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Diffusion-weighted post-mortem magnetic resonance imaging of the human fetal brain in situ

Ioanna Papadopoulou[a], Dean Langan[a], Neil J. Sebire[a,b], Thomas S. Jacques[a,b], Owen J. Arthurs[a,b,*]

[a] Great Ormond Street Hospital for Children NHS Foundation Trust, London WC1N 3JH, UK
[b] Institute of Child Health, UCL, London, UK

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ABSTRACT

Purpose: To evaluate perinatal brain apparent diffusion coefficient (ADC) values at postmortem MRI (PMMR) in order to evaluate post mortem changes.
Materials and methods: Postmortem brain MRI was performed with diffusion gradient values b = 0, 500, and 1000 s/mm^2 on 43 fetal cases. Mean ADC values were calculated from 7 regions of interest (ROIs) throughout the brain.
Results: 43 fetuses were evaluated with median gestational age 36 weeks (range 21–41). Overall, fetal brain ADC varied with maceration score, but not with gestational age or post mortem interval. The best single predictor of brain ADC was maceration score, which accounted for 52% of data variation for frontal cortex ($p < 0.001$) and 44% in basal ganglia ($p < 0.001$), and between 24% and 32% in all five of the other included brain areas. Gestation was only significantly associated with occipital ADC changes and post mortem interval only significantly associated with basal ganglia ADC changes. Median intra-observer and inter-observer variability was 6.0% (95% range 1.0%–18.1%) and 8.0% (95% range 0.2%–33.9%) respectively.
Conclusion: DWI characteristics in different fetal brain areas following death are multifactorial, with maceration the strongest predictor in most anatomical areas. Deep grey matter areas are also affected by gestation and post mortem interval. With better models, brain ADC may be useful to estimate the degree of maceration where gestation and post mortem interval is unknown.

1. Introduction

Post mortem magnetic resonance imaging (PMMR) has been shown to have high diagnostic accuracy for most perinatal abnormalities and forms a key component of a less-invasive fetal and neonatal post mortem service [1,2]. PMMR can be used to guide minimally invasive tissue sampling or offer an imaging approach to examination after death when consent for an invasive autopsy is declined [3]. PMMR performs well at diagnosing congenital anatomical and most brain abnormalities, but many normal post mortem changes, including those affecting the brain, are difficult to interpret on conventional sequences even by experienced neuroimagers [4–6].

Diffusion-weighted imaging (DWI) is an MR sequence that assesses water motion and diffusivity through tissues, quantitatively expressed as the apparent diffusion coefficient (ADC) value [7]. As there are several changes anticipated in the brain tissue following death, with initial tissue ischaemia followed by cell lysis and fluid redistribution [8], these changes should be observable using DWI PMMR imaging. DWI parameters in adult brains change post mortem, and ex-vivo studies suggest a strong correlation between ADC values and post mortem interval [9,10]. Similar changes in rat brain diffusion tensor imaging appear to correlate with histopathological autolysis [11,12]. DWI PMMR may also give better signal-to-noise and contrast than conventional sequences in fixed tissue [13].

Post mortem DWI may therefore be useful to evaluate post mortem interval in the perinatal brain, which could be useful in medicolegal settings when the time of death is unknown, or to assess for potential timing of intra-uterine demise in stillbirth. However, perinatal brain PMMR is complicated by other factors

Abbreviations: ADC, apparent diffusion coefficient; DWI, diffusion weighted (magnetic resonance) imaging; (PM)MR, (post mortem) magnetic resonance imaging; ROI, region of interest.

* Corresponding author at: Consultant Paediatric Radiologist, Great Ormond Street Hospital for Children NHS Foundation Trust, London, WC1N 3JH, UK.
E-mail addresses: ioapapadopou@gmail.com (I. Papadopoulou), d.langan@ucl.ac.uk (D. Langan), Neil.sebire@gosh.nhs.uk (N.J. Sebire), t.jacques@ucl.ac.uk (T.S. Jacques), owen.arthurs@gosh.nhs.uk (O.J. Arthurs).

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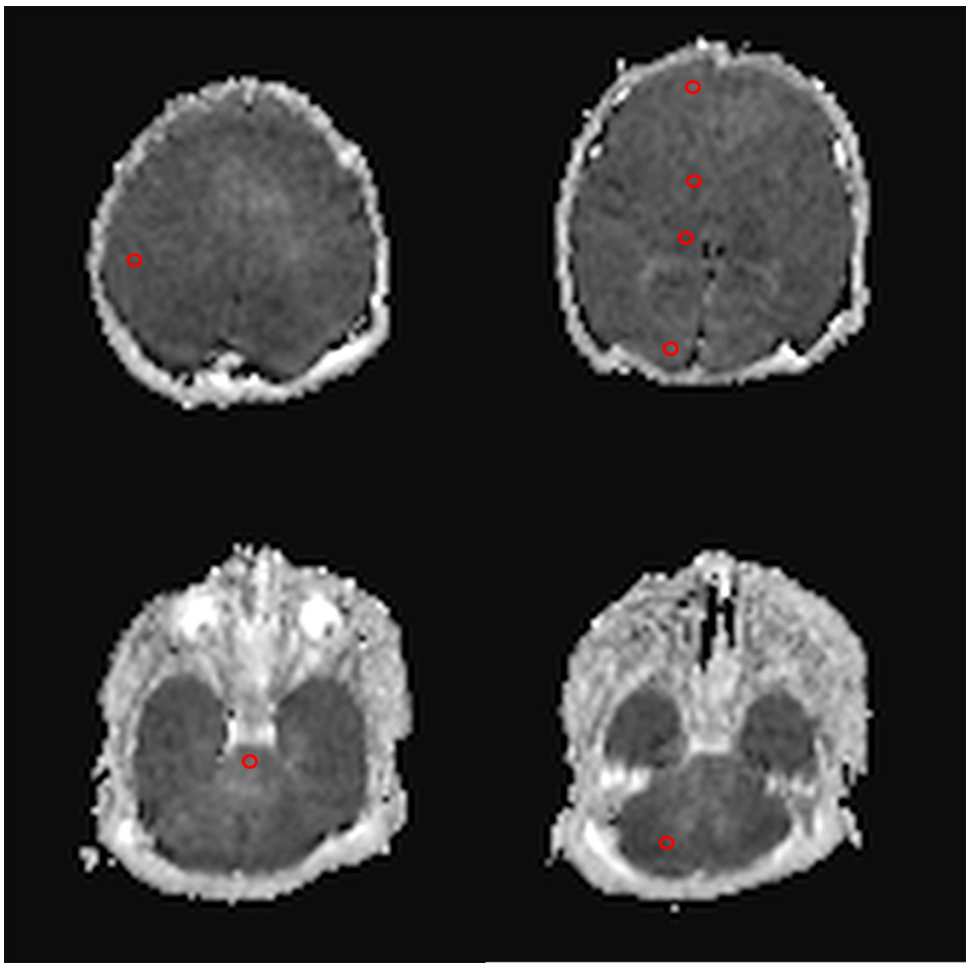

Fig. 1. Fetal brain post mortem diffusion-weighted imaging.
Example of axial ADC maps of the perinatal brain with 7 circular regions of interest (ROIs) plotted on the motor cortex (a), frontal lobe, occipital lobe, thalamus and basal ganglia (b), pons (c) and cerebellum (d).

including maceration and gestation-dependent changes. Maceration is the term given for tissue degeneration as a consequence of retention within a fluid filled cavity (amniotic fluid following in-utero death), and is currently assessed at autopsy by external appearances, including skin changes, umbilical cord discoloration and cranial collapse, and used as a surrogate for estimating intra-uterine death interval (IUD) [14]. Together, these processes may have different effects on tissue appearances at autopsy or at post mortem imaging, on a background of gestational-dependent progressive myelination changes.

The purpose of this study was therefore to establish:

(a) whether fetal brain DWI changes are detectable by PMMR in situ.
(b) whether PMMR DWI changes following death are related to variables such as post mortem interval or maceration (as surrogate markers of tissue autolysis) in a predictable manner.

2. Methods

2.1. Study cohort

2.1.1. Postmortem cases

We prospectively collected DWI sequences on all post mortem fetal and stillbirth cases referred to our institution from February 2012 to January 2014. We excluded cases in which DWI was of inadequate quality or incomplete datasets, and those in whom the brain was abnormal on imaging or at autopsy. Written informed consent was obtained for all patients for clinical pre-autopsy PMMR as part of our institution's clinical post mortem assessment. Bodies were stored in a mortuary at 4 °C and PMMR was performed out of the scheduled appointments causing least disturbance to clinical services.

Demographic data acquired from the clinical notes included age (gestation, in weeks), estimated intra-uterine interval (IUI, number of days of intra-uterine retention if stillborn or termination of pregnancy, to delivery), maceration score (MAC), and post mortem interval (PMI, days from delivery or death to imaging). PMI did not include the estimated IUI, largely because of the difficulty in collecting reliable IUI data from the clinical notes, and thus PMI in this study referred to ex-utero time interval between delivery and MRI examination. The autopsy maceration score was a visual index assessed by pathologist at autopsy from 1 to 4 (none, mild, moderate and severe maceration), based on standard criteria involving external evaluation of the fetus including skin slippage, skin discoloration and overlapping of the skull structures [14].

2.2. Magnetic resonance imaging

All MR imaging was performed at 1.5 T (Avanto, Siemens Medical Solutions, Erlangen, Germany), with a conventional phased array head coil. Post mortem brain imaging included conventional 3D T_1-weighted and T_2-weighted sequences for clinical