

Contributors to contrast between glioma and brain tissue in chemical exchange saturation transfer sensitive imaging at 3 Tesla

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Purpose: Off-resonance saturation transfer imaging has emerged as a potentially important tool for localizing¹⁻⁴ and evaluating treatment response in brain tumors⁵⁻⁶. Interpretation of the contrast between glioma and normal brain tissue is complicated, however, by the presence of multiple sources of exchanging magnetization including chemical exchange from amide, amine, and hydroxyl protons, magnetization transfer contrast (MTC) from macromolecules, and nuclear overhauser enhancement from protons in the aliphatic spectral region. We report a study targeted at separating these components and identifying their relative contributions to contrast in glioma.

Methods: 6 healthy controls (age, 31-52 years) and 6 patients (age, 48-65 years) with high grade glioma were scanned on a 3T GE whole-body MRI scanner. Single-slice saturation transfer images were acquired using CW RF saturation followed by a single shot EPI readout [TR/TE=2000/16ms, FOV=24cm, matrix=96x96, slice=8mm]. Z-spectra were acquired with several RF powers ($B_1=0.5, 1.5, 3, \text{ and } 6\mu\text{T}$) and durations ($T_{\text{sat}}=140\text{ms}, 240\text{ms}$) at 64 frequency offsets up to $\pm 40\text{ppm}$ (scan time=35min). SAFARI⁷ images (NEX=6) were acquired at 3.5ppm with pulsed RF saturation [pw=9ms, $TR_{\text{RF}}=15\text{ms}$, $T_{\text{sat}}=3\text{s}$] followed by a single shot EPI readout [TR/TE = 4000/16 ms] (scan time=1.5min). All images were motion corrected and z-spectra were corrected for B_0 shifts using the WASSR⁸ method. Amide and aliphatic proton peaks were identified by fitting the $0.5\mu\text{T}$ z-spectrum⁹⁻¹⁰. Saturation transfer was quantified by magnetization transfer ratio: $MTR=1-S_{\text{sat}}(\omega)/S_0$, by asymmetry analysis: $MTR_{\text{asym}}=[S_{\text{sat}}(-\omega)-S_{\text{sat}}(+\omega)]/S_0$ at RF offsets corresponding to amine protons ($\omega=2.5\text{ppm}$), amide protons ($\omega=3.5\text{ppm}$) and broad MTC ($\omega=20\text{ppm}$) and by SAFARI: $MTR_{\text{SAFARI}}=[S_{\text{sat}}(+3.5\text{ppm})+S_{\text{sat}}(-3.5\text{ppm})-2S_{\text{sat}}(\pm 3.5\text{ppm})]/S_0$. In patients, ROIs were selected in the tumor ASL hyperintensity and the contralateral normal appearing brain.

Results and Discussion: Figure 1 shows an example of the saturation transfer images obtained in a patient with a glioblastoma. $MTR_{\text{asym}}(3.5 \text{ ppm}, 1.5\mu\text{T})$ was significantly ($P=0.003$) higher in tumors ($0.32 \pm 0.22\%$) than the contralateral brain ($-0.83 \pm 0.13\%$) as has been observed in other studies with similar B_1 power^{4,11}. However, $MTR_{\text{asym}}(20 \text{ ppm}, 1.5\mu\text{T})$ was less negative ($-0.32 \pm 0.06\%$ vs. $-0.74 \pm 0.04\%$, $P=0.0002$) and $MTR(+20 \text{ ppm})$ was also decreased ($14.32 \pm 1.28\%$ vs. $21.79 \pm 0.68\%$, $P=0.002$) in all tumors compared to the contralateral brain. Therefore, the increased MTR_{asym} in glioma coincides with decreased saturation transfer from broad macromolecular MTC and loss of MTC asymmetry from the normal brain. At $0.5\mu\text{T}$, saturation peaks corresponding to amide and aliphatic protons could be seen in the tumor and contralateral regions (Figure 2). There were no statistically significant differences in the amide and aliphatic peak integrals between glioma and brain tissue. At $B_1 \geq 3\mu\text{T}$ a broad MTR_{asym} peak attributed to amine exchange became more dominant but there was no significant difference between $MTR_{\text{asym}}(2.5\text{ppm}, 6\mu\text{T})$ in tumors and contralateral tissue. MTR_{SAFARI} , which has signal from amide and aliphatic protons while being insensitive to non-saturated lines such as amine protons and broad MTC also showed no significant differences between glioma and contralateral brain.

Conclusion: Contrast between glioma and normal brain tissue is dominated by macromolecular magnetization transfer asymmetry, rather than chemical exchange from mobile protons. Amide exchange could be detected with low RF power, but it was a weak signal source with no significant contrast from normal brain tissue. At high RF power, amine proton exchange was a major contributor to the signal but showed no significant difference from normal brain.

References: ¹Zhou et al. MRM 2003;50. ²Jones et al. MRM 2006;56. ³Wen et al. Neuroimage 2010;51. ⁴Zhao et al. Mol Imaging Biol 2012. ⁵Zhou et al. Nat Med 2011;17. ⁶Wang et al. Int J Radiat Oncol Biol Phys 2012;83. ⁷Scheidegger et al. MRM 2011;66. ⁸Kim et al. MRM 2009;61. ⁹Jin et al. MRM 2012. ¹⁰Jones et al. MRM 2012;67. ¹¹Zhao et al. MRM 2011;66.

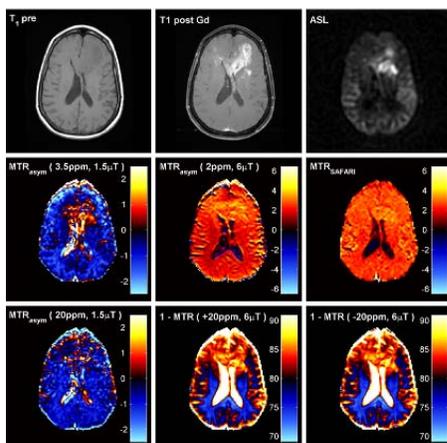


Fig. 1: Saturation transfer maps compared with standard MR images for a patient with a glioblastoma.

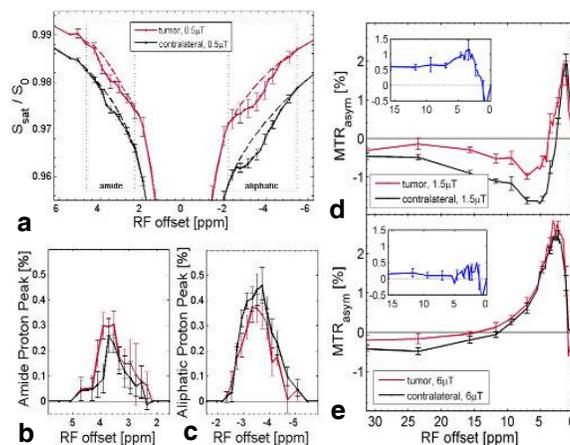


Fig. 2: a) $0.5\mu\text{T}$ z-spectrum ($N=6$). b) Amide and c) aliphatic peaks after subtracting the z-spectrum fit from the data. d) MTR_{asym} at $1.5\mu\text{T}$ and e) $6\mu\text{T}$. Insets show ΔMTR_{asym} between the tumor and contralateral regions.