Wills Eye Hospital

Believing is Seeing

840 Walnut Street
Philadelphia, PA 19107
215-928-3000
1-877-AT-WILLS
www.willseye.org

visuALL Validation Study 1.2

Principal Investigator: M. Reza Razeghinejad, MD

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IRB# 18-768E

Study Protocol
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Protocol Number	001
Principal Investigator (PI)	M. Reza Razeghinejad MD
PI email	mrazeghi@willseye.org
Coordinating Center	Wills Eye Hospital; 840 Walnut Street, Philadelphia, PA 19107
Protocol Version	1.2
Date	October 1, 2018; rev. November 6, 2018
Protocol Authors	L. Jay Katz, MD Dr. Alberto Gonzalez Garcia
Liaison/Olleyes	Dr. Alberto Gonzalez Garcia gonzalezao@olleyes.com
Sponsor	Olleyes, Inc. 11 Hillcrest Dr, Randolph NJ 07869 973-567-8068

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Study Objective	To determine age-adjusted reference values of the visuALL Field Analyzer (vFA), to assess the repeatability for each parameter and correlate them with a Standard Automatic Perimetry (SAP) parameters.
Study Rationale	Standard Automatic Perimetry (SAP) is the gold standard test for the evaluation of different diseases of the visual pathway like glaucoma. Its main goal is to measure the differential light sensitivity at several locations of the central field of vision. Nevertheless, the accuracy of the current device is limited by several factors like the inherent inconsistency of the psychophysical test, stressful examinations and frequency of testing among others.[1,2] Several devices have been developed since the advent of the Octopus Perimeter[3-5] and the Humphrey Field Analyzer (HFA),[6,7] in an effort to improve the early detection glaucoma.[8,9] Examples of these visual field test variants are implemented using laptops and iPads and virtual reality headsets.[10-13] These modalities bring portability but the lack of fixation methods, environmental control and hardware standardization may limit its wide usage. The main goal of this study is to evaluate the repeatability of a novel psychophysical platform that takes advantage of a Head Mounted Device (HMD) with eye tracking capabilities. Other objectives of this study include the development of an initial reference database and the evaluation of its correlation with HFA parameters.

Study Design	visuALL-1 is a cross-sectional observational study. The primary endpoint of the study will be at end of the recruitment phase.
Participants	A group of healthy subjects and patients with glaucoma; between 21 and 80 years old will be invited to participate in the study. A total of 50 healthy eyes and an additional 50 eyes with glaucoma will be recruited for this study. All subjects will undergo a complete ophthalmologic examination at the glaucoma department of Wills Eye Hospital. Each examination will include refraction, slit lamp biomicroscopy of the anterior segment, IOP measurement, BCVA, visual field and visuALL Field Analyzer (vFA) testing, gonioscopy and dilated stereoscopic fundus examination of the retina and optic nerve head. Data about family history of glaucoma will also be recorded.

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<table>
<tr><td></td><td>
Study Groups:
1. Control group: Healthy eyes (n=50)
2. Glaucoma group: Chronic Open Angle Glaucoma (COAG) eyes (n=50)
- 30 eyes with mild COAG
- 20 eyes with moderate COAG
The recruitment process of healthy subjects will include a stratification based on age as indicated in the table below.
<table>
<tr><th>Age Group (years)</th><th>Eyes</th></tr>
<tr><td>30 - 39</td><td>10</td></tr>
<tr><td>40 - 49</td><td>10</td></tr>
<tr><td>50 - 59</td><td>10</td></tr>
<tr><td>60 - 69</td><td>10</td></tr>
<tr><td>70 and more</td><td>10</td></tr>
</table>
Individuals of different races will be included but no single ethnic group will encompass more than 50%. 15% of gender differences will be allowed.
The clinical study plan will be reviewed and approved by Wills Eye Hospital Institutional Review Board (IRB).
</td></tr>
<tr><td>Healthy criteria</td><td>
• Normal appearing optic nerve and retina
• IOP < 19 mmHg.
• Normal SAP results in both eyes. (See SAP criteria)
</td></tr>
<tr><td>COAG criteria</td><td>
• Glaucomatous appearing optic nerve and/or retina (i.e. increased cup to disc area ratio, rim thinning or RNFL defects indicative of glaucoma)
• Abnormal SAP results in the study eye. (See SAP criteria)
</td></tr>
<tr><td>Exclusion criteria</td><td>
1. A spherical refraction outside ± 3.0 D and cylinder correction outside 2.0 D.
2. Unreliable SAP (false positives, fixation losses and false negatives >25% and/or observable testing artifacts).
3. Unreliable vFA (>25% false positive, excessive fixation losses)
4. SAP abnormality with a pattern of loss which is consistent with a neurologic and/or other ocular diseases than glaucoma.
</td></tr>
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	5. Intraocular surgery in the study eye (except non-complicated cataract or refractive surgery performed more than 6 months before enrollment and without posterior capsule opacification). 6. History of systemic condition known to affect visual function. 7. History of medication known to affect visual function.
Instrumentation	1. Refraction (autorefractor) 2. Tonometry (Goldmann) 3. SAP Humphrey Field Analyzer (HFA) 24-2, Swedish Interactive Threshold Algorithm (SITA) Standard Strategy (Carl Zeiss Meditec, Inc. Dublin, CA) (single session). 4. visuALL *Pro* (Olleyes, Inc. Randolph, NJ) (single session).
Within Normal Limits SAP criteria	Pattern Standard Deviation significant within 95% normal limits, Glaucoma Hemifield test within normal limits, and no other pattern of loss which is consistent with a neurologic and/or ocular disease.
vFA reliability criteria	False positives, fixation losses and false negatives >25% and/or observable testing artifacts
vFA Description	vFA *Pro* will be used for this validation study. The visuALL system is composed of two main parts - the hardware and the software. The hardware includes three main components: A Head Mounted Device (HMD) also known as Virtual Reality (VR) headset, a Laptop and a Bluetooth connected handpiece. The HMD is powered by FOVE (Fove, Inc. Tokyo, Japan). This HMD weight 520g and includes a Wide Quad High Definition Organic Light Emitted Diode (WQHD OLED) display with a resolution of 2560x1440 pixels with a refresh rate pf 70Hz. The display is divided in two halves (one for each eye) with a resultant resolution of 1280x1440 pixels on each half. The display measures 125.4 x 70.56 mm and it is placed at a distance to subtend a field of view (FOV) up to 100 degrees. The HMD includes several tracking systems, inertial measurement units (IMUs) consisting of gyroscopes and accelerometers, in addition to infrared-based (IR) position tracking with two arrays of 6 IR sensors. The HMD uses 2 eye-tracking system including infrared cameras with a frame rate of 120fps. The eye-tracking system has a resolution of less than 1 degree. The main PC components are a graphic processing units (GPU) NVIDIA GeForce GTX 970, a central processing unit (CPU) Intel Core i7 7th Gen 7820HK (2.90 GHz), random access memory (RAM) of 32GB, a hard disk

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<table>
<tr><td></td><td>drive (HDD) of 1 TB and 3 main interfaces: one High Definition Media Interface (HDMI), one Universal Serial Bus (USB) 3.0 and two USB 2.0. The PC runs and Operating System (OS) WINDOWS 10 64-bit. The PC networking protocols are Killer Ethernet E2400 10/100/1000 Gigabit Ethernet LAN (RJ-45 port), Wi-Fi Dual-Band (WLAN) 2.4GHz and 5GHz and Bluetooth 4.1
The visuALL software includes three main testing protocols.
<table>
<tr><td>Parameters</td><td>SupraT</td><td>NormalT</td><td>FlickerT</td></tr>
<tr><td>Range (degrees)</td><td>24</td><td>24</td><td>24</td></tr>
<tr><td>Background Illumination (cd/m^2)</td><td>10</td><td>10</td><td>50</td></tr>
<tr><td>Stimulus Locations</td><td>54</td><td>54</td><td>54</td></tr>
<tr><td>Stimulus Size (degrees)</td><td>0.43</td><td>0.43</td><td>5</td></tr>
<tr><td>Stimulus Duration (ms)</td><td>150</td><td>150</td><td>Up to 200</td></tr>
<tr><td>Stimulus Intensity (cd s/m^2)</td><td>100</td><td>Variable</td><td>50</td></tr>
<tr><td>Inter-stimulus Time (ms)</td><td>Random</td><td>Random</td><td>Random</td></tr>
<tr><td>Fixation Control</td><td colspan="3">Eye tracking with dynamic stimulation-grid adjustment within a threshold area, otherwise paused. Blinking control</td></tr>
</table>
</td></tr>
<tr><td>vFA Outcome Measurements</td><td>• Retinal sensitivity at each location
• Mean retinal sensitivity at each quadrant
• Mean retinal sensitivity at each hemifield
• Mean retinal sensitivity</td></tr>
<tr><td>Analyses</td><td>1. Descriptive statistics and demographics
2. References values
3. Reliability indexes for HFA and vFA variables
4. Agreement between HFA and vFA variables</td></tr>
<tr><td>References</td><td>1. Heijl A, Lindgren A, Lindgren G. Test-retest variability in glaucomatous visual fields. Am J Ophthalmol. 1989;108:130-135.
2. Russell RA, Crabb DP, Malik R, Garway-Heath DF. The relationship between variability and sensitivity in large-scale longitudinal visual field data. Invest Ophthalmol Vis Sci. 2012;53:5985-5990.
3. Spahr J, Fankhauser F, Bebié H. Advances in the automation of perimetry. Klin Monbl Augenheilkd. 1976;168:84-6.
4. Spahr J, Fankhauser F, Jenni A, Bebie H. Practical experiences with the Octopus automatic perimeter. Klin Monbl Augenheilkd. 1978;172:470-7.
5. Portney GL, Krohn MA. Automated perimetry: background, instruments and methods. Surv Ophthalmol. 1978;22:271-8.</td></tr>
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	6. Beck RW, Bergstrom TJ, Lichter PR. A clinical comparison of visual field testing with a new automated perimeter, the Humphrey Field Analyzer, and the Goldmann perimeter. Ophthalmology. 1985;92:77-82. 7. Brenton RS, Phelps CD. The normal visual field on the Humphrey field analyzer. Ophthalmologica. 1986;193:56-74. 8. Bosworth CF, Sample PA, Johnson CA, Weinreb RN. Cur- rent practice with standard automated perimetry. Semin Ophthalmol 2000;15:172–181. 9. Delgado MF, Nguyen NTA, Cox TA et al. Automated perimetry: a report by the American Academy of Ophthalmology. Ophthalmology 2002;12:2362–2374. 10. Wu Z, Guymer RH, Jung CJ, et al. Measurement of retinal sensitivity on tablet devices in agerelated macular degeneration. Trans Vis Sci Tech. 2015;4:13. 11. Tahir HJ, Murray IJ, Parry NRA, Aslam TM. Optimization and Assessment of Three Modern Touch Screen Tablet Computers for Clinical Vision Testing. PLoS ONE 2014;9: e95074. 12. Vingrys AJ, Healey JK, Liew S, et al. Validation of a tablet as a tangent perimeter. Trans Vis Sci Tech. 2016;5:3. 13. Prea SM, Yu Kong YXG, Mehta A, He M, Crowston JG, Gupta V, Martin KR, Vingrys AJ. Six-month Longitudinal Comparison of a Portable Tablet Perimeter With the Humphrey Field Analyzer. Am J Ophthalmol 2018;190:9–16.
Proposed Due Date for Analysis of Primary End Point Data:	February 2019
Planned Publications & Abstract Submissions:	The Study will plan to submit abstracts for 2019 ARVO. Subsequently two manuscripts will be written and submitted to Journal of Glaucoma and Ophthalmology.

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