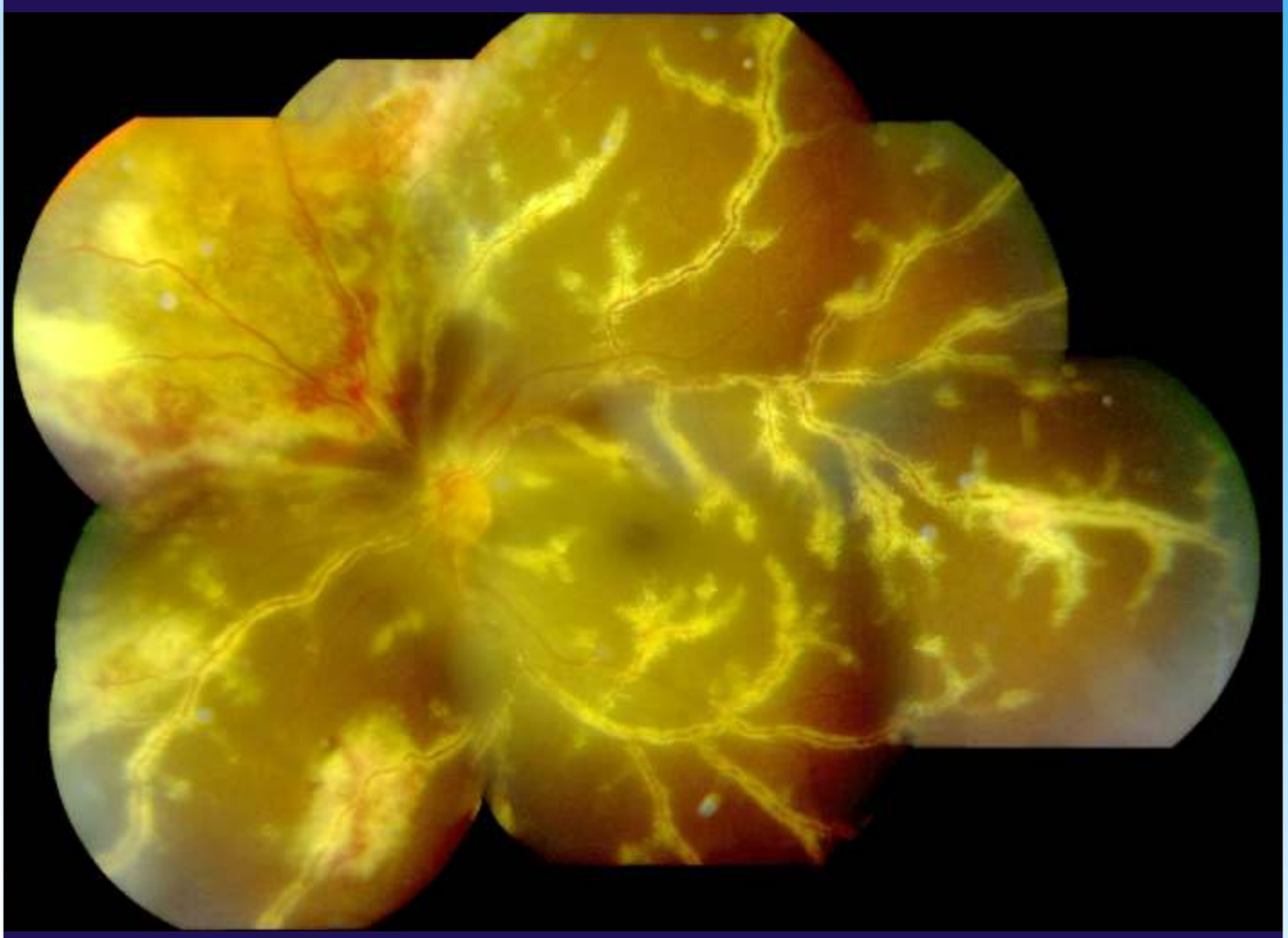
MARCH 2019

The Official Newsletter of the

VITREO RETINAL SOCIETY-INDIA



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Contents

From the President's Desk

Dr. Shobhit Chawla
Medical Director and Chief - Vitreo Retinal Services
Prakash Netra Kendr
Lucknow
shobitchawla1412@gmail.com

Dear Friends

Best wishes at the start of the new year. The first VRSI Newsletter is here by the efforts of Dr. Anand Rajendran, the Scientific Convenor. Let us all contribute with enthusiasm and think of the best possible ways for keeping the pace with which our society has grown, going and achieve new milestones.

I encourage all the young VR surgeons to contribute to the Society and the Newsletter, We welcome all suggestions. This year the VRSI annual meeting is in Lucknow from 5th to 8 th December 2019. Our organizing secretary Dr Mohit Khemchandani and his team have already started the preparations for the meeting , to make the Awadhi experience a rich one for all in every way.

Warm regards

Dr. Shobhit Chawla
President
VRSI

From the Honorary Secretary's Desk

Dr. Raja Narayanan
Director-Head, Clinical Research Consultant
Smt. Kanuri Santhamma Centre for Vitreo Retinal Diseases
Kallam Anji Reddy Campus, Hyderabad
narayanan@lvpei.org

Dear Friends

Greetings from VRSI! The first issue of VRSI Newsletter 2019 has been compiled by Dr. Anand Rajendran. I am sure that you will find the articles extremely valuable for your daily practice, and to provide the best care to your patients. I take this opportunity to request you all to submit your interesting cases, articles and innovations to the VRSI newsletter, which will help improve the scientific knowledge base of our members.

Preparations for our XXVIII annual meeting at Lucknow from Dec 5 to Dec 8, 2019 are under way. Dr. Shobhit Chawla and Dr. Anand Rajendran are putting together an excellent program. I request you all to participate enthusiastically in the activities of VRSI.

Regards

Raja Narayanan
Hon. Secretary
VRSI

From the Convenor, Scientific Committee's Desk

Dr. Anand Rajendran
Professor & Head
Vitreo-Retinal Service,
Aravind Eye Hospital, Chennai
anandrjn@gmail.com | convener.scientificcom.vrsi@gmail.com

Dear Friends and Colleagues

It gives me great pleasure in bringing out this inaugural edition of the VRSI Newsletter of 2019. As of going into print, we are now a 1000-strong Retina Society and VRSI is on the cusp of becoming one of the largest Retina societies in the World. This edition and future ones will hope to address the needs and aspiration of a growing society endowed with energetic, talented, young retina specialists as well as experienced doyens in the field.

The Current issue begins with a celebration of our Awardees – Dr. Mangat Dogra for the SS Hayreh Award chronicling his lifetime saga, pioneering first, and then championing the cause of ROP - spreading awareness, developing treatment protocols and spurring generations of young retina consultants in his institute and around the country to take up this mission. Dr. Jay Chhablani, the very deserving first recipient of the Prof Namperumalsamy Young Researcher Award, has been prolific in publishing over the last few years and has numerous research efforts to his credit. He is perhaps better known for his work in imaging Choroidal Pathology and has captured this in his article. We have an excellent article on Intraoperative OCT by Dr.Ramandeep Singh and workers in the RetinaTech Corner. Stats for Starters from Dr. Sabyasachi Sengupta in the Writer's C(r)amp Section hopes to provide a leg-up for young researcher's looking to kickstart their publishing career by demystifying and clarifying some basic concepts in Statistics. Dr.Ashish Ahuja, a young retina specialist, with an innovative bent of mind and an awardee at the APVRS and AIOC, shares his trials and tribulations in bring forth his innovations.

Hope you enjoy this Newsletter as much as we did in bringing this to you. We look forward to contributions from all members to future issues.

Dr. Anand Rajendran
Convenor
Scientific Committee
Vitreo-Retina Society India

Guidelines - Manuscript Submission for VRSI Newsletter

Original articles:

These include randomized controlled trials, intervention studies, studies of screening and diagnostic test, outcome studies, cost effectiveness analyses, case-control series, and surveys with high response rate. The text of original articles amounting to up to 3000 words (excluding Abstract, references and Tables) should be divided into sections with the headings Abstract, Key-words, Introduction, Material and Methods, Results, Discussion, References, Tables and Figure legends.

Case reports / Challenging case /Innovations / Instruments /Techniques :

New, interesting, challenging, rare cases, innovations, instruments and techniques can be reported. They should be unique and providing learning point for the readers. Manuscripts with clinical significance or implications will be given priority. These communications could be of up to 1000 words (excluding Abstract and references) and should have the following headings: Abstract (unstructured), Key-words, Introduction, Case, Discussion, Reference, Tables and Legends in that order.

The manuscript could be of up to 1000 words (excluding references and abstract) and could be supported with up to 10 references. Case Reports could be authored by up to four authors.

Mail to anandrjn@gmail.com, convener.scientificcom.vrsi@gmail.com

"The SS Hayeh Award"
- Dr. MANGAT R DOGRA

My Journey with Retinopathy of Prematurity

Dr. Mangat R Dogra
Professor and Head
Advanced Eye Centre
PGIMER Chandigarh
India

I am extremely grateful to Vitreo-Retinal Society of India for bestowing me the most prestigious S S Hayreh Award. I consider it a greatest honour ever bestowed on me. Prof. S S Hayreh is a living legend in ophthalmology. He started his initial carrier at medical college Patiala which is very close to our institute in Chandigarh. He is tallest figure of Indian origin in world ophthalmology. I feel greatly humbled to receive this award named after him.

Retinopathy of prematurity (ROP) is a new and fast emerging disease due to increased survival of extremely low birth weight babies in developing country like India. My journey with ROP started in University of Maryland Hospital Baltimore, USA in 1989 where I did my vitreo-retinal fellowship for two years. It was Dr Lingam Gopal from Sankara Nethralaya Chennai in 1990 at American Academy of Ophthalmology Meeting in Atlanta who advised me to concentrate more on ROP as he had already started seeing some cases of ROP in Chennai. I consider him as father of ROP in India as he was first person to start screening and treatment of ROP in 1990. Subsequently, Prof. R V Azad from Dr RP centre AIIMS New Delhi has made major contributions in scaling up the ROP services in India. He introduced the concept of paired work shop comprising ophthalmologist and neonatologist. He was instrumental in including ROP in National Programme for Control of Blindness.

ROP screening and treatment program was started by me for the first time in Post Graduate Institute of Medical Education and Research (PGIMER) Chandigarh in July 1991. This was the time when premature babies started surviving in India in some well equipped neonatal intensive care units (NICU) and ROP started emerging. PGIMER at Chandigarh had one of the first and largest Neonatal Care Unit of the country. This centre trained 60% to 70% of the neonatologists for India. At that time there was no awareness of ROP among ophthalmologist, neonatologist, pediatrician, obstetrician, nurses and parents. Prof O N Bhakoo who is considered as father of neonatology in India and Prof Narang both from PGIMER supported me whole heartedly in this initiative in to this uncharted territory.

We chose single nodal person in NICU who communicated with parents, nurses, neonatologist and ophthalmologist and identified premature babies for screening of ROP. We arbitrarily fixed birth weight <1700gms and/or <32 weeks period of gestation for screening of ROP in the beginning as no guidelines were available in India. Pupils of eligible premature infants were dilated with 2.5% phenylepherine and 1% cylopentolate eye drops instilled twice after a gap of 15 minutes. Excess drops were wiped from medial canthus. Once in a week time was fixed in NICU area for screening of ROP. Screening was started at 4 weeks (day 30) after birth and was always performed once before discharge from NICU. Subsequent ROP screening was performed in Ophthalmology out-patients Department (OPD) on same day as follow up for neonatal problems by neonatologist in their unit. Initially all cases of ROP were screened personally by me and later resident doctors and younger faculty members were trained and involved. We also trained ophthalmologists from various parts of India for screening and treatment of ROP.

Hand written wall charts regarding whom to screen, when to screen and how to dilate were pasted in NICU, Nursery, Neonatal Clinic and OPD.

Indirect ophthalmoscopy with 20D lens was performed and eyelids were prized opened with fingers and oculocephalic reflex was used to examine retinal periphery. Infant eye speculum with wire vectis was used for indentation or rotation of the globe where ever required.

Anterior segment was examined for tunica vasculosa lentis, neovascularisation and pupillary abnormalities with magnification offered by indirect ophthalmoscope and 20D lens. After noting media clarity of fundus, posterior pole was examined for plus disease. Subsequently all four quadrants and clock hours of peripheral retina were examined for extent of involvement with avascular retina or stage of ROP. Documentation of ROP was done according to International Classification of ROP (ICROP). Location of disease in zones and extent of involvement in clock hours along with stage of ROP were noted as per ICROP classification. Immature retina or any stage of ROP was drawn in a chart and compared at subsequent follow up. Screening for ROP was continued till complete vascularisation of retina or spontaneous regression or treatable stage of ROP reached.

First prospective study from India on ROP was published in 1995 by us that reported incidence of 47.27% which was comparable to Western studies. (Charan R, Dogra M R etal. Indian J Ophthalmol 43:123-126; 1995). This was my first thesis as a chief guide which was allotted by me to Dr Rohit Charan in 1992. After this we concentrated on training manpower and clinical research in ROP relevant to our country.

Some of the contributions from us in publications highlighted issues related to ROP in India. These made significant impact on practice of ROP and formulating guidelines for screening and treatment of ROP in this country. Retinopathy of prematurity in Asian Indian babies weighing greater than 1250 grams at birth ten year data from a tertiary care centre in

a developing country (Vinekar A, Dogra M R etal. Indian J Ophthalmol 55:331-336; 2007). This article is one of the highest cited (87 citations) publications ever published in Indian Journal of Ophthalmology. This was a thesis submitted by Dr Anand Vinekar under my guidance for MS ophthalmology in PGIMER, Chandigarh. This article for the first time highlighted why western ROP screening guidelines are not suitable for developing country like India. In this study threshold or worse ROP was observed in 16.1% babies with birth weight >1750 grams, 6.5% were >2000 grams and 22.6% of babies were >32 weeks of gestational age. This had major contribution to convince neonatologist, pediatricians and ophthalmologist to change ROP guidelines for screening in India to include all premature babies with birth weight 2000 grams and 34 weeks of period of gestation.

40% to 50% of severe treatable ROP encountered in India is aggressive posterior ROP (APROP) in higher birth weight babies which has different spectrum and outcome. This is also contrary to western countries where APROP is observed rarely and in extremely low birth weight babies. We reported and highlighted this aspect in several landmark publications including hybrid ROP (combination of APROP and staged ROP) nomenclature given by us for the first time in literature. Recently we reported the spectrum and outcome after laser treatment of ROP in posterior zone 1(Deeksha K, Dogra M R etal. Can J Ophthalmol, article in press)

1. Sanghi G, Dogra M R etal. Aggressive posterior ROP in Asian Indian babies: Spectrum of disease and outcome after laser treatment. Retina 2009:29;1335-1339
2. Sanghi G, Dogra M R etal. A hybrid form of retinopathy of prematurity. Br J Ophthalmol 2012:96; 519-522.
3. Sanghi G, Dogra M R etal. Aggessive posterior ROP in infants >1500 grams birth weight. Indian J Ophthalmol 2014:62; 254-257
4. Sanghi G, Dogra M R etal. Aggressive posterior ROP: Risk factors for retinal detachment despite confluent laser photocoagulation. Am J Ophthalmol 2013:155; 159-164

Cryotherapy was performed under general anaesthesia by me for threshold ROP from 1991-1997 as per CRYO-ROP Study guidelines. Later from 1997 onwards diode laser delivered through laser indirect ophthalmoscope (LIO) delivery system was used for treatment of threshold ROP.

In 2003 laser treatment earlier than threshold ROP was started as per ETROP guidelines. Detailed written consent was always taken before cryotherapy / laser treatment. Laser treatment was performed for all treatable ROP under topical anaesthesia in NICU area under monitoring by a neonatologist. We had major contributions in laser treatment of ROP relevant to our country. These were as follows:

Laser treatment was possible inside the incubator through the sloping transparent wall in extremely unstable premature infants with severe ROP (Dogra etal Ophthalmic Surg Lasers imaging 2008:39; 350-352). This was presented as a video in all major ophthalmic conferences in India and around the globe. We compared frequency doubled Nd: Yag (532 nm

green) versus diode laser (810 nm) in treatment of ROP.(Sanghi G, Dogra M R etal. Br J Ophthalmol 2010 :94;1265) Outcome in this study was comparable in both groups even in eyes with tunica vasculosa lentis, vitreous or preretinal hemorrhage without inducing any cataract, ischemia or hyphema. After this 532nm green laser has become standard of care in treatment of ROP in developing countries. 532nm green laser is usually available in most hospitals to treat other vitreo-retinal disorders. Separate diode laser only for ROP is not affordable and cost effective.

Most babies for cryo/laser treatment were initially from our NICU as premature babies were not surviving in other places. However, at this time majority of babies for laser treatment at our institute are out born and are referred to us for laser treatment from neighboring states. These babies are referred from states of Jammu & Kashmir, Himachal Pradesh, Punjab, Haryana, Rajasthan, Uttranchal, Utter Pradesh and Madhya Pradesh. Incidence of ROP has reduced from 47% to 26% despite increased survival of extremely low birth weight babies in our centre. This is the result of close collaboration and dialogue between neonatology and ophthalmology teams. It is my dream to see that this get replicated all over India.

We published demographic profile of infants with stage 5 ROP in North India: Implications for screening (Sanghi G, Dogra M R etal. Ophthalmic Epidemiology 2011; 18; 72-74). In this study median age of presentation with stage 5 to ophthalmologist was 7 months. 86% were never screened for ROP. 74% were self referred by parents when they realized that child is not seeing. The number of stage 5 babies are on rise due to lack of awareness and timely screening for ROP. This is area of major concern and needs to be addressed at national level.There is increasing ROP blindness in India due to highest preterm birth in the world, increasing numbers of NICUs/SNCUs, neonatal care not being optimal, heavier babies develop severe ROP in India and ROP screening and treatment program are not in place.

I made firm resolution to myself in 1991 that I will never refuse invitation to participate in all activities related to ROP from any place in the country. I have visited all states of India to either hold a workshop or deliver a talk on ROP. I have delivered 207 presentations on ROP in India and abroad since 1991. We have 45 peer reviewed publications in national and international journal and 27 book chapters on ROP. This helped to create awareness about timely screening and referral of treatable ROP among ophthalmologist, pediatrician and neonatologist. These steps in long run may help to reduce blindness due to ROP.

Dr Lingam Gopal, Dr Subhdra Jalali, Dr Anand Vinekar and I are all products of same institution as we did our residency from Department of Ophthalmology PGIMER Chandigarh. Maximum numbers of ophthalmologist for India in ROP were trained by four of us. There is some unknown connection between ROP and PGIMER, Chandigarh.

ROP surgery for stage 4a and 4b is being done in PGIMER for the last 11 years. We have adequate capacity to train large numbers of

ophthalmologists for screening, laser treatment and vitreo-retinal surgery of ROP.

I am extremely grateful to Prof Amod Gupta, Prof Jagat Ram and my ROP team at advanced Eye centre, PGIMER for their encouragement, help and co-operation which helped me to work with passion and make ROP the biggest mission of my life.

"Prof Namperumalsamy Young Researcher Award"
-Dr. JAY CHHABLANI

Choroidal Imaging Biomarkers

Dr. Niroj Kumar Sahoo
Dr. Jay Chhablani
LV Prasad Eye Institute,
Kallam Anji Reddy Campus,
Banjara Hills, Hyderabad - 500 034

Introduction

The choroid signifies the vascular layer of the eye that is involved in the nourishment of the outer retinal layers. Histologically, it is comprised of Bruch membrane, layer of choriocapillaris (CC), Sattler and Haller layers, and the suprachoroidal lamina. It has been implicated in various retinal diseases and of late, has become the center of focus of numerous ophthalmologists.

Imaging modalities

Optical coherence tomography

Since its inception, OCT has been instrumental in diagnosing a multitude of retinal diseases. While the older generation of OCT machines provided excellent layer by layer sections of retina, poor penetration beyond the RPE resulted in the lack of acquisition of the choroidal layers. This resulted in underestimation of the role of choroid in various retinal pathologies. The longer wavelength of light used in swept source technology has enabled the ophthalmologist to image the choroidal details with greater accuracy.

Choroidal thickness

The increased penetration of the enhanced depth OCT has resulted in the acquisition of the outer choroid in most of the cases. Choroidal thickness (CT) is measured from the choroid-scleral interface to the outer limit of the hyper-reflective band representing the retinal pigment epithelium (RPE) and Bruch's membrane complex.[1] It is one of the most commonly used choroidal parameter and has been used to diagnose many macular disorders. CT can vary with age, ethnicity, gender, refraction, axial length.[2, 3] An increased CT has been seen with conditions like CSCR, PCV, VKH while AMD, pathological myopia and retinal dystrophies have reduction in CT.[4-8]

Choroidal volume

Although CT found a meaningful place as a diagnostic tool, it was a cross-sectional measurement and thus hardly ever provided any information about global variations and

distribution along the whole of choroid. Choroidal volume mapping has been made possible by the help of manual segmentation of the inner and outer boundaries of the choroid using in-built retinal segmentation software on EDI-SD-OCT.[9] Variations in choroidal volume have been demonstrated on the basis of age, sex, axial length and thus could prove to be an essential tool in distinguishing various macular pathologies.[10]

The above two parameters provide an extensive information about the overall choroidal profile with both proven physiological and pathological variability.

Then what was lacking??

Choroidal vascularity

Considering the fact that choroid is composed of both vessels and surrounding stroma, measurement of solely the thickness or the volume barely reflects on the alterations occurring in the choroidal vasculature. In an attempt to quantify this parameter, Sonoda et al. took the help of binarization of the OCT images. With the help of Niblack auto-local thresholding technique, the images were first binarised into dark pixels (choroidal vessels) and white pixels (choroidal stroma)using public domain ImageJ software. This was followed by segmentation of the choroid in order to quatify the total vascular area and stromal area. This was further refined by Agarwal et al by introducing the concept of choroidal vascularity index which is the ratio of area dark pixels to white pixels.[11]The CVI provided an approximate estimate of the choroidal vascular profile. Subsequently, an automated method of binarization, segmentation and CVI estimation was developed by Vupparaboina et al. which made the calculation of CVI rapid and reproducible.[12] The rapid acquisition and calculation of this technique enabled us to construct a database of these indices in a number of conditions like myopia,[13] CSCR[14] and

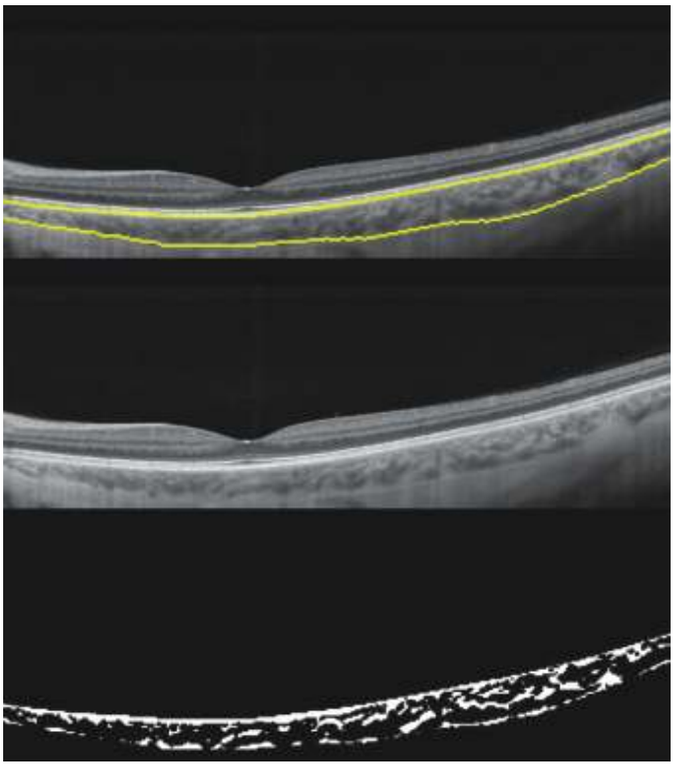

Figure 1 : Choroidal vascularity measurements of a normal healthy eye

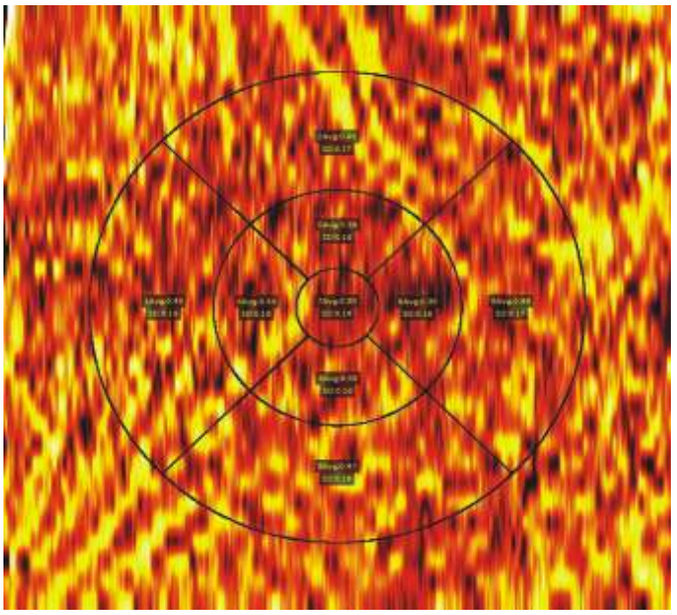

Figure 2: Choroidal vascularity map of a healthy eye

retinitis pigmentosa[15]. Mapping of the CVI values across the macula has also been attempted to determine its distribution across the macula along with its relationship with each other (article under review).With the help of wide field imaging, acquisition of scan from the mid-periphery has also been tried.[16] Individual choroidal vessel layer thickness analysis is another modality that can be used to analyze the choroid in various diseases as it has been seen in a study that there occurs a significant reduction in the size of medium sized vessels in non-pathological myopia[17]whereas an increase occurs in CSCR. Similarly, acquisition of scans from mid-peripheral retina has been used to generate a wide-field image of the choroidal vessel layer thickness.[16] Also, the segmentation of the Haller's layer has been made faster and easy by the development of automated segmentation algorithms.[18] Figure 1 shows CVI measurements of a normal healthy eye. Figure 2 shows CVI map of a healthy eye.

En-face choroidal Vascularity

En-face OCT provides a coronal or en-face topographical map of the choroidal in contrast to a cross-sectional OCT scan. The higher scanning speed of the SS-OCT results in higher number of scans and thus provides a better en-face view of the choroid. It has been shown to be useful in determination of size and distribution of the choroidal vessels.[19]It finds its application in diseases like PCV, where an irregularity in the pigment epithelial detachment has been described. Also, abrupt tapering of the choroidal vessel caliber has been described in diseases of the pachychoroid spectrum in contrast to a slow taper seen in normal eyes.[20, 21]Figure 1 shows CVI measurements of a normal healthy eye.

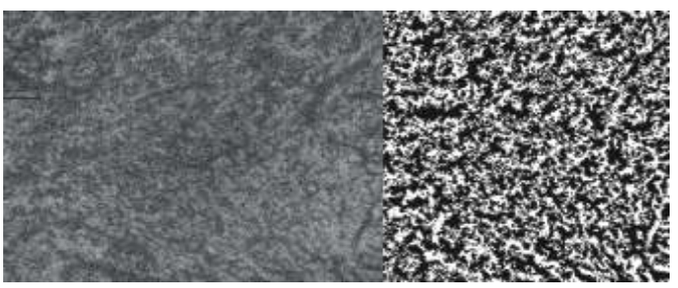

Figure 3: En-face choroidal vascularity of a healthy eye

Optical coherence tomography angiography (OCTA)

Introduction of OCTA has added a new frontier to the way choroid is being imaged. Its ability to capture blood flow characteristics without the need for a dye injection is one of its biggest assets. It is based on the principle of detection of OCT reflectance signal produced by flow of red blood cells through vessels. Some of the commonly used algorithms include split spectrum amplitude decorrelation angiography (SSADA), OCT microangiography (OMAG) and optical coherence tomography ratio analysis (OCTARA).[22]Easy and non-invasive detection of CNV is one of its notable features. It is of particular importance in the detection of non-exudative CNVM as these cases have been shown to have higher progression to exudation than eyes with dry ARMD.[23]Also, quantitative assessment of CNV on the basis of area measurement has been seen to be useful in analyzing CNV regression following treatment.[24]Among the various other advantages of OCTA, analysis of choriocapillary layer in particular is gaining interest. Dark areas on the choriocapillary slab are believed to represent area of flow void. These void areas have been demonstrated to be

affectedbyincreasing age, myopia, pachychoroidspectrum disorders, diabetes mellitus and, various other degenerative and inflammatory diseases.[25-28]

Conclusion

Choroidal imaging hasimproved significantly since the introduction of high penetrance optical coherence tomography. Although it has resulted in greater understanding of choroidal dynamics in healthy and diseased eyes, the resolution obtained from these techniques allow us to only make an estimate of the pathology. Hence these choroidal biomarkers can be seen as a stepping stone towards the unfolding of much more advanced techniques of the future.

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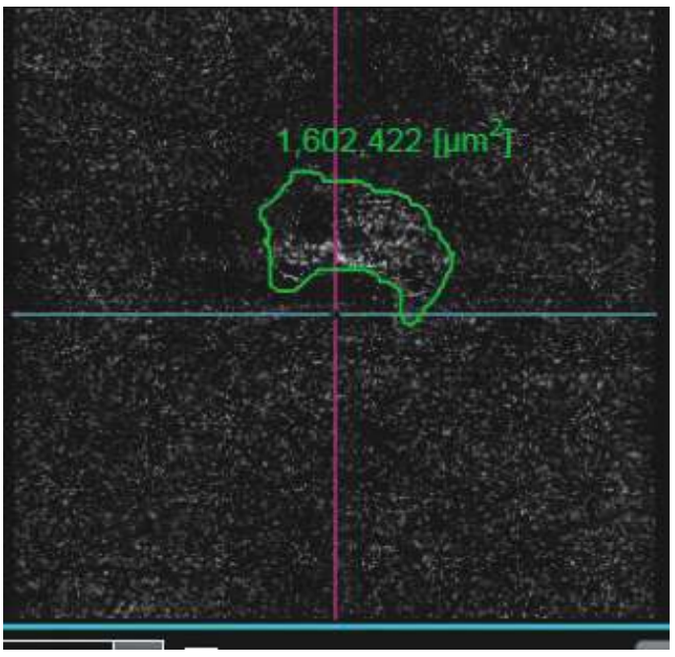

Figure 4: Choroidal neovascular membrane measurements on OCT angiography scan

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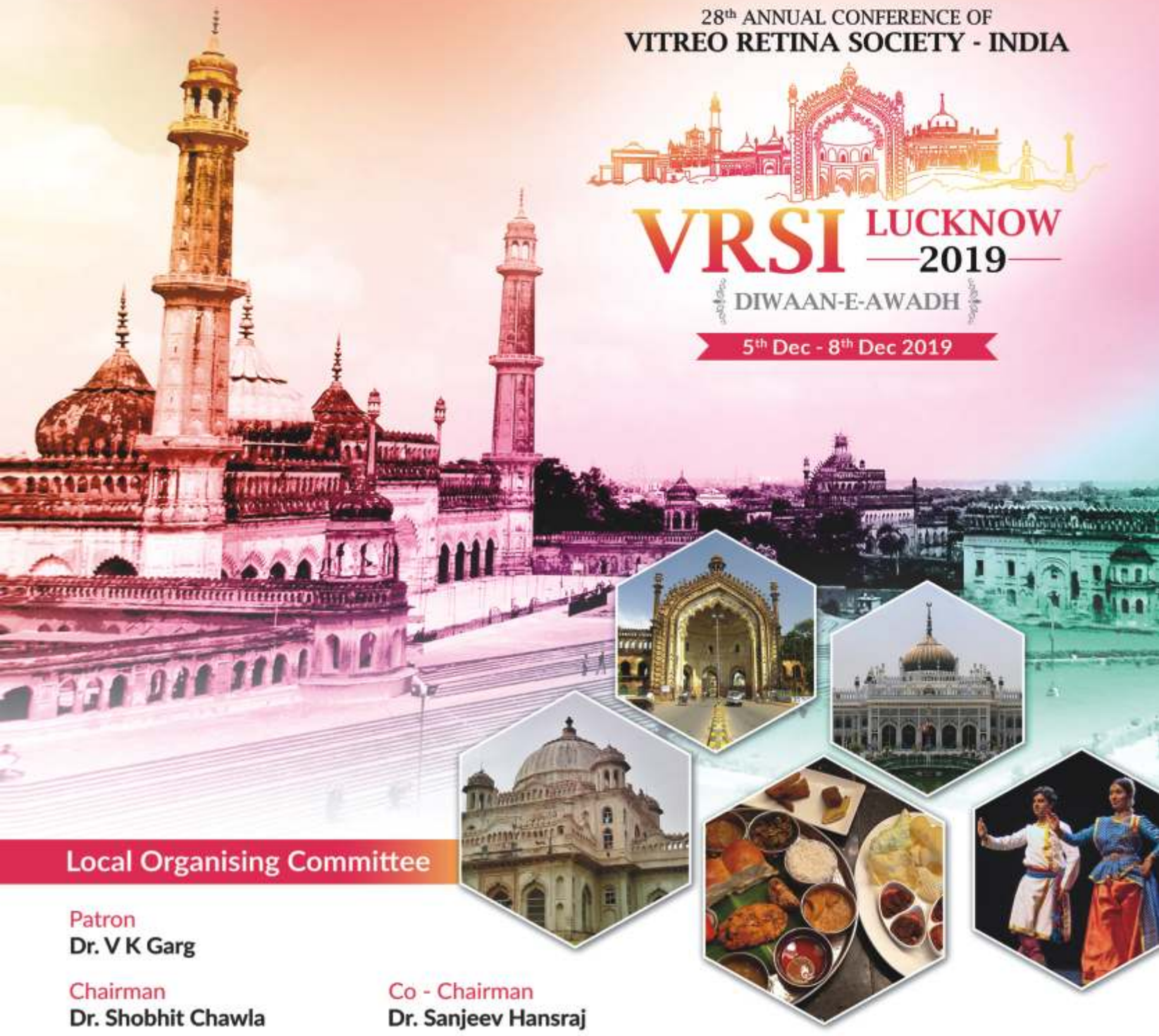

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Role of intraoperative OCT in Posterior Segment Surgeries

Dr. Ankur Singh
Dr. Bruttendu Moharana
Dr. Ramandeep Singh
Correspondence:
Dr. Ramandeep Singh
Professor, AEC, PGIMER, Chandigarh | mankoo95@yahoo.com

Introduction

Since the introduction of OCT in ophthalmology, it has proven to be a vital diagnostic and therapeutic surveillance tool. It has become an integral part of clinical retina practice. But it lacked portability in the past making it unavailable for operation theatres as well as intraoperative use. The need for portability led to the development of newer devices in the form of handheld OCT probes. Handheld OCT was first developed by Bioptigen (Research Triangle Park, NC). This novel technology had the benefit of bedside, non-sedated, noncontact imaging ability. Handheld OCT could image infants and young children during supine examination under anesthesia which was not possible in standalone OCTs [1].In adults, it was used in a various vitreoretinal procedure which included surgeries for macular hole, epiretinal membrane, vitreomacular traction, and optic disc pit related maculopathy [2,3]. Though it was being portable, there was difficulty in obtaining high-quality images due to motion artifacts. This necessitated further research and improvements, which led to the development of a microscope-mounted OCT, and subsequently, microscope integrated intraoperative OCT (MI-OCT). MI-OCT can provide real-time visualization of ocular anatomy and the same was displayed to the surgeon on head-up display or eyepiece of the microscope. This allowed the surgeon to perform image-assisted or image-guided surgeries for better postoperative results. MIOCT has bettered the understanding of tissue behavior during various surgical procedures and thereby improving the predictability of surgical outcome. Though an emerging technology, numerous studies have reported the usefulness and value of MI-OCT in retinal surgeries.

In a recently published study [4] which evaluated the utility of MI-OCT both in anterior and posterior segment surgeries, had found MI-OCT led to the revision of surgical plan in around one-third of their patients undergoing posterior segment surgeries (n = 593 eyes). For this trial they had used three different microscope-integrated OCT prototypes: the RESCAN 700 prototype, the EnFocus prototype

(Bioptigen/Leica Microsystems, Wetzlar, Germany), and an integrated prototype internally developed at the Cole Eye Institute, Cleveland Clinic Foundation (Cleveland, Ohio)[4].The Zeiss RESCAN 700 is a microscope integrated OCT that provides a heads-up surgical view of real-time OCT images. It has an axial resolution of 5.5 µm in tissue with scan length adjustable 316 mm and 360° scan rotational capabilities.

Intraoperative OCT has reported to be used in various posterior segment procedures that includes epiretinal membrane (ERM) peeling, and surgeries for proliferative diabetic retinopathy (PDR) sequelae, rhegmatogenous retinal detachment, macular hole, optic disc pit associated retinoschisis, chorioretinal biopsy, subretinal TPA injection, Argus (Second Sight Medical Products, Inc., Sylmar, CA) prosthesis implant, in diagnostic procedures for panuveitis and Primary intraocular lymphomas.

The benefits of MIOCT will be discussed under various sub headings.

Indications:

1. MI-OCT in of the vitreoretinal interface disorder

While tackling vitreoretinal interface disorders, MI-OCT provides the ability to successfully visualize and delineate the ERM, at the beginning of surgery itself. It allows real-time visualization of intraoperative changes in retinal architecture during ERM peeling (Fig.1A). Completeness of ERM peeling can also be confirmed intra-operatively without the use of any dye. However, the visualization of the posterior hyaloid and ILM is not possible in a reproducible manner. It has been observed thatuse of chemo-adjunct during surgical procedure enhances the visualization of posterior hyaloid as well as ILM.

Leisser et al.in their study visualized a subfoveal hyporeflective zones during ERM peeling which were absent in the post-operative period [5]. These subfoveal hyporeflective zones were subtle, temporary neuro-sensory retinal detachments which developed intra-operatively resultant from traction forces generated during the procedure. The anatomy of the retinal surface was also observed to change after ERM peel; corrugations were observed intra-operatively on the retinal surface post-ERM peel. (Fig 1 B).

In macular hole surgeries, intraoperative OCT aids in the visualization of changes in macular hole architecture during the surgical procedure. While performing internal limiting membrane

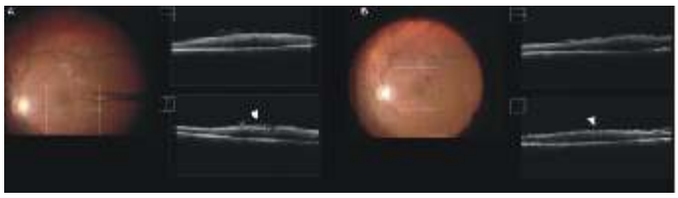

Fig-1. Intraoperative OCT (iOCT) images and photographs obtained during epiretinal membrane (ERM) peeling (A) Visualisation of ERM in real time on iOCT identifying pick areas. (B) Intraoperative visualization of corrugation in the inner retinal surface (arrowhead) post ERM removal with the residual membrane in the temporal periphery.

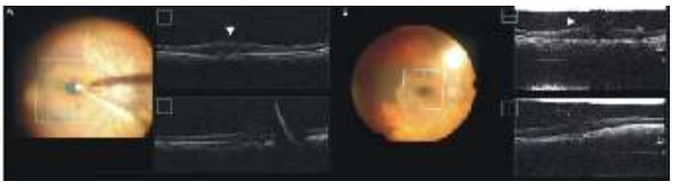

Fig-2. Intraoperative OCT (iOCT) images and photographs obtained during macular hole surgery. (A) Visualization of Internal limiting membrane ILM graft in the macular hole after it being tucked in, real-time visualization of instrument and tissue interaction. (B) Intraoperative OCT image obtained after air-fluid exchange showing properly tucked ILM graft (arrowhead).

peeling (hinged / free flap technique) for macular hole, MI-OCT visualizes the graft in a distinct manner (Fig 2A). Any displacement of the graft after fluid air exchange can also be ascertained on MI-OCT, which would prevent any postoperative surprises (Fig 2B). Development of large areas of hyporeflectivity / lucency during the procedure may be attributed to suboptimal visual outcome post-surgery[6].

2. MI-OCT in proliferative diabetic retinopathy sequelae

MI-OCT is of great use while tackling the cases of PDR with vitreous hemorrhage. Vitreous hemorrhage precludes preoperative planning and complete evaluation of retinal architecture. After clearance of the hemorrhage, MI-OCT can identify optimal surgical dissection planes. Real-time visualization of retina below the vitreous cutter tip can prevent inadvertent retinal tissue damage (Fig 3A&B). Presence of residual traction, partial hyaloid removal due to vitreoschisis, underlying epiretinal membranes and macular edema are best visualized on intraoperative OCT (Fig 3C&D). Removal of these inapparent tractions sites improves the outcome of the procedure, thus reflecting in better and early visual gain. MI-OCT also aids in the identification of occult retinal breaks, confirmation of the absence of a retinal break and differentiation between schisis or traction and retinal detachment, thereby improving clinical decision making of the surgeon. Kahn et al found that in more than 50% of PDR sequelae cases, the surgeon reported obtaining valuable feedback from the intraoperative OCT. In addition, in 26% of these cases, the surgeon felt the feedback from intraoperative OCT was

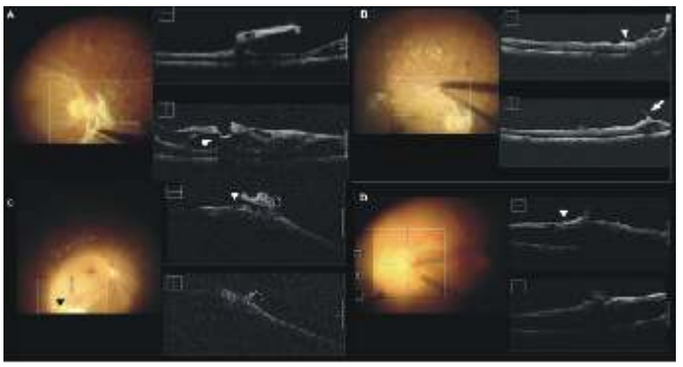

Fig-3. Photographs and intraoperative OCT (iOCT) images obtained during posterior segment surgery for proliferative diabetic retinopathy (A) Real-time iOCT image visualizing a potential dissection plane below the fibro-vascular proliferation(FVP). The lower edge of the aperture of the cutter visualized (arrowhead), thereby allowing the real-time visualization of the distance of cutter tip from the retina. (B) Presence of vitreoschisis membrane after FVP dissection (arrowhead); the stump of dissected FVP (arrow). (C) Visualization of residual membrane (arrowhead) post FVP dissection in a case of combined retinal detachment. (D) Visualization of the residual membrane (arrowhead) even after careful membrane dissection.

discordant with his or her subjective impression, resulting in a change in the surgical plan[7].Formation of subclinical full-thickness or lamellar macular hole may also occur during vitrectomy for diabetic macular edema associated with a thickened and taut posterior hyaloid membrane, identification of these subclinical changes may alter the immediate surgical approach, such as prompting the use of gas tamponade, and potentially preventing the need for reoperation[8].

In retinal detachment surgeries, MIOCT aids in localization of occult membranes (e.g.,

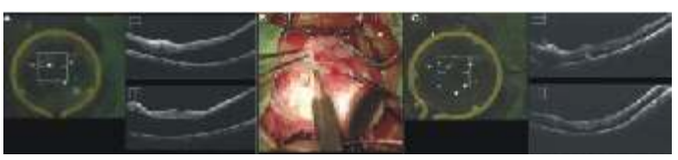

Fig-4. Intraoperative OCT (iOCT) images and photographs obtained during scleral buckling for retinal detachment. (A) Visualization of sub-retinal fluid at the beginning of surgery (B) Intraoperative photograph with surgeons view shows creation of sclerotomy to drain subretinal fluid in the bed of the buckle. (C) Decrease in the subretinal fluid at the end of surgery.

subretinal, preretinal), retinal breaks, residual pre-retinal or sub-retinal perfluorocarbon liquid, as well as differentiation between retinoschisis and detachment. It can assess the presence or absence of macular hole intraoperatively. At the end of surgery, assessment of residual sub-retinal fluid if any can also be assessed by MI-OCT even in cases undergoing scleral buckling procedure (Fig 4 A,B&C). MI-OCT distinctly visualizes breaks in the intercalary membrane in coloboma associated retinal detachment.

3. MI-OCT in other posterior segment surgeries

In cases of neo-vascular age-related macular degeneration with of shallow hemorrhagic retinal detachment, MI-OCT can benefit in visualizing the ideal depth and location for cannula penetration while giving sub retinal tissue plasminogen activator(tPA) injection (Fig 5A&B). Inadvertent intra-retinal or sub-RPE injection of tPA can be prevented. Real-time visualization of the portion of this 39-gauge cannula can prevent unexpected consequences.

Malignancies and other infiltrative disease processes can masquerade as ocular inflammatory conditions. Biopsy of the choroid and retina may be required to obtain a definitive clinical diagnosis in the above cases. MI-OCT can provide details on the relative thickness of sub-retinal lesions, therefore, helping in localizing the biopsy sites as well as identifying surgical landmarks.

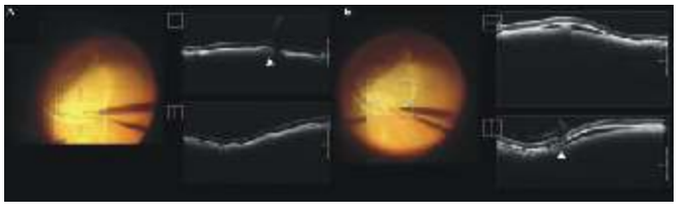

Fig-5. Intraoperative OCT (iOCT) images and photographs obtained during sub-retinal tissue plasminogen activator injection(tPA) (A) Assessment of the placement of sub-retinal cannula tip while giving subretinal tissue plasminogen activator injection(TPA) ; a hypo-lucent area seen below the retina as soon as tPA was injected(arrowhead) (B) hypo-lucent area increase on successful injection.

Intraoperative OCT has been used while implanting Argus II Retinal Prosthesis by Runkle et al.[1]. They placed three Argus II implants for retinitis pigmentosa utilizing MI-OCT feedback. In all 3 cases, intraoperative imaging provided information regarding array positioning and provided feedback to the surgeons to assess retina array apposition. The positioning of the implant was also confirmed by iOCT before and after retinal tack placement.

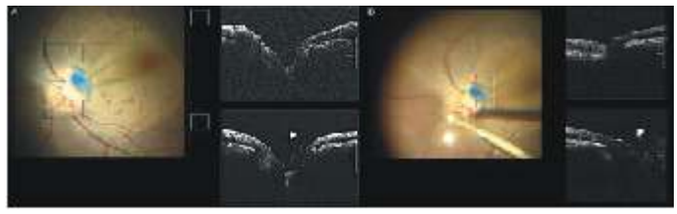

Fig-6. Intraoperative OCT (iOCT) images and photographs obtained during Optic disc pit surgery. (C) Visualization of Internal limiting membrane (ILM) graft in the optic-disc pit, with associated neuro-sensory detachment. (B) Intraoperative OCT image obtained after the air-fluid exchange showing no displacement of the graft (arrowhead).

MI-OCT aids in the intra-operative visualization of optic disc pit in patients of optic disc pit associated maculopathy. Autologous ILM flap position can be visualized before and after fluid air exchange for any potential dislodgement (Fig 6 A&B). MIOCT's ability to visualizes these free graft can help in the proper posting of graft thereby preventing any post-operative displacement.

Treatment of myopic foveoschisis warrants complete removal of hyaloid, which is difficult in

myopes and requires repeated staining. Intraoperative visualization of foveal architecture in cases of myopic traction maculopathy can improve surgical outcome by assuring complete hyaloid removal, preventing inadvertent break formation, and also avoiding the requirement for repeated staining to achieve the optimum surgical result [9, 10].

Our experience with MIOCT

We studied the efficacy of MI-OCT (RESCAN 700; Carl Zeiss Meditec, Inc., Oberkochen, Germany) in surgical decision makingfor various posterior segment surgical procedures. For this, we evaluated all the patients who underwent posterior segment surgery with MIOCT imaging. For the ease of quantification of results, these patients were divided into four groups.

Group A - Patients in whom intraoperative OCT was used as an alternative to surgical steps that required surgical adjutants like various dyes; triamcinolone; proportional reflux hydro-dissection etc. Group B - Patients in whom MI-OCT acted as a guiding tool duringa specific surgical step to provide surgical endpoint, as in cases of sub retinal TPA injection, macular hole surgeries with autologous neurosensory retinal auto graft.

Group C - Patients in who mintraoperatively a new surgically important finding was picked up by MI-OCT, that led to an additional surgical maneuver/change of plan /altered the post-operative care. Group D - MI-OCT acted as a diagnostic tool in pediatric patients undergoing examination under anesthesia (EUA).

A total number of 41 eyes underwent posterior segment procedures where MIOCT was used. MI-OCT was successfully able to image and provided useful information in 92.68% eyes. In Group A, in 85.95% of eyes, MI-OCT was able to visualize the tissue of interest and aid in the completion of the surgical steps without the need for any surgical adjuvants. In Group B which had four eyes, MI-OCT was able to provide Anatomical Delineation for all eyes. Anatomical Delineation provided by MIOCT was enough to guide the surgeon with surgical end point for that particular surgery. There was no complication in any surgical step in this group. In Group Chad 27.27% of total surgical cases, where MIOCT was able to provide additional information that led to change in the surgical management or required additional surgical step (e.g. residual ERM, vitreoschisis, visualization of break) . In Group D, successful image acquisition was possible in 80% of eyes at time of EUA; all these eyes had normal foveal anatomy. In our experience, MIOCT proved to be a promising tool in surgical decision making. Real-time visualization of the area of interest aided in achieving better surgical results, but at the cost of increased surgical time. MIOCT does have the potential to reduce the use of various surgical adjuvants to a reasonable extent.

In our pioneer work to evaluate the feasibility and utility of MIOCT in patients undergoing full

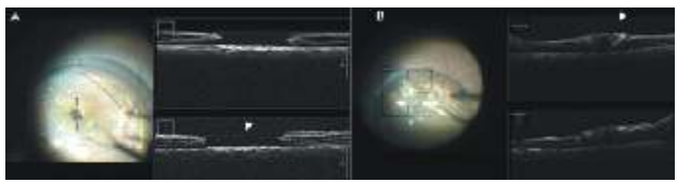

Fig-7. Intra-operative OCT of neurosensory retina graft for macular hole associated with retinal detachment A) Shows actual size of the macular hole under PFCL [both upper and lower OCT frames] B) MIOCT shows graft being tucked within the macular hole and the presence neurosensory retinal overlap inferiorly [arrowhead].

thickness neurosensory retinal autograft for refractory macular hole associated retinal detachment. We found that MIOCT provided intra-operative visualization of macular holes and provided real-time feedback regarding dimensions of the macular holes, thus aiding in accurate sizing and positioning of graft on/in the macular hole (Fig 7 A&B). This ensured the proper fitting of the autograft and also prevented any postoperative displacement, thereby achieving adequate macular hole closure.

Discussion

MI-OCT is a novel device that provides real-time high-resolution visualization of posterior segment anatomy. This device is especially useful for posterior pole surgeries that require meticulous tissue dissection. Its ability to provide real-time feedback to the surgeon not only improves surgical maneuverability but also improves the surgical outcome. MI-OCT has also opened a new paradigm in understanding the behavior of retinal tissue during surgical procedures. A large prospective, study, Discover had recently published their three-year results, in which they found that iOCT in posterior segment surgery was able to add valuable information in approximately 60% of cases and might alter surgical decision making in approximately 30% of cases, making this device a very important tool in vitreoretinal surgical procedure.

Like any other investigative procedure, MI-OCT also has limitations. The limitation is the inability to continuously track the movement of the instruments during the procedure. Shadowing caused by the metallic instrument is another potential problem. Manually tracking the area of interest leads to a potential increase in surgical time. Small transparent scans projected in the eyepiece of the microscope are difficult to read during the surgical procedure, which compels the surgeon to visualize the OCT information on the screen rather than through the microscope oculars.

Although a very useful technology, additional research is needed to develop better understanding of the implications of this information provided by this novel device on outcomes of surgery. Improvement surgical safety by decreasing re-operation rates, better anatomic results, and the role in postoperative care (ideal postoperative positioning) needs to be further researched. Although there are several indicators that suggest that technology may reduce unnecessary surgical maneuvers, enhance surgical safety, improving surgical efficiency, more trials are also required to prove the same.

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WRITER'S C(R)AMP

Stats for Starters

Dr. Sabyasachi Sengupta
Affiliation:
1. Future Vision Eye Care and research Centre, Mumbai, India
2. Sengupta's Research Academy, Mumbai, India
www.senguptasresearchacademy.com

In todays' ever-evolving world, we are confronted with clinical trials on a weekly basis and are expected to constantly adapt our practice patterns based on published literature. A major part of interpreting these trials is interpreting the statistics given in these papers. Sometimes this can be taxing, especially since clinicians are not well versed with statistical terms and analysis.

Additionally, with a lot of pressure to publish articles in top notch journals these days, as well as guiding postgraduate thesis regularly, we are called upon to advise and perform statistics on our own data regularly. This write up intends to orient you with some basic statistical terms that will be useful in your own research endeavours as well as help you in interpreting published literature and review manuscripts for journals.

Like biology and medicine is based on building blocks called "Cells" and material sciences are built on "atoms", the science of biostatistics is based on "Variables".

Variables are of two main types:

1. Continuous variables - are ones, which can take any value from zero to infinity and have a unit to it. For example: age, BCVA in logMAR, retinal thickness in microns etc.

2. Categorical variables - are the ones which as expressed as proportions or percentages (n, %). For example: gender, grades of diabetic retinopathy, outcomes of surgery (% of success) etc.

Once we classify variables into one of these two fundamental types, we can proceed towards describing them (i.e. Descriptive statistics) and analysing them (i.e. Analytic Statistics).

Descriptive Statistics:

Descriptive statistics deals with describing variables that were measured during a study. The metrics used to describe continuous variables are different from those used to describe categorical variables.

Continuous variables are described with

their measure of central tendency (i.e. mean, median or mode) and spread (i.e. standard deviation, interquartile range and variance). If a continuous variable has a normal distribution, it is best described using mean with standard deviation and if the distribution is not normal, it is best to use the median (the 50th percentile with interquartile range) to describe it. The box and whisker plots are the best ways to graphically display continuous variables.

Categorical variables are described using percentages alone (i.e. n, %) and these are best represented using bar diagrams.

Analytic Statistics

Once we describe each individual variable well, it is time to analyse them. Analytic statistics can be broadly classified into the following three types:

1. Differences between variables
2. Correlation between variables
3. Association between variables

Differences between variables

The following table gives an overview of the statistical tests to be used to analyse differences between variables

Type of variable	Number of groups	Distribution	Statistical test
Continuous	2	Normal	Student t test
Continuous	2	Not - Normal	Ranksum test*
Continuous	3 or more	Normal	ANOVA test
Continuous	3 or more	Not - Normal	Kruskall Wallis test
Categorical	2 or more	---	Chi square test
Categorical	2 or more	Small percentages	Fischer's exact test

* Also called Man – Whitney test

As you will see, the test used to analyse differences in variables between variables depends upon the fundamental type of variable, number of groups and the normalcy of their distribution.

Correlation between variables

This deals with how one variable behaves when the values of the other are either increased or decreased and are expressed as correlation coefficients. The coefficients vary from -1 to +1 and are interpreted as follows: O= no correlation, +1 means a strong positive correlation and -1 means a strong negative correlation. Pearson's correlation coefficient is the commonly used metric to represent this. Correlation coefficients are mainly used when continuous variables are being studied. For example: correlation between central retinal thickness at baseline and 3 months post Anti-VEGF injections. The scatter plot with a locally weighted smoothening curve (LOWESS) is the best way to graphically show correlations.

Association between variables

This is done using regression analysis. It is important to understand that correlation does not indicate causality. To establish causality i.e. a cause and effect relationship, we need to perform regression analysis. The type of regression analysis depends upon the nature of

Type of outcome	Type of regression	Type of output
Continuous variable	Linear regression	Beta coefficients
Categorical variable	Logistic regression	Odds ratios
Counts data	Poisson regression	Regression coefficient
Time to event	Survival analysis	Hazard ratios

the outcome measure. The following table summarizes types of regression analysis

Most of the IOL calculation formulae such as the SRK-T are derived using linear regression. Odds ratios show the likelihood of the outcome happening when the influencing variable is increased or decreased. When the outcome depends upon the time from exposure to occurrence, a survival analysis is used. For example, hazards ratios are used in the AREDS studies, 5-year survival rates in cancer are calculated using survival analysis etc.

As you will notice, the first step to understanding biostatistics is classifying the variable correctly. Then you can describe it well and analyse outcomes using appropriate statistical tests.

Dr Sabyasachi Sengupta is the current Associate Editor of the Indian journal of Ophthalmology and Director of Sengupta's Research Academy.

INNOVATOR'S ISLE

Frugal Innovations in Retina
- Think globally, act locally.

Dr. Ashish Ahuja
Sadhu Kamal Eye Hospital, Mumbai
Address for communication : Sadhu kamal Eye Hospital
Room 104, 105, Building No.2, Navjivan Society, Lamington Road, Mumbai Central.
Co-Author: Lavina Utamani, Director at Design way company, Malad, Mumbai
The author has been awarded for Innovations at APVRS and AIOC Meets

Retina subspeciality requires very expensive equipments to practise which restricts service delivery across the country and hence we need to work on ways to develop low cost solutions.

Innovation in healthcare can take many forms, ranging from drug therapies, surgical procedures, devices and tests, through to new forms of health professional training, patient education, and management, financing and service delivery models. 'Innovation' is widely assumed to be positive in its effects, to the extent that the term 'innovative' usually expresses unqualified praise.[1] Research and innovation in science require failure, which must be taught , nurtured, understood, and incorporated in one's scientific paradigm.[2] The aim of this article is to stimulate innovative research and to use the currently available technology to provide more effective and higher quality of care.

Indirect ophthalmoscope can be modified using the currently available technology for better documentation and patient education. We have made a prototype of a low-cost uniocular video indirect ophthalmoscope (IO) using an IO, telephoto lens and a small spy camera (Mini Wireless HD 1080P SPY Hidden Camera Wifi Module video recorder) [Image 1]. We also used a butter paper over the light source to create a diffuse illumination. We obtained good resolution of images using this technique of the posterior pole as well as the peripheral retina

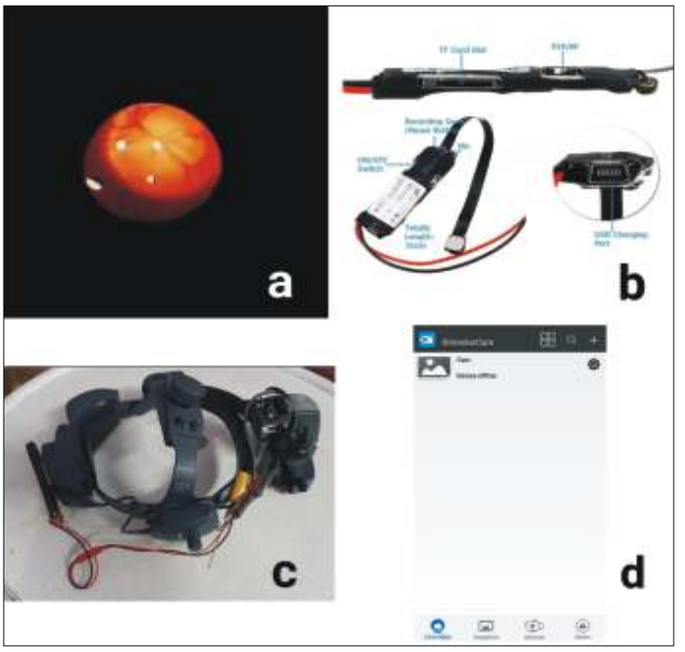

IMAGE 1 :
a. Retieye fundus image captured through the video I.O.
b. Components of the wifi HD spy camera.
c. spy camera mounted on the video indirect ophthalmoscope .
d. ShirestarCam application on the mobile device for viewing the image over a wireless network.

and the data can be directly viewed via an application using the smartphone, which can be transferred via Wifi.

The device cost ranges from Rs 1500 - Rs 8,000. We can record high-definition videos or capture still images using this technique.[3] Image quality can be improved by using a higher resolution camera with an auto focus ability and ability to control the ISO settings. The telephoto lens used is 2X in our device, but if we can use a 4X telephoto lens the image captured would be much better. This device works best with a white LED light indirect ophthalmoscope. Google glass has also been used for indirect ophthalmoscopy with a small modification of attaching an external illumination source. [4]

Recent technological advances in 3D printing have resulted in increased use of this technology in the medical field, where it is beginning to revolutionize medical and surgical possibilities.[5] 3D printing may be used to make a Fundus simulator for different pathologies. 3D doodling may be used which is a pen which extrudes a PLA or ABS filament at a high temperature which can be given any desired shape. Using the aurolab retieye, different retinal diseases may be simulated for better training of doctors. The image shows proliferative diabetic retinopathy with vitreous haemorrhage. [Image 2]

Face-down positioning (FDP) is recommended after vitrectomy and gas tamponade for rhegmatogenous retinal detachments (RRDs). [6,7] Vitrectomy surgery requires a patient to maintain a prone position for 12-14 hours a day for a period of 2 weeks. The real world scenario is that it is very difficult for the patient

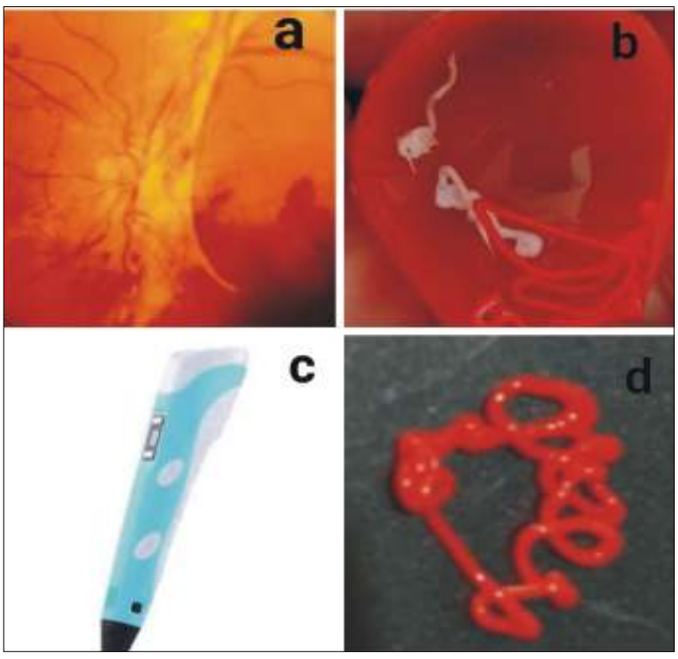

IMAGE 2 :
a. Left Eye Fundus image of high risk PDR with fibrous proliferation noted along the arcade with VH .
b. A modified retieye model (aurolab) with 3D printing to simulate Fundus image a.
c. 3D printing pen which extrudes a filament made of PLA or ABS .
d. Neovascular frond made from 3D printing.

to maintain prone position due to various reasons, maybe a back problem, uncomfortable posture giving chest pain. Challenge is to help patients improve their quality of life and provide early rehabilitation post surgery while providing face down positioning support in the sitting or in lying down position.

A survey of 69 patients with MH found a mean adherence rate of 88.3%, and failure of the MH closure was observed in the one patient who showed the poorest adherence (33.3%). [8] We have come up with a solution to help patients maintain a face down posture in the immediate postoperative period by providing supportive devices which will come in 3 different designs to provide support while the patient is in lying down or in sitting position. This device would come along with an angled mirror which will help patients interact with their surroundings

without a change of posture as the image will reflected by 90 degrees so they can see straight while maintaining a prone position. [Image 3]

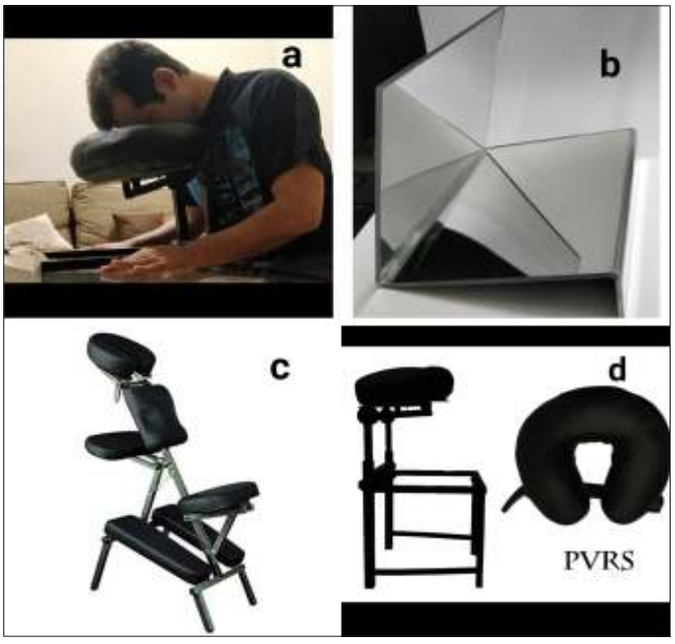

IMAGE 3 :
a. Table top model of PVRS , which can be used on any flat surface .
b. Specialized mirror for viewing objects in front of the observer while maintaining prone position.
c. Seating unit model of PVRS.
d. Bedside model to be used while sleeping with an adjustable height .

In addition we have developed a customised sensor to track the body posture over 24 hours period ,so we can determine the compliance of the patient to maintain prone posture post surgery. The sensor will be a part of the PVRS and would maintain data on a memory card or relay the information via a sim card to the doctor so that we know on daily basis, how many hours the patient maintained prone position. This is a novel device which would have a big impact in vitreo-retina services. If the patient compliance is improved for prone positioning we might be more comfortable going for a gas tamponade instead of silicone oil for some patients and it will reduce the cost of re surgeries and the morbidity related to silicone oil use. PVRS becomes a temporary seating mechanism to help patients relax while writing, reading, eating, socializing or watching TV while facing down from Vitrectomy surgery. With a 2-Way angled Mirror it is easier to watch television On The Table, Desk or TV Tray.

One of the treatment protocols for central retinal artery occlusion requires a gonio massage to be given over a period of 10-15 minutes. We have developed a customised mobile application with a built in timer at design way company to help doctors precisely perform

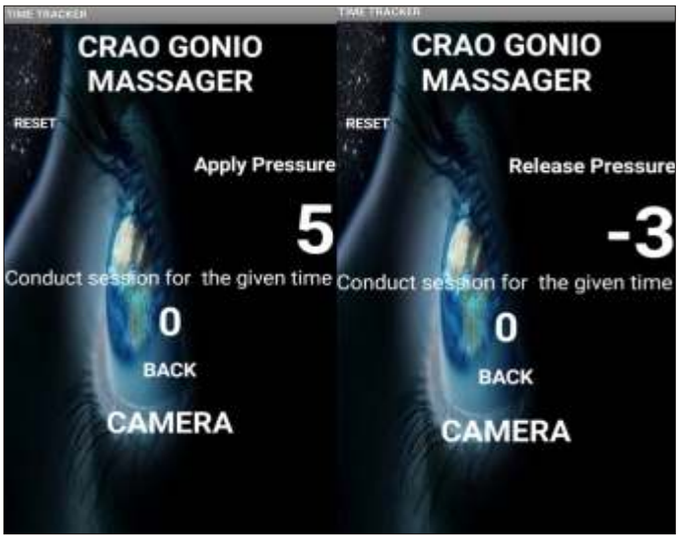

IMAGE 4 :
screenshot of the smartphone based customised app with a timer to assist in gonio massage. (Developed at Design way, Mumbai)

the gonio massage by voice assistance for alternate gonio pressure (10 secs) and release (5 secs) over a 15 minute period so that the doctors can focus on the optic nerve head during the procedure. [Image 4]

We have developed a customised multi lens carry case (developed at design way) for our diagnostic lenses along with a scleral depressor. [Image 5] The case can be modified as per the type of lenses required by the user.

IMAGE 5 :
Customised multi lens case to keep 20D, 90D, 78D lens along with the scleral depressor in a common case. (Developed at Design way, Mumbai)

Innovations need to be focused on improving the quality of care, reduce the cost and increase the access of vitreo retina services across the nation.

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CASE REPORT

A case of IRVAN syndrome treated with Adalimumab

Dr. Sanjana B. Singh
Dr. V. K. Anuradha
Dr. V. R. Saravanan
Aravind Eye Hospital, Coimbatore.

Abstract :

Idiopathic retinal vasculitis, Aneurysms and neuroretinitis syndrome (IRVAN) is seen in young individuals with no systemic involvement. It is characterised by bilateral retinal vasculitis aneurysmal dilatation at the arterial bifurcation, neuroretinitis with macular exudation. Various treatment modalities has been described in literature for the treatment of IRVAN, however, no consensus exists on the medical management. We report a case of IRVAN syndrome in a 13 year old girl who seems to be responding well to subcutaneous Adalimumab and oral Azathioprine after having transient response to Ozurdex and Mycophenolate Mofetil.

Case Report :

A 13 year old female presented to us with complaints of central scotoma both eyes for past 10 months. She had no history of systemic illness. Initially she had defective vision in left eye which was diagnosed as neuro-retinitis and was treated with oral steroids and Doxycyline. Right eye developed visual complaints 6 months after the initial episode. She had received multiple courses of oral steroids with poor response.

When she presented to us her BVCA was 6/24 both eyes. Anterior segment examination was normal. Posterior segment evaluation showed vitreous cells 1+, with bilateral disc edema, hard exudates in macula, retinal vasculitis and aneurysmal dilation of retinal arterioles. OCT revealed macular edema with subfoveal hard exudates in both eyes. Fundus Fluorescein angiography(FFA) showed aneurysmal dilatation of the arteries on the disc and along the arterial arcade. There was vascular leakage suggestive of active vasculitis with no evidence of capillary non-perfusion areas. Serum P-ANCA, C-ANCA, Anti DsDNA, RA factor, Quantiferon TB and, S.Angiotensin converting enzyme were negative. HRCT was normal. S.ANA was positive. She was evaluated by a rheumatologist who ruled out systemic collagen vascular disorders.

Because of patient's reluctance to take oral

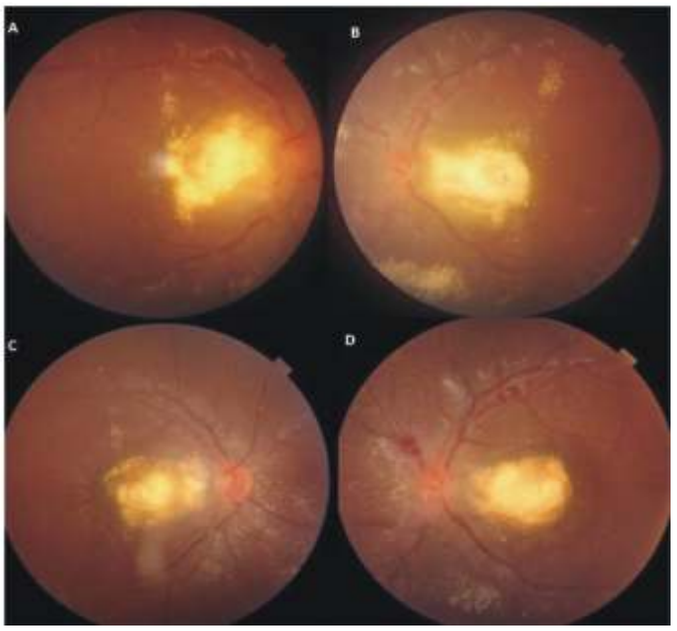

Fig-1. A and B-Fundus picture of our patient at presentation showing macular exudation with aneurysmal dilatation of the arterioles; Fig 1 C and D - latest fundus picture of our patient after treatment showing reduction of size of exudates and also decrease in the size of aneurysmal dilatations.

steroids and poor response with prior treatment, she was treated with sequential Intravitreal dexamethasone implantation (Ozurdex) Right then Left eye with oral Mycophenolate Mofetil (MMF) 1g BD. She responded well to intravitreal dexamethasone implantation (Ozurdex) with reduction in the size of macular hard exudates, disc edema and vascular cuffing. However as the effect of implant wore off a recurrence in disease activity was noted in both eyes.

Since the inflammation was not controlled even after 6 months of combination therapy with MMF and Ozurdex she was referred to the rheumatologist for biologicals. She was started on subcutaneous Adalimumab 40 mg 2 weekly and Tablet Azoran 50mg BD. With the current regime she is showing a good response to treatment with decrease in macular exudation and vascular cuffing. Her BVCA of 6/12 in Right Eye and 6/18P in Left eye. Patient is on regular follow-up.

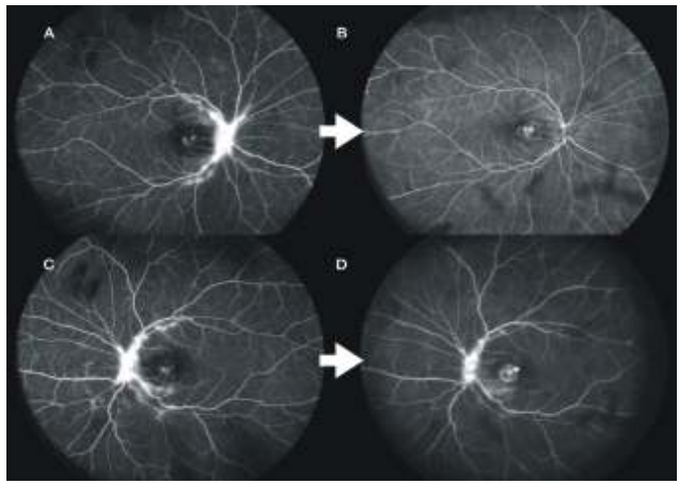

Fig2A and 2B: Fundus fluorescein angiography of right eye before and after a month of Ozurdex implantation showing decrease in leakage at the sites of aneurysmal dilatations after ozurdex indicating reduction of active inflammation. Fig 2C and 2D Fundus fluorescein angiography of left eye before and after 3 months of Ozurdex implantation showing early recurrence of active inflammation due to weaning of steroid effect.

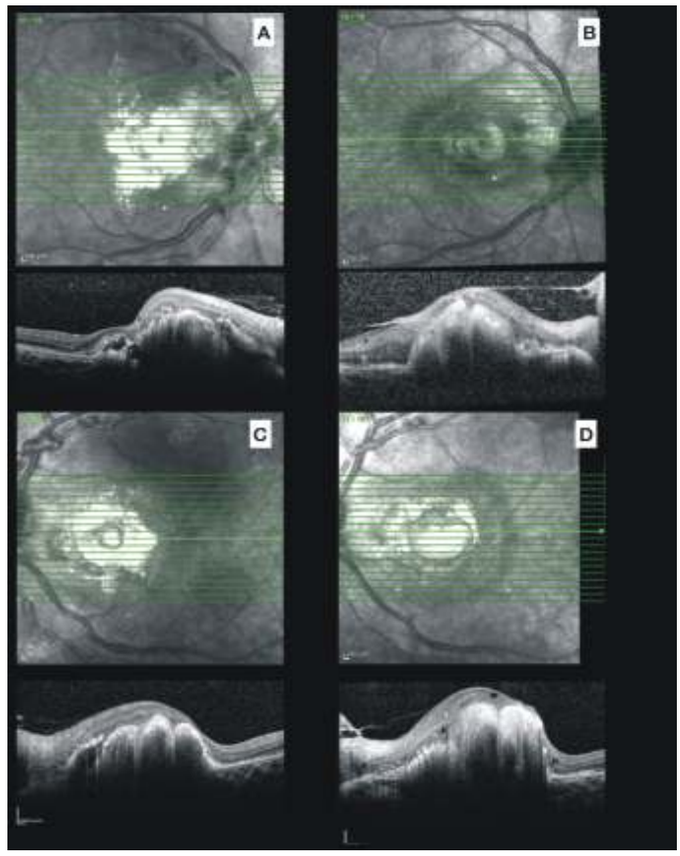

Fig-3 A ,B and 3 C, D shows OCT of the right eye and left eye respectively before and after treatment. Though the retinal thickening and the size of exudation has decreased, sub foveal hard exudates still persists.

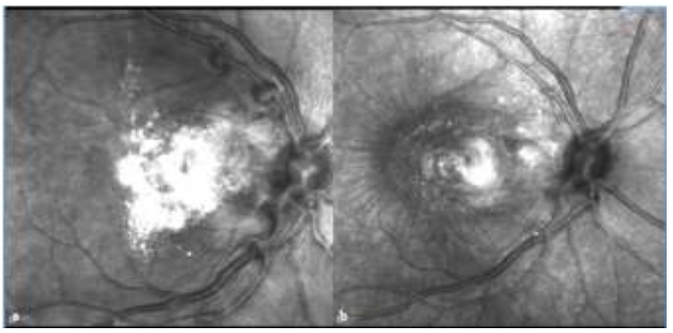

Fig-4 a and 4b IR images of right eye before and after treatment which shows reduction in the size and number of aneurysmal dilatation along with the size of macular exudation after treatment.

Discussion :

IRVAN syndrome is a rare clinical entity of unknown etiology. Change et [1] described the diagnostic criteria for IRVAN. Our patient fulfills all 3 major criteria and 1 minor criteria of this disease.

Major Criteria	Minor Criteria
Retinal vasculitis	Peripheral capillary nonperfusion
Neuroretinitis	Retinal neovascularization
Aneurysmal dilations of the optic nerve head and retinal arterioles at or near their major branching sites	Macular exudation

Table-1 : Criteria for diagnosis of IRVAN syndrome[1]

Although the pathogenesis of the diseases though not clear, it is believed to be of autoimmune origin. Various case reports have shown an association of P-ANCA[2] and APLA[3] antibodies with IRVAN syndrome, however majority of these patients have no systemic illness.

Untreated, IRVAN syndrome passes through various stages ending with irreversible vision loss due to neovascular complications. Samuel et al[4] who coined the acronym IRVAN, has also described the stages of the disease.

STAGE	OCULAR FINDINGS
1	Macroaneurysms, exudation, neuroretinitis and retinal vasculitis
2	Capillary nonperfusion with angiographic evidence
3	Posterior segment neovascularization of disc or elsewhere and / or vitreous hemorrhage
4	Anterior segment neovascularization (rubeosis iridis)
5	Neovascular glaucoma

Table-2 : Staging of IRVAN syndrome[4]

The treatment modalities which has been tried for controlling the inflammation in IRVAN includes oral steroids, steroid implants, conventional immunosuppressives and biologics. There are few case reports of IRVAN syndrome treated with Ozurdex implantation [5,6] and only one case report of IRVAN responding to Infliximab therapy [7] .Lasers photocoagulation or cryotherapy is indicated when the patient has capillary non-perfusion areas or neovascularization. Surgery is required in case of complications like vitreous hemorrhage.

TNF-a inhibitors like Infliximab, and Adalimumab are very effective for treating various subtypes of refractory uveitis and retinal vasculitis. Adalimumab is the first FDA approved biologic for treatment of uveitis in both adults and children. It is humanised monoclonal antibody administered as a subcutaneous injection every 2 weeks. Studies comparing Adalimumab with Infliximab has found it be be more effective, better tolerated and easier to administer, making it the first choice when biologics are indicated in treatment of uveitis [8,9,10].

Because of the rarity of disease no guidelines exist for treatment of IRVAN. Our patient showed good but transient response to

Intravitreal dexamethasone implantation but this was not sustained in spite of concurrent use of oral mycophenolate mofetil. Hence she was switched over to Adalimumab SC 40 Mg 2 weekly along with oral Azathioprine 50 mg BD with promising results.

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Thane, -400607 Maharashtra India. E-mail : medicalinfo.india@bayerzyduspharma.com

ABBREVIATED PRESCRIBING INFORMATION

EYLEA™ SOLUTION FOR INTRAVITREAL INJECTION IN VIAL. Approved name(s) of the active ingredient(s) One ml solution for intravitreal injection contains 40 mg aflibercept. Each vial provides a usable amount to deliver a single dose of 50 l containing 2 mg aflibercept. Indication. EYLEA™ is indicated for the treatment of neovascular (wet) age-related macular degeneration (wetAMD). Dosage Regimen wAMD The recommended dose for EYLEA™ is 2mg aflibercept , equivalent to 50l. EYLEA™ treatment is initiated with one injection per month for three consecutive months, followed by one injection every 2 months. There is no requirement for monitoring between injections. Long term (after the first 12 months of treatment), it is recommended that patients continue to be treated with EYLEA™ every 2 months. Method of administration Intravitreal injections must be carried out according to medical standards and applicable guidelines by a qualified physician experienced in administering intravitreal injections. Following intravitreal injection patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g. eye pain, redness of the eye, photophobia, blurring of vision) without delay. Each vial should only be used for the treatment of a single eye. Contraindications Know hypersensitivity to aflibercept or to any of the excipients, active or suspected ocular or periocular infection, active severe intraocular inflammation. Special warnings and special precautions for use Endophthalmitis and retinal detachments may occur following intravitreal injections. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Increases in intraocular pressure have been seen within 60 minutes of an intravitreal injection. There is a potential risk of immunogenicity and arterial thromboembolic events following intravitreal use of VEGF inhibitors. EYLEA™ should not be used in pregnancy unless the potential benefit outweighs the potential risk to the foetus. Women of childbearing potential have to use effective contraception during treatment and for at least 3 months after the last intravitreal injection of aflibercept. Undesirable effects Very common: Conjunctival hemorrhage, eye pain. Common: Retinal pigment epithelial tear, detachment of the retinal pigment epithelium, cataract, cataract cortical, cataract nuclear, cataract sub capsular, corneal erosion, corneal abrasion, intraocular pressure increased, vision blurred, vitreous floaters, vitreous detachment, injection site pain, foreign body sensation in eyes, lacrimation increased, eyelid edema, injection site hemorrhage, punctate keratitis, conjunctival hyperemia, ocular hyperemia. For full listing of undesirable effects, please refer to the full product insert. For further prescribing information, please contact Bayer Zydus Pharma Private Limited, Bayer House, Central Avenue, Hiranandani Estate, Thane, Maharashtra, India Pin-400607. Email: medicalinfo.india@bayerzyduspharma.com. Source: Based on CCDS / Version 10 / 19 Apr 2016, PI Rev 03 Nov 2016. Date of revision of API, 17 Nov 2016. For the use of healthcare professionals only.

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