MR Monitoring of Non Contrast-enhanced brain infusions with MRI T1 Mapping

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Introduction: Convection-enhanced delivery (CED) [1] is a method for the targeted delivery of high molecular weight agents into the brain parenchyma that would otherwise not cross the blood-brain barrier. This technique allows for the direct, targeted infusion of a drug over a larger area than previous methods with a roughly spherical distribution and uniform concentration within the target volume. In order to verify that the correct target volume has been treated, therapeutic agents are typically co-infused with a Gadolinium (Gd)-based T_1 shortening agent and monitored using T_1-weighted MRI [2,3]. This is an important step to verify that the correct dose of a drug or agent has been administered to have a therapeutic effect. CED has been proposed as a method for the delivery of agents to treat Parkinson's disease. However, it is known that heavy metal exposure may be a factor for increased risk for Parkinson's [4], and it would be prudent to have a method for tracking infusion without introducing Gd into the brain parenchyma. Unlike T_1 weighted imaging, quantitative T_1 mapping removes the confounding effects of receiver coil sensitivity and proton density [5], and is proportional to infusion concentration [6]. We present the use of T_1 mapping to track infusion distribution and relative concentration of an infusion without the co-infusion of a Gd contrast agent.

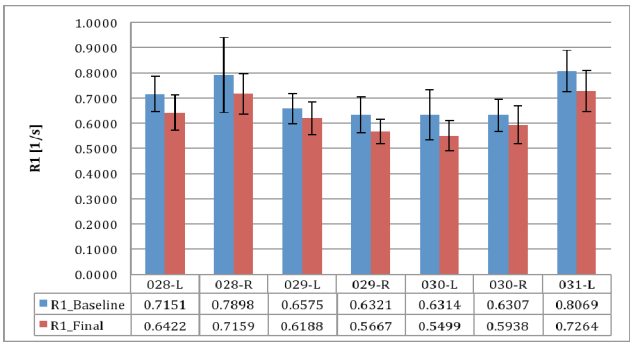

Fig 2: Putamen R_1 pre-infusion (blue) and post-infusion (red) over the infusion region of interest. Error bars indicate ± 1 standard deviation.

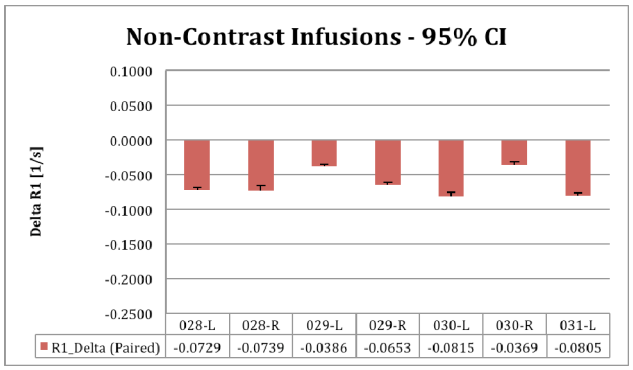

Fig 3: ΔR_1 values over the infusion region of interest. Error bars indicate a 95% confidence interval as computer from a paired student's t-test.

Methods: Four rhesus macaque *(Macaca mulatta)* underwent *in vivo* CED delivery of a therapeutic contrast agent in phosphate buffered saline without the use of a Gd contrast agent. All experiments were performed according to the federal guidelines of animal use and care and with approval of the local IACUC. Infusions of 30µl were performed into the caudal putamen (8-10mm in depth) under MRI guidance using the Navigus catheter navigation system and a fused silica cannula. Three animals underwent infusion (three bilateral, one unilateral) for a total of 7 infusions.

Scans were acquired on a GE Discovery MR750x (GE Healthcare; Waukesha, WI) using a 3-inch diameter surface coil placed on the dorsal surface of the head. Spoiled gradient echo (SPGR) scans were acquired with TR/TE=21/6ms, NEX=1, and alternating flip angles = [6 20]° over the course of the infusion. Scans were acquired at 256x256x64 matrix and 0.55x0.55x0.8 mm^3 voxel size. After the infusion, a region of interest (ROI) was drawn on the final (30µL) time point, covering the area of observed infusion. Quantitative T_1 mapping was then performed on a pre-infusion and 30µL images in the series using a linearized version of the DESPOT1 equation [5].

Results: Figure 1 illustrates an R_1 maps pre and post-infusion, and the corresponding infusion mask. Figure 2 shows pre and post-infusion R_1 (=1/T_1) values in each of the 7 infused caudate nuclei. Unlike the case of co-infusion with a T_1-shortening agent such as Gd, infusion of saline increases the water content of tissue, and thus makes T_1 longer (R_1 shorter). Figure 3 shows the change in R_1 measured over the infusion mask, with a 95% confidence interval as computed by a paired student's t-test. Differences in R_1 vary from subject to subject, with a mean ΔR_1 of 0.064 s^{-1}.

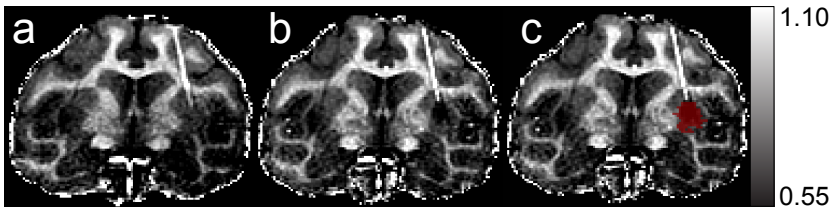

Fig 1: R_1 (=1/T_1) maps of a non-contrast putamen infusion (a) pre-infusion and (b) post-infusion, as well as an example infusion mask (c).

Discussion: A small but measureable reduction in R_1 was observed from the infusion of phosphate buffered saline without a co-infusion of Gd contrast agent. These changes are small in comparison to image noise; however statistically significant differences are still observed over the region of infusion for all cases. Future work will focus on the application of flip angle correction to CED monitoring, as well as increased signal averaging to improve the noise of parameter maps.

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References: [1] Bobo R. et al. Proc Natl Acad Sci 1994; 91:2076 [2] Nguyen T.T et al. J Neurosurg 2003;98:584 [3] Emborg M.E. et al. Cell Transpaln 2010;19:1587 [4] Seidler A. et al. Neurology 1996;46:1275 [5] Deoni S.C.L. et al. MRM 2003;49:515 [6] Tweedle M.F. et al. MRM 1991;22:191