Target Audience: Researchers and clinicians with an interest in BOLD effects in skeletal muscle and in methods for dynamic quantification of tissue relaxation rates.

Purpose: The time-courses of MR relaxation rates have traditionally been assessed using echo planar imaging (EPI) based dynamic measurements of $R_2^*$ and $R_2$ from separate image acquisitions. Subtraction of these rates yields an estimate of $R_2'$, which can be used for image-based calculation of muscle oxyhemoglobin saturation. This approach requires subjects to repeat functional tasks such as contractions or cuff occlusion. Recently, an EPI based multiple spin- and gradient-echo (SAGE) method has been developed for brain perfusion imaging that permits the simultaneous measurement of $R_2^*$ and $R_2$. We applied the SAGE sequence to measurements of relaxation rates in skeletal muscle during maximal and submaximal isometric dorsiflexion contractions.

Methods: With local IRB approval, SAGE, multi-gradient echo (MGE), and multi-spin echo data (MSE) were acquired from the legs of 5 subjects [4 female, Age=29(4) years, Height=165.4(4.3) cm, Mass=62.0(11.9) kg] using a 3T Interia Achieva MRI (Philips Healthcare, Cleveland, OH) and an 8 channel knee coil. SAGE imaging parameters were: TR=2.5s, TE=4.9, 14, 29, 38, 47, FOV=180x180 mm$^2$, Voxel Size = 2.81x2.81x7.6 mm$^3$. $R_2^*$ and $R_2$ from the SAGE acquisition were compared to those from MGE (TR=2.5s, TE=2.5ms, ESP=2.5ms, NE=30) and MSE (TR=2.5s, TE=10.77ms, ESP=10.77ms, NE=8) acquisitions. Subjects then performed two 10s duration maximal voluntary isometric dorsiflexion contractions and one 120s duration submaximal isometric dorsiflexion contraction (40%) while SAGE data were acquired. On a separate day, near-infrared data were acquired (model 96208; ISS, Inc., Champaign, IL) from the tibialis anterior muscle of 3 of the 5 subjects [2 female] while the isometric contraction protocol was repeated.

Results and Discussion: There was fairly good agreement between relaxation rate measurements derived from EPI SAGE and those derived from MGE and MSE sequences. SAGE $R_2^*$=40.23 [35.59, 45.45] (mean [95% confidence interval]); MGE $R_2^*$=37.35 [37.13, 37.57]; SAGE $R_2$=37.50 [32.90, 42.10]; and MSE $R_2$=32.80 [31.62, 33.97]. It is notable that agreement was good even when comparing SAGE EPI rates to the non-EPI multi-echo rates. The post-contraction decrease in $R_2^*$ and $R_2$ characteristic of the muscle BOLD effect is clearly visible (Fig 1) with a 1.6% decrease in $R_2^*$ occurring 25.0s post-contraction and a 3.0% decrease in $R_2$ occurring 22.5s post-contraction. The data in figure 2 suggest that the magnitude and kinetics of the $R_2'$ are influenced by a combination of changes in proton density and deoxyhemoglobin. At present, we were unable to achieve such results for submaximal contractions, however, patient populations such as those with diabetes may tolerate brief maximal contractions better than longer submaximal contractions. Additional data collection will allow more quantitative analysis of the observations in the present study.

Conclusion: Baseline SAGE $R_2^*$ and $R_2$ measurements generally agree with more conventional multi-echo measurements. SAGE allows simultaneous measurement of changes in $R_2^*$ and $R_2$ related to the BOLD effect in skeletal muscle induced by isometric contractions. These simultaneous measurements allow a more direct calculation of $R_2'$ that is related to the change in muscle oxygen saturation when maximal isometric contractions are performed.