# Calibration of the amplitude of fMRI contrast (β) using fractional volume of gray matter: the spatial and inter-subject β calibrations

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## Introduction

Blood oxygenation level dependent (BOLD) contrast has been widely used in fMRI study to investigate neuronal functionality. While the amplitude of BOLD contrast during the brain activation (commonly called β) is widely used to monitor neuronal activity in group analyses, β usually varies over subjects because BOLD contrast depends on a number of physiological and biophysical parameters [1]. These inter-subject β variations have been studied recently and several approaches have been proposed to calibrate these variations [2-4]. However, the calibrated fMRI is still in challenge. In this study, we propose a calibrated fMRI method based on fractional volume of gray matter (GM) measurement using FRASIER method [5], in which the spatial β variations and the inter-subject β variations are calibrated to improve sensitivity in detecting brain activation.

## Methods

FRActional Signal mapping from InvErsion Recovery (FRASIER): FRASIER provides volume fractions of GM, white matter (WM), and cerebrospinal fluid (CSF), based on a recently developed fast $T_1$ mapping method using inversion recovery Look-Locker echo-planar-imaging at a steady state (IR LL-EPI SS) [6]. Using an inversion recovery (IR) time-series acquired from a single-shot Look-Locker sequence [7], the measured voxel-wise signal was fitted into a three-compartment (WM, GM, and CSF) exponential model. The detailed technical information is described in the reference [5].

MRI experiment: Ten healthy subjects were scanned using a single-shot IR LL-EPI SS sequence for FRASIER: non-selective IR, TR/TE=400/13 ms, α=16°, matrix=64x64, and 15 slices. Five FRASIER measurements were acquired in 1 min including the preparation time of 10 s. A visual stimulation paradigm with 8 Hz flashing checkerboard (30s on and off) was used in a BOLD experiment acquired with TR/TE=3s/27ms, matrix=64x64, 39 slices, and total running time = 5:32. The center slice locations of IR LL-EPI SS and fMRI images were aligned so that the direct voxel-wise comparison between the two scans was feasible because the FRASIER method used the same gradient-echo EPI kernel as the fMRI acquisition (similar geometric distortions).

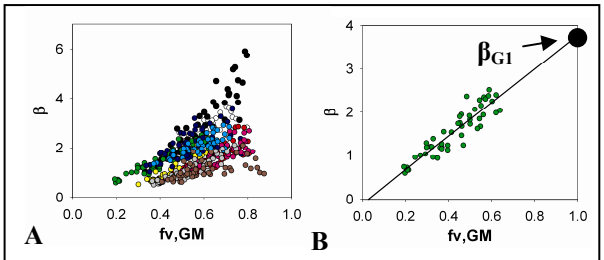


**Fig 1**. (A) Voxel-wise comparisons between β and fractional volume of GM ($f_{v,GM}$) of the activated voxels in a ROI. Different color dots represent individual subjects (N = 10). (B) Linear fitting between β and $f_{v,GM}$ and demonstration of $\beta_{G1}$ calculation.

Group analysis: Recently, we observed that the spatial β variations within a subject during brain activation are strongly correlated with fractional volume of GM ($f_{v,GM}$). Fig.1A shows the correlation between β and $f_{v,GM}$ in the activated ROI (defined by the top 50 highest t-value voxels) over 10 subjects. Therefore, the spatial calibration was performed using individual β maps divided by voxel-wise corresponding $f_{v,GM}$ maps in the Talairach space. Note that the spatial calibration method provides voxel-wise β per GM. To calibrate the inter-subject β variations, we introduce $\beta_{G1}$, or the estimated β value with $f_{v,GM}$ =1 (all GM in the voxel). $\beta_{G1}$ was measured from fitting the data that were obtained from the individual activated ROI, demonstrated in Fig. 1B. Finally, the inter-subject calibration method was performed using individual β maps divided by $\beta_{G1}$ in the Talairach space. Four different group analysis methods were used: 1) the conventional method using uncalibrated β maps, 2) the spatial calibration method, 3) the inter-subject calibration method, and 4) the method using both the spatial and inter-subject calibrations. Statistical tests (t-test) were performed respectively on the data from the four methods.

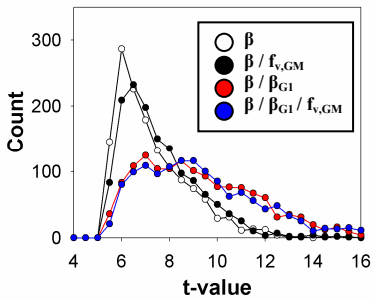


**Fig 2**. Distributions of t-scores of the activated voxels in a common ROI (p<0.001) from the four analysis methods (white dots: the conventional method; black dots: the spatial calibration method; red dots: the inter-subject calibration method; and blue dots: the combination of both the spatial and inter-subject calibration method).

## Results and Discussion

Fig.2 shows the t-score distributions of the activated voxels (p<0.001) in the common ROI of activation from the four different methods. Compared with the conventional method (white dots), the spatial calibration method slightly improved the statistical power (black dots). Large improvements were observed with the inter-subject calibration method, (red dots) and the combination of inter-subject and spatial calibration methods (blue dots). Fig.3 demonstrates the t-maps in the activated ROIs obtained with the four different methods. The activated ROI was defined separately (p<0.001) with each method. Activation was detected consistently in all four methods. However, inter-subject calibration method (Fig. 3C) and the combination method using both inter-subject and spatial β calibration (Fig.3D) show significant increase in t-values, while the spatial calibration method (Fig. 3B) shows slight improvement, compared with the original group analysis result (Fig. 3A).

In this study, we present a new calibrated fMRI method to correct the spatial and the inter-subject β variations using voxel-wise GM volume fraction and $\beta_{G1}$ (extrapolated β value when the voxel is 100% GM) across subjects. Inter-subject $\beta_{G1}$ correction resulted in much larger improvement in t-scores, compared with the spatial correction, suggesting that the inter-subject $\beta_{G1}$ differences account for more variations in the group analysis. We demonstrated here the feasibility of the calibrated fMRI to improve sensitivity in detecting brain activation in a visual task. It would be interesting to further examine the possibility of the calibration in other brain systems. FRASIER provides efficient measurement of GM volume fraction (1 min scan) and can be implemented easily in most fMRI protocols.

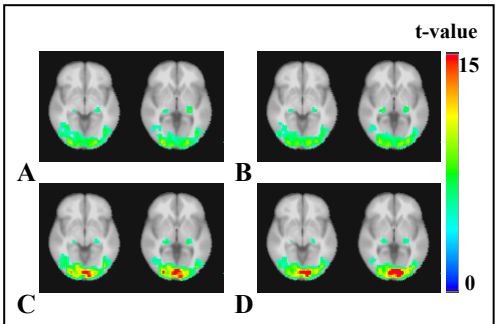


**Fig 3**. Group analysis (t-test) results ($p$<0.001) from the four analysis methods (n=10). (A) conventional method; (B) the spatial calibration method; (C) the inter-subject calibration method; and (D) the spatial and inter-subject calibration method.

## Acknowledgements

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## References

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