Towards Quantitative Dynamic Vessel Size Imaging in Humans

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Introduction

The brain microvasculature can only be characterized indirectly by means of MR. A common characterization bases on the assumption, that the tissue in a given voxel is populated by monosized, cylindrical vessels at a low volume fraction. The regime where the diffusion length of the measured protons is small in comparison to the radius of the above cylinders is called the static dephasing regime (SDR) [1]. In this regime, an analytical expression can be computed that relates the relaxivity changes of the gradient-echo to that of the spin echo signal, yielding the cylinder radii, the so called Vessel Size Index (VSI) [2]:

$$VSI = 1.734\,(\zeta D)^{1/2}\frac{\Delta R_{2GE}}{\Delta R_{2SE}^{3/2}}$$

From the dynamic measurement of a contrast agent (ca) bolus passage with a multi-echo EPI sequence, the time course of the induced relaxivity changes in the gradient- and spin-echo signals can be deduced on a voxel by voxel basis. A linear fitting of the above equation yields the VSI that is expected to be a good surrogate parameter for tumor staging. It is a well known fact [2] that the VSI has overestimates the true vessel caliber. Another strong limitation on the quality the VSI is that for capillaries under the diffusion conditions in the brain in a typical measurement the SDR prerequisites are violated as the diffusion length approaches the vessel diameter and the derived relation does not hold any more. Beyond the SDR an analytical relation of the two relaxivity changes can not the derived yet. The approach presented in this work is based on the theory of transverse signal relaxation in a vascular network as introduced in [3]. The theory is still based on the monosized cylinder model, but overcomes the limitations of SDR. Using this theory, the relaxivity of a given tissue composition at a given ca concentration can be simulated without the knowledge of an analytical expression beyond the SDR. In this work we present an approach to fit such a tissue model to the measured relaxivity time courses yielding a more accurate vessel caliber.

Method

The tissue was modeled to consist of monosized capillaries (c), arterioles (a) and venules (v), at the Diffusion constant D=0.8 μ^2 /s. For such a tissue the relaxivity timecourse can be simulated as a function of vessel radius ($R_{a,v,c}$), volume fraction ($\xi_{a,v,c}$) , and concentration (ca). An accurate description of all parameters with their values can be found in [4]. In order to fit this model to experimental data, one needs a cost function that is minimized with respect to the free parameters of the model, that are here reduced to R_c and the ca concentration at each measured time point. R_a was set to 100 µm and R_v to 120 µm at ξ_a = 0.005 and ξ_v = 0.01. ξ_c can be determined from conventional rCBV determination normalized to 6% blood volume fraction in the whole brain. For a densely sampled linearly increasing concentration function the induced relaxivity changes can be simulated at fixed $R_{a,v,c}$ and $\xi_{a,v,c}$ for both, the GE and SE signal. In order to cover the real ca concentration range, the maximum concentration has to be set much higher than reported values [2]. The sum of the squared distances of the measured points to their closest points on the simulated function can then be used as a cost function for the remaining parameters R_c and ξ_c. The minimization of this cost function yields the desired best fit values for the mean vessel radius. The cost function was minimized using the Nelder-Mead simplex direct search algorithm as implemented in MATLAB for the *fminsearch* function. As a start value for the minimum search the SDR evaluation was used in order to stabilize the fit.

The patient data was measured on a 3T Siemens scanner with a GE/SE multiecho EPI at a matrix size of 64x64x16 for 40 timepoints at $TE_{GE/SE}$ = 25 ms / 85 ms and TR = 1800 ms. The acquisition was started 10s before the ca injection, a protocol that is typically used for VSI measurements.

Results

During the bolus passage, the solid curve in Fig. 1 describes a loop. The loop is due to the transit of the bolus from the arterial to the venous pool. This time dependence is not yet considered in the model which leads to the interpolation of the simulated relaxivity curve. The application of the fit yields vessel radii by a factor of 1.7 below the SDR approach. The factor was formerly found by comparison of VSI computed from patient data to physiologically expected values as well as by simulations [2] to be of the same order. Fig. 2 shows the distribution of the vessel radii for a whole patient dataset. Fig. 3 shows the correlation map between VSI fitted and VSI SDR for the whole dataset.

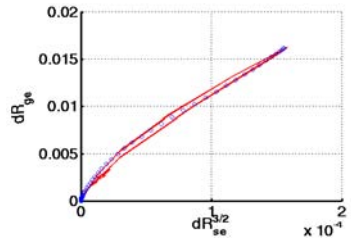

Fig. 1: Relaxivity changes during the bolus passage (mean over the whole brain). The circles indicate the fitted values.

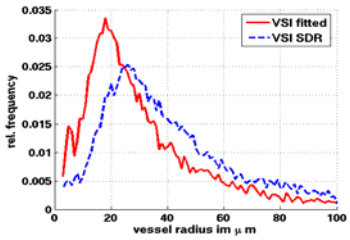

Fig. 2: Relative frequency of the vessel radii computed with the fit (solid line) and with the SDR formula (dashed line).

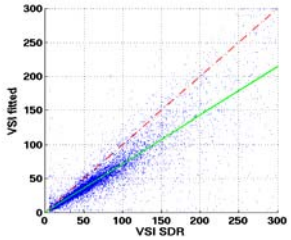

Fig. 3: Correlation plot of the fitted VSI to the SDR VSI for a patient dataset. The solid line indicates the regression line.

Discussion

The new approach seems to remove at least a major part of the expected overestimation of VSI although the visual impression of the corresponding maps (not shown) does not differ a lot. Even though the assumed tissue parameters have to be calibrated more accurately the results show an improvement on the determination of the VSI. For a further improvement various physiologically well determined tissue types that can be segmented in anatomical images have to be modeled as presented here for the whole brain. The mEPI measurement needed for this fitting approach is more limited in resolution than conventional perfusion measurements, but shows a path to the quantitative tissue description.

References

[1] Yablonskiy et al, MRM 32:749-763 (1994) **[2]** Kiselev et al, MRM 53:553-563 (2005) **[3]** Kiselev et al, MRM 41:499-509 (1999)