Consequences of Multi-echo Fits in Perfusion MRI for the Determination of MTT in Presence of T1-Effects.

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INTRODUCTION – Although it was already pointed out that T_1-shortening can be a considerable confounder in DSC-PWI [1], it has been heavily underestimated so far by the community. While practitioners are aware of potential *CBV* underestimation due to T_1-shortening [1], time-based perfusion parameters are widely deemed to be immune against confounding effects that primarily influence the calculation of the time course of contrast concentration. In this study, we demonstrate in simulations and on clinical data that current DSC-PWI approaches can also lead to incorrect estimates of *MTT*, specifically in areas of contrast agent (CA) leakage due to a compromised blood-brain barrier. This can be seen as a confirmatory study for the predictions in [1]. With the current trend of neuroimaging migrating towards higher fields and shorter sampling rates, T_1 shortening warrants even more attention as these effects will be increased. Here, we show that T_1-effects can have considerable consequences for the estimation of *MTT*, whereas T_{max} is more robust against this confounder.

METHODS – First, simulations based on numerical models as described in [1] were executed to predict MR signal properties in situations with and without dominating T_1-effects. The simulation parameters for tissue and tracer properties were taken from [1], and imaging parameters were set as described in the following. To confirm findings from the simulations, a human brain was imaged at 3T scanner (gradients: 50mT/m, 200T/m/s) using 5-echo spin- and gradient-echo (SAGE) PWI acquisition [2] with echo times TE = {16.6, 34.0, 61.8, 79.2, 97.0} ms, 15 slices, in-plane resolution of 84^2, 5 mm slice thickness and FOV = 24 cm. A 90° spectral-spatial RF excitation pulse was followed by a 180° spin echo refocusing pulse. PWI was based on the subsequent acquisition of 60 EPI volumes with *TR* = 1.8 s and the administration of a single-dose bolus (0.1 mmol/kg of body weight) of Gd-DTPA tracer. All perfusion parameters were obtained using the RAPID post-processing toolbox [3]. SAGE PWI allows estimating both the changes in T_2 and T_2* simultaneously, ultimately leading to contrast agent concentration derived from absolute $T_2(t)$ and $T_2^*(t)$ and decoupled from T_1-effects [4, 5], as opposed to relative approaches used in conventional single-echo gradient-echo (GE) or spin-echo (SE) PWI. The multi-echo SAGE-PWI sequence can be used to investigate the effect of T_1-shortening by looking at *MTT* and T_{max} from individual echoes (e.g. GE TE = 34.0ms; SE TE = 97.0ms), as well as from the fully corrected multi-echo fit T_2 and T_2* data [6].

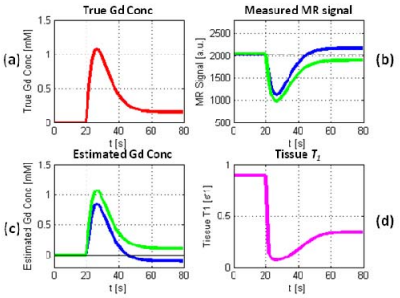

***Fig. 1** - Simulations of time curve properties with and without T_1-shortening effects. (a) True bolus*

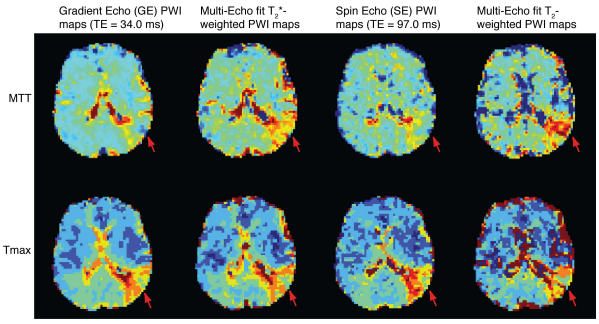

***Fig. 2 -** Comparison of MTT and T_{max} using single echo GE and SE PWI maps, as well as PWI maps computed from multi-echo estimates of T_2 and T_2*.*

RESULTS – Fig. 1 shows results of numerical modeling of the signal time-curves in cases with and without dominant T_1-effects. Estimated values of *MTT* in presence of T_1-effects were 50% higher compared to situations in which T_1-effects were removed, however, T_{max} values did not show any significant differences (data not shown). A very similar behavior was observed in the scanned data. Presence of T_1-shortening in a scan performed at 3T and at high temporal resolution (TR = 1.8sec) resulted in considerable differences between multi-echo T_2 and T_2* DSC-PWI maps and those derived from conventional single-echo GE or SE methods. Specifically, both single-echo GE and SE derived *MTT* maps did not show significant increase in the region of the subacute stroke (accompanied by noticeable T_1 extravasation), whereas T_{max} maps derived from these methods clearly showed alterations in hemodynamics (Fig. 2, columns 1 and 3). Corresponding maps derived from multi-echo fits resulted in a much better match between perfusion abnormalities expressed in *MTT* and T_{max} (Fig. 2, columns 2 and 4). Most notably, while *MTT* differed considerably, T_{max} remained almost unchanged regardless of the method that was chosen (single-echo *vs.* multi-echo fit).

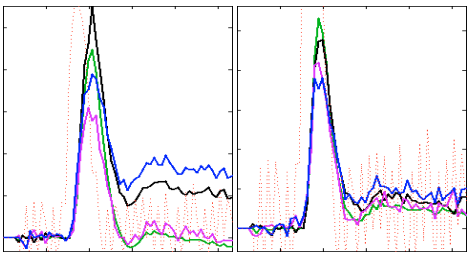

***Fig. 3 -** Tracer concentration time-curves obtained using the 4 methods as described here (green: GE PWI, purple: SE PWI, black: T_2* fit, blue: T_2 fit, red: AIF). Left: curves from a location in subacute stroke lesion. Right:curves from a location contralateral to the stroke.*

DISCUSSION – In assessment of stroke, the T_1-shortening can severely limit the veracity of *MTT* maps (derived using bolus tracking methods) when not accounted for. This is due to errors in the estimation of contrast agent concentration; to some degree immediately before and during the first pass of the bolus, but to a much greater extent after the first pass (cf. Fig. 3). The results shown here might be exaggerated because the GEs were acquired with a 90° flip angle, which could be adjusted towards lower flip angles to reduce the T_1 sensitivity. To eliminate this T_1 sensitivity entirely and to leverage higher SNR from more optimal flip angles, a SAGE approach as described in this work should be used, ultimately leading to more accurate estimates of tracer concentration and therefore *MTT*. On the other hand, T_{max} appears not to be affected by T_1 effects. This is mostly because it is an AIF-corrected bolus arrival map; T_{max} is not sensitive to erroneous signal changes predominantly occurring at the tail end of the bolus, but these signal changes are mainly responsible for *MTT* estimation errors. In summary, when reporting clinical *MTT* values in addition to T_{max}, caution should be exercised, as regions with prolonged *MTT* might be severely underestimated.

REFERENCES – [1] Calamante *et al.*, MRM 58:544-553, [2] Newbould *et al.*, Proc ISMRM 2007, p1451, [3] Straka *et al.*, JMRI 32:1024-1037, [4] Jochimsen *et al.*, NMR Biomed 20:429-438, [5] Newbould *et al.*, MRM 58:70-81, [6] Schmiedeskamp *et al.*, Proc ISMRM 2010, p2962,

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