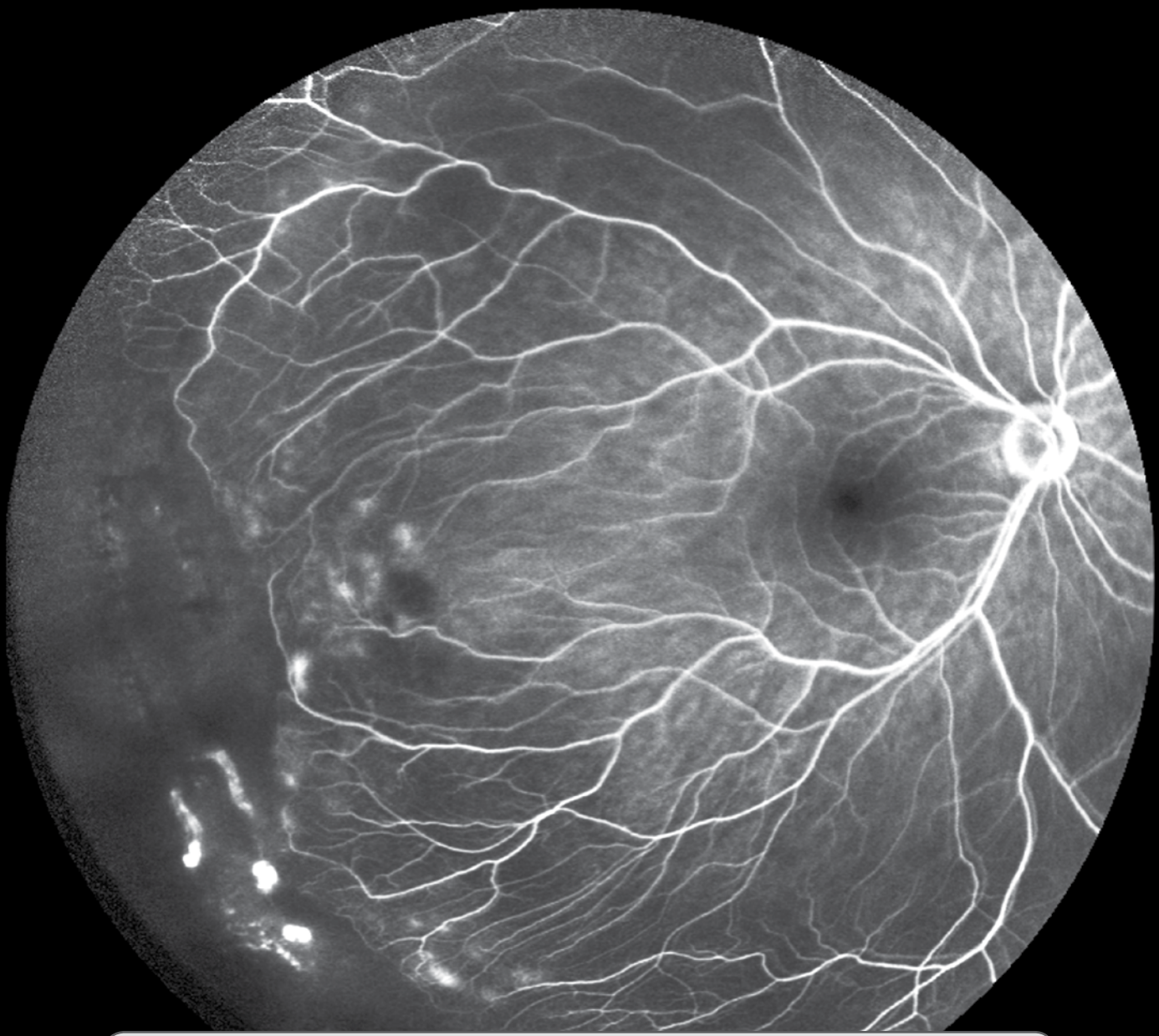
The official Newsletter of the

VITREO RETINAL SOCIETY - INDIA

May 2014



"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."

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From the President's Desk

Dear Friends

On behalf of Vitreo-Retinal Society of India (VRSI), I extend warm greetings to all our members. This issue of news letter focuses on recent advances in vitreoretinal diseases and surgery. I would like to thank all contributors of articles for this issue. I would like to put on records the efforts of Dr Aditya Kelkar for excellent organisation of the last Annual Conference of VRSI from December 12 to 14, 2013 at Lavasa near Pune. Dr S Natarajan deserves all the credit for bringing Frankfurt Retina Group Dry Lab Course headed by Dr. Frank Koch to train our young ophthalmologists in vitreoretinal procedures during this conference. Due to incorporation of new innovations, our speciality is already in forefront to change the face of vitreo retinal practice in India. We all need to think out of the box to further improve annual meeting and growth of speciality in our country.

It is a matter of great pride for all of us that one our former president of VRSI Prof. Amod Gupta was conferred with Padmashree Award by President of India this year. On behalf of all members of VRSI I would like to congratulate him for this honour.

This issue announces the next Annual VRSI conference to be held between December 5th to 7th 2014 at Jaypee Palace Hotel and Convention Centre Agra. This year, Nataraja Pillai Oration Award has been awarded to Dr Richard F. Spaide of Vitreous-Retina-Macula Consultants of New York, USA. Dr Cyrus Shroff from Shroff Eye Centre, New Delhi has been nominated for VRSI Hayreh Award. Both of them would deliver their award lectures at the next VRSI conference at Agra.

I would like to appreciate the efforts of Dr V Narendran Convener Scientific Committee VRSI for bringing out these issues of news letter regularly. We are interested in your feedback regarding the news letter. This will help us to bring further improvement in the future issues.

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From the Honorary Secretary's Desk

Dear Colleagues:

Greetings from the Vitreo Retinal Society-India.

This is the first issue of the newsletter for the year 2014. We did a very successful meeting at Lavasa, Pune which also saw the largest number of delegates ever attending the VRS-I conference. One of the important features of the Lavasa meeting was the Dry Lab conducted by the Frankfurt Retina Group. This was a big success and all the participants were extremely happy with the hands-on experience. There is a very strong request that this should be repeated and we are trying to work out the modality by which we could have this Dry Lab again at Agra.

In the year 2013, we had enrolled 31 new members in the Society.

Some of the major decisions that we have taken during the last year in the Governing council were (i) to encourage associate membership in the VRS-I for those who have done short term medical retina fellowship for less than one year. Earlier members who have done a short term medical retina fellowship of 3 months were not given associate membership because the minimum requirement was fellowship for a period of one year. It was decided in the Governing Council that they can be given associate membership but they will not be eligible for any award in the Society and also they will not be in a position to participate in the elections and contest for any posts of the Society (ii) We have also decided to institute Life Time Achievement Awards to very senior members who have made significant contributions towards the development of vitreo retina in India. The first two recipients of the award are (1) Dr. Namperumalsamy, Chairman-Emeritus, Aravind Eyecare System, and (2) Dr S.S. Badrinath, Chairman-Emeritus, Sankara Nethralaya, Chennai. You will all agree that these two stalwarts were the pioneers along with Dr. Nagpal and late Dr Patnaik to bring modern Vitreo Retina to this part of the world. The Life Time Achievement Awards to these gentlemen will be presented during the next annual conference at Agra.

I would also like to share with you all some of the major achievements of our members during the year 2013.

1. Dr S Natarajan and Dr Taraprasad Das received the Padmashree Award from the Government of India.
2. Our senior member Dr Alay Banker received the Col. Rangachari Award from the All India Ophthalmological Society. He also received the Senior Achievement Award from the American Academy of Ophthalmology, and Senior Honour Award from American Society of Retina Specialists.
3. Dr Mahesh Shanmugam received the Dr. P. Siva Reddy Oration Medal from the Andhra Pradesh Ophthalmological Society.
4. Dr. Ramasamy Kim has been elected as a member in the Beckman's New International AMD Classification Committee.

This year we have also conducted two CME programmes under the aegis of the VRS-I viz. one on Medical Retina at JIPMER, Pondicherry and the other a Post Graduate training Programme by NIO, Pune. We have two more CMEs coming up – one in September at Mangalore and the other at Ranchi. I would appreciate if members could conduct interesting and educative CME programmes for the comprehensive ophthalmologists in smaller towns to improve awareness on Vitreo Retinal diseases among general ophthalmologists.

This year's conference will be held at Agra. We have initiated the efforts to make this conference a memorable one. We already have a list of international participants and hopefully it would be a good conference and I will appreciate if the members come in a large number to make this conference a success.

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From the Convener Scientific Committee Desk

Greetings! To colleagues and members.

Last year we had seen record abstract submissions for 22nd annual conference of VRSI at Lavasa, Pune. We had arranged extensive scientific session for which we had received good reviews. This year for VRSI Agra submissions are already open. The abstract submission website is www.vrsi.co.in and submissions are till 31st June 2014. We are hopeful for the same this year too.

I invite all the VRSI member to 23rd annual conference at AGRA during 5th to 7th of December. Egyptian vitreoretinal society has accepted our invitation. Scientific sessions moderated by renowned national and international faculty have been planned. Confirmed international faculty includes Richard Spaide (USA), Anna Ells (Canada), Timothy Lai, Xia Xin LI (China), and Akito Hirakata.

Visit to Taj Mahal is also planned. The weather during that period would be amiable to visit other tourist destinations around Agra too.

VRSI members can also avail opportunity to publish articles in VRSI newsletter.

See you all at Agra.

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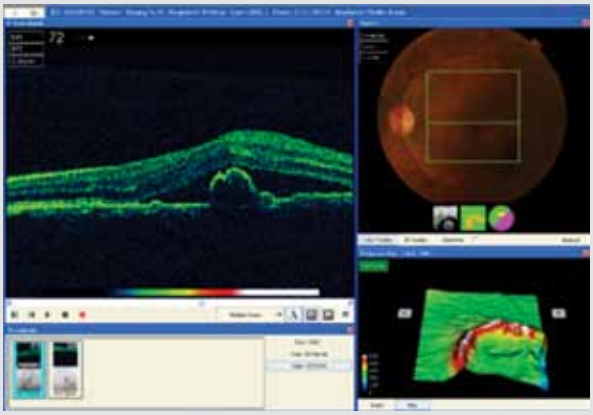
Polypoidal Choroidal Vasculopathy, Present Scenario

Polypoidal choroidal vasculopathy (PCV) is characterized by the presence of polypoidal subretinal, vascular lesions associated with serous and hemorrhagic detachments of retinal pigment epithelium. It shows focal hyperfluorescence in the early phase of indocyanine green angiography (ICGA) and may be associated with a branching vascular network (BVN) and clinically visible orange-red subretinal nodule(s).1 It was first described by Yannuzzi in 1982 American Academy of Ophthalmology meeting and initially used to be called as idiopathic polypoidal choroido-vasculopathy.2 The natural course of PCV is variable. It may be relatively stable or there may be repeated bleeding and leakage with vision loss and chorioretinal atrophy with or without scarring. Uyama et al reported that half of the study eyes had hemorrhagic episodes, recurrent leakage, or severe RPE atrophy after a long follow-up period (24–54 months).3 The prevalence of PCV in Asian population is much more compared to the white populations. Prevalence rate is upto 9.8% reported in Caucasian populations.4 Maruko et al, reported PCV incidence of 54.7% in presumed neovascular age related macular degeneration.5 Thus the PCV is a disease of paramount importance in Indian populations with presumed exudative AMD.

The quest for the exact diagnostic and treatment protocols are going on. The consensus about the diagnostic criteria and the therapy are slowly building up. Fluorescein Angiography may give a suspicion of the polyp with increased hyperfluorescein but it is never conclusive. Indocyanine green absorbs and emits near infra-red lights which readily penetrates the retinal pigment epithelium and in addition it has higher binding affinity to protein so that it does not leak readily from the choroidal capillaries. The gold standard is Indocyanine Green Angiography (ICGA) and highly recommended as it helps to visualize the choroidal circulations providing direct evidence of the choroidal polyps.6 The confocal scanning laser ICGA and video angiography provides better visualization and delineates the exact areas to be treated. It also helps to differentiate PCV from the choroidal neovascularization.7

The clinical features suggestive of PCV and thus needing an ICGA include a serosanguinous maculopathy with one of the following features: Clinically visible orange-red subretinal nodules; spontaneous massive subretinal hemorrhage; notched or hemorrhagic pigment epithelium detachment (PED) in OCT; a lack of response to anti VEGF therapy.8



Based on ICGA findings, PCV is defined as the presence of single or multiple focal nodular areas of hyperfluorescence arising from the choroidal circulation within the first 6 minutes after injection of Indocyanine green, with or without an associated choroidal interconnecting vascular network.9 Yang et al published that in optical coherence tomography enhanced depth imaging technique, there is a thickened sub-foveal choroid, dilated choroidal vessels, double layer signs in RPE – Bruch membrane-choriocapillary complex, hyper-reflectivity between RPE and Bruch`s membrane and the choroidal macular swelling is associated with vascular engorgement and dilatation.10

Diagnosis Synopsis based on above literatures:

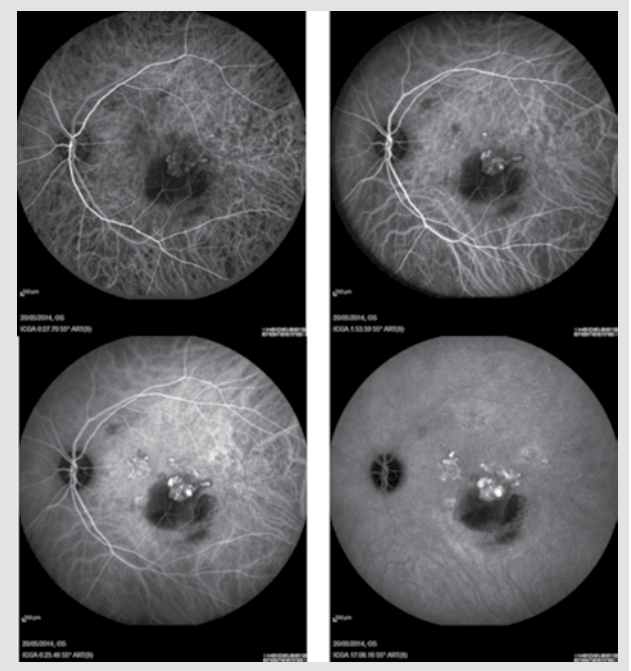
STEP1. Routine retina examination showed suspicion of PCV should be there if serous or sero-sanguinous macular changes with one of the followings occurs:

-Submacular haemorrhage

-Clinically visible orange subretinal nodules

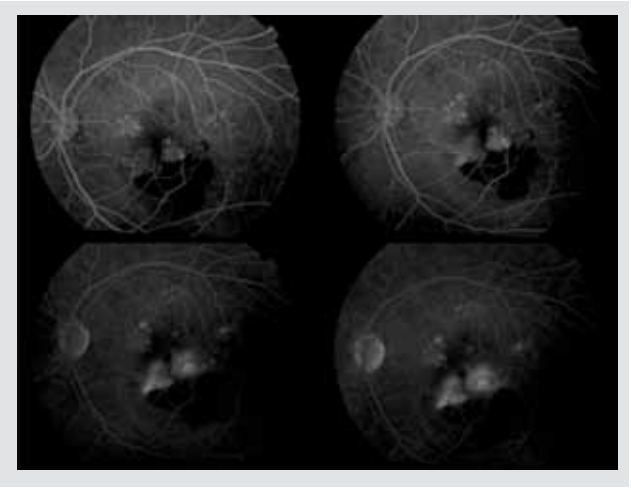
-Haemorrhagic PED or notched PED

- Lack of response to Anti VEGF



STEP2. Indocyanine Green Angiography to diagnose the PCV: Single or multiple focal nodular areas of hyperfluorescence from choroidal circulation in first 6 minutes with or without BVN. There may be associated stereoscopic nodules in ICG, may be a hypofluorescent halo surrounding the hyperfluorescent area or even pulsation in the polyp in video angiography.

STEP3. Treatments considered for active PCVs. Activity is considered if there is any of the one : Drop of ETDRS chart 5 letters due to PCV or subretinal fluid or subretinal haemorrhage or PED or leak in Fluorescene angiography.



Different treatment modalities are described in literature. Verteporfin photodynamic therapy seems to be promising with complete regression of polyps in quiet a number of cases.11,12 Intravitreal anti vascular endothelial growth factor (Anti VEGF) therapy also reported to be able to decrease the exudations and increase the vision though not able to make the polyps disappear.13,14 The combined use of anti-VEGF and Verteporfin PDT therapy showed that it improves the visual outcome along with decrease in PDT frequency and decrease in exudations.9,15,16 There was reported success with thermal laser and also transpupillary thermotherapy in extrafoveal PCVs.17

The only multicentered double masked randomized controlled trial published was the Everest Trial. It was done in 61 Asian Patients and the results were analysed upto 6 months. As per this study results,

the Verteporfin PDT alone or in combination with ranibizumab 0.5 mg was superior to ranibizumab monotherapy in achieving complete regression of polyps in this 6-month

study in patients with symptomatic macular polypoidal choroidal vasculopathy. 77.8% regression with verteporfin PDT and ranibizumab combinations and 71.8% regression with Verteporfin-PDT monotherapy alone Vs. 28.6% in ranibizumab alone. There was mean change ± standard deviation in best-corrected visual acuity (letters) was 10.9 ± 10.9 (verteporfin PDT + ranibizumab), 7.5 ± 10.6 (verteporfin PDT), and 9.2 ± 12.4 (ranibizumab).9

Based on these reports this treatment can be summarized grossly as below:

Extra-foveal PCV (not on papillomacular areas): Can be treated with Thermal laser

Subfoveal or Juxtafoveal PCV: It can be treated initially with Verteporfin-PDT therapy along with 3 doses of Injection Ranibizumab, once every month. Bevacizumab has been used also with good effects.15 If PDT is not possible due to any reason, then the anti VEGF monotherapy is the only choice. Continuously active PCV has to be re-treated with combination therapy. PDT is usually applied only after a minimum of 3 months period.

Follow Up: Visual acuity measurements, Amsler`s chart self monitoring along with, clinical examination, periodic OCT, and if required FA and ICG are the methods to be used for detection of recurrence or persistence of activity. Treatment decision to be taken by the surgeon case to case basis based on patient`s condition and chance of improvement9

However few grey areas still remains to be solved. Akaza et al showed that there was 77% recurrence with Verteporfin PDT therapy in 3 years time and the 2nd and 3rd year visual outcome were inferior to the 1st year visual outcomes.18 There are concerns that repeated PDT may result RPE atrophic changes and choroidal nonperfusion. Ricci et al showed improved visual stability or improvements in 95% of cases and also decrease in mean macular thickness with reduced fluence PDT along with intravitreal Ranibizumab.19 There are approaches with selectively targeting the PCV with small PDT spots for retreatment and using anti VEGF initially or in different schedules along with thermal lasers where possible to decrease the number and the spot size of PDT with reportedly good result at 3 year.20

The search is on for that ideal treatment with maximum effects with least or no side effects. It is the beginning of a journey to conquer the PCV and to prevent severe visual disability and we can only say `` And miles to go before I sleep and miles to go before I sleep`` (Robert Browning).

References:-

1. Yannuzzi LA, Ciardella A, Spaide RF, et al. The expanding clinical spectrum of idiopathic polypoidal choroidal vasculopathy. .Arch Ophthalmol 1997; 115:478–485.

2.Yannuzzi LA. Idiopathic polypoidal choroidal vasculopathy. Macula Society Meeting, 1982, Miami, FL.

3.Uyama M, Wada M, Nagai Y, et al. Polypoidal Choroidal Vasculopathy: natural history, Am J Ophthalmol 2002;133;639-648

4.Scassellati-Sforzolini B, Mariotti C, Bryan R et al. Polypoidal Choroidal Vasculopathy in Italy. Retina 2001;21:121-125

5.Maruko I, Iida T, Saito M, et al. Clinical characteristics of exudative age related macular degeneration ion Japanese patients. Am J Ophthalmol 2007; 2007; 144:15-22.

6.Stanga PE, Lim JI, Hamilton P. Indocyanine Green Angiography in choroidal diseases: indications and interpretation: an evidence based update. Ophthalmology 2003; 110:15-21.

7.Yuzawa M, Mori R, Kawamura A. The origins of polypoidal choroidal vasculopathy. Br J Ophthalmol 2005; 89:602–607.

8.Koh H.C. Adrian, on Behalf of the Expert PCV Panel. Polypoidal Choroidal Vasculopathy; Evidence based

guidelines for clinical diagnosis and treatment. Retina 2013;33:686-716.

9.Koh A, Lee K W,Chen J L et al. Everest Study. Efficacy and Safety of Verteporfin Photodynamic Therapy in Combination with Ranibizumab or Alone Versus Ranibizumab Monotherapy in Patients with Symptomatic Macular Polypoidal Choroidal Vasculopathy. Retina 2012; 32:1453-1464.

10.Yang L H, Jonas B J,Wei W B. Optical Coherence Tomographic Enhanced depth Imaging of Polypoidal choroidal vasculopathy. Retina.2013; 33:1584–1589.

11.Gomi F, Ohji M, Sayanagi K, et al. One-year outcomes of photodynamic therapy in age-related macular degeneration and polypoidal choroidal vasculopathy in Japanese patients. Ophthalmology 2008;115:141–146.

12.Spaide R F, Donsoff I, Lam D L, Yanuzi L A, Jampol M L, Slakter J, Sorenson J, Freund K B. Treatment of polypoidal choroidal vasculopathy with photodynamic therapy. Retina. 2002; 22: 529-535.

13.Marcus D M, Singh H, Lott M N, Singh J, Marcus M D.Intravitreal ranibizumab in polypoidal choroidal vasculopathy in non-Asian patients. Retina 2013; 33:35-47.

14.Cheng C K, Peng C H,Chang C Kl , Hu C C, Chen L J. One year outcome for intravitreal Bevacizumab (Avastin) therapy for polypoidal choroidal vasculopathy. Retina 2011; 31: 846-856.

15.Sato T, Kishi S, Matsumoto H, Mukai R. Combined photodynamic therapy with verteporfin and intravitreal bevacizumab for polypoidal choroidal vasculopathy. Am J Ophthalmol 2010; 149:947–954.

16.Tomita K, Tsujikawa A, Yamashiro K, et al. Treatment of polypoidal choroidal vasculopathy with photodynamic therapycombined with intravitreal injections of ranibizumab. Am J Ophthalmol 2012; 153:68–80.

17.Ananthraman G, Ramkumar G, Rajput A. Clinical Features , management and visual outcomes of polypoidal choroidal vasculopathy in Indian patients. Indian J Ophthalmol.2010 Sep-Oct; 58(5):399-405.

18.Akaza E, Yuzawa M, Mori R. Three-year follow-up results of photodynamic therapy for polypoidal choroidal vasculopathy. Jpn J Ophthalmol 2011; 55:39–44.

19.Ricci F, Calabrese A, Regine F, Missiroli F, Ciardella A P. Combined reduced fluence photodynamic therapy and intravitreal ranibizumab for polypoidal choroidal vasculopathy. Retina 2012; 32:1280-1288.

20.Jeon S, Lee W K,Seop K. Adjusted retreatment of polypoidal choroidal vasculopathy after combination therapy. Results at 3 years. Retina 2013; 33: 1193-1200.

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Medical Retina – A Dynamic New World

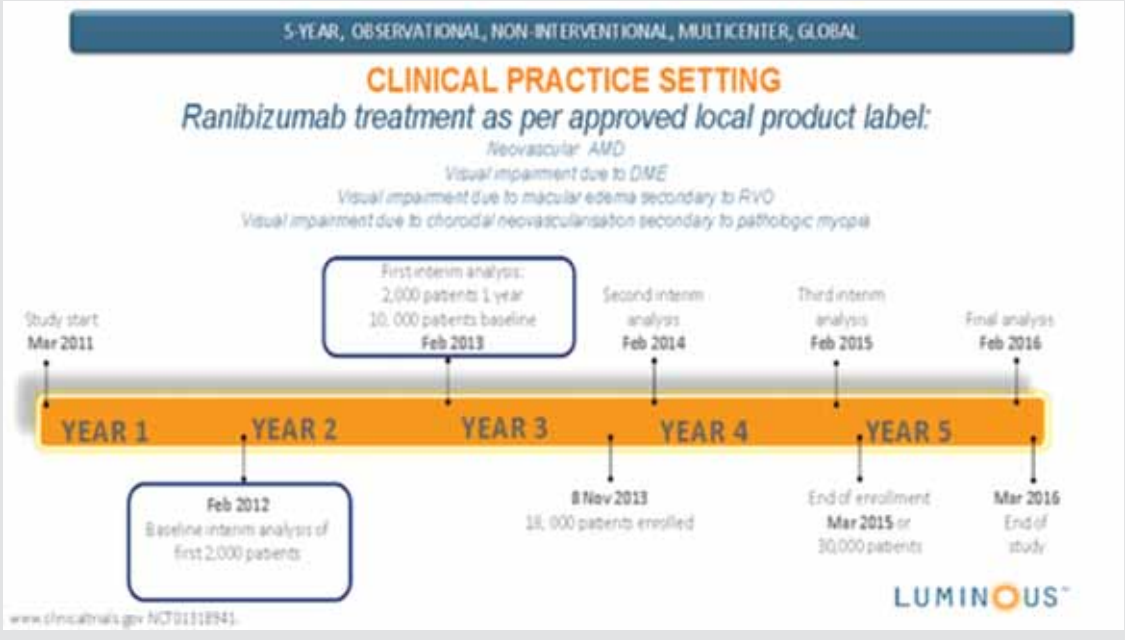
The arrival and establishment of Intravitreal injections as a standard of care has led to the emergence of a new sub-specialty in Ophthalmology – Medical Retina.

Medical Retina refers to the management of all retinal diseases which are better managed by non-surgical techniques. These disorders are varied, most common being wet and dry Age-related macular degeneration (AMD), Diabetic Macular Edema (DME), retinal vein and artery occlusions, idiopathic polypoidal vascular coagulopathy, central serous retinopathy, Idiopathic juxtafoveal telangiectasia and uveitis.

Out of the various weapons in the armamentarium of a medical retina specialist, Laser has always been the mainstay for the past 30 years. In 1998, the U.S. Food and Drug Administration (FDA) approved the use of the first agent for intravitreal injections, Fomivirsen sodium (Vitravene; Isis Pharmaceuticals, Carlsbad, CA), for the treatment of CMV retinitis.

Approval of Anti-Vascular Endothelial Growth Factor (Anti-VEGF) intravitreal injections in the decade after 2000 has transformed the treatment protocols throughout the world in the management of multiple retinal and uveal diseases and now being used as a primary therapy. Avastin (Bevacizumab), Lucentis (Ranibizumab) and Eylea (Aflibercept) are the BIG THREE Anti-VEGFs in Medical Retina.

Lucentis (Ranibizumab) is the only Anti-VEGF injection approved by regulators world-wide and in India for 5 indications i.e. wet AMD, DME,



BRVO (Branch Retinal Vein Occlusion), CRVO (Central retinal Vein Occlusion) and Myopic CNV. It is the most researched molecule in this group with cumulative exposure of 1.7 million patient years. Over 10,000+ patients have been enrolled in randomized controlled trials and 21000+ patients are currently enrolled in the LUMINOUS registry1. LUMINOUS is a 5 year observational study involving 41 countries, 600 sites and target of 30000 patients.

Figure 1: LUMINOUS TRIAL

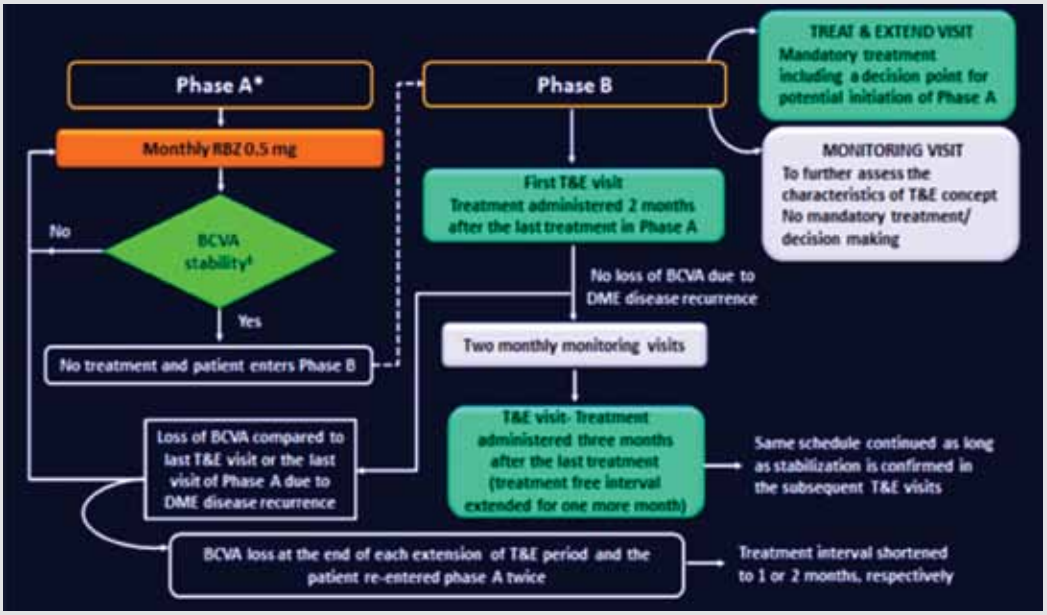
The largest observational trial of Ranibizumab in wet AMD in 650 Indian patients – UNVEIL2(Utilizing raNibizumab intravitreal Injection in a reaL-world setting) is on the verge of publication and confirms the effectiveness and safety of Ranibizumab in real-world in Indian population using 3 loading + PRN regimen with a median of 3-4 injections/year.

Head to head studies of off-label Avastin and approved Lucentis3, 4, 5 (CATT/IVAN /GEFAL) in wet AMD demonstrated non-inferiority of Avastin in terms of efficacy but were not powered for safety comparisons. Wide real-life clinical experience in India and abroad with Avastin suggests similar efficacy to Lucentis but issues of safety with respect to endophthalmitis and cardiovascular events3 seen with Avastin are known and need to be carefully considered.

Recently, Eylea has been approved in wet AMD and launched in many countries (not yet available in India) and has demonstrated similar efficacy to Ranibizumab in its VIEW studies6 as well as case reports .Larger Phase 4 studies would be required to confirm these early positive results . The proposed regimen with Eylea is 3 monthly loading doses followed by bi-monthly injections and monitoring for 1 year. However the VERO28 survey conducted in the US demonstrated that doctors preferred to follow the time-tested Ranibizumab regimen of 3 loading + PRN with monthly monitoring rather than bi-monthly even for Eylea.

In DME, Ranibizumab studies7, 8 (DRCR, RESTORE) set the benchmark for use of Anti-VEGF injections and demonstrated superiority over LASER and Steroids in terms of effectiveness as well as safety. Management guidelines such as European9, Canadian10, DRCR11 and Asia-Pacific12 all have Ranibizumab as the first line of treatment in centre involving DME.

A new regimen of Treat and Extend was proposed based on outcomes of RETAIN13 study with Ranibizumab in DME. In this regimen, after monthly injections when the vision is stable, the follow up duration can be extended by 1 month every time for better compliance and benefit of patients. This led to significantly lower follow up



visits for the DME patients without compromising on VA outcomes.

Figure 2: RETAIN STUDY Methodology

Avastin has large usage experience but only 1 clinical trial – BOLT14 which demonstrates superior effectiveness of Avastin over laser.

Eylea has presented their Phase3 VIVID and VISTA15 trial results at international conferences last year which demonstrate superiority over laser in center involving DME. A prior Phase 2 DA VINCI16 study with 3 arms of Eylea and 1 arm of Ranibizumab did not show any difference in efficacy between the 2 drugs.

In BRVO and CRVO, wait and watch approach has given way to use of Anti-VEGF injections. Again this was pioneered through BRAVO17 and CRUISE18 studies of Ranibizumab which clearly demonstrated that use of monthly Intravitreal Ranibizumab gave superior outcomes to sham (wait and watch) at all time- points up to 1 year. The ongoing SHORE19 trial will help to define a treatment regimen/algorithm with Ranibizumab in BRVO and CRVO.

Avastin has been used in RVO patients reporting of its good efficacy. However, use of Avastin in vascular disorders on the backdrop of its known cardiovascular risks is debatable and needs to be evaluated.

Eylea has been recently approved in CRVO on the basis of COPERNICUS20 and GALILEO21 Phase 3 studies. Phase 4 studies and real-world evidence is awaited.

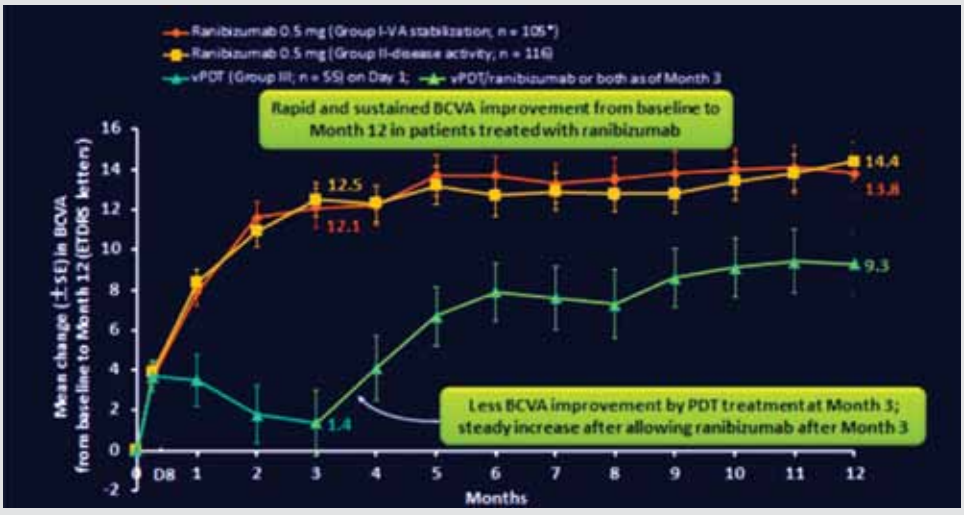
Last year Ranibizumab was the first Anti-VEGF to receive world-wide approval in myopic CNV. In April this year Ranibizumab received Health authority approval for mCNV in India. This approval was received on the basis of the Phase3 RADIANCE22 study which demonstrated significantly superior effectiveness of Lucentis over V PdT over a period of 1 year with a median of just 2 Lucentis Injections per year. This study included Indian patients as well.

Figure 3: RADIANCE Study BCVA outcomes

Avastin experience in myopic CNV has not been well documented however anecdotal reports from doctors suggest a possible higher number of injections required for Avastin as compared to Lucentis.

Eylea has an ongoing trial in myopic CNV i.e. MYRROR23. The 6 month results were shared last year which showed good vision outcomes. However final results are awaited.

Macugen (Pegaptanib) is an intravitreal injection which is approved only in wet AMD. However it did not meet favor among retina specialists since it did not improve visual acuity but only stabilized



vision24 and Lucentis was found to be a more effective option. National Institute of Clinical Excellence (NICE) in 2008 issued a statement – "Pegaptanib is not recommended for treatment of wet AMD but ongoing treatment may continue until the patient or clinician deems it appropriate to stop."

Visudyne PDT was the mainstay of treatment in wet AMD prior to era of Anti-VEGFs. Today it is rarely used in wet AMD but finds application in some off-label disorders such as Idiopathic polypoidal choroidal Vasculopathy25 (IPCV) and Central Serous Retinopathy 26(CSR). Use of low fluence PDT26 is being considered to reduce the potential damage to the macula.

Intravitreal Injections also include the use of steroids like Triamcinolone and long-acting implants such as Ozurdex (dexamethasone) and Illuvein (Fluocinolone).

DRCR.net trial demonstrated that use of Intravitreal triamcinolone led to large number of enrolled patients developing cataracts and glaucoma.

Figure 4: DRCR.net Triamcinolone Arm–Incidence of Cataract Surgery

However in pseudophakic eyes, at the end of 1 year, the Triamcinolone+laser arm had similar vision outcomes to the Ranibizumab arms. The vision outcomes deteriorated towards the end of 2nd year even in pseudophakic eyes possibly due to progression of glaucoma.

Ozurdex has been approved as a sustained release dexamethasone implant in the management of RVO.

The Geneva Study27 demonstrated a peak response i.e. improvement in BCVA by 2 months and significant drop in BCVA after that to reach the baseline VA by 6 months. The makers of the implant also now agree that the duration of action for Ozurdex is 3 months rather than 6 months are previously believed. Ozurdex is also being used off-label for DME either alone or as maintenance following vision stabilization by Anti-VEGFs.

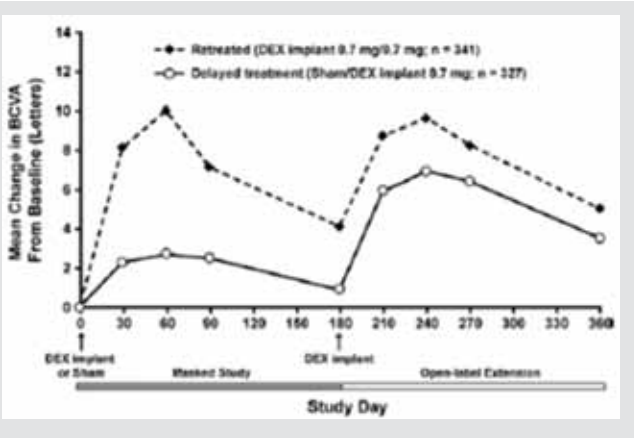


Figure 5: GENEVA Study VA outcomes

Illuvien is a long acting implant (36 months) which has been approved in many countries forchronic refractory DME29. However the studies show high incidence of cataracts (87%) and glaucoma (37%) over a period of 3 years. It is not available in India.

It has been recommended in various guidelines to use steroids as second line if the DME does not respond to Anti-VEGFs9, 10, 11, 12 (refractory edema). The DRCR guidelines11 typically describe a non-responder to Anti-VEGFs (Ranibizumab) as a patient of DME who has received at least 6 Anti-VEGF injections and the resultant BCVA is stable but worse than 20/20 or the edema is visible on OCT.

The other reason behind the explosion of Intravitreal therapies for retinal disorders is the contemporary availability of a diagnostic tool- Optical Coherence Tomography or OCT .No other advancement in the past few decades in diagnosis of retinal diseases matches up to the invention of the OCT.

OCT has now become the mainstay in diagnosis and monitoring of retinal disorders and treatment and is crucial for decision making i.e. whether to do Laser, give intravitreal Anti-VEGFs, administer steroids or perform surgery.

The term – "Clinically significant macular edema" was used in the pre-OCT era defined as edema in the center of the macula or threatening the center. In the post-OCT era –we have a rapid, non-invasive, objective and standardized way of assessing

macular status which is reproducible (coefficient of repeatability about 10%)

Macular edema is now defined as center involvement (CSF thickening), or non-central DME (inner or outer subfield thickening).OCT thickness is now used to monitor response and guide re-treatment, rather than "CSME". The preference now is to define macular edema by location and severity involved among the 9 subfield map with 6 mm diameter.

The field of Medical Retina is ever changing. The advent of "less destructive " lasers such as 'yellow laser' could cause a shift in the way we manage retinal conditions in the future . There are various intravitreal agents under different phases of clinical research. In the meanwhile Anti-VEGF injections are fast becoming standard of care in medical retinal disorders.

References:

1. www.clinicaltrials.gov NCT 01318941

2. Novartis data on file

3. Martin, DF et al, NEJM 2011

4. Chakravarthy U, et al. Ophthalmology 2012

5.http://clinicaltrials.gov/ct2/show/NCT01170767?term=GEFAL&rank=1

6. Heier JS et al, Ophthalmology. 2012 Dec;119(12):2537-48

7. Elman et al, Ophthalmology 2011;118:609–614

8. Mitchell P et al. Ophthalmology 2011;118:615-25

9. Bandello et al, Eye (2012) 26, 485–493

10. Hooper et al, Ophthalmologica 2014;231:2–15

11. Bressler et al, Ophthalmology. 2011 December; 118(12): e5–e14.

12. Mitchell and Wong,Am J Ophthalmol 2013.

13. Christian Prunte et al , presented at AAO 2013

14. Michaelides et al, Ophthalmology 2010;117:1078–1086

15. Ursula Schmidt et al, abstract presented at Euretina 2013

16. Do et al , Ophthalmology 2012;119:1658–1665

17. Campochiaro PA et al. Ophthalmology 2010;117: 1102-112

18. Brown DM et al. Ophthalmology 2011;118:1594-602

19. http://clinicaltrials.gov/show/NCT01277302

20. Brown et al, Am J Ophthalmol. 2013 Mar; 155(3):429-437.e7.

21. Korobelnik et al, Ophthalmology. 2014 Jan;121(1):202-8

22. Wolf S et al, Ophthalmology. 2014 Mar;121(3):682-92.e2

23.http://www.clinicaltrials.gov/ct2/show/NCT01249664

24. Ishibashi et al, Jpn J Ophthalmol. 2013 Sep; 57(5):417-23.

25. Maugat- Faysse et al ,Eur J Ophthalmol. 2006 Sep-Oct;16(5):695-704.

26. So Hyun Bae et al , Ophthalmology 2014;121:558-565

27. Haller et al , Ophthalmology 2011;118:2453–2460

28. Holekamp, NM et al. ARVO 2012 abstract 4179

29. Sanford et al , Drugs. 2013 Feb;73(2):187-93

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Update on Anti-VEGF (Bevacizumab) Use in ROP

Laser treatment, that was initially reported to halt progression to retinal detachment, is currently the standard of care for ROP (1). It has distinct advantages over Cryotherapy (2) that was the first proven therapy for prevention of retinal detachment in ROP (Table 1). Laser was also found useful in preserving vision and macular status if done early enough before the retinopathy progressed to a vitreoretinopathy (3). Laser works, as in other ischemic retinopathies, by destroying the VEGF producing cells (RPE/Astrocytes) of the growing avascular retina, and stops the disease progression. However, it cannot counter the already secreted VEGF that creates ongoing retinal damage. Therefore, prompt, confluent and complete laser ablation is needed, with no skipped avascular areas that could continue to spew the VEGF (4). Hence, laser ablation works best only if done in the earliest phase of the disease so that the amount of secreted VEGF in the vitreous cavity is not enough to continue damage while the laser starts working. The secreted VEGF slowly moves out of the eye and only then does the disease show regression. Clinically, this is seen as the High-risk pre-threshold disease and also the earliest phase of Aggressive-posterior ROP, where laser treatments are most effective. Once the ROP regresses with laser, sometimes needed in more than one session (5), it does not recur except in very rare cases (6) and the condition can be considered as fully cured which happens within 2-3 weeks of complete laser therapy. However the expertise needed to do this complete treatment and sometimes repeated sessions is very high and requires a steep and prolonged labour intensive learning curve. This is especially so for the APROP/ Zone 1 disease where treatment successes are less optimum both due to delayed treatment and/or inadequate laser application (7). Laser failed eyes may show progressive traction on the retina and require vitreoretinal surgery to prevent evolving retinal detachments.

Adverse Ocular events immediately after laser therapy have been reported from various cohort studies and randomized clinical trials. These include rare and isolated instances of cataract, anterior segment ischaemia, exudative retinal detachment, transient rise of intraocular pressure, inadvertent foveal damage, hyphema and vitreous haemorrhage. Long-term side effects include peripheral field constriction and Myopia (Table 1and 2). No long-term systemic effects are envisaged or reported as the treatment is local.

In recent years, there are increasing reports of use of Anti-VegF intravitreal injections, primarily Bevacizumab, in Retinopathy of Prematurity. The ease of administration, less stress on the baby, possibly less expensive and less expertise needed could make this an ideal choice of treatment. However, before this becomes standard of care there is a strong requirement of understanding the drug, what it does and how, the long and short term concerns and the literature knowledge so far about this new treatment modality (Table 2). The current write-up attempts to provide update practical knowledge about use of these drugs for ROP.

Efficacy issues: The anti-VEGF drugs neutralize the abnormal high levels of VEGF in the eye and hence prevent new vessel formation and propagation of the ongoing neovascular process. In various studies it has been found to be highly efficacious in causing

regression of prethreshold and threshold ROP new vessels and plus component (8-11). It is also found to have good efficacy in causing regression of plus component as an adjunct to failed laser eyes or eyes needing surgery in preparation of the surgery to reduce bleeding during or after the surgery. (11,12) However Anti-VEGF drugs also prevent normal retinal vascularization of the immature retina in the preterm baby, because the natural vascularization requires low and sustained levels of VEGF till the retina completely matures. Since the Anti-VEGF do not destroy the avascular retina and do not promote, but in fact halt the natural vascularization, recurrences sooner or later are high. Once the effect of the anti-VEGF drug decreases as it is washed out from the vitreous cavity, the avascular retina continues to produce VEGF and also the eye develops deranged angiogenic signaling (13). Hence severe and 'rebound' recurrence of neovascular ROP are reported anywhere from 4 weeks to as long as 74 weeks (even one and a half years!) after injection (10, 11, 14). These recurrences can lead to very bad and incurable retinal detachments and loss of vision. This puts a lot of responsibility on the doctor injecting the drug and the parents and neonatologists to ensure and provide periodical, close and long-term follow-up even upto a year or more for the baby, before declaring that the baby is 'Cured'.

Adverse Events: Ocular and systemic adverse events with Anti-VEGF in ROP are slowly being reported and constant vigil and reporting are desirable. (8, 15, 16). Besides reactivation mentioned above, these include retinal break formation, rapid worsening of traction, choroidal injury, transient vasculitis, cataract, vitreous haemorrhage, and deranged Liver enzymes.

Laser versus Bevacizumab (Table 2): The BEAT-ROP trial (10) reported anti-VegF Monotherapy treatment in ROP to be better than laser especially for zone I threshold disease. Eyes with bevacizumab did exceptionally well with preservation of peripheral retina, retinal vascularization and less recurrences. However, some issues have been raised regarding the methodology of laser delivery, high rate of laser failure and safety issues in this trial (17, 18). Recent laser protocols show very good anatomic outcomes in 70-87% cases of Zone I disease when treated early, and adequately as per ETROP guidelines and remain the standard of care currently (5,7,19,20). In the BEAT-ROP study, systemic intubation rates (37.5%) were far beyond those reported in current literature on ROP laser treatment (10, 19). In the combined data from two Indian studies (7,20), a total of only three babies had apnoea during or after laser treatment done under topical anaesthesia and so laser therapy, though induces stress on babies and surgeons, is actually very safe.

Role of combination Therapy: Since anti-VegF drug kills preexisting VegF in the vitreous cavity and may not have mucheffects on matured new vessels once pericytes are laid down, a combination therapy of anti-VEGF and laser could be a logical mode of treatment. Theoretically, combination treatment would take care of the secreted VegF and the upcoming secretion of any additional VegF and protect against late recurrences while still reducing the peripheral field loss or myopia. Some reports have found good results with the combination therapy. Lee et al reported early regression of the plus disease and faster peripheral vessel growth in the eyes treated with a combination of laser and intravitreal Bevacizumab (0.5mg/0.02ml) as compared to Laser alone (21). Nazari et al also reported similar observations with the use of combination therapy in more advanced disease (22). Recently Kim et al have reported in a small sample of eyes, the efficacy of the lowest effective dose of intravitreal Bevacizumab (0.25mg/0.01ml) in combination with Zone 1 sparing Laser for Zone 1 type 1 ROP. None of these eyes showed any unfavourable structural outcomes or recurrence requiring retreatment following combination therapy (23). Visual and refraction outcomes of combination therapy are awaited. Combination therapy may provide a new direction in the treatment of ROP that may reduce the disadvantages of each of the treatment modality and possibly enhance efficacy. Safety issues would still continue to require consideration. All such treatments need

to be provided with detailed informed consent to parents regarding lack of information about the pharmacokinetics and tissue/organ effects of Anti-VEGF drugs in the developing newborns.

Dosage Issues: The least effective dose that can be safely used in preterm infants' eyes without spill over into systemic circulation is as yet unknown. Bilateral simultaneous injections, pre-treatment with laser (which breaks down the blood retinal barrier), and more immature tissues could all potentially lead to more drug in the systemic circulation. The dose of intravitreal bevacizumab used in various reports, which showed effective regression of new vessels in ROP, has ranged from 0.40 mg to 0.75 mg, about half the adult dose (7-12, 15, 16, 21, 22, 24). The smallest effective dose recently reported is 0.25mg in 0.01ml (23) and so consideration should be given to using smaller doses than being used currently. Because even a total of 0.50 mg of intravitreal bevacizumab was reported to reduce the serum levels of VEGF significantly and for prolonged duration, consideration should be given to decreasing the systemic exposure by injecting a lower effective dose.

Systemic safety and drug Pharmacokinetics: VEGF is required in the developing baby for maturation of critical organs including alveoli, renal glomeruli, brain and liver. Animal models show reduced growth, increased mortality and longterm hepatic and cartilage dysfunctions after Anti_VEGF administration. (13, 25) Intravitreal Anti-VEGF cause significant suppression of systemic VEGF levels lasting upto 8 weeks (25). Every doctor administering Bevacizumab to infants must know that the off-label use of Bevacizumab or other AntiVEGF drugs has been introduced for ROP treatment without adequate clinical and animal data on its dosage, pharmacokinetics and safety in premature babies. (25) More deaths (five) were reported in the bevacizumab group than in the laser group (two) in the BEAT-ROP study (10) and all were related to cardio-pulmonary problems. It would be very difficult to diagnose adverse effects of these drugs especially on worsening of bronchopulmonary dysplasia in the presence of preexisting condition which is not uncommon in these preterm babies. Administration of VEGF in animal models has been shown to improve lung alveolar maturation and reduce respiratory distress. Assessment of adverse effects on renal tissues such as altered Glomerular filtration rates or development of hypoplastic kidneys could take decades. Worsening of hepatic function has been reported by us (12) but Liver enzyme studies have not been undertaken in most reports of Bevacizumab in ROP to assess its safety.

Indian Babies: The ocular, systemic and neonatal care characteristics of Indian babies with ROP are different from the western literature and so India specific screening criteria have been laid out (26, 27). Larger and more mature babies, especially from suburbs and level II NICU, show very unusual and severe ROP with extensive avascular retina, in our population (28, 29, 30). Safe and effective least Bevacizumab dose, rates of recurrence, and management outcomes of recurrence etc in our such ROP population are still not reported. In our population, we need more prospectively collected safety and efficacy data on Bevacizumab use in such babies before we can consider it as a standard of care. It is the responsibility of all users in India to collect and publish Ocular and systemic safety data so that realistic and accurate safety information can be collected and disseminated for better and safer care of ROP babies. The least systemic safety data that is desirable should include pulmonary, renal, and hepatic assessments including laboratory and clinical work up in the short term and neuro-developmental and renal Glomerular filtration rate data in the long term.

Does this mean that we should not use Bevacizumab injections in ROP? Or that we should frighten the parents so much that they will be scared of accepting anti-VEGF drugs even at the risk of losing the eye to ROP? No! That is not the message that this write-up gives. The message is, use it judiciously only where there is no alternative, use minimal dose as being reported now (example 0.25mgm), discuss with parents that we are using the least dose needed and will need to monitor baby

for long term just as for any other new modalities of treatments in any disease, collect samples for renal and liver function parameters, and report any adverse events. Academic centers of course will continue their responsibility to provide further prospectively collected safety, efficacy and strategy data for enhanced knowledge to the community at large.

Table 1. Comparison between Cryotherapy and Laser photocoagulation

	CRYOTHERAPY	LASER
Mechanism of action	Destroys source of VEGF; does not neutralize already secreted VEGF	Destroys source of VEGF; does not neutralize already secreted VEGF
Efficacy in treatment of ROP	Proven	Proven
Availability	Common, affordable	Less common, but more widespread now , expensive
Pain	+++	+
Bradycardia / need for re-intubation	+++	+
Anesthesia	Always general anaesthesia; rarely subconjunctival anaesthesia	General or Topical anaesthesia with or without sedation/ analgesics
Ease of posterior treatment	Difficult ; needs conjunctival dissection	Relatively Easier to treat posterior disease
Ease of anterior treatment	Easily achieved	Needs practice and expertise
Development of Exudative RD	Not uncommon	Rare ; occurs with intense burns
Treatment	Shorter duration	
Easier even in small pupils and Tunica vasculosa lentis	Longer duration	
Requires skill and expertise		
Difficult in pupil rigidity		
Multiple sessions	Very difficult due to difficulty in repeat general anaesthesia at short intervals and adnexal edema	Can be repeated easily every 3-7 days
Post treatment evaluation	Difficult till adnexal edema regresses, usually more than a week	Easily done from next day due to minimal adnexal edema
Visual outcomes	More myopia BCVA <20/200	Less myopia BCVA >20/50

Table 2. Comparison between Laser photocoagulation and intravitreal Bevacizumab injection

	LASER	Bevacizumab
Mechanism of action	Destroys source of VEGF	Neutralizes existing VEGF in vitreous
Efficacy in treatment	Proven	Regression of new vessels proven
Ease of treatment	Requires skill, expertise	
Long sessions ; effect appears after few weeks	Easily administered	
Less time, skill required		
Immediate effect		
Recurrence of new vessels once regressed after completion of retinal ablation	Rare	Late and early severe rebound recurrences ++. Risk factors for recurrence need study
Rapid worsening of preexisting tractional component	Less common	Quite common and so is a relative contraindication
Safety	Safe with known well studied ocular side effects; No long-term systemic safety issues	Ongoing studies
Visual field	Destructive so reduces visual field	Preserved visual field as not destructive
Refractive outcome	More myopia	Less myopia (ongoing studies)
Current status	Standard of care	Rescue in laser failed eyes. Preoperative preparation. Ongoing evaluation as a Primary Monotherapy or Combination therapy

References:

1. McNamara JA, Tasman W, Brown GC et al. Laser photocoagulation for stage 3+ Retinopathy of prematurity. Ophthalmology 1991; 98(5): 576-580.

2. Multicentre trial of Cryotherapy for Retinopathy of Prematurity: Ophthalmological outcomes at 10 years. Arch Ophthalmol 2001; 119: 1110-1118.

3. Jalali S, Hussain A. We can aim at better results in coming years. Arch Ophthalmol, 2006; 124 (4): 604-605.

4. Hurley BR, McNamara JA, Fineman MS, et al. Laser treatment for retinopathy of prematurity:evolution in treatment technique over 15 years. Retina 2006; 26(7suppl):S16-17

5. Jalali S, Azad RV, Trehan HS et al. Technical aspects of laser treatment for acute retinopathy of prematurity under topical anaesthesia. Ind Jl Ophthalmol 2010; 58: 509-515.

6. Dave VP, Jalali S, Rani PK et al. Characteristics and outcomes of anterior hyaloidal fibrovascular proliferation in lasered ROP. The Indian twin Cities ROP study report 4. Int Ophthalmology. 2013; 14 (epub ahead of print)

7. Jalali S, Kesarwani S, Hussain A. Outcomes of a protocol based management for zone I retinopathy of prematurity. The Indian twin cities ROP screening program report number 2. Am J Ophthalmol 2011; 151(4):719-724.

8. Miciell A, Surkont M, smith AF. A systematic analysis of the off-label use of Bevacizumab in severe ROP. Am J Ophthalmology 2008; 148; 536-542?

9. Quiroz-Mercado H, Martinez-Castellanos MA, Hernandez-Rojas ML et al. Antiangiogenic therapy with intravitreal bevacizumab for Retinopathy of prematurity. Retina 2008; 28(3suppl):S19-25

10. Mintz-Hittner HA, Kennedy KA, Chuang AZ; BEAT_ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. N Engl J Med 2011; 364: 603-615.

11. Law JC, Recchia FM, Morrison DG, et al. Intravitreal bevacizumab as adjunctive treatment for retinopathy of prematurity. JAAPOS 2010;14:6 –10

12. Jalali S, Balakrishnan D, Zeynalova Z et al. Serious adverse events and visual outcomes of rescue therapy using adjunct bevacizumab to laser and surgery for ROP. The Indian twin Cities ROP screening database report number 5. Arch Dis child Fetal Neonatal ed. 2013; 98 (4) F 327-333.

13. McCloskey M, Wang H, Jiang Y et al. Anti-VEGF antibody leads to later atypical intravitreous neovascularization and activation of angiogenic pathways in a rat model of ROP. IOVS 2013; 54: 2020-2026.

14. Hu J, Blair MP, Shapiro MJ et al. Reactivation of Retinopathy of prematurity after Bevacizumab injection. Arch Ophthalmol 2012; 130: 1000-1006.

15. Atchaneeyasakul L-O, Trinavarat A. Choroidal ruptures after adjuvant intravitreal injection of bevacizumab for aggressive posterior retinopathy of prematurity. J Perinatol 2010; 30:497-499.

16. Chhabalani J, Rani PK, Balakrishnan D et al. Unsusual adverse Choroidal reaction to intravitreal Bevacizumab in aggressive posterior Retinopathy of Prematurity, the ITCROPS data base report number 7. Semin Ophthalmol Oct 2013 (epub ahead of print)

17. Azad R, Dave V, Jalali S. Use of intravitreal anti-VEGF: ROP surgeon in Hamlets' dilemma? Ind J Ophthalmol 2011; 54 (6): 421-422. Erratum Ind Jl Ophthalmol 2012; 60 (1): 40.

18. Darlow BA, Ells AL, Gilbert CE et al. Are we there yet? Bevacizumab therapy for Retinopathy of Prematurity. Arch Dis child Fetal Neonatal ed. 2013; 98 (2): F170-174.

19. Early treatment for retinopathy of prematurity cooperative group. Revised indications for the treatment of retinopathy of prematurity. Results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol 2003; 121:1684-1696.

20. Sanghi G, Dogra MR, Das P, Vinekar A, Gupta A, Dutta S. aggressive Posterior ROP in asian Indian babies: spectrum of disease and outcome after laser treatment. Retina 2009; 29(9): 1335-1339.

21. Lee JY, Chae JB, Yang SJ et al. Effects of intravitreal bevacizumab and laser in retinopathy of prematurity therapy on the development of peripheral retinal vessels. Graefes Arch Clin Exp Ophthalmol 2010; 248:1257 –1262.

22. Nazari H, Modarres M, Parvaresh MM et al. Intravitreal bevacizumab in combination with laser therapy for the treatment of severe retinopathy of prematurity (ROP) associated with vitreous or retinal hemorrhage. Graefes Arch Clin Exp Oph-thalmol 2010; 248:1713 –1718.

23. Kim J, Kim SJ, Chang YS et al. Combined intravitreal bevacizumab injection and zone I sparing laser photocoagulation in patients with zone I retinopathy of prematurity. Retina. 2014 Jan; 34(1):77-82.

24. Wu WC, Yeh PT, Chen SN et al. Effects and complications of bevacizumab use in patients with retinopathy of pre maturity: a multicenter study in Taiwan. Ophthalmology 2011; 118:176–183.

25. Hard A, Hellstrom A. On safety, pharmacokinetics, and dosage of bevacizumab in ROp treatment- a review. Acta Paediatrica 2011; 100 (12): 1523-1527.

26. Jalali S, Matalia J, Hussain A, Anand R. Modification of screening criteria for retinopathy of prematurity in India and other middle income countries. Am J Ophthalmol 2006; 141:966-968.

27. National Neonatology forum (NNF). Clinical practice guidelines (Cpg) 2010 (India). Retinopathy of Prematurity. www.nnfpublication.org. Pages 253-263.

28. Sanghi G, dogra MR, Katoch D et al. Aggressive posterior ROP in infants >1500grams birth weight. Ind J Ophthalmol 2014; 62(2); 254-257.

29. Sanghi G, Dogra MR, Dogra M et al. A hybrid form of ROP. Br J Ophthalmol 2102; 96(4): 519-522.

30. Shah PK, Narendran V, Kalpana N et al. Severe ROP in big babies in India: History repeating itself? Ind J Paediatr 2009:76 (8): 801-804.

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INTRAOCULAR FOREIGN BODIES

Intraocular foreign bodies (IOFB) form a unique subset of trauma cases that presents a diagnostic and therapeutic challenge to the treating ophthalmologist. IOFB occur in 18-41% of the open globe injuries. Most are young men, in there twenties to forties. The commonest scenario is workplace accidents, commonly involving hammering metal/ stone 2,4

A majority of the foreign bodies(FB) lodge in the posterior segment of the eye.1-4 Smaller, sharp FB are less destructive and easier to remove but difficult to detect; while larger FB have risk of proliferative vitreoretinopathy(PVR) and retinal detachment(RD).1,6 Most FBs are metallic(80-90%). Some like gold, silver, platinum and tantalum are inert while iron, copper, lead etc, are toxic. Inorganic non-metals like stone, glass, plastic, porcelain and rubber are relatively inert 5 Organic FB(wood, vegetable matter) can result in severe infection and poor outcome

All open globe injuries may potentially harbor IOFB. In children, subtle signs like sealed corneal tear, iris hole and localized conjuctival chemosis must be looked for. Visual acuity, RAPD, FB size, number, route of entry, location and extent of collateral damage to ocular tissue are important factors that alter the prognosis.

The damage to ocular tissue caused by IOFB can be due to mechanical trauma/ inflammation/ infection/ chemical(metallosis) or a combination of the above.

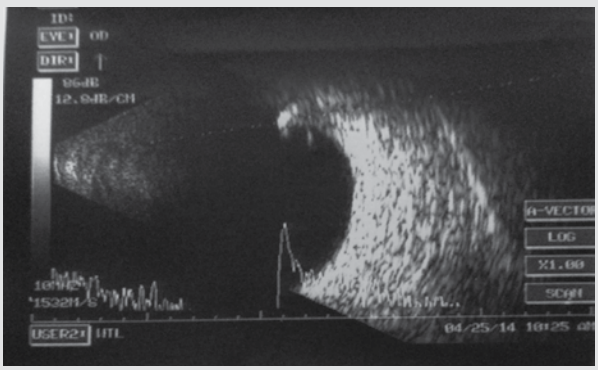
Siderosis is caused by intracellular deposition of trivalent iron ions, especially in Muller cells and retinal pigment epithelium. Clinical features include corneal dusting, rusty iris, sluggish pupil, yellow cataract, pigmentary retinal degeneration, vascular attenuation and optic atrophy. ERG changes are useful in monitoring and prognosticating and partly reversible by FB removal.2,5

Chalcosis is caused by IOFBs with copper content 85-95%; whereas pure copper produces rapid suppurative endophthalmitis. Copper gets deposited extracellularly on limiting membranes in cornea, lens and retina. Clinical features include Kayser–Fleischer ring, greenish-brown sunflower cataract; greenish hue of iris, sluggish pupil, copper particles in aqueous, vitreous and along retinal blood vessels.2,5

Plain-film radiography/X-ray is a valuable screening tool for radio-opaque FB, especially in opaque media but may miss small IOFB. FB location may be difficult to ascertain without additional aid of limbal ring.

CT scan is a more sensitive tool for IOFB detection; especially in suspected cases where X-ray turned negative. It can also detect FB location, composition and globe rupture('flat tire sign'), but falls short when it comes to organic FB and soft tissue damage.10

USG is very effective in detecting and locating radiolucent IOFB, assessing the status of retina, choroid, vitreous and optic nerve, and detecting globe perforation. IOFB typically shows high



reflectivity and shadowing of the RCS complex. It is to be avoided in open globe lacerations.2

Electroretinogram(ERG) is of special value in cases of metallosis bulbi for prognostication. Initially a- and b-waves are normal/supernormal, then gradually b-wave amplitude reduces and in final stages ERG becomes flat. Upto 40% reduction in b-wave amplitude is reversible by IOFB removal.7

Magnetic resonance imaging (MRI) though more sensitive than CT-scan for organic/plastic IOFB, is contraindicated if ferromagnetic FB is suspected7 Ultrasound biomicroscopy (UBM) is useful to detect small/non-metallic IOFBs in the anterior chamber angle or behind the iris root.

Management

All suspect cases of IOFB must be referred to a vitreo-retinal surgeon as early as possible. Systemic medications must be started to control pain, nausea, coughing, and anxiety. Broad-spectrum systemic antibiotics (oral or intravenous depending on the case) are routinely used. Tetanus immunization should be supplemented if reqired. The injured eye should be patched and covered with shield before referring.2,7

The primary goal in surgical handling of the injured eye is anatomic restoration of the globe and prevention/ treatment of infection. IOFB in general constitutes an emergency. The presence of other factors like endophthalmitis, retinal detachment, organic FB material or contaminated wound calls for earlier intervention as prognosis deteriorates with time.

The IOFB can be removed ab externo, by scleral cutdown and applying a strong external magnetic field; or ab interno, by pars plana vitrectomy(PPV) using forceps or intraocular magnets.7 Ancillary procedures like corneoscleral tear repair and removal of traumatic cataract are frequently required at the same sitting. An intraocular lens implantation may be deferred for later. Retinopexy by cryotherapy/laser barrage at the retinal impact site of the IOFB is controversial. But any traumatic retinal break needs retinopexy(laser or cryo) if surgery is delayed. Scleral buckling may benefit some eyes with peripheral tears.

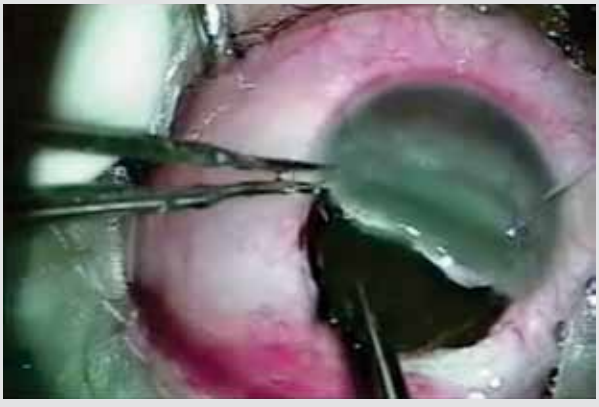
There are certain situations where intervention may be more traumatic than retained IOFB. A chronic, inert, encapsulated IOFB without clinical/ electrophysiological evidence of toxicity in a quiet eye may be left alone, with periodic ERG monitoring.7 Once ERG is extinguished in an eye with established metallosis, IOFB removal may not improve the outcome. Small FBs in the corneal stroma(eg.blast injury) that are inert and asymptomatic, should not be removed unless they project into the chamber or out through the epithelium.7 Large IOFBs in a phthisical eye with no perception of light(PL) are better left alone.

Though generally eyes with no PL are deferred for surgical intervention, exploratory surgery may be considered in some cases such as altered mental status, media opacity, commotio retinae, RD, subretinal hemorrhage etc. Morris et al in a series of eyes with no PL, reported visual recovery in 64%, and claimed that even a non-recordable bright-flash ERG is compatible with visual recovery

Surgical techniques

Anterior chamber foreign bodies are generally removed through a secondary limbal incision(after repairing the primary laceration). Intralenticular IOFBs are removed during cataract surgery. Visual prognosis is excellent in anterior segment IOFBs.

The posterior segment foreign bodies are removed by vitrectomy or by trans-scleral route. External electromagnet exerts a powerful magnetic pull that can be employed after scleral cutdown either directly over the IOFB(direct approach) when it is anterior and accessible; or at the pars plana(indirect approach) when it is posterior but intravitreal and away from retina. IOFB movement may damage



retina or crystalline lens. Small [<3 mm], anterior, visible, intravitreal, magnetic IOFB in a fresh case may yield good results.3

For large, posterior, invisible, non-magnetic, intra/subretinal or encapsulated IOFBs (Figure 3), or those associated with RD, endophthalmitis or significant vitreous hemorrhage, pars plana vitrectomy(PPV) is the only option. Induction of posterior vitreous detachment (PVD) eliminates ERM and PVR. Retinopexy is done for peripheral / iatrogenic breaks. The IOFB is picked up with intraocular magnet/forceps after removing its adhesions and taken out by enlarging the sclerotomy/via limbal section, with prior lensectomy.

Prognosis

Anatomic and visual outcome after IOFB removal is limited by infection, PVR and RD.1 Endophthalmitis occurs in 8-13% of eyes with IOFB. Incidence quadruples if IOFB removal is delayed >24 hours.11 For PVR and RD, the main risk factors are the size of IOFB, retinal injury and traumatic cataract.

Final visual outcome depends on size, shape, nature and location of IOFB, size and location of entry wound, RAPD, patient's age and visual acuity at presentation. With modern surgical techniques, open-globe lacerations with foreign bodies have a better visual prognosis; a final visual acuity of 6/12 or better can be expected in up to 71% of the eyes with early and appropriate intervention.3

Prevention is better than cure. According to a survey on work-related injuries, only 3% of those with IOFBs were actually wearing protective glasses. A majority of ocular injuries can be prevented by adequate eye protection. There is a need for occupation-based counseling on safety measures, and legislations to make them mandatory, supplementing the advances in surgical management to effectively reduce foreign body-related ocular morbidity.

References

1. Jonas JB, Knorr HLJ, Budde WM. Prognostic factors in ocular injuries caused by intraocular or retrobulbar foreign bodies. Ophthalmology 2000;107:823–828

2. Mester V, Kuhn F. Intraocular foreign bodies. Ophthalmol Clin N Am 2002;15: 235-42

3. Greven C, Engelbrecht N, Slusher M, Nagy S. Intraocular foreign bodies. Management, prognostic factors, and visual outcomes. Ophthalmology 2000; 107:608-12.

4. Williams DF, Mieler WF, Abrams GW, Lewis H. Results and prognostic factors in penetrating ocular injuries with retained intraocular foreign bodies. Ophthalmology 1988; 95:911-6.

5. Bustros SD. Posterior segment intraocular foreign bodies. In: Shingleton BJ, Hersh PS, Kenyon KR, editors. Eye trauma. St. Louis: Mosby, 1991. pp 226-237

6. Chiquet C, Zech J, Gain P, Adeleine P, Trepsat C. Visual outcome and prognostic factors after magnetic extraction of posterior segment foreign bodies in 40 cases. Br J Ophthalmol 1998;82:801.

7. Mary Elizabeth Harnett. Trauma (part IV). In: Schepens CL, Harnett ME, Hirose T, editors. Schepens' retinal detachment and allied diseases,2nd edition.. Woburn: Butterworth-Heinemann; 2000. pp 679-705

8. Bettman JW: Seven hundred medicolegal cases in ophthalmology. Ophthalmology 1990;97:1379-84.

9. Bryden FM, Pyott AA, Bailey M, McGhee CNJ. Real time ultrasound in the assessment of intraocular foreign bodies. Eye 1990;4:727-31.

10. Zinreich SJ, Miller NR, Aguayo JB, Quinn C, Hadfield R, Rosenbaum AE. Computed tomographic three-dimensional localization and compositional evaluation of intraocular and orbital foreign bodies. Arch Ophthalmol 1986; 104:1477-82.

11. Thompson JT, Parver LM, enger CL, Mieler WF, Liggett PE. Infectious endophthalmitis after penetrating injuries with retained intraocular foreign bodies. Ophthalmology 1993; 100:1468-74.

12.Kuhn F, Morris R (editorial): Posterior segment IOFB-management in the vitrectomy era. Ophthalmology 2000; 107:821-2.

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MICROPERIMETRY

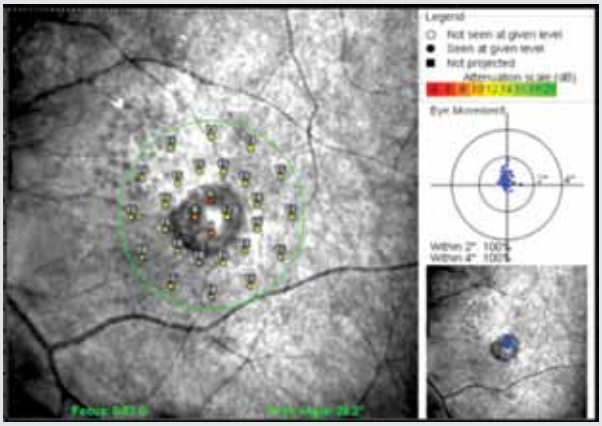
Ever Expanding Frontiers of Knowledge, New Epoch making inventions and technological innovations have brought New Armamentarium in the hands of Ophthalmologists to provide better care to our ailing population.

It is an ardent task for an Ophthalmologist to not only be abreast of latest developments but also to invest in latest high-tech equipments. Affordability , user friendly and every investigative procedure needs to be evaluated based on information it gives during investigation and treatment of the patient, its relevance in day to day care.

Microperimetry is one such investigation modality which with the advent of SCANNING LASER OPHTHALMOSCOPY AND OPTICAL COHERENCE TOMOGRAPHY has proved itself to be useful patient friendly and yields important relevant information in the hands of Ophthalmologist to provide better care and evidence based care.

Perimetry is the measurement of the extent of visual field which is the space an Eye can see while remaining fixed. This is standard test done to diagnose treat & follow up Glaucoma patients.,and Neurological conditions affecting visual pathways.

Microperimetry as name suggests is a Localised field testing . It evaluates the function of Focal area of retina accurately. This ability helps us to evaluate the functional involvement of retinal function at a desired location of Retina . With this we can better understand the retinal pathologies, its natural history, progress,response to treatment. This investigative modality has a very High level of Sensitivity and Specificity.

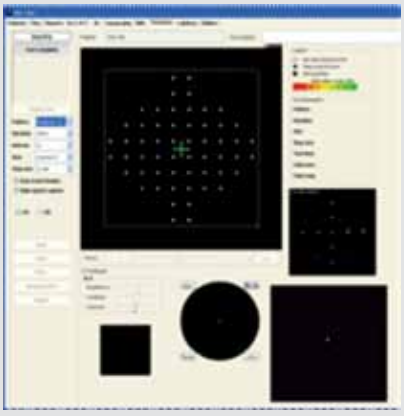


The SLO-OCT multimodality with Microperimetry mode is used to generate Fundus image simultaneously and a sensitivity testing is performed on the desired area of lesion. Correlation of OCT findings and the patient response to the stimulus pattern at the spot gives in depth information about the type and nature of disease process affecting the retina. This is simultaneously done and recorded matching the target with pixel

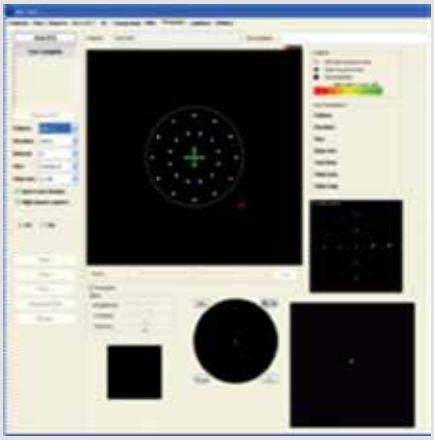
to pixel correlation giving it accuracy, repeatability and reproducibility.

The Multimodality of the machine can superimpose finding of two or more procedure done simultaneously and superimpose findings to incorporate your results.

PROCEDURE - This is exceptionally simple . Patient is primed by explaining the nature of stimulation signals and how to press the button on seeing the same. Various sizes and shapes of stimulus pattern are available depending on the location , size and shape of the retinal pathology one wishes to evaluate.



Humphry 10 Pattern



Peripapillary Pattern.

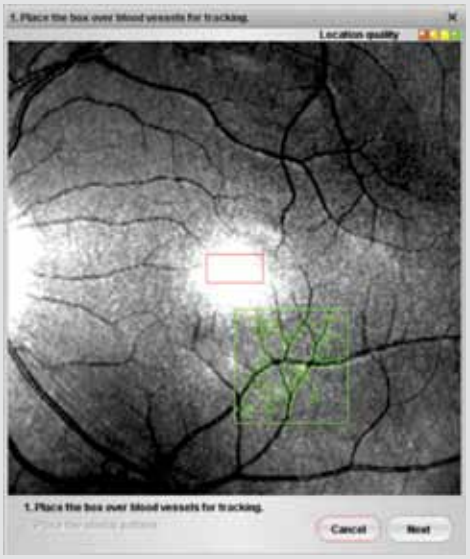
So we can select an area and than select the pattern which shall be suitable to evaluate the function of that area . This incanny ability to not only Objectively assess the lesion but simultaneously Subjectively evaluate the function makes MIcroperimetry a unique tool capable of providing quality information for betterment of Eye care.

US FDA has approved this investigation as Standard of care and hence a recent surge in its applications.

We at Retina Care Hospital have been using this modality for patient care since last Five years and have been very satisfied with the results and information it provides.

The versatility of this procedure is the freedom to choose the Pattern,Determine the duration of stimulus,Choose the interval between the stimulus , and choose the Size of the stimulus.

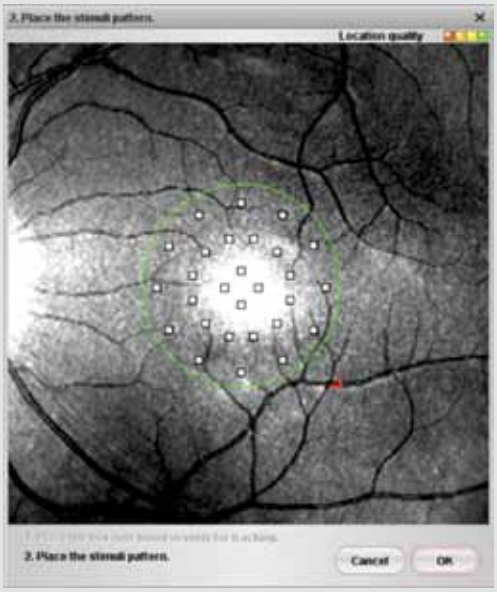
Another hallmark of this procedure is repeatability. When we prime the patient Software selects a vascular structure that will be used to track the retina during the Microperimetry test. So when we retest the location is already stored and accurately realigned to make the information analysis perfect.

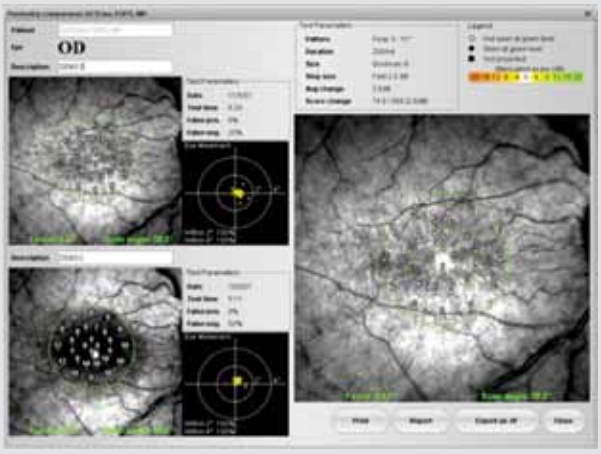


The user can select the location of the box over the blood vessel. The Retinal Blood vessel tracking is visible to the clinician throughout the exam.

We can select the location of test by dragging or placing the test pattern to a location of interest.

This is another feature which helps us to accurately compare the same test location functionality done at different time frame. So we can evaluate progress





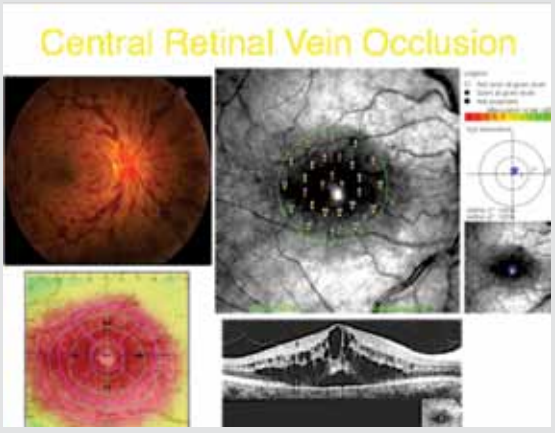
of lesion , responsiveness to the treatment and evaluate our understanding of the disease process.

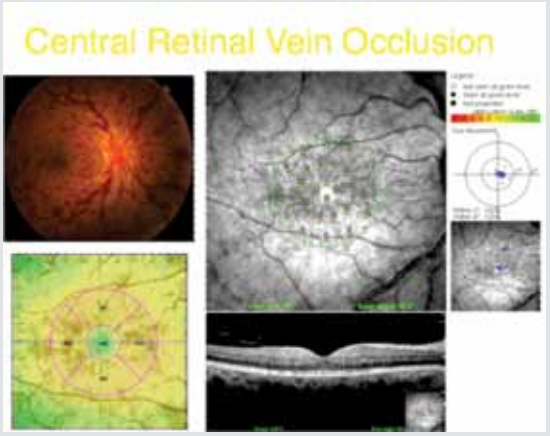
Clinical cases and relevance of this test can be better explained by sharing with you our experiences in treating some of the common disorders we face in our day today practice using this Multimodality approach.

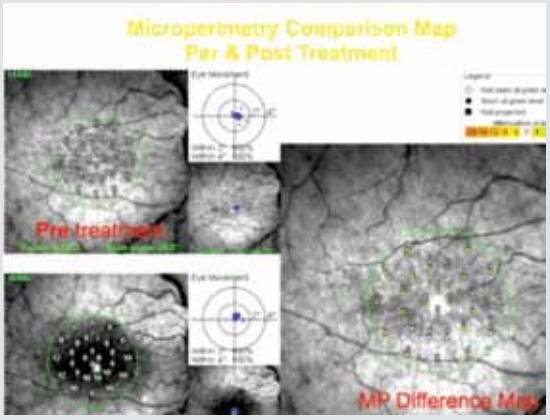
This is a pretreatment evaluation both OCT & Microperimetry results on the same page.

This is the post Treatment analysis of the same patient after AntiVegf treatment.

This is the Microperimetry Comparison Map Pre & post treatment.



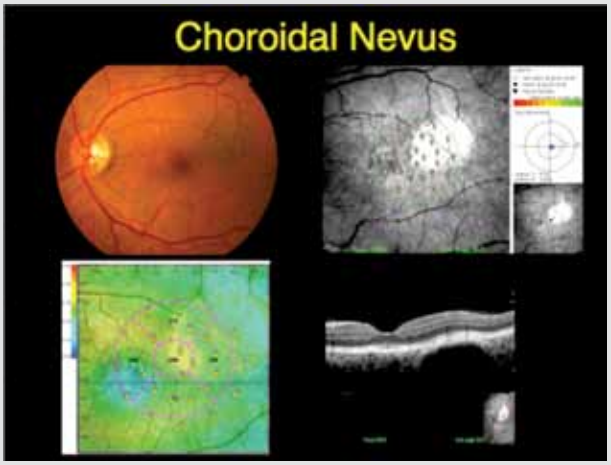




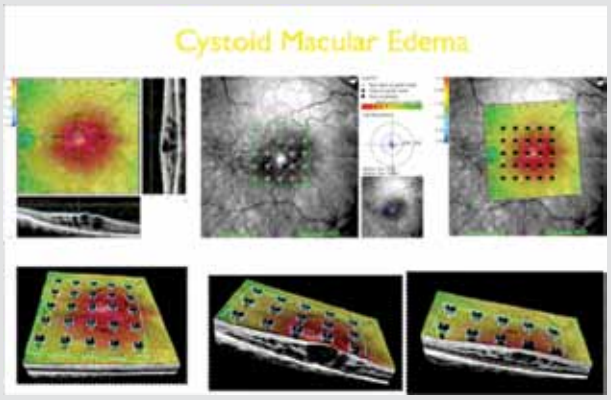
A case of Choroidal Naevus which can be evaluated over a period of time more accurately to see for the progress and possibility of its turning malignant.

A case of Cystoid Macular oedema where the threshold values over the Cystic spaces demonstrated reduced values.

Retinal thinning over the cicatricial CNV correlated with reduced threshold sensitivity.

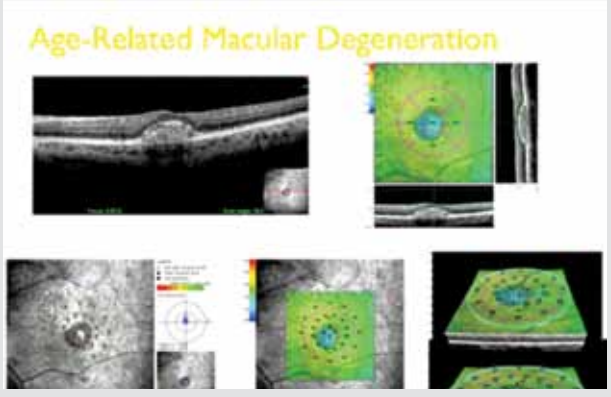


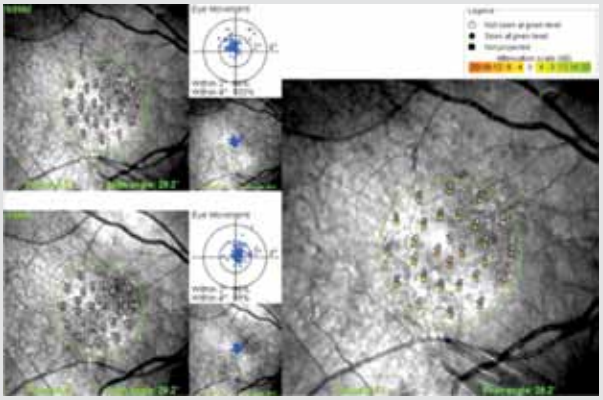
The accuracy and the repeatability of this test also gives us a useful tool to evaluate No Improvement and assess our treatment protocol in this example where over the period of treatment the functionality



didn't improve on the contrary started worsening when the line of management is altered.

Our observation over the last few years with this modality have educated us with these Pearls of wisdom.





Large cystic areas and Retinal thinning consistently correlates with decreased threshold sensitivity so patients can be preinformed of the prognosis before starting the treatment.

Cystic changes involving inner retinal layer appear to influence threshold sensitivity negatively more than similar size cyst in outer layers of Retina.

Small cysts in outer layers have minimal effect on threshold.

Areas of Normal OCT thickness with decreased Threshold suggest Ischaemic Vascular Effect and have poor prognosis. This is a very important information to be shared with the patient before starting any intervention to avoid uncomfortable Patient Doctor Relation in future.

Spectral OCT /SLO with integrated MICROPERIMETRY offers an additional functional dimension to High Resolution Anatomic Imaging which may enhance our Diagnostic Evaluation of retinal Diseases and our ability to predict visual outcomes from OCT

The ability of Spectral OCT/SLO to image and measure different aspects of a particular Macular lesion with precise registration promises to further our understanding of the complex relationship between structure and function.

In Conclusion it can be emphatically said that MICROPERIMETRY is a useful and informative investigation which should be judiciously used to interpret evaluate and provide Evidance Based Medical Care to our patients.

CME NEWS

The National Institute of Ophthalmology(NIO) under the aegis of **The Vitreo-Retinal Society –India** and Poona Ophthalmological Society had organized a symposium titled 'Retina, Keeping an Eye' on the most relevant topics in retina for postgraduate students in Ophthalmology, at Pride Executive Hotel, Pune.

The event was inaugurated by Dr Pran Nath Nagpal, the Father of Retina Surgery in India. The occasion was graced by the presence of eminent ophthalmologists in and around Pune such as

Col. Dr M Deshpande (Medical Director, H V Desai Hospital, Pune),

Brig. Dr V. S. Gurunadh (HOD, Dept of Ophthalmology, AFMC, Pune),

Dr Suvarna Gokhale (HOD, Dept. of Ophthalmology,

Smt Kashibai Navale Medical College, Pune) ,

Dr Madhav Bhatt (HOD, Dept of Ophthalmology, Deenanath Mangeshkar Hospital, Pune).

The event was attended by about 50 postgraduate students from various medical colleges and hospitals in and around Pune. The speakers included vitreoretinal surgeons from all over the city , lending their expertise and experience in the field of ophthalmology. The talks were based on various topics covering the entire spectrum of retina, including various clinical and theoretical aspects. The highlight of the day was the talk on Dry AMD by Dr Pran Nagpal and a practical demonstration of Indirect Ophthalmscopy by Dr Subhash Gokhale. The lectures followed by panel discussion and case presentations by postgraduate students.

The event received positive feedback from both dignitaries and students attending it. To sum up, the endeavour was a huge success and the students hope that more such educational events would be organized in the future.

XXIIND ANNUAL MEET OF
VITREO RETINAL SOCIETY -INDIA
12TH – 14TH DECEMBER 2013,
LAVASA, PUNE.

REPORT

Dear Colleagues,

The ***22nd ANNUAL VITREO RETINA SOCIETY OF INDIA MEET***,was held on 12th – 14th December 2013, at the beautiful location ***Lavasa International Convention Centre***, in the new and controversial city of Lavasanear Pune. It was organized by the Retina Conglomerate, under the aegis of the Maharashtra Ophthalmology Society and the Pune Ophthalmology Society. The planning and organizing of the details for the conference was capably spearheaded by the local organizing secretary Dr Aditya Kelkar of the National Institute of Ophthalmology.

The planning and ground work began nearly a year ahead. The brochure designing, printing and posting was done well in time. The posting was only for the VRSI members, but an e-brochure was mailed to the POS, MOS and AIOS members. The conference website was up and live, as were the online registrations.

We got an excellent response for the submission of abstracts for the papers, posters and videos. The selection of the papers, posters and careful planning of the scientific programme was done painstakingly by Dr V Narendran.

This year, we added an interesting and much appreciated partner in the conference, initiated by Dr S Natarajan of Adityajyot Hospital – the VRS Frankfurt team, integrated in this prestigious annual meeting of VRSI with lectures and lab education with Virtual Reality DryLabs. Each session equipped with simulators and vitrectomy machines.This was an excellent opportunity for Residents / Fellows to train surgical Skills with this International Faculty.The simulators were given by Alcon, Appaswamy, and VRmagic from Frankfurt. The simulator was imported with the ATA Carnet, which enabled us to get it without paying the import duty.

Posters, slides and presentations were made to be displayed at the various meetings held, to promote the conference and get registrations

By October the total no. of registrations for the conference was already 250! The final registrations had nearly touched 500, the highest in the history of VRSI!!

The challenge had been to accommodate this huge number at the venue city,

which had limited options for accommodation. We had taken all the rooms available in all the hotels, and even the camping site which had a/c tents! Inspite of this, some of the delegates had to stay in Pune and transport was provided daily to pick and drop them back.

All the delegates and faculty were provided transport from Pune station and Pune Airport on arrival, and back after the conference ended.

The program started on time, and went on very well. The advantage of having the conference in an isolated valley location was that most of the delegates attended the lectures. The Drylab sessions were well appreciated and attended. We had 24 applicants who were selected carefully depending on their qualifications and experience in the field.

The inauguration was followed by dinner and an entertaining musical program.

The conference got a tremendous response from the industry! Our prime sponsors were Novartis, Alcon and Allergan. All the sponsors were given an adequate exposure to all the delegates, and have been satisfied with the opportunity to showcase their products and services, and have supported us generously. We had 30 companies participating during the conference.

The banquet was preceded by an enthralling dance performance by Mrs A Kelkar and her troupe

The conference ended on a positive note, and delegates were satisfied with the knowledge, different

viewpoints and approaches to add to their own practices. The abstract book/souvenir with the presentations of the participants has been printed and distributed. The conference participation certificates and the paper, poster and video presentation certificates were given to the delegates before departure itself.

Vitreo Retinal Society-India

Vitreo Retinal Society - India

XXIII Annual Conference 2014, Agra

December 5th to 7th, 2014

Venue : **Jaypee Palace Hotel & Convention Centre,** Fatehabad Road, Agra

Chairperson
Prof. Hem K Tiwari
Prof. Saran K Satsangi

Organizing Secretaries
Dr. Lalit Verma
Dr. Gunjan Prakash

Conference Secretariat

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VITREO RETINAL SOCIETY - 2014

Scientific Highlights

Life Time Achievement Awards:

1. Dr. P. Namperumalsamy, Chairman-Emeritus, Aravind Eyecare System, Madurai.

2. Dr. S. S. Badrinath, Chairman-Emeritus, Sankara Nethralaya, Chennai.

Nataraja Pillai Oration Award

Dr. Richard F. Spaide, New York, USA.

VRSI Hayreh Award

Dr. Cyrus Shroff, New Delhi.

Special Sesions:

Egyptian Vitreo Retinal Society.
Uveitis Society of India.

International Faculty

1. Dr. Michael Stewart, Florida, USA.
2. Dr. Veeral Sheth, Chicago, USA.
3. Dr. Akito Hirakata, Tokyo, Japan.
4. Dr. Anna Ells, Canada.
5. Dr. Timothy Lai, Hong Kong.
6. Dr. Xia Xin Li, China.
7. Dr. Sunil Srivastava, USA.

XXIIIND ANNUAL MEET OF
VITREO RETINAL SOCIETY -INDIA
5TH – 7TH DECEMBER 2014, AGRA

ABSTRACT SUBMISSION CLOSED ON **31st JULY 2014**

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Treatment is given monthly and continued until maximum visual acuity is achieved, confirmed by stable visual acuity for three consecutive monthly assessments performed while on Lucentis® treatment. • Treatment is resumed with monthly injections when monitoring indicates a loss of visual acuity due to wet AMD, DME or macular edema secondary to RVO and continued until stable visual acuity is reached again for three consecutive monthly assessments. • Lucentis and laser photocoagulation in DME or in branch RVO: Lucentis has been used concomitantly with laser photocoagulation in clinical studies. When given on the same day, Lucentis should be administered at least 30 minutes after laser photocoagulation. Lucentis can be administered in patients who have received previous laser photocoagulation. • Lucentis must be administered by a qualified ophthalmologist using aseptic techniques. Broad-spectrum topical microbicide and anaesthetic should be administered prior to the injection. • The patient should be instructed to self-administer antimicrobial drops four times daily for 3 days before and after each injection. • Not recommended in children and adolescents. **Contraindications:** Hypersensitivity to ranibizumab or to any of the excipients; patients with active or suspected ocular or periocular infections; patients with active intraocular inflammation. **Precautions/Warnings:** • Intravitreous injections have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. Therefore proper aseptic injection techniques must be used. Patients should be monitored during the week following the injection to permit early treatment if an infection occurs. • Transient increases in intraocular pressure (IOP) have been seen within 60 minutes of injection of Lucentis. Sustained IOP increases have also been reported. Intraocular pressure and the perfusion of the optic nerve head must be monitored and managed appropriately. • There is a potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors. A numerically higher stroke rate was observed in patients treated with ranibizumab 0.5 mg compared to ranibizumab 0.3 mg or control, however, the differences were not statistically significant. Patients with known risk factors for stroke, including history of prior stroke or transient ischemic attack should be carefully evaluated by their physicians as to whether Lucentis treatment is appropriate and the benefit outweighs the potential risk. • As with all therapeutic proteins, there is a potential for immunogenicity with Lucentis. • Lucentis has not been studied in patients with active systemic infections or in patients with concurrent eye conditions such as retinal detachment or macular hole. • There is limited experience with treatment of patients with prior episodes of RVO and of patients with ischemic branch RVO (BRVO) and central RVO (CRVO). In patients with RVO presenting with clinical signs of irreversible ischemic visual function loss, treatment is not recommended. • Should not be used during pregnancy unless the expected benefit outweighs the potential risk to the fetus. For women who wish to become pregnant and have been treated with ranibizumab, it is recommended to wait at least 3 months after the last dose of ranibizumab before conceiving a child; use of effective contraception recommended for women of child-bearing potential; breast-feeding not recommended. • Following treatment patients may develop transient visual disturbances that may interfere with their ability to drive or use machines. Patients should not drive or use machines as long as these symptoms persist. **Interactions:** No formal interaction studies have been performed. **Adverse reactions:** • **Very common adverse reactions are:** intraocular inflammation, vitritis, vitreous detachment, retinal hemorrhage, visual disturbance, eye pain, vitreous floaters, conjunctival hemorrhage, eye irritation, foreign body sensation in eyes, lacrimation increased, blepharitis, dry eye, ocular hyperemia, eye pruritus, intraocular pressure increased, nasopharyngitis, headache, arthralgia. • **Common adverse reactions are:** retinal degeneration, retinal disorder, retinal detachment, retinal tear, detachment of the retinal pigment epithelium, retinal pigment epithelium tear, visual acuity reduced, vitreous hemorrhage, vitreous disorder, uveitis, iritis, iridocyclitis, cataract, cataract subcapsular, posterior capsule opacification, punctuate keratitis, corneal abrasion, anterior chamber flare, vision blurred, injection site hemorrhage, eye hemorrhage, conjunctivitis, conjunctivitis allergic, eye discharge, photopsia, photophobia, ocular discomfort, eyelid edema, eyelid pain, conjunctival hyperemia, stroke, influenza, urinary tract infection*, anemia, anxiety, cough, nausea, allergic reactions (rash, pruritus, urticaria, erythema) **Uncommon** • **adverseeactions are:** blindness, endophthalmitis, hypopyon, hyphema, keratopathy, iris adhesions, corneal deposits, corneal edema, corneal striae, injection site pain, injection site irritation, abnormal sensation in eye, eyelid irritation. • **Serious adverse events** related to intravitreal injections included endophthalmitis, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. *observed only in the DME population **Packs:** Pack of 1 vial Before prescribing, please consult full prescribing information available from Novartis Healthcare Private Limited, Sandoz House, Dr. Annie Besant Road, Worli, Mumbai- 400 018. 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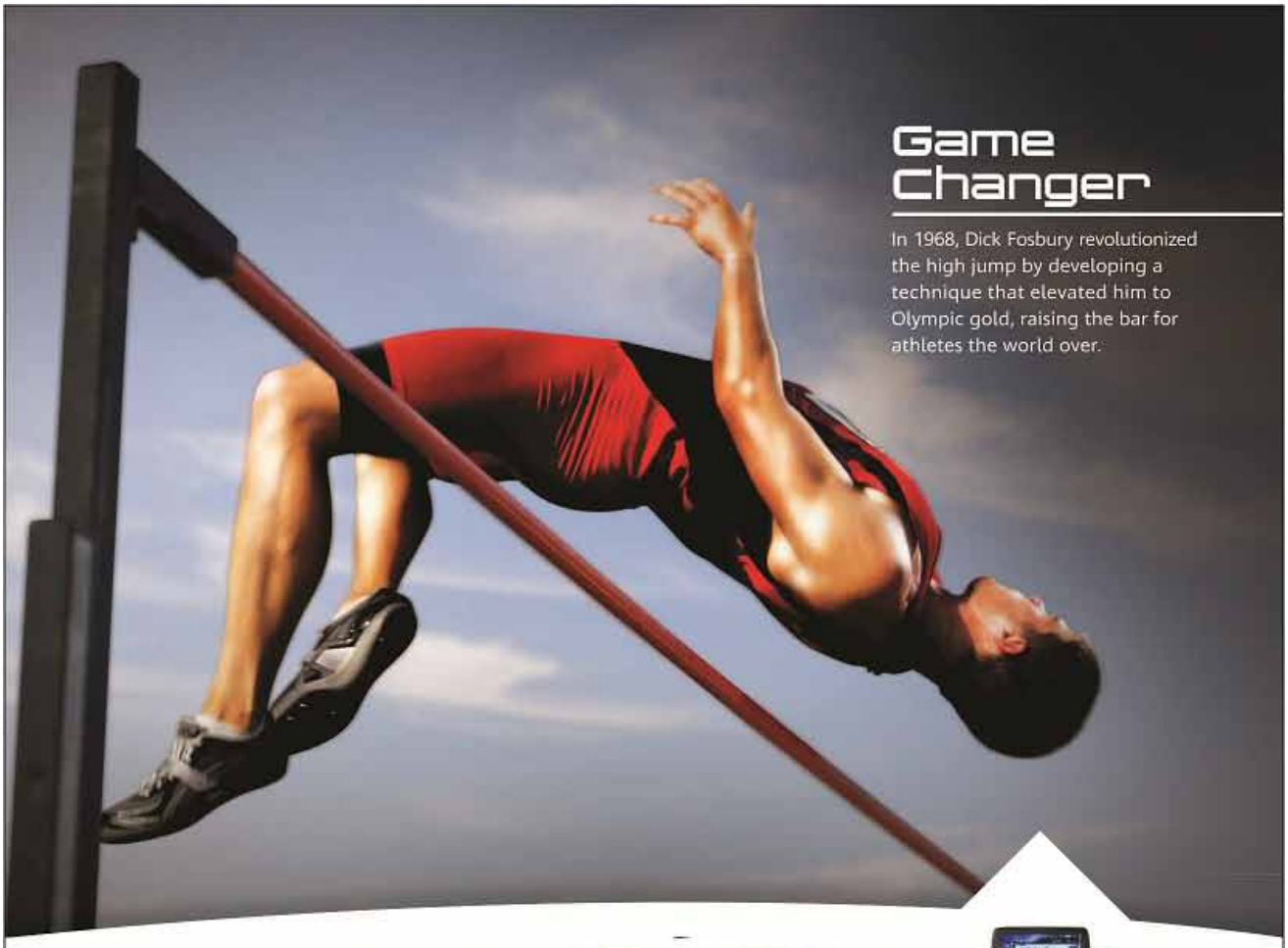

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1. Rizzo S, *et al*. Comparative Study of the Standard 25-gauge Vitrectomy System vs the New Ultra-high-speed Vitrectomy System. *Retina Today*. September Insert, 2010. 2. Data on File, Alcon Research 954-2020-003. 3. Nagpal M, Wartikar S, Nagpal K. 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.

Indications for Use: The CONSTELLATION® Vision System is an ophthalmic microsurgical system that is indicated for both anterior segment (i.e., phacoemulsification and removal of cataracts) and posterior segment (i.e., vitreoretinal) ophthalmic surgery. **Caution:** Federal (USA) law restricts this device to sale by, or on the order of, a physician. **Warnings and Precautions:** The disposables used in conjunction with Alcon instrument products constitute a complete surgical system. Use of disposables and handpieces other than those manufactured by Alcon may affect system performance and create potential hazards. Attach only Alcon supplied consumables to console and cassette luer fittings. Do not connect consumables to the patient's intravenous connections. Mismatch of consumable components and use of settings not specifically adjusted for a particular combination of consumable components may create a patient hazard. Vitreous traction has been known to create retinal tears and retinal detachments. The closed loop system of the CONSTELLATION® Vision System that adjusts IOP cannot replace the standard of care in judging IOP intraoperatively. If the surgeon believes that the IOP is not responding to the system settings and is dangerously high, this may represent a system failure. **Note:** To ensure proper IOP Compensation calibration, place infusion tubing and infusion cannula on a sterile draped tray at mid-cassette level during the priming cycle. Leaking sclerotomy may lead to post operative hypotony. **Important Safety Information: Warnings and Cautions:** A complete listing is available in the CONSTELLATION® Vision System Operators Manual. To obtain a copy, please contact Alcon Customer Service. **Attention:** Reference the Directions for Use for a complete listing of indications, warnings, and precautions.