Portable System to Monitor Astronaut Ocular Health and the Development of the VIIP Syndrome

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Abstract—**We propose to utilize a previously developed, deployed, and clinically tested comprehensive visual field test and diagnosis system to investigate the relationship between intracranial pressure (ICP) and intraocular pressure (IOP) elevations that occur during long-term space travel and visual field loss. Recent data describing this phenomenon, now called the Visual Impairment/Intracranial Pressure (VIIP) Syndrome raise concerns that it could impact the visual health of astronauts both during long-duration space travel, potentially causing an impact to the mission, and after flight, causing significant morbidity. A non-invasive, easily-deployable, user-friendly visual field test system can provide early detection of changes in vision in flight as well as a screening and research tool to help develop countermeasures to prevent/alleviate this problem and to identify at-risk astronauts.**

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1. INTRODUCTION

We propose to utilize a previously developed, deployed, and clinically tested *comprehensive visual field test and diagnosis system* [1-3] to study and reveal the relationship between *intracranial pressure (ICP)* and *intraocular pressure (IOP)* elevations that occur during long-term space travel and associated visual field loss. Recent data describing this phenomenon, now called the *Visual Impairment/Intracranial Pressure (VIIP) Syndrome* raise concerns that it could impact the visual health of astronauts both during long-duration space travel, potentially causing an impact to the mission, and after flight, causing significant morbidity. Perturbations in the difference between IOP and ICP (i.e., translaminar pressure) affect the optic nerve, and the consequence of changes in either of these pressures can be dropout of signals carried from the retina to the visual system. This can result in the loss of the high resolution central visual field (i.e., the macular region).

We have developed a Web-based, integrated, and comprehensive visual field test & diagnosis system to assess the visual performance of astronauts and crewmembers [2-5]. At the core of the system is the 3D Computer-automated Threshold Amsler Grid (3D-CTAG) test [1]. In multiple clinical studies 3D-CTAG has proven to be innovative and successful for fast (<5 minutes per eye), easy (intuitive use of finger), accurate (<1 degree spatial resolution), non-invasive, and comprehensive visual field testing. Conditions, such as glaucoma [6], ocular hypertension [7], age-related macular degeneration (AMD) with distinction between wet and dry AMD [8, 9], macular edema [10], ethambutol toxicity [11], anterior ischemic optic neuropathy and optic neuritis [12] have been successfully detected. 3D-CTAG allows for an unprecedented characterization of the structure of visual field defects in three dimensions [1, 4]. This non-invasive, easily-deployable, user-friendly visual field test system can provide early detection of changes in vision in flight as well as act as a screening and research tool to help develop countermeasures to prevent/alleviate VIIP and to identify at-risk astronauts [13, 14].

A beneficial spin-off of this effort is the potential development and deployment of a portable, wireless visual field test system with diagnostic capability onboard the International Space Station (ISS). This system could enhance the diagnostic ophthalmological capabilities during future long-duration human space travel. The comprehensive visual field test and diagnosis system has application in routine astronaut assessment (Clinical Status Exam), pre-flight, in-flight, and post-flight monitoring, interplanetary operations, and astronaut selection.

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2. NASA RELEVANCE

Human-machine interfaces depend on the visual system for proper input and feedback during all phases of spaceflight. Degradation in vision can result in loss of mission or loss of life; thus, it is critical to be able to understand the adverse effects of the spaceflight environment on the ocular system. In order to be able to determine the onset and progression of ocular compromise, a robust device is needed to monitor the health of the visual system. Such a device needs to be accurate, give reproducible results, have high sensitivity, and have minimal impact on crew time and payload stowage.

Because of the importance of the ocular system to mission success, astronauts are carefully screened prior to selection. Despite being free of significant ocular pathology at the time of selection, astronauts are subject to the development of visual problems with normal aging, such as the formation of cataracts, presbyopia, retinal drusen and floaters. In addition, the spaceflight environment with microgravity or low gravity conditions, increased radiation exposure, toxic contamination, nutritional changes, and changes in oxygen/carbon dioxide levels can cause accelerated damage to the visual system.

The "Longitudinal Study of Astronaut Health" (LSAH, [15]) revealed the occurrence of the following ocular problems: cataracts, ocular hypertensives, glaucoma suspects, retinal detachments, retinal drusen, retinal degenerations, and hypertensive retinopathy. The development of ocular/retinal disease is well-described in the astronaut corps. Post-flight interviews after shuttle and ISS missions indicate that 34% of astronauts have noted some sort of visual change during their missions. However, this probably is an underestimate of the actual number because of under-reporting bias and subclinical changes that were not noticed. Changes, such as decreased visual acuity, increased farsightedness (i.e., hyperopic shift), and even visual field loss have been reported in up to 50% of long-duration mission astronauts (LSAH, [15]). Such changes, if not accompanied by appropriate intervention, can have important impacts on crew safety, such as has been seen when crews have been unable to read checklists on reentry.

The putative cause of VIIP has been derangements in the relationship between IOP and ICP, most likely due to cephalad fluid shifts during spaceflight and during reduced gravity conditions, although other mechanisms have been proposed. Although initial increases in IOP that occur shortly after reaching orbit appear to ameliorate after two days in reduced gravity conditions, elevation of pressures appear to persist throughout the mission and have been noted well after landing. Thus far, at least fifteen US astronauts who have flown on the International Space Station (ISS) have shown findings that are associated with this syndrome, including hyperopic shift, cotton wool spots, globe flattening, and optic disc edema or even frank papilledema [16, 17, 13]. While some of these changes have been seen on previous, short-duration missions and are relatively benign, some findings could have an important impact on the mission and on long-term astronaut visual health. It is likely that this phenomenon is synergistic with other visual hazards that astronauts encounter during extended missions. These include ultraviolet light exposure, thermal damage to the retina from solar viewing, radiation throughout the electromagnetic spectrum, hypoxia, increased carbon dioxide levels, and exposure to toxins or irritants due to release of toxic materials during flight [18]. Each of these hazards could be potentiated by pre-existing visual problems that an astronaut might have before flight.

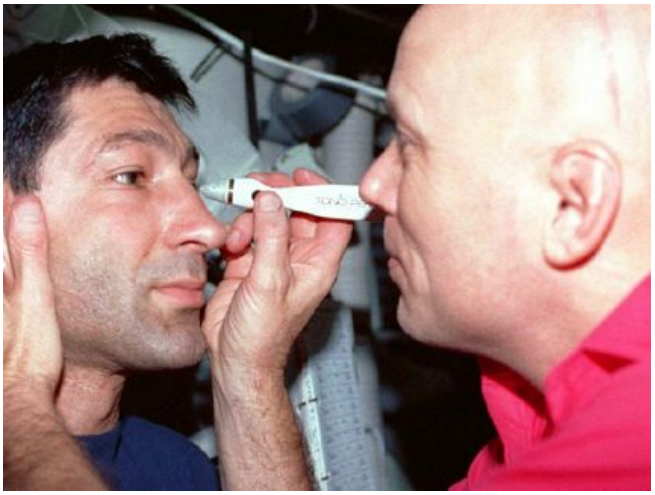

Figure 1. Intraocular pressure measurement with a Tonopen device aboard the Space Shuttle. [Image courtesy NASA]

These conditions pose an important risk to crew ocular health and underscore the importance of early detection and intervention. Current equipment carried onboard the ISS, and before then on the Space Shuttle, such as the "Tonopen Intraocular Pressure Device" (Fig. 1), can measure IOP but requires local anesthesia and is not able to detect functional changes in visual acuity or visual fields.

NASA's Human Research Program has multiple ongoing research projects to address one of their top health risk, which is space-related ICP elevation. The proposed 3D-CTAG approach is unique in exploring the relationship of ICP and IOP changes to visual pathology. Moreover, to date, no automated or semi-automated test of visual performance exists for on orbit human spaceflight. Therefore, there is an operational need for an easy-to-use, Internet-based or autonomous in-situ comprehensive visual field test and diagnosis system for (1) assessing visual fields, (2) characterizing and diagnosing visual field defects/ocular pathology, and (3) detecting the onset of eye conditions to implement timely countermeasures.

3. SPACE OPERATIONS

State-of-the-art perimetry devices are bulky (Fig. 2), thereby precluding application in a spaceflight setting. In contrast, 3D-CTAG requires only a touchscreen-equipped computer

(Fig. 3) or touchpad device (e.g., iPad [3], Fig. 4), which may already be in use for other purposes (i.e., no additional payload), and custom software [5].

Figure 2. Zeiss-Humphrey Visual Field Analyzer setup: oblique view (left) and patient perspective (right).

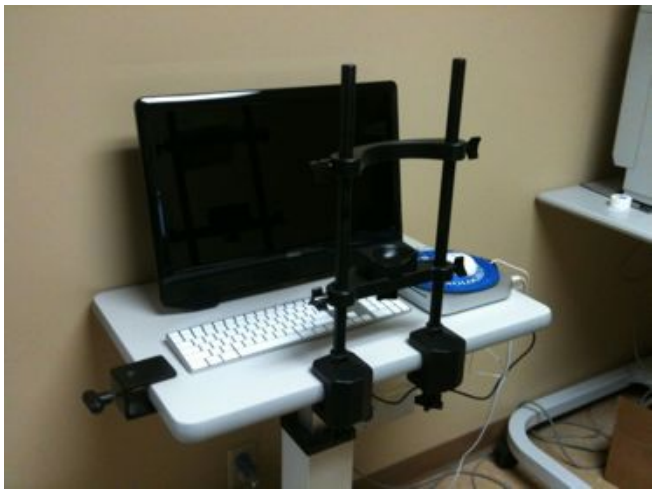

Figure 3. Examination station setup for 3D-CTAG consisting of an Apple Mac mini computer, a head-chin rest, and a touch-sensitive computer monitor.

Operationally, the impact of the 3D-CTAG examination is minimal [5]. The exam requires less than 5 minutes per eye. Setup, teardown, and stowage are projected to take only up to an additional 5 minutes, including turning on the touchscreen device (e.g., iPad) and launching the 3D-CTAG software.

For consistency of results, it is important that the head position relative to the screen remains fixed and that the crewmember remains stabilized during testing. An ideal location for the device would be a site where the level of ambient lighting can be maintained at a pre-determined reference for each test (e.g., the crew sleep station onboard the ISS), as contrast sensitivity can vary with the level of background light. Both lower extremity and torso stabilization are ideal as some reactive force may be encountered when the screen is touched in reduced gravity. The torso could be stabilized with a hand-hold for the hand that is not in use. While the device could be securely attached directly to the head in microgravity conditions, fixed mounting to a bulkhead or rack would minimize reactive forces and maximize stabilization.

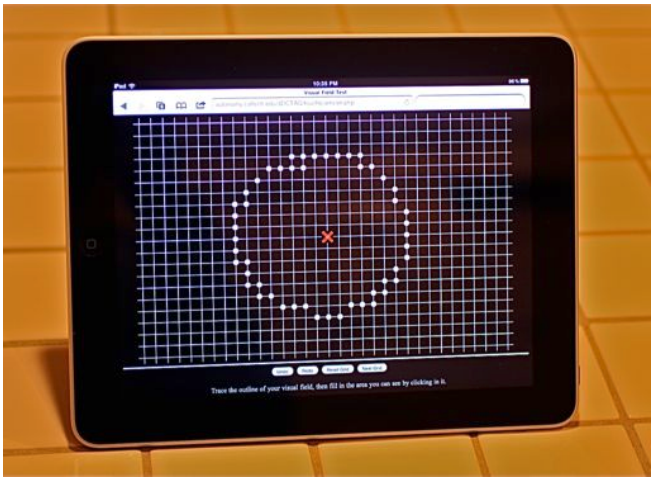

Figure 4. Visual field test and diagnosis system administered on an Apple iPad.

While the volume of the International Space Station can easily accommodate the small dimensional requirements of this experiment, spacecraft in transit to an interplanetary destination or to the ISS will be more volume-constrained. In these situations, temporary mounting to a convenient structure with adequate lower extremity and torso stabilization or a head-mounted device may be a more viable option. For example, the screen could be secured to a convenient spot on the spacecraft interior with Velcro. For reduced-gravity planetary applications, the Velcro could be supplemented by simple mechanical fasteners. Head mounting could be accomplished by a suitable brace that maintains a fixed distance between the screen and the viewer's eyes and is adequately secured to prevent slippage or undesired movements during the experiment. These principles will be similar in low-gravity environments such as Martian or lunar outposts, although stabilization may be more easily accomplished.

Depending on the urgency of diagnosing a condition affecting the visual performance of an astronaut/crewmember, and depending on the communication bandwidth and delay, the comprehensive visual field test and diagnosis system provides for two distinct modes of operation [5]:

- *True telemedicine*: 3D-CTAG examination data is sent back to Earth for evaluation and the resulting diagnosis is returned;

- *Autonomous in-situ*: 3D-CTAG examination data is analyzed by the integrated auto-characterization system, and visual field defects are objectively identified, characterized, and classified, resulting in a probabilistic diagnosis in the absence of expert input.

4. EARTH OPERATIONS

With one eye covered, the subject is positioned at a fixed distance in front of a touch-sensitive computer screen on a

head-chin rest (Fig. 3), and the finger traces the areas of an Amsler grid missing from his field of vision (Fig. 5). The Amsler grid [19, 20] represents a standard means of evaluating the central vision surrounding the fovea (~10 degrees radially from fixation). However, the 3D-CTAG presents Amsler grids at various degrees of contrast across a visual field area determined by the dimensions of the touch-screen by repeating the test at different grayscale levels, thereby enabling detection of even subtle visual field defects. 3D-CTAG records contrast sensitivity across the tested visual field. Contrast sensitivity is a functional measure of the performance of the visual system including retina, optic nerve, and visual cortex.

An integrated auto-characterization system analyzes 3D-CTAG visual field data and objectively identifies and characterizes the occurring visual field defects (i.e., scotomas) in accordance with the following numerical methods [3-5]: (1) *visual field data transforms* include area and volume of visual field loss, lost and preserved area grades, and slope distribution; and (2) *scotoma data transforms* include scotoma perimeter/scallopedness and scotoma center location. These data transforms enable the qualitative and quantitative analysis of temporal changes of a subject's visual field [5, 21].

5. Improvements for Earth Operations

Guide-screen/mask for 3D-CTAG

When testing patients with the 3D computer-automated threshold Amsler grid test the need for confining the patient's finger movement on the touch-sensitive computer screen/monitor (Fig. 5, left) to the testable area of the displayed Amsler grid becomes apparent.

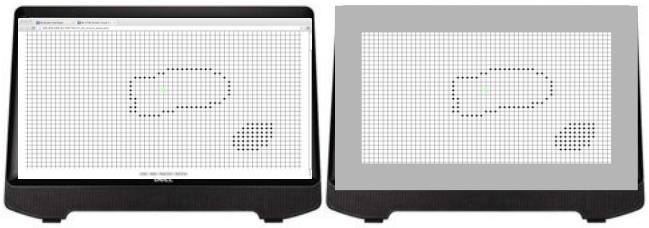

Figure 5. *Left:* Touchscreen without screen, mask, mat, safeguard, etc. mounted, displaying an Amsler grid. *Right:* Same touchscreen with a translucent or opaque screen, mask, mat, safeguard, etc. (here an opaque mask displayed in gray) mounted on top of the touchscreen to allow finger touch access to only a portion of the entire touchscreen display/Amsler grid area.

In one instantiation, this can be accomplished by mounting a screen, mask, mat, safeguard, etc. around the touch-sensitive area of the touchscreen (Fig. 5, right), to allow finger touch access to only the intended portion of the touchscreen (i.e., the Amsler grid itself), thereby preventing the subject from accessing areas of the display that are not part of the actual Amsler grid (e.g., menu items, navigation bars, etc.).

Fluorescent Eccentric Fixation Markers for 3D-CTAG

For large test screens (Figs. 3 and 5) it is beneficial to introduce eccentric fixation markers, especially for subjects with central visual field defects who have an inherent difficulty to maintain fixation if at all possible (Fig. 6).

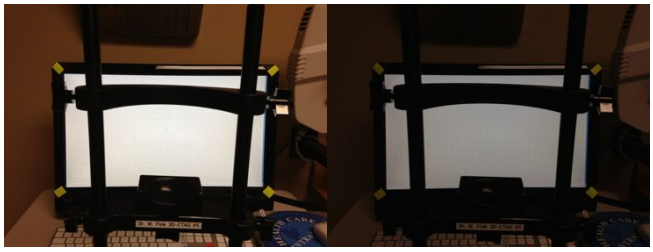

Figure 6. *Left:* Eccentric fixation markers in yellow before the testing (i.e., lights on). *Right:* Fixation markers fluoresce after the test procedure has begun (i.e., lights out).

In one embodiment, this can be realized by placing fluorescent fixation markers in the four corners of the touchscreen, or, alternatively, by affixing fluorescent tape along the four edges of the touchscreen.

6. Proposed VIIP Study Procedure and Parameters

The 3D-CTAG testing will be done at the Biomedical Innovations for Space and Earth facility at the Center for Space Medicine at Baylor College of Medicine (Fig. 7, top) with the following methodology:

- Transiently elevate ICP and IOP in normal subjects (comparable to astronaut population) using accepted techniques (head down tilt, carbon dioxide elevation, etc.), while noninvasively monitoring ICP and IOP and other physiologic parameters.

- Employ the 3D Computer-automated Threshold Amsler Grid (3D CTAG) test [1] to assess visual field changes in test subjects with induced ICP and IOP elevation.

We will utilize a Mac mini computer in conjunction with a 21-inch touch-sensitive Dell computer monitor (Fig. 7, top). The brightness level will be well defined and graded systematically throughout each study and between separate trials. The monitor will not be re-calibrated but will be kept at the same brightness and contrast settings both throughout and between separate trials for consistency. Moreover, the ambient light in the examination room will be kept constant.

Each subject will be positioned in font of the computer monitor on a chin-head rest (Fig. 7, left). The angle of visual field will be determined by seating the patient at the fixed distance of 12 inches from the central fixation marker on the computer screen (i.e., 0 deg. horizontally and 0 deg. vertically from fixation). An eye cover will be used to occlude the eye not being examined. Refractive correction

will be used with the subject's eyeglasses if need be. Additional corrective lenses will not be used.

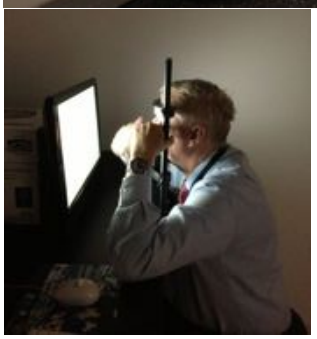

Figure 7. 3D-CTAG test setup at NSBRI on height-adjustable table in a room with controlled lighting (top). Test subject on chin-head rest in front of touchscreen at a fixed distance performing the visual field test (left).

The computer will display an Amsler grid of a pre-selected gray scale (i.e., contrast) level and a pre-selected angular resolution on the 21-inch touch screen. The pre-selected angular resolution for all subjects will be determined by the distance between the monitor and the patient, and also the Amsler grid spacing on the monitor. It will be consistently set to 1 deg., i.e., the standard Amsler grid spacing between lines. This setting expands to represent about 89 deg. (horizontal) x 49 deg. (vertical) of tested visual field for the entire test.

The subject will be asked to focus on a changing fixation marker at the center of the grid. To suppress the central Troxler effect (i.e., fading of peripheral objects during central fixation) and keep the subject's attention, the shape of the fixation marker will be regularly changed. Given the instability of fixation in subjects with central scotomas, the subjects will be instructed to use the four corners of the rectangular monitor as an additional reference frame for fixation.

The subjects will be asked to mark the areas on the Amsler grid that are *missing* from their field of vision by tracing the border of this region with their finger on the touch screen while maintaining fixation. The subjects' responses will be recorded by the computer program. This test modality screens for *scotomas*, i.e., visual field defects manifested as missing Amsler grid lines.

In a second test modality the subjects will be asked to mark the areas on the Amsler grid that are *distorted* (but not missing) in their field of vision by tracing the border of this region with their finger on the touchscreen while maintaining fixation. The subjects' responses will be recorded by the computer program. This test modality screens for *metamorphopsia*, i.e., non-straight, distorted Amsler grid lines.

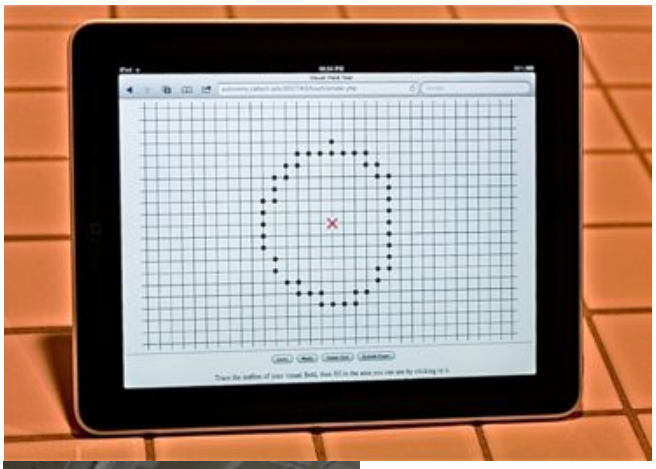

Figure 8. Head down tilt table setup at NSBRI with test subject performing 3D-CTAG testing on hand-held iPad (left). 3D-CTAG test running on iPad (top).

In a second orientation, the 3D-CTAG test will be performed during a 15 deg. head down tilt position (Fig. 8, left) on an iPad (Fig. 8, top). The iPad will be affixed to the tilt table above the subject's face and kept at a fixed distance from the subject using a standoff attached to the iPad. The ambient brightness in the test room will be controlled and kept constant throughout the examination. Current iPad generations (1 through 4) allow for about 33 deg. (horizontal) x 21 deg. (vertical) of tested visual field. With Apple's recent announcement (as of October 2013) of the development of an iPad with a size greater than 12", it will be possible to test a visual field of about 43 deg. (horizontal) x 31 deg. (vertical) according to NASA's onboard visual field testing requirements.

7. 3D-CTAG DATA ANALYSIS

The following analyses, detailed in [5], on the gathered 3D-CTAG data will be performed:

- Visual field raw data extraction from 3D-CTAG database in machine-readable form.

- Characterizing indices that describe scotomas (i.e., visual field defects) will be calculated from the visual field raw data, gathered with the 3D-CTAG test, for each test subject for the entire performance test period. These include the following:

    - *Area of Visual Field Impaired at XX% Contrast*: number of Amsler grid points marked as not visible at a given Amsler grid contrast;

    - *Relative Area of Visual Field Impaired at XX% Contrast*: number of Amsler grid points marked as not visible at a given Amsler grid contrast divided by the total # of tested Amsler grid points at that given Amsler grid contrast in [percent];

    - *Absolute Hill-of-Vision Volume Lost*: total number of Amsler grid points marked as not visible across all tested Amsler grid contrasts;

    - *Relative Hill-of-Vision Volume Lost*: absolute # of test-locations not seen divided by the total # of tested Amsler grid points in [percent];

    - *Lost Area Grade (LAG)*: existing scotoma area at highest tested contrast level divided by existing scotoma area at lowest tested contrast level;

    - *Preserved Area Grade (PAG)*: existing preserved visual field area at lowest tested contrast level divided by existing preserved visual field area at highest tested contrast level.

  These characterizing indices will be used to assess/visualize visual field changes over time for each subject during the test period [5, 21].

- Feature vectors will be generated from these characterization indices. These feature vectors are characteristic for and representative of the respective 3D-CTAG examination results [21].

- The feature vectors enable both qualitative and quantitative analyses of temporal changes of a subject's visual field. These temporal changes will be assessed by calculating the following comparative quantities amongst different 3D-CTAG examination results for each subject [5, 21]:

    - *Overlap Parameter*: defined as the N-dimensional scalar product between two feature vectors, ranging from -1 to +1, with -1 representing the case that two visual fields are completely opposite/dissimilar from each other, 0 representing the case that two visual fields are orthogonal to each other, and with +1 representing the case that two visual fields are the same – and of course all continuous variations in between these values. The Overlap Parameter is a measure of similarity between two feature vectors.

    - *Hamming Distance*: defined as the sum of squared differences between the feature vector components, divided by the dimension N of the feature vector. The Hamming Distance is always >= 0 and is a measure of similarity between two feature vectors.

    - *Euclidian Distance*: defined as the square root of the sum of squared differences between the feature vector components. The Euclidian Distance is always >=0 and is also a measure of similarity between two feature vectors.

8. DISCUSSION & CONCLUSIONS

The 3D-CTAG system is a versatile, robust, and portable tool that can be adapted to a variety of space-related applications. It has the advantage of combining a standard Amsler grid with adjustable contrast sensitivity thus giving a "three-dimensional," functional evaluation of the optical system. It has been shown to be a sensitive screening test for ocular diseases such as glaucoma, macular degeneration, drug and environmental toxicity, optic neuritis, etc., and thus can be used as part of the screening process for initial selection into the astronaut program. It can be used during the preflight period for baseline data collection, during long-duration space flights to assess for the development of ocular pathology such as the VIIP syndrome and its progression, and post-flight to evaluate the effects of the space environment on visual fields. The life-long impact to ocular health of extended operations in reduced gravity conditions and exposure to radiation and other space hazards can be studied longitudinally with this system.

In August 2013, the 3D-CTAG system was presented [22] at the National Space Biomedical Research Institute (NSBRI) Sensorimotor Workshop "Towards Integrated Countermeasures", in Houston, TX, and is currently being considered by NASA as a technology for visual field testing in space.

One of the authors (DCH) was a crewmember on four NASA space missions. From an experienced astronaut's perspective this system has a number of desirable characteristics. First, it has a low up-mass and a small footprint that minimizes the impacts to mission performance

and stowage. Secondly, it requires very little crew time to deploy and set up, probably less than 5 minutes. Testing requires a minimum of crew time, approximately less than 5 minutes, is not tedious and can provide near real-time results. Proper fixation to a bulkhead, to a work station, or to the subject's head will insure that activities in zero or reduced gravity conditions will not affect its operation or its interfaces with the crew. Existing foot loops and/or hand-holds should be all that is necessary to provide proper stabilization. Since the device can provide rapid feedback to the crew as to ongoing visual changes, it can be correlated with subjective observations (e.g., increased hyperopia or developing scotomas) that the crew may have noted. This information can be used to inform upcoming mission operations, allow the deployment of countermeasures (e.g., corrective lenses), and give the crew warning of pathologic changes that may affect visual health. Finally, the device can either be kept permanently mounted or rapidly deployed without adversely affecting on-going crew operations, and there are no foreseeable risks to crew safety.

In summary, we propose to use the 3D-CTAG, a well-tested, portable and versatile system, to evaluate the causes, onset, and progression of visual problems during long-duration spaceflight. The discovery of the VIIP syndrome makes the deployment of this system more timely and relevant. However, the flexibility of the system lends itself to a wide range of applications to the space program, including the selection of astronauts, pre-flight, monitoring during missions, post-flight and longitudinally to follow ocular health through the remainder of the astronaut's life.

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AUTHOR DISCLOSURE STATEMENT

One of the authors (WF) may have a financial interest in the technology presented here as several Caltech patents on the visual field testing and associated evaluation technologies are issued and currently pending. Authors DCH and MAT have no financial interest in the technology presented.

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BIOGRAPHIES

Wolfgang Fink *is currently an Associate Professor and the inaugural Edward & Maria Keonjian Endowed Chair of Microelectronics with joint appointments in the Departments of Electrical and Computer Engineering, Biomedical Engineering, Systems and Industrial Engineering, Aerospace and Mechanical Engineering, and Ophthalmology and Vision Science at the University of Arizona in Tucson. He is a Visiting Associate in Physics at the California Institute of Technology, and holds concurrent appointments as Visiting Research Associate Professor of Ophthalmology and Neurological Surgery at the University of Southern California. Dr. Fink is the founder and director of the Visual and Autonomous Exploration Systems Research Laboratory at Caltech (http://autonomy.caltech.edu) and at the University of Arizona (http://autonomy.arizona.edu). He was a Senior Researcher at NASA's Jet Propulsion Laboratory from 2000 till 2009. He obtained a B.S. and M.S. degree in Physics and Physical Chemistry from the University of Göttingen, Germany, and a Ph.D. in Theoretical Physics from the University of Tübingen, Germany in 1997. Dr. Fink's interest in human-machine interfaces, autonomous/reasoning systems, and evolutionary optimization has focused his research programs on artificial vision, autonomous robotic space exploration, biomedical sensor/system development, cognitive/reasoning systems, and computer-optimized design. Dr. Fink is a Fellow of the American Institute for Medical and Biological Engineering (AIMBE). His work is documented in numerous publications and patents. Dr. Fink holds a Commercial Pilots License for Rotorcraft.*

David C. Hilmers *is an Associate Professor in the Departments of Internal Medicine and Pediatrics and the Center for Space Medicine at the Baylor College of Medicine in Houston, Texas. In addition to clinical instruction, he teaches medical school courses in tropical medicine, malnutrition, global health, and space medicine. His clinical pursuits have included experiences in international HIV, pediatrics special needs, outpatient pediatrics and internal medicine, emergency medicine, tropical medicine, nutrition, and as a hospitalist in internal medicine. His research interests include micronutrient deficiencies, food fortification programs, food insecurity, metabolic syndrome, tropical diseases, aerospace medicine, and the influence of malnutrition on infectious diseases such as HIV, TB, malaria, and rickets. He is a member of the National Space Biomedical Research Institute's User Panel advisory board. He has done international volunteer medical service and disaster relief work in more than 50 countries. Prior to going to medical school he was a Marine Corps Colonel, aviator and electrical engineer and served*

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Mark A. Tarbell *is currently a Senior Research Scientist at the University of Arizona, a Visiting Scientist at Caltech, and Senior Software Specialist with more than 25 years of satellite and ground-based command and control system architecture design and development. Mr. Tarbell designed and implemented the ground data processor control infrastructure for JPL's SRTM mission, and was involved with JPL's Jason JTCCS project, which supports real-time telecommanding of Earth-orbiting satellites from wireless handheld devices. In collaboration with the Visual and Autonomous Exploration Systems Research Laboratory at Caltech, he recently co-designed and implemented a remote telecommanding control system for an outdoor test bed for autonomous surface exploration, and a biomedical Artificial Vision Support System, which uses various vision processing algorithms to interface to blind patients' implanted retinal microelectrode array in real time.*