

A Fingerprinting Approach to Compute Blood Volume, Vessel Diameter and Blood Oxygenation Maps in the Human Brain

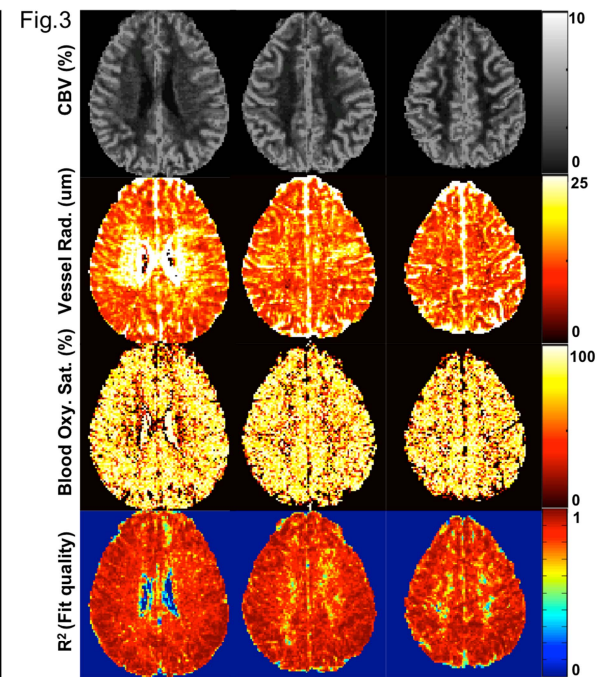
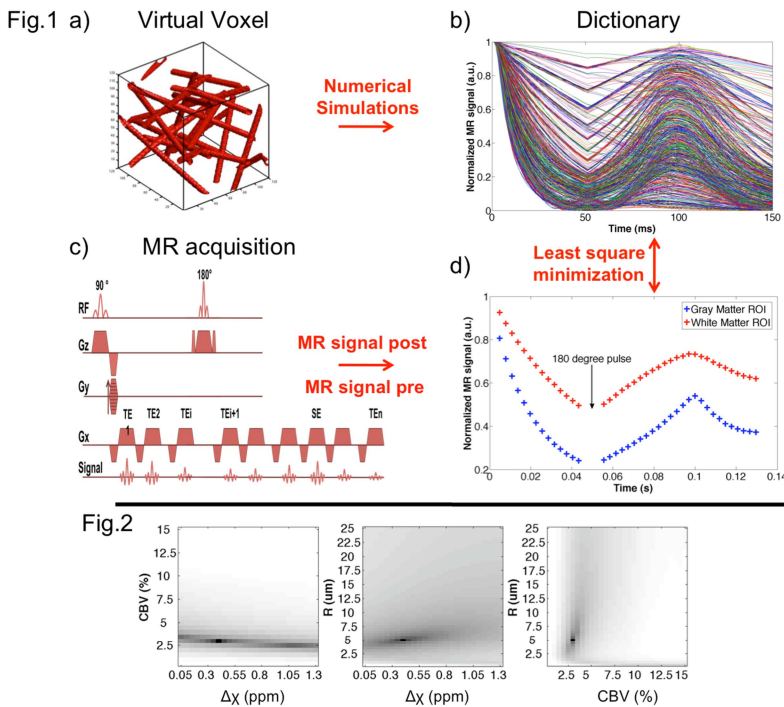
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Introduction: In vivo, the MR signal contains various information about the vascular network such as blood volume fraction, blood vessels geometry, and blood oxygenation. All these parameters are important biomarkers for studying angiogenesis or hypoxic processes in cancer or stroke. Quantitative BOLD approaches [1] have tried to extract blood oxygen and blood volume information by analyzing the formation of the spin echo (SE) signal using a mathematical model. While the results were encouraging, recent studies [2] have shown that the use of an analytical model was inadequate due to the complex influence of the water diffusion process. In the present study, we used a fingerprinting approach to analyze the time evolution of the FID and SE (Fig.1). The MR signal evolution was sampled voxelwise with a Gradient Echo Sampling of the FID and SE (GESFIDE) sequence (Fig.1c). Because other parameters such as B0 inhomogeneities and T2 also influence the signal evolution in vivo, we used in this work the ratio between GESFIDE signal pre and post injection of an iron based contrast agent (Feraheme, AMAG Pharmaceuticals, Inc., Cambridge, MA) as a fingerprint. We then simulated the same experiment with an advanced numerical tool and varied the parameters inputs to obtain a dictionary of curves (Fig.1a b). Fingerprint and dictionary were finally compared with a least square minimization approach.

Materials and Methods: The local IRB committee approved all studies. 4 volunteers were scanned at 3T (MR750, GE Healthcare Systems, Waukesha, WI) with an 8-channel head coil. The protocol included a 3D T1-weighted fast spoiled gradient echo sequence used to acquire high-resolution structural information of the whole brain. A GESFIDE sequence (TR=2000ms, 40echoes, SE=100ms, FOV=20*20cm, ST=1.5mm, 128*128, 12slices, Tacq=4min) was acquired pre- and post-injection of a full dose of Feraheme (7 mg Fe/kg). Data from the scanner were imported into Matlab (MathWorks Inc., Natick, MA, USA) and SPM8 was used for co-registration of the images. The numerical simulation tool uses a Fourier based approach to compute the magnetic field distribution inside the voxel and a deterministic approach to account for relaxation and diffusion processes [3]. This allows high computation time efficiency and a free choice for the geometry of the vascular network and tissue. For sake of simplicity, straight cylinders were used here as blood vessels. 54000 individual simulations were performed to compute the dictionary by changing blood volume [0.5,0.5,...10]%, blood vessel radius R=[0.5,0.5,...25] μ m and magnetic susceptibility of blood $\Delta\chi$ = [0.05,0.1,...1.35]ppm (SI) (with or without presence of contrast agent). After least square minimization, $\Delta\chi$ was converted to blood oxygen saturation (SO2) using $(1 - \Delta\chi / (4*\pi * \Delta\chi_0 * Hct)) * 100$ with $\Delta\chi_0=0.264$ (difference of magnetic susceptibility between fully oxy and fully deoxygenated blood) and $Hct=0.85*0.42$ (microvascular haematocrit).



Results: Fig.1d presents the signal evolutions in a gray matter (GM) and white matter (WM) ROI in a volunteer, showing similar characteristics to the dictionary curves. Fig.2 shows 3 orthogonal planes for the Root Mean Square Error (RMSE) between one curve of the dictionary and all other curves. The presence of a single minimum in the 3 maps indicates that a unique solution can be found during the minimization process. Also, these same RMSE plots without contrast agent (not shown) indicate that only the vessel radius can be properly estimated. Parametric maps obtained in one volunteer are presented in Fig.3. Three slices were averaged (equivalent 4.5mm slice thickness) to increase SNR. CBV maps show a good contrast between GM and WM, while Vessel Radius and Blood oxygen saturation maps are more homogeneous. The fit quality maps show low values only in CSF, low SNR white matter regions and highly vascularised area such as sagittal sinus vein. The numerical values (CBV_GM=3.6 \pm 0.6%, CBV_WM=2.5 \pm 0.7%, SO2_GM=69 \pm 5%, SO2_WM=65 \pm 2%) averaged over the volunteers are consistent with previous report using PET [4]. Vessel radius values (R_GM=15 \pm 1 μ m, R_WM=15 \pm 2 μ m) are higher than histological reports [5] but inline with MR vessel size imaging results [6].

Conclusion: This study suggests that quantitative maps of microvascular parameters can be obtained with this fingerprinting approach. Several improvements of the method can easily be realized: realistic vessel geometry simulation, presence of only few large blood vessels with preferential orientation, incorporation of ADC information, magnetic susceptibility estimates using MR phase information. A similar approach, which combines several MR sequences and does not necessitate the use of contrast agent, will also be investigated.

References: [1] He et al, MRM 2007. [2] Dickson et al., JMR 2011. [3] Christen et al, MRM, 2012. [4] Leenders et al, Brain, 1990. [5] Lauwers et al., Neuroimage 2008. [6] Kiselev et al, MRM 2005. **Acknowledgements** Supported in part by the National Institute of Health (NIH 1R01NS066506, NIH 2R01NS047607, NCR R5P41RR09784).