Numerical Approach for quantitative BOLD with Vessel Size Estimate – Validation on Phantom.

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Introduction: MRI is a powerful tool to investigate the microvasculature. Various techniques benefit from the entanglement of the contrasts that arise within a voxel and provide relevant biomarkers such as vessel size index or oxygenation [1-2]. However, the analysis relies on analytical models [3-5] that present a discrepancy with Monte Carlo simulations [6]. Furthermore recent results showed that classical qBOLD models actually fail to distinguish oxygenation and blood volume [7-8]. In this work, to overcome the analytical model assumptions, we present a versatile approach directly based on simulations (termed NumVox). We evaluated our approach on phantom data where vessels are mimicked by polyamide (PA) strings embedded in a medium. We compared our model with analytical ones and we demonstrated that this approach could provide a mean to estimate the radius of the vessel without the use of contrast agent (CA).

Methods: ***Model –*** We designed an algorithm that simulates the MR signal within a voxel taking into account the diffusion of the water molecules within the magnetic field perturbations induced by the susceptibility interfaces. The voxel contains vessels of radius R that occupy the volume fraction Vf. The magnetic susceptibility difference between the vessels and the tissue is $\Delta\chi$. The diffusivity of water molecules is ADC and diffusion is restricted to the outside of the vessel. To enhance computation time, this algorithm was designed for 2D lattices but the magnetic field perturbation was computed in a way that mimics 3D [9]. The lattice was 256x256 points, 96 vessels were randomly spread out and the voxel size was adapted in order to maintain the constraint on Vf. ***Phantom –*** Four phantoms (P1, P2, P3 and P4) with PA strings immersed in a NiSO4 solution were used. The radius of the PA strings were respectively R=27µm, 63 µm, 89 µm and 245µm with volume fraction Vf=2-3% [7]. ***MRI –*** A gradient-echo sampling of the spin-echo (GESSE) sequence was used to acquire the MR signal in the vicinity of the spin echo (T_E = 68ms, 32 echoes, 3x3x6mm^3). Multi-SE (CPMG) and multi-GE (MGE) sequences were used for T_2 and B_0 evaluation. Water diffusion was assessed by diffusion weighted EPI sequence. ***Analysis –*** The CPMG signal was fitted with the extended phase graph algorithm [10] using the Levenberg-Marquardt minimization (LM) and assuming a single T_2 component. The derived value was used to correct the GESSE signal from the T_2 decay. The GESSE signal was further corrected by removing the B_0 contribution to the decay [11]. The resulting signal was then fitted using a LM minimization and the seed point was initialized with a lookup table (LT) built up with the range of parameter values: R= [1,3,…99]µm, Vf= [0.2,0.4,…10]% and $\Delta\chi$= [0.05,0.07,…2]ppm (SI) (245000 individual simulations). For comparison, two analytical models were also fitted in the same way: KP [4] and SY [5]. R, Vf, and $\Delta\chi$ were estimated either on averaged ROI or voxel wise. Voxels with r^2<0.8 were rejected.

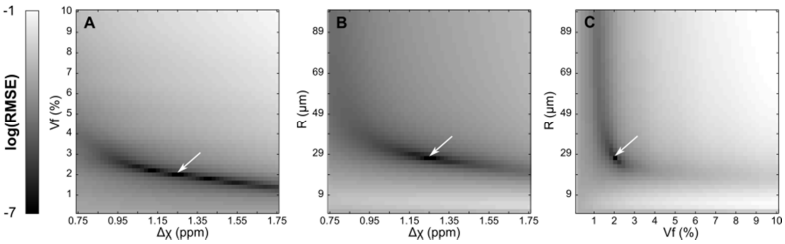

Fig 1 – Three orthogonal planes of the RMSE between the MR signals simulated for the range of parameters values and a reference signal chosen here to match the expected value of P1 (white arrow, R=27µm, Vf=2%, $\Delta\chi$=1.2ppm).

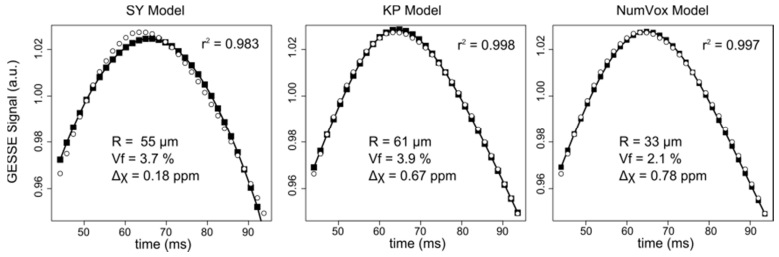

Fig 2 – Illustration of the fit obtained on the P1 data for the 3 different approaches on ROI. o : data, : fit. The best agreement with the expected values is obtained for the NumVox approach.

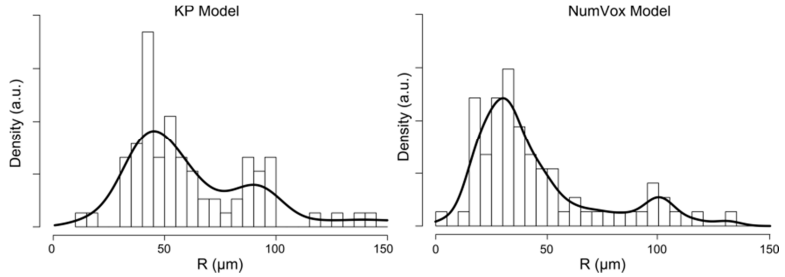

Fig 3 – Histograms of the estimates of R obtained voxel wise in P1 with the KP Model (left) and the NumVox model (right).

Results: Figure 1illustrates 3 orthogonal planes for the Root Mean Square Error (RMSE) between a reference MR signal and the MR signals simulated for the range of parameters values. While Fig1A presents a long minimum valley, Fig1B and C exhibit narrow ones that indicates that R can be assessed with accuracy. ***ROI –*** Figure 2 presents the fits obtained for the ROI data of P1 for the 3 different approaches. The KP and NumVox approaches perform better than the SY approach. The estimates obtained with the NumVox are the closest from the expected values. For higher radii the estimates get worse. ***Voxel –*** Histograms of R obtained in P1 for the KP and NumVox models are displayed in Figure 3. About 20% of the voxels were rejected in both approaches. The density of R is narrow with a maximum at 30µm in good agreement with the expected value. Using KP model tends to overestimate R (47 µm) with r^2=0.67 compared to the NumVox approach. Rejected voxels and wide distribution of the radii can be ascribed to the inhomogeneity of the phantom.

Conclusion: This study demonstrates that our numerical model can properly describe the MR signal. LT initialization enhances the robustness of the fit and may be sufficient in most cases. Our approach provides a mean to estimate the vessel radii without the use of CA. However, T_2 correction is critical and may lead to inaccurate estimates. This approach will be pursued in vivo studies.

Reference: [1] Tropres et al., MRM, 2001, 45:397-408. [2] An et al., Stroke, 2009, 40:2165-2172. [3] Yablonskiy et al., MRM, 1994, 6:749-763 [4] Kiselev et al., MRM, 1999, 41:499-509 [5] Sukstanskii et al., JMR, 2004, 167:56-67 [6] Dickson et al., JMR, 2011, 212:17-25 [7] Sohlin et al, JMRI, 2011, 33:417-425. [8] Sedlacik et al., MRM, 2010, 63:910-921, 1991 [9] Pannetier et al., ISMRM 2012, #1957. [10] Hennig, Conc Mag Res, 1991,3:125-143. [11] He et al., MRM, 2007, 57:115-126.