NASA Investigator's Workshop, Human Research Program
February 8-11, 2016 Galveston, TX
Poster Session A: VISUAL IMPAIRMENT AND INTRACRANIAL PRESSURE
Abstract 7304

Space Biosciences
NASA AMES RESEARCH CENTER

National Aeronautics and Space Administration

ANALYSIS BY NASA'S VESGEN SOFTWARE OF RETINAL BLOOD VESSELS BEFORE AND AFTER 70-DAY BED REST: A RETROSPECTIVE STUDY

Sneha Raghunandan[1*], Ruchi J. Vyas[1*], Gianmarco Vizzeri[2], Giovanni Taibbi[2], Susana B. Zanello[3], Robert Ploutz-Snyder[3] and Patricia A. Parsons-Wingerter[1]

[1]Ames Research Center, NASA, Mountain View CA, patricia.a.parsons-wingerter@nasa.gov,
[2]Department of Ophthalmology and Visual Sciences, University of Texas Medical Branch, Galveston TX,
And [3]Universities Space Research Association, NASA Johnson Space Center, Houston TX. *Authors contributed equally.

INTRODUCTION AND BACKGROUND

Significant risks for visual impairment associated with increased intracranial pressure (VIIP) are incurred by microgravity spaceflight, especially by long-duration missions [1]. We hypothesize that microgravity-induced fluid shifts result in pathological changes within the retinal blood vessels that precede development of visual and other ocular impairments. Potential contributions of retinal vascular remodeling to VIIP etiology are therefore being investigated by NASA's innovative VESsel GENeration Analysis (VESGEN) software [2,3] with two studies: (1) human subjects before and after 70 days of bed rest (BR) with head-down tilt (HDT), and (2) U.S. crew members before and after ISS missions. One goal of our VESGEN HDT study was to develop the analysis of 30° Heidelberg Spectralis images in preparation for our astronaut study [IWS Abstract 7324]. VESGEN analysis previously identified surprising new opportunities for regenerating retinal vessels during early-stage, potentially reversible progression of a visually impairing and blinding disease supported by the US National Institutes of Health [2].

METHODS

For the NASA NRA award, we are analyzing with VESGEN the clinical ophthalmic images of retinal blood vessels obtained by 30° infrared (IR) Heidelberg Spectralis® (average image resolution, 11.4 μm/px). The 40 images were collected in the two eyes of six healthy subjects before, during and after 70 days of bed rest at 6° HDT. For this NASA IRB-approved retrospective study of NASA Bed Rest Campaign 11, the VESGEN retinal analysis is being conducted in a randomized fashion without knowledge of the subjects' identity or temporal sequence of the images. VESGEN (NASA patent pending) is a mature, automated software developed as a translational and basic vascular research discovery tool [3,4], particularly for retinal vascular disease [2,3]. Binary branching patterns of venous and arterial trees extracted from the Spectralis® images with Adobe Photoshop® are automatically mapped by VESGEN into vessel branching generations (G_x) and quantified by parameters that include generation-dependent densities of vessel length (L_v), area (A_v), number (N_v) and fractal dimension (D_f).

RESULTS AND DISCUSSION

VESGEN analysis of the venous branching in one image for each of the 12 eyes of the six study subjects is complete. Two results for our preliminary study are reported here: (1) Two populations were detected by VESGEN analysis that are distinguished primarily by the presence or absence of small veins (Figure 1). Results for the 12 arterial trees are in progress. (2) The smaller vessels are not easily extracted from the grainy image background. However, small blood vessels are of critical importance because generally they remodel more actively than large vessels during progression of vascular-dependent diseases [2,3]. To estimate more objectively any differences in small vessel patterning before, during and after HDT, we therefore plan to complete the study by using the first 12 images as masking templates. We will investigate whether our image masking approach offers higher confidence in accurate vessel segmentation of the remaining HDT images prior to performing the automated VESGEN analysis. We note that HDT subjects remained asymptomatic throughout the duration of BR. Clinically relevant ocular structural or functional changes were not observed.

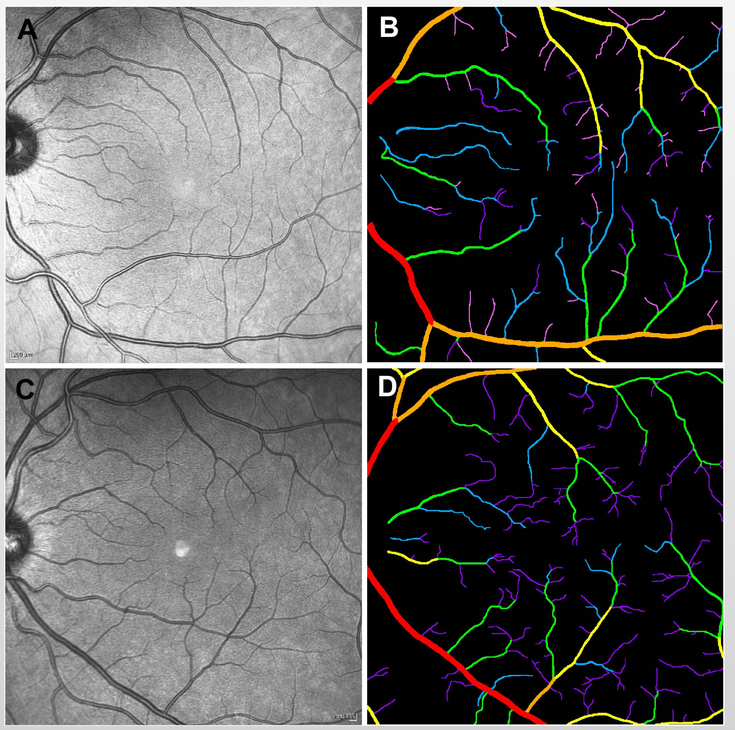

Figure 1 Two Populations of HDT Study Subjects Differ in Small Veins

The presence or absence of small veins ($G_{\geq 7}$) distinguish two populations identified by VESGEN analysis from 12 retinas of six subjects that participated in a 70-day HDT campaign. Representative Spectralis® images of the two populations identified by VESGEN (*A,C*) are displayed together with the VESGEN generational mappings of venous (*B,D*) trees extracted from the images. For example, $L_{v\geq 7}$ and $A_{v\geq 7}$ are 2.7 ± 1.3 E-4 μm/μm² and 7.2 ± 3.6 E-4 μm²/μm² for venous density in six retinas displaying smaller vessels, but zero in the other six retinas (mean ± SD). Nonetheless, the space-filling properties of the entire venous trees are quite uniform in both populations by all parameters, such as D_f = 1.56 ± 0.02 for 6 retinas with $G_{\geq 7}$ and 1.55 ± 0.02 for retinas without $G_{\geq 7}$.

CONCLUSIONS

By VESGEN analysis, two populations of the 12 subject retinas clearly differed in the presence or absence of small veins. These differences may result from: (1) effects of HDT, (2) pre-existing variation in the retinal vessels of the HDT subjects, or (3) limits in the resolution capabilities of the IR Spectralis® imaging. Final results of our investigation will be completed later this year that should help determine which explanation for the two populations is correct.

Modified retinal vascular patterning may offer early-stage predictions of downstream ocular changes that result in decreased visual acuity. Novel insights provided by VESGEN may help to guide new etiological insights into the progression of VIIP and consequently, future development of successful countermeasures.

REFERENCES

1. Mader T.H., Gibson C.R., Pass A.F., Kramer L.A., Lee A.G., Fogarty J., Tarver W.J., Dervay J.P., Hamilton D.R., Sargsyan A., Phillips J.L., Tran D., Lipsky W., Choi J., Stern C., Kuyumjian R. and Polk J.D. (2011) *Ophthalmology* 118:2058-2069.
2. Parsons-Wingerter P.A.,* Radhakrishnan K.,* Vickerman M.B. and Kaiser P.K. (2010) *Inv Ophthal Vis Sci* 51(1):498-507 (2010). *Co-authors contributed equally.
3. Vickerman M.B., Keith P.A., McKay T.L., Gedeon D.J., Watanabe M., Montano M., Karunamuni G., Kaiser P.K., Sears J.E., Ebrahem Q., Ribita D., Hylton A.G. and Parsons-Wingerter P.A. (2009) *Anat Rec* 292:320-332.
4. [4] Chen X., Yang G., Song J.H., Xu H., Li D., Yang X., Zeng H., Parsons-Wingerter P.A., Reinecker H.C. and Kelly C.P. (2013) *PLOS ONE* 8(5):e64227 (May 13, 2013).