Assessment of liver and brain volumes at post-mortem fetal MRI – comparison to organ weights at conventional autopsy.

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Introduction

Post-mortem MRI has been proposed as a non-invasive alternative when parents decline consent for conventional perinatal autopsy [1,2]. Although most stillborn fetuses will appear normally formed, intrauterine growth restriction (IUGR) is implicated in many stillbirths [3]. Evidence of IUGR at autopsy may include an elevated brain weight/liver weight ratio [4], reflecting the fetal "brain-sparing" adaptive response to hypoxia. Such information can however only be obtained by invasive autopsy. We investigated whether comparable information could be obtained by using post-mortem MRI to estimate fetal brain and liver volumes and compared these estimations to organ weights obtained at conventional perinatal autopsy.

Methods

20 fetuses underwent 'whole-body' post-mortem MRI prior to conventional autopsy with parental consent and ethical approval. Fetal weights ranged from 113g – 3270g, with corresponding gestational ages of 17 – 40 weeks. The fetuses were imaged at 1.5T (EX, Excite GEHT Milwaukee) using head, knee or wrist receiver coils according to fetal size. When time permitted, FSE-XL T2 weighted sequences in the 3 anatomical orthogonal planes covering the whole fetal body were performed. Typical body sequence parameters were TE effective 102ms, TR 4000-6500ms, ETL 13-24, bandwidth 20.83kHz, FOV 16-28cm, slice thickness 2-3mm with no gap, matrix 512x256 (384x256 for axial) and a minimum of 4 NEX. Phase field of view of 0.5 is used to reduce time for the axial and sagittal sequences. Scan times for each plane were between 5-8 minutes. Typical head parameters were TE 102ms, TR 15000ms, ETL 32, bandwidth 20.83kHz, FOV 12-16cm and slice thickness 2mm with no gap. Conventional autopsies were performed by specialist perinatal pathologists according to UK Royal College of Pathologists' guidelines, which include the weighing of major fetal organs.

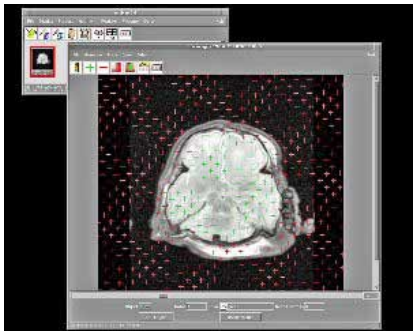
Organ volumes were estimated independently by two investigators: a fetal medicine research fellow (ACGB) and a senior radiology resident (FAG) with a special interest in MRI. Volumes were measured using the ANALYSE software package (Mayo Foundation, Minnesota, USA) on a GE Workstation with the stereology application. This employed a grid superimposed over the axial sections (or coronal sections when axial sections were not available) through the fetal brain and liver (figures 1a, 1b) and the number of grid points overlying the organ of interest were recorded thereby giving an estimate of the volume. A grid size was selected to ensure a minimum of 400 test points per organ. Organ volumes for each observer were compared to the autopsy organ weights, R^2 values were calculated and the gradient compared to recorded density measurements [5]. Inter-observer agreement was assessed using Bland-Altman analysis.

Results

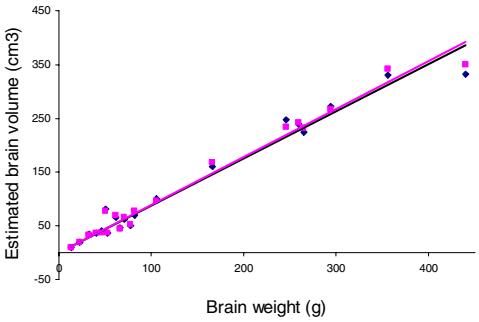
There was a high linear correlation between organ volume estimation and measured weights ($R^2 > 0.97$ for both observers; figures 2a, 2b). The reciprocal of the gradients gave an average organ density which was compared with known paediatric standards [5]: calculated liver density 1.11 g/cm3 (6% overestimate); calculated brain density 1.03 (0.5% underestimate). Bland-Altman analysis demonstrated a high inter-observer agreement (figures 3a, 3b). Organ size does not appear to significantly affect inter-observer variability.

Conclusions

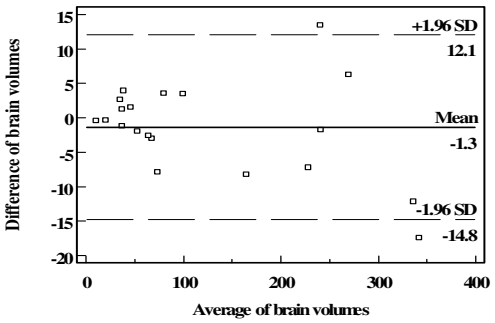
The study demonstrates that *ex utero* fetal organ volume measurements of both the liver and brain are highly correlated to pathological organ weight, with a calculated density that corresponds well to published reference standards. The calculated density is more accurate for the brain which may reflect the larger size of this organ relative to the liver and its more clearly defined boundaries on MR. Furthermore, there may be metabolic differences in the fetal and paediatric livers which contribute to differences in density. The technique we have described has low inter-observer variability and may therefore provide useful information about fetal growth status when conventional autopsy is declined by parents. Further work assessing its utility in the prenatal assessment of IUGR is required.



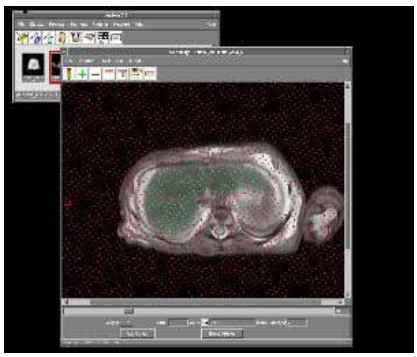
Figures 1a and 1b. Screen grabs demonstrating stereology grid used in ANALYSE .

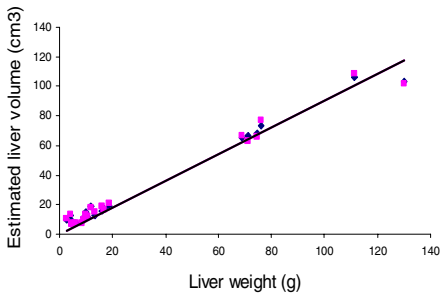


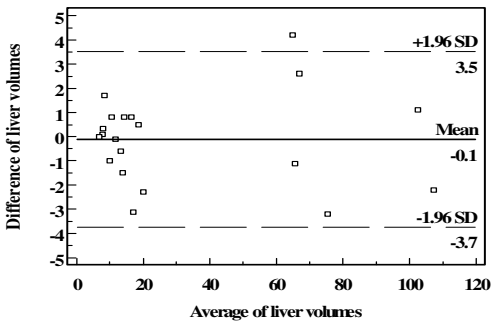
Figures 2a and 2b. Estimated organ volumes for both observers with linear regression lines



Figures 3a and 3b. Bland-Altman plots of both the organs comparing the two observers.







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References

[1] Alderliesten et al *BJOG* 2003;**110**:378
[2] Griffiths PD et al *Lancet* 2005;**365**:1271
[3] Kady et al *Best Pract Res Clin Obstet Gynaecol* 2004;**18**:397
[4]Anderson *J Clin Pathol* 1972;**25**:867
[5] ICRU 1992: Bethesda, MD. Report 46