Introduction

The retinal subspecialty is growing by leaps and bounds as evidenced by the explosion of treatment options for disease entities that were previously left to progress to irreversible blindness. Gone are the days when this specialty was taken up only by a choice few who were willing to have a special relationship with their perpetually dissatisfied patients with irrevocable retinal damage and the maximum that could be done was the prescription of a placebo and needless to say a stiff dose of counseling. Most multidisciplinary hospitals thought twice before planning to finance and equip a retina vitreous clinic as the expenses incurred were far beyond the maximum returns that could be expected. The 3 factors that waved a magic wand over this barren area of ophthalmology were.

1. Advancement in Imaging Technology
2. Advent of Intravitreal Phacomacotherapy
3. Availability of Small Gauge Vitrectomy

These 3 advances in technology are not only available in elite institutions but are also available in each and every nook and cranny and their effects are translated into benefits in terms of anatomical and structural outcomes for our patients. Majority of the available treatment options are covered by insurance policies, a factor that increased their acceptability. To understand this magic let us take a journey through history—visit the past, …live in the present and …….dream of an even brighter tomorrow!!!

History of retinal imaging

Imaging the retina has always been the most commonly performed diagnostic test for both vascular and non-vascular retinal pathologies. Fundus photography and fluorescein angiography (FA) have long served to aid the retinal physician in the evaluation, management and documentation of these disorders. With technology advancing by leaps and bounds we are at present in the golden era of imaging where the retinal layers can be studied in microscopic detail, the vitreo-retinal interface analysed and an enhanced depth imaging of the choroid is possible. Our quest for perfection which began with a simple fundus camera providing a 20° fundoscopic view, has been a highly successful journey. In its present state of evolution we have scaled a significant pinnacle of perfection where wide field 200° imaging is the norm and the IS-OS function or External limiting membrane integrity can be studied. We still have miles to go……with no end of the road in sight, to a future that is bright with better prospects.

Historical perspective

The first reliable fundus camera¹, providing a 20° field of view was developed by Carl Zeiss and J.W Nordensen in 1926 which was later developed further to give a 30° field of view. Around the same time in 1961 Novotny and Alvis² discovered the technique of fluorescein angiography, a technique that was popularised by Gass (1962)³. Since then the diagnostic test of ‘Fluorescein Angiography’ has served to compliment fundus photography. This wonderful technique has with stood the test of time and is still done today albeit in fewer situation. Its indication have gradually shrunk to a mere few in comparison to its use when this technique topped the list of investigations for diagnostic confirmation of a retinal pathology.

While fundus imaging of the posterior pole became common place, obtaining more peripheral views became challenging due to restraints imposed by the physical properties of the eye. Improvisations to obtain a wider view occurred in the form of

1. Equator plus camera (1970;Pomerantzeff)⁴ was a wide angle camera that utilized scleral trans-illumination and a contact lens to obtain a 148° field of view of poor image quality thanks to the glare at the site of trans-illumination.

2. Obtaining a mosaic of image by performing multiple photographic sweeps and combining the images⁵, adding upto about a 100° field of view.

3. 75° Montage Images⁶: The Early Treatment Diabetic retinopathy study (ETDRS) research group combined multiple 30° fundus images to obtain a 75° Montage which has served as the standard image used in the evaluation of most retinal vascular disorders.

Availability of digital imaging and improved computer software has made the creation of montages and mosaics easier, but this technology is not ideal for a dynamic imaging process such as a fluorescein angiography as the images from different phases of the angiogram have to be combined.
In addition to traditional film and digital cameras, another retinal imaging technology, the scanning laser ophthalmoscopy was developed in the early 1980s. When this technology was coupled with a confocal aperture, the combination provided an excellent performance compared to conventional systems. With this advancement in technology, evolved the techniques video angiography and simultaneous FA (fluorescein angiography) and ICG (Indocyanine green angiography) angiography.

4. Using special lenses in conjunction with a small angle camera: Accessorily contact and non contact lenses have been used to increase the field of view of both conventional cameras and the SLO system since 1980s. Recently, the combination of the ocular Staurenghi 230 SLO retina lens (Ocular instrument, Bellevue, WA) and a SLO system has been used to provide a 150° field of view. When used with the Heidelberg Spectralis (Heidelberg Engineering, Dossenheim, Germany) it is possible to obtain wide field fluorescence images.

5. The Retcam first introduced in 1997 used a fibre optic light source and contact lens and with its widest angle attachment can provide a 1300° field of view. This technology is thus suited for neonatal and infants and it has been extensively used in the evaluation of paediatric disorders such as retinopathy of prematurity and familial exudative vitreo retinopathy. The Retcam has limited utility in adults because even a minor lens opacity can degrade the image quality.

6. Panoret – 1000: uses scleral trans-illumination similar to Equator – Plus camera, has less difficulty with lens opacity and is therefore suitable for use in adults.

7. Another wide field imaging device, the Optos-Optomap (Optos, Dunfermline, United Kingdom) developed in 2000 was the first camera capable of producing a 2000 field of view (roughly 82.5% of the total retinal surface area). Thus ultra wide field image is obtained in Optos device by utilizing an ellipsoid mirror and SLO technology. This device utilizes both a red and green laser. The Optos wide field device when combined with the Staurenghi lens is capable of obtaining fluorescein and indocyanine green angiography as well as fundus auto fluorescence. Let us take a look at how UWFA has expanded our treatment options in retinal vascular pathologies.

The role of wide field angiography in the management of retinal diseases:

1. Identifying peripheral proliferative diseases earlier, especially in patients with diabetic retinopathy and retinal vein occlusion which can be easily missed with small angle cameras and conventional FA.

2. Recent studies have significantly co-related peripheral retinal ischemia with macular oedema in eyes with DME and RVO. Studies have shown that patients with refractory macular oedema, who show minimal response to anti VEGF and steroids, may have peripheral ischemia. Treatment of these ischemic area with laser should improve treatment response in these patients.

3. WF-FFA is used to develop an “ischemic index” (amount of non perfused to total visualized retina) patients who develop proliferative disease have a significantly higher ischemic index. Hence if peripheral ischemia is diagnosed earlier with wide field angiography earlier initiation of laser coagulation could improve outcomes in these patients.

4. In retinopathy of prematurity, wide field imaging with the retcam shows co- relation with indirect ophthalmoscopy for treatment of ROP. Incorporating WF imaging with telemedicine in ROP management will reduce the cost of care.

Indocyanine Green Angiography
The main advantage of using Indocyanine Green Angiography (ICGA) is that it provides an additional imaging modality to access the choroidal circulation below the retinal pigment epithelium. ICG compliments fundus fluorescein angiography which images the retinal circulation above the RPE.

ICGA is not replacement for FFA, but it provides important adjunctive information that assists in defining the choroidal circulatory involvements in macular diseases. The commonest indications for the use of ICGA are:

1. In the diagnosis and management of a wet AMD like picture when an IPCV is suspected. ICGA is considered as a gold standard for diagnosing PCV.

2. In the diagnosis and management of retinal angiomatous proliferation and central serous chorioretinopathy.

OPTICAL COHERENCE TOMOGRAPHY: A RETINA ODYSSEY!!!!

The advent of optical coherence tomography in 1991 was associated with a prediction that this technology would never be commercially viable. The technology was developed by researchers of Massachusetts institute of technology (MIT) headed by Fujimoto. MIT technology licensed by MIT to Humphery systems (Now CARL ZEISS MEDITECH incorporated, Dublin, California) Although OCT
was developed in the early 90’s, it took more than 10 years before it became clinically accepted with the third generation technology — the ZEISS Stratus. But this technology grounded in sound scientific principles with stood the rest of time. Its acceptability both by the clinicians and the afflicted patients is so high, that it now occupies the coveted position “at the top”, in retinal diagnostics. a place were FFA was enthroned for years. We now routinely gazes deep inside the retina, the IS-OS junction and more recently the choroid without thinking twice about the “ magic” that we are performing on our patients.

Initial devices utilized ‘Time Domain’ (TD) technology which was monopolized by Carl Zeiss Meditech. Their prototype machines Stratus III and later Stratus IV OCT were the only ones in the market for nearly 10 years.

This technology employed a mobile reference arm mirror that sequentially measures light echoes from time delays with acquisition speed of 400 A scans/second and axial resolution of 8 – 10 µm. The images obtained were described as an “OPTICAL BIOPSY” and was akin to a histopathological section of the retina.

The introduction of Fourier / Spectral Domain OCT improved imaging speed, which is now several times higher than in previous OCT technology. Resolution has improved and 3-D rendering imaging of selected layers and segmented 3-D images are now possible. More than seven companies have introduced OCT into the Ophthalmic market. The Indian market have 5 of them. The acquisition speed varies from 25000-52000 A scans/second with an axial resolution of 3-7µm significantly improving the signal –to- noise ratio and allowing the detection of individual retinal layers and lesion components.

Thus spectral domain OCT represents a significant improvement over TD-OCT in axial resolution and image acquisition, reduction of motion artifacts, increased area of retinal coverage, and the ability to produce three dimensional data sets to create topographic maps with precise registrations.

Despite superior advantages, SD-OCT is still subject to some elements of motion artifacts, segmentation artifacts, and inter instrument comparability.

Known limitations of TD and SD-OCT include limited resolution due to infrared radiation absorption by the anterior segment structures and the ocular media, “speckle noise” due to image scattering from ocular structures and limited lateral resolution due to restricted numerical aperture of the optical system.

The last few years have witnessed mind boggling advances in imaging technology. we will take a look at these “impossible” advances. Some a never leave the work bench, but the few that will reach the clinical “bed side” will definitely change how we diagnose and treat retinal diseases in the future. OCT technology that is still under development includes:

1. Swept-source OCT (SS-OCT), another form of FD-OCT uses a narrow band light source with central wavelength of 1,050 nm, and a short cavity-swept laser (instead of a super luminescent diode laser) that can emit light of different frequencies and can be rapidly tuned over a broad band width. A high speed complementary metal oxide semi conductor (CMOS) camera and two parallel photo detectors are used to achieve 100,000 -400,000 A Scans/second. With 5.3 µm tissue axial resolution over a 4 mm imaging range. Extensive B Scan averaging reduces speckle noise artifact. The small area, high density image allows imaging of individual photo receptors when coupled with adaptive optics. SS-OCT scores over SD-OCT in terms of reducing fringe wash out, better sensitivity with imaging depth, longer imaging range, higher detection effeminacy and dual balanced detection. Hence there is less patient introduced artifacts from movement and breathing, better penetration through media opacities and a longer imaging range (7.5 mm) that allows anterior segment imaging with ease.

2. ADAPTIVE OPTICS – OCT (AO-OCT) Adaptive optics corrects higher order ocular aberrations during image acquisitions, thereby allowing “near –cellular level” resolutions. AO-OCT limits motion artifacts, increases lateral resolutions, reduces speckle and enhances sensitivity. With a pupil diameter >6 mm, a lateral resolution of 2-3 mm and an axial resolution of 3.5µm enables imaging of individual cones on a 3- D basis.

3. Full –Field OCT (FF-OCT): is based on spatial coherence grating. A narrow band of illumination with high numerical aperture objectives and a liquid crystal retarder to minimize defocusing and dispersion effects are used to produce three dimensional ultra high resolution imaging.

4. Intra operative OCT (IO-OCT) augments intra operative microscopy to help surgeons delineate tissues, reducing surgical time and excessive illumination as well as limiting the need for potentially toxic stains. IO-OCT can be microscope mounted (MM) or hand held (HH). Metallic surgical instruments are detected as highly reflective with total shadowing below the instrument, while poly amide materials are moderately reflective with sub total shadowing and silicone instruments are moderately reflective with minimal shadowing.
5. **Widefield OCT (WF-OCT):** employs ultra high speed SS-OCT technology. Using a 1050 – 1060 nm FD mode locked laser to collect 1900 * 1900 A Scan with roughly 70° angle of view in 3-6 seconds. The image acquisition speed varies between 684,000 – 1,368,700 A can /second. WF - OCT can achieve good choroidal and scleral interface penetration with an axial resolution of 6.7 to 19 µm.

In combination with Optical Microangiography technology (OMAG) vascular perfusion mapping down to the capillary level is possible. OMAG technology utilizes 840 nm wave length with an A scan rate of 27000 Hz and axial resolution of 8µm to image a 7.4 * 7.4 mm² area of the posterior segment. A volumetric map acquisition comparable to fluorescein and indocyanine green angiography is possible.

6. **Doppler OCT** can be used to access blood flow velocity. In patients with perimetric glaucoma decrease, retinal blood flow access by Doppler OCT (840 nm wave length, axial resolution 5µm, and transverse resolution 20 µm). was evident even in the absence of RNFL changes.

**Functional OCT** is a method of functional tissue assessment by means of light polarization evaluation. PS-OCT allows individual retinal layer identification by measuring cross-sectional and volumetric birefringence, contrasting between birefringent layers and other retinal layers. PS-OCT simultaneously measures intensity (conventional OCT images), retardation, and optic axis orientation to distinguish polarization - preserving tissue, birefringent tissue, and polarization scrambling tissue. Birefringent tissues include the RNFL, Henle’s layer, sclera, or any fibrotic tissue that increase phase retardation. The RPE is a polarization-scrambling layer. Light transmitted through the RPE maintains the same polarization state and degree of retardation as images below and above the RPE layer, allowing assessment of RPE damage, which is specially useful in the context of pigment epithelial detachments and pseudovitelliform dystrophy.

In summary, a variety of emerging OCT technologies are poised to expand significantly the scope of OCT imaging and to enhance significantly our approach to the diagnosis and management of patients with retinal disease. An in depth understanding of these technologies and their potential advantages and disadvantages will aid retinal specialists in using these new methods for optimum benefit.

**THE USE OF MACULAR MICROPERIMETRY IN THE ASSESSMENT AND DIAGNOSIS OF MACULAR DISEASE**

Although BCVA remains the gold standard assessment tool for measuring visual function, it is widely recognized that conventional tests of vision, such as high-contrast BCVA, underestimate the actual level of visual impairment, particularly in older patients. As a result, other clinical assessment tools, such as contrast sensitivity, macular recovery function, and reading speed tests, are often employed to assess visual function in an individual, particularly when changes occur in visual function after an intervention. Although the Humphrey Field Analyzer (HFA) can be used to measure central macular sensitivity, its role in monitoring macular disease has been limited by its inability to quantify retinal threshold accurately over small and discrete retinal lesions and to retest these areas accurately over time. In response to these limitations, the scanning laser ophthalmoscope (SLO) microperimeter was developed. The SLO integrates fundus imaging with computerized threshold perimetry to achieve an exact correlation between macular and corresponding functional defects. This device was, however, very time-consuming and cumbersome to use and did not easily facilitate automated follow up examinations. Consequently, its use remained the preserve of a few academic institutions, and it never gained widespread popularity as an assessment tool.

The desire for a more practical, user friendly alternative led to the development of the Nidek MP1 microperimeter. The later version of microperimeters incorporates a color fundus camera for image registration and an auto tracking system to facilitate the accurate measurement of retinal sensitivity within the central visual field, even in patients with unstable or extrafoveal fixation. Although the MP-1 has an array of test strategies, in clinical practice, it has two principle modes of use: fixation localization and threshold testing. By analyzing the relationship among MPI, OCT and autofluorescence data, we now know that, in the context of AMD at least, stable and central fixation correlates well with preservation of the outer retinal signal on OCT.

Conversely, the presence of fibrosis, RPE atrophy, and loss of foveal autofluorescence are associated with a much higher rate of unstable eccentric fixation.

Perhaps the most exciting potential with microperimetry is that it allows investigators to assess the relationship between functional and structural changes accurately. For example, recent data have revealed that progressive loss of macular function over time, which involves not only expansion of the absolute scotoma but also reduced sensitivity in the perilesional area and a loss of fixation stability. This loss of perilesional retinal sensitivity appears to be unrelated to progressive atrophy but is associated with progressive decreased fundus autofluorescence.
FUNDUS AUTOFLUORESCENCE: AN EMERGING WINDOW ON THE RETINA

Fundus autofluorescence (FAF) has emerged in the past 10 years as an effective means of identifying lipofuscin distribution in the retinal pigment epithelium cell monolayer plus other fluorophores associated with disease in the outer retina and subneurosensory space. What makes FAF clinically effective is that excessive accumulation of lipofuscin granules within the RPE represents a common downstream pathological pathway in various hereditary and complex retinal diseases, notably AMD.

Common Ocular Fluorophores are
A: Lipofuscin in the retinal pigment epithelium (RPE) (A2E)
B: Extracellular vitelliform material
C: Crystalline lens
D: Optic nerve head drusen
E: Astrocytichamartoma
F: Sclera

HOW FAF WORKS:
FAF depends on the use of ultraviolet light to visualize lipofuscin with fluorescence microscopy. One difficulty in detecting FAF is that its intensity is about two orders of magnitude lower than the background of a fluorescein angiogram. Autofluorescent properties of structures anterior to the retina further confound the clinical picture. This means existing camera systems as well as new imaging devices must be adjusted to record FAF. Confocal scanning laser ophthalmoscopy (cSLO) and fundus photography are the two chief clinical means of capturing the FAF signal.

SCANNING LASER OPHTHALMOSCOPY: Confocal SLO addresses the limitations of the low intensity signal of FAF and the interference of the crystalline lens. The confocal optics ensure the reflectance and fluorescence come from the same optical plane. Light originating in the light beam, but out of the focal plane, is greatly suppressed, which in turn reduces autofluorescence from structures anterior to the retina.

FUNDUS PHOTOGRAPHY: The fundus camera differs from a cSLO in that the former uses a single flash and captures the entire retinal area in a single frame. The fundus camera does not have confocal optics, which means the signal it detects comes from all tissue levels with fluorescent properties within that light beam. So also, light scattering both anterior and posterior to the plane of interest can disrupt the detected signal. These are serious drawbacks. What's more, the fundus camera lens itself contributes significantly to the fluorescence signal. This is particularly the case with older patients who have yellowing of the lens with nuclear sclerosis. One way around this problem is to modify the fundus camera by moving the excitation and emission wavelengths toward the red end of the spectrum. Longer wavelengths are thought to exhibit much less contribution from nuclear sclerosis and macular pigment, compared with shorter wavelengths.

Because cSLO and fundus photography use different wavelengths, it stands to reason that the two techniques might record fluorescence from a different set of fluorophores. An example is that macular pigment absorption is observed at a much lesser extent and the signal is less decreased over blood, retinal vessels, and the optic nerve head using the fundus camera system compared with the cSLO. A head to head comparison of the two systems is lacking.

FAF’S CLINICAL CONTRIBUTION:
Fundus autofluorescence imaging allows topographic mapping of lipofuscin distribution in the retinal pigment epithelium cell monolayer as well as other fluorophores that may accompany disease in the outer retina and sub neurosensory space. FAF imaging yields diagnostic data otherwise unobtainable through fundus photography, FA, and OCT, and therein lies its special clinical value.

Fundus Autofluorescence Imaging in Clinical Practice
A: Detect and follow geographic atrophy
B: Follow hereditary retinal diseases
C: Monitor for drug toxicity (hydroxychloroquine)
D: Disease signatures (acute zonal occult outer retinopathy [AZOOR], A3243G, ABCA4, pseudoxanthomaelasticum, cuticular drusen, acute exudative polymorphous vitelliform maculopathy)
E: Distinguish vitelliform lesions from other material
F: Identify RPE tears
G: Identify optic disc drusen
H: Identify subretinal fluid
I: Diagnose and follow posterior segment inflammatory disease (MEWDS, PIC/MFC, AZOOR, acute posterior multifocal placoid pigment epitheliopathy)

Identifying Choroidal Pathology With Enhanced Depth Imaging OCT
Better imaging reveals new anomalies. What is their clinical significance? The technique of enhanced depth imaging (EDI)-OCT, which involves placing the objective lens of the Spectralis SD-OCT(SD-OCT) device (Heidelberg Engineering) closer to the eye so that an inverted image is obtained. This maneuver allows deeper structures to be placed closer to the zero delay, thereby allowing for better visualization of the choroid. Combining high speed scanning, eye-tracking, image-averaging technology, reduced noise and greater coverage of the macular area, high-resolution OCT images of...
the choroid can now be created.60,51,

Due to the choroid’s chief functions of supplying metabolic support to the RPE 52 and outer retina and the preliminary portion of the optic nerve 53, and because it contains melanocytes that absorb excess light and prevents damage to surrounding structures54, it may be involved in several important diseases of the retina, RPE and optic nerve. With the development of EDI-OCT, the understanding of the choroid using noninvasive imaging techniques has grown significantly. Margolis and Spaide65 analyzed normal eyes and found that the choroid was thickest underneath the fovea, with a mean thickness of 287µm. Given that the choroid is the most vascular structure within the eye and the fovea, is situated at the center of the macula, and has the highest photoreceptor density and metabolic activity, it is not unexpected that the choroid is thickest in this region.

Interestingly, Margolis and Spaide66 found a statistically significant correlation with age and choroidal thickness, in which the choroid thinned with age. Using regression analysis they showed that the subfoveal choroidal thickness decreased 1.56µm for each year of age or that, over the course of an 80 year lifetime, an eye would lose approximately one-third of its subfoveal choroidal thickness. This in vivo measurement of subfoveal choroidal thickness using EDI-OCT correlated with similar previous studies with eye bank and autopsy eyes, which found that choroidal thickness was correlated negatively with age and decreased by 1.1µm per year of age.

On examination, individuals with ARCA 57 (Age Related Choroidal Atrophy) demonstrate pigmentary changes, a tessellated fundus and a paucity of visible choroidal vessels. These clinical and EDI-OCT imaging observations may help explain the age related decrease in visual acuity and function commonly seen with aging.

The introduction of EDI-OCT has opened up a new world of imaging the choroid, using commercially available SD-OCT machines. Before the introduction EDI-OCT, SD-OCT imaging of the choroid was quite limited. Now, with this technology, noninvasive, in vivo measurements of this vascular structure can be repeatedly and reliably performed. EDI-OCT has allowed the identification of ARCA, which may explain certain macular pathologies, other possible pathophysiologic mechanism, such as peripapillary atrophy58 and glaucoma59, and Focal Choroidal Excavations60,61,62. ARCA and FCE represent two new choroidal entities that may provide more insight into the pathogenesis and management of retinal disease.

EDI-OCT of Choroid in Clinical Practice:

A: Quantitative analysis with EDI of the choroid is critical for baseline diagnosis and response to therapy of various retinal disorders. This type of analysis is unavailable with traditional modalities such as fluorescein and indocyanine angiography.

B: Diagnosis of CSR and differentiation from PCV and AMD is improved with EDI, and EDI is important for monitoring response to therapy of CSR.

C: Diagnosis of inflammatory disease is improved with EDI. A thick choroid is seen with VKH and thin choroid is seen with birdshot chorioretinopathy. EDI is helpful in assessing response to therapy of VKH.

D: EDI offers a higher resolution modality for analysis of choroidal tumors and potentially greater accuracy in measurement of choroidal tumors.

E: Qualitative analysis of each of the different layers of the choroid is possible with EDI and is evolving, and this may impact diagnosis, therapy, and understanding of retinal and choroidal diseases.

Future of Imaging

The Future of Imaging includes not only new OCT instruments and techniques but also innovations in other novel optical and non-optical technologies. These new technologies include

1. Hyperspectral imaging63 for visualization of retinal oxygenation and other metabolites,

2. Multispectral imaging64 for measurement of rhodopsin concentration,

3. Photoacoustic imaging65 for visualization of melanin and blood vessels,

4. Magnetic resonance imaging (MRI)66 for characterization of retinal function in the setting of media opacity.

In addition to novel imaging technologies, one can expect new advances in imaging techniques. For example, wide-field imaging strategies, currently used for fluorescein angiography, fundus autofluorescence, and color imaging, will likely be expanded to new areas including indocyanine angiography, near infrared imaging, and OCT.

Indeed, OCT-related technologies can be expected to dominate the future of imaging in both research and clinical practice. The morphologic biopsy of the retina provided by OCT will likely be enhanced by the incorporation of robust, low-cost adaptive optics solutions, which should make commercial clinical application feasible. The improvements in resolution will enable better visualization and understanding of the various retinal bands. As a result, one can expect continued refinement of the classification of these structures over time.

A final expected advance in imaging is improvements in automation. Automated segmentation and classification of features on imaging data will increase with a more complete delineation and quantification of all disease findings. Automated diagnosis and monitoring of disease may
availability of beautifully descriptive 3D imaging has definitely improved the diagnostic capabilities in retinal diseases and we will now move on to the vista of therapeutic option available for managing these conditions.

Ischemia and VEGF in Different Retinal Diseases and Therapies: How does One Influence the Other?

Retinal diseases have undergone a metamorphosis over the last seven years. Age related macular degeneration, retinal vein occlusion and diabetic macular edema, which were once primarily treated with laser, are now predominantly being treated with anti VEGF or corticosteroid based therapies. This switch to newer treatments is due to our better understanding of free intraocular VEGF levels and the role they play in retinal diseases. Currently, there are four different anti VEGF medications to choose from. If we include the three major corticosteroids – triamcinolone, dexamethasone and flucinolone, our armamentarium is significantly enhanced. There has been many studies in literature comparing one anti VEGF medication to another, yet there are many questions that remain unanswered.

The one year results of the CAT	extsuperscript{2} study showed that monthly injections of Bevacizumab vs Ranibizumab were equally efficacious when treating wet AMD. These findings although true for AMD, are not consistent with other retinal diseases, such as RVO and DME, which have much higher levels of free intraocular VEGF. Case reports in the literature have also suggested that persistent macular edema due to vein occlusions that are nonresponsive to one anti VEGF agent can have complete resolution after switching to another agent with a higher affinity for VEGF	extsuperscript{30}. In the coming years, studies such as CRAVE for RVO and the DRCR.net Protocol T for DME may answer these questions.

VEGF LEVELS IN ISCHEMIA

Why would there be differences among these diseases when they share abnormal VEGF levels as a basis for their pathology? The answer may lie in the degree of ischemia, as well as in the corresponding levels of VEGF expression. The levels of VEGF in central RVO are higher than in branch, RVO and are almost 100 times higher than the VEGF levels in wet AMD	extsuperscript{30}. This fact demonstrates that diseases with higher levels of ischemia result in higher intraocular levels of free VEGF.

VEGF AND REBOUND EDEMA

The exact duration of effect of these anti VEGF medications on any given retinal diseases is still unknown. The concept of rebound edema in RVO patients	extsuperscript{70} when occurring after injections with anti VEGF agents, tends to be much greater than on initial presentation. Prior experience have shown that nearly 41% of our patients who responded to bevacizumab at two weeks rebounded by four weeks. In many instances, the edema may be related to significant peripheral ischemia, which is often difficult to image	extsuperscript{12,13}. Using widefield fluorescein angiography, such as with the Optos device, may provide clues about some of these diseases, as well as potential therapies to block this cycle of rebound edema from going forward.

Anti VEGF and drugs acting on the angiogenesis cascade: The future in the management of Exudative AMD and retinal vascular diseases

The last decade has been a remarkable period for the treatment of neovascular AMD. We have gone from having no effective treatment and simply watching our patients go blind to providing anti VEGF monotherapy, allowing for some, albeit temporary, stabilization of vision.

Looking at present – day therapies for exudative AMD the role of VEGF in AMD has been well established and that blocking VEGF has been a good idea. Turning to the cascade of VEGF activity, we are aware of the fact that Macugen, Avastin, Lucentis, all block VEGF in the extracellular space and before it binds to its receptors. Thus till end of 2011 we had mainly 3 major players in the arena of VEGF inhibition.

Year 2011: Enter Eylea (Aflibercept, Regeneron)

Eylea’s Roaring Rollout has taken the retinal world by storm.

By any fiscal reckoning, the launch of Eylea (Aflibercept, Regeneron) exceeded expectations. Wall Street forecasters initially predicted sales of the new anti VEGF agent for wet AMD would total $5 million in the final quarter of 2011. Instead, it took in $24 million. Enthusiasm is tempered by the second-year VIEW results	extsuperscript{71} and recent case reports of inflammation. Many had hoped Eylea would outperform Lucentis in its anti-VEGF punch, a point as-yet unresolved by the data available in the literature. Additionally, one of aflibercept’s main selling points, its reduced dosing schedule—just five injections in the first year of treatment—wasn’t maintained in the year 2 VIEW data submitted to the FDA. Finally, a cluster of post-injection inflammation events	extsuperscript{15}, though well within established incidence rates for intravitreal injections, prompted a company notification to the FDA to take a precautionary look at injection protocols.

Real-world testing will tell whether Eylea truly offers longer biologic activity. Furthermore, nine cases in the cluster of inflammation events occurred in a single physicians practice, a trend suggesting a localized problem and not a drug – specific issue. No other reports of such a cluster have since
arisen. The Aflibercept solution\textsuperscript{31} has higher viscosity than other anti-VEGF agents, and whether this variable might have played a role in these events, is debated. This unfortunate complication was not seen in the pivotal trials.

For the past seven to 10 years, we have focused our attention and finances on blocking VEGF in the extracellular space to fix the “chronically leaking boat”. At first, we believed this led to blockade of VEGF induced angiogenesis, as was shown in the preclinical animal models. But as more and more data appeared, it seemed that anti-VEGF agents largely work by reducing vascular leakage and drying the retina, not by eliminating choroidal neovascularization. Therefore, we are just patching leaks, and not fixing the problem.

We are all well aware of the downsides of intravitreal Anti-VEGF pharmacotherapy …………. An overwhelming treatment burden, coupled with a suboptimal treatment response with little hope for a definite treatment end point. This has led to the exploration of newer anti-VEGF agents, and other molecules to target different areas of the angiogenesis cascade.

Some other VEGF related compounds under investigation. Among these VEGF related compounds was KH902\textsuperscript{32}, a VEGF-blocking fusion protein from China, which showed impressive results in phase I trials.

In addition, MP0112\textsuperscript{26}, a recombinant fusion protein based on DARPin technology, is important because it theoretically can prolong the durability of the chemical, providing a long intravitreal half-life. MP0112 is currently in phase 1 studies in the United States.

Another VEGF-related approach is to have body produce its own anti VEGF therapy using genetics. For instance, AAV2-sFLT01\textsuperscript{27} uses a viral vector to deliver a gene to the back of the eye, where “infected” cells then produce sFLT01. The drug’s effects lasted at least 12 months in animal studies A phase 1 trial is currently under way.

Returning to the VEGF cascade, upstream of the extracellular space, there is a long list of events that result in VEGF production. Compounds that could be effective against VEGF in this part of the cascade include Sirolimus\textsuperscript{34} and Palomid 529\textsuperscript{35}. Palomid 529 is currently being investigated in a phase 1 trial.

Turning to the VEGF cascade downstream of the extracellular space, blockade of VEGF receptors is one way to approach the problem. Integrins are transmembrane proteins that help regulate and modulate the downstream kinase signaling pathways, and hence using Integrin antagonist may prove useful.

The drug being investigated along this route is an α5β1 integrin inhibitor\textsuperscript{36}, which via its blockade can lead to vessel regression, allowing for the destruction of choroidal neovascularization. In addition, volociximab\textsuperscript{37}, a monoclonal antibody against α5β1, showed inhibition of CNV on fluorescein angiography in a phase 1 trial.

Further downstream, once VEGF has bound to its receptors, another cascade of events occurs and targeting this area also could stop angiogenesis.

These chemicals include the Tyrosine Kinase Inhibitors (TKIs), which if blocked could stop the growth of vessels. Pazopanib\textsuperscript{38}, which is topically administrated, is a TKI that, in a phase 2 study, resulted in a mean 4.3 letter increase in VA, with patients with the CFHTT genotype exhibiting the best response.

Beyond the VEGF cascade: Can Anti-PDGF Drug Targets Heart of Angiogenesis? Amid the justifiably positive excitement and fanfare surrounding the birth of anti-VEGF therapy, one important fact went largely unnoticed. In the pioneering ANCHOR\textsuperscript{39} and MARINA studies, (which laid the foundation for anti VEGF AMD therapy) patients in general did not experience neovascular membrane regression and a significant number (20% in ANCHOR and 15% in MARINA) saw their choroidal neovascular lesions grow over the course of the study, despite strict adherence to monthly injections.

At the time, visual acuity benefits were cause enough for celebration with angiograms clearly showing reduced vascular permeability, leakage, and edema. But the actual structures underlying exudative disease remained untouched by the treatment. Also worth remembering is that despite functional outcomes unimaginable at that time, most patients did not regain three or more lines of vision\textsuperscript{40}.

Then there is treatment burden, a more widely acknowledged anti-VEGF challenge. It is widely accepted that we get the best outcomes with a strict monthly injection schedule, and any deviation from that schedule resulted in decreased vision, even among patients who maintained disciplined monthly visits for years.

Angiogenesis involves hundreds of chemical factors of which VEGF is an important factor, but perhaps not the most vital. Angiogenesis occurs over many stages: initiation, progression, differentiation, maturation, and remodeling\textsuperscript{40a}. Numerous cell types including pericytes, in addition to endothelial cells, contributes to vascular growth during these
In the initial stage of angiogenesis, a group of endothelial cells, known as tip cells, set the trail for this process, proliferating and expanding the size of the neovascular membrane. These cells shape the leading edge of the angiogenic sprout. They also secrete platelet-derived growth factor B (PDGF-B), which in turn recruits pericytes to proliferate and migrate along the growing neovascularization. The presence of pericytes is a hallmark of vascular maturation; pericytes protect and stabilize the endothelial cells that constitute to the vascular wall.

While this process is unfolding, the tip endothelial cells continue to build new sprouts. Pericyte attachment and maturation and endothelial cell protection lag behind endothelial cell proliferation. Throughout angiogenesis tip cells are the only endothelial cells unprotected by a shield of pericytes, and this could be one of the main factors responsible for anti VEGF resistance. Current anti VEGF therapy only impacts the leading tip cells, temporarily reducing the vascular permeability, leakage, and edema that causes vision loss, but leaving the pericyte guarded neovascular complex intact. Soon after anti VEGF therapy ceases or slows down, the pericyte protected endothelial lesions stand ready to sprout new vessels. Platelet derived growth factor (PDGF) is a key cytokine involved in this recruitment. Blockade of Platelet derived growth factor (PDGF) only blocks pericytes, it is not going to be successful as monotherapy but instead will need to be combined with anti-VEGF agents.

Ophthotech Corp, Princeton, NJ, recently developed an anti PDGF aptamer, formerly known as E100300 and now called Fovista. The to using, dose-escalating, multicenter, uncontrolled, single and multiple-dose study included 22 patients who were given three monthly intravitreal injections of combination therapy, Lucentis (Ranibizumab, Genentech, South San Francisco, CA) with Fovista.101. No dose-limiting toxicities nor any adverse events were reported and all of the patients displayed some degree of neovascular regression, with an 86% average magnitude of regression.

Based on these results, a phase 2b clinical trial was designed involving 449 patients. Three groups received one of three treatments every four weeks: Fovista 1.5 mg combined with Lucentis 0.5; or a placebo combined with Lucentis 0.5 mg.91

Results for this phase 2 study mirrored the earlier trial results with a mean +10.6 letters of vision improvement at six months, or a 62% improvement over Lucentis monotherapy.

With any luck, we have here a combination therapy that inhibits pericyte recruitment, strips pericytes from the neovascular complex without negatively affecting host non cardiovascular vessels, and causes both inhibition and regression of the neovascular complex.

Combination anti VEGF and anti PDGF therapy offers hope that we may provide our patients with a more permanent and sustainable treatment model to combat the blinding effects of this common disease.

ANTI VEGF THERAPY: Can Anti-VEGF Trigger GA?

While anti VEGF drugs have improved the vision and quality of life for hundreds of thousands of patients with retinal disease, these drugs do have some shortcomings. Patients and retinal specialists understandably chafe under the treatment burden that regular anti VEGF intravitreal injections entail. In addition, some patients are not responsive to anti VEGF therapy.

One of the most puzzling and controversial findings to come out of the 2-year CATT study data is the presence of geographic atrophy (GA) in 30% of patients who received monthly doses of Ranibizumab during the trial. Some patients who received Bevacizumab monthly or either drug on a PRN basis also showed signs of geographic atrophy, but not at the high levels seen in the Lucentis monthly arm of the trial.

The association of GA with the most potent arm of the trial has led to a concern that repeated anti VEGF injectors can serve as a trigger mechanism for GA. Hence given the current lack of effective treatment for GA. Anti VEGF therapy should be used judiciously following a “treat-and-extend protocol…a Goldilocks approval.92 We don’t want too much or too little VEGF inhibition…we want just enough!!!

Given that opportunities exist to improve upon ant VEGF monotherapy, numerous efforts are underway to find better drugs or less invasive delivery systems. In the investigational pipeline for wet AMD are such concepts as pills, eye drops, sustained-release delivery systems, radiation treatments, and other innovative drug-development efforts too numerous to mention here.

But in terms of what new therapies are deemed most promising, early stage clinical trials have shown that combination drugs may have the best chance of early approval. Three combinations worth mentioning are:

1. Ophthotech’s anti platelet derived growth factor (PDGF) drug Fovista in combination with ranibizumab93 has shown excellent results in phase 1 clinical trials of 22 patients who were not responsive to anti VEGF monotherapy. In a large phase 2 study encompassing 449 patients, investigator
is designed to improve the precision of treatment with the use of a mouse or touch screen. A joystick definition color or IR images. The surgeon easily designs the treatment plan with the use of a mouse or touch screen. A joystick is utilized to position and control the device and provides a micromanipulator. The software allows the surgeon to place caution zones over the foveal avascular zone (FAZ) and the optic nerve area in order to highlight these sensitive regions during laser application. The surgeon is able to effectively plan a comprehensive treatment with the Navilas system targeting all microaneurysms and nonperfused areas with unprecedented accuracy due to this unique live imaging system.

To perform panretinal laser photoablation, a PRP objective is utilized along with a specifically designed contact lens. The contact lens and Navilas optical head must be centered to each other with optical axes aligned. The image of the patient’s retina is brought into focus by moving the optical head axially using a joystick until a sharply illuminated image appears. Unlike a slit lamp microscope where only a small part of the aerial image can be sampled with narrow slit and microscope, Navilas instantly samples a static field of 630 X 500 (800 diagonal). By moving the Navilas optical head laterally, the full equatorial field may be sampled.

The PRP contact lens forms a real aerial image of the retina up to the equator. For covering the retina up to the equator, no or minimal tilt of the lens is required minimizing astigmatic changes of the image and of the projected laser spot. This leads to uniform and consistent laser uptake with round spots from the posterior pole to the periphery.

PRP using the Navilas Laser System appears to be safe, well tolerated and achieves a high rate of efficacy. Distribution of laser spots across the retina is even and very precisely placed due to the unique navigational capabilities of the Navilas device. Panretinal laser treatment can be efficiently completed with less pain than with the more traditional laser approach.

Why navigated laser?
The answer, is that navigated laser may offer increased accuracy and a lower retreatment rate. 91.5 % of the treatment delivered vs 71.5 % with conventional laser and the treatment rate was decreased by 50 % when compared to conventional slit lamp laser.

The ability to utilize live imaging to plan, navigate and execute precise laser treatments with one multi-functional platform represents a tremendous technological advance. An entirely new level of safety, efficacy and stability is anticipated with expanded use of the Navilas Laser System as a stand alone treatment or in combination with anti-VEGF therapy.

Pattern Scanning Laser (PASCAL)

The excellent results demonstrated thus far by Fovista, the DARP in and ALG-1001 appear to indicate that a next generation of combination drugs to combat retinal disease may be just over the horizon.

ADVANCES IN LASER TECHNOLOGY
New Breakthroughs in Laser Technology /Advances in Laser Technology for Photo coagulation: Delivering faster, safer and more accurate LASER treatment.

Laser photocoagulation has been the mainstay of retinal practice, having been validated as an effective treatment for clinically significant macular edema associated with Diabetic Retinopathy & retinal vein occlusion in landmark studies such as ETDRS & BVOS. The technology for laser photocoagulation has evolved through several prototype instruments. Three important advances in laser photocoagulation technology has resulted in more accurate and effective treatment that is less painful to the patients. The xenon arc coagulator, the huge water cooled argon & krypton gas laser, solid state semiconductor diode red and frequency doubled 532nm Yag green laser have been in use till date. Dye laser, TTT and PDT lasers had only transient popularity and are rarely used in the present day scenario.

1. The Navilas is designed to improve the precision and efficacy of retinal photocoagulation by means of an integrated live imaging system that uniquely enables the surgeon to plan, “navigate” and execute the treatment. The Navilas device is a multifunctional system that combines fundus photography, fluorescein angiography and laser to effectively aid in the diagnosis and treatment of ocular pathologies in the posterior segment of the eye.

Throughout treatment, an LCD monitor provides live high definition color or IR images. The surgeon easily designs the treatment with the use of a mouse or touch screen. A joystick is utilized to position and control the device and provides a micromanipulator. The software allows the surgeon to place caution zones over the foveal avascular zone (FAZ) and the optic nerve area in order to highlight these sensitive regions during laser application. The surgeon is able to effectively plan a comprehensive treatment with the Navilas system targeting all microaneurysms and nonperfused areas with unprecedented accuracy due to this unique live imaging system.

To perform panretinal laser photoablation, a PRP objective is utilized along with a specifically designed contact lens. The contact lens and Navilas optical head must be centered to each other with optical axes aligned. The image of the patient’s retina is brought into focus by moving the optical head axially using a joystick until a sharply illuminated image appears. Unlike a slit lamp microscope where only a small part of the aerial image can be sampled with narrow slit and microscope, Navilas instantly samples a static field of 630 X 500 (800 diagonal). By moving the Navilas optical head laterally, the full equatorial field may be sampled.

The PRP contact lens forms a real aerial image of the retina up to the equator. For covering the retina up to the equator, no or minimal tilt of the lens is required minimizing astigmatic changes of the image and of the projected laser spot. This leads to uniform and consistent laser uptake with round spots from the posterior pole to the periphery.

PRP using the Navilas Laser System appears to be safe, well tolerated and achieves a high rate of efficacy. Distribution of laser spots across the retina is even and very precisely placed due to the unique navigational capabilities of the Navilas device. Panretinal laser treatment can be efficiently completed with less pain than with the more traditional laser approach.

Why navigated laser?
The answer, is that navigated laser may offer increased accuracy and a lower retreatment rate. 91.5 % of the treatment delivered vs 71.5 % with conventional laser and the treatment rate was decreased by 50 % when compared to conventional slit lamp laser.

The ability to utilize live imaging to plan, navigate and execute precise laser treatments with one multi-functional platform represents a tremendous technological advance. An entirely new level of safety, efficacy and stability is anticipated with expanded use of the Navilas Laser System as a stand alone treatment or in combination with anti-VEGF therapy.

Pattern Scanning Laser (PASCAL)
The launch of the pattern scanning laser technology\textsuperscript{46} by Topcon Medical Laser Systems, Inc in 2006 marked a major breakthrough in laser treatment for retinal diseases. By rapidly applying 532nm laser pulses (56 spots is approximately 0.6 seconds) in predetermined patterns, the PASCAL photocoagulator enables physicians to target specific pathologies with less scatter and to create multiple rapid, sequential burns. This results in reduced treatment duration and less pain for the patient. When compared to traditional single spot laser photocoagulation as well as less collateral damage. The Pascal photocoagulator features the following preset patterns for various pathologies.

1. Square arrays for proliferative diabetic retinopathy
2. Triple areas for retinal tears lattice degeneration & PDR
3. Modified Macular Grid: for diffuse DME

Pattern specific controls such as spot spacing, enable further customization so that patterns can be matched to retinal disease states & anatomical features.

**SURGICAL RETINA**
**DOES SURGERY HAVE A FUTURE IN RETINA CARE?**

Advancements in medical treatments mean less time in the OR for retina specialists.

It’s no secret that the treatment of retinal disease is changing. With the pharmacological advances that have been made, retina specialists face the choice of continuing to use the standard surgical techniques they have relied on for years, or the newer, less invasive medical treatments that are evolving at a rapid pace.

**MEDICAL TREATMENT NOW STANDARD FOR AMD:**
Surgical management of AMD, including vitrectomy and removal of sub retinal choroidal neovascular membrane\textsuperscript{102}, macular translocation\textsuperscript{103}, and RPE transplantation\textsuperscript{104} are rarely being done now.

Now for a patient with wet AMD, and with salvageable vision, anti VEGF injection is the first line of therapy, and treating a macular degeneration patient with laser or PDT has become rare in the past five years.

However, some retina specialists still find a place for PDT, and even thermal laser, in select AMD patients - PDT is a component of treatment for subtypes of macular degeneration, and occasionally laser is still performed for an area of choroidal neovascularization outside of the fovea itself. There still is an occasional surgical case, where someone comes in with a massive sub retinal hemorrhage that warrants surgery.

**TREATMENT OF RETINAL DETACHMENT:**
Retinal detachment, to a large degree, still requires a surgical treatment. The tendency has been more and more to go toward vitrectomy. In the past sclera buckles were performed primarily in patients who were phakic. Or a combination of a buckle with vitrectomy was performed for rather extensive pathology in the inferior periphery. The exception to the rule were pseudophakic patients who have had previous cataract surgery and a lens implant. In this subgroup generally buckles were avoided\textsuperscript{105}.

Surgery for repair of retinal detachment is becoming less invasive\textsuperscript{106,107}. Some of the retinal detachments that were fixed with surgery in the past can now be done in the office with less invasive procedures such as pneumatic retinopexy. But pneumatic retinopexy\textsuperscript{108} is also being done less, mainly because of the reliance it places on the postoperative positioning.

**ADDITION OF OCRIPLASMIN:**
Ocriplasmin, (Jetrea, ThromboGenics, Iselin, NJ)\textsuperscript{109} recently received FDA approval for treating symptomatic vitreomacular adhesion (VMA). While it isn’t a treatment for retinal detachment, it might aid in helping to close macular holes and in the release to traction in VMA in some eyes that develop macular holes.

Ocriplasmin could lead to fewer surgeries for symptomatic VMA and macular holes - just as the surgical volume was already dropping off when we began using anti VEGF agents for AMD.

The studies that were done with ocriplasmin certainly showed that patients who had relatively small macular holes or well defined VMAs responded favorably. Forty to 45% of cases had resolution of the abnormality with a single injection. However surgery has a 90% success rate or better for all conditions proposed for treatment with ocriplasmin. The drug has no application in retinal detachment and is rarely indicated for vitreomacular traction cases...\textsuperscript{110,111,112}

A select group of patients may be ideal for treatment with ocriplasmin especially patients with vitreomacular adhesions that focally elevate the posterior pole, resulting in the type of configuration more likely to progress to macular hole or already causing an early-stage hole. Those patients can be easily identified by the characteristic anatomic appearance on SD-OCT. It is very difficult to reliably determine if there is vitreous adherent to the margins of macular hole using OCT, the so-called stage 2 macular hole, said to be an indication for ocriplasmin. If there is no vitreous adherence, which is usually the case, the agent is not indicated.
The cost, expected to be around $4,000 in the United States, also is prohibitive. It is “Over twice the cost of Lucentis (Ranibizumab, Genetech, South San Francisco, CA) or Eylea (aflibercept, Regeneron, Tarrytown, NY), and about the cost of surgery in an ASC.

**A MATTER OF CONVENIENCE AND LESS INVASIVENESS:**
What are the reasons for retina specialists moving in the direction of injection of pharmaceutical medications rather than a surgical procedure?

The greatest advantages is convenience for the patient and the retina specialist. If there is an agent that does the same job but in a less invasive way, or if the invasiveness is similar but the treatment is more effective, that option is always chosen.

Certainly in general, pharmacologic treatments are less invasive and is safer than a surgical procedure and can often be considered as an alternative at an earlier stage of disease to preserve or improve the patients vision.

**TEACHING OUTGOING METHODS**
As treatment evolve and older procedures are used less frequently, is there any need to continue teaching the old way to incoming students and residents? The need for surgery will never go away and the problem facing future generations is maintaining a certain level of expertise while the volume of a procedure may diminish. However if a newer, better approach replaces on older one the need to continue teaching the old method decreases.

**ALWAYS A ROLE FOR SURGERY**
Despite the advances in medical therapy and the discoveries certain to occur in the future, the need for surgery will continue. Looking at the future where stem cell research will be the next paradigm shift in retina therapy we may come full circle and may have to sharpen our surgical skills. Let us look at some of the newer indications for surgery.

**Floatarctomies: Should it Be a Routine Part of the Surgeon’s Armamentarium: Fact or Fiction**
The management options for a patient with vitreous floaters were Observation (The treatment of choice in almost all cases - Efficacy: High patient satisfaction / Safety: No associated risks), and Nd: YAG laser vitreolysis¹¹³ / photodisruption (Procedure rarely performed/ Efficacy: Most patients have no improvement; many patients report the continued presence of smaller floaters, moderately effective primary treatment conferring clinical benefit in one third of patients. Safety: Risks include retinal hemorrhage, retinal pigment epithelial damage, and choroidal hemorrhage) **Vitrectomy surgery**¹¹⁴ a procedure occasionally performed previously but is being advocated now as an out-patient procedure for vitreous floaters (27G vitrectomy)

- **a:** Efficacy: High patients satisfaction; surgical removal of vitreous floaters is not expected to improve visual acuity.
- **b:** Safety: Risks include those associated with vitrectomy for other conditions, such as cataract, vitreous hemorrhage, macular edema, retinal detachment, choroidal hemorrhage, and endophthalmitis.

Vitrectomy may be indicated in a select group of patients with visually disabling vitreous floaters, although objective assessment of visual dysfunction from vitreous floaters requires further evaluation.¹¹⁴ Vitrectomy, while offering superior results (compared to laser vitreolysis), should be reserved for patients who remain marked symptomatic following vitreolysis, until future studies further clarify its role.¹¹⁵

Patients should be informed about the risk of cataract progression, unexpected inflammatory reaction and an increased risk for retinal detachment several years after vitrectomy (5.5%). The idea that vitrectomy for floaters is simple and less dangerous than vitrectomy for other indications should be banned. Despite these risks, a small section of patients with persistent and debilitating symptoms can consent to treatment by vitrectomy.¹¹⁶

**Endoscopy-assisted surgery**
Current technology for ophthalmic endoscopy delivers undoubtedly advantages in certain surgical situations. Endoscopy allows for viewing in 360° through nontransparent media, at a high magnification and tangential approach to the anterior “Zonular” vitreous base, involved in anterior posterior vitreoretinopathy and cyclitic membranes¹¹₇. It facilitates excellent PRP in patients with peripheral ischemic retinopathies. It allows endoscopic cyclophotocoagulation in patients with glaucoma.¹¹₈

A long learning curve, absence of stereopsis and limited view with current 23G probes are the main drawbacks. In the future we can look forward to increased functionality of 23G endoscopic probe. This reduced gauge probe may also be used for retinal vessel cannulation, delivery of stem cells or other therapeuctic agents.¹¹₉

**The preferences & Trend Survey of ASRS (American Society of Retinal Specialists)** showed that most surgeons are using 23G & 25G instrumentation for vitrectomy surgery. 72.5% for respondents perform 23G vitrectomy & 60% perform 25G Vitrectomy.

 Concerns that were raised when 25G instrumentation was first introduced included
1. poor illumination & flow through tiny instruments
2. unacceptable flexibility of instruments
3. risk of hypotony
4. unpredictable gas fills due to leakage from sclerotomy
5. concern over possibility of higher incidence of Endophthalmitis with unsutured wounds
6. an inability to perform certain manoeuvres such as lens extraction
7. loss of many elegant hand held instruments that were designed for 20G technology. Some of these instruments have still not been replicated in 25G

Presented with these concerns about the early 25G technology, the Ophthalmic profession and industry attempted to address them in a no of ways:
1. B & L, Alcon & other manufacturers worked to improve & resolve the limitation of 25G
2. Claus Eckardt along with DORC worked on the 23G platform
3. Others retained the 20G platform with which they were familiar & tried to adapt it to a sutureless transconjunctival approach.
4. Shift to an even smaller 27G
5. Rizzo and co workers introduced a novel design of guillotine of the inner sleeve. Adding a sharp edged hole on the inner sleeve of the guillotine cutter allows the device to cut vitreous both on the downs stroke and return stroke. This doubles the cut rate, increase the flow and potentially reduces traction on the vitreous by the probe.

Presently vitrectomy is performed with variety of gauges & a combination of gauges of instrumentation. Selection of Gauges depends on the level of difficulty expected with the case with the finer gauge instrumentation being used for less complicated cases.

Continuing Development of 27-gauge Vitrectomy Systems: Where Are We Now?
Since Eugene de Juan, MD, first introduced the concept of transconjunctival sutureless vitrectomy with a trocar-cannula system and 25-gauge instrumentation, microincision vitrectomy systems (MIVS) with 25 or 23 gauge instruments have evolved radically over the past several years.\(^{120,121}\)

There is no doubt that MIVS has simplified the vitrectomy procedures and that it offers numerous potential advantages over traditional 20 gauge surgery, including shorter operating time, reduced corneal astigmatism, diminished conjunctival scarring, improved patient comfort, and in some cases, earlier visual recovery.\(^{122}\)

Recent innovations and improvements seem to have settled several concerns that were raised in the early years of MIVS. Stiffer instruments and wide-angle viewing systems have eliminated the frustration with tool fragility. A more powerful light source combined with a chandelier system have improved the endoilluminating brightness through a small gauge optic fiber. The new generation of vitrectomy machines have dramatically improved the cutting efficiency of small-gauge vitrectomy probes.\(^{123,124}\)

CRITICISMS OF SMALL GAUGE VITRECTOMY
The most serious criticisms regarding the current 23 and 25 g systems have focused on complications related to wound sealing, such as leakage, hypotony, and postoperative infectious endophthalmitis. Although the recent refinement of trocar-cannula systems has ergonomically improved their self-sealing architectures, special techniques are still required. Complete self-sealing wounds are not yet achievable in every case, even with 25g systems, especially in patients who have thin scleras or who have had extensive peripheral vitreous shaving.\(^{125}\)

On the basis of the above-mentioned aspects of modern MIVS, the gauge size for MIVS will likely decrease in the future. Recent, innovations, such as the advent of powerful light sources, techniques for building up stiffer instrumentation, and high-performance vitrectomy systems, have also encouraged the development of a 27 g vitrectomy system over the past several years.\(^{126,127}\)

CURRENT STATUS OF THE DEVELOPMENT OF 27-G VITRECTOMY SYSTEMS
In 2008, reports on preliminary results using a first generation 27-g system were released. Although at that time it was used only in the selected cases, mainly macular disease and simple vitreous hemorrhage, both the anatomical and visual results were promising.

Remarkably, there was no need to transition to a larger gauge, no suturing was required, and no hypotony was observed in any of the study cases.\(^{128}\)

Commercially available 27-gauge system packages include a 2,500-cpm high-speed pneumatic vitreous cutter, a wide-angle illuminating light pipe, an infusion tube with a trocar-cannula system, and a micro membrane forceps. The system from DORC is compatible with two vitrectomy machines, the Accurus (Alcon) and Associates (DORC). The system from synergetics can be used with the Accurus only.

When developing a smaller-gauge vitrectomy system, the most crucial concerns may be about reduced endoilluminating and cutting efficiency through small-gauge lumen. The introduction of powerful light sources, using xenon light and mercury vapor light, which have been featured in the new-generation vitrectomy machines as the standard illumination light sources, had fortunately enabled us to develop smaller gauge illumination tools.
Currently, not only the 27-g wide-angle illuminating light pipe packaged in the 27-g pack, but also the 27-g chandelier endoilluminating optic fibers, are commercially available from several manufacturers for use with 27-g systems for more challenging cases, such as a 27-gauge twin light chandelier system (Dorc International, Zuidland, Netherlands) and a 29-/23-gauge dual chandelier fiber system (Synergetics, O'Fallon, MO)\textsuperscript{129,130}

Both types of 27-g chandelier fibers\textsuperscript{131} have maximum output reaching to more than 20 lumens, which is sufficient to endoilluminate the fundus. Development of a practical 27-g vitreous cutter is also a key step for establishing a 27-g vitrectomy system.

Very recently, the second generation spring/pneumatic 27 g cutter from DORC and Medical Instrument Development Laboratories, Inc., (San Leandro, CA) have become commercially available, featuring a normal shaft length (32 mm) and a maximum cutting rate of up to 2,500 cpm with higher duty cycles.

**TECHNIQUES, INDICATIONS, AND CLINICAL EXPERIENCE WITH 27-GAUGE SYSTEMS**

The most distinctive characteristic of the 27-g system that makes it superior to the larger-gauge MIVS systems is the simplicity of creating rigid, self-sealing wounds. The surgeon can begin 27-g vitrectomy immediately after creating sclerotomies at the paraplana by one-step vertical insertion. Complex techniques for creating a self-sealing wound, such as angled-insertion techniques or two step entry methods are no longer required.

Also, because of the small size and multifunctionality of the 27-g cutter, reducing the use of various instruments for manipulation in complex cases will minimize the time wasted in instrument exchanges and, as result, also contribute to the reduction of total operating time.

After simple removal of all instruments, surgeons can close at once, and all sclerotomies can self seal completely without the need for suturing, even in cases with thin scleras, extensive peripheral vitreous shaving, or multiple surgeries. It is no doubt feasible that this system will supersede the current 25 and 23 g systems, at least for treating macular diseases and simple vitreous hemorrhages.

The 27-gauge cutter can be much more easily inserted into the tiny space between the membrane and the retina. Through wide-angle fundus viewing, it is also easy to carry out bimanual membrane dissection with a 27-g system and it goes without saying that the 27-g cutter with a single hand is sufficient for several roles.

**FUTURE PERSPECTIVE**

The final goal of trans conjunctival surgery is to achieve perfect, self-sealing wounds with stable postoperative IOP from the first day after surgery, with tiny changes on the ocular surface-limited subconjunctival hemorrhages and scars and acceptable operating time with minimal intra and postoperative complications- as well as favorable anatomic success and early visual rehabilitation.

The 27-g system may have advanced one step closer to these final goals, compared with the current 23 and 25 g systems. Although the development of 27 g vitrectomy is an ongoing project, and it has not yet been established as a widely accepted system.

The new generation machines, featuring dual-pneumatic driven technology, allow for ultrahigh cutting rates with duty cycle control. The 27 g systems, with this new technology in the near future, will achieve much higher performance.

The recent evolution in 23 and 25 g systems, further development and refinement of 27-g instruments functionality are under way and will continue over the coming years, allowing us in the future to establish this system for ultra minimally invasive surgery for the full spectrum of vitreoretinal pathologies.

**Endophthalmitis after parsplana small gauge vitrectomy**

Several hypothesis have been put forward to explain the higher incidence of endophthalmitis after small gauge vitrectomies. These include

1. **Poor wound stability:** Unsutured wounds that lead to early post operative hypotony may allow intraocular influx of extraocular fluid and micro organisms.
2. **Infusion rate with reduced influx & efflux** of fluid may allow greater bacterial inoculum to remain in the eye.
3. **Residual vitreous skirt** may facilitate bacterial adherence and sequester bacteria from normal immunological factors &extraocular antibiotics.
4. **Vitreous wick prolapse** through sclerotomy sites may create a potentially open conduit through conjunctival and scleral wound, facilitating entry of bacteria into the eye.

Currently prevailing evidence emphasizes the importance of the following measures to reduce the risk of endophthalmitis.

1. **lid scrubbing**
2. direct povidone iodine application
3. conjunctival displacement and angled beveled incision
4. more complete vitreous removal adjacent to sclerotomies
5. air tamponade
6. repositing potential extra conjunctival vitreous wick
with light pipe assisted canula removal & subconjunctival antibiotic injection
7. extra insufflation of air/gas if necessary to stabilize IOP
With refinement of technology we can look forward to water tight sutureless closure and a lower complication rate

New Instrument Update: The list of new instruments released this year resembles science fiction components with ability to outperform older ones as well as make seemingly impossible procedures possible.A peep into the future will not be complete without a mention of these
1. Retidyne132 : is a dye with low potential for phototoxicity due to the addition of small amounts of antioxidant Lutein to a low concentration of Brilliant Blue.This is an intense green dye which has affinity for both the posterior hyaloid and the ILM.(L/2 0.3% + BB 0.2%)
2. Rezzo Pocket Cryo with a small nitrous oxide canister.
3. UltravitProbe with 7500 cuts /min
4. 27 Gauge accessories
5. Edge Plus valved Trocar cannula
6. Versa Vit133 the small compact complete vitrectomy system
7. EVA Phacovitrectomy system with vacuum flow based vitrectomy mode, and LED light source with the first titratable colour source
8. Bausch & Lomb Stellaris with yellow green and amber filters
9. Ehab el Raes Suprachoroidal catheters
10. Tornabe “s temporary winged wedge scleral buckle for 2-8 wks
11. Disposable BIOM
The list goes on ………

GENE THERAPY IN RETINAL DISEASES
 Gene Therapy: Where Are We Now?
A major misconception about gene therapy is that its application is limited to genetic disease. Gene therapy is simply a delivery system for drugs (bioactive substances). Any disease that would benefit by the local production of a genetically engineered protein, peptide, RNA, or RNA fragment would be a potential candidate for gene therapy133.
Proof of principle has been established in animal models for a variety of genetic and non-genetic retinal diseases. For example:
A: Acquired: retinal neovascularization, choroidal neovascularization134
1: Anti-VEGF strategies (eg, using RNAi, antisense RNA)
2: Production of pigment epithelium derived factor
B: Genetic: retinitis pigmentosa, Leber congenital amaurosis135,136, retinal/macular dystrophies
1: For recessive diseases, replacement with “wild-type” gene or gene correction resulting in production normal enzyme:
eg, RPE-65, peripherin / RDS(Prph2)137
2: For dominant disease, neutralization of toxic “dominant” substance (eg, ribozyme therapy for rhodopsin mutants causing dominant RP)

Technique of Retinal Gene Therapy
As with any other drug, the gene therapy agent (ie, vector) has to somehow be applied in order to work. Systemic (eg, intravenous) administration of vectors increases toxicity by enhanced exposure to the immune system; furthermore, it will not result in any appreciable uptake in the retina. Vectors need to come in direct contact with their target cells as they do not cross tissue planes. They are engineered not to replicate and therefore do not spread beyond the field of administration. In addition, since retinal neurons do not replicate, the vector does not become diluted over time.

Administration procedures and the cells types that are transduced:
1: Subretinal injection: retinal pigment epithelium photoreceptors, Muller cells
2: Intravitreal injection: ganglion cells, optic nerve, Muller cells, ciliary body, anterior chamber structures
3: Ex vivo gene therapy can be used to create encapsulated implants; site of “drug” delivery depends on site of surgical implantation.

To date, the genes for some 35 ocular disorders have been identified, and a few of these diseases will be discussed below. The four ocular diseases that have received the most attention are Leber’s congenital amaurosis (LCA), wet AMD, Stargardt disease, and Usher syndrome.

Leber’s Congenital Amaurosis:
In treating LCA135,136, the majority of the work has been focused on RPE65, the RPE specific 65-kDa protein that is involved in the conversion of all trans retinol to 11-cis retinal during phototransduction and that has been implicated as a genetic defect in LCA. When loaded onto the AAV2 virus, the product becomes AAV2-RPE65.

Wet AMD: Another major area of emphasis in gene therapy is treatment of wet AMD. Although anti VEGF drugs are currently successfully treating wet AMD, the cost and time involved monthly or semimonthly injections can be troublesome. As a one time treatment the promise of gene therapy (the “for-ever fix”) is attractive. In wet AMD, VEGF plays a critical role because blockade of VEGF is sufficient to suppress the development of choroidal neovascularization. A variety of antiangiogenic proteins oppose the actions of proangiogenic factors, such as VEGF. Gene transfer to augment expression of these endogenous inhibitors or related engineered proteins is a potential alternative to
suppress CNV and avoid frequent intraocular injections. Considerable preclinical and emerging clinical data suggest this approach may be feasible.

The secreted extracellular domain of VEGF binding protein that consists of domain 2 of Flt-1 linked to a human immunoglobulin B1 (IgG) heavy chain Fc fragments (sFLT01). Intravitreous injection of AAV2.sFLT01 is being evaluated in a phase ½ clinical trial of wet AMD137,138.

**Stargardt Disease:**
The gene identified in the treatment of Stargardt disease is ABCA4139. This gene produces a protein involved in energy transport to and from photoreceptor cells in the retina. Mutations in the ABCA4 gene produce a dysfunctional protein that cannot perform its transport function. As a result, photoreceptor cells degenerate and vision loss occurs.

**PHARMACOGENOMICS AND TREATMENT OF NEOVASCULAR AMD**
How genotype can affect response to treatment.
Age related macular degeneration is a genetically heterogeneous condition in which the mainstay of local anti VEGF treatment also produces widely varied outcomes.

**GENETIC VARIATION TREATMENT RESPONSE:**
It has been long understood that there is a significant genetic component to AMD, based on family history studies. The advances in our ability to analyze the human genome have paralleled the advances in intraocular neovascular inhibitors. Single-nucleotide polymorphisms (SNPs) associated with AMD were first characterized in genes involved in the alternate complement pathway140. Subsequently, disease-associated SNPs have been associated with the genes that are involved in tissue remodeling, as well as oxidative and cholesterol metabolism.

By combining haplotype odds ratios of these multiple SNPs, smoking history, drusen size, our ability to predict the risk of individuals with AMD to progress to advanced sight-threatening AMD is so advanced that it approximates the level of correlation between tobacco smoking and the development of lung cancer, with an odds ratio >17.141

There was no correlation of overall risk score with response to anti VEGF treatment in terms of visual acuity change, OCT thickness change, or treatment number. There were no independent associations of SNPs within the CFH,C3 or ND2 genes with response to anti VEGF therapy based on these three parameters. However, at least one insertion/deletion polymorphic iste, indel (NM_001099667.1:c.372_815del1443ins54), within the ARMS2 gene was found in 63 patients who had an average improvement in log MAR visual acuity, compared to a visual deterioration in those with the ancestral genotype which indicates both a clinically and statistically significant association.

This indel polymorphism in the ARMS2 gene did not appear to be related to a significant difference in the treatment number of anatomic response based on OCT thickness. Patients with or without deletions did not differ by age or presenting visual acuity. The positive treatment response related to this mutation was similar in patients who were treated with either bevacizumab or ranibizumab.

**ANTI VEGF RESPONSE AND ARMS2 GENE STRUCTURE**
Many groups have reported linkage of AMD markers that may predict response to anti VEGF treatment and photodynamic therapy, which include genetic polymorphisms CC(rs1061170,Y402H) in the complement factor H gene (CFH) and the APOE gene. Variable response to AMD therapy was initially studies for PDT, in which visual acuity change was linked to the Y402H SNP in complement factor H.142-146 First report of a relationship between treatment response and polymorphisms within the LOC387715/ARMS2 gene147-150. The reported relatively strong association of the indel deletion of the ARMS2 gene with vision protection following 12 months of anti VEGF treatment, in a population that is representative of typical anti VEGF response, provides a framework for the development of confirmatory prospective studies and for the possible design of novel ocular antiangiogenic strategies.

Two of the central issues in the treatment of neovascular AMD remain optimizing the results of anti VEGF treatment with the lowest treatment burden. The next advances in treatment of neovascular AMD will likely be contingent upon the ability to predict the response of antiangiogenic treatment better and to develop neovascular inhibitors with novel mechanisms of action. Genetic analyses of patients undergoing anti VEGF treatment have the potential to help to accomplish these two advances.

Pharmacogenomics of AMD is therefore a rapidly evolving field, and initial studies of patients with neovascular lesions have provided both interesting results and the rationale for large studies to allow ultimately for better individualized patient care and the design of new therapies.

**Future Treatments for Retinal Degenerations: Neuroprotection**
Photoreceptor cell death is the ultimate cause of vision loss in many eye diseases, including AMD, retinitis pigmentosa, and retinal detachment (RD), which together affects tens of millions of people worldwide. While therapies exist for some of these eye diseases, there are currently no treatments...
that effectively prevent photoreceptor cell death. Much research has focused on the mechanisms of cell death in hopes of identifying therapeutic targets in degenerative retinal diseases. Apoptosis is the most characterized form of programmed cell death, and was previously thought to be the main mechanism of photoreceptor degeneration. Indeed, the caspase enzymes (which play a central role for inducing apoptosis) are activated in dying photoreceptor cells in experimental models of RD151. Paradoxically, inhibiting caspases does not sufficiently protect against photoreceptor cell loss. This suggests that other mechanisms of cell death are involved. Recent accumulating evidence demonstrates that non-apoptotic forms of cell deaths, such as autophagy and necrosis, are also regulated by specific molecular machinery, such as autophagy-related proteins and receptor-interacting protein (RIP) kinases,152 respectively. By identifying alternative cell death pathways and understanding how to inhibit them, we can prevent vision loss in multiple eye disorders.

Classification of Cell Death: Apoptosis, Autophagy, and Necrosis

The morphological features of apoptotic, autophagic, and necrotic cells are quite distinct and still the gold standard in distinguishing the various forms of cell death. Genetic / biochemical features have been now recognized, but there is a lot of interplay and cross talk.

Caspase signaling is initiated by either external death signals such as tumor necrosis factor (TNF)153 or Fas ligand (FasL) or intrinsic signals such as mitochondria damage and reactive oxygen species (ROS)154. First identified as the key player of cell death in development, apoptosis also has strong evidence supporting its central role in disease. Caspases are also involved in pyroptosis, a distinct mechanism of cell death associated with inflammation. The role of caspase-dependent apoptosis in photoreceptor cell death has been established in many models.

3: Apoptosis-Inducing Factor (AIF)-Mediated Mitochondrial Pathway

Apoptosis-inducing factor (AIF) is an intrinsic factor involved in initiating a caspase-independent pathway of apoptosis. It moves from the mitochondrion into the nucleus and has been shown to play a role in photoreceptor cell death after RD153.

RIP kinase (RIPK) signaling is closely connected to both the extrinsic caspase signaling pathway and the NF-KB survival pathway. Caspases inhibit RIPK signaling and limit necrosis. However, when caspases are blocked, the RIP kinases are activated, and increased necrosis compensates for the inhibition of apoptosis.

4: Autophagy-Related Protein (Atg) Family

Autophagy (from the Greek word auto meaning “self” and phagein meaning “to eat”) is a process/mechanism in which the cell degrades unnecessary or dysfunctional cellular components to ensure cellular survival during starvation by maintaining cellular energy levels. Depending on the system and the levels of activation autophagy can promote either cell survival or cell death.

5: Neuroprotection Strategies

A: Caspase inhibition

Early on it was shown in experimental RD that apoptotic photoreceptor cell death is associated with caspase activation. In addition, Zacks and colleagues155 have shown that the Fas-mediated apoptosis pathway becomes activated after RD, and inhibition of Fas activation (with anti-FAS-receptor antibodies) can decrease caspase-9 activity (Zacks, et al., 2004). However, when pan-caspase inhibition was tested as a neuroprotection strategy, caspase inhibitors were unable to prevent cell death. In contrast activation of the endogenous X-linked inhibitor of apoptosis (XIAP) 155as been shown to have protective qualities in rodent models of retinitis pigmentosa (Leonard, et al., 2007)156 and in RD Zadro-Lamoureux, et al., 2009)157, and it may be a useful strategy for neuroprotection.

B: Combined inhibition of apoptosis and necroptosis

We found that in photoreceptor degeneration after experimental RD, RIPK-mediated necrosis is also a significant mode of cell death; furthermore, when caspase are inhibited, RIP-mediated necrosis become the predominant form of death. (Trichonas, et al., 2010)158. This may explain why caspase inhibition has been unsuccessful in preventing photoreceptor cell death. RIPK-mediated programmed necrosis and apoptosis and redundant mechanism of photoreceptor cell death, and simultaneous inhibition of RIP kinases and caspase is essential for effective neuroprotection.

C: Ciliaryneurotrophic factor (CNTF)

CNTF159, which may act through the IL-6 receptor, is a potential neuroprotective treatment. Significant in vitro and animal studies have shown CNTF to be a potent survival factor for neurons and oligodendrocytes, and it may reduce tissue destruction resulting from inflammation. Neurotech has devised a technology using encapsulated human cells (NT-501) genetically modified to secrete CNTF. In the early stage clinical trials for retinitis pigmentosa and geographic atrophy secondary to AMD, this treatment appeared to be rather well tolerated with some hints of benefit.

D: Brimonidine: Brimonidine 160(Allergan; Irvine, Calif., USA) is a selective alpha 2-adrenergic agonist well known
for reducing aqueous production that has been shown to increase the production of neurotrophic factors, protecting cells from degeneration with unknown mechanism. Allergan is investigating a brimonidine intravitreal implant in patients with geographic atrophy in a Phase 2 clinical trial.

6: Pathway to Clinical Trials
To date, neuroprotection has been unsuccessful in ophthalmic clinical trials. Proof-of-concept studies could be undertaken in RD to test whether visual outcomes can be improved in acute settings. For chronic diseases like AMD and IRDs, slow-release formulation should be developed. The local delivery and tolerability to intravitreal injections will facilitate our efforts to easily integrate neuroprotective treatments into standard patient care.

Photoreceptor cell death is the ultimate cause of vision loss in RD and other retinal degenerative disorders, and apoptosis is the best-characterized form of programmed cell death. However, despite more than a decade of work, attempts to achieve neuroprotection by pharmacologically targeting apoptosis have largely failed. We and others have shown that not only apoptotic but also nonapoptotic pathways contribute to photoreceptor cell death and that simultaneously targeting key mediators in both pathways (eg, inhibiting both caspases and RIP kinases) is effective in preventing photoreceptor cell loss. Further dissection of the complex molecular mechanisms of photoreceptor cell death will lead to novel strategies for preventing vision deficits in retinal degenerative diseases.

And more to come in future……….
Trials on topical eye drops in AMD, advancement in the bionic eye, individualized treatment options based on genetic component, advancement in imaging technology and newer and better drug delivery systems to deliver drugs to the posterior segment are being evaluated and will soon reach the bedside.
The practice of RETINA has never been so exciting and rewarding ……. and with no end of the road in sight we can look forwards to a brighter tomorrow.

Telemedicine’s Role in Posterior Segment Eye Care
Making eye care more accessible to patients and decreasing unnecessary visits

The advent of telemedicine heralds a new era in ophthalmology to bridge the gap between physician and patient and offering many benefits for the screening, diagnosis, monitoring and management of eye disease. Advances in computing and telecommunications technology enable ophthalmologists and optometrists to offer a higher standard of care despite geographic distance. Significant cost savings can be realized by using telemedicine instead of annual eye exams.

THE PROS OF TELEMEDICINE
Telemedicine provides a reliable, cost-effective means of screening diabetic patients and premature babies for retinopathy, which can lead to blindness. Since the number of diabetics in the United States is growing fast, and the supply of eye-care practitioners is not, healthcare resources are strained and becoming more so. Certainly, not every diabetic now receives the standard of care, an annual eye exam, but that situation will likely worsen unless alternative healthcare delivery systems are employed to address it. With new, easy to-use, non-mydriatic cameras, nurse and medical assistants without any ophthalmic training can learn to take excellent fundus photographs. These images can be transmitted to a reading center where they can be expertly assessed. This new methodology has already been adopted in a number of high profile institutions and also is part of the HEDIS standards for comprehensive diabetic care.

Two new technologies that work seamlessly together are the PRN Referral cloud based telemedicine software and the nonmydriatic fundus cameras.

References


43. Oh J, Kim SW, Kwon SS et al. Correlation of fundus autofluorescence grey values with vision and microperimetry in resolved central serous chorioretinopathy.
47. Spaide RF. Fundus autofluorescence and age-related macular degeneration. Ophthalmology. 2003;110: 392-399
72. Roth DB et al. The Incidence of noninfectious intraocular inflammation after intravitreal Aflibercept Injection. Verbal communication of ASRS annual meeting, Las

74. Peter K Kaiser Editorial. Retinal Physician 2012 OCTOBER.


76. Molecular partners report positive results from its clinical studies on MP 0112, its lead macular targeting VEGF-A. April 28, 2011, Eastern Daylight Time. Abstract ARVO Fort Lauderdale, FL (May 1st -5th 2011)


Dr Meena Chakrabarti did her MBBS & MS Ophthal from Medical College Trivandrum and was trained at Aravind Eye Hospital, she is now Vitreo Retinal Surgeon and Director of Chakrabarti Eye Care Centre.