# Detection of X-Linked Juvenile Retinoschisis

Jeremy Zhang
Graduate Student
Computer Engineering
George Mason University

***Abstract* – A child's education during adolescence is essential for mental and confidence development. As one is exposed to a constantly changing learning environment, unaccounted factors are extremely detrimental. One such factor is X-Linked Juvenile Retinoschisis (XLRS). In general, retinoschisis is a condition in which cysts form within the layers of the retina, causing separation of said layers [1]. Photoreceptor cells within the inner layer are permanently damaged, which ensures near complete blindness. XLRS is a genetic disease that affects an estimated 1 in 5000 males during (pre)adolescence. It causes mutation of the RS1 gene, responsible for creating a retina developmental protein named retinoschisin [2]. The absence of retinoschisin results in an underdeveloped outer layer, causing light to pass through, thus forming the cysts. The disease is incurable, and common visual enhancements cannot be applied to improve conditions [2]. Currently, detection followed by proper accommodation is the only viable prevention method. Such detection methods are genetic testing for the RS1 gene mutation, ocular echography (ultrasound), electroretinography (ERG), and optical coherence tomography (OCT). In this paper, we will mainly discuss ERG and OCT [3][4]. The initial diagnostic tool was electroretinography (ERG), in which a darkness adapted retina is exposed to flashes of light [3]. The photoreceptor cells produce an electrical potential that is measured. The aspects of these measurements will be discussed in this paper. As for recent advancements, OCT is the current method for commercial use, and subsequently generates high resolution 2D or 3D images [4]. This method involves utilizing long wavelength light to penetrate organic tissue. The light contacting the desired scan area is reflected and is processed through a signal receiver, while the other light waves are scattered [4]. In this research paper, we will review the various detection methods along with the complications these methods have on XLRS. Relevant information and data will be obtained and complied to determine the most viable methods, as well as the advantages and disadvantages of each. As XLRS is currently incurable and unpreventable, the importance of precise detection and observation is significant for the betterment and accommodation for those affected.**

**Keywords—X-Linked Juvenile Retinoschisis, XLRS, retina, retinoschisin, photoreceptor, RS1 gene, electroretinography, ERG, optical coherence tomography, OCT**

## I. INTRODUCTION

The purpose of the RS1 gene is to produce a protein called retinoschisin. This protein binds to and develops cells within the retina prior to adolescence [1]. Mutation of RS1 gene is hereditary and is linked through the X-chromosome [2]. This mutation causes the absence of retinoschisin, thus resulting in an underdeveloped retina. The underdevelopment occurs within the outer layer in most cases but can also sometimes occur within the inner layers. Common light can pass through the layers unfiltered and damage the sensitive cells beneath, forming cysts in the absent locations of the damaged cells [2]. Once these cysts form, it is irreversible, and all forms of surgical procedures are rendered useless [2]. As such this being the case, only early detection and subsequent accommodations are the only viable solution, limited by the optical and genetic advancements of our time. The victim will generally be considered legally blind when they reach their teenage years [2]. Prior to this, it was surveyed that approximately 10% of those affected would report deterred visions during adolescence [1]. The other 90% would report their case ranging from teenage years to late 40s [1]. As with the 90%, it was reported that a majority were subjected to common childhood vision tests, but were prescribed only common glasses [1]. The glasses would only improve the situation by a minuscule amount, but in-depth testing of the retina is not performed. The 90% would go through most of their grade school education with a significant hinderance, and no proper accommodations for their near legal blindness [1]. As such, the importance of these detection methods will be emphasized and will hopefully be mandated testing for those with any hinderance to their vision.

## II. METHODS

There are currently four methods that can allow detection of diseases such as XLRS. Two are less commonly used, while the other two are widely used for in depth analysis of regions such as the retina. The two less common methods are genetic testing for mutation of the RS1 gene, and ocular echography (ultrasound) [3]. The genetic testing is considered too specific a test, and is not a viable efficient method. Ocular echography is not widely used due to low resolution images produced, as images are produced with sound, and not light. Electroretinography (ERG) is widely known as the initial tool to detect retinal damage. The test involves electrodes on the surface of the cornea [3]. The eye is adapted to darkness, although some minor tests involve the eye to be adapted to light [3]. The eye is then exposed to flashes of bright light. These can be singular flashes, or can be flickers (to test for consistency). The photoreceptor cells within the retina react to the light, and subsequently produce an electrical potential response that can be measured through the electrodes [3]. The electrical potential is measured in microvolts or nanovolts as a function of time [3]. What is generally observed is an immediate decrease in voltage, the negative peak of this decrease is known as the a-wave amplitude. The a-wave is subsequently followed by an immediate increase, and the peak of said increase is known as the b-wave amplitude [3]. For a patient not affected by XLRS, the b-wave amplitude is much larger than the a-wave amplitude. For an XLRS affected patient, the b-wave is much more miniscule and can even come close to being absent [3]. The amplitude for both the a-wave and b-wave are also generally much smaller. The characteristics of these waves are observed and analyzed for purposes of detecting retinal damage, and not just XLRS. Optical coherence tomography (OCT) is the more recently commonly used tool for detection of XLRS and other retinal degeneration disorders [5]. OCT is a low coherence light imaging test. Long wavelength light is used to penetrate

organic tissue [5]. For the desired scan area, the light is reflected and is subsequently processed through a signal receiver [6]. As for the undesired light waves, those are scattered, and are of no use for processing [6]. With the processed reflected light waves, high resolution images can be produced to display cross sections of the retina [6]. OCT can be utilized in various domains [7]. Currently, time domain OCT and spectral domain OCT are the widely used domains, although advancements for other domain types are constantly being made [7]. OCT is system that involves reference mirrors and light beam splitters to process the light through the signal receiver [7]. The resulting data is then modulated and received by a computing system for analysis [7]. We will look at tests done with ERG and OCT and review the data in the results section.

## III. Results

The data we will look at first is ERG data. There are two test sets that we will analyze, which generally covers the extent of the disease. In Figure 1, a 48-year-old man is tested with ERG and we will review the responses from the photoreceptor cells (rods and cones) [3]. As a side note, the rod and combined rod-cone test were performed with a darkness adapted eye, and the cone with a light adapted eye. With the rod test, only the b-wave should be present, and in comparison, the rod response for the XLRS patient is essentially absent [3]. With the combined test, the a-wave is present, albeit much more decreased in comparison, while the b-wave is completely absent [3]. As such with the cone test, it is concluded that the man has severe rod photoreceptor cell damage. With rod damage, mainly perihelial vision and night vision is significantly hindered [3]. The present a-wave ensures that partial vision during daylight is present, but is not prevalent as the amplitude is much less in comparison. For the second test, seven patients with XLRS ranging from 10 to 35 years old are tested in comparison to a control group (Figure 2) [3]. Just as the first test, it can be seen that the rod and combined test are where we see the biggest discrepancies. The electrical response after the b-wave amplitude fluctuates, but the a-wave and b-wave amplitude are generally consistent [3]. The flicker test is also performed for consistency. As displayed, peaks and negative peaks are prevalent in the control group, while the XLRS patients display more curvature and less amplitude in their test data. OCT, in comparison is an imaging test, and does not rely on measurable data for displayed results, as said results can be analyzed visually [5]. In Figure 3, six different cross section images of XLRS affected retinas are shown [7]. In images A, C, and E, the macula region of the retina is displayed. The space shaded with black within the layers are the cysts that form [7]. The size of these cysts varies by patient, and as such bigger cysts results in an increased number of damaged cells [6]. In images B, D, and F, cross sections of other locations of the retina are shown [7]. The cysts formed in areas other than the macula are more minor in comparison, but still add onto the visual impairment of the patients in general. In Figure 4, a top-down image of the macula region is shown in three different patients [7]. Image A displays the macula of a non-XLRS patient, while image B and C display the macula of XLRS patients. Image B displays a hole in the outer layer of the retina, with cysts forming in the surrounding areas, while image C displays cysts only, and no hole is present. The patient in image B is observed to have complete legal blindness, with the inability to perform vision necessary tasks.

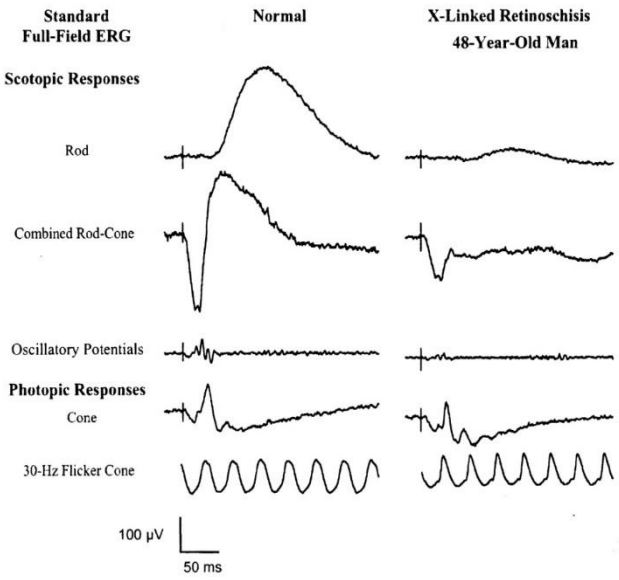


Figure 1: Test of a 48-year-old man affected by XLRS. General cell response is shown with the rod and combined cone response having a more prevalent difference. [3]

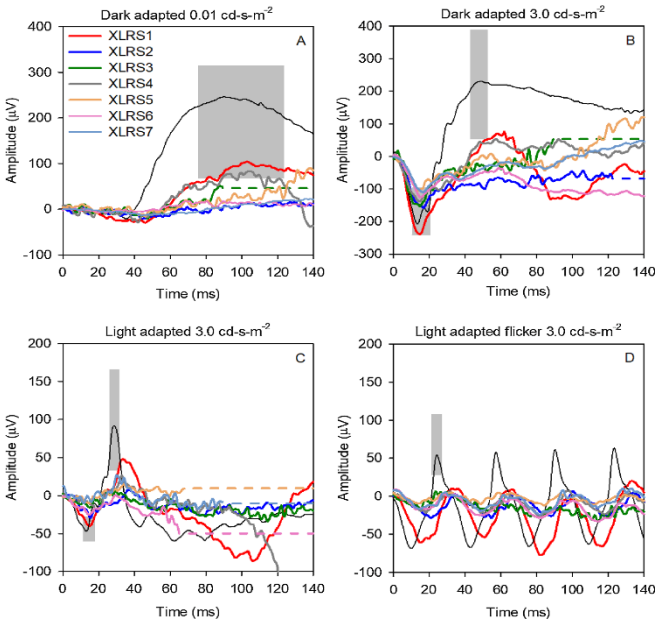


Figure 2: ERG test of seven patients affected with XLRS compared to a control group. The first graph displays a rod

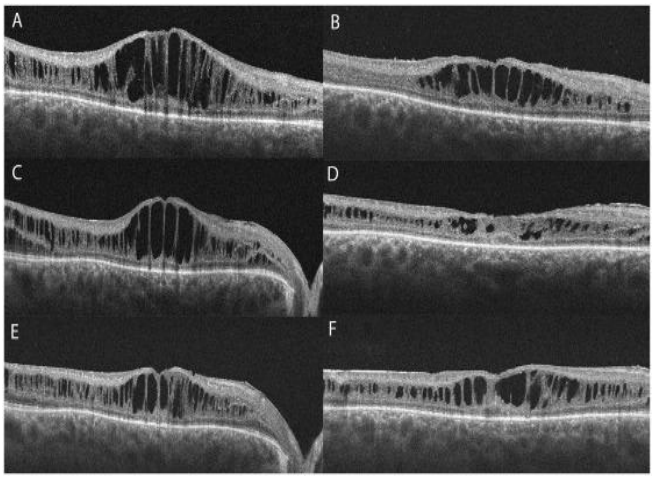


Figure 3: OCT scans of a retina. In images A, C, E, the macula region of the retina is shown. In images B, D, G, other areas of the retina are shown. [7]

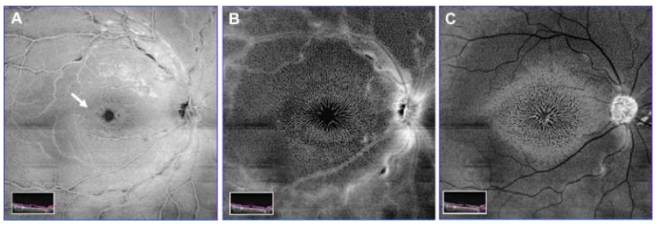


Figure 4: OCT scans of the macular region in the retina. [7]

## IV. Discussion

In terms of both ERG and OCT, more advancements are being made for OCT. Several factors include the ease of having a visual result versus a measurement result. The high-resolution images are significant for observing the root cause of one's visual impairment, as many other diseases and disorders can cause retina damage, and not just XLRS or retinoschisis in general. Some advancements being made for OCT include full-field OCT and line-field OCT [6]. The respective methods emphasize their own unique mechanism, with full-field OCT using advanced cameras without beam splitting for multiple image capture to be phase shifted, and line-field OCT using line illumination and detection with a line-scan camera [6]. In a general invasiveness sense, OCT does not involve any contact in comparison to ERG, thus making OCT the method to be improved upon by researchers in the field [3][6].

## Conclusion

The importance of these detection methods is emphasized through the idea that most XLRS affected victims live most of their early life with no knowledge of the severeness of this disease. As XLRS is incurable and damage is irreversible, detection of this disease and proper accommodations are necessary for the betterment of the children affected, both for everyday life purposes and educational purposes. With advancements in both engineering and genetic research, it is hoped that the disease will eventually become preventable and be subject to common visual testing.

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