Measuring Venous Blood Oxygenation in Fetal Brain using Susceptibility Weighted Imaging

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Introduction: A major issue in studying fetal hypoxic ischemic injury (HII) in-utero in humans is that identification of the fetal brain injury is difficult and in some cases the diagnosis has to wait until the post neonatal period when injury becomes evident in behavioral tests or neuroimaging. Hence, non-invasive imaging methods for assessing hypoxic-ischemic brain injury in-utero are of clinical interest which may help in better prediction of long-term outcome [1]. Ability to measure fetal blood oxygenation helps in assessing fetal brain oxygen utilization [2]. Along with blood flow parameters, it is possible to assess the metabolic rate of oxygen utilization by the fetus which can in turn help identify hypoxia in the fetus. As a first step towards this ability, in this study, we use magnetic resonance (MR) susceptibility weighted imaging (SWI) to evaluate fetal cerebral oxygenation levels in human fetus.

$$Y_v = 1 - \frac{6 \cdot |\Delta\varphi|}{\Delta\chi_{do} \cdot Hct \cdot (3\cos^2\theta - 1) \cdot (|\gamma B_o| \cdot TE)} \quad -Eqn.(1)$$

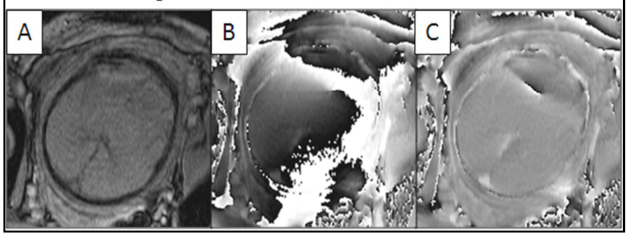
Table 1: MR Imaging Parameters

Sequence Mode	TR (ms)	TE (ms)	Flip Angle in degrees	In plane reconstructed voxel size (mm)	Slice Thickness (mm)	BW (Hz/pixel)	# of Slices
2D	250 to 280	15 to 18.7	32°	0.78 x 0.78 mm^2 or 0.85 x 1.70 mm^2	3.5mm	199	10 or 11
3D	20 to 23	13.5 to 17.3	10°	0.78 x 0.78	3 to 3.5mm	219	16

Material and Methods: ***Theory:*** SWI phase data ($\Delta\varphi$) provides a direct measure of the field perturbation (ΔB) within a tissue relative to its immediate background. Due to the paramagnetic nature of deoxyhemoglobin in the venous blood, it has different magnetic susceptibility ($\Delta\chi_{vein}$) compared to the surrounding parenchyma which is dependent on its oxygen saturation [3-5]. This difference in the magnetic susceptibility of the venous blood has a direct relation to the oxygen saturation (Y_v), which is given by the Eq. (1). Here, $\Delta\chi_{do}$ is the magnetic susceptibility difference between fully deoxygenated and fully oxygenated blood, Hct is the blood hematocrit (which varies as a function of gestational age (GA) as $Hct = 0.285 + GA*0.0064$) [6], TE is the echo time of the experiment, θ is the angle made by the long axis of the cylinder with the main magnetic field B_o, and γ is the proton gyromagnetic ratio. Measuring $\Delta\varphi$ from an approximately straight section of a vein, Yv was obtained using Eq. 1. ***MR Imaging:*** 2D and 3D fetal-SWI data (see Table 1 for sequence parameters) from 5 pregnant subjects (mean GA = 33.7±3.6 weeks) with singleton pregnancies were analyzed. Subjects were recruited and scanned on a 3T Siemens Verio system, in accordance with local IRB guidelines after written informed consent was obtained. Fetuses included in this study were considered normal for brain development based on their routine ultrasound (US) examinations. SWI data was acquired axial to the fetal brain, under maternal breath-hold condition (2D and 3D SWI acquisition time: 22-24 seconds) [7].

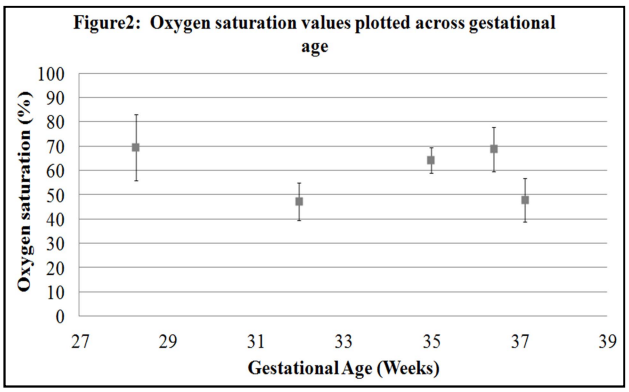
Data Analysis: Raw phase images from the fetal-SWI data were filtered using a mild homodyne high pass filter [8] of size 32x32 to remove background field inhomogeneities. Mean and standard deviation of, $\Delta\varphi$, vessel phase measurements within relatively straight sections of the superior sagittal sinus (SSS) in 5 subjects were obtained. Phase in white matter of the fetal brain was used as reference tissue relative to which $\Delta\varphi$ was measured. The angle θ, that the vessel segment's long axis makes with Bo, was ascertained using image orientation information from the DICOM header. Substituting the values of $\Delta\varphi_{sss}$, θ, TE, Hct, $\Delta\chi_{do}$, γ and Bo in Eq. (1), the value of Y_v was obtained. Error in measured cerebral venous oxygen saturation is obtained by propagating error in phase to error in $\Delta\chi_{vein}$ and consequently error in Y_v. A $\Delta\chi_{do}$ value of 0.18ppm cgs units [3] from adult blood, was assumed for fetal blood.

Figure 1: A. Magnitude Image; B. Original phase image; C. High pass filtered Phase image



Results: Figure.1 shows representative SWI magnitude and phase images of the fetal brain. Figure.2 shows the putative oxygen saturation measured from five fetal brain SWI data plotted across their GA. The square points (■) indicate measurements from superior sagittal sinus. The mean cerebral venous oxygen saturation across the five fetuses with mean gestational age 33.9±3.3 weeks was 59.44±11.58 %. The standard deviation here represents across subject variability. These values are in close agreement with the fetal cerebral venous oxygen saturation, (61±14%), measured using trans-abdominal near infrared spectroscopy (NIRS) by Vintzileos et al [9].

Figure2: Oxygen saturation values plotted across gestational age



Discussions: Although this susceptometry approach could be done easily in this situation, susceptibility mapping methods were not viable due to the low image resolution. In this work, a $\Delta\chi_{do}$ of 0.18ppm cgs units was uesd to evaluate putative fetal venous oxygenation. Recently, it has been suggested that $\Delta\chi_{do}$ is 0.27-ppm cgs units [11]. Using this value for fetal blood however leads to Yv values comparable or larger than arterial oxygenation values (SaO2) in the umbilical vein reported in the literature [12], which is physiologically unreasonable. It may also be possible that $\Delta\chi_{do}$ for fetal blood may be different from that of adult blood due to the changing proportions of fetal hemoglobin. However, this remains to be studied. With future developments in speed and high resolution, we expect that the use of quantitative susceptometry or mapping will play an important role in the future study of oxygen saturation in the fetus. In summary, we report in-vivo measurement of putative cerebral venous oxygen saturation in the human fetus using magnetic resonance imaging. To our best knowledge this is the first such report in the human fetus. This MR technique potentially has the advantage of measuring cerebral venous oxygenation at younger gestational terms as well, compared to the other noninvasive techniques existing today [9], which can only be employed at late gestational ages of 36 weeks and older. Along with fetal blood flow measurements, MR based assessment of fetal blood oxygenation could open the doors for studying fetal brain hypoxic ischemic injury in-utero.

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