HHSN268201000050C, RECOVERY
Quantitative Imaging Biomarkers Alliance (QIBA)

PROPOSED METHODOLOGY

QIBA will conduct its work under the NIBIB contract through frequent **conference calls**, **email** communications among the PI, PD, RSNA Staff and various participants. **In-person meetings** are held at the RSNA Annual Meeting in late November, or early December, and in May of each year. Specific work on data collection projects funded with NIBIB contract money will be conducted by the sub-contractors, usually at academic sites.

The QIBA Steering Committee meets monthly by conference call. The Modality committees and Task groups meet frequently as needed, often weekly.

To begin, we have grouped the contract tasks into several thematic categories, labeled A through E below.

A. MANAGING RELATIONSHIPS AND OPTIMIZING COMMUNICATIONS

These tasks will be accomplished through periodic conference calls and occasional workshops or other in-person meetings of the key individuals representing the groups and organizations described.

Create a collaborative, multidisciplinary environment that fosters communication among imaging groups and other medical disciplines involved in the research, approval, and use of QIBs:

- Build on the foundational activities of the TQI and Imaging Biomarker Roundtable efforts, and implement their recommendations relating to quantitative imaging biomarkers.
- Conduct a strategic planning process to determine how QIBA can best be supported and over what period of time into the future.
- Determine what relationship (if any) with IHE would be constructive.

B. DETERMINING AND MANAGING PROCESS

These tasks will be accomplished through monthly Steering Committee conference calls, consultations with biostatisticians and imaging scientists, and occasional workshops or other in-person meetings of the key individuals as needed.

Develop standards, methods, hardware, and/or software that significantly reduce variance in quantitative results from images.

Adopt a statistically rigorous framework for determining sources of variation in quantitative results from imaging methods, and for developing subsequent QA procedures to minimize such variations.

Utilize principles from imaging science to understand the content and analytical framework for quantitative imaging assessments. Specifically, use available data from phantom and clinical studies to characterize the sources of error attributable to the sensor parameters, image quality, the clinical environment, the patient's condition, the image processing techniques, etc.

Educate stakeholders about how Profiles are documented and used to organize the activity and capture the results (including incorporation into UPICT).

Lay out a process for certification of compliance with the Profile and how this relates to the regulatory pathway.

C. WORKING TO ESTABLISH REGULATORY PATHWAYS

These tasks will be accomplished through meetings and discussions with relevant FDA staff members, and subsequent workshop implementation as required.

Clarify and optimize the regulatory pathway by which QIBs enter the market, working with the FDA.

Plan and hold workshops with FDA; topics to include methodology to evaluate and approve computer-assisted diagnosis (CAD) software and new tracer issues (where such issues interface with quantitative imaging). This task is subject to the willingness and availability of FDA to engage with us on this topic.

D. RELATING BIOMARKERS TO DISEASE AREAS

These tasks will be accomplished through occasional conference calls with subject matter experts to set up a Delphi consensus process for each disease area, and occasional workshops or other in-person meetings of the subject matter experts as needed.

Set the clinical context for the disease area:

- Link to relevant research programs for QIB development (e.g., determining disease staging, clinical manifestations, etc).
- Define outcome measurements and surrogate endpoints
- Identify, research, validate, and quantify measures as necessary for such issues as:
    - Early stratification for risk
    - Symptom evaluation
    - Risk assessment for events
    - Staging and characterizing disease state
    - Prediction of intervention outcome
    - Delivery of intervention
    - Disease and Intervention Surveillance
- Based on the clinical context, identify and prioritize what biomarkers to pursue.
- For each biomarker, determine what Profiles to pursue.
- Characterize/Understand the Currently Accepted Standard (e.g., RECIST).
- Articulate Claims that express how the new imaging biomarker will do better.

E. COORDINATING QUANTITATIVE IMAGING BIOMARKER EVALUATION

These tasks will be accomplished through daily RSNA staff support activities, weekly operational calls to include the PI, PD and RSNA staff, additional staff conference calls as needed (sometimes as often as daily), frequent QIBA Technical Committee and other (e.g., ad hoc) committee conference calls, and occasional workshops or other in-person meetings of the key individuals as needed.

Create a collaborative, multidisciplinary infrastructure to foster research, approval, and use of QIBs.

- determine levels of accuracy and reproducibility that are required for clinical trials of oncologic drugs,
- establish Profiles incorporating those levels,
- implement Profiles for the first three imaging biomarkers [Volumetric Imaging Analysis using CT, SUV using FDG-PET, and K_3 using DCE-MRI in Oncology applications] in active industry-sponsored clinical trials and
- begin work on additional markers such as, but not limited to, density in CT, COPD measurements on CT, functional MRI (fMRI), and FLT in PET.

Develop and maintain a national repository of QIB image data and associated metadata.

The general approach to be used for each quantitative imaging biomarker is given here. Actual projects funded will be selected by the QIBA Steering Committee, which meets by monthly conference call. Depending on the project, financial support will be needed for clinicians and scientists for individual project plan development, phantom purchases or construction, imaging scientists, physicists and technologists for data collection, site support (e.g., scanner time), radiologists for image interpretation, and data analysis.

E. COORDINATING QUANTITATIVE IMAGING BIOMARKER EVALUATION (CONTINUED)

Potential tasks include:

I. Image analysis infrastructure.
II. Technical Characteristics and Standards Groundwork:
    a. Systems engineering analysis of sources of variability, including consideration for co-variates.
    b. Phantom development:
        i. Maintain inventory of currently available phantoms
        ii. Assess applicability of existing phantoms
        iii. If new one is required, pursue development as defined by the Technical Committee
    c. Assessment of intrinsic scanner variability – same scanner, scanners from same manufacturer, scanners from different manufacturers:
        i. Prospective Single- and multi-center phantom studies
    d. Assessment of intra- and inter-reader bias and variance of measurements on phantom and clinical images:
        i. Phantom images from prospective single- and multi-center studies
        ii. Clinical images from no-change (“coffee break”) conditions on patients
        iii. Clinical images from retrospective clinical serial studies
III. Document Profile Details to include explicit coverage of:
    a. Quality Control and Covariates
    b. Acquisition protocols
    c. ROI definition
    d. Quantification computation
    e. Data transfer and storage issues
    f. Longitudinal measurements
    g. Establish and implement a system for software version tracking / mitigation so as to accommodate changes in software version during clinical trial period
IV. Synthetic digital reference object (i.e., pseudo-data created to facilitate performance assessment for candidate implementations of the biomarker):
    a. Create synthetic digital reference object to support algorithm performance testing and certification activities
V. Clinical Performance Groundwork:
    a. Begin with a single expert per software package (or method) working under ideal conditions, and use data obtained from clinical trials that used the QIBA Profile:
        i. For each new imaging biomarker and its reference standard, determine the sensitivity and specificity for individual expert readers using appropriate outcome measure, such as prediction of survival at relevant established time-point (e.g., 6 month survival for advanced lung cancer)
        ii. Compare correlations between new and standard biomarkers with outcome measures
    b. Progress to multiple image analysts for each software package (or method)