Analysis of BOLD Sensitivity in Matched Filter fMRI

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INTRODUCTION Matched-filter fMRI was recently proposed [1] as a means of increasing BOLD sensitivity by matching acquisition density in k-space to the desired spatial response – which is a Gaussian kernel in the vast majority of statistical fMRI analyses. Theory predicts a significant SNR benefit from such acquisitions, which is maximal when thermal noise dominates and expected to be reduced with increasing physiological noise contributions. In this work, we explore the validity of this argument for different regimes of physiological noise in the brain and report robust and replicable SNR increases of 30-40 % compared to uniform EPI acquisitions. For task-based fMRI, we observe a corresponding increase in BOLD-sensitivity of 30 % (average t-value), and show reproducibility both within and between subjects (N=4).

METHODS *Matched-filter Trajectory:* We designed a 2D Gaussian density weighting for a matched-filter EPI by varying traverse duration in phase encoding direction ([1], Fig. 1B) and modulating the frequency encoding gradient, such that $\dot{\boldsymbol{k}} \propto \mathbf{1}/\boldsymbol{d}(\boldsymbol{k})$ with $\boldsymbol{d}(\boldsymbol{k}) \propto \boldsymbol{exp}(-\boldsymbol{k}^2 \cdot \boldsymbol{\sigma}_r^2)$ ([2], Fig. 1B), where $\boldsymbol{\sigma}_r^2$ determined a smoothing kernel of 4.5 mm FWHM. This trajectory was compared to a uniform reference EPI of equal TE (35 ms), readout duration (40 ms) and bandwidth (375 kHz). Both acquisitions shared all geometry parameters: FOV 230 mm, SENSE 2.5, resolution 1.8 mm, 5 slices (thickness 3 mm, gap 3 mm).

Concurrent Field Monitoring & Image Reconstruction: Data was acquired on a Philips 3 T Achieva system equipped with a concurrent magnetic field monitoring setup [3,4]: 16 ^{19}F NMR probes were mounted on an 8-channel head coil, allowing for simultaneous acquisition of imaging data and temporal field evolutions up to 3rd order spatial spherical harmonics. Global field fluctuations and 1st order k-space trajectory information entered image reconstruction in an iterative, gridding-based CG-SENSE reconstruction [5] with B0-correction using a B0-map for multi-frequency interpolation [6,7].

Experiments: The signal-to-fluctuation-noise ratio (SFNR) of matched-filter and uniform EPI sessions was assessed in a spherical $CuSO_4$-doped water phantom (TR 6.25 s, 95 dynamics) and brain images of 4 healthy volunteers (TR 3 s, 48 dynamics). These sessions were repeated using 9 excitation flip angles (0-90°) for imaging. This allowed to evaluate SFNR differences for varying contributions of signal-dependent image fluctuations, e.g. physiological noise.

To assess BOLD-sensitivity in task-based fMRI, we ran a visual paradigm with the same subjects (N=4) stimulating quarter-fields of the visual cortex: 2 uniform EPI and 2 matched-filter sessions were acquired (120 dynamics, order counterbalanced between subjects) to test for consistent inter-modality differences in BOLD sensitivity as well as intra-modality reproducibility of both acquisition schemes. Data was preprocessed and analyzed using SPM8. Peak- and average t-values as well as cluster sizes of activated voxels in the contrast images were considered as performance measures.

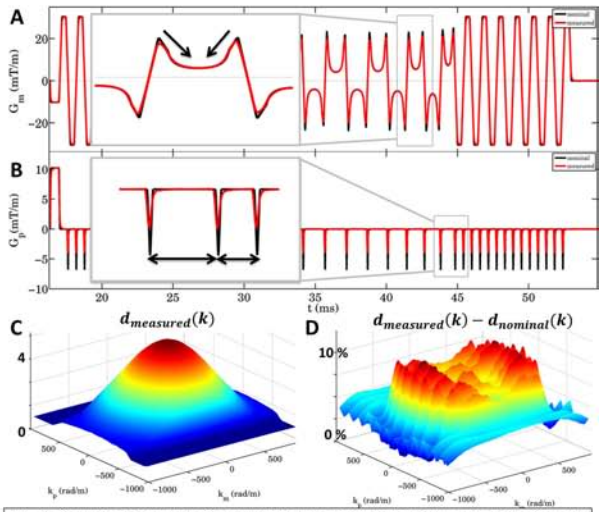

FIG. 1: GRADIENT DESIGN AND CONCURRENT FIELD MONITORING RESULTS OF A 2D GAUSSIAN DENSITY WEIGHTED EPI. **(A)** FREQUENCY AND **(B)** PHASE ENCODING GRADIENT (BLACK = NOMINAL; RED = MEASURED) **(C)** MEASURED K-SPACED DENSITY AND **(D)** DEVIATION FROM NOMINAL GAUSSIAN DENSITY

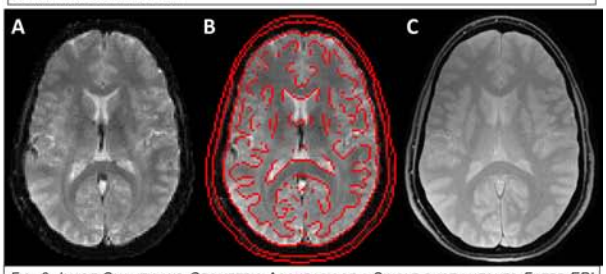

FIG. 2: IMAGE QUALITY AND GEOMETRIC ACCURACY OF A SINGLE-SHOT MATCHED-FILTER EPI RECONSTRUCTED WITH FIELD MONITORING DATA, SENSE (2.5) & B0-CORRECTION. **(A)** MATCHED-FILTER EPI RECONSTRUCTION, VIRTUALLY ARTIFACT-FREE. **(B)** GEOMETRIC ACCURACY: OVERLAY OF (C) ON (A). **(C)** SPIN-WARP IMAGE USED AS GEOMETRIC REFERENCE

RESULTS Trajectory assessment revealed successful implementation of a Gaussian density weighting (Fig. 1C) with minor deviations due to common eddy current delay behavior (Fig. 1D). Based on full monitoring and B_0 information, we were able to reconstruct artifact-free and fully geometrically congruent EPI images (Fig. 2).

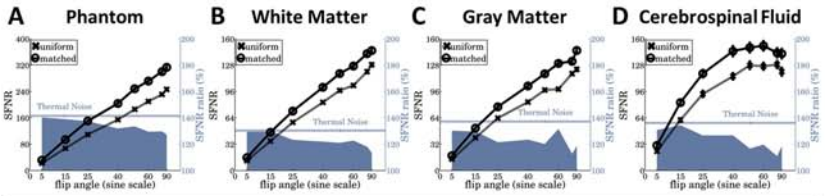

FIG. 3: DEPENDENCE OF MATCHED-FILTER SFNR ADVANTAGE ON FLIP-ANGLE. **(A)** PHANTOM DATA: LINEAR SFNR INCREASE FOR UNIFORM AND MATCHED-FILTER EPI (BLACK CURVES; STANDARD ERROR OF THE MEAN SMALLER THAN DOT SIZE). SFNR ADVANTAGE RATIO (BLUE SHADE) OF MATCHED-FILTER EPI DROPS BELOW THE THERMAL LIMIT OF 40 % FOR HIGHER FLIP ANGLES. **(B)-(D)** IN-VIVO RESTING STATE SFNR FOR DIFFERENT BRAIN REGIONS: THE MATCHED-FILTER SFNR ADVANTAGE DECREASES FOR HIGHER SIGNAL AND IN REGIONS WITH INCREASING PHYSIOLOGICAL NOISE (WM<GM<CSF), BUT STILL EXCEEDS 20 % IN GRAY MATTER.

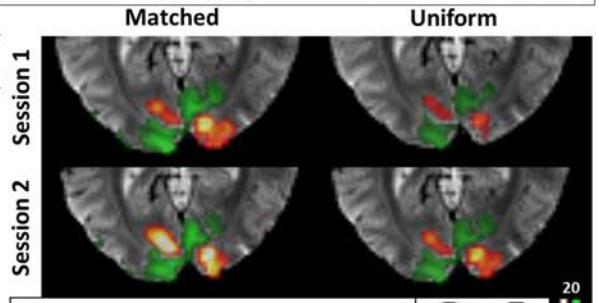

FIG. 4: SINGLE SUBJECT ACTIVATION MAPS FOR TASK FMRI STIMULATING THE QUARTER-FIELDS (UNDERLAY: MEAN EPI OF EACH SESSION) **(TOP)** MATCHED-FILTER ACQUISITION IMPROVES BOTH CLUSTER EXTENT AND PEAK T-VALUE COMPARED TO UNIFORM EPI. **(BOTTOM)** HIGH REPRODUCIBILITY OF THE BOLD SENSITIVITY INCREASE IN A 2ND SESSION WITH THE SAME SUBJECT

The SFNR maps confirmed the expected benefit of a matched-filter acquisition for time series of smoothed images (Fig. 3). SFNR gains reached as high as 45 % in the phantom and low flip angle in-vivo cases, where thermal noise dominates. For higher flip angles the SFNR ratios evolved differently in white, gray matter and CSF, corresponding to their relative susceptibility to physiological noise. Even for peak levels of physiological noise, the SFNR gain for matched-filter EPIs was about 30 % in the gray matter regions relevant for fMRI.

This SFNR gain for "resting-state" conditions translated into similar gains in BOLD sensitivity for task-based fMRI, as measured by contrast t-values: we observed the known topological organization of the visual cortex when stimulating opposite quarter-fields (Fig. 4). Both cluster extent and peak t-value increased for all subjects in both t-maps contrasting the opposite stimulations. To quantify this effect for all voxels in the brain, we computed an orthogonal regression for the t-value changes between different pairs of sessions (Fig. 5). This yielded reproducible average t-value increases of 35 % in matched-filter compared to uniform EPI sessions, while t-values in sessions with identical acquisition technique varied by less than 7 %.

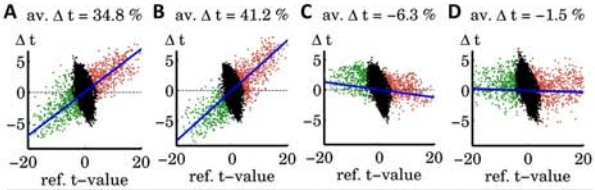

FIG. 5: WHOLE BRAIN SUMMARY OF BOLD SENSITIVITY CHANGES USING A TOTAL LEAST SQUARES FIT OF ALL VOXEL T-VALUES BETWEEN SESSIONS. POSITIVE SLOPES INDICATE HIGHER MEAN BOLD SENSITIVITY COMPARED TO THE REFERENCE SESSION. **(A)** MATCHED-FILTER VS UNIFORM ACQUISITION IN SESSION 1 AND **(B)** SESSION 2 **(C)** REPRODUCIBILITY OF T-VAUES BETWEEN SESSIONS IN UNIFORM AND **(D)** MATCHED-FILTER EPIS.

DISCUSSION Matched-filter fMRI combined with concurrent magnetic field monitoring has proven to be an fMRI acquisition technique recovering artifact-free, geometrically accurate images, temporal SFNR gains of up to 40 % and resulting BOLD sensitivity increases in the same range – that are robust and reproducible both within and between subjects. The proposed matched-filter technique is versatile to accommodate any assumption about the spatial response function of the BOLD signal and can be generalized to optimize SNR for non-Gaussian kernels.

REFERENCES [1] Kasper et al. *Proc. ISMRM 11*, p. 1634, 2011. [2] Greiser & von Kienlin, *MRM 50*, 2003 [3] Barmet et al., *Proc. ISMRM 10*, p. 216, 2010. [4] Barmet et al., *MRM 60*, 2008. [5] Pruessmann et al., *MRM 46*, 2001. [6] Man et al., *MRM 37*, 1997. [7] Sutton et al., *IEEE Trans Med Imaging 22*, 2003.