

## **Astronaut preflight cardiovascular variables associated with vascular compliance are highly correlated with post-flight eye outcome measures in the Visual Impairment Intracranial Pressure (VIIP) syndrome following long duration spaceflight.**

### Methods:

The detection of the first VIIP case occurred in 2005, and adequate eye outcome measures were available for 31 (67.4%) of the 46 long duration US crewmembers who had flown on the ISS since its first crewed mission in 2000. Therefore, this analysis is limited to a subgroup (22 males and 9 females). A “cardiovascular profile” for each astronaut was compiled by examining twelve individual parameters; eleven of these were preflight variables: systolic blood pressure, pulse pressure, body mass index, percentage body fat, LDL, HDL, triglycerides, use of anti-lipid medication, fasting serum glucose, and maximal oxygen uptake in ml/kg. Each of these variables was averaged across three preflight annual physical exams. Astronaut age prior to the long duration mission, and inflight salt intake was also included in the analysis. The group of cardiovascular variables for each crew member was compared with seven VIIP eye outcome variables collected during the immediate post-flight period: anterior-posterior axial length of the globe measured by ultrasound and optical biometry; optic nerve sheath diameter, optic nerve diameter, and optic nerve to sheath ratio- each measured by ultrasound and magnetic resonance imaging (MRI), intraocular pressure (IOP), change in manifest refraction, mean retinal nerve fiber layer (RNFL) on optical coherence tomography (OCT), and RNFL of the inferior and superior retinal quadrants. Since most of the VIIP eye outcome measures were added sequentially beginning in 2005, as knowledge of the syndrome improved, data were unavailable for 22.0% of the outcome measurements. To address the missing data, we employed multivariate multiple imputation techniques with predictive mean matching methods to accumulate 200 separate imputed datasets for analysis. We were able to impute data for the 22.0% of missing VIIP eye outcomes. We then applied Rubin’s rules for collapsing the statistical results across our 200 multiply imputed data sets to assess the canonical correlation between the eye outcomes and the twelve astronaut cardiovascular variables available for all 31 subjects.

### Results:

A highly significant canonical correlation was observed among the canonical solutions ( $p < .00001$ ), with an average best canonical correlation of .97. The results suggest a strong association between astronauts’ measures of cardiovascular health and the seven eye outcomes of the VIIP syndrome used in this analysis. Furthermore, the “joint test” revealed a significant difference in cardiovascular profile between male and female astronauts ( $\text{Prob} > F = 0.00001$ ). Overall, female astronauts demonstrated a significantly healthier cardiovascular status. Individually, the female astronauts had significantly healthier profiles on seven of twelve cardiovascular variables than the men ( $p$  values ranging from  $< 0.0001$  to  $< 0.05$ ). Male astronauts did not demonstrate significantly healthier values on any of the twelve cardiovascular variables measured when compared with the female astronauts.