MOTION CONTRAST USING OPTICAL COHERENCE TOMOGRAPHY

Thesis by

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ABSTRACT

Diagnosis of ophthalmic diseases like age-related macular degeneration is very important for treatment of the disease as well as the development of future treatments. Optical coherence tomography (OCT) is an optical interference technique which can measure the three-dimensional structural information of the reflecting layers within a sample. In retinal imaging, OCT is used as the primary diagnostic tool for structural abnormalities such as retinal holes and detachments. The contrast within the images of this technique is based upon reflectivity changes from different regions of the retina.

This thesis demonstrates the developments of methods used to produce additional contrast to the structural OCT images based on the tiny fluctuations of motion experienced by the mobile scatterers within a sample. Motion contrast was observed for motions smaller than 50 nm in images of a variety of samples. Initial contrast method demonstrations used Brownian motion differences to separate regions of a mobile Intralipid solution from a static agarose gel, chosen in concentration to minimize reflectivity contrast.

Zebrafish embryos in the range of 3-4 days post fertilization were imaged using several motion contrast methods to determine the capabilities of identifying regions of vascular flow. Vasculature identification was demonstrated in zebrafish for blood vessels of all orientations as small as 10 μm in diameter. Mouse retinal imaging utilized the same motion contrast methods to determine the contrast capabilities for motions associated with vasculature within the retina. Improved contrast imaging techniques demonstrated comparable images to fluorescein angiography, the gold standard of retinal vascular imaging. Future studies can improve the demonstrated contrast analysis techniques and apply them towards human retinal motion contrast imaging for ophthalmic diagnostic purposes.

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INTRODUCTION

1.1 Introducing Age-related Macular Degeneration

Age-related macular degeneration (AMD) is the most common form of vision loss in the western world for people over the age of 50. Approximately 9 million people in the United States suffer diminished vision due to AMD, with a prevalence that increases with the age of patients. While 7% of the population between the ages of 60-69 have this disease, the percentages increase to approximately 14% for the ages of 70-79 and over 35% for the population over the age of 80 [1,2]. With the aging population in this country (the first baby boomers turn 65 in 2011), the number of people in the high-prevalence age ranges increases over time [3]. The occurrence of AMD is estimated to double within approximately the next 15 years [4].

To understand the source of age-related macular degeneration, changes occurring within the retina of the eye over time must be understood. The retina is a thin layer of tissue in the inner eye responsible for vision. With the front of the eye defined as the location of the pupil and lens, the retina is located in the inner globe at the back of the eye. There are many layers in the retina, but the region of interest is the outermost layers extending from the photoreceptors to the choroid, the ocular blood supply.

Light entering the eye is focused by the lens onto the retina at the back of the eye, including the central vision region called the macula. The light passes through the top layers of the retina which contain blood vessels to supply the retina as well as the nerve fibers which combine to form the optic nerve to the brain. The light then arrives on the photoreceptors, the light sensitive cells which translate photons into electrical signals interpreted by the brain as vision. The highly pigmented membrane called the retinal pigment epithelium (RPE) reduces any incoming light penetrating deeper into the retina.

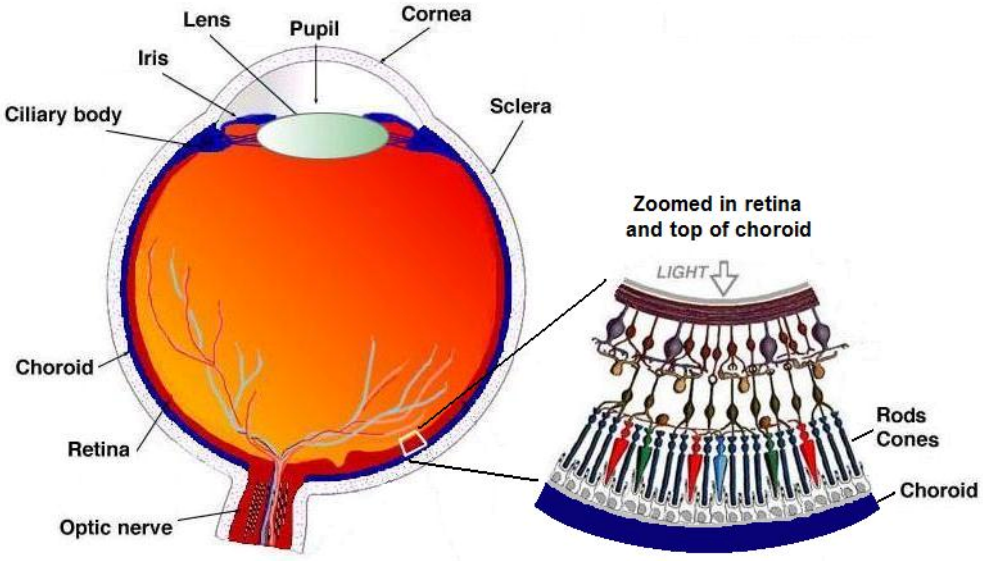

Figure 1.1: Schematic of a human eye with a zoomed-in region of the retina. Image reproduced from [5].

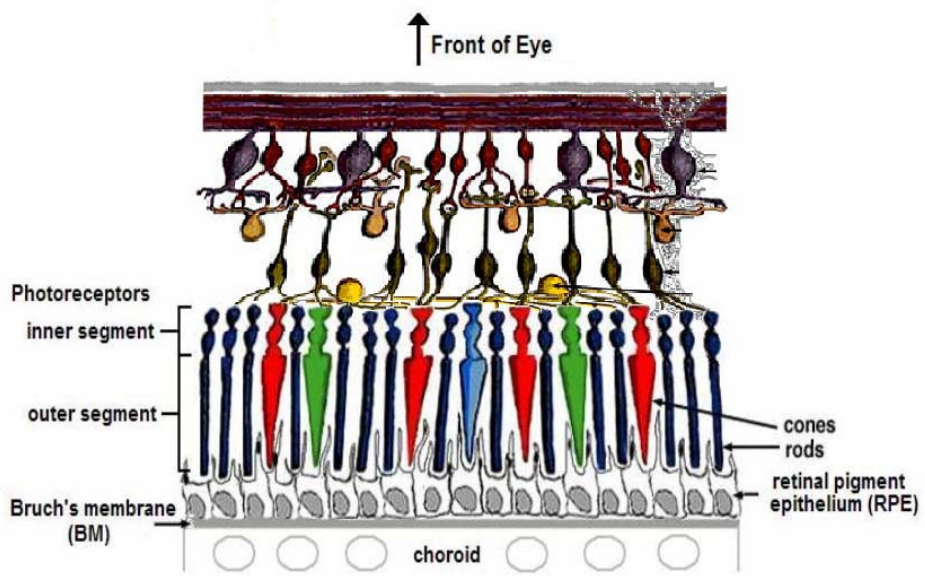

Figure 1.2: Schematic image of the major structures of the lower retina. Image reproduced from [5].

There are two types of photoreceptors, defined as rods and cones. Rods are extremely light-sensitive cells responsible for vision in low-light scenarios requiring night vision. Cones are the main cells responsible for daylight vision, less sensitive than cones and with three types differentiated by the three different spectral sensitivities of the cells. The variety of spectral sensitivities of the cones and the lack of color differentiation of the rods are the reasons normal vision is experienced in color but night vision is only in black and white.

High-resolution imaging occurs in the central part of the macular region of the retina, called the fovea. For this region, the cells located above the photoreceptors are thinned and contain no blood vessels. This allows minimal image signal degradation before arriving at the photoreceptors. While for most of the retina, the photoreceptors contain a mixture of rods and cones, the central fovea region contains only a tightly packed region of cones.

The process of converting incoming light into nerve signals in the photoreceptors is accomplished through photosensing pigments called rhodopsin. Disc-shaped lipid membranes containing rhodopsin are packed into the outer segments of the photoreceptors. As the chemical in the discs becomes bleached over the course of a day, the spent photoreceptor outer segment discs must be removed to maintain vision quality [6,7]. Approximately 10% of all outer segment discs are shed each day while the same amount of new discs is produced by the inner segment of the photoreceptors.

Phagocytosis is a process by which a cell engulfs and digests microorganisms and cellular debris. The RPE cells undergo the process of phagocytosis, in which the cells extend out and pinch off the outermost discs of the photoreceptors [8,9]. This circadian process is synchronized with the end of the daily cycle of the rods and cones separately [10,11]. (Early morning for rods and beginning of nightfall for cones) Metabolic waste produced by the cells passes from the RPE through Bruch’s membrane (BM) to the choroidal blood supply for disposal.

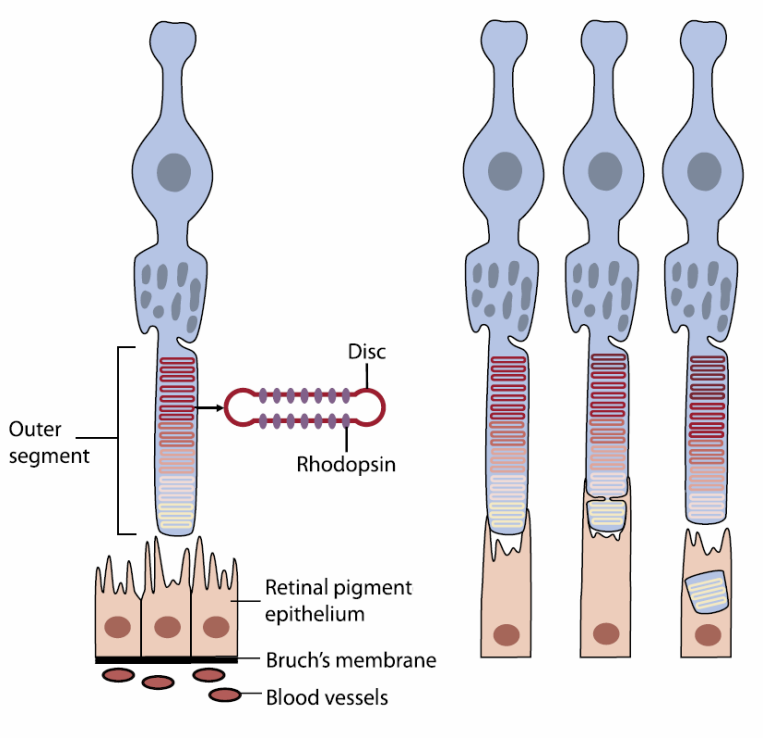

Figure 1.3: Schematic of daily phagocytosis process: RPE cells pinching off the used outer segments of photoreceptors while new segments grow in their place.

Bruch's membrane is a five-layer matrix separating the RPE from the choroid [12]. The collagenous fibers that compose these layers create a basket-weave-type structure. A decline in the RPE phagolysosomal processing associated with the accumulation of lipid-based molecules called lipofuscin within the RPE cells occurs over time within the eye [13,14,15]. Also occurring over time, a portion of the sticky lipid waste product passing through Bruch's membrane attaches itself to the structure. As the ability of the RPE to break down and metabolize the lipids of the photoreceptor discs decreases over time, the amount of "sticky" lipids that are likely to attach themselves to Bruch's membrane increases as well. With an increased amount of lipids attached to BM, there is an increased chance that future metabolitic waste will also become blocked from passing through the membrane.

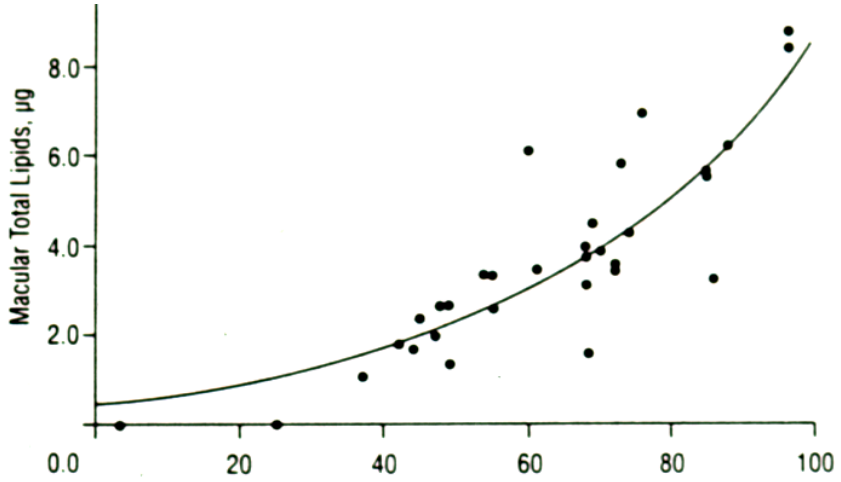

Figure 1.4: The total lipid content present in the macular region of Bruch's membrane as a function of the patient age. Data reproduced from [16].

With the decreased metabolism of the RPE cells and the increased blocking of waste passage by Bruch's membrane, the expected rate of lipids getting stuck to Bruch's membrane should increase in time. If this rate increases linearly with time, the resulting amount of lipids attached to BM should be an exponential increase over time. Using histological sections of human retinas and analyzing the total lipid content of Bruch's membrane of the macular region, this trend has been experimentally verified [16]. The rate of lipid deposition on Bruch's membrane depends on the amount of metabolitic waste passing through the membrane. With the highest density of photoreceptors located within the macular region of the retina (high resolution central vision region), this region accumulates the largest amount of lipids over time.

The accumulation of lipids on and within Bruch's membrane does not change the fundamental structure of the membrane itself. Excised Bruch's membrane tissue of an aged eye has been demonstrated to contain an increased amount of lipids. Electron microscopy images of the tissue from an aged eye visualized a lipid-filled Bruch's membrane. Removal of the lipids using ethanol reveals the collagenous layered structure of Bruch's membrane as shown in Figure 1.5. The lipid accumulations which occur on and within Bruch's membrane are referred to as basal linear deposits and basal lamellar deposits. The build up

of these deposits thickens the membrane over the lifetime of patients. Histological measurements of excised retinal tissues have determined a typical thickness change of Bruch's membrane to more than double over ten decades of patient age [17].

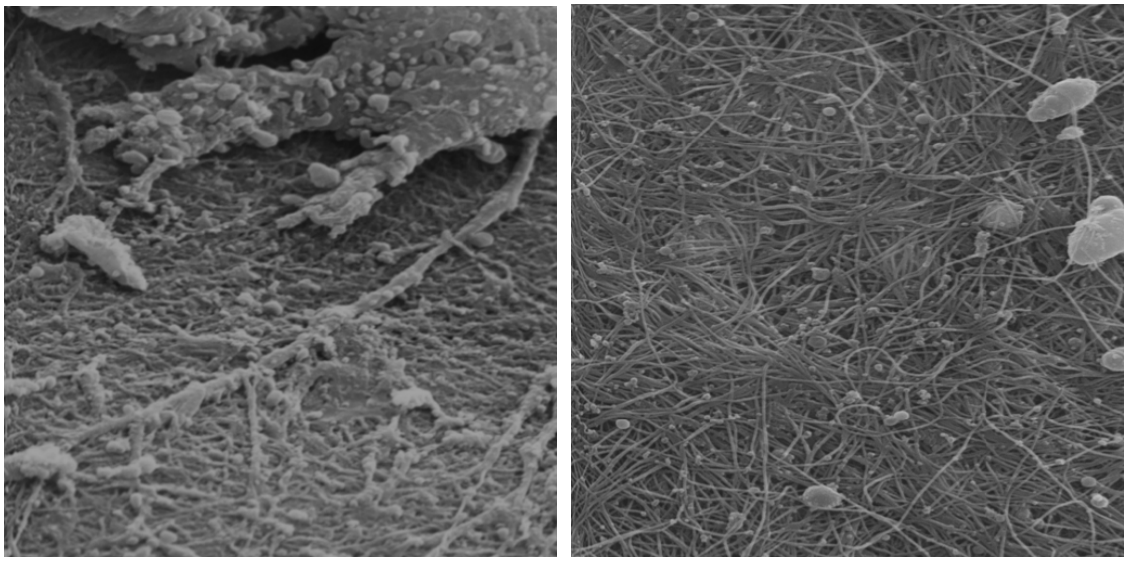

Figure 1.5: Electron micrograph images of Bruch's membrane with lipids before (left) and after (right) the application of ethanol. Images reproduced from [8].

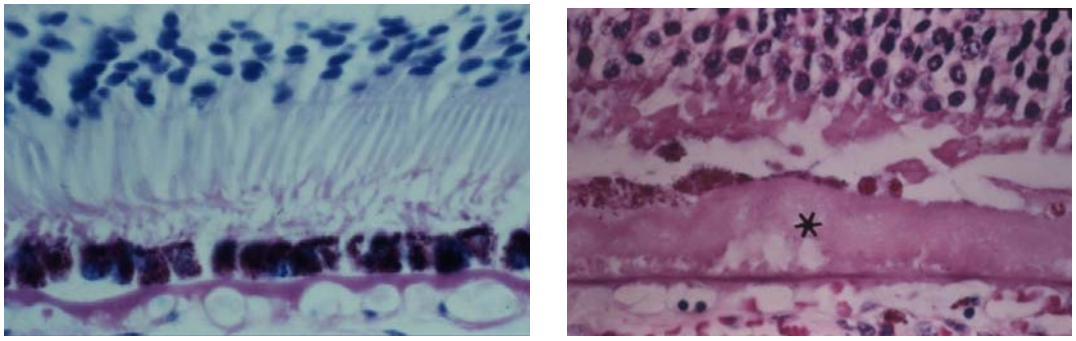

Figure 1.6: Histology images of normal retina (left) and retina containing thickened Bruch's membrane (right). Images reproduced from [18].

The result of this thickening does not only affect the amount of future metabolitic waste that can pass through the membrane. The flow of nutrients and oxygen passing from the choroidal blood vessels through Bruch's membrane to supply the retina is also adversely

affected. [19,20] Experiments have demonstrated a measurable drop in the permeability of macromolecules and hydraulic conductivity through Bruch's membrane as a function of patient age. Limited sampling and variability between human subjects and experimental setups could be a cause for discrepancies to the functional form of the decrease over time (i.e., linear versus exponential decrease with respect to patient age).

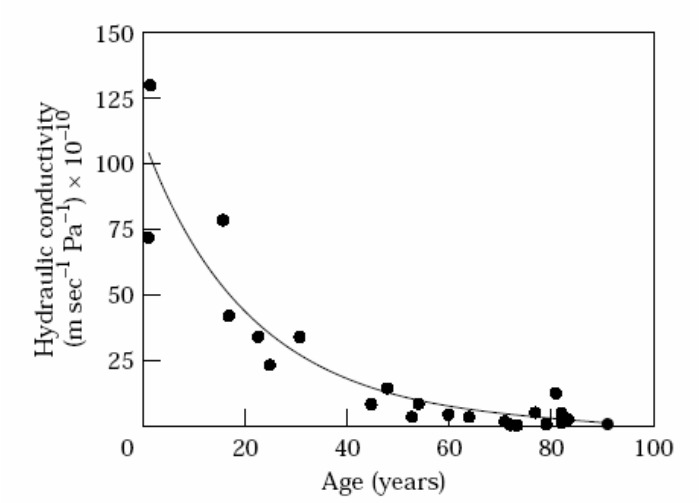

Figure 1.7: Decrease of the hydraulic conductivity of Bruch's membrane over patient age. Data reproduced from [19].

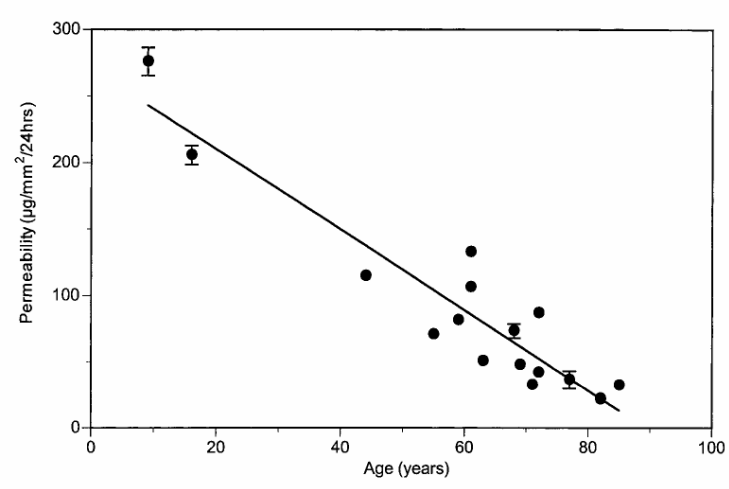

Figure 1.8: Decrease of the macromolecular permeability of Bruch's membrane over patient age. Data reproduced from [20].

With a decreased supply of oxygen from the choroidal blood vessels as Bruch's membrane becomes filled with lipids, there is an increased reliance on the retinal blood vessels which lie on top of the retina. These vessels are supplied directly from the optic nerve head, the ocular connection of blood and nerve signals to the rest of the body. Fundus photography takes a picture of the globe of the retina taken through the pupil of the eye. The shadowing of the reflected light due to the major retinal blood vessel absorption can be seen in this type of picture. The foveal region of the retina which produces the highest visual resolution does not have any major blood vessels on the top of the retina.

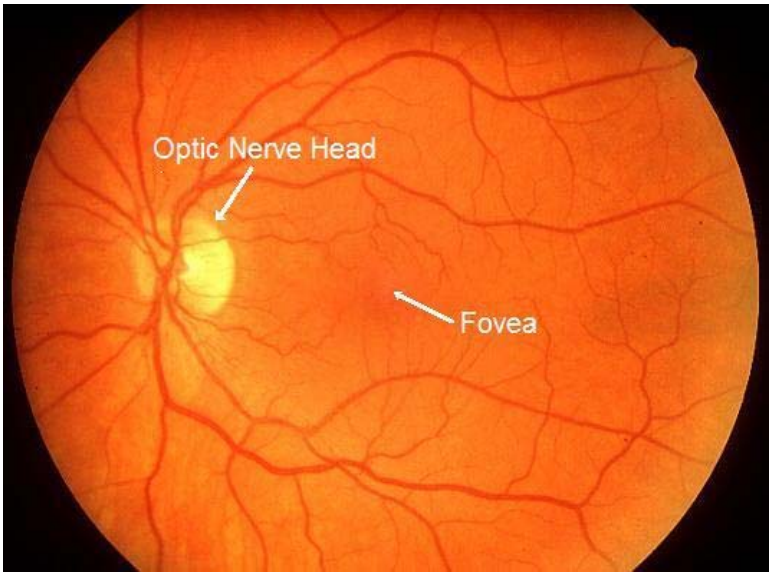

Figure 1.9: Fundus Photography image of normal healthy eye. The darker image regions demonstrate retinal blood vessel absorption. The fovea is the high-visual-resolution central vision region of the eye and the optic nerve head connects the eye to the rest of the body.

The oxygen deprivation of the photoreceptors in the fovea causes a decrease of photoreceptor operation in the central vision of the patient. The form of the disease causing vision loss due to the accumulation of lipids is called dry AMD. Over time, the lack of oxygen in dry AMD can result in death of retinal cells such as the RPE in the foveal region. For this form of the disease the majority of peripheral vision is maintained, allowing for a fraction of the original vision to be maintained.

Figure 1.10: Simulated images of normal vision (left) and AMD vision (right). Images reproduced from the National Eye Institute.

In many cases, once the photoreceptors have experienced enough of a decrease of oxygen, the retina will produce signaling to induce creation of new blood vessels to supply more oxygen to this region of the retina. These new blood vessels would extend from the choroid, breaking through Bruch's membrane in order to feed the retina. This form of the disease is called choroidal neovascularization (CNV), also referred to as wet AMD. VEGF (vascular endothelial growth factor) is a substance made by cells to stimulate the formation of blood vessels, a process called angiogenesis. VEGF was first discovered as occurring in cancerous situations in which blood vessels were created to improve tumor growth [21]. This factor was found to be expressed in human retinas during choroidal neovascularization [22,23,24].

Wet AMD is the major source of severe vision loss for AMD patients. The problem with this form of the disease is that the new blood vessels being created are very fragile and susceptible to leaks or bursting. As fluid leaks into the retina, distortions to vision can occur as the retinal layers are locally lifted up. This can lead to detaching retinal layers, killing photoreceptors and destroying regions of vision completely. Scar tissue can also form to affect regions of vision as well. While the vision loss associated with dry AMD can progress over the course of years, once the transition to wet AMD has been diagnosed the progression to severe vision loss can occur over the course of weeks [25].

Age-related macular degeneration is classified in three regimes: early, intermediate, and advanced. Early-stage AMD is difficult to identify without professional diagnosis because it occurs without any symptoms or vision loss. Intermediate AMD is the stage where the permeability of Bruch's membrane has decreased enough that there is a noticeable change in vision of the eye. Since most cases of AMD do not have identical disease progressions in both eyes, patient vision may not notice a change in one eye right away. Advanced AMD is the progression of the disease which can cause severe vision loss. This includes the advanced form of dry AMD as well as wet AMD. There are no early or intermediate stages of wet AMD.

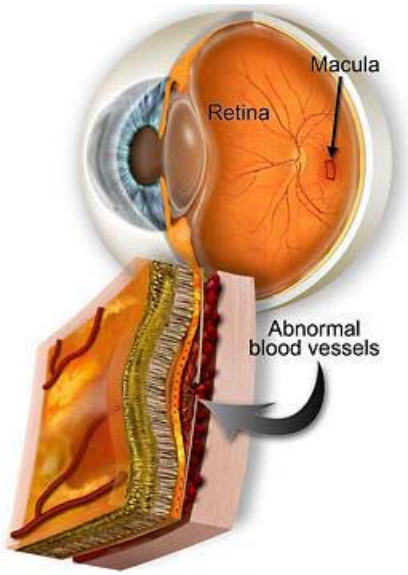

Figure 1.11: Wet AMD produces abnormal blood vessel growth which tries to break through the retinal layers, damaging the retina.

Looking at the prevalence of the disease is the best way to determine the age groups most at risk. Ophthalmologists generally diagnose patients who are suffering from a form of vision impairment so the prevalence of early stage AMD is not well accounted for. Statistics used by the National Eye Institute for the eye disease prevalence for the population over 60 (as well as the estimated population in the US currently in this category) are shown in Figure 1.12 [1].

Age Group	Advanced AMD prevalence estimated for age group	Intermediate AMD prevalence estimated in age group
60-69	0.7% (147,000 people in US)	6.4% (1,290,000 people in US)
70-79	2.4% (388,000)	12.0% (1,950,000)
≥80	11.8% (1,080,000)	23.6% (2,160,000)

Figure 1.12: AMD prevalence statistics for the United States [1].

In considering current US statistics of AMD prevalence, about 90% of all classified AMD cases are dry AMD versus wet AMD. But, if only advanced forms of AMD are considered, about 2/3 of cases are wet AMD.

1.2 Current Approaches to Disease Treatment

There are two main approaches in current treatment options for age-related macular degeneration: preventative and stop-gap measures. Preventative treatments attempt to delay the progression of early stage AMD with no vision loss to intermediate and advanced AMD stages where vision loss occurs.

The latest developments on the study of preventative management come from the National Eye Institute supported Age-Related Eye Disease Study (AREDS). AREDS is a 10-year study on the effects of a regimented daily supplement of vitamins and minerals on the progression of AMD for an at-risk patient group already presenting with intermediate stage AMD.

The results, according to NEI director Paul A. Sieving, M.D., Ph.D [26]: “This study found that high-dose antioxidant vitamins and minerals (vitamins C and E, beta-carotene, zinc, and copper), taken by mouth by people at risk of developing advanced AMD, reduced the risk of progression to advanced AMD by 25 percent and the risk of moderate vision loss by 19 percent. People at risk for AMD are advised to not smoke and to maintain a healthy lifestyle, with a diet including leafy green vegetables and fish".

The dietary recommendations come from multiple studies which suggest that while many foods do not seem to have any impact on the progression of AMD, a couple of specific foods have shown very promising results. Consumption of dark leafy green vegetables like spinach, which contain lutein, have demonstrated a decrease in incidences of late stage AMD. Certain types of fish containing omega-3 fatty acids have also shown similar beneficial effects [27].

The NEI has just launched a nationwide study to see if a modified combination of vitamins, minerals, and fish oil can further slow the progression of vision loss from AMD. This new study, called the Age-Related Eye Disease Study 2 (AREDS2), will build upon results from the earlier AREDS study [28].

Stop-gap measures are the only way to describe the treatments for people who are currently suffering from wet AMD. Early treatments of this disease used photodynamic therapy (PDT) to photocoagulate leaking vessels in the eye to prevent future leakage damage from those vessels. To avoid laser damage to the central vision during treatment, only a fraction of wet AMD patients with particular locations of vessels qualified for treatment. Even for the treated patients, within 18 months nearly all had a reoccurrence of wet AMD.

The current popular approach for treatment is to produce drugs which can target the VEGF signaling of the retina. The assumption is that if VEGF was blocked, the retina would not grow any new vessels and wet AMD would not occur. Recent drugs including Avastin (Bevacizumab), Macugen (Pegaptanib), and Lucentis (Ranibizumab) have been designed towards this purpose with varying degrees of success. For all of these type of anti-VEGF drug treatments, there is one consistent trend: Once treatment is stopped, wet AMD progression will continue.

A primary concern with these drug treatments is the cost associated with them. Some of these drugs, which may need to be injected as often as once a month, can cost as much as $2000 per injection. If money were not a concern, the next major issue is related to the drug delivery system, which is accomplished through an injection directly into the patient’s eye.

Approximately 1% of patients following a 2-year regiment of eye injections will suffer an infection in the eye as a result. This type of infection generally leads to a complete loss of vision in the eye.

Developments of future treatments will be helped by the diagnostic capabilities of visualizing the disease progression. AREDS was a 10-year study which had effectiveness determined by visual acuity measurements. With the ability to measure the more subtle changes associated with the transitions in AMD, the effectiveness of treatments can be determined in shorter times and adjustments can be made to ineffective treatment regimes for patients.

1.3 Current Diagnostic Technologies and Limitations

AMD treatments are partly limited by the availability of diagnostic technologies able to screen the general population for disease management. An ideal screening tool for AMD needs to be able to:

a) Identify the earliest stages of AMD before patient has visual symptoms so that preventative treatments can be applied

b) Identify the earliest transitions from dry AMD to wet AMD to improve the efficiency of treatments directed towards wet AMD

c) Monitor quantitative changes of disease progression and treatment efficacy to improve future disease treatments

The earliest symptoms of AMD do not usually cause noticeable changes in a patient's vision. It is important to be able to have an instrument which is quick, easy to operate, cheap, comfortable, carries no risk to the patient, and provides quantitative information about the disease. This would allow a diagnostic to be incorporated into a regular eye examination for determining at-risk patients to be referred for further study or treatment.

There are many technologies currently in use for diagnostic purposes for ocular exams. Each has its own benefits and limitations that need to be discussed in order to determine which one has the greatest potential of being the primary screening diagnostic for AMD.

1.3.1 Histology

Histology has always been a valuable tool for understanding tissue morphology over the course of a disease progression. Most of the structural models of the retina have been developed through study of the excised retinal tissues using optical microscopy. Histological staining combined with microscopy adds an additional level of contrast for improved visualization at a very high resolution. Unfortunately, biopsy of the retina to get the excised tissue would have a severe negative impact on the vision of any living eye so this technique is limited to post-mortem subjects only. Monitoring progress of a disease within one individual is not possible with this method.

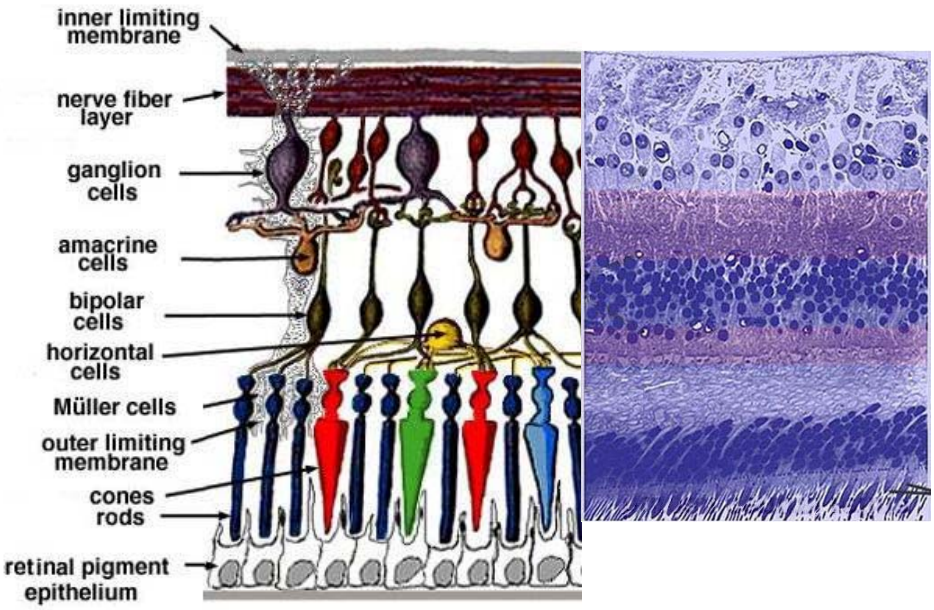

Figure 1.13: Histology image of retina compared to labeled schematic image.

1.3.2 Visual Acuity

Visual acuity is a coarse measurement of the sharpness of the retinal focus within the eye. It is the standard measurement used by optometrists to determine prescriptions for glasses. Used in AMD diagnostics, visual acuity has been used to determine wet AMD drug effectiveness. As sub-retinal fluid accumulates in wet AMD, the lifting of the retina causes a change in the patient's visual acuity.

There are two main issues with using visual acuity as the main diagnostic measurement [29]. First, as a coarse measurement of the mean visual acuity over the fovea, visual acuity is not designed to quantify very small localized changes due to disease progression [30]. Large visual acuity drops measured with this method correspond very well with the progression of the disease. Improvements of visual acuity measured over time for a patient could correspond to an improvement of the disease progression. They could just as easily be explained by a patient adapting to their current vision or adapting to the test itself. Without additional diagnostics, it would be difficult to discern the true scenario.

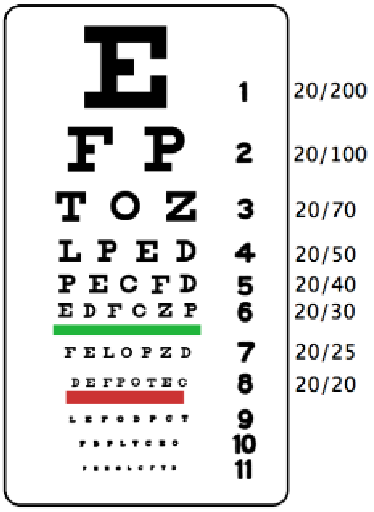

Figure 1.14: Scaled picture of traditional Snellen chart used for visual acuity tests.

1.3.3 Amsler Grid

The Amsler grid is a simple grid composed of horizontal and vertical lines with a dot in the center. When a patient focuses on the dot and observes any of the lines as distorted or missing, this might identify the existence of locations of sub-retinal fluid associated with a leak from choroidal neovascularization.

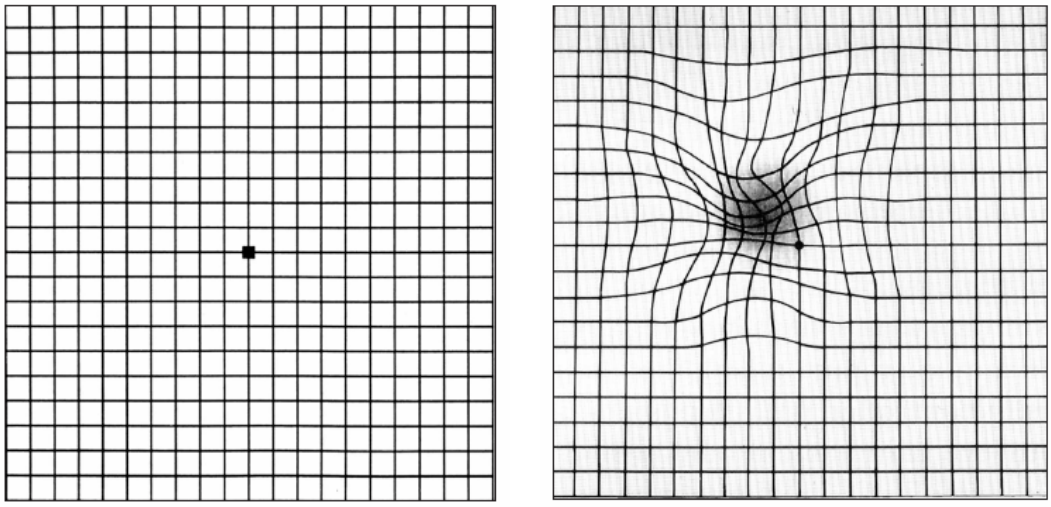

Figure 1.15: Amsler grid viewed under normal vision versus simulated wet AMD leak.

This test is user-based and very qualitative, making it a poor diagnostic tool by itself. The Amsler grid is ideal for directing to an eye care professional potential wet AMD patients who otherwise may not have gotten an examination until much later in the progression of the disease.

1.3.4 Fundus Photography

The most common diagnostic technique is based on the ophthalmoscope, an instrument which allows a doctor the ability to look through the pupil of a patient's eye to view the back globe of their eye, called the fundus. Fundus photography uses the exact same principle while transferring the image of the fundus to a camera for acquisition. The earliest stages of AMD are characterized using the images of this technique.

Early stages of dry AMD are roughly linked to the appearance of localized fatty deposits called drusen. By identifying the color, size, and number of drusen which appear on the fundus image, the early stage of AMD can be classified. Fundus photography is capable of visualizing many aspects of AMD progression including pigment abnormalities, regional cell death in the retina (called geographic atrophy), and choroidal neovascularization (CNV). With blood contrast occurring due to the regional light absorption for the image, the earliest stages of CNV may experience limited contrast in this technique.

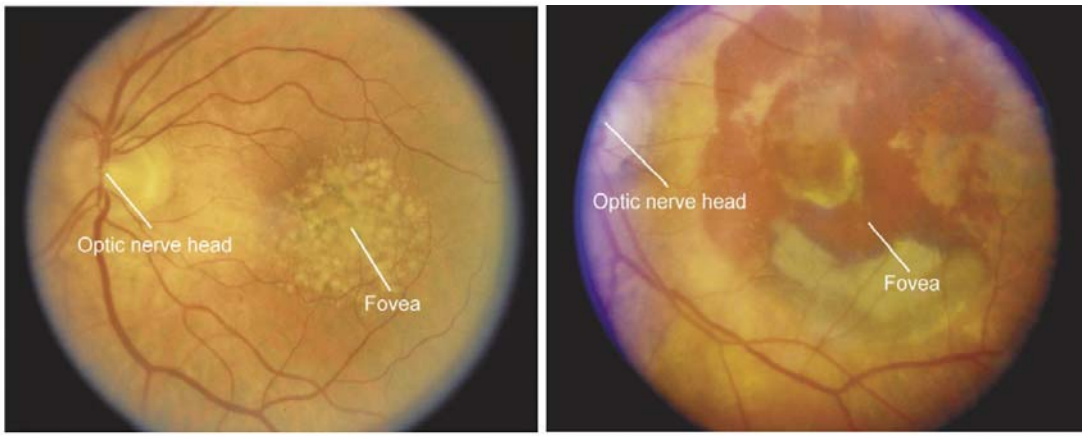

Figure 1.16: Fundus photography images for AMD eyes. Drusen deposits in the fovea region are associated with dry AMD (left) and observed blood vessel leaks are caused by wet AMD (right). Images reproduced from [8].

Fundus photography has a lot of characteristics that make it ideal as a screening tool: It is quick, easy, risk-free, and relatively comfortable for patients. Until the relationship between the drusen observed in AMD patients and the progression of the disease can be understood, this technique will remain a qualitative measure for early AMD diagnostics. With absorption as the main blood contrast observed, the earliest stages of wet AMD will remain very difficult to discern.

1.3.5 Fluorescein Angiography

Fluorescein angiography (FA) is one of the gold standards for visualizing vasculature in the retina, as well as leaks caused by wet AMD. A fluorescein solution is injected into the patient's blood stream and the retina is viewed using an altered fundus photography

system. Fluorescein is a molecule which will fluoresce green at a wavelength around 521 nm while undergoing absorption of blue light at a wavelength around 494 nm. Fundus photography with blue light illumination and a green filter on the camera will allow visualization of the fluorescein as it circulates through the retinal vasculature.

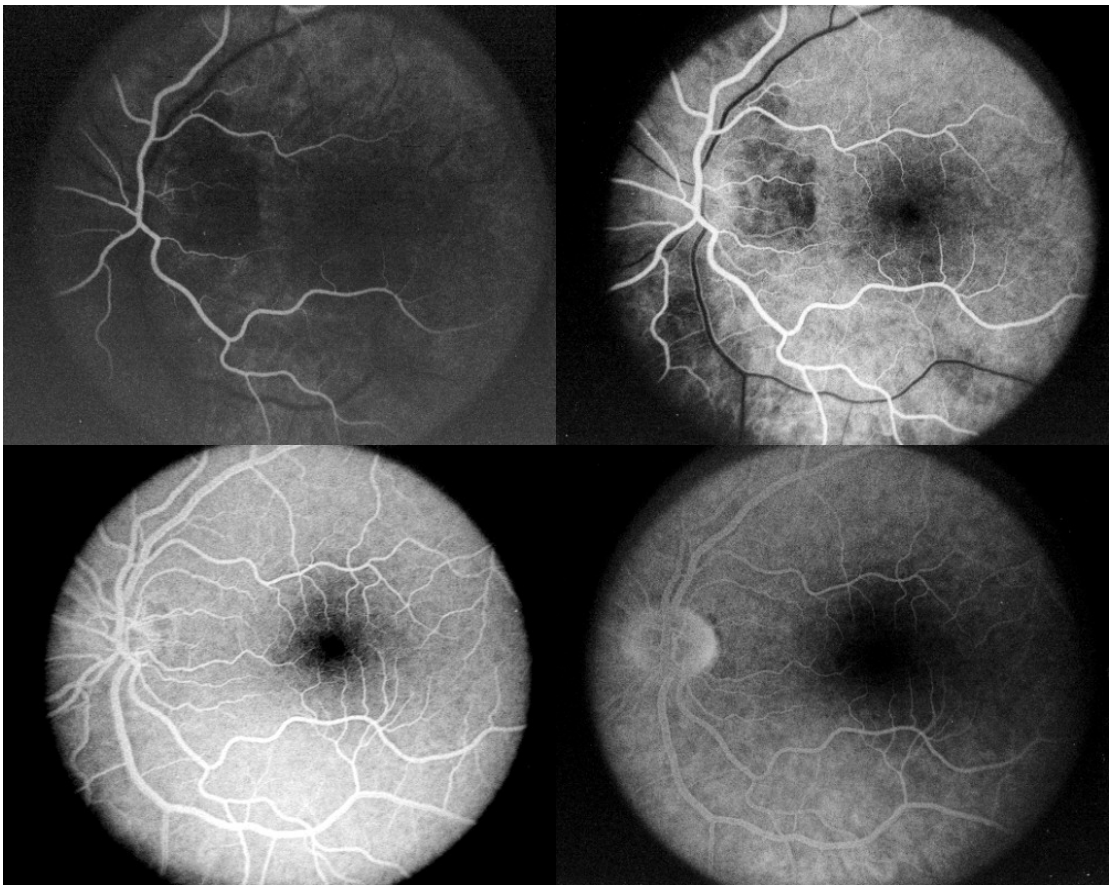

Figure 1.17: Fluorescein angiography images taken at different time points after dye injection. The time sequence of stages are the arterial stage (upper left), the venous stage (upper right), the mid phase (lower left), and the late phase (lower right).

By taking angiography images at different time points, the arteries and veins in the retina can be identified as well as any leaks caused by CNV [31]. The lack of retinal blood vessels in the fovea region can also be visualized using this method. Another form of angiography utilizing indocyanine green uses higher-wavelength light to illuminate the molecules, allowing for deeper penetration of the light into the retina. Indocyanine green angiography

(ICGA) allows improved visualization of the deeper choroidal blood vessels as well as the retinal vessels.

The injections required for this technique limit the general screening capabilities of this technique. Possible adverse reactions to injections or to the fluorescein sodium solution used are the main concerns with this method [32,33]. If the diagnostic capabilities of the angiography techniques were possible without the injections, it would be an ideal screening tool for identifying the earliest stages of wet AMD.

1.3.6 Ultrasound

Ultrasound uses sound waves to identify interfaces within the sample. Each depth reflection is separated from each other by the differing travel times of the sound waves reflecting back to the detector. Typical high-resolution ultrasound is capable of separating distinct layers 20 microns from each other. To allow the sound waves to propagate to the retina, the sound wave transducer must be placed in physical contact on the eye which may not be comfortable for all patients. Ultrasound is commonly used to assess the retina for cases with dense cataracts which limit the optical accessibility of the retina. Optical imaging is generally preferable to ultrasound as a screening instrument.

1.3.7 Scanning Laser Ophthalmoscope

The major limitation to optically image the retina depends on the optical properties of the eye. With the sclera considered optically opaque, the retina is accessible by imaging through the cornea and lens of the eye. The aqueous humor is the fluid which fills the globe of the eye between the lens and the retina, which optically can be considered as water. The absorption profile of water limits the available wavelengths to use for retinal imaging.

With a total path length that illumination and collected light travels in the eye being approximately 5 cm (twice the length of the eye), absorption coefficients of greater than 0.2 cm^{-1} will allow < 70% of the light to propagate through the medium. The additional

absorption of the light in these cases limit the usefulness of certain wavelength ranges of illumination light sources.

The scanning laser ophthalmoscope (SLO) performs confocal microscopy imaging of the retina, using the lens of the eye as the focusing element. By scanning a laser transversely across the retina and measuring the reflected light, an image comparable to fundus photography is created. In this system, the image is created from monochromatic laser light. Through the appropriate selection of laser wavelength and illumination power levels, image contrast can be adjusted with a higher level of flexibility than standard fundus photography [34].

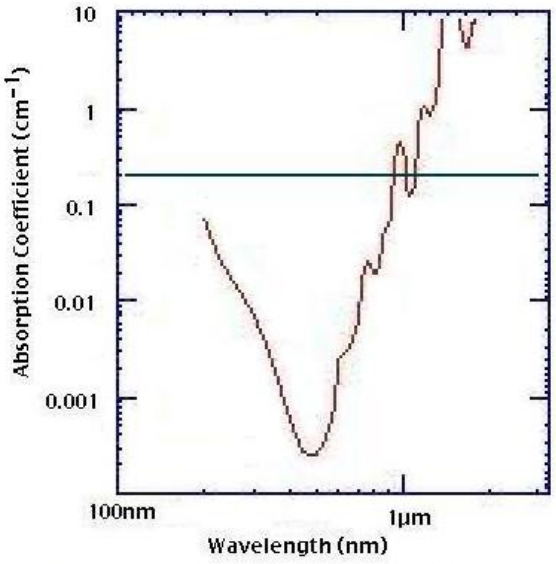

Figure 1.18: Wavelength absorption spectra of water. Horizontal line corresponds to absorption of 0.2 cm^{-1}.

1.3.8 Optical Coherence Tomography

Optical coherence tomography (OCT) is a relatively new technology. Incorporation into regular clinical use for ophthalmologists has been increasing steadily over the past 10 years as the instrumentation capabilities have been improving. OCT can be considered as the optical analogue of ultrasound: light reflecting off of each retinal layer in the eye will be delayed based on the distance the light has traveled. With the speed of light so much faster

than the speed of sound in tissue, it is technologically challenging to temporally separate out the reflections. Instead of pushing technology to attempt to distinguish femtosecond temporal resolution, an interferometric technique was developed which allows the separation of retinal layers through spatial discrimination.

OCT is sometimes considered in vivo optical histology because it is capable of producing 3D structural information of a sample. The most popular OCT retinal imaging system (Stratus OCT, created by Carl Zeiss Meditec) demonstrates a depth resolution in retinal images of 10 μm in tissue [35]. While it is has not reached the resolution level of current histology imaging capabilities, this technique creates images which correlate to expected histological measurements.

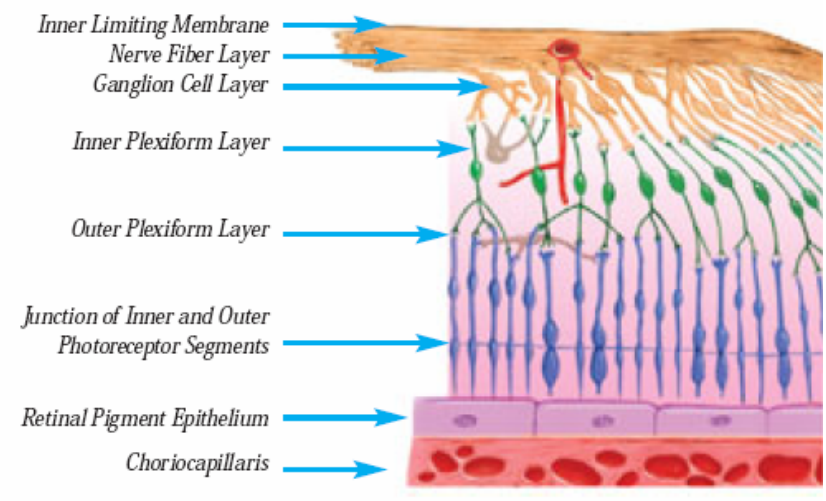

Figure 1.19: Schematic image of retina with the retinal layers identified. Image reproduced from reference [34].

Current usages of retinal OCT are primarily limited to structural abnormalities such as macular holes and retinal detachments. With imaging improvements and clinical studies with current systems, additional functionality for this technique will be applied to clinical eye examinations.

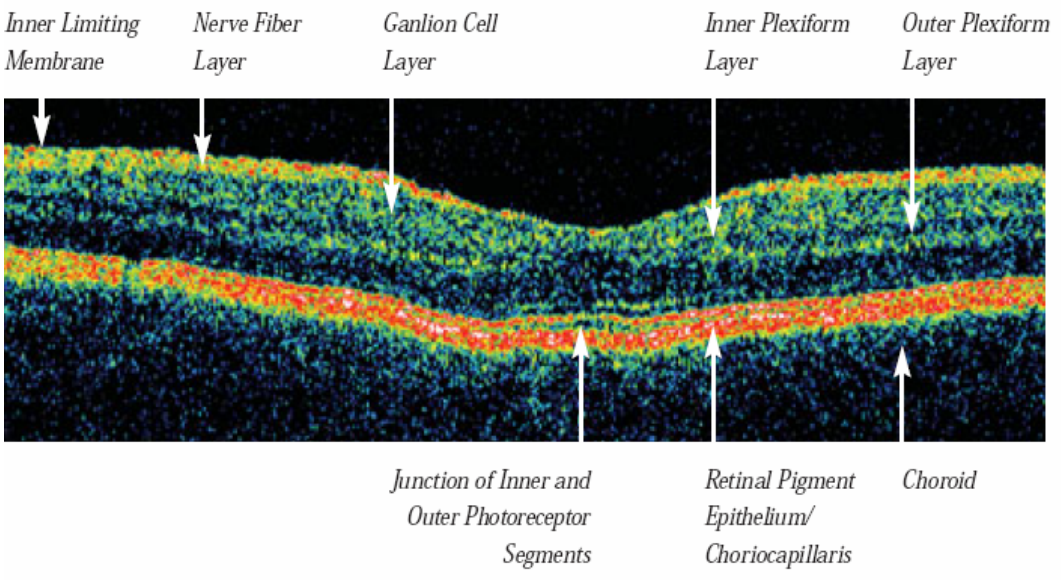

Figure 1.20: OCT Image acquired with Carl Zeiss Meditec Stratus OCT system, with labeling of identified retinal layers. The structure is consistent with the expected layering of the schematic of the retina in Figure 1.19. Image reproduced from [34].

1.3.9 Summary of Diagnostic Technologies

Optical imaging techniques are very capable as a quick and risk-free screening tool for patients. For AMD diagnostics, fundus photography and fluorescein angiography are currently the most valuable diagnostic tools available. The diagnostic capabilities would be enhanced further with additional quantitative information of the fundus images as well as the possibility of achieving fluorescein angiography images without requiring the dye injection.

Optical coherence tomography is a non-invasive method capable of three dimensional structural imaging. Commercially available systems are capable of nearly real time two-dimensional images which can separate out retinal layers of interest. With resolution and speed improvements, this technique can add accessibility as a screening tool. Functional improvements also have the possibility of improving the capabilities to diagnose AMD disease progression.

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