SPT Thesis

An Observational Study to assess the ability of Low-Vision Multi-Parameter Test (LVMPT) to evaluate functional vision.

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Abstract

Research Question: For patients with ultra-low vision, it is difficult for clinicians and researchers to evaluate visual function. Background: While there are several established tests meant to test single parameters of vision for these patients, functional vision requires multiple parameters. For accurate evaluation of true visual ability, multiple parameters need to be evaluated to assess a patient's visual ability, both for the detection of disease, and the evaluation of treatment effectiveness. Vision disorders are extremely impactful both for individual patients, but also society at large. If clinicians and researchers are able to develop treatments for patients who have significant visual impairment, there needs to be a simple and effective way to evaluate functional vision. Our project aims to answer the following question: Does the 2nd generation 3D Low Vision Multi-Parameter Test (LVMPT) accurately assess visual function in ultra-low vision patients, and how does it compare to established tests such as the logMAR eye chart? Materials and Methods: Our study separated our participants into two cohorts based on their logMAR scores. We then evaluated each participant using the LVMPT that Nanoscope Technologies has created. The parameters tested by the LVMPT were 3D shape recognition under different light conditions. These measurements were then compared with Visual Acuity (VA) and Visual Field (VF) for each patient. Results: The results of the study include the LVMPT having a Pearson's Correlation Coefficient of -0.9 for participants in both groups when compared to their logMAR eye chart scores. The LVMPT also had a correlation of -0.921 when compared to their Humphrey Visual Field test. Conclusion: This study provides evidence the LVMPT can be an effective tool to measure vision in patients with ultra-low vision by showing its correlation with established evaluation tools. More research needs to be done to determine how effective it is in determining functional visual ability.

Research Question:

Does the 2nd generation 3D Low Vision Multi-Parameter Test (LVMPT) accurately assess visual function in ultra-low vision patients, with greater efficacy compared to the established logMAR visual acuity test?

We hypothesize the 2nd generation 3D LVMPT will be able to depict visual ability on an equal or greater level than the logMAR.

Introduction, Significance, and Rationale

Introduction

Vision is a dynamic sensory experience involving many different aspects including light sensitivity, depth perception, color, movement tracking, sharpness, and what is seen in one's visual field. [1] Clinically, vision is mainly tested using a Snellen eye chart for the general patient population. For patients with low vision, there are several widely used vision assessments that aim to test relevant parameters. Visual acuity is often assessed by an Early Treatment for Diabetic Retinopathy Score (ETDRS) which uses a similar chart to the more popular Snellen eye chart, but is intended for patients with low vision. Sensitivity to different thresholds of light has been tested using the Full-Field Stimulus Threshold test (FST). [2] Electroretinography is used to gather objective data on a patient's rods and cones' ability to sense light. [3] The Humphrey visual fields test is used to assess a patient's visual field detection ability. [4] There are also other visual tests used. [5,6,7] While these tests have been commonly used, they all test only one parameter of vision. Testing all these parameters individually can be difficult concerning effective training to reliably administer a given test and are time-consuming. There exists a need for a visual test that can assess multiple parameters accurately and conveniently.

A standard eye chart can not be used for ultra-low vision patients because their vision is so poor they are not able to see the largest letters on the chart. For ultra-low vision, the Freiburg Visual Acuity Test (FrACT) assesses a patient's ability to count fingers, detect hand movement, and light perception. [8] However, it is unclear if the FrACT draws any correlation to clinically meaningful outcomes. The Low Vision Multi-Parameter Test (LVMPT) developed by Nanoscope Instruments enables assessment of a variety of different visual parameters, but also tests for clinically significant variables.

The LVMPT tests 3D object identification under different thresholds of light. It is important to evaluate a patient's ability to detect objects at different light levels to understand their ability to see things in well-lit vs. low-light environments. 3D object identification is an important skill to

have; from choosing the right utensils to eat with, to dressing oneself in the right clothing, to interacting with technology such as phones and remote controls. By packaging these different parameters into one testing device, evaluators will have a convenient and accurate way to assess patients' real-world visual ability.

Significance

Vision disorders have a significant impact on the quality of life of the patient. Visual problems can range from seeing floaters, blurriness, light sensitivity, or even blindness. It is estimated the economic impact of vision disorders on the United States is 35.4 billion per year. [9] The impact of complete or near-complete loss of vision to patients and society is immense, and goes far beyond vision alone. Low vision patients are at high fall risk leading to hip and extremity fractures. There have been significant advances in regenerative medicine over the last decade, focusing on halting cellular degeneration and introducing therapies to generate new cells into the retina.[10] With the number of resources dedicated to treating visual disorders being so high, there needs to be accurate ways to assess visual acuity before and after treatment. The availability of a vision test that accurately measures functional visual ability will allow better assessment of patients with ultra-low vision as their disease progresses. It will also allow assessment of how effective treatment for ultra-low vision is when patients undergo experimental or established treatment options.

Rationale

A multi-parameter vision test that assesses clinically relevant parameters has not been validated. The 3D LVMPT will allow researchers and clinicians to accurately assess low-vision patients' improving vision. This will require hardly any training to administer the test because it is mostly all automated.

Two cohorts will be chosen based on BCVA score and will be able to test the accuracy and validate the 3D LVMPT as a reliable and efficient standardized test of visual function in patients with severely depleted vision. The study is designed to be able to validate the LVMPT by correlative measurements using logMAR visual acuity. The highest vision patient group will be used as a control.

Materials and Methods

General Study Details and Resources

Our study tests the overall hypothesis that the 2nd generation LVMPT will accurately depict visual ability in patients with impaired vision as reliably as other validated tests of visual acuity; the logMAR visual acuity test. The hypothesis was tested by execution of the following specific aims:

Specific Aim 1: From a population of subjects, we separated them into two cohorts based on their Best Correlated Visual Acuity (BCVA) as demonstrated by their logMAR score. Those cohorts are 1) logMAR better than 0.3 or normal vision, 2) logMAR worse than 1.6 or legally blind.

Specific Aim 2: In each study participant, we assessed the relative performance of the LVMPT compared to the logMAR eye chart. This is done once at baseline.

Specific Aim 3: Determine the correlation between the LVMPT and logMAR.

Cohort Groups:

From a population of subjects, we separated them into two cohorts based on their Best Correlated Visual Acuity (BCVA) as demonstrated by their logMAR score which were measured by a trained technician. The first cohort (Cohort 1) consisted of 10 subjects with clinically normal ocular findings and a Best Corrected Visual Acuity better than logMAR 0.3 in each eye. The second cohort (Cohort 2) consisted of 25 subjects with advanced visual impairment (Best Corrected Visual Acuity worse than or equal to logMAR 1.6 in the better seeing eye and worse than logMAR 1.9 in the worse seeing eye, and a clinical diagnosis of advanced retinitis pigmentosa (See Figure 1).

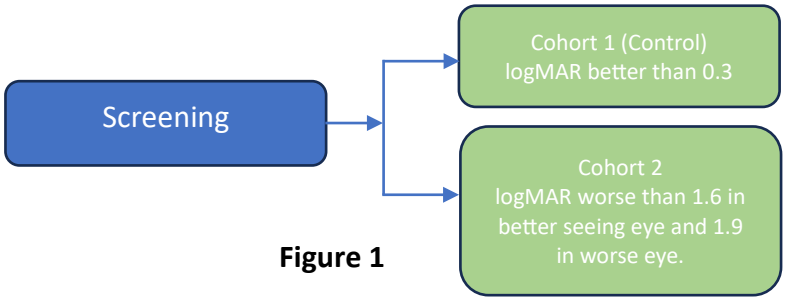

Figure 1

Instruments used:

The 3D-LVMPT measures 3D shape recognition using shapes including a cylinder, sphere, cube, brick, donut, and pyramid. These shapes are placed on pressure censors in an illuminated box that features adjustable illumination (See Figure 2). Other instruments used as part of the LVMPT test included a laptop with software, a light meter, a measuring string marked with 30 cm, and an eye patch.

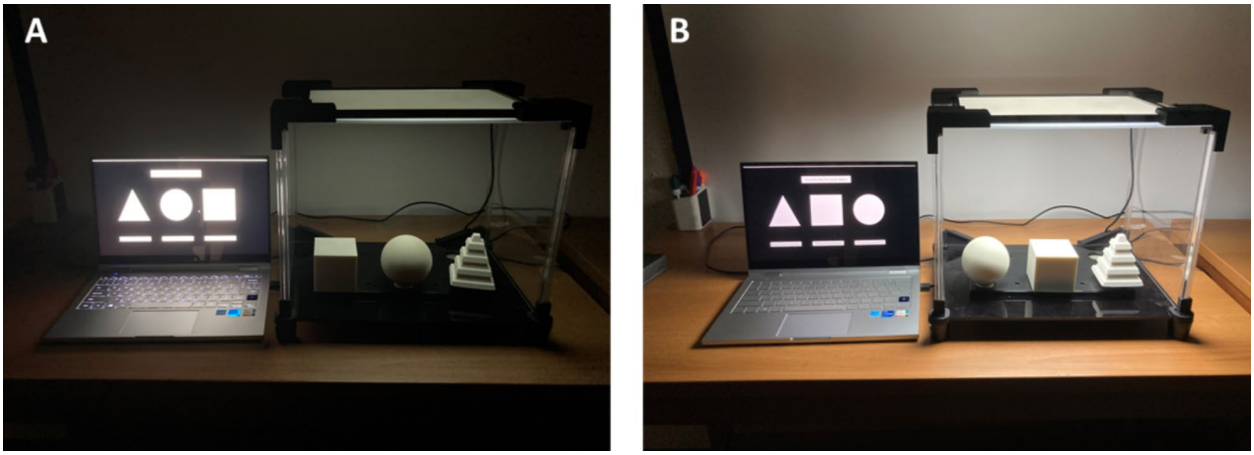

Figure 2. 3D-LVMPT in multiple luminance settings. (A) Low-luminance (0.2 lux); (B) High luminance (21 lux) measured at 30 cm from the device at subject's eye level.

Shapes were selected based on commonly encountered objects that subjects would encounter in real-life. The size of objects was approximately 6-7 cm.

When screening patients, a logMAR chart (See Figure 3) and Humphrey Visual Field machine (See Figure 4) were used. A trained clinician administered both tests for participants.

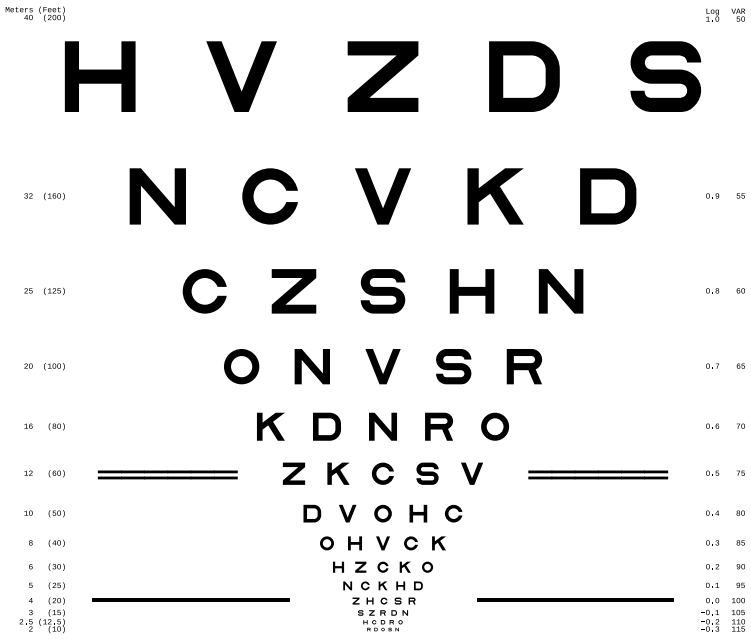

Figure 3: logMAR chart used to assess patient's Visual Acuity.

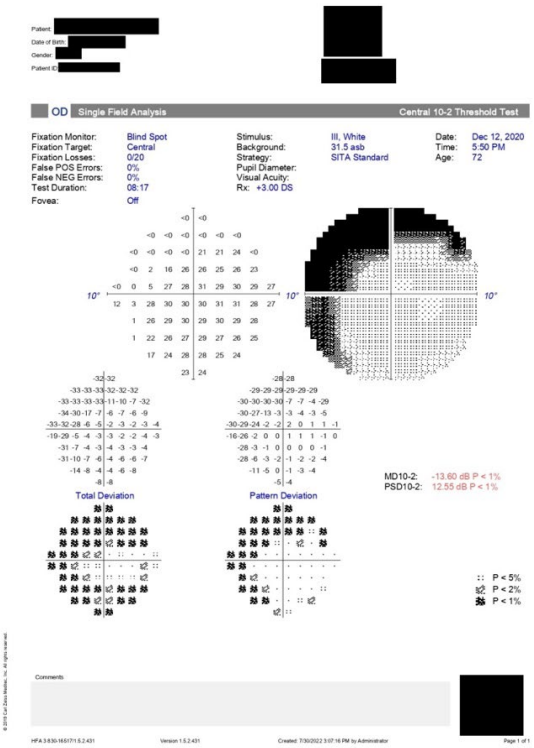

Figure 4: Sample readout from a Humphrey Visual Field test[12].

Parameter set-up

Patients with significantly low vision who have Retinitis Pigmentosa have constricted visual fields. Since the 3D-LVMPT apparatus is intended to treat patients with such visual defects, objects in the apparatus were placed no further than a 45-degree angle to the patients. Placing the objects 30 cm away, which simulates the viewing distance for near activities, we limited the length of the apparatus to 25 cm which limits the viewing angle to 45 degrees.

Being able to identify objects at different illumination levels is instrumental for real-world vision. The 3D-LVMPT is designed to evaluate visual ability at different light levels. We choose illumination levels equally spaced on a semi-log scale of 0.2 lux, 0.7 lux, 2.1 lux, 7 lux, and 21 lux. This encapsulates a range of illumination including near darkness, an outdoor parking lot at night, and a well-lit room.

A main object of the 3D-LVMPT is to achieve a simple way for a relatively untrained person to measure visual ability in patients. To accomplish this, the 3D-LVMPT uses an automated-scoring method to avoid any bias or lack of ability in the proctor. It is therefore necessary to design the apparatus to allow subjects to pick up individual objects while not hitting others. A 3x1 configuration was implemented to fill enough objects at the previously discussed size of 6-7 cm and within a 25 cm total length with adequate spacing (~3cm) (See Figure 5).

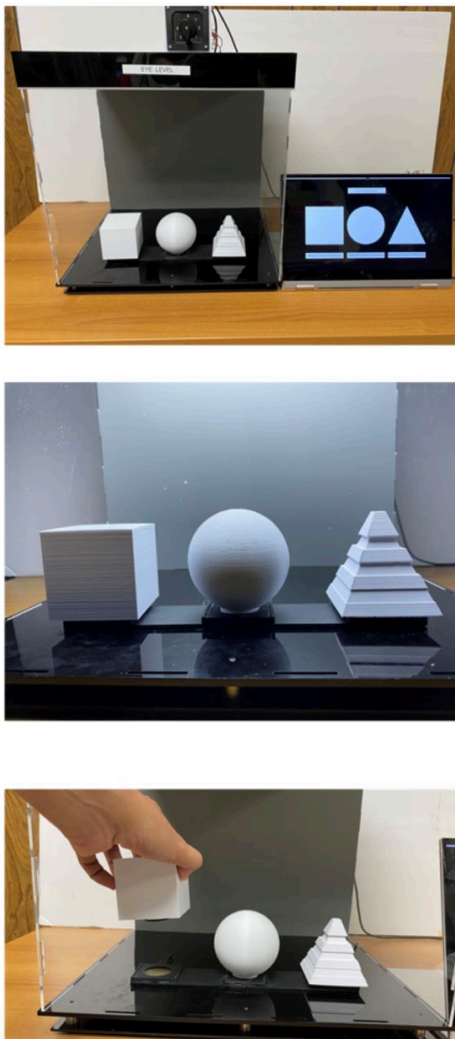

Figure 5: Final iteration of the 3D-LVMPT included a cube, sphere, and pyramid spaced approximately 3 cm apart.

Methods:

The study involved participants, some with normal vision and others with impaired vision, who were given the task of correctly identifying and retrieving a specified object in the quickest time possible. For individuals with vision at logMAR of 0.3 or better, the tests within the 3D-LVMPT system were expected to be easily completed. To evaluate the precision of object recognition, the assessment covered different levels of brightness. Within the system, the requested object for the user to select was randomized, as was the placement of objects within the box, aiming to eliminate any potential bias.

To comprehensively understand participants' object recognition abilities, performance was analyzed under varied lighting conditions. All assessments were conducted monocularly, with one eye occluded before the test began. The test proctor, positioned opposite the subject, had access to a graphical user interface (GUI) displayed on a monitor. The subject, however, did not have access to the GUI or the screen display, as the monitor's light intensity was lowered to maintain a controlled low luminance environment (e.g., <1 lux ambient room light) during testing.

The GUI provided instructions regarding the sequence in which objects were to be placed on the 3D LVMPT platform. Once arranged by the proctor, the specific object to be picked up was announced either by the proctor following the procedure or by an automated voice in the GUI. A pressure sensor (or camera sensor) ensured the correct arrangement of the 3D objects. Participants were instructed to pick up the designated object within a time limit (15 seconds) and were not permitted to change their decision after touching an object, considering that the texture could influence their choice. Each trial concluded when the subject picked up an object, irrespective of its correctness. The pressure sensor in the 3D LVMPT device provided feedback to the software and recorded the shape picked up in that trial. Each test was repeated a set number of times at the same light level before advancing to higher illumination intensities.

The scoring method used to assess subjects' accuracy was as follows. For each light level (5 levels), participants were instructed to pick up the correct object 5 times. Ensuring there were 5

trials for each light level decreased the chance of false positives from randomly picking up the correct object. For each trial, the software on the provided laptop gives instructions to the proctor for object positioning. The software then instructs the subject to pick up a specific object, records the time taken to pick up that object, and records which object was selected. The software then instructs the proctor to rearrange the objects in a random order that is shown on the screen again, and the test continues in a repeating pattern. The overall score for each participant is based on the lowest light intensity that the participant was able to pick up each of the 3 objects correctly. A score of "1" was assigned to a participant if they were only able to correctly pick up the correct object 5 times on the highest light intensity (21 lux), a score of "2" was assigned if the participant was able to correctly pick up the objects 5 times at the highest and second highest intensities (21 and 7 lux), and so on until a maximum score of "5" would be achieved with a participant able to pick up the correct object 5 times at all light intensities.

Data gathering and interpretation:

Data was collected by staff at a clinical site in Dallas and stored in the cloud using encrypted software. Collected Data included patient's demographics, BCVA, adverse events, and response times for each LVMPT test. Accuracy of the LVMPT will be evaluated and compared with Visual Acuity (VA) and Visual Field (VF).

Results:

Cohorts 1 (control) and 2 (impaired vision) had results as shown in Figures 6 and 7. Each participant in Cohort 1 had perfect LVMPT scores for each eye. Cohort 2 had a majority of participants score a zero on the LVMPT, with a few participants getting scores from 1-5.

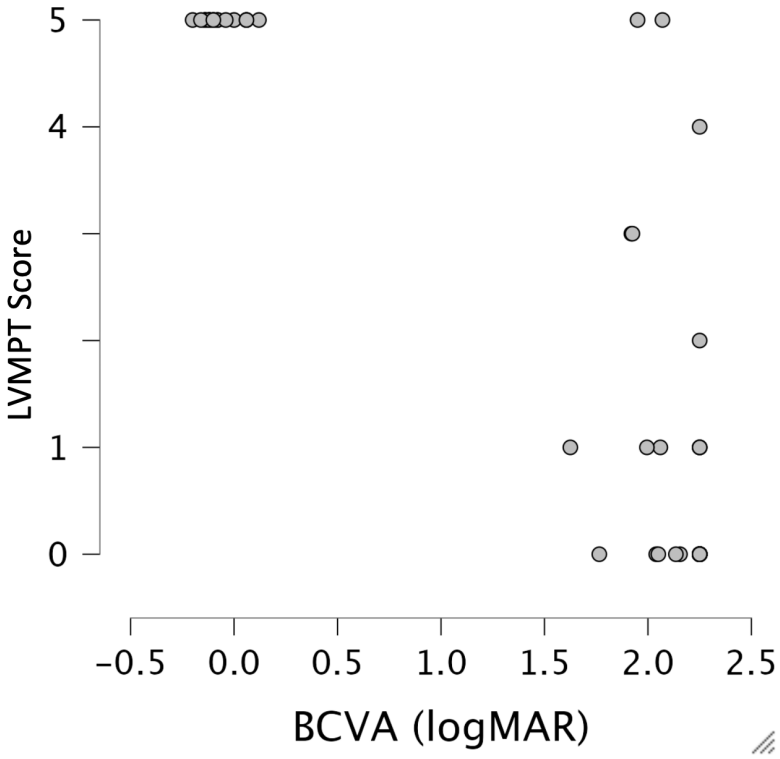

Figure 6

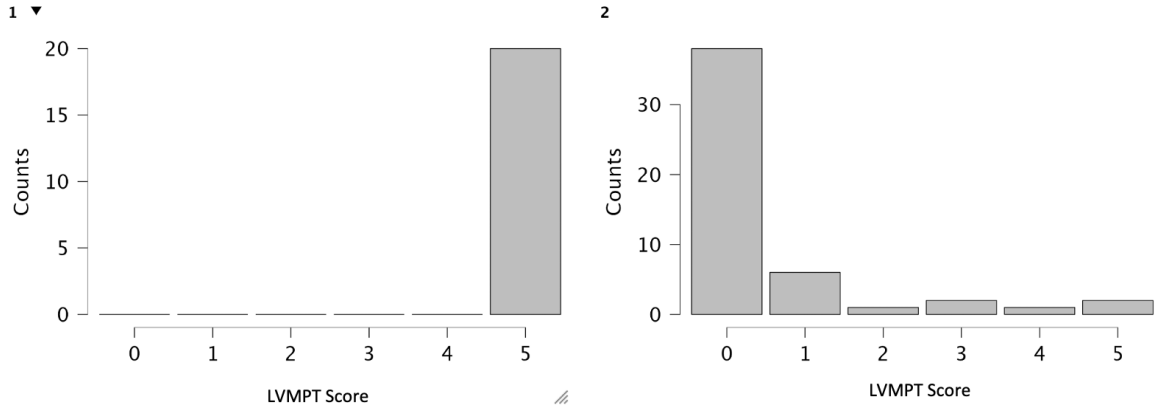

Figure 7: Counts show results for both eyes of participants.

Correlation to visual acuity and visual field tests:

For all participants, the LVMPT had a Pearson's Correlation coefficient of -0.9 in comparison to their logMAR scores with a p value of <.001.

Additionally, when comparing the LVMPT to a patient's Humphrey Visual Field test measured in dB, the LVMPT had a Pearson's Correlation coefficient of -0.921 when compared to the mean deviation (MD) with a p value of <.001.

Discussion:

The results of our study suggest the LVMPT was successful in evaluating a person's visual ability as compared to a more traditional method such as a logMAR chart as evidenced by the Pearson's Correlation of -0.9 and very small p-value. The results provide evidence that the LVMPT can be promising as an evaluation tool for patients with ultra-low vision. An interesting finding was for some subjects with almost identical logMAR scores, their LVMPT scores differed by as much as the maximum five points. This suggests patients used different abilities when using the LVMPT compared to the logMAR chart, potentially showing the LVMPT's ability to measure a different, more functional, vision.

The LVMPT also had high correlation when compared to the Humphrey Visual Field test, signifying it could potentially be a clinically useful tool to measure a patient's visual field. Combining the correlation of the logMAR chart and Humphrey Visual Field test suggests the LVMPT can be a useful tool to measure both a patient's visual acuity and visual field with good accuracy.

A major appeal to the LVMPT is how simple it is to operate due to its automation and ease of use. There were no technical difficulties reported by the proctor, and we anticipate there being few, if any, in future use.

A limitation of our study was the small sample size of patients, as well as the single date of evaluation. Another limitation was the single group of subjects representing people with ultra-low vision. While they all were legally blind, there is greater variability amongst the population of people with ultra-low vision from conditions such as retinitis pigmentosa than was represented in our study, so having more cohorts of patients with poor vision would have been more helpful to answer our hypothesis. Another weakness is though the study showed good correlation to visual acuity and visual field tests, there wasn't a method associated with functional vision that we compared it to, thus limiting our study's conclusions.

Future Direction:

While the results of the study were promising because the LVMPT showed good correlation with more established tests, further research needs to be done to evaluate its effectiveness in measuring functional vision in ultra-low vision patients. Additional studies with a larger sample size, more cohorts of patients with poor vision, and comparisons to functional vision assessments could provide more insight into the effectiveness this evaluation tool can have. Comparing the LVMPT to a patient survey that assesses their visual abilities in their day-to-day lives would also be useful.

Conclusions:

The LVMPT showed close correlation to established visual ability tests which satisfied a primary aim in the study. Since the LVMPT requires real-life skills to evaluate a person's vision, it represents a new evaluation tool for clinicians and researchers to use for patients with low vision.

Compliance:

The LVMPT project is an observational study using human subjects. As such, Nanoscope Therapeutics obtained IRB approval for the project before any testing of the apparatus began. Patient data was de-identified and kept on secure servers.

All technology and research used in this study is the property of Nanoscope Technologies.

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