Simultaneous MR Angiography and Perfusion (MRAP): Application in Lower Extremity MRA and Skeletal Muscle Perfusion

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Introduction: Examination of both large and small vessels requires two techniques: MR angiography and perfusion. While non-contrast options are available, robust methods for both MRA and perfusion often require contrast and thus the two exams cannot be performed in the same setting. Moreover, in the case of perfusion, dynamic contrast enhanced (DCE) analysis is typically performed on single, thick slices. Contrast enhanced time resolved MRA (trMRA) data sets contain not only arterial enhancement time-courses, but also high resolution 3D T_1-weighted data on tissue enhancement, i.e., perfusion. However, there are competing needs for the two exams. trMRA requires high spatial resolution and DCE-perfusion measurements require high temporal resolution and SNR for modeling accuracy. If sufficient SNR and temporal resolution for modeling the arterial input function (AIF) and tissue perfusion curves could be achieved while maintaining the necessary spatial resolution for MRA, a single trMRA data set could conceivably be used for both purposes, thus requiring a single contrast agent dose, in a single exam setting, with reduced scan time and with superior resolution for the DCE exam. In this work, a technique for simultaneous MR Angiography and Perfusion (MRAP) is demonstrated, which allows this dual use of trMRA data. MRAP is initially applied in the legs, as the lower extremities are prone to peripheral arterial disease. While MRA is commonly used for non-invasive imaging of large vessels, no robust method for evaluating muscle perfusion is in routine clinical use. The feasibility, quantitative accuracy, repeatability, and ability to measure physiological changes in perfusion due to exercise are demonstrated on asymptomatic volunteers.

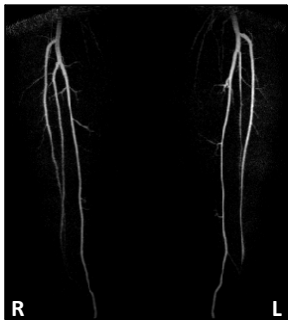

Figure 1. MIP of a single frame from a trMRA exam of the legs.

Methods: Ten asymptomatic volunteers underwent a unilateral exercise challenge (performing a three minute flexion/extension exercise at the ankle with an exercise resistance band) to provide a physiologically generated perfusion change relative to the contralateral leg which remained at rest to serve as a baseline control. Immediately following exercise, the MRAP experiment was initiated. The experiment was performed on each subject on two separate days at least one week apart. All imaging was performed at a field strength of 3.0 T (Magnetom Verio, Siemens Healthcare, Erlangen, Germany). To acquire trMRA images with a high temporal resolution and a high spatial resolution, data sharing across frames with Time-resolved angiography With Interleaved Stochastic Trajectories (TWIST) [1] was combined with GRAPPA [2] and a partial Fourier acquisition (pA: 20%, pB: 33%, R_{phase}xR_{par}=2x2, PF_{phase} 6/8). Combining these rapid imaging techniques minimizes image quality degradation that would occur from using any technique alone (i.e. temporal blurring related to view sharing and decreased SNR related to GRAPPA) [3] while achieving a spatial resolution of 1.3x1.6x1.5 mm and a temporal resolution of less than 4 s/frame. Contrast enhanced trMRA exams were performed on the volunteers after administration of a single dose (0.1 mmol/kg) of Gd-DTPA (Magnevist; Bayer, Berlin, Germany) followed by a 25 ml injection of saline at an injection rate of 3 ml/s. A FLASH readout was used with the following parameters: TR 2.97 ms, TE 1.48 ms, FA 10°, BW 1120 Hz/pixel, FOV 430x403x96 mm. Direct, quantitative pharmacokinetic analysis was performed in using a two- compartment model and K^{trans} (a direct measure of perfusion) was obtained [4]. Due to the high spatial resolution of the acquired data, the AIF could be directly estimated from an arterial region of interest (ROI) and modeled using a gamma variate exponential function [5]. Perfusion analysis was performed using a ROI approach in the tibialis anterior, gastrocnemius, and soleus muscles, and also via pixel-wise mapping. Error propagation due to noise in the acquired images was determined, and variation in K^{trans} was calculated. The effects of exercise, each imaging session, and their interaction on the measured K^{trans} were evaluated using a two-way repeated measures ANOVA (α=0.05, two-tailed). Bland-Altman analysis was performed to evaluate repeatability of the perfusion measurement on the same subject in the two sessions [6].

Figure 2. Representative muscle (soleus) signal intensity time course and model fits (rest/exercise).

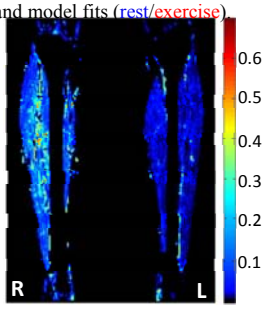

Figure 3. Pixel-wise perfusion map (K^{trans},min^{-1}).

Results/Discussion: A maximum intensity projection (MIP) of a representative frame from a trMRA data set is shown in Figure 1. Figure 2 is shows time-course data and pharmacokinetic modeling fit for the gastrocnemius muscle in resting (blue) and exercising (red) legs. Mean error in measured K^{trans} was 0.001 min^{-1}. The mean K^{trans} ± sd (over 10 subjects) were 0.14 min^{-1} ± 0.13, 0.15 min^{-1} ± 0.14, 0.19 min^{-1} ± 0.14 in rested tibialis anterior, gastrocnemius, and soleus muscles, respectively, and 0.29 min^{-1} ± 0.24, 0.27 min^{-1} ± 0.16, 0.34 min^{-1} ± 0.15 with exercise. Physiological variation in K^{trans} was thus much larger than measurement error. The two-way repeated measures ANOVA shows a strong significant effect of exercise on the measured K^{trans} (p= 0.016, 0.001, and <0.001 in the tibialis anterior, gastrocnemius, and soleus muscles, respectively), demonstrating the ability to measure a physiological change in perfusion. This is also easily seen in the pixel-wise perfusion maps (Figure 3; right leg was exercised). There was no significant difference in K^{trans} between sessions 1 and 2. The measured K^{trans} were converted to perfusion [4], and the perfusion values obtained at rest with MRAP agree well with recently published data on resting muscle, using an ASL technique [7]. While the amount of exercise was not quantified in this study, the magnitude of difference in perfusion between resting and exercised muscle was also similar to that previously reported with similar exercise [7]. A Bland Altman plot analyzing K^{trans} measurements in resting gastrocnemius in the two imaging sessions is seen in Figure 4. This shows good inter-session agreement of K^{trans} for 9 of the 10 volunteers with a near zero mean difference and only one volunteer falling outside two standard deviations from the mean. Results in other muscle groups for exercise and rest (not shown) were extremely similar. Especially given that perfusion on two separate days could vary due to simuli such as activity levels, caffeine intake, etc., the results show good agreement between the perfusion measurements from the two sessions.

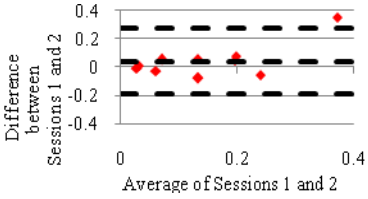

Figure 4. Bland Altman plot of K^{trans} in resting gastrocnemius muscle. Expect zero mean difference (central dashed line) between imaging sessions for each volunteer and all points to fall within 2 sd of mean (outer dashed lines) assuming similar perfusion between sessions.

Conclusion: MRAP is a viable method for simultaneous high resolution MRA and quantitative DCE exams, thus assessing small and large vessels with a single contrast dose. The technique is demonstrated in skeletal muscle and results show accurate, repeatable perfusion measurements at rest and with exercise.

References: [1]Vogt, et al. ISMRM, Berlin 2007, p92. [2]Griswold, et al. *MRM* 2002; 47:1202-10. [3] Wright, et al. ISMRM, Stockholm 2010, p. 2740. [4]Tofts, et al. *JMRI* 1999; 10:223-32. [5]Feng, et al. *Int J Biomed Comput* 1993; 32:95-110. [6] Bland, et al. *Lancet* 1986; 1:307-10. [7] Elder, et al. MRM 2010, 64: 852-61.

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