

ADC Changes with Temperature in Neonatal Porcine Brain

A. N. Priest^{1,2}, A. Bainbridge¹, J. S. Thornton³, O. Iwata⁴, S. Shanmugalingam⁴, S. Iwata⁴, R. Ordidge³, J. S. Wyatt⁴, E. B. Cady¹

¹Department of Medical Physics, UCL Hospitals NHS Trust, London, United Kingdom, ²Department of Radiology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany, ³Department of Medical Physics, University College London, London, United Kingdom, ⁴Department of Paediatrics, University College London, London, United Kingdom

Introduction

Hypothermia has been demonstrated to delay the onset of secondary energy failure (SEF) following perinatal hypoxia-ischaemia (HI) and may be an effective neuroprotective therapy in the longer term [1–3]. Brain cooling can be accurately and non-invasively monitored using ¹H MR spectroscopy thermometry [4,5]. In normothermic brain, local pathology during SEF can be observed using diffusion-weighted imaging (DWI) as apparent diffusion coefficient (ADC) changes evolve with time in affected brain regions [6]. However, ADC also changes with temperature [7]. It is therefore necessary to characterise the temperature dependence of ADC in the normal brain in order to understand the significance of ADC changes seen post-ischaemia during hypothermia. Although the temperature dependence of ADC has been determined in phantoms, this variation may be different *in vivo* because the activation energy is tissue specific [8]. Using an established animal model [9] we report measurements of ADC in the normal neonatal piglet brain during hypothermia, in conjunction with simultaneous local temperature measurements using an invasive fibre-optic probe. Hypothermia was induced with both whole-body cooling, which gives an approximately uniform brain temperature, and a water-cooled cap which generates strong temperature gradients across the brain.

Methods

Diffusion-weighted images were acquired on a 7T Bruker Biospec scanner using a using a 5 cm home-made doubly tuneable surface coil in the crown position. Images were acquired using a trace-weighted, single-shot, spin-echo EPI sequence [10] with b-values of 53 and 908 mm²s⁻¹; TE = 85 ms, TR = 2.5 s, readout length 49 ms, matrix 64×64, FoV 5 cm x 5 cm. 24–28 signal averages were taken at the lower b-value, with 3× as many averages at the high b-value. Data for each average were stored and reconstructed separately. Measurements were repeated if motion was visible over the time-series of images, and the magnitude images were averaged to avoid phase errors caused by more subtle inter-shot motion. ³¹P spectra were monitored to confirm that cerebral energetics were not compromised by the prolonged anaesthesia.

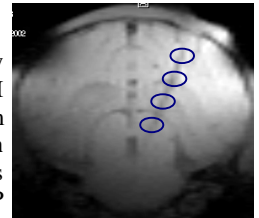


Fig 1: Image showing probe location with representative ROIs

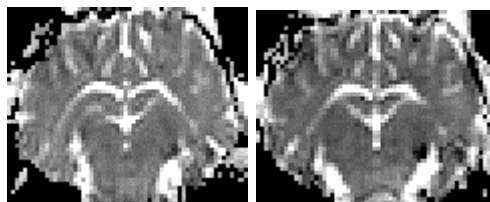


Fig 2: ADC images for approximately uniform brain temperatures of (a) 38°C and (b) 30°C

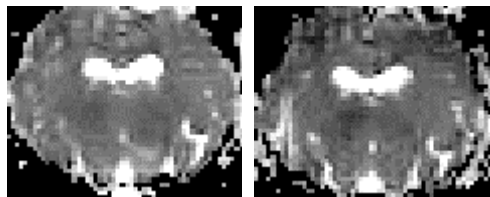


Fig 3: ADC images at (a) without and (b) with cooling cap (at 10°C).

4 neonatal large white piglets, of age < 24 h, were anaesthetised and subjected to hypothermia using a water mattress (for whole-body cooling). This was combined with a water-cooled cap (for selective head cooling) in 2 of the animals. ADC images were acquired without hypothermia and for whole-body temperatures down to 30°C or cooling cap temperatures down to 8°C (giving cortical temperatures of around 20°C). A fibre-optic temperature probe (Luxtron) with four probes was inserted into the brain and *in vivo* measurements were taken 0.5 cm, 1.0 cm, 1.5 cm and 2.0 cm below the surface. The probe was positioned close to the imaging slice, and its position was confirmed by conventional imaging (Fig 1). ADC maps were calculated, and ADC values measured in ROIs corresponding to the probe positions. The work was approved by the UK home office and local research ethics committee.

Results

Figs 2 and 3 show examples of ADC images with whole-body and cap cooling, demonstrating the fall of ADC with decreasing temperature. Fig 4 shows a plot of ADC against the corresponding *in vivo* temperature measurement. Eight sets of measurements were fitted to a straight line with $R^2 > 0.9$ and for these the average change in ADC was 2.0 %°C⁻¹. The remaining measurements were excluded because they coincided with a ventricle, because of imaging artefacts e.g. visible distortion introduced by the probe.

Discussion and Conclusions

We have measured the change in cerebral ADC with temperature in a neonatal animal model which we intend to employ for further studies of cerebral hypothermia. The magnitude of the observed changes *in vivo* is ~10% less than that seen in phantoms [8]. This pulse sequence has a rather short diffusion time of ~7 ms, so these results should be interpreted with caution when comparing with measurements at longer diffusion times.

Future work should determine whether the ADC changes are dependent on anatomical location. There was no evidence for this in our study although the data are limited by the small number of usable measurement points and the locations of the probes. This issue may be addressed using chemical shift imaging to map temperature non-invasively *in vivo*, allowing more detailed determination of the anatomical dependence of temperature-induced ADC changes.

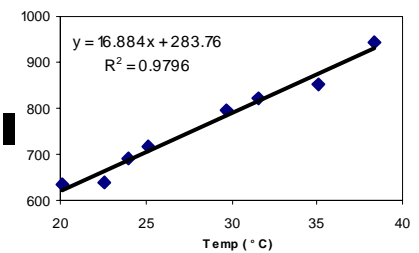


Fig 4: Example plot of ADC vs temperature

References

- [1] Amess et al. *Pediatr Res* 1997;41:803–8.
- [2] Brooks KJ et al. *Neurochem Res* 2002;27:1599–604.
- [3] O'Brien F et al. *Proc ESPR* 2000; 66.
- [4] Cady EB et al. *Magn Reson Med* 1995;33:862–7.
- [5] Thornton JS et al. *Proc ISMRM* 2003;263.
- [6] Thornton JS et al. *Magn Reson Med* 1998;39:920–7.
- [7] Le Bihan D et al. *Radiology* 1989;171:853–7.
- [8] Włodarczyk et al. *Phys Med Biol* 1999;44:607–24.
- [9] Lorek A et al. *Pediatr Res* 1994;36:699–706.
- [10] Cercignani M et al. *J Magn Reson* 1999;140:58–68.