# HHSN268201300071C
# Quantitative Imaging Biomarkers Alliance (QIBA)

## PROGRESS REPORT: AS OF MARCH 2014

This progress report is stated in terms given in the accepted Work Plan. This progress report is organized in the same subsections as used in the approved workplan:

A. Review of activities responsive to each objective.

B. Status for each groundwork project approved by steering committee with respect to funding approval and start.

C. Additional descriptions of general committee progress.

## A. REVIEW OF ACTIVITIES RESPONSIVE TO EACH OBJECTIVE.

An update on Objectives 1-6 is given below. *Note that in general the data from each of these efforts is available for uploading to the Quantitative Imaging Data Warehouse identified in the Methodology for Objective 5.*

### OBJECTIVE 1. DEVELOP AT LEAST 2 NEW PROTOCOLS AND QIBA PROFILES PER YEAR THAT ADDRESS DISEASES OF SIGNIFICANT BURDEN TO THE US POPULATION.

The work of the six QIBA Technical Committees follows a defined, coordinated process described below to develop solutions and promote their adoption.

The **CT volumetry** committee has a subgroup called the Lung Nodule Assessment in CT Screening Writing Group. This subgroup has created a QIBA Profile for lung cancer screening, and is preparing to make it available for public comments. The group is finalizing the language of the claims.

**PET – AMYLOID** writing group: The NM Modality group has initiated a new Profile writing group on PET Amyloid imaging tracers. Starting in the summer and fall of 2013 there were several discussions with leaders in this rapidly emerging field, and in December 2013 the QIBA Profile Writing Group focusing on PET-Amyloid / brain imaging was formed. The first meeting was in January 2014, and has continued roughly bi-weekly. It is anticipated that this Profile will leverage the efforts of the recently published FDG-PET Profile.

The **fMRI** TC is working on V1.0 of its Profile for Pre-surgical Mapping of Eloquent Brain Tissue. The TC has incorporated findings from funded projects 1 & 2 (2012-2013) – refining its claims (Profile Section 2) and providing methodological detail in Profile section 3 (Profile Details). The committee has started its draft of Profile section 4 (Compliance) which will be informed by currently funded projects.

### OBJECTIVE 2. PERFORM INDIVIDUAL GROUNDWORK DATA COLLECTION AND ANALYSIS PROJECTS TO FILL GAPS IDENTIFIED DURING WORK DEVELOPING AT LEAST 6 QIBA PROFILES.

Groundwork data are extracted from the literature, and in that process gaps in the data necessary to understand the sources of variability are noted.

**CT Volumetry**: For the clinical data 3A challenge, results were received from participants in September 2013. There are 12 participating sites testing 13 algorithms. All data is saved in the QI-Bench database. Analysis of the data is underway, and a preliminary report has been presented to the group by the statistician Dr. Kjell Johnson. Elucid Bioimaging is continuing statistical analysis. Final analysis will include an individual report for each participating algorithm, as well as a cross-algorithm comparison.

**FDG-PET** – Profile implementation data collection (field test project) is underway at two sites and a third site will begin data collection as soon as funding is approved. Groundwork data (i.e. phantom calibrations scans) will be collected as part of the field test project for the FDG-PET Profile.

**SWS US**: The US SWS committee has tested the first set of prototype phase II phantom materials, obtained additional support from the FDA, initiated further phantom development, and outlined the study to generally

follow that of the first study performed with elastic phantoms. Drs. Palmeri, McAleavey and Jiang are using and making available numerical simulation software for hepatic SWS measurements. This will reveal our level of understanding of the reasons for the results of study 1 and allow future assessment of the various possible methods of achieving consistent reported results from the various commercially available systems, or the largest possible subset thereof. Progress in evaluating and discarding the dominant Voigt model for SWS estimation in visco-elastic media has been significant. These advances with expensive and custom modeling software are being implemented in free or less expensive software. Codes for producing simulated data have been posted. Dr. Samir will initiate a pilot study of effects of steatosis & inflammation on SWS US for liver fibrosis, examines two possible major confounders in achieving discrimination of fibrosis stage. Another goal is analysis of the literature to estimate the effects of various confounders for the initial Profile drafting. The Mendeley reference database of ~1533 manuscripts on elastography of the liver includes 106 on the primarily targeted acoustic radiation force measurement or imaging method. Eighty of these have been analyzed.

## OBJECTIVE 3. DEVELOP PROCEDURES AND PROCESSES FOR HARDWARE AND SOFTWARE MANUFACTURERS AND USERS TO DEMONSTRATE COMPLIANCE WITH QIBA PROFILES.

A key focus for the various profiling efforts this year is to address issues of compliance with QIBA Profiles, including the processes and procedures to demonstrate it. Additionally, some of the funded projects specifically include development of predictive metrics for use in calibration and quality control programs and development of evaluation procedures to verify compliance by vendors and providers of service with QIBA Profiles. Selected specifics for effort in this reporting period:

**CT**: Compliance with the profile for volumetry of advanced disease has been divided into three subsections: patient preparation and handling, scan acquisition and reconstruction, and image analysis. Each subsection has been assigned to a specialized subgroup of the committee. Each subgroup is constructing a checklist, and these will be assembled into Section 4 (Compliance) of the profile.

**fMRI**: Ongoing identification of hardware and software properties at each participating clinical test site for compatibility concerns. Data Analysis questionnaires have been created and are in the process of being refined for documenting image processing algorithms, parameters, and activation thresholding methods used at each site. Questionnaire development is on track to be ready when the first DRO's are available for distribution to sites.

**FDG-PET:** The specifications listed in the publicly-reviewed FDG-PET Profile have been extracted into a draft checklist for Compliance. Two sites in the US (Duke and JHU) are being funded under this contract to test the feasibility of this checklist for Compliance. A third site in Europe will also test the checklist, when funding is approved.

**DCE-MRI:** The specifications listed in the publicly-reviewed DCE-MRI Profile are being extracted into a draft checklist for Compliance. When this is completed the checklist will be disseminated for field testing.

## OBJECTIVE 4. DETERMINE FROM EXPERT CONSENSUS THE DESIGN REQUIREMENTS FOR PHYSICAL AND VIRTUAL (DIGITAL) REFERENCE OBJECTS NEEDED FOR DETERMINATION OF IMAGING BIOMARKER VARIABILITY OR TO DEMONSTRATE COMPLIANCE.

The following projects are funded to develop and/or utilize phantoms and their support for QIBA Profiles.

The **CT volumetry** group has designed a physical anthropomorphic liver phantom that includes liver lesion reference objects. This phantom will be used to extend the current lesion volumetry profile claims to lower contrast liver lesions. The phantom is based on a commercial CIRS phantom that has a uniform density liver region. In our modified design, the liver is split into two density regions with one region representing an arterial phase enhanced liver and the second a venous phase enhanced liver. The reference objects include spherical, elliptical and lobulated lesions of various sizes and densities representing the range of expected clinical lesions for each contrast phase. The liver region of the phantom is removable, and we have also requested an empty liver shaped insert that can be used to design custom, non-uniform backgrounds (e.g., fatty infiltrated liver or vascular anatomy) representing more realistic clinical scans.

The **FDG-PET/CT** Digital Reference Object (DRO) Extension project will provide necessary extensions (i.e. features) to the FDG-PET/CT Digital Reference Object (DRO) to expand the testing capabilities. These capabilities will include measurements of Region of Interest (ROI) fidelity, SUVpeak, and PET-CT display alignment. After these extensions are incorporated and validated, the DRO will be field-tested at multiple sites and display stations as successfully done previously.

**fMRI**: We have assembled existing fMRI data sets to use as DRO templates. Each DRO includes a high-resolution whole brain T1-weighted anatomical scan. First fMRI datasets have been selected for use as DRO templates and sources of noise and task signals. DRO synthesis software design is partly completed. Some design features are still under discussion and will likely require initial use of the first revision software in order to complete specification. Design of a “library” of empirical signals has just begun.

**SWS US**: The codes for generating raw SWS ultrasound data will be compared on posted raw data sets (DROs), and this software will be made available for use by manufacturers in getting their systems to achieve the QIBA SWS and other goals. The phase II phantom materials being developed and evaluated will likely be needed for demonstration of compliance.

## OBJECTIVE 5. COLLECT IMAGES AND ASSOCIATED CLINICAL DATA FOR THE RSNA-QIBA IMAGE WAREHOUSE OR OTHER LOCATIONS, AND PERFORM ANALYSES ON THE DATA TO SERVE QIBA COMMITTEES AND THE BROADER IMAGING COMMUNITY.

Selected specifics:

**PET**: The committee is evaluating the potential of using the RSNA-QIBA Image warehouse to host the FDG-PET/CT DRO. Potential de-identified clinical data sets will also be recruited.

**fMRI**: An initial “phantom” DRO has been generated and de-identified at the MCW site. It is expected to be released to the Duke site for evaluation within the week. This should allow us to test initial data formats and transfer procedures. In parallel we are working with data warehouse personnel on uploading fMRI data to QIDW. Plan is to use the QIDW database for DRO distribution to collaborating test sites.

**SWS US**: Many of the human liver study results will be made available in the image data warehouse. Work is continuing to define the processing stage of the images stored and the degree of quantitative information that can be obtained from them. Most such commercial images now in the USA do not show quantitative information throughout the image but only in regions of interest selected before image storage.

## OBJECTIVE 6. PROVIDE SUPPORT FOR QIBA STAFF, SCIENCE ADVISER, SCIENTIFIC DIRECTOR, PROGRAM DIRECTOR, PROJECT MANAGEMENT, MEETINGS, TRAVEL, AND CONFERENCE CALLS.

Support for all of the above committee work, funded project management meetings, conference calls and travel continues to be administered and provided by the RSNA/QIBA staff, Science Adviser, Scientific Director, and Program Director.

## B. QIBA/NIBIB ROUND-3 FEDERALLY FUNDED PROJECT STATUS

**Executed Subcontracts**

| | | | | |
|---|---|---|---|---|
| B | CHENEVERT | 47,960 | U Mich | Software Development for Analysis of QIBA DW-MRI Phantom Data |
| C3 | LODGE | 28,000 | JHMI | FDG-PET/CT Profile Field Test |
| E | KINAHAN | 48,453 | U Wash | FDG-PET/CT Digital Reference Object (DRO) Extension |
| F | BUCKLER | 22,066 | Elucid Bio | Second 3A statistical and image processing analysis |
| K2 | McALEAVEY | 16,775 | U Rochester | Numerical Simulation of Shear Wave Speed Measurements in the Liver |
| K3 | JIANG | 16,775 | Mich Tech U | Numerical Simulation of Shear Wave Speed Measurements in the Liver |
| N | KITWARE | 40,000 | Kitware | Support and Development of the Quantitative Imaging Data Warehouse (QIDW) |

**Subcontracts with RSNA/Inst Contract Officers (have already received Federal COA)**

| | | | | |
|---|---|---|---|---|
| C1 | TURKINGTON | 34,000 | Duke | FDG-PET/CT Profile Field Test |
| D | HALL | 20,460 | U Wisc | Phase 2 Phantom Study with Inelastic, SWS-dispersive Media |
| G1 | DEYOE | 52,749 | Med Col Wisc | fMRI Digital Reference Objects for Profile Development and Verification |
| G2 | VOYVODIC | 31,033 | Duke | fMRI Digital Reference Objects for Profile Development and Verification |
| I | SAMIR | 62,982 | Mass General | A Pilot Study of the Effect of Steatosis and Inflammation on Shear Wave Speed for the Estimation of Liver Fibrosis Stage in Patients with Diffuse Liver Disease |
| K1 | PALMERI | 10,450 | Duke | Numerical Simulation of Shear Wave Speed Measurements in the Liver |
| L | ZHAO | 37,000 | Columbia | Phantoms for CT Volumetry of Hepatic and Nodal Metastasis |
| M | JORDAN | 26,865 | Case Western | Test / re-test Reproducibility of CT Volumetry in Liver Lesions in an Animal Model |

**International Subcontracts awaiting Federal COA/ State Department Approval**

| | | | | |
|---|---|---|---|---|
| C2 | BOELLAARD | 28,000 | VUMC | FDG-PET/CT Profile Field Test |
| H | PERSIGEHL | 13,200 | U Cologne | DCE-MRI Phantom Study to Evaluate the Impact of Parallel Imaging and B1 Inhomogeneities at Different MR Field Strengths of 1.0T, 1.5T, and 3.0T |
| J | LAUE | 24,657 | Fraunhofer | Development of a Tool to Evaluate Software Using Artificial DCE-MRI Data and Statistical Analysis |

**Purchase Orders awaiting Federal COA**

| | | | | |
|---|---|---|---|---|
| A | BOSS | 4,154 | NIST | DW-MRI ADC Phantom |

## C. GENERAL PROGRESS ON ACTIVITIES BEYOND FUNDED PROJECTS

Additional updates from the committees are as follows.

**DCE-MRI**

Profile v1.0 Compliance: A detailed description of, and checklist for demonstrating, profile compliance is in preparation and will address actions and requirements specified by each actor involved in data acquisition, data processing, and data analysis.

Profile v2.0 Development: Extensions of the v1.0 Profile to address 3.0T field strength and parallel imaging acquisition modes depend on the results of two selected groundwork projects to be supported by NIBIB Phase 3 funding when approved by NIH.

Clinical Validation / Field Testing: The field testing of Profile v1.0 principles is ongoing in collaboration with ACRIN via clinical trial 6701, which addresses DCE and DWI in prostate. As of February 2, 2014, five institutions were fully qualified by RSNA QIBA DCE-MRI Phantom scans and DWI Phantom scans, and two sites had accrued at least one patient.

T1 Digital Reference Object (DRO) Project: Data analyses, determinations of limits of parameter space to be used in software package comparisons and compliance testing continue. Additional data are being provided by software companies. Optimal test report formats and contents to be provided to the software providers are also being addressed.

**DWI-MRI**

Profile v 1.0 Development: The effort started with a decision to review published DWI data from different organ systems in detail. Draft imaging protocols are now available for Philips and Siemens scanner families; GE protocols are under development at two sites. Each set of protocols will undergo review by the respective vendor.

Isotropic ADC Phantom: A v1.0 phantom has been designed, manufactured, and tested by QIBA and European IMI project groups. An abstract on the initial work has been accepted for presentation at the 2014 ISMRM Annual Meeting. A second abstract has been submitted to the Quantitative Imaging Track of the 2014 AAPM Annual Meeting.

Next Generation Phantom: The fabrication, multicenter testing, and data analyses depend on groundwork projects to be supported by NIBIB Phase 3 funding, when approved by NIH.

**COPD/Asthma**

Radiation Dose Project – Project Completed – December 2013: The goal of this project was to use automatic exposure control (AEC) acquisition to achieve constant pixel noise across various scanners and subject size. A constant pixel noise is required to control measurement bias. The Committee determined that using an (AEC) would be premature because the CT vendors use various methods. Consequently, a uniform pixel noise from various vendors could not be achieved. Likewise, dose reduction reconstruction will not be included in the QIBA lung density Profile. Rather, the Profile will specify a pixel noise value in the COPDGene Phantom. The specified pixel noise will be determined for each scanner model by varying the tube currents to achieve the specified pixel noise.

Lung Density Profile – Continuing: The draft acquisition and reconstruction specifications have been completed. Careful specification is required to control measurement bias. A compliance checklist will be developed after March 15th, 2014. A presentation of the Profile status will be made during the Lung CT Symposium before the Society of Thoracic Radiology. The presentation will emphasize the actions required by radiology departments planning a QCT service to evaluate COPD. This discussion will provide the Committee feedback about suitability of the stringent specifications in the Profile.

The Committee will evaluate methods to correct effects of inspiration variation on lung density lung density measurements. By June 2014, the Committee will specify the method to correct effects of inspiration variation on longitudinal measurement of lung density. Members of the Technical Committee are developing a model of the lung histogram that will include effects of inspirational variation. The goal is to have a final draft of lung density Profile by July 2014.

**SWS US**

The purpose of this effort is to improve consistency of shear wave speed (SWS) estimates from available systems for noninvasive grading of liver fibrosis. The clinical group at Massachusetts General Hospital, led by Dr. Anthony Samir, has an active clinical protocol for estimating SWS in livers, and that protocol is being converted into the current QIBA protocol template. The QIBA Profile is still in data gathering and outlining phase. A multicenter phantom study of all commercially available shear wave ultrasound and MR imaging systems has been completed, with some analysis continuing. Submission of a manuscript, solicited by Radiology as a result of 2013 RSNA exposure, is planned, and numerous presentations and two proceedings articles have been submitted. Some manufacturers are already using the results of that study to modify their commercial software for more robust SWS estimation. There is hope that the ability to discriminate F0-F2 from F3-F4 grade fibrosis can be system-independent and perhaps that some or all systems will be able to discriminate individual grades F1 to F4. Results of one spin-off from that study with a set of the QIBA/CIRS phantoms have been submitted as a paper directed at SWS ultrasound imaging systems in pediatrics and other applications closer to the skin than is typical for adult livers.

The main impediment to achieving the goals is the dependence of shear wave speed on shear wave frequency, which varies in commercial systems from 50 Hz to 500 Hz and, in some research systems, 2000 Hz. To assess this frequency dependence, a second set of phantoms (phase II) is being developed that, unlike the first set of phantoms, have significant variation in SWS with frequency and a relatively large loss component of their complex elastic moduli, simulating those of livers of various fibrosis stages.