Application for QIBA Project Funding

Title of Proposal: Evaluation of FDG-PET SUV covariates, metrics, and response criteria		
QIBA Committee/Subgroup: Quantitative PET		
NIBIB Task Number(s) which this project addresses: 1, 3, 10		
Project Coordinator or Lead Investigator Information:		
Last Name: Yap	First Name: Jeffrey	Degree(s): PhD
e-mail:	Tel #:	
Institution/Company: Dana-Farber Cancer Institute / Harvard Medical School		
Amount Requested:		

Please check the primary category for this proposal from among the following: **1a** and **3b**

- ☐ 1. Identification of Technical Characteristics and Standards
  - ☐ a. Creation and refinement of protocols for image acquisition, analysis, quality control, etc., for specific clinical utility
  - ☐ b. Phantom development and testing
  - ☐ c. Identification and assessment of intra-reader bias (1) and variance across scanners and centers
  - ☐ d. Identification and assessment of inter-reader bias and variance across scanners and centers
  - ☐ e. Other
- ☐ 2. Clinical Performance Groundwork
  - ☐ a. Assessment of intra-reader sensitivity and specificity
  - ☐ b. Assessment of inter-reader sensitivity and specificity
  - ☐ c. Other
- ☐ 3. Clinical Efficacy Groundwork
  - ☐ a. Assessment of correlation between new biomarker and 'accepted-as-standard' method
  - ☐ b. Characterization of value in clinical trials
  - ☐ c. Characterization of value in clinical practice
  - ☐ d. Development/merger of databases from trials in support of qualification
  - ☐ e. Other
- ☐ 4. Resources (money and/or people) committeed from other sources.

Additional collaborators and staff will participate without request for salary support. The existing IT infrastructure and research databases will be utilized with the exception of additional hardware and software listed in the budget.

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.[1] 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 SUVmax vs. SUVmean (Figure 1) and SUV patient size normalization using lean body mass vs. body weight (Figure 2).[2,3,4] 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 image analyses will be performed to generate normal tissue ROIs (e.g. liver) as well as multiple tumor ROIs for studies that only included single tumor per patient in the original analysis. A software package will be developed in IDL to establish a DICOM server research archive and automatically extract and compare various PET metrics (e.g. SUVmax, SUVmean, SUVlbm) from previously performed ROI analysis. This will address a major limitation in commercial software that only allows the use of a single metric and/or response criteria for a given study and facilitate the automated generation and comparison of different PET metrics and response criteria. Lastly statistical analysis will be performed on the results of multiple clinical trials in order to evaluate the impact of covariates, PET metrics, and response criteria on the performance of FDG-PET SUV as an imaging biomarker of therapeutic response. This will yield critical results for supporting claims in the QIBA profile with such as the variability in response assessment using different methods as well as justify consensus recommendations in the UPICT protocol, e.g. with regards to image analysis and response assessment.

Primary Goals and Objectives:

1) Identify the impact of covariates (e.g. body weight, height, lean body mass, dose) on PET SUV quantification.
2) Compare and evaluate the correlation between different PET metrics including SUVmax, SUVmean, SUVpeak, SUVlbm and metabolic response assessment using these metrics.
3) Compare different PET response criteria (EORTC, PERCIST, RECIST) and correlate with anatomic response (e.g. RECIST) and clinical outcome (time to progression, overall survival) in 2 clinical trials
    a) GIST patients naïve to tyrosine kinase inhibition therapy treated with imatinib.[5]
    b) imatinib-resistant non-GIST soft tissue sarcomas treated with sunitinib.[6,7]
    c) Phase I and Phase III imatinib-resistant GIST patients treated with nilotinib.[8] (optional)

Note: Due to QIBA funding limits, this proposal has been separated into two phases. Phase 1 will have duration of 6 months. Phase 2 will commence after the completion of Phase 1 and is contingent on availability of QIBA funding.

Deliverables:

Phase 1 - A research archive and standardized database that supports FDG-PET imaging results, covariates, and clinical outcome data will be created. A report or draft manuscript will be written summarizing the results. Software will be developed to facilitate retrospective analysis of previously defined ROIs and automate the comparison of different PET SUV metrics and response criteria. Where possible, numerical results comparing FDG-PET imaging metrics from multiple studies will be presented.

Phase 2 - The standardized database will be populated with results of FDG-PET imaging metrics and relation to covariates and clinical outcome data as described above in primary goals and objectives. A report and draft manuscript will be written summarizing the results.

Timelines:

Phase 1

1) **Months 0-3: Initiate software development and data collection. Milestones: Compilation of clinical trial images for analysis, establish project research archive and connectivity, extraction and migration of metadeta.**
2) **Months 3-6: Compile outcome data for clinical trials. Perform additional tumor ROI analysis of images. Milestones: Initial software prototype for testing and evaluation. Preliminary results to design formal analysis plan.**

Phase 2 (For follow-up funding application from QIBA)

3) Months 0-3: Complete software development and analysis of tumor and liver ROIs. Preparation of interim results summary for RSNA QIBA sub-committee. Milestones: Dissemination of relevant findings to RSNA QIBA subcommittee chairs for discussion/inclusion in RSNA annual meeting session(s).

4) Months 3-6: Perform formal statistical analysis of covariates, PET SUV metrics, and clinical outcome. Provide interpretation of quantitative results in individual clinical trials and overall meta-analysis. Summarize findings. Milestones: Submission of scientific abstract (SNM, RSNA), authorship of scientific report and draft manuscript.

Figures:

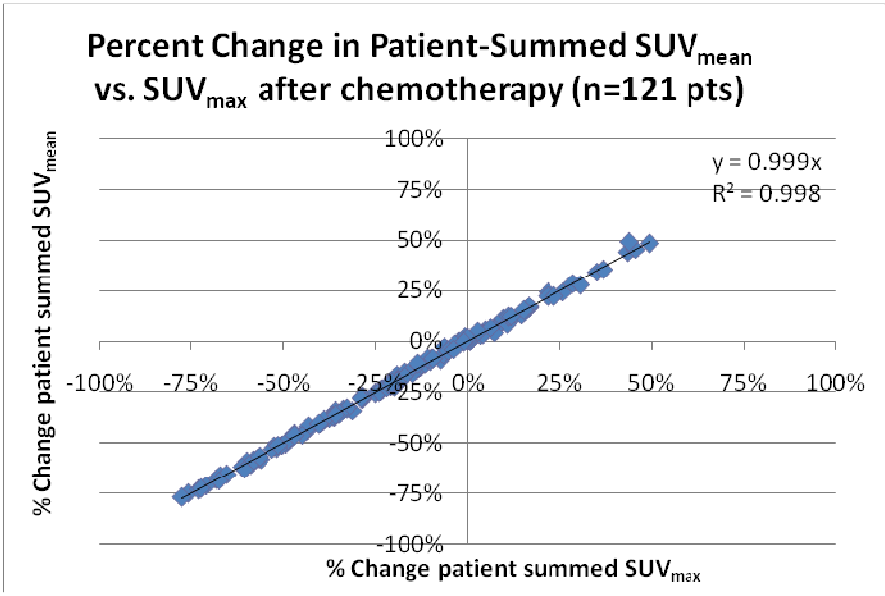

Figure 1: Comparison of response assessment with patient summed SUVmax vs. 70% SUVmean.

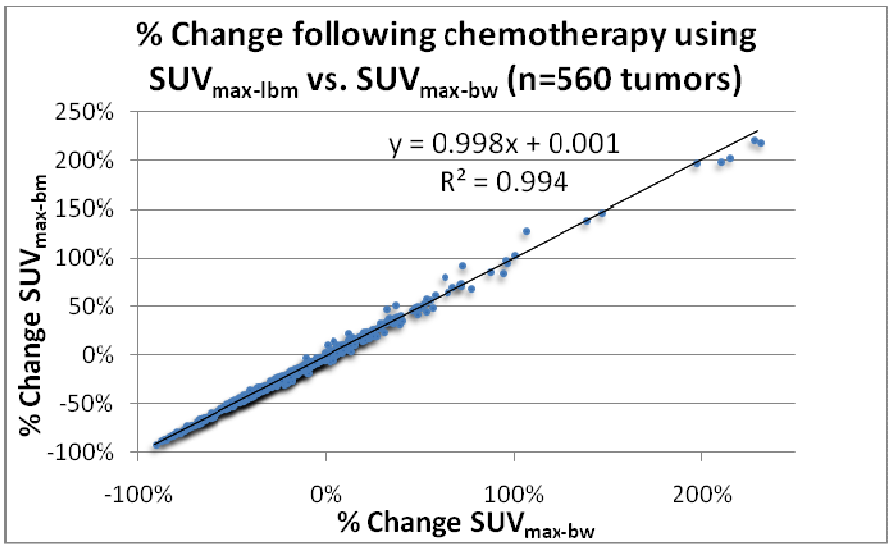

Figure 2: Comparison of response assessment using $SUV_{max\text{-}lbm}$ vs. 70% $SUV_{mean\text{-}bw}$

References

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