#### DIFFERENCES IN PRE AND POST VASCULAR PATTERNING OF RETINAS FROM ISS CREW MEMBERS AND HDT SUBJECTS BY VESGEN ANALYSIS

M. C. Murray<sup>1,2</sup>, G. Vizzeri<sup>3</sup>, G. Taibbi<sup>3</sup>, S. S. Mason<sup>4</sup>, M. H. Young<sup>5</sup>, S. B. Zanello<sup>6</sup>, P. A. Parsons-Wingerter<sup>1</sup> <sup>1</sup>Ames Research Center, NASA, Mountain View CA, <sup>2</sup>Blue Marble Science Institute of Space, <sup>3</sup>Department of Ophthalmology and Visual Sciences, University of Texas Medical Branch, Galveston TX, <sup>4</sup>MEI Technologies, <sup>5</sup> NASA Johnson Space Center, Houston TX, <sup>6</sup>KBRwyle.

# INTRODUCTION AND BACKGROUND

Accelerated research by NASA [1] has investigated the significant risks for visual and ocular impairments Spaceflight Associated Neuro-Ocular Syndrome /Visual Impairment/Intracranial Pressure (SANS/VIIP) incurred by microgravity spaceflight, especially long-duration missions. Our study investigates the role of blood vessels in the incidence and etiology of SANS/VIIP within the retinas of Astronaut crewmembers pre-and post-flight to the International Space Station (ISS) by NASA's VESsel GENeration Analysis (VESGEN). The response of retinal vessels in crewmembers to microgravity was compared to that of retinal vessels to Head-Down Tilt (HDT) in subjects undergoing 70-Day Bed Rest. The study tests the proposed hypothesis that cephalad fluid shifts missions, resulting in ocular and visual impairments, are necessarily mediated in part by retinal blood vessels, and are therefore accompanied by significant remodeling of retinal vasculature.

# METHODS

Vascular patterns in the retinas of crew members and HDTBR subjects extracted from  $30^{\circ}$  infrared (IR) Heidelberg Spectralis<sup>®</sup> images collected pre/postflight and pre/post HDTBR, respectively, were analyzed by VESGEN (patent pending). a mature, automated software developed as a research discovery tool for progressive vascular diseases in the retina and other tissues [2]. The weighted, multi-parametric VESGEN analysis generates maps of branching arterial and venous trees and quantification by parameters such as the fractal dimension ( $D_f$ , a modern measure of vascular space-filling capacity), vessel diameters, and densities of vessel length and number classified into specific branching generations by vascular physiological branching rules [2,3]. The retrospective study approved by NASA's Institutional Review Board included six HDT subjects (NASA Flight Analogs Research Unit [FARU] Campaign 11; for example, [4]) and eight ISS crewmembers monitored by routine occupational surveillance who provided their study consents to NASA's Lifetime Surveillance of Astronaut Health (LSAH). For the initial blinded VESGEN phase, ophthalmic retinal images were masked as to subject identity and pre- and post-status. In the second unblinded phase, VESGEN results were analyzed according to the pre- and post-status of left and right retinas matched to each subject. To complete our study, vascular results will be subjected to NASA biostatistical analysis and correlated with other ophthalmic and medical findings.

# RESULTS

Preliminary results for changes in the pre- to post-status of vascular patterning in the retinas of crewmembers and HDT subjects are strikingly opposite. By  $D_f$  and other vascular branching measures, the space-filling capacity of arterial and venous trees decreased in a substantial subset of crewmembers (11/16 retinas). In contrast, vascular densities increased in a substantial subset of HDT subjects by the same parameters (6/10 retinas, currently excluding one anomalous subject). To conclude the study, biostatistical and medical analyses will be of critical importance for investigating the validity of these vascular findings.

## CONCLUSIONS

Vascular densities appeared to decrease in the retinas of crewmembers following ISS Missions, and increase in subjects after HDT. The vascular increases and decreases most likely derive primarily from limits of resolution to the ophthalmic imaging that does not capture the smallest vessels, rather than from vessel growth or atrophy. Differences in arterial and venous response to cephalad fluid shifts induced by ISS and HDT may have resulted from a long-duration conditioning phenomenon (for example, 6-month ISS missions compared to 70-day HDT), or the presence of gravity in HDT compared to microgravity onboard the ISS. To conclude our study, the biostatistical and medical analyses will be of critical importance for investigating the validity and significance of the VESGEN findings.

## REFERENCES

[1] Mader et al (2011) *Ophthalmology* 118:2058-2069 [2] Parsons et al (2010) *IOVS* (2010) 51(1):498-507

[3] Vickerman et al (2009) Anat Rec 292:320-332 [4] Taibbi et al (2016) IOVS 57(2):495-501

ACKNOWLEDGMENTS Contributions by former IRB Team Members R Vyas, S Lim, M Predovic, and K Askin are gratefully acknowledged.