Simultaneous quantification of perfusion, intravascular venous oxygen saturation, and skeletal muscle $T_2^*$ during reactive hyperemia in the leg using an interleaved PASL and multi-echo GRE sequence

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INTRODUCTION

• Peripheral arterial disease (PAD), generally a systemic manifestation of atherosclerosis, is a debilitating disease affecting many people, particularly the elderly.
• Risk factors include smoking, diabetes, older age, and high blood pressure.
• Patients present with low ankle-brachial index (ABI) and claudication.
• PAD is an independent risk factor for heart attack and stroke.

PAD results in structural as well as functional impairments.

• Structural - Flow-limiting stenoses in large arteries and compensatory collateralization [2].
• Functional - Endothelial dysfunction, decreased perfusion, and blunted hyperemic response [3].
• Many current MRI-based methods for assessing PAD require an ischemia/reperfusion paradigm to investigate the functional reserve of the vasculature.
• MR oximetry to assess dynamic parameters of venous oxygen saturation (SvO₂) [5,6].
• Measurement of skeletal muscle $T_2^*$ as a marker of muscle oxygenation status [7,8].

No previous study has been able to concurrently measure all functional parameters.

We propose to develop and validate an interleaved PASL/multi-echo GRE (PASL/Ox-BOLD) pulse sequence, capable of simultaneously measuring perfusion, venous oxygen saturation, and skeletal muscle $T_2^*$ during reactive hyperemia in the leg.

THEORY & METHODS

Perfusion - Saturation Inversion Recovery

Perfusing blood is labeled by alternating between non-selective (NS) and slice selective (SS) adiabatic inversion pulses [4].

Perfusion is calculated as:

$$ f = \frac{\lambda}{T} \left( M_0 - M(t) - M_b(t) \right) $$

[Eq 3]

Where $\lambda$ is perfusion in classical units (ml/min/100g)

$\lambda$ is the tissue partition coefficient (mL/ml/4)

$T$ is the post labeling delay (PLD) + TE

$M_0$, $M(t)$, and $M_b(t)$ are the magnitude signal intensities

$T_{iso}$ = 1420 ms

Partial-Fourier GRE-EPI readout following NS and SS inversions with the following parameters:

• FOV = 250 x 250 mm², ST = 10 mm

• Matrix = 80 x 50, Reconstructed matrix = 80 x 80


Oximetry and $T_2^*$ - Multi-echo GRE

Oximetry - MR Susceptometry

• Magnetic susceptibility induced differences in phase accumulation between blood and surrounding tissue are used to calculate hemoglobin oxygen saturation [6, 10-11] from phase images acquired at $T_1$ and $T_2$, as:

$$ \frac{\Delta \phi}{\phi_0} = \gamma \chi_B H_c \cos \beta \left( \cos \theta - \frac{3}{5} \right) $$

[Eq 2]

Where $\chi_B$ is the susceptibility difference between fully oxygenated and deoxygenated blood (0.27 ppm)

• Hematocrit (Hct) is taken to be 0.45

• $\beta$ is measured from axial scout images

Skeletal muscle $T_2^*$

• Magnitude $S_{T1} - T1E$ are fitted to a monoexponential to calculate $T_2^*$.

• Multi-echo GRE readout with keyhole acquisition (central 1/3 of k-space acquired every PLD of PASL) and:

• FOV = 96 x 96 mm², ST = 10 mm, slice location located 3 cm in the foot direction

• Matrix = 96 x 96, Reconstructed matrix = 96 x 96 using reference image acquired after dynamic scan.

Experimental Design

• To validate PASL/Ox-BOLD, measured perfusion, $S_{O2}$, and $T_2^*$ data were compared to an otherwise identical PASL-only, or a keyhole Ox-BOLD-only version of the sequence.

• 5 subjects were scanned on two separate days to assess accuracy and reproducibility.

• For each subject, two PASL/Ox-BOLD, one PASL, and one Ox-BOLD sequence were run in a randomized order. The protocol was repeated in the same order on the second day.

• All imaging was performed on a Siemens 3T scanner with the calf centered in an 8 cm x 12 cm knee coil (miso), and a cuff (thiokonan) placed around the thigh

• Each scan lasted 10 min, with 1 min baseline, 3 min arterial occlusion with cuff inflated to >205 mmHg, and 6 min recovery. 1 min of rest was given before the next scan.

Image Analysis

• Perfusion - Temporal matching of NS and SS images was achieved by averaging adjacent NS time points.

• Regions of interest (ROIs) were drawn in the gastrocnemius, soleus, peroneus, and tibialis anterior (TA) muscles with voxel-based perfusion calculated for each ROI.

• Parameters extracted from the perfusion time course data include peak perfusion and peak time to peak perfusion (TPP).

• Ox-BOLD - For each Ox-BOLD image, high spatial frequency data was fitted to the average of reference images acquired immediately after the scan.

• Only data acquired following SISV inversion was used for analysis, though the Ox-BOLD interleave was run every PLD to control for magnetization transfer effects.

• OXIMETRY - A phase map was generated for each of the images and the baseline phase accumulation was subtracted [12].

• The larger of the peroneal veins was selected for $S_{O2}$ analysis and an ROI was drawn in this vein. The reference tissue was selected in an ROI immediately surrounding the peroneal vein and $S_{O2}$ was calculated from Eq. 2.

• Washout time (time to minimum $S_{O2}$), and overshoot (peak $S_{O2}$ - baseline $S_{O2}$) were recorded from the $S_{O2}$ time course.

• $T_2^*$ calculation

• Signal intensity in each of the 5 echoes in a homogeneous region of the soleus muscle was extracted and fitted to a monoexponential function.

RESULTS

CONCLUSIONS

• Perfusion - Good intra-scan reproducibility, but relatively poor inter-scan reproducibility of the perfusion parameters measured with PASL/Ox-BOLD.

• Perfusion varies physiologically with time of day, hydration, caffeine intake, hormonal fluctuations, and exercise.

• Oximetry and $T_2^*$

• It is possible to measure venous oxygen saturation in the peroneal vein with keyhole oximetry in less than one second.

• $T_2^*$ is similar for PASL/Ox-BOLD and Ox-BOLD, though $T_2^*$ differs between PASL/Ox-BOLD and Ox-BOLD.

• Although the order of the scans was randomized, one of the PASL/Ox-BOLD scans was first in all but one subject. This could explain the decreased $T_2^*$ in the other subject.

• Owing to non-homogeneous samples this method is useful for investigating tissue oxygenation.

• $T_2^*$ was normalized to his baseline value.

• Simultaneous acquisition of PASL, oximetry, and $T_2^*$ has no effect on the quantification of perfusion, $S_{O2}$, or $T_2^*$.

• The data demonstrate the feasibility of a combined PASL/Ox-BOLD method for simultaneous measurement of perfusion, venous oxygen saturation, and skeletal muscle $T_2^*$ during reactive hyperemia.

• There are striking differences in the measured parameters between healthy subjects and PAD patients.

• Further exploration of these functional parameters in PAD patients could:

• Help to better characterize pathophysiologic mechanisms underlying the functional impairment in PAD.

• Provide a new, noninvasive tool for the diagnosis, evaluation, and monitoring of PAD disease progression and response to therapy.

REFERENCES & ACKNOWLEDGEMENTS


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