MEASUREMENT OF BRAIN WATER IN CHILDREN DURING AND AFTER TREATMENT FOR DIABETIC KETOACIDOSIS

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Introduction: Cerebral edema is a potentially life-threatening complication of diabetic ketoacidosis (DKA) in children and is the most frequent diabetes-related cause of death in childhood. Severe, clinically-apparent cerebral edema occurs in approximately 1% of children with DKA, but mild, sub-clinical cerebral edema likely occurs in the majority of patients [1]. Even sub-clinical DKA-related cerebral edema may be associated with subtle cerebral injury resulting in lasting deficits in learning and memory. Cerebral ischemia prior to DKA-treatment and the effects of reperfusion during DKA treatment are likely involved in this injury [2]. Measurement of brain water content during DKA treatment (with concurrent ADC measurement) will help determine if DKA-related cerebral edema is strictly vasogenic or is both vasogenic and cytotoxic, and provide an accurate time course of edema formation and resolution [3].

Methods: Brain water was measured on a 3.0T MRI system (Excite HDx, Ver.12x, GE Healthcare, Waukesha, WI) with a 8-channel RF head coil (In-vivo, Inc. Gainesville,FL) using 3D fast spoiled gradient echo (FSPGR) scans (8.76 ms TR, 2.80 ms TE, 24.0 cm FOV, 256x256 matrix, 2.0 mm thickness, 32 slices) with five different flip angles (3, 6, 9, 12, 15, 29°), followed by non-linear curve fitting for generation of proton density (M0) and T1 maps, and finally by calculation of regional brain water by division of M0 map values by the reference average signal values in four 100% water reference vials attached to the RF coil. An FSPGR scan with 6° flip angle using the body coil for signal reception was also obtained, and post-processing algorithms were developed to estimate the RF coil sensitivity and the B1 field (flip angle) spatial distributions to refine the curve fitting for M0 and T1 maps [4,5]. Total scan time was 15 minutes. IRB approval and written informed consent was obtained for all children. Seven children admitted to the hospital for DKA underwent MRI at three time points: 3 to 6 and 9 to 12 hours after initiating treatment for DKA, and after recovery from DKA, 72 or more hours after initiating treatment. All children were treated for DKA in accordance with international consensus guidelines.

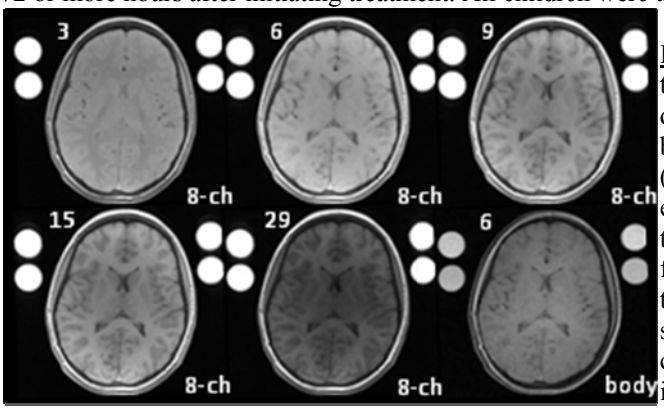


Fig. 1: FSPGR images used to derive first M0 map

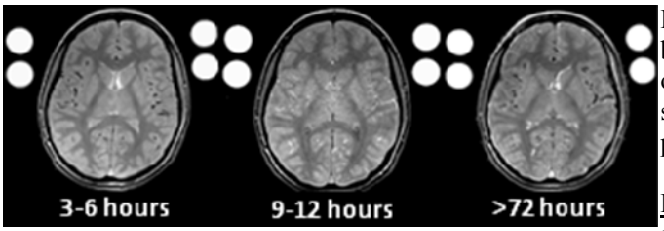
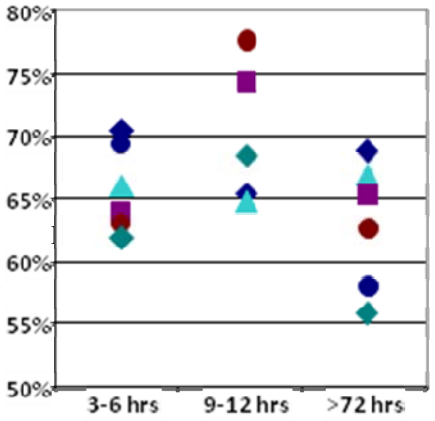


Fig. 2: M0 maps for regional brain water measurement

Results: Fig. 1 shows example axial FPSGR images at one slice location through the thalamus, and Fig. 2 shows derived M0 maps. Fig. 3 displays the apparent brain water measurements in the thalamus bilaterally from the seven patients. Compared with the post-recovery (baseline) brain water content, children in acute DKA demonstrated elevated brain water content at the start of therapy, which further increases during therapy. This suggests subclinical or asymptomatic cerebral edema develops early in the therapy for DKA, and worsens during therapy before resolving after recovery from DKA. Other regions of the brain (basal ganglia, frontal and occipital cortices) show a similar pattern but less pronounced changes.



Discussion/Conclusion: The brain water measurements are not absolute percentages, but apparent percentages that are comparable across patients and across time points. Sources of inaccuracies in the percentages include 1. increased RF coil sensitivity at the brain periphery, and at the vial locations, using the 8-ch coil, and 2. B1 field spatial distribution with higher B1 field at the center of the imaged volume resulting in biased T1 estimates if not accounted for. Correction for the RF sensitivity function and the B1 field distribution improves the accuracy of the brain water measurements. However, this study suggests that the protocol without these corrections can also be successfully used for clinical assessment of brain water. Use of reference vials with 100% water placed in fixed locations, and consistent head placement in the RF coil and relative to these vials, are important procedures to insure that the brain water measurements can be compared across patients and time points.

References: [1] Glaser NS, et. al., Pediatr Diabetes 2006 Apr; 7(2): 75-80. [2] Glaser NS, Pediatr Diabetes, 2009 Oct 10 (e-pub). [3] Glaser NS, et. al., J Pediatr. 2008 Oct; 153(4): 541-6. [4] Venkatesan R, et. al., Magn Reson Med 2008; 40: 592-802. [5] Tofts P Editor, Quant. MRI Brain, 2004 J Wiley, W Sussex, UK. **Acknowledgement:** This research is supported by R01-NS048610.