Quantitative Imaging Biomarkers Alliance RSNA

Application for QIBA Round-2 Project Funding

Title of Proposal: Validation of Breath Hold Task for Assessment of Cerebrovascular Responsiveness and Calibration of Language Activation Maps to Optimize Reproducibility.		
QIBA Committee/Subgroup: fMRI		
NIBIB Task Number(s) which this project addresses: 1,3,6,7,9		
Project Coordinator or Lead Investigator Information:		
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e-mail:	Tel #:	
Institution/Company: Johns Hopkins Univ. School of Medicine		
Amount Requested:		

Please check the primary category for this proposal from among the following:

- ☐ 1. Identification of Technical Characteristics and Standards
  - ☐ a. Creation and refinement of protocols for image acquisition, analysis, quality control, etc., for specific clinical utility
  - ☐ b. Phantom development and testing
  - ☐ c. Identification and assessment of intra-reader bias (1) and variance across scanners and centers
  - ☐ d. Identification and assessment of inter-reader bias and variance across scanners and centers
  - ☐ e. Other
- ☐ 2. Clinical Performance Groundwork
  - ☐ a. Assessment of intra-reader sensitivity and specificity
  - ☐ b. Assessment of inter-reader sensitivity and specificity
  - ☐ c. Other
- ☐ 3. Clinical Efficacy Groundwork
  - ☐ a. Assessment of correlation between new biomarker and 'accepted-as-standard' method
  - ☐ b. Characterization of value in clinical trials
  - ☐ c. Characterization of value in clinical practice
  - ☐ d. Development/merger of databases from trials in support of qualification
  - ☐ e. Other
- ☐ 4. Resources (money and/or people) committeed from other sources.

Ongoing or completed IRB approved studies will provide datasets for this project. Existing personnel are available for study design, data processing/analysis and report generation but will have to be partially re-tasked to support this project.

Project Description

Assessment of the integrity of cerebral vascular responsiveness (CVR) is a critical problem in clinical applications of fMRI brain mapping, and must be addressed in any attempt to quantitate fMRI results in patients. Neurovascular uncoupling (NVU) associated with brain tumors and other brain diseases may result in regional variations in CVR that affect the ability to generate a BOLD signal and thereby reliably and reproducibly localize eloquent cortex during presurgical mapping. Multiple studies have demonstrated that a breath-hold (BH) hypercapnia task is a reliable tool for assessing CVR and normalizing BOLD response among different subjects, different brain regions and various features of the scanning environment. In this project we plan to 1) validate use of a BH task for mapping of brain CVR and 2) use such maps to calibrate language task-based BOLD activation maps in order to both reduce intersubject variability and increase intrasubject reproducibility across scan sessions.

For the first objective, we will compare BH CVR maps with T2* DSC MR perfusion imaging maps using quantitative region of interest analysis to assess concordance of regions of decreased CVR with regions of abnormal perfusion in a cohort of 10 brain tumor patients. For the second objective, we plan to apply the normalization/calibration technique described by Thomason et al. (2007) to an existing dataset of approximately 10 normal right-handed native English speaking subjects who performed two BOLD language tasks--silent word generation and sentence completion--in addition to a breath hold (BH) task, as well as to a cohort of a similar number of brain tumor patients who performed similar tasks. Furthermore, for the patient cohort, analysis of multiple runs of the same language activation paradigms will assess intrasubject BOLD activation variability utilizing CVR-calibrated activation maps. The results of this study will help fill the high priority gaps of evaluation of neurovascular responsiveness, reproducibility and protocol optimization, defined by the QIBA fMRI subcommittee, and address NIBIB Tasks 1, 3, 6, 7, and 9 in the context of fMRI as a biomarker of brain function/dysfunction.

Primary goals and objectives

1) To validate BH CVR mapping by comparison of areas of regional pathologically reduced CVR to areas of regional perfusion abnormality.

2)To evaluate BOLD CVR in a cohort of 10 normal volunteers for establishment of a normative standard prior to application of a recently described BH CVR-based BOLD normalization/calibration technique (Thomason et al, 2007) to cortical language mapping in both normal volunteer and brain tumor patient cohorts.

3)To assess whether BH CVR-calibrated BOLD language activation maps can reduce both intersubject and intrasubject variability (and thus enhance reproducibility) compared to standard BOLD language activation maps.

Deliverables

1) Completion of ROI-based analysis of T2*DSC perfusion images and BH- CVR maps to compare perfusion metrics to CVR percentage signal change (PSC) within brain tumors.
2) Generation and optimization of algorithms/scripts for automated generation of BH-CVR maps and CVR-normalized/calibrated language BOLD activation maps in both normal volunteer and brain tumor cohorts.
These algorithms will be made available for sharing across centers within the fMRI subcommittee for future testing across different analysis platforms.

Timeline

Months 1-3: Comparison of BH CVR maps to T2* DSC perfusion maps in a brain tumor cohort; Months 4-6: Optimize the calibration method for utilization of BH CVR maps in a volunteer cohort and generate AFNI and MATLAB-bases scripts for automated application of this method; Months 7-9: Comparison of standard BOLD language activation maps to BH CVR-calibrated CVR maps in both volunteer and brain tumor patient cohorts using ROI-based single subject and group analysis to assess inter-subject and intra-subject BOLD variability; Months 10-12: Manuscript preparation.

Dr. Pillai, Project PI, will supervise and assume overall responsibility for performance of single subject and group analysis, including both semiautomated voxelwise and ROI analysis, of BOLD and MR perfusion data in this project. Analysis will include generation of BOLD breath-hold (BH) cerebrovascular reactivity (CVR) maps that will be used to both evaluate neurovascular responsiveness and normalize/calibrate language activation maps in both a cohort of brain tumor patients and in a group of normal volunteers. MR perfusion imaging will be used to initially validate BH CVR mapping in a cohort of brain tumor patients.

Dr. Zaca, postdoctoral fellow, will perform BOLD analyses of both the BH CVR data and the language activation maps, and along with Dr. Pillai, will perform ROI-based analysis as well as statistical thresholding of the BOLD data and analysis of MR perfusion maps. Overall statistical analysis and quality control analysis will be primarily performed by Dr. Zaca.