INTRODUCTION: Intracranial pressure (ICP) is currently monitored invasively and is a clinically important measurement for trauma and neurosurgery patients. ICP may also be an important factor in conditions resulting from physiological fluid shifts, such as symptoms of space adaptation syndrome that occur during the first few days in a microgravity environment. Fluid shifts similar to those experienced during exposure to microgravity have been simulated on Earth using head-down tilt (HDT) bedrest studies. Although the skull is often assumed to be a rigid container with a constant volume, many animal studies have demonstrated that the skull moves on the order of a few microns (µm) in association with changes in ICP due to arterial pulsations. The described noninvasive technique is based upon detecting these small skull movements which occur with fluctuations in ICP.

PURPOSE: These studies were designed to develop an in-vitro calibration and characterization tool for this ultrasonic technique for measuring ICP and to apply the technique in-vivo to evaluate the effect of 30 days of head-down tilt (HDT) bedrest on cranial dynamics.

CURRENT STATUS OF RESEARCH

Methods: This noninvasive ultrasound technique detects skull pulsation and is based upon a modification of a pulse phase lock loop (PPLL) design, making it possible to measure slight changes in distance between an ultrasound transducer and a reflecting target. A 500 kHz ultrasonic tone burst is transmitted through the cranium via a transducer placed on the head. The wave passes through the cranial cavity, reflects off the inner surface of the opposite side of the skull, and is received by the same transducer. The instrument compares the phase of emitted and received waves and alters the frequency of the next stimulus to maintain a 90° phase difference between the output of the device and the received signal. A change in pathlength (diameter) results in a phase shift and the voltage of the instrument output signal reflects this phase difference that occurs due to changes in cranium dimensions.

A portable, in-vitro system was designed to calibrate the PPLL instrument output prior to in-vivo measurements. The ultrasound transducer was mounted to a stepper motor assembly and submersed in a water bath. The pathlength, magnitude of displacement, and oscillation frequency were user adjustable and computer-controlled. Clinically relevant parameters were studied to establish sensitivity and to calibrate the instrument output as a function of frequency and displacement.

In-vivo measurements were performed on four sets of healthy, male, identical twin volunteers as part of a larger, 30-day HDT bedrest protocol simulating fluid shifts that occur in microgravity. The patients were in a supine position and the ultrasound transducer was secured to the temporal region of the skull. The arterial blood pressure was monitored via a cuff transducer placed on a finger. Measurements were performed at the beginning and the end of the bedrest period to evaluate effects of 30 days simulated microgravity on the magnitude of cranial oscillations. PPLL instrument output voltage and digit blood pressure were measured continuously and digitized under computer control for subsequent analysis.

Results: The in-vitro studies demonstrated that the PPLL instrument output voltage was proportional to displacement amplitude as measured from 1-50µm (Fig. 1). The output voltage amplitude tracked the displacement oscillations, increasing when pathlength increased and decreasing during pathlength reduction. The output signal oscillation frequency matched that of the stepper motor frequency over the expected physiological range (0.5 – 2 Hz). In-vivo results showed that PPLL signal output frequency corresponded to the measured heart rate of the subject and the signal amplitude was highest during systole and lowest during diastole. The measured amplitude was 25 ± 9 mV (mean ± std dev) before HDT bedrest (Fig. 2). Following the 30-day bedrest period, the amplitude was significantly reduced by approximately 60% to 9 ± 4 mV (Wilcoxon test, p = 0.01). Applying the results obtained from the calibration measurements
(-1.5mV/µm), the displacement amplitude was approximately 16µm before bedrest and 6µm following bedrest, a decrease on the order of 10µm.

**Conclusion:** The calibration system provides a useful tool for instrument characterization and development, and for quantifying the relationship between signal amplitude and magnitude of displacement. In-vivo measurements estimate cranial displacements of 6-16µm at frequencies corresponding to those of the arterial blood pressure oscillations, supporting previously published observations made using invasive techniques. A normally upright subject placed in a supine posture experiences an increase in measured cranial oscillations believed to be due to gravity-induced physiologic fluid shifts toward the upper body. In an upright position, measured displacements are typically reduced by >50% as compared to supine position. Following a 30-day period in supine position, skull pulsation amplitudes decreased by 60%, suggesting that there are physiological adaptations to these fluid shifts which reduce amplitudes to values similar to those found in an upright position. Detailed studies of the early time course of ICP adaptation to microgravity may provide insights into potential mechanisms and development of countermeasures for space adaptation syndrome.

**FUTURE PLANS:** The calibration system will be used to characterize further the instrumentation and to evaluate modifications. In-vivo experimentation will be performed in normal volunteers to investigate physiological fluid shifts further and explore potential medical applications.

**INDEX TERMS:** instrumentation, intracranial pressure, bedrest, microgravity, adaptation, skull

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