Parameter Optimization and Demonstration of Simultaneous Time Resolved Angiography and Perfusion Measurement in the Lower Extremities at Rest and with Exercise

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Introduction: Time resolved magnetic resonance angiography (trMRA) allows dynamic anatomic assessment of large vessels, while dynamic contrast enhanced MRI (DCE-MRI) assesses small vessels, providing a quantitative measurement of tissue perfusion. Typically these require two doses of contrast and two separate acquisitions. If both analyses could be performed in a single acquisition, large vessel/anatomical pathology (via trMRA) and small vessel/functional pathology (via perfusion) could be evaluated with one dose of Gadolinium, decreased table time, and improved patient comfort. The challenge in a simultaneous approach is to maintain high spatial resolution to visualize the vasculature while also achieving high temporal resolution to accurately capture the changes in contrast agent concentration to make a perfusion measurement. In this study, Time resolved angiography WIth Stochastic Trajectories (TWIST) [1] was used with parallel imaging and partial Fourier acquisitions to achieve high temporal and spatial resolutions. The effects of undersampling and reconstruction techniques on image quality and accuracy of perfusion quantification were optimized to determine an acceptable range of parameters to be utilized. The acquisition parameters were applied in the lower extremities to measure perfusion in exercising and resting legs, demonstrating the ability to measure physiological perfusion changes.

Methods: TWIST is a 3D view-sharing technique where a central region of k-space is fully sampled in every time frame while the outer region is undersampled, and images are reconstructed by sharing information between neighboring frames. Data can be further undersampled using parallel imaging and partial Fourier acquisitions and reconstructed using GRAPPA [2] and POCS [3]. The effects of varying the undersampling parameters on the acquisition were studied in simulation: pA (fractional size of central region) was varied between 20, 25, 33, and 50%, outer regions of k-space were shared across 2-5 frames, and GRAPPA acceleration factors were set at 1, 2, or 3 along the phase and partition encoding dimensions. A 6/8 partial Fourier acquisition was used in the phase encoding direction. A simulated 4D phantom with dynamic signal intensity similar to that observed *in vivo* and coil sensitivities which mimic those of the Siemens run-off coil were simulated and undersampled. Following TWIST view-sharing and reconstruction, signal intensity curves were manually segmented for blood and muscle tissue. Pharmacokinetic analysis was performed on the resulting curves: the arterial input function (AIF) was fit using a gamma variate function [4], and the signal intensity curves were fit using a two-compartment model to find the transfer constant (K_{trans}) that is directly proportional to perfusion [5]. The effects of the acquisition and reconstruction parameters on angiography images and perfusion measurements were assessed by measuring artifact power in the images and percent error in K_{trans}. Sampling parameters for imaging were selected based on these results. *In vivo* IRB approved studies were performed on 2 asymptomatic volunteers at 3T (Siemens Magnetom Verio) after informed written consent. Unilateral flexion/extension exercise was performed prior to imaging. Initial T_1 values of muscle and blood were taken from literature values. Two different TWIST examinations were performed on the volunteers after administration of a single dose of Gd-DTPA (Optimark; Mallinckrodt Inc). TWIST imaging parameters: TR/TE/FA: 3ms/1.47ms/19°, TA: 3.7s/frame, BW: 1090 Hz/pixel, Resolution: 1.49x1.38x1.5 mm, FOV: 381x342x96 mm, pA=0.2(0.25), pB=0.33(0.5), PF_{phase}=6/8, R_{phase}=2(3), R_{par}=2, ACS=24. Perfusion analysis was performed as for the simulations.

Results/Discussion *Simulation*: Fig 1 depicts results from the subset of simulations in which temporal resolution was <5s/frame. Whether accelerating with GRAPPA or view-sharing, a higher temporal resolution leads to higher artifact power. The trade-off between the two TWIST parameters is less important than the choice between acceleration using GRAPPA or view-sharing. In general, R=6 with GRAPPA reconstruction led to more accurate images than R=4 with more view-sharing for a given temporal resolution; however, when moving to R=9, accuracy decreased due to inaccurate GRAPPA reconstructions. The simulations where K_{trans} error was less than 10% are circled in Fig 1. The optimal parameters chosen from the simulation (bold circles) were used in the two *in vivo* experiments as described above. *In vivo*: Fig 2 shows signal intensity curves generated by ROIs in the *tibialis anterior* muscle and the popliteal artery for the R=4 volunteer. There is earlier bolus arrival and a clear increase in perfusion for the exercised leg in comparison to the non-exercised leg. Figure 3 shows a single time frame maximum intensity projection (MIP) image, and a qualitative perfusion difference between exercised (L) and non-exercised (R) limbs is even visible here. Quantitative perfusion measurements yielded K_{trans} of 0.255 min^{-1} in the exercised leg, compared to 0.144 min^{-1} in the resting leg. Similar results were obtained for the second volunteer. Potential clinical applications of this technique could be assessment of large and small vessel status in pathologies such as atherosclerosis and diabetes mellitus, assessment of physiological reserve, and vascular response to pharmacological challenges.

Conclusion: Using simulation results, optimal TWIST parameters and GRAPPA undersampling were selected to optimize image artifact power and errors in K_{trans}. The *in vivo* exercise experiment demonstrated that this technique provides a quantitative means for identifying physiological perfusion changes.

References [1] Song, et al. *MRM* 2009; 61:1242-8. [2] Griswold et al., *MRM* 2002; 47:1202-10. [3] Haacke, et al. *JMR* 1992; 92:126-45. [4] Feng, et al. *Int J Biomed Comput* 1993; 32:95-110. [5] Tofts, et al. *JMRI* 1999; 10:223-32.
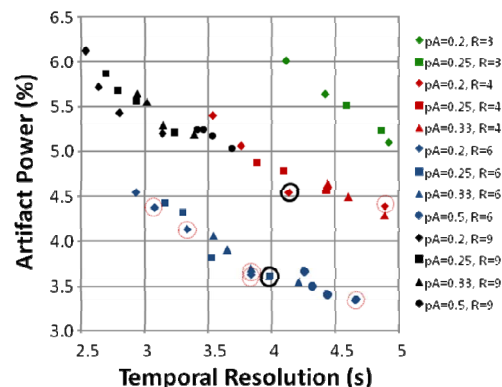
Figure 1: Artifact power vs. Temporal Resolution for the TWIST simulations. Different TWIST parameters are shown using different shapes, and different GRAPPA factors are shown in different colors. Reconstructions with K_{trans} errors of less than 10% are circled, and parameters used for in vivo acquisitions are circled in bold.
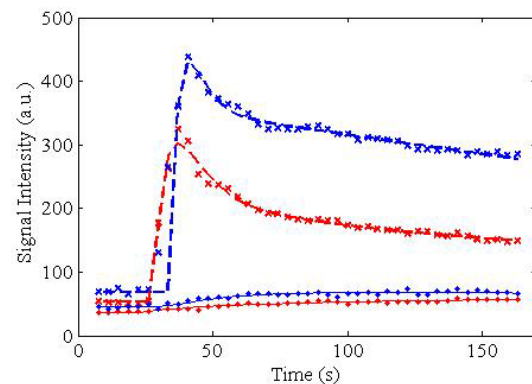

Figure 2. Signal intensity curves for resting (red) and exercising (blue) legs. X: Measured AIF. •: Measured muscle signal intensity. --: Fit of AIF. -: Fit of muscle tissue.

Figure 3. MIP of single frame of subtraction images.