

# Physiological Noise Effects on the Flip Angle Selection in BOLD fMRI.

J. Bodurka<sup>1</sup>, and P. Bandettini<sup>1,2</sup>

<sup>1</sup>Functional MRI Facility, National Institute of Mental Health, NIH, Bethesda, MD, United States, <sup>2</sup>Section on Functional Imaging Methods, National Institute of Mental Health, NIH, Bethesda, MD, United States

**INTRODUCTION:** Physiological noise is present in gradient echo BOLD fMRI data. Its strength varies across brain tissue compartments [1-2]. It has been shown that this noise depends on the MRI signal strength [1] causing a nonlinear dependence of the temporal-signal-to-noise (TSNR=mean voxel time course signal/time course standard deviation [2]) versus signal-to-noise (SNR). This results in diminishing gains in TSNR as SNR increases [1-2]. In BOLD fMRI studies it is a common practice for a given repetition time (TR) to use the Ernst angle[3] for T<sub>1</sub> of gray matter (around 1.3 sec at 3T[4]) in order to maximize gray matter MRI signal. Here we have considered theoretically and experimentally the physiological noise effects on the flip angle selection. We show that for given TR, TSNR versus flip angle plots are significantly affected by the physiological noise. For situations where available SNR is high and physiological noise dominates over system/thermal noise [2] the selection of Ernst angle does not result in significant improvements in TSNR. It is possible to select a much smaller flip angle and have similar TSNR as for the Ernst angle, however, smaller flip angles have important benefits of reducing possible inflow effect [5].

**THEORY:** In a spoiled gradient echo EPI acquisition it can be shown that TSNR as a function of flip angle ( $\alpha$ ) is given by equation 1, and where:  $R1=\exp(-TR/T_1)$ ,  $SNR_0=M_0\exp(-TE/T_2^*)/\sigma_0$ ,  $SNR_0$  is signal to noise ratio computed from the first image in the time series,  $\sigma_0$  is thermal/system noise and  $\lambda$  is constant specific to different brain tissue compartments [1-2].

$$TSNR = \frac{SNR}{\sqrt{1+\lambda^2 SNR^2}} = \frac{SNR_0 \frac{(1-R1)\sin(\alpha)}{1-R1\cos(\alpha)}}{\sqrt{1+\lambda^2 SNR_0^2 \left[ \frac{(1-R1)\sin(\alpha)}{1-R1\cos(\alpha)} \right]^2}} \quad (1)$$

**MATERIAL and METHODS:** MRI Imaging: Three subjects were scanned in a 3T General Electric HDx MRI Scanner. Sixteen-element receive-only brain array (Nova Medical Inc) and Gradient Echo single shot full-k-space EPI were used. Resting fMRI scans at two different resolutions (20 axial slices, FOV=24cm, High-Res: 128x128, 2mm slice, gap=2mm; Low-Res 64x64, 4mm slice, no gap) to modulate physiological and thermal/system noise contribution were conducted as a function of flip angle. Other relevant parameters: TR=3s, TE=30ms, 62 volumes. Also similar experiments were conducted on phantom (silicon oil, T<sub>1</sub>=1.0s). All data analysis was performed with AFNI. Processing steps: (1) motion correction to 4<sup>th</sup> volume, (2) tissue segmentation over EPI volumes using method described in [2], (3) calculate TSNR values for white and gray matter and CSF compartments.

**RESULTS:** The physiological noise affected TSNR versus flip angle plots (TSNR( $\alpha$ )) in all subjects. Representative single subject data for GM, WM, and CSF for both High-Res (red) and Low-Res (black) are shown on Figure 1A, 1B, and 1C, respectively. Number of voxels in GM, WM and CSF compartments for (High-Res, Low-Res) were (13084, 3069)<sub>GM</sub>, (13973, 3629)<sub>WM</sub>, and (11570, 3430)<sub>CSF</sub>, respectively. Figure 1D shows corresponding phantom experiments. All symbols represent experimental data, solid lines computed from equation (1) with experimental SNR<sub>0</sub> and  $\lambda$  taken from [2] (Fig 1A: GM: T<sub>1</sub>=1.3s; Low-Res SNR<sub>0</sub>=652,  $\lambda$ =0.0067; High-Res: SNR<sub>0</sub>=113,  $\lambda$ =0.0125; Fig 1B: WM: T<sub>1</sub>=1.0s; Low-Res SNR<sub>0</sub>=516,  $\lambda$ =0.0053; High-Res: SNR<sub>0</sub>=92,  $\lambda$ =0.0053; Fig 1C: CSF: T<sub>1</sub>=3.5s; Low-Res SNR<sub>0</sub>=734,  $\lambda$ =0.0095; High-Res: SNR<sub>0</sub>=155,  $\lambda$ =0.0213; Fig 1D: Silicon Oil: T<sub>1</sub>=1.0s; Low-Res SNR<sub>0</sub>=440,  $\lambda$ =0.00154; High-Res: SNR<sub>0</sub>=67,  $\lambda$ =0.00154). Error bars represent StDev computed for each ROI at each flip angle. For low resolution human data partial volumes were accounted for to estimate  $\lambda$ . All dotted lines show theoretical TSNR versus flip angle plots for cases of system/thermal system noise only. Figure 2 shows simulations of the equation (1) in GM, where effects of physiological noise on TSNR versus flip angle plots are computed for different TR (TR: 3s red, 2s blue, 1s green, 0.5s black). Figure 2A, and 2B show High-Res, and Low-Res case, respectively.

**DISCUSSION and CONCLUSIONS:** We have shown that the physiological noise strongly influences the TSNR versus flip angle plots. Physiological noise introduces non-linear dependence of TSNR versus flip angle. Due to this effect, it is possible to use much lower  $\alpha$  than Ernst angle to achieved comparable TSNR( $\alpha$ ) to maximum of TSNR(Ernst). In the presence of signal dependent noise, the TSNR still reaches maximum at Ernst angle, however TSNR versus flip angle curve is flattened as shown on Figure 1A, 1B, 1C, and 2A, 2B. The degree of flatness reflects the level of physiological noise, more noise causes bigger deviations. As shown on Fig 1C, and as expected, Low-Res CSF has the strongest physiological noise contribution and the biggest deviation from TSNR( $\alpha$ ) where thermal/system noise dominates [2]. Except for phantom experiments only at WM compartment and High-Res condition, TSNR( $\alpha$ ) deviates only slightly from the case where system/thermal noise dominates. Specifically for TR=3s and gray matter

we have found that for flip angles 30-45 degrees TSNR level is very close to obtained at 84 flip angle (Ernst angle for T<sub>1</sub><sub>GM</sub>=1.3s). Interestingly, for the Low-Res case (typical fMRI voxel volume) simulation shows (Fig 2A, 2B) that TSNR( $\alpha$ ) for  $\alpha$  smaller than 90 deg, is relatively insensitive on TR choice. However, when TR is reduced and the corresponding Ernst angle is used, inflow effects are getting larger [5]. Therefore, the ability to reduce flip angle to reduce inflow effects and to keep TSNR at a similar level is desirable. Our results suggest that it is possible to use a much lower flip angle than the Ernst angle for typical BOLD fMRI studies as long as physiological noise dominates (or for voxel volumes larger than suggested voxel volume [2]). The use of the lower flip angle can reduced the inflow effect [5] as well can be also beneficiary for fMRI at ultra high field strengths (7T and beyond).

**References:** [1] Kruger et al. (2001): MRM 46:631; [2] Bodurka et al. (2007): Neuroimage 34:542; [3] Ernst et al. Rev. Sci. Instrum. (1966): 37:93; [4] Wanasapura et al. (1999): JMIR 9:531; [5] Glover et al. (1996): MRM 35:299.

