HHSN268201300071C,
Quantitative Imaging Biomarkers Alliance (QIBA)

PROPOSED WORKPLAN

Consistent with the Proposed Methodology approved by the NIBIB Project Officer, QIBA has completed an initial project planning exercise covering the scope of work in the NIBIB award. The plan has been composed at two levels, the first level comprising work by the several subcommittees to define profiling activities and groundwork projects for submission to the steering committee, and review/approval by the steering committee of those projects deemed most likely to provide results against the contract objectives. This workplan is therefore arranged in the following subsections:

A. Review of activities responsive to each objective.

B. Combined list of groundwork projects approved by steering committee across the objectives.

C. For each modality and technical committee, a graphical representation of the timeline and summary narratives for the projects identified thereon.

A. REVIEW OF ACTIVITIES RESPONSIVE TO EACH OBJECTIVE.

Those projects associated with Objectives 1-4 are identified below. It should be noted that many of the projects are responsive to multiple objectives. In some cases a given project is listed twice but in general projects are referenced in the objective where they have the strongest contribution.

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, and that the committee work and funded projects are administered by the QIBA staff, Science Adviser, Scientific Director, Program Director, as identified in the Methodology under Objective 6.

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. QIBA has completed three profiles to date: CT Volumetry for Advanced Disease, DCE-MRI for Solid Tumors, and FDG-PET for whole body studies.

The following Profiles are expected in 2014 or early 2015:

CT: Starting from the released profile for use of CT volumetry as a response marker for drug development in advanced disease, a working group has been formed to develop a Profile for assessment of small nodules in the context of lung cancer screening. They are developing document text to define evidence-based consensus standards and processes for CT imaging in the setting of lung cancer screening, to allow for quantification of biologically meaningful longitudinal volume changes, with acceptable range of variance across vendor platforms. This activity is expected to release a Profile in 2014. In parallel, groundwork projects focused on volumetry of liver masses are being undertaken by the main committee for the purposes of extending the first version of the CT volumetry Profile early in 2015.

fMRI: The QIBA BOLD Profile 1.0 has been developed to provide a systematic approach for optimizing Blood Oxygen Level Dependent (BOLD) fMRI brain mapping for treatment planning prior to surgery or invasive treatment intervention. Whereas the primary purpose of this Profile development is for individual patient care, application of the best practice guidelines it creates has application to clinical trials as well. This Profile makes claims about the precision with which hemodynamic response in eloquent cortex can be measured and displayed under a set of defined image acquisition, processing, and analysis conditions.

MRI: DCE Profile v2.0 will extend DCE Profile v1.0 by addressing 3.0T field strength-specific issues as well as parallel imaging acquisition issues impacting quantitative imaging. DWI Profile v1.0 is being drafted to address a test-retest claim (or claims) for multiple organ systems.

Ultrasound: An initial outline for the Shear Wave Speed (SWS) Profile has been sketched. The literature review for the Profile will be drafted this year. The approach to reducing differences between the different SWS-measuring systems, US imaging/non-imaging and MRI, will depend on the studies to be done with the

new viscous phantom and on simulations. An initial Profile for public review is targeted for Late 2014 or early 2015.

Radionuclides: There are two Profiles under development by the Nuclear Medicine modality Group. The first is the FDG-PET/CT Profile, for which the initial draft was distributed for the public comment phase on January 17, 2013, which was closed on May 24th, 2013. At this point the FDG-PET/CT Profile is being readied for distribution as a 'Publicly Reviewed Profile'. In addition suggested modifications to the DICOM PET standard are being prepared. The next phase for the FDG-PET/CT Profile is field-testing, which is being initiated at multiple sites. The output of the 1 year field testing will likely lead to suggested changes to the Publicly Reviewed Profile, as well as a checklist of procedure steps. It is planned that these changes will lead to a later revision of the FDG-PET/CT Profile. The second Profile, initiated in November of 2013, is for amyloid plaque neuroimaging with PET. It is anticipated that Profile will take a year or longer to complete, and will utilize the framework of the FDG-PET/CT Profile and the recent efforts of the amyloid plaque neuroimaging community.

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 gaps in the data necessary to understand the sources of variability are noted. These gaps lead to QIBA projects to obtain such data. The following are examples of groundwork tasks:

CT: *Test-retest Reproducibility of CT Volumetry in Liver Lesions in an Animal Model.*

MRI: *DW-MRI ADC Phantom, 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.*

Radionuclides: *FDG-PET/CT Profile Field Test.*

Ultrasound: *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, Numerical Simulation of Shear Wave Speed Measurements in the Liver.*

See section C for narrative descriptions of projects.

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, 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:

CT: *Second 3A Statistical and Image Processing Analysis.*

Radionuclides*: FDG-PET/CT Profile Field Test.*

MRI*: Software Development for Analysis of QIBA DW-MRI Phantom Data.*

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 Profiles:

CT: *Phantoms for CT Volumetry of Hepatic and Nodal Metastasis*.

fMRI: *fMRI Digital Reference Objects for Profile Development and Verification.*

MRI: *Development of a Tool to Evaluate Software Using Artificial DCE-MRI Data and Statistical Analysis.*

Ultrasound: *Phase 2 Phantom Study with Inelastic, SWS-dispersive Media*.

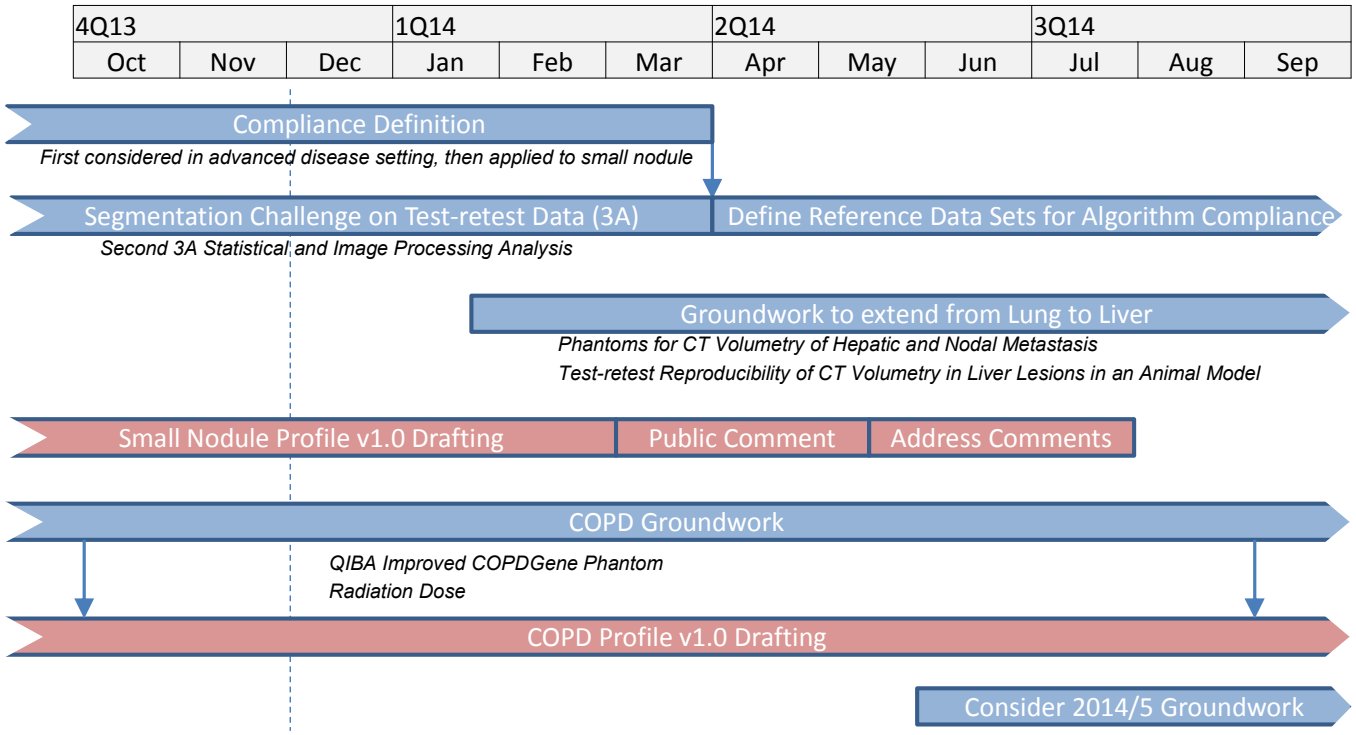
B. COMBINED LIST OF GROUNDWORK PROJECTS APPROVED BY STEERING COMMITTEE ACROSS THE OBJECTIVES.

Project ID	Tech Ctte	Project Title	Investigator
A	DW-MRI	**DW-MRI ADC Phantom**	Michael Boss, PhD University of Colorado, Boulder/NIST
B	DW-MRI	**Software Development for Analysis of QIBA DW-MRI Phantom Data**	Thomas Chenevert, PhD University of Michigan
C-1	FDG-PET	**FDG-PET/CT Profile Field Test**	Timothy Turkington, PhD Duke University
C-2	FDG-PET		Ronald Boellaard, PhD VU Medical Center
C-3	FDG-PET		Martin Lodge, PhD Johns Hopkins University
D	US SWS	**Phase 2 Phantom Study with Inelastic, SWS-dispersive Media**	Tim Hall, PhD University of Wisconsin, Madison
E	FDG-PET	**FDG-PET/CT Digital Reference Object (DRO) Extension**	Paul Kinahan, PhD University of Washington
F	Vol CT	**Second 3A Statistical and Image Processing Analysis**	Andrew Buckler, MS Elucid Bioimaging Inc.
G-1	fMRI	**fMRI Digital Reference Objects for Profile Development and Verification**	Edgar DeYoe, PhD Medical College of Wisconsin
G-2	fMRI		James Voyvodic, PhD Duke University
H	DCE-MRI	**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**	Thorsten Persigehl, MD University Hospital Cologne, Germany
I	US SWS	**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**	Anthony Samir, MD, MPH Massachusetts General Hospital
J	DCE-MRI	**Development of a Tool to Evaluate Software Using Artificial DCE-MRI Data and Statistical Analysis**	Hendrik Laue, PhD Fraunhofer MEVIS, Germany
K-1	US SWS	**Numerical Simulation of Shear Wave Speed Measurements in the Liver**	Mark Palmeri, MD, PhD Duke University
K-2	US SWS		McAleavey U Rochester
K-3	US SWS		Jiang Mich Tech U
L	Vol CT	**Phantoms for CT Volumetry of Hepatic and Nodal Metastasis**	Binsheng Zhao, DSc Columbia
M	Vol CT	**Test / re-test Reproducibility of CT Volumetry in Liver Lesions in an Animal Model**	David Jordan, PhD Case Western

C. FOR EACH MODALITY AND TECHNICAL COMMITTEE, A GRAPHICAL REPRESENTATION OF THE TIMELINE AND SUMMARY NARRATIVES FOR THE PROJECTS IDENTIFIED THEREON.

CT

Starting from the released Profile for use of CT volumetry as a response marker for drug development in advanced disease, a working group has been formed to develop a Profile for assessment of small nodules in the context of lung cancer screening. They are defining the document text to define evidence-based consensus standards and processes for CT imaging in the setting of lung cancer screening, to allow for quantification of biologically meaningful longitudinal volume changes, with acceptable range of variance across vendor platforms. This activity is expected to release a Profile in 2014. In parallel, the groundwork projects being undertaken by the main committee are for the purposes of extending the first version of the drug development Profile early in 2015. The following figure sets out a timeline for the committee work, inclusive of Profiling activities as well as funded groundwork projects:



The projects are described below.

Second 3A Statistical and Image Processing Analysis: Quantifying changes in lung tumor volume is important for diagnosis, therapy planning and evaluating response to therapy. Computer algorithms have been developed in order to measure such volume changes in clinical settings. The aim of the first QIBA 3A study was to estimate the inter-algorithm variability on phantom data. The algorithms were applied to FDA acquired CT scans of synthetic lung nodules in anthropomorphic phantoms. Using FDA-supplied physical measurement values as ground truth, we calculate the algorithm measurement accuracy bias and variability. The study was organized as a public "challenge" and consisted of two phases, the pilot and the pivotal one. Both the pilot and the pivotal used anonymous participants from academic and commercial developers associated with QIBA. The participants downloaded High Resolution CT images from QI-Bench, an open source software infrastructure that supports the development of quantitative imaging biomarkers.

Phantoms for CT Volumetry of Hepatic and Nodal Metastasis: The aim of this project is to assess the measurement performance of lesion sizing tools in estimating the volume of liver lesions in liver phantoms. Phantoms to be used include simple uniform phantoms such as lesions embedded in gelatin, as well as anthropomorphic phantoms that more accurately reproduce the radiographic texture and morphological complexity of the liver. Synthetic nodules will be embedded in the phantom, simulating lesions of different sizes, shapes, and radiological densities. The phantoms will be scanned on multiple systems (multiple models

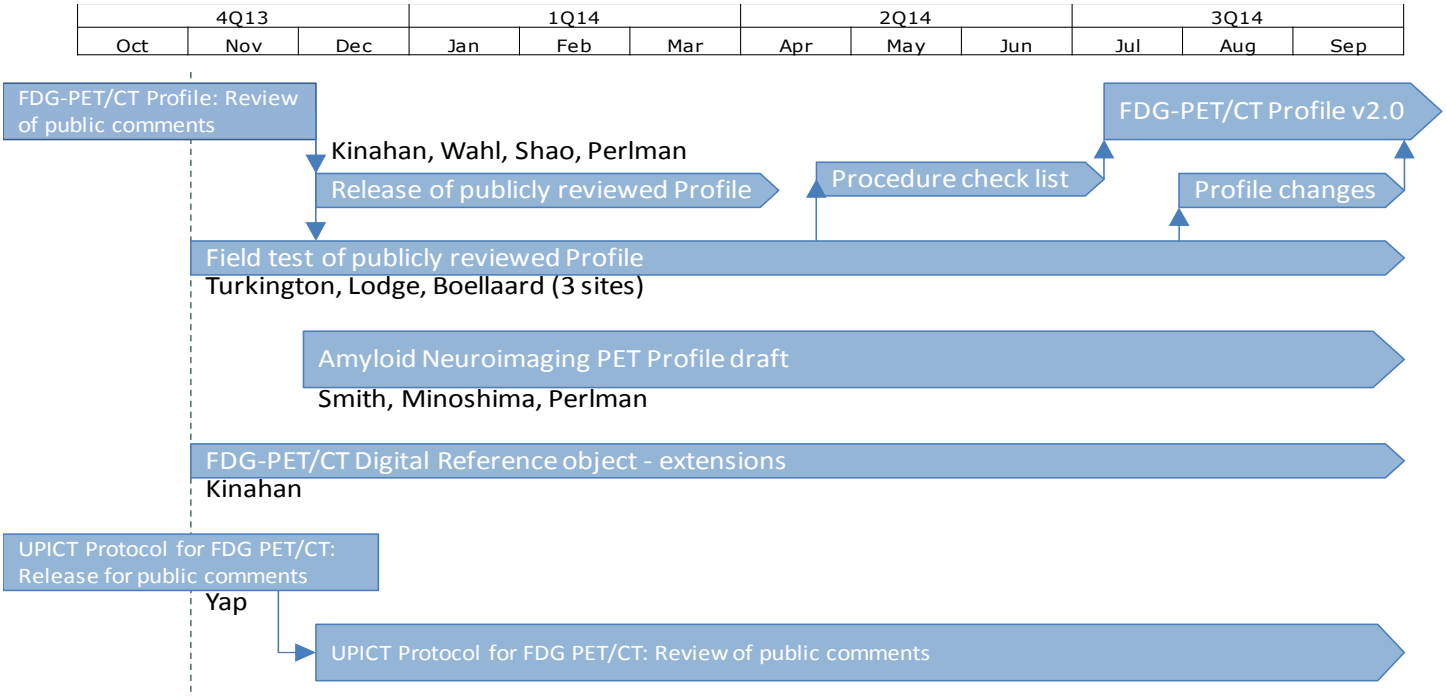
and manufacturers), using a variety of scanner settings. The scans will be segmented using automated and semi-automated tools that have been used in previous QIBA activities to segment lung lesions. Initially, only two or three tools will be used. In the subsequent program year, the project can be extended to a public challenge, in which multiple participants receive data and submit their segmentation results for independent analysis and comparison. Analysis of the data will include statistical comparison of biases to determine accuracy, and comparison of reproducibility to assess precision. ANOVA will be used to identify important factors (lesion characteristics, scan technique, scanner models) that affect volume measurements.

Test / re-test Reproducibility of CT Volumetry in Liver Lesions in an Animal Model: An animal (pig) model of liver metastases has been developed, and will be used in this project to characterize the test/re-test variability in a manner similar to the 1B study previously done with lung lesion data. The pilot study will be conducted on a single animal. The animal will undergo implantation of samples of a modified fibroblast cell line into the liver, and then must be kept immunosuppressed to permit implant growth. An estimated 3 lesions can be expected per animal. Tumors will be allowed to grow over approximately 2 months, with occasional checks by ultrasound to estimate lesion size. The animal will be anesthetized and CT scans will be performed at several intervals after injection of IV contrast. The animal will be allowed to wake up, a period of time (approximately 12 hours) will pass to allow complete washout of contrast, and then the scans will be repeated, taking care to keep all contrast injection parameters (volume, rate, timing of scan) the same. The entire process will then be repeated once more, for a total of 3 sets of scans obtained over approximately 24 hours. The goal is to obtain a dataset containing multiple scans of multiple lesions, which can be used for analysis following the same approach as used in the previous QIBA CT volumetry 1B project.

COPD: There are two active projects in COPD, one to improve the COPDGene phantom, and another to evaluate effects of radiation dose. Additionally, profile development continues, focusing on reproducibility of lung density from literature and COPDGene duplicate scans; volume correction to determine method to assess precision and bias of volume corrections; and determining the utility of reference standards included in exam. An outreach effort is planned through sponsoring of a one day conference on QCT of the lung before Annual meeting Society of Thoracic Radiology in March 15, 2014.

RADIONUCLIDES

The following figure sets out a timeline for the committee work, inclusive of Profiling activities as well as funded groundwork projects:



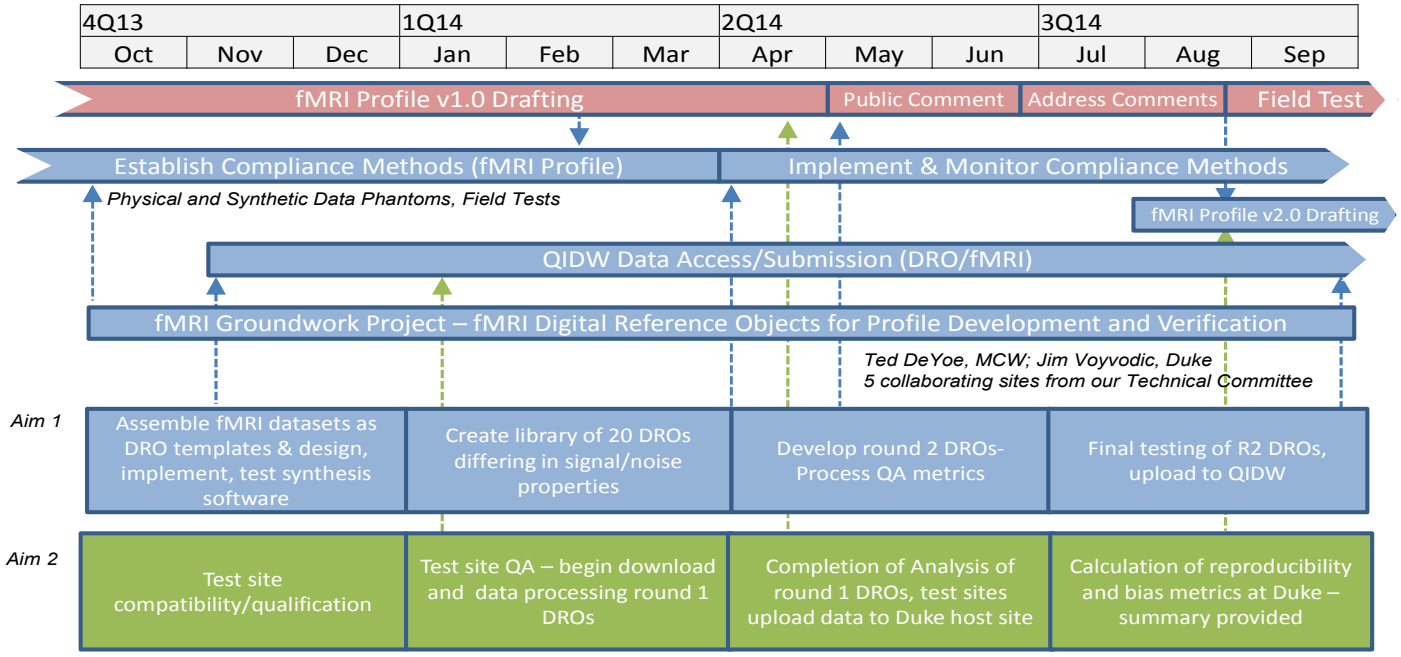
The projects are described below.

FDG-PET/CT Profile Field Test: The primary goal is to determine the feasibility of the FDG-PET/CT Profile as standard to test against for compliance. This data will be used to revise the Profile to improve its utility and establish efficacy. A step-by-step list of compliance tests will be generated as documentation for compliance testing for PET/CT scanners from each of the major manufacturers. Areas in which compliance cannot be achieved will be identified and documented. The secondary goal is to measure test-retest scan SUV variability and bias at different points in the image processing chain across multiple sites using real and digital phantoms. This will also be done, as much as feasible, with patient scans within the validation workflow. It is anticipated that the acquisition, processing, display and analysis phases will be tested with at least one scanner at each site in the first phase.

FDG-PET/CT Digital Reference Object (DRO) Extension: This 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 ROI (region of interest) fidelity, SUVpeak, and PET-CT display alignment. After these extensions are incorporated and validated, the DRO will be field-tested and at multiple sites and display stations as successfully done previously. The multiple testing sites will be selected from FDG-PET/CT Technical Committee members. The primary site will coordinate testing procedures, DRO distribution, and data analysis. The project will start with experienced quantitative imaging centers first (partnering with core labs if possible), then expand to community centers (if budget and time allow).

FMRI

The QIBA BOLD Profile 1.0 has been developed to provide a systematic approach for optimizing Blood Oxygen Level Dependent (BOLD) fMRI brain mapping for treatment planning prior to surgery or invasive treatment intervention. Whereas the primary purpose of this Profile development is for individual patient care, application of the best practice guidelines it creates has application to clinical trials as well. It is expected to provide specifications that may be adopted by users as well as equipment developers (hardware and software devices) to meet targeted levels of clinical performance in identified settings. This Profile makes claims about the precision with which hemodynamic response in eloquent cortex can be measured and displayed under a set of defined image acquisition, processing, and analysis conditions. The following figure sets out a timeline for the committee work, inclusive of Profiling activities as well as funded groundwork projects:



The projects are described below.

fMRI Digital Reference Objects for Profile Development and Verification: Previous work by this committee has identified many possible sources of variance in fMRI and has established metrics of reproducibility for one representative image analysis protocol. However, methods used for clinical fMRI typically vary from site to site

and it is not known: (1) which methodological factors significantly affect reproducibility, sensitivity and bias, (2) which methods in current use are best suited for obtaining consistent quantitative results, or (3) how our methodological considerations impact clinical performance of fMRI as a biomarker. The current proposal covers the first year of a 2 year project to address these issues. The centerpiece of the project will be to create standard datasets or “digital reference objects”

(DROs) with realistic known signal qualities and noise features. Aim 1 will combine existing human fMRI data sets plus simulation software to create a range of DROs that will allow us to manipulate sources of variance and systematically assess the technical performance of different fMRI data analysis methods. These DROs will be used in Aim 2 to compare the performance of different fMRI data processing methods in current use at different experienced clinical sites. As optimal existing methods are identified, we will begin the process of isolating and characterizing specific individual sources of variance by comparing reproducibility, sensitivity, bias, and linearity for Aim 1 DROs that vary systematically in signal and noise properties.

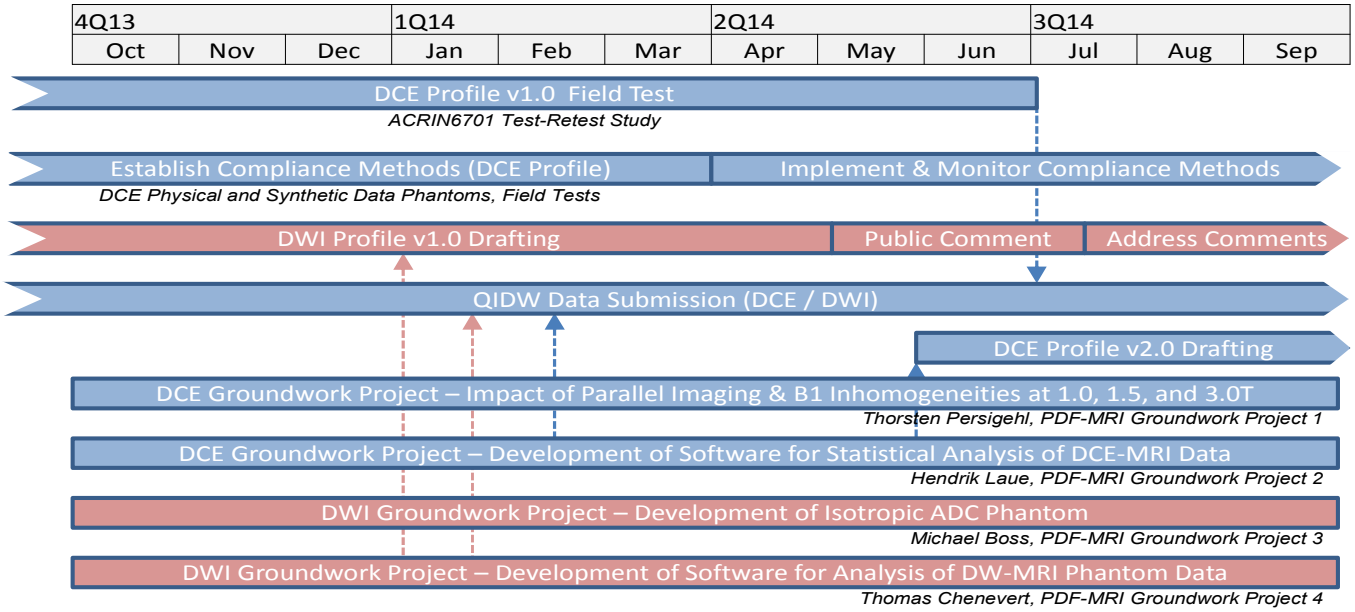
MRI

The DCE Profile v1.0, addressing the claim "Quantitative microvascular properties, specifically transfer constantand blood normalized initial area under the gadolinium concentration curve, can be measured from DCE-MRI data obtained at 1.5T using low molecular weight extracellular gadolinium based contrast agents with a 20% within subject coefficient of variation for solid tumors at least 2 cm in diameter.", is currently in the field test phase. The field test for this profile is in the form of a multi-center, multi-vendor, test-retest prostate DCE-MRI study. The trial is ACRIN6701 and is a clinical trial jointly sponsored and funded by RSNA QIBA and ACRIN. Currently, five sites have been qualified and three additional sites are in the qualification process.

DCE Profile v2.0 will extend DCE Profile v1.0 by addressing 3.0T field strength-specific issues as well as parallel imaging acquisition issues impacting quantitative imaging. Two of the funded groundwork projects in the current funding cycle (PIs Persigehl and Laue) will provide the information necessary to develop v2.0 of the DCE Profile.

DWI Profile v1.0 is being drafted and two of the currently funded groundwork projects will provide information necessary to finalize of the profile draft. This Profile will address a test-retest claim (or claims) for multiple organ systems. The two groundwork projects are focused on development and validation of a NIST-traceable multi-ADC isotropic diffusion MRI phantom (PI: Boss) and the associated software for analysis of multi-field strength, multi-vendor, multi-center data acquired using the phantom (PI: Chenevert).

The following figure sets out a timeline for the committee work, inclusive of Profiling activities as well as funded groundwork projects:



The projects are described below.

DW-MRI ADC Phantom: we will build a robust phantom that is suitable for rapid characterization in multicenter trials. Initial prototyping will be performed at NIST in Boulder, CO and at the University of Michigan, while phantom construction will be outsourced to a third party with previous phantom experience. This phantom will blend the best characteristics of the NIST and NCI prototypes by containing an array of ADC components, as well as temperature control via an ice bath, and possibly *in situ* MR thermometry. NIST will retain a subset of phantom insets for long term testing of phantom stability and accuracy. The phantom will allow characterization of inter-scanner variation of ADC measurements, intra-scanner variation over time, optimization of pulse sequence choice, and spatial dependence of ADC due to uncompensated non-linear gradient effects.

Software Development for Analysis of QIBA DW-MRI Phantom Data: Collection of DWI and derived quantities, such as ADC, are being incorporated into clinical trials as a potential diagnostic or therapy response biomarkers. Unfortunately, several essential elements of DWI quality control across multiple institutions are still lacking. Deficiencies include: a multi-component DWI phantom design; consensus on system testing procedures; definition of systems performance metrics; and availability of DWI performance analysis software to assess these metrics. A multi-compartment PVP-based DWI phantom has been proposed for QIBA support by Michael Boss at NIST, and is herein referred to as “NIST PVP DWI Phantom”. This project will provide the means to measure key system DWI performance metrics for cross-vendor/site comparison thereby forming the basis of DWI site certification and quality control utilizing NIST PVP DWI Phantom data.

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: For this project, we are planning to acquire T1 maps using the variable flip angle technique and the QIBA DCE-MRI phantom (MD Anderson Cancer Center) at 1.0 Tesla (Philips Panorama), 1.5 Tesla (Philips Achieva), and 3.0 Tesla (Philips Achieva) at the University Hospital Cologne (Germany). The DCE-MRI phantom will be scanned using the Qbody coil and surface coil with and without parallel imaging. The MR protocol will be re-measured after repositioning of the phantom and the surface coil. B1 maps will be acquired to correct for the flip angle on a pixel-by-pixel basis. MR data will be exported as PAR/REC and DICOM, and provided for an open image archive. T1 maps will be calculated by using the Philips permeability software (Version 5.2, based on PAR/REC) with and without B1 correction. The measured T1 data of the various imaging techniques and field strengths, as well as the T1 mapping with and without B1 correction, will be used to measure the individual and population biases, and the reproducibility coefficient (RDC); 95% Confidence Intervals (CIs) will be constructed. The bias and precision of the imaging techniques will be compared using repeated measures analysis and variance component analysis, respectively. DICOM data will also be analyzed by using DynaLab software (Fraunhofer MEVIS, Germany). Moreover, for analysis of variance across different MR scanners, the QIBA DCE-MRI phantom will be also measured at 1.5 Tesla and 3.0 Tesla MR scanners from Siemens (Franhofer Institute Bremen and University Hospital Freiburg, Germany) and GE (MGH and University of Wisconsin, USA). Corresponding Philips, Siemens, and GE DICOM data will be compared by using DynaLab software (Frauenhofer MEVIS, Bremen).

Development of a Tool to Evaluate Software Using Artificial DCE-MRI Data and Statistical Analysis: Artificial data based on underlying pharmacokinetics and MR physics allows for the evaluation of the accuracy and performance of complex analysis software for dynamic contrast enhanced (DCE-) MRI and similar measurement techniques, such as diffusion weighted imaging (DWI) and native T1 mapping. Besides the creation of test data, it is important to evaluate and compare the results from the different software packages tested. This is especially relevant since the results will most likely show deviations, even for more or less identical implementations, resulting from the underlying numerics and differing initial values.

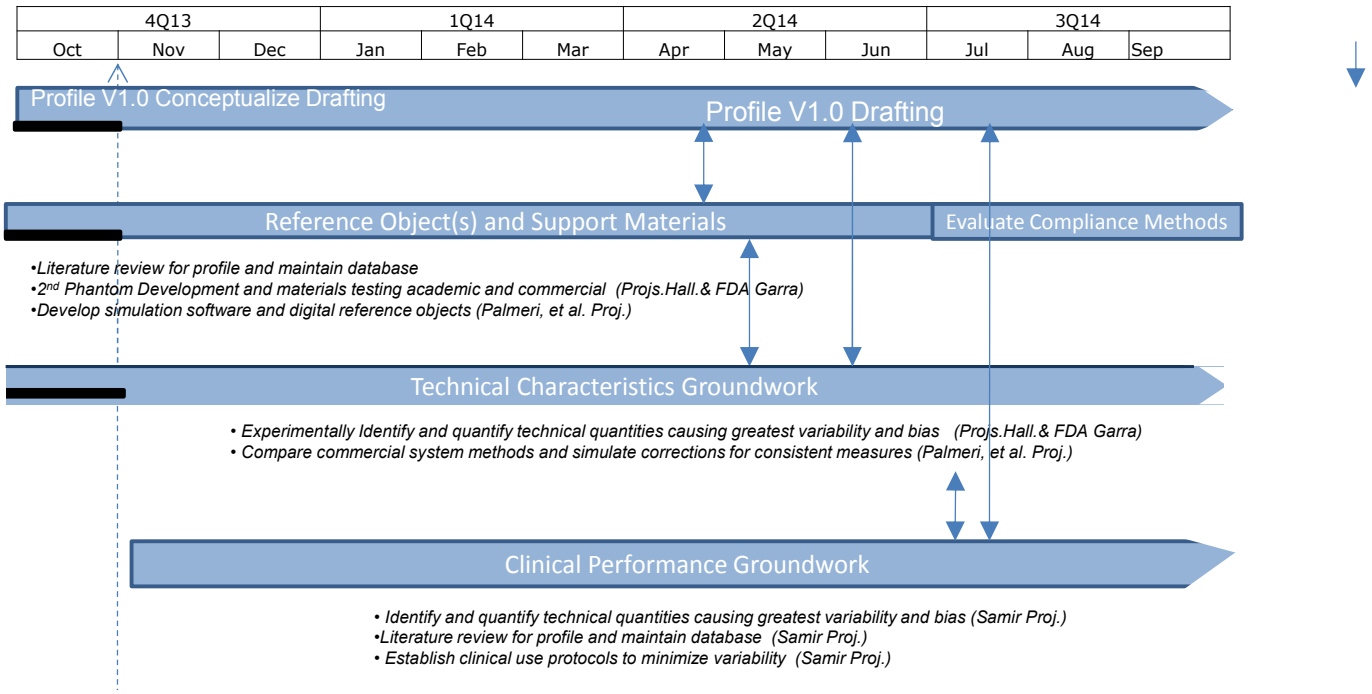
Consequently, it is not sufficient to simply compare the equality of parameter maps: a statistical comparison is needed, and we propose to build a tool to compare the results of parameter maps from different software packages with the reference parameter maps from the test data.

ULTRASOUND

For the Shear Wave Speed (SWS) Ultrasound Imaging Profile, co-chair Brian Garra has sketched an initial outline. The literature review for the Profile will be drafted this year in the A. Samir clinical project, where experimental information will be obtained on several of the main anticipated confounding factors. The approach to reducing differences between the different SWS-measuring systems, US imaging/non-imaging

and MRI, will depend on the studies to be done with the new viscous phantom and on simulations. An initial Profile for review is targeted for Late 2014 or early 2015.

The following figure sets out a timeline for the committee work, inclusive of Profiling activities as well as funded groundwork projects:



The projects are described below.

Phase 2 Phantom Study with Inelastic, SWS-dispersive Media: the viscoelastic properties of liver [1]. We expect larger differences in SWS estimates from different system vendors, and that data will form a basis to begin investigation of the system-related causes for bias in SWS estimates (such as frequency content of the shear wave, details of the shear wave tracking strategy, etc.). Several approaches to accounting for these sources of bias have been proposed, but the differences have to be measured in order to make corrections. Inter-laboratory tests in known media, such as this, are essential for achieving that goal. Test samples will be created at the time these phantoms are manufactured so that independent dynamic mechanical testing can be performed on equivalent materials over time. The phantoms will be shipped serially to the sites involved (a subset of those involved in the Phase 1 study) for SWS estimation with various systems and participants. Data analysis will follow that established in the Phase 1 study.

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: This project has two components: **(1)** a comprehensive review of the existing SWE and transient elastography (TE) literature to identify and rank – in order of perceived clinical importance – clinical factors that potentially influence the speed of shear waves within the liver parenchyma. **(2)** A pilot study focused on the effect of liver steatosis and inflammation on shear wave speed. Evaluation of these two factors, particularly steatosis, is also of value for possible inclusion of these critical conditions in future QIBA ultrasound profiles.

Numerical Simulation of Shear Wave Speed Measurements in the Liver: By leveraging freely available software resources (i.e. VMTK [geometry creation], Tetgen [mesh generation], FEBio1 [FEM]), one of our objectives is to develop a freely available shear wave imaging simulation tool. Concurrently, a finite-difference code base will be developed in OpenCL that can be run with less computation overhead. These mechanical simulation tools will be coupled with the freely available acoustic simulation tools, Field II and FOCUS, to simulate acoustic radiation force excitations and ultrasonic displacement tracking. Further development will be focused on streamlining FEA simulations of shear wave propagation in the liver through a simple text file passing mechanism.