Quantitative Imaging Biomarkers Alliance RSNA

Version 3 (Oct 2011) Application for Round-2 QIBA Project Funding

Title of Proposal: *PERCIST Validation*		
QIBA Committee/Subgroup: FDG PET		
NIBIB Task Number(s) which this project addresses:		
Project Coordinator or Lead Investigator Information:		
Last Name: Hoekstra	First Name: Otto S.	Degree(s): MD
e-mail:	Tel #:	
Institution/Company: VU University Medical Center		
Amount Requested:		

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

Resources
VUmc Dept of Nucl Med & PET research (analysis software, Boellaard)

Please provide a one-page summary that includes the following information:

Project Description and Primary goals and objectives

Project aim:
Validate PERCIST metrics using peer-reviewed patient cohorts**.**

Background and aims:
PERCIST proposes to use (a). peak SUV and (b). a combination of relative change and absolute differences between serial scans. This approach certainly has face-validity but it lacks clinical evidence to support it, as was acknowledged by its inventor (Dr Wahl). Valid, uniform metrics are crucial for clinical acceptance of PET in the context of response evaluation, as well as for its implementation as a read-out of response in drug development.

Until now, several SUV variants are used in the literature, and the concept of applying a combined relative and absolute change to the data-analysis has not yet been validated. Since many authors (including us) did not use the SUVpeak method, and since one (mainly within QIBA) has proposed (and seem to agree on) technical modifications to it, this is the time to embark on re-analysis of existing PET scans using studies that passed quality control of peer-review or internal quality standards (in case of VUmc: Boellaard, Lammertsma).

As a first step, we propose to validate the PERCIST metrics in a single tumor type treated with the currently prevailing different types of therapy, using survival as clinical outcome measure. Since one of the main obstacles for new metrics may be acceptance in the field, we will develop a teaching module to explain the methodology of the quantitative procedures.

Ideally, to expand the validation, other types of cancer and observer variation of data-analysis should be performed in a follow-up project, and the teaching module should be embedded in an competence-based adaptive e-learning system.

Methods:
1. re-analysis of PET datasets available at VUmc, in non-small cell lung cancer treated with systemic therapy using the PERCIST metrics
2. comparison with the original methodology used in the publications, and vs their reference tests (pathology or survival)

Materials:
VUmc FDG PET response database NSCLC:
- Platinum based chemotherapy (Hoekstra CJ, JCO 2005) ~ 150 scans
- sorafenib/erlotinib (Lind, manuscript in preparation) ~ 100 scans
- bevacizumab/erlotinib (de Langen, JNM 2010) ~ 85 scans
- erlotinib (Zander, JCO 2011) ~ 100 scans

  i.e., a total ~ 435 [18F]-FDG PET scans (335 dynamic)

Outcomes/deliverables:
1. accuracy of PERCIST vs conventional PET quantitative approaches, and robustness in context of different systemic treatment modalities
2. teaching module

Timeline [must include intermediate measureable milestones]
April 01, 2012– September 29, 2012
- End of month 2: analysis beva/erlotinib completed & 50% of sorafenib/erlotinib
- End of month 4: analysis sorafenib/erlotinib and erlotinib completed
- End of month 6: analysis cisplatinum completed, teaching module available