The official Newsletter of the

VITREO RETINAL SOCIETY - INDIA

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From the President's Desk

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Dear Friends

My dear Vitreo-Retinal Society of India (VRSI) members, accept my heartiest greetings. This issue of news letter from Vitreo Retinal Society of India highlights recent developments in vitreoretinal diseases and surgery. I would like to thank Dr S Natarajan, Dr Gopal Lal Verma, Dr Mahesh Shanmugam, Dr Anand Vinekar, Dr Praveen Sen and Dr Annie Mathai for contributing articles for this issue.

Given the paradigm shift in the vitreoretinal field, biggest challenge lie in keeping abreast with the changes. This news letter and next Annual VRSI Conference between December 12 to 14, 2013 at Lavasa are the steps in that direction. Our speciality is already in forefront to change the face of vitreo retinal practice in India. We need to work with sincerity, devotion and dedication to serve the vast population of India. We all need introspection as to how we can contribute to the progress and growth of this speciality in our country.

It is a matter of great pride for all of us that two of our former presidents of VRSI Prof. Amod Gupta and Prof. R V Azad are heading Advanced Eye Centre, PGIMER, Chandigarh and Dr R P Centre, AIIMS, New Delhi respectively. These two public sector institutions are apex centres and contribute maximum and best manpower in ophthalmology including vitreoretina for the entire country. Prof. Amod Gupta is a world leader in intraocular tuberculosis and Prof. Azad in retinopathy of prematurity. Other two illustrious former presidents of VRSI, Dr T P Das and Dr S Natarajan were bestowed with Padmashri Awards by President of India this year. This was also highlighted in last issue of news letter. They have all made us proud and we pay our respect to all these devoted leaders of VRSI. They also have set a very high benchmark for all of us to follow.

I would like to thank Dr V Narendran Convener Scientific Committee VRSI and all the contributors for this issue. I hope you will find this issue of news letter educational and enjoyable. We will be very much interested in your feedback regarding the news letter. This will help to further improve the issues in future.

"Inviting submissions for next VRSI newsletter. Kindly send your submissions along with your passport sized photograph to Dr. V. Narendran at vrsiscicom@gmail.com. Categories are Case Report or Original Article or Review Article. The word count for Case Report is upto 1,000 words, upto 10 references and upto 4 Figures/Tables. For Original/Review Article upto 2000 words, 25 references and 7 Figures/Tables. All the articles will be peer reviewed before publishing it in the VRSI newsletter."

Dr. A Giridhar
Honorary Secretary

From the Honorary Secretary's Desk

Greetings from the Governing Council of the VRS-I.

I would like to inform you all that we are likely to have a wonderful conference at Lavasa, Pune. The local Organizing Secretary Dr Aditya Kelkar is working very hard to make this conference a big success. The response to the free papers and videos has been amazing and this conference will also give us an opportunity to interact with the Frankfurt Retina Group.

Looking forward to participation of every member in the 23rd Annual Conference of the VRS-I at Pune.

With best wishes
Dr A Giridhar
Honorary Secretary

Dr. V. Narendran
Convener Scientific Committee
VRS-I

From the Convener Scientific Committee Desk

Dear Colleagues,

Greetings from the VRSI Scientific Committee Office!

At the outset I thank all the VRSI members for the overwhelming response we got for abstract submissions for the forthcoming 22nd Annual VRSI to be held in Lavasa in December 12-14 2013. We got a record number of submissions this year. We will be sending all the abstracts for external evaluation and will send the response by 15th September.

From next issue onwards, we invite articles from any VRSI member who are interested in publishing their articles in the VRSI newsletter. Kindly send your submissions along with your passport sized photograph to vrsiscicom@gmail.com. Categories are Case Report or Original Article or Review Article. The word count for Case Report is upto 1,000 words, upto 10 references and upto 4 Figures/Tables. For Original/Review Article it is upto 2000 words, 25 references and 7 Figures/Tables. All the articles will be peer reviewed before publishing it in the VRSI newsletter.

Hope to see you all in Lavasa.

Warm regards,

Dr. V. Narendran
Convener Scientific Committee, VRS-I.

Guest Editorial

Prof Dr S Natarajan

Dear Friends,

I am absolutely honored as a founder member of the Vitreo Retinal Society of India and delighted to write this guest editorial for this issue of the news letter.

I'm sure that we, our colleagues and our residents have benefitted from several programs conducted by the Vitreo Retina Society of India since its inception. On a global level we need to continue the collaboration with similar societies for enhancing and widening the opportunities for the gaining more educational materials and training programs.

In this issue I like to address few advanced concepts and developments in the vitreo retinal speciality like the 27 G Vitrectomy, Use of Endoscopes for vitrectomy , AC maintainer during vitreous surgery and Intrector. I am happy to say that i am the pioneer in using this type of advanced techniques in vitreo retinal surgery since 1984.

27 G Vitrectomy

A major difference between 25-g, 23-g and 27-g surgery vs conventional 20-g Pars Plana Vitrectomy is that these micro-incision techniques 1, 2 (ie, 25-g, 23-g and 27-g) are transconjunctival approach, with self-sealing wound. As peritomy is not performed and as conjunctival and scleral sutures are often not required, operative time is shorter. In addition, this may result in less astigmatism, less postoperative inflammation, and improved postoperative comfort.The rationale behind using 27-g surgery is that smaller is better than larger wounds. They are more likely to self-seal and prevent hypotony. Smaller wounds are less prone to vitreous prolapsed also. The 27-g was first introduced in 2007, when Oshima et al. introduced a 27-g chandelier light. Later Sakaguchi et al. published their experience performing 27-g nonvitrectomy for epiretinal membranes. The potential indications are given in table.1.

Table:1

Potential Indications for 27G PPV
Macular Hole
Macular pucker
Vitreomacular traction
Vitreous hemorrhage
Focal tractional retinal detachment

Recent introductions of 253 and sub 25 G vitrectomies are important advances in the evolution of microincision vitreous surgery. However, the incidence of cataract progression, a major postoperative complication of vitrectomy, is still high with small-gauge instrumentation. The following link will help in watching this type of surgery performed by me and hosted in www.vitreousurgery.in (http://vitreousurgery.in / PlayVideo.aspx? SeriesId=14)

The 27-gauge chandelier endoilluminator

The tip is introduced about 3 mm into the vitreous cavity, so the reflected glare from the tip is mostly blocked by the iris during surgery. The tip of the light fiber is shaped-like a cone for wide-angle illumination. A polyamide sleeve (arrow) covers the microfiber to prevent thermal burn-induced scleral damage. A footplate and a malleable sleeve keep the chandelier in contact with the eyeball.

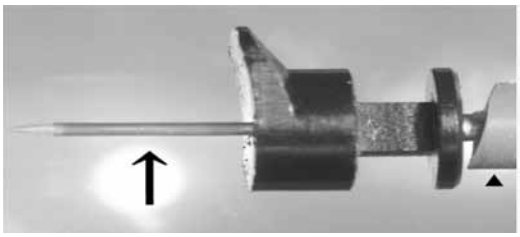

Figure 1: 27-gauge chandelier endoilluminator(DORC)

27/29 - Gauge Chandelier Light Fiber Mercury Vapor Illuminator offer several advantages. Compared with other commercially available illumination systems, the mercury vapor light source combined with the 27/29 - gauge chandelier probe has several advantages. The 27/29 - gauge chandelier illumination has a green yellowish hue, when illuminated by a mercury vapor light source and is comfortable to surgeons' eyes. The use of an ultraviolet and blue light cutoff filter reduce phototoxicity with higher hazard efficiency. Insertion through a 27- gauge (0.35 mm) sclerotomy, facilitates surgical entry and closure, and conjunctival peritomy and suture placement are not needed. The 27- gauge chandelier endoilluminator, combined with a xenon light source, is particularly useful during cases requiring a panoramic viewing system. The retracted needle wall serves as an optical shield to minimize the reflected glare and as a heat shield to prevent thermal burns on the sclera

View of the 29/27- gauge one-step chandelier probe. The device consists of a retractable 27- gauge thin-walled needle socket through which the 29- gauge light fiber passes. The tip of the 29- gauge light fiber can be exposed easily by fully retracting the outer needle wall

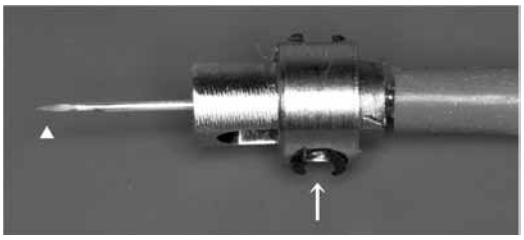

Figure 2: 27-gauge one-step chandelier probe(Synergetics Inc)

27 - gauge transconjunctival instruments for epiretinal membrane removal are designed effectively for comfortable intra ocular manipulation.The size of the shaft - 0.40 mm in diameter. The shaft of the microforceps is rigid and thin enough for intraocular manipulation. The shape of the grasping end is asymmetric. The distance between the two tips of the grasping end is 750 microns when opened and is wide enough to grasp tough and thick proliferative epiretinal tissue.

Intrector System

Intrector system 4 is a new surgical equipment which helps in single port trans conjunctival 23G Vitrectomy. I am happy that I am the first person who introduced this in India. This has the advantage of managing many vitreous surgeries in a less invasive manner. The procedure involves the use of a portable single entry step of 23 G vitrectomy instrument for simultaneous drug delivery, infusion nd aspiration, vitreous cutting all with the use of a single tip. The aspiration and injection are performed by an assistant, thereby allowing for an anterior, core and central vitrectomy with any desired volume being removed.

This is an extremely simple and quick operation. It incorporates 23G needle tip. It is portable and battery operated. It has a guillotine type cutter with adjustable speed. The other advantages are it is less expensive, a single step entry with no cannulas, there is separation of injection, infusion and aspiration, cutting utilizing two individual channels in the probe tip. In my personal experience, the results were good in endopthalmitis cases which I have treated.

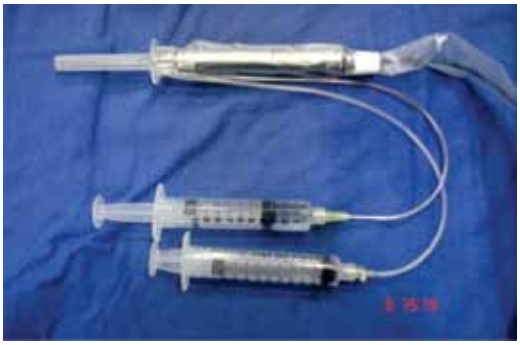

Figure 4.Intrector.

Endoscopic Vitrectomy

The first endoscope was described by Thorpe in 1934. Several types of endoscopes were introduced with variable results reported. The endoscopes currently used commonly, employ two different modes of transmission. Fused fibre optic endoscopes transmit segmented images through single fibres, allowing a long distance transmission. The second type is Gradiant index endoscopes which transmit whole images through a single rod of varying refractive indices allowing for refraction and transmission of light. The applications include visualization and manipulation of vitreous cavity through opaque media,Intraoperative inspection of wounds and other difficult areas, Endophthalmitis, proliferative diabetic retinopathy (complicated by hyphema and miosis), to view anterior retina and ciliary body in posterior vitrectomy patients undergoing large retinectomies, in subretinal choroidal neovascular membrane dissection, Complicated cataract surgery with retained lens fragments in the vitreous, Complicated dislocated IOL removal etc.

Figure 5 - Ocular Endoscope(Ref.5)

Two types of endoscopes are available. The most commonly used one is the Wide Angle endoscope (110 0) 19 G depth of focus 3-35mm. The other one is the Sub retinal endoscope (50 0) 20 G with probe depth of focus 0-5mm. Ocular endoscopy is limited by a fairly steep initial learning curve as a new proprioceptive sense must be developed, before one can comfortably operate in the vitreous cavity. The depth perception and shadows cast by instruments onto the retinal surface from eccentric incident light will be lost, therefore, it is important that the retinal surface be approached slowly. Despite its current limitations, endoscopy can be a significant help in the management of patients with retinal detachment in whom the retina is poorly visualized.

Two port Vitrectomy with AC maintainer

Anterior Chamber manger can be used during vitrectomy in pseudophakic and aphakic eyes, with two port pars plana approach. The advantages using AC maintainer are that it avoids entry through the vitreous base, avoids sub retinal entry when it is difficult to visualize the posterior segment due to thick exudates and membranes. It helps in preventing hypotony also.

Recent developments in surgical, medical and diagnostics of retinal disorders is promising and it throw light for the future possibility of more effective treatment outcome and benefits for the patients. The world

wide acceptance of the Argus II retinal prosthesis system in advanced cases of retinitis pigmentosa and the FDA approval is promising. The recent results in clinical studies shows that the system helped subjects to identify the location or movement of objects and people, to recognize large letters, words and also helped in daily activities of life such as walking on a sidewalk without stepping off and detecting street curbs.

The newer developments with reported improved anatomic response in treatment of refractory AMD patients with aflibercept has been reported recently. The reduction in number injections remains as challenge in treating refractory cases. The interesting developments in this field is quite promising in terms of reducing the burden of care on patients.

The Adaptive optics technology which was used to improve the performance of optical systems by reducing the wave front distortions helps in better retinal imaging also. The correction of higher order aberrations by measuring the wavefront and compensating for them with the technology that helps in better analysis and better retinal imaging at cellular levels.

Ref:

1.*Oshima Y, Awh CC, Tano Y. Self-retaining 27-gauge transconjunctival chandelier endoillumination for panoramic viewing during vitreous surgery. Am J Ophthalmol. 2007,143:166-167.*

2.*Sakaguchi H, Oshima Y, Tano Y. 27-gauge transconjunctival nonvitrectomizing vitreous surgery for epiretinal membrane removal. Retina. 2007;27:1131-1132*

3.*Biju Raju, NSD Raju. 25 gauge vitrectomy under topical anesthesia: A pilot study,Indian Journal of Ophthal. 2006 Vol 54:3;185-188*

4.*Koch FH, Koss MJ. Microincision vitrectomy procedure using Intrector technology.Arch Ophthalmol. 2011 Dec;129(12):1599-604.*

5. *Sabti KA, Raizada S .Endoscope-assisted pars plana vitrectomy in severe ocular trauma.Br J Ophthalmol. 2012 Nov;96(11):1399-403.*

Obituary

Dr. Stephen J Ryan

Stephen J Ryan passed away on April 29, 2013 on his 70th year. He was the President of Doheny Eye Institute, Los Angeles, USA and author of 9 books including RETINA which is in its 5th Edition.

Dr. Morton S Cox Jr.

Morton S Cox Jr. passed away on April 21, 2013 on his 79th year. He was a world expert in retinal ocular trauma and optic pit macular disease practicing in Michigan, USA.

Dry ARMD and upcoming drug trials

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Dr. GopalLalVerma

Introduction

The pathogenesis of drusen formation and geographic atrophy is poorly defined and so is the role of therapy.There is no single pathway, several key processes are involved in drusen formation and progression of geographic atrophy (GA).

Role of AMD candidate genes and environment

Research in dry ARMD have implicated role of 12-15 abnormal genes mainly CFH, ARMS2, C2, C3, CFB,CFI etc. In a recently published study by Yu and coworkers1 Markov model of AMD disease progression CFH and ARMS2 act to drive the transition from AREDS2 to AREDS3 disease. CFB, ,LIPC and CEPT are most significant genetic driver of AREDS3 disease to CNV, while CFI is asignificant driver of progression from AREDS3 to GA. Simillarly elevated body - mass index is significant for the transition from AREDS3 to GA but not for development of CNV. Smoking affects transition to GA and CNV but not significant for development of AREDS3 disease. Age is an important driver of CNV but does not influence progression of AREDS3 to GA. The Known polymorphism of above genes and environmental factors like smoking, diet, sunlight exposure help to predict individual`s risk of progressing to GA or CNV. The Macula Risk NXG (Arctic DX,Inc.) test guides regarding individual`s inherited risk of developing vision loss due to ARMD with smoking and body mass etc. RetnaGene (Sequenom,Inc.) test determines the probability of developing CNV. These test are not routine screening test but helps in early detection of treatable advanced ARMD.

Progression ofdrusen to ARMD -Clinicopathological evidence

Although fundus color photo, fundus auto fluorescence have been the standard for measurement of drusen and RPE activity but recent incorporation of software for volumetric measurement of drusen and registration of area of GA in OCT has paved way for accurate analysis of progression of dry ARMD changes in various clinical drug trials. In AREDS2 Ancillary SD - OCT study Christenbury and coworkers2 studied axial distribution of hyper reflective foci on SD-OCT in intermediate ARMD through 2 years followup and showed that SD-OCT hyperreflective foci proliferation and migration may serve as important biomarkers for AMD progression.

Is there any light at the end of tunnel

Currently there are at least dozen promising clinical trials to address dry form of AMD which has lacked effective treatment. Investigational strategies for treatment of atrophic AMD include vitamin A visual cycle modulators, oral nutraceutical formulations, and injectable molecular interventions altering complement system to retard the progression of GA. The aim of these investigational interventions is to prevent photoreceptor and retinal pigment epithelial (RPE) cell loss, reduce the load of toxic metabolites in these cells, and suppress inflammation.

Another approach under investigation in relation to preventing photoreceptor and RPE cell loss in GA is cellbased therapy—the harvesting and transfer of stem cells to support or replace diseased cells.

The main sources for the cells used in cell-based therapies include embryonic stem cells, adult stem cells. The following ongoing clinical trials in dry ARMD are worth mentioning.

Oral formulations

SEATTLE study : Safety and efficacy Assessment Treatment Trials of Emixustat. (ACU- 4429) in geographic atrophy. Emixustat hydrochloride is a visual cycle modulator. Emixustat orally given inhibit activity of RPE65resposible for conversion of all- retinal esters to11-cis retinol and reduces levels of 11 - cis and all-transretinal thereby reducing accumulation of A2E in RPE. A2E (product of two molecule of all - trans retinal and ethanolamine) is a cytotoxin having several deleterious effect on REPE cells including impairment of lysomal degradation 3, induction of proapopticproteins,complement activation and upregulation of VEGF in RPE and choroid. Reducing load of A2E in RPE could rescue RPE cells. The response of emixustat is dose related. Emixustat is in phase 2b/3 trial. The enrollment is of 440 participants to determine if emixustat reduces the rate of progression of GA compared to placebo. The downside of emixustat is that it reduces rod photoreceptor activity.

Nutriceuticals Study

Effect of Omega3 - fatty Acids on blood levels of Omega3 fatty acids in patients with AMD.100 participants AREDS category 3 or 4 are under study.

I-TEAM study : Intervention Trial in Early Age - related Macular degeneration. In this study 120 participants AREDS 2 category will receive lutein rich beverage (lutein from egg enriched in carotenoids and Omega3 fatty acids). Lutein and zeaxanthin act as free radical quencher.

TOGA study : Treatment with Oracea for Geographic Atrophy. Doxycycline is known to inhibit matrix mettaloproteinasesenzymes, cytokine production and inhibit caspase activation preventing cell death.246 study participants will receive 40 mgm of oral Doxycycline and placebo in ratio of 1:1 daily for 24 months.

Topical formulation.

MC1101 1% TID drops (MacuClear,Inc.). The drug increases choroidal blood flow. Safety and efficacy in 60 participants of mild to moderate nonexudative ARMD vision better than 20/80 have been studied. Phase3 trials study started.

Intravitreal Injections.

Sirolimus study: NEI sponsored pilotstudy of the evaluation of intravitreal Sirolimus in the treatment of bilateral Geographic Atrophy (GA) associated with Age-Related Macular Degeneration. Study investigators believe that GA may be partly caused by inflammation. Sirolimus is a drug that can help

prevent inflammation. Researchers want to see if sirolimus can help prevent vision loss in people with GA. Participants initially received a (440 μgm) intravitreal injection sirolimus in the study eye at baseline and every two months thereafter. Studyresults are awaited.

FluocinoloneAcetonideIntravitreal inserts in Geographic atrophy:. Interventional randomised double blind study in 40 participants with bilateral GA secondary to AMD of ≥ 0.5 and ≤ 7 disc areas.

Intravenous infusions

COMPLETE: Complete inhibition with eculizumab (C5 inhibitor) for the treatment of non exudative AMD.Participants 60 divided in drusen and GA cohort in ratio of 2:1 to evaluate the safety and efficacy of eculizumab for the treatment of dry AMD as evaluated by the change in drusen volume and area of geographic atrophy. patient will receive eculizumab 600 mg or 900 mg via IV infusion over approximately 30 minutes once a week (7 ± 2 days) for 4 weeks followed by 900 mg or 1200 mg every 2 week untill 24 week. Study completed.

RN6G: anti - Aβ40/42 (Anti - Amyloid therapy) Randomised double blind intravenous treatment in 24 participants of advanced dry ARMD including GA.

GSK933776:Study participants 162.A Phase 2, Multi-centre, Randomised, Double - masked, Placebo-controlled, Parallel-group Study to Investigate the Safety, Tolerability, Efficacy, Pharmacokinetics and Pharmacodynamics of GSK933776 Intravenous infusion in Adult Patients With Geographic Atrophy (GA) Secondary to Age - related Macular Degeneration (AMD)

Sub retinal Injections

CNTO2476 : Participants 56. Phase 1/2a, Multicenter, Randomized, Dose Escalation, Fellow - Eye Controlled, Study Evaluating the Safety and Clinical Response of a single, subretinalinjection of Human Umbilical Tissue - Derived Cells (CNTO 2476) delivered through microcatheter system in subjects with visual acuity no better than 20/200 in each eyewith Geographic Atrophy area at least 2.6mm 2 involving foveasecondary to ARMD.

Human central nervous system stem cells (Hu - CNS-SC) in AMD.Participants 16.

MA09 - hRPE : subretinal transplantation of human embryonic stem cell derived RPE cells 50000-150000 in 12 participants. Estimated study completion date July 2014.

Reasearch in dry ARMD is a dynamic field,unlike wet form of ARMD amenable to anti vascular endothelial growth factor therapy there is no effective therapy for dry ARMD till date.

References

1. Yu Y,Reynolds R,Rosner B. Daly MJ,Seddon JM. prospective assessment of genetic effects on progression to different stages of age related macular degeneration using multivariate Markov models.InvestOphthal Vis Sci.2012:53:1548-1556.

2. ChristenburyJG,Folgar A et al. progression of Intermediate Age-related macular Degeneration with proliferation and inner retinal migration of hyper reflective foci.Ophthalmology 2013; 120:1038-1045.

3. Bermann,Schutt F et al.Does A2E,a retinoid component of lipofuscin and inhibitor of lysosomaldegradativefunction,directly affect the activity of lysosomalhydrolases? Exp Eye Res. 2001; 72: 191-195.

4.A Study of the safety and efficacy of CNTO2476 in patients with age-related macular degeneration. http://clinicaltrials.gov/ct2/show / NCT01226628.

Role of Intravitreal Chemotherapy for Refractory Retinoblastoma

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Retinoblastoma tumors not confined to the retina in an eye with salvageable vision are treated primarily with multiple cycles of triple drug systemic chemotherapy.

Tumors with focal subretinal or vitreous seeding (International classification of retinoblastoma group C) have 90% eye salvage rate with systemic chemotherapy. However more than 50% of eyes with diffuse vitreous or subretinal seeding (International classification of retinoblastoma group D) may have to be enucleated despite systemic chemotherapy.[1] Vitreous seeds may be recalcitrant to radiation as well.

Kaneko et al. in 1987 were the first to attempt treating eyes with recalcitrant vitreous seeding in retinoblastoma with local chemotherapy. They delivered the chemotherapeutic agent in to the affected eye using 2 routes – one by catheterizing the ipsilateral carotid artery with a balloon catheter and injecting the drug in to the ophthalmic artery and the second by an intravitreal injection.[2] They injected 8microgram (mcg) of Melphalan in to the vitreous cavity of eyes with residual vitreous seeds, persisting despite radiation and managed to salvage nearly 50% of the treated eyes.

Indications:

Intravitreal chemotherapy is presently employed to treat recalcitrant or recurrent vitreous disease in eyes that have failed conventional, maximum treatments. Typically these eyes have visual potential and would have been treated with full course of regular or hi-dose systemic chemotherapy, multiple local treatments (laser, cryotherapy, TTT) and often with radiation as well, prior to being treated with intravitreal chemotherapy.

Drugs:

1. Melphalan is currently the most commonly used intravitreal chemotherapeutic agent. Dosages varying from 8mcg – 50mcg have been employed to treat vitreous seeding, with 8mcg being the most commonly employed dosage. Rabbit experiments have shown that intravitreal melphalan up to 40mcg can be administered without risk of changes in the electroretinogram.[3]

2. Carboplatin has also been employed to treat recalcitrant vitreous disease at doses of 3-6mcg. Animal experiments indicate that carboplatin up to 8mcg may be safe to the rabbit retina.[4]

Intravitreal injections are most often repeated once in 4 weeks, though injections as often as 1week have been employed.[5,6]Munier et al report the largest number of injections – 122 injections in 23 eyes over a median of 22 months, injections repeated once every 7-10 days until complete disappearance of the vitreous disease.[6]

Intravitreal methotrexate has also been used to treat retinoblastoma and intravitreal topotecan is an emerging option.[7,8]

Concerns with intravitreal injection in retinoblastoma

Intravitreal injections invade the eye and retinoblastoma being a friable tumor can seed the needle track thereby converting an eye with intraocular disease and excellent prognosis to an eye with extraocular retinoblastoma associated with poor prognosis for life. This concern has been the barrier to adapting intravitreal injection of retinoblastoma as a form of treatment except in exceptional situations.

Another important concern is the risk of endophthalmitis with intravitreal injections. This risk assumes particular significance when treating retinoblastoma. An endophthalmitis has to be treated with repeated intravitreal injection of antibiotics, some cases needing a therapeutic vitrectomy. These therapeutic maneuvers assume lethal significance in the presence of an active retinoblastoma that can seed the orbit through the needle tracts or the sclerotomy wound. Hence an infection following an intravitreal injection in retinoblastoma may in all probability result in loss of the eye to enucleation.

Technique of injection

While the technique of administering an intravitreal injection in retinoblastoma is no different from any other intravitreal injection, some precautions are to be followed to decrease the risk of orbital seeding through the needle tract.

1. Use of a small gauge needle such as 30 -32 gauge needle
2. Injection in the quadrant where there are no or minimal vitreous seeds
3. Performing an aqueous tap to lower the intraocular pressure prior to the injection decreases the risk of needle tract seeding. Aqueous tap obviously has to be avoided in the presence of anterior chamber disease. A special technique of paracentesis has been described prior to intravitreal injection in retinoblastoma. In brief, it involves creating a clear corneal track up to the descemets membrane using a 25gauge MVR blade and entering the anterior chamber through this using a 32 gauge needle. This technique results in a self sealing paracentesis tract.[9]
4. Single or triple freeze thaw cryotherapy applied to the injection site as the needle is withdrawn to kill cells that may be spilt at the site of injection.
5. Vigorous shaking of the eye to disseminate the drug within the eye
6. We usually employ pre-injection 5% povidone applied to the conjunctival cul-de-sac 5 and 10 minutes before and also post injection. Though we do not routinely use pre and post injection prophylactic topical antibiotics, using them may further minimize the risk of infection in these sensitive eyes.

Complications

Complications such as preretinal hemorrhage, retinal vasculitis and retinal pigment epithelial alterations may occur without adversely affecting vision. More serious complications such as cataract, vitreous

hemorrhage, subretinal hemorrhage, severe hypotonia have been reported with higher doses of melphalan.[2,5,6]

Fortunately no cases of orbital extension have as yet been reported even in the series of patientswith the longest follow-up, reported by Kaneko et al.

Results

Results of eye salvage vary from 40-87% up to a medium follow-up ranging from 6-22 months.[2,5,6] We however need to realize that these are eyes with end-stage disease with no other treatment option available and would have otherwise be enucleated. Considering these factors, the results are rather encouraging. (Fig 1,2)

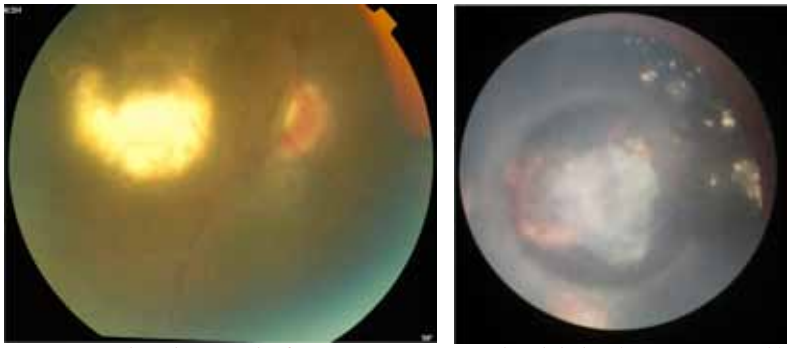

Fig 1,2: Fundus photograph of 2 eyes post intravitreal melphalan (2 injections each) showing disappearance of vitreous seeds in one eye (Fig 1) and inactive seeds in the other (Fig 2). The central opacity in Fig 2 is due to radiation induced cataract.

To conclude, intravitreal injection to treat retinoblastoma iscurrently used to treat recalcitrant vitreous disease after exhausting other safer modes of treatment such as systemic chemotherapy and often, external beam radiation. Special precautions and technique have to be employed when administering the injections and serious complications resulting in loss of vision and eye may occur. In the absence of long-term results, intravitreal injections have to be used with extreme caution in select situations to treat extra-retinal retinoblastoma in eyes with visual potential.

References:

1. *Shields CL, Fulco EM, Arias JD, Alarcon C, Pellegrini M, Rishi P, Kaliki S,Bianciotto CG, Shields JA. Retinoblastoma frontiers with intravenous, intra-arterial, periocular, and intravitreal chemotherapy. Eye (Lond). 2013 Feb;27(2):253-64.*

2. *Kaneko A, Suzuki S. Eye-preservation treatment of retinoblastoma with vitreous seeding. Jpn. J. Clin. Oncol. (2003) 33 (12): 601-607.*

3. *Ueda M, Tanabe J, Suzuki T, Sakai H, Mochizuki K, Kitano K, Inomata M, Kaneko. Conservative therapy for retinoblastoma--effect of melphalan on in vitro electroretinogram]. Nihon Ganka Gakkai Zasshi. 1994 Apr;98(4):352-6.*

4. *Pochop P, Darsova D, Uhlik J, Lestak J, Kukacka J, Kodetova D, Klapkova E, Malis J, Vajner L. Retinal toxicity after repeated intravitreal carboplatin injection into rabbit eyes. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2012 Dec 10. [Epub ahead of print]*

5. *Ghassemi F, Shields CL. Intravitreal melphalan for refractory or recurrent vitreous seeding from retinoblastoma. Arch Ophthalmol. 2012. Oct;130(10):1268-71.*

6. *Munier FL, Gaillard MC, Balmer A, Soliman S, Podilsky G, Moulin AP, Beck-Popovic M. Intravitreal chemotherapy for vitreous disease in retinoblastoma revisited: from prohibition to conditional indications. Br J Ophthalmol. 2012 Aug;96(8):1078-83.*

7. *Kivelä T, Eskelin S, Paloheimo M.Intravitreal methotrexate for retinoblastoma. Ophthalmology. 2011 Aug;118(8):1689, 1689. e1-6.*

8. *Buitrago E, Del Sole MJ, Torbidoni A, Fandino A, Asprea M, Croxatto JO, Chantada GL, Bramuglia GF, Schaiquevich P. Ocular and systemic toxicity of intravitreal topotecan in rabbits for potential treatment of retinoblastoma. Exp Eye Res. 2013 Mar;108:103-9.*

9. *Munier FL, Soliman S, Moulin AP, Gaillard MC, Balmer A, Beck-Popovic M. Profiling safety of intravitreal injections for retinoblastoma using an anti-reflux procedure and sterilisation of the needle track. Br J Ophthalmol. 2012 Aug;96(8):1084-7.*

Spectral Domain Optical Coherence Tomography in Retinopathy of Prematurity – What we still don't see!

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Although Spectral Domain Optical Coherence Tomography (SD-OCT) has become an essential tool for a VR-surgeon, its utility and popularity in pediatric retinal conditions is interestingly limited at this time. The most important reasons for this have been the limitation (and until a while ago, unavailability) of hand-held devices, and the fact that pediatric patients remain largely uncooperative and require either sedation or anesthesia for good image acquisition.1Recently the FDA approved hand held device, Bioptigen (Research Triangle, NC, USA) and newer techniques of imaging supine infants haveenhanced our understanding of OCT in infants.Spectral Domain OCT, particularly scores over the older Time-Domain OCT in pediatric imaging, by providing faster and more accurate scans, an obvious advantage while imaging an uncooperative patient.

This article will summarize the author's experience in imaging infants, particularly premature infants with and without Retinopathy of Prematurity (ROP).[1-9,11]

The utility of OCT in detecting features of advanced ROP such as preretinal structures, retinoschisis and retinal detachment not identified on clinical exam has been reported.10 However, OCT changes in acute ROP in early stages, particularly those that 'spontaneously resolve' are not well studied.[2-4]

We described the modification of a table-top, 'adult' OCT device, namely the Spectralis (Heidelberg Engineering, Germany) into a hand-held device for office use.[2] In a two-step disassembly, the camera is freed and is pointed downwards in alignment with the infant's eye. Using the infrared window the retina is focused and the desired OCT images are captured. To image the periphery, the camera is tilted and the resulting laterally inverted images must be remembered while localizing the pathology. Using this modification we were able to map flat neovascularization (FNV) in aggressive posterior ROP, that were not easily discernible clinically and target selective laser photoablation to these structures. Despite the absence of 'image registration', the same area was re-imaged on subsequent visits and the regression of the FNV was documented on the OCT scans.

While we were concentrating on imaging the peripheral FNV, we serendipitously observed, abnormal foveal changes, resembling 'macular edema' of adults in some of our babies. This led to our second report,3wherein we reported a cohort of 146 eyes of 74 premature infants, of which 27 eyes had stage 1, 79

had stage 2 ROP and 40 had no ROP. The mean central fovealthickness of these 3 groups was 157µ, 206µand 136µ respectively ($p < 0.001$). Post-hoc test revealed that the difference was due to stage 2 ROP. In 29% of stage 2 eyes (and none in stage 1 and eyes without ROP), we found abnormal fovealchanges which we categorized into 2 groups – Pattern A and B. All foveae were 'normal' on clinical appearance and on Retcam imaging.Pattern A, (Fig 1*)had a dome shaped elevation in the center of the foveae with intraretinal cystoid spaces, highly reflective vertical septae between the roof and floor of the dome and complete disruption of the foveal depression with an average macular thickness of 406µ. Pattern B, (Fig 2*)had multiple, confluent, vacuolated, optically empty spaces within the inner retina with fewer septae and some preservation of the foveal depression with an average thickness of 224µ ($p < 0.001$).Interestingly, both patterns in all eyes, spontaneously resolved to 'normal' configuration on OCT by the 52nd week of corrected age, which coincides with the 3rd month from the expected delivery date.

We hypothesized that these transient foveal changes could be due to an increased concentration of VEGF or due to the greater mechanical forces in stage 2 compared to stage 1 eyes.[3] Although literature is replete with adults who have had historical mild ROP who 'do not see as well as they should' and it is tempting to suggest that these foveal changes, albeit transient, may influence fovealization and hence long term vision, the truth is that there is insufficient data at this time to pass judgment on the significance of these findings. In our limited follow-up of these 'edema' babies (unpublished), we have not found any difference in visual acuities at the end of the first year, although there is a significantly higher proportion of hyperopia in infants who suffered from edema than those who did not.

More recently we used the Bioptigen to study the foveal development in infants.[3-7]It is very interesting to learn that infants are not born with the normal 'OCT morphology' of their adult counterparts. In comparing the layers between a 38-year-old male (Fig 3*) with a 36-week-old (corrected age) infant(without ROP)(Fig 4*), we noticed that the infant's fovea is 'immature'. Owing to the difference in reflectivity of the retinal layers that stack one over another, substructure differentiation is possible and even quantifiable. With the advent of 3D scans it is now possible to reconstruct the foveal microanatomy (Fig 5*).[5,6]

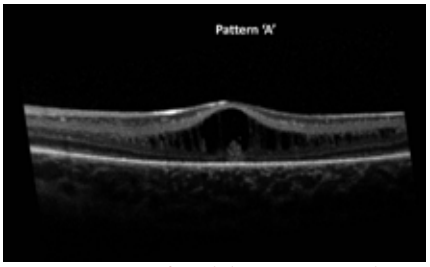

Fig 1: Pattern Afoveal disruption noted in 52% of those with macular changes.*

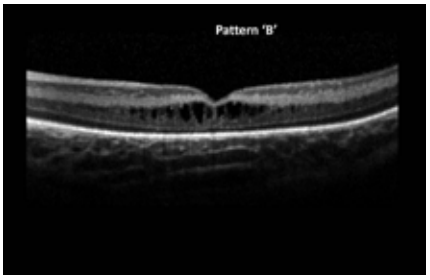

Fig 2: Pattern B with less severe changes in the foveal contour was seen in the remaining 48% of infants with macular changes.*

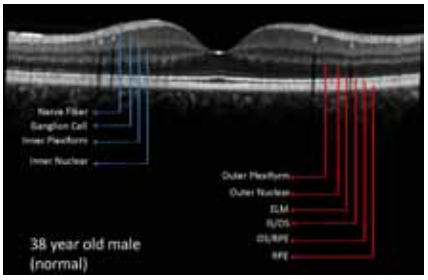

Fig 3: SD-OCT image of an adult male showing the normal 'mature' layers of the retina*

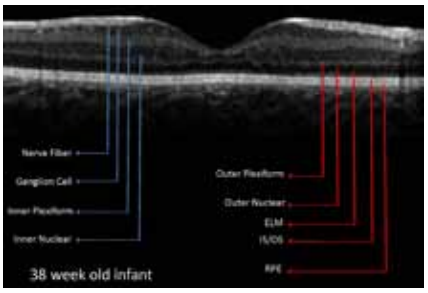

Fig 4: 36 week old infant with a birth weight of 1250 grams and 31 weeks of gestation showing 'immature' layers*

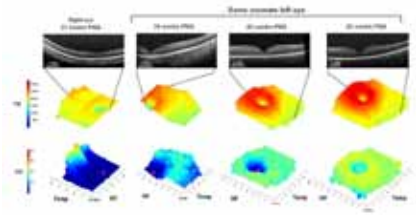

Fig 5: Three-dimensional map of retinal layers with their dynamic changes in a growing neonate*

Firstly, it is important to understand some of the key terms that are used in describing these layers:[5,6]

a. Central foveal thickness – refers to the layers extending from the inner aspect of the inner limiting membrane (ILM) to the inner aspect of the RPE at the foveal center.

b. Inner retina: refers to layers from the inner aspect of the ILM to the outer border of the inner nuclear layer (INL)

c. Outer retina: refers to layers extending from the inner aspect of the outer plexiform layer (OPL) to the inner border of the RPE

d. Photoreceptor layer: refers to the layers from the outer aspect of the OPL to the inner border of the RPE.

The premature eye differs from older children and adults in having: [5,6]

1) Shallower foveal depression

2) Presence of one to many IRLs at the foveal center

3) Thinner retinal layers overall and

4) Attenuation of the PRL with absence of the photoreceptor sub-layers relative to the adult.

The most immature foveae show the presence of ganglion cell layers (GCL), inner plexiform layers (IPL) and INL in the foveal center. These layers 'migrate' centrifugally to eventually result in a single thin hyperreflective band.Interestingly, in premature infants, the PRL subcellular layers have not developed into a visible structure on OCT as yet. These include the external limiting membrane (ELM) and the inner-segment outer segment (IS-OS) junction. It is fascinating to observe on serial OCT images, that the IS-OS layer progressively approaches the foveal center in a centripetal growth pattern between the 33rd and the 48th week corrected age.[6]

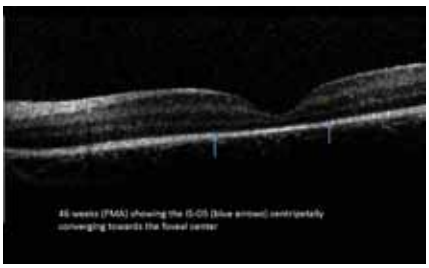

Fig 6: At 46 weeks PMA, the IS-OS is seen as two separate points converging at the foveal center*

(Fig 6* and Fig 7*). The ELM has been 'imaged' at variable ages and we observed it at 40 weeks.[4]

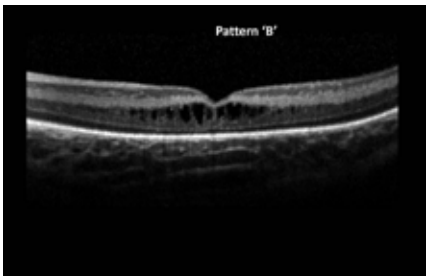

Fig 7: The same infant imaged 2 weeks later (48 weeks) now shows that the IS-OS has centripetally grown to fuse at the foveal center.*

There is a second hyperreflective band between the RPE and the IS-OS, attributed to the outer segments of the photoreceptors and the RPE microvilli. This so called, "OS-RPE" layer is currently poorly understood, but its maturity certainly appears after the IS-OS fusion at the foveal center. The upward sloping 'tent' of the foveal center also accentuates with increasing age and is believed to coincide with the lengthening of the foveal cones and more dense cone packing.

It has been our attempt to correlate visual acuity with these subcellular layers and in our ongoing study (unpublished) we noted that critical events such as IRL migration and appearance and maturation of the PRL subcellular layers influence vision in these growing infants.[11] Also the presence of ROP, even mild, spontaneously regressing disease, does influence some of these layers negatively and thus impacts vision as well.

The other more obvious utility of OCT in ROP would be itsrole in imaging Stage 4 ROP.[9] A clinically 'on' macula (Stage 4A) imaged on OCT could help detect the 'extension of the detachment' into the foveal center and hence 're-classify' it to a stage 4B. This can help plan surgery and prognosticate the outcome more accurately.

We are currently experiencing an exciting phase of OCT imaging in pediatric retina. With improved devices and techniques, our understanding of diseases and its management has undergone a sea-change. Further research will help us unravel some of the hitherto unknowns to help us visualize what we still do not see!

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References:

1. Vinekar A. Imaging an infant on optical coherence tomography. In Vinekar A, Avadhani K. (Eds).Spectral Domain Optical Coherence Imaging of the Eye. New Delhi:Elsevier;2013.p.351-353.

2. Vinekar A, Sivakumar M, Shetty R, et al. A novel technique using spectral-domain optical coherence tomography (Spectralis, SD-OCT+HRA) to image supine non-anaesthetized infants: utility demonstrated in aggressive posterior retinopathy of prematurity. Eye 2010;24(2):379-82

3. Vinekar A, Avadhani K, Munusamy S et al. Understanding Clinically Undetected Macular Changes in Early Retinopathy of Prematurity on Spectral Domain Optical Coherence Tomography. Invest Ophthalmol Vis Sci. 2011 Jul 15;52(8):5183-8

4. Vinekar A, Avadhani K, Munusamy S et al. Macular Edema in Premature Infants. Ophthalmology, 2012 Jun;119(6):1288-1289.e1

5. Vinekar A, Maldonado R, Toth C. Foveal layers in an infant. In Vinekar A, Avadhani K. (Eds).Spectral Domain Optical Coherence Imaging of the Eye. New Delhi:Elsevier;2013.p.354-356.

6. Vinekar A, Maldonado R, Toth C. Foveal maturation in infants. In Vinekar A, Avadhani K. (Eds).Spectral Domain Optical Coherence Imaging of the Eye. New Delhi:Elsevier;2013.p.357-360.

7. Vinekar A, Avadhani K. Retinopathy of Prematurity – Macular changes. In Vinekar A, Avadhani K. (Eds).Spectral Domain Optical Coherence Imaging of the Eye. New Delhi:Elsevier;2013.p 377-378

8. Vinekar A. Pai H, Anaspure H. ROP – Neovascularization. In Vinekar A, Avadhani K. (Eds).Spectral Domain Optical Coherence Imaging of the Eye. New Delhi:Elsevier;2013.p 379-380

9. Vinekar A, Yadav NK. ROP – Postvitrectomy. In Vinekar A, Avadhani K. (Eds).Spectral Domain Optical Coherence Imaging of the Eye. New Delhi:Elsevier;2013.p 381-383.

10. Chavala SH, Farsiu S, Maldonado R, et al. Insights into advanced retinopathy of prematurity utilizing handheld spectral domain optical coherence tomography imaging. Ophthalmology. 2009;116:2448–2456.

11. Vinekar A, Avadhani K, Munusamy S et al. Influence of photoreceptor sub-elements on visual acuity in premature infants with and without ROP. Best Poster at the 3rd, World ROP Congress, October, 2012, Shanghai, China.

Ocular Electrophysiology: Present Status

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Electrophysiology of the eye is a non invasive method which allows functional assessment of retina as well as the whole visual pathway. Where **full field electroretinogram** (ffERG) is a mass electrical potential generated by the retinal cells in response to a flash of light newer technique like the **multifocal electroretinogram** (mfERG) can stimulate various focal areas of the retina and pick up focal disease as well as map the disease distribution. MfERG was developed by Erich Sutter.[1] According to ISCEV standards2 it is recorded monocularly using Burian Allen or DTL electrodes in a light adapted state after pupillary dilatation with refractive error correction in place. A special pseudo-random m- sequence is used to control the order of flicker of the unique multi-hexagonal stimulus created for mfERG. Good fixation is vital throughout the procedure and is monitored by the use of an infrared fundus camera. Since, the testing is done in a light adapted state the responses are primarily cone driven evaluating the function of the fovea, parafovea and some part of the peripheral retina.

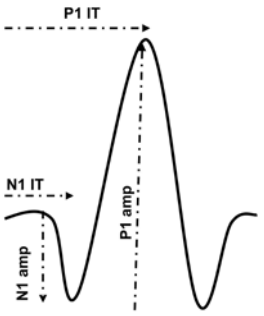

Figure 1: Normal waveform of multifocal ERG showing P1 and N1 amplitudes (amp) and implicit times (IT).

The mfERG waveform is a mathematical extraction of signals. A typical waveform of the first order response/kernel of mfERG response consists of an initial negative wave (N1) followed by a positive peak (P1) and sometimes there may be a second negative deflection after the positive peak (N2). These appear similar to the ff ERG photopic 'a wave' and 'b wave', but they are not identical.

Data is displayed in form of 3-dimensional topographic plots, group averages or trace arrays. Group averages evaluate the distribution pattern and topographic plot reflects the overall signal strength per unit area of retina. The 3-D plots are best seen along with corresponding mfERG trace arrays for correct interpretation of results.

Since mfERG is easy to interpret and well tolerated by the patient it is extensively used in **various hereditary retinal disorders**. Early cases of **Retinitis pigmentosa (RP)** who have a preserved central island of vision may have a discernible foveal response on mfERG even when ff ERG is extinguished. In segmental or perivenous RP the responses are lost in the affected regions and grossly normal in the unaffected retina. In **X-linked juvenile retinoschisis (XLRS)**, mfERG shows multi-area amplitude decrease with reduction of central peak amplitude. The P1/N1 ratio of mf ERG is different from the b/a ratio of ffERG3 because of

the difference in the cellular origin of the waveforms. Though, ffERG with the typical negative waveform in scotopic bright flash still remains essential to establish the diagnosis in XLRS, mfERG is useful in identifying the degree and extent of damage. MfERG can easily map the specific areas of chorioretinal atrophy4 in **Bietti's Crystalline Dystrophy** even when ffERG may be only mildly affected. In congenital maculopathies like **Stargardt's macular dystrophy** and **Vitelliform macular dystrophy (VMD)** the central responses on mfERG are markedly diminished surrounded by near normal responses. In contrast in **cone dystrophies** the mfERG-responses across the entire retina are markedly decreased or lost. Difference in the extent of the central lesion as well as degree of peripheral involvement in different diseases helps in diagnosis of the disease. For example, in **chloroquine retinopathy** the responses are markedly diminished in the ring of 2–7 degree eccentricity with recordable responses in the fovea and midperiphery.

Decrease in amplitudes as well as increase in the implicit time of mfERG responses in **Central Serous chorioretinopathy (CSC)** is not confined to the area of subretinal fluid alone; suggesting a global affection of the retina in this disease. This has improved our understanding of the disease. MfERG can be also be used as a tool for post treatment follow-up of patients with **Choroidal neovascular membrane (CNVM)** or macular hole. In vascular disorders like Central retinal vein occlusion, Hemi Central Retinal Vein Occlusion and Branch retinal vein occlusion reduced amplitude of mfERG corresponding to the area of occlusion are seen. Implicit time delays are more useful indicators of retinal edema than mfERG amplitudes 5. Role of mfERG in early stages **retinotoxicity** due to various drugs like Chloroquine,hydroxychloroqiune, Deferoxamine and Ethambutol is vital6. It is now a part of the new standard protocol for diagnosis of retinal toxicity due to these drugs.

MfERG plays little role in optic nerve disorders because the ganglion cells do not contribute to it.

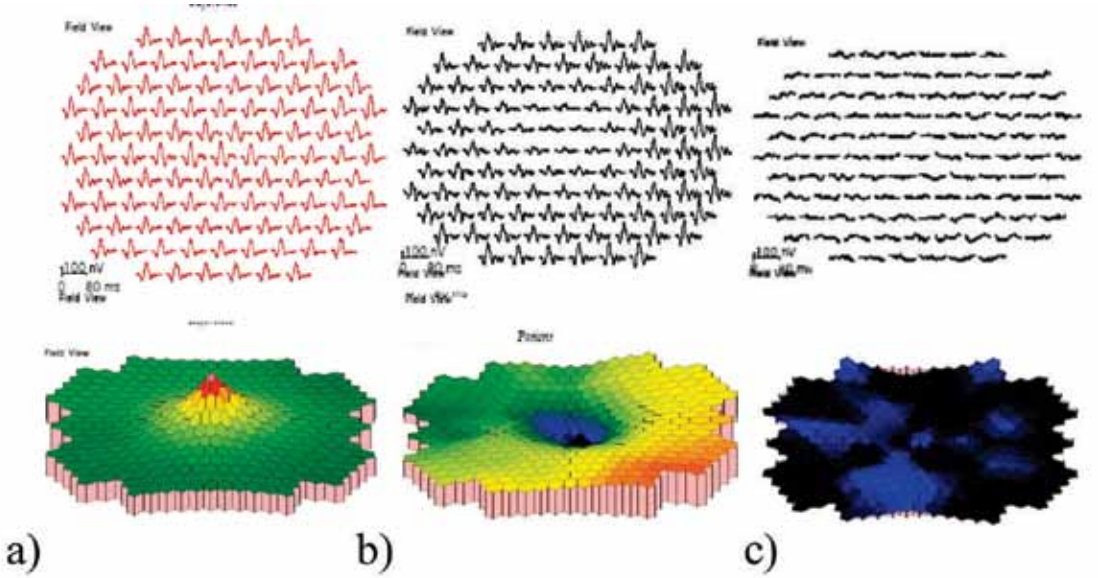

Figure 1: Normal waveform of multifocal ERG showing P1 and N1 amplitudes (amp) and implicit times (IT).

Flash and Pattern Visual evoked potentials (VEP)

Flash and Pattern VEP have been recorded to evaluate the optic nerve function. Their use is limited by the fact that bright flash VEP is a mass response and Pattern VEP is dominated by responses from

macular area. **The multifocal VEP (mfVEP)** as developed by Baseler and Sutter et al7 measures VEP responses from the focal areas of the visual field and is useful in picking up distribution of the optic nerve dysfunction. Interocular comparison of mfVEP recordings is a sensitive indicator of optic nerve pathology. MfVEP follows the visual fields and can also be effectively done in subjects not cooperative for HVF 30-2 and in children. This has been particularly found to be useful in patients with glaucoma.

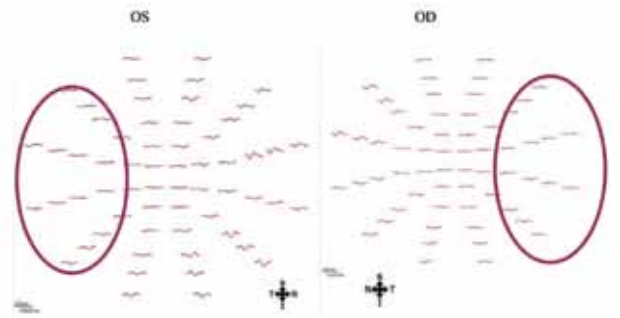

Figure 3: MfVEP responses showing bilateral non-recordable temporal field waveforms in a 48-year female with bitemporal hemianopia on HVF 30-2. MRI imaging revealed a pituitary adenoma.

Photopic negative response (PhNR) which originates from retinal ganglion cells has also been used as an indicator for ganglion cell function in early glaucomatous neuropathy. The PhNR is a slow negative potential that is seen after the b-wave of a light adapted ffERG. It can be recorded as full-field PhNR, focal PhNR and mutifocal PhNR. The full-field PhNR reflects the overall retinal ganglion cell function and can be used to assess the generalized optic nerve damage while focal PhNR can reflect early damage in the central ganglion cells as seen in glaucoma8.

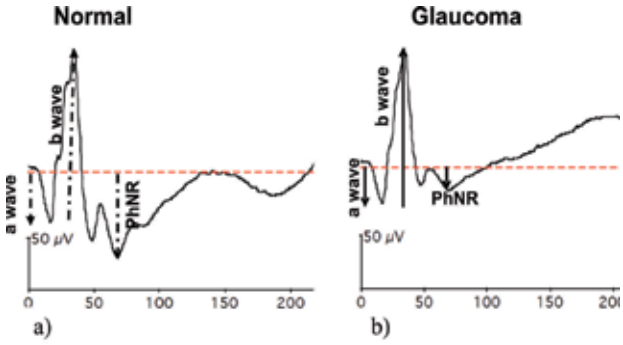

Figure 4: The amplitude of PhNR (photopic negative response) is reduced in a glaucomatous (b) eye as compared to a normal waveform (a).

To differentiate between the reduced VEP because of optic nerve disease or macular disorder newer investigation protocol like the **pattern ERG (PERG)** is being increasingly used. Transient PERG is a retinal biopotential that is produced by alternating reversal of a checkerboard pattern at a reversal rate of 6. Normal transient PERG has two main components: P50 (positive component appearing at 45-60 ms) which shows macular function and N95 (larger negative component appearing at 90-100 ms) which shows ganglion cell function. Since PERG has very low amplitude (0.5-8 micro V) special recording techniques are needed to differentiate it from noise.

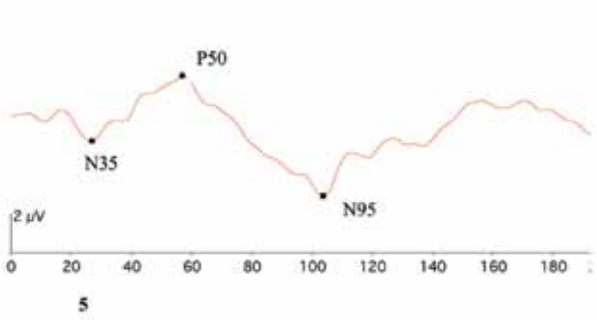

Figure 5: Normal waveform of PERG showing N35, P50 and N95 components.

It is recorded as per ISCEV standards 9 using the DTL electrodes. Binocular recording are usually taken without pupillary dilatation with refractive error correction in place. Normal ffERG with a decrease in the P50 amplitude depicts localized macular dysfunction as seen in patients with Stargadt's disease, macular hole and age related macular degeneration. An abnormal ERG with an abnormal PERG points towards a

generalized retinal disorder as seen in cone rod dysfunction with macular involvement. Selective affection of the N95 component, with a near normal P50 wave points towards optic nerve pathology. N95/P50 ratio remains unaltered in macular disease but decreases in optic nerve disorders. Acute phase of optic neuritis shows a loss of visual acuity; hence, PERG waveforms can be non-recordable. In chronic phase of optic neuritis as the initial optic nerve edema resolves P50 recovers while N95 abnormality persists with significant reduction in the N95:P50 ratio 10. This can be associated with the retrograde degeneration of the ganglion cells seen in the chronic stages of optic neuritis. Subnormal N95 component is also seen in Leber hereditary optic neuropathy (LHON) and Kjer-type dominant optic atrophy (DOA) and in optic nerve compression. Though PERG can differentiate between a retinal and an optic nerve disorder it does not give us the topography of the disease process.

Hence, a combination of these new investigation modalities can give us a better understanding of the physiology of the various ocular diseases and help in their management.

References:

1. Sutter, E. E. (2001). Imaging visual function with the multifocal m-sequence technique. Vision Research, 41, 1241-1255

2. Marmor MF, Hood DC, Keating D, et al. Guidelines for basic multifocal electroretinography (mfERG). Doc Ophthalmol 2003; 106:105–115

3. Huang S, Wu D, Jiang F, et al: The multifocal electroretinogram in X-linked juvenile retinoschisis Doc Ophthalmol. 2003 May;106(3):251-5.

4. Sen P, Ray R, Ravi P. Electrophysiological findings in Bietti's crystalline dystrophy. Clin Exp Optom. 2011 May; 94(3):302-8. doi: 10.1111/j.1444-0938.2011.00602.x. Epub 2011 Apr 13

5. Maturi RK, Yu M, Weleber RG: Multifocal electroretinographic evaluation of long-term hydroxychloroquine users. Arch Ophthalmol. 2004 Jul;122(7):973-81

6. Dolan FM, Parks S, Keating D, et al: Wide field multifocal and standard full field electroretinographic features of hemi retinal vein occlusion. Doc Ophthalmol. 2006 Jan; 112 (1):43-52.2001 Sep-Oct;45(5):516-22.

7. Baseler HA, Sutter EE, Klein SA, et al. The topography of visual evoked response properties across the visual field. Electroencephalogr Clin Neurophysiol. 1994; 90:65–81.

8. Viswanathan S, Frishman L, Robson J G, Walters J W. The photopic negative response of the flash electroretinogram in primary open angle glaucoma. Invest Ophthalmol Vis Sci. 2001, 42, 514-522.

9. Holder GE, Brigell MG, Hawlina M,Meigen T,Vaegan, Bach M. ISCEV standard for clinical pattern electroretinography—2007 update. Doc Ophthalmol (2007) 114:111–116

10. Holder GE: The incidence of abnormal pattern electroretinography in optic nerve demyelination. Electroenceph Clin Neurophysiol 1991; 78:18–26.

Sympathetic ophthalmia following vitreoretinal surgery. Is it a cause for concern?

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Sympathetic ophthalmia (SO), first described by Mackenzie in 1840 is characterized by bilateral diffuse granulomatous panuveitis that follows penetrating trauma or surgery in one eye.[1] The pathophysiology is postulated to be an autoimmune and inflammatory response directed against ocular antigens exposed to the lymphatic system in the conjunctiva. The antigens are believed to be located in the uveal tissue, retina or choroidal melanocytes. Though penetrating trauma was thought to be the commoner precipitating event, recent reports have shown that ocular surgery, particularly vitreoretinal surgery has become a major risk factor.[2-6]

Changing trends in epidemiology: The true incidence of SO is difficult to establish due to its rare occurrence, varying reports in literature and the fact that diagnosis is based most often on clinical findings rather than histopathology. In 1979, incidence of SO following intraocular surgery was reported to be 0.01%, while open globe injuries had an incidence of 0.2 – 0.5%.[7] In 1982, Gass reported the incidence of SO to be 0.01% following pars plana vitrectomy and 0.06% after penetrating ocular trauma.[8] In 2000, a prospective study of SO conducted in UK and Ireland reported the incidence of SO as 0.03 per 100,000 population. This study also demonstrated ocular surgeries as the most common cause of SO. Following retinal surgical procedures, either pars plana vitrectomy (PPV) or external retinal detachment repair, the calculated risk was 1 in 1152, while the risk following PPV alone was 1 in 799.[2,9]

Case report: A 52-year old male presented with gradually progressive diminution of vision in the left eye since 2 years. He had undergone right eye cataract surgery with IOL 4 years earlier with a satisfactory visual outcome.

On examination visual acuity was 20/20, N6 in the right eye and 20/60 in the left eye. Examination showed right eye PCIOL and left eye grade III nuclear sclerosis, non-dilating pupil and pseudoexfoliation. Fundus was normal in both eyes. He underwent SICS, sphincterotomy and PCIOL in the left eye. On post-op day 1, he had corneal edema, AC inflammation, IOP of 34 mm Hg, aphakia and fundus examination showed dislocated IOL in the vitreous. After control of IOP and inflammation, he underwent pars plana vitrectomy + IOL removal + scleral fixated IOL (SFIOL) in the left eye. At 6 weeks post surgery, the left eye had a visual acuity of 20/30, quiet AC, well centered SFIOL, IOP of 14 mm Hg and normal fundus.

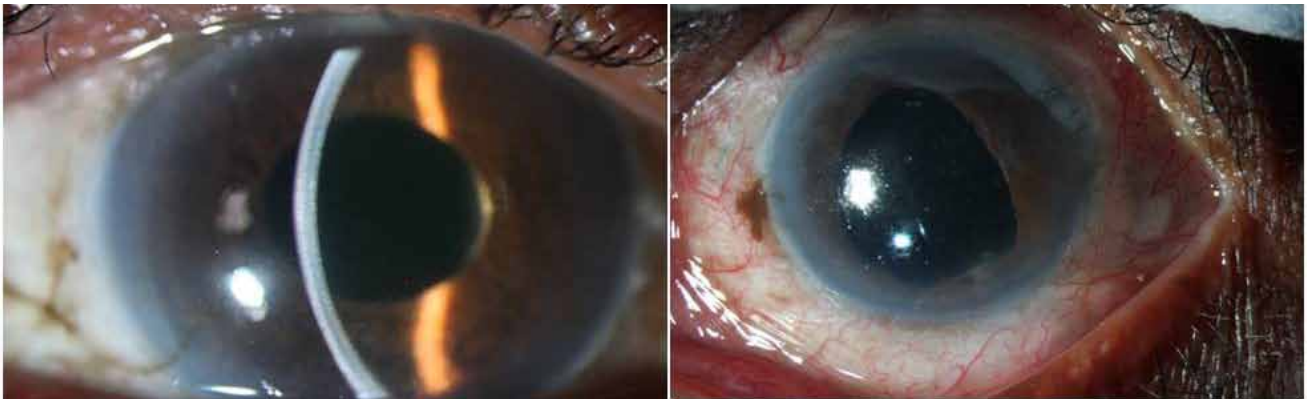

Figure 1: Right eye: sympathizing eye with round pupil. Left eye: exciting eye with irregular pupil

He presented 3 months later with complaints of pain, watering and decrease of vision since 2 weeks in both eyes. Visual acuity was 20/200 in both eyes. There were medium to large keratic precipitates, 2+ cells and flare in both eyes. The right eye pupil was round, regular and left eye had an irregular pupil. Both were sluggishly reacting to light. Both eyes had PCIOL, the left eye had deposits on the IOL (Figure 1). Fundus examination showed 3+ vitreous cells and hazy view due to vitritis in both eyes (Figure 2).

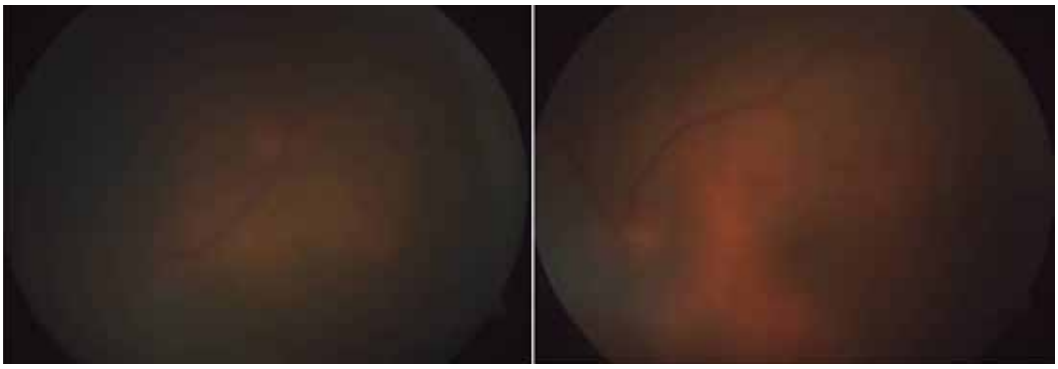

Figure 2: Right and left eye fundus showing hazy view due to vitritis

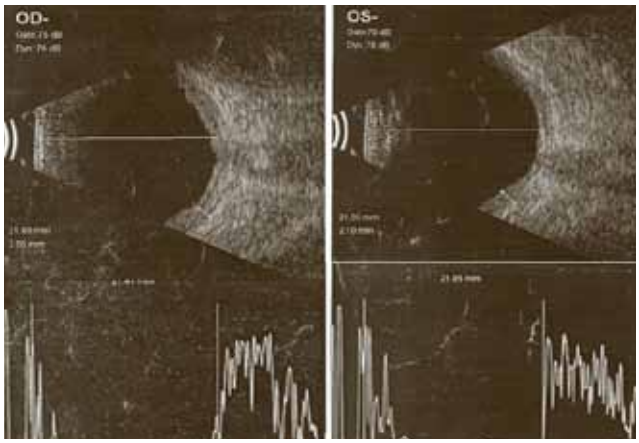

Figure 3: Ultrasonography showing choroidal thickening in both eyes

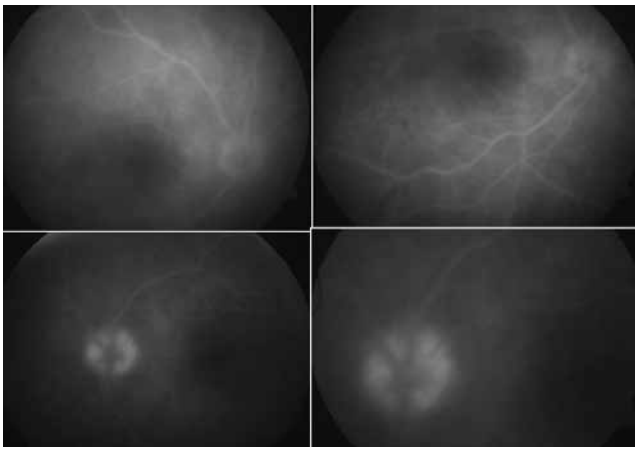

Figure 4: Fluorescein angiography showing patchy hyper and hypofluorescence with disc leak in both eyes

B-scan showed increased choroidal thickness of 2.05 mm and 2.10 mm in the right and left eye respectively (Figure 3). Fundus fluorescein angiography showed multiple patchy areas of hypo and hyperfluorescence and disc leakage (Figure 4). Based on the clinical findings, ultrasonography and fluorescein angiography, a diagnosis of sympathetic ophthalmia, status post vitreoretinal surgery was made. The patient was given IV methyl prednisolone for 3 days followed by oral steroids and azathioprine. He was also started on topical steroids and cycloplegics. The oral steroids were tapered over 4 months and azathioprine continued for 9 months. At the last visit, the best corrected visual acuity was 20/25 N6 and 20/30 N6 in the right and left eye respectively and both eyes are quiet.

Discussion: Sympathetic ophthalmia following vitreoretinal surgery has no gender predilection and is increasingly seen in older patients.[2,5] The onset is variable, appearing between 3 weeks to 6 months or even after few years.[2-4] The immunogenic risks of PPV are likely to be due to increased retinal manipulation and breakdown of the blood-retinal barrier, with release of previously sequestered retinal antigens, and possibly subclinical uveal incarceration at the wound site.[9]

The clinical presentation is variable and the inflammation may be rapid or insidious in onset. Both eyes present with photophobia, epiphora, pain and blurring of vision due to paresis of accomodation. Anterior segment findings include cells, flare, keratic precipitates and posterior synechiae. Pupils are usually mid-dilated and poorly responsive to light. Posterior segment shows a moderate to severe vitritis, yellow-white sub retinal pigment epithelial lesions (Dalen-Fuch's nodules), papillitis, choroiditis or exudative retinal detachment.[1,2,3,5]

Ancillary diagnostic tests include B-scan ultrasonography for choroidal thickening, OCT for retinal elevation and neurosensory detachment, fluorescein and ICG angiography. Fluorescein angiography shows multiple hypo or hyperfluorescent spots at RPE level in the early phase with late leakage and disc leak. ICG angiography shows areas of hypofluorescence where subretinal lesions are located.[1-3,5]

Differential diagnosis of SO include Vogt-Koyanagi-Harada (VKH) syndrome. Though similar to SO on presentation, a history of trauma or surgery can rule out VKH syndrome. Other diagnoses to consider are tuberculosis, sarcoidosis and syphilis and may be ruled out with appropriate systemic work-up.[1]

Initial therapy consists of IV pulse steroid therapy (1 gm/day x 3 days) followed by oral steroids

(1–1.5 mg/Kg/day). As steroid therapy often needs to be continued for 6 months or more, immunomodulatory agents (eg.azathioprine, cyclosporine, mycophenolate) can be initiated along with steroids, followed by a slow taper of steroids.

Symapthetic ophthalmia has also been reported following 23-gauge vitrectomy. Lack of wound closure leading to a disturbed blood-retinal barrier and exposure of ocular antigens has been postulated to be the likely cause. [10, 11]

Conclusions: SO can manifest with diverse clinical presentations. Any bilateral uveitis following vitreoretinal surgery should alert the surgeon to the possibility of SO. A successful vitrectomy does not preclude the development of SO. However the risk is higher in those undergoing multiple procedures and one may consider counselling such patients about the risk of SO. Early recognition, prompt and prolonged immunosuppression can result in good visual prognosis.

References:

1. *Chu XK, Chan Chi-Chao. Sympathetic ophthalmia: to the twenty-first century and beyond. J Ophthalmic Inflamm Infect. 2013;3:49*
2. *Kilmartin DJ, Dick AD, Forrester JV. Prospective surveillance of sympathetic ophthalmia in the UK and Republic of Ireland. Br J Ophthalmol 2000;84:259-263*
3. *Pollack AL, McDonald HR, Ai E, Green WR, et al. Sympathetic ophthalmia associated with pars plana vitrectomy without antecedent penetrating trauma. Retina. 2001;21:146-154*
4. *Ozbek Z, Arikan G, Yaman A, Oner H, Bajin MS, Saatci AO. Sympathetic ophthalmia following vitreoretinal surgery. Int Ophthalmol. 2010;30:221-227*
5. *Vote BJ, Hall A, Cairns J, Buttery R. Changing trends in sympathetic ophthalmia. Clin Experiment Ophthalmol. 2004;32:542-545*
6. *Jonas JB, Holbach LM, Schonherr U, Norman GO Sympathetic ophthamia after three pars plana vitrectomies without prior ocular injury. Retina 2000;20:405-406*
7. *Marak GE. Recent advances in sympathetic ophthalmia. Survey Ophthalmol 1979;24:141-156.*
8. *Gass JD. Sympathetic Ophthalmia following vitrectomy. Am J Ophthalmol 1982;93:552-558.*
9. *Kilmartin DJ, Dick AD, Forrester JV. Commentary: sympathetic ophthalmia risk following vitrectomy: should we counsel patients? Br J Ophthalmol 2000;84:448-449.*
10. *Cha D, Woo , Ahn J, Park K. A case of sympathetic ophthalmia presenting with extraocular symptoms and conjunctival pigmentation after repeated 23-gauge vitrectomy. Ocul Immunol Inflamm.2010;18:265-267.*
11. *Haruta M, Mukuno H, Nishijima K, Takagi H, Kita M. Sympathetic ophthalmia after 23-gauge tranconjunctival sutureless vitrectomy. Clin Ophtalmol 2010;4:1347-1349*

Eye Doctor ' Out of the box '

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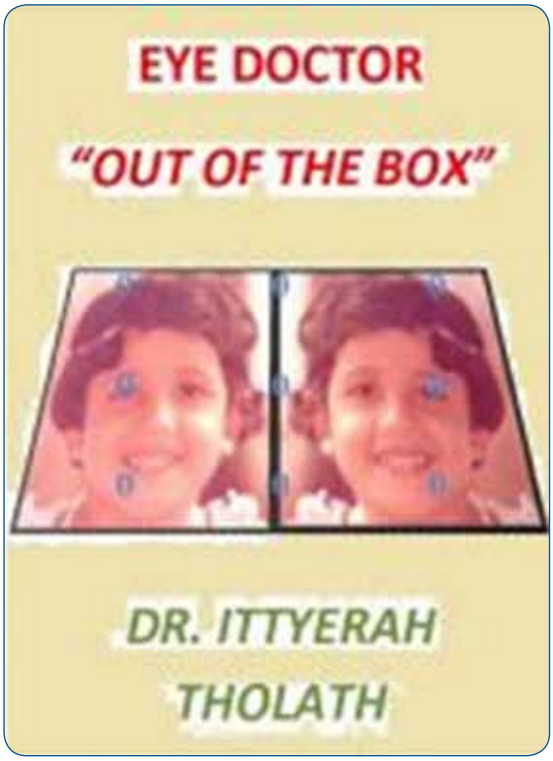

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1. Rizzo S, *et al*. Comparative Study of the Standard 25-gauge Vitrectomy System vs the New Ultra-high-speed Vitrectomy System. *Retina Today*. September Insert, 2010. 2. Data on File, Alcon Research 954-2020-003. 3. Nagpal M, Wartikar S, Nagpal K. Comparison of clinical outcomes and wound dynamics of sclerotomy ports of 20, 25, and 23 gauge vitrectomy. Retina. 2009;29(2):225-231. 4. Alcon data on file 954-0000-004.

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