

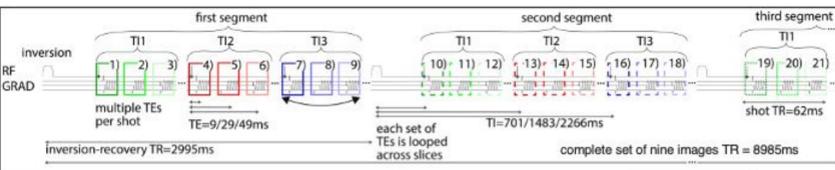
INTRODUCTION

- Dynamic cerebrospinal fluid (CSF) acts as a clearance system in the human brain, removing waste and toxins, especially during sleep¹⁻³.
- Most functional CSF tracking with fMRI has focused on CSF flow⁴⁻⁵, where sensitivity and efficiency is difficult; CSF volume may be more straightforwardly measured.
- CSF volume changes can be a contributor and contaminant in Vascular Space Occupancy (VASO)⁹⁻¹³.
- We use a VASO-like inversion recovery (IR) sequence to capture CSF volume changes. Specifically, our novel inversion recovery 7T 3D-EPI protocol uses CSF's specific relaxation "fingerprint" to capture voxel-specific CSF volume fractions independent of dynamic changes in cerebral blood volume (CBV) and BOLD.

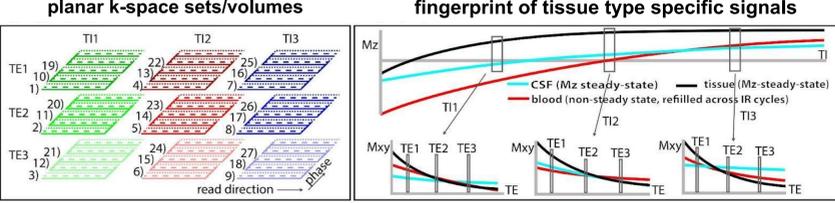
METHODS

- Multi-echo, multi-TI approach combining three echo times and three inversion times.
- 7T (N=11 sessions at 7T (Siemens, Germany), 8Tx/32Rx head coil (Nova, USA)), 3D-EPI with Skipped-CAIPI¹⁴. FRISGO⁸ is used to capture images in time scales of T1.
- Representative values: TE1/TE2/TE3=9/29/49ms, TI1/TI2/TI3=731/1573/2416ms.
- Assumed T1 values (Bloch modeling): GM/blood/CSF = 1950/2100/4000ms, T2* GM/blood/CSF/WM = 33.2/37.5/4000ms/26.8¹⁵⁻¹⁸.
- 12-14 minute block design (30sec blocks) with flashing checkerboards.
- Physiological recording to track changes in respiration¹⁹ (BIOPAC) and in-scanner eye tracking (EyeLink-1000Plus, SR-Research) were done simultaneously to fMRI
- Image processing: AFNI, LayNii, SPM, FSL and NORDIC.
- Scan parameters: https://github.com/nimh-sfm/mapping_CSF_volume

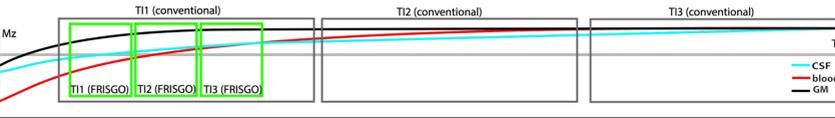
Proposed sequence - one partition is depicted as part of a 12 slice 3D-EPI sampling scheme, segmentation across IR-cycles and 2 phase encoding dimensions



Grouping of 27 shots to nine echo planar k-space sets/volumes

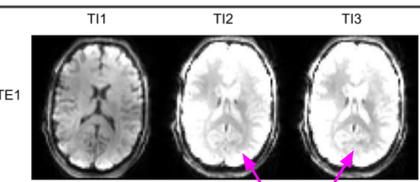


Segmentation across IR cycles + advanced readout acceleration (FRISGO) is needed to capture dynamics of inversion recovery

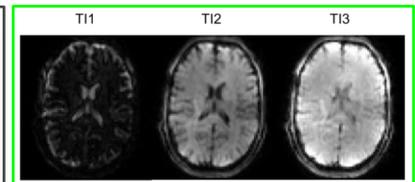


RESULTS

Conventional EPI is not fast enough to fully capture multi-exponential T1 relaxation

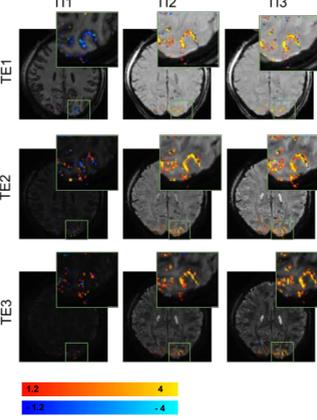


FRISGO⁸ captures multiple echo brain multi-echo images in time scales of T1

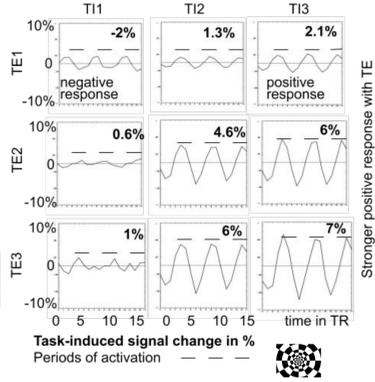


FRISGO, a method that allows for more rapid sampling of data⁸, can capture the relevant T1-relaxation in the range of TIs that separate CSF and blood

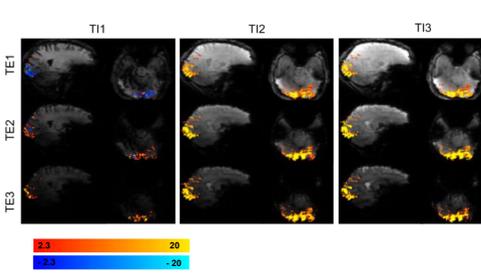
Task-locked fluctuations



Time courses



Feasibility of 3D whole brain mapping at low resolution (2.6mm) with GRAPPA 21



- Task-induced activation in the visual cortex can be seen at high resolution, in time courses and at whole brain resolution
- Negative signal changes seen with the early TI, while later TIs resulted in increasingly positive signal changes
- Functional responses are stronger at later echo times, as expected from GE-BOLD

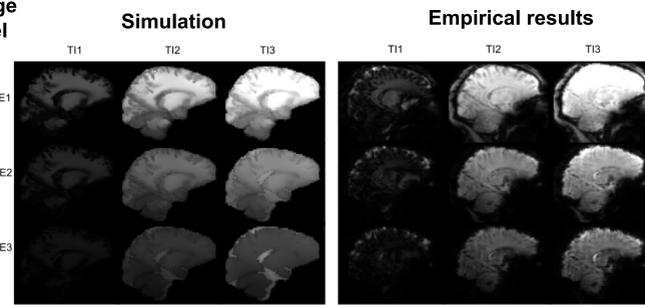
We developed a Bloch model that can predict the image contrast of the used TEs and TIs; inverting this model allows dynamic tracking of CSF volume and CBV

	T11	T12	T13
CSF	0.0005	0.20	0.34
TE1	0.09	0.32	0.47
TE2	0.0005	0.19	0.34
TE3	0.0005	0.19	0.34

Bloch model used for each tissue type:

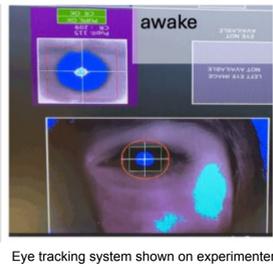
$$S(TI, TE) = \left[1 - e^{-\frac{TI}{T_1}} \left(1 - \frac{\chi}{M_0} \right) \right] e^{-\frac{TE}{T_2}}$$

Fingerprinting: Expected signal intensities/contrasts for CSF and blood at different TI/TE combinations



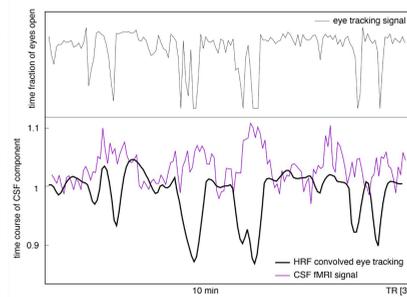
Comparing predicted tissue contrasts and the contrasts seen in the empirical data shows that overall our predictions match the empirical results

Tracking vigilance: Eye tracker for pupil measurement in the scanner room



In-bore eye tracker to obtain an imaging-independent measure of alertness

Time course of "sleepy" eyes vs. CSF volume (picked one section of three runs)

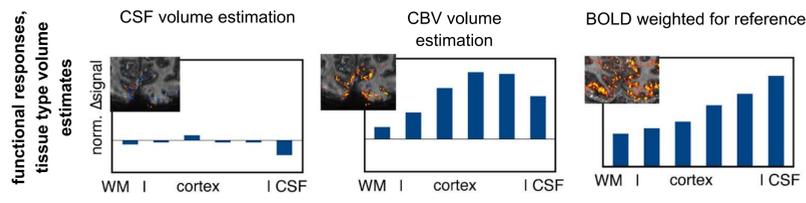
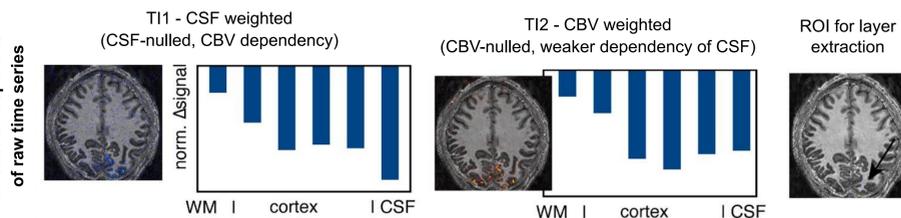
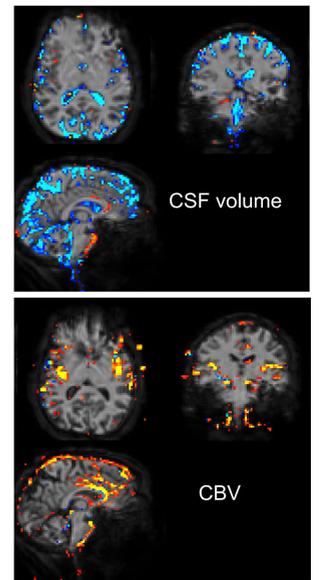


As eyes get more drowsy, CSF volume increases

In the time course, we see that drowsiness seems to modulate CSF volume quite a bit

In the maps of the correlates of alertness, we see that CSF shows a decrease with alertness and CBV shows an increase with alertness

Preliminary maps of CSF and CBV correlates of alertness, at both high resolution and low resolution



scan parameters: 0.8mm iso, 12 slices, TR_{IR}= 3s, TR_{vol}=8.8s, to confirm spatial signature of CSF (not possible with whole brain protocol)

- Using high-resolution data, confirmation that this method can spatially map CSF
- There are indications of a small CSF volume reduction in voxels above the cortical ribbon consistent with previous work⁹⁻¹²
- CSF-weighted signal changes are largest above the cortex, while CBV and BOLD show relatively more signal changes within GM
- GE-BOLD exhibits a signal increase towards the cortical surface, as expected from draining vein effects

Although a bit noisy, this layer analysis shows that we are seeing the greatest signal changes for CSF, CBV and BOLD where we would expect

CONCLUSIONS

- Our novel sequence can dynamically track functional changes of CSF, CBV, and BOLD concomitantly. Our multi-inversion and multi-echo data can track how the signal of blood differs from the signal of CSF across the spectrum of echo time and inversion time combinations, at both high resolution and whole brain low resolution.
- We see indications of CSF volume change during functional activation and even more so during changes of drowsiness.

FUTURE DIRECTIONS

- Future work will include further validations of the Bloch model (converting 9 TI-TE combinations → CSF, CBV, BOLD) with ground truth CSF modulation tasks.
- We plan to obtain more data where participants get sleepy to replicate the relationship between "sleepy eyes" and CSF volume.

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ETHICS

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