THE IDOS - News & Views

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*(Volume 2, Issue 2)*

*"The only way of discovering the limits of the possible is to venture a little way past them into the impossible."*

***- Arthur C. Clarke***

# *FROM THE EDITOR'S DESK.....*

Editorial Team is proud to present RETINA Issue of THE IDOS (News and Views). This issue has 16 review articles and 4 case reports which provide current information on diagnostic and therapeutic techniques to manage various vitreo retinal disorders and the tips given can be easily applied to our clinical practice.

We would like to express our gratitude to all the authors, for their support, contribution and cooperation to release this issue on Retina.

As the editorial team works harder to propel THE IDOS to greater heights, carving out academics to learn something about everything and everything about something, we are hopeful that this issue is appreciated and well read by all members of the society.

Wishing all a wonderful and prosperous Happy New Year.

With warm regards

***Dr ( Prof) Shweta Walia***

**Editor IDOS**

***Dr. Neetu Kori***

***Dr. Sumeet Agrawal***

**Co-Editors**

# *Ophthalmologist in 2022 and beyond....*

***Dr. Rajiv Raman***

India is ready to assume a more significant leadership role in the global health agenda. The enormous medical human resource development in the form of various health care professionals (78,000 registered medical practitioners per annum) that India generates may prove to be an invaluable asset in solving many challenges that global health is facing. The same is true for Ophthalmology too. Ophthalmology training and practice have changed over the last decade. The number of ophthalmologists practising medical retina, surgical retina & Uveitis has increased in the previous few years.

We were the lucky generation of ophthalmologists who have witnessed rapid strides of changes in the way retinal diseases are treated. These changes have equipped us to make better diagnoses and surgical results. The present generation of retina specialists will witness changes they must be prepared for. The following characteristics will equip him for these changes. He must be a "Learning" Ophthalmologist, ready to adapt to rapid developments in science and technology. The skill set which will help him are:

1. **An "Empathic" Ophthalmologist :** Last few years have seen rapid mechanisation of Medicine. With improvement in imaging, the basic skills of clinical acumen seem to have reduced. In this era, when the patient has become "more aware" and the trust in treating the doctor appears to be dwindling, empathy is the only skill that can create trust in our patients. The decision maker for an investigation or treatment a patient needs for their disease is the "Patient". An empathic ophthalmologist will provide the best possible care for illness.
2. **A "Tech-savvy" Ophthalmologist :** Use of newer technologies, newer software, image processing tools, AI, and metaverse, are all part of our life now. Even as a doctor, we cannot shy away from it. We must adapt to these changing times and adopt these technologies for better patient care.
3. **A "Connected" Ophthalmologist :** Distances are no longer a barrier. Covid times have taught us to relate to the world even at home. We need to nurture these technologies and stay connected. Stay connected with peers and your patients. An ophthalmologistneeds to create a "Shared Vision" with his team to achieve more quickly. Practising "retina" is predominantly a referral practice. Staying connected is an essential prerequisite in improving your clinical practice.
4. **A "Multitasker" Ophthalmologist :** The modern-day ophthalmologist has to multitask.

   The task of a treating doctor, the job of technician, Manager, multimedia guy, teacher, researcher and so on. There is no way he completes one task and takes another. They must, however, learn to prioritise the tasks so that all of them can be done elegantly.
5. **An "Ethical" Ophthalmologist :** The decision between ethical and unethical is a very grey zone. In the current age where investments by ophthalmologists to set up a good Retina set-up have increased, and the pharmaceutical industry's influence on medical care is overgrowing, there is a need to self-evaluate the decisions we make with a conscious effort to do the ethical practice.
6. **A "Communicator" Ophthalmologist :** It is not the result of a surgery or a procedure which makes a patient happy. It is the way you communicate with them. So effective communication is a need rather than an option. However, counsellors may help to some extent. Spending that extra 5 min to comminate makes a difference among the treating doctors.

These six facets will equip ophthalmologists to provide better patient care, become better educators and help them become better researchers.

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# Indirect Opthalmoscopy and Condensing Lenses - An Overview

***Preeti Rawat***

One of the leading causes of vision loss and blindness worldwide, particularly in underdeveloped nations, is vitreoretinal disease.

Governments in poor countries pay close attention to all that can be done to lower the occurrence of vitreoretinal diseases, especially in the early detection of these conditions.

This is where the role of diagnostic tools and the accessibility of knowledgeable specialists in lowering prevalence comes into play.

The fundus is illuminated during indirect ophthalmoscopy by light travelling through a powerfully positive lens, returning light enters the lens and is refracted to create between the lens and the retina, a genuine, inverted, and laterally reversed image of the fundus. The image will be roughly in the bio lens's focus.

In light of this, a +90D lens will provide a fundus image at about 11mm from thelens.

The excellent field of view, the superior illumination, the stereoscopic picture, and the capacity to detect minute diffuse fundus color changes are the advantages of BIO over direct.

Investigating symptoms including photopsia and/or rapid onset floaters, posterior vitreous detachment, suspected retinal tears or retinal detachments, and excessive myopia requires the use of indirect ophthalmoscopy. This facility could be very helpful in management programmes that monitor post-operative detachment surgery or the surveillance of peripheral lesions that could be prone to detachment, like lattice degeneration.

## BIO (BINOCULAR INDIRECT OPHTHALMOSCOPY) LENSES :

Binocular Indirect Ophthalmoscopy (BIO) is a diagnostic procedure by which a practitioner uses a condensing lens and a head mounted ocular system to look at the retinal structures. This technique has a greater scope for dynamic examination due to the mobility offered by the oculars not being fixed to a table top. The patient can be in a supine position or sat with the head tilted at a comfortable angle. The condensing lenses used for BIO examination have a higher magnification and lower field of view profile when compared to slit lamp biomicroscopy lenses. As the names suggests, the image formed is indirect in nature meaning it is inverted and reversed. The distance at which the lens needs to be held in front of the patient's eye varies depending on the power of the lens. As a general rule of thumb, as the dioptric power of the lens increases, the field of view increases, magnification decreases and the working distance decreases. It is general practice to dilate patients for a BIO exam, in cases where dilation is not possible, or patients inherently have small pupils (neonates or geriatrics) higher power lenses are appropriate.

For an emmetropic eye, head-band or spectacle indirect ophthalmoscopes with a +20D power lens will provide an approximate x 3 magnification and a static field of view of about 40 degrees. Up to 240 degrees can be seen in the complete dynamic field of view. Lenses with powers above +20D are helpful for wide-field inspection, but they do not provide enough magnification to view fundus detail.


**Figure 1 : Different BIO lenses available (Image source:https://www.volk.com/collections/bio-lenses)**

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**Table 1 : The range of view and magnification of the various ophthalmoscopic procedures.**

| LENS POWER [D] | STATIC FIELD OF VIEW [degrees] | TRANSVERSE MAGNIFICATION | TYPICAL WHOLE SYSTEM MAGNIFICATION | WORKING DISTANCE FROM CORNEA [MM] |
|---|---|---|---|---|
| Direct ophthalmoscope | 12 | 15 | 15 | 25 |
| Head band BIO + 20 LENS | 30 | 3.25 | 3 | 50 |
| Head band BIO + 30 LENS | 40 | 2.1 | 2 | 33 |
| SLM BIO + 60 LENS | 67 | 1.09 | 15 | 11 |
| SLM BIO + 78 LENS | 73 | 0.87 | 12 | 7 |
| SLM BIO + 90 LENS | 69 | 0.72 | 10 | 6.5 |
| SLM BIO + 90 super field lens | 120 | 0.72 | 10 | 6.5 |
| SLM BIO + 132 Ultra view SP lens | 99 | 0.45 | 7 | 3.0 |

The static field of view with the SLM BIO and a Volk lens of +120D is up to 120°, while the dynamic field is up to 180°.

Additional SLM magnification is necessary when a practitioner needs the precise view of a fundus to examine the fine lesions present in diabetics, such as microaneurysms, intra-retinal micro-vascular abnormalities (IRMA), lipid, small hemorrhages, and neovascularization. Headband BIO will not provide enough magnification to observe minute fundus details until a lens of roughly +14 Diopter's is used.

This technique has the following benefits: (a) a great field of view (about 40 degrees); (b) the capacity to move around the patient and so increase the field of view; (c) a stereoscopic view; (d) superb illumination; and (e) scleral indentation.

## WORKING PRINCIPLE OF THE CONDENSING LENS :

Condensing lenses work by gathering and focusing the shadow cast by the instrument's light beam (the illumination beam), which is then received by the examiner's eyes. Focus of this light beam can pass through turbid refraction medium, similar to an early cataract situation.[3]

A condensing lens works by making the eye hyper myopic so that the focal point is in front of the retina. This focus point then sends a beam of light to the retina. A shadow is created between the condensing lens and the examiner when this light beam is reflected by the retina and refocused by it.[4]

Between the condensing lens and the examiner, the fundus casts a shadow that is both genuine & inverted. To determine that a shadow formed, the proper interpretation is required. Only the light beam that is not reflected goes through the lens's centerin order to pinpoint the exact location of the fundus. Midpoint parts are fully reversed from one another, with upper parts on the bottom, right parts on the left, and vice versa.[3]

## MAGNIFICATION OF CONDENSING LENS :

The ratio of a huge aerial fundus shadow is magnification in relation to the patient's fundus size. In this ratio, proportionate to the ratio of the focal length of the lens to length of the patient's eye's focus. Using a formula, a ratio can bebe developed to calculate magnification depending on the effectiveness of the lens, assuming diopter power (D) emetropia is as large as 60 D from the eyes.[5]

The two main parts of the examination's magnification when employing a condensing lens are the magnification from the patient's fundus to the focal point and the magnification from the focal point to the examiner. The strength of the diopters determines the first magnification, while the examination distance determines the second. The magnitude of the total magnification is obtained by combining lens power with inspection distance.[3,5]

**Magnification Formula :**

shadow large $= f_{lensx} \sin á = D_{eye} = 60$

## WIDE FIELD VIEW OF THE CONDENSING LENS :

A beam of light that emanates from the patient's eye and can be caught by the equipment determines the wider field of view. A wider field of view is created by a lens with a larger diameter because it can capture a larger portion of the light beam.

The fundus shadow is perfectly generated when the condensing lens is positioned correctly. The distance between the patient's eye and the lens is nearly identical to the distance between the lens and the focal point, which is the location where the lens shadow develops. larger field of view and closer focal point generated.

The fundus shadow is perfectly generated when the condensing lens is positioned correctly. The distance between the patient's eye and the lens is nearly identical to the distance between the lens and the focal point, which is the location where the lens shadow develops. larger field of view and closer focal point generated.

Based on forementioned hypothesis, a formula may be

created to calculate the field of view's size. The lens's diopters' strength and width directly relate to how wide the field of vision is. It can be concluded that a lens's field of view can be made wider by increasing its diameter and dioptric power.[2,3]

**Wide field of view formula :**

Lens diameter/focal point length = lens diameter * lens power

The general idea can be applied by combining a broad field of vision and the condensing lens's strength at magnification at various sizes. Wider field of view, reduced magnification, and stronger lens diopters. High dioptric strength lenses are comparatively more useful for examinations with tiny dilated pupils due to the wide field of view they produce. Additionally, when dioptric strength increases, the distance from the lens to the patient's eye will decrease, bringing the inspection distance closer. This occurs as a result of the closer focal point that high dioptric strength lenses have.[6]

Between the instrument and the patient's eye, the condensing lens is positioned, roughly 1-2 cm in front of the patient's eye. The tip of the index finger and the thumb's surface are used to hold the lens. The patient's eyelids or brows are employed as the lens fixation with the third or fourth finger.

The wrist of the examiner is just somewhat flexible. By increasing or decreasing the index finger's flexion, the lens can be moved up and down. Some condensing lenses exhibit a silver or white circle on the side facing the patient, especially when examined with an indirect binocular ophthalmoscope.[7]

Because the lighting and observation beams follow the same path, reflection on the lens may occur.

The creation of the fundus shadow will be hampered by this reflection. Reflections that arise can be removed by slightly tilting condensing lens. By tilting lens, reflections arising on anterior surface of the lens will be kept away from reflections arising on posterior surface of the lens.[4,7]

## INTERPRETATION OF FUNDUS EXAMINATION WITH CONDENSING LENS :

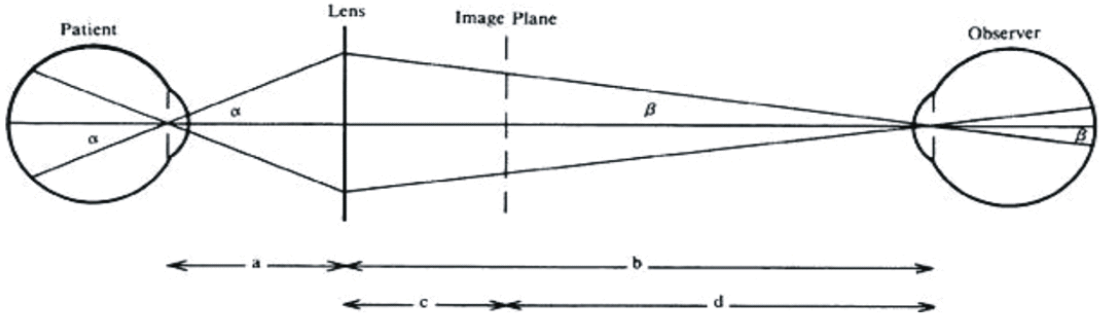


**Figure 2 : Inspection distance schematic on condensing lens**

The generated condensing lens picture is real and reversed. The midpoint portion is entirely completely inverted such that

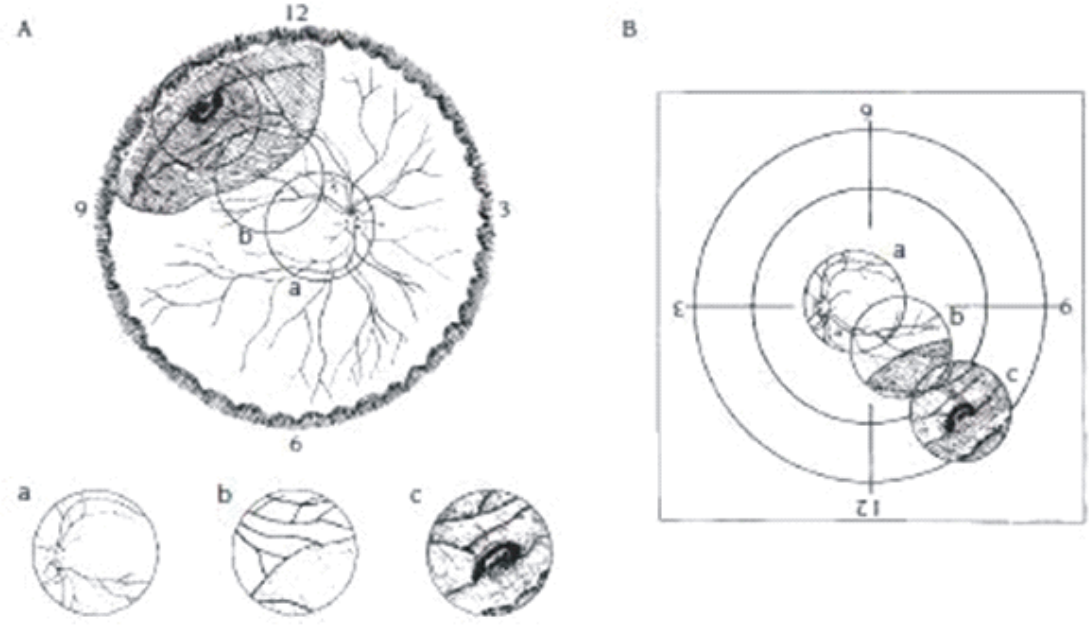


**Figure 3. (A) Abnormalities position on fundus (B) Picture on fundus chart**

**TABLE 2 : COLOR CODING ON RETINAL DRAWING8**

| CODING USED | RETINAL ABNORMALITIES |
|---|---|
| Blue | Retinal arterioles, elevated neovascularization, vascular abnormalities/anomalies, vascular tumors, vortex veins, attached retina, hemorrhages (pre-retinal and intraretinal, sub hyaloid), the open interior of conventional retinal breaks (tears, holes)Retinoschisis(line)<br>Lattice degeneration (cross-hatched)<br>Retinal vein<br>Inner layer of retinoschisis, white with or without pressure, detached pars plana epithelium anterior to the separation of ora serrate, rolled edges of retinal tears (crossed lines) |
| Green | Turbidity of vitreous- e.g. floaters, bleeding<br>Turbidity of refraction media- e.g. cornea, cataract(solid lines)<br>Asteroid hyalosis, frosting or snowflakes on cystoid degenerations, retinoschisis, or lattice degeneration (stippled lines) |
| Red | Retinal breaks (blue outline)<br>Retinal bleeding<br>Microaneurysms ,microaneurysms<br>Retinal vascularization<br>the open interior of conventional retinal breaks (tears, holes)<br>macula (dot)<br>Open portion of a giant retinal tear or large dialyses, inner portion of CRA, inner portions of thinned retinal areas, open portions of retinal holes (crossed-lines) |
| Brown | Hypopigmentation<br>Photocoagulation<br>Choroid/ retinal pigmentation<br>pigment epithelial detachment, outline of posterior staphyloma, malignant choroidal melanomas |
| Yellow | Optic disc edema<br>Retinal edema |
| Orange | Cotton wool spots<br>Exudates |
| Black | Scar, degenerations, dystrophy, foreign bodies |

the higher half is at the bottom right portion is on left side and vice versa for each side. In outlining the area, the meridian's customary use is based on the distance from the rear and its clockwise direction, based on the optic disc's diameter, or it can also be based on a more regional area, like the fundus equator and ora serrata.

## FUNDUS CHART :

A fundus chart is required for discussing results of fundus abnormalities. Three enormous concentric circles and a smaller circle in the centre make up this diagram. The inner circle of the large concentric circle depicts the fundus equator, the middle circle the ora serrata, and the outer circle the ciliary process. Optic disc may be seen in the middle little circle.

Orientation is the main issue when describing anomalies in the fundus chart. The representation of the fundus will be challenging due to the inverted shadows created by condensing lenses. Rotating the fundus chart by 180 degrees is one technique that can be used. A wide field of view on the patient's fundus may present a unique challenge when presenting anomalies in a reversed fundus chart. It's important to remember that just the fundus image of the condensing lens is flipped; the location of the abnormality stays as it is in reality. Drawing irregularities on a chart in accordance with the orientation of the discovered meridians is what must be done.

## COLOR CODING ON FUNDUS CHART :

Because colour is utilised to describe a variety of abnormalities detected in the fundus, writing information on abnormalities discovered is still required. The use of colour codes to indicate abnormalities obtained does not have a

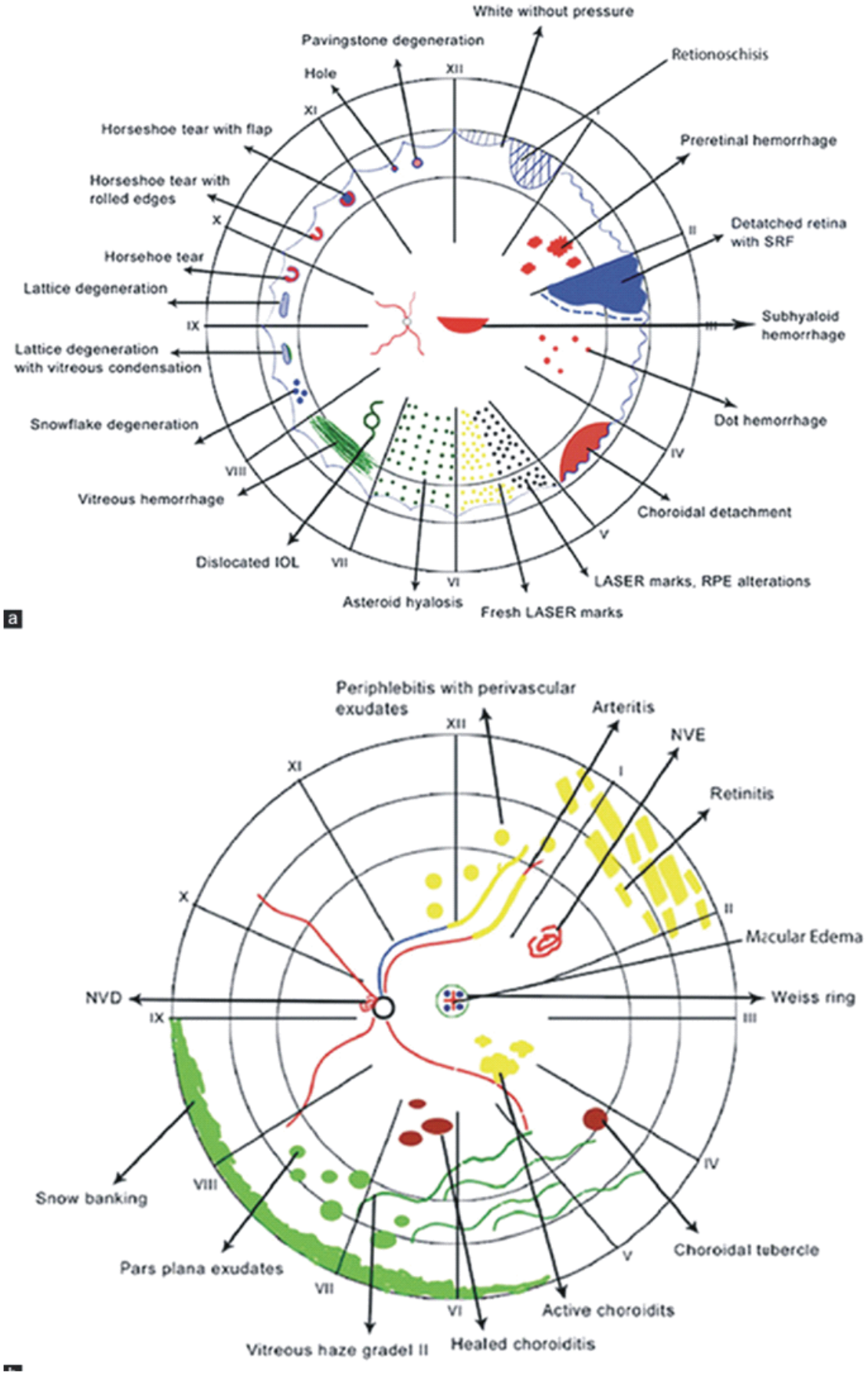


**FIGURE 4: INTERPRETATION OF VARIOUS FUNDUS PATHALOGIES USING DIFFRENENT COLOUR CODINGS (image source:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9675514/#!po=50.0000)**

universally accepted standard.

## CONCLUSION :

The primary function of the condensing lens is to increase myopia, to move the retina's focal point in front of the pupil. The resulting fundus shadow is actual, aerial, and upside down. Diopter diameters vary for condensing lenses. Greater lens diopter power and closer examination distance result in a lesser image magnification. Wider fields of view are generated the higher the dioptric power and lens diameter.

There are benefits and drawbacks to examining the condensing lens using slit-lamp biomicroscopy and binocular indirect ophthalmoscopy. The indirect binocular ophthalmoscope has the advantages of being portable and usable on recalcitrant individuals.

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***Dr. McPherson*** *with Charles L. Schepens, MD Alice R. McPherson, MD, is a recognized retina leader and philanthropist. She is the founder of two leading vision research institutions The Retina Research Foundation (RRF) founded in 1969 and the McPherson Eye Research Institute at the University of Wisconsin (UW) in 2005. She was first female vitreoretinal fellow of Charles L. Schepens, MD, and the first full-time female retina specialist in the world. She pioneered a number of treatments for retinal diseases, including scleral buckling procedures, cryotherapy and xenon arc and laser photocoagulation. While initially controversial, her early advocacy for photocoagulation for the treatment of diabetic retinopathy was later supported by the National Eye Institute Diabetic Retinopathy Study.*

# Fundus Fluorescein Angiography

*Sumeet Agrawal*

The retinal and choroidal vascular anatomy can be basically divided into 3 parts :

1. Retinal and choroidal vasculature 2. Superficial and deep capillary plexus 3. Inner and outer blood-retinal barriers.

The retina receives its nutrition from two discrete circulatory systems the retinal and the choroidal blood vessels. Both are derived from the ophthalmic artery, which is the first branch of the internal carotid artery.

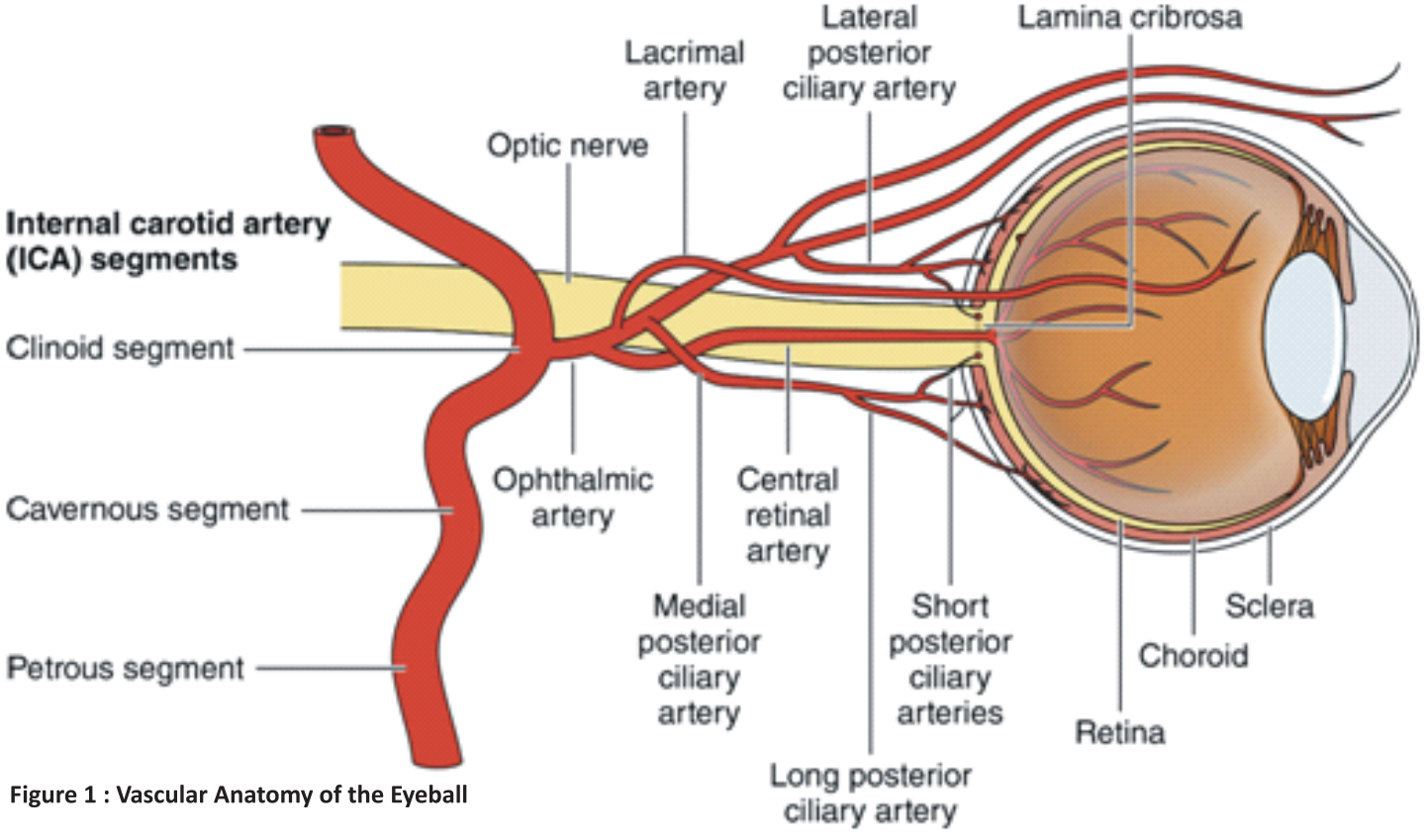


**Figure 1 : Vascular Anatomy of the Eyeball**

The major branches of the ophthalmic artery are the posterior ciliary arteries, the central retinal artery, and the muscular branches. [1] The posterior ciliary arteries branch out proximal to the central retinal artery. This explains the early filling of the dye in the choroidal circulation (˜1-2 sec prior) in comparison to the retinal circulation.

The choroid receives its blood supply via two posterior ciliary arteries (medial and lateral). The choroidal watershed area, which represents the area between the supply of each posterior ciliary artery, is usually a vertically oriented zone situated between the optic disc and macula. [1]

The posterior ciliary arteries further divide into two long posterior ciliary arteries and numerous short posterior ciliary arteries. The posterior choriocapillaris is supplied by these short posterior ciliary arteries, which enter the choroid in the peripapillary and submacular region. The outer choroid, known as Haller's layer, is composed of large caliber, non-fenestrated, vessels. The inner choroid is referred to as Satler's layer and is composed of significantly smaller vessels. [1]

## Principle of Fundus Fluorescein Angiography :

Fundus Fluorescein angiography (FFA) is a diagnostic technique that allows the sequential visualization of blood flow simultaneously through retina and choroidy. The fluorescein dye is injected into the bloodstream via a vein in

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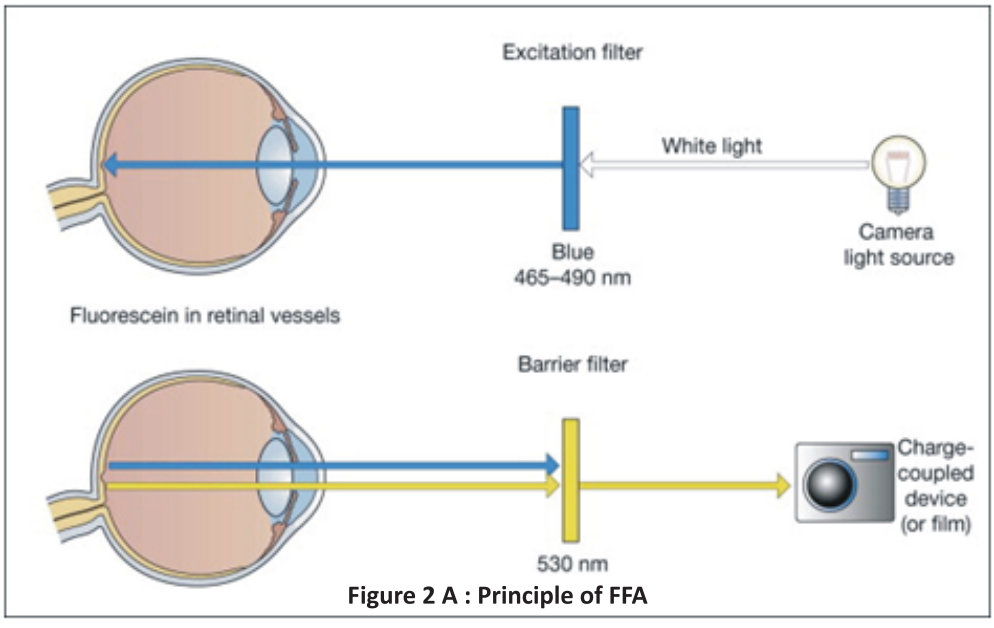


**Figure 2 A : Principle of FFA**


**Figure 2 B : Sodium Fluorescein Dye**

the arm. FFA is based on the principle of fluorescence. Fluorescence is the luminescence that is maintained only by continuous excitation i.e. excitation at one wavelength occurs and is emitted immediately through a longer wavelength.[2]

Fluorescein sodium is an orange red water-soluble dye, moleular weight of 376 Da and pH of 8 - 9.8. Normal adult dose is- 500mg - 3ml of 20%, 5ml of 10% or 10 ml of 5%. Paediatric dose is 35mg/ 10 pounds of body weight. Oral dosage 30 mg/ kg. pH 8 to 9.8. 80% of molecules bind to plasma proteins. It is metabolised by liver & eliminated by kidney in 24-36 hrs. The dye absorbs light in blue range of visible spectrum, peaking at 465-490nm and emits light in yellow-green range of visible spectrum, peaking at 520-530nm.[2]

**Pseudo fluorescence :** It occurs when nonfluorescent light passes through the entire filter system. If greenyellow light penetrates the original blue filter, it will pass through the entire system. If blue light reflected from nonfluorescent fundus structures penetrates the greenyellow filter, pseudo fluorescence occurs.

## Equipment and Technique :

**1. Camera and Auxiliary Equipment :** In clinical retinal practice, cameras ranging from 35° to 200° are routinely used. Regardless of range, a camera with the ability to yield high resolutions of the posterior pole is essential for most macular problems especially when laser treatment is to be done, as with background diabetic retinopathy, branch vein occlusion, or choroidal neovascularization.

**2. Fluorescein Solution :** Fluorescein (sodium fluorescein) is an orange water-soluble dye and has a low molecular weight (376.27 Da), and when injected intravenously, remains largely intravascular (>70% bound to serum proteins). It is excreted in the urine over 24-36 hours. It readily diffuses through most of the body fluids and through the choriocapillaris, but it does not diffuse through the retinal vascular endothelium or the pigment epithelium.

**3. Matched Fluorescein Filters :** Cobalt blue excitation filter. Incident white light from the camera is filtered so that blue light enters the eye, exciting the fluorescein molecules in the retinal and choroidal circulations. Yellow-green barrier filter blocks any blue light reflected from the eye, allowing only yellow-green emitted light to pass.

**4. Injecting the Fluorescein :** A 23-gauge intracath or scalp-vein needle is used for injection. Injection of the fluorescein is coordinated with the photographic process and is done after the first photographs have been taken. Rapid injection of 2 or 3 seconds delivers a high concentration of fluorescein (5ml of 10%) to the bloodstream in a short time and yields somewhat better photographs than a slower injection.[3]

**Contraindications of FFA**

**Absolute contraindication**

Allergic reaction in past.

**Relative contraindications**

Cardiac disease, Renal impairment, Uncontrolled hypertension and Pregnancy.

**Adverse Reactions** [4]

Nausea (5%) & vomiting (0.3-0.4%)- usually seen 30-60s after injection and lasts 2-3 minutes Extravasation of dye transient yellowish discoloration of skin (cold compresses for 5-10 minutes usually settles the discoloration).

Inadvertent arterial injection Pruritis, urticaria Bronchospasm, laryngeal edema, anaphylaxis Hypotension, syncope, myocardial infarction, cardiac arrest Seizures tonic clonic type.

**Normal Fluorescein Angiography :**

The angiogram consists of the following overlapping phases :

**The choroidal (pre-arterial) phase** typically occurs 9-15 seconds after dye injection longer in patients with poor general circulation and is characterized by patchy lobular filling of the choroid due to leakage of free fluorescein from the fenestrated choriocapillaris. A cilioretinal artery, if present, will fill at this time because it is derived from the posterior ciliary circulation.

**The arterial phase** starts about a second after the onset of choroidal fluorescence, and shows retinal arteriolar filling and the continuation of choroidal filling.

**The arteriovenous (capillary) phase** shows complete filling of the arteries and capillaries with early laminar flow in the veins in which the dye appears to line the venous wall leaving an axial hypo fluorescent strip. This phenomenon reflects initial drainage from posterior pole capillaries filling the venous margins, as well as the small vessel velocity profile, with faster plasma flow adjacent to vessel walls where cellular concentration is lower.

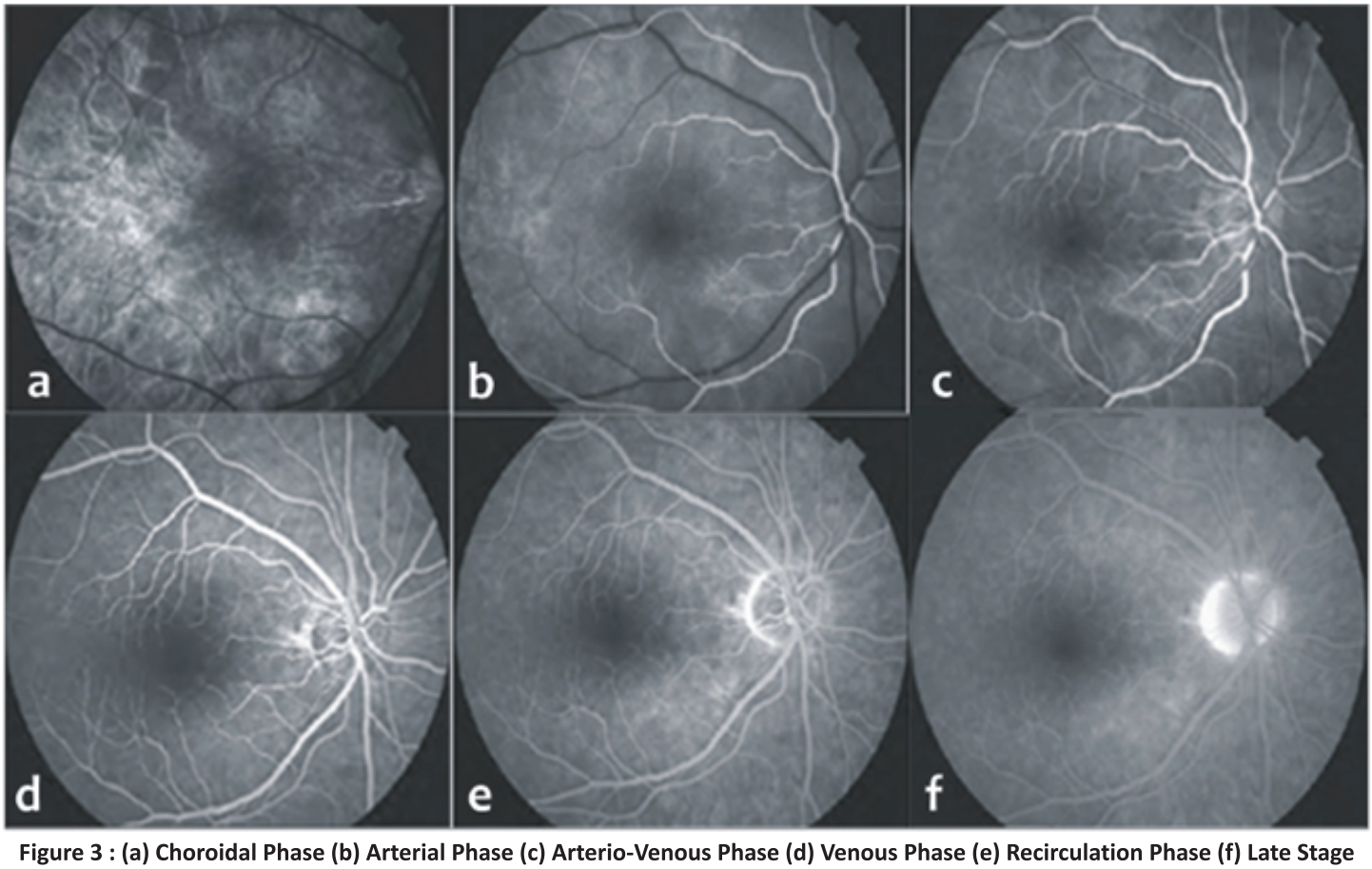


**Figure 3 : (a) Choroidal Phase (b) Arterial Phase (c) Arterio-Venous Phase (d) Venous Phase (e) Recirculation Phase (f) Late Stage**

**The venous phase.** Laminar venous flow progresses to complete filling, with late venous phase featuring reducing arterial fluorescence. Maximal perifoveal capillary filling is reached at around 20-25 seconds in patients with normal cardiovascular function, and the first pass of fluorescein circulation is generally completed by approximately 30 seconds.Perifoveal capillary network best visualised at the peak venous phase **The late (recirculation) phase** demonstrates the effects of continuous recirculation, dilution, and elimination of the dye. With each succeeding wave, the intensity of fluorescence becomes weaker although the disc shows staining. Fluorescein is absent from the retinal vasculature after about 10 minutes.[5][6]

## Appearance of the foveal avascular zone (FAZ) :

Fovea appers dark in a normal FFA. The dark appearance of fovea is caused by three factors: a) absence of blood vessels in the FAZ; b) blockage of background choroidal fluorescence due to the high density of xanthophyll at the fovea and c) blockage of background choroidal fluorescence by the RPE cells at the fovea, which are larger and contain more melanin and lipofuscin than elsewhere in the retina. In macular ischemia, there is distortion and enlargement of the FAZ.[6]

## Abnormal fluorescence patterns on fluorescein angiography :

Interpretation of the fluorescein angiogram follows a simple

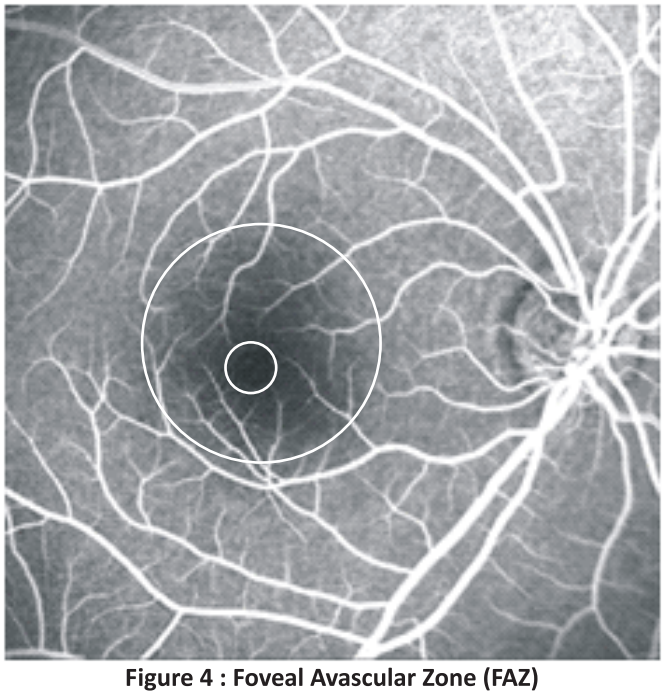

**Figure 4 : Foveal Avascular Zone (FAZ)**

and logical progression. The first step is to recognize areas of abnormal fluorescence and determine if they are hypo fluorescent or hyperfluorescent.

**Hyperfluorescence:**[7]

Hyperfluorescence is any abnormally light area on the positive print of an angiogram, that is, an area showing fluorescence in excess of what would be expected on a normal angiogram. Hyperfluoroscence can be noted in the absence of dye injection (autofluorescence and pseudo fluorescence) or after dye injection (true hyperfluoroscence).

Autofluorescence is an inherent property of a lesion to spontaneously fluoresce even in the absence of dye.

Pseudo fluorescence occurs when nonfluorescent light passes through the entire filter system. If green-yellow light penetrates the original blue filter, it will pass through the entire system. If blue light reflected from nonfluorescent fundus structures penetrates the green-yellow filter. Basically, the pseudo fluorescence occurs due to the mismatch filters.

There are four possible causes of abnormal true hyperfluorescence: (1) Transmitted fluorescence; (2) Staining (3) Pooling and (4) Leakage.[8][9]

**A) Transmitted hyperfluorescence (Window defects) :** This is a type of early hyperfluorescence due to RPE atrophy. In this type of hyperfluoroscence, there is increased visualization of the normal choroidal fluorescence due to the defects/atrophy of the overlying RPE. There is increased early hyper-fluoroscence which fades during the late stages of the angiogram.

**B) Staining :** This is a type of late hyperfluoroscence which occurs due to the retention of the dye by the tissue e.g. disciform scar, drusens etc.

**C) Pooling :** In this type of hyperfluoroscence, there is an accumulation of the dye in a closed space e.g. cystoid macular edema and retinal pigment epithelial detachment.

**D) Leakage :** This type of hyperfluoroscence occurs due to the leakage of the dye into an open space e.g. NVE (where the dye leaks into the preretinal space), CSCR leak (where the dye leaks into the subretinal space) and choroidal neovascular

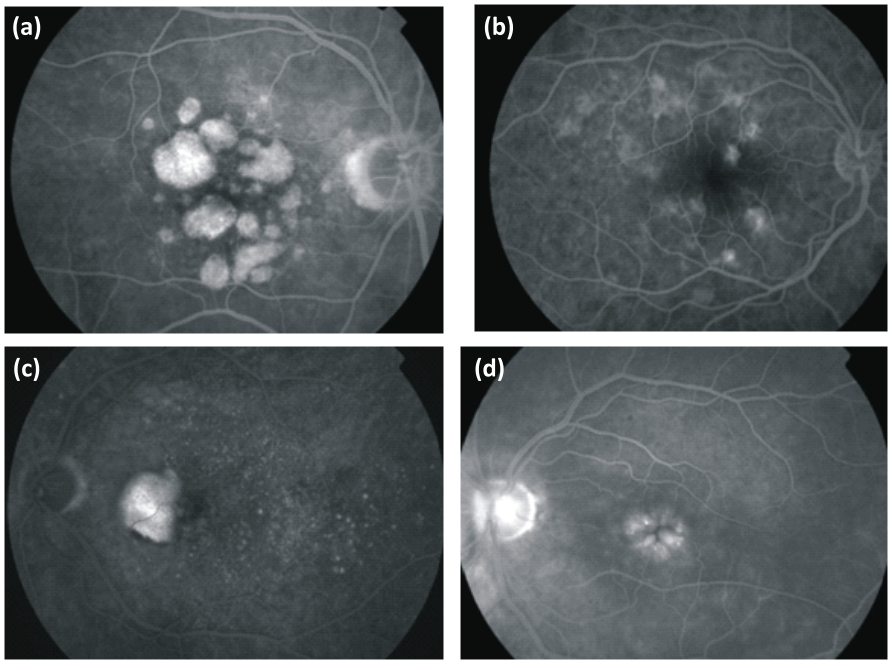


**Figure 5 : (a) Window Defect due to Geographic Atrophy of RPE (b) Staining of lesions in APMPPE (c) Pooling of Dye in CSCR (d) Leakage of Dye in Cystoid Macular Edema**

membrane (where the dye leaks into the sub-RPE or subretinal space).

## Hypo Fluorescence :

Hypo fluorescence is any abnormally dark area on the positive print of an angiogram. The key to differentiating blocked fluorescence from a vascular filling defect is to correlate the hypofluroscence on the angiogram with the ophthalmoscopic view. If there is material visible ophthalmoscopically that corresponds in size, shape, and location to the hypo-fluroscence on the angiogram, then blocked fluorescence is present. If there is no corresponding material on the colour photograph, then it must be assumed that fluorescein has not perfused the vessels and that the hypofluroscence is caused by a vascular filling defect.[9][10]

**Non perfusion/filling defects**

Ischemic retinal vascular disease Ophthalmic artery occlusion Giant cell arteritis Hypertensive choroidopathy - choroidal infarcts Loss of vascular bed as in myopic degeneration and choroidemia

**Blocked Fluorescence**

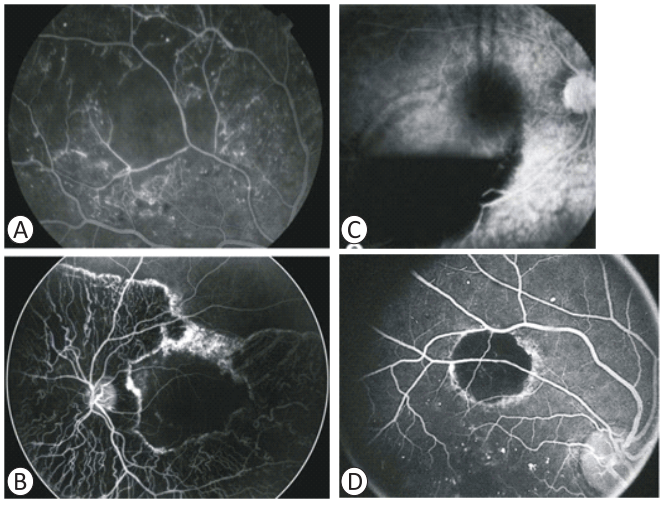


**Figure 6 : (a) Hypofluorescence due to capillary non-perfusion Blocked fluorescence due to (b) Hypofluorescence due to blocking by Meretinal Hemouhage (c) Hypofluorescence due to loss of vascularity in Choroidermia (d) Hypofluorescence due to blocking of choroidal fluorescence in CHRPE**

1. Masking of retinal fluorescence- Pre retinal lesions pre retinal bleed (vitreous haemorrhage, subhyaloid haemorrhage, sub inner limiting membrane haemorrhage)

2. Masking of background choroidal fluorences - Intra retinal / Subretinal bleed Hard exudates, soft exudates Melanin-choroidal nevus Xanthophyll-RPE hypertrophy Lipofuscin

**Reporting FFA findings**

Most of the FFA can be reported in this pattern :

Arm to Retina time (normal/delayed)

AV transit time (normal/delayed)

FAZ shape and size (enlarged/broken)

Abnormal Fluorescence areas (Hypo or hyper) and their course in the late phase (like capillary non-perfusion areas, microaneurysms, etc.)

Late phase findings: leakage/ staining especially of the disc.

FFA is a valuable tool in the retina specialist's armamentarium to diagnose and prognosticate several pathologies.

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# Optical Coherence Tomography

*Keshav Lahoti*

## INTRODUCTION :

Optical Coherence Tomography is a powerful noninvasive imaging modality that yields high resolution, micron-scale, cross-sectional imaging of the retina. Originally developed in 1991 by Huang et al,[1] OCT technology has continuously evolved and has been explored in a wide range of clinical applications. With the introduction of Spectral/ Fourier Domain OCT (SD-OCT, FD-OCT) and Swept Source OCT (SS-OCT), there is greater tissue resolving power, significantly higher scan density, and faster data acquisition than original Time Domain OCT. Thus, OCT has revolutionized the practice of ophthalmology and, in particular the diagnosis and management of patients with retinal diseases.

## WORKING PRINCIPLE :

OCTs operate on the principle of low-coherence interferometry, in which a beam of light is directed into the retina, and the resulting back-scattered light travels an unknown distance to a detector, which is compared to a reference beam of a known length to calculate the echo time delay of light. TD-OCT employs near-infrared light for better penetration of ocular structures. When the distance between the light source and retinal tissue equals the distance between the light source and reference mirror, the reflected light and the reference mirror interacts to produce an interference pattern. The interference measured by the photodetector is then converted to an A-scan signal.[2-6]

## EVOLUTION OF OCT Technology :

OCT technology has evolved across 3 major developmental milestones. Swept Source- OCT (SS-OCT) which is the latest in this regard uses longer wavelength (1050 nm) to overcome scattering by the RPE and employs photodetectors instead of earlier CCD cameras to further increase the resolution. With faster scan acquisition rates using SD-OCT and SS-OCT, the diagnostic accuracy has been enhanced by eliminating the use of alignment algorithms to correct patient movement in "lengthy" TD scans. As a result, significant motion artifacts are avoided and multiple measurements can be taken in a short time enabling the three-dimensional retinal scanning.[7,8]

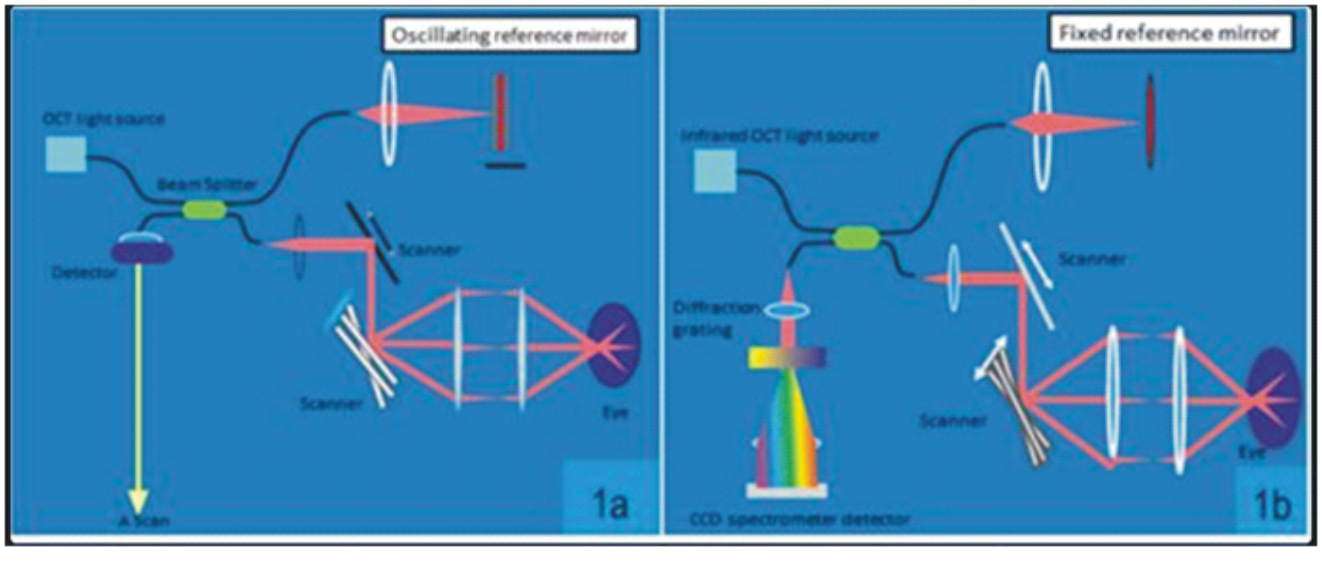


**Fig 1a.Schematic representation of the working principle of TD- OCT. Here the beam splitter directs the 830 nm beam into the reference mirror and the area to be scanned. The photodetector receives the interference signal. Here the position of the reference mirror is kept constantly changing which limits the speed of scanning. Fig 1b.In SD-OCT, the reference mirror is kept stationary. The spectral pattern of the interference between the sample and reference reflections is measured using a spectrometer**

## INTERPRETATION OF OCT :

SS-OCT illustration of the various layers of retina and choroid. Retinal layers from inside out are ILM- Internal limiting membrane, NFL- Nerve fiber layer, GCL- ganglion cell layer, IPL-

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*Retina Speciality Hospital, Indore*

| | TD- OCT | SD- OCT | SS- OCT |
|---|---|---|---|
| Features | Movable reference mirror | Fixed reference mirror Spectrometer | Swept source laser |
| Wave length | 810 nm | 840 nm | 1052 nm |
| A Scan Speed / Sec | 512 scans/ sec | 50000 scans/sec | 100000 scans/ sec |
| Axial resolution | 10 µ | 8 µ | 6 µ |
| Lateral resolution | 20 µ | 20 µ | 20 µ |
| Artifacts | More | Less | Less |
| Length of line scan | 6mm | Up to 9mm | Up to 12 mm |

**Table 1 : Differences between various OCT systems**

agreed on the adequate nomenclature for the outer retinal bands depending on the reflectivity of the layer.The recent nomenclature of the outer retinal bands and their anatomic feature attributions are described below, from the innermost to the outermost.

**The external limiting membrane band (ELM) -** is located at the boundary between the cell bodies (nuclei) and the inner segments (IS) of the photoreceptors and comprises clusters of junctional complexes between the Müller cells and the photoreceptors.

**Myoid zone (MZ) -** the hyporeflective region between ELM and ellipsoid zone (EZ) corresponds to the innermost segment of photoreceptors. The reduced reflectivity of this zone is due to the lower packing density of mitochondria.

**Ellipsoid zone (EZ) -** the hyperreflective region adjacent to the

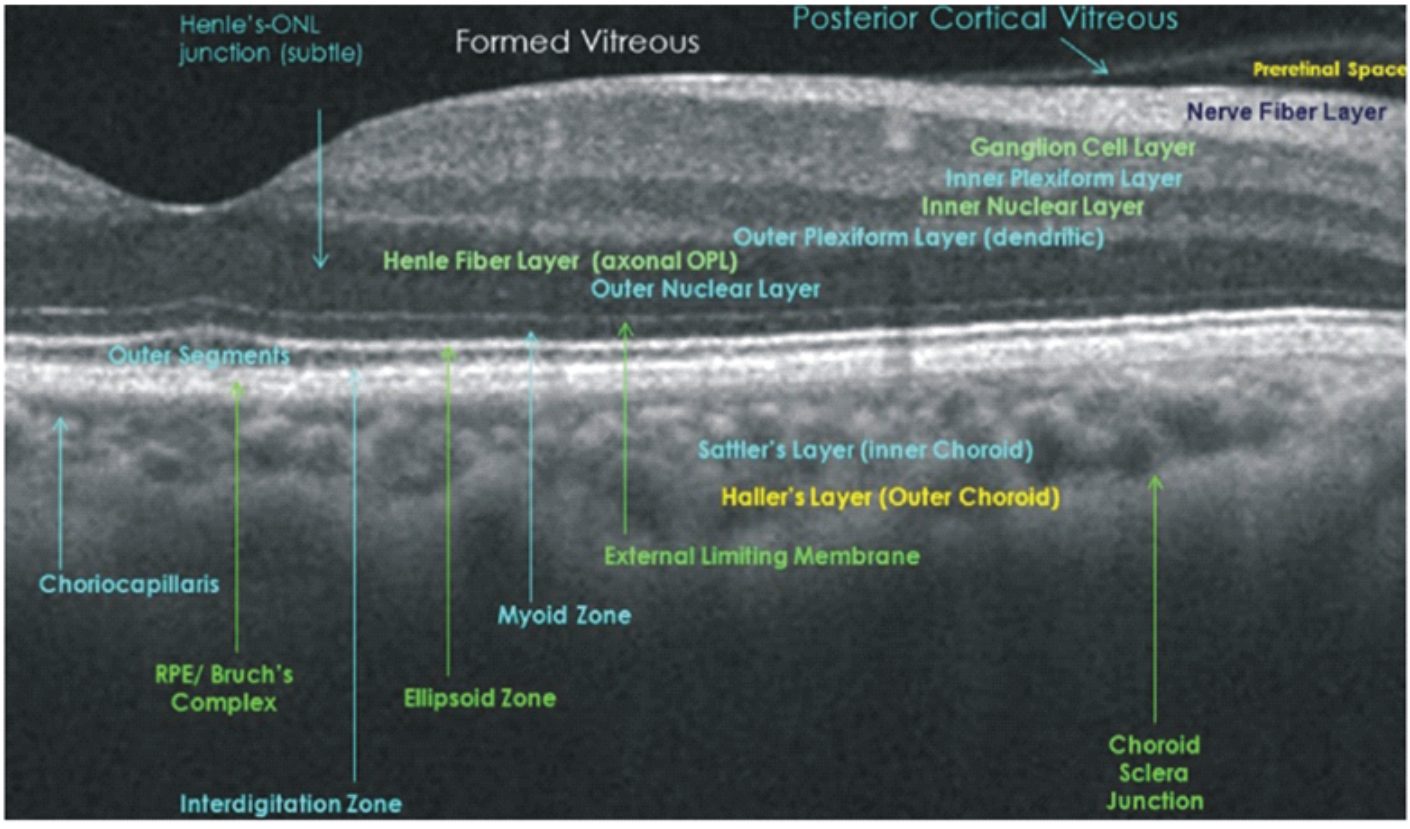



**Figure 2 : Normal OCT scan of the Macula**

inner plexiform layer, INL- inner nuclear layer, OPL- outer plexiform layer, ONL- outer nuclear layer, ELM- External limiting membrane, IS-OS junction- Inner segment- outer segment junction and RPE- Bruch's Complex.

## Revised nomenclature for OCT :

International Nomenclature for Optical Coherence Tomography panel (INOCT, 2014) has proposed and adopted a standardized nomenclature for the classification of retinal and choroidal layers and bands visible on SD- OCT[9].The INOCT

MZ is the interface between inner and outer photoreceptors (previously referred as IS-outer segments [OS] junction). They are packed with mitochondria and have the potential for high reflectivity.

**The interdigitation zone (IZ) -** corresponds to the contact cylinder represented by the apices of the RPE cells that encase the cone OS. This layer was previously referred to as cone outer segment tips/Verhoeff's membrane, or rod outer segment tips, and it is not always distinguishable from the underlying RPE layer.

**RPE- Bruch's complex -** The outermost band in the retina previously described as the RPE has now been realized to be formed of 2 hyperreflective bands separated by a hyporeflective layer. These 2 hyperreflective bands correspond with the RPE and Bruch's membrane which are often not separable under normal conditions. Therefore the term RPE Bruch's complex was proposed.

Photoreceptor disruption can be visualized on OCT as the loss of integrity or absence of the outer retinal layers: The ELM, EZ, and IZ. Disruptions of these layers on OCT have been shown to correlate with worse visual acuity and retinal sensitivity in many retinal diseases.

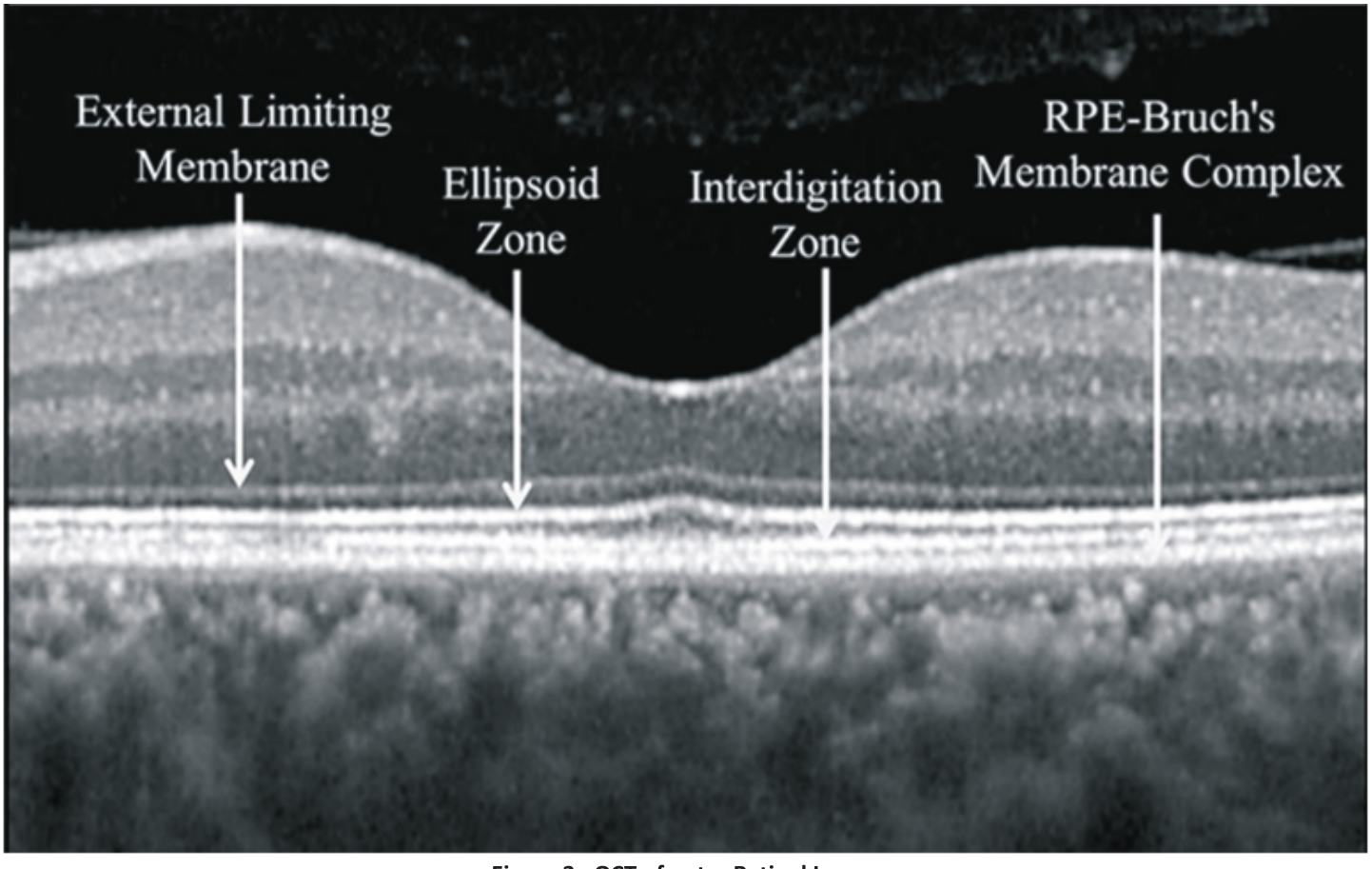



**Figure 3 : OCT of outer Retinal Layers**

## CLINICAL APPLICATIONS OF OCT :

Optical coherence tomography provides both qualitative (morphology and reflectivity) and quantitative (thickness, mapping, and volume) analyses of the examined tissues in-situ. Qualitative data can be in the form of identification of retinal pathologies like vitreomacular traction, macular holes, cystoid macular edema, and choroidal neovascularmembrane. Quantitative data such as foveal thickness are used to make treatment decisions like in conditions such as age-related macular degeneration, diabetic macular edema, and retinal vein occlusions. It is indicated in various retinal disorders; however it should not be interpreted independently in reference to any ocular disease.[10, 11] Clinical applications of OCT include :

1. Clinical aid in diagnosis and prognostication
2. To plan treatment
3. Monitor response to treatment

In general, lesions in the macula are easier to image than lesions in the mid and far periphery. OCT can be particularly helpful in diagnosing:

- Macular hole
- Macular pucker/epiretinal membrane
- Vitreomacular traction
- Macular edema and exudates
- Detachments of the neurosensory retina
- Detachments of the retinal pigment epithelium (e.g. central serous retinopathy or age-related macular degeneration)
- Retinoschisis
- Pachychoroid
- Choroidal tumors

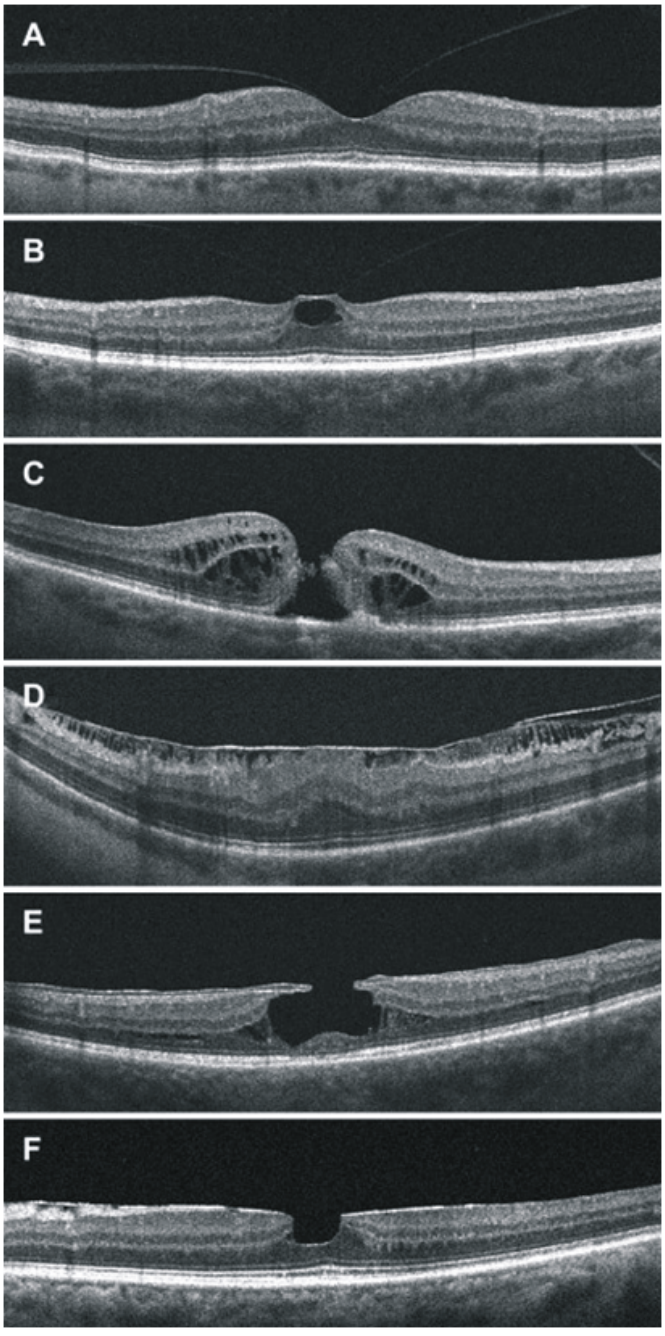
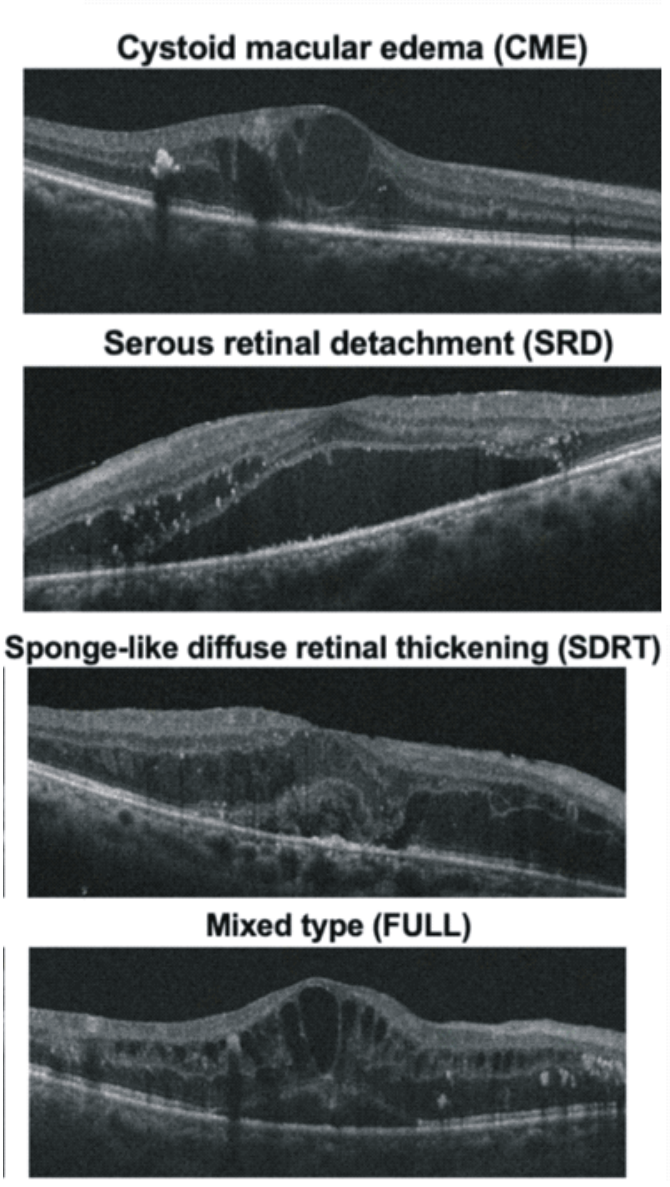



**Figure 4 : Vitreo macular interface disorders (a) Vitreo macular adhesion (b) Vitreo macular traction (c) Macular Hole (d) Epiretinal membrane (e) Lauellar Macular (f) Pseudo hole of the macula**

## ARTIFACTS in OCT :

Artifacts are defined as anomalies in the scan that are not accurate images of actual physical structures, but are rather the result of an external agent or action. The artifacts can be a result of software errors (misidentification of retinal layers, mirror artifact, cut edge artifact), operator related error (degraded image scan, out of register artifact, off-center artifact) or patient-related factors (motion artifact, off-center




**Diabetic macular edema (DME): representative images of four types of DME morphology**

artifact, degraded image scan, mirror artifact). [12] Knowledge about the possible artifacts in an OCT image and its avoidance will aid in better interpretation of the disease condition.

## Widefield OCT :

Widefield OCT system developed in Optovue (Fremont, CA) Avanti RTVue-XR uses SD technology and can obtain 70,000 A-scans/second. It can create 12 mm x 9 mm B-scans and offers 3-µm digital resolution, providing detailed imaging of both the choroid and the retina. In clinical practice it aids visualization of macular disorders that span greater areas than standard scan widths. Second, application of this OCT technology to the retinal periphery would aid in the diagnosis and follow-up of peripheral retinal disorders. [13, 14]

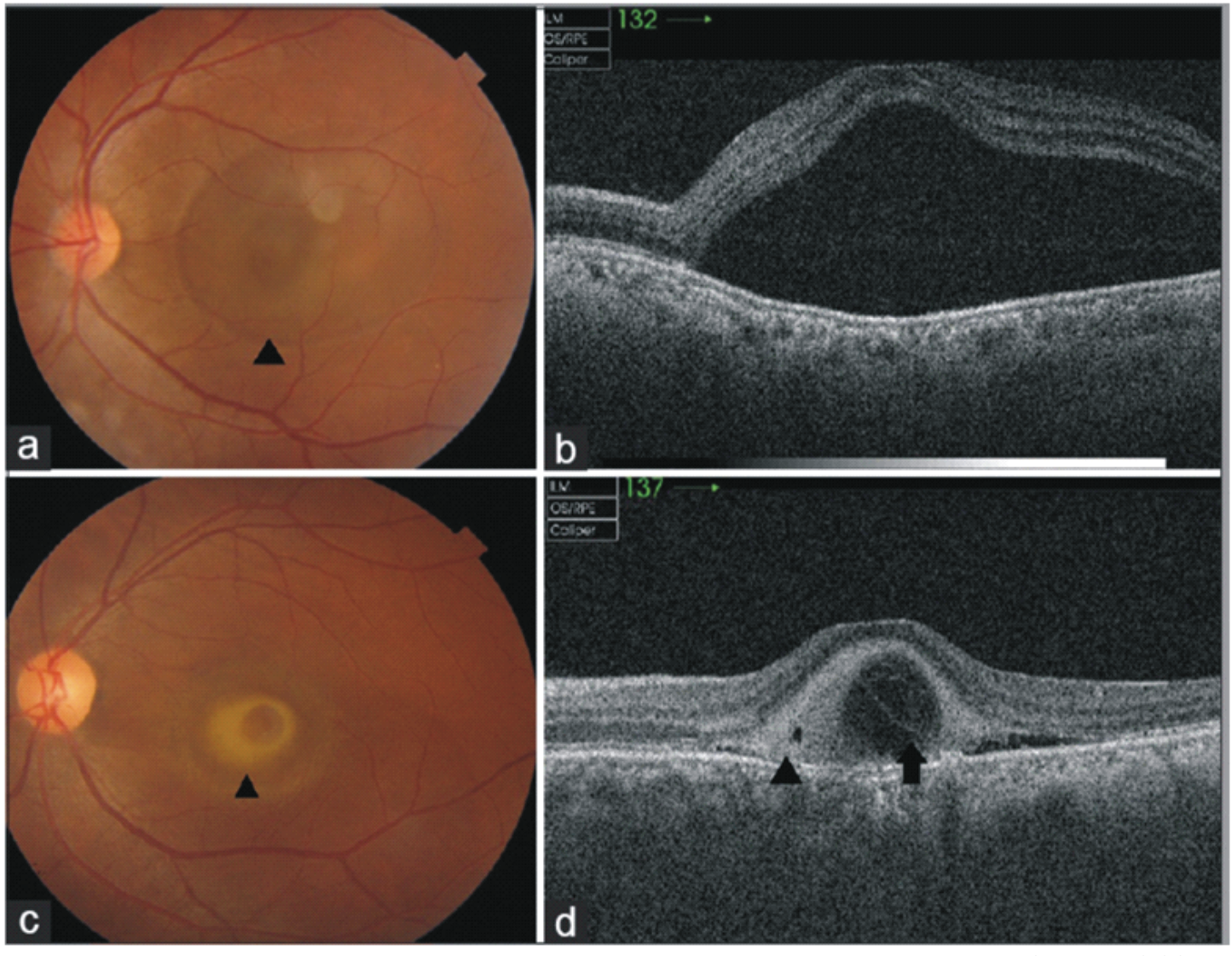



**Figure 5 : Acute Central serous chorioretinopathy showing serous macular detachment at the posterior pole (arrowhead), (a) OCT image showing bullous elevation of neurosensory retina due to presence of serous fluid, (b) Atypical CSR with yellowish subretinal fibrin deposition (arrowhead), (c) OCT image showing hyperreflective deposits in subretinal space (arrowhead) due to fibrin with hyporeflective space within fibrin clump (arrow) (d)**

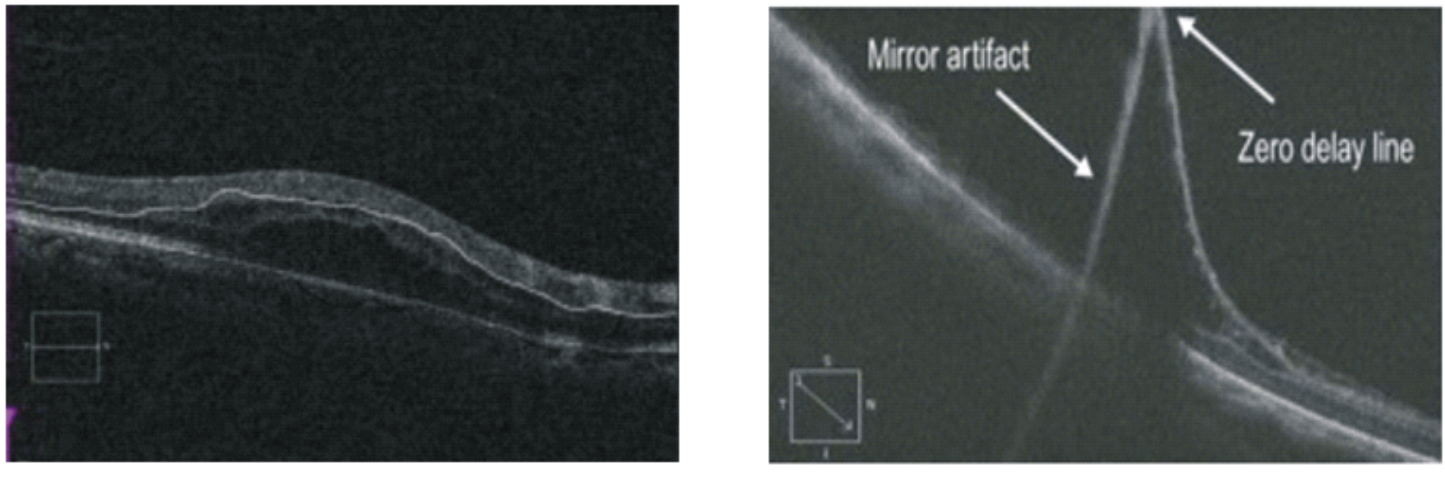



**Figure 6 : Common artifacts on SD-OCT (a) Segmentation artifact- here the outer and inner boundaries are misidentified leading to artifact (b)Mirror artifact occurring in a case of retinoschisiswhen the area of interest to be imaged crosses the zero delay line**

## OCT Angiography :

OCT angiography (OCTA) is a noninvasive, dye less method of retinal imaging based on motion contrast imaging to generate angiographic images in a matter of seconds. OCTA compares the decorrelation signal scans taken at precisely the same cross-section in order to construct a map of retinal and choroidal blood flow. It provides information of vascular perfusion at superficial inner retina, deep retina, outer retina and choriocapillaries levels. OCTA has been shown to be a useful imaging modality for the evaluation of common ophthalmologic diseases such as age-related macular degeneration, diabetic retinopathy, and vascular occlusions. Constrains of this technology include a limited field of view,

**Figure 7 : A 23mm wide field OCT B-scan image of a normal fundus**

inability to view leakage, increased potential for artifacts and inability to detect blood flow below the slowest detectable flow.[15]

## Intraoperative OCT :

Microscope integrated OCT (MIOCT) devices designed to enable simultaneous surgical viewing and high-resolution SD-OCT imaging are based on folding of the optical OCT path into the full beam path of the operating microscope to enable high resolution imaging.[16] This system is confocal with surgical microscope allowing multimodal imaging in supine patients.The shared optical path of the MIOCT and surgical microscope enabled OCT imaging simultaneous with surgical manipulations.[17]

The RESCAN 700 (Carl Zeiss Meditec, Germany) is a MIOCT system that has been used clinically to visualize steps of surgeries “real time”. It is an SDOCT that provides in vivo imaging which can help the surgeon in decision making at the time of surgery and modify his surgical plan. This system is based on the Lumera 700 (Carl Zeiss Meditec, Germany) platform and the RESIGHT lens system is used for posterior segment imaging.This system provides the surgeon with options to select the scan length, angle, and location either using the foot pedal control or through the video monitor display system.

## Adaptive optics OCT :

Adaptive Optics is not an imaging modality, but rather a technology that can be used in combination with imaging modalities to improve their performance. AO works by measuring and correcting ocular aberrations in real-time.AO provides improved lateral resolution and OCT provides improved axial resolution.In combination with an adaptive optics slit lamp ophthalmoscope, AO-OCT can acquire both OCT and SLO (Scanning Laser Ophthalmoscope) images in vivo with a resolution of 3.5 μm. [18]

## Limitations :

Because OCT utilizes light waves (unlike ultrasound which uses sound waves) media opacities can interfere with optimal

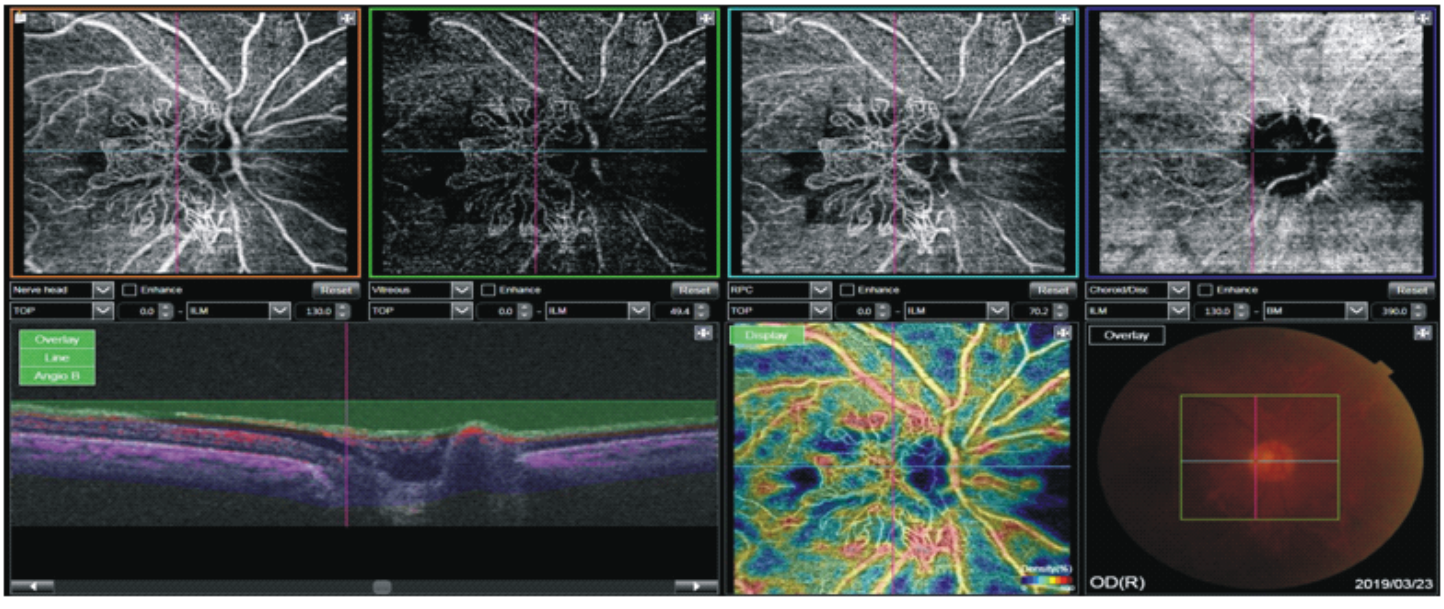



Figure 8 : OCTA showing neovascularization at disc in a case of proliferative diabetic retinopathy

imaging. As a result, the OCT will be limited the setting of vitreous hemorrhage, dense cataract or corneal opacities.As with most diagnostic tests, patient cooperation is a necessity. Patient movement can diminish the quality of the image. With newer machines, acquisition time is shorter which may result in fewer motion related artifacts.

The quality of the image is also dependent on the operator of the machine. Early models of OCT relied on the operator to accurately place the image over the desired pathology. When serial images were acquired over time (e.g. during treatment for AMD with anti-VEGF therapy), later images could be taken that were off axis compared to earlier images. Newer technologies, such as eye tracking equipment, limit the likelihood of acquisition error.

## Conclusion :

OCT technology has revolutionized the management of patients with vitreorertinal diseases and has become an integral part of the clinical practice. A systematic method of interpretation and an awareness of the possible errors, limitations, and artifacts are vital. Advances in OCT technology including choroidal imaging, OCT angiography has improved understanding of various chorioretinal disorders. OCT technology appears to be an ever-evolving field with a much bright future and leading to better patient care.

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***Gholam A. Peyman,*** *a world-renowned ophthalmologist, retina surgeon and inventor.In 2013, he received National Medal of Technology and Innovation from President Obama for, “Invention of LASIK surgery, development of intraocular drug delivery and expanding the field of vitreoretinal surgery.” He also received the Gold Medal of Ophthalmology from the Iranian Ophthalmological Society and an honorary Doctorate of Medicine from the University of Cordoba/Argentina (2014).*

# Clinicial Interpretation of OCT-A

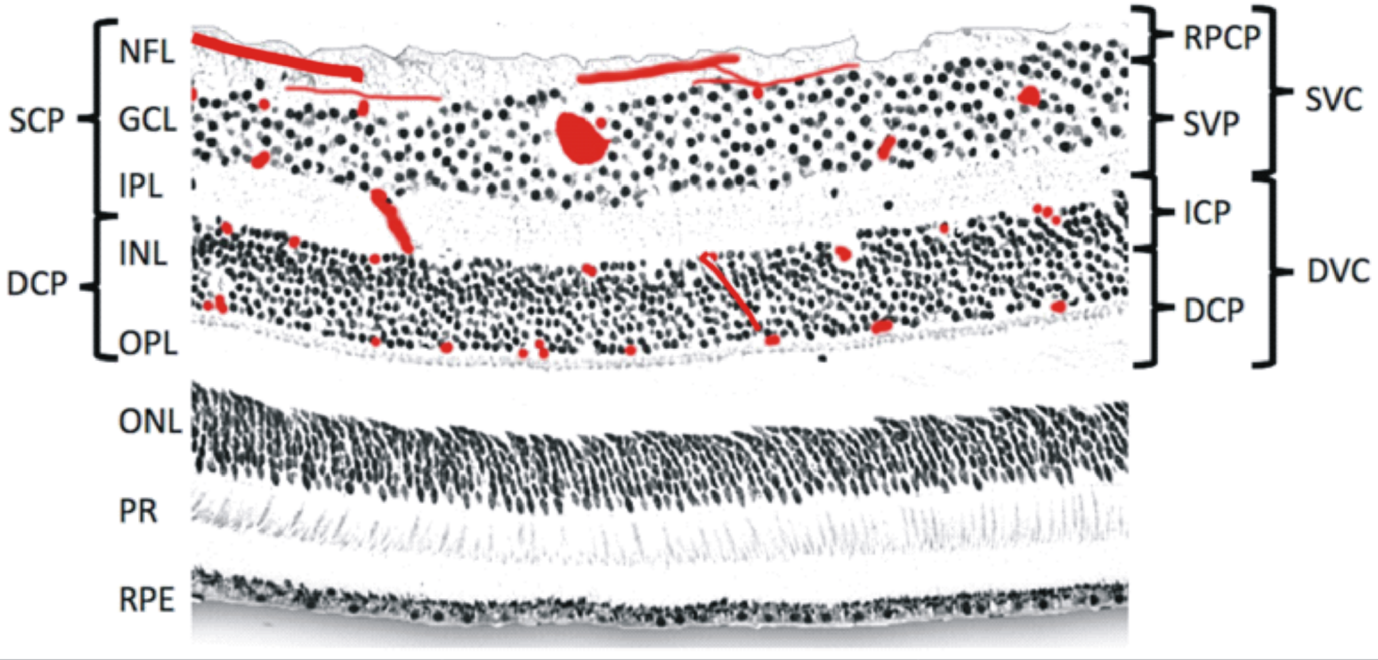
*Dhaivat Shah*

The modern era retina practice was revolutionized by the discovery of Optical Coherence Tomography (OCT) in the late 20th century. A decade down the lane in the early 21st century, with the uncovering of AntiVEGF injections in the armamentarium, a rebellion was established in the way we manage major retinalpathologies. A similar kind of revolution that is changing our preferred practice patterns today is OCT-Angiography (OCT-A).

OCT-A has recently emerged as a non-invasive technique for imaging the microvasculature of the retina and the choroid. It uses laser light reflectance of the surface of moving red blood cells to accurately depict vessels through different segmented areas of the retina. It hence eliminates the need for intravascular dyes, and enhances repeatability. The OCT scan of a patient's retina consists of multiple individual A-scans, which when compiled into a B-scan provides cross-sectional structural information of the retina and choroid. With the advent of OCT-A, the same tissue area is repeatedly imaged and differences are analysed between scans over time, thus allowing one to detect zones containing high and low flow rates, which will be similar among serial scans. [1]

For interpretation of OCT-A, the blood flow network of the retina and choroid has to be clearly understood, because the analysis is done slab-wise (Superficial, Deep, Outer retinal and RPE complex- ORCC, Choriocapillaris and Choroid).[2] The

**Figure 1 : Nomendature of retinal layers**




| Current OCTA Nomenclature | Anatomic Layers | Proposed OCTA Nomenclature | |
|---|---|---|---|
| SCP | NFL | RPCP | SVC |
| | GCL | SVP | |
| | IPL | | |
| DCP | INL | ICP | DVC |
| | OPL | DCP | |

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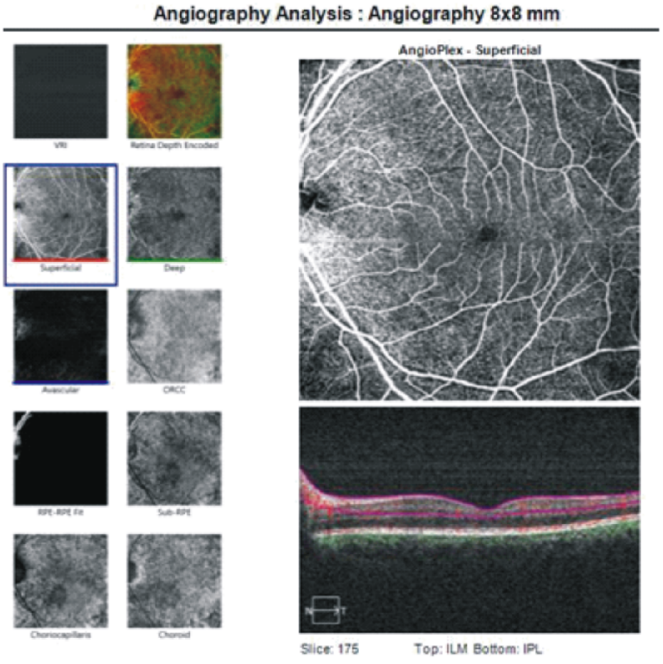
*Joint Medical Director,*
*Choithram Netralaya, Indore, India*

segmentation and slab nomenclature might vary from company to company, but the conceptual core basics remain static.

The representative normal image on Angioplex Cirrus 5000, Carl Zeiss (Germany) OCT-A is given below.

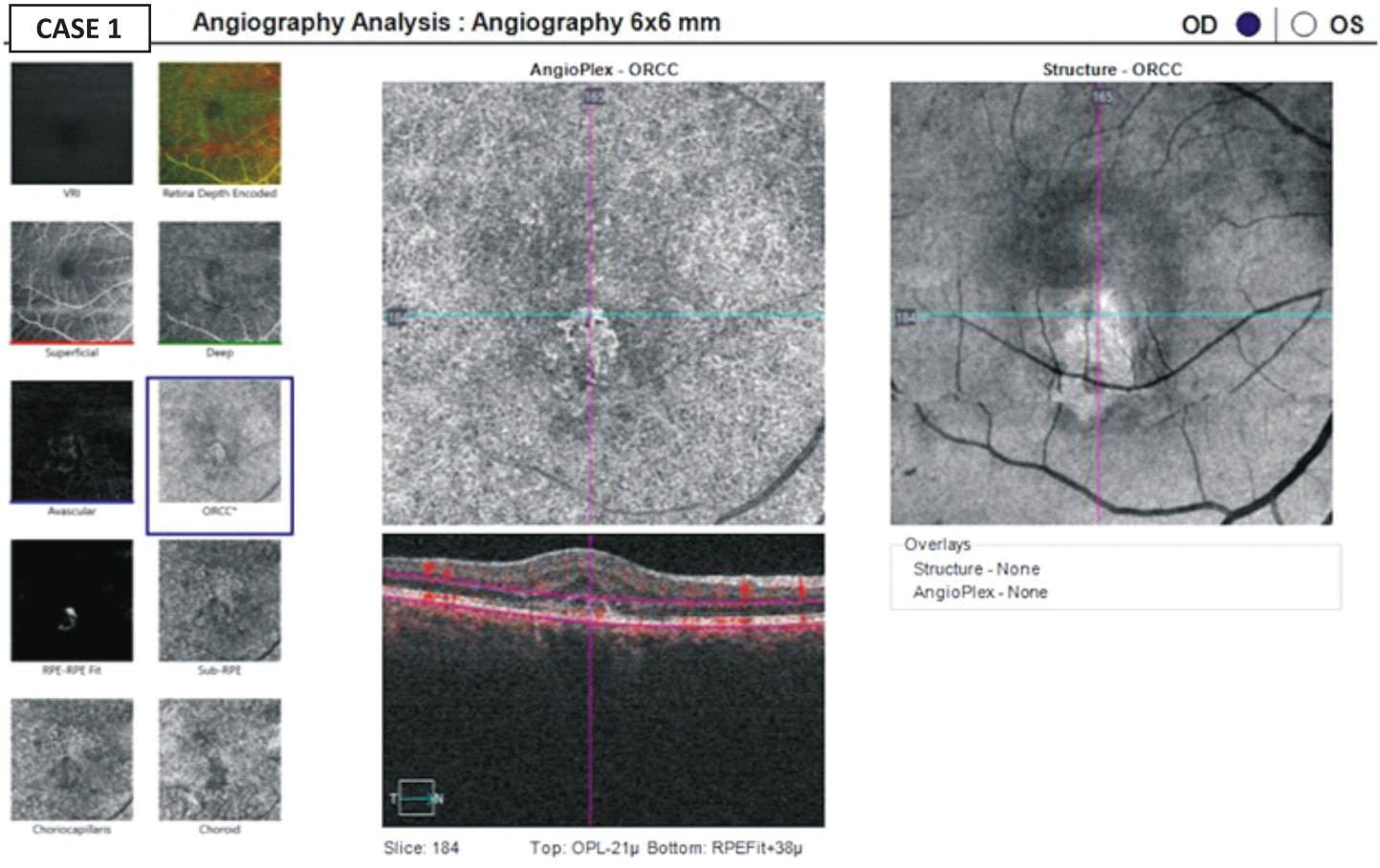



Now let's interpret some OCT-Ascans by going through a bunch of different case scenarios:-

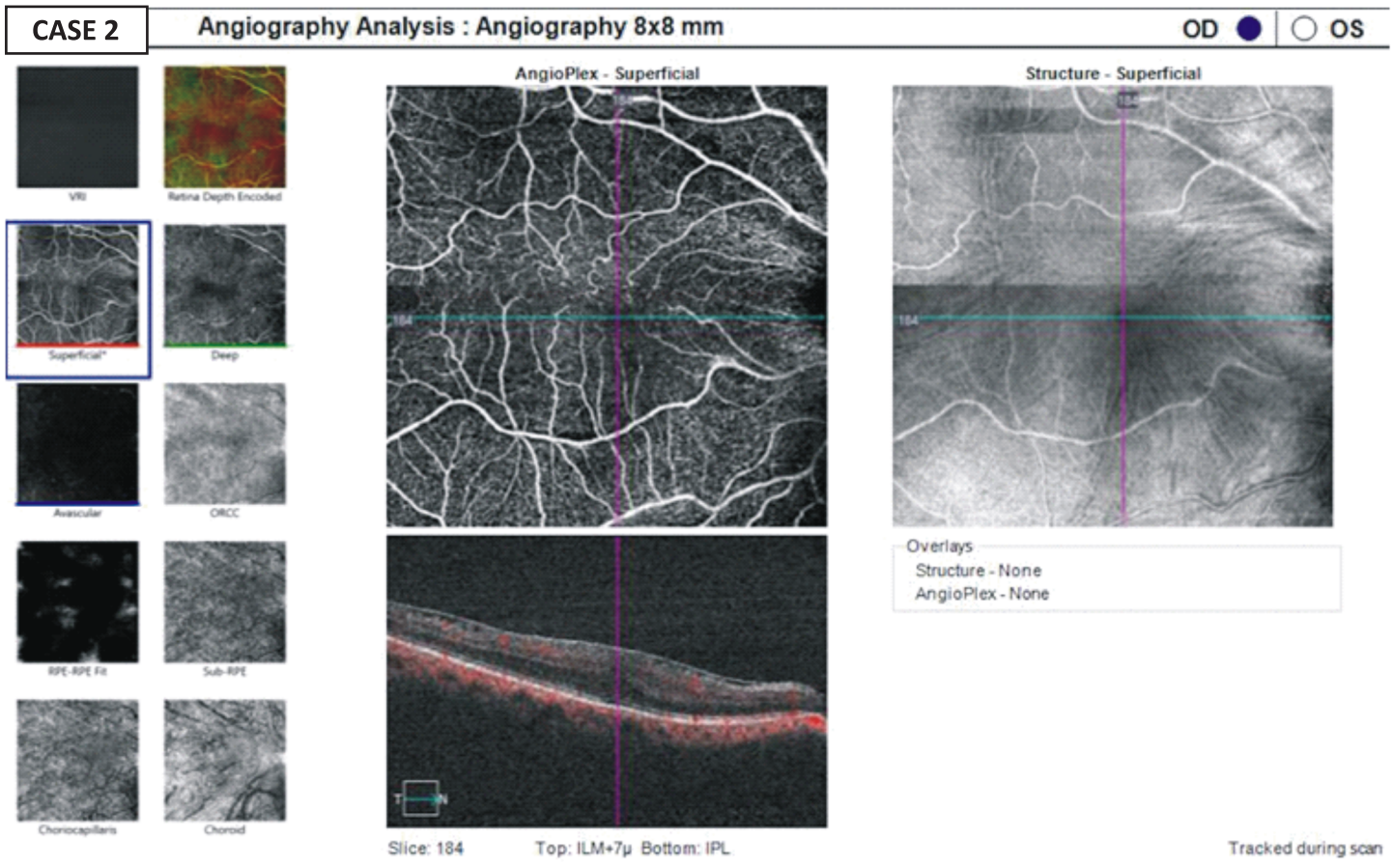
**CASE 1 : Choroidal NeoVascular Membrane (CNVM) :** A 40 year old smoker presented with complains of metamorphopsia and decreased vision in the right eye for 2 weeks (BCVA: 6⁄18). On OCT-A imaging in the ORCC slab, a membrane complex is clearly seen with an increased flow signal indicative in red. This correlates with the pigment epithelial detachment (PED) with underlying hyperreflectivity noted on the structural OCT scan. Hence, a diagnosis of Type 1 CNVM can be evidently established in a quick non-invasive manner, without subjecting the patient to a fundus fluoresceine angiography (FFA).

**CASE 2 : EpiRetinal Membrane (ERM) :** A 52 year old female patient presented with complaints of metamorphopsia post blunt injury with a stick before 3 months BCVA: 6⁄18). On OCT scan, a hyperreflective membrane was seen over the retinal surface, with an absent foveal contour. On OCT-A analysis in the superficial as well as En-face scan, the vessels tortuosity and rarefaction is clearly visible, indicative of decreased arterial perfusion. Hence, if such a case is to be taken up for surgery, the OCT-A will help in prognosticating the case and counseling the patient accordingly.

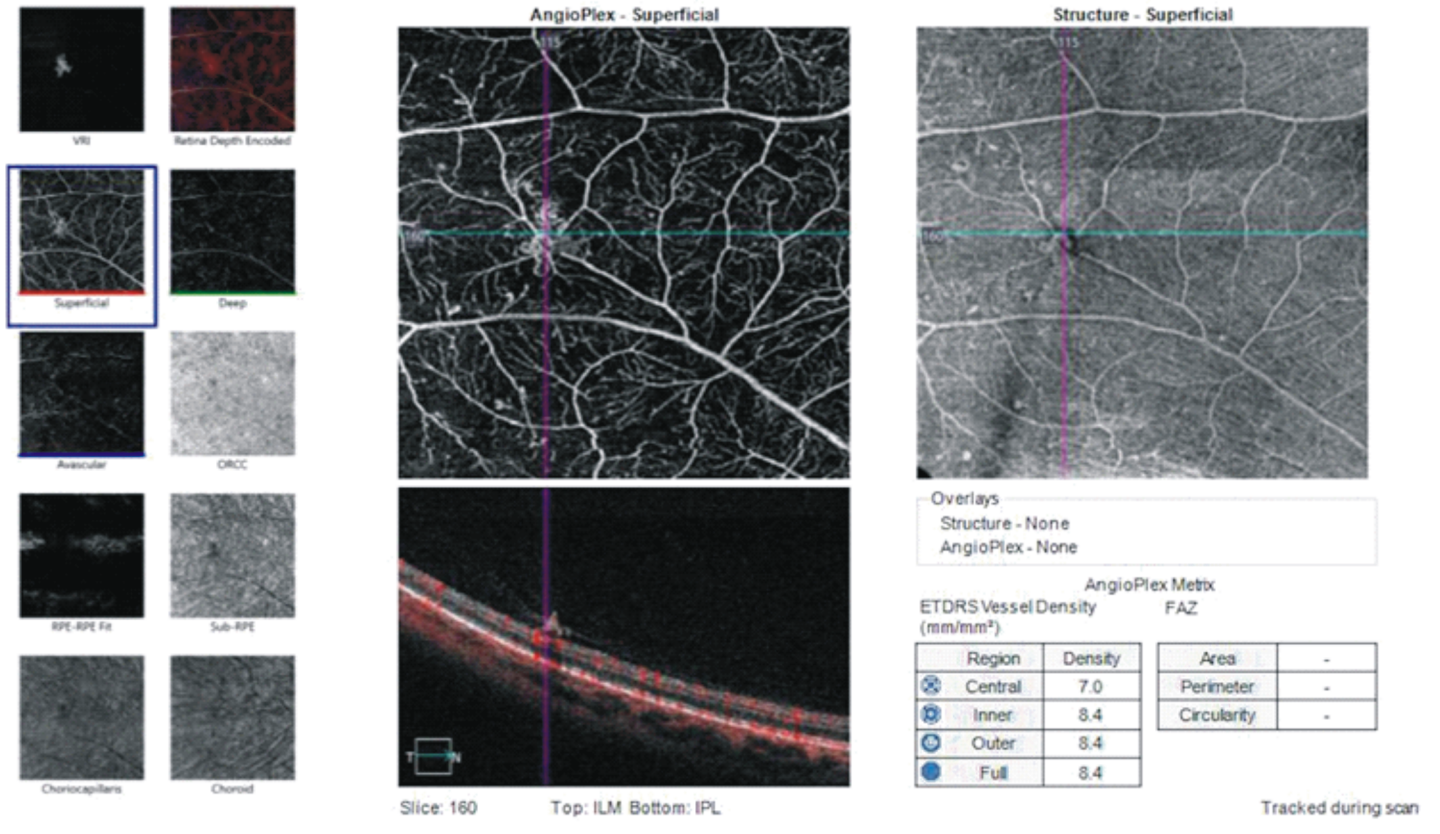
**CASE 3 : Proliferative Diabetic Retinopathy (PDR) :** A 54 year



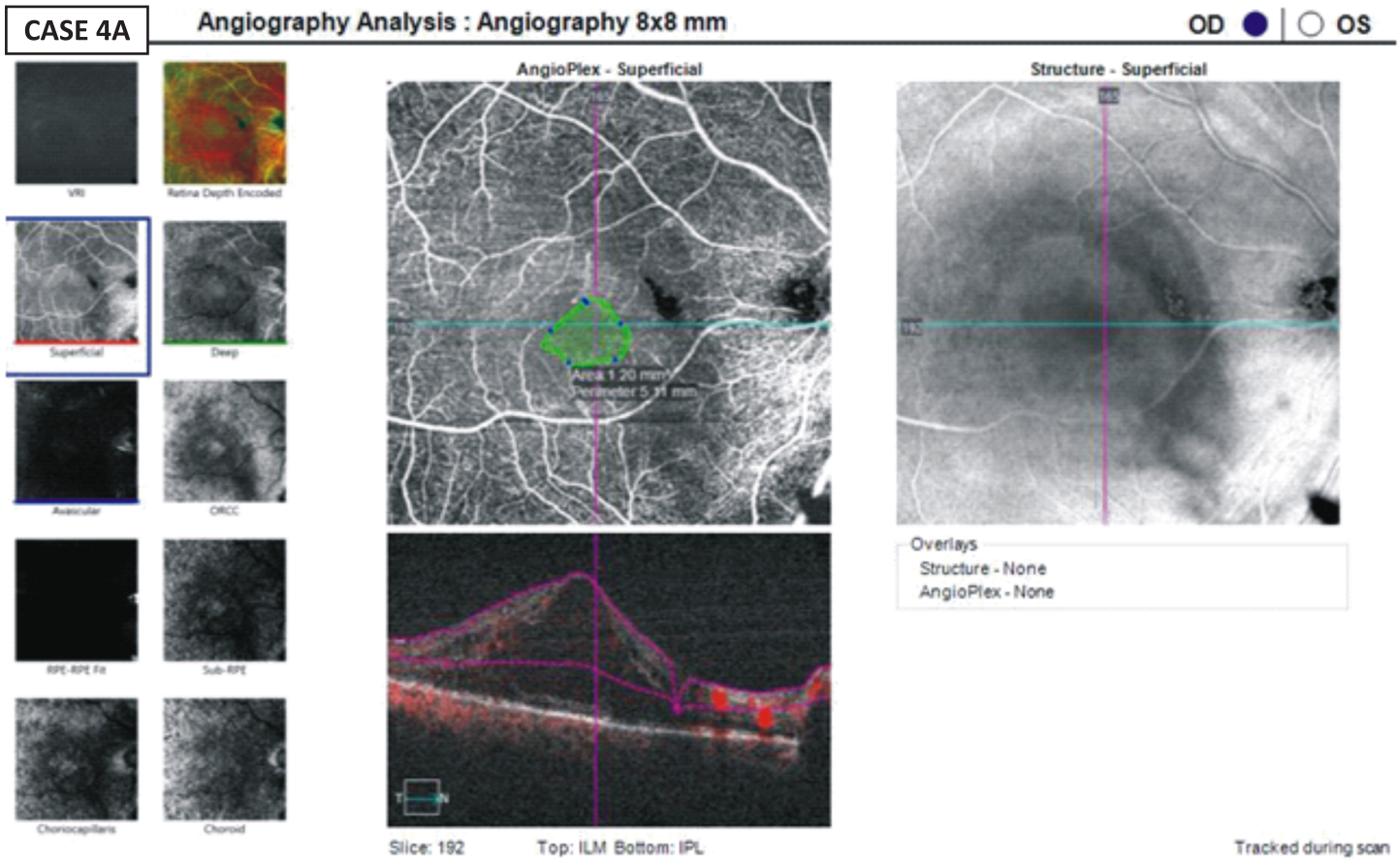
**CASE 2**


Angiography Analysis : Angiography 8x8 mm
OD
OS
AngioPlex - Superficial
Structure - Superficial
VRI
Retina Depth Encoded
Superficial*
Deep
Avascular
ORCC
RPE-RPE Fit
Sub-RPE
Choriocapillaris
Choroid
Overlays
Structure - None
AngioPlex - None
Slice: 184
Top: ILM+7µ Bottom: IPL
Tracked during scan

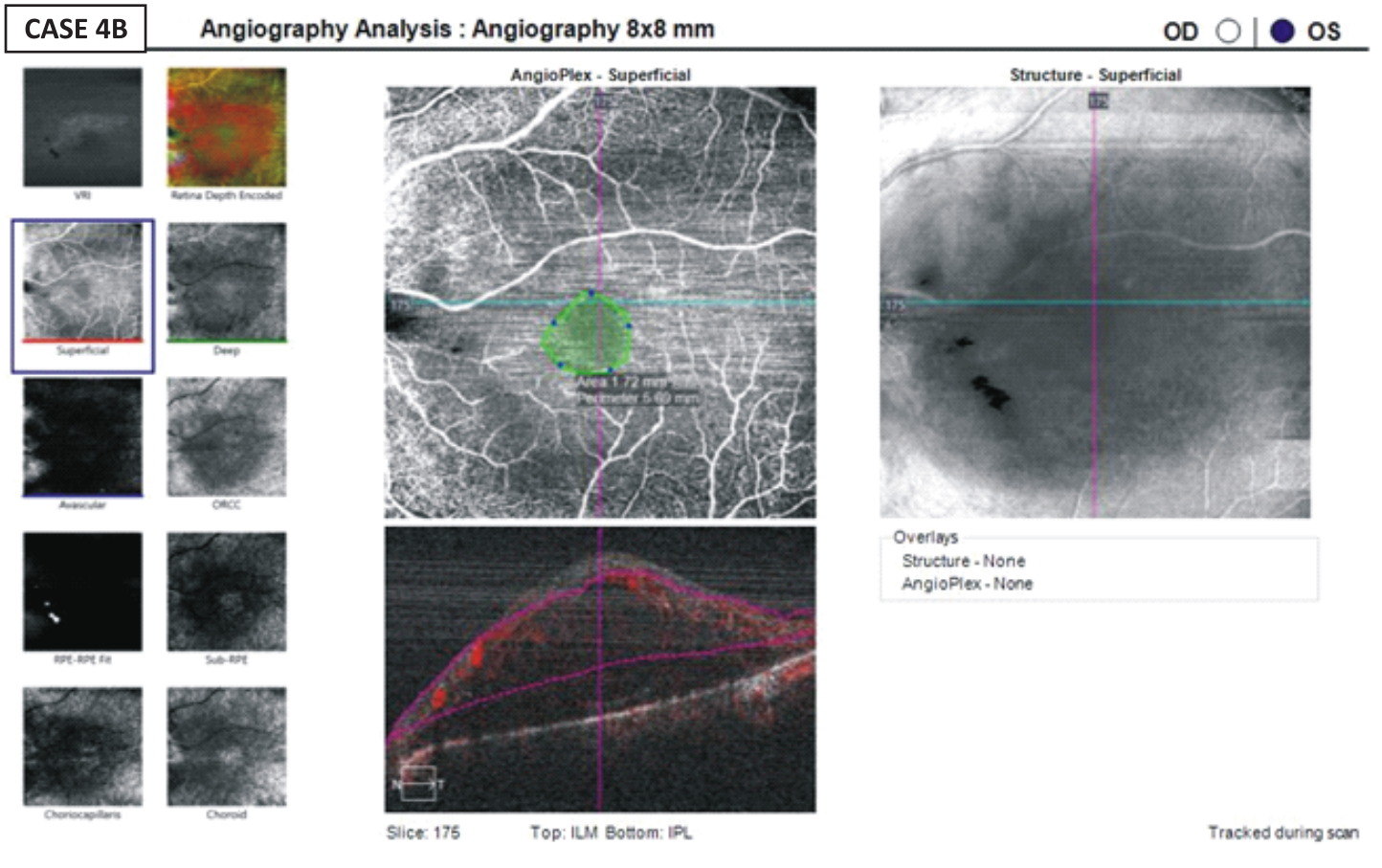
**CASE 3**


Angiography Analysis : Angiography 6x6 mm
OD
OS
AngioPlex - Superficial
Structure - Superficial
VRI
Retina Depth Encoded
Superficial
Deep
Avascular
ORCC
RPE-RPE Fit
Sub-RPE
Choriocapillaris
Choroid
Overlays
Structure - None
AngioPlex - None
AngioPlex Metrix
ETDRS Vessel Density (mm/mm²)
Region
Density
Central
7.0
Inner
8.4
Outer
8.4
Full
8.4
FAZ
Area
-
Perimeter
-
Circularity
-
Slice: 160
Top: ILM Bottom: IPL
Tracked during scan

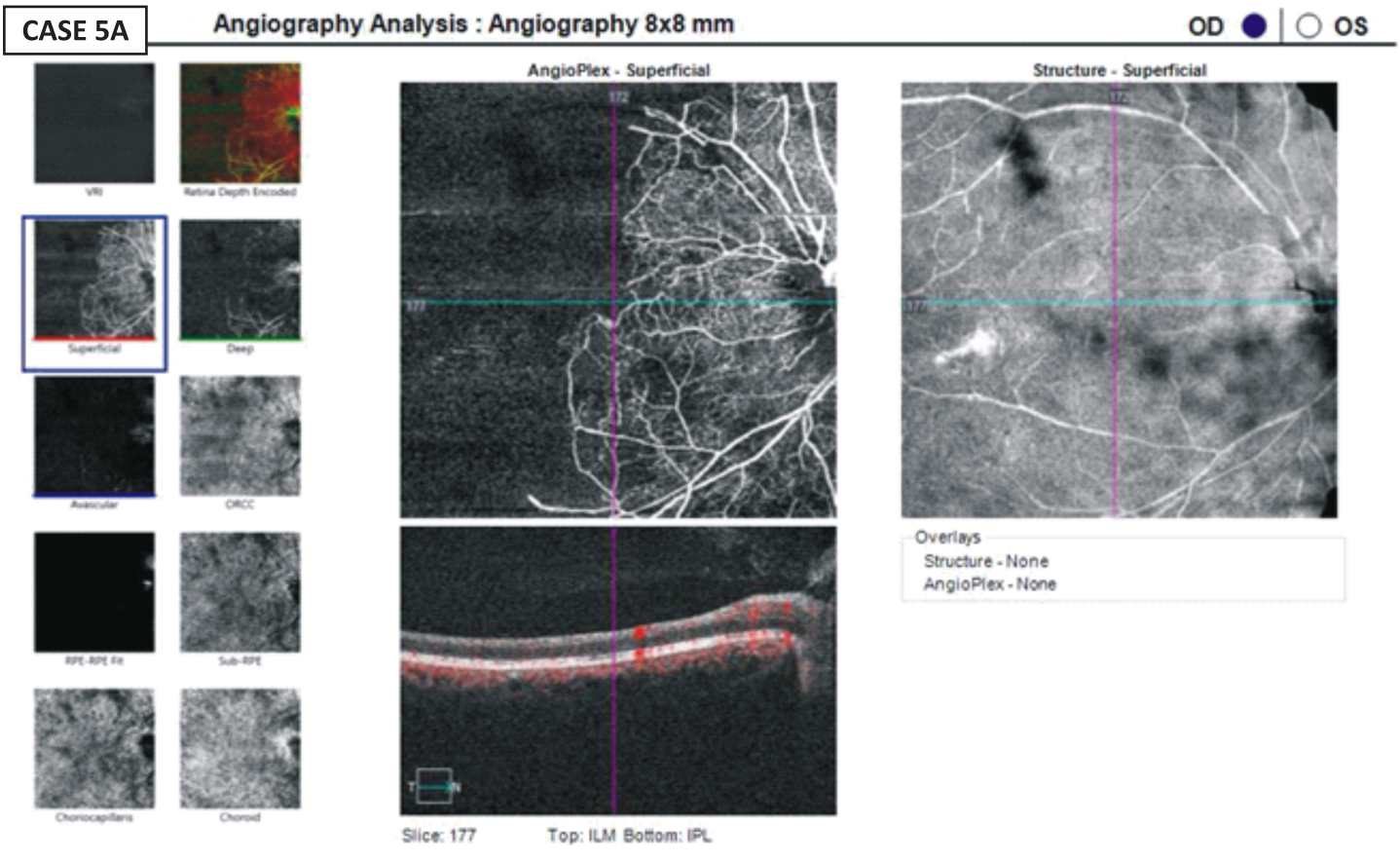
**CASE 4A**



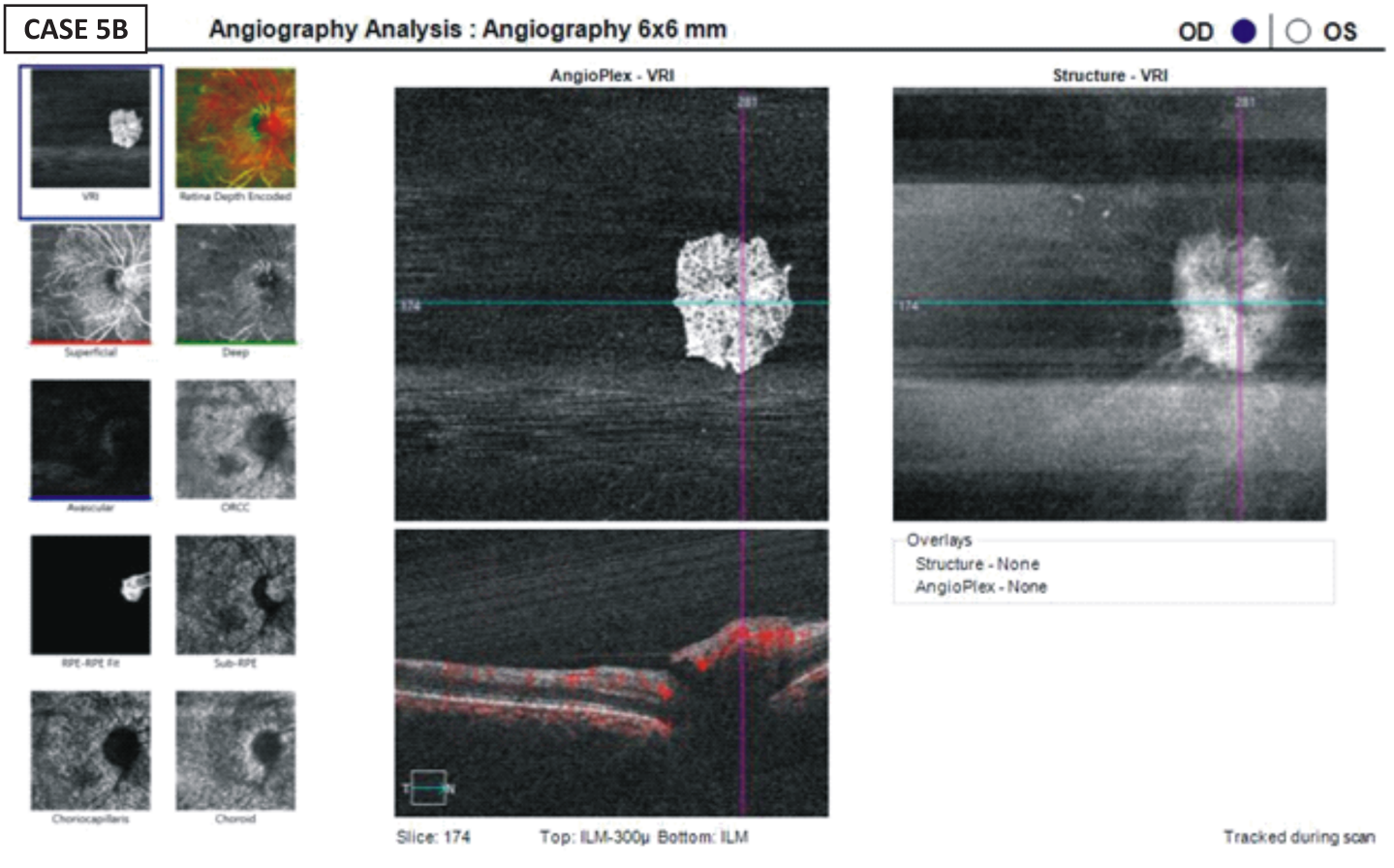

**CASE 4B**

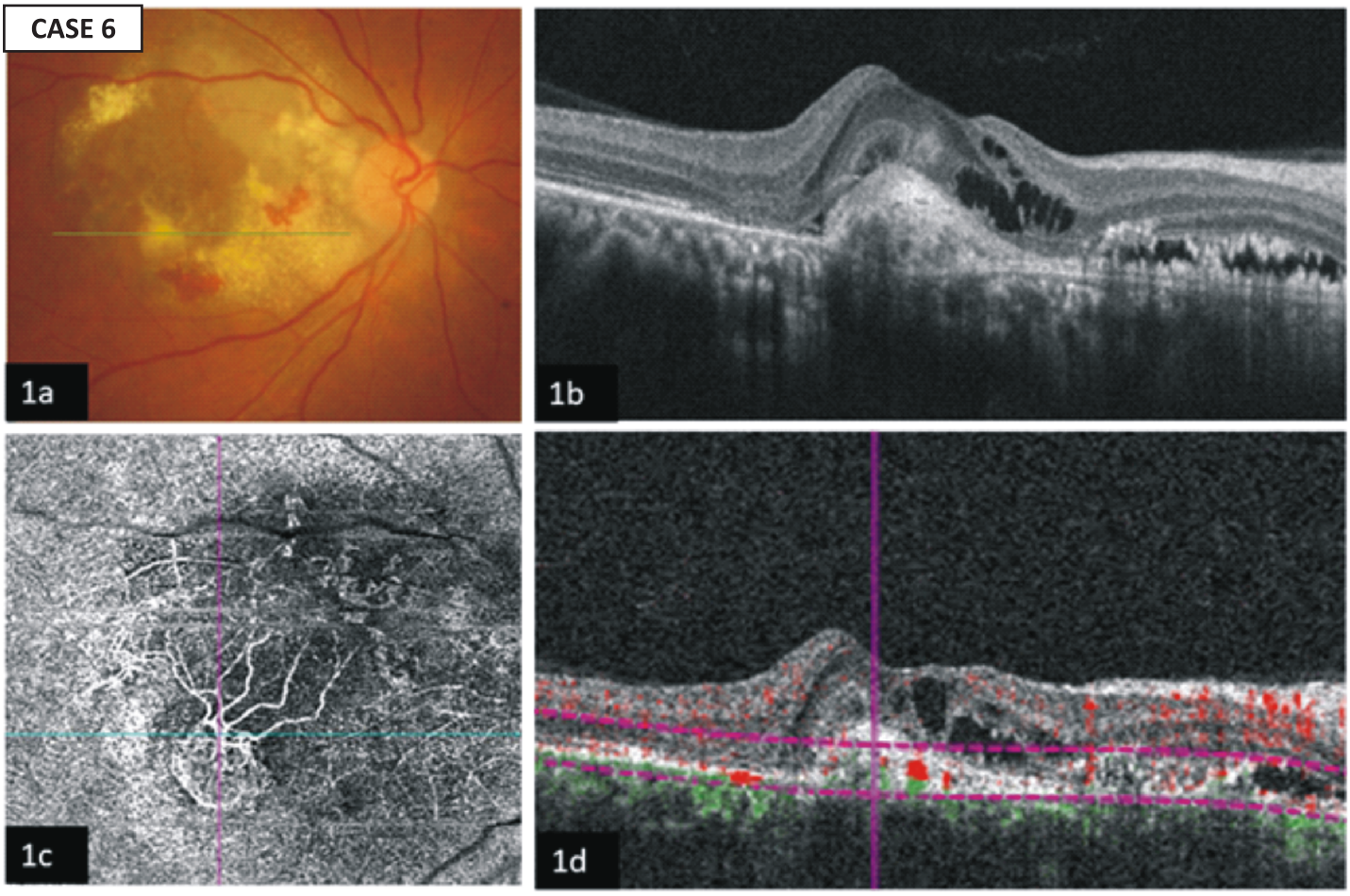


**CASE 5A**




**CASE 5B**






old diabetic male, came for a routine ocular examination (BCVA: 6/6). On clinical examination, a few microaneurysms and an abnormal vascular loop were noted, hence an OCT and OCT-A wereadvised. On structural analysis, the fovea appeared to be within normal limits. But on OCT-A scan, the abnormal looking loop appeared in the Vitreo-Retinal Interface (VRI) slab, with increased flow intensity (indicated in red), thus proving to be a neovascular membrane (NVE). This changed the diagnosis of a simple clinically looking mild NPDR to an early PDR, hence completely changing the line of management.

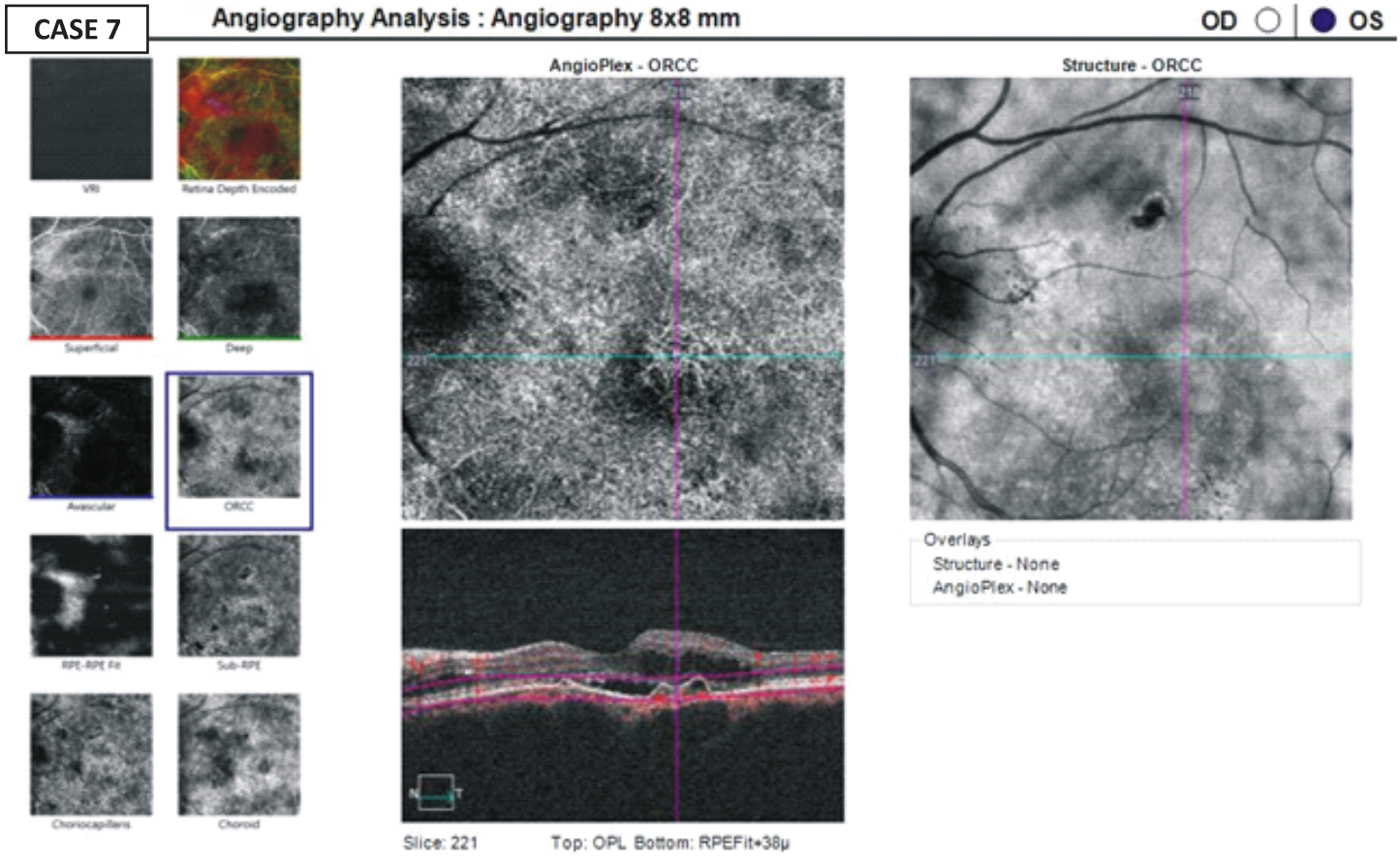
**CASE 4 : Macular Ischemia :** A 60 year old chronic diabetic and hypertensive entered our OPD for a second opinion. He was diagnosed as both eyes PDR with CME, for which multiple Anti VEGF injections and laser PRP had already been done. The BCVA in both eyes was 6/60. He was subjected to an OCT diagnosis of chronic CME with hard exudates and was advised a steroid implant. We performed an OCT-A in this case, and the superficial and deep slabs showed a clearly enlarged foveal avascular zone (FAZ). Meaning, even if the edema subsides here, the visual acuity is unlikely to improve.

**CASE 5 : Vasculitis and Uveitis :** A 22 year old girl complained of floaters in her right eye for the past 2 months after a bout of fever (BCVA: 6/36). On clinical examination, a dull foveal reflex with minimal retinal vasculature was noted temporally. On OCT-A, this area was clearly seen in the superficial slab as a capillary non-perfusion area which correlated to inner retinal thinning on the OCT. A membrane complex was seen clinically over the optic nerve head, which was diagnosed as NVD as it lit up in the VRI slab.She was eventually diagnosed as a case of lupus vasculitis and was subjected to laser under immuno-modulator cover.

**CASE 6 : Retinal Angiomatous Proliferation (RAP) :** A 58-year-old male patient, a chronic smoker, came to our OPD with complaints of diminution of vision in the right eye (BCVA: 2/60). On clinical examination, he had severe exudation and haemorrhages, that were evident on the structural OCT. The patient had financial constraints for ICG-A, hence an OCT-A was performed. The ORCC slab showed a well-defined membrane complex and feeder vessels supplying it, suggesting a diagnosis of Type 3 CNVM (RAP).

**CASE 7 : Central Serous Retinopathy :** A 41 year old male complained of chronic metamorphopsia in left eye for the past 2 years (BCVA: 6/36). He had consulted multiple doctors, and had gone through multiple medical treatments including focal lasers for a suspected CSR. On presenting to us, an OCT-A was

**CASE 7**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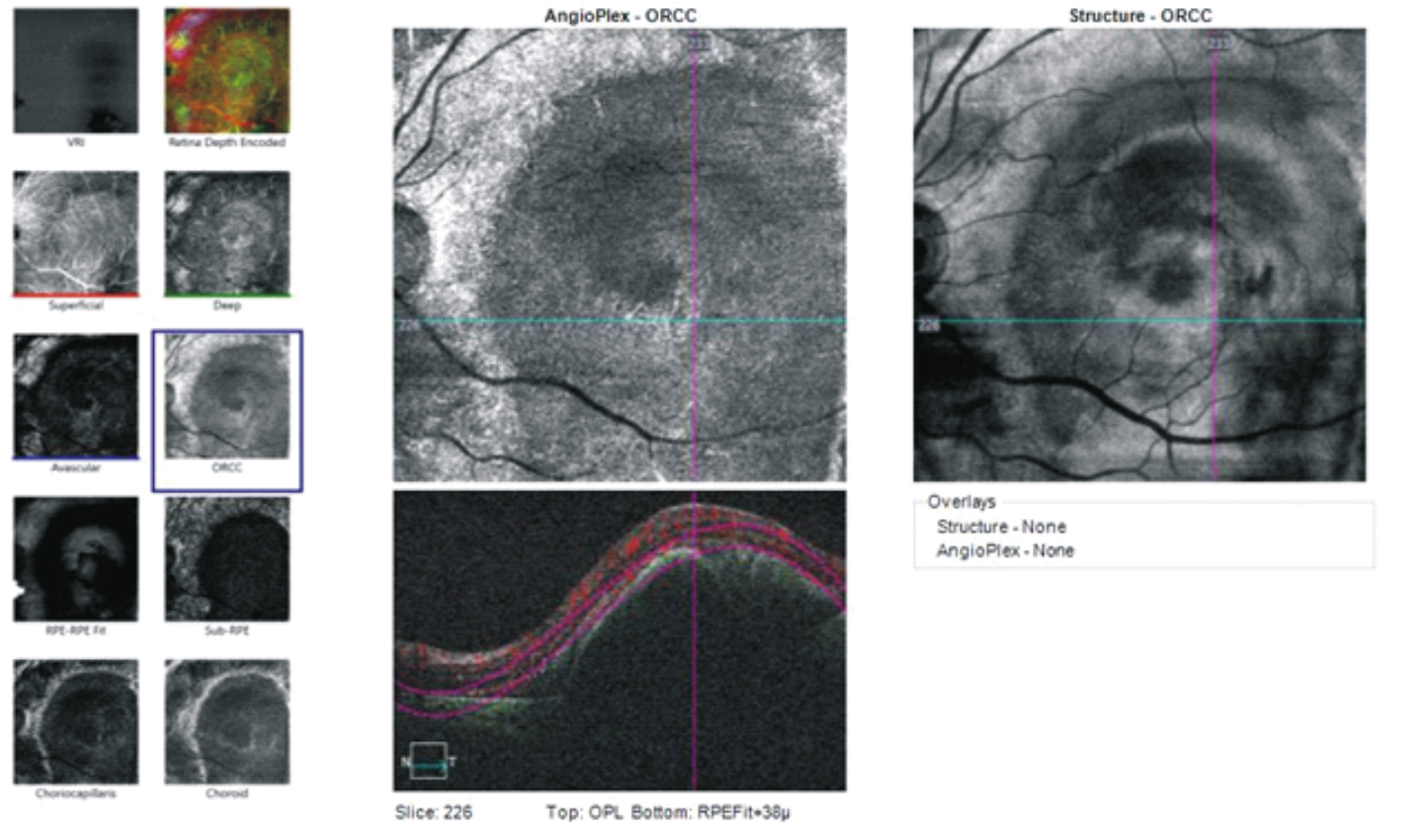
OS
AngioPlex - ORCC
Structure - ORCC
VRI
Retina Depth Encoded
Superficial
Deep
Avascular
ORCC
RPE-RPE Fit
Sub-RPE
Choriocapillaris
Choroid
Overlays
Structure - None
AngioPlex - None
Slice: 221
Top: OPL Bottom: RPEFit+38µ

**CASE 8**


Angiography Analysis : Angiography 8x8 mm
OD
OS
AngioPlex - ORCC
Structure - ORCC
VRI
Retina Depth Encoded
Superficial
Deep
Avascular
ORCC
RPE-RPE Fit
Sub-RPE
Choriocapillaris
Choroid
Overlays
Structure - None
AngioPlex - None
Slice: 226
Top: OPL Bottom: RPEFit+38µ

performed and multiple findings were noted. A double layer sign was seen on the OCT, and in the OCT-A, a Type 1 membrane was noted below it in the ORCC slab with a positive flow. Also, a pachychoroid was seen in the OCT, and the En-face slab of OCT-A showed multiple hyporeflective areas, indicative of previously present fluid. A superior dark spot was also seen on the En-face, which was indicative of a dense laser burn. Hence, with the above findings, a diagnosis of pachychoroid-neovasculopathy was made, and he was treated with a combination of low fluence PDT and Anti VEGF injections.

**CASE 8 : Polypoidal Choroidal Vascularization :** A 60 year old hypertensive complained of sudden onset loss of vision in his left eye for the past 3 days (BCVA: HM+). The OCT showed multiple peaked haemorrhagic PEDs, and subretinal hyperreflective matter. The OCT-A here showed an increased flow signal at the apex of the PEDs, indicative of an active polyp. Hence, without the aid of an ICG-A, the patient was diagnosed to have a PCV and was treated with Anti VEGF monotherapy.

The machine algorithm and acquisitions are in an evolving phase, hence we do get artifacts like motion, stretch, displacement, projection, masking, unmasking, segmentation etc. Significant research is being done towards enhancing the field of view of OCT-A and reducing the artifacts. Deep learning algorithms are being tested to increase the accuracy of automated segmentation protocols, with promising results so far. The future also beholds the incorporation of artificial intelligence and adaptive optics.[3]

Hence, we believe that OCT-A is going to revolutionize the diagnosis, management and prognostication of retinal diseases in the years to come.

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2. Campbell, J., Zhang, M., Hwang, T. et al. Detailed Vascular Anatomy of the Human Retina by Projection-Resolved Optical Coherence Tomography Angiography. Sci Rep 7, 42201 (2017).https://doi.org/10.1038/srep42201
3. https://www.eophtha.com/posts/optical-coherence-tomography-angiography-made-simple


***J. Donald M. Gass,*** *MD 1928-2005 widely recognized as the father of macular diseases. He made significant contributions to the diagnosis and treatment of macular diseases and in the interpretation of fluorescein angiography of the macula and retina. As Harry W. Flynn, Jr., MD, FASRS, stated, "He described It first and described It best."*

# Diabetic Retinopathy

*Ashutosh Agarwal*

## I. Introduction :

Diabetes mellitus (DM) has become a modern pandemic with significant morbidity. Diabetic retinopathy (DR) is a microvascular complication of DM and affects 1 in 3 persons with DM. It remains a leading cause of vision loss in the adult population. Patients with vision loss due to DR have a poorer quality of life and reduced levels of physical, emotional, and social well-being. Studies have shown that optimal control of blood glucose, blood pressure, and lipid profile can reduce the risk of developing retinopathy and slow its progression. Early diagnosis and timely treatment with laser photocoagulation, and anti- vascular endothelial growth factors (anti-VEGFs) can prevent visual loss in vision-threatening retinopathy. Since visual loss may not be present in the earlier stages of retinopathy, regular screening of persons with diabetes is essential to enable early intervention.

### 1.1 Epidemiology of Diabetic Retinopathy :

A Global meta-analysis study reported that 1 in 3 (34.6%) had any form of DR in the US, Australia, Europe and Asia. It is also noted that 1 in 10 (10.2%) had Vision Threatening DR (VTDR) i.e., PDR and/or DME. In 2010 amongst world diabetic population, more than 92 million adults had any form of DR, 17 million had PDR, 20 million had DME and 28 million had VTDR.DR develops with time and is associated with poor control of blood sugar, blood pressure, and blood lipids. The longer someone has had DM, and the poorer their control, the higher their risk of developing DR. It is estimated that more than 3 million people aged 40 years or above have VTDR in India.[1]

### 1.2 Classification of Diabetic Retinopathy[2] :

Retinal lesions of DR include microaneurysms, hemorrhages, venous beading (venous caliber changes consisting of alternating areas of venous dilation and constriction), intraretinal microvascular abnormalities, hard exudates (lipid deposits), cotton-wool spots (ischemic retina leading to accumulations of axoplasmic debris within adjacent bundles of ganglion cell axons), and retinal neovascularization.

#### 1.2.1 Nonproliferative Diabetic Retinopathy (NPDR) :

Eyes with nonproliferative DR (NPDR) have not yet developed neovascularization, but may have any of the other classic DR lesions. Eyes progress from having no DR through a spectrum of DR severity that includes mild, moderate and severe NPDR. Correct identification of the DR severity level of an eye allows a prediction of risk of DR progression, visual loss, and determination of appropriate treatment recommendations including follow-up interval.

#### 1.2.2 Proliferative Diabetic Retinopathy (PDR) :

Proliferative diabetic retinopathy (PDR) is the advanced stage of DR and represents an angiogenic response of the retina to extensive ischemia from capillary closure. Retinal neo-vascularization is typically characterized as being new vessels on the disc (NVD) or new vessels elsewhere (NVE) along the vascular arcades. NVE usually occur at the interface of perfused and non-perfused areas of retina.

#### 1.2.3 Diabetic Macular Edema (DME) :

Diabetic macular edema (DME) is an important cause of visual morbidity that is assessed separately from the stages of retinopathy, as it can be found in eyes at any DR severity level and can run an independent course. Currently, diabetic eyes are generally classified as having no DME, noncentral-involved DME, or central-involved DME. The determination of DME severity based on these 3 categories will determine the need for treatment and follow-up recommendations.

Previously, the ETDRS classification was widely used to classify diabetic retinopathy. ETDRS gave the definition of clinically significant macular edema (CSME). Now, with the advent of OCT and widespread use of anti-VEGFs, this classification is being sparingly used since the newer classification helps define treatment protocols.

## 2. Detailed Ophthalmic Assessment of Diabetic Retinopathy :

### 2.1 Initial Patient Assessment :

Detailed patient assessment should include a complete ophthalmic examination, including visual acuity and the identification and grading of severity of DR and presence of DME for each eye. The patient assessment should also include the taking patient history focused on diabetes and its modifiers.

#### 2.1.1 Patient History :

- Duration of diabetes
- Past glycemic control (hemoglobin A1c)

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**Table 1: International Classification of Diabetic Retinopathy and Diabetic Macular Edema**

| Diabetic Retinopathy | Findings Observable on Dilated Ophthalmoscopy |
|---|---|
| No apparent DR | No abnormalities |
| Mild non-proliferative DR | Microaneurysms only |
| Moderate non-proliferative DR | Microaneurysms and other signs (e.g., dot and blot hemorrhages, hard exudates, cotton wool spots), but less than severe non-proliferative DR |
| Severe non-proliferative DR | Moderate non-proliferative DR with any of the following:<br>- Intraretinal hemorrhages (=20 in each quadrant);<br>- Definite venous beading (in 2 quadrants);<br>- Intraretinal microvascular abnormalities (in 1 quadrant);<br>- and no signs of proliferative retinopathy |
| Proliferative DR | Severe non-proliferative DR and 1 or more of the following:<br>- Neovascularization<br>- Vitreous/preretinal hemorrhage |
| **Diabetic Macular Edema** | **Findings Observable on Dilated Ophthalmoscopy#** |
| No DME | No retinal thickening or hard exudates in the macula |
| Noncentral-involved DME | Retinal thickening in the macula that does not involve the central subfield zone that is 1mm in diameter |
| Central-involved DME | Retinal thickening in the macula that does involve the central subfield zone that is 1mm in diameter |

- Medications (especially insulin oral hypoglycemics, antihypertensives, and lipid-lowering drugs)
- Systemic history (e.g., renal disease, systemic hypertension, serum lipid levels, pregnancy) Ocular history

**2.1.2 Initial Physical Exam (Key Elements) :**

- Visual acuity
- Measurement of intraocular pressure (IOP)
- Gonioscopy when indicated (e.g., when neovascularization of the iris is seen or in eyes with increased IOP)
- Slit-lamp biomicroscopy
- Fundus examination

**2.1.3 Ancillary Tests :**

- OCT is the most sensitive method to identify DME. OCT can provide quantitative assessment of DME to determine the severity of DME. Retinal map scan is useful in locating the area with retinal thickening; single scan is useful in detailing the types of DME as diffuse, cystic changes, sub-retinal fluid/detachment, and vitreoretinal traction.
- Fluorescein angiography is not required to diagnose DR, proliferative DR or DME, all of which are diagnosed by means of fundus examination.
- Fluorescein angiography can be used as a guide to evaluate retinal non-perfusion area, presence of early retinal neovascularization, and microaneurysms or macular capillary non-perfusion in DME.
- OCTA is quicker, noninvasive, and harbors no risk of allergic reaction (no intravenous fluorescein infusion) as well as the ability to visualize structural morphology and microvasculature in one test.

## 3. Treatment of Diabetic Retinopathy :

i. Optimize medical treatment : Improve glycemic control if HbA1c >7% as well as associated systemic hypertension, heart disease or dyslipidemia.

ii. No DR, Mild or Moderate NPDR : Follow up at recommended intervals with dilated eye examinations and retinal imaging as needed. Treat DME as needed (see below).

iii. Severe NPDR: Follow closely for development of PDR. Consider early panretinal photocoagulation for patients at high risk of progression to PDR or poor compliance with follow-up. There are benefits of early panretinal photo-coagulation at the severe NPDR stage for patients with type 2 diabetes. Other factors, such as poor compliance with followup, impending cataract extraction or pregnancy, and status of fellow eye will also help in determining the timing of the panretinal photo-coagulation.

iv. PDR: Treat with panretinal photocoagulation (PRP). There is increasing evidence from clinical trials demonstrating anti-VEGF injections as a safe and effective treatment of PDR through at least 2 years. PRP laser does have minor side effects as far as quality of vision is considered, but remains the gold standard for treatment of PDR in the Indian scenario.

**3.3.1 Pre-treatment Discussion with Patients :**

- Patients usually need numerous follow-up visits and may require supplementary laser treatment.
- PRP reduces the risk of visual loss and blindness.
- Although laser treatment is effective, some patients may still develop vitreous hemorrhage. The hemorrhage is caused by the diabetes and not by the laser; it may mean the patient needs more laser treatment.
- Laser treatment sometimes leads to reduced peripheral and night visionand increase in dark adaptation time.

**3.3.2 Technique for PRP :**

i. The pupil should be fully dilated and topical anesthesia is used.

ii. Typical initial settings on the Double Frequency Nd : VAG laser would be 500 μm spot size, a 0.2 second exposure and 100-150 mw power. The power is gradually increased until a whitish reaction is obtained on the retina. The lesions are placed 1 burn width apart.

iii. A total of 1600-3000 burns are placed in 1 or more sittings, carefully avoiding the macular area and any areas of tractional elevation of the retina. The burns are placed 2 to 3 disc diameters away from the center of the macula and 1 disc diameter away from the disc, usually outside the arcades and extended peripherally up to the equator and beyond.

iv. Laser treatment should not be applied over major retinal veins, preretial hemorrhages, darkly pigmented chorioretinal scars, or within 1 DD (200-300 ìm) of center of macula, so as to avoid risk of hemorrhage or large scotomas.

Alternatively, PRP can also be done with laser indirect ophthalmoscope (LIO). The settings are the same except that there is no spot size in LIO.

## 4. Treatment for Diabetic Macular Edema :

i. DME without central involvement: May observe until there is progression to central involvement, or consider focal laser to leaking microaneurysms if thickening is threatening the fovea. No treatment is applied to lesions closer than 300-500 ìm from the center of the macula. Modified grid laser can also be done in cases of diffuse macular thickening / gross circinate maculopathy.

ii. Central-involved DME and good visual acuity (better than 6⁄9 or 20⁄30): 3 treatment options being evaluated in an ongoing clinical trial: (1) careful follow-up with anti-VEGF treatment only for worsening DME; (2) intravitreal anti-VEGF injections; or (3) laser photocoagulation with anti-VEGF, if necessary.

iii. Central-involved DME and associated vision loss (6⁄9 or 20⁄30 or worse): intravitreal anti-VEGF treatment (e.g., with ranibizumab [Lucentis] 0.3 or 0.5mg, bevacizumab [Avastin] 1.25mg, or aflibercept [Eylea]) 2mg therapy). Treatment with aflibercept may provide the best visual outcomes over 1 year, especially in eyes with baseline visual acuity of 6⁄15 (20⁄50) or worse. However, by 2 years of therapy, ranibizumab-treated eyes achieve similar visual results to those given aflibercept. Brolucizumab is a promising new molecule for DME and real world data is slowly emerging for the use of Brolucizumab in DME.

**Laser Technique for Diabetic Macular Edema :**

i. Modified ETDRS guidelines recommends focal laser treatment of microaneurysms and grid treatment of areas of diffuse leakage and focal nonperfusion within 2DD of center of the macula. There is increasing evidence that laser for microaneurysms is not recommended and multiple re-treatments of microaneurysms can lead to heavy retinal laser burns and future laser scars and central scotomas.

ii. Laser parameters used are 50-100 μm spot size, 120-150 mW energy and very light gray intensity of the burn. Care is taken to demarcate and avoid the foveal avascular zone.

iii. If DME is associated with large areas of macular ischemia, only the areas of retinal thickening are treated.

## 5. Indications for Vitrectomy :

i. Severe vitreous hemorrhage of 3 months duration or longer that does not clear spontaneously. Earlier intervention may be warranted in low-/intermediate resource settings as the underlying PDR disease may have been previously untreated and highly advanced. In these settings it may be reasonable to perform vitrectomy in eyes with vitreous hemorrhage of 4 -6 weeks duration that has not cleared spontaneously.

ii. Advanced active proliferative DR that persists despite extensive PRP. Surgery is reasonable in eyes with recurrent episodes of vitreous haemorrhage from PDR due to persistent vessels despite PRP or mechanical traction on NV.

iii. Traction macular detachment of recent onset. Fovea-threatening or progressive macula-involving traction detachments benefit from surgical management.

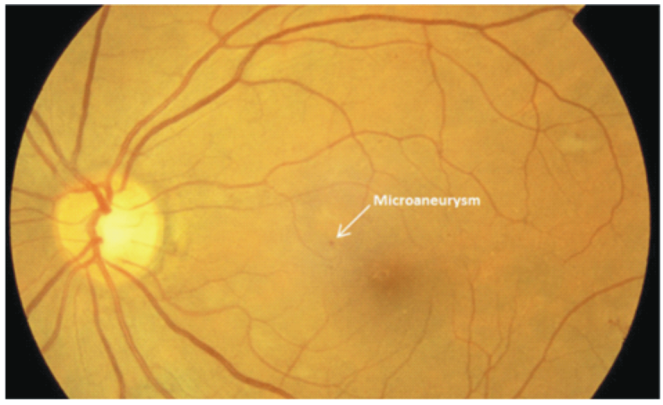


Figure 1 : Mild NPDR with microaneurysms

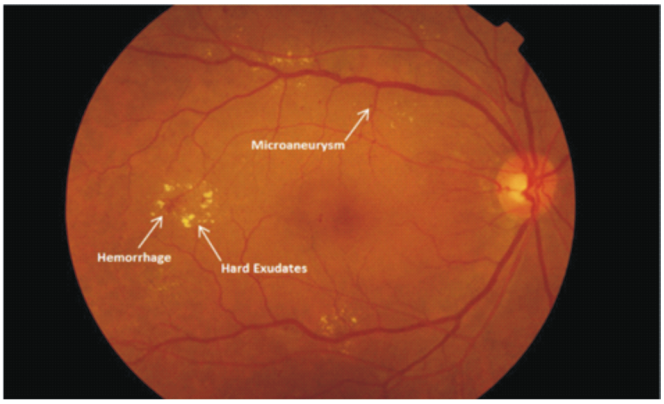


Figure 2 : Moderate non proliferative diabetic retinopathy with hard exudates

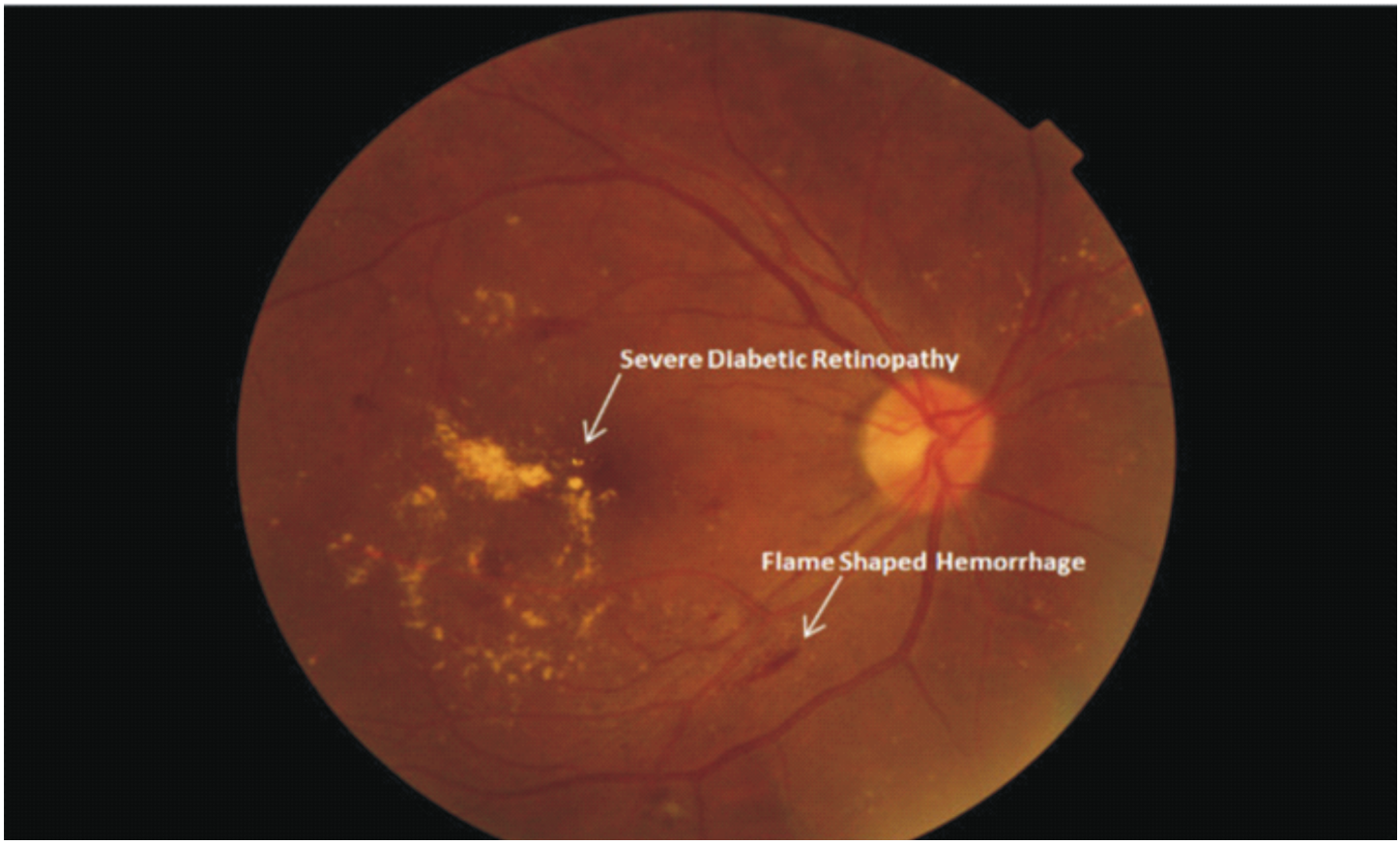


Figure 3 : Moderate NPDR with circinate maculopathy.

iv. Combined traction-rhegmatogenous retinal detachment.

Tractional macular edema or epiretinal membrane involving the macula. This includes vitreomacular traction.

## 6. Management of Cataract :

DR progresses faster after cataract surgery, so principles of management are as follows -

i. Mild cataract - carefully assess DR status. Patients without vision loss with clear fundus view may not require cataract surgery.

ii. Moderate cataract - carefully assess DR status. Attempt to treat any severe NPDR with laser PRP, and/or DME with focal/grid laser or anti-VEGF therapy, before cataract surgery. Once DR/DME is stable, consider cataract surgery to improve vision.

iii. Severe to advanced cataract with poor fundus view - if DR status cannot be adequately assessed, consider early cataract surgery followed by assessment and treatment as necessary. If DME is present, consider anti-VEGF before surgery, at the time of surgery, or after surgery if DME is discovered when the media is cleared.

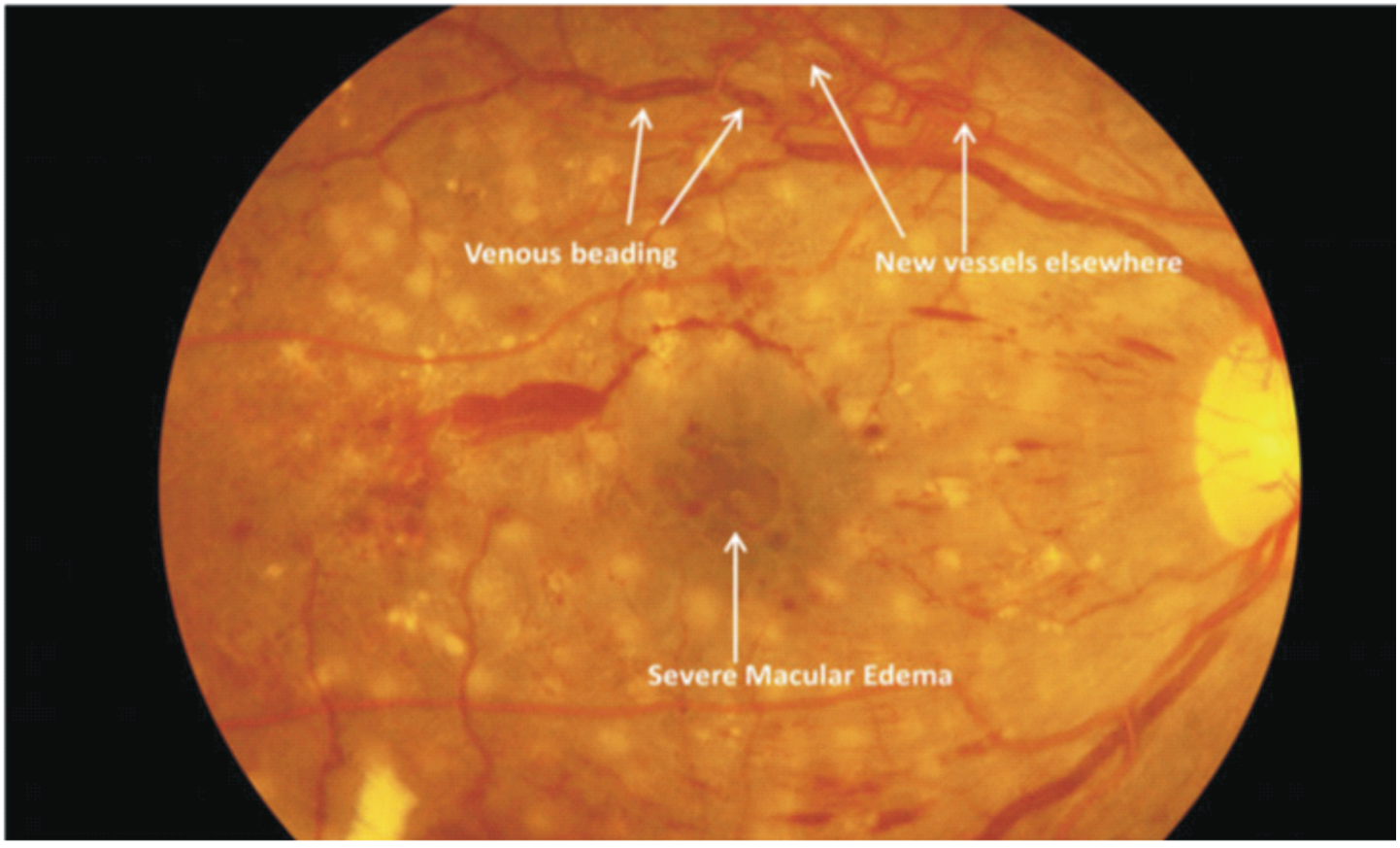


**Figure 4 : Proliferative diabetic retinopathy with venous beading, NVEs and DME**

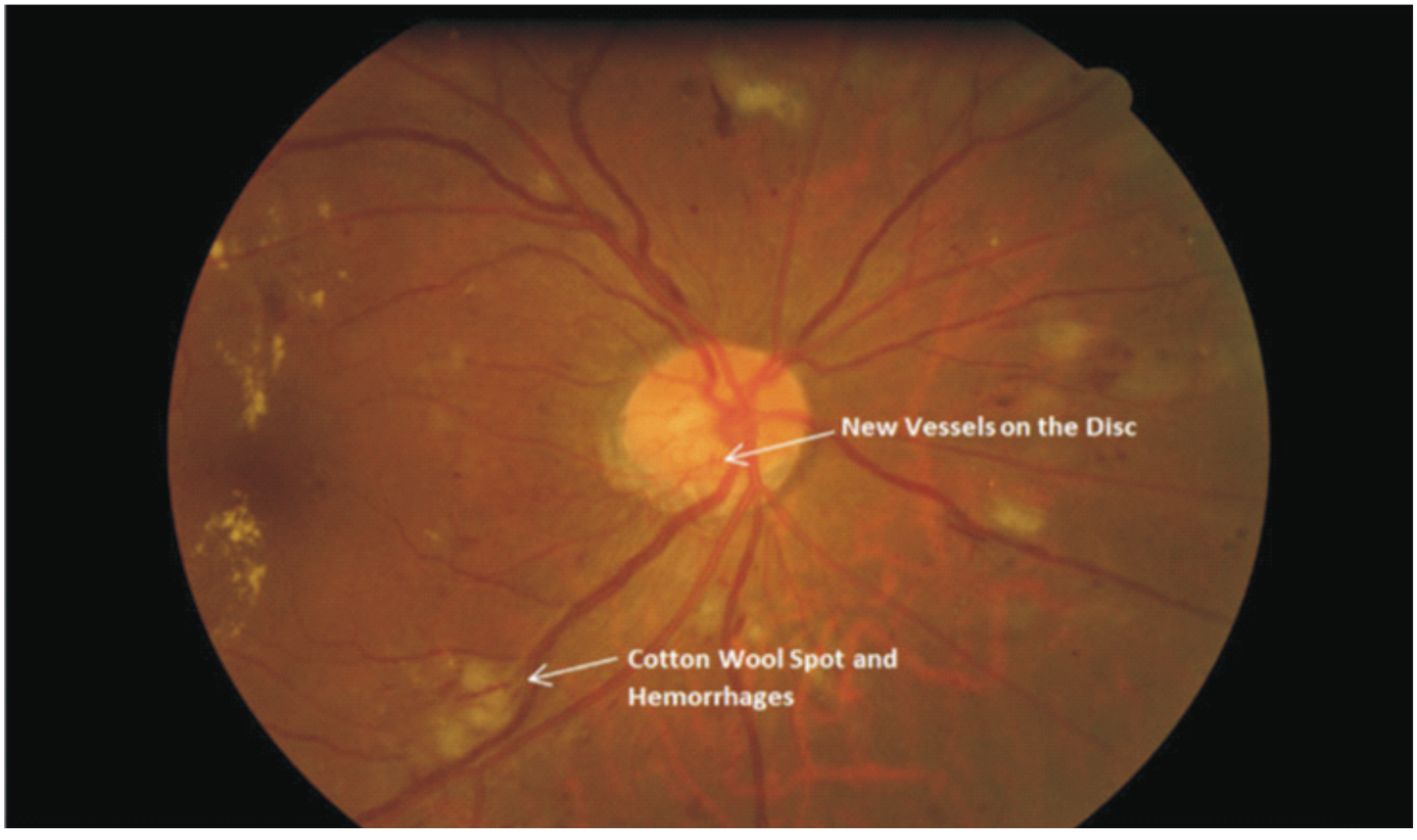


**Figure 5 : PDR with neovascularisation at the disc (NVD)**

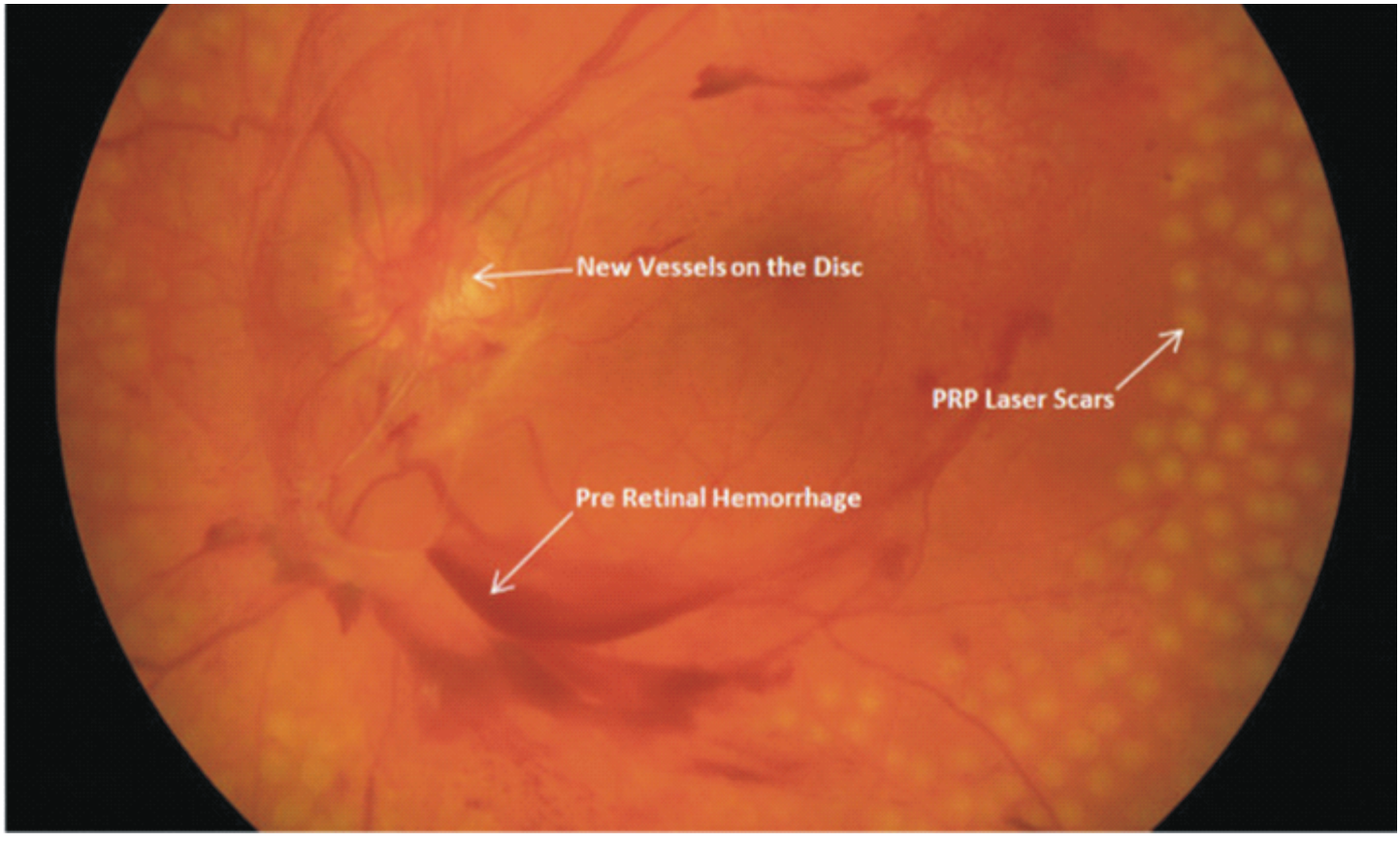


**Figure 6 : High risk PDR with fresh PRP marks**

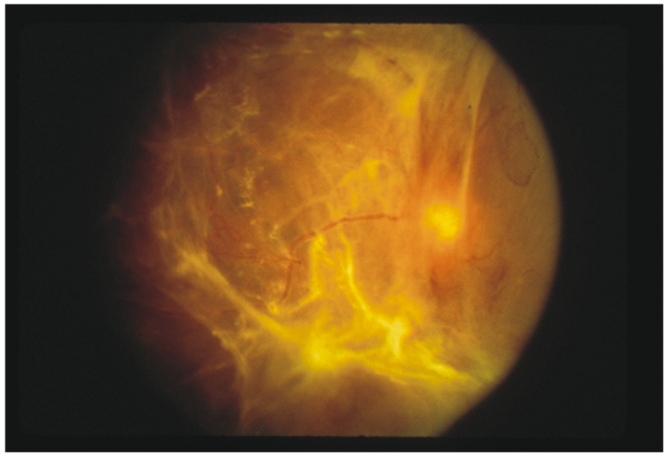

**Figure 7 : Tractional retinal detachment**

iv. In cases with PDR and operable cataract, it is most important to treat PDR first. Untreated PDR can land up in neovascular glaucoma after any intraocular surgery and lead to severe and permanent vision loss.

## 7. Conclusion :

Diabetic retinopathy is a leading cause of vision loss in the adult population. With prevalence of diabetes on the rise throughout the world, it is important to screen for diabetic retinopathy and treat vision threatening diabetic retinopathy in a timely fashion to get favourable outcomes in this disease.

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# Retinal Vein Occlusion : Recent Trends in Management

*Sonam Verma[1], Kishan B Verma[2]*

If there is one international Indian origin figure that influenced the way we understood retinal vascular disease monumentally, it was Dr SS Hayreh who ascended to heavenly abode this year. We can only imagine impact of its clinical significance by the fact that the only site in body to visualize occlusion directly and warn us of impending adverse cardiovascular events is fortunately retina. The disease being blockage of veins needs to be investigated thoroughly for:

- Prevention of recurrences and visual loss, and
- Timely detection of systemic coagulopathies thereby prevention of potentially morbid and/ or life threatening complications

In order to have best and long term effective outcome in management of any disease identification and prompt control of causative systemic and coexisting ocular conditions acts as founding stone. As for retinal vein occlusion (RVO), hypertension, cardiovascular diseases, and glaucoma are those to be watched for and well managed. Certain investigations which are a must are complete blood count with haemoglobin, lipid profile, coagulation profile, serum homocysteine, carotid Doppler ultrasound, blood urea, serum creatinine and electrocardiography alongwith urgent referral to cardiologist for simultaneous needful management.

Currently, no treatment is available to reverse retinal vein occlusions. However, all treatment is advocated in order to limit complications from RVO.

## Then what are we primarily treating in RVO and looking for ?

In RVO patients, macular oedema (MO) is the most common cause of visual loss, caused by physical destruction of the inner blood-retinal barrier due to elevated venous pressure as a result of vein occlusion at the arteriovenous crossing site. Its morphological destructive effects which better explain the loss of physiological functioning are much appreciated with the advent of ocular coherence tomography (OCT).

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## Role of OCT in RVO with MO :

The following features are prognostically useful over the course of long term follow ups and not merely on a single or first visit [1]:

1. Macular thickness and quality of internal retinal layers,
2. Changes in intraretinal cysts (size, content, location and numbers),
3. Accumulation of subretinal fluid, and
4. Photoreceptor damage

**A Step Ahead with Role of Ocular coherence tomography angiography (OCTA) in RVO with MO**

The underlying findings are more often associated with cases showing recurrences [1]:

1. Widened foveal avascular zone in superficial capillary plexus (SCP) and deep capillary plexus (DCP)
2. Perifoveal capillary ring loss in SCP and DCP
3. Hemi vascular density disparity in SCP

**The Age Old Friend: Fundus fluorescein angiography (FFA)**

The chances of developing neovascularization are as high as 80% risk with 75 to 150 disc area (DA) of non-perfusion as compared to no risk with less than one DA of non-perfusion area detected hence aids us in prognosticate and tailor our management. The use of wide-field FFA offers easier image acquisition in single view of larger area even in lesser cooperative patients and saves time spent instead in creating manual montage for visualizing capillary non-perfusion. [2]

## Evidence based guiding lights: The studies related to RVO in a gist :

Where SCORE 1 (Standard Care Vs corticosteroid for Retinal vein occlusion) conveyed to us 1 injection of preservative free triamcinolone acetonide (TA) is adequate to reduce macular oedema being safer than 4mg dose, it is however more likely associated with risks to cause rise in intraocular pressure and cataract. Hence soon alleviating worry of these two side effects, anti-vascular endothelial growth factor (anti VEGF) gained more popularity. [3]

Question remained in daily practice as to which is the best anti VEGF?....answered not very late by the SCORE 2 study which

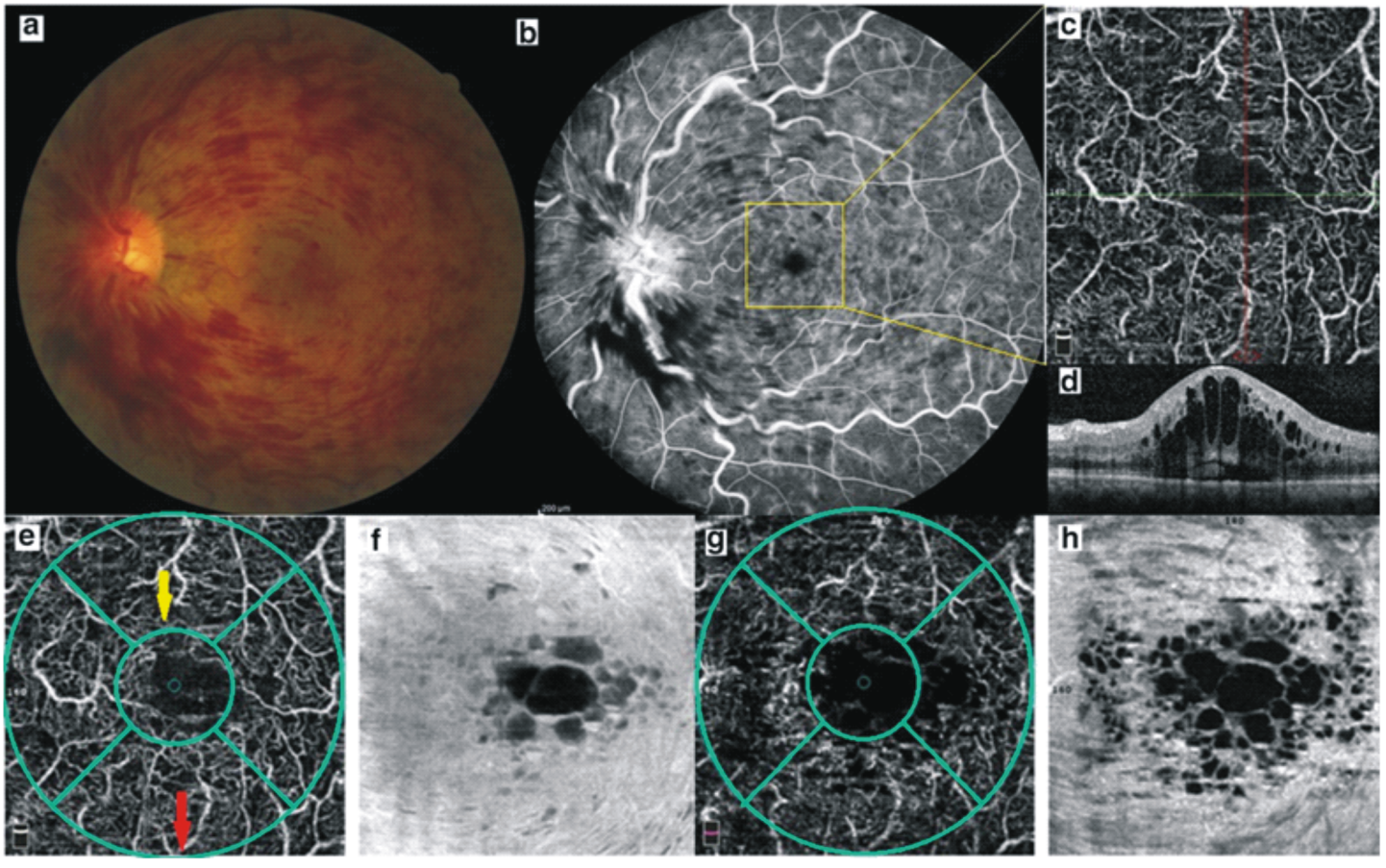


**Figure 1. A patient with central retinal vein occlusion. a Fundus photograph, b fluorescein angiography, c optical coherence tomography angiography (OCTA) in superficial capillary plexus, d cystoids macular edema is observed in optical coherence tomography (OCT). e, g Whole vascular density (larger green circle: red arrow), foveal vascular density (small green circle: yellow arrow) and parafoveal vascular density (difference between 2 circles) were calculated in superficial and deep capillary plexuses in OCTA. f, h En face OCT at the level of superficial and deep capillary plexuses showed cystoids macular edema (Image source: Khodabandeh, A., Shahraki, K., Roohipoor, R. et al. Quantitative measurement of vascular density and flow using optical coherence tomography angiography (OCTA) in patients with central retinal vein occlusion: Can OCTA help in distinguishing ischemic from non-ischemic type?. Int J Retin Vitr 2018.4, 47.**

emphasized effectiveness of treatment in terms of good visual outcome with any choice of intravitreal anti VEGFs when injected early and consistently until sufficient. This way vessel closure due to leukocytes is best checked. [4, 5]

So what becomes of those presenting late or with a chronic macular oedema secondary to retinal vein occlusion?

Risk factors for suboptimal response include:

1. older age,
2. shorter occlusion distance from the optic nerve,
3. longer pre-treatment duration, and
4. larger areas of non-perfusion

The recent upsurge in use of dexamethasone implant (DEX implant; Ozurdex, Allergan, Irvine, CA, USA) owes to its benefit of controlled continuous delivery of anti inflammatory action in single injection working over 2 to 3 months as compared to need of multiple monthly anti VEGF injections.[6] On the other hand, in comparison to intravitreal TA, implants exhibited lesser rates of cataract formation and rise in IOP.[7]

When cases are presenting late, discovered incidentally or as a result of recurrence, they are more often having inflammatory mechanism or partial perfusion area with a dilated and irregular capillary net was a source of macular edema. Hence steroid implants work better here .

**What is the take on LASER: focal, panretinal or should not?: Evidence vs. Experiential**

In the RELATE study, although it was exhibited of not much significance when given with ranibizumab in real time clinical practice once oedema is resolved many practitioners on identifying non perfusion areas on fluorescein angiography have better managed to combat another anticipated future complication of neovascularization. [8]

It is also more reasonable in cases where macular ischemia has been identified instead of giving intravitreal injections, where visual improvement has practical limits but the retina needs to be protected from complications arising from unchecked neovascularization, especially in CRVO cases. Although LASER therapy alone is not as beneficial as when given timely with anti VEGF. [9]

**The first line avengers in MO due to RVO: Anti VEGFs**

The BRAVO and CRUISE trials have been respectively prominent in proving role of ranibizumab in improvement by three lines in patients of BRVO and CRVO, although many cases may require LASER therapy as adjunct.[11, 12] Similarly aflibercept with its VEGF trap eye mechanism of action has been proven to be efficacious, safe and has shown three line gain in patients of RVO.[13, 14]

**Anti VEGF biosimilars in RVO: which one to trust?**

They give results non inferior to the main stream generic anti VEGFs and their safety and efficacy is best assessed by either FDA and/ or DCGI approval (Razumab taking the lead in being first one to get approved), add to it, confidence from own experience also.[15, 16]

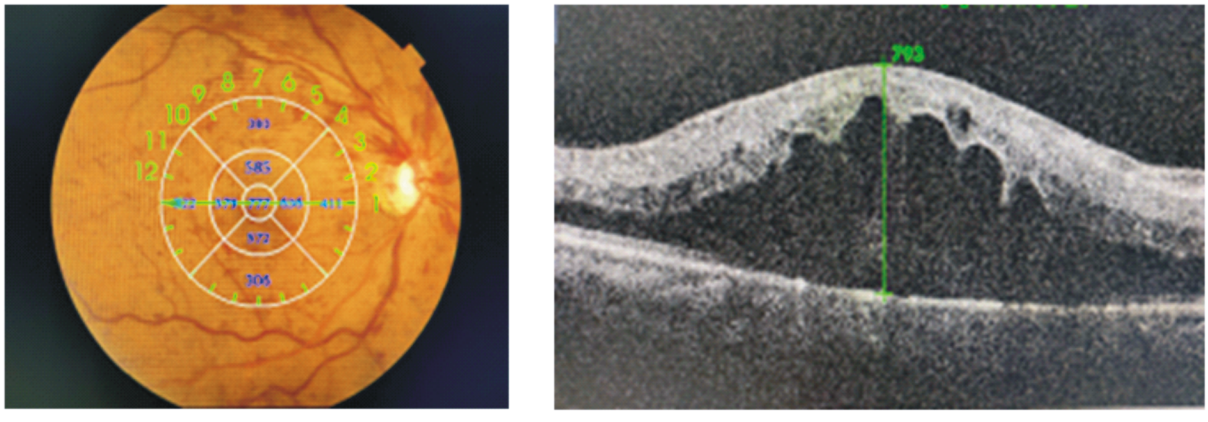


**Figure 2 (a). Clinical fundus picture and OCT of a CRVO case on presentation**

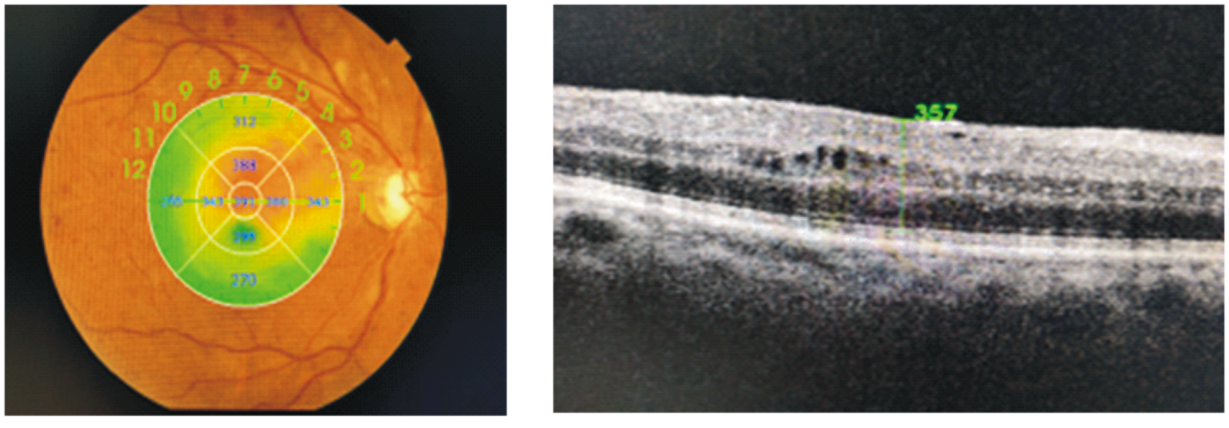


**Figure 2 (b). Clinical fundus picture and OCT of same CRVO case 1 month post intravitreal Razumab**

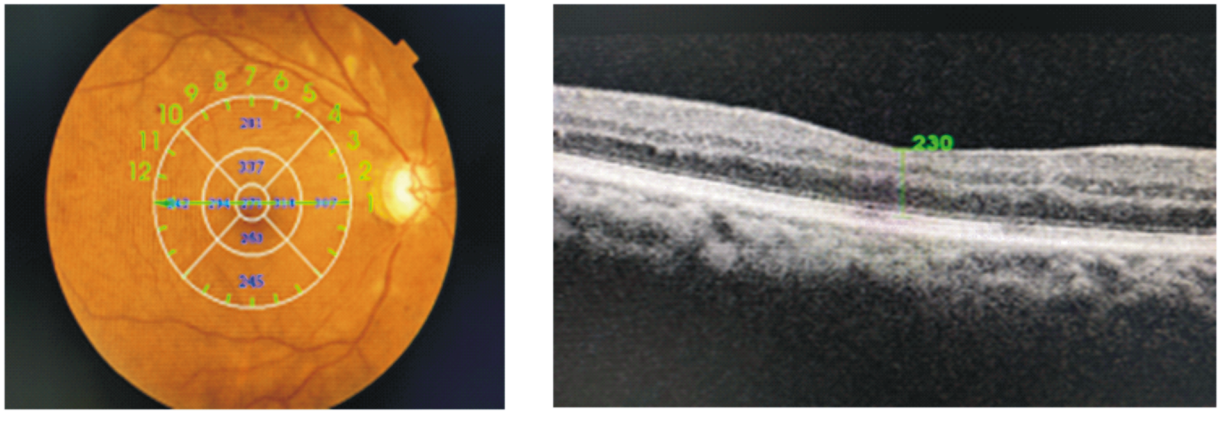


**Figure 2 (c). Clinical fundus picture and OCT of same CRVO case 1 month after second intravitreal Razumab**

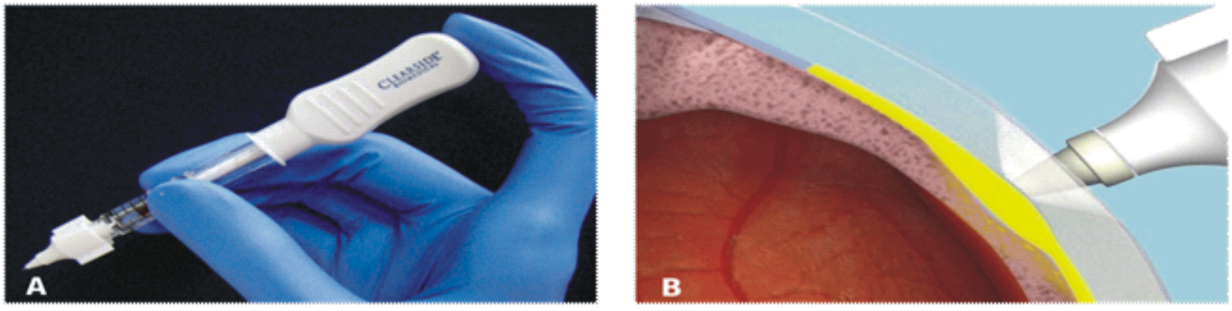


**Figure. A) Maintaining constant, firm pressure on the plunger throughout the injection is key to using the Xipere microinjector. B) Holding the Xipere microinjector needle perpendicular to the sclera, dimple down on the sclera 4 to 5 mm from the limbus. (*Images courtesy Clearside Biomedical*)**

**Figure 3**

They can be a more economic and safer option if bevacizumab's non approval or safety in using or preserving aliquots is questionable. Demonstrating a case of CRVO here in figure 2 a, b, c where Razumab (first DCGI approved biosimilar since 2015) was used.

**The newest approach of Suprachoroidal injection of Triamcinolone Acetonide**

Instead of combining the anti VEGF and steroid injections through intravitreal injections recent focus is to utilize the suprachoroidal space. It does need good precision and dexterity but by this way being in suprachoroidal space, side effect of steroid is minimized and steroid therapy remains cost effective. Through clinical trials it has been demonstrated to be well tolerated and significantly reduces the need for additional intravitreal aflibercept injections over a 3-month period in patients with RVO. This combination therapy may sustain edema resolution and improve visual outcomes.[17] In order to make this technique easier a microinjector has been launched which carries microsuspension of TA shown in the illustration (figure 3). Surgical treatments and use of newer anti VEGF like conbercept and brolucizumab are underway trials for use in RVO and are present grounds of research.

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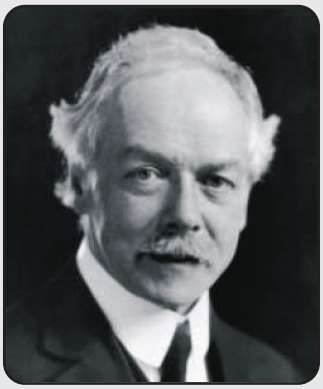

***Jules Gonin*** *1870-1935. 1913 First treatment of traumatic retinal detachment using ignipuncture procedure 1916 First treatment of idiopathic retinal detachment using ignipuncture procedure 1928 Awarded the Benoit Prize, highest scientific honor in Switzerland 1929 Received worldwide recognition at the International Ophthalmological Congress in Amsterdam 1930, 1934, 1935 Nominated for the Nobel Prize in Medicine 1934 Published his book on retinal detachment, called "Le decollement de la retine" 1938 Establishment of the Gonin medal by the University of Lausanne and Swiss Ophthalmological Society.*

# Eales Disease

*Vineet Mutha*

## Introduction :

Eales disease was first described in 1880 by Sir Henry Eales as a spectrum of recurrent vitreous hemorrhage along with headache, constipation and epistaxis. Wardsworth, in 1887 found the cause of recurrent vitreous hemorrhage to be retinal inflammation and vasculitis. It most commonly affects young males and Asian population, mostly Indian subcontinent. Association with Tuberculosis is controversial and some clinicians prefer giving anti- Tubercular regimen along with eye treatment. Eales disease is considered to be an immunological reaction to an exogenous antigen. Treatment mainly involves Steroids and retinal laser, and if diagnosed early, prognosis is very good.

## Epidemiology :

Eales disease is usually seen in young males most commonly affecting 20-40 years age group. It is rarely seen in western world and 90% of disease load is in Asian population, most commonly affecting Indian subcontinent. Disease is usually bilateral and asymmetric presentation is not uncommon. Rarely disease has been reported in females as well as paediatric population.

## Etiology :

The causative factors of Eales disease are poorly understood and controversial. Many theories have been proposed for the same but predominantly etiology of Eales disease is considered multifactorial. Most often, etiology of Eales is linked with Tuberculosis, atypical mycobacteria or their hypersensitivity (Table 1).

## Pathogenesis and Classification :

Eales vasculitis involves inflammation of mid peripheral retinal veins resulting in perivascular infiltrates which manifest as sheathing of blood vessels. This periphlebitis in turn leads to obliteration of vessel lumen which causes ischemia in the retinal area perfused by the latter. Ischemia leads to increased secretion of VEGF which causes neovascularisation. All types

**Table 1 - Etiology of Eales disease and literature evidence.**

| | Possible associations of Eales | Supporting literature |
|---|---|---|
| 1 | Idiopathic | Most commonly patients have no underlying cause |
| 2 | Mycobacterium chelonae and M. fortuitum | -M. fortuitum was found in aqueous of patient with Eales<br>-DNA of both species were found in ERM of patients with Eales on semi nested polymerase chain reaction |
| 3 | M. tuberculosis | -Gene MPT64 and MPB64 was found on PCR of vitreous sample in patients with Eales<br>-M. tuberculosis was found in ERM of Eales patients<br>-M. tuberculosis was found in nested PCR testing of enucleated eyes in patients with history of Eales<br>-Few patients were found to have signs of Ocular TB such as choroidal tuberculoma years after primary diagnosis of Eales<br>*Mantoux positivity does not have higher prevalence in patients with Eales |
| 4 | Immunological mechanisms | -T cells<br>-HLA B5, DR1, DR4<br>-Combination of Haptoglobin, Complement C3 and Galectin-1 can be considered as a biomarker for Eales disease<br>-Vascular endothelial growth factor (VEGF), platelet- derived growth factor (PDGF), insulin-like growth factor (IGF), epidermal growth factor (EGF), transforming growth factor (TGF) and urokinase may be involved in neovascularization of eye |

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*Medical Director - ASG Eye Hospital, Indore*

of neovascularisation can occur in Eales disease out of which neovascularisation elsewhere (NVE) is the most common followed by Neovascularisation in and around one disc diameter of optic nerve (NVD) and rarely neovascularisation of iris (NVI) and angle (NVA) occurs in advanced and untreated cases. These new vessel walls are weak and result in recurrent hemorrhages, which must be treated as early as possible in today's era. Based on this, stages of Eales disease was classified by Charmis et al. (old classification) and Saxena and Kumar et al. (new classification).

| Eales disease was classified by Charmis into the following stages (Not followed now) | |
|---|---|
| Stage I | Mild periphlebitis - Peripheral small retinal capillaries are affected. |
| Stage II | Large veins are inflamed. |
| Stage III | Neovascularisation with vitreous and retinal hemorrhages. |
| Stage IV | Tractional retinal detachment |

| Eales classification by Saxena and Kumar | |
|---|---|
| Stage 1a | Superficial retinal hemorrhages with inflammation of small calibre vessels |
| Stage 1b | Superficial retinal hemorrhages with inflammation of large calibre vessels |
| Stage 2a | Capillary non perfusion (leading to ischemia) |
| Stage 2b | Neovascularisation of disc/elsewhere |
| Stage 3a | Fibrovascular proliferation |
| Stage 3b | Vitreous hemorrhage |
| Stage 4a | Tractional or secondary rhegmatogenous retinal detachment |
| Stage 4b | Neovascularisation of iris, neovascular glaucoma, complicated cataract or optic atrophy |

## Clinical Examination :

Initially in the disease process patient may be asymptomatic for months. Usually the first symptoms of Eales disease are floaters and painless diminution of vision with a usual presenting visual acuity of 6/12 (20/40) or better. In patients with macular edema or vitreous hemorrhage visual acuity ranges from 20/40 to hand movement close to face with accurate projection of rays. No light perception may develop in patients with extensive TRD or optic atrophy or neovascular glaucoma corresponding to Stage 4b of Saxena and Kumar classification.

On examination, anterior uveitis is less common and even if present, despite association with tuberculosis, is generally non granulomatous. Granulomatous uveitis should prompt to think of other differentials like Sarcoidosis or Tuberculosis. Neovascularisation of iris and angle are found in late disease stages. Synechia are less common in patients with Eales disease. Posterior subcapsular cataract may be present in patients with recurrent episodes of vitreous hemorrhage. Retrolental cells may be present but retrolental RBC and pigments are more common, thus must be carefully examined.

Retinal inflammation is characterised by periphlebitis (84% patients) of mid peripheral veins which appears as venous cuffing (fluffy yellow exudates around vein Figure 1) in activestage while pigmentation around veins, venous sheathing (Figure 2) and vascular anastomosis are seen in healed vasculitis. If similar picture is seen in veins at posterior pole, another differential or disease process should be considered.

If untreated or not spontaneously resolved, stage of ischemia follows, leading to capillary non perfusion areas with vascular anastomosis. There may be cystoid macular edema during this phase as VEGF levels are high due to ischemia. Stage of proliferation signifies development of neovascularisation (occurs in 80% patients with Eales disease) leading to vitreous hemorrhage (34% patients) (Figure 3, 4). Tractional retinal detachment, secondary rhegmatogenous retinal detachment, optic atrophy and neovascular glaucoma are of rare occurrence. Healed chorioretinitis patches are present in few patients with Eales disease usually those associated with tuberculosis.

## Ocular investigations :

Fundus fluorescein angiography (FFA) is the gold standard investigation for diagnosing Eales vasculitis at an early stage. Early venous phase shows staining of vessel wall due to sheathing while late phase may show leakage due to inflammation. Inflammation leads to increase in gap junctions on the vessel endothelium. In the stage of ischemia, large areas of capillary non perfusion are visible starting from equatorial region to periphery of retina. Vascular shunts may

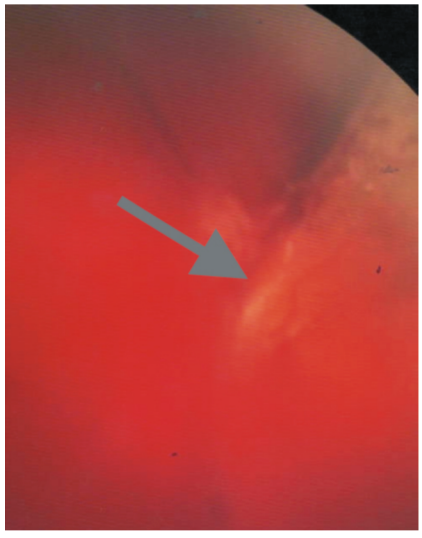

Figure 1 - Perivenous exudates (cuffing) with vitreous haemorrhage

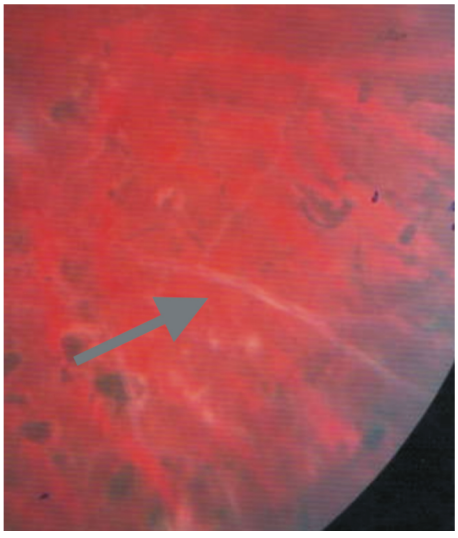

Figure 2 - Healed lasered vasculitis with perivenous sheathing

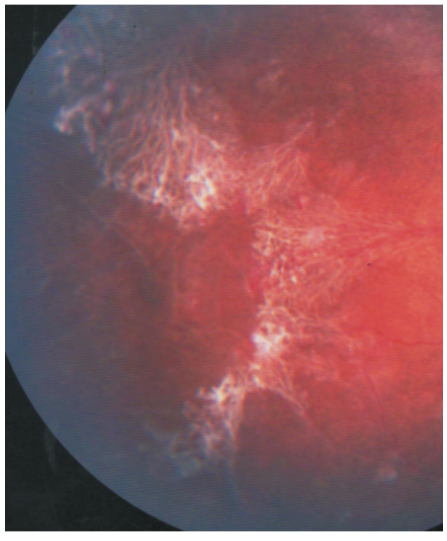

Figure 3 - Neovascularisation at mid peripheral retina

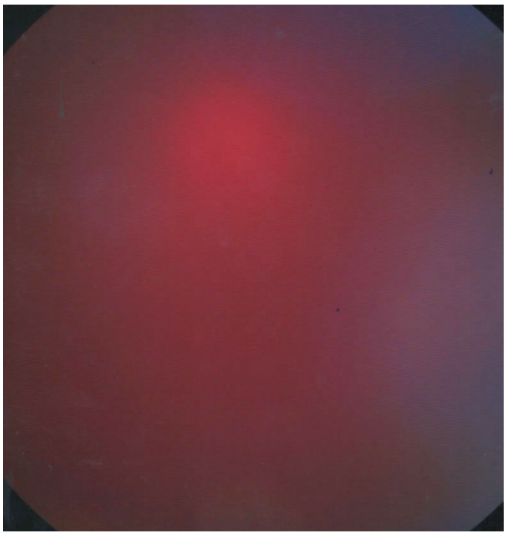

Figure 4 - Vitreous haemorrhage obscuring fundus visualisation

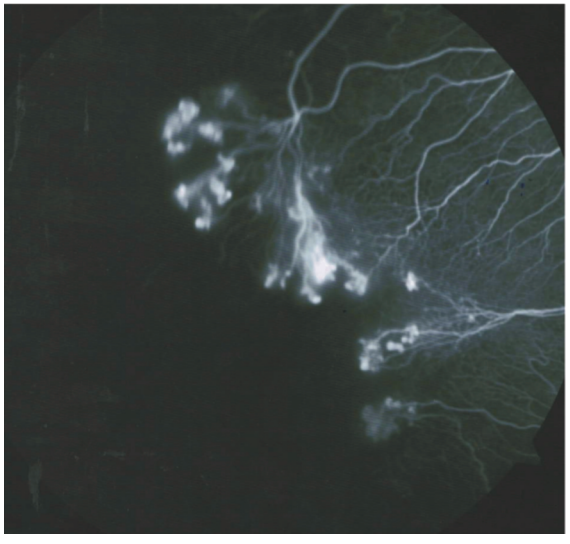

Figure 5 - Fundus fluorescein angiography showing leakage and capillary non perfusion areas

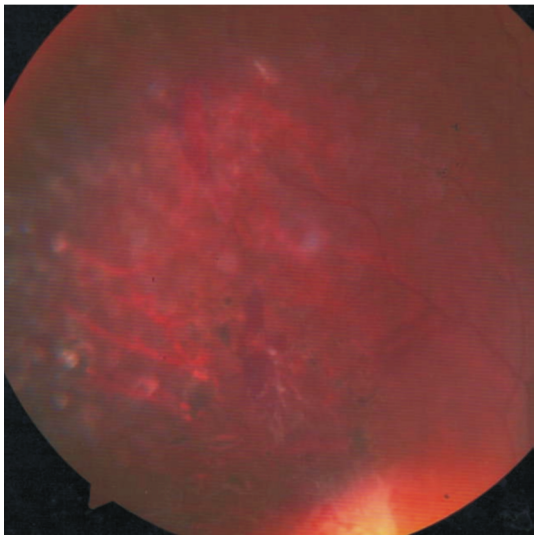

Figure 6 - Rebleeding in previously lasered areas

also be visible in this stage. Cystoid macular edema leads to petalloid leakage in the foveal avascular zone. In proliferative stage, there are multiple areas of neovascularisation with leakage usually at equatorial region. There can be areas of blocked fluorescence corresponding to areas of vitreous hemorrhage. In patients with extensive hemorrhage in one eye should also be advised angiography to look for capillary non perfusion areas and neovascularisation in the fellow eye. In patients with chorioretinal scarring, window defect may be visible. In scenario of Eales disease, ultra wide field angiography (UWF) is of special consideration. It provides picture of more than 80% retina in one go if properly performed thus better capturing capillary non perfusion areas and peripheral neovascularisation. This can also assist in targeted laser photocoagulation of the affected areas. (Figure 5)

**B scan (Ultrasonography)** is a must in cases of vitreous hemorrhage obscuring fundus view. In cases on going observation for resolving vitreous hemorrhage, retina as well as vitreoretinal interface changes can be easily picked up on USG. In such patients, serial ultrasonography two weekly is advisable. If retinal detachment is present, then immediate surgical intervention should be considered for the same.

**Optical coherence tomography (OCT)** must be advised in cases of macular edema or epiretinal membranes, which may be present although rare. Also OCT retina may pick up neurosensory detachment, pachychoroid or intraretinal or subretinal septae etc. which aid in considering other differentials.Among other ocular investigations, serial fundus photographs should be considered and in patients with elevated IOP Ultrasound biomicroscopy and/or gonioscopy should be done to rule out NVA.

**Laboratory Investigations -** Purpose of laboratory testing is to confirm associated diagnosis like tuberculosis or its hypersensitivity. Complete blood count, erythrocyte sedimentation rate, C- reactive protein, Mantoux test, Chest X Ray or HRCT chest must be done. Accessory investigations to rule out TB are IGRA (Interferon gamma release assay) or Quantiferon TB gold test.

## Differential Diagnosis :

All causes of vitreous hemorrhage and neovascularisation in young patients become the differentials of Eales disease. Most common differentials are other causes of inflammatory vasculitis preferentially involving veins such as Bechet disease, sarcoidosis, multiple sclerosis and pars planitis. Infectious vasculitis due to syphilis, tuberculosis, HIV and cytomegalovirus retinitis may have similar presentation. Causes of proliferative retinopathy such as Diabetic retinopathy (type 1 diabetics fall into similar age groups), retinal vein occlusion in young and rarely sickle cell retinopathy and radiation retinopathy may have similar clinical presentation. Rare diseases which should be kept in mind are frosted branch angitis, familial exudative vitreoretinopathy, coat's disease and leukemia.

## Management and Treatment :

Best suited treatment modality is based on the presentation of Eales disease. As the disease is usually asymptomatic in early phase, patients present to hospital at the stage of vitreous hemorrhage with slight diminution of vision and floaters. Fellow eye may be asymptomatic. Thus, it is very important to examine fellow eye in such cases.

**1) Observation :** In cases of resolving vitreous hemorrhages with inactive disease suggested by no active perivenous cuffing, no retrolental cells and old pigmentary changes, observation is the preferred modality. If disease worsens then active treatment can be done with steroids and laser photocoagulation. After partial resolution of hemorrhage, angiography can be performed for further treatment plan.

**2) Steroid (Mainstay of treatment in inflammatory stage) :** In cases of active inflammatory stage, steroids remain the gold standard of treatment. If bilateral perivascular cuffing is present, then oral steroids (1 mg per kg body weight) can be considered in tapering dose. In unilateral cases or in cases with cystoid macular edema, posterior sub tenon triamcinolone acetonide or intraocular dexamethasone implant can be considered with explained risks of cataract and glaucoma, which is although minimal but must be discussed prior. If extensive inflammation is present bilaterally, then even initial intravenous pulse steroids for 3 days can be given. Inpatients who have undergone long term steroid treatment or those with adverse effects related to steroid use can be given immunosuppressants like azathioprine (50 mg twice or thrice daily for 6 months atleast) or methotrexate (10-15 microgram once per week with folic acid alternate days). Immuno-suppressants must be cautiously given with appropriate lab testing prior and during the course of therapy monthly or bimonthly.

**3) Laser Photocoagulation (Mainstay of treatment in proliferative stage) :** Double frequency Nd:YAG laser (green laser) must be considered in cases of ischemia and neovascularisation. Active inflammation should be ruled out prior to laser and if present, steroids should be given prior for at least a week or two. If macular edema is present than it should be treated first as laser may increase macular edema. Pan retinal photocoagulation (done in 3 sittings) is done in cases of neovascularisation of optic disc and neovascularisation of iris or angle. Sectoral laser or angiography guided laser is done in cases of capillary non perfusion areas or

neovascularisation elsewhere. In cases of vitreous haemorrhage, laser photocoagulation is done in visible areas of funds which can be augmented as haemorrhage starts clearing. Further sittings of retinal laser may be required later on if recurrent vitreous haemorrhage or recurrent neovascularisation occurs (Figure 6).

**4) Surgery :** Pars plana vitrectomy is done in patients with

a) Non resolving vitreous hemorrhage for 4 to 6 weeks. These days due to advances in retina surgeries, early intervention can also be considered if there is no active inflammation.

b) Tractional retinal detachment involving or threatening fovea and secondary rhegmatogenous retinal detachment.

c) Extensive vitreous membranes or vitreous opacities, epiretinal membrane leading to diminution of vision or metamorphopsia.

d) Ghost cell glaucoma.

Surgical results are considered better than that of diabetic retinopathy and other proliferative retinopathies.

**5) Other treatment modalities :** Association of Eales disease with tuberculosis is controversial so is the addition of Anti tubercular treatment (ATT) to the ongoing treatment regimen. In cases of positive findings on HRCT or chest X ray and positive lab tests such as Quantiferon gold or Interferon gamma release assay, ATT can be started. In doubtful scenarios, physician consultation can be sought. Intravitreal anti VEGF injections can be considered in ischemic stage with cystoid macular edema and early proliferative stage with neovascularisation. Any traction in retina should be ruled out before treatment with anti VEGFs as they may increase the same. Role ofvitamin C and serratiopeptidase is controversial. Anterior retinal Cryotherapy can be considered in cases with neovascular glaucoma not responding with anti VEGF and laser photocoagulation.

**Prognosis :** If treatment is done earlier in the disease process, the prognosis is very good and patients can achieve near normal visual acuity. In patients who have received long term oral steroid treatment may develop systemic side effects such as moon face, osteoporosis, peptic ulcer, obesity, impaired glucose tolerance or diabetes and/or hypertension. Patients who underwent intraocular or periocular steroid treatment may develop cataract or glaucoma, which must be discussed with patient prior. If untreated, disease may worsen and may lead to sequelae such as neovascular glaucoma and tractional retinal detachment which carry a worse prognosis.

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# Pathogenesis and Management of Macular Hole : Review of Current Advances

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## INTRODUCTION :

Macular hole (MH) is a vitreoretinal interface disease characterized by a partial or full-thickness neurosensory retinal defect in the center of the macula. The diagnosis and treatment plan has been dramatically changed in the last two decades. A new classification system based on morphology and vitreoretinal interface pathology has convincingly revealed the pathways related to the formation of a macular hole.[1] Due to central foveal involvement, metamorphopsia and visual deprivation are the common presenting symptoms that may be reversible after successful anatomical closure following surgery. Full thickness macular hole(FTMH) have a prevalence rate of 0.02 % to 0.33% with 5% to 20% nonsimultaneous bilateral involvement.[2]

FTMHs are classified as either primary or secondary. The majority of FTMHs are primary also known as idiopathic macular hole, resulting from vitreomacular traction (VMT). Risk factors associated with primary FTMH are female gender and older age . Secondary MHs are caused by other pathologic conditions, such as trauma, high myopia, macular schisis, macular telangiectasia Type 2, occlusion of the central retinal vein, diabetic macular edema, uveitis, and age-related macular degeneration.

## PATHOPHYSIOLOGY :

**a) Vitreomacular Traction :** Vitreomacular traction has long been suspected to be a cause of MH formation, but until the advent of OCT it was difficult to visualize the vitreofoveal interface routinely. In 1952, Grignolo et al provided histologic evidence of strong vitreomacular adherence to the fovea. Later on anteroposterior traction of vitreous fibers on the fovea found to be major factor involved in the formation of MH.

**b) Contraction of the Premacular Vitreous Cortex :** In 1988, Gass revised the biomicroscopic description of MH and proposed a new interpretation of the role of the vitreous in the pathogenesis of MH.[3] He also proposed a MH staging system, from impending to FTMH. Gass suggested that the tangential contraction of the prefoveal posterior hyaloid membrane resulted in the detachment of the central photoreceptors and then opening of the fovea.

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**c) Foveal Cyst :** The existence of a foveal cyst in the fellow eye of an eye with MH was shown histologically by Kornzweig and Feldstein in 1950.[4] later on Ocular Coherence Tomography (OCT) for the first time showed, the vitreous cortex attached to the roof of a foveal cyst. The foveal cyst appeared then to be an initial change in the foveal structure that predisposes to the risk of progression to MH.

**d) Stages of Posterior Vitreous Detachment :** The process of posterior vitreous detachment (PVD) is not yet clear, but its understanding has progressed immensely because of OCT. OCT studies and ultrasonographic observations established that in normal individuals, the process of PVD starts gradually at the posterior pole, around the fovea, and it occurs relatively early in life, long before detachment of the Weiss ring . The attachments of the posterior hyaloid to the foveal center and optic disc are the last to be released.

## CLASSIFICATION :

Four Clinical stages of Macular Hole have been described by Gass.3 These are :

1. **Stage 1a : (Impending Hole):** 100- 200-micron, foveolar detachment- Yellow Spot
2. **Stage 1b : (Occult Hole):** 200-300-micron, foveal detachment- Yellow Ring
3. **Stage 2 :** Small full-thickness macular hole less than 400 micron
4. **Stage 3 :** Full-thickness macular hole more than 400 microns with or without an operculum. No Posterior Vitreous Detachment (PVD)
5. **Stage 4 :** Full-thickness macular hole with complete PVD. May be associated with anterior displacement of pseudo-operculum.

**The International Vitreomacular Traction Study Classification System (IVTS) -** Classification for Vitreomacular Adhesion, Traction, and Macular Hole (5)

- Vitreomacular adhesion (VMA) - Size: focal (<1500 ìm) or broad (>1500 ìm), isolated or concurrent
- Vitreomacular traction (VMT) - Size: focal (<1500 ìm) or broad (>1500 ìm), isolated or concurrent
- Full-thickness macular hole Size - small (<250 ìm), medium (>250-400 ìm), or large (>400 ìm) Status of vitreous: with or without VMT, Cause- primary or secondary

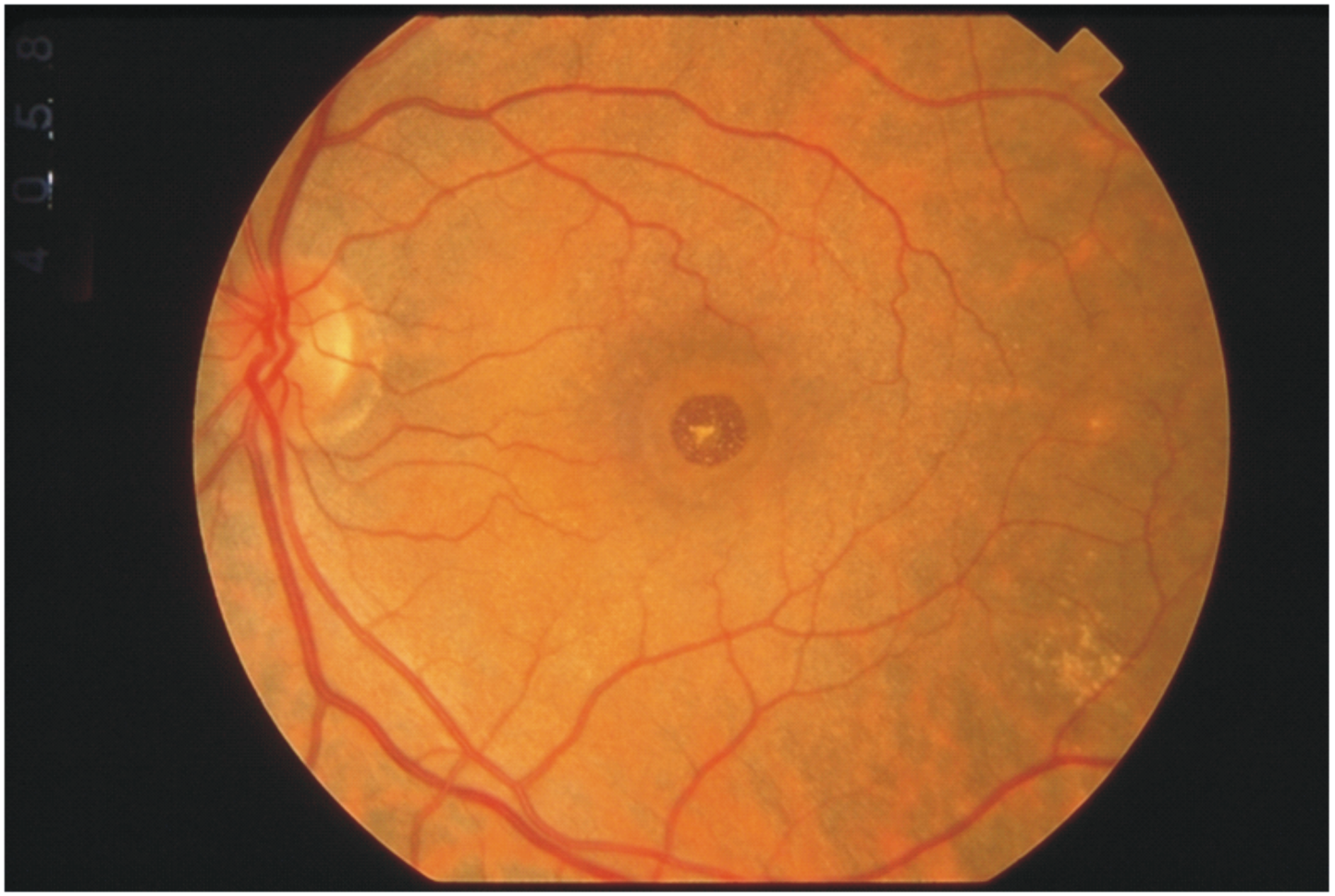

**Figure 1 : Medium size full thickness macular hole with cuff of subretinal fluid and hyper reflective yellow spots at its base**

**Ocular Coherence Tomography (OCT) IMAGING :**

OCT is the current gold standard for the diagnosis, staging, and monitoring of FTMH. Swept-Source Ocular Coherence Tomography (SSOCT) gives a high-resolution image of vitreoretinal interface, neurosensory retina and retinal pigment epithelium (RPE). This helps to identify surrounding epiretinal membrane (ERM), cuff of fluid, vitreo-foveal adhesion, operculum or pseudo-operculum, and status of RPE. It also allows calculation of various macular hole indices that have a role in prognosis.

OCT based macular hole classification -

**Grade 0 macular hole -** Vitreous separation on OCT but with persistent attachment to the fovea. Grade 0 is present in 29% of the contralateral eyes of patients with macular holes. 46% of eyes with Grade 0 progress to macular hole at 2 years compared with 6% in those with no vitreous attachments.

**Grade 1 hole -** The posterior hyaloid pulls on the fovea causes an intraretinal cyst.

**Grade 2 hole -** The retina ruptures produces a small full-thickness hole often with the vitreous still attached to one edge which causes an eccentric opening of the roof of the hole by traction from the posterior hyaloid [6].

**Grade 3 hole -** the vitreous is often separated (but too close to the retina to see biomicroscopically) while the hole gets enlarge. Two different types of opercula have been described in stage 3 full-thickness macular hole.[6]

1. Pseudo-opercula (61%) - contains only glial tissue (Müller cells and fibrous astrocytes). Anatomical closure rates were better compared to true opercula, but visual outcomes were similar once the macular hole closed, though chances of a final vision of at least 20/40 were higher in the pseudo-opercula group.
2. True opercula (39%) - contains both glial tissue and neural tissue (cones) due to avulsion of neuroretinal tissue from full-thickness foveal tear. This also suggests that direct foveal traction has a role in the pathogenesis of macular holes.

With OCT imaging many macular hole indices has been proposed based on both the MH diameter and the status of the vitreous attachment at the hole edge.

- The minimum linear diameter is measured at the narrowest hole point in the mid-retina, using the OCT caliper function, as a line parallel to the retinal pigment epithelium.. It is used in FTMH staging and prognostic for anatomical success after surgery. (7)
- Another prognostic FTMH feature is base diameter which is defined as the distance between two retinal edges at the level of RPE.
- Both base diameter and minimum linear diameter are negatively correlated with postoperative visual outcomes

quadrants of the fundus. Use of preservative free triamcinolone has been demonstrated to be safe and effective for improving visualization during PPV with or without membrane removal.[9]

**Chromovitrectomy -**

The use of dyes to stain the ERM and internal limiting membrane (ILM), also known as "chromovitrectomy," has made the peeling of the retinal surface more precise, more complete, and less traumatic. Indocyanine green (ICG) was introduced by in 2000 for ILM staining and is still widely used,

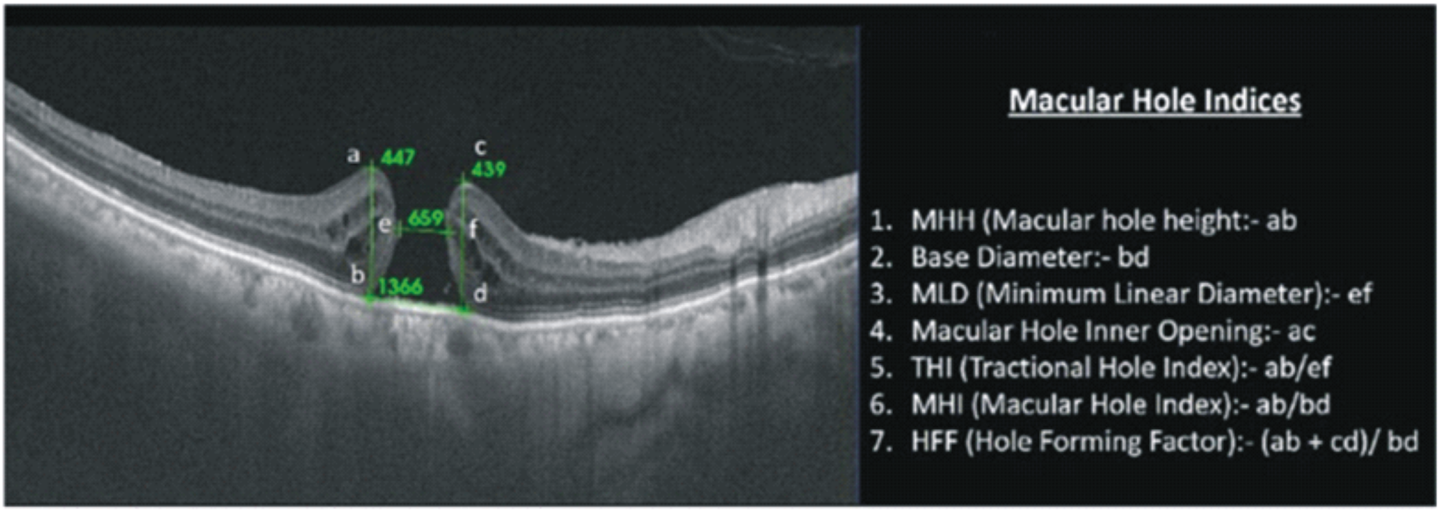


**Figure 2 : Macular hole indices**

## TREATMENT :

Kelly and Wendel[8] first initiated successful surgery for MH and reported their results for 52 cases in 1990. Their success rate was 58% with a technique combining extensive vitrectomy, detachment of the posterior vitreous cortex, peeling of any epiretinal membrane (ERM) around the hole, thorough fluid gas exchange, and postoperative face-down positioning. This formed the basic concept of Macular hole surgery. Various modifications have been made to this and are associated with improved anatomical and visual outcomes.

**Posterior Hyaloid Detachment :**

Detachment of the posterior hyaloid (PH) is a crucial step in MH with vitreo-macular traction (VMT) in which the vitreous still adheres to the hole edge and optic disc, but also in MH in which the vitreous still adheres to the optic disc. The 23/25/27-G vitreous probes, with an aspirating port that is narrower and closer to the tip of the probe, are very effective for firm aspiration and detachment of the posterior hyaloids. Preoperative OCT helps in detecting the exact location of attachment of vitreous to retina. Direct aspiration of the vitreous fibers attached to the Weiss ring appears to be the most effective way of lifting the vitreous cortex en bloc and gradually extending its detachment to the equator in all the

despite concern in some quarters regarding its safety.(10) It can be used at the minimal concentrations of 0.025 to 0.05% (0.250.5 mg/mL) and for a short exposure time when other dyes cannot be used. Trypan blue (TB) stains the ERM well but the ILM poorly. Trypan blue ophthalmic solution 0.15% (is commonly used to help visualize the epiretinal membrane and assist in peeling the internal limiting membrane.[11] In most studies, TB showed no signs of toxicity to the RPE or neuronal tissue. Brilliant blue (BBG) has a selective affinity for the ILM and gives a good staining in an iso-osmolar solution of 0.25 mg/mL (0.025%). The staining occurs after a brief contact with the dye injected onto the retinal surface. Schumann et al[12] have reported that the damage caused to Müller cells during the mechanical peeling of the ILM is significantly lesser in BBG-stained specimens as opposed to ILMs stained with ICG.

Acid violet is a recently introduced dye for use in MH surgery. Since this dye is specific to ILM, it gives superior staining and better contrast when compared to BBG.Further studies need to be done to establish its safety.

## Internal Limiting Membrane Peeling :

ILM peeling as a method of improving the MH closure rate was first described by Eckardt et al in 1997. ILM peeling is supposed to relieve the tangential traction. Pinch technique by using the

end gripping forceps or needle method to create a rip in ILM or diamond duster to create a tear in ILM are the methods used for ILM peeling. The ILM is then peeled off in a circular movement, thus creating a "maculorrhexis." The optimal size of the peeling area is still controversial. It is recommended to keep the size of peel to as minimum as possible, just enough to relieve the tangential traction around the hole and maximize the functional outcome without compromising the anatomical success rate of surgery for idiopathic MH repair. Modi et al[13] studied significant improvement in visual acuity in smaller peel group better than in larger peel group. While small MH can be operated without ILM peeling with a good success rate, ILM peeling techniques are modified for improving the success rate of larger macular holes.[14]

**Role of microscope integrated optical coherence tomography (Mi-OCT) :**

Mi-OCT is a useful intraoperative adjunct in MH surgery. Mi-OCT gives high resolution, real time imaging of ILM peeling. This has a specific role in cases where visualization of ILM is difficult. Mi-OCT also allows visualization in thinned out retina, and thereby helps guide ILM peeling to avoid intra-op break formation. It also helps in identification of residual ILM, epiretinal membrane (ERM), and adequacy of inverted ILM flaps .[15]

## Problems with ILM Peeling :

Recent studies have found that ILM peeling is associated with mechanical trauma to retinal nerve fibre layer (RNFL). Direct mechanical damage to retina while grasping the ILM and damage to Muller cell endplates that are attached to ILM during ILM peel leads to swelling of arcuate nerve fibre layer which can be seen as hyperreflective swelling on SSOCT. Some patients develop small spindle shaped splitting of nerve fibre layer in ILM adjacent to peeled edge. This is known as dissociated Outer nerve fibre layer (DONFL).[16] Tadayoni[17] made an interesting observations that ILM peeling reduces retinal sensitivity, and increases the incidence of microscotomas and went on to suggest that it is justified to avoid peeling the ILM when its potential benefit seems unproven, and when and if peeling is performed, we should limit the surface peeled to the minimum. Internal limiting membrane peel is associated with significant alteration in inner retinal architecture, especially in ganglion cell layer, which can adversely influence functional outcome of the surgery.

## Modifications of ILM peeling :

**1) Inverted ILM flap technique :** In 2010, Michalewska et al [18] introduced the inverted flap technique, thus providing a new surgical approach for ILM peeling. They reported a 98% closure rate of large macular holes (defined as > 400 μm) compared to conventional ILM peeling (88%).

In this technique, after core vitrectomy and dye staining, the ILM is not completely removed from the retina but is left in place, attached to the edges of the MH. This ILM remnant is then inverted to cover and fill the MH. Finally, fluid-air exchange is performed. The authors have found the inverted ILM flap technique to be a safe and successful procedure for treating large idiopathic full thickness MHs and myopic MHs. The inverted ILM, containing Müller cell fragments, may induce glial cell proliferation, filling the MH and supporting MH closure. It may also work as a scaffold for tissue proliferation, creating a microenvironment that encourages correct photoreceptor positioning and finally improving postoperative anatomic and functional outcome. Peel can be done in one or two flaps. A very tiny amount of viscoelastic material on top of the flaps to anchor them in place, can be used. The tip of the flute at the lower boundary of the optic nerve should be kept while doing fluid gas exchange ( FGE). In this way, the fluid will flow towards the needle across the flap (hinged on the temporal side) and it will help to keep the flaps in the correct position.

**2) Fovea sparing ILM Peeling (FSP) :** In this technique ILM is grasped several times near the arcades and pulled in a centripetal fashion toward the edge of MH with the maneuver ending at the point where the orange pigmentation of the fovea is first visible (this area approximately corresponds to the parafoveal area). A disk of ILM measuring about one papillary diameter is left in place over the MH. The remaining peripheral floating ILM flap is trimmed using a vitrectome . No attempt are made to place the inverted ILM flap within MH. FSP has shown to be effective and safe in terms of both morphological and functional outcomes in patients with all sizes of MHs.[19]

**3) Multi layer ILM flap (ML-ILM) technique :** For large macular hole (diameter >600 μm) Agrawal et al[20] reported multi layer ILM flap technique under PFCL which is a safe and easily reproducible technique and offers distinct advantages over all the currently described ILM peeling technique in terms of flap-related complications. In their study, they achieved 100% anatomical closure after vitrectomy with ML-IILM flap technique that was higher compared to 93.33% anatomical closure after vitrectomy with standard ILM peeling.

Narayana et al[21] showed inverted ILM flap does not seem to be substantially more beneficial than conventional ILM peeling in large macular holes more than 800 μm in diameter.

## USE OF HEALING ADJUVANTS :

Soon after MH surgery was introduced, attempts were made to improve MH closure by applying healing adjuvants. The rate

of persistent MH varies between 8% and 44% and has been found to be positively correlated with the size of the initial MH and the absence of an elevated cuff of subretinal fluid at the margin of the MH.

Autologous serum, thrombin and autologous whole blood have also been used. Autologous platelet concentrate was reported to be a highly effective adjuvant in few studies.[22]

Amniotic membrane plugs have been proposed to increase the closure rate of MH with a poor outcome, but their mechanism of action, safety, and indications remain to be clarified.[23]

In patients with a lack of ILM around the MH for further peeling in secondary surgery, Morizane et al[24] described the technique of autologous transplantation of the ILM. A small piece of the ILM was peeled from the area of residual ILM to make a free flap with a diameter similar to that of the MH to be repaired. The flap was then placed inside the MH with the aid of viscoelastics to anchor the flap, followed by gas tamponade and postoperative posturing.

In few studies Autologous retinal transplantation found to be helpful to rebuild the macular structure resulting in functional improvement for eyes with primary chronic large macular hole and refractory macuar hole. The entire neurosensory retina was harvested after bimanual dissection with scissors and forceps; the diameter of the donor retina was approximately 1,500 µm. The harvested retina was placed in the macular hole under perfluorocarbon liquid and carefully positioned under the macular hole with a diamond-dust scraper. The internal limiting membrane was not removed during the procedure. The retinal tear created during the harvesting process was later closed with a laser photocoagulation, the harvested retina was confirmed to be correctly oriented.[25]

Autologous and allogenic Lens capsular flap transplant combined with/without whole-blood application showed 96 % MH closure rate for refractory macular holes in one study. [26]

Inducing macular hole detachment, macular laser photocoagulation and radial retinal incisions are other procedures tried by few authors to increase MH closure rate.

## TYPE OF GAS IN MACULAR HOLE SURGERY :

If the hole is small and a 3-day tamponade is assumed to be sufficient, 20% SF6-air, or even air alone, might be enough, provided the patient avoids the supine position. Holes larger than 500 µm may require longer-acting gas mixture, such as 12 - 15 % C3F8, and face-down positioning for few days.

## POSTOPERATIVE POSITIONING :

If the gas mixture injected is able to cover the macula for a week, even in the upright position, MH with a diameter up to 400 µm may be a candidate for nonface-down positioning. In such cases, the patient will only be advised to avoid the supine position, even during the night. This could be achieved by fixing a tennis ball on the back of the nightshirt during sleep to prevent the patient from sleeping in a supine position.

The success rate is probably increased by postoperative posturing in larger MH. Ablerti et al[27] proposed Non Supine Position as standard of care in most FTMH cases. Poor gas fill, improper gas concentration or sclerotomy leakage are the factors responsible for nonclosure of MH.

Use of the Swept Source -OCT protocol to determine when to halt the prone positioning can significantly decrease the duration of the prone positioning after MH surgery compared with that based on the conventional protocol.[28]

## OCT PROGNOSTIC FACTOR :

Macular hole minimum diameter, base diameter, diameter of choroidal hypertransmission, and diameter of Ellipsoid zone (EZ) disruption measured from foveal B-scans on SD-OCT are few factors, can be used for predicting visual outcome after macular hole surgery.[29] Increasing width of choroidal hypertransmission was found to be associated with worse vision. EZ disruption on SD-OCT is useful to predict current vision but is not predictive of future postoperative photoreceptor health.

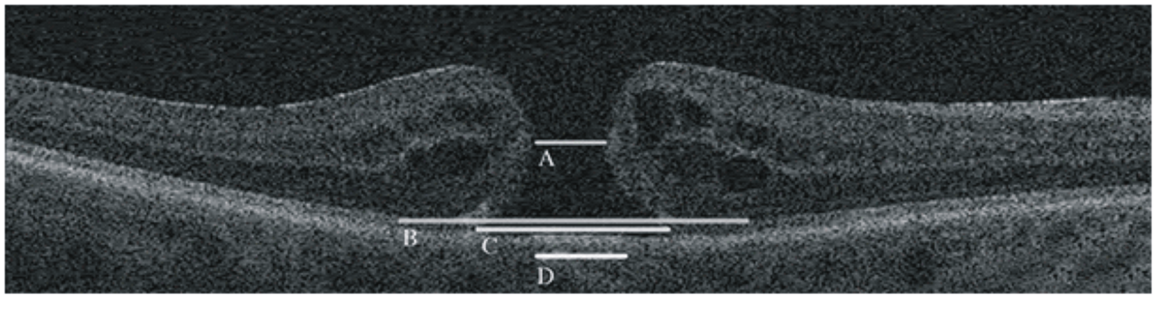


**Figure 3 : Sample presenting foveal B-scan with representative lines highlighting the measured parameters. A. Macular hole minimum diameter. B. Ellipsoid zone loss diameter. C. Macular hole base diameter. D. Choroidal hypertransmission width.**

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