**BACKGROUND**

Visual Impairment/Intracranial Pressure (VIP) is a top human spaceflight risk for which NASA does not currently have a proven mitigation strategy. Thigh cuffs and lower body negative pressure (LBNP) devices have been or are currently being evaluated as a means to reduce VIP signs and symptoms, but these methods alone may not provide sufficient relief of cephalic venous congestion and VIP symptoms. Additionally, current LBNP devices are too large and cumbersome for their systematic use as a countermeasure. Therefore, a novel approach is needed that is easy to implement and provides specific relief of symptoms. This investigation will evaluate an impedance threshold device (ITD) as a VIP countermeasure.

The ITD provides up to 7 cm H2O (~5 mmHg) resistance to inspiratory air flow, which upon each inhalation effectively turns the thorax into a vacuum pump that lowers the intrathoracic pressure (ITP) to facilitate venous return to the heart. The ITD is FDA-approved and was developed to augment venous return to the heart and increase cardiac output in patients with hypotension and during cardiopulmonary resuscitation (CPR). While the effect of ITD on CPR survival outcomes is controversial, it’s ability to lower ITP with a concomitant decrease in intracranial pressure (ICP) is well documented. A similar concept that creates negative ITP during inhalation (intrathoracic pressure regulator; ITPR) decreased ICP in 16 of 20 patients with elevated ICP in a hospital pilot study. ITP and central venous pressure (CVP) have been shown to decrease in microgravity. However, ITP drops more than CVP, indicating an increased transmural CVP. This could explain the paradoxical distention of jugular veins (JV) in microgravity despite lower absolute CVP and also suggests that JV transmural pressure is not dramatically elevated. Use of an ITD may lower JV pressure enough to remove or relieve cephalic venous congestion.

During spaceflight experiments Braslet thigh cuffs reduced cardiac preload but only reduced the internal jugular (IJV) cross sectional area by 23%. The addition of modified (open-glottis) Mueller maneuvers resulted in an IJV area reduction of 48%. This project will test the ITD’s ability to lower ITP in each respiratory cycle, acting to: 1) reduce venous congestion in the head and neck and 2) reduce ICP based on noninvasive indicators. The expected mechanism of action for relief of venous congestion is that in microgravity (or an analog), blood is relocated toward the heart from vasculature in the head and neck. Reduction of ICP would occur as a result of reduced ITP.

Once validated, the ITD would be an exceptionally easy countermeasure to deploy and test on the ISS. Dosage could be altered through 1) duration of application and 2) inspiratory resistance set point. Effects could be additionally enhanced through co-application with other countermeasures such as thigh cuffs or LBPN.

**SPECIFIC AIMS**

Using a supine and head down tilt (HDT) model, this investigation will:

1. Determine if an ITD can reduce venous congestion in the head and neck
2. Determine if an ITD can reduce indicators of elevated intracranial pressure

**METHODS**

The experimental approach is to use a battery of tests that are currently being used to evaluate the effects of other interventions. Healthy test subjects (n=15) will participate in two sessions, one with an ITD and one with a sham ITD (placebo). Subjects will be evaluated in the seated and supine positions as well as 6° and 15° HDT postures. Measures taken at each posture will include IJV cross sectional area, carotid artery Doppler, measures of cardiac preload, transcranial Doppler (TCD), optic nerve sheath diameter (ONSD), superior ophthalmic vein (SOV) Doppler, facial soft tissue thickness, IJV pressure (VeinPress), optical coherence tomography (OCT), cochlear and cerebral fluid pressure analysis (CCFP), otocoustic emissions (OAE), and intracranial pressure (IOP). Blood pressure, ECG, heart rate, and transcutaneous PO2 and PCO2 will be monitored throughout the experiment. Blood samples will be drawn and archived for potential one carbon pathway analysis.

**REFERENCES**


**PILOT RESULTS**

Figure 3: Effect of ITD breathing on UV cross-sectional area in the supine position. A: M-mode across the UV without ITD, B: B-mode (2D) image of the UV without ITD, C: M-mode across the UV with ITD, D: B-mode image of the UV without ITD. In panels A and C ECG is the green trace and respiration in red.

Figure 4: Effect of ITD breathing on UV time-weighted cross sectional area in different postures (n=1). UV cross sectional area was time-averaged over one full respiratory cycle at 15° (head up tilt (HUT)), Supine, and 15° head down tilt (HDT), each posture with and without ITD breathing.

Figure 5: Noninvasive indication of ICP changes in response to ITD breathing at different postures. Tympnic Membrane Displacement (TMD) values in n=2 trials each panel. A: subjects at 15° head up tilt (HUT), Supine, 15° head down tilt (HDT), and Supine with ITD breathing (Supine+ITD). B: subjects at 30° head up tilt (30HUT), Supine, 15° head down tilt (30HDT), and 15° head down tilt with ITD breathing (15HDT+ITD). Higher TMD displacement values indicate lower ICP.

**DISCUSSION**

Pilot data demonstrate substantial reductions in UV cross sectional area and in estimated ICP as measured by CCFP. Human subject testing is planned for February 2017.

The investigation team recognizes that ITD use as a routine countermeasure during spaceflight may not be particularly comfortable in its current form and function. The purpose of the planned work is to 1) use the ITD as a tool to further understand VIP, and 2) establish the effectiveness of this methodology before embarking on more in-depth investigations to develop and validate a countermeasure with optimized crewmember acceptability.

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