# Utilizing Virtual Reality Guided Multi-Luminance Orientation and Mobility Testing for Assessment of Visual Function

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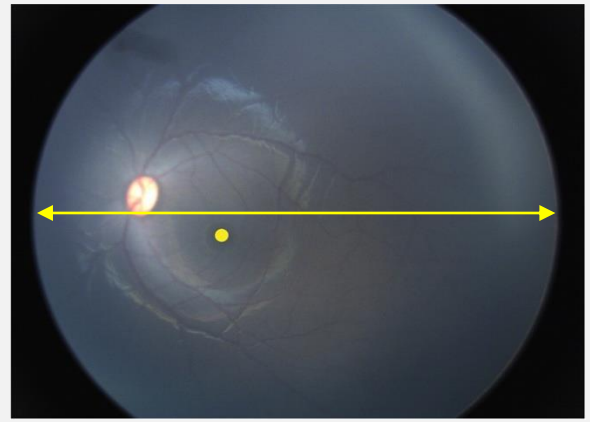
Braydon,
*RDH12* patient

# Functional Vision is the Patient's Use of Vision to Perceive Their Environment

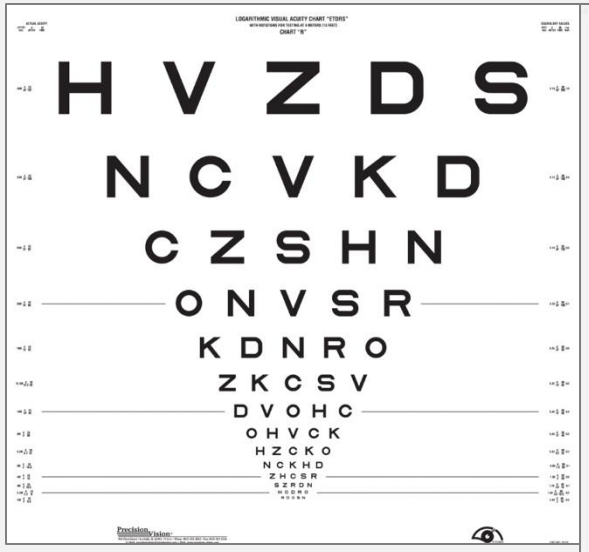
## An unmet need exists for a functional vision test that:

- Screens vision in a variety of retinal disease states (e.g., inherited retinal degeneration, macular degeneration)
- Accommodates various ages and disease stages
- Evaluates function of the entire retina
- Is easy to deploy
- Is sensitive, accurate, reproducible, and clinically meaningful
- Provides rapid and objective readouts
- Can document clinical meaningfulness of an intervention

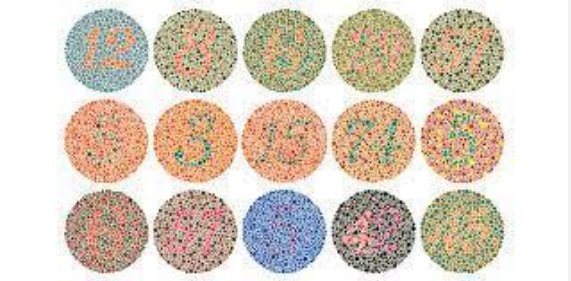
The total area of the retina is 2,500 times larger than the area of the fovea

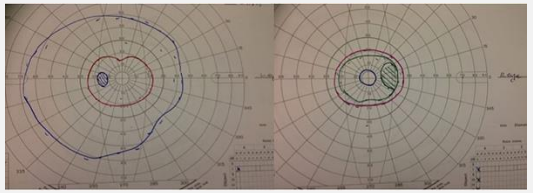


# Traditional Assessments of Vision are Not Relevant Outcome Measures for Many Patients with Advanced Vision Loss





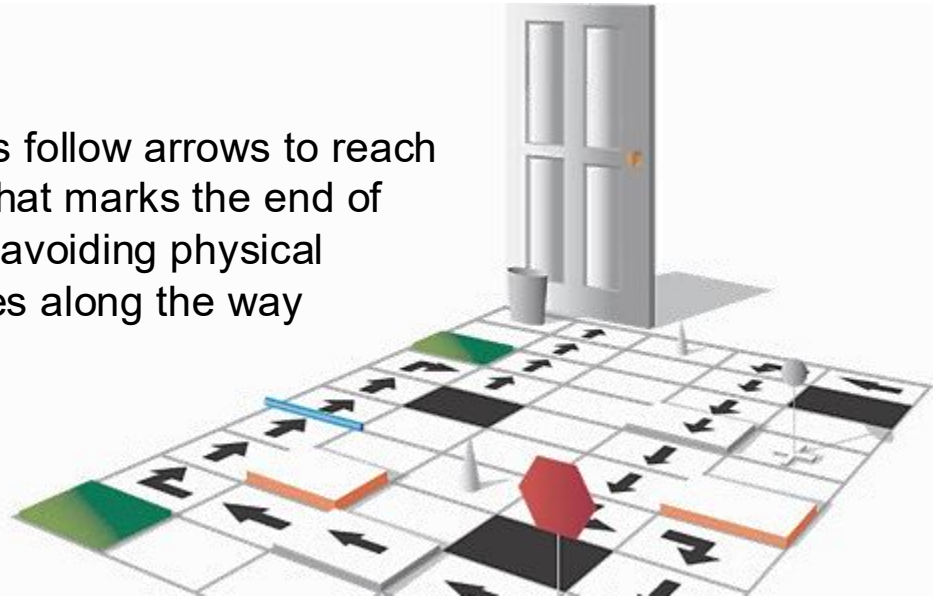


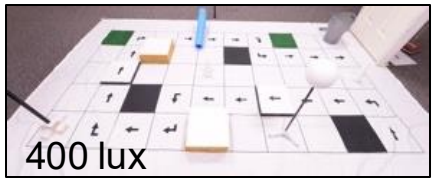
# Development of the Multi-Luminance Mobility Test® (MLMT ®) for the Luxturna® Clinical Trial was Groundbreaking

## MLMT physical course detects changes in functional vision across a range of light levels

Subjects follow arrows to reach a door that marks the end of course, avoiding physical obstacles along the way







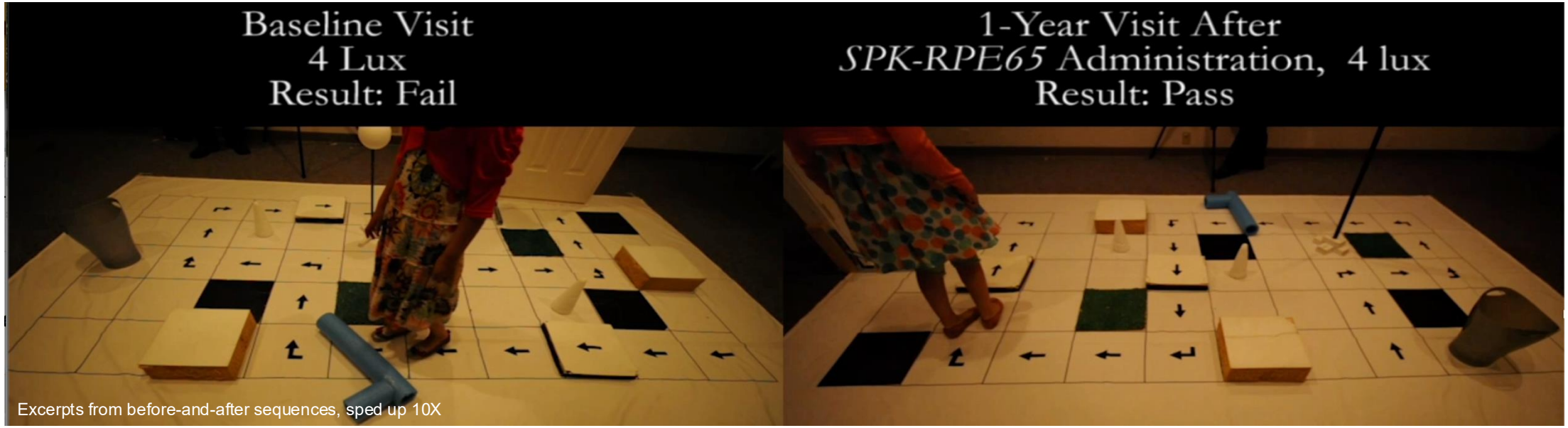

**Rationale for MLMT in the Luxturna Clinical Trial**

Other FDA-validated endpoints were not effective for measuring vision changes in patients with mutations in the *RPE65* gene

Speed and accuracy of navigation are evaluated under different levels of light

MLMT® and Multi-Luminance Mobility Test® are registered trademarks of Spark Therapeutics, Inc.
*MLMT physical course was utilized in the FDA registrational studies for Luxturna.
Luxturna® is a registered trademark of Spark Therapeutics, Inc.
FDA, Food and Drug Administration; MLMT, Multi-luminance mobility test.
Chung DC, et al. Clin Exp Ophthalmol 2018; 46(3):247-259.

# MLMT is Effective, but has Several Limitations



Excerpts from before-and-after sequences, sped up 10X

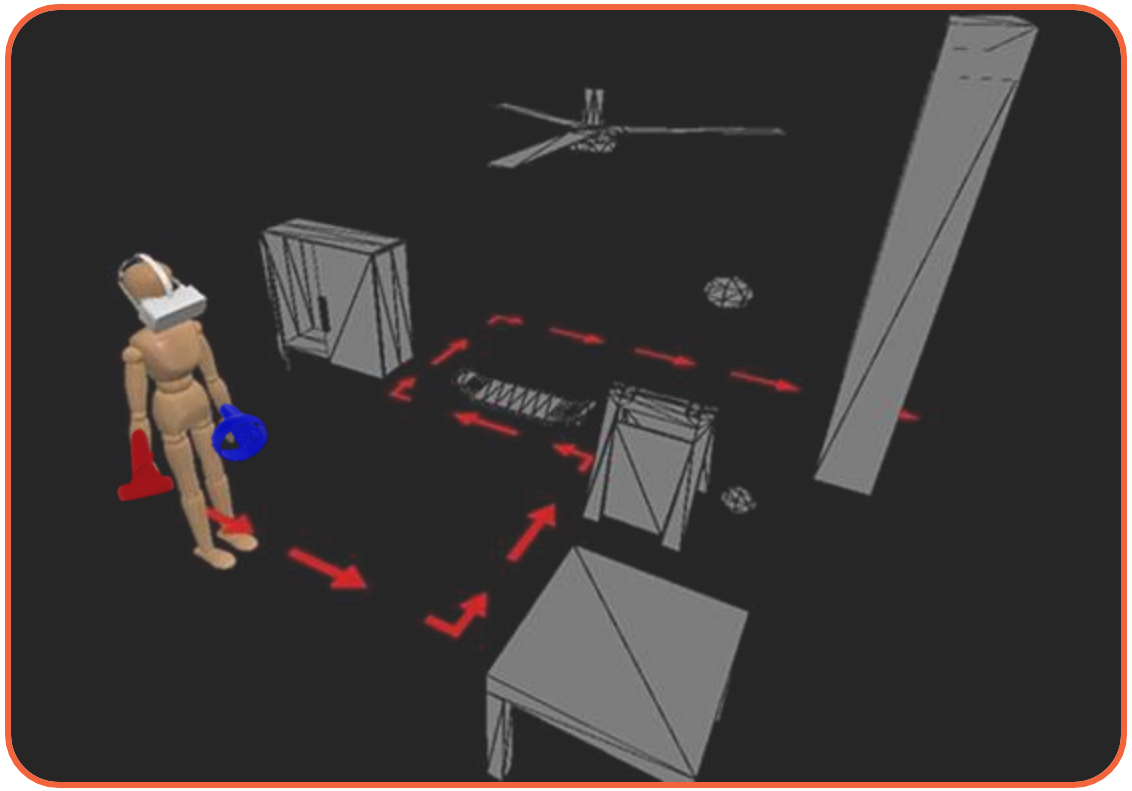
## Drawbacks of MLMT

- Tripping hazards for patient
- Requires a large designated space
- Time-consuming to set-up and reconfigure
- Difficult to ensure uniform illumination
- Limited number of tests per session
- Potential for echolocation
- Subjects with good visual acuity do well
- Requires a reading center (potential for bias)
- Long wait time for analysis
- Risk of confidentiality breech (videotaped date)


MLMT, Multi-luminance mobility test.

# Functional Vision Assessment with a Multi-Luminance Orientation and Mobility Test Overcomes the Limitations of Physical Settings

- MLoMT utilizes a readily available VR headset with body trackers to navigate a virtual course
- Household objects are presented at increasing illumination while the subject follows a path of red arrows
- Subject identifies and “touches” obstacles while following the path
- Establishes a threshold of functional vision that may be used to assess impact of disease and treatments
- Enormous amount of data automatically collected
- Relates well with clinical readouts (visual acuity, visual fields, and visual sensitivity)



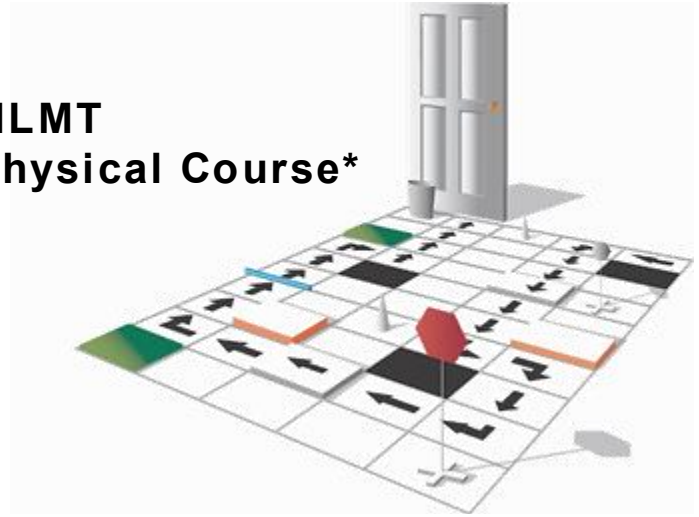
MLoMT, multi-luminance orientation and mobility test; VR, virtual reality.

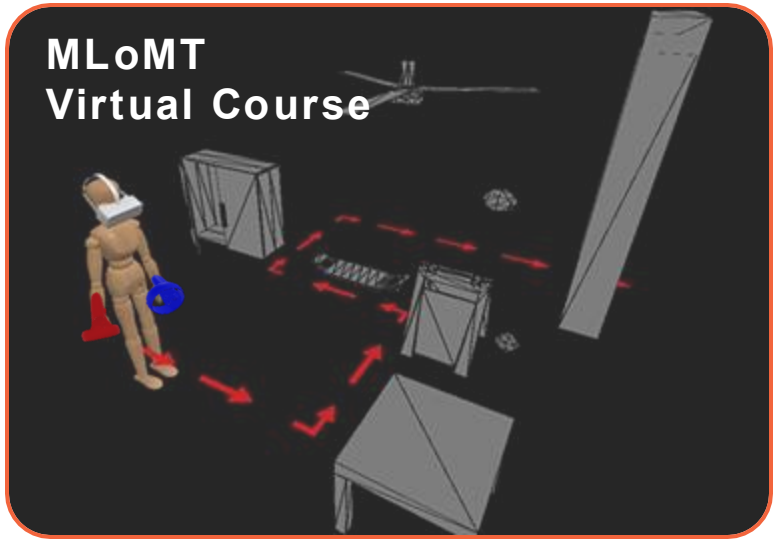


Bennett J, et al. *Transl Vis Sci Technol.* 2023;12:28.

# MLoMT Builds Upon the Success of MLMT

- Endlessly-randomizable: can conduct numerous tests over a broader range of lighting levels and in a quicker timeframe
- Ability to duplicate test across sites
- Minimal equipment and room requirements
- No physical obstacles that could cause harm in a collision
- Ability to test one or both eyes
- Automated capture of quantitative parameters (no requirement of a reading center)



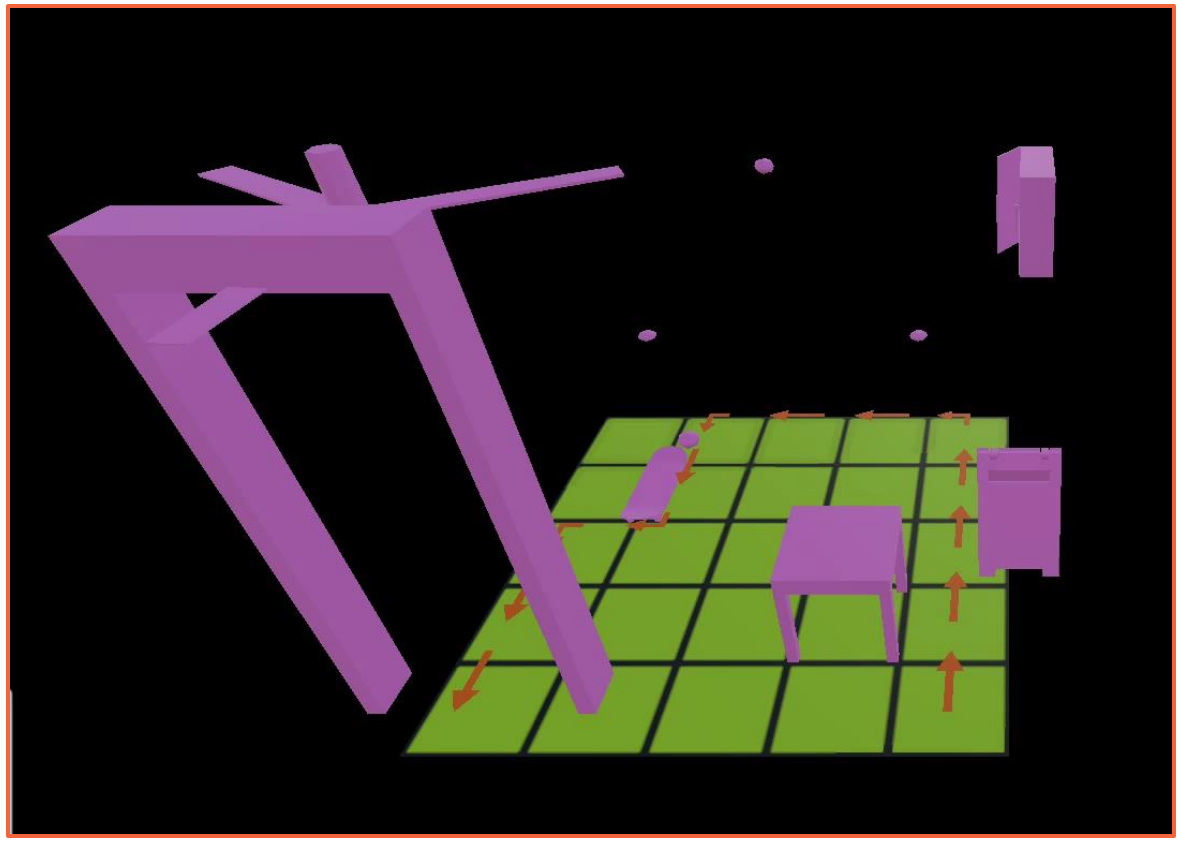

FDA, Food and Drug Administration; MLoMT, Multi-luminance orientation and Mobility Test; MLMT, Multi-Luminance Mobility Test.



**1.** Bennett J, et al. *Transl Vis Sci Technol.* 2023;12:28; **2.** Aleman et al. *Clin Ophthalmol.* 2021;15:939

# Virtual Reality Test Design of MLoMT

## No mechano-sensory feedback and no possibility for the subject to echo-locate an object

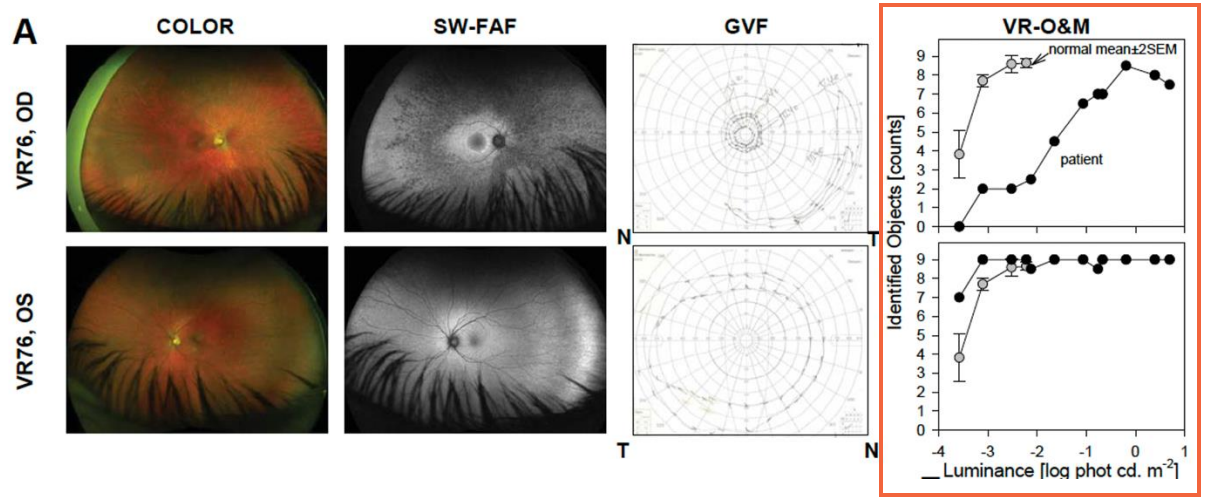


- Ability to follow a path of red arrows at increasing levels of luminance
- Ability to identify (“tag”) objects at differing heights/sizes (similar to those found in daily living) while following arrows on a path at increasing levels of luminance

# MLoMT Validation Studies are Underway

- Study completed in 49 subjects:
  - Distinguished normally-sighted subjects from those affected by LCA, RP, choroideremia, and cone-rod dystrophy
  - Distinguished level of functional vision, and results were correlated to visual acuity, visual fields, and full-field stimulus testing
- **FDA deemed MLoMT a "nonsignificant risk" and approved its use in clinical studies in subjects 8 years and older**

VR can distinguish the performance from each eye of a patient with uniocular RP (interocular differences)




FDA, Food and Drug Administration; GVF, Goldmann visual field; LCA, Leber congenital amaurosis; MLoMT, multi-luminance orientation and mobility test; SW-FAF, short-wavelength fundus autofluorescence; RP, retinitis pigmentosa; VR, virtual reality.

Bennett J, et al. *Transl Vis Sci Technol.* 2023;12:28.

# MLoMT is Being Utilized to Assess Functional Vision in an Ongoing Phase 1/2 Study of OPGx-LCA5

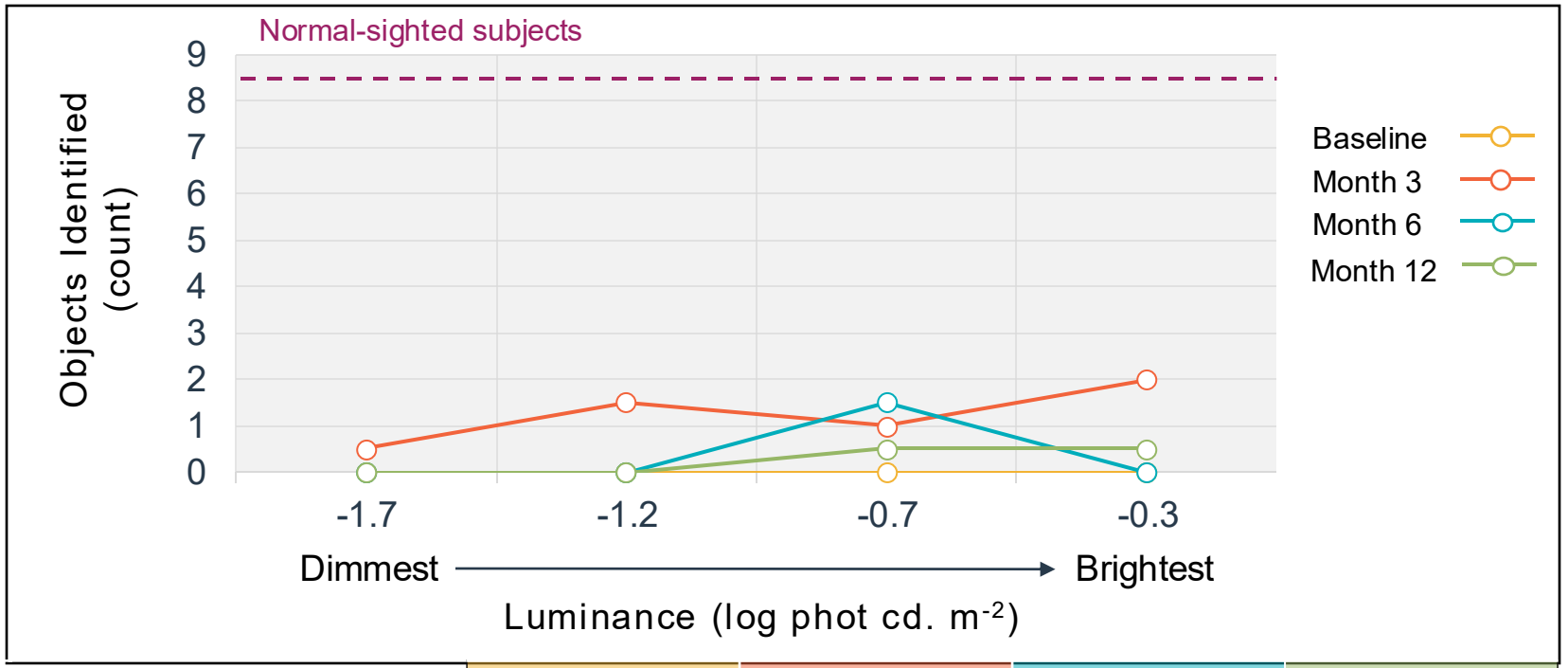
## OPGx-LCA5

- Designed to address mutations in the LCA5 gene, which encodes for the lebercilin protein
- Clinically derisked AAV8 vector delivers a functional *LCA5* gene directly to photoreceptor cells
- Same promoter technology as Luxturna
- Validated surgical delivery method via subretinal injection

- Open-label, non-randomized, single ascending dose escalation study of a subretinal injection of OPGx-LCA5 in participants with *LCA5*-IRD
  - LCA5 is an early-onset, severe hereditary retinal degeneration
- MLoMT is an exploratory efficacy endpoint
  - Subjects evaluated at baseline, 1-month, 3-months, 6-months, 1-Year, 1.5-Years, 2-Years, and 3-Years
- **In Cohort 1, improvement in MLoMT was observed in all three adult patients at 3, 6, and 12 months and in the first pediatric patient at 1-month**


IRD, inherited retinal disease; MLoMT, multi-luminance orientation and mobility test.

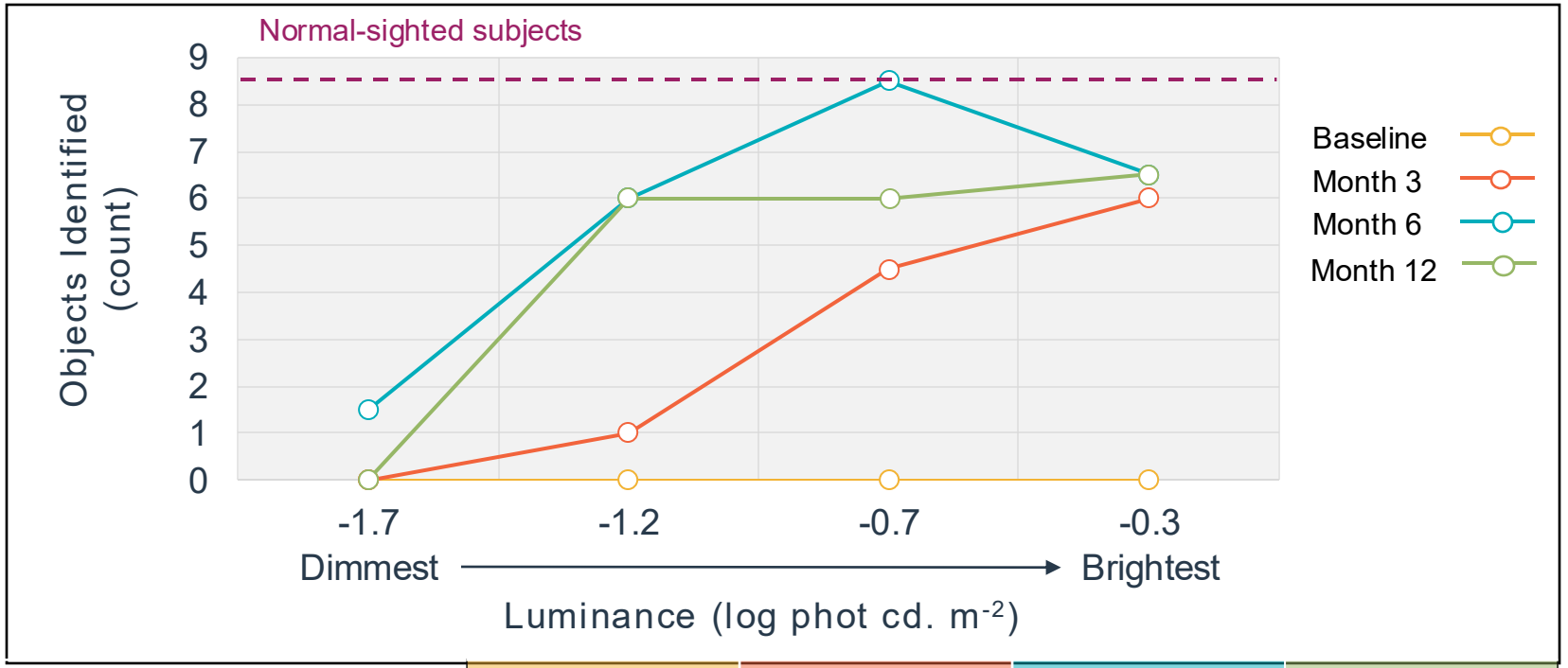
# MLoMT: Study Eye of Subject 01-03
## 26-Year-Old Male




| Luminance | BL | Month 3 | Month 6 | Month 12 |
|---|---|---|---|---|
| -1.7 (dimmest) | 0 | 0.5 | 0 | 0 |
| -1.2 | 0 | 1.5 | 0 | 0 |
| -0.7 | 0 | 1 | 1.5 | 0.5 |
| -0.3 (brightest) | 0 | 2 | 0 | 0.5 |
| | Count of Objects Identified (Max=9) | | | |


BL, baseline; MLoMT, multi-luminance orientation and mobility test.
Data on file.

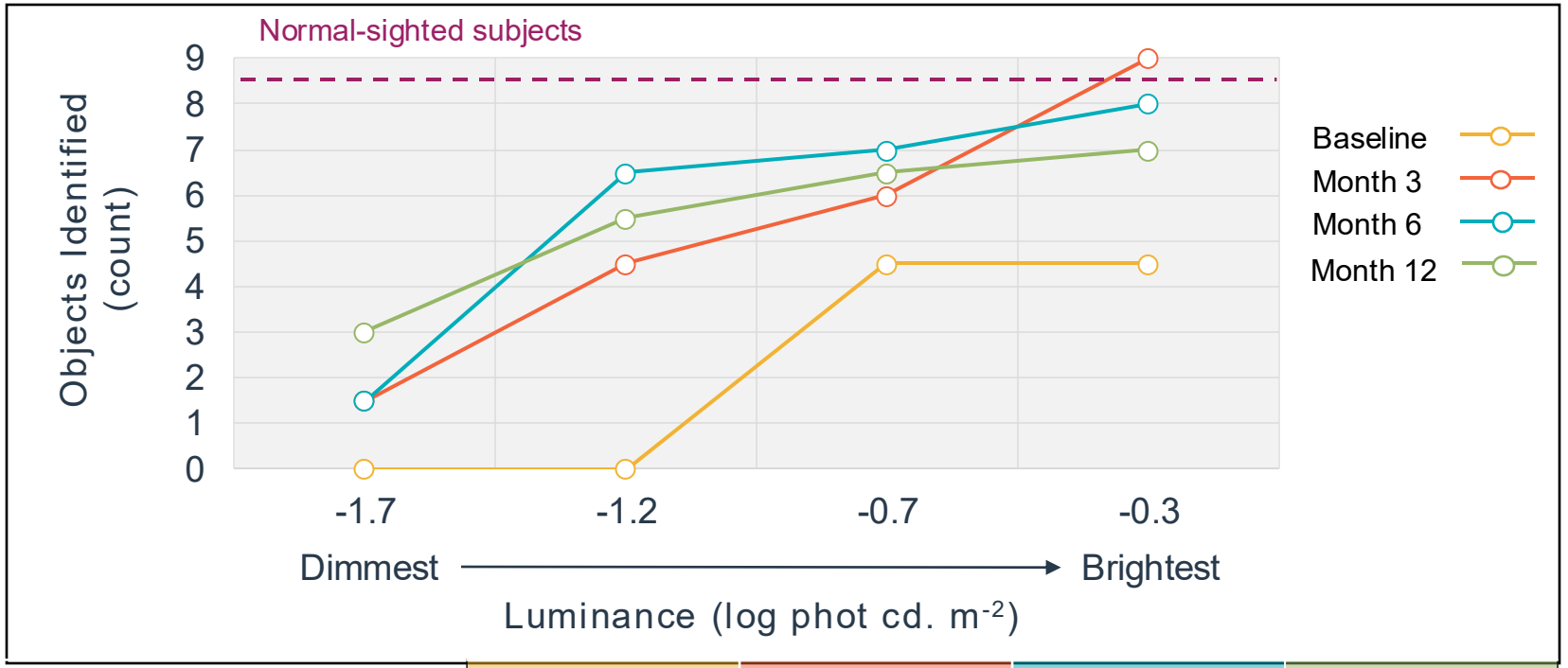
# MLoMT: Study Eye of Subject 01-01
## 34-Year-Old Female




| Luminance | BL | Month 3 | Month 6 | Month 12 |
|---|---|---|---|---|
| -1.7 (dimmest) | 0 | 0 | 1.5 | 0 |
| -1.2 | 0 | 1 | 6 | 6 |
| -0.7 | 0 | 4.5 | 8.5 | 6 |
| -0.3 (brightest) | 0 | 6 | 6.5 | 6.5 |
| | Count of Objects Identified (Max=9) | | | |


BL, baseline; MLoMT, multi-luminance orientation and mobility test.
Data on file.

# MLoMT: Study Eye of Subject 01-04
## 19-Year-Old Female



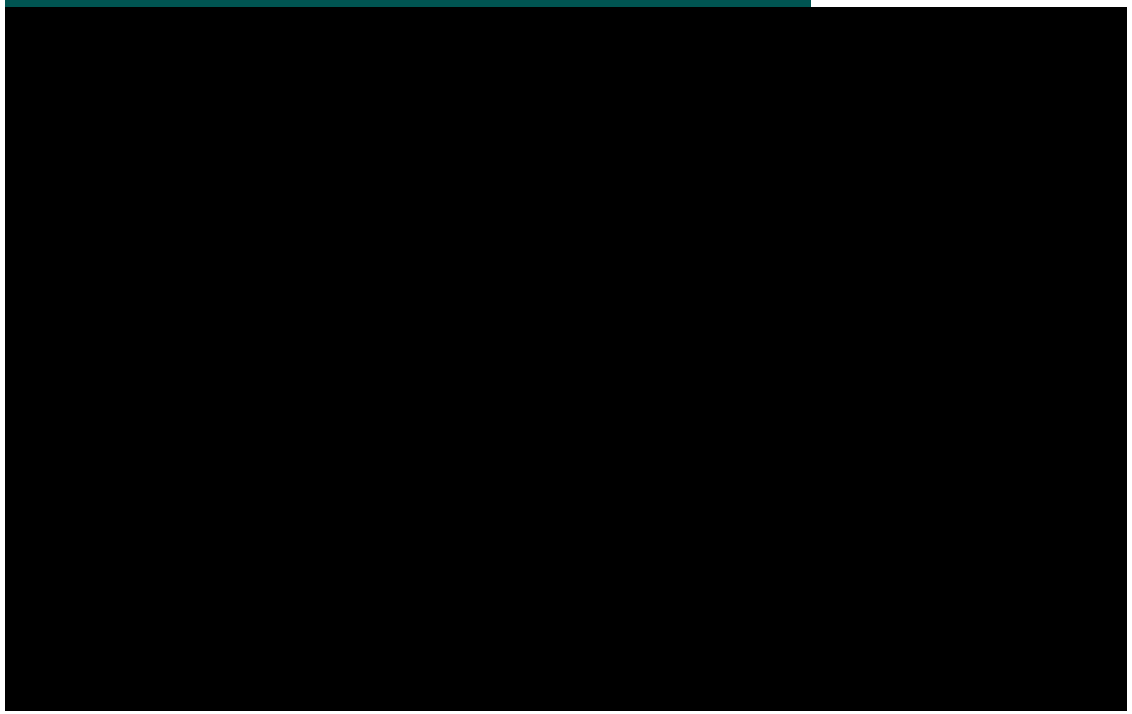

| Luminance | BL | Month 3 | Month 6 | Month 12 |
|---|---|---|---|---|
| -1.7 (dimmest) | 0 | 1.5 | 1.5 | 3 |
| -1.2 | 0 | 4.5 | 6.5 | 5.5 |
| -0.7 | 4.5 | 6 | 7 | 6.5 |
| -0.3 (brightest) | 4.5 | 9 | 8 | 7 |
| | Count of Objects Identified (Max=9) | | | |


BL, baseline; MLoMT, multi-luminance orientation and mobility test.
Data on file.

# MLoMT: Study Eye in Subject 01-01

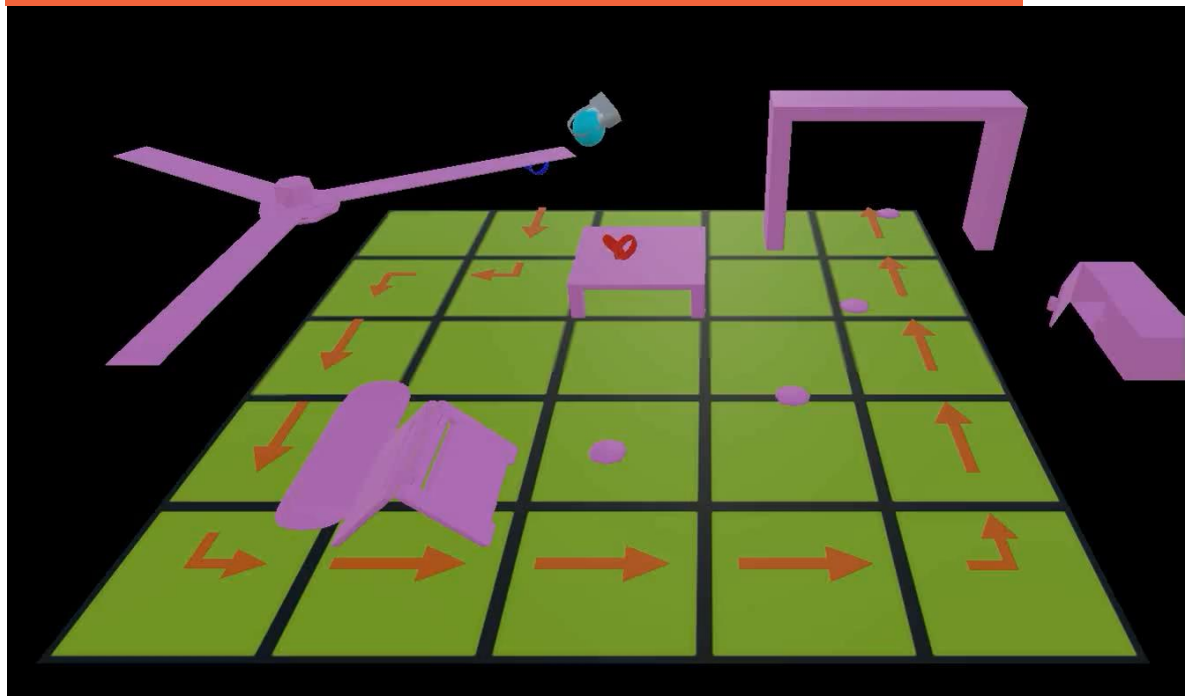
## Object Luminance 0.7 (log phot cd. m-2)

**Baseline**



Subject ended the test prematurely by raising both hands after ~45 seconds; Subject could not follow the path, identify any objects, or exit the door

**1-month post OPGx-LCA5 treatment**



Subject follows the path, identifies nearly all the objects, and finds the exit door

Baseline Video: Colorization not possible.
1-month video: Objects are colorized for presentation purposes.
MLoMT, multi-luminance orientation and mobility test.

# MLoMT is a Validated, VR-Based Functional Vision Test Being Used in a Phase 1/2 Clinical Trial of OPGx-LCA5

- MLoMT provides several key advantages over traditional physical mobility courses for vision evaluation in clinical trials, especially for IRDs including:
  - Precision, flexibility, safety, consistent and repeatable testing conditions, and automated data collection
- In an ongoing Phase 1/2 clinical trial of OPGx-LCA5, three treated adult subjects identified more objects on the MLoMT through 12 months compared to baseline
- The study is currently enrolling pediatric subjects; The first treated pediatric subject identified more objects on the MLoMT at 1 month compared to baseline



IRD, inherited retinal disease; MLoMT, multi-luminance orientation and mobility test.
Data on file.