Imaging of Oxygen Extraction Fraction Using Velocity Selective Excitation with Arterial Nulling (VSEAN)

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Introduction: Oxygen Extraction Fraction (OEF) is thought to be a more specific indicator of ischemic penumbra in stroke than contrast based perfusion MRI [1]. The Cerebral Metabolic Rate of Oxygen ($CMRO_2$), which can be calculate from OEF and CBF provides a quantitative measure of brain metabolism, and can be used to study brain physiology and function. These provide strong motivation for robust non-invasive measures of OEF. Bolar *et al* [2] introduced a new imaging method to differentiate the post-capillary venular (PCV) blood from other tissues using velocity-selective (VS) pulses [3], and used T2 measurements in the PCV blood to estimate OEF. Here we introduce a strategy to image the PCV blood with higher signal to noise ratio (SNR) using VS Excitation with Arterial Nulling (VSEAN).

Theory: The source of signal in brain can be classified into static and moving spins, the latter consisting primarily of arterial and venous blood. Since venous blood is the target in OEF experiments, static tissue and arterial blood should be removed. In this new method, a slab selective inversion pulse is applied just below the imaging plane as in a typical PASL experiment, and the inversion time is chosen so that arterial blood is nulled during image acquisition. To remove the static tissue signal, a modified Velocity-Selective BIR4 pulse train [4] with Mz response proportional to $sin(v)$ (VS-sin) is applied. For cutoff velocity v_{cut}, the longitudinal magnetization can be expressed as: $Mz(v) = \sin(\pi v_{cut})$, note that the spins with positive and negative velocities have opposite phases. A second VS-sin module can be applied to create sin^2 modulation: $Mz(v) = \sin^2(\pi v_{cut})$. Because of this symmetric and quadratic response near zero velocity, static and slow moving spins are well suppressed. We use as a second VS-sin module simple diffusion gradients in the imaging sequence to shorten the preparation time and most importantly, to keep the flowing spins out of phase with residual static tissue signal, allowing for additional phase sensitive suppression of static tissue. Compared to this method, QUIXOTIC subtracts out static tissue signal, and filters venous blood signal based on deceleration. However, after the first VS module, an in-plane inversion pulse is applied in QUIXOTIC to null partially recovered arterial blood signal. This pulse also inverts venous blood, and the signal of venous blood is reduced due to inversion recovery (**Fig. 1**). The magnetization of venous blood with VSEAN is 0.86, compared to 0.47 in QUIXOTIC with TR=3s, $T1_{arterial}$=1664ms, $T1_{venous}$=1500ms, $T1_{tissue}$=1200ms. Since no subtraction is used in VSEAN, another factor of $\sqrt{2}$ improvement of SNR per unit time is achieved. Because static tissue is suppressed in VSEAN, it may be less sensitive to physiological noise. Assuming that venous spins are distributed across a large velocity range, up to half of the signal is lost in VSEAN due to the $\sin^2(\pi v_{cut})$ modulation, however, the overall SNR improvement per unit time is still 1.29 times that of QUIXOTIC. The measurement of oxygenation of venous blood can either be carried out with T_2 prep or multiple spin echo acquisition, and the latter is used in this study.

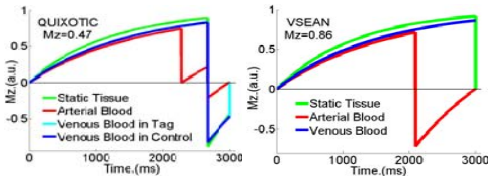

Fig 1. Mz evolution in QUIXOTIC and this method, only the signal from spins that will be imaged are shown. Venous signal in QUIXOTIC is 0.47 in every two TRs, compared to 0.86 in this method in only one TR

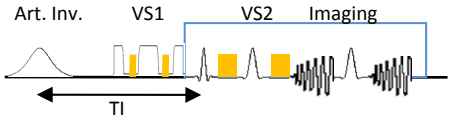

Fig. 2 Pulse sequence diagram

Pulse Sequence and Methods: As shown in **Fig. 2**, a proximal sech pulse is applied at TI to invert arterial blood. The first VS module is applied right before image acquisition, the second VS module is incorporated into the image acquisition, and multiple spin echoes are collected with spiral readout. To collect reference images, the first VS pulse train has $\cos(\pi v_{cut})$ modulation, while in actual data acquisition, VS-sin modulation is applied. The diffusion gradients in the imaging part remain the same for reference and data collection. A young male subject was scanned on GE 3T system with 8-channel head coil. The imaging parameters were: single slice with FOV=220mm*8mm, TR=4s, TE=21/41/61ms, TI=1013ms, v_{cut}=2cm/s, gradients along S/I direction, inversion band=15cm, 10mm gap between inversion and imaging region, spatial spectral excitation with sinc 180° CPMG refocusing pulses, spiral read out with matrix size 32, interpolated to 64; 80 images plus 4 reference images were collected.

Data Processing and Results: The data from each coil was complex-reconstructed individually in order to preserve the phase information, then spatially smoothed by a 3*3 Gaussian kernel and projected onto the axis perpendicular to the phase estimated from reference image with the same TE. The projected signal from coils were combined using the sensitivity map for coil j estimated also from the reference images: $S_{comb} = \sum_j S_{j,data}\, sen_j$, where $sen_j = \frac{|S_{j,ref}|}{\sum_i |S_{i,ref}|}$. With this type of signal combination, the noise has zero mean and does not bias the T2 estimates. A T2 map was calculated using echoes 1 and 3 because of the even echo rephasing phenomenon [5]. A threshold from the relative venous blood volume map (**Fig. 3d**) after T2 calculation masked out the regions in which mean T2 value and its standard deviation are estimated.

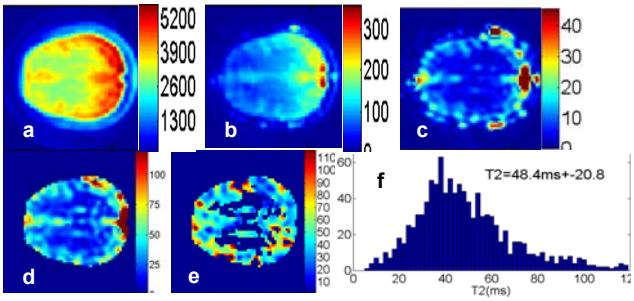

Fig. 3 A. reference image; B. acquired data; C. venous blood signal after projection; D. estimated relative venous blood volume; E. T2 map; F. histogram of T2 values in E.

As shown in **Fig. 3b**, the VS-sin module suppressed the static to <5%, and after projection (**Fig. 3c**) the static tissue signal was below 0.1%, leaving venous blood signal (since arterial blood was nulled at this acquisition time). The calculated venous T2 values were 48.4±20.8ms, giving a venous oxygen saturation of 58% using a T2/Yv calibration curve [6], and an OEF of 42% assuming fully oxygenated arterial blood. Note that the high T2 values in **Fig. 3e** were at the low relative blood volume region, which may be contaminated by noise.

Discussion: Other strategies could be considered to further reduce the static signal: 1) alternate the sign of the moving spin signal every TR without affecting the static tissue signal, either by adding an extra 0/π phase shift to the VS-sin module, or by changing the sign of the diffusion gradients in the imaging sequence; 2) apply a tip-down pulse right before the readout gradients to tip the static tissue signal onto longitudinal axis.

In conclusion: the main advantages of this method are: 1) higher SNR due to more relaxed venous blood; 2) no subtraction gives higher time efficiency; 3) insensitive to physiological noise; 4) a T2 map is generated every TR from multi-echo acquisition.

Acknowledgement: **NIH R01 EB002096**

Reference: 1) Sobesky et al, Stroke 36;980 2005. 2) Bolar et al, ISMRM, 2009, 628. 3) Wong et al, MRM 55:1334-41 (2006). 4) Wong et al, ISMRM, 2010, submitted. 5) Kucharczyk et al, Radiology, 157:95-101 (1985). 6) van Zijl & Clingman, personal communication.