LHON OUTCOME METRICS IFOND FUNDING REQUEST

Abstract

Leber Hereditary Optic Neuropathy (LHON) is a genetic mitochondrial optic nerve condition that damages retinal ganglion cells, leading to loss of vision. People with LHON often struggle with everyday tasks such as reading, facial recognition, and navigating their environment.[1] However, standard vision tests used in clinics mainly measure how well someone can see high-contrast letters on a chart.[2] These tests do not fully reflect the real-world challenges faced by patients.

Standard clinical testing has been used for clinical trials and so far no treatment has shown a statistically significant improvement in standard clinical testing, as a result no therapy has been approved by the Food and Drug Administration. Gene therapy for a retinal dystrophy caused by RPE65 has been approved by the FDA and functional vision was assessed in the clinical trials by using the Multi-Luminance Mobility Test (MLMT). The MLMT requires a large room with set luminance's and lighting patterns, which makes the test difficult to administer outside of a few clinical centers.

The MLMT has been adapted to use a virtual reality (VR) headset and forms part of a group of outcome metrics that form part of the Diagnosys Eidolon VR Headset. The headset also has the ability to measure contrast sensitivity using a FrACT protocol, and a proprietary reaching task which can provide a more realistic and comprehensive way to assess vision. While wearing the VR Headset, participants will complete four types of tasks: (1) Identifying symbols of various sizes, (2) seeing objects in low contrast conditions, (3) reaching out to touch visual targets (combining vision and movement), and (4) navigating through a virtual environment. These tasks are designed to better reflect real-life situations in a safe and controlled setting. Combine this test with FrACT and the MLMT can help establish each task as a potential outcome metric for patients with low vision such as LHON.

The goal of this study is to determine whether this VR-based testing is practical, reliable, and more meaningful than standard vision tests. If successful, this approach could improve how vision loss is measured in LHON and provide a portable method for assessing functional outcomes in a measurable way which has already been accepted by the FDA as a clinical outcome metric.

Study Rationale

Assessment of visual function in LHON remains limited by an over reliance on static, high-contrast visual acuity measures, which do not adequately reflect the functional impairments experienced by patients.[3] LHON is characterized by degeneration of retinal ganglion cells, leading to central vision loss and reduced contrast sensitivity.[4] As a result, patients often experience significant challenges with everyday tasks such as navigation and interacting with dynamic environments, despite relatively stable findings on conventional tests.

Visual acuity testing (VA) assesses how clearly a person can see at various distances, including near, intermediate, and far.[5] Distance visual acuity is specifically measured by having the patient read the smallest line of letters they can at 20 feet using a standardized optotype chart, most commonly the Snellen chart.[6] Contrast sensitivity testing is a recognized measure that can provide additional insight into visual dysfunction.[3] However, it is not routinely incorporated into standard clinical assessments. Additionally, standard visual acuity testing does not capture the integration of vision and motor function required for real-world activities. These limitations underscore the need for more sensitive and functionally relevant assessment tools.

Virtual reality (VR) technology offers a promising approach by enabling controlled, immersive, and interactive testing environments.[7] VR headsets can simulate low-light conditions in a standardized manner, allowing for more consistent contrast sensitivity assessment. They also support the development of dynamic tasks, such as combined visual acuity and motion-based testing (e.g., reaching out to touch visual targets), which better reflect real-world functional demands.[8]

Furthermore, VR has emerging applications as a navigation aid for individuals with visual impairment; however, its application in patients with LHON remains limited.[9] At the same time, its potential as an integrated platform for both assessment and functional evaluation remains underexplored.

This study aims to evaluate the feasibility and utility of the Diagnosys Eidolon VR Headset as a multimodal tool to assess visual acuity, contrast sensitivity, combined visual acuity-motion performance, and navigation ability in LHON patients. By providing a more comprehensive and functionally relevant evaluation of vision, this approach may improve sensitivity to disease-related deficits and support the development of targeted interventions.

Purpose and Objectives

In this study, we will evaluate the performance of the Diagnosys Eidolon VR Headset as a multimodal tool for functional vision assessment in patients with LHON. Specifically, we will assess its ability to replicate and extend beyond conventional testing by implementing and comparing the following protocols:

1. Visual Acuity
2. Contrast Sensitivity Test (FrACT)
3. Combined Visual Acuity and Motion Task (object interaction test)
4. VR based MLMT (VR-based orientation and mobility tasks)

The objective of this study is to determine the feasibility, usability, and validity of VR-based testing in a clinical setting, and to evaluate whether these protocols provide a more functionally relevant assessment of vision compared to current standard of care testing.

Clinical Significance:

The goal of this study this to enhance the detection of clinically meaningful deficits and improvements, improve enhance patient engagement, and support more comprehensive functional vision assessment in LHON.

Contrast sensitivity testing within a VR environment allows for standardized simulation of low-light conditions while minimizing variability associated with ambient lighting in clinical settings. This approach may improve the detection of visual deficits and changes that are not captured by high-contrast visual acuity testing alone.

The combined visual acuity and motion task integrates visual perception with motor response, offering a more realistic assessment of visuomotor function required for daily activities. This may better reflect the functional limitations experienced by LHON patients.

The MLMT protocol leverages existing VR capabilities as an assistive and evaluative tool, allowing for controlled assessment of spatial awareness and mobility. This approach may improve the relevance of visual function testing to daily life by simulating real-world challenges in a safe and reproducible manner. It is based on the standard MLMT protocol which has been FDA accepted for clinical trial outcomes and adapts it to a VR system. This VR system has been developed and benchmarked against the original MLMT by the Children's Hospital of Philadelphia.

Testing visual acuity within the VR headset provides a standardized baseline that can be compared with traditional clinical visual acuity measurements obtained using a Snellen chart at 20 feet. This comparison will help assess the validity of VR-based assessments for the use of measuring visual function in patients with LHON.

Collectively, these VR-based protocols represent a new method for assessing functional vision.

Study Design

This is a prospective study that will be conducted by the Department of Ophthalmology at The Ottawa Hospital (TOH).

The Diagnosys Eidolon VR Headset (which utilizes the Pico 4 Ultra VR Headset as its base platform) consists of a head-mounted device and interactive tracking capabilities. The testing protocol will be loaded on an app installed in the headset.

We will establish two participant groups:

1. LHON Group: Consists of adults (≥ 18 years old) diagnosed with LHON who are actively seen at the Department of Ophthalmology at TOH or are attending an LHON conference in Canada.
2. Randomly Selected Group: Consists of general ophthalmic patients ≥ 18 years old seen at the Department of Ophthalmology at TOH.

All participants will complete the four VR-based tasks. Participants recruited at the LHON Conference will undergo visual acuity testing in addition to completing the VR assessments.

Primary outcomes/measures/endpoints:

The primary outcome of this study is to evaluate the feasibility of the VR-based testing platform by determining whether patients with low vision, specifically those with LHON, can successfully complete the proposed visual and navigation tasks.

Secondary outcomes/measures/endpoints:

Secondary outcomes include comparing performance on the VR-based Visual Acuity, Contrast Sensitivity, and Object Interaction tasks with standard clinical visual acuity testing to evaluate agreement and potential added functional value.

Overall anticipated public and/or scientific benefit of the study:

This study is anticipated to benefit clinicians, researchers, and individuals with LHON by providing a more comprehensive and functionally relevant way to assess vision in a standardized, controlled setting. The VR-based platform may reveal deficits and improvements that are missed by conventional testing and better reflect the real-world challenges experienced by patients. This could improve clinical understanding of LHON, support the evaluation of emerging treatments, and inform more targeted rehabilitation strategies. In the future, this approach may also be adapted for other low vision populations, offering a practical and sensitive method for assessing visual function across a broad range of eye conditions.

Funding request

The purpose of this funding request is to allow us to complete this study and run a patient recruitment session at the LHON Canada Conference in September 2026. This session will allow us to recruit patients who are not typically seen at our eye institute, increasing patient involvement and understanding of outcome metrics and measurement. There is no cost associated with the equipment and licensing of the MLMT test which is being provided with support by Diagnosys. Should the testing be successful, we would build on this project and may requesting additional funding from IFOND, along with other patient advocacy groups, and industry to run a similar study at the 2027 LHON Conference

adjacent to ARVO, next year. This grant would serve as start up funds to test this new technology in the LHON patient population.

Budget

ITEM	COST	UNITS	TOTAL
STAFF TO PERFORM AND COMPLETE PATIENT ASSESSMENTS.			
1. CERTIFIED OPHTHALMIC MEDICAL TECHNOLOGIST	$3,000.00	1	$3,000.00
2. STUDENT STIPEND	$9,500.00	1	$9,500.00
TRAVEL AND TRANSPORTATION COSTS FOR TESTING AT THE CONFERENCE			
1. TRAVEL, INCLUDING EQUIPMENT TRANSPORTATION	$1000.00	1	$1000.00
2. ROOM RENTAL	$500.00	1	$500.00
3. ACCOMMODATION FOR STAFF	$250.00	2	$500.00
TOTAL			
			$14,500.00

The main expense is to support a certified ophthalmic technician trainee who will be helping to perform the testing at the LHON Canada conference and at The Ottawa Hospital. There is a small cost associated with travel, setup and fees to allow us to test patients at the meeting.

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