Simultaneous Acquisition of Quantitative ASL and T2* (SQUAB) for Characterization of Skeletal Muscle Hemodynamics.

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Introduction: Simultaneous measurements of both perfusion and BOLD have the potential to improve assessment of tissue oxygen and metabolism across a range of applications, including skeletal muscle in peripheral arterial disease (PAD)[1,2]. We have developed a pulse sequence, Simultaneous Quantitative Arterial perfusion and BOLD imaging (SQUAB), for simultaneous acquisition of quantitative perfusion maps with arterial spin labeling (ASL) and high SNR T2* maps to monitor BOLD changes at rest and following exercise. As shown in Fig. 1, SQUAB consists of two multi-echo EPI readouts blocks. The first block (B_1) is preceded by a selective saturation and a FAIR preparation using an alternating selective or non-selective inversion pulse while the second block (B_2) is preceded only by a slice selective saturation. B1 and B2 are acquired sequentially within a single repetition period, TR1. This sequence design offers several advantages over previous simultaneous BOLD and ASL acquisition schemes. First, a high SNR T2* map can be calculated from B2 which is acquired after a long recovery period (TR2) and contains increased initial magnetization. Secondly, using a selective saturation pulse prior to the FAIR preparation allows for increased accuracy when subtracting alternatively selective and non-selective inversion prepared B1 readout blocks for blood flow measurements. Finally, this sequence allows for an estimate of T1 and Mo as B_1 and B_2 are acquired after different saturation recovery times. These values can be used in the blood flow calculations as they dynamically change following recovery from exercise[1].

Methods: All experiments were performed using a Siemens 3.0T Verio system with a 32 channel knee coil (*Invivo,Gainesville, Fl*) for calf imaging. RF Excitation was accomplished with a 90º water selective pulse and slice selective saturation was accomplished through a train of three 90º pulses each followed by a spoiling gradient. Inversion recovery was performed with either a selective or non-selective 10.2ms, 180º hyperbolic secant pulse. Other MRI parameters included: TI 1200ms, TR1 4000ms, TR2 2400ms, matrix size 64 x 64, FOV 16cm, phase Partial Fourier 7/8, TE1=19ms, and TE2 = 52ms.

Volunteers (n=3, 2 M, mean age 31.7y) and a 76 year old female patient with bilateral intermittent claudication were rested for 20 minutes prior to the exercise protocol. In 2 volunteers, experiments were conducted bilaterally on the same day while in a third volunteer and the patient, exercise was conducted unilaterally. Baseline SQUAB imaging was performed over 2 min. Next, subjects performed exercise within the scanner, consisting of repeated ankle dorsi- and plantar-flexion as rapidly as possible until exhaustion was reached. An elastic resistance band (Thera-Band, Akron, OH) was applied to the dorsum of the foot, such that dorsiflexion was performed against resistance and the anterior compartment calf musculature was isometrically exercised. SQUAB imaging was commenced immediately on cessation of exercise for 20 minutes.

Signal intensities used to calculate blood flow, T1, and Mo were measured by placing an ROI in the anterior compartment. T2* values were calculated from B2 as $(TE_1 - TE_2)/ln(B_{2(TE1)}(x,y)/B_{2(TE2)}(x,y))$. T1 could be calculated by finding the T1 value that minimizes the function $B_1(x,y)/B_2(x,y) - (1 - exp((-TI)/T1(x,y)))/(1 - exp((-TR2)/T1(x,y)))$ and based on the results, $M_o(x,y)$could be calculated as $B_1(x,y)/(1 - exp(-TI/T1(x,y)))$. Therefore, blood flow, *f*, could be calculated from ΔM, the difference between selective and nonselective inversion prepared block, B1, T1, and M_o as $f = (\Delta M(x,y)\lambda/(2TIMo(x,y)))exp(TI/T1(x,y))$where λ is assumed to be .09g/ml. T2* values were used to correct the signal intensities required to calculate T1, Mo, and blood flow.

Results and Discussion: The SQUAB sequence was successfully implemented showed demonstrable changes in muscle signal on T2* and perfusion images in the tibialis anterior as shown in Figure 2. The time course of changes in perfusion and T2* in the tibialis anterior and gastrocnemius muscle groups over the average of all volunteers and a patient is shown in Figures 3 and 4 respectively. In both volunteers and the patient, increases in both perfusion and T2* are observable in the tibialis anterior. In volunteers, perfusion in the tibialis anterior increased from undetectable levels to a maximum of 40.42±14.39ml/min/100g, while BOLD signal increased from 26.29±1.03ms to 34.25±2.25ms maximally. In the PAD patient, exercise resulted in an increase of blood flow in the tibialis anterior from undetectable levels to 8.7ml/min/100g and T2* from 24.12ms to 25.83ms demonstrating delayed and lower responses, indicating restricted post-exercise hyperemia. In the gastrocnemius muscle, which was minimally exercised in this protocol, perfusion in the volunteers and the patient remained relatively unchanged from baseline, while T2* values were slightly reduced from baseline.

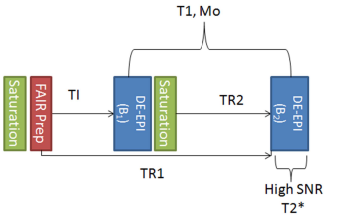

Fig. 1 SQUAB Pulse Sequence Design. Each EPI readout block (B_1 and B_2) contains a Dual Echo (DE) readout. A high SNR T2* map can be calculated from B_2. T1 and Mo can be calculated from B_1 and B_2. The subtraction of two alternatively selective and nonselective inversion prepared B_1 blocks can be used to calculate muscle blood flow.

In conclusion, our results show the feasibility of acquiring simultaneous T2*maps and perfusion measurements in skeletal muscle. SQUAB offers: high temporal resolution dynamic imaging, quantitative blood flow values, and simultaneous, high SNR T2* maps. Future work will include performance of the technique in a larger clinical population, to determine its efficacy in PAD evaluation, including response to intervention.

Ref: [1]Boss et al NMR Biomed, Feb 19(1) 2006 [2]Ledermann et al Radiology, Nov 241(2) 2006

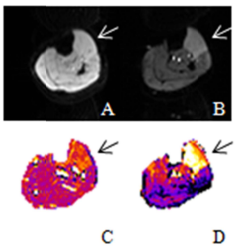

Fig. 2 Example images of the lower extremity. A.) First and B.) second echo images, C.) Blood Flow map, and D.) T2* map 2 minutes after exercise in a volunteer. The arrow points to areas of enhanced perfusion and T2* localized to the tibialis anterior muscle.

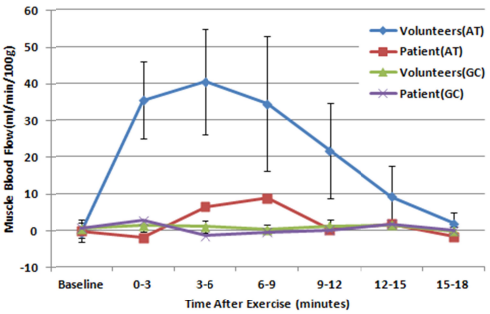

Fig. 3 Time course of the tibialis anterior and gastrocnemius muscle blood flow averaged over all volunteers and in a patient over the specified time period. The bars depicted at each time point represent the standard deviation.

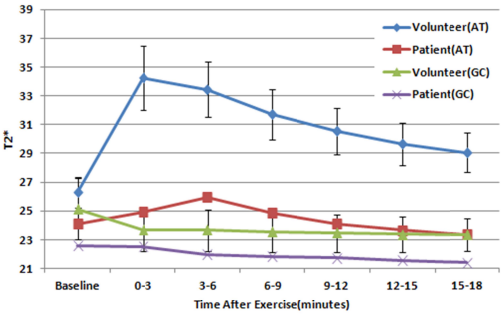

Fig. 4 Time course of changes in tibialis anterior and gastrocnemius muscle T2* values averaged over all volunteers and in a patient over the specified time period. The bars depicted at each time point represent the standard deviation.