Cerebrovascular compliance quantification with non-gated, velocity encoded projections

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INTRODUCITON: MR-based methods offer a robust, non-invasive approach to quantifying cerebrovascular compliance (CVC), a measure of microvascular distensibility equal to the change in volume (the pulse volume) divided by the change in pressure (the pulse pressure) of the brain microvasculature over a cardiac cycle: $CVC = \Delta V/\Delta P$ [Eq. 1]. CVC quantification requires resolving arterial inflow and venous outflow waveforms, which are temporally offset due to the dampening or "compliance" of the microvasculature. Subtracting these waveforms gives net flow, half of which must be inflow and half outflow, so that ΔV can be quantified by integrating half of absolute net flow over the cardiac cycle: $\Delta V = 0.5 \cdot \int_{cc} |Q_a - Q_v|\, dt$ [Eq .2].[1] Division by cuff-measured ΔP then gives CVC.

CVC can be thought of as the microvascular analogue of pulse wave velocity (PWV), but unlike PWV, development and application of CVC quantification methods is surprisingly limited. Existing methods[1,2] have used prospectively cardiac gated (PCG) PC-MRI to produce arterial and venous flow waveforms. PCG may results in overly smoothed flow waveforms due to temporal averaging, especially in subjects with unsteady heart rates. To address this limitation, we have explored CVC quantification with retrospectively cardiac gated (RCG) PC-MRI as well as a new non-gated projection (NGP) PC-MRI method. These techniques will allow investigation of CVC as a new marker of cerebral microvascular function and viability.

METHODS: Method 1 – *RCG-Oblique:* A single oblique axial slice was selected for RCG PC-MRI to capture all inflow arteries (basilar and internal carotids) and the superior sagittal sinus (SSS), the largest outflow vein, as near to the microvascular bed as possible to avoid macrovascular contribution to CVC.[3] Acquisition time was ≈100s. Because the SSS represents ≈50% of central venous outflow, its waveform must be scaled to the same average flow as the arterial waveform before applying Eq. 2. This RCG approach is a potential "gold standard" method for CVC quantification, *when* gating is available and the subject's heart rate is steady.

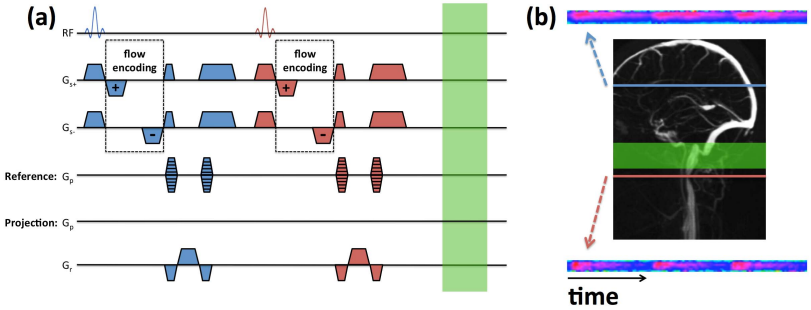

Figure 1: (a) pulse sequence diagram of the phase encoded reference sequence and non-phase encoded projection sequence used to quantify venous flow in the head (blue) and arterial flow in the neck (red) along with a saturation band (green) to prevent venous contamination of the neck slice; **(b)** sagittal MIP demonstrating relative locations of the head and neck interleaves and saturation band with the arrows indicating 1D projection flow waveforms corresponding to 3 cardiac cycles in the SSS (above) and right ICA (below).

Method 2 – NGP: A two-slice interleaved, velocity-encoded GRE sequence was developed to simultaneously resolve flow waveforms in the carotid and vertebral arteries of the neck and superior sagittal sinus (SSS) of the head (Figure 1a). A two-slice approach is required to prevent overlap of arterial and venous vessels in the projection direction. Immediately before the non-phase encoded projection sequence, a fully phase-encoded but otherwise identical reference sequence is used to acquire positive and negative velocity encoded 2D phase maps. The center k-space line of these 2D images, with vessels of interest (VOI) masked, represents the contribution of the background (non-VOI) signal to the projection images, which can be subtracted from the corresponding positive or negative velocity encoded projection lines to obtained background-free velocity encoded projections.[4] Taking the phase difference between consecutive projections produces a stack of time-resolved velocity projection images (Figure 1b) with 30ms temporal resolution. To obtain sufficient SNR, 5 consecutive waveforms (≈5s of data) are averaged through peak alignment, resulting in some temporal averaging but considerably less than gated methods.

Method 3 – RCG-2Slice: An identical RCG sequence as in the RCG-Oblique method was applied to the same slice locations used in the NGP method to investigate whether a lower arterial measurement slice location will affect CVC via macrovascular contribution to ΔV.

Pilot Study – In a single young healthy subject, methods 1, 2, and 3 were applied consecutively. In these initial investigations, ΔP was not measured, but could be easily obtained in future studies during the scan with an MR-compatible blood pressure cuff.

RESULTS: Figure 2 shows arterial, venous, and net flow waveforms and corresponding ΔV for each method.

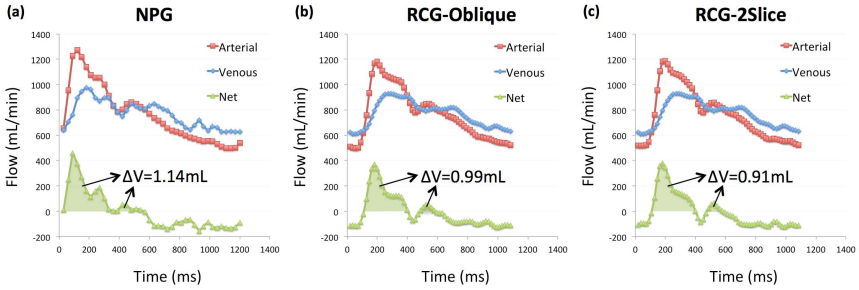

Figure 2: Arterial, venous, and net flow waveforms for NPG **(a)**, RCG-Oblique **(b)**, an RCG-2Slice **(c)**.

DISCUSSION: The sharpness of the arterial peak in Figure 2 relative to previous investigations with PCG (not shown) suggests the advantage of reduced temporal averaging using RCG and NGP. The similarity of waveform shape and ΔV in 2a & 2b suggests the projection method is capable of accurately resolving flow waveforms, despite using data acquired in one-tenth the time and without gating. The similarity of 2b & 2c suggests that the lower arterial slice location of the NGP method does not significantly impact ΔV.

CONCLUSIONS: We have demonstrated the feasibility of both gated and non-gated CVC quantification techniques. These investigations must be repeated in more subjects to determine accuracy, precision, and intra/inter subject repeatability of these CVC measurement methods. We are especially interested in applying the methods to the study of Alzheimer's disease (AD) because despite emerging evidence supporting a significant microvascular contribution to AD progression,[5] few non-invasive methods exist for probing cerebral microvascular function and testing such hypotheses. Furthermore, these methods offer a potential non-invasive alternative to transcranial methods for monitoring changes in intracranial pressure in traumatic brain injury (TBI), critical for prognosis and treatment of TBI.

REFERENCES: [1] Bateman et al., *AJNR* 21:1574-1585 (2000); [2] Bateman et al., *J. Clin. Neurosci.* 13:563-568 (2006); [3] Tain et al., *JRMI* 30:878-883 (2009); [4] Langham et al., *MRM* 64:1599-1606 (2010); [5] J.C. de la Torre, *Neurodegener. Dis.* 1:116-121 (2010).

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