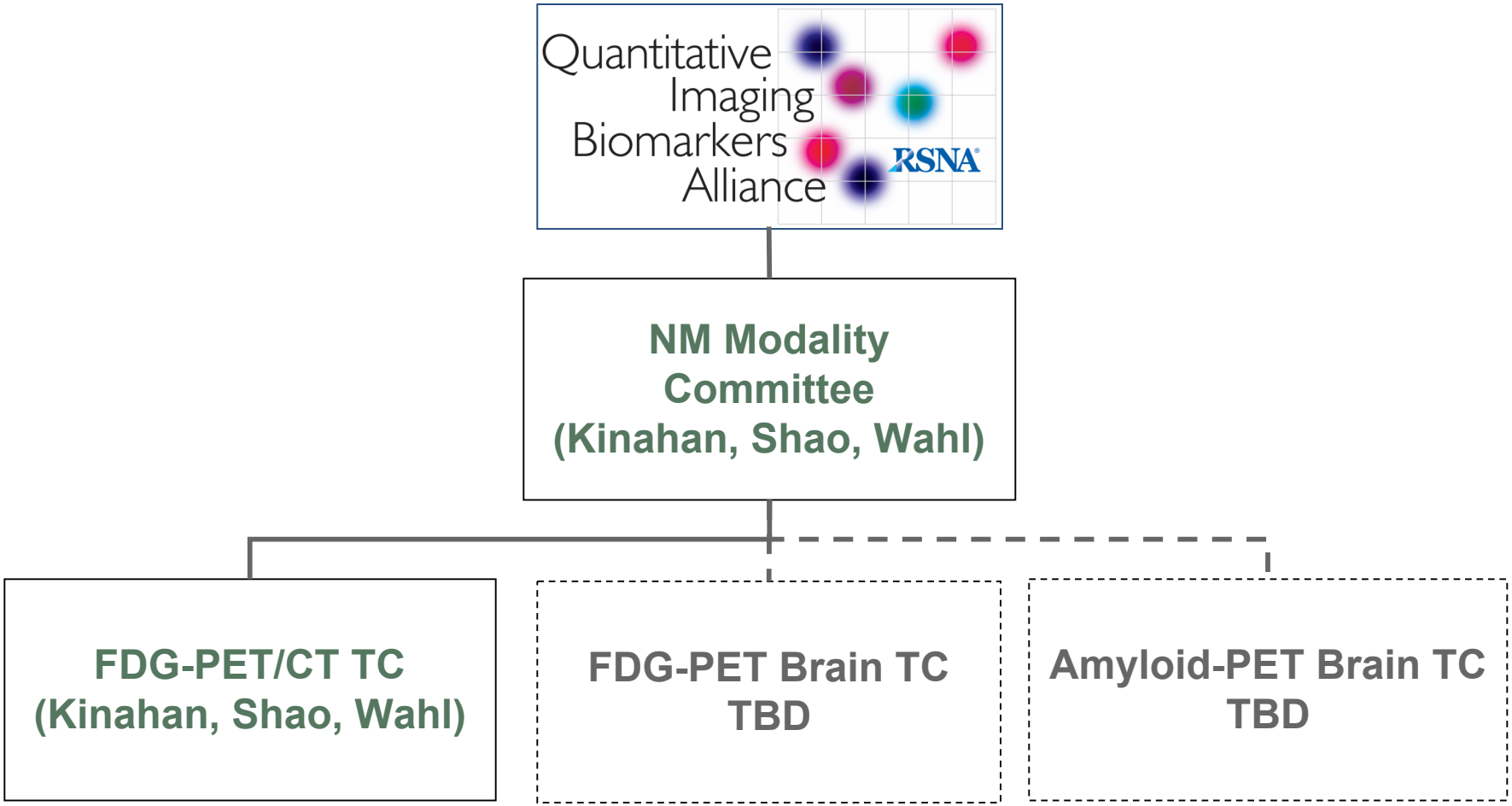
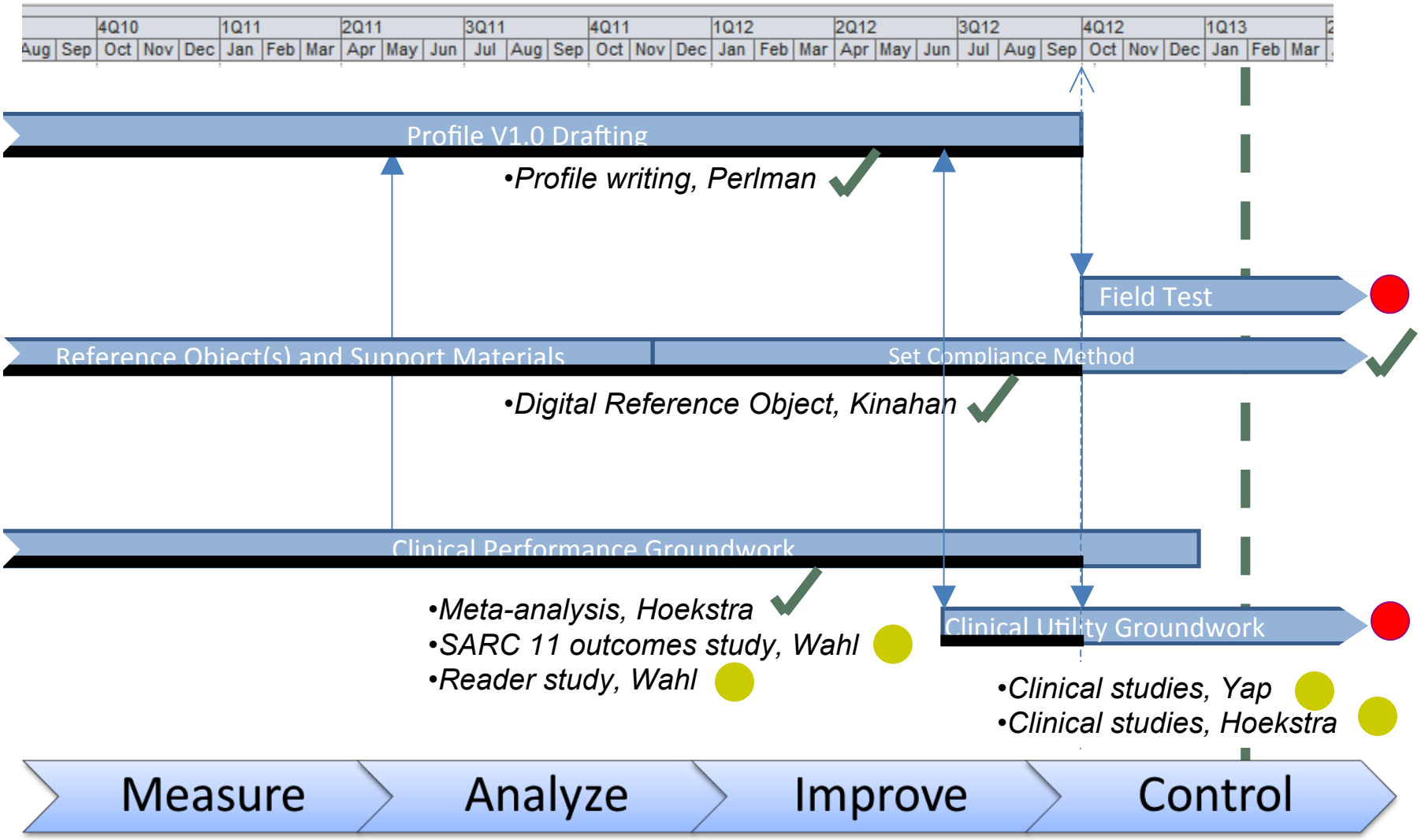
NM Committee Update



NM Committee

- Members
  - To date effectively the same as the FDG-PET TC
  - Approximately 115 TC members
  - Approximately 20 NM Committee members
- Activities
  - meetings every 1-2 weeks
  - regular attendance about 25
  - last several months entirely focused on Profile
  - Now starting discussions on leveraging FDG-PET/CT whole-body oncology profile for Brain PET TCs

Progress for Quantitative FDG-PET/CT: 9/12



QIBA FDG-PET/CT Profile

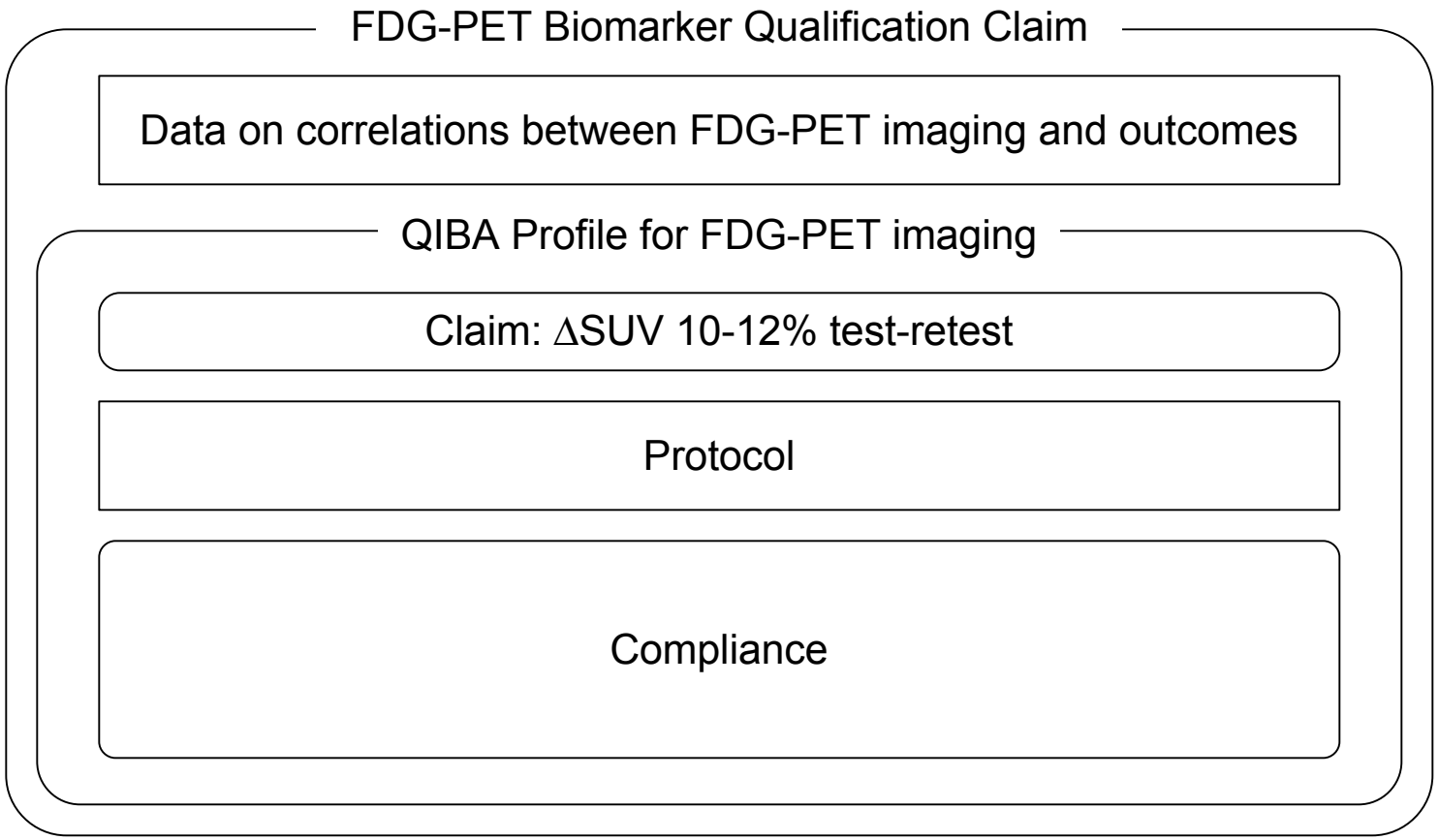
- Draft released for public comment till February 15
  - About 70 pages, good level of detail
  - Much work by many people
  - Profile editor identified: Eric Perlman
  - Thanks to RSNA staff for critical support
- Remaining Items
  - Coordination with DICOM WG3 (David Clunie)
  - Conversion to publications / editorials etc.

QIBA FDG-PET/CT TC Projects

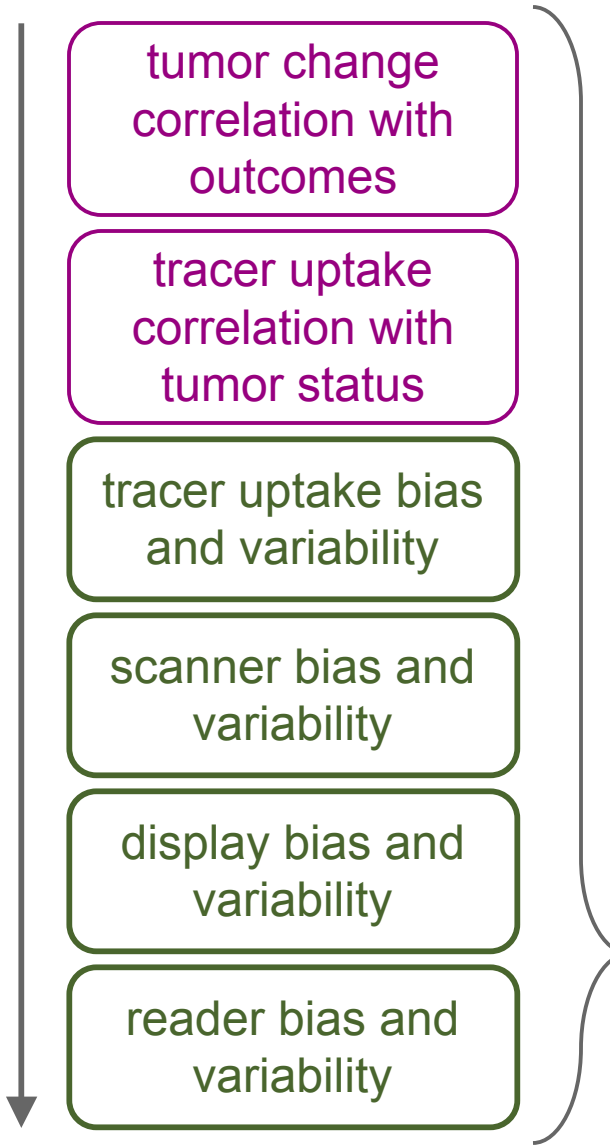
	Title	PI	Status
11a	Meta-analysis to analyze the robustness of FDG SUV changes as a response marker, post and during systemic and multimodality therapy, for various types of solid extracerebral tumors.	O. Hoekstra, U of the Netherlands	**Completed**
12a	QIBA FDG-PET/CT Digital Reference Object Project	P. Kinahan, U of Washington	**Completed**
13a	Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes	R. Wahl, Johns Hopkins	Close to completion
20a	Personnel Support for FDG-PET Profile Completion	E. Perlman, PAG & P. Kinahan, U of Washington	**Completed**
21a	Evaluation of the Variability in Determination of Quantitative PET Parameters of Treatment Response Across Performance Sites and Readers	R. Wahl, Hopkins	In Progress
22a	Evaluation of FDG-PET SUV Covariates, Metrics and Response Criteria	J. Yap, Dana Farber	In Progress
23a	Integration of Retrospective Reviews of 2-3 Groupings of Clinical Trial Datasets (This includes the current Hoekstra proposal) Will utilize the PERCIST analysis	O. Hoekstra, Netherlands	In Progress

Round 1: $198,740 (3 projects)
Round 2: $200,000 (4 Projects)

Project Relevance



Project Relevance - Conceptual Model



Assumptions

- Ignoring bias for ΔSUV metrics
- Variabilities add in quadrature
- If true tracer uptake variability has COV of 10%

Then

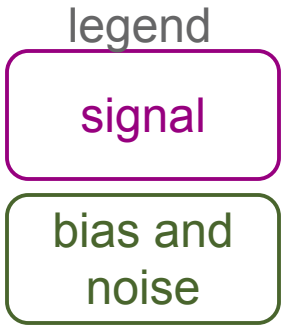
- All other sources of variability must be below, say, 5%, to avoid increases in SUV variability

Furthermore

- If we can determine the signal (correlation of tracer uptake with outcomes)

Then

- We can predict confidence intervals on QIB utility



QIBA FDG-PET/CT TC Project 11a

Project 11a: Hoekstra

- Title: Meta-analysis to analyze the robustness of FDG SUV changes as a response marker
- Amount:
- Aim: Develop a model of quantitative FDG PET to predict response of neoadjuvant chemo- (ChT) or chemoradio-therapy (ChRT) in solid extracerebral tumors.
- Status: Completed
- Conclusion: FDG change (end of treatment vs baseline) and pathological response are associated; this association seems to be a function of treatment (best results with ChT) and baseline FDG uptake. The apparent effect-modification by low baseline uptake values may (at least in part) relate to repeatability issues.
- Supported QIBA activity: Claims to FDA and others for FDG PET as a QIB

QIBA FDG-PET/CT TC Project 12a

Project 12a: Kinahan

- Title: QIBA FDG-PET/CT Digital Reference Object Project
- Amount:
- Aim: Construct a common reference DICOM PET/CT test image to be read on PET/CT display stations to check SUV computation fidelity, region of interest analysis performance and PET-CT image alignment.
- Status: Completed
- Conclusion: 13 sites with 18 different display systems participated. In general the core functions of measuring mean and maximum SUV were accurate. There were, however, differences in truncation of negatives values, and reporting of standard deviation values. Has good potential for becoming a standard, but does not test everything.
- Supported QIBA activity: Profile and claims to FDA and others for FDG PET as a validated assay

QIBA FDG-PET/CT TC Project 13a

Project 13a: Wahl

- Title: Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes
- Amount:
- Aim: Quantitatively and qualitatively analyze FDG PET data prospectively obtained at up to three time points in the SARC 11 trial (311 patients accrued). The analyses will focus on linkage of PET findings to clinical outcomes of response, PFS and survival
- Status: In progress - near completion
- Supported QIBA activity: Claims to FDA and others for FDG PET as a QIB (quantitative imaging biomarker)

QIBA FDG-PET/CT TC Project 20a

Project 20a: Perlman/Kinahan

- Title: Personnel Support for FDG-PET Profile Completion
- Amount:
- Aim: Provide expert support over 2-3 months as a 'Profile Editor' to convert the considerable amount of material accumulated by the FDG-PET TC into a draft QIBA Profile.
- Status: Completed
- Conclusion: Provided critical support to get current profile started
- Supported QIBA activity: Profile

QIBA FDG-PET/CT TC Project 21a

Project 21a: Wahl

- Title:
- Amount:
- Aim: Determine how reproducible quantitative analysis of PET parameters are across sites and readers. Primary metric will be % change in SUV max, determined pre- and post-Rx in the "hottest tumor" as defined by the reader. Secondary metrics will include absolute SUV peak, SUL max, SUL peak, and TLG (as determined by site), normal liver SUV and SUL in a 3 cm diameter sphere, as well as SD of this region of interest
- Status: In progress
- Supported QIBA activity: Claims to FDA and others for FDG PET as a QIB (quantitative imaging biomarker). May lead to Profile revision

QIBA FDG-PET/CT TC Project 22a

Project 22a: Hoekstra

- Title: PERCIST Validation
- Amount:
- Aims: 1. Validate the PERCIST metrics in a single tumor type treated with the currently prevailing different types of therapy, using survival as clinical outcome measure. 2 develop a teaching module to explain the methodology of the quantitative procedures
- Status: In progress - near completion
- Conclusion: None yet
- Supported QIBA activity: Claims to FDA and others for FDG PET as a QIB

QIBA FDG-PET/CT TC Project 23a

Project 23a: Yap

- Title: Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes
- Amount:
- Aim: A research archive and standardized database that supports FDG-PET imaging results, covariates, and clinical outcome data will be created. Where possible, numerical results comparing FDG-PET imaging metrics from multiple studies will be presented.
- Status: In progress - near completion
- Supported QIBA activity: Claims to FDA and others for FDG PET as a validated assay. May lead to Profile revisions

- Note: In Phase 2 (contingent on NIBIB funding) the database will be populated with results of FDG-PET imaging metrics and relation to covariates and clinical outcome data.

Other Activities

- FDG SUV Digital Reference Object presentations
  - Presented at SNM and as part of QIRR at RSNA
  - Presented to NEMA/MITA group at RSNA
  - Presented to PET/CT display manufacturers at RSNA
  - Possible presentation at SNM?
- UPICT FDG-PET/CT Protocol
  - Presentation at SNM of near-final version
  - Stalled but recently charged Jeff Yap with completion
- FDA BMRT
  - Materials on validated assay aspect of FDG-PET/CT sent to Dr Higley to respond to FDA comments

QIBA Nuclear Medicine - Gap Analysis

- Motivation for quantiative FDG-PET/CT not clearly defined
- FDG-PET/CT Profile based on data / publications where the studies may not have been in compliance with the Profile
  - Would ideally re-estimate the 10-12% test-retest values of claim using Profile compliant studies, but this is expensive
  - Correlation between ΔFDG and outcomes might be better than estimated if studies had been Profile complaint
- Multi-center data is minimal
  - Publishing of the ACRIN 6678 / Merck data is in the works
    - Results appear to be consistent with single-center claim of Profile
  - May be possible to evaluate Profile-compliance of these studies
- How do we test compliance with Profile
  - DRO provides an explicit test of one portion of profile
  - ACRIN and NEMA standards provide for testing of a few other components
- ROI testing / definition still not complete
- How do we better tie outcomes of projects to support the QIBA mission
  - Can we couple to signal and error propagation concept
  - Can we convert QIBA results (profile, projects, etc.) to publications

QIBA Nuclear Medicine - 2 year plan

- Proposals for new projects if additional NIBIB funding (match to conceptual process based on gap analysis?)
- Formalize the DRO as a standard
  - needs improvement
  - host on QIBA/RIC server
- Transition FDG-PET/CT Profile to next phase release 1
- Plan for release 2
- Can images from projects be hosted on QIBA/RIC server?
- Coordination with DICOM WG3 for proposing changes to standard
- Conversion of Profile and projects to publications / editorials etc.
- New Profiles
  - FDG-Brain TC
  - Amyloid Brain TC
  - Consensus that these TCs should go ahead regardless of NIBIB funding