% for PPV.¹⁵

Distortion and retinal displacement after retinal detachment repair

Image distortions such as metamorphopsia and micropsia are common complaints after surgery for retinal detachment. In 2010 Shiragami et al were the first to demonstrate hyper-fluorescent lines, adjacent to the retinal blood vessels in Fundus auto-fluorescence imaging (FAF) of the retina after retinal detachment (RD) repair surgery²⁶. They proposed a theory in which these lines which are called also Retinal Vessel Printing (RVP) correspond to the area where the retinal blood vessels were located before the retinal detachment. According to this theory the RVP in FAF imaging is due to increased metabolic activity of RPE cells. Prior to surgery these RPE cells were obscured to light rays by retinal blood vessels while after surgery, due to displacement of the retina, these RPE cells became exposed to the light which leads to increase in the cells metabolic activity. This increase in metabolism is thought to be the cause for the hyper fluorescence seen in FAF imaging. Displacement of the retina after RD repair surgery can serve as anatomy basis of vision distortion. Moreover, these reference lines allow us to quantify the displacement of the retina after retinal detachment surgeries. By doing this, we can compare retinal displacement of different retinal detachment repair surgeries and may reduce post operation visual distortion.

Since Shiragami's first report, several other studies looked into retinal displacement after RD repair²⁶⁻³², epiretinal membrane³³ and macular hole³⁴. Codenotti et al have shown that retinal displacement ratio is higher in patients with intravitreal gas compare to patients with silicon oil (71.4% vs. 22.2%)²⁷. Lee et al proposed a way of quantifying the rotational displacement of the retina²⁸. They showed that there is more than a simple rotation and probably also a temporal stretch of the retina. Dell'omo described additional OCT and FAF changes after RD repair such as outer retinal folds and IS/OS skip reflectivity abnormalities²⁹. Recently Dell'omo

published the biggest study so far of 125 patients after pars plana vitrectomy (PPV) with 35.2% of patient showed signs of retinal displacement³⁰.

Recently we showed in PIVOT trial that patients after pneumatic retinopexy has less vertical distortion than patients after PPV. To the best of our knowledge, no study so far looked into retinal displacement after Pneumatic Retinopexy. Moreover, wide field FAF was not used in previous studies. We think there is a reason to believe that Pneumatic Retinopexy will cause less retinal displacement than PPV. Thus, we propose a prospective cohort study which will compare retinal displacement of patients after RD repair by PPV versus Pneumatic Retinopexy.

II. Aim

To compare retinal displacement and visual distortion of primary retinal detachment repair following pneumatic retinopexy (PnR) versus pars plana vitrectomy (PPV).

III. Study design

(i) Hypothesis The primary study hypothesis is that pneumatic retinopexy will cause less retinal displacement and less visual distortion at the first 12 months for patients with primary retinal detachment.

(ii) Experimental design A prospective, cohort trial, comparing two surgical interventions (PnR versus PPV) for patients with primary retinal detachment.

(iii) Participants Patients presenting to St. Michaels Hospital retinal service with rhegmatogenous retinal detachment. Eligibility for study participation will be ascertained by the examining physician at the time of presentation:

Inclusion criteria:

- Age \geq 18
- Diagnosis of macula off primary rhegmatogenous retinal detachment

Exclusion criteria:

- Previous retinal detachment and/or retinal detachment repair surgery in the study eye
- Retinal detachment with macula on.
- Patients with other retinal pathologies causing structural changes to the retina in the study eye, such as diabetic retinopathy, previous vascular occlusion (artery or vein occlusion), macular dystrophy, among others.
- Previous vitreoretinal surgery in the study eye
- Inability to come for follow ups up to 12 months.
- Inability to take FAF imaging due to neck stiffness or other medical issue.

- Inability to maintain post operation head positioning
- Mental incapacity
- Inability to sign on informed consent.
- Patient is unwilling or unable to follow or comply with all study related procedures or to sign informed consent form

Criteria for participant withdrawal from study: - Patient withdraws consent

(v) Interventions

Participants will undergo either: PnR + laser/cryotherapy

or PPV + laser/cryotherapy depending on the treating physician's recommendation, regardless their participation in the study.

For patients undergoing PPV, the use of adjunctive surgical techniques such as placement of a scleral buckle, use of silicone oil, or combined cataract extraction are at the discretion of the treating surgeon. All patients undergoing the vitrectomy arm, regardless of the additional steps done during the procedure, will be considered as one group for data analysis.

In the event of primary intervention failure (i.e. failure of retinal re-attachment following primary intervention), the decision to proceed with secondary intervention, and the nature of such intervention, will rest with the treating physician in conjunction with the patient. Secondary intervention may involve any surgical procedure, as deemed clinically appropriate.

Note: Additional laser retinopexy, cryotherapy, gas injection or head positioning are not considered a failure.

(vi) Timing of observations See flow diagram (Appendix 1)

(vii) Outcome measures

Primary outcome:

- retinal displacement by the presence of retinal vessels printing on FAF imaging.

Secondary outcome:

- Visual Distortion measured with M chart.
- Anisokenia testing.
- Optical Coherence Tomography (OCT) changes.
- Metamorphopsia according to the patient symptoms.
- Visual acuity (ETDRS 12 months post intervention)
- Metamorphopsia questionnaire

imaging

Fundus AutoFluorescence (FAF)

Fundus autofluorescence (FAF) imaging is a noninvasive imaging method and requires relatively little time. It highlights the fluorophores accumulating in lipofuscin (LF) within retinal pigment epithelium cells (RPE). No radiation is involved therefore this imaging method is safe without any clear contraindications.

M Chart

Recently, several tools have been developed for quantification of metamorphopsia severity including M-CHARTS (Inami Co., Tokyo, Japan). In the patients with metamorphopsia, a straight line appeared curved or irregular. On M-CHARTS, straight lines are replaced with dotted lines, and the dot intervals (range: 0.2° - 2.0°) are changed from fine to coarse. With increasing dot interval, the line distortion decreases until the dotted line becomes straight. The visual angle that denoted the dot interval of the line seen as straight was considered as the patient's M-CHARTS score. When a patient was tested with vertical dotted lines, the result was defined as the vertical M-CHARTS score. After the M-CHARTS were rotated 90° , the horizontal M-CHARTS score also was measured according to horizontal dotted lines³⁵.

Aniseikonia test

Aniseikonia is a phenomenon in which the size or shape of perceived images differs between eyes. The anomaly is reported to be associated with interocular differences in refractive error and some retinal diseases. Following successful repair for rhegmatogenous retinal detachment, some patients have complained that objects appeared distorted in size or shape. The Aniseikonia Test measures the ratio of image size difference between the 2 eyes³⁶.

(viii) Recruitment plan

Recruitment will begin in March 2018 after Research Ethics Board approval has been granted and will continue until the required number of patients are enrolled and have completed the study. Patients visiting the St. Michael's Hospital's retina clinic with primary RRD will be given the option to participate if they meet the criteria. Based on our clinic's routine volume, we anticipate recruiting approximately 4 patients per sub-study per week, with complete recruitment over a 12-month period. Each patient will be followed for 12 months.

(ix) Screening Procedures

Patients will be screened by the investigators in the same manner as standard patients. The tests to be performed are typically used for diagnosis and follow-up of retinal detachment: best-corrected Snellen visual acuity assessment, slit-lamp exam, tonometry, fundoscopy, and Optical Coherence Tomography (OCT) at every visit. ETDRS visual acuity (ETDRS - 'Early treatment of Diabetic Retinopathy Study' – this study defined a method of visual acuity assessment that has become the gold

standard for use in eye research) will be assessed at 12 months after the treatment for RRD.

Assessment of Clinical Parameters:

The following clinical data will be obtained from each patient: age, gender, extent of the detachment (quadrants), duration of subjective symptoms (days), vitreous status (presence/absence of vitreous hemorrhage), macular status (attached/on or detached/off), the location of main retinal tears (fundus sketch), refractive power (emmetropic, hyperopic, myopic <6 or > 6 diopters, lens status (phakic or pseudophakic) and medications in use.

(x) Sample size

Sample sizes for each sub-study were calculated for a 5% level of statistical significance with 80% power. Assuming displacement ratio of 35% and 15% in the vitrectomy and pneumatic groups respectively, A total sample size of 80 subjects will be required for each group. Anticipating a dropout rate of 10%, we calculated a total of 180 patients in the study.

IV. Data management

Initial data collection (clinical examination findings, visual acuity, questionnaire data) will take place in a paper format. Subsequently, this data will be transferred to a digital database (Microsoft Excel). Paper data will be stored in a locked filing cabinet in the principal investigator's office and away from the study data, and will be destroyed once digital data entry has taken place. The digital spreadsheet will be held on a password protected computer in a locked room, and an encrypted memory stick. At recruitment, each patient's name and date of birth will be obtained to facilitate onward administration of follow-up appointments and safety

monitoring, and stored on a face sheet (master linking log). The face sheets will be stored in a locked filing cabinet, away from the study data. Each patient will be allocated a unique study identification number, which will be used to label all paper and digital data pertaining to that patient. The face sheets (master linking log) and all paper/electronic data will be destroyed once publication takes place. The de-identified study data will be destroyed five years after publication has taken place.

V. Consent:

Written, informed consent will be obtained from each participant. *On no occasion should consent be obtained by the treating physician or study investigator.* During working hours: The study will be introduced to the patient by the examining physician. Interested patients are directed to Philip To (Research Technician) who will obtain informed consent.

Late evenings / weekends: Our Research Technician (Philip To) will generally be available to obtain informed consent from potential study patients outside normal working hours, on an 'on call' basis. However, on occasions when he is unavailable, informed consent may instead be obtained by the Ophthalmology resident or fellow (assuming that they are not the treating physician and will not be involved in the patient's surgery). The resident/fellow will be familiar with both interventions (PnR and PPV), the nature of the study and trained to the consent discussion and obtaining written informed consent. Since retinal detachments are usually unilateral conditions, patients can still read the informed consent. If the patient has any bilateral visual impairment, the research technician will be available to help and read the consent to the participant. In this situation, a witness, usually being the accompanying relative of the patient or a SMH staff member not

involved in the study, will also be present.

VI. Data Analysis:

Continuous data: Data will be checked for normality. Normal data will be compared using a non-paired t-test.

Non-normal data will be compared using non parametric tests. Categorical data: Chi squared test.

Coefficients with 95% confidence intervals will be reported. A p-value of 0.05 will be considered for statistical significance. Data will be analyzed using SPSS (SPSS Inc., Chicago, IL). Per protocol analysis will be used.

VII. Safety Monitoring Plan

This study will be conducted in accordance to the Declaration of Helsinki. The local principal investigator will meet monthly with study team members to review the progress of the study. Furthermore, to ensure that all members are performing their roles in accordance with the professional obligations described in this Ethics Application, the Principal Investigator will randomly check on the study coordinators and participants. Patients will be made fully aware of the risks and benefits of the procedures. Patients will be assessed before and after the treatment and will be closely monitored throughout the study. Complications will be managed by highly trained hospital staff including ophthalmologists, nurses, allied health professionals and technicians as per standard of care.

VIII. Funding

All aspects of clinical care, including procedures visits and exams, carried out as part of the study represent standard of care.

Support staff: Our research technician (Philip To) is already a salaried employee within the department. Part of his existing job description is assisting Fellow's research, and therefore no additional funds will be required.

Expenses with printing and copying will be absorbed by the principal investigator's (Dr. Rajeev Muni) office.

VII. References:

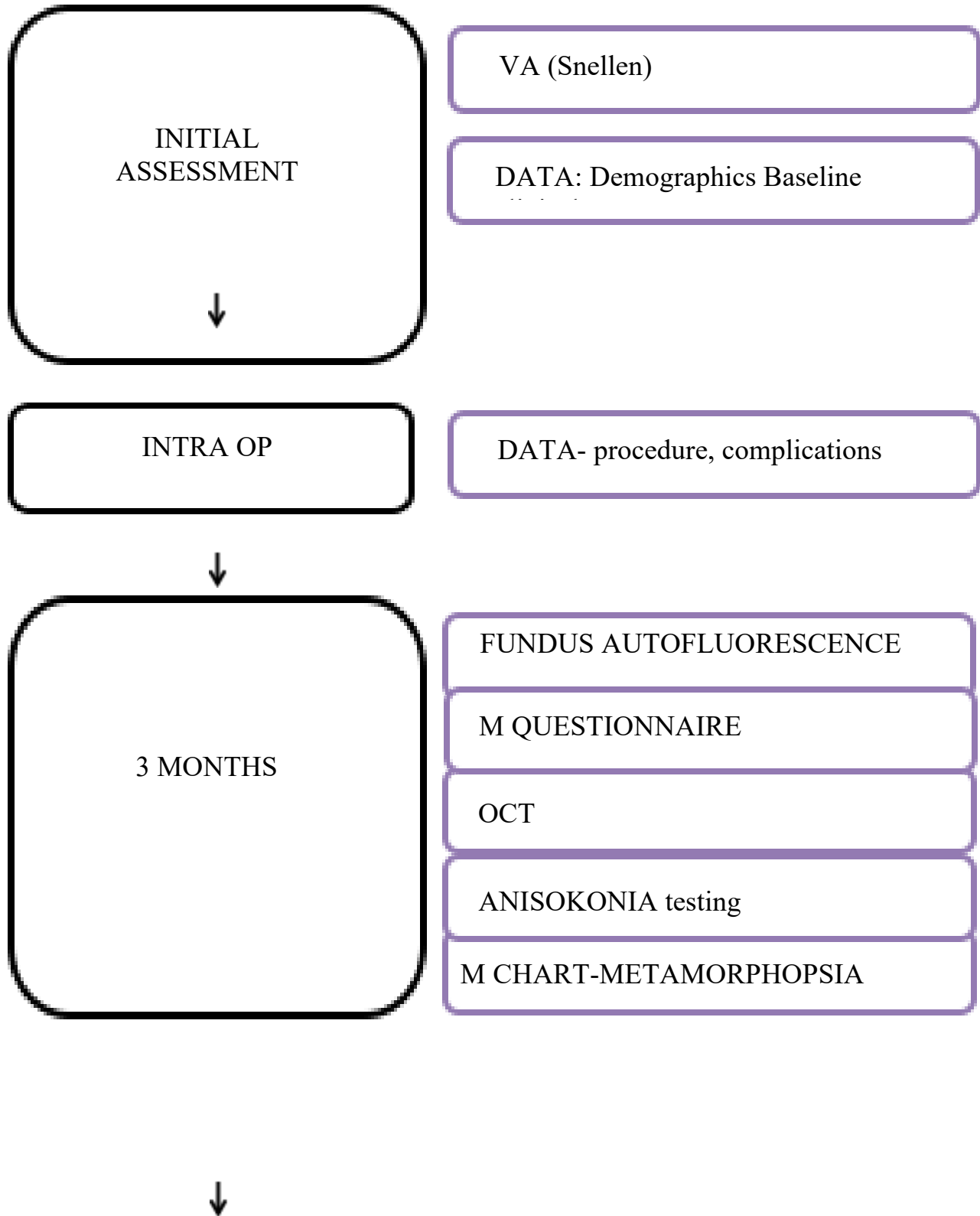
1. Mitry D, Chalmers J, Anderson K, Williams L, Fleck BW, Wright A, et al. Temporal trends in retinal detachment incidence in Scotland between 1987 and 2006. *Br J Ophthalmol*. 2011 Mar;95(3):365–9. 2.
2. Mitry D, Charteris DG, Fleck BW, Campbell H, Singh J. The epidemiology of rhegmatogenous retinal detachment: geographical variation and clinical associations. *Br J Ophthalmol*. 2010 Jun;94(6):678–84.
3. Rezar S, Sacu S, Blum R, Eibenberger K, Schmidt-Erfurth U, Georgopoulos M. Macula-on versus macula-off pseudophakic rhegmatogenous retinal detachment following primary 23-gauge vitrectomy plus endotamponade. *Curr Eye Res*. 2016 Apr;41(4):543-50.
4. Saw S, Gazzard G, Wagle AM, Lim J, Au Eong K. An evidence-based analysis of surgical interventions for uncomplicated rhegmatogenous retinal detachment. *Acta Ophthalmologica Scandinavica*. 2006 Oct 1;84(5):606–12.
5. Kulkarni KM, Roth DB, Prenner JL. Current visual and anatomic outcomes of pneumatic retinopexy. *Retina (Philadelphia, Pa.)*. 2007 Oct;27(8):1065–70.
6. Tornambe PE. Pneumatic retinopexy: the evolution of case selection and surgical technique. A twelve-year study of 302 eyes. *Trans Am Ophthalmol Soc*. 1997;95:551–78.
7. Schaal S, Sherman MP, Barr CC, Kaplan HJ. PRIMARY RETINAL DETACHMENT REPAIR: Comparison of 1-Year Outcomes of Four Surgical Techniques. *Retina (Philadelphia, Pa.)*. 2011 Sep;31(8):1500–4.
8. Hilton GF, Grizzard WS. Pneumatic retinopexy. A two-step outpatient without conjunctival incision. *Ophthalmology*. 1986;93(5):626-41.
9. Goldman DR, Shah CP, Heier JS. Expanded criteria for pneumatic retinopexy and potential cost savings. *Ophthalmology*. 2014;121:318-326.
10. Tornambe PE, Hilton GF, Kelly NF, Salzano TC, Wells JW, Wendel RT. Expanded indications for pneumatic retinopexy. *Ophthalmology*. 1988;95(5): 597-600.
11. Tornambe PE, Hilton GF, Brinton DA, Flood TP, Green S, Grizzard WS, et al. Pneumatic retinopexy. A two-year follow-up study of the multicenter clinical trial comparing pneumatic retinopexy with scleral buckling. *Ophthalmology*. 1991 Jul;98(7):1115–23.
12. Mendrinós E, Dang-Burgener NP, Stangos AN, Sommerhalder J, Pournaras

- CJ. Primary vitrectomy without scleral buckling for pseudophakic rhegmatogenous retinal detachment. *Am. J. Ophthalmol.* 2008 Jun;145(6):1063–70.
13. Brazitikos PD, Androudi S, Christen WG, Stangos NT. Primary pars plana vitrectomy versus scleral buckle surgery for the treatment of pseudophakic retinal detachment: a randomized clinical trial. *Retina (Philadelphia, Pa.)*. 2005 Dec;25(8):957–64.
 14. Mougharbel M, Koch FH, Böker T, Spitznas M. No cataract two years after pneumatic retinopexy. *Ophthalmology*. 1994 Jul;101(7):1191–4.
 15. Heimann H, Bartz-Schmidt KU, Bornfeld N, Weiss C, Hilgers R-D, Foerster MH. Scleral Buckling versus Primary Vitrectomy in Rhegmatogenous Retinal Detachment: A Prospective Randomized Multicenter Clinical Study. *Ophthalmology*. 2007 Dec;114(12):2142–2154.e4.
 16. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD. Development of the 25-item National Eye Institute Visual Function Questionnaire. *Arch. Ophthalmol.* 2001 Jul;119(7):1050–8.
 17. Okamoto F, Okamoto Y, Fukuda S, Hiraoka T, Oshika T. Vision-Related Quality of Life and Visual Function after Vitrectomy for Various Vitreoretinal Disorders. *Investigative Ophthalmology & Visual Science*. 2010 Feb 1;51(2):744 –751.
 18. Okamoto F, Okamoto Y, Hiraoka T, Oshika T. Vision-related quality of life and visual function after retinal detachment surgery. *Am J Ophthalmol.* 2008 Jul;146(1):85–90.
 19. The SF Community - SF-36® Health Survey Update [Internet]. [cited 2012 Apr 14]; Available from: <http://www.sf-36.org/tools/SF36.shtml>
 20. Tranos PG, Ghazi-Nouri SMS, Rubin GS, Adams ZC, Charteris DG. Visual function and subjective perception of visual ability after macular hole surgery. *Am J Ophthalmol.* 2004 Dec;138(6):995–1002.
 21. Ghazi-Nouri SMS. Visual function and quality of life following vitrectomy and epiretinal membrane peel surgery. *Br J Ophthalmol.* 2006 May 1;90:559–62.
 22. Saxena S, Lincoff H. Finding the retinal break in rhegmatogenous retinal detachment. *Indian J Ophthalmol* 2001;49:199-202
 23. Wickham L, Bunce C, Wong D, McGurn D, Charteris DG. Randomized controlled trial of combined 5-Fluorouracil and low-molecular-weight heparin in the management of unselected rhegmatogenous retinal

- detachments undergoing primary vitrectomy. *Ophthalmology*. 2007 Apr;114(4):698–704.
24. Azad RV, Chanana B, Sharma YR, Vohra R. Primary vitrectomy versus conventional retinal detachment surgery in phakic rhegmatogenous retinal detachment. *Acta Ophthalmol Scand*. 2007 Aug;85(5):540–5.
 25. Rosser DA, Cousens SN, Murdoch IE, Fitzke FW, Laidlaw DAH. How sensitive to clinical change are ETDRS logMAR visual acuity measurements? *Invest. Ophthalmol. Vis. Sci*. 2003 Aug;44(8):3278–81.
 26. Unintentional displacement of the retina after standard vitrectomy for rhegmatogenous retinal detachment. Shiragami C, Shiraga F, Yamaji H, Fukuda K, Takagishi M, Morita M, Kishikami T. *Ophthalmology*. 2010 Jan;117(1):86-92.
 27. Influence of intraocular tamponade on unintentional retinal displacement after vitrectomy for rhegmatogenous retinal detachment. Codenotti M, Fogliato G, Iuliano L, Querques G, Maestranzi G, Prati M, Ramoni A, De Benedetto U, Bandello F. *Retina*. 2013 Feb;33(2):349-55.
 28. Macular displacement following rhegmatogenous retinal detachment repair. Lee E, Williamson TH, Hysi P, Shunmugam M, Dogramaci M, Wong R, Laidlaw DA. *Br J Ophthalmol*. 2013 Oct;97(10):1297-302.
 29. Early simultaneous fundus autofluorescence and optical coherence tomography features after pars plana vitrectomy for primary rhegmatogenous retinal detachment. Dell'Omo R, Mura M, Lesnik Oberstein SY, Bijl H, Tan HS. *Retina*. 2012 Apr;32(4):719-28
 30. Incidence and relation with anatomical and functional variables of postoperative macular displacement in rhegmatogenous retinal detachment. Cobos E, Rubio MJ, Arias L, Caminal JM, Garcia-Bru P, Català J, Jordan S, Vidal M, Gutiérrez L. *Retina*. 2016 May;36(5):957-61.
 31. Incidence and Factors Influencing Retinal Displacement in Eyes Treated for Rhegmatogenous Retinal Detachment With Vitrectomy and Gas or Silicone Oil. dell'Omo R, Scupola A, Viggiano D, Sammarco MG, De Turris S, Romano MR, Grimaldi G, dell'Omo E, Costagliola C. *Invest Ophthalmol Vis Sci*. 2017 May 1;58(6):BIO191-BIO199.
 32. Metamorphopsia and outer retinal morphologic changes after successful vitrectomy surgery for macula-off rhegmatogenous retinal detachment. Okuda, Tetsuhiko MD, PhD; Higashide, Tomomi MD, PhD; Sugiyama, Kazuhisa MD, PhD. *Retina*. 2018 Jan;38(1):148-154.

33. Measurement of retinal displacement and metamorphopsia after epiretinal membrane or macular hole surgery. Rodrigues IA, Lee EJ, Williamson TH. *Retina*. 2016 Apr;36(4):695-702.
34. Retinal displacement toward optic disc after internal limiting membrane peeling for idiopathic macular hole. Ishida M, Ichikawa Y, Higashida R, Tsutsumi Y, Ishikawa A, Imamura Y. *Am J Ophthalmol*. 2014 May;157(5):971-7.
35. Clinical parameters related to metamorphopsia outcome in patients with resolved central serous chorioretinopathy using M-CHART: retrospective cohort study. Bae S, Jin K, Kim H, Bae SH. *BMC Ophthalmol*. 2015 Dec 18;15:180.
36. Aniseikonia Following Pneumatic Retinopexy for Rhegmatogenous Retinal Detachment. Lee HN, Lin KH, Tsai HY, Shen YC, Wang CY, Wu R. *Am J Ophthalmol*. 2014 Nov;158(5):1056-61.

Appendix 1: STUDY FLOWCHART (ALL PATIENTS)



12 MONTHS

- FUNDUS AUTOFLUORESCENCE
- VA (ETDRS)
- M CHART-METAMORPHOPSIA
- ANISEIKONIA
- OCT
- M QUESTIONNAIRE