

## MT effect of Q2TIPS in multiple inversion time ASL acquisitions

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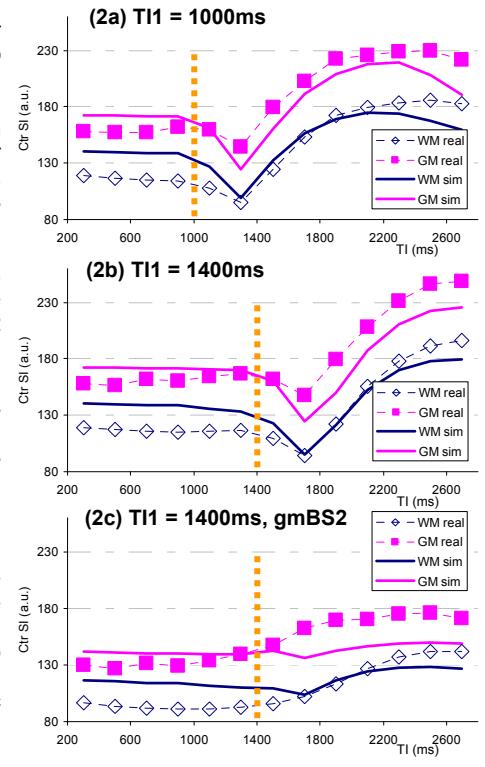
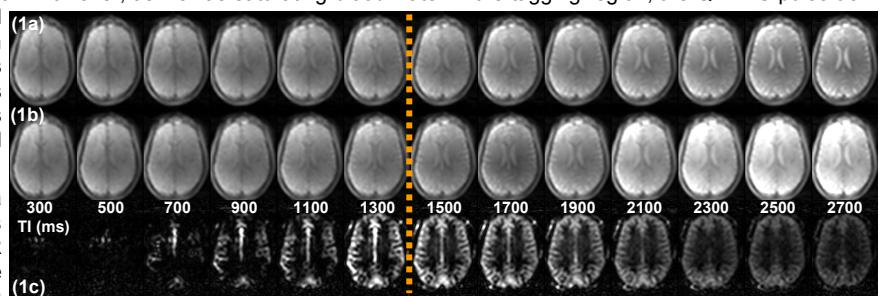
**Introduction.** In arterial spin labelling (ASL) the delay between the application of the tag and the arrival of the tagged blood into the tissue (bolus arrival time, BAT) is a potential source of systematic error in perfusion quantification, as it varies widely across individuals and brain regions. Q2TIPS [1] (and its predecessor QUIPSS II [2]) is a modified pulsed ASL (PASL) technique designed to eliminate the confounding effect of BAT on cerebral blood flow (CBF) estimates. In practice, the effectiveness of Q2TIPS depends on BAT values being within a specific range, and this assumption may be violated in some neurovascular diseases, compromising the accuracy of CBF estimates. A more robust approach is to acquire PASL images with a range of post-labelling delay times (TI) [3,4]. Simultaneous estimates of local cerebral blood flow (CBF) and BAT can then be obtained using Buxton's general kinetic model [5]. Even with this multi-TI approach, it is useful to employ Q2TIPS saturation pulses for the longest TI acquisitions, in order to precisely define the temporal width of the tagged bolus and facilitate quantification. However, as well as saturating blood water in the tagging region, the Q2TIPS pulse train will potentially have an indirect effect on the tissue and blood signal in the imaging volume via magnetisation transfer (MT) effects. In this work, we examine this undesired, and not yet studied, effect of the Q2TIPS pulses on multi-TI ASL, in particular how it alters the effectiveness of background suppression (BS) [6] of static tissue and therefore impacts on the SNR of the ASL measurement.

**Methods.** Data were acquired on a Siemens 3T Trio with a 32-channel head-coil on 2 informed healthy volunteers according to the local research ethics protocol. FAIR Q2TIPS with a 3D-GRASE readout [7] was used. Image volume pre-saturation was optimised using WET with parameters as in [8]. Inversion for FAIR and BS used 10.2ms FOCI pulses (Foci factor 2,  $\beta=12$ ,  $\mu=800$ ). Non-selective BS pulses (BS1, BS2) were made optional and their position calculated for each TI as in [7] (to minimise signals with  $T1=700\text{ms}$ ,  $1400\text{ms}$ ). TI was varied from  $300\text{ms}$  to  $2700\text{ms}$  in  $200\text{ms}$  steps. The echo/repetition times were  $14.82/3300\text{ms}$ . For Q2TIPS we used  $5.12\text{ms}$  sinc-shaped pulses, cosine modulated to produce saturation bands (thickness  $4\text{cm}$ ) on either side of the imaging slab. The readout (bandwidth  $2790\text{Hz/pixel}$ ) used GRAPPA acceleration factor 2 (21 lines, 18 pts/line), in-plane matrix  $64\times 31$  and 24  $6\text{mm}$  thick partitions (partial Fourier 6/8) in the head-feet direction, field of view  $288\text{mm}\times 163\text{mm}$  (nominal resolution  $4.5\times 4.5\times 6\text{mm}^3$ ), 2 averages. BS was turned either on (BSon) or off (BSoff) and  $T1=0\text{ms}$ ,  $1000\text{ms}$ ,  $1400\text{ms}$ ,  $2700\text{ms}$  used. BSoff data (not shown) was fitted to estimate tissue parameters  $T1$ ,  $M0$  ( $T1=2700\text{ms}$ ) and  $T1\text{sat}$ ,  $M0\text{sat}$  ( $T1=0$ ) in regions of interest (ROIs) in grey (GM) and white matter (WM). For each ROI the saturation recovery with double inversion was then simulated assuming instantaneous ideal inversions using calculated  $M0$ ,  $T1$  for  $T1 < T1$ , and  $M0\text{sat}$ ,  $T1\text{sat}$  thereafter to predict the behaviour of BSon data. Based on the simulations in GM for subject 1 (Table: 1-GM), a shift of BS2 to minimise signal intensity (SI) variation in the GM Ctr images (gmBS2) was computed for each TI and used in subject 2.

**Results and Discussion.** Figure 1 shows the Ctr images of a single slice at all TIs for  $T1=2700\text{ms}$  (a) and  $1400\text{ms}$  (b). Fig. 1c shows the perfusion (Ctr-tag) signal for  $T1=1400\text{ms}$  and gmBS2. Fig. 2 shows actual (real) and predicted (sim) ROI SI vs TI for  $T1=1000\text{ms}$  (a),  $1400\text{ms}$  (b),  $1400\text{ms}$  with gmBS2, with fitted parameter reported in the Table (2-GM, 2-WM). For  $T1=2700\text{ms}$  (fig 1a) the WM intensity in background tissue is stable whilst GM increases only slightly for the longer TIs. However when Q2TIPS is introduced (orange line in fig. 1b, 2a, 2b), the MT effect associated with the Q2TIPS pulses results in a reduction of the effective  $T1$  and  $M0$  ( $T1\text{sat}$ ,  $M0\text{sat}$ ) for  $T1 > T1$ , which disrupts the BS scheme: for all tissues we see a SI 'dip' followed by an increase. As the effectiveness of the BS of static signal deteriorates, the relatively small perfusion signal difference (Ctr-tag) becomes less precise as it is more affected by physiological noise in the tissue signal (plus potential subject motion). Moreover, this happens exactly when the perfusion signal starts to decrease especially in GM (Fig. 1c). This behaviour can be simulated (the residual discrepancy in predicted vs real data is likely to be due to the assumption of instantaneous pulses). Fig. 2c demonstrates that by re-running the sequence with recalculated BS2 position the background SI variation can be reduced (both BS pulses can be shifted to minimise variations over a larger range of  $T1$ ,  $T1/T1\text{sat}$ ,  $M0/M0\text{sat}$  values). Whilst we have modelled the MT effect of the Q2TIPS pulses on background tissue signal, perfused tissue and labelled blood will also be affected; this will influence the actual perfusion signal and affect CBF estimation; this effect is more complex to model as the tagged blood spins (characterised by  $M0_{\text{blood}}$ ,  $M0\text{sat}_{\text{blood}}$ ,  $T1_{\text{blood}}$ ,  $T1\text{sat}_{\text{blood}}$ ) can exchange with tissue spins ( $M0$ ,  $M0\text{sat}$ ,  $T1$ ,  $T1\text{sat}$ ) at different times relative to the FAIR inversion pulse, and depends on brain region. To minimise the overall Q2TIPS MT effect one could: (i) use pulses requiring lower power; (ii) increase the spacing of the Q2TIPS pulses (here, the cut-off velocity  $v_c$  associated with the Q2TIPS pulses [4] is  $\sim 280\text{cm/s}$ ; e.g. by doubling the spacing  $v_c$  becomes  $140\text{cm/s}$ , still sufficient to saturate flowing blood in the Q2TIPS slab).

**Conclusions.** Q2TIPS pulses have an MT effect on tissue and blood  $T1$  and  $M0$  and thus have a detrimental effect on BS efficiency. Though BS schemes can be adjusted to prevent a reduction in perfusion signal to noise ratio, this MT effect should also be taken into account when estimating CBF.

**References.** [1] Luh W-M et al., MRM 41:1246 (1999); [2] Wong EC et al., MRM 39:702 (1998); [3] Petersen ET et al., Neuroimage 49:104 (2010); [4] MacIntosh BJ et al., JCBFM 28:1514 (2008); [5] Buxton RB et al., MRM 40:383 (1998); [6] Ye FQ et al., MRM 44:92 (2000); [7] Günther M et al., MRM 54:491 (2005); [8] Golay X et al., MRM 53:15 (2005).



	$T1$ (ms)	$T1\text{sat}/T1$	$M0\text{sat}/M0$
1-GM	$1520\pm 10$	.70 $\pm$ .02	.61 $\pm$ .01
2-GM	$1410\pm 10$	.66 $\pm$ .02	.57 $\pm$ .01
2-WM	$1050\pm 10$	.63 $\pm$ .02	.53 $\pm$ .01