fMRI Biomarker Development: Progress Report 2018

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Quantitative Imaging Biomarkers Alliance RSNA

BOLD fMRI as a Quantitative Biomarker

The aim of the QIBA fMRI Biomarker Committee is to establish detailed Profiles for using functional MRI as a quantitative biomarker for imaging brain function. The primary context of use for the fMRI biomarker Profile is diagnostic fMRI to map critical brain areas for neurosurgical planning. The focus of Profile v1.0 is mapping of hand motor regions. Profile v2.0 will address mapping of brain regions involved in language processing.

Profile Status

fMRI Profile v1.0 establishes the claim that the intensity-weighted center of mass of activation (CMA) for a motor task can be localized reproducibly in brain activation maps.

Biomarker measurand: The location, CMA, of local T2*-weighted BOLD fMRI signal evoked by a hand movement task.

Precision claim: If XYZ is the measured location of the CMA of a single focus of fMRI hand motor activation, then the 95% confidence interval for the true CMA is XYZ +/-5mm.

Status: This Profile has received public comment and is in the process of technical confirmation to ensure that the Profile's procedures can be implemented. When followed, the results will satisfy the precision claim. To this end we have developed a conformance checklist to help fMRI sites implement the Profile.

Conformance testing: We have developed two sets of realistic synthetic fMRI data as digital reference objects (DROs) for use in the conformance testing process. A smaller set helps sites test the completeness of their analysis methods. A larger set can be used to test that their methods satisfy the Profile's claim. Both sets can be downloaded from QIBA's data warehouse at: https://bit.ly/2O001B6

Head Motion DRO Projects

This past year we have completed two groundwork projects, both designed to assess the quantitative impact of head motion as a source of variance in fMRI. Both projects involved creating synthetic DRO data sets with known BOLD activity signals and then adding different patterns of image motion. One project used a large database of human fMRI scans to extract empirical head movements and brain activity signals; its goal was to examine the variability of real head movements and the effectiveness of motion correction software. The other project synthesized head motion using random models in order to systematically assess how quantitative metrics of motion could predict fMRI results. Here, we present results from both of these head motion DRO projects.

Empirical Motion DROs

We used 1000 different empirically-derived sets of motion parameters to test a broad range of head motions. Using 2 different tasks (language and motor), 2 different task timings (block-design and event-design), and images from 2 different scanners (GE and Siemens) we created and analyzed over 12,000 DROs.

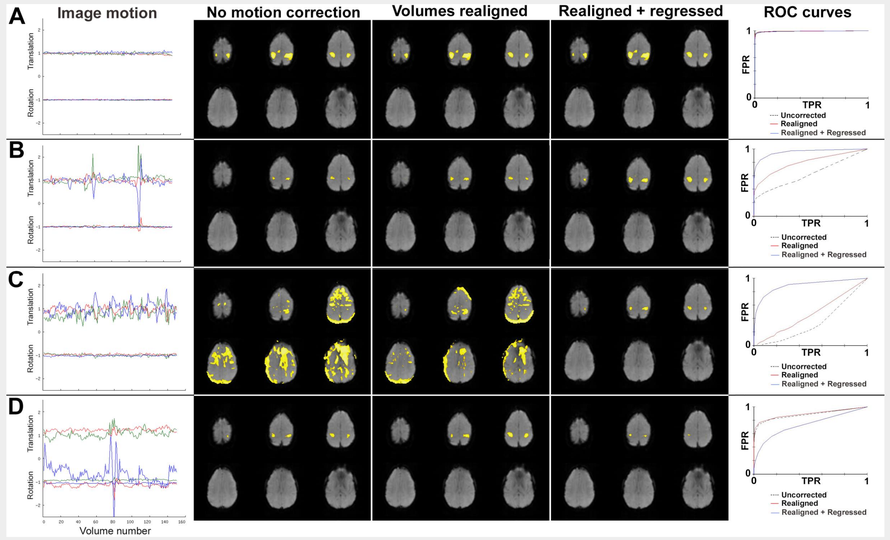

Figure 1. Examples of DROs with same brain activity but different patterns of head motion. Maps show detected activity without and with image realignment, and with realignment and motion regression. ROC curves compare voxels detected to true activation for the 3 maps.

FSL, AFNI, and SPM compared for motion estimation and image realignment
All 3 programs produced very similar results:

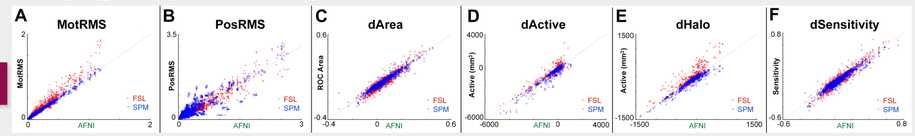

Figure 2. Scatterplots comparing FSL, SPM, and AFNI results for all 12000 DROs. Summary motion metrics (MotRMS & PosRMS) are similar, as are image realignment changes in area under ROC curves (dArea), number of active voxels (dActive), number of voxels outside the brain (dHalo), and cluster detection (dSensitivity). Image realignment improves some results and degrades others, similarly for the 3 packages.

Quantitatively reliable activation maps (ROC area > 0.9) are attained if QA metric MotRMS (root-mean-squared volume-to-volume motion) is <= 0.2 before motion correction, and after correction Halo (voxels outside edge of brain) < 20, and the most active brain voxels have t-values >= 8 (i.e., half-maximum t >= 4.0).

Under those QA conditions fMRI activation maps satisfy the QIBA fMRI Profile claim for detecting true clusters of brain BOLD activation.

Note: Motion metric **MotRMS** is almost identical to **$SSDM_{rms}$** developed in Project 2.

Random Motion DROs

Methods: In this project, a high-resolution MPRAGE data set was used to create a high-resolution T_2*-weighted image volume. Block-design activation was assigned to a cluster in brain area M1, random motion was applied to induce inter-slice motion, and the data set was downsampled to $4 \times 4 \times 4$ mm^3 to induce partial volume effects (see Soltysik, 2017 for more detail). Across DROs, random motion was applied with different maximum cumulative motion values (up to 4 mm). In total, 768 fMRI DROs were created. Summary motion metrics were calculated and plotted against both the true positive fraction and the deviation from the true center of mass.

Results: Scatter plots showed that as the summary motion metric $SSDM_{rms}$ increased, the sensitivity decreased exponentially (Fig. 3A). In addition, the exponential decay constant was found to be different across different cortical areas (not shown). Scatter plots also showed that as the motion metric increased, the deviation from the true center of mass increased until it reached a plateau (Fig. 3B). For the simulated data set, the 95% confidence intervals showed that the deviation from the true center of mass was less than 12 mm.

Discussion: Because of the gradual decrease in sensitivity in the plot against the motion metric, it is not viable to use a single summary motion metric for deciding whether to discard data. However, the center of mass was found to be very stable even for cases of extremely high random head motion.

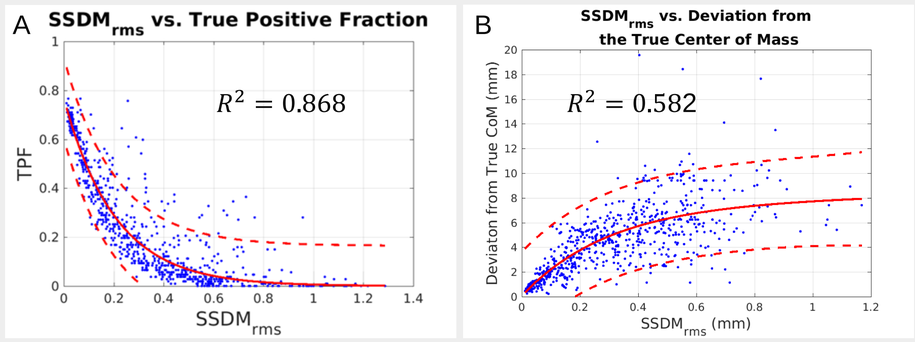

Figure 3. Scatter plots of the summary motion metric vs. (A) the true positive fraction and (B) the deviation from the true center of mass. (Dashed lines are 95% confidence intervals.)

Overall Conclusions:

1) Head motion is highly variable; different patterns of motion affect fMRI maps differently, and respond to different correction methods (alignment, regression)
2) Major motion correction packages produce very similar results
3) While head motion can greatly affect sensitivity, the calculated center of mass can be located consistently if statistically significant activation is present

References:

Soltysik, DA. Simulating the effect of head motion in fMRI. Proceedings of the 23rd Annual Meeting of the Organization of Human Brain Mapping, Vancouver, Canada, June 2017.

Voyvodic J. and Cruz P.R. Quantitative assessment of fMRI head motion metrics and motion correction methods using digital motion phantoms. Proceedings of the 26th International Society of Magnetic Resonance in Medicine, Paris, France, June 2018.

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