

**NASA's VESsel GENeration  
Analysis (VESGEN) Software  
as Research Discovery Tool**



**Differences in Pre and Post Vascular Patterning  
within Retinas from ISS Crewmembers  
and HDT Subjects by VESGEN Analysis**

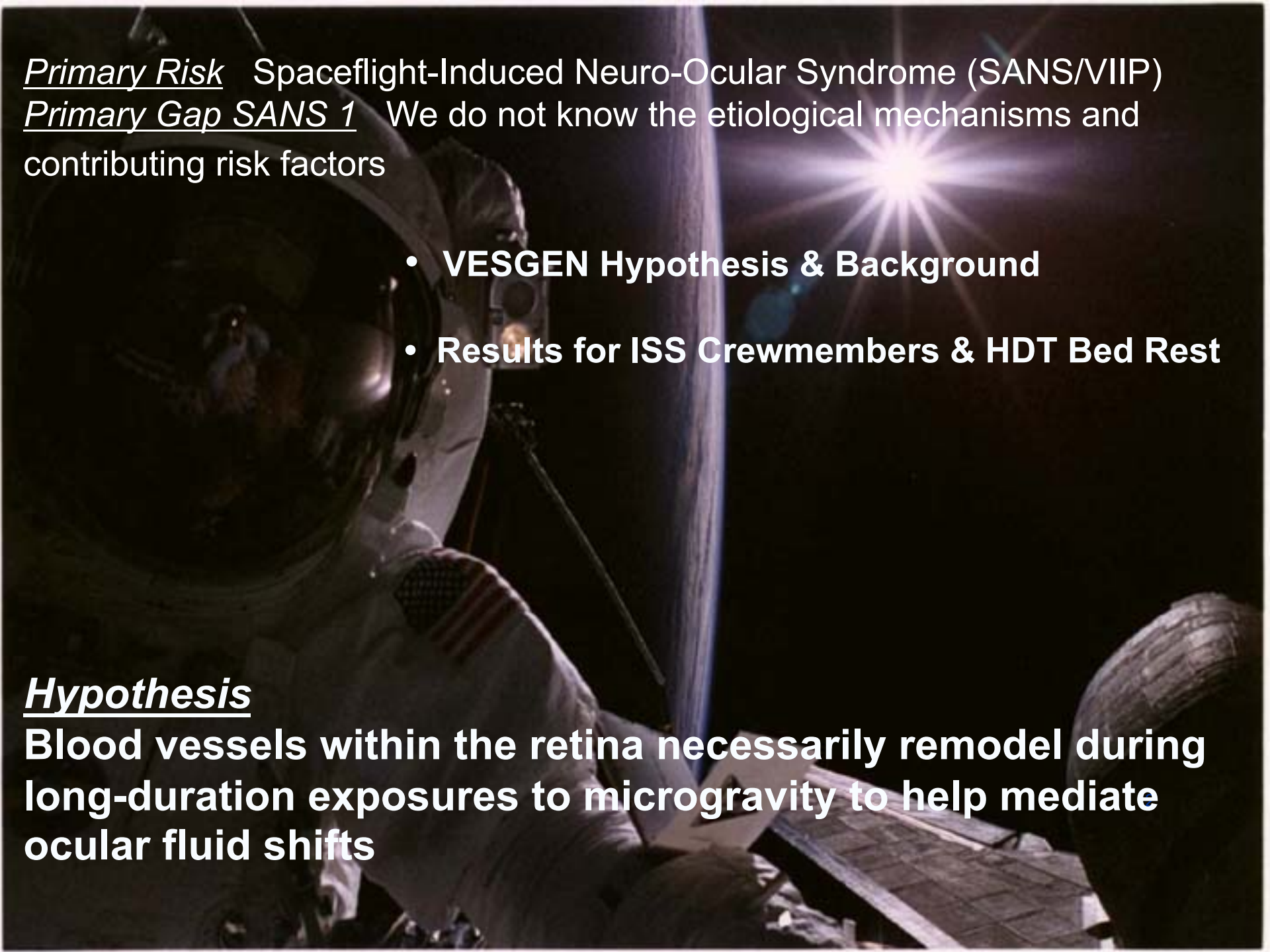
**M. C. Murray<sup>1,2</sup>, G. Vizzeri<sup>3</sup>, G. Taibbi<sup>3</sup>, S. S. Mason<sup>4</sup>, M. Young<sup>5</sup>,  
S. B. Zanello<sup>6</sup>, P. Parsons-Wingerter<sup>1</sup>**

<sup>1</sup>NASA Ames Research Center, Mountain View CA, <sup>2</sup>Blue Marble Space Institute of Science,

<sup>3</sup>Department of Ophthalmology and Visual Sciences, University of Texas Medical Branch,

Galveston TX, <sup>4</sup>MEI Technologies, NASA Johnson Space Center, <sup>5</sup>Human Health and Performance,  
NASA Johnson Space Center, Houston TX, <sup>6</sup>KBR Wyle, NASA Johnson Space Center, Houston TX

Supported by NASA HRP NRA, Human Health & Countermeasures

A photograph of an astronaut in a white spacesuit working on the exterior of a spacecraft. The astronaut is in the foreground, looking towards the right. The background shows the dark void of space with a bright sun or starburst light source in the upper right, creating a lens flare effect. The curvature of the spacecraft is visible in the center.

**Primary Risk** Spaceflight-Induced Neuro-Ocular Syndrome (SANS/VIIP)

**Primary Gap SANS 1** We do not know the etiological mechanisms and contributing risk factors

- **VESGEN Hypothesis & Background**
- **Results for ISS Crewmembers & HDT Bed Rest**

**Hypothesis**

**Blood vessels within the retina necessarily remodel during long-duration exposures to microgravity to help mediate ocular fluid shifts**

# *Proof-of-Concept Study Design*

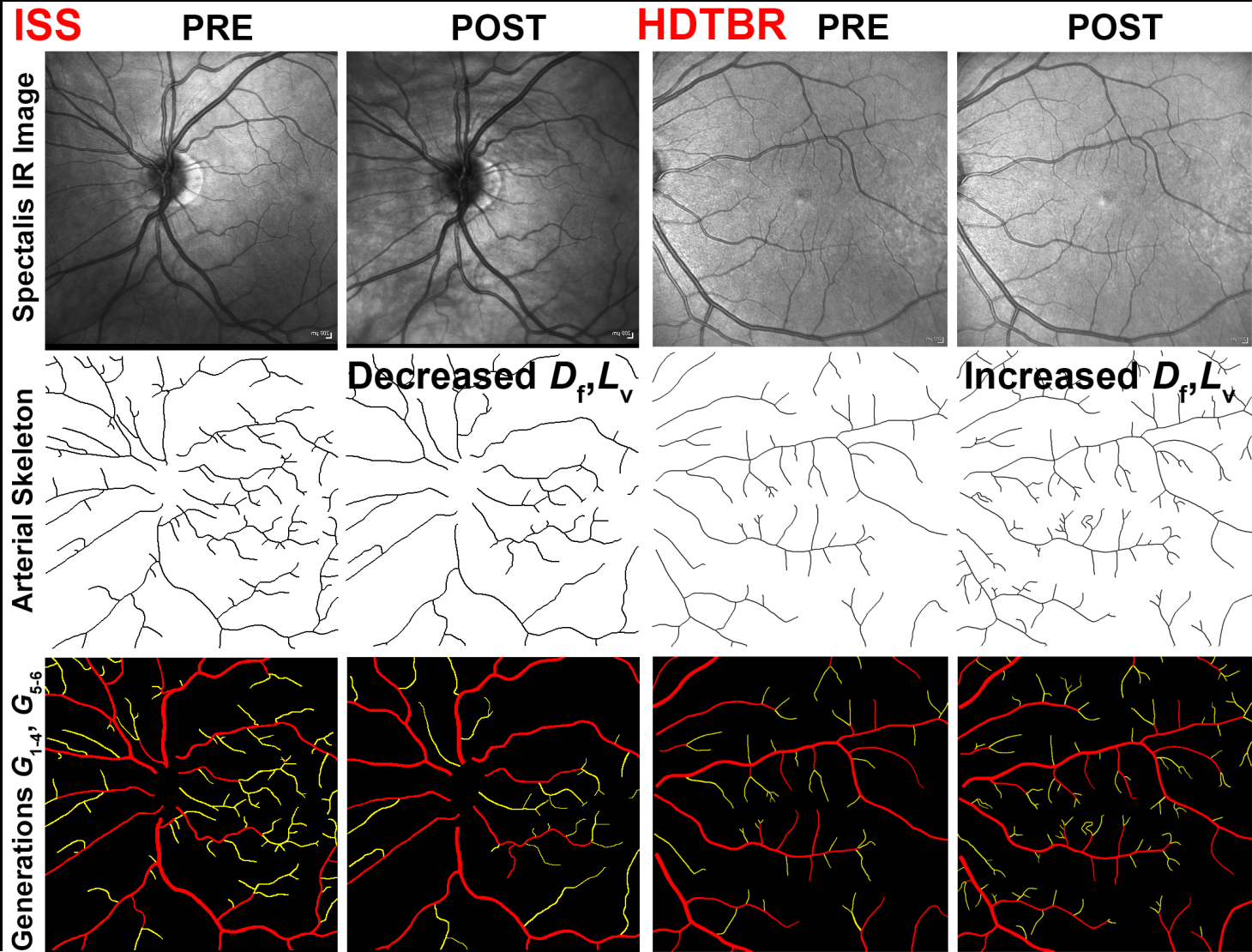
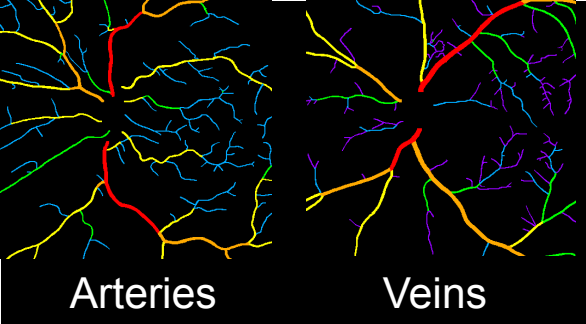
## **Pre and Post Analysis of ISS Crewmembers Compared to HDT Bed Rest**

- Eight Crewmembers (16 retinas) from 6-Month NASA ISS Missions
- Six Bed Rest Subjects at 6° HDT (12 retinas) for 70 Days, FARU Campaign 11
- Prospective study of males and females approved by NASA's Institutional Review Board, Lifetime Surveillance of Astronaut Health (LSAH): gender, age not released
- Retinal imaging by Heidelberg Spectralis 30° Infrared (IR) at somewhat different scanning conditions
- Crew Member images, centered on optic disc; HDT images, on macula
- **Phase 1** Blinded VESGEN analysis of pre and post retinal images
- Extraction of binary arterial and venous patterns from Spectralis grayscale images followed by automated mapping and quantification by VESGEN
- **Phase 2** Unblinding of subject pre/post image status and correlation with other ocular, visual and cardiovascular parameters



# VESGEN

Automated Mapping and Quantification of Fractal-Based Pattern into Vascular Branching Generations by Physiological Branching Rules





# Decreased Arterial and Venous Density Measured Post-Flight by VESGEN in Right Retina of ISS Crew Member

Associated with optic disc edema, abnormal change in peripapillary area, and choroidal folds, compared to no change in other 15/16 retinas

**ISS**

**PRE**

**POST**

**Spectralis IR Image**



# Decrease of Vascular Density in Retinal Images of ISS Crew Members [ $n=8$ ] Compared to Increase in HDT Bed Rest [ $n=5$ ]

Subpopulation Incidence

Population Analysis

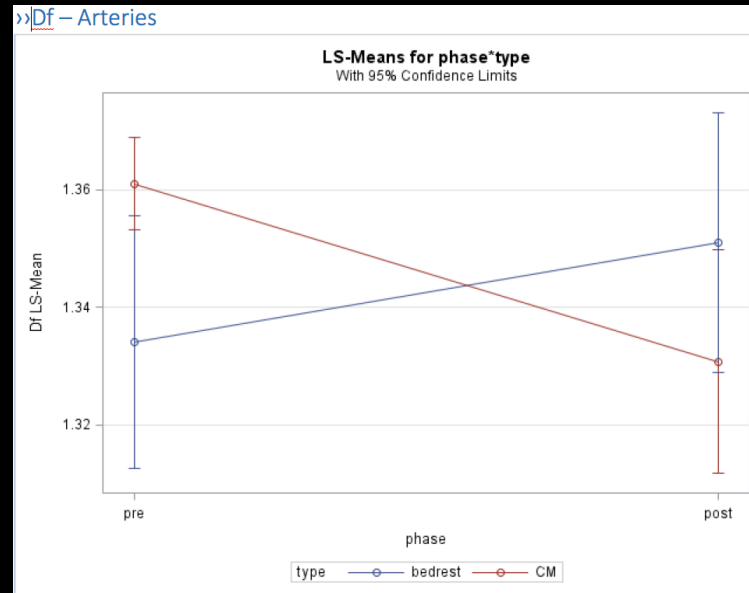
$p$

$\geq D_f$

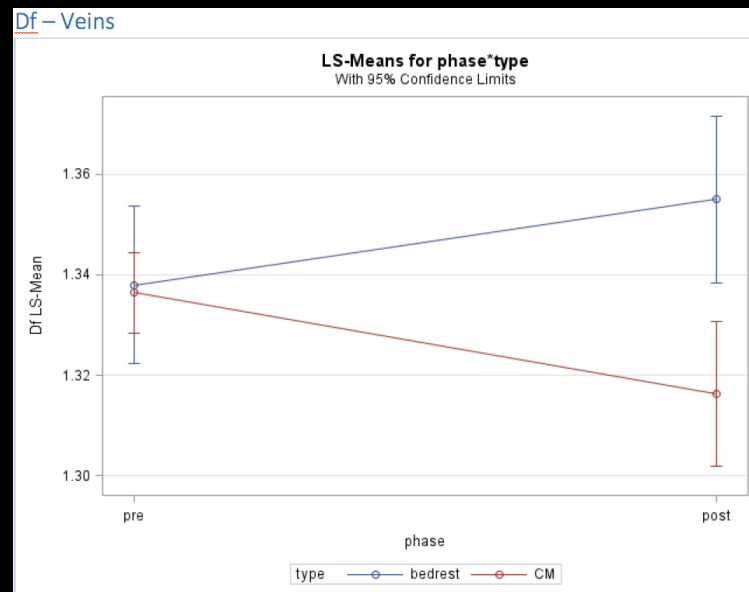
7/16 Retinas  
6/8 Crew Members

$\leq D_f$

5/10 Retinas  
3/5 HDT Subjects  
[6<sup>th</sup> Subject, anomalous imaging]



ISS 0.006  
HDT 0.27



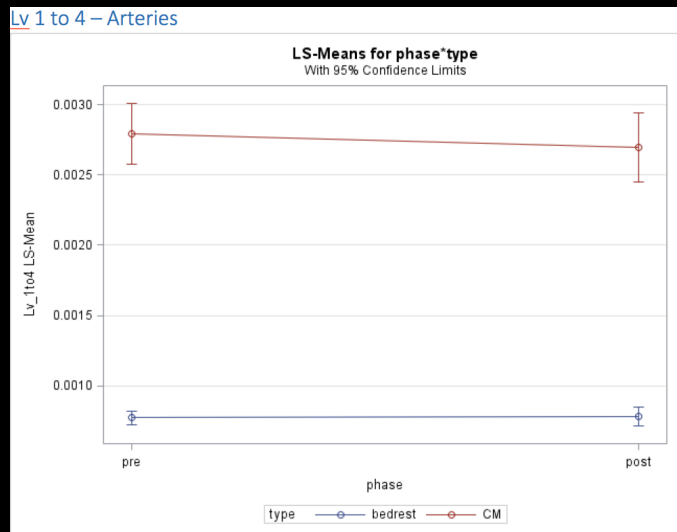
ISS 0.02  
HDT 0.14

Millennia  
Young, PhD

# Population Analysis for $L_V$ Decreased Density of Small but not Large Vessels in Retinal Images of ISS Crew Members compared to Increase in HDT Bed Rest

## Large Vessels, $L_V 1-4$

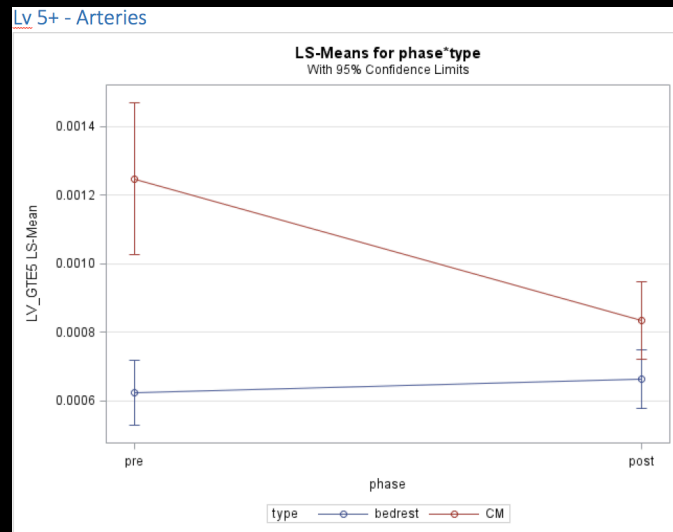
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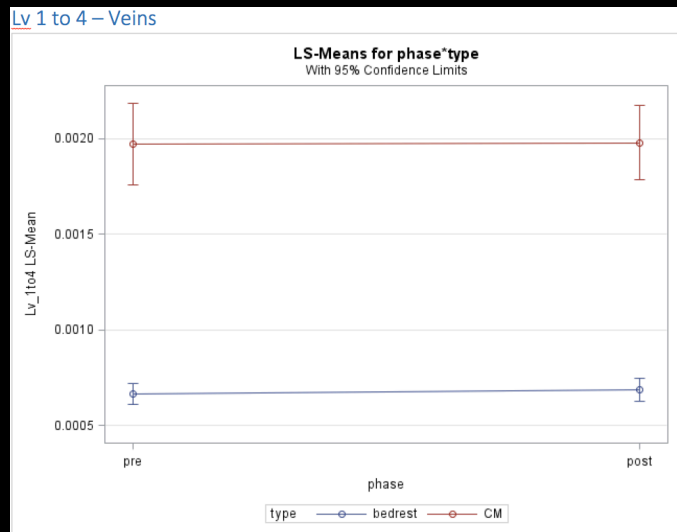
ISS 0.54  
HDT 0.85

## Small Vessels, $L_V \geq 5$

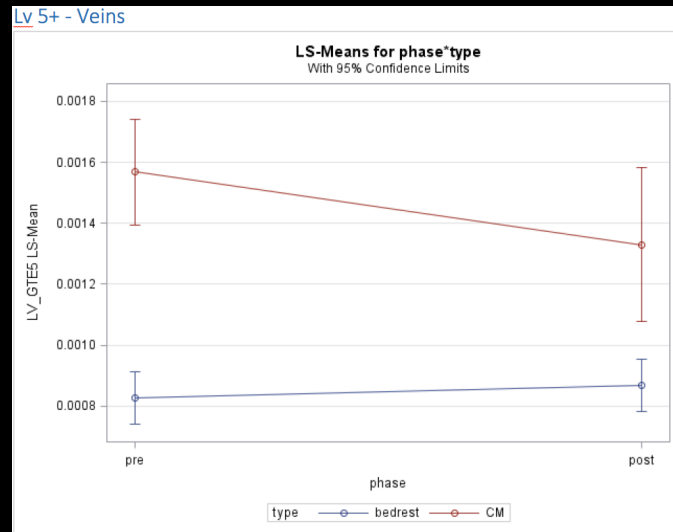
$p$



ISS 0.002  
HDT 0.53



ISS 0.97  
HDT 0.58

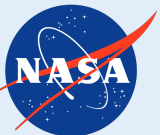


ISS 0.12  
HDT 0.49

## Summary of Results

### Vascular Analysis by VESGEN of Pre and Post Retinal Images of ISS Crewmembers Compared to 70-Day HDT Bed Rest

- **First Proof-of-Principle Study of Structure-Function Relationships**  
**Opposite Trends in Adaptations of Vascular Density in Crew Members after 6 Month ISS Missions Compared to HDT Subjects after 70 Days of Bed Rest**
  - ***Statistically significant decrease in vascular density*** in grouped analysis of eight crewmembers; subset of 6/8 Crew Members [7/16 retinas]
  - ***Trend toward increased vascular density*** in subset of 3/5 HDT subjects [5/10 retinas], although not statistically significant
- To better define SANS Risk Factors – Currently examining Subpopulation associations of vascular decrease incidence with specific SANS factors such as increased RNFL, TCT, choroidal folds, compared to Overall Population Results
  - Left and right retinas of 1 Crew Member: ± choroidal folds, optic disc edema, abnormal peripapillary area
- Observations include presence and absence of a few small vessels within images and perhaps some vessel ‘ghosting’
- Limitations in Spectralis image resolution acknowledged as secondary reason for some differences in detection of small vessels



# Conclusions

## Vascular Analysis by VESGEN of Pre and Post Retinal Images of ISS Crewmembers Compared to 70-Day HDT Bed Rest

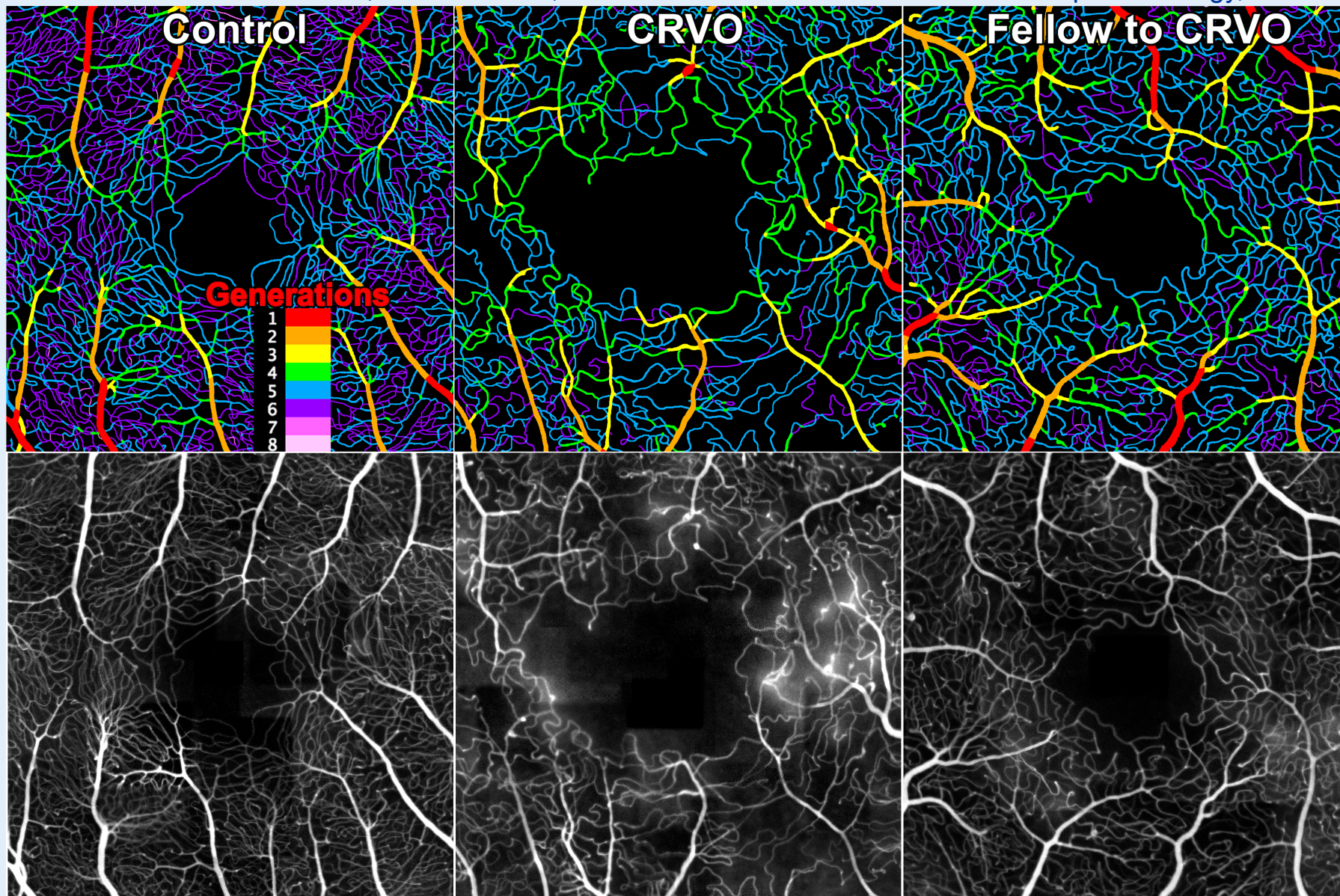
- **Statistical significance in proof-of-principle study of ISS crewmembers**  
Preliminary validation of hypothesis that blood vessels in the retina necessarily remodel to help mediate fluid shifts resulting from microgravity exposure
- **Opposite trends in adaptations of vascular density in Crew Members after 6 Month ISS Missions compared to HDT Subjects after 70 Days of Bed Rest**
- **Most Probable Explanation?** Hypothesize change in vascular density due to decreased ('constriction') and increased ('dilation') vessel diameter **below** and **above** image resolution for Crew Members and HDT Bed Rest
  - Relatively low resolution by Heidelberg Spectralis IR
  - Probably not vascular remodeling such as angiogenesis or vascular dropout?





# VESGEN mapping of retinal blood vessels for FA-AOSLO and OCT-Angiography

P Parsons with A Pinhas, R Rosen et al, Association for Research in Vision and Ophthalmology, 2014



# Recommendations

## Vascular Analysis by VESGEN of Pre and Post Retinal Images of ISS Crewmembers Compared to 70-Day HDT Bed Rest

- Recommend analysis of images from 30, 60 and 90 days on ISS  
Do differences between Crewmembers and HDT result from **differences in temporal response**, or **presence and absence of gravity** acting together with fluid shifts to upper body?
  - More advanced imaging such as OCT-Angiography now available  
For more complete understanding of the structure-function role of blood vessels in mediation of SANS
- More extensive testing of hypothesis that blood vessels necessarily remodel in with both healthy and pathological adaptations to accommodate fluid shifts incurred in microgravity

