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

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Supported by NASA HRP NRA, Human Health & Countermeasures
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

<table>
<thead>
<tr>
<th>ISS</th>
<th>PRE</th>
<th>POST</th>
<th>HDTBR</th>
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<tbody>
<tr>
<td>Spectral IR Image</td>
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<td>Arterial Skeleton</td>
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<td>Decreased $D_f L_v$</td>
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<td>Increased $D_f L_v$</td>
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<tr>
<td>Generations $G_{1,4}, G_{5,6}$</td>
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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
Decrease of Vascular Density in Retinal Images of ISS Crew Members \( [n=8] \) Compared to Increase in HDT Bed Rest \( [n=5] \)

### Subpopulation Incidence

\[ \geq D_f \]

7/16 Retinas
6/8 Crew Members

\[ \leq D_f \]

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

### Population Analysis

\[ p \]

\begin{align*}
    &\text{ISS} & 0.006 \\
    &\text{HDT} & 0.27 \\
    &\text{ISS} & 0.02 \\
    &\text{HDT} & 0.14
\end{align*}

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, $L_v^{1-4}$

- ISS: 0.54
- HDT: 0.85

Small Vessels, $L_v^\geq5$

- ISS: 0.002
- HDT: 0.53
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

VESGEN Patent Pending
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