# Initial Clinical Application of Simultaneous MR Angiography and Perfusion (MRAP) in Peripheral Arterial Disease

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**Target Audience:** This work targets those interested in the application of MR Angiography (MRA), quantitative dynamic contrast-enhanced (DCE) MRI, and peripheral arterial disease (PAD).

**Purpose:** The purpose of this study was a preliminary evaluation of MRAP for assessing the severity of PAD.

**Introduction:** Lower extremity peripheral arterial disease (PAD) results from the development of occlusive atherosclerotic plaque in arteries that supply the lower limbs. The symptoms (leg weakness, claudication) result from a constellation of physiological changes secondary to reduced tissue perfusion. Existing methods for following PAD are limited to crude, non-spatially resolved measures such as the ankle-brachial index (ABI, a simple ratio of blood pressures in the lower and upper limbs), evaluation of large vessel pathology only (again ABIs) and indirect measures such as skin oxygenation. The ability to evaluate treatment success is even poorer and thus there is an open need for disease biomarkers for PAD. The vascular pathology in PAD could result from inflow (i.e. large vessel) or true perfusion deficits (i.e. small vessel disease), which may require different treatments. MRI can be used to assess both large and small vessels, with MRA exams and for measuring perfusion with DCE-MRI, respectively. MRA has been extensively applied to large vessel peripheral atherosclerotic disease. However, despite the long history of accurate MR perfusion measurements elsewhere in the body, application of DCE-perfusion MRI to PAD has been limited. This is partially because the enhancement in muscle is slow and relatively weak, and thus perfusion quantitation in muscle is difficult. Nevertheless, semi-quantitative measurements of a perfusion index (upslope ratios of muscle and arterial enhancement) were found to be extremely promising for PAD[1]. A second problem is that MRA and DCE-MRI each require a dose of contrast agent. Thus these exams should be performed on separate days to avoid contamination of either study or double-dosing the patient. This effectively precludes performing both an MRA and DCE-MRI clinically. Recently, it was shown that by using an optimized, high spatio-temporal resolution acquisition, MRA and Perfusion (MRAP) measurements can be performed simultaneously using a single dose of contrast agent[2]. Here, pilot results using MRAP to assess PAD are presented.

**Methods:** All imaging was performed at 3.0T (Magnetom Verio, Siemens Healthcare, Erlangen, Germany) in this HIPAA-compliant and IRB-approved study. Five subjects with PAD were imaged following written informed consent. To achieve the required high spatiotemporal resolution, Time-resolved angiography With Interleaved Stochastic Trajectories (TWIST)[3] was combined using optimized acceleration with GRAPPA[4] and partial Fourier (pA: 20%, pB: 33%, $R_{phase}$,$R_{par}$=2, $PF_{phase}$ 6/8)[5], yielding a spatial resolution of 1.3x1.6x1.5 mm and a temporal resolution of less than 4 s/volume. In order to image during a physiological stress on the skeletal muscle, volunteers were asked to perform a plantar flexion exercise on both legs to exhaustion, in order to measure maximal perfusion in the limbs. Immediately following exercise completion, MRAP exams were performed after administration of a single dose of Gd-DTPA (0.1 mmol/kg, Magnevist; Bayer, Berlin, Germany). A FLASH readout was used with the following parameters: TR/TE/FA: 2.97 ms/1.48 ms/10°, BW 1120 Hz/pixel, FOV 430x403x96 mm. To display trMRA data, subtracted maximum intensity projection (MIP) images were reconstructed in the coronal orientation. To perform the perfusion estimation, a quantitative pharmacokinetic analysis was performed using signal intensity curves from both ROI and pixelwise approaches. Data were fit using a Tofts compartment model, and $K^{trans}$ (a direct measure of perfusion) was obtained[6]. Due to the high spatial resolution of the acquired data, the arterial input function could be directly estimated from an arterial region of interest (ROI) and was modeled using a gamma variate exponential function[7]. Pixelwise parameter maps were created at a lower spatial resolution (2.6x3.2x3 mm). Prior to the MRI exam, all subjects had an ankle brachial index (ABI) measured as part of routine clinical care. $K^{trans}$ measurements from three muscles – gastrocnemius, soleus, and tibialis anterior were correlated against ABI values, and the Pearson correlation coefficient (α=0.05) was calculated.

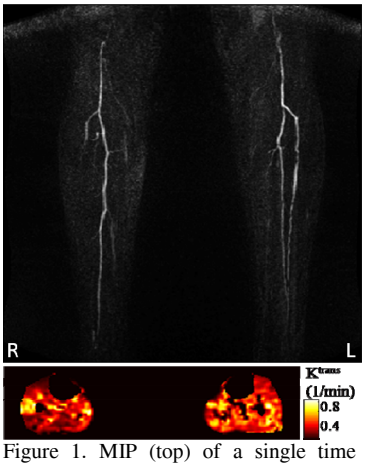


Figure 1. MIP (top) of a single time frame from a subject with PAD and unequal ankle-brachial indices (0.35 and 0.68 on the right and left, respectively). Axial perfusion ($K^{trans}$, $min^{-1}$) map (bottom). Note higher global $K^{trans}$ values in the left leg, which has the higher ankle-brachial index.

**Results:** A representative MIP image from a single frame of an MRAP exam is shown in Figure 1 above an axial $K^{trans}$ map for the same subject. Similarly, an axial reconstruction of a perfusion map for a second patient is shown in Figure 2. Group analysis (N=10 legs) for the soleus muscle showed a linear relationship between ABI and perfusion ($K^{trans}$, $min^{-1}$), $R^2$=0.43, Pearson correlation coefficient of 0.66, p=0.03, statistically significant at p<0.05. No significant correlation was found for the gastrocnemius or tibialis anterior (TA) muscles.

**Discussion:** The perfusion difference between the unequally affected limbs is clearly visible in the perfusion maps from both patients in Figures 1 and 2, with the less affected leg showing lower perfusion. There is a significant relationship between ABI and perfusion in the soleus muscle, but not in the smaller gastrocnemius, or in the anteriorly located TA. While preliminary and on a small set of patients, these data indicate that perfusion deficits in PAD are likely to be geographic and therefore require spatially resolved analysis, for which MRAP (and imaging in general) is ideally suited. Moreover, the ability to reliably map tissue perfusion and therefore quantitatively assess small vessel pathology (unlike ABI or MRA) provides a window into a factor of PAD pathophysiology that could not be reliably assessed previously. Further work is needed to evaluate the role of perfusion measurements in PAD follow-up.

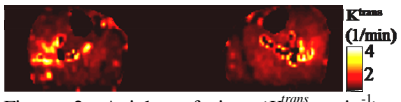


Figure 2. Axial perfusion ($K^{trans}$, $min^{-1}$) map. Note diffusely higher $K^{trans}$ values in the left leg, particularly posteriorly. The left and right ABIs are 0.82 and 0.49, respectively.

**Conclusion:** This preliminary study shows the feasibility of applying MRAP in subjects with PAD. The results indicate that perfusion deficits in PAD may be geographic, and not all muscles may be equally affected.

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