

Application for QIBA Project Funding

Title of Proposal: <i>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.</i>		
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, PhD
Institution/Company: VU University Medical Center		

Please check the primary category for this proposal from among the following:

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) committed from other sources.

VUmc Dept of Nucl Med & PET research (2nd reader in meta-analysis, electronic tools)

Statistical support needs to be hired from other institute

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

Project Description

Meta-analysis on the association between FDG uptake changes and histopathological response (details see below goals and objectives).

Primary goals and objectives

Validated qualitative and quantitative statistical model of quantitative FDG PET to predict response of neoadjuvant therapy in solid tumors.

Methods, tasks and timelines:

- Task 1. Febr-April 2011: update and extend VUmc *databases* containing data on individual patients in prospective VUmc and peer-reviewed studies, in > 800 patients on cytotoxic therapy. Contexts: baseline & end-of-treatment FDG PET; baseline & during treatment FDG PET
- Task 2a. May-June 2011: study quality estimation using (modified) QUADAS;
- Task 2b. July – Sept 2011: *model development*: multivariable mixed effects logistic regression analysis accounting for precision as a function of repeatability (using results of meta-analysis on repeatability, now in final stage), tumor type, timing of PET, type of therapy (e.g. drug type, radiotherapy vs. chemo-radiotherapy), criteria of responsiveness.
- Task 3. Oct –Nov 2011: *model validation* using point estimates (and distribution measures) of the remaining peer-reviewed observational FDG PET studies to be obtained via updated systematic literature search (which will also focus at studies cf. task 4)
- Task 4. Dec-Jan 2012: *applicability of the model with targeted agents*
 - extend the database (task 1) with patient data in the context of targeted agents
 - explore validity and precision of the initial model.
- Task 5. comparison with RECIST where available (throughout Tasks 1-4)

Deliverables

1. open-access database of individual patient data and FDG PET (tasks 1,4)
2. explorative statistical model on FDG uptake (change) vs pathology in cytotoxic therapy (task 2), using individual patient data
3. validation of the model using aggregated published data.
4. validation of the model in the context of of targeted agents (task 4)

Timeline [must include intermediate measurable milestones.]*

- Task 1. End of April 2011; **Milestone:** *database containing study and test characteristics for modeling*
- Task 2a. End of June 2011; **Milestone:** *QUADAS overview*
- Task 2b. End of Sept 2011; **Milestone:** *statistical model describing the quantitative association between FDG uptake change and probability of histopathological response*
- Task 3. End of Nov 2011; **Milestone:** *validation result*
- Task 4. End of Jan 2012; **Milestone:** *open access availability of extended database; model validation result.*