Monitoring of T2 with application of diffusion gradients to remove microcirculation contributions to signal for optimisation of diffusion protocols and generation of flow-free T2 maps

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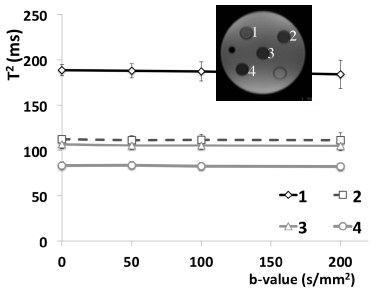
Introduction: The bi-exponential IVIM model used in diffusion-weighted magnetic resonance imaging (DW-MRI) separates self diffusion from a second, faster, pseudo-diffusion component that is often equated to perfusion or flow (1); with applied diffusion gradient b-values of 200 s/mm^2 or higher, this flow component is considered essentially absent from the image. Maki (2) describes the varying types of microcirculation that may be present within an imaging voxel, and that diffusion gradients induce either phase shift or phase dispersion in various forms of microcirculation leading to signal attenuation. Commonly in DW-MRI, diffusion gradient parameters δ and Δ are calculated by the scanner and vary with TE, but explicitly controlling these parameters allows further investigation of complex diffusion phenomena (3). Using explicit δ and Δ control to acquire DW-MRI at varying TE, we investigate the effect of applied diffusion gradients to T_2 measurements. Where T_2 is often considered in MRI as a simple exponential decay, there is evidence it reflects a more complex picture regarding tissue structure (4). For highly vascular tissue (vascular fraction *f*), where blood has a known T_{2blood}, flow desensitization with applied diffusion gradient gives the potential to generate T_2 maps that eliminate the flow component and more accurately reflect the intrinsic tissue T_2:

$$S=S_0(f.\exp(-bD^*).\exp(-TE/T_{2blood}) + (1-f).\exp(-bD).\exp(-TE/T_{2tissue}))$$

where D and D* are the apparent diffusion coefficients of the tissue (random) and microcirculatory (pseudo-random) components, and a sufficiently large b-value is used to reduce the first term to zero; the decay curve then reduces to a single exponential, where the (1-*f*).exp(-bD) scaling factor is constant and can be absorbed into S_0. Incomplete removal of the flow term would necessitate fitting the full five parameters (f, D, D*, T_{2blood}, $T_{2tissue}$) and may best be accomplished in tandem with IVIM diffusion modeling; conversely, monitoring changes in T_2 with increasing applied b-value has the potential to unambiguously identify the minimum threshold beyond which microcirculatory components can be considered absent, which may aid in modeling diffusion data.

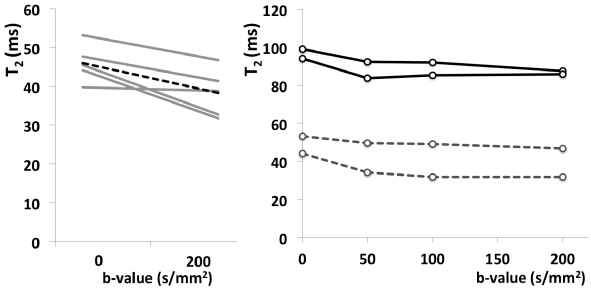
Method: Five volunteers were recruited and consented. Coronal free-breathing DW-MRI images of the abdomen were acquired on a MAGNETOM Avanto 1.5T scanner (Siemens AG, Healthcare Sector, Erlangen, Germany). Three echo times were acquired (71.2 – 130 ms), with either four (0, 50, 100, 200 s/mm^2, n=2) or two (0, 200 s/mm^2, n=3) b-values, with multiple averages (6 to 8), TR 4500 ms, δ 17.6 ms and Δ 30 ms. A diffusion phantom with multiple physiological T_2 compartments (no flow component) was also scanned with matched b-values and TEs. ROIs were drawn for different regions in the phantom, for each kidney, and homogenous tissue regions in the liver and spleen; for each b-value series of TE the data were fitted with a mono-exponential decay model using in-house software (ADEPT, ICR, UK). Results are given as mean ± s.d., with significance from comparison using 2-tailed paired t-test set at 0.05.

Figure 1: T_2 of simple diffusion phantom (inset) is unaffected by application of diffusion gradients.



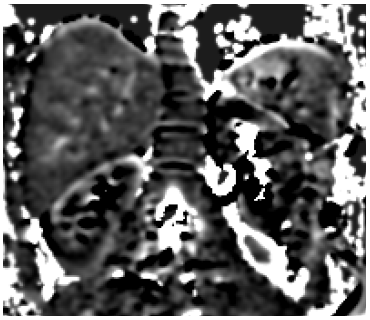
Results: Single-compartment phantom data shows that the presence of the diffusion gradient has no effect on T_2 estimates over a relevant range of b-value and TE (**figure 1**) as expected, whereas the mono-exponential model applied to liver and spleen (**figure 2a** for ladder plots of liver) shows a systematic variation in observed T_2 in the presence of the b=200 s/mm^2 gradient pulses, decreasing from 46.0 ± 4.9 to 38.3 ± 6.2 ms in the liver (p=0.024), and from 85.8 ± 13.8 to 78.9 ± 11.3 ms in the spleen (p=0.037). **Figure 3** shows an example map of ΔT_2, showing structure visible within the liver, kidney, and spleen. In the kidney ROIs, exclusion of an apparent outlier gives a significant decrease in T_2 from 103.0 ± 12.5 to 94.8 ± 10.2 ms (p<0.001). In the subset where acquisitions at b=50 and 100 s/mm^2 were acquired, the decrease observed occurs predominantly for b=0 to 50 s/mm^2 (**figure 2b** for spleen and liver, n=2), leveling off from b=100 to 200 s/mm^2.

Figure 2: (left) ladder plot of liver T_2 with applied b=0 and 200, mean in black, and (right) plots for liver (grey) and spleen (black) for b=0, 50, 100, 200.



Discussion: The observed T_2 changes for mono-exponential T_2 fit with applied diffusion gradients are consistent with the removal of fast microcirculatory components of the voxel and their contribution to the overall T_2 decay curve. The necessarily increased TE to allow for the gradient pulses does not preclude sufficient sampling of the (now simplified) signal decay curve, whereas attempting to resolve components of the T_2 decay curve from a standard multi-echo acquisition remains problematic when the composition of tissue voxels is unknown and/or complex. We demonstrate the potential use of diffusion gradients to produce microcirculatory-free T_2 maps, as well as suggesting that an applied b-value of 200 s/mm^2 appears large enough to remove the pseudo-diffusion component modeled in IVIM DWI. Limitations of the current protocol are the sparse sampling of TE and the long echo times used for T_2 estimation in abdominal organs; further exploration of the TE/b-value space will allow a more confident assignment of an optimal protocol. Vascular properties that vary on a short timescale, particularly in highly vascular organs or heterogeneous tumours, may confound the use of T_2 as a biomarker; the ability to modulate or remove the vascular component of the observed T_2 may provide a more robust measure of tissue water environment.

Figure 3: Subtraction map for T_2(b0) – T_2(b200), showing structure within abdominal organs.



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