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Research Article

Multi-Luminance Y-Mobility Test for Assessment of Functional Vision in Patients with Severe Vision Impairment

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Abstract

Existing methods for measuring functional vision in low-vision individuals may not capture clinically meaningful outcomes. The Multi-luminance Y-Mobility Test (MLYMT) is developed to assess the ability to navigate around obstacles lighted at various luminance levels and accurately touch randomly switched lighted panels by individuals with severe vision loss, especially in the periphery. This test is designed to measure the patient's ability to navigate at different light levels, providing valuable information about the progression of as well as evaluating therapeutic efficacy. MLYMT seeks to gauge severe-vision loss subjects' visually guided navigational skills and their ability to effectively move through a course, making informed decisions while encountering obstacles at varying lighting conditions. MLYMT assay evaluates the ability of a subject to navigate under different luminance levels, which is relevant to patients suffering from photoreceptor degeneration. The assay's multi-luminance design aligns with clinical standards, enabling meaningful interpretation of outcomes within a clinical context and facilitating comparisons with existing benchmarks in the field of functional vision assessment. By incorporating a simple Y-shaped configuration of light panels and light-scattering large obstacles, the MLYMT aims to create a controlled, yet real-life environment that simulates everyday scenarios of luminance-gradient encountered by individuals with severe vision loss. The assay focuses on participants' ability to adapt to changing luminance levels (while navigating in a luminance gradient) and make navigation decisions based on visual cues and obstacles, mirroring the different real-world environments. The MLYMT can serve as a standard tool for monitoring and quantifying functional vision changes over time, allowing for evaluation of the impact of interventions aimed at enhancing the subject's vision. Overall, the MLYMT represents a promising new approach for the evaluation of functional vision in severe vision loss patients.

Keywords: *Multi-Luminance Y-Mobility Test; Vision Assessment Tool; Low Vision; Functional Vision Assessment; Vision Guided Navigation*

Introduction

Retinal degenerative diseases such as retinitis pigmentosa (RP) involve the progressive loss of visual field in affected individuals due to degeneration of outer retinal cells, primarily photoreceptors [1]. Loss of peripheral vision occurs first due to the degeneration of rod photoreceptor cells, which are primarily responsible for dim light and peripheral vision [2]. In RP, as the disease progresses, the visual field narrows, leading to a restricted field of view, followed by the death of cone photoreceptors resulting in severe to total vision loss. The ability to conduct visually dependent activities of daily living (ADL) independently is a key component of overall quality of life (QoL) [3]. The progressive loss of visual field in RP can have a profound impact on the daily lives of affected individuals. Difficulty in visually guided mobility leads to limitations in personal independence and social interactions [4]. Mobility of RP patients is correlated with vision, measured by Pelli-Robson contrast sensitivity and residual visual field [5]. The mobility performance was however not found to be correlated to psychological variables in RP patients [5]. Assessment in retinal prosthetic clinical trials showed that mobility performance did not improve with electrical prosthetics implanted over the macula [6].

Conventional vision testing charts have limitations in measuring vision below a certain threshold, encompassing counting fingers (CF), hand movements (HM), and light perception (LP) categories [7]. Vision within this range is often challenging to accurately assess and quantify. As a result, these measures are not as well-defined and understood in terms of their impact on an individual's quality of life. The lack of precision in evaluating CF, HM, and LP vision levels can hinder effective treatment planning and limit the ability to fully comprehend the functional implications for patients with such visual impairments [8]. Hence, there arises a need for more refined and comprehensive evaluation methods to address these challenges and enhance patient care. Traditional measures of mobility performance showed that RP subjects travel more slowly than the normally sighted subjects. While both normally-sighted and RP subjects travel more slowly under reduced illumination, RP subjects are five times more likely to have a mobility incident under reduced illumination than the normally-sighted subjects [9]. However, standardization based on speed is difficult as the ambulatory measure is confounded by age and other comorbidities. The presence of distractors, as well as visual function and age, have been observed to influence orientation, mobility errors, and walking speed [10]. Reduced illumination levels have been found to negatively impact the mobility of older visually impaired adults [11]. Further, the vision of off-ETDRS chart patients is difficult to evaluate in existing mobility tests including MLMT [12]. Moreover, the ability of currently available tests to gauge clinically meaningful outcomes in ultra-low-vision studies remains uncertain. Consequently, there arises a pressing demand for the creation of a visually guided multi-luminance mobility test, considering the baseline characteristics of patients with severe vision loss. Such a test would not only address the limitations of existing methods but also offer a more robust and reliable assessment of functional vision in individuals with low vision. This development would significantly contribute to advancing low-vision research and enhancing the efficacy evaluation of potential interventions and treatments.

The Multi-luminance Y-Mobility Test (MLYMT) is a novel visual function test developed for the evaluation of individuals with severe vision loss. The concept of a visually guided Y-Mobility test is derived from forced 2-choice Y-maze that has previously been used to confirm rescue of visual function following corrective gene therapy in a canine model of X-linked RP [13,14]. The primary purpose of the development of the MLYMT is to comprehensively assess and quantify functional vision capabilities in individuals with severe vision loss. MLYMT aims to replicate real-world scenarios and challenges by evaluating participants' ability to navigate a mobility course under varying levels of illumination in the presence of obstacles. Based on results and discussions with low-vision experts, we believe that the visually guided MLYMT is appropriate to evaluate severe low-vision subjects.

Materials and Methods

Best corrected visual acuity using monitored Freiburg visual acuity

Visual acuity was measured in "logarithm of the minimal angle of resolution" (logMAR) units by Freiburg Acuity (FrACT) measurements. Freiburg Vision Test (FrACT) [15] is a computer-based test developed to assess patients down to the LP level. Freiburg visual acuity can provide objective, quantifiable, and reproducible visual acuity assessments for low-vision subjects and has been independently validated to correlate with Early Treatment Diabetic Retinopathy Study (ETDRS) [7,16] and Snellen visual acuity [7]. This test has been recommended for clinical trials in individuals with low vision, including optogenetics, by the International HOVER Taskforce (Harmonization of Outcomes and Vision Endpoints in Vision Restoration Trials [16]). A lower logMAR score denotes better visual acuity.

MLYMT design considerations

Illumination level: The selection of specific light levels in the MLYMT design is based on a meticulous consideration of factors that contribute to the assessment's practicality, and applicability to varying real-world scenarios. These chosen light levels, measured at the start position of the subject and away from the lighted panel, play a critical role in ensuring that the assessment accurately evaluates participants' functional vision. The MLYMT incorporates a range of illumination levels to simulate various real-world scenarios. These levels are 0.3 lux, 1 lux, 3 lux, 10 lux, 32 lux, and 100 lux, which cover illumination from moonless night to the interior of a shopping mall measured at the starting position of the assay. The goal is to simulate different luminance conditions (with luminance-gradient), such as moving inside a home or exiting a public gathering, to assess advanced RP subjects' ability to navigate effectively in dimmer light environments. Further, these luminance levels include various times of the day, twilight, nighttime to mid-day conditions. Starting with the lowest light level and increasing emulates the natural changes in lighting conditions that individuals with low vision encounter as they transition from dimly lit (home) to well-lit (outside) environments. Further, by progressively increasing light levels in MLYMT, the learning effect (by being able to see obstacles at higher light intensity) is minimized. The gradual increase in light levels provides insights into participants' ability to adapt to changing luminance conditions. This assessment component evaluates their responsiveness to light variations and their capacity to efficiently navigate while accommodating these changes, which is crucial for individuals with low vision.

Multiple light panels with random activation: The primary objective of the MLYMT is to replicate real-world scenarios faced by individuals with low vision, particularly those with retinitis pigmentosa. The MLYMT employs a dynamic feature involving multiple light panels, one of which is randomly illuminated during the test. This design adds an element of unpredictability, requiring participants to identify the lighted path and walk toward the lighted panel. This aligns with real-world scenarios, where lighting conditions in a pathway may change from left to right. The choice to position the illuminated panels in a Y-shape configuration within the MLYMT is based on several considerations. Utilizing a Y-shaped configuration for the illuminated panels closely imitates the diverse lighting conditions encountered in everyday life, such as navigating through corridors, doorways, and sidewalks. By placing the illuminated panels in a Y-shaped configuration, the assessment requires very low-vision subjects to make accurate visual discriminations between two or more potential paths. This challenges their ability to differentiate between illuminated and non-illuminated paths, and obstacles within illuminated paths-both crucial aspects of functional vision. Maintaining a consistent light gradient across the assessment at multiple light levels ensures a controlled testing environment, minimizing confounding variables and facilitating accurate comparisons. A Y-shaped arrangement standardizes the illumination variables across trials, sites, participants, and time points, allowing us to isolate the participants' visually guided navigational performance. In summary, the decision to position the illuminated panels in a Y-shaped configuration within the MLYMT is driven by the need for practical considerations, and control over testing conditions. This arrangement effectively demands accurate visual discrimination and ensures a standardized evaluation that aligns with the objectives of the assessment.

Due to the limitation of two oppositely placed light sources (e.g. two sides in a pathway), a stringent pass criterion has to be implemented to avoid a false positive outcome. Requiring subjects to pass all consecutive trials at each light level sets a stringent pass criterion. Even if a subject were to guess correctly on one trial, the chances of consistently guessing correctly on all trials are significantly reduced. For example, in a 3-trial test scenario, success is measured by 3/3 consecutive choice of correct lighted path and touching of lighted panel, such that the probability of passing by chance is .

Obstacle integration: Recognizing that patients with even light perception (LP) might detect the LED panel at baseline, the inclusion of multiple obstacles enhances the test's ability to differentiate the vision of LP with and without projection. Large obstacles introduce barriers that replicate real-world situations (such as a table in a room, or a person on a sidewalk) where individuals with severe vision impairment need to avoid such barriers to reach their destination safely. The gap between multiple large obstacles can simulate a doorway and the navigation of a subject through the obstacles' gap allows evaluation of the patient's ability to see the obstacles and avoid collision. This replicates the activities of daily living in individuals with severe vision loss. Further, avoidance of additional obstacles in the hallway mimics personnel encountered while standing, walking, or sitting. By presenting various placements of obstacles in the mobility course, challenges encountered by low-vision subjects might be replicated. This exposure to diverse obstacles enhances their ability to adapt and navigate through different environments effectively. Additionally, working with multiple obstacles encourages the development of improved spatial awareness, problem-solving skills, and sensory processing, ultimately enhancing the individual's overall mobility and confidence in their daily activities. In conclusion, the MLYMT's incorporation of multiple obstacles, navigational avoidance requirements, and multi-luminance environments serves to enrich its comprehensiveness, and relevance in the severe vision loss patient population.

Multi-luminance Y-mobility test configurations

Different configurations based on the placement of multiple obstacles were used to test the performance of normal-vision and low-vision individuals. Supplementary figure 1A shows the arrangement of obstacles and 3 light panels in MLYMT V0.0. Supplement figure 1B-1D shows time-lapse images of a low-vision subject performing the MLYMT V0.0 test monocularly, navigating through an obstacle course. As can be seen in supplement figure 1B-1D, when the middle light panel is randomly switched on, the center obstacle in front of the light is illuminated and light intensity reaching the subject's eye is much lower and non-directional, leading to difficulty in navigation even for a subject with ~20/200 vision. Further, when the subject is near the illuminated obstacle, instead of touching the lighted panel, the subject touches the lighted center obstacle. In addition, for such a less severe vision loss subject, 100 lux (measured at the starting point) was found to be too bright near the lighted panel which blinded the subject from touching the LED panel. Therefore, in the next versions of MLYMT, 100 lux was set as the upper limit for luminance and 2 light panels on two sides were used instead of 3 lighted panels.

A schematic of the visually guided mobility test V1.0 setup is shown in figure 1A. The visually guided mobility setup requires a dark empty room (≤ 1 lux determined by a light meter) with at least 10 ft by 10 ft for the test setup. The LED panels are positioned on top of height adjustable tripod at a height of 5 feet measured from the floor to the middle of the screen, and the two LED panels were placed 5 feet apart (measured from the poles of the tripods). The subject is positioned in the midline, 10 ft away from both the LED panels. The center obstacle is positioned in the middle, 2 feet from the LED panels toward the subject, and left obstacles, and right obstacles are placed 4 feet from the subject with left obstacles and right obstacles 4 feet from the subject with a gap of 4 feet between the left and right obstacles. One of the two LED panels is randomly switched ON and MLYMT is videotaped for review and assessment of score. The MLYMT has 6 preset light illumination levels (0.3 lux, 1 lux, 3 lux, 10 lux, 32 lux, and 100 lux) measured at the subject's eye level at the start position. In this version of the visually guided mobility test, the subject (1006) is asked to walk towards a lighted Light Emitting Diode (LED) panel (1001 or 1002) at different levels of illumination avoiding obstacles (1003, 1004, 1005). Videos of subjects undergoing visually guided mobility tests are recorded using camera(s) (1008) that are mounted on a tripod for front view and/or in the ceiling for top view. The height of the camera position on the tripod could be adjusted to account for the different heights of the subjects performing the test. The camera is equipped with infrared LEDs to enable imaging in low-luminance (or dark) environments. The synchronized video recording, switching ON/OFF of the LED panels, and LED panel light intensity are controlled by PC (1007). Figure 1B illustrates an example of visually guided mobility test performance. The subject is positioned at the starting position and a random LED panel is turned on to produce the desired light intensity level. The subject navigates around the obstacles and the test ends when the subject touches the lighted LED panel.

MLYMT graphical user interface

Supplementary figure 2 shows the graphical user interface for the visually guided Y mobility test. In the "Testing Eye" tab, the proctor provided inputs on which eye-open condition for the subject (Monocular: OS-left eye, OD-right eye, or Binocular: OU-both eyes) is to be tested. In the "light control" tab, the proctor manually checked if the LED panels were functioning or not. According to the test protocol, desired light intensity and light color are selected in the "intensity control" and "color control" tabs respectively. The upper tabs are designed to include the controllable parameters of individual test trials by a proctor. Once the subject is positioned at the starting line, the proctor starts the test in the test control tab. Once the start button is pressed, the timer starts as well as recording of the video as shown in the bottom right tab. During the test, the proctor inputs which obstacles are hit by the subject in the obstacle tab. The timer ends when the end button in the test control tab is pressed, and the proctor records the input parameters and results in the save tab.

MLYMT procedure

A visually guided mobility test is implemented to assess and discriminate subjects with different levels of functional vision by adjusting the levels of difficulty in performing/passing the test. This includes adjustment of the range (lowest and highest) of light intensity levels and the location of different obstacles within the test. In addition to physical adjustments of the components and configuration of the test, various scoring systems are assigned to adjust the sensitivity as well as the dynamic range of the assay considering different functional vision levels.

Supplementary figure 3 illustrates a sequence of procedures in a visually guided Y-mobility test. First, the test instruction is provided to the subject (1001), and the lowest light intensity is selected (1002). When the test starts (1003), the synchronized video and timer start (1004) and the randomly selected LED panel is lit (1005). The subject navigates around the obstacles to touch the lighted LED panel, while the proctor records in the software any obstacle(s) hit during the test. The motion sensor(s) associated with the obstacle(s) also records obstacle(s) hit in software independently and/or alternatively. The test ends when the subject finds the lighted (correct) LED panel or pre-set timer runs out (1006). After completing a trial, repeated tests are performed at the same light intensity level where a new randomized LED panel is lit up on each trial (1007). After completing the predetermined number of trials for each light level, the proctor changes the light intensity level (1008) and repeats the test protocols until reaching the maximum light intensity level.

Supplementary figure 4A describes the scoring system of the visually guided mobility test. First, individual penalty weights for obstacle-hit(s), repositioning (required when the subject is completely off the mobility course), cut-off test time as well as pass/fail threshold score is assigned (1001). Repositioning of the subject (within the pre-determined cut-off time) is conducted when there is a safety issue and /or when the subject is completely lost in a visually guided task and touches the non-lighted (wrong) panel. Once penalty weights are assigned, the final score is computed from data collected within each trial (1002). The computed score of each trial is compared to the pass/fail threshold score (1003). Depending on the proportion of trial pass criteria set for overall passing of a light level, the subject's trial performance is evaluated for pass/fail of the specific light level (1004). When all calculations are finished for all tested light intensity levels, the lowest light illumination level (1005) that the subject passed (light intensity level in which the proportion of trial pass criteria is met) is determined.

MLYMT trial scoring

Supplementary figure 4B shows an example of a scoring system for the visually guided Y mobility test. The penalty weights of any obstacle(s) hit, going out of the boundary such as hitting the boundary of the test area (such as the wall of the room), and repositioning are assigned differently. In this scoring system, left and right obstacle hits have a weight of C1, center obstacle hit has a weight of C3, out of boundary has a weight of C4, and repositioning has a weight of C5. N1 through N5 represents the number of hits with a corresponding obstacle(s) and the number of other penalties during the test. The subject earns a Screen Touch Score (e.g., 100 points) if he/she touches the lighted LED panel, and the final score is calculated by an equation, Accuracy Score = Screen Touch Score – C1*N1 – C2*N2 – C3*N3 – C4*N4 – C5*N5. If the trial score is higher than X, which is the pass/fail threshold value, the subject is considered to have passed that specific trial.

Figure 1C-1E depict several scenarios of scoring by the subject in the visually guided mobility test. In figure 1C, the left LED panel is lighted, and the subject navigates and touches the lighted LED panel without bumping any obstacles. Number of Left/Right obstacle(s) hit = 0; Number of Center obstacle(s) hit = 0; Number of Out of boundary = 0; Number of Repositioning = 0; Touched lighted panel = Yes. Using the scoring system described earlier, the accuracy score is calculated as Score = 100 (Screen Touch) –C1*0 – C2*0 – C3*0 – C4*0 – C5*0 = 100. In figure 1D, the left LED panel is lighted, and the subject bumps the left obstacle(s) once, then navigates to touch the lighted LED panel without bumping any additional obstacle(s). Number of Left/Right obstacle(s) hit = 1; Number of Center obstacle(s) hit = 0; Number of Out of boundary = 0; Number of Repositioning = 0; Touched lighted panel = Yes. Similarly, the accuracy score is calculated as Score = 100 (Screen Touch) – C1*1 – C2*0 – C3*0 – C4*0 – C5*0 = 100 – C1.

In figure 1E, the right LED panel is lighted, however the subject bumps left obstacle(s) once, then bumps into the center obstacle (s) once and never finds/touches the lighted LED panel. Number of Left/Right obstacle(s) hit = 1; Number of Center obstacle(s) hit = 1; Number of Out of boundary = 0; Number of Repositioning = 0; Touched lighted panel = No. In this case, the accuracy score is calculated to be Score = 0 (No Screen Touch) – C1*1 – C2*1 – C3*0 – C4*0 – C5*0 = – C1 – C2. In this scoring system, left and right obstacle(s) weights are assigned the same but different weights are assigned for left and right obstacle(s) depending on which LED panel is lighted for other mobility test configurations. If the value of C1 is 20, the value of C2 is 30, and pass accuracy score threshold is higher than 0 points, the subject in figure 1C passes the trial with an accuracy score of 100, the subject in figure 1D passes the test with a score of 80, but the subject in figure 1E fails the trial with an accuracy score of -50.

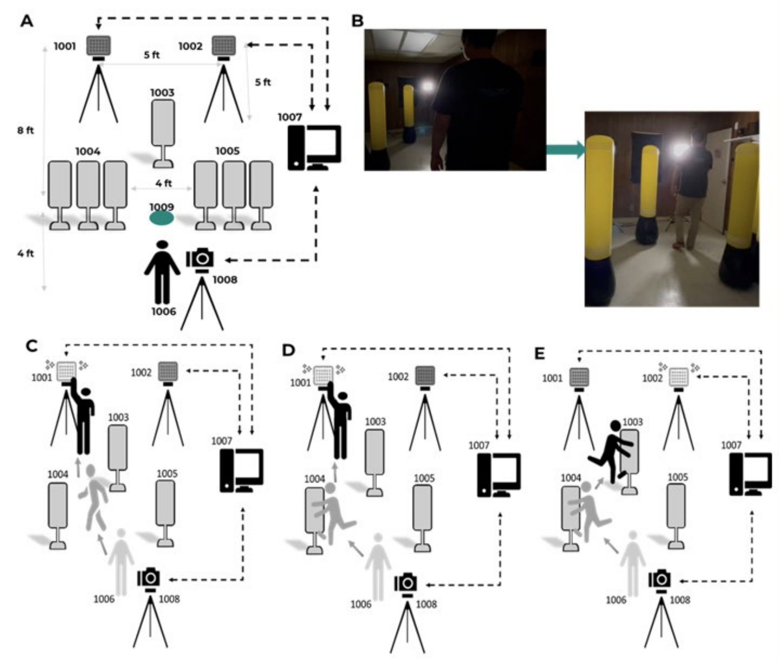


Figure 1: *Multi-luminance Y-mobility test V1.0 Setup. And Scenarios (A) Schematic of the YMT V1.0 Setup. 1001: LED light panel 1; 1002: LED light panel 2; 1003: Center obstacle(s); 1004: Left obstacle(s); 1005: Right obstacle(s); 1006: Subject start position; 1007; PC and monitor/laptop/tablet; 1008: Video camera; 1009: Restart position following repositioning. (B) Images of Visually Guided Y-Mobility Test procedures. Beginning of the test: The subject is positioned at the start line, and the LED panel is randomly lit. End of the test; Subject finding/touching correct lighted LED panel after navigating through obstacles. (C) The subject navigates and touches the lighted LED panel without bumping any obstacles. Number of Left/Right obstacle(s) hit = 0; Number of Center obstacle(s) hit = 0; Number of Out of boundary = 0; Number of Repositioning = 0; Touched lighted panel = Yes. (D) The subject bumps the left obstacle(s) once and then navigates to touch the lighted LED panel without bumping any additional obstacle(s). Number of Left/Right obstacle(s) hit = 1; Number of Center obstacle(s) hit = 0; Number of Out of boundary = 0; Number of Repositioning = 0; Touched lighted panel = Yes. (E) The subject bumps into the left obstacle(s) once, then bumps into the center obstacle(s) once, and never finds/touches the lighted LED panel. Number of Left/Right obstacle(s) hit = 1; Number of Center obstacle(s) hit = 1; Number of Out of boundary = 0; Number of Repositioning = 0; Touched lighted panel = No.*

MLYMT scoring based on luminance level

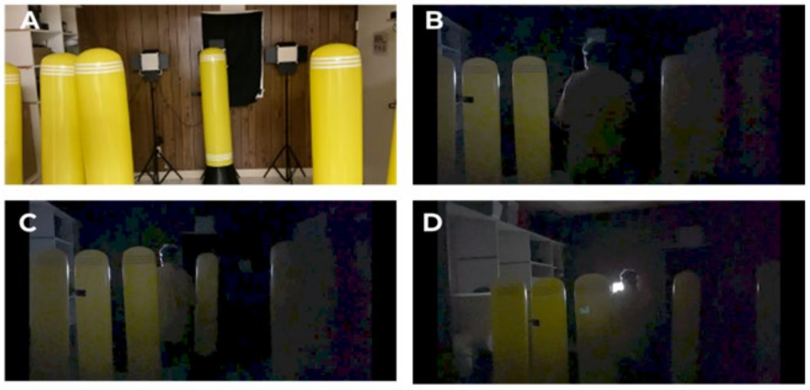
Subjects are given an overall MLYMT score of 5 (0.3 lux), 4 (1 lux), 3 (3 lux), 2 (10 lux), 1 (32 lux), or 0 (100 lux) to the lowest light level they can pass the test. A score of -1 was assigned to those who could not pass the test at 100 lux. For each test trial at a specific light level, the accuracy score was generated based on their assessment of errors (e.g., contacting obstacles). The maximum allotted time is 60 seconds per trial. Accuracy score was calculated as following: (i) 100 points are given for completing the primary task (i.e. touching the lighted panel), and no points are given for not touching the lighted panel; (ii) 20 points are deducted for each of the following occurrences: hitting the left obstacle, the right obstacle, tripod, wall, or touching the wrong (non-lighted) panel; (iii) The center obstacle hit is assigned a greater penalty (40 points) for MLYMT V1.0 and V1.1 since it is most proximal to the lighted panel and the easiest obstacle to avoid; (iv) In MLYMT V1.2, 20 points are deducted for hitting any obstacle. To pass a light-level trial, an accuracy score of > 0 must be achieved in 3/3 trials at that light level.

Results

Discriminant validity of MLYMT

Subjects with normal vision and low vision provided written, informed consent. Figure 2A shows the arrangement of obstacles and 2 light panels (the middle light panel from MLYMT V0.0 is being removed). Figure 2B-2D show time-lapse images of a low-vision subject performing the MLYMT V1.0 test monocularly, navigating through the obstacle course, and ending with touching the (randomly)-lighted panel. The test performance was found to be improved (measured by fewer obstacles hit and correct identification of the lighted panel) with increasing luminance. The ceiling was observed for subjects with a visual acuity of logMAR 1.9 (measured by Freiburg visual acuity). A subject with tunnel vision (having better visual acuity but impacted peripheral vision) could perform the test at the lowest luminance level (0.3 lux). No light perception (NLP) subject could not perform the test at bright luminance levels. The NLP subject did not feel confident to move from the starting position of the test without the use of a cane or holding the hand of the caregiver. The MLYMT V1.0 videos are graded by multiple independent masked graders, with high inter-rater reliability, and strong test-retest correlation.

Figure 2E shows the sensitivity analysis of MLYMT in normal vision and low-vision subjects having different levels of vision. The measured MLYMT score as a function of BCVA (at baseline) of eyes demonstrates that a change of 2 light levels was associated with 0.3 logMAR (measured by FrACT) in individuals with severe vision loss due to RP. Therefore, a 2-light level change in MLYMT aligns with a 0.3 logMAR improvement supporting this increment as clinically meaningful. Further, the test-retest variability of MLYMT score in individuals with severe vision loss due to RP was estimated in the Observational study to be < 2. Moreover, considering the score range of MLYMT (-1 to 5, or 7 levels) a 2-unit change in MLYMT score is nearly one-third of the entire range in MLYMT scores and therefore, a stringent criterion.



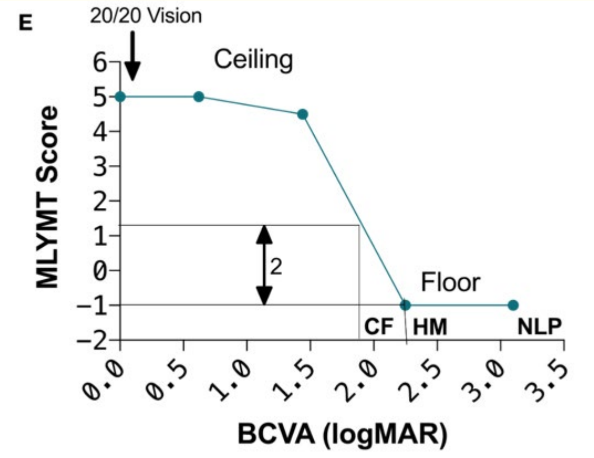


Figure 2: *Images of a visually guided Y-Mobility Test V1.0. (A) Picture showing the arrangement of obstacles and 2 light panels. (B-D) Time-lapse images of a low-vision subject (CF 1') performing the test, navigating through the obstacle course, and ending with touching the (randomly)-lighted panel. (E) Variation of MLYMT score with BCVA and discriminant validity. N=8.*

Mapping of light distribution in MLYMT

Obstacles' scattering map: To measure the obstacle visibility at the start position, when one of the LED panels is turned ON, a light meter (Dr. Meter LX1330B) was positioned (attached to a post, at average subject height) at the starting location of the test, oriented (faced) toward each obstacle. The luminance was measured at different luminance conditions. As shown in figure 3A, at the lowest luminance level (0.3 lux), the visibility of the obstacles remains poor, and the visibility increases as the LED intensity increases. As expected, the left-side obstacle visibility is higher when the left LED panel is ON compared to the right obstacles, and the same is true when the right LED panel is ON.

MLYMT light intensity map: To measure the luminance level, a 10 x 10 grid was used on the floor of the MLYMT V1.0 setup. Intensity (measured at the subject height facing toward the light in the presence of the obstacles) was measured at each grid and an intensity map was generated. The process was repeated for all luminance levels. The map portrays the light distribution from a single light source within the MLYMT course in the presence of obstacles. After setting up the MLYMT V1.0 on top of the grid, the LED panel was switched ON. The light meter was anchored at eye level (5 ft) to a camera post. The light meter was then positioned in the center of each pixel in the grid, oriented to the light source. A total of 9 x 10 measurements per luminance level were made excluding the top row where the light panel is located.

Overlay: The two maps, the light intensity map, and the obstacle scattering map, were then overlaid to represent what a subject would see at a given position navigating through the MLYMT. The luminance map across different areas within the room for MLYMT V1.0, as measured from the subject's perspective using a light meter, is presented in figure 3B for different luminance levels (0.3 to 100 lux, measured at the starting position).

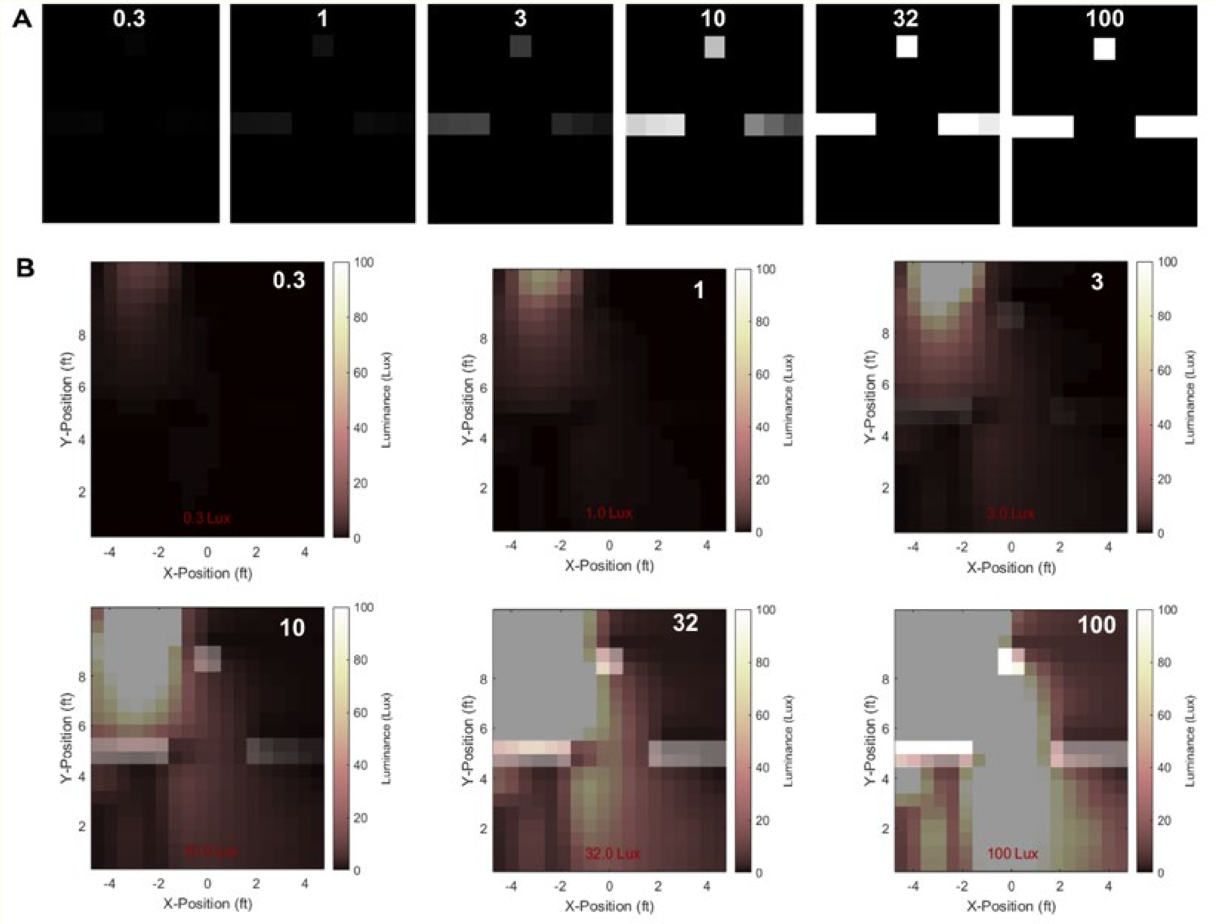


Figure 3: *Mapping of luminance in MLYMT. (A) Scattered light map of the obstacles at the starting position under different luminance levels. Left to Right: 0.3, 1, 3, 10, 32, 100 Lux, measured at starting position at eye level. This mapping data was collected when the left LED panel was ON. (B) Luminance distribution in the MLYMT as measured by light meter. Map of luminance in the room from the light source and scattered light from the obstacles as seen by the subject. The non-uniformity of the illumination path (created by obstacles and their reflection) for different light levels. Scale bar: lux.*

Performance of low vision subjects in MLYMT

In the MLYMT assay, the subject is tasked with navigating around these obstacles while successfully adhering to the correct path leading to the lighted panel. The MLYMT assessment is tailored to evaluate the navigational vision of individuals with visual impairment. This evaluation effectively mirrors real-life scenarios in which such individuals must navigate towards or away from a light source, recognize a lighted train door on a platform, respond to traffic lights while crossing roads, pinpoint exits within public spaces, and more. Multiple possible configurations of the Visually Guided Y-Mobility Test are shown in supplement figure 5. These configurations include different arrangements and several obstacle(s), to adjust the difficulty level of the mobility test. The visually guided mobility setup design is adapted to the vision status and mobility of the subject population. To evaluate if the dynamic range of the test can be improved, additional obstacles were used and arranged (as shown in figure 4A). Normal vision and low-vision individuals were tested in the MLYMT 1.1 setup. Figure 4B-4D shows time-lapse images of a low-vision subject performing the MLYMT V1.1 test, navigating through an obstacle course, and ending with touching the (randomly)-lighted panel.

Similar to MLYMT V1.0, the test performance in MLYMT 1.1 improved with increasing luminance in low-vision individuals, however, the ceiling could not be improved above the visual acuity of logMAR 1.9. It was noted that such low-vision subjects exhibit visual acuity variability (due to measurement or other physiological reasons), and therefore, the determination of a ceiling with high accuracy may not be possible with a limited number of subjects. The complexity of the MLYMT setup was increased by additional obstacles and positioning of the obstacles in a checkerboard pattern as shown in figure 4E. Normal vision individuals (VA better than 20/50) could attain perfect scores in the MLYMT 1.2 setup without hitting any obstacle at the lowest luminance level, unlike subjects with severe vision impairment. Figure 4F-4H shows time-lapse images of a low-vision subject performing the MLYMT V1.2 test, navigating through the obstacle course, and ending with touching the (randomly)-lighted panel. Subjects with 1.9 logMAR vision could perform the test albeit with obstacle hit(s). Therefore, it is possible to increase the ceiling of the test with stringent pass/fail criteria. However, in this version, difficulties in recording obstacle-hit events were observed due to the high density of obstacles. This may lead to difficulties in grading and higher inter-rater variability as compared to MLYMT V1.0. Further, the light was occluded by the obstacles in MLYMT V1.2 (as seen in figure 4G), which can contribute to variable performance by the individuals based on their height and the initial path taken.

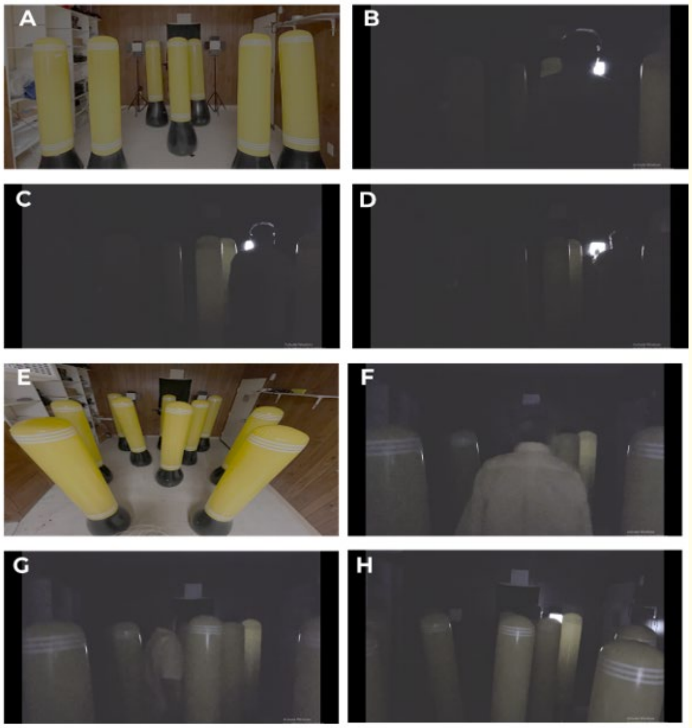


Figure 4: *Images of a visually guided Y-Mobility Test V 1.1 and V1.2. (A) Picture showing the arrangement of obstacles and 2 light panels. (B-D) Time-lapse images of a low-vision subject (CF 1') performing the test, navigating through an obstacle course, and ending with touching the (randomly)-lighted panel. (E) Picture showing the arrangement of obstacles and 2 light panels. (F-H) Time-lapse images of a low-vision subject performing the test, navigating through the obstacle course, ending with touching the (randomly)-lighted panel.*

Sensitivity analysis of different versions of MLYMT

Figure 5 shows a sensitive analysis of different versions of MLYMT. Variation of MLYMT score with BCVA while using different MLYMT versions (V1.0, 1.1, 1.2). Adding more difficulties by introducing more obstacles in MLYMT had an impact on the dynamic range of the outcome score for a set of subjects with different visual acuity measured by BCVA. Therefore, different versions of MLYMT can be used to target a specific range of low-vision subjects effectively.

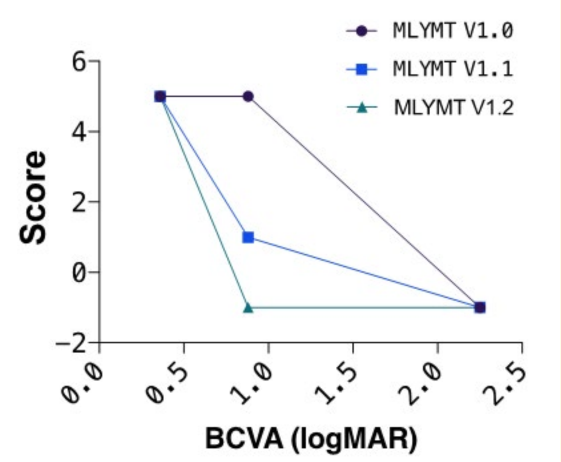


Figure 5: *Sensitive analysis of different versions of MLYMT. Variation of MLYMT score with BCVA while using different MLYMT versions (V1.0, 1.1, 1.2).*

Discussion

Vision-guided mobility tests have been utilized in previous clinical trials in the form of obstacle courses to simulate daily vision-guided activities [17]. Based on the mobility test (MLMT) in previous ocular gene therapy trials and approval [17] involving IRD patients with RPE65 mutation, a clinically meaningful change in vision was defined by passing the mobility test at two dimmer light levels after treatment. The multi-luminance Y-mobility test (MLYMT) is a specialized assessment tool designed by Nanoscope to evaluate functional vision in individuals with low vision, particularly those with retinitis pigmentosa (RP). The test aims to measure changes in functional vision by assessing the ability of subjects to navigate a course accurately and efficiently under different levels of illumination. The MLYMT builds upon the earlier Y mobility test (YMT) and incorporates enhancements suggested by regulatory agencies and relevant research findings. By replicating real-world lighting transitions, and adapting to changing luminance, the MLYMT offers a comprehensive evaluation of participants' functional vision abilities in various lighting scenarios, accurately simulating their experiences and challenges. In summary, the decision to employ two light panels in the MLYMT design is rooted in the need for simplicity, cognitive manageability, and limited vision (visual field) of advanced RP patients.

The decision to employ two light panels in the MLYMT design, as opposed to utilizing more than two light panels, is driven by several key considerations that prioritize the practicality of implementation. While incorporating more light panels may seem advantageous at first glance, the following points demonstrate why the use of two light panels is a more suitable choice. Using multiple light panels would introduce an increased cognitive load on participants, requiring them to rapidly process and respond to a higher number of lighting cues. This could result in heightened stress and reduced accuracy in navigation, compromising the reliability of the assessment. The use of two light panels strikes a balance between challenge and manageability, allowing participants to focus on key navigation tasks without becoming overwhelmed. The development of the MLYMT is motivated by several compelling reasons that underscore its significance in the realm of functional vision assessment. Simple navigational routes featuring gentle, yet substantial barriers (eliminating the risk of stumbling) enable individuals with severe visual impairment (who rely on canes, guide dogs, or caregivers) to attempt to move independently, without the need for extra assistance, while ensuring their safety. This targeted approach ensures that the assessment remains relevant and directly applicable to the population it aims to serve.

The MLYMT effectively simulates the scenario of walking towards a lighted window, assessing subjects' ability to not only detect a light source and direction but to identify and avoid obstacles as well as to localize the finite light panel with certainty. Further, the MLYMT extends the assessment's relevance by introducing varying levels of illumination and light locations-factors closely mirroring the environment encountered in real-world navigation scenarios. Tasks such as avoiding other pedestrians while walking on a street, navigating unfamiliar hallways, or passing through doorways are simulated within the test. These features enable the MLYMT to evaluate not only basic light detection but also navigational skills under dynamic lighting and obstacle-rich conditions. By incorporating additional illumination levels, the MLYMT captures mobility performance over a wider range of light intensities than YMT and AMT, increasing the dynamic range to determine clinically meaningful changes in participants' visually guided navigation. MLYMT offers a comprehensive assessment that evaluates multiple dimensions of functional vision. It assesses basic light detection, navigational accuracy, ability to perceive scattering cues needed for obstacle avoidance, adaptation to varying light intensities, and accurately determining the definite boundary of the light panel -an aggregation of factors crucial for holistic functional vision assessment. The MLYMT introduces a refined scoring system that aligns with its expanded complexity. The scoring, which incorporates multiple levels of illumination and obstacle interaction, offers valuable insights into participants' performance and captures their adaptability to a range of navigational challenges.

Each component of the visually guided mobility test can be chosen to have different properties. Different size and shapes of LED panel can be used, and the LEDs can emit different colors (red, green, blue, and white) that allows the assessment of color-specific functional vision. Also, different elements or arrays of LED within the LED panel can be lit to generate specific spatial frequencies of LED stripes and patterns. For further control of the dynamic range of light intensity from the LED panel, a polarizer and/or neutral density filter can be used to attenuate the light. The height of the LED panel position on the tripod could be adjusted. The reflectivity from the obstacles could be changed by the use of a polarizing film. Potential sources of error are: (i) hallucinations faced by the severe-vision loss subjects, and (ii) variability in the availability of vitamin A (all-trans-retinol) which is required for the natural visual transduction process. The limitations of the assay include (i) performance ceiling at vision of ~logMAR 1.7 (i.e., CF 1'), and (ii) floor of performance at light perception (LP) without projection (~ logMAR 2.8). The mobility performance of visually impaired adults may improve after orientation and mobility training [18]. The learning effect in the MLYMT can be minimized by: (i) having a gap between the time points for performing the assay, (ii) conducting the trials from low to high Lux levels; (iii) randomly switching the lighted panels; and (iv) non-training of any subject at any time points.

Conclusion

The multi-luminance Y-mobility test's design and objective is to provide a meaningful assessment of functional vision changes in clinical studies. The MLYMT performed at multiple luminance levels is a sophisticated assessment tool developed by Nanoscope to evaluate the functional vision of individuals with low vision, particularly those with retinitis pigmentosa. Through the incorporation of various illumination levels, obstacles, dynamic lighting scenarios, and real-world challenges, the MLYMT offers a comprehensive evaluation of subjects' navigational abilities and their capacity to overcome obstacles under diverse conditions, although the inclusion of too many obstacles may occlude the view of the subject and lead to difficulty in finding the light. The ceiling of the MLYMT assays was found to be approximately CF 1', while the floor was determined to be at LP. The MLYMT performance was found to be disease dependent, i.e. variation of mobility scores with BCVA for RP is different from other IRDs or vascular atrophy. However, the MLYMT has shown promise as a reliable tool for the measurement of visual function in low-vision subjects and may provide valuable data for the evaluation of the effectiveness of therapy. Improvement of MLYMT performance, measured by the ability to perform tests at lower luminance and/or with a smaller number of obstacle hits will serve as an indicator for improvement, while the opposite will indicate worsening of vision. However, validation of the visually guided YMT is required to provide an appropriate key end-point assessment, in the absence of any established mobility test for subjects with advanced vision loss.

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Conflict of Interest

SK, MC, and SM have an equity interest in Nanoscope Instruments Inc. SM also has an equity interest in Nanoscope Technologies LLC. SK, MC, SB, and SM are employed by Nanoscope Technologies LLC.

Ethical Approval

The procedures performed in this observational study involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in this observational study.

Bibliography

1. Hartong DT., *et al*. “Retinitis pigmentosa”. *Lancet* 368.9549 (2006): 1795-1809.
2. Sugawara T., *et al*. “Relationship between peripheral visual field loss and vision-related quality of life in patients with retinitis pigmentosa”. *Eye (London)* 24.4 (2010): 535-539.
3. Chen CS., *et al*. “Vision-related quality of life in patients with complete homonymous hemianopia post stroke”. *Topics in Stroke Rehabilitation* 16.6 (2009): 445-453.
4. Pundlik, S., *et al*. “Evaluation of a portable collision warning device for patients with peripheral vision loss in an obstacle course”. *Investigative Ophthalmology and Visual Science* 56.4 (2015): 2571-2579.
5. Haymes S., *et al*. “Mobility of people with retinitis pigmentosa as a function of vision and psychological variables”. *Optometry and Vision Science* 73.10 (1996): 621-637.
6. Geruschat DR., *et al*. “Orientation and mobility assessment in retinal prosthetic clinical trials”. *Optometry and Vision Science* 89.9 (2012): 1308-1315.
7. Schulze-Bonsel K., *et al*. “Visual acuities “hand motion” and “counting fingers” can be quantified with the Freiburg visual acuity test”. *Investigative Ophthalmology and Visual Science* 47.3 (2006): 1236-1240.
8. Gordois A., *et al*. “An estimation of the worldwide economic and health burden of visual impairment”. *Global Public Health* 7.5 (2012): 465-481.

9. Geruschat DR., *et al*. "Traditional measures of mobility performance and retinitis pigmentosa". *Optometry and Vision Science* 75.7 (1998): 525-537.

10. Leat SJ and JE Lovie-Kitchin. "Visual function, visual attention, and mobility performance in low vision". *Optometry and Vision Science* 85.11 (2008): 1049-1056.

11. Kuyk T., *et al*. "Visual correlates of mobility in real world settings in older adults with low vision". *Optometry and Vision Science* 75.7 (1998): 538-547.

12. Chung DC., *et al*. "Novel mobility test to assess functional vision in patients with inherited retinal dystrophies". *Clinical and Experimental Ophthalmology* 46.3 (2018.): 247-259.

13. Beltran WA., *et al*. "Successful arrest of photoreceptor and vision loss expands the therapeutic window of retinal gene therapy to later stages of disease". *Proceedings of the National Academy of Sciences* 112.43 (2015): E5844-E5853.

14. Beltran WA., *et al*. "Optimization of retinal gene therapy for X-linked retinitis pigmentosa due to RPGR mutations". *Molecular Therapy* 25.8 (2017): 1866-1880.

15. Bach M. "[The Freiburg Vision Test. Automated determination of visual acuity]". *Ophthalmologe* 92.2 (1995): 174-178.

16. Ayton LN., *et al*. "Harmonization of outcomes and vision endpoints in vision restoration trials: recommendations from the international HOVER taskforce". *Translational Vision Science and Technology* 9.8 (2020): 25.

17. Maguire AM., *et al*. "Safety and efficacy of gene transfer for Leber's congenital amaurosis". *New England Journal of Medicine* 358.21 (2008): 2240-2248.

18. Soong GP., *et al*. "Does mobility performance of visually impaired adults improve immediately after orientation and mobility training?" *Optometry and Vision Science* 78.9 (2001): 657-666.

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