Analysis of Conventional Imaging Techniques Used in Grading Diabetic Macular Edema

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Abstract— The most common and first among other disorders caused due to prolonged and untreated diabetic are retinopathy and maculopathy. These disorders effect the visual ability of human eye. India stands second contributing 30% population being affected by diabetes. This fact motivates towards the study of problem associated in this domain to design and assert the solutions through engineered technology. The present work is towards building a knowledgebase to understand the existing technology used in diagnosis by the ophthalmologist. The work acquaints with the commonly used imaging techniques, their advantages and disadvantages to support the future research to be carried out in right and efficient direction. The retinal diagnosis involves non-invasive procedures. The patients are administered with eye drops to dilate the pupil for better visualization of the internal structure of the eye. The most preferred imaging tools used by ophthalmologist are fundus imaging, fluorescein angiography, and optical coherence tomography. These tools are used for visualization of retinal pathologies such as microaneurysms, exudates (both hard and soft), hemorrhages, neovascularization, retinal thickness among others. Automating the diagnosis process aids the ophthalmologist in accurate and timely diagnosis as India suffers a drastic mismatch in the ratio of ophthalmologist to the population (1: 1,00,000).

Index Terms— Diabetic Retinopathy, Color Fundus Photography, Fluorescein Angiography, Optical Coherence Tomography, Diabetic Macular Edema

1 Introduction

One of the primary causes of eye disorder leading to blindness is diabetes. World Health Organization reports the required ratio of ophthalmologist to the population as 1 per 20,000 in the world and in particular, for India, there is an estimated 9,000 to 10,000 ophthalmologists that presents a ratio of 1:100,000 populations, which is a serious shortage of manpower in this sector. The pervasiveness of Diabetic Retinopathy (DR) is 56% and Diabetic Macular Edema (DME) is 42% in Type 1 diabetes and 30.3% and 53% in Type 2 diabetes subjects according to the UK National diabetic retinopathy screening service [1]. So, to facilitate the tele-medicine concepts and to aid Ophthalmologists for treating the patients with less manpower and time-consuming procedures there is a need to use images for grading DME. Analysis of retinal images helps in screening, evaluation, diagnosis, and treatment of diabetic retinopathy and maculopathy.

Microaneurysms (MA), hard exudates (HEx), cotton wool spots (CWS), retinal thickness (RT) and hemorrhages (HE) are the characteristic features of DR and DME. MAs are red spots on the retina's surface caused by injury to the retinal blood vessels [2], [3]. Microaneurysms are tiny enlargements of capillary walls that can leak fluid, causing intraretinal edema and haemorrhages. Hemorrhages do not have proper clearly distinguishable specific sharp edges. HEx and CWS are the fat deposits and HEs are the serious damage to blood vessels [4]. Exudates can be seen from initial stages of diabetic retinopathy to advanced stage of maculopathy. Hence exudates are an important feature to consider for diagnosis of retinal disorders. The retinal thickness is caused due to liquid accumulation between the layers. The extent of presence and distribution of these pathologies in the human eye are the parameters to grade the disorders as DR or DME.

1.1Diabetic Retinopathy

Diabetic Retinopathy (DR) is the early stage of disorder characterized by MA, Hard exudates and soft exudates. Diabetic retinopathy is classified as Non-proliferative and Proliferative as shown in Figure 1 and the images relevant to DR classification is shown in figure 2. At NPDR stage the blood vessels in the retina are weakened and various pathologies are observed in lower count. In PDR abnormal blood vessels growth called as Neovascularization are observed. These pathologies are found scattered all over the retina and are less in numbers in NPDR and gradually increases in PDR [5].

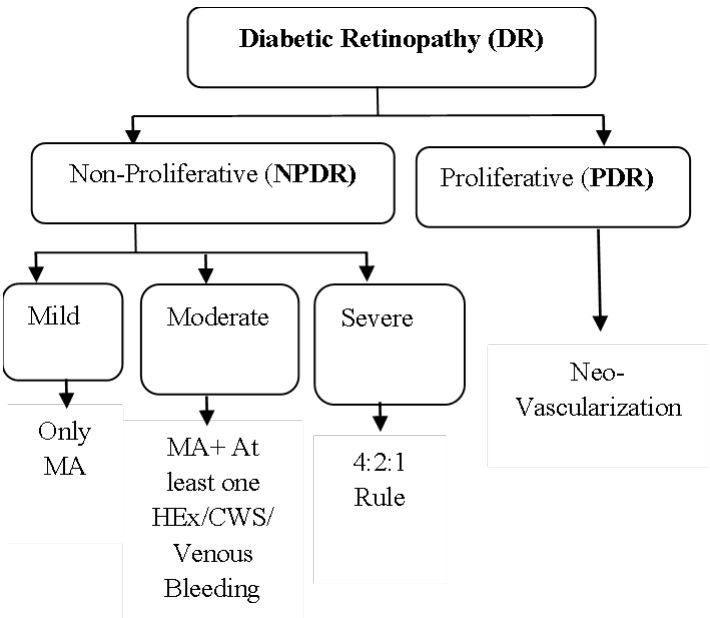


Figure 1: Classification of Diabetic Retinopathy

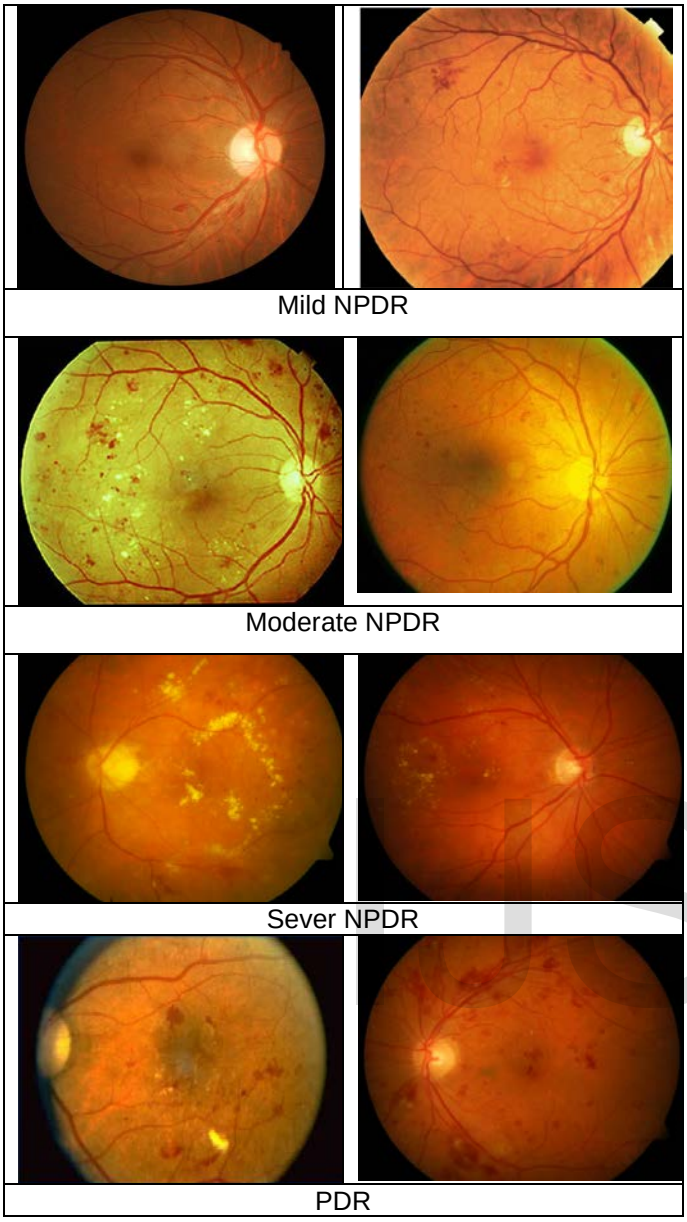


Figure 2: Sample fundus images with various levels of Diabetic Retinopathy

1.2 Diabetic Maculopathy

Diabetic maculopathy affects the macula, causing central vision loss and is a potential cause of legal blindness in people with type 2 diabetes [6]. The retinal thickness, retinal morphology, macular traction, larger hard exudates and foveal photoreceptor status can be some of the parameters or the findings that can be considered to classify the DME [7]. Based on the severity of macular edema, the DME can be classified as Clinically Significant Macular Edema (CSME), Mild DME, Moderate DME and Severe DME (Figure 3).

CSME is defined by the presence of hard exudates in the middle of the retina within 500 µm of the fovea's centre and retinal thickening in at least one disc area within 1500 µm of the fovea's centre. DME can also be classified as mild (retinal thickening or HEx between1500 and 3000 µm from the foveal center), moderate (retinal thickening or HEx between 500 and 1500 from the foveal center approaching the center of the macula), or severe (retinal thickening or HE in the center of the macula within 500 µm of foveal center) [8] - [10].

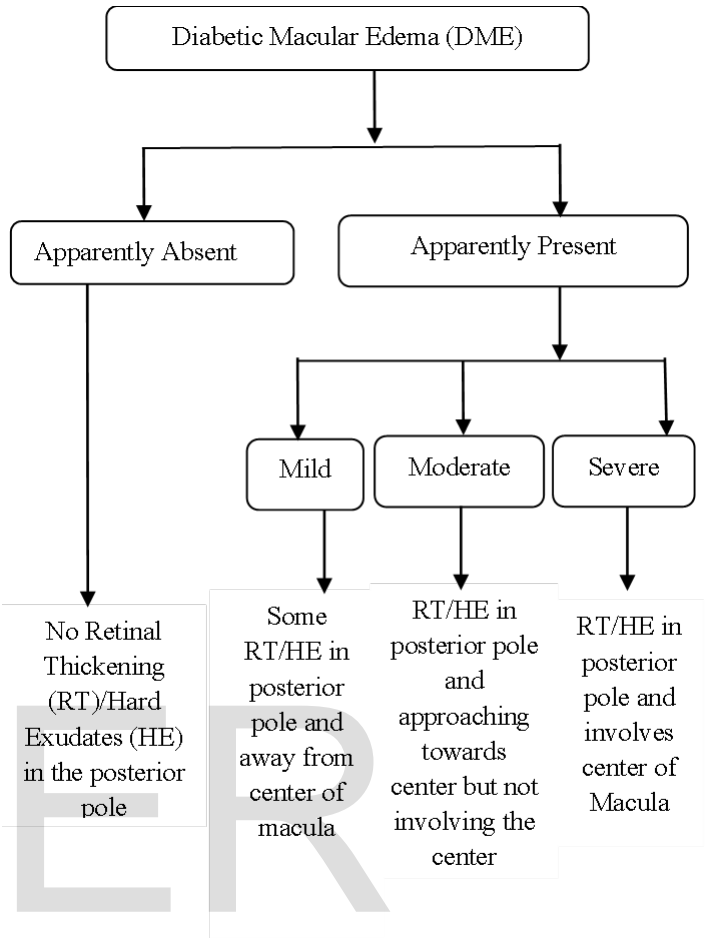
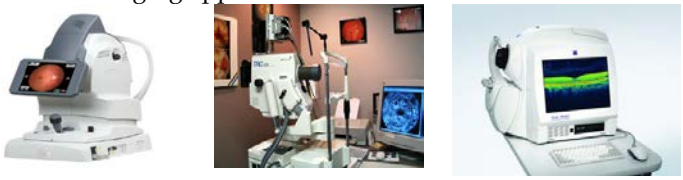


Figure 3: Classification of Diabetic Maculopathy

2 IMPORTANCE OF IMAGING TECHNIQUE FOR GRADING DME

Ocular imaging is crucial in the diagnosis and management of diabetic eye disease. The imaging techniques can be invasive and non-invasive. The invasive techniques extract the systemic features while non-invasive techniques capture deep structural changes in the body parts. Ophthalmologists and retina specialists are in need of obtaining accurate and highly reproducible information on retinal disorders. Thus, non-invasive techniques like Fundus photography, fluorescence angiography and Optical Coherence Tomography are used to detect and evaluate eye diseases. These techniques are more advantageous for the ophthalmologists to diagnose, evaluate and provide early treatment with less time and effort. In this work imaging techniques used in grading DR and DME are extensively explored. Figure 4 depicts a few of the devices utilised in various imaging approaches.

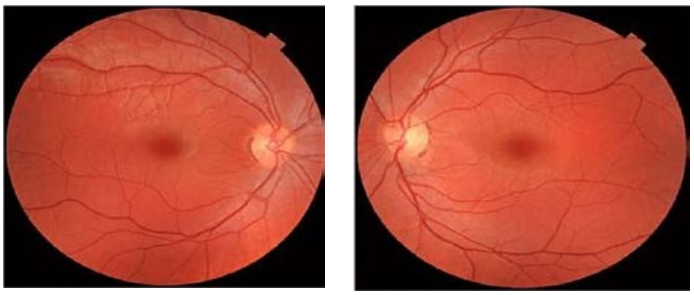


Fundus Camera Device FA Camera OCT Device

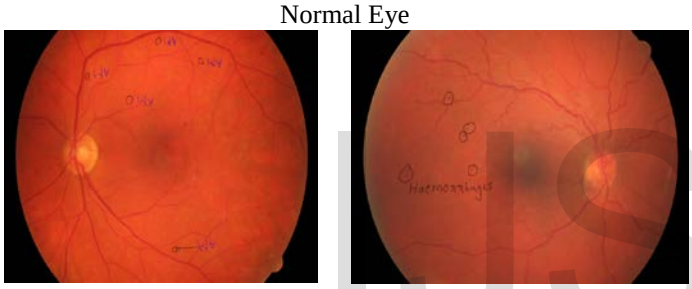
Figure 4: Retinal Imaging Techniques

2.1 Fundus Imaging Technique

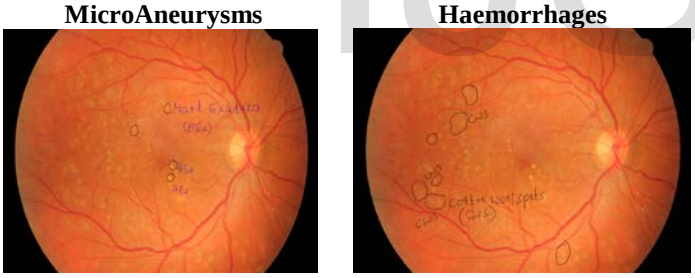
The fundus photography provides clearly evident visualization of initial pathologies, anatomical structures like blood vessels, optic nerves. This does not need any specific knowledge to study fundus imaging. This imaging technique is cost effective and very helpful in the initial stages of diagnosis of retinopathy.



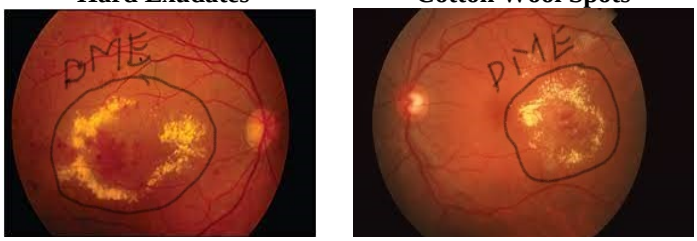
Normal Eye



MicroAneurysms **Haemorrhages**



Hard Exudates **Cotton Wool Spots**



DME

Figure 5: Sample fundus images with presence of different Lesions

Figure 5 depicts the specifics of several lesions that can be diagnosed by fundus photography as well as their appearance [11][12]. The Microaneurysms are seen as Small circular deep-red dots (with radius) on side walls of blood vessel found in the retina of eye, in the posterior pole. Hemorrhages range from smallest red color dot and blot, creates circinate patterns, and are found in all the quadrants of fundus images. Hard exudates are yellow patches made up of lipid and proteinaceous material that form in the outer layers of the retina. Soft Exudates are yellow-white (with indistinguishable edges) lesion in the superficial retina that usually occupies an area less than one fourth that of the optic disc [13].

With the above benefits fundus photography has several limitations. The Cross-sectional visualization is not supported as it presents the information in 2D which makes it incapable to capture the cross-sectional details of pathologies. Additional methods are required to classify the structures sharing the common properties such as color, contrast and the intensity. For example, Optic Disk (OD) and hard exudates share same color shape and size with well-defined edges as shown in figure 6 [14]. Hence there might be increase in false positive results. Color fundus photography can be used to detect retinopathy, but it can't detect other ocular illnesses including glaucoma, cataracts, macular edema, or retinal neovascularization. Due to imaging imperfections or low image quality, image interpretation can be hampered at some times. Often, the cloudiness, dullness or any kind of opacity in the media will not provide clear/proper images and hence it can be difficult to get good images.

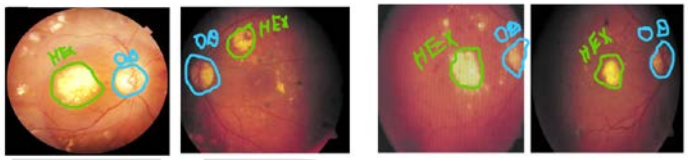


Figure 6: Optical discs and Hard exudates in Fundus Images [25] - [27]

2.2 Fluorescein Angiography

The Fluorescein Angiography (FA) provides retinal circulation details that are useful in assessing retinal disorders generally influenced by diabetes. This technique is generally used for treatment planning [15]. An ophthalmologist injects a vegetable dye or sodium fluorescein into a vein in the arm or hand, and as the dye goes through the eye, photographs are taken at various stages to spot any blockages or leaking. The injection of sterile fluid may lead to transient nausea, vomiting, and allergic reactions [16]. FA can detect changes in blood flow, vascular permeability, retinal and choroidal vascular patterns, retinal pigment epithelium, and a range of other things [17]. The identification of the macular center, leaking vessels or internal blockages can be observed and detected properly by FA than Fundus Photography.

The most common way to describe deviations from the typical FA is in terms of relative fluorescence. Hypo fluorescence is a decrease in fluorescence compared to what is expected, whereas hyper fluorescence is an increase in or aberrant fluorescence. The lesions responsible for DR and DME can be seen in figure 7 based on fluorescence relativeness. Microaneurysms are filled with contrast early during the angiogram, presenting itself as a fusiform hyper fluorescence dot in the shape of a light bulb. Dot- blot hemorrhages appear as Hypo fluorescent spots. Hard exudates are identified as Non focal hypo fluorescent areas. cotton-wool spots are elongated as compared to hard exudates. Increased brightness and blurring of vessels indicate leakage from vessel segments [18]. Diffuse hyper fluorescence at macular area represents Macular Edema.

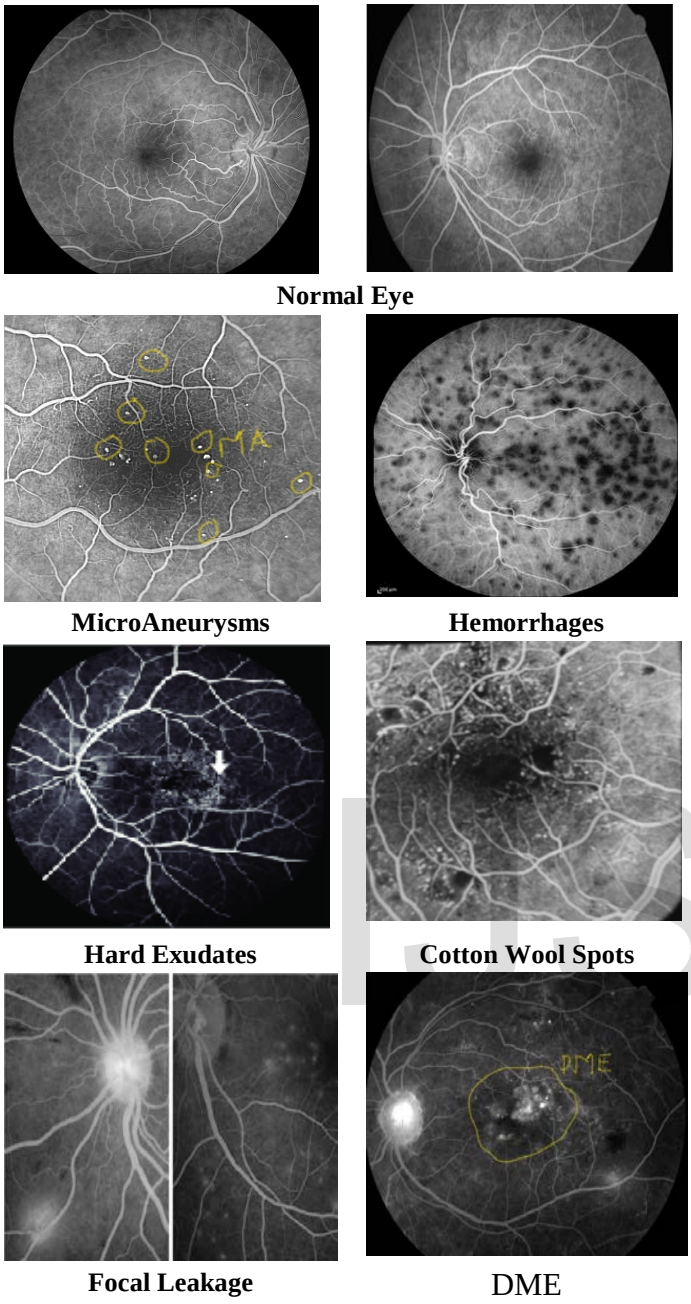


Figure 7: FA images with presence of different Lesions

FA are important for detecting clinically hidden Neovascularization, especially before cataract surgery and in eyes with unexplained vision loss. The FA is useful for determining a diagnosis, formulating a treatment strategy, and monitoring afflicted blood vessels. The infusion of fluorescent dye into the bloodstream to highlight blood vessels in the back of the eye causes allergic symptoms in subjects, which is a major disadvantage of FA. It's possible that HEx and optical discs are misidentified in fundus pictures. The use of FA limits the visibility of deep retinal and choroidal arteries. Quantifying and classifying macular edema, evaluating outer retinal structural damage, and ensuring proper follow-up are all made easier with optical coherence tomography [19], [20].

2.3 Optical Coherence Tomography (OCT)

OCT is a noninvasive imaging technique that produces high-resolution volumetric cross-sectional images of the retina. To aid in the early detection and diagnosis of retinal disorders and ailments, the layers within the retina can be separated and retinal thickness can be quantified [21]. OCT images help in identifying small changes in layer thickness and severity of the diseases can be properly diagnosed. Thus, OCT is well suited and recently used imaging technique to assist ophthalmologist in identifying retinal diseases for early detection and diagnosis. OCT is most beneficial in diabetic individuals for measuring and quantifying macular edema.

The spectral domain OCT (SDOCT) has considerably reduced acquisition time and permitted imaging at speeds approaching video rate. This has benefits for real-time eye tracking. The SDOCT can give better description of the structural changes and the presence of various lesions in the individual retinal layers. A Type-II diabetic patient can have increase in the retinal thickness at the central portion of the retina which is called as Edema. The thickness can be observed due to the accumulation of the fluid which can be extracellular, intracellular or a combination of both. The Retinal thickness can be increased mainly in the Inner Nuclear Layer (INL). Around 79% increase in retinal thickness is shown in the INL. There were also increases in the Outer Nuclear Layer (ONL) and Inner Segment (IS) layers but in the Outer Plexiform Layer (OPL) retinal thickness is less frequent. Cystoid spaces can be seen in INL and OPL. Hyperreflective foci in the subretinal fluid can accompany serous retinal detachment, exacerbating the pathophysiology at the photoreceptor-Retinal Pigment Epithelium interface (RPE). The disruption of the external limiting membrane or the junction between the inner and outer segment lines represents photoreceptor injury at the fovea, which is associated to visual impairment. On SD-OCT pictures, hyperreflective foci can also be seen in the outer retinal layers.

The presence of lesions can be observed in different layers of retina using OCT. The structural findings, as well as multiple lesions with their layers, are depicted in Figure 8. Microaneurysms appear as hyperreflective rings usually located in the middle retinal layers. Hemorrhages are Dense, dark red, sharply outlined, moderately hyperreflective masses, may be located in the inner retinal layers. the hemorrhages can be Intraretinal, Subretinal and Sub-RPE. Intraretinal Dot and blot hemorrhages, found within the INL and OPL of the retina. Deep red in color and broader in shape with diffuse margins subretinal hemorrhages occur between the photoreceptor layer and RPE. The dark red Sub-RPE Hemorrhages have well-defined sharp boundaries and are found between the RPE and the Bruch membrane [22]. HEx with accompanying retinal thickening appear within 500 microns of the fovea's center in highly hyperreflective and irregular pictures with posterior shadowing. Exudates accumulate at the OPL level in SDOCT. Foveal, Temporal, Superior, Nasal and Inferior inner/outer thickness along with macular thickness can be observed.

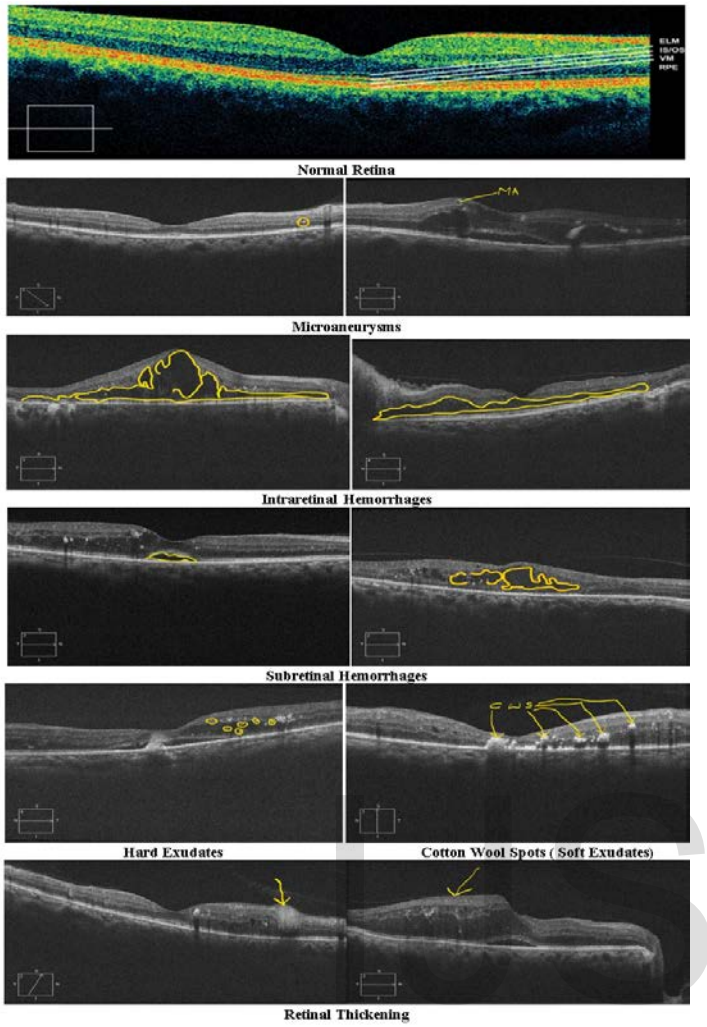


Figure 8: Structural Findings of Multiple Lesions with Their Layers

OCT is currently the utmost essential test in the evaluation and therapy of DME because it can tell if the patient has center-involving or non-center-involving DME. OCT reveals a variety of micro-anatomical aspects in DME, including loss of distinct layers of the retina, such as photoreceptors or nerve fiber layer, which helps to explain vision loss in those who don't have any other macular abnormalities [23][24]. The ophthalmologist may quickly see structural changes and the presence of various lesions in the separate retinal layers using an OCT, which aids in early diagnosis and therapy. Increased scan speed and three-dimensional data production are two advantages of OCT. Each volumetric output using OCT can take as little as 6 seconds, compared to 10-30 minutes for procedures like fluorescein tomography, which only offers two-dimensional images. OCT is safer than FA because it does not involve radiation, X-rays, or fluorescent injection. It is painless and comfortable for the patients.

3 CONCLUSION

The survey on research focuses on the several imaging modalities that are used to grade Diabetic Macular Edema. The three procedures, fundus, fluorescein angiography, and Optical Coherence Tomography, are discussed, along with a comparison of their results. The presence of retinopathy and maculopathy-causing lesions is discussed, as well as their size, shape, color, location, and appearance. Fundus photography is used to diagnose retinopathy, while FA measures microvascular alterations, focal leakage, and neovascularization. Clinical distinctions between microaneurysms and hemorrhages, hard exudates, and optical discs are difficult to distinguish using fundus and FA imaging techniques since these diseases have similar color, shape, and intensity. Fundus and FA do not support structural, cross-sectional, or retinal layer thickness measurements. As a result, OCT is the most widely accepted tool for ophthalmologists to observe any structural changes. The distinct layers of the retina may be easily identified for thickness and lesion diagnosis. This is the most effective method for further classifying DME based on severity levels.

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