Quantitative Imaging of eXtraction of Oxygen and Tissue Consumption (QUIXOTIC) using velocity selective spin labeling

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INTRODUCTION: While oxygen extraction fraction (OEF) and cerebral metabolic rate of oxygen (CMRO2) are fundamental quantitative parameters in neuropathological and functional neuroactivation, a robust MRI-based OEF/CMRO2 mapping technique has not been established. A key hurdle in OEF/CMRO2 imaging is absolute quantification of venular oxygen saturation (Yv), which requires isolating signal exclusively from post-capillary venular (PCV) blood on a voxel-by-voxel basis. We propose and demonstrate a novel, voxel-wise method to address this signal-dependence problem using velocity selective spin-labeling. We subsequently estimate T2 of isolated PCV blood, convert T2 to Yv with a calibration curve, compute OEF from Yv, and estimate baseline CMRO2 from OEF and an additional cerebrovascular blood flow (CBF) measurement. This approach is dubbed QUantitative Imaging of eXtraction of Oxygen and Tissue Consumption (QUIXOTIC) MRI.

THEORY: QUIXOTIC MRI is adapted from velocity-selective arterial spin labeling [1], and uses nearly identical velocity selective (VS) modules to saturate blood spins above a given velocity. The pulse sequence (Fig 1) is played for both tag control acquisitions. The tag acquisition applies a user-defined cutoff velocity (Vc) for both VS Module I (VS1) and VS Module II (VS2), while the control uses Vc for VS1, but disables velocity selection for VS2 (i.e. moving spins are unaffected). Incorporated into VS2 is a T1-preparation module [2], allowing acquisition at multiple echo times. An important feature of the sequence is an inversion pulse at TINV, which compensates for T1 relaxation. To introduce properties of this sequence, we first neglect T1 relaxation and the TINV inversion pulse. At t=0, before VS1, all blood (arterial, venous, capillary) is relaxed. Strong velocity weighting (low Vc) is then applied during VS1 for both tag and control, selecting for slow moving spins in small arterioles, capillaries and small venules (VcVc), but saturating faster moving spins in larger vessels (Vc>Vc). Notably, this large-vessel signal is eliminated on both sides of the circulation. After VS1, the inflow term (TI) allows the targeted blood to flow out of the small vessel compartments and accelerate into larger venular vasculature. VS2 is then applied at TI. This time, however, the tag and control acquisition experience different velocity weightings; the tag sees velocity selection at Vc, but the control experiences no velocity weighting. Spins that have accelerated above Vc during TI are saturated by the tag acquisition, but left unaltered in the control. As imaging starts immediately after VS2, subtraction of tag from control yields an image weighted to blood that has accelerated from below Vc, to above Vc during TI. Assuming unidirectional flow (arterial to capillary to venous), these spins are venous only. Other spins (static, CSF, non-venular blood) are eliminated via subtraction. If Vc and TI are chosen properly, signal from PCV blood is exclusively targeted. Of course, T1 relaxation complicates this idealized model. Spins saturated at VS1 at t=0 experience recovery. Because velocity selection via VS2 occurs only for the tag and not control, spins from unwanted compartments will partially recover in the control, and fully saturate in the tag at TI. Without compensation, these unwanted spins will not subtract completely, and QUIXOTIC loses venous selectivity. We place an inversion pulse at TINV to null recovering blood at TI, so spins in this unwanted population are saturated in both control and tag at TI, leaving only desired PCV blood upon subtraction.

METHODS & RESULTS: Four healthy volunteers (2 M, 2 F, 21 to 27 years) were scanned at 3T (Siemens Tim Trio, 32-ch head coil) with QUIXOTIC MRI to image PCV blood (Vc=2.4 cm/s, x-directed, TINV=400 ms assuming T1blood=1664 ms at 3T [3], TI=722 ms, T1CPAG of T2-prep = 10 ms). A GRE-EPI readout (TE/TR = 12/3000 ms, 4 slices, 3.9x3.9x10 mm3) was used for tag/control image acquisition. Eighty measurements were acquired. The raw data series were motion corrected and smoothed; pairwise subtraction was then performed. The subtraction series was averaged to produce mean PCV-weighted images. Here, mean PCV images at 8 effective TEs (ΔTE = 17.4 ms) were acquired (in principle only two are necessary). A double inversion recovery sequence yielded gray-matter-only (GM) images; these were used as GM ROI, from which venular blood signal intensity (SI) could be measured (with an exception of anterior regions which suffer from signal-dropout artifacts, possibly due to gradient imperfections/eddy currents in GM). GM PCV-blood SI was plotted versus TE, and fit to measure T1, T2 and OEF during block-design and event-related fMRI. One such study is described in Table 1. Separately, the T1-prep module was incorporated into the PASL sequence; experiments targeting arterial blood were performed as described in [4], with T2arterial>150 ms, indicating complete arterial oxygen saturation, supporting validity of the QUIXOTIC approach to measure oxygen saturation of deoxygenated venous blood.

DISCUSSION: Values reported for Yv and OEF agree with those acquired by other PET/MR studies, and fall within normal physiological range [4-6,11]. Prior GM CMRO2 measurements are more scarce in the literature; those reported in PET studies [10,11] are lower than those reported here, perhaps due to substantially lower baseline CBF reported by PET imaging, thereby causing an underestimate in CMRO2.

We have shown the feasibility of using QUIXOTIC MRI to isolate PCV blood signal and subsequently measure Yv, OEF, and CMRO2. Advantages of this method are: 1) QUIXOTIC maps venous-only blood, with CSF, static tissue, and capillary/arterial blood eliminated; 2) QUIXOTIC analysis can be performed on a voxel-by-voxel basis, allowing creation of Yv, OEF, and CMRO2 maps; and 3) QUIXOTIC generates images every TR, making the technique amenable to functional imaging of Yv and OEF during block-design and event-related fMRI. One such study is described in [12]. To our knowledge, no currently available technique offers these three features. Future studies will explore optimal parameter settings (Vc, TI), employ a spin-echo EPI for rapidly acquiring multi-echo data, and focus on employing selection velocity in the control VS2 module to enable flexible “velocity bracketing” i.e. targeting venous blood in a specific velocity range, offering better PCV targeting via elimination of blood in larger draining veins.

REFERENCES:

ACKNOWLEDGEMENTS: NIH R01EB006647, NIH R01EB005742, NNC N01RR141047, HST Martinos Catalyst Fund, T Banner, T Reese