

# HHSN268201000050C, RECOVERY Quantitative Imaging Biomarkers Alliance (QIBA)

PROGRESS REPORT: AS OF FEBRUARY 29, 2012

## **EXECUTIVE SUMMARY**

During the first 18 months QIBA has made significant progress toward creating and implementing a process for the development, validation, qualification and use of accurate, repeatable quantitative imaging biomarkers across instruments and settings. The paradigm that has evolved is to create, for each imaging biomarker, documents referred to as the UPICT Protocol and the QIBA Profile. Definitions of these documents can be found on the QIBA wiki at

[http://qibawiki.rsna.org/index.php?title=What\\_Are\\_Profiles\\_and\\_Protocols%3F#Definitions\\_and\\_Descriptions\\_of\\_QIBA\\_Profiles\\_and\\_Protocols](http://qibawiki.rsna.org/index.php?title=What_Are_Profiles_and_Protocols%3F#Definitions_and_Descriptions_of_QIBA_Profiles_and_Protocols). To create these documents, QIBA coordinates broadly with various

stakeholders, including professional imaging societies, academic centers, imaging device manufacturers, the pharmaceutical industry and federal agencies. Profiles have been completed for CT volumetry and DCE-MRI, and are in development for FDG-PET SUV, lung CT densitometry and airway measurements for COPD, and fMRI for pre-surgical mapping. Also during Year 1, in partnership with the FNIB Biomarkers Consortium, we completed and submitted Briefing Documents to the FDA for qualification of quantitative FDG-PET and CT volumetry as imaging biomarkers for drug development. We met with the FDA Biomarker Qualification Review Teams (BQRT) in June 2011 (FDG-PET) and August 2011 (CT volumetry).

To further improve the accuracy and precision of imaging biomarkers, more research is needed regarding sources of variability and the impact of various proposed mitigation strategies. We have solicited, reviewed, approved and implemented 26 projects funded from the NIBIB contract award to address some of these research needs. Status reports on all those projects are given below. QIBA is thus creating a collaborative, multidisciplinary infrastructure to foster research, approval, and use of quantitative imaging biomarkers,

This progress report is stated in terms given in the accepted Work Plan. Work Tasks 11-19 in the SOW are associated with the overall program. Some of these do not lend themselves to scheduling in Gantt chart format, but are associated with specific events during the contract term. A status report on those activities is given in Section A below.

Work tasks 1-10 generally comprise the elements of our roadmap for each biomarker. Section B lists specific experimental groundwork projects that are ongoing and/or have been allocated NIBIB contract project funding. Sections C-E provide 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.

## **A. OVERALL PROGRAM TASKS 11-19 (FOR REPORTING PERIOD OCTOBER 1, 2011 THROUGH FEBRUARY 29, 2012).**

Our initial plan with respect to each numbered task is given in italics, and the status is given in BOLD font:

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.*

**The RSNA Annual Meeting held in November/December 2011 provided opportunities for both formally scheduled as well as informal meetings related to QIBA. Formally scheduled sessions included Special Interest Session - Quantitative Imaging Biomarkers for Clinical Care and Research and a Technical Committees Working Meeting.**

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

**At the 2011 RSNA Annual Meeting, our technical committees each prepared and presented a poster associated with our QIBA Kiosk exhibit. General updates were also provided in a Special Interest Session on Monday, November 28<sup>th</sup> 2011.**

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

**The December 2011 “QIBA Newsletter” included the following articles: How QIBA Will Benefit Medical Device Innovation, by SANDEEP N. GUPTA, PhD; Software Development for Analysis of QIBA DCE-MRI Phantom Data, by EDWARD ASHTON, PhD; a review of RSNA 2011: Quantitative Imaging/Imaging Biomarkers and QIBA Meetings and Activities; and a PubMed Search on How QIBA Will Benefit Medical Device Innovation.**

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.*

**Our technical committees continue to have broad involvement from the supplier community, including medical device as well as software companies.**

**In the technical committees, several projects involve key supplier participation. In FDG-PET and DCE-MRI, synthetic data objects have been created and are being evaluated by a number of companies. In CT Volumetry, an algorithm performance “Challenge” has been organized with the following participants:**

- Median Technologies
- Vital Images, Inc.
- Fraunhofer Mevis
- Siemens
- Moffitt Cancer Center
- Toshiba
- GE Healthcare
- Icon Medical Imaging
- Columbia University
- INTIO, Inc.
- Vital Images, Inc.

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

**During the current reporting period, we worked closely with the Pharma Imaging Group in the evaluation and collection of comments in response to the FDA’s public comment period for “Standards for Clinical Trial Imaging Endpoints.” We solicited and collated comments from the QIBA membership as well as produced a matrix with detailed remarks on paragraphs within the guidance and observations as well as suggestions from the vantage point of our experience with UPICT protocol and QIBA profile authorship.**

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 the process and to promote the venue of the Uniform Protocols for Imaging in Clinical Trials (UPICT) to discuss details for specific consensus protocols. The most active project in this regard during the first contract year is working 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, 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.*

**During the current reporting period we have formalized a process to disseminate program documents, including an inclusive list of professional societies, trade groups, and other organizations. We have begun to use this process to engage stakeholders in the review of our documents through the public comment process.**

**Additionally, we have taken steps to gather and organize interested parties to form an Ultrasound Modality Committee, with several meetings associated with this effort held both in person and by phone. We have also been responsive to the feedback we have heard on our current biomarkers and proposals for new ones. For example, we have compiled and vetted proposals for formation of a DWI-MRI committee that will be organized associated with our DCE-MRI effort.**

- b. *For consensus related to formal FDA qualification of imaging biomarkers, we will work with the FNIH 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.*

**Since the two Biomarker Qualification Review Team (BQRT) meetings last June and August, we have corresponded with the FDA regarding questions they raised, questions we have raised, as well as the process and logistics for updating the briefing documents and reconvening the BQRTs to review them.**

**With respect to the FDG-PET BQRT:**

- Briefing document submitted Spring, 2011
- Meeting with FDA BQRT June 17, 2011
- Key issues in FDA response:
  - Prefer that we be more specific regarding variant of SUV being considered
  - Request systematic consideration of errors for lesion size, instrumentation factors, and calibration
  - Require randomized clinical trial (RCT) designs to establish the degree to which SUV captures treatment effect; the CALGB Lymphoma trial design is of this type, ACRIN 6678 is not an RCT
- Current Status/Plans:
  - A template for the full data package that merges qualification guidance has been composed
  - Study reports for QIBA groundwork may be submitted as they complete
  - Pharma company donations of trial data may provide additional study reports for retrospective re-analysis

- Responses to agency issues are being considered to determine the scale of effort going forward, including whether prospective RCTs will be needed and how limits of generalizability may be determined

**With respect to the CT Volumetry BQRT:**

- Briefing document submitted June, 2011
- Meeting with FDA BQRT Aug. 31, 2011
- Key issues in FDA response:
  - Prefer that we tie to clinical benefit (rather than compare to unidimensional assessments)
  - Prefer that context for use be more specific
  - Prefer that thresholds not be trial dependant
  - Encourage use in early phase trials
- Current Status/Plans:
  - A template for the full data package that merges qualification guidance has been composed
  - Study reports for QIBA 1A (phantom reader study), 1B (minimum detectable change), and 1C (site- and scanner-variability) may be submitted now for review, 3A (inter- and intra-algorithm variability) and 3B (correlation with clinical outcome) may be submitted as they complete
  - Pharma company donations of trial data may provide additional study reports for retrospective re-analysis
  - Responses to agency issues are being considered to determine scale of effort going forward, including whether prospective RCTs will be needed and how limits of generalizability may be determined

**We have also continued our engagement of potential data donors, presently including active discussions with Merck, Astra Zeneca, and Genentech/Roche. An approach whereby we prepare and submit quarterly updates to the Briefing Documents highlighting additional study designs and data sets has been assembled.**

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.*

**We have held monthly teleconferences with the Steering Committee as well as a face-to-face meeting in Chicago on February 1, 2012.**

b. *The Modality Committees convene on an as-needed basis.*

**We have formed a new Modality Committee for Ultrasound in the current reporting period, and the MR Modality Committee has proposed an extension of their work to include DWI-MRI that has been approved by the Steering Committee.**

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 by phone at least biweekly, and many meet 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).*

**During the current reporting period, we reviewed and consolidated process and structure including authoring, review, and testing of documents; imaging biomarker roadmap and approach to groundwork; as well as team structure & governance. We also compiled and reviewed various models for QIBA compliance.**

**Also during the current reporting period, we formed two *ad hoc* workgroups to address key issues associated with our work. One is associated with metrology terminology and statistical approach. This group has three active subgroups working to prepare for an upcoming in-person workshop scheduled for April 3-4, 2012. The other is the joint QIBA/RIC committee, which began in the last reporting period but converged proposals to form an image warehouse with associated capability that is presently being considered by the RSNA board. This latter workgroup utilized input derived from the NIBIB funded project to engage the technical committees on requirements and issues associated with data resources.**

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

**As detailed above under Task 13, we have corresponded with the FDA regarding questions they raised, questions we have raised, as well as the process and logistics for updating the briefing documents and reconvening the BQRTs to review them.**

**Additionally during the current reporting period, we produced a detailed response to the FDA's public comment period for "Standards for Clinical Trial Imaging Endpoints." We solicited and collated comments from the QIBA membership as well as produced a matrix with detailed remarks on paragraphs within the guidance and observations as well as suggestions from the vantage point of our experience with UPICT protocol and QIBA profile authorship.**

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,*

**During the current reporting period, we have formed a new Modality Committee for Ultrasound, and the MR Modality Committee has proposed an extension of their work to include DWI-MRI that has been approved by the Steering Committee.**

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).*

**During the current reporting period and in response to a panel of experts convened by the RSNA Board of Directors and chaired by Carolyn Meltzer, MD, Emory University, we have taken the following steps: we have reorganized the UPICT effort to now be part of QIBA, and we have formalized a leadership succession planning process consistent with RSNA's approach to other sustained committees. This process includes both formal approval of leaders as well as defined terms of service.**

*b. In partnership with NCCR/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.*

**Leadership of and responsibility for the CTSA Imaging Working Group has been transferred to the RSNA Research Development Committee (RDC), in part because of the NIH reorganization involving NCCR and resulting uncertainties around the CTSA program. The RDC has created a Vice Chairs of Radiology committee, and that committee has created three sub-groups that are now addressing the issues initiated within the CTSA IWG.**

*c. We have created an 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.*

**The *ad hoc* Open Image Archives (OIA) Committee of QIBA was formed to assess what could be done to improve the creation and sustained growth of imaging archives. These efforts have transitioned to a committee of combined QIBA, OIA and Radiology Informatics Committee (RIC) members which was formed to provide a platform of collaboration, to optimize synergy between overlapping areas of expertise and interests, and, in particular, to support and augment the OIA activities by drafting a plan for potential RSNA involvement for imaging data warehouses going forward.**

**Four classes of QIBA use cases were defined: A. Comparative Evaluation of Imaging Biomarker Performance versus Gold Standard; B. Public Resource Shared Data (e.g., Image Processing Algorithm Development); C. FDA Approval of Clearance of Imaging Tests; and D. Pharma Clinical Trials with Imaging Biomarkers as Endpoints; for two quantitative imaging biomarker projects: 1) CT volumetric image analysis for management of patients with lung cancer, and 2) quantification of tumor metabolism using FDG-PET standardized uptake value (SUV) image analysis.**

**Imaging data warehouse needs for each of the QIBA Technical Committee Working Groups (DCE-MRI, FDG-PET, Volumetric-CT, fMRI, and COPD-Asthma) were summarized and common features noted. These included the requirement to accommodate different image and non-image data formats (including, in addition to DICOM image files, a variety of other file formats such as XML, TIFF, NiFTI, etc.) and a wide variety of relevant clinical metadata. In addition, the following needs were identified: data input and search and query-retrieve capabilities; image de-identification, data security and user authentication with group sharing; and data output statistics and analytics functions, though not necessarily image display applications.**

Existing tools and databases, including The Cancer Imaging Archive (TCIA), the National Biomedical Image Archive (NBIA), Laboratory of Neuroimaging (LONI), eXtensible Neuroimaging Archive Toolkit (XNAT), and MIDAS, were examined, and current limitations detailed. Of concern is the lack of and/or need for a "trusted third party", the need to promote a culture of sharing perhaps with a reward system or participation, and a business model for long-term sustainability. Additional limitations of existing image data archives include ease-of-use regarding tool downloads, data uploading, tool configurability and functional enhancements. The need for front-end image and metadata collection tools, security control, advanced search, and back-end data analytics components was also noted.

A way forward is to perform a proof-of-concept implementation using projects from each of the QIBA work groups demonstrable at the RSNA 2012 Annual Meeting, by beginning with one existing image data archive with the most flexible, modular architecture deemed to be MIDAS. Next steps would be to enhance and/or create an easy-to-use input portal as well as a back-end analytics portal, with the aim of augmenting the architecture to be generalizable to other data archives. The benefits of having the RSNA as convener of the imaging data warehouse are manifold. Direction is needed from the RIC regarding development, implementation and service models (e.g., open-source by committee, industry development or RSNA in-house development similar to MIRC activities). In addition, funding will be sought to support ongoing and future QIBA-RIC imaging data warehouse efforts.

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

**Staff has successfully met 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.**

**B. ONGOING AND NEWLY FUNDED PROJECTS (FULL 18 MONTH SUMMARY)**

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

**CT, round 1:**

Biomarker	Title	Amount Awarded	Submitter	TimeLine (contract)	Project Description (Abstract)
VolCT	Inter-scanner/Inter-clinic Comparison of Reader Nodule Sizing in CT Imaging of a Phantom	\$14,000	Michael McNitt-Gray, PhD (UCLA)	04/01/2011 - 03/31/2012	Project Description Inter-scanner/inter-clinic comparison of reader nodule sizing in CT imaging of a phantom.
VolCT	Inter-scanner/Inter-clinic Comparison of Reader Nodule Sizing in CT Imaging of a Phantom	\$11,000	David Clunie, MBBS (CoreLab Partners)	04/01/2011 - 03/31/2012	Project Description Inter-scanner/inter-clinic comparison of reader nodule sizing in CT imaging of a phantom (reader mark-up services).
VolCT	Assessing Measurement Variability of Lung Lesions in Patient Data Sets	\$13,185	Michael McNitt-Gray, PhD (UCLA)	04/01/2011 - 03/31/2012	Project Description The purpose of this project is to perform the statistical analysis of data collected under QIBA Volumetric CT committee's 1B experiment, which is investigating the minimum detectable
VolCT	Validation of Volumetric CT as a Biomarker for Predicting Patient Survival	\$62,495	Binsheng Zhao, DSc (Columbia Univ)	04/01/2011 - 09/29/2012	Project Description Unidimensional measurements have become a de-facto standard for assessing a patient's response to therapy. In essence, the RECIST measurement is a "surrogate" for tumor burden and change in this metric is used to guide drug discovery. We and other groups have demonstrated that the unidimensional measurement and change in the unidimensional measurement do not always correlate with change in tumor burden. The actual change in tumor burden is better assessed by change in tumor volumes as measured on CT. We plan to retrospectively analyze tumor burden change in patients enrolled on an already completed large, multicenter Phase II/III clinical trial in metastatic colorectal cancer. We are in an excellent position to validate CT volumetric response assessment technique using our computer algorithms and the clinical data in this trial. 451 patients have been enrolled in this trial and have measurable target lesions in the liver as well as in the lungs and lymph nodes. Each patient underwent an average of 5 CT scans (baseline and follow-ups at every 6-week after the treatment and every 3-month starting 49 months until disease progressed or patient died). The trial also collected a number of tissue biomarkers (e.g., markers in the IGF-1R or EGFR signaling pathway) before and at 6-week after the treatment and tumor genotype from
VolCT	Development of Assessment and Predictive Metrics for Quantitative Imaging in Chest CT	\$50,000	Ehsan Samei, PhD (Duke)	04/01/2011 - 09/29/2012	Project Description: Previous work in our laboratory has developed a framework for predicting quantitative imaging performance from basic system performance measurements. <sup>1</sup> These figure of merits (FOM) included metrics that characterize the resolution (modulation transfer function, MTF) and noise (noise power spectrum, NPS) of the image. It was shown that the precision with which medical images can be used to estimate volume of lesions can be predicted from these simpler FOM. By extending this framework to CT, we expect to be able to evaluate how well clinical CT systems perform various quantitative imaging tasks based on measurements of system FOMs (i.e., noise, contrast, and spatial resolution) via conventional QA phantoms. The goal of this project is to utilize these models in the evaluation of existing phantoms in the characterization of quantitative performance of CT and further develop a calibration procedure to assess compliance of quantitative imaging technique in volumetric CT. As part of this project, we anticipate the collaboration with existing QIBA efforts (1a, 1b, and 1c).
VolCT	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, MD (U Colorado)	04/01/2011 - 03/31/2012	Recently released initial results of the National Lung Screening Trial (NLST) show mortality reduction by 20% in the CT arm compared with CXR. If screening becomes widely adopted in those at high risk, follow-up investigation of positive scans will impose a major burden on the health care system. In patients with positive scans, a risk stratification strategy or quantitative analysis of lung nodules could reduce this burden by reducing the rate of follow-up in those who are determined to be at lower risk. Quantitative CT analysis for solid nodules has been attempted previously, however there is no significant data available for subsolid nodules.
<b>TOTAL CT FUNDING AWARDED</b>		<b>\$192,750</b>			



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CT, round 2:

Biomarker	Title	Budget request	Submitter	TimeLine (contract)	Project Description (Abstract)
VolCT	Validation of Volumetric CT as a Biomarker for Predicting Patient Survival (Carry-over from Round-1)	\$62,495	Binsheng Zhao, DSc (Columbia Univ)	04/01/2011 - 09/29/2012	
VolCT	Development of Assessment and Predictive Metrics for Quantitative Imaging in Chest CT (Carry-over from Round -1)	\$25,000	Ehsan Samei, PhD (Duke)	04/01/2011 - 09/29/2012	
VolCT	Extension of Assessing Measurement Variability of Lung Lesions in Patient Data Sets: Variability Under Clinical Workflow Conditions	\$14,110	Michael McNitt-Gray, PhD (UCLA)	08/01/2011 - 07/31/2012	<p>Project Description</p> <p>The purpose of this project is to extend the data collection and statistical analysis of the QIBA Volumetric CT committee's 1B experiment, which is investigating the minimum detectable change in lesion size from patient datasets imaged on CT. That project used: (a) "Coffee Break" CT image datasets from 32 NSCLC patients who were imaged twice over a short (15 minute) interval on the same scanner using thin (1.25 mm) slices; (b) one lesion was identified for each patient, (c) Image data was marked up by five radiologists at RadPharm (now CoreLabs); (d) each reader marked the lesions on each of the repeat scans to obtain measures of volume, single longest diameter and bi-dimensional diameters. This data was previously collected and initial analyses have been performed.</p> <p>In that previous project, each reader performed the image markup as an independent reading, with no access to the results or images of their markup of any previous session. This was done because the only data used in that study were limited to "Coffee Break" experiment cases. If readers were allowed to both: (a) know that these were cases with no change and (b) see their markings on one scan while making markings on the second scan, then those results would be considered very biased as readers would know what the answer should be (they would inherently know that the markings should match and that change should be zero). Using that independent reading paradigm, the initial results indicated that there were significant amounts of variation in measurement.</p>
VolCT	Extension of Assessing Measurement Variability of Lung Lesions in Patient Data Sets: Variability Under Clinical Workflow Conditions (reader mark-up)	\$13,125	David Clunie, MBBS (CoreLab Partners)	08/01/2011 - 07/31/2012	<p>Project Description</p> <p>The purpose of this project is to extend the data collection and statistical analysis of the QIBA Volumetric CT committee's 1B experiment, which is investigating the minimum detectable change in lesion size from patient datasets imaged on CT. That project used: (a) "Coffee Break" CT image datasets from 32 NSCLC patients who were imaged twice over a short (15 minute) interval on the same scanner using thin (1.25 mm) slices; (b) one lesion was identified for each patient, (c) Image data was marked up by five radiologists at RadPharm (now CoreLabs); (d) each reader marked the lesions on each of the repeat scans to obtain measures of volume, single longest diameter and bi-dimensional diameters. This data was previously collected and initial analyses have been performed.</p> <p>In that previous project, each reader performed the image markup as an independent reading, with no access to the results or images of their markup of any previous session. This was done because the only data used in that study were limited to "Coffee Break" experiment cases. If readers were allowed to both: (a) know that these were cases with no change and (b) see their markings on one scan while making markings on the second scan, then those results would be considered very biased as readers would know what the answer should be (they would inherently know that the markings should match and that change should be zero). Using that independent reading paradigm, the initial results indicated that there were significant amounts of variation in measurement.</p>
VolCT	Comparative Study of Algorithms for the Measurement of the Volume of Lung Lesions: Assessing the Effects of Software Algorithms on Measurement Variability	\$35,500	Michael McNitt-Gray, PhD (UCLA)	08/01/2011 - 07/31/2012	<p>Project Description</p> <p>QIBA 1A study investigated the bias and variance using CT images of an anthropomorphic phantom and obtained measurements using only one algorithm. However, image processing algorithms have been developed in many organized activities from a number of groups using many different approaches with varying amounts of human interaction and different levels of segmentation success. This study proposes to investigate the effects of different algorithms in bias and variance using reference data sets of both phantoms and patients; in addition, this study proposes to investigate the performance of different methods and degree of automation in the algorithm.</p> <p>This study can increase knowledge for the QIBA Profile and to provide a context in which multiple parties have incentives to participate. (1) manual analysis in which sites perform required measurement task and manually supply data back to QIBA 3A project personnel and (2) scripted analysis that would apply to multiple data sets to invest in a re-usable infrastructure for large-scale algorithm testing</p> <p>This project extends other QIBA Volumetric CT committee experiments investigating measurement variability by specifically looking at: (a) the effects of measurement variability due to the measurement-algorithms (b) the effects of the degree of automation and by algorithm method, assessing measurement variability between algorithms (c) apply to multiple data sets by creating a re-usable infrastructure for large-scale algorithm testing. This will allow us to understand variability across algorithms in large datasets.</p> <p>This project proposes three specific bases to assess the overall variability due to algorithms and by the degree of automation and by the algorithm method:</p>
COPD	Impact of Dose Saving Protocols on Quantitative CT Biomarkers of COPD and Asthma	\$49,754	Sean Fain, PhD (Univ of Wisconsin)	08/01/2011 - 07/31/2012	<p>Project Description</p> <p>Longitudinal clinical research studies that depend on quantitative measures of CT (qCT) number and structures depend on stable and reproducible image fidelity in often young, radiation sensitive, populations. Quantitative image measures of CT number and structural dimensions in ongoing lung studies, such as parenchymal density and airway wall thickness, have been shown to vary substantially according to the CT scanner make and model due to factors that differentially affect image noise, artifacts, and other image quality parameters, such as low contrast detectability and MTF. Imaging at the lowest possible dose, while maintaining diagnostic accuracy, is important to reduce the patient's risks from radiation. While image noise is normally adversely affected by adjusting scan parameters to decrease radiation dose, there now exist methods that allow decreased dose with no significant effect on image quality. However, there are significant questions as to effects of these techniques on qCT measures. These dose reduction techniques include automatic exposure control (AEC) systems, such as Smart mA on the GE systems, which produce mA modulation in the Z and angular directions, and iterative reconstruction (IR) techniques such as ASIR (GE).</p> <p>Additionally, the effects of simple dose reduction, with or without the use of the AEC and IR, on the qCT</p>
<b>TOTAL CT FUNDING AWARDED</b>		<b>\$199,984</b>			

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### MR, round 1:

Biomarker	Title	Amount Awarded	Submitter	TimeLine (contract)	Project Description (Abstract)
DCE-MRI	DCE-MRI Phantom Fabrication, Data Acquisition and Analysis, and Data Distribution	\$60,347	Edward Jackson, PhD (MD Anderson CC)	04/01/2011 - 03/31/2012	<p><b>Project Description</b> The DCE-MRI Technical Committee has developed a prototype DCE-MRI phantom that is proposed for use in DCE-MRI clinical trial site qualification as well as ongoing quality control processes. When it was initially formed, the DCE-MRI Technical Committee identified the need for such a robust DCE-MRI contrast response phantom as a top priority. Since that time, the committee developed a "generic" DCE-MRI acquisition protocol, developed a protocol for quality control / initial site qualification, each process a key component of the first DCE-MRI Profile, and has evaluated the use of a modified ADNI MagPhan phantom and, upon initial multicenter testing of two copies of this phantom design, found the phantom to be insufficiently robust to shipping and handling, too limited in its evaluation of R1 (longitudinal relaxation rate) contrast response assessment, and not time efficient in routine application. A new phantom design was proposed to address each identified weakness of the modified ADNI MagPhan phantom for DCE-MRI contrast response characterization, relaxometry, and quality control.</p>
DCE-MRI	Software Development for Analysis of QIBA DCE-MRI Phantom Data	\$29,975	Edward Ashton, PhD (VirtualScopics)	04/01/2011 - 03/31/2012	<p><b>Project Description</b> This project will address the development of a distributable software package to allow the analysis of QIBA DCE-MRI phantom data.</p>
DCE-MRI	Digital Reference Object for DCE-MRI Analysis Software Verification	\$57,763	Daniel Barboriak, MD (Duke)	04/01/2011 - 09/29/2012	<p><b>Project Description</b> One barrier to implementation of dynamic contrast-enhanced (DCE) MRI in multi-center clinical trials is that available software packages used to analyze the images may differ in their approach and implementation, causing variability in the extracted quantitative parameters. Because no standardized image analysis method is available, results obtained using DCE-MRI in different laboratories are difficult to compare, and the rational choice of one software implementation over any other for use in a multi-center trial is exceedingly challenging. As a first step in providing a standardized analysis process, it is necessary to ensure that software implementations are extracting parameters accurately. In this project, we propose to create digital reference objects (DROs) using synthetic data in order to help verify software packages for use in DCE-MRI analysis, and to initiate the development of verification protocols as a method to qualify software packages for use in clinical trials of DCE-MRI.</p>
fMRI	Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning	\$19,411	Edgar DeYoe, PhD (Med College of Wisconsin)	04/01/2011 - 03/31/2012	<p><b>Project Description</b> This subproject will provide quantitative measures of reproducibility for a unique set of vision- and motor-related fMRI brain maps using a set of data manipulations, computations, and the AMPLE normalization algorithm that will be standardized in coordination with subproject 1. In addition, this subproject will provide a unique analysis of the reproducibility of fMRI functional specificity and will compare reproducibility measures over different time durations both within and across subjects. The results of this study will help address NIBIB Tasks 1, 3, 6, 7, and 9 in the context of fMRI as a biomarker of brain function/dysfunction.</p>
fMRI	Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning-Development of Reproducibility Metrics	\$33,423	James Voyvodic, PhD (Duke)	04/01/2011 - 07/31/2012	<p><b>Project Description</b> This sub-project will develop metrics for quantifying reproducibility within and across fMRI scans, and it will apply those metrics to existing data sets to assess the reproducibility of fMRI results both within and across scanning sessions. The metrics to be developed will be based on using the AMPLE normalization algorithm (Voyvodic, 2006) to assess reproducibility and will include both voxel-wise and ROI-based measures of the consistency of fMRI activation maps over time. The results of this study will help address NIBIB Tasks 1, 3, 6, 7, and 9. Demonstration and quantification of reproducibility is an essential step in the development of the QIBA Profile for fMRI.</p>
<b>TOTAL MR FUNDING AWARDED</b>		<b>\$200,919</b>			

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**MR, round 2:**

DCE-MRI	Test-Retest Evaluation of Repeatability of DCE-MRI and DWI in Human Subjects	\$175,000	Mark Rosen, MD, PhD (ACR/U Penn)	08/01/2011 - 07/31/2012	<p><b>Project Description</b>                      In order to evaluate the profile claims for the repeatability of tumor DCE-MRI metrics, it is ultimately necessary to evaluate the performance of the QIBA DCE-MRI protocol in human subjects with tumors. This process would include not only implementing the imaging protocol, but also introducing site imaging personnel to proper procedures for magnet qualification, the selection of tumor-bearing human subjects, and the implementation of the proper DCE-MRI imaging exam to these subjects. Through discussions within the DCE-MRI subcommittee, it has been decided to seek a partnership with the American College of Radiology Imaging Network (ACRIN) to facilitate the development and ultimately the implementation of the test-retest DCE-MRI human study. The overall project, including the completion of the protocol, selection of participating sites, central and site regulatory approval, and implementation is expected to last two years.</p>
fMRI	Validation of Breath Hold Task for Assessment of Cerebrovascular Responsiveness and Calibration of Language Activation Maps to Optimize Reproducibility	\$29,376	Jay Pillai, MD (Johns Hopkins MC)	08/01/2011 - 07/31/2012	<p><b>Project Description</b>                      Assessment of the integrity of cerebral vascular responsiveness (CVR) is a critical problem in clinical applications of fMRI brain mapping, and must be addressed in any attempt to quantitate fMRI results in patients. Neurovascular uncoupling (NVU) associated with brain tumors and other brain diseases may result in regional variations in CVR that affect the ability to generate a BOLD signal and thereby reliably and reproducibly localize eloquent cortex during presurgical mapping. Multiple studies have demonstrated that a breath-hold (BH) hypercapnia task is a reliable tool for assessing CVR and normalizing BOLD response among different subjects, different brain regions and various features of the scanning environment. In this project we plan to 1) validate use of a BH task for mapping of brain CVR and 2) use such maps to calibrate language task-based BOLD activation maps in order to both reduce intersubject variability and increase intrasubject reproducibility across scan sessions.                      For the first objective, we will compare BH CVR maps with T2* DSC MR perfusion imaging maps using quantitative region of interest analysis to assess concordance of regions of decreased CVR with regions of abnormal perfusion in a cohort of 10 brain tumor patients. For the second objective, we plan to apply the</p>
<b>TOTAL MR FUNDING AWARDED</b>		<b>\$204,376</b>			

**NM, round 1:**

FDG-PET/CT	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, MD (VU Med Ctr, NL)	04/01/2011 - 03/31/2012	<p><b>Project Description</b>                      Meta-analysis on the association between FDG uptake changes and histopathological response.                      Validated qualitative and quantitative statistical model of quantitative FDG PET to predict response of neoadjuvant therapy in solid tumors.</p>
FDG-PET/CT	QIBA FDG-PET/CT Digital Reference Object Project	\$68,240	Paul Kinahan, PhD (U Washington)	04/01/2011 - 03/31/2012	<p><b>Project Description</b>                      Construct a common reference DICOM PET/CT test image (Digital Reference Object or DRO) as if generated by each vendor's PET/CT scanner. This will then be read on PET/CT display stations to check SUV computation fidelity and region of interest (ROI) analysis performance. This is motivated by the vendor-specific variations in the standardized uptake value (SUV) calculations. It is well known that variations in the implementation of DICOM standards produce substantial quantitative differences in SUVs for the same image on different display stations. In addition, the behavior of ROI analysis tools, (e.g., due to image interpolation) is rarely, if ever, quantitatively understood.</p>
FDG-PET/CT	Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes	\$57,500	Richard Wahl, MD (Johns Hopkins MC)	04/01/2011 - 03/31/2012	<p><b>Project Description</b>                      The insulin-like growth factor (IGF) pathway plays an important role in a variety of physiological processes in humans and animals, including normal growth and development. Additionally, this pathway has been shown to play an important role in the development of conditions like cancer. IGF signaling has been proposed to play a major role in the very aggressive nature of certain sarcomas, like Ewing's sarcoma family of tumors (ESFT) and synovial sarcomas                      The SARC 11 trial prospectively evaluated the utility of an anti Insulin like Growth Factor Human Monoclonal Antibody (R1507) as monotherapy for Sarcomas of several types (Recurrent or Refractory Ewing's Sarcoma, Osteosarcoma, Synovial Sarcoma, Rhabdomyosarcoma and Other Sarcomas). All patients received R1507 9mg/kg i.v. This single arm study evaluated the efficacy and safety of R1507 in patients with recurrent or refractory sarcoma. Clinical efficacy of the trials was judged by: Objective response rate [ Time Frame: Week 24, and every 12 weeks thereafter ], Progression-free survival in patients with Ewing's sarcoma [ Time Frame: Week 18 ], Duration of response, PFS, and overall survival.                      In this multicenter study, a baseline PET scan was obtained as well as a PET scan at approximately 9 days post therapy initiation. A follow up scan at 12-18 weeks was obtained in those remaining on study. A total of 311 patients entered the study. Importantly, the PET was not used to alter the therapy. Thus, the PET data can be used to determine prognostic ability. Accrual to the study is now complete and the full PET data set have been collected and are available in DICOM form for analysis. Details of the SARC 11 trial and the rationale for anti IGF antibody therapy are detailed at ClinicalTrials.gov and the SARC website.</p>
<b>TOTAL NM FUNDS AWARDED</b>		<b>\$198,740</b>			

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### NM, round 2:

Biomarker	Title	Budget request	Submitter	TimeLine (contract)	Project Description (Abstract)
FDG-PET/CT	Personnel Support for FDG-PET Profile Completion	\$16,000	Eric Perlman, MD (Perlman Advisory Group)	10/01/2011 - 12/31/2011	Project Description This is a proposal for expert support as a 'Profile Writer' to convert the considerable amount of material accumulated by the FDG-PET TC into a QIBA Profile.
FDG-PET/CT	Evaluation of the Variability in Determination of Quantitative PET Parameters of Treatment Response across Performance Sites and Readers	\$100,000	Richard Wahl, MD (Johns Hopkins MC)	10/01/2011 - 09/29/2012	Project Description There is very limited data on the performance of varying readers and quantitative imaging workstations in determining cancer treatment response using FDG PET/CT. We propose a study design using well-defined anonymized pre-treatment and post-treatment FDG PET scans of cancer patients as an analysis set. All
FDG-PET/CT	PERCIST Validation	\$50,000	Otto Hoekstra, MD (VU Med Ctr, NL)	04/01/2012 - 09/29/2012	Project Description Validate PERCIST metrics using peer-reviewed patient cohorts.
FDG-PET/CT	Evaluation of FDG-PET SUV Covariates, Metrics, and Response Criteria	\$34,000	Jeffrey Yap, PhD (Dana-Farber Cancer Institute)	02/01/2012 - 07/31/2012	Project Description We have developed a large database of more than 25,000 PET oncology studies, which includes critical acquisition parameters, patient information, and DICOM CT and PET images. Many of these studies are from multi-center trials that included PET scanner qualification, phantom imaging, central review and PET SUV analysis, and collection of clinical outcome data. We propose to perform a retrospective meta-analysis to compare different PET metrics, response assessment criteria (EORTC, PERCIST), PET SUV covariates (FDG dose, glucose, fasting time, patient size, etc.), and clinical outcome. A small component of this activity has already been performed in a subset of data comparing the impact of metabolic response assessment using SUV <sub>max</sub> vs. SUV <sub>mean</sub> (Figure 1) and SUV patient size normalization using lean body mass vs. body weight (Figure 2). The requested resources that are needed to complete this work include the compilation of images, meta-data, and clinical trial outcome measures from a research miniPACS archive, multiple clinical trial MS Access databases, a clinical PET database, and various sources of clinical trials results such as Excel spreadsheets. In addition to the existing results, additional
<b>TOTAL NM FUNDING AWARDED</b>		<b>\$200,000</b>			

### Cross-modality:

Biomarker	Title	Amount Awarded	Submitter	TimeLine (contract)	Project Description (Abstract)
Cross Modality	Groundwork for QIBA Image Reference Database	\$10,250	Gudrun Zahlmann, PhD (Roche)	04/01/2011 - 03/31/2012	Project Description QIBA profiles of all technical committees describe what the imaging process for a certain quantitative imaging biomarker should look like in order to fulfill the profile claims. The claims state how accurate and reliable the respective quantitative imaging biomarker can be expected if the profile is followed. The so-called bull's-eye principle is used for describing ideal, target and acceptable quality. All teams deal with phantom imaging to assess the scanner quality. In addition clinical images are captured and analyzed in order to define the claims. It would be beneficial to support the QIBA profiles with a repository of phantom and clinical images illustrating the QIBA understanding of ideal, target and acceptable quality in real life image examples.
Cross Modality	Groundwork for QIBA Image Reference Database	\$16,000	Rick Avila, MS (Kitware)	04/01/2011 - 03/31/2012	Project Description QIBA profiles of all technical committees describe what the imaging process for a certain quantitative imaging biomarker should look like in order to fulfill the profile claims. The claims state how accurate and reliable the respective quantitative imaging biomarker can be expected if the profile is followed. The so-called bull's-eye principle is used for describing ideal, target and acceptable quality. All teams deal with phantom imaging to assess the scanner quality. In addition clinical images are captured and analyzed in order to define the claims. It would be beneficial to support the QIBA profiles with a repository of phantom and clinical images illustrating the QIBA understanding of ideal, target and acceptable quality in real life image examples.
<b>TOTAL CROSS FUNDS AWARDED</b>		<b>\$26,250</b>			

## C. PROGRESS FOR QUANTITATIVE CT (CURRENT SNAPSHOT AS OF FEBRUARY 2012)

Snapshot at this time:

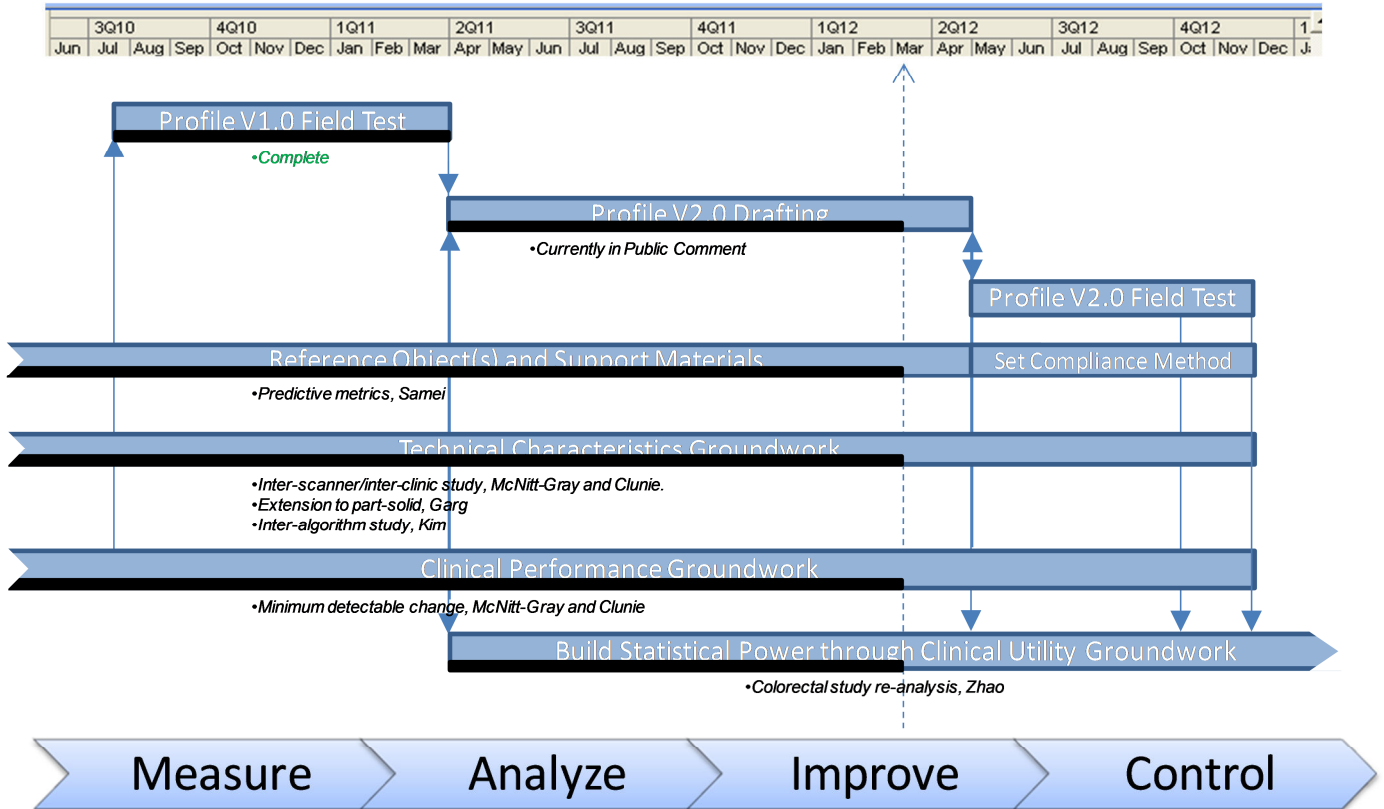
- With respect to CT volumetry:
  - Experimental groundwork:
    - **Inter-scanner/Inter-clinic Comparison of Reader Nodule Sizing in CT Imaging of a Phantom** (Fenimore): All data has been acquired, reads are done, and currently documenting results.
    - **Validation of Volumetric CT as a Biomarker for Predicting Patient Survival** (Zhao): Completed preparation work for retrospective re-analysis of clinical study donated by

pharma including a research agreement with donor, IRB waiver, consensus reading, subset image data selection for the variability study, etc. Submitted an abstract to ASCO meeting in early Feb 2012. The abstract described the variability study performed between Sept 2011 - Feb 2012.

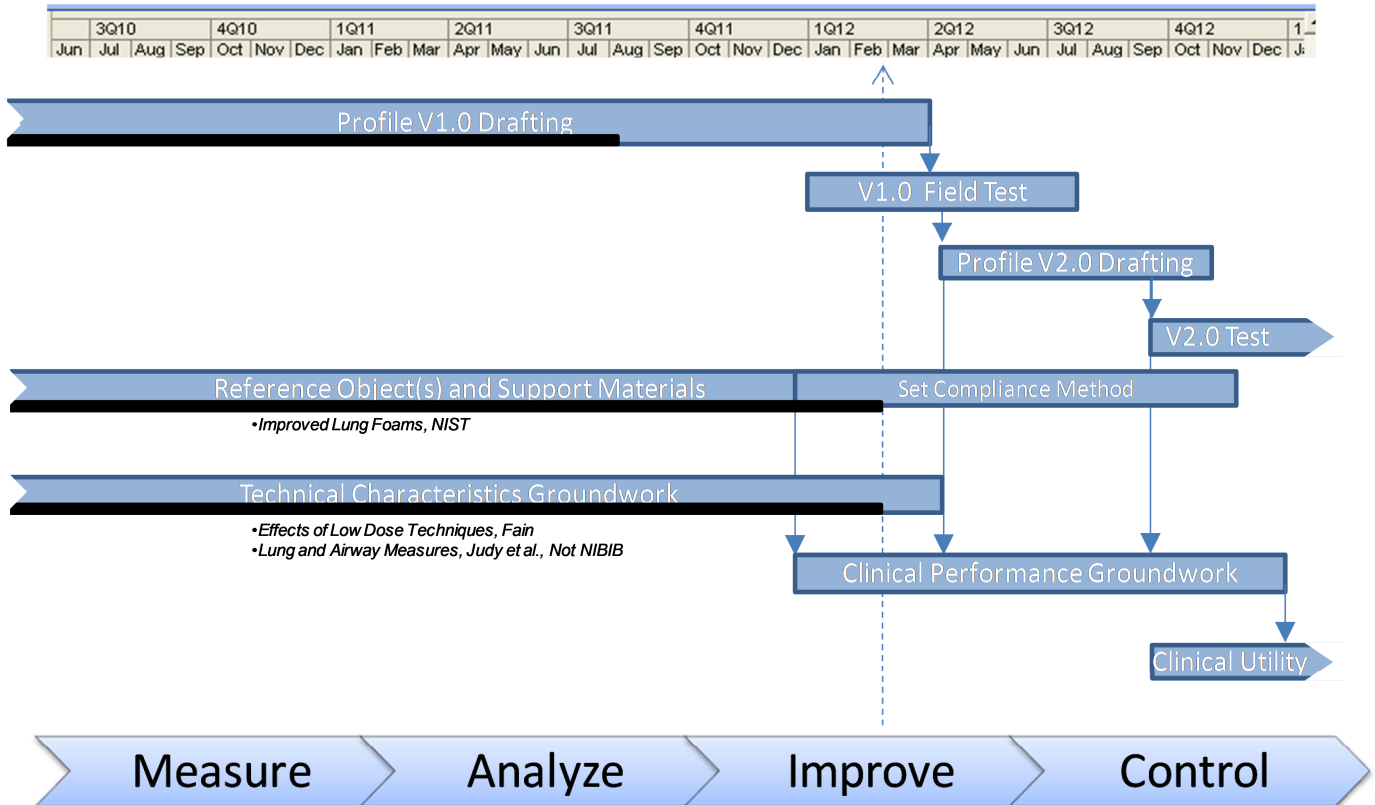
- **Development of Assessment and Predictive Metrics for Quantitative Imaging in Chest CT** (Samei): Thus far the project has achieved the development of a robust modeling framework to predict volumetric performance of a CT scanner from its basic performance characteristics of 2D resolution and noise. Methods have also been developed to measure those characteristics using a newly-designed phantom that accounts for the influence of patient size, mA modulation, and feature contrast. Ongoing work includes extension of the model to 3D, new task and volumetric operators, and the design of standard methods to ascertain quantitative conformance.
- **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** (Garg): Phantom nodules have been ordered and will arrive early April; have imaged some solid nodules and plan to start measurements in coming days, once the INTIO software is installed; INTIO is tuning up their algorithm for the part-solid nodules using clinical cases provided by our team; and have reviewed the statistical analysis plan.
- **Assessing Measurement Variability of Lung Lesions in Patient Data Sets: Variability Under Clinical Workflow Conditions** (McNitt-Gray and Clunie): Have determined reader study design for the extension, and presented poster at RSNA for first phase results.
- **Comparative Study of Algorithms for the Measurement of the Volume of Lung Lesions** (statistical analysis Kim): Assessing the Effects of Software Algorithms on Measurement Variability: pilot study results for 12 participating groups have been collected and statistical analysis is underway to power the pivotal study.
- Profiling:
  - The team is presently converging response to comments received during a 90-day public comment period for revision 2 of the Profile and Protocol.
  - The team expects to return to its “Small Pulmonary” nodule Profile for neoadjuvant clinical trials in the next period.
- 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.
  - **Impact of Dose Saving Protocols on Quantitative CT Biomarkers of COPD and Asthma** (Fain): Using the COPD Lung phantom the team has produced scans under conditions of varying the pitch, the mA, the scan FOV, and the beam collimation, and have reconstructed these scans using various reconstruction algorithms that do not use edge enhancement and have performed the reconstructions with and without GE’s iterative reconstruction algorithm, ASIR. With the mA variations/ reductions and the application of ASIR we are investigating the usefulness of low dose techniques for our protocols. We have measured effects of changing these scan and reconstruction parameters on the CT numbers of water, lung and air in the phantom, and will be looking at the effects on airway measurements.

- First draft Profile.
- NIBIB funds have been allocated to one project as outlined above in section B.

The following updated Gantt chart reflects the CT volumetry Technical Committee progress and plan adjustments through the reporting period:



The following updated Gantt chart reflects the COPD/Asthma Technical Committee progress and plan adjustments through the reporting period:



#### D. PROGRESS FOR QUANTITATIVE FDG-PET (CURRENT SNAPSHOT AS OF FEBRUARY 2012)

Snapshot at this time:

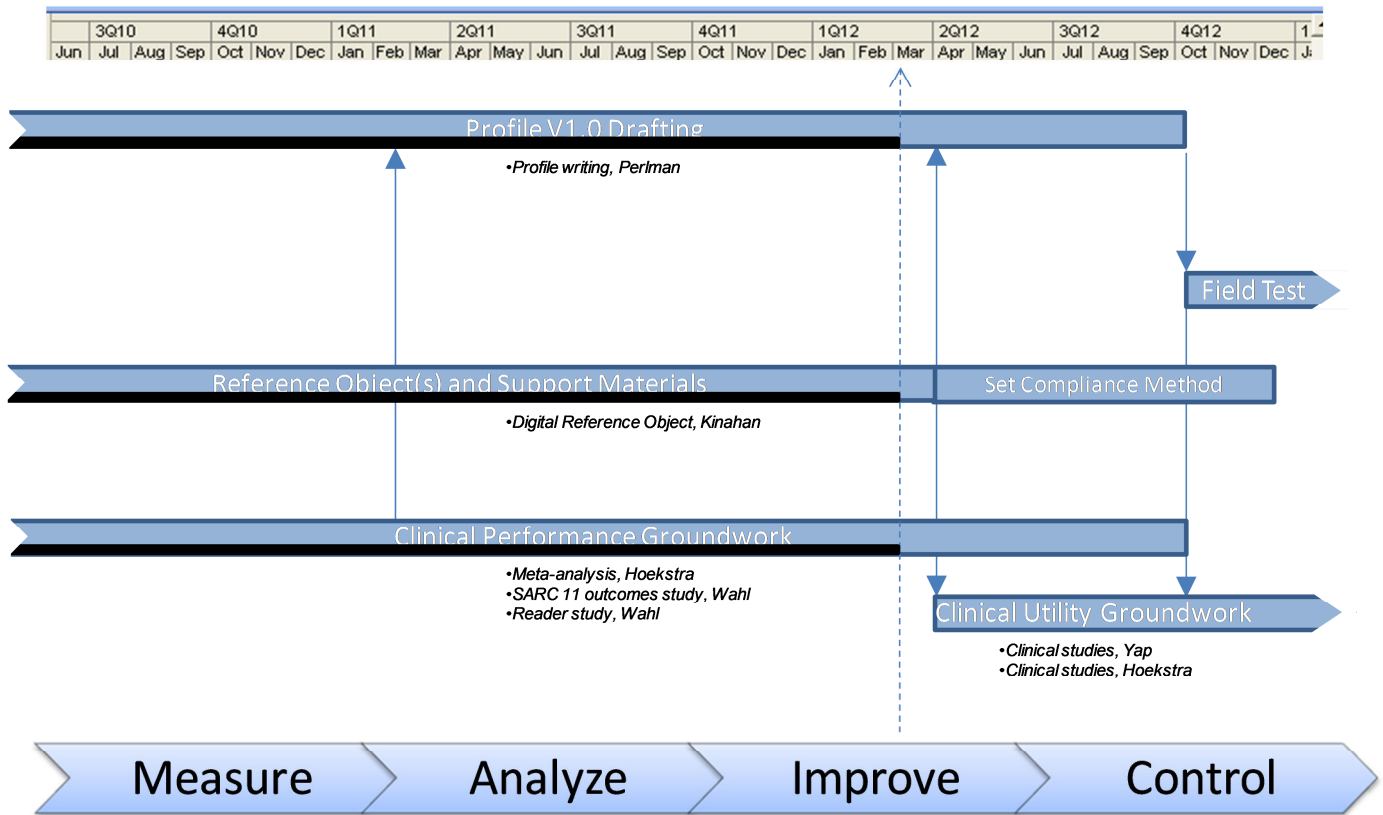
- Experimental Groundwork:
  - **Meta-analysis to Analyze the Robustness of FDG SUV Changes as a Response Marker, Post and During Systemic and Multimodality Therapy, for Various Types of Solid Extracerebral Tumors** (Hoekstra): Literature search complete, model created and validated, interim analysis reported in December. Have responded to input received in that session. Intend to finalize on schedule. Have indicated that we are in the process of extending the database by inviting authors to provide additional data. Formally, this is beyond the deliverables which refer to use of data as they appeared in the literature. That process depends on speed of replies. We are now working on the interim PET analyses.
  - **QIBA FDG-PET/CT Digital Reference Object Project** (Kinahan): Created and extensively tested a 'generic' DRO. Placed the generic DRO on a website for QIBA FDG-PET/CT TC

members to download and test. Developed user guide. Requested TC member feedback using a testing survey. Completed development of the first vendor-specific DRO (using GE formats), which is currently undergoing testing.

- ***Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes*** (Wahl): At present, two physician readers are analyzing the data to be certain the auto PERCIST tool has functioned properly. In addition, TLG will be determined and SUV max extracted. Once data have been classified by PERCIST, the worksheet will be locked and provided to SARC for comparison to the clinical data on each patient on trial in whom response could be assessed. Notable will be the baseline to 15 day changes which we believe are most important as they are the most actionable. The locking of the PERCIST data before transfer to SARC for comparison is essential to assure the independence of our analysis. From these prospectively collected data we expect to link early response or non response on PERCIST PET to survival. These data should be highly informative as regards efforts to qualify FDG-PET and changes post Rx as a biomarker. Following are examples of a responder and a non responder (imaging) and preliminary data showing the responders and non responders graphically.
- ***Evaluation of the Variability in Determination of Quantitative PET Parameters of Treatment Response across Performance Sites and Readers*** (Wahl): Early organizational work in the period with majority of effort to follow in next period.
- ***PERCIST Validation*** (Hoekstra): Early organizational work in the period with majority of effort to follow in next period.
- ***Evaluation of FDG-PET SUV Covariates, Metrics, and Response Criteria*** (Yap): Early organizational work in the period with majority of effort to follow in next period.
- Profiling:
  - A robust working draft of the QIBA FDG-PET Profile for the therapeutic area of oncology was completed as per the approval of the chairpersons of the QIBA PET Technical group's Internal Review Committee (IRC) and RSNA staff. The document was presented to the full PET Technical Committee by the Profile Editor on February 3, 2012 at which time the document was posted to the RSNA QIBA wiki. The Profile Editor also provided a slide presentation which outlined the document format and conventions as well as its relationship to the FDG-PET UPICT Protocol. Additionally, a roadmap, timeline and strategy to perform PET Technical Committee review and subsequently provision of the document for public comment and version 1.0 finalization were provided.
- NIBIB funds have been allocated to four projects to build evidence for the biomarker, as outlined above in section B, and to author the Profile. Three additional projects are under consideration.



The following updated Gantt chart reflects the FDG-PET Technical Committee progress and plan adjustments through the reporting period:



**E. PROGRESS FOR QUANTITATIVE MRI (CURRENT SNAPSHOT AS OF FEBRUARY 2012)**

Snapshot at this time:

- DCE-MRI, progress has been exceptional on all fronts:
  - Experimental groundwork:
    - **DCE-MRI Phantom Fabrication, Data Acquisition and Analysis, and Data Distribution** (Jackson): The project is nearly complete. Four copies of the QIBA DCE-MRI phantom have been manufactured successfully by The Phantom Laboratory. Data from multiple MR scanner vendors are being acquired and analyzed.
    - **Software Development for Analysis of QIBA DCE-MRI Phantom Data** (Ashton): The work is complete. We are currently monitoring reports from user testing, and will make any required software revisions as they become apparent.

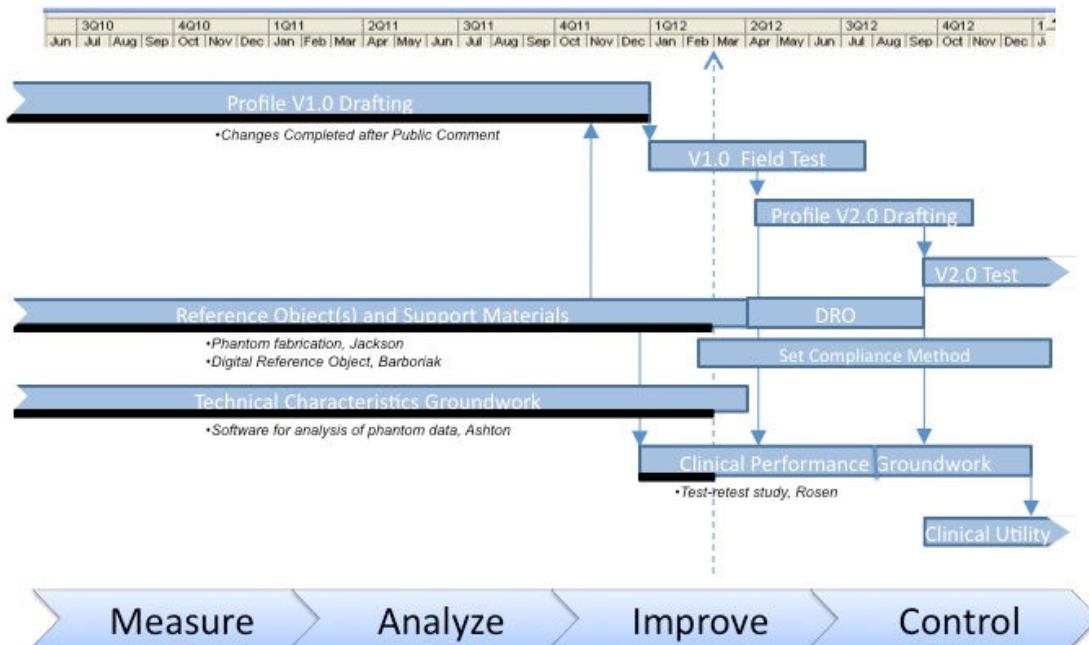
- **Digital Reference Object for DCE-MRI Analysis Software Verification** (Barboriak): Synthetic text objects (Tofts DCE-MRI data and T1 data, with and without added noise) have been created and posted. Presently they are under evaluation by users.
- **Test-Retest Evaluation of Repeatability of DCE-MRI and DWI in Human Subjects** (Rosen): Work with ACRIN on the test-retest protocol has progressed. ACRIN protocol 6701 has been submitted to CTEP for second round review. The original DCE-MRI image acquisition protocol was considered too general. A version with minor revisions will be drafted by Dr. Rosen and put forward as the first UPICT DCE-MRI protocol.
- Profiling:
  - The team completed authoring of the DCE-MRI Profile, ran it through a Public Comment period, and is presently finalizing responses to comments received and issuing the first version of the file for field test.
- The fMRI committee has developed provisional core details for a Profile and has defined tasks and approach to characterize reproducibility in the measurements. The first draft of the Profile and a release for public comment are targeted for July 2012.
  - **Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning-Development of Reproducibility Metrics** (Voyvodic): Generated AMPLE normalized activation maps for all subjects who underwent multiple scan sessions in our local data collections and the FBIRN Phase 1 data. Motor and language maps in the local data collections have been compared and submitted for publication (the QIBA-supported language reproducibility paper has been accepted with minor revisions by JMRI and those revisions are currently being reviewed). The FBIRN data analysis is still underway. Developing automated processing scripts to analyze AMPLE temporal stability for all functional data sets. We anticipate that these normalized stability metrics will be strongly correlated with fMRI scan quality in general and reproducibility in particular. These automated scripts will be applied to all data sets. The relational imaging database has been improved to include clinical and behavioral meta-data for each scan session, with appropriate links to the associated imaging data. This makes the data set collections more useful in general; it also allows our local image processing software (fScan) to find image data sets and run automated analysis scripts based on database queries of arbitrary subject or scan session properties. Both the DeYoe lab in Wisconsin and the Pillai lab in Maryland have installed fScan software and have been using it to perform AMPLE normalization analyses on their own data sets. We discuss these results in our biweekly reproducibility calls. QIBA supported publication: J.T. Voyvodic (2012 in review) "Reproducibility of single-subject fMRI language mapping with AMPLE normalization", J. Mag. Res. Imaging. QIBA supported presentation: J.T. Voyvodic (March 2012) "Quantitative reproducibility of clinical fMRI mapping of language and motor function", oral abstract presented at the Amer. Soc. Func. Neuroradiol. Annual meeting
  - **Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning** (DeYoe): Selected, tested and installed standardized computational sequences including the AMPLE algorithm coordinated with the Voyvodic project. Data for 8 subjects successfully organized in local imaging data base with table entries to facilitate scripted data queries and analysis. Registration of MRI scans with standard atlas brain, generation of brain activation maps, and calculation of image-based quality assurance QA metrics (image motion, signal drift, signal spikes, task activation) was completed. Reproducibility metrics were calculated for all repeat

scans, including the # of active voxels and center-of-mass metrics. Reproducibility metrics for fMRI activation cluster centers-of-mass (CM) are now available. Overall reproducibility of this metric across several variations in post-processing was quite good. The standard deviation of the CM location within the brain of single subjects is 3.1, 3.0, 6.53 mm in the left-right, posterior-anterior, and inferior-superior dimensions respectively. These measures can be improved slightly to 2.8, 2.3, 5.9 using Dr. Voyvodic's AMPLE normalization. Currently in progress efforts to complete analysis for spatial extent metric. We also are making good progress on developing more refined metrics to describe the spatial extent of an fMRI activation cluster based on discussions during some of the recent technical subcommittee conference calls. QIBA supported presentation - DeYoe, EA et al (2011) "Reproducibility of Functional MRI – Progress Towards Profile Development", poster presented at RSNA 2011 Annual meeting.

- **Validation of Breath Hold Task for Assessment of Cerebrovascular Responsiveness and Calibration of Language Activation Maps to Optimize Reproducibility** (Pillai): Assessment of cerebrovascular responsiveness in the presence of pathology has progressed on schedule. Two of the three phases have been accomplished.
- NIBIB funds have been allocated as outlined above in section B.

The following updated Gantt chart reflects the DCE-MRI Technical Committee progress and plan adjustments through the reporting period:

## Progress for DCE-MRI as of 3/2012



The following updated Gantt chart reflects the fMRI Technical Committee progress and plan adjustments through the reporting period:

## Progress for fMRI as of 3/2012

