

Serial and 2 TE-Acquisition ^{23}Na MRI for Assessment of Therapy Response in Pediatric Glioma

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INTRODUCTION

Pediatric gliomas have shown high heterogeneity with zones of proliferation, necrosis and therapy response intermixed at the site of lesion [1]. Use of single quantum sodium (^{23}Na) MR imaging, while sensitive to changing total sodium concentration (TSC) in tissue, may not be able to differentiate spatial and temporal heterogeneous tumor response in the setting of ongoing therapy. In this study, we used serial single quantum ^{23}Na imaging acquired at two echo times to study pediatric astrocytomas, and to help distinguish between proliferation and therapy response. Serial single quantum ^{23}Na imaging has been used before to study tumor progression [2]. Based on methodology first proposed by Hilal [3], the dual echo sodium is a novel technique developed to measure protein-bound ^{23}Na , which is predominantly associated with intracellular sodium. Two ^{23}Na images are acquired, one at (a) ultrashort echo time, and the other at (b) long echo time. The bound sodium measurement is calculated by deducting the intensity values of long echo ^{23}Na image (dominated by free sodium) from image acquired at ultrashort echo time (contributed by total sodium concentration).

METHODS

A total of 8 pediatric astrocytoma patients (low grade (n=1), and high grade (n=5) supratentorial gliomas; brainstem glioma (2); median age=14 years) at different points of therapy were prospectively recruited and scanned with a 3T TIM Trio (Siemens AG, Erlangen, Germany) using a dual-quadrature (^1H - ^{23}Na) volume head coil (Advanced Imaging Research, Cleveland, OH, USA), and twisted projection imaging with sequence [4] parameters: FOV=220mm, voxel size=3.44mm (isotropic), matrix size=64x64x64, TR=100ms, and TE1/TE2=0.44/5ms (for ultrashort/long TEs). All patients received two (n=4), or three (n=1) additional follow-up dual echo scans conducted from 1 to 6 months after the initial scan. The images were linearly calibrated using CSF TSC (145 mM), and noise-only background (0 mM). After the calibration, the region of interest (ROI) quantification was performed for normal appearing Grey Matter (GM) and White Matter (WM) for both ultrashort and long echo images. For each patient, the follow-up images were registered to the initial images using rigid body 6 degrees of freedom transformation in MIPAV [5].

RESULTS

Sodium averages for ultrashort echo sodium: GM=52.40 \pm 6.10 mM, and WM=41.75 \pm 3.55 mM. Averages in long echo scans: GM=38.60 \pm 6.17 mM, and WM=27.65 \pm 2.75. The average TSC difference between total sodium and free sodium (associated with extracellular sodium) in GM was 13.80 \pm 8.67 mM. This average value (13.80mM) was used as a base line intensity-concentration difference between total and unbound sodium in healthy GM tissue. Multiple of the standard deviation (SD) of this normal GM measurement (8.67 mM) was used as a relative scaling factor for comparison purposes. Six of the 8 patients showed no change in tumor course by conventional MRI criteria. One patient (high grade) showed response to immunotherapy (Figure 1A). One patient (high grade) showed tumor progression (Figure 1B). The bound sodium image derived from the subtraction showed a sodium intensity decrease (below 1 SD from average) for the lesion showing response to therapy (Figure 1A), and an increase (1-2 SD) above average difference was observed for the tumor which progressed, uncovering possible focal areas of cell proliferation (Figure 1B).

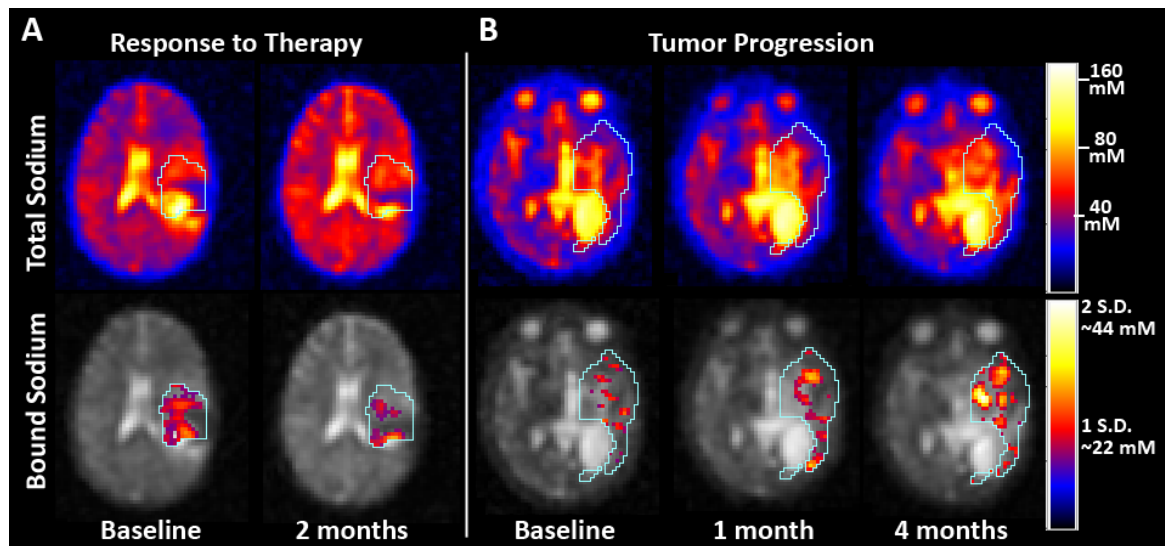


Figure 1. ^{23}Na images of total sodium (top row). Pixels showing at least 1 standard deviation (SD) above the average difference threshold ($\sim 22\text{mM}$) within the tumor (outlined) overlaid on total sodium images (bottom row). (A) Tumor showing response to therapy, and (B) tumor which progressed.

DISCUSSION

This study demonstrated that serial ^{23}Na imaging combined with the 2 TE-acquisition technique can characterize the difference between tumor progression and response to therapy. The

high intensity spots within the outlined tumor region on the total sodium were sometime difficult to interpret. (Figure 1 top row). It could be unclear whether total sodium intensity was due to CSF, or cellular proliferation. Our methodology provided an alternative to obtain improved clarity of the true proliferative nature of the tumor parenchyma. This methodology may provide value in the assessment of molecularly targeted –based innovative treatment of pediatric brain tumors in which pseudoprogression and/or heterogeneous treatment response (i.e. necrosis) may be an issue.

REFERENCE: [1] Panigrahy A, et al. AJNR 2006; 27.3:560-572. [2] Laymon, CM., et al. MRI 2012; 30:1268-1278 [3] Hilal SK, et al. SMRM 1985; p797. [4] Boada F.E., et al. MRM 1997; 37:706-715. [5] McAuliffe MJ, et.al., IEEE CBMS 2001: 381-386.