



Evaluation of an Impedance Threshold Device as a VIIP Countermeasure

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BACKGROUND

Visual Impairment/Intracranial Pressure (VIIP) is a top human spaceflight risk for which NASA does not currently have a proven mitigation strategy. Thigh cuffs (Braslets) and lower body negative pressure (LBNP; Chibis) devices have been or are currently being evaluated as a means to reduce VIIP signs and symptoms, but these methods alone may not provide sufficient relief of cephalic venous congestion and VIIP 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 VIIP countermeasure.



Figure 1: ITD and face mask

The ITD works by providing up to 7 cm H₂O (~5 mmHg) resistance to inspiratory air flow, effectively turning the thorax into a vacuum pump upon each inhalation that lowers the intrathoracic pressure (ITP) and facilitates venous return to the heart. The ITD is FDA-approved and was developed to augment venous return to the central circulation and increase cardiac output during cardiopulmonary resuscitation (CPR) and in patients with hypotension. While the effect of ITD on CPR survival outcomes is controversial, the ITD's ability to lower ITP with a concomitant decrease in intracranial pressure (ICP) is well documented¹. A similar concept that creates negative ITP during exhalation (intrathoracic pressure regulator; ITPR) decreased ICP in 16 of 20 patients with elevated ICP in a hospital pilot study². ITP and central venous pressure (CVP) have been shown to decrease in microgravity^{3,4}. 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.

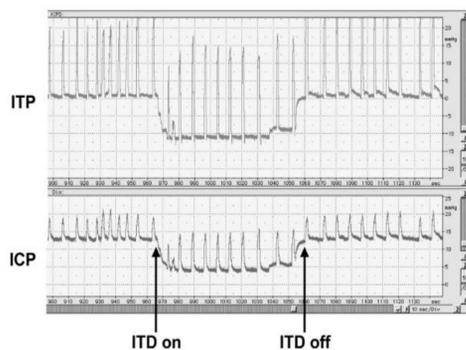


Figure 2: Effect of ITD use on ITP and ICP in a porcine model (from Convertino et al.)¹

During spaceflight experiments with Braslet thigh cuffs and modified (open-glottis) Mueller maneuvers, Braslets alone reduced cardiac preload but only reduced the internal JV (IJV) cross sectional area by 23%. The addition of Mueller maneuvers resulted in an IJV area reduction of 48%⁵. This project will test if ITD essentially applies a Mueller maneuver with added negative ITP in every respiratory cycle, acting to: 1) reduce venous congestion in the neck and 2) potentially lower ICP. The expected mechanism of action is that in microgravity (or an analog), blood is relocated toward the heart from vasculature in the head and neck.

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 LBNP.

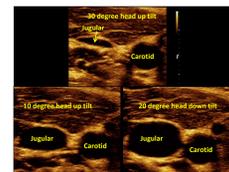
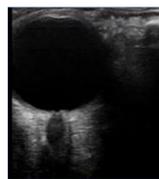
SPECIFIC AIMS

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

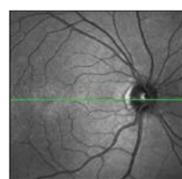
1. Determine if an ITD can reduce venous congestion in the head and neck
2. Determine if an ITD can reduce indicators of elevated intracranial pressure

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). Blood pH and pCO₂ measures will be made immediately prior to and following each session. Subjects will be evaluated in the seated and supine positions as well as head down tilt (HDT) postures, including 6 and 15 degree HDT. Measures taken at each posture will include IJV cross sectional area, IJV and carotid artery Doppler, measures of cardiac preload, transcranial Doppler (TCD), optic nerve sheath diameter (ONSD), superior ophthalmic vein (SOV) Doppler, optical coherence tomography (OCT), cochlear and cerebral fluid pressure analysis (CCFP), otoacoustic emissions (OAE), intraocular pressure (IOP), facial soft tissue thickness and hyperemia, arterial blood pressure, ECG, and heart rate.



Posture	Time
Upright (seated)	15 min
Supine	15 min
Upright, mask off (washout)	5 min
6° HDT	15 min
Upright, mask off (washout)	5 min
15° HDT	15 min
15° HDT, no data collection	30 min
15° HDT	15 min



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PILOT RESULTS

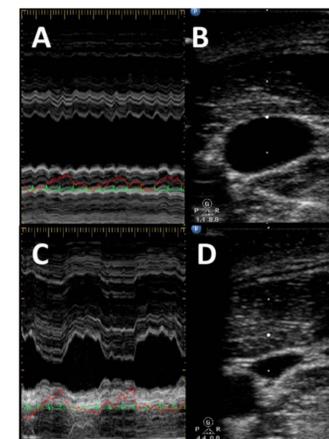


Figure 3: Effect of ITD breathing on IJV cross-sectional area in the supine position. A: M-mode across the IJV without ITD, B: B-mode (2D) image of the IJV without ITD, C: M-mode across the IJV with ITD, D: B-mode image of the IJV with ITD. In panels A and C ECG is the green trace and respiration in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

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

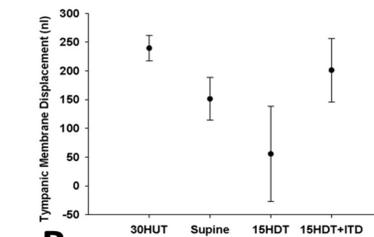
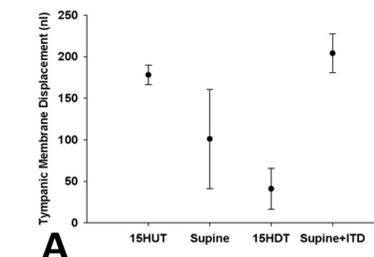
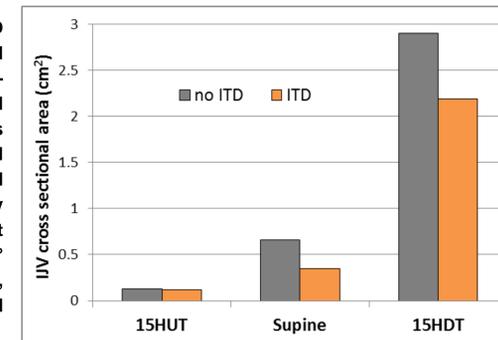


Figure 5: Noninvasive indication of ICP changes in response to ITD breathing at different postures. Tympanic Membrane Displacement (TMD) values in n=2 trials each panel. A: subjects at 15° head up tilt (15HUT), Supine, 15° head down tilt (15HDT), and Supine with ITD breathing (Supine+ITD). B: subjects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

DISCUSSION

Pilot data demonstrate substantial reductions in IJV cross sectional area and in estimated ICP as measured by CCFP. Study funding commenced in November 2015 with human subject testing planned for spring 2016.

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 VIIP, and 2) establish the effectiveness of this methodology before embarking on more in-depth investigations that could optimize acceptability to crewmembers as a countermeasure.

ACKNOWLEDGEMENTS

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