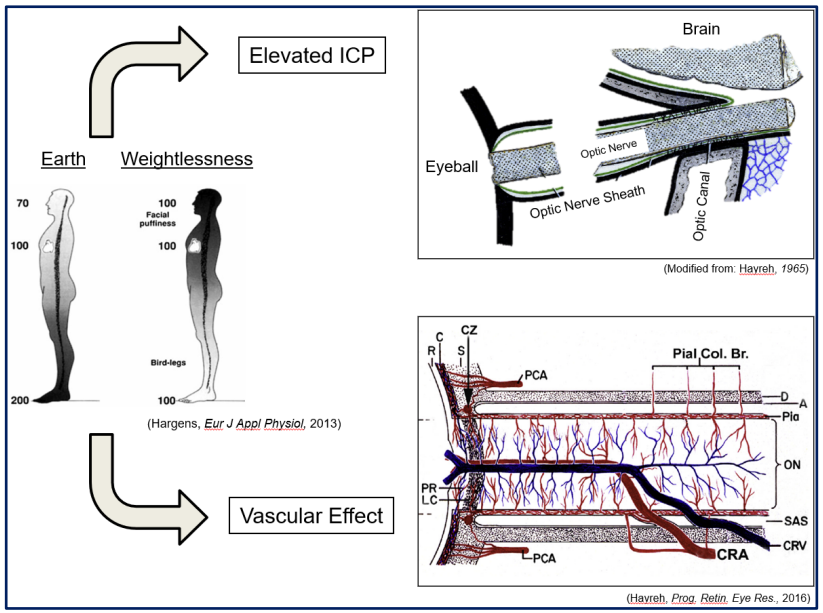
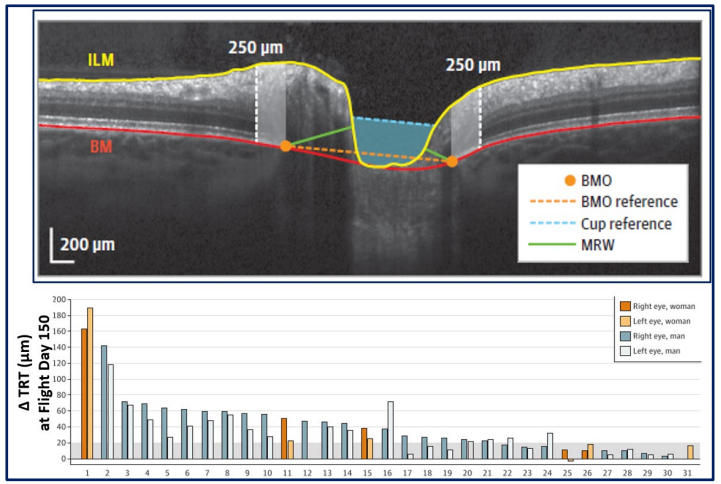
# Human Research Program (HRP) Approach - SANS

**Hypothesis: Headward fluid shift affects both cerebral spinal fluid (CSF) dynamics and blood (mostly venous) drainage. This leads to changes in the structure and function of the eye and brain, as seen in Total Retinal Thickness (TRT), Chorioretinal Folds and Brain Ventricle Expansion.**

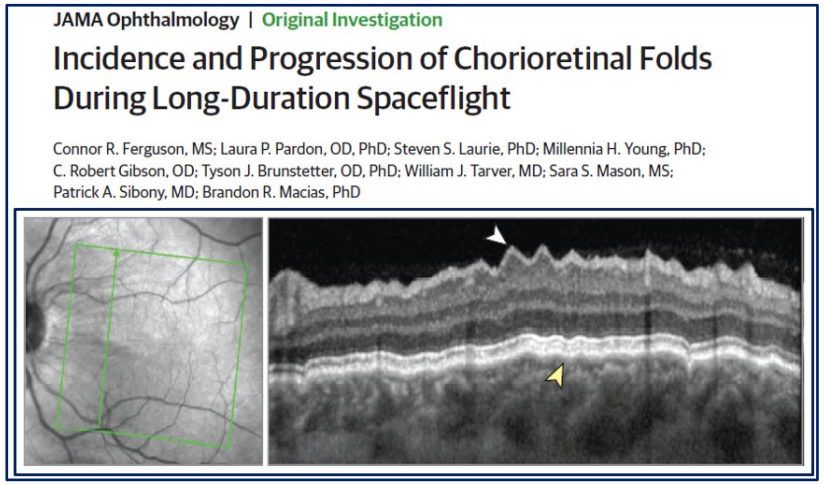
## Headward Fluid Shift



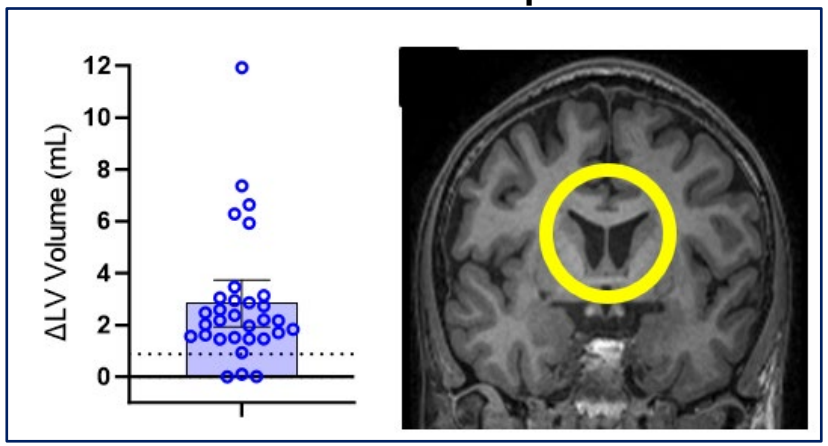

## Optic Disc Edema (TRT)




## Chorioretinal Folds




## Brain Ventricle Expansion



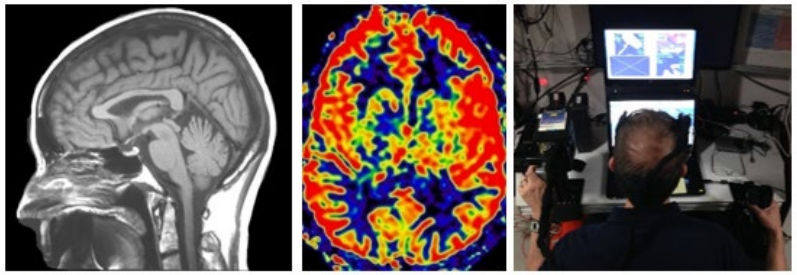

## HRP Research Strategy focuses on:

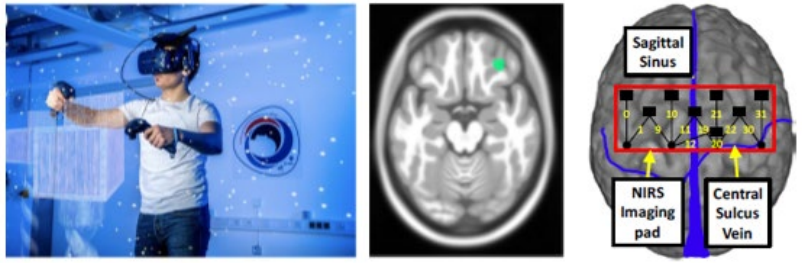
- **Characterizing morphological changes and determining clinical significance.**
- **Developing preventative or treatment countermeasures as necessary.**

# SANS Characterization Studies

## Long-Term Health

Goal: To quantify the long-term changes in (1) brain and (2) eye structure that remain or develop after long-duration spaceflight and to characterize associated changes in functional outcomes.





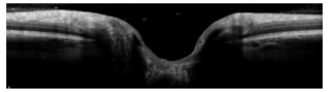

**Collaboration with HFBP Element to characterize Long Term Health consequence of spaceflight.**

**Includes novel biomarkers of brain health.**

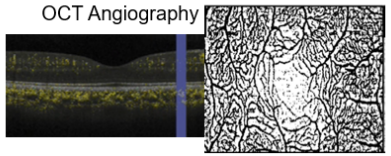
## CIPHER iSAFE

**Retinal Structure and Function**

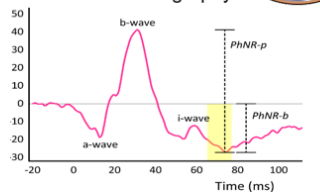
Optical Coherence Tomography (OCT)



OCT Angiography

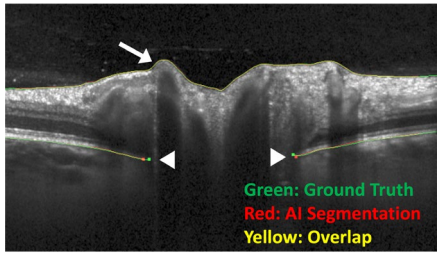


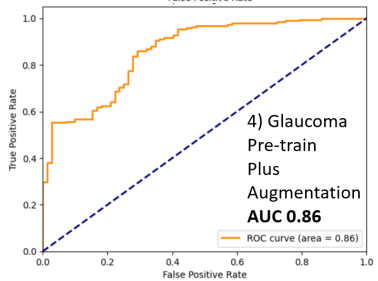
Electroretinography




Goal: Identify underlying SANS mechanisms and characterize progression and recovery.

## Artificial Intelligence



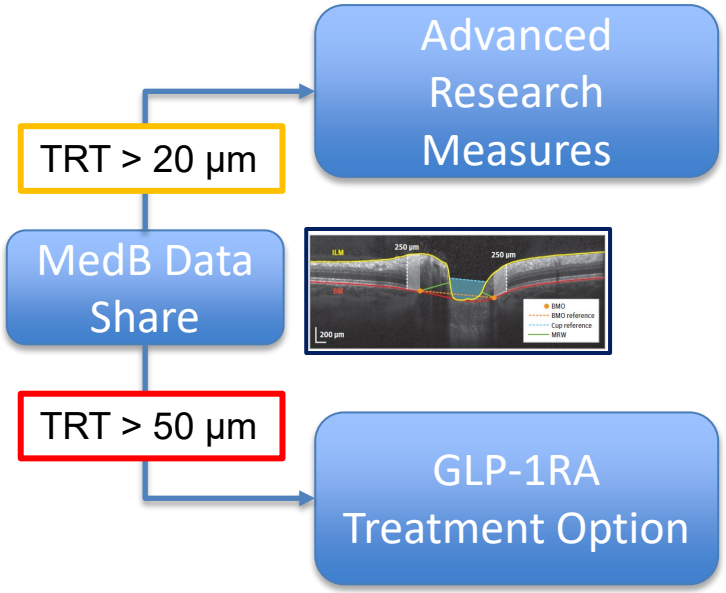




Machine learning approach to train model to recognize key anatomical features relevant to SANS

**Artificial Intelligence may be able to predict who is at risk for developing SANS.**

## SANS DSO/DCO

Goal: (1) Increase sample size of advanced research measures and (2) offer potential treatment for clinically significant cases.

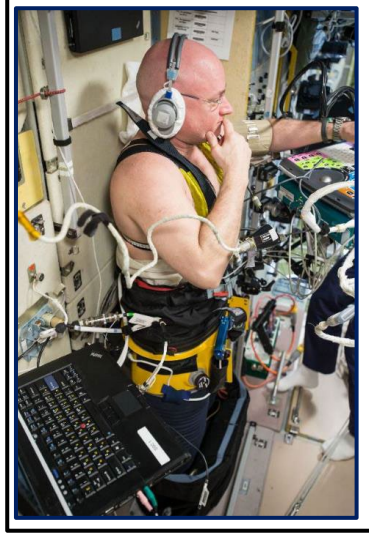




GLP-1 Receptor Agonist

# SANS Countermeasure Studies

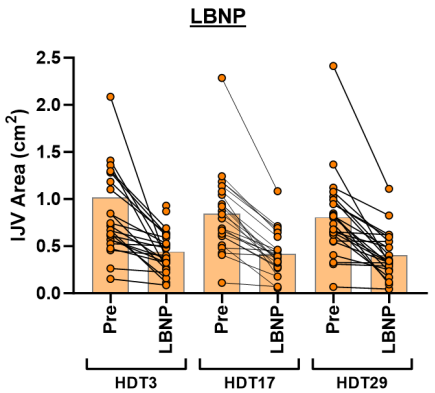
## Lower Body Negative Pressure



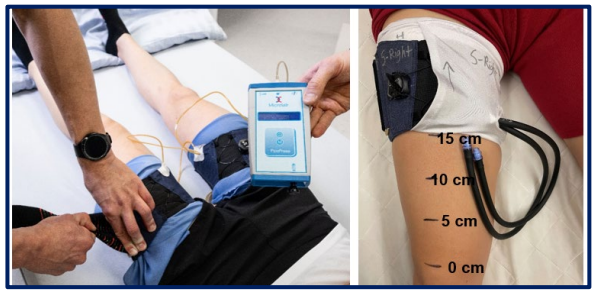
Proven to reduce headward fluid shift.

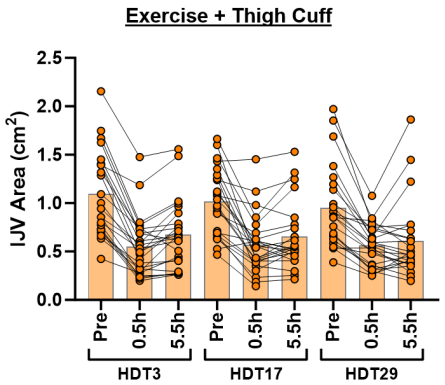
Prescription as an inflight countermeasure needs to be determined.

**Mobile Flight Unit in development.**



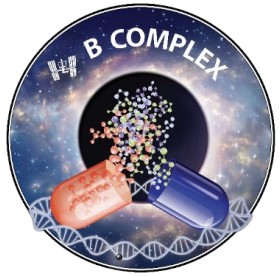

## Veno-constrictive Thigh Cuffs



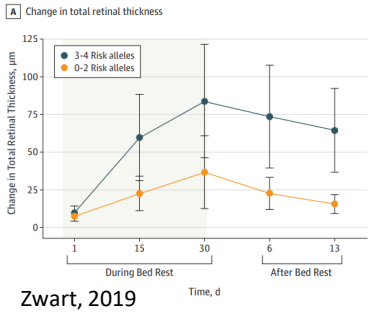




Proven to reduce headward fluid shift.
Prescription as an inflight countermeasure needs to be determined.
**Current ongoing flight study evaluating safety, comfort and efficacy.**

## Antioxidants / B-Vitamins




Single Nucleotide Polymorphisms (SNPs) in the 1 Carbon nutrition pathway may predispose individuals to optic disc edema via a vascular dysfunction mechanism.




Zwart, 2019

**Current flight study ongoing to evaluate B-Vitamin supplementation as a countermeasure.**

## GLP-1R Agonist / ICP Bed Rest


GLP-1RA's have been shown to reduce ICP in IIH patients. Exenatide will be tested as a SANS countermeasure at the DLR :envihab facility.

**This will be the first study to measure ICP (lumbar puncture) in a spaceflight analog.** Study approved and planned to start next year.

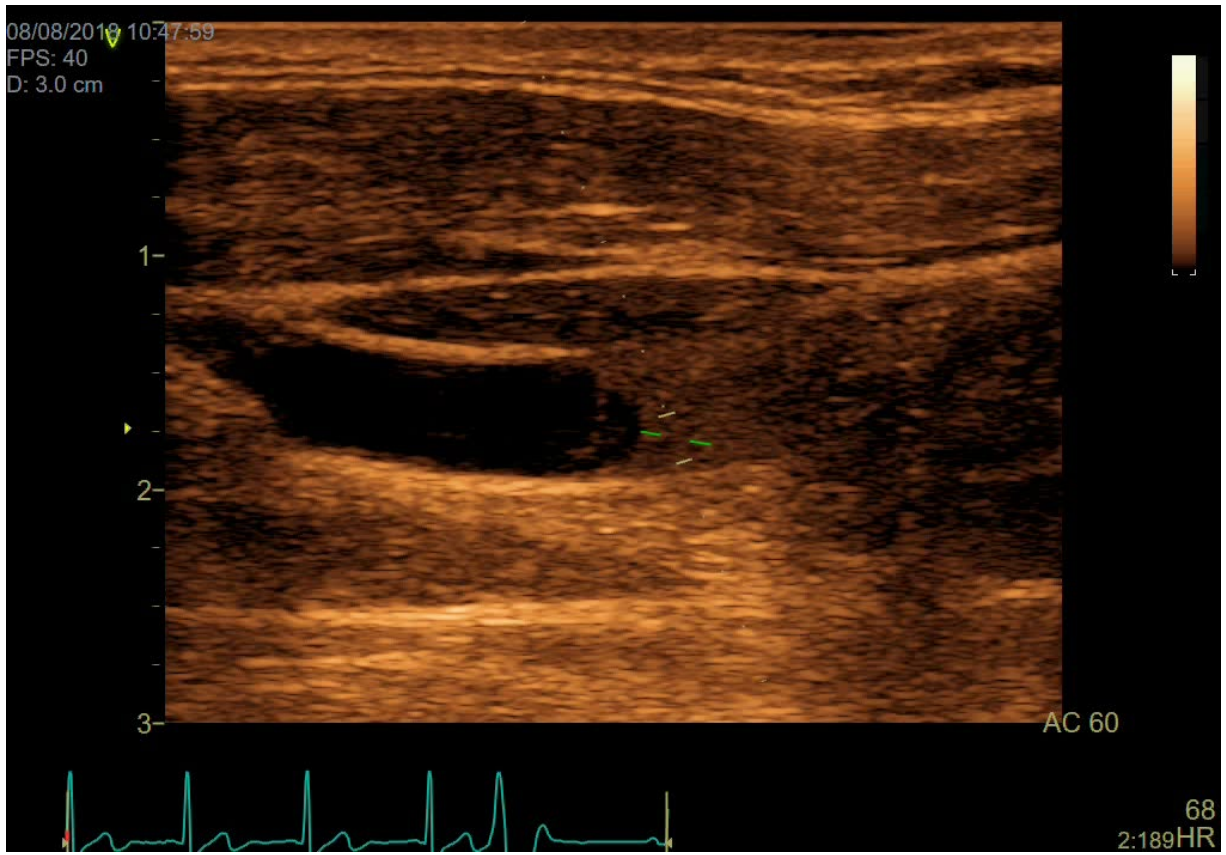
# Human Research Program (HRP) Approach - VTE

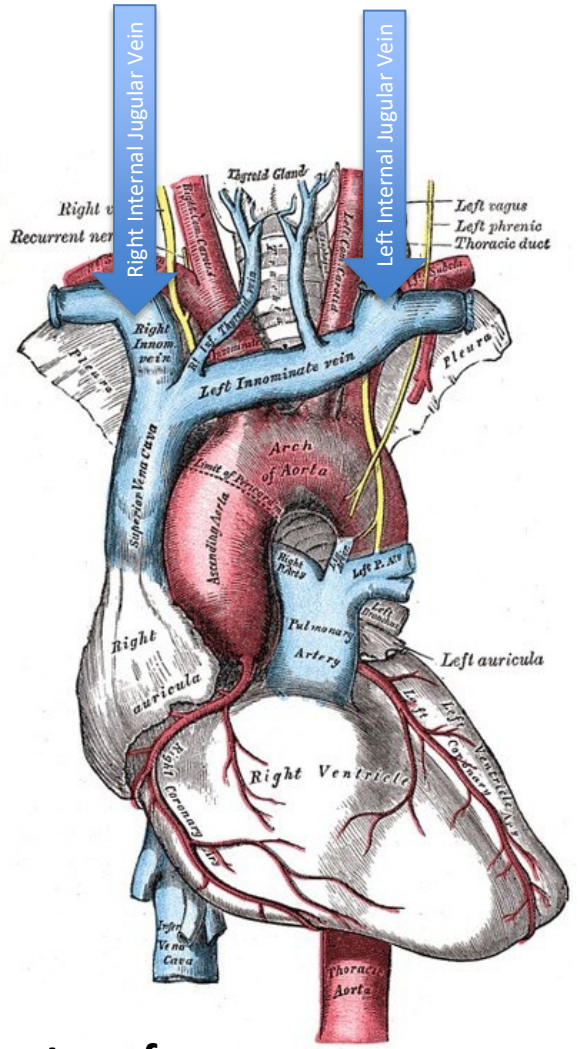
JAMA Network | Open

Original Investigation | Cardiology

## Assessment of Jugular Venous Blood Flow Stasis and Thrombosis During Spaceflight

Karina Marshall-Goebel, PhD; Steven S. Laurie, PhD; Irina V. Alferova, MD, PhD; Philippe Arbeille, MD, PhD; Serena M. Auñón-Chancellor, MD; Douglas J. Ebert, PhD; Stuart M. C. Lee, PhD; Brandon R. Macias, PhD; David S. Martin, MS; James M. Pattarini, MD; Robert Ploutz-Snyder, PhD; L. Christine Ribeiro, JD; William J. Tarver, MD; Scott A. Dulchavsky, MD; Alan R. Hargens, PhD; Michael B. Stenger, PhD




**HRP Research Strategy focuses on:**

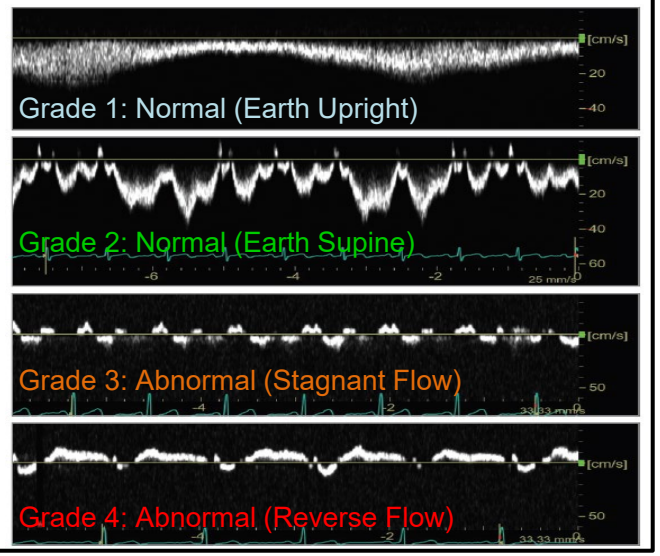
- **Characterizing venous stasis and thrombus formation.**
- **Developing preventative countermeasures.**

# Venous Thrombus Research Studies

## Parabolic Flight Assessment of Venous Flow

**Stagnant blood flow can occur with only brief periods of weightlessness, even at partial gravity levels.**

**Thus, clotting risk may exist in Lunar/Martian gravity.**




## Bed Rest Surveillance

Upcoming Spaceflight Analog study at DLR :envihab facility (60 day head-down bed rest)

Jugular vein flow stasis has only been seen a few times during bed rest studies.

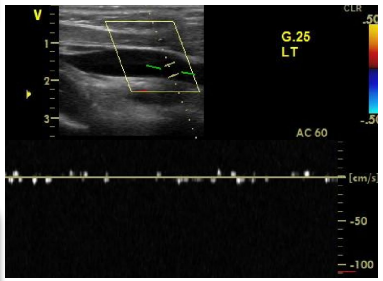
Periodically, Ultrasound will be used to determine if flow stasis occurs. If detected, further ultrasound and MRI assessment of vascular anatomy will be pursued to investigate possible anatomical phenotype.

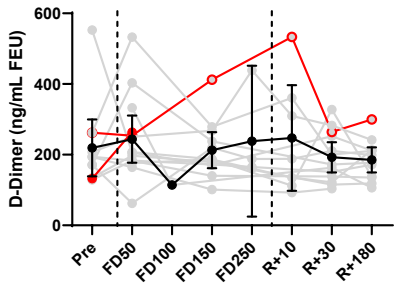
## Venous Thrombus Flight DSO

MedB Data Share

Flow Stasis

Additional Ultrasound & Biomarkers






<u>Goal:</u> Increase sample size of advanced research measures and to better characterize venous thrombus risk.

## HERO Research Solicitation

National Aeronautics and Space Administration
Johnson Space Center
Human Exploration and Operations Mission Directorate
Human Research Program
Houston, TX 77058

Human Exploration Research Opportunities (HERO)
NNJ23ZSA001N-FLAGSHIP
Appendix E: Venous Thrombosis Concern during Spaceflight

NASA Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions

HRP Research Solicitation will be released in May 2024.

Purpose is to fund research to identify:

- Causes of flow stasis / thrombus formation
- Novel biomarkers of flow stasis / thrombus risk
- Countermeasures to flow stasis / thrombus risk

# Schedule


ISS Retirement

Ground Study

Flight Study

| | FY23 | FY24 | FY25 | FY26 | FY27 | FY28 | FY29 | FY30 | FY31 | FY32 | FY33 | FY34 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **SANS Characterization Studies** | SANS Long Term Health | | | | | | | | TBD on CLDs | | | |
| | CIPHER iSAFE | | | | | | | | | | | |
| | SANS DSO | | | | | | | | | | | |
| | AI SANS Prediction | | | | | | | | | | | |
| **SANS Countermeasure Studies** | SANS DCO (GLP-1) | | | | | | | | TBD on CLDs | | | |
| | Lower Body Negative Pressure | | | | | | | | | | | |
| | Veno-constrictive Thigh Cuffs | | | | | | | | | | | |
| | Anti-oxidants/B-vitamins | | | | | | | | | | | |
| | GLP-1R Agonist/ICP Bedrest | | | | | | | | | | | |
| **Venous Thrombosis Research Studies** | Parabolic Flight Assessment of Venous Flow | | | | | | | | TBD on CLDs | | | |
| | Venous Thrombosis Bedrest Surveillance | | | | | | | | | | | |
| | Venous Thrombosis Flight DSO | | | | | | | | | | | |
| | Venous Thrombosis HERO Research Solicitation | | | | | | | | | | | |