Quantitative magnetization transfer imaging of rodent glioma using selective inversion recovery

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Target Audience: Investigators who are interested in probing tumor microenvironment using quantitative magnetization transfer (qMT) imaging.

Purpose: Magnetization transfer ratio (MTR) provides an indirect means to detect variations in macromolecular contents in biological tissues non-invasively, but it is also sensitive to various user-dependent experimental parameters, which reduces the specificity to pathological changes. Quantitative MT (qMT) can in principle avoid some of the limitations of MTR measurements, but so far, there have been only a few qMT studies reported in cancer, all of which used pulsed saturation methods[1,2]. The current work describes the first implementation of a different qMT approach, selective inversion recovery (SIR)[3], for characterizing tumor microenvironment *in vivo*. In addition, a new SIR-EPI sequence was developed to accelerate the acquisition but retain the fitting accuracy of qMT parameters.

Methods: *SIR*: Distinct from steady-state approaches, the SIR is a transient, on-resonance qMT technique, in which an on-resonance RF pulse is applied to selectively invert the free water protons. The resulting longitudinal magnetization can be measured and fit to a bi-exponential recovery from which the intrinsic MT parameters can be estimated[3-5].

SIR-EPI with saturation pulse train: In the current study, a new SIR-EPI sequence was introduced to combine the advantages of the fast acquisition of EPI and short pre-delay time. Specifically, the EPI readout was followed by a saturation pulse train consisting of multiple 180° pulses (see Fig.1). The EPI readout ensures fast acquisitions, while the train of saturation pulses saturate longitudinal magnetization so that a short repetition time can be used. Such a sequence can further accelerate the acquisition of SIR-qMT experiments compared to previously reported SIR-FSE methods[4] but preserve the ability to estimate qMT parameters without bias.

Animal and cancer model: Eight F344/Hsd rats were injected with 9L cancer cells in their right brain hemispheres to develop intracranial rat gliomas.

In vivo imaging: All experiments were performed on a 9.4T Varian MRI scanner. A 1ms hard inversion pulse was applied to invert the longitudinal magnetization of the free water pool. There were 20 inversion times used in the current study which were logarithmically distributed over the range from 5ms to 10sec, while the pre-delay time t_d was kept constant at 3.5sec. The saturation pulse train had 10 refocusing pulses with an echo spacing of 10ms. Computer simulations confirmed that longitudinal magnetization will be saturated at the end of the echo train.

Results and Discussion: Fig.2 shows representative SIR signals of 3 typical ROIs, i.e. tumor, gray matter (GM) and white matter (WM), and the corresponding fitted curves obtained using the SIR theory[3,4]. All signals were normalized by the corresponding signals at the longest inversion time 10 sec. Fig.2 shows excellent agreement between the SIR-qMT data (markers) and the SIR model fits (solid lines). It is clear that the tumor shows a very different bi-exponential recovery behavior in addition to its different recovery rate R_1.

Fig.3 summarizes the results of measured PSR (pool size ratio of the macromolecular pool vs. the free water pool), k_{mf} and k_{fm} (MT exchange rates from water to macromolecules and reverse) of ROIs in all eight rats. Balanced one-way ANOVA analyses suggested the mean differences of qMT parameters of different type of tissues were highly significant (all p values < 10^{-7}). In addition, all Bonferroni-corrected p values are much smaller than 0.05, suggesting all three qMT parameters provide highly reliable ways to differentiate tissue types from each other.

Conclusion: The results show that PSR is significantly lower in tumors compared with normal tissue, which suggests PSR may be a sensitive imaging biomarker for assessing cancer. Despite being less robust, the estimated MT exchange rates also show clear contrast that can differentiate different types of tissue. Unlike conventional continuous-wave and pulsed saturation qMT methods, the SIR qMT approach does not require extra mapping of B_0, B_1, and conveniently, T_1 and qMT parameters can be fit simultaneously. The results presented here not only assist better understanding of the changes in the macromolecular contents of tumors, but also are important for better interpreting other imaging contrasts such as chemical exchange saturation transfer (CEST) of tumors.

References: (1) Yarnykh. MRM. 2002 (2) Tozer. NBM. 2011 (3) Gochberg. MRM 2003 (4) Gochberg. MRM 2007 (5) Li. MRM 2010

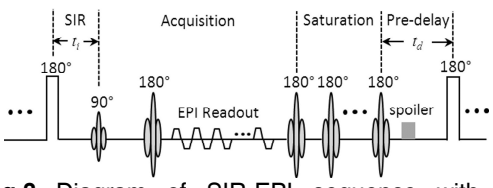

Fig.3 Diagram of SIR-EPI sequence with a saturation pulse train applied after the EPI readout to saturate the free and macromolecular pools.

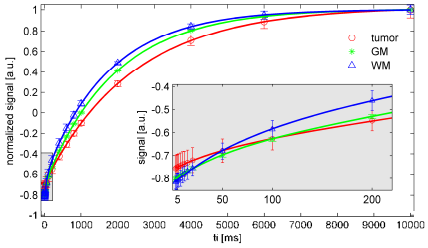

Fig.2 Representative SIR signals of tumor, GM and WM ROIs, and the corresponding model fits (lines).

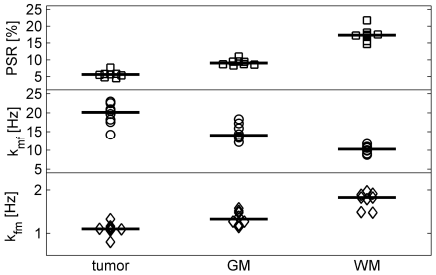

Fig.1 Summary of fitted PSR, k_{mf} and k_{fm} (MT exchange rate) of all eight animals.