fMRI as a Biomarker – Clinical Context

- BOLD fMRI can be used clinically as a biomarker for functionally eloquent brain tissue at risk of damage from invasive procedures used to treat brain cancer or other focal pathologies
- Clinical utility and acceptance of fMRI as a biomarker is dependent on reproducibility and validity of brain activation patterns - primary measure produced by fMRI exams - from which secondary quantitative measures are derived
- Current methodology is variable at all stages (exam administration, data acquisition, analysis, report of results) - best described by a model of integration across acquisition systems, MR and analysis platforms.
Groundwork for Profile Development

- **Claims Construction** – Describe the Biomarker and establish performance expectations (what are readout measures? What is achievable?)
- **System Characterization** describes the ‘system’ required to successfully implement the Biomarker (what steps must be taken to support claimed behavior?) – variance in workflow/methodology
- **Transition to Practice** – guidance to imaging professionals to facilitate consistent implementation of the Biomarker (Industry, standards groups, clinical practice professionals) – DICOM synergies

Use Case: fMRI as a biomarker of healthy brain tissue for guiding tumor surgery

Brain surgery? What's at risk?

Day 1

- Tumor
- Risk Zone

Day 2

- Vision fMRI
Proposed Claims Concerning the Reproducibility of fMRI Brain Maps

1. Location of centroid of activation for motor, language, and vision areas is reproducible and quantifiable
2. Spatial extent of activation for motor and language areas is reproducible and quantifiable
3. Language laterality is reproducible and quantifiable

Successful implementation of the fMRI biomarker will promote successful brain surgery - minimizing neurological side-effects.

Improved implementation will facilitate adoption as standard of care and promote industry-wide acceptance.

NIBIB Funding for Modality Projects

RSNA received a 2-year contract from the National Institute for Biomedical Imaging and Bioengineering (NIBIB) and established an RFP distributed to all QIBA Technical Committees.

“To establish a coordinated process structured to meet previously-identified scientific needs for quantitative imaging biomarkers. The long-term objective is to establish processes and profiles that will lead to acceptance by the imaging community, clinical trial industry, and regulatory agencies of quantitative biomarkers as proof of biology, proof of changes in pathophysiology, and surrogate endpoints for changes in the health of patients”.
1st Round - Quantitative measures of fMRI reproducibility for pre-surgical planning
Development of reproducibility metrics
Jim Voyvodic (Duke) & Ted DeYoe (MCW)

- To derive quantitative measures of variability and reproducibility in healthy individuals and a select group of patients.
- These measures will be compared across fMRI paradigms including motor, language, vision and audition.
- The strength of the two projects is the use of standardized post processing sequences to enhance the comparability of the results from the two sites.
- This study is designed to fulfill a critical gap in our knowledge concerning reproducibility as it pertains to presurgical mapping, the context of use in our profile.

Reproducibility of single-subject motor mapping with fMRI
James T. Voyvodic
Brain Imaging and Analysis Ctr., Radiology Dept., Duke University Medical Ctr
Reproducibility of Vision mapping with fMRI
Edgar A. DeYoe
Dept. Radiology, Medical College of Wisconsin, Milwaukee

Validation of Breath Hold Task for Assessment of CVR and Calibration of Language Activation to Optimize Reproducibility
Jay Pillai & Domenico Zaca – Johns Hopkins

- Neurovascular uncoupling (NVU) may result in variations in cerebral vascular reactivity (CVR) that affect BOLD signal.
- Accurate assessment of NVU is essential for accurate and reproducible assessment of underlying neuronal activity.
- Comparison of BOLD cerebrovascular reactivity mapping and DSC MR perfusion imaging for prediction of neurovascular uncoupling potential in brain tumors. Accepted for publication in *Technology in Cancer Research & Treatment* (2012; in press).
- Optimize the calibration method for utilization of BH CVR maps in a volunteer cohort and generate AFNI and MATLAB-based scripts for automated application of this method.
fMRI clinical practice

- Why evaluate the current clinical practice?
  - Reproducibility depends upon workflow stability
  - Considerable variability in best practices
  - Many workflows are home grown

- What is the current clinical practice of fMRI like?
  - Surveyed QIBA-fMRI member sites
  - Collected free-form information from clinicians
  - Distributed to attendees at ASFNR BOLD Study Session
fMRI Profile Development

• Why endorse best practice guidelines?
  – Promote interoperability/Standardization should enhance reproducibility

• How to develop best practice guidelines?
  – Use existing standards where applicable (e.g. DICOM)
  – Work with current efforts – professional societies, etc.
  – Make a unique contribution where feasible
    = quantitative biomarker

Survey of Common Elements of the Clinical Workflow
Used by Current Practitioners of fMRI Brain Mapping
(to what extent is practice consistent across facilities?)
fMRI and DICOM

- The fMRI workflow already employs DICOM
  - MR scans are universally available as DICOM MR
- Examples of potential fMRI DICOM elements
  - Enhanced MR multi-frame = more efficient communications
  - Real World Values = encoding of t, r etc. parameter maps
  - Network Time Protocol = reliable sync of scans vs stimuli
  - Enhanced MR palettes = quantifiable color mapping
- Examples of unmet needs
  - Paradigm descriptions and execution records
  - Non-imaging fMRI results (patient performance)

fMRI: Paradigms

- No single ‘standard paradigm library’
  - Local best practices: experience = confidence
  - Professional organization work (e.g. ASFNR)
  - Goal is not to recommend the paradigms to use
- Recommend methods for QA and interpretation
- Establish power & limitations of fMRI as a biomarker
- Guidelines that define an effective paradigm?
  - duration, # epochs, control period
  - stimulus resolution
fMRI: Post Processing

- A few basic algorithms (e.g. GLM) with many variations, parameters
- Variety of processing tools
  - in-house versus open-source versus proprietary
  - freeware versus commercial
  - FDA-cleared or not

fMRI: Best Practices

- Clinical Best Practices = quality in healthcare
  - Should be established by professional organizations
  - Deal with decision-making
  - Based on meta-studies of clinical trials

- How to help: fMRI as a biomarker
  - Define the best ‘tactical’ approach to fMRI
  - Document the strengths and limitation
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