The T_1 of Macromolecular Protons in Human Brain at 3T and 7T.

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Introduction

Magnetization Transfer (MT) experiments, which measure the transfer of saturation from the (invisible) macromolecular hydrogen pool (MP) to the MRI-visible water hydrogen pool (WP), are influenced by the longitudinal relaxation time constant of the MP ($T_{1,MP}$). Correct estimation of MT rates and MP fraction therefore require an estimate of $T_{1,MP}$. As the MP cannot easily be directly observed due to its short T_2, estimates of $T_{1,MP}$ (or $R_{1,MP}$=1/$T_{1,MP}$) are hard to obtain. Most MT studies therefore assume $R_{1,MP}$ to be similar to the $R_{1,WP}$, i.e. around 1/s. Here we estimate $R_{1,MP}$ by joint analysis of pulsed MT and inversion recover (IR) data based on a 2-pool model of MT, and derive an estimate for $R_{1,MP}$ by assuming both $R_{1,MP}$ and $R_{1,WP}$ to be constant over the brain.

Methods

MT and inversion recovery (IR) data were acquired at 3T and 7T (n=10) under a local IRB approved protocol. Following a single preparatory MT or inversion pulse, five slices through the center of the brain were acquired in succession with EPI, with variable delay after the preparatory pulse. The EPI parameters were: resolution: 1.5x1.5x2mm, TE: 30ms (3T), 24ms (7T), SENSE rate 2, TR: 4s for IR, 3s for MT. MT delay times were 10, 72, 138, 258 and 600ms, IR delay times were 9, 71, 147, 283 and 1200ms. Twenty averages were acquired for MT, fourteen for IR, in each case the first four without preparation pulses as reference signal for normalization. The MT pulse consisted of a series of 16 hard pulses with a total time of 6ms, a B_1 of 833Hz and an flip angle of 60,-120,120,...,120,-60 (1). The IR pulse was a 5ms adiabatic hyperbolic secant type, maximum B_1 of 833Hz, and a β of 1400/s (2).

Analysis

The IR and MT data were analyzed with the same two pool exchange model, which can be formulated as (3-4):

$$\frac{dM_{z,WP}}{dt} = -(R_{1,WP}+k_{WP})M_{z,WP}+k_{WP}M_{z,MP} \quad [1]$$

$$\frac{dM_{z,MP}}{dt} = k_{MP}M_{z,WP}-(R_{1,MP}+k_{MP})M_{z,MP} \quad [2]$$

where the magnetization is normalized to 1 for each compartment, *k* is the exchange rate, expressed as fraction of the volume it refers to. The solution of this set of equations is:

$$S_{WP}(t) = a_1e^{-\lambda_1}+a_2e^{-\lambda_2} \quad [3]$$

$$S_{MP}(t) = a_1\frac{(R_{1,WP}+k_{WP}-\lambda_1)}{k_{WP}}e^{-\lambda_1}+a_2\frac{(R_{1WP}+k_{WP}-\lambda_2)}{k_{WP}}e^{-\lambda_2} \quad [4]$$

where the magnetization is converted to saturation levels, $S=1-M_z/M_0$. The decay rates are given by:

$$2\lambda_{1,2} = R_{1,WP}+R_{1,MP}+k_{WP}+k_{MP} \pm \sqrt{(R_{1,MP}-R_{1,WP}+k_{MP}-k_{WP})^2+4k_{WP}k_{MP}} \quad [5]$$

while the amplitudes (*a*) follow from the initial condition of the system, ie. the saturation levels at *t*=0:$S_{WP}(0)$ and $S_{MP}(0)$. As only $S_{WP}(t)$ is observable, one experiment yields four parameters (2 amplitudes and 2 rates) by fitting Eq. [3] to the normalized signal. There are however 6 unknowns, $R_{1,WP}$, $R_{1,MP}$, k_{WP}, k_{MP}, $S_{WP}(0)$, $S_{MP}(0)$. To solve this problem, we assumed the $R_{1,WP}$ and $R_{1,MP}$ are uniform over the brain and combined MT and IR data.
In every voxel, both the MT and IR data were fitted with Eq. 3, using the same two decay rates for both experiments. Then the combined data of all 10 subjects were used to calculate the distribution of the initial MP saturation levels ($S_{MP}(0)$) for both experiments as function of the global $R_{1,WP}$, $R_{1,MP}$ values. This distribution was converted to a 2D histogram, showing the number of voxels as function of the MT_$S_{MP}(0)$ and IR_$S_{MP}(0)$ values. This distribution shifts as function of $R_{1,WP}$ and $R_{1,MP}$, so prior knowledge about the position of the 2D $S_{MP}(0)$ distribution can be used to select the most likely $R_{1,WP}$ and $R_{1,MP}$ values. The prior knowledge consisted of: 1) MT_$S_{MP}(0)$ < 1; 2) IR_$S_{MP}(0)$ < 1; 3) IR_$S_{MP}(0)$ < MT_$S_{MP}(0)$; 4) IR_$S_{MP}(0)$ > 0.7 MT_$S_{MP}(0)$. The first two reflect that MP can be saturated, but not inverted (due to their short T_2), the last two are based on the relative power levels of the MT and inversion pulses. Together this defines an area in the 2D histogram where the peak of the peak of the $S_{MP}(0)$ distribution is expected to occur.

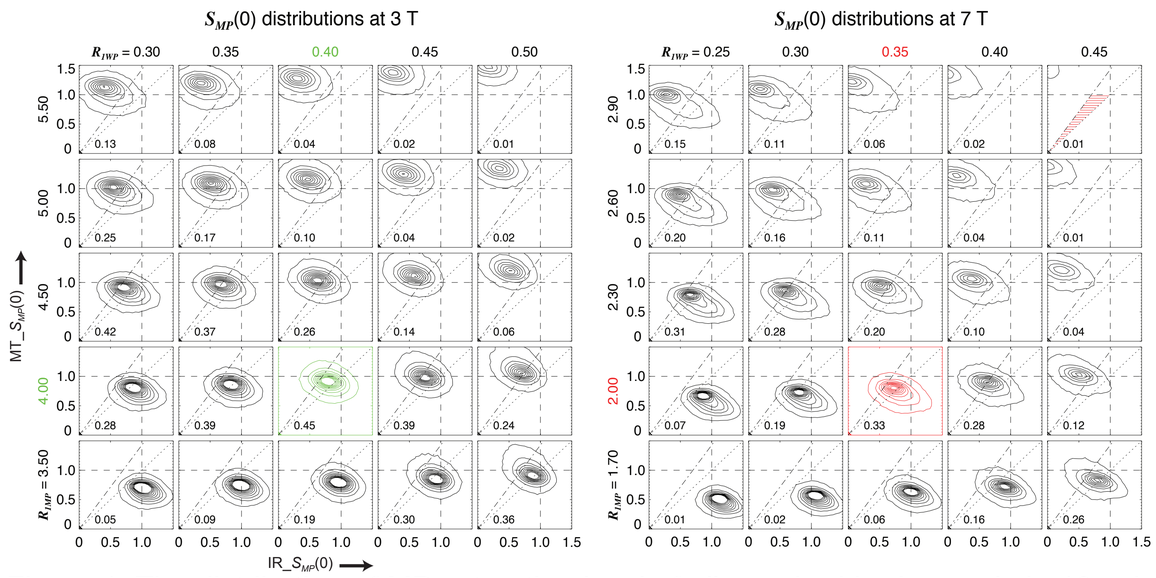

Figure 1: The distribution of MP saturation level of all acquired brain voxels in 10 subjects as function of $R_{1,WP}$ and $R_{1,MP}$ values, for 3T and 7T field strength. The shaded triangle in the top right plot reflects the area of the expected center of the distribution, the four dashed lines show the constraints forming this area. The plots in color show the best fit, used to determine the best $R_{1,WP}$ and $R_{1,MP}$ values for this data. In the final analysis a smaller step size was used for $R_{1,WP}$ and $R_{1,MP}$ than shown here.

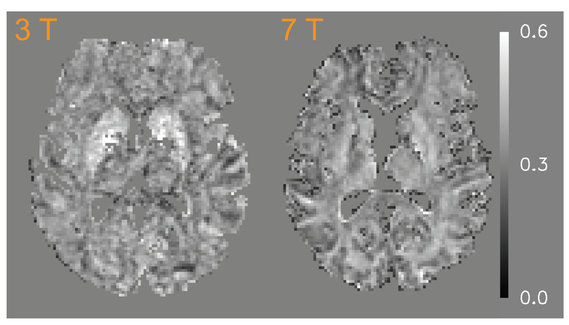

Figure 2: The $R_{1,WP}$ values at 3T and 7T for one subject recalculated from the IR and MT data with the assumption the MT_$S_{MP}(0)$ and $R_{1,MP}$ are constant in space. The small amount of contrast in these maps supports the assumption that the $R_{1,WP}$ is constant, with exception of some iron rich brain structures.

Results & Discussion

The contours plots in Fig. 1 show dependence of the $S_{MP}(0)$ distribution on the global $R_{1,WP}$ and $R_{1,MP}$ values. The optimal values for $R_{1,WP}$ and $R_{1,MP}$ were found to be 0.40/s and 4.0/s at 3T, while the 7T data showed 0.35/s and 2.05/s respectively. Based on the sensitivity of the MP distribution to changes in $R_{1,WP}$ and $R_{1,MP}$, the precision of these values is estimated to be about 20% for $R_{1,WP}$ and 10% for $R_{1,MP}$. The assumption of a (spatially) constant $R_{1,WP}$ is supported by the lack of contrast found in Fig.2 and consistent with the model that the T_1 contrast in the brain is primarily the result of variations in MP fraction (5-7). The field dependence of the $R_{1,MP}$ is consistent with the trend found in the literature: 5/s at 1.5T (6), 3/s at 3T and 2.3/s at 7T (5). This field dependence indicates MT effects should increase with field strength, as there is more time for exchange ($R_{1,MP}$ becomes small compared to k_{MP}).

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