INTRODUCTION
NASA’s Human Research Program is focused on addressing health risks associated with long-duration missions on the International Space Station (ISS) and future exploration-class missions beyond low Earth orbit. Visual acuity changes observed after short-duration missions were largely transient, but now more than 50% of ISS astronauts have experienced more profound, chronic changes with objective structural findings such as optic disc edema, globe flattening and choroidal folds. These structural and functional changes are referred to as the visual impairment and intracranial pressure (VIIP) syndrome. Development of VIIP symptoms may be related to elevated intracranial pressure (ICP) secondary to spaceflight-induced cephalad fluid shifts, but this hypothesis has not been tested. The purpose of this study is to characterize fluid distribution and compartmentalization associated with long-duration spaceflight and to determine if a relation exists with vision changes and other elements of the VIIP syndrome. We also seek to determine whether the magnitude of fluid shifts during spaceflight, as well as any VIIP-related effects of those shifts, are predicted by the crewmember’s pre-flight status and responses to acute hemodynamic manipulations, specifically posture changes and lower body negative pressure.

METHODS
We will examine a variety of physiologic variables in 10 long-duration ISS crewmembers using the test conditions and timeline presented in the figure below. Measures include (1) fluid compartmentalization (total body water by D₂O, extracellular fluid by NaBr, intracellular fluid by calculation, plasma volume by CO rebreathe, interstitial fluid by calculation); (2) forehead/eyelids, tibia, and calcaneus tissue thickness (by ultrasound); (3) vascular dimensions by ultrasound (jugular veins, cerebral and carotid arteries, vertebral arteries and veins, portal vein); (4) vascular dynamics by MRI (head/neck blood flow, cerebrospinal fluid pulsatility); (5) ocular measures (optical coherence tomography; intraocular pressure; 2-dimensional ultrasound including optic nerve sheath diameter, globe flattening, and retina-choroid thickness; Doppler ultrasound of ophthalmic and retinal arteries and veins); (6) cardiac variables by ultrasound (inferior vena cava, tricuspid flow and tissue Doppler, pulmonic valve, stroke volume, right heart dimensions and function, four-chamber views); and (7) ICP measures ( tympanic membrane displacement, otoacoustic emissions). Pre- and post-flight, acute head-down tilt will induce cephalad fluid shifts, whereas lower body negative pressure will oppose these shifts. Controlled Mueller maneuvers will manipulate cardiovascular variables. Through interventions applied before, during, and after flight, we intend to fully evaluate the relationship between fluid shifts and the VIIP syndrome.

DISCUSSION
Ten subjects have consented to participate in this experiment, including the recent One-Year Mission crewmembers, who have recently completed R+180 testing; all other subjects have completed pre-flight testing. Preliminary results from the One-Year Mission crewmembers will be presented, including measures of ocular structure and function, vascular dimensions, fluid distribution, and non-invasive estimates of intracranial pressure.