

HHSN268201000050C, RECOVERY Quantitative Imaging Biomarkers Alliance (QIBA)

PROGRESS REPORT: AS OF MARCH 2011

This progress report is stated in terms given in the accepted Work Plan. Work tasks 1-10 generally comprise the elements of our roadmap for each biomarker. Section A lists specific experimental groundwork projects that are ongoing and/or that have been allocated NIBIB project funding. Sections B-D give a high-level statement of what has been done in the period since last report and present updated Gantt charts to reflect the progress and any plan adjustments for CT, FDG-PET, and MRI respectively.

NIBIB Tasks 11-19 are associated with the overall program. Some of these comprise ongoing activities that do not lend themselves to scheduling in Gantt chart format, but will be associated with specific events during the contract term. Our initial plan with respect to each numbered task is as follows:

NIBIB Task 11. Stimulate an interest in disseminating and implementing QIBA solutions to assess their feasibility and efficacy more broadly.

- a. *We will schedule two QIBA meetings per year, one in May and the other at the RSNA Annual Meeting in November, with agenda set for this purpose.*

Since last report we held well-attended public and working meetings during the RSNA Annual Meeting, as well as 5 vendor meetings (Siemens, GE, Philips, Toshiba, and smaller suppliers). An additional meeting is scheduled for late May.

- b. *We will schedule educational content in the RSNA Annual Meeting to disseminate information to a wide audience.*

At the RSNA Annual Meeting, our technical committees each prepared and presented a poster associated with our “Quantitative Imaging Reading Room” exhibit. A general updates was also provided in a Special interest Session on Monday, November 29th.

- c. *We also publish a quarterly QIBA Newsletter electronically.*

Our most recent “QIBA Quarterly” was issued in December 2010.

NIBIB Task 12. Encourage adoption, integration and clinical education of validated QIBA solutions by the research and industry community.

- a. *We have begun to schedule company-specific meetings with managers of medical device companies to explain QIBA, and solicit their feedback.*

In addition to the vendor meetings at RSNA Annual Meeting, we have completed on-site visits with CT, NM, and MR business units at GE in Waukesha, WI; with the MR business unit at Philips in Cleveland, OH. (with video conference feed to Best, NL); and the MI business unit at Siemens in Knoxville, TN.

- b. *We will work with the Pharma Imaging Group to get QIBA solutions integrated into pharmaceutical industry drug trials.*

We have placed our first controlled document, a protocol for volumetric image analysis in lung cancer, into Field Test in cooperation with the “extended Pharma Imaging Group” (e-PIG). We also have a monthly status report and discussion with the group.

- c. *We will work with ACRIN, the SNM Clinical Trials Network, and other academic organizations to get QIBA solutions integrated into clinical trials.*

We continue to refine process and to promote the venue of the Uniform Protocols for Imaging in Clinical Trials (UPICT) to discuss details for specific consensus protocols. In this reporting period, intensive work has progressed first to collect protocol elements and then to work towards a consensus protocol for quantitative FDG-PET.

NIBIB Task 13. Develop an initial consensus on quantitative imaging biomarkers qualification by coordinating broadly with various stakeholders, including professional imaging societies, academic centers, and imaging device manufacturers, and drug industry.

- a. *We will use breakout groups at the annual "Imaging Biomarkers Roundtable" to achieve this objective, as well as collective input from the Pharmaceutical Imaging Group, meetings with individual medical device manufacturers, and recommendations from relevant academic workshops.*

We held specific discussions with these groups associated with our September 2010 Imaging Biomarkers Roundtable, with targeted break-out sessions considering neurological diseases and regulatory issues related to contrast agents (in addition to the prior subjects we have raised in that meeting). Additionally, we invited and received reports from the FDA as well as the Critical Path Institute, and also featured a discussion regarding Ultrasound (a modality in which we have not yet started technical committees but which we may at some point choose to establish).

- b. *For consensus related to formal FDA qualification of imaging biomarkers, we will work with the FNHI Biomarkers Consortium and the Critical Path Institute as well. This collaboration will occur by monthly conference calls, as well as collective work on the Briefing Documents and Data Packages to be submitted to the FDA.*

In this reporting period we have concluded and submitted a 100+ page briefing document to FDA for qFDG-PET. We are also nearing conclusion of the corresponding package for volumetric image analysis using CT.

NIBIB Task 14. Organize and manage relationships in a collaborative, multi-disciplinary environment that fosters communication among imaging groups and other medical disciplines involved in the research, approval and use of quantitative imaging biomarkers.

- a. *The QIBA Steering Committee meets once per month by phone and in person twice a year.*

In this reporting period we have increased the number of times we have met in person so as to administer the allocation of NIBIB project funds. In that regard we have completed the first year allocations and set up a project selection process for year 2.

- b. *The Modality Committees meet monthly.*

In this reporting period we focused the modality committees on evaluation of funding requests and the recommendations to steering committee on funding.

- c. *The Technical Committees meet biweekly, with groundwork subgroups meeting as needed, often weekly. All of these QIBA groups are composed of individuals from the named stakeholder groups.*

All of the teams meet at least biweekly and many more frequently.

NIBIB Task 15. Create and implement a process by which standardized and harmonized systems emerge that are sufficient for the development, validation, qualification and use of accurate, repeatable quantitative imaging biomarkers across instruments and settings.

The QIBA Steering Committee, with input from the Technical Committees, has begun to develop such processes. These will be documented in a process manual by the end of year 1 (Sept 30, 2011). We will provide a feedback (public comment) mechanism with a formal update mid-way through year 2 (March 30, 2012).

A preliminary version of the Process Manual has been posted to the QIBA Wiki and different steps of the process are being refined through experience by the various teams. Also in the

reporting period, we created means for sharing of content between protocols and Profiles as well as refined formats and writing methods.

NIBIB Task 16. Clarify and optimize the regulatory pathway by which quantitative imaging biomarkers enter the market.

- a. *We have authored a Special Report that will be published in Radiology during the Spring of Year 1 (2011).*

In this reporting period, two Special Reports have been published in Radiology:

Article "A Collaborative Enterprise for Multi-Stakeholder Participation in the Advancement of Quantitative Imaging" has been published by Radiology. This paper is available online at <http://radiology.rsna.org/cgi/content/abstract/258/3/906>.

Article "Quantitative Imaging Test Approval and Biomarker Qualification: Interrelated but Distinct Activities" has been published by Radiology. This paper is available online at <http://radiology.rsna.org/cgi/content/abstract/radiol.10100800>.

- b. *We have also initiated formal efforts with FDA/CDER to qualify two biomarkers utilizing these ideas as of this year. We expect to meet with the FDA in a collaborative process and then transition to the formal review phase. As these processes are new to both FDA and ourselves, we are not able to indicate a schedule at this time but will update in our periodic reports. Additionally, early in Year 2, we anticipate formal discussions related to the use of data accumulated for qualification to be contributory to CDRH filing and will update as we get closer to that engagement.*

As per the reference to work with the fNIH above, we are presently scheduling a meeting with the FDA Biomarker Qualification Review Team, at the FDA's invitation, for quantitative FDG-PET for late April or early May.

NIBIB Task 17. Establish a process for relating biomarkers to disease areas, setting the clinical context and, based on the clinical context, identifying and prioritizing what biomarkers to pursue.

We will use breakout groups at the annual "Imaging Biomarkers Roundtable" to achieve this objective,

In addition to what has already been noted regarding specific topics and breakouts at the Imaging Biomarker Roundtable, the Steering Committee has developed criteria and a procedure for considering and prioritizing new biomarkers to address.

NIBIB Task 18. Create a collaborative, multidisciplinary infrastructure to foster research, approval and use of quantitative imaging biomarkers, including development and maintenance of a national repository of quantitative imaging biomarker data, representation at a variety of workshops and meetings, and provide project management and staff support for same.

- a. *The QIBA committee structure and leadership constitutes one component of a collaborative, multidisciplinary infrastructure to foster research, approval and use of quantitative imaging biomarkers. A plan for long-term sustainability will be developed over the next year. (See Task 19).*

A panel of experts, chaired by Carolyn Meltzer, MD, PHD, Emory University, has been convened by the RSNA Board of Directors to consider this strategy.

- b. *In partnership with NCRR/NIH, RSNA provides support for a CTSA Imaging Working Group which constitutes another component of a collaborative, multidisciplinary infrastructure to foster research, approval and use of quantitative imaging biomarkers.*

The CTSA Imaging Working Group convenes by telephone every month to facilitate communication and sharing of best practices among funded CTSA sites on issues relevant to imaging in clinical research. On alternate months, the CTSA Steering Committee meets. In-person educational sessions have been planned by CTSA at the SCTS meeting in May and at the in-person ACRIN meeting in September.

- c. *We have created and Ad Hoc Committee on Open Image Archives which will provide in approximately 6 months a report containing recommendations for creating one or more national repositories of quantitative imaging biomarker data.*

This committee has continued to meet and has produced proposals presently being considered by the Steering Committee. The task force's intent is to deliver several 'use cases' that can be used for archive implementation.

- d. *RSNA staff supported by this NIBIB contract will provide project management and staff support for same.*

The staff has successfully transitioned to meet the challenges as well as the opportunities afforded by this contract assignment.

NIBIB Task 19. Explore self-funding models to maintain forward progress of the infrastructure and effort described in task 18 above.

We will create an Ad Hoc Task Group to conduct strategy discussions on this topic during Year 1 and will develop a draft proposal by year end. Based on the nature of that proposal we will lay out actions and a plan for Year 2.

As noted in Task 18a.

A. ONGOING AND NEWLY FUNDED PROJECTS WITHIN MODALITIES

Follows is a listing of projects that contribute to the summary tasks identified in the charts and information in Sections B-D. They are presented here to demonstrate use of the first year project funds in the context of on-going activities.

	Biomarker	Title	Budget request	Submitter
CT	VIA for response assessment in oncology	Evaluation of 1D, 2D and 3D nodule size estimation by radiologists for spherical and non-spherical nodules through CT thoracic phantom imaging	N/A	Nick Petrick, FDA
CT	VIA for response assessment in oncology	Assessing Measurement Variability of Lung Lesions in Patient Data Sets	\$13,185	Michael McNitt-Gray, UCLA
CT	VIA for response assessment in oncology	Inter-scanner/inter-clinic comparison of reader nodule sizing in CT imaging of a phantom	\$35,000	Charles Fenimore, NIST
CT	VIA for response assessment in oncology	Validation of volumetric CT as biomarker for predicting patient survival	\$62,366	Binsheng Zhao, Columbia NY

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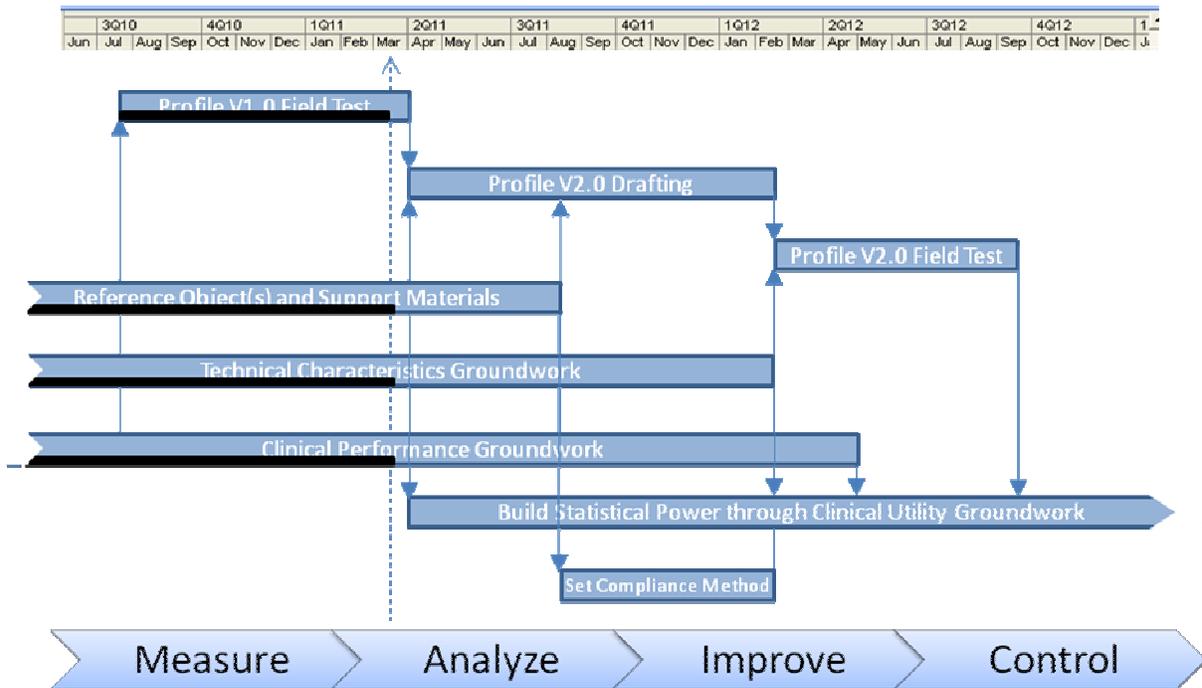
CT	various phenotypic features for various indications	Development of assessment and predictive metrics for quantitative imaging in chest CT	\$40,000	Samuel Richard and Ehsan Samei, Duke University
CT	VIA for response assessment in oncology	Quantifying variability in measurement of pulmonary nodule (solid, part-solid and ground glass) volume, longest diameter and CT attenuation resulting from differences in reconstruction thickness, reconstruction plane, and reconstruction algorithm.	\$42,070	Kavita Garg, David Miller, Ann Scherzinger, University of Colorado, Denver
		Year 1 CT Project Funding	\$192,621	
MR	DCE-MRI for response assessment in oncology	Inter-scanner/inter-clinic comparison of DCE-MRI imaging of a phantom	N/A	Edward Jackson, MDACC
MR	DCE-MRI for response assessment in oncology	DCE-MRI Phantom Fabrication, Data Acquisition and Analysis, and Data Distribution	\$60,347	Edward Jackson, MDACC
MR	DCE-MRI for response assessment in oncology	Software Development for Analysis of QIBA DCE-MRI Phantom Data	\$29,975	Edward Ashton, VirtualScopics
MR	DCE-MRI for response assessment in oncology	Digital Reference Object for DCE-MRI analysis software verification	\$46,210	Daniel Barboriak, Duke University
MRI	fMRI for pre-surgical mapping	Quantitative measures of fMRI reproducibility for pre-surgical planning	\$19,411	Edgar DeYoe, Medical college of Wisconsin
MRI	fMRI for pre-surgical mapping	Development of reproducibility metrics in fMRI	\$26,400	James Voyvodic, Duke University
		Year 1 MR Funding	\$182,343	
NM	Covariates, ROI, Software version tracking, SUV, and QC subcommittees	Derive specifications and requirements for FDG-PET imaging devices in each key area	N/A	Various
NM	FDG-PET/CT for response assessment in oncology	Meta-analysis to analyze the robustness of FDG SUV changes as a response marker, post and during systemic and multimodality therapy, for various types of solid extracerebral tumors.	\$73,000	Otto Hoekstra, University of the Netherlands
NM	FDG-PET/CT for response assessment in oncology	QIBA FDG-PET/CT Digital Reference Object Project	\$68,240	Paul Kinahan, UWashingon
NM	FDG-PET/CT for response assessment in oncology	Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes	\$57,500	Richard Wahl, Johns Hopkins
		Year 1 NM Funding	\$198,740	

B. PROGRESS FOR VOLUMETRIC CT AS OF MARCH 2011

Since our last formal report:

- With respect to volumetric CT:
 - The project “Evaluation of 1D, 2D and 3D nodule size estimation by radiologists for spherical and non-spherical nodules through CT thoracic phantom imaging” has completed and been reported at SPIE 2011.
 - The team has prepared for the collection of feedback on the field test of our initial lung cancer protocol.
 - The team has updated its “Small Pulmonary” nodule Profile.
- The COPD/Asthma committee has characterized various foam inserts and other aspects of phantom design for effective calibration and quality control in lung densitometry studies.
- NIBIB funds have been allocated to six projects, as outlined above in section A.

The following updated Gantt chart reflects this progress and plan adjustments in the period.

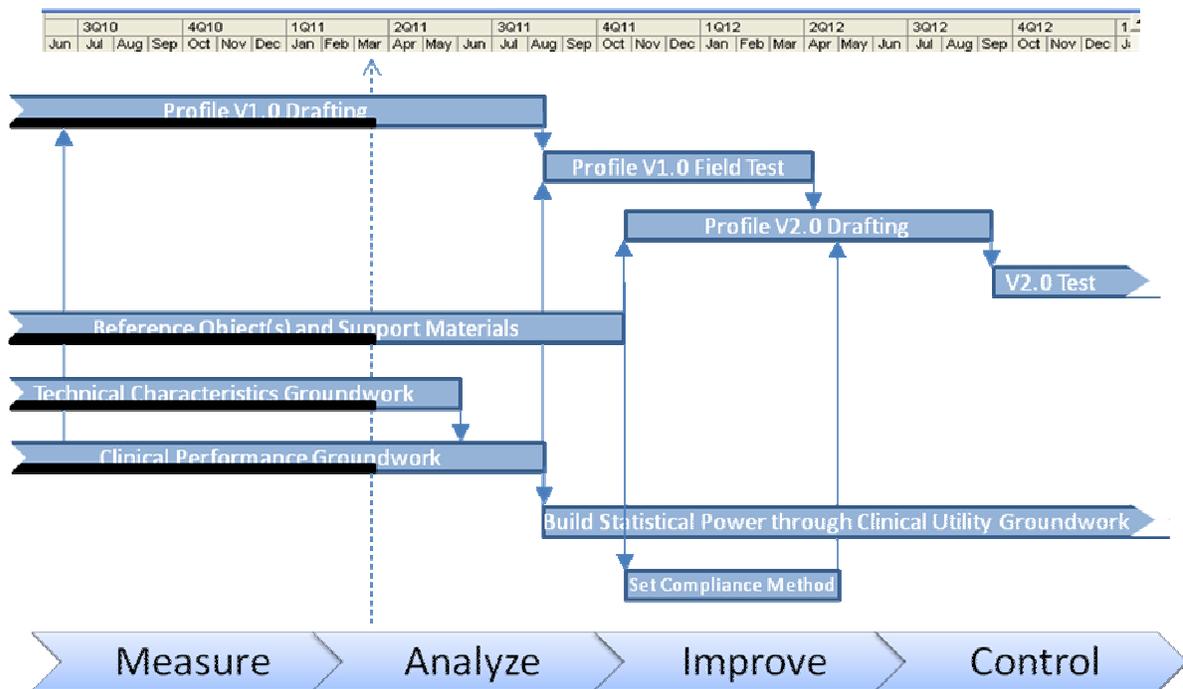


C. WORKPLAN FOR FDG-PET

Since our last formal report:

- The work of the covariates, ROI, Software version tracking, SUV, and QC subcommittees have completed a list of requests that represent requirements to be incorporated into the Profile and have concluded their activities.
- Considerable progress has been made on a consensus protocol for quantitative FDG-PET in collaboration with people from many societies and geographies.
- The team has draft Profile text and is continuing to refine it.
- NIBIB funds have been allocated to three projects to build evidence for the biomarker, as outlined above in section A.

The following updated Gantt chart reflects this progress and plan adjustments in the period.



D. WORKPLAN FOR MRI

Since our last formal report:

- With respect to DCE-MRI:
 - The project inter-clinical and inter-scanner study has completed data acquisition and is presently analyzing the results.
 - Specifications for a new phantom design that incorporates experiences from the inter-clinic study have been documented.
 - The team is nearing completion of its DCE-MRI Profile and will release it for Public Comment soon.
- The fMRI committee has developed provisional core details for a Profile and has defined tasks and approach to characterize reproducibility in the measurements.
- NIBIB funds have been allocated to four projects, as outlined above in section A.

The following updated Gantt chart reflects this progress and plan adjustments in the period.

