QIBA fMRI Biomarker Committee (BC) Call

Wednesday, September 2, 2020 at 11 a.m. (CT)

Call Summary

In attendance			**RSNA staff**
Feroze Mohamed, PhD (Co-chair)	Ping Hou, PhD	David Scott, PhD	Susan Stanfa
Jay Pillai, MD (Co-chair)	Ho-Ling (Anthony) Liu, PhD	James Voyvodic, PhD	
David Soltysik, PhD (Co-chair)	Nancy Obuchowski, PhD	Francisco Zamorano, PhD	
Lee Baugh, PhD			

Moderator: Dr. Soltysik

Review of Previous Call Summary

- The 08.19.2020 call summary was approved as presented

Dr. Voyvodic's Round-1 DRO Project: Comparing clinical fMRI analyses

- Dr. Francisco Zamorano, PhD (Universidad del Desarrollo - Santiago, Chile) completed his analysis of the data and will send the link to Dr. Voyvodic

Groundwork Project Ideas

- A strategy to apply for grants and contracts to help support continued QIBA activities is being developed
- QIBA leadership is seeking information about currently unfunded groundwork and clinical studies that could help advance Profiles through the Technically Confirmed and/or Claim Confirmed stages
- Ideas are being requested from BCs in the format of brief, structured abstracts of the type used by many medical journals (about 100-to-250 words is typical)
- QIBA Leadership already has some ideas about potential sources of financial support but would like to approach them with specific examples related to current quantitative imaging biomarkers and potential benefits
- Dr. Sullivan noted that August 31st was a soft deadline; groundwork ideas encouraged across all MR BCs which will need adequate time to draft, review and discuss
- BC Co-chairs were encouraged to discuss this on upcoming BC calls and reach out to CC leadership with questions
- SBIR grants funded by NIST and DOD for phantom and analysis software may be relevant to QIBA projects
- Suggestion to initiate a project based on fMRI reproducibility data of normal subjects from multiple sites
    - Dr. Voyvodic just completed a study comparing the metrics Laterality Index (LI), cluster location and cluster size of language activations in 600 human subjects who have performed more than one sentence or word generation language task
    - The data were easily collected, but challenges remain regarding analysis
    - Due to the degree of complication involved in comparing details of multicenter language scans, this project was not selected for groundwork project submission

- Discussion re: revisiting the project proposal, "Reproducibility of task-free (resting-state) fMRI as a clinical brain biomarker," submitted to 39 Pharma/iCRO contacts in May 2019
    - Proposal to use fMRI scan data from patients and volunteers who have undergone either task-free resting-state (rs) fMRI scans alone or active task-based fMRI as well as resting-state fMRI scans, to quantitatively assess the reproducibility of rs-fMRI and the concordance of the two methods in determination of the sensorimotor network (SMN) and the language network (LN)
    - Existing data published in the literature would mainly be relied upon, but some funds for multicenter data acquisition may be needed

- rs-fMRI may be scalable for use in interrogation of any sensory or cognitive brain network in the future for pharmacological intervention or other types of clinical trials

- fMRI BC members to define exactly what groundwork needs to be done to inform Language-Mapping Profile v2.0 reproducibility Claim development
  - Dr. Voyvodic has cross-session (between subjects) and within-session (to assess within-subject variability) data for the same tasks and different tasks; he offered to collect additional task-based fMRI data if needed to inform v2.0

- Dr. Scott added an imaging CRO (iCRO) perspective and noted that pharma has supported many trials that have used rs-fMRI
  - Regulatory agencies have started to reassess the idea that an endpoint needs to be clinical in nature and are beginning to accept that a biomarker alone can be sufficient evidence for registering a compound
  - Reliability demonstrated in a study would be really powerful and cited for years to come
  - Gold standard normative data set and top line image acquisition and analysis procedures are needed to demonstrate longitudinal efficacy and may generate interest from pharma
  - Challenges relating to rs-fMRI implementation include complete absence of standardization of image acquisition, preprocessing and postprocessing methods, and absence of commercially available software
  - The dynamic nature of functional connectivity is not completely understood, and most currently implemented rs-fMRI analysis methods ignore the important confound of dynamic connectivity with respect to assessment of intra-network and inter-network connectivity
  - The need to prioritize standardization of rs-fMRI analysis techniques was emphasized; due to methodological differences, the neurologic and psychiatric rs-fMRI literature is replete with varied and conflicting disease-specific results

- Discussion on which biomarker/resting state network to quantify; rs-fMRI to eventually be pursued following Profile v2.0
  - Due to inter-subject variability, language mapping deemed more complicated than motor mapping; there are many intricacies of language-mapping with task-based fMRI
  - Advantage of using rs-fMRI is that multiple neural networks can be interrogated in a single image acquisition session; this will allow analysis of multiple networks beyond language alone, which may be valuable for longitudinal intervention studies
  - Recommendation to approach this not only from an application standpoint, but also from a feasibility one
  - fMRI functional connectivity efforts are currently being focused on comparisons between task-based fMRI vs. rs-fMRI data, but there are some fundamental differences between these techniques in terms of interrogated networks and their identification
  - The language network was deemed important, as it is a conglomeration of different resting state networks; any guidelines offered re: acquisition, analysis and reporting would be useful due to scalability making the Profile more appealing to end users
  - It was agreed that the fMRI BC will use the "Reproducibility of task-free (resting-state) fMRI as a clinical brain biomarker" project description as a starting point and modify as needed based on additional BC input
  - It was noted that it had been over a year since original project PIs, Jay Pillai, MD (Johns Hopkins University), Ho-Ling (Anthony) Liu, PhD (UT MD Anderson Cancer Center) and James Voyvodic, PhD (Duke University) had volunteered to assist with this project and that their availability may have since changed

Action Items

- Dr. Pillai to circulate "Reproducibility of task-free (resting-state) fMRI as a clinical brain biomarker" project description for feedback from fMRI BC members

Next call: Wednesday, September 16, 2020 at 11 a.m. CT (1st & 3rd weeks of each month)

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