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● *Original Contribution*

TISSUE PULSATILITY IMAGING OF CEREBRAL VASOREACTIVITY DURING HYPERVENTILATION

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Abstract—Tissue pulsatility imaging (TPI) is an ultrasonic technique that is being developed at the University of Washington to measure tissue displacement or strain as a result of blood flow over the cardiac and respiratory cycles. This technique is based in principle on plethysmography, an older nonultrasound technology for measuring expansion of a whole limb or body part due to perfusion. TPI adapts tissue Doppler signal processing methods to measure the "plethysmographic" signal from hundreds or thousands of sample volumes in an ultrasound image plane. This paper presents a feasibility study to determine if TPI can be used to assess cerebral vasoreactivity. Ultrasound data were collected transcranially through the temporal acoustic window from four subjects before, during and after voluntary hyperventilation. In each subject, decreases in tissue pulsatility during hyperventilation were observed that were statistically correlated with the subject's end-tidal CO_2 measurements. (E-mail: kucewicz@u.washington.edu) **© 2008 World Federation for Ultrasound in Medicine & Biology.**

Key Words **Ultrasound, Tissue pulsatility imaging, Brain imaging, Tissue Doppler imaging, Hyperventilation, Hypocapnia, Cerebral vasoreactivity.**

INTRODUCTION

Over the past two decades, there has been growing research and clinical interest in developing ultrasound (US) methods to measure tissue displacement and strain. Of particular interest have been the measurement of myocardial contractility (Heimdal et al. 1998; Kanai et al. 1999; Kowalski et al. 2001; McDicken et al. 1992) and the measurement of tissue mechanical properties (Gao et al. 1996; Ophir et al. 1991, 1999). Over this period, there have been relatively few publications describing applications of these methods to brain imaging. Moehring et al. (1999) describe a method for measuring brain shifts to detect intracranial bleeding, Selbekk et al. (2005) describe an elastographic method for tumor margin detection during brain surgery and Kucewicz et al. (2007) describe a method for measuring tissue displacement for functional brain imaging.

Some of the earliest work with measuring tissue motion with US, however, was done on the brain. Comprehensive reviews of this work can be found in Campbell et al. (1970) and White (1992). It was first observed by Leksell (1956) that the amplitude of the US signal from the cerebral midline pulsated synchronously with the cardiac cycle. Later it was observed that the cerebral hemispheres pulsated 180° out of phase with each other because of the opposing, centripetal movement of the two hemispheres (Taylor et al. 1961; de Vlieger and Ridder 1959). Campbell et al. (1970) described the influence of various physiological manipulations including breath-holding, hyperventilation, Valsalva maneuver and jugular vein compression on brain motion. Much of this early work was limited, however, by the US hardware available at the time and was not extensively pursued after the 1970s as research and clinical interests shifted to US blood flow measurement.

At the University of Washington we are developing a Doppler US technique referred to as tissue pulsatility imaging (TPI) that measures the natural pulsatile motion of tissue due to blood flow as a surrogate for blood flow

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itself (Beach et al. 1992, 1993, 1994; Kucewicz et al. 2004, 2007). During systole, blood flows into the arterial vasculature faster than it leaves through the venous vasculature, causing blood to accumulate and the tissue to expand by a fraction of a percent. During diastole, venous drainage dominates, allowing the tissue to return to its presystolic volume (Campbell et al. 1970; Strandness and Sumner 1975). As with other perfused tissues, changing blood volume causes the brain to expand and relax over the cardiac cycle. Because the volume of the brain is constrained by the fixed volume of the skull, expansion of the brain early in the cardiac cycle compresses the cerebral ventricles, forcing cerebrospinal fluid (CSF) out of the skull. Later in the cardiac cycle, brain blood volume decreases, drawing CSF back into the skull. This expansion of the brain and compression of the cerebral ventricles causes the brain to move medially during systole and laterally during diastole (Campbell et al. 1970). In addition, the changing blood volume pushes the brain posteriorly and caudally toward the foramen magnum during systole followed by a rebound during diastole (Maier et al. 1994; Poncelet et al. 1992).

Cerebral vasoreactivity (CVR) is the ability of the cerebral arterioles to respond to changes in arterial CO_2 partial pressure ($PaCO_2$) to regulate blood flow and oxygen delivery to the brain. Under normal conditions, hypercapnia, an increase in $PaCO_2$, will cause the cerebral arterioles to dilate, reducing vascular resistance and increasing cerebral blood flow (CBF). Hypocapnia, a decrease in arterial $PaCO_2$, will cause the cerebral arterioles to constrict, increasing vascular resistance and reducing CBF.

Cerebral vasoreactivity is most commonly tested by having subjects breathe increasing concentrations of CO_2 or administering acetazolamide to increase $PaCO_2$, or by having subjects voluntarily hyperventilate to decrease $PaCO_2$ (Manno and Koroshetz 1999). Measurement of CVR has been used to evaluate cerebral vascular function over a broad range of clinical applications, including to monitor the severity of brain damage after an ischemic event (Dohmen et al. 2007), to predict the risk of a cerebral ischemic event in patients with carotid occlusive disease (Diehl 2002; Kleiser and Widder 1992; Markus and Cullinane 2001; Vernieri et al. 1999; Webster et al. 1995; Yonas et al. 1993), to assess the efficacy of a carotid endarterectomy (Herzig et al. 2004) and to study anxiety disorders (Giardino et al. 2007; Mathew and Wilson 1997) and migraine attacks (Akin and Bilensoy 2006).

Magnetic resonance imaging (MRI) (Kassner and Roberts 2004; Kastrup et al. 2001; Posse et al. 1997), positron emission tomography (PET) (de Boorder et al. 2006; Steiner et al. 2003) and near infrared spectroscopy (NIRS) (Smielewski et al. 1995) techniques have all been used to monitor changes in CBF with changes in $PaCO_2$. The most common method used to assess CVR, though, is transcranial Doppler ultrasonography (TCD) (Dahl et al. 1994; Markwalder et al. 1984; Ringelstein et al. 1988; Settakis et al. 2003). TCD provides a low-cost, noninvasive means to measure blood flow velocities in the larger cerebral blood vessels in real time.

A study was conducted to test the feasibility of using TPI to assess CVR. Brain tissue pulsatility was measured in four subjects through the temporal acoustic window using a standard, general-purpose US scanner. Tissue pulsatility was measured before, during and after voluntary hyperventilation, and the results were correlated with the subjects' end-tidal CO_2 measurements collected concurrently with US acquisition.

MATERIALS AND METHODS

Subjects

Four male subjects age 29, 33, 41 and 52 participated in the study. No effort was made to control day of week, time of day or caffeine intake. Written informed consent was obtained from all subjects. The research protocol was approved by the University of Washington Human Subjects Committee.

Protocol

During the study, the subject lay supine on a massage table (Stronglite Inc., Cottage Grove, OR, USA) with his head stabilized in a custom-built, padded fixture. Before the study, ECG leads were attached to the subject's arms, and a cannula was placed in the nostrils to collect expired air. A Terason 4V2 phased-array transducer (Teratech Corp., Burlington, MA, USA), held by an articulated clamp (Manfrotto, Bassano del Grappa, Italy) securely mounted to the table, was positioned over the right US temporal window, slightly anterior and superior to the ear. Before locking the clamp in place, the transducer was positioned by an experienced sonographer to image a nearly transverse plane through the cerebral peduncles.

Each study consisted of three phases, a prehyperventilation phase lasting 6 min 40 s, a voluntary hyperventilation phase lasting 20 min and a posthyperventilation phase lasting 20 min. During the pre and posthyperventilation phases, the subject was instructed to breathe normally through his nostrils to maintain an end-tidal CO_2 around 40 mm Hg. During the hyperventilation phase, the subject was instructed to breathe rapidly (approximately 1 breath every 2 s) through his nostrils to maintain an end-tidal CO_2 around 20 mm Hg. Although not explicitly instructed to do so, subjects maintained a relatively constant depth of respiration throughout the hyperventilation phase.