# MR Fingerprint assessment of capillary with quadratic coefficient and falling down parameter

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Purpose: MR high resolution measurement of capillary radius r and blood volume fraction v is of great importance for understanding tumor angiogenesis. However, It is difficult to derive an analytical formula to describe MR signal because of multiple de/rephasing mechanisms such as slow diffusion, motional narrowing, T2/T2* relaxation, echo rephasing, magnetic diffraction etc. working together in shaping the signal characteristics. After investigating MR signal shapes with GESFIDE[1] sequence, we propose two biomarkers, quadratic coefficient q and falling down parameter f, which are measured before TE and can preserve more microstructural information than signals measured at TE. Because q-f parameters are sensible to and can continuously vary with geometry changes, MR Fingerprint (MRF) can be used to resolve the geometrical parameters r-v by searching the dictionary database with k Nearest Neighbor (kNN) approach in q-f feature space. The 3D SE-EPI sequence is used to acquire feature parameters q-f with four TRs for data acquisition, while traditional GESFIDE requires 64 TRs for phase encoding, and consumes 10 folds more scanning time. In addition, with the asymmetrical weighting strategy, q-f enhanced MRF (qf-MRF) can improve the r-v estimation accuracy by 59% as compared with the identical weighting MRF (iw-MRF)[1], which resolves r-v by identically weighting 40 signal readout across whole signal temporal range.

Method: The MR fingerprint is in a form of fractional signal acquired pre- and post-injection of a superparamagnetic iron oxide contrast agent (AMI-227). Figure 1 displays the 3D SE-EPI sequence used for four EPI acquisitions at $T_{readout}$ of 42, 58, 79, 100 ms, with 10ms acquisition window (AW). Siemens Trio 3T scanner, 12-channel head coil, TE/TR = 100/1000ms. Spatial resolution was $1\times1\times1mm^3$, $128\times128\times64$, $N_{ex}=2$. SPM8 was used to register to the structural image. Monte Carlo[3] (MC) Simulation was used to generate virtual voxel signals with following parameters: virtual voxel size $1mm^3$, iteration interval 2ms, 60 simulation iterations, tissue microvascular parameters r-v, isotropic distributed microvessels, diffusion coefficient $D=2.88\times10^{-9}$ m^2/s at normal tissue temperature of 37°C, susceptibility difference of tissue- plasma $\Delta\chi=4\times10^{-7}$ (cgs units) achieved by injection of an agent dose

Figure 1

derived by subjects' height and weight. White noise was added to achieve tissue SNR=15. At the end of each MC iteration, MR signal was calculated by summing magnetization of each random-walk proton. For each voxel, the feature parameter f was calculated by averaging fractional signals at readout time 42ms and 58ms; feature parameter q was the quadratic coefficient fitted by second order polynomial regression to signals readouts at 58, 79 and 100ms. Then MRF dictionary containing 400 records of (r-v;q-f) was built by MC simulations with microvascular parameters independently random sampled from r(2μm,8μm) and v(1%,4%). q-f values were obtained for each voxel after taking MR scan, then kNN (k=20) was used to calculate geometrical parameters r-v.
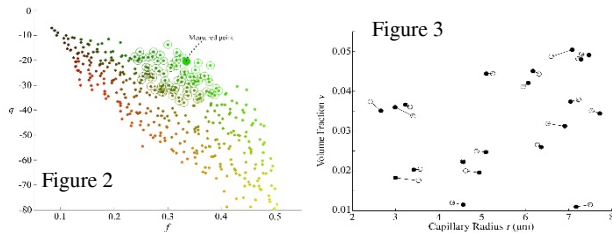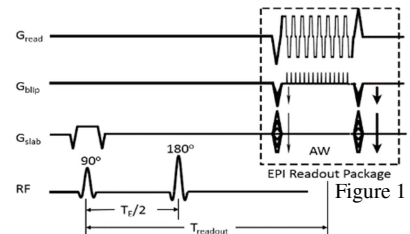
Figure 2

Figure 3

Results: Figure 2 shows the 400 records of MRF dictionary in the q-f feature space, colored by red and green representing capillary radius and volume fraction. The feature space can be approximately classified into 5 regimes: black points regime represents small r and small v; similarly, red, green, yellow and brown points regime represent different r-v combinations. Note that the r-v color changes continuously with q-f variation, which is the base for application of statistical inference. We performed one measurement with q = -20.05 and f = 0.34, which is mapped as the measured point. The kNN approach was used to infer the measured point's radius and volume fraction by polynomial surface fitting of the 20 nearest neighbors. The calculated result, r = 2.34μm and v = 4.38% is close to the true value r = 2.21μm and v = 4.52%. Figure 3 demonstrates the first 20 qf-MRF results from 500 MC testing simulations with independently random sampled tissue parameters. Established microvascular parameters (hollow circles) are close to their corresponding true parameters (filled circles). The results show that radius have the bias of -2.71×10^{-2} μm and the standard deviation of 0.27 μm, while the volume fraction is more accurate with the bias of -1.16×10^{-3}% and the standard deviation of 0.10%. We also tested the same microvascular parameter sets with the identical weighting strategy[1], whose standard deviation is 0.43 μm, 59% less accurate than qf-MRF even though iw-MRF used 10 times more signal readouts.

Discussion: Figure 4 displays signal trends generated by MC simulations with red and green representing 2μm and 4μm radius, thickness representing 2%, 4%, and 6% volume fractions. Note three observations: 1) rephasing peak containing the primary structure modulation information occurs before echo time. 2) Capillaries with larger radius have stronger ability to reverse back the rephasing peak. 3) At TE/2, signals fall down greater when there are higher volume fraction

Figure 4

Figure 5

but size unchanged. Figure 5 are the phase evolution plots with different combination of r-v. In each subplot, the phase density (color brightness) evolution can be observed along readout time (y-axis). It also demonstrates that larger volume fraction tends to have small brightness head, indicating a faster dephase process in the early stage; while larger radius tends to have a thinner bright tail, indicating stronger rephase process in the late stage. So identically adding more late stage readouts would destroy instead of favor v estimation, while weighting more late stage readout could benefit r estimation as what quadratic coefficient q implies.
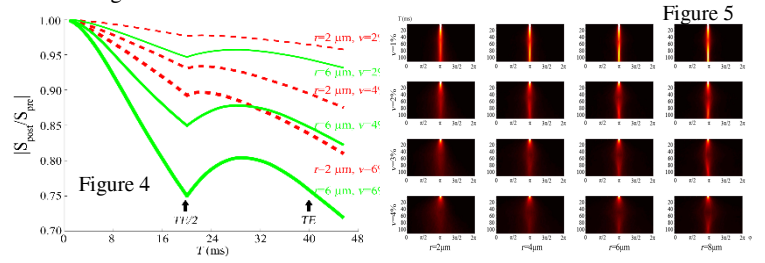
Reference: [1] T. Christen et al., NeuroImage, 2014. [2] F.Qi, ISMRM, 2015. [3] J.L. Boxerman et al., MRM, 1995.