Reliable Measurement Techniques for Motion Corrected Fetal Brain Volume

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Introduction: Although ultrasound (US) remains the main imaging modality to examine the fetal brain in-vivo, MRI is increasingly used to study human brain development in the 2nd and 3rd trimester. However, fetal MRI is challenging due to fetal motion. Although retrospective motion correction is now possible for MRI based investigations of the fetal brain, segmentation techniques are still being developed to extract brain structures and compartments of interest and there remains an important role for the manual application of unbiased and efficient stereological methods for estimating fetal brain measurements with predictable precision. We applied a HASTE (Half Fourier Single Shot Turbo Spin-Echo) protocol to image fetal brain with multiple planes and applied a between-slice head motion correction technique[1] available in the SLIMMER tool. Subsequently, the reconstructed 3D brain datasets can be sampled to enable convenient application of stereological methods such as the Isotropic Cavalieri (IsoC), Invariator (InV) and Nucleator (Nuc) designs. These are approaches for whole brain, brain compartment, brain structure volume and surface area measurement, which hitherto were impossible to apply using standard MRI or with US due to challenges in performing appropriate image sampling strategies for a moving 'target'. We describe the first application of IsoC, InV and Nuc for estimating fetal brain volume (includes ventricular CSF) on motion corrected 3D fetal brain images. In particular, we investigated the practicality, time efficiency and precision of the stereology designs and compared the volume estimates obtained with corresponding values obtained from the same MR image series without motion correction.

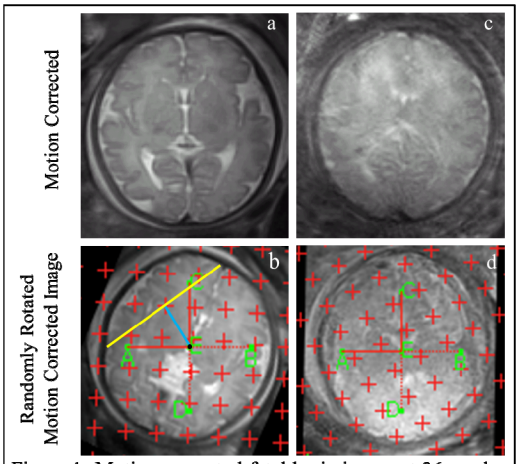

Figure 1: Motion corrected fetal brain image at 36 weeks. (a and b) Fetal brain had clear delineation of gyri and sulci, (c and d) Gyri and sulci were not clear due to poor motion correction resulting from excessive fetal motion. The yellow line defines the distance between edges of the brain (invariator) and the blue line defines the distance from the center of the brain to the test grid (nucleator).

Methods: Scanning: 15 pregnant women were recruited: 9 at 24–26 weeks and 6 at 36–37 weeks gestation. All subjects gave informed consent. Imaging was performed on a Magnetom Verio 3T system (Siemens AG, Germany) using body and spine matrix coil elements. Women lay in the left decubitus position to avoid vena caval compression; all scans were conducted with a specific absorption rate of <2.0 W kg^{-1}. HASTE acquisitions of the fetal brain were obtained (25–45 slices, TE = 94 ms and TR = 4200 ms, 0.55×0.55×3 mm^3 voxels) 3 times in each of axial, sagittal and coronal scanning directions. Analysis: The image series were motion corrected to form a single 3D high resolution brain image (1×1×1 mm^3 voxels) using the Slice MRI Motion Estimation and Reconstruction (SLIMMER) tool.[1] The resulting 3D datasets were inputted to Analyze 10.0 software (MAYO Foundation, USA) and fetal brain volume estimated using stereology methods[2], namely the IsoC, InV and Discretized Nuc. Beginning from a random starting position, the IsoC method involves exhaustively sampling the brain with a series of images a constant distance T apart along a random orientation in 3D. Sections were analyzed using point counting, $\sum P_i$, whereby fetal brain volume = $T \times A \times \sum P_i$, where A is the area associated with each point in the test system.[2] Unlike IsoC, the InV requires a single isotropic section to be obtained through a fixed point in the 3D image volume and a T-shaped InV measurement tool is laid down to join this center point to each lattice point of a point counting test system. Orthogonal chord lengths (yellow line on Fig. 1b) within the brain are measured for each test point. Total chord length is calculated, $\sum R_i$ and fetal brain volume = $A \times \sum R_i$.[2] The measuring procedure for the Nuc method is similar to InV, but the length of the radial arm of the T-shaped measurement tool (blue line in Fig. 1b) is measured from the center point to each test point lying within the brain. Total radial arm length is calculated, $\sum L_i$ and fetal brain volume = $2 \times A \times \sum L_i$. All methods were applied in three random mutually orthogonal orientations. The Cavalieri method was also applied directly to the original axial, sagittal, and coronal HASTE datasets, in which case the MR image series in each orientation exhibiting the least motion was chosen for measurement.

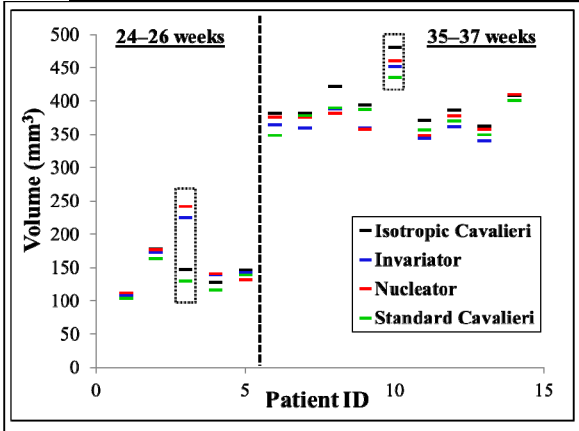

Figure 2: Average fetal brain volume measured using different stereological methods. Dotted boxes represent subjects with excessive motion.

Results: The fetal brain volume measurements obtained using IsoC, InV, Nuc and standard Cavalieri methods are presented in Fig. 2. Reconstruction of the fetal brain was possible in all cases except for one dataset acquired at 25 weeks, which exhibited excessive fetal motion. Efficiency measures (time, precision) was lowest for the InV (10–15 minutes, 2%–37%), followed by IsoC and Nuc (both 5–10 minutes, 0%–5% and 4%–37% respectively). There was excellent agreement between the fetal brain volume estimates obtained from each of the orthogonal IsoC series. As expected, there was greater variation between the fetal brain volume estimates obtained from the 3-orthogonal InV or Nuc sections, but the mean was always close to the results obtained using the IsoC method. The estimates obtained by applying the Cavalieri method to the uncorrected datasets were widely variable depending on the scale of motion (Fig. 2).

Discussion: The intrauterine environment plays an important role in determining health in later life and it is important to be able to monitor fetal brain development in utero. The quality of the fetal head motion correction using SLIMMER depends greatly on the degree of fetal motion. Motion was greater during the 2nd trimester and more challenging to correct for than in the 3rd trimester when the fetal head is engaged in the maternal pelvis. However, in some cases the gyri and sulci of the fetal brain may still not be clearly depicted on the reconstructed 3D image. This affects the ease of performing surface area measurement (Fig. 1d), which as well as being interesting in their own right, are a prerequisite for being able to apply the mathematical formula developed by Cruz-Orive[2] for directly predicting the precision of volume estimates obtained using the IsoC method.

Conclusion: We have shown high levels of agreement between fetal brain volume measurements obtained by applying three new stereological methods to 3D MR images of the fetal brain corrected for fetal motion. The IsoC method is the most precise and time efficient stereological method and is recommended to be applied in a single scanning direction prescribed with random orientation for detailed studies in individual subjects. In contrast, InV and Nuc could find a place in studying differences in mean brain volume between different groups of subjects or in the same group at different time points. On these occasions analysis of a single MR image section prescribed isotropically through a fixed reference point could be an attractive and convenient proposition.

References: [1] Kim (2010), IEEE Trans. Med. Imaging, **29 (1)** 146-158, [2] L.M.Cruz-Orive (2010), Journal of Microscopy **240** 94-110.