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fMRI Digital Reference Object Development: Preliminary Results

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Quantitative Imaging Biomarkers Alliance RSNA

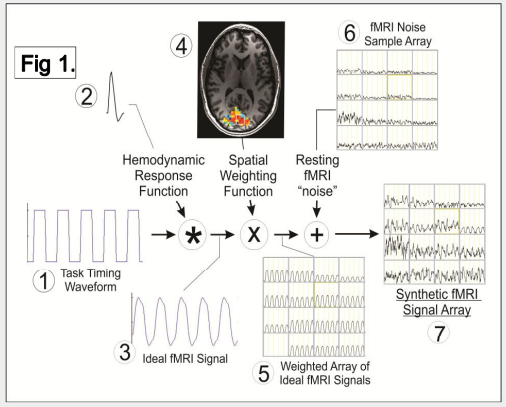
BOLD fMRI as a Quantitative Biomarker and Digital Reference Objects

The aim of the QIBA fMRI technical committee is to establish quantitative standards for functional MRI. Previous work by this committee has identified many possible sources of variance in fMRI and has established metrics of reproducibility for one representative image analysis protocol. However, methods used for clinical fMRI typically vary from site to site and it is not known: (1) which methodological factors significantly affect reproducibility, sensitivity and bias, (2) which methods in current use are best suited for obtaining consistent quantitative results, or (3) how our methodological considerations impact clinical performance of fMRI as a biomarker.
In our recent work the committee has focused on creating standard datasets or "digital reference objects" (DROs) with realistic known signal qualities and noise features. To create DROs, existing human fMRI data sets plus simulation software are used to create a range of synthetic data sets that allow us to manipulate sources of variance and systematically assess the technical performance of different fMRI data analysis methods.

In the first year of this project we have created two types of DROs. In Phase 1 we concentrated on extracting empirical temporal and spatial MRI signals from real human fMRI scans and then recombining these empirical signals to create synthetic data with known signal components. In Phase 2 we combine empirical signal components with synthesized artificial spatial and temporal signals to systematically manipulate common sources of fMRI signal variance.
We have begun to use these DROs to compare the performance of different fMRI data processing methods currently in use at different experienced clinical sites. Our goal is to identify optimal existing methods and then begin the process of isolating and characterizing specific individual sources of variance by comparing reproducibility, sensitivity, bias, and linearity for DROs that vary systematically in signal and noise properties. Here we report the DRO design and construction methods, our simulation software and some preliminary results from analyses of our Phase 1 DROs processed at multiple clinical fMRI sites across the country.

DRO Design, Construction & Simulation Software

DRO construction is outlined in Figure 1. The ON/OFF timing (1) of a simple sensory or motor task is temporally convolved with a hemodynamic response function (2) which models the vascular response to the task-evoked neural activity. This model can be used both to identify and extract empirical task signals from real human EPI scans, and to create Ideal fMRI signals (3) with amplitude multiplied by a spatial weighting factor (4 and 5). DROs are then generated by adding either extracted empirical or ideal synthetic task-signals to empirical samples of fMRI "noise" (6) obtained from a real subject EPI scan with no significant signal at the task frequency. This yields a fMRI DRO with synthetic signals (7) containing realistic noise with task- related signals whose true locations and amplitudes are known. Such a Digital Reference Object can then be used to test fMRI analysis methods and determine the accuracy with which the known task-related signals can be recovered. Future work will introduce specific sources of variance such as variable hemodynamic response functions, head movements, cardiac, respiratory and other signals to create a library of DRO's with known fMRI signals plus known artifacts.



DRO Multi-Site Processing Comparison Study

The first phase of the fMRI DRO project involved generating 10 standard reference data sets based on empirical scan data, each comprised of 3 semi-synthetic brain scans (a whole-brain high-resolution T1-weighted brain volume plus a sentence-completion language fMRI scan and a bilateral hand movement fMRI scan). The 20 empirical fMRI DROs plus their T1 scans were uploaded to RSNA's Quantitative Imaging Data Warehouse (QIDW) from where they could be downloaded by 8 QIBA test sites involved in clinical fMRI scanning and/or research. Each scan was uploaded in both DICOM and NIfTI file formats. Each site downloaded and then processed the DRO data using their standard clinical fMRI processing methods. The resulting functional activation maps were then returned to a central collection site for comparison. In returning their maps, each site identified their processing methods and their standard automated activation thresholding criteria. Where appropriate, they also identified any manual threshold adjustments they would typically perform to create optimal clinical fMRI results.

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DRO Preliminary Results

Here we present the fMRI mapping results from 8 sites that all analyzed the same bilateral hand motion DRO, but with each site using their own standard clinical fMRI analysis methods. The "standard threshold" maps (Fig 2 - left) were obtained from each site using their standard default threshold setting (no manual threshold adjustments). "AMPLE normalized" (Fig 2 – right) is the same maps after applying the automated AMPLE threshold normalization algorithm (Voyvodic, 2006 MRI 24:1249-61) to show the 50% most-active voxels in each region.
These preliminary results show:
1)Different software packages and user settings result in generally similar maps but with significant variability in spatial extent of brain activations.
2)Differences in anatomical and functional registration methods, and/or motion correction methods, introduce some site-based variability in the locations of centers of activation.
3)AMPLE normalization reduces the variability in spatial extent of activation across analysis methods that use similar statistical parameters (i.e., t-values).
This DRO project will continue to explore multiple sources of variability in fMRI due to scanning, behavior, and analysis methods.

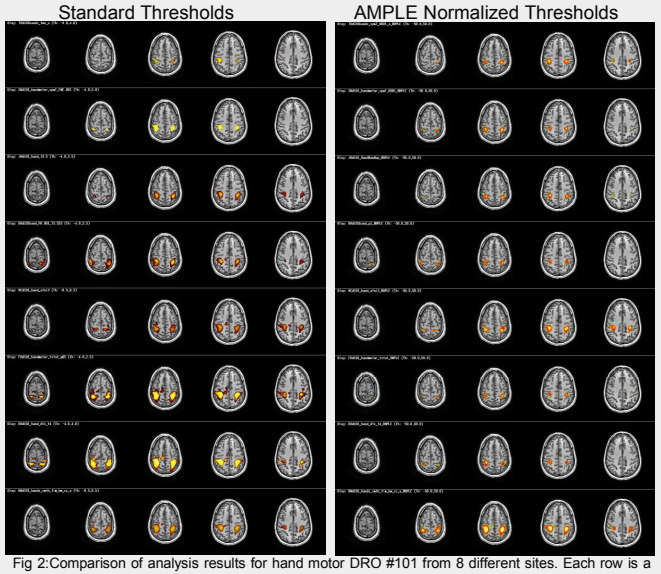

Fig 2:Comparison of analysis results for hand motor DRO #101 from 8 different sites. Each row is a different site; the 2 panels show the same fMRI maps with the site's standard automated threshold and an AMPLE normalized threshold. Software packages were SPM, AFNI, BrainEx, Prism, and fScan. The first 7 sites generated t-value maps; the 8th site created correlation coefficient maps. AMPLE normalization was performed using the unthresholded versions of the maps in the left panel.

DICOM WG-16 Collaboration - Update

Goal: To prioritize the storage and transmission of fMRI data within an industry-wide DICOM standard.
Progress: 2013 - QIBA fMRI workflow was presented to DICOM working group WG-16
May 2014 - WG-16 established an fMRI subcommittee
Immediate fMRI needs can be mostly met using existing elements in DICOM's Enhanced MR standard.
Current Plans: WG-16 will propose new elements to represent task paradigms, execution, and results.
QIBA & WG-16 will co-operate to develop an IHE profile promoting use of the fMRI DICOM standard.