On the Importance of T1 Estimation for SAGE Perfusion MRI Data

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Target audience – Researchers and clinicians with an interest in perfusion and leakage quantitation in stroke and brain tumors.

Purpose – The spin- and gradient-echo (SAGE) EPI sequence was developed to estimate cerebral blood flow (CBF) and cerebral blood volume (CBV) from estimates of absolute R_2 and R_2^*, rather than relative changes in signal intensity [1], to provide T_1-independent perfusion-weighted imaging (PWI) maps in the presence of contrast leakage. Contrast leakage into the extravascular-extracellular space (EES) occurs commonly in patients suffering from high-grade brain tumors, subacute strokes, or inflammation. Even after accounting for T_1-effects, in the presence of contrast leakage, the contrast distribution volume is no longer the plasma space alone and, thus, simple area under the curve (AUC) measurements for CBV are on error if no proper corrections for leakage are applied. To correctly estimate perfusion and blood volume, contrast agent leakage should therefore be addressed by using a pharmacokinetic modeling approach. However, both DCE and SAGE-based leakage correction require a separately acquired pre-bolus T_1 map to determine native tissue T_1 (T_{10}) [2]. Given a prebolus T_{10} map, the parameters CBV, CBF, as well as mean-transit-time (MTT) and tissue permeability (K^{trans}) can be estimated. An unsolved conundrum is the required additional T_{10} mapping and how T_{10} errors/noise propagate into SAGE parameter estimation. Hence, the purpose of this work was to assess to what degree estimation errors in T_{10} influence the resulting SAGE parameters.

Methods – To estimate the effects of an incorrect T_{10} map contrast kinetics in SAGE was simulated by employing the 2-compartment pharmacokinetic model [2]. Assuming parameters close to values obtained in real experiments (TR=1.8s, T1=1.75s, MTT=5s, CBV=5ml/100g, CBF=60ml/100g/min), concentration time course for tissue and arterial signal were simulated assuming different permeability values (K^{trans} = [0, 0.3, 0.6, 0.9, 1.2] min^{-1}). The concentration time courses were subsequently converted into SAGE MR echo signals *vs.* time and served as input into the SAGE post-processing pipeline, which first computes R_1-based tissue concentration (C_T^{R1}), K^{trans}, and an estimate of the residue function (R(t)). Thereafter, perfusion parameters are determined. The computation of C_T^{R1} requires an estimate of T_{10}, which we varied in a range of +/- 10% of its original value (1,600 ms) [3]. This is an accepted error range for T_1 relaxometry. For each T_{10}, K^{trans} as well as R(t), CBF, CBV, and MTT were computed and compared to the ground truth.

Results – Our results show that leakage-corrected perfusion parameters derived from SAGE data are not independent of T_{10} maps, however, they are also not very sensitive to incorrect T_{10} maps. In a direct comparison between the estimated and simulated contrast agent concentration, C_T^{R1} shows only a slight deviation with T_{10} deviation from the truth (**Fig. 1**). Underestimation of T_{10} leads to larger changes in the resulting CBV, MTT, and K^{trans}. CBF is essentially independent of T_{10} effects; it was underestimated by less than 2% in our simulations. Depending on the tissue permeability, an underestimation of T_{10} can lead to a significant under- or overestimation of CBV and MTT, see **Fig. 2**. The values for MTT are not presented here, as the changes in MTT are directly proportional to CBV via the central volume theorem (MTT=CBV/CBF). Overestimation of T_{10} leads to an underestimation of CBV and MTT. Even in the extreme case when T_{10} is assumed to be 10% too long, CBV/MTT are underestimated by less than 5%. The estimated tissue permeability values show a similar behavior, although the estimates are much worse. An underestimation of T_{10} by only 5% leads to an overestimation of K^{trans} by 10% for the given range of true K^{trans} values (0.0-1.2 min^{-1}) (**Fig. 3**). The residual function R(t), depicted in **Fig. 4**, shows almost no difference between different with respect to T_{10}.

Discussion – The simulation shows that a good T_{10} map leads to the best results with respect to the estimation of CBV, MTT, and K^{trans}. CBF is not affected by incorrect T_{10}, as CBF determination using the model shown in [2] is T_{10}-independent. Overall, a slight misestimation of T_{10} has little effect on the estimation of the perfusion parameters CBF, CBV, and MTT. However, K^{trans} depends more on the accurate determination of T_{10} as even relatively small T_{10}-estimation errors result in large deviations of K^{trans}. In fact, the K^{trans} error is propagated into the estimation of the other perfusion parameters. In case of a too highly estimated tissue concentration, K^{Trans} is overestimated, whilst an underestimated concentration (compared to the ground truth) leads to a higher plasma/EES gradient and a lower underestimated K^{Trans}. A similar behavior can be also expected from regular DCE as it utilizes the same modeling approach.

Conclusion – Leakage correction on multi-echo data, in particular SAGE, can compensate for estimation errors in CBV and MTT caused by the effects of contrast extravasation. To facilitate leakage correction, a prebolus T_{10} map is acquired. The presented results, however, showed that mis-estimations of T_{10} have only a significant effect on CBV and MTT, while CBF is entirely T_{10} -independent. Thus, leakage correction could potentially be applied to multi-echo data that lack a properly determined prebolus T_{10} map without significantly compromising CBV and MTT estimates. However, K^{trans} values will be less reliable. T_{10} errors should also be considered in DCE.

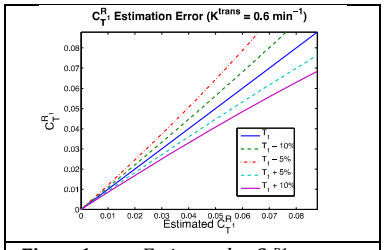

***Fig. 1**: Estimated C_T^{R1} versus simulated C_T^{R1}.*

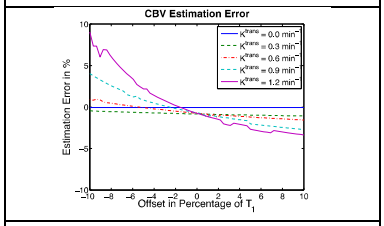

***Fig. 2**: CBV estimation using SAGE and leakage correction whilst assuming under- or overestimation of T_1.*

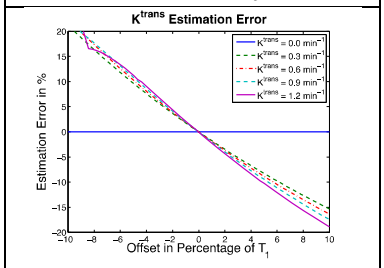

***Fig. 3**: K^{trans} estimation using SAGE and leakage correction whilst assuming under- or overestimation of T_1 map.*

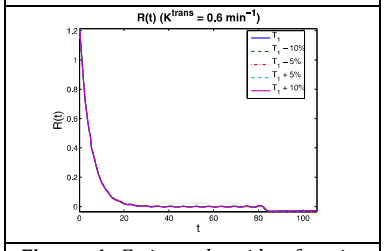

***Figure 4:** Estimated residue function R(t).*

References – [1] Schmiedeskamp, et al., Magn Reson Med. 2012 Jul;68(1):30-40 - [2] Schmiedeskamp, et al., ISMRM Workshop on Perfusion MRI, Amsterdam, 2012 - [3] Ostergaard, et al. MRM 1996 Nov;36(5):726-36.

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