Do gadolinium-based contrast agents alter 23Na T1 relaxivity in glioma?

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Synopsis

Incomplete fluid suppression on fluid-attenuated inversion-recovery ^{23}Na-MRI (IR-^{23}Na-MRI) was observed in three patients undergoing IR-^{23}Na-MRI after gadolinium contrast injection, as part of a brain tumour imaging study. To evaluate this, ^{23}Na-MRI T_1 maps were acquired before and after injection of a gadolinium-based contrast agent on a grade IV glioma (GBM) patient, which showed a statistically significant change of ^{23}Na-MRI T_1 within the peritumoral oedema (p=0.0095). Gadolinium contrast-enhanced ^{23}Na-MRI could potentially add further applications for sodium imaging and probe tumour tissue structure in new ways to investigate proliferation and treatment response.

Introduction

Gadolinium-based contrast agents (Gad) are commonly used for the diagnosis and monitoring of changes in perfusion and blood-brain barrier integrity in neurological conditions using clinical ^{1}H-MRI. It has previously been demonstrated that Gad can alter ^{23}Na chemical shift.[1] The effect is however small compared to dedicated ^{23}Na chemical shift reagents that can be utilized to separate intra and extracellular sodium. Separation of intra and extracellular sodium is of clinical interest, however dedicated ^{23}Na contrast agents are based on heavy metals and are toxic in humans. Triple quantum filtered (TQF) ^{23}Na-MRI is the gold standard for separating intra from extracellular sodium using MRI, but is limited by low resolution and long acquisition times.[2] *In vivo* studies have recently employed inversion-recovery sodium fluid attenuation (IR-^{23}Na-MRI), due to its ease of implementation and short acquisition times compared to TQF.[3,4]

However, the effect of Gad on these IR sequences is unknown. This study has assessed the effects of clinical concentrations of Gad in IR-^{23}Na-MRI of brain tumors.

Methods

Three patients with brain tumors (2 glioblastoma (GBM), 1 metastases) were imaged between 15 and 60 minutes after Gadobutrol (Bayer Schering Pharma AG, Berlin, Germany) injection on a 3T GE MR750 (GE Healthcare, Waukesha, WI) using a dual-tuned ^{1}H/^{23}Na volume head coil (Rapid Biomed, Germany) using a 3D-cones sequence[5] (TE=0.5ms, TR=112-130ms,resolution=3.75mm isotropic, 30cm FOV, 500µs hard-pulse excitation, adiabatic inversion pulse with TI=30ms, 3 averages, total scan time 12-15.5 minutes). One GBM patient was scanned before and after Gad injection (1 mmol/kg) in addition with 4 inversion times (TI=0,20,30,40ms) for T_1 estimation using a shorter lower resolution protocol to make the total scan duration clinically feasible (TE=0.5ms, TR=100ms, resolution=4.5mm isotropic, 30 cm FOV, 500µs hard-pulse excitation, adiabatic inversion pulse, 3 averages, total scan time per TI = 1.5 minutes). This patient study is ongoing. ^{23}Na-T_1 maps were fitted in Matlab 2016a (the MathWorks, Natick, MA).[6] Regions-of-interest (ROIs) were drawn in Osirix 8 (Pixmeo SARL, Switzerland) by a neuroradiologist on contrast-enhanced ^{1}H T_1-weighted images (3D, magnetization prepared FSPGR, TE=3.18ms, TR=8.16 ms, resolution=1.5mm isotropic, reconstructed to 1mm, 25cm FOV, 5.5 minutes). ^{23}Na-MRI was co-registered to the contrast-enhanced ^{1}H-T_1-weighted volume using SPM12 (UCL, London, UK). Statistical significance was assessed using the paired sample t-test at the 5% significance level.

Results

Figure 1 shows incomplete fluid suppression in the patients in IR-^{23}Na-MR images after Gad injection. Residual sodium signal is detected in the necrotic/cystic region. Images show successful suppression of cerebrospinal fluid. Figure 2 shows post-contrast ^{1}H-T_1-weighted imaging of the patient who had ^{23}Na T_1 maps acquired before and after gadolinium injection. White matter (40 ± 5.5 vs. 45 ± 7 ms), enhancing tumor (30 ± 2 vs. 29 ± 1 ms) and gray matter (30 ± 3 vs. 32 ± 4.5 ms) ^{23}Na-T_1 values were similar before and after contrast injection and showed no statistically significant change. Within the edema however, ^{23}Na-T_1 was significantly reduced from 31.5 ± 1.5 to 27 ± 1 ms after contrast injection (p = 0.0095).

Discussion

We expected to see the largest effect of ^{23}Na-T_1 shortening in the enhancing part of the lesion and the necrotic/cystic core, as in the latter, gadolinium would slowly diffuse and essentially be trapped. As this GBM atypically lacked a necrotic/cystic core, we were unable to test this hypothesis and no ^{23}Na-T_1 changes were observed in the enhancing tumor. ^{23}Na-T_1 shortening was observed in peritumoral edema only, which normally would not enhance on ^{1}H-MRI. This effect is interesting and could be due to the atypical patient or a different effect of gadolinium in ^{23}Na-T_1 compared to ^{1}H-T_1. We are currently investigating in a wider pool of patients. ^{23}Na-T_1 changes were also observed in the white matter ROI, albeit were not statistically significant. The white matter ROI was placed in the centrum semiovale and could have been influenced by partial volume from ventricular cerebrospinal fluid.

Conclusion

It was shown that a Gadolinium-based contrast agent alters ^{23}Na-T_1 relaxivity in peritumoral edema. Further subjects will be studied to investigate the effect on large necrotic/cystic regions as well as the relationship between time of injection and imaging. Investigation of other gadolinium formulations at different concentrations and charge distribution may demonstrate other effects. More pronounced effects may be observed at higher field strengths.

Acknowledgements

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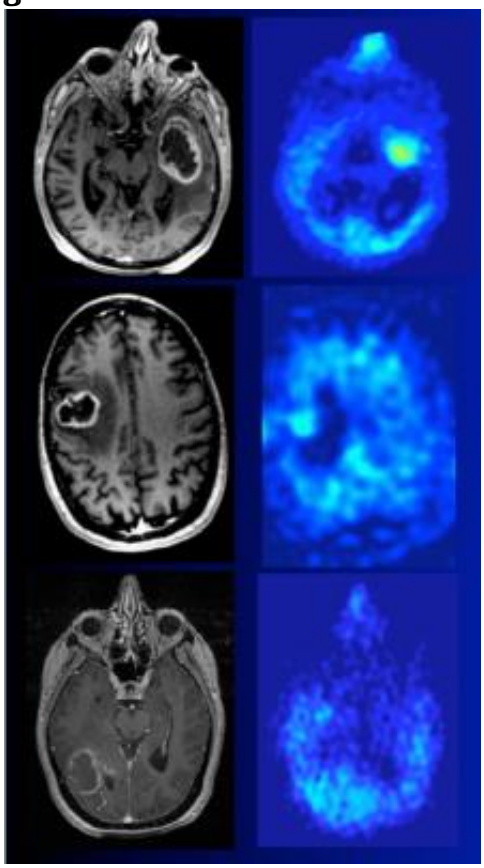
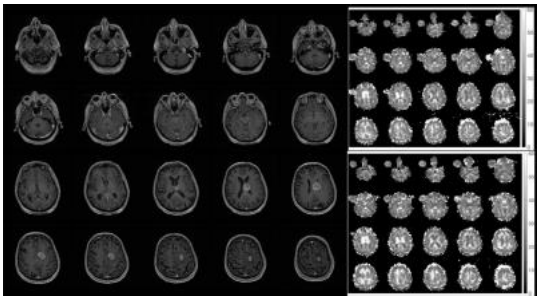
Figures



Top row: Contrast enhanced ^{1}H-T_1 imaging of a temporal lobe GBM on the left, fluid suppressed ^{23}Na-MR on the right showing a strong signal in the necrotic/cystic part of the lesion. Middle row: Contrast enhanced ^{1}H-T_1 imaging of a high grade serous carcinoma metastases on the left, fluid suppressed ^{23}Na-MR on the right also demonstrating a strong signal in the necrotic/cystic part of the lesion. Bottom row: Contrast enhanced ^{1}H-T_1 imaging of a occipital/parietal lobe GBM on the left, fluid suppressed ^{23}Na-MR on the right showing a strong signal in the necrotic/cystic part of the lesion again.



Contrast-enhanced ^{1}H-T_1-weighted imaging of GBM patient showing position and extent of lesion. ^{23}Na-MRI-T_1 maps of the same patient on the right pre (top) and post (bottom) contrast injection. Scale bar in milliseconds.