Application for QIBA Project Funding

Title of Proposal: Validation of Volumetric CT as a Biomarker for Predicting Patient Survival		
QIBA Committee/Subgroup: Volumetric CT Technical Committee		
NIBIB Task Number(s) which this project addresses: **Task 10** - Compare correlations between imaging biomarkers and standard biomarkers with outcome measures		
Project Coordinator or Lead Investigator Information:		
Last Name: Zhao	First Name: Binsheng	Degree(s): DSc
Institution/Company: Columbia 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) committeed from other sources.

Resources have been committed from other sources and will be used in this proposed research. These include, but are not limited to: (1) imaging, tissue biomarkers and tumor genotype data collected from a large, multicenter clinical trial sponsored by a pharmaceutics company, and (2) advanced image analysis algorithms developed for volumetric segmentation of solid tumors and metastases by the PI's group over the past decade.

Project Summary

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 blood sample taken pre- and every 6-week post-treatment.

Volumetric (as well as unidimensional and bidimensional) measurements of target lesions on all scans of all patients will be calculated using our in-house computer-aided (CA) methods developed for segmentation of lung, liver and lymph node metastases. Intra- and inter-reader variability of the three measurements will be explored in a subset of patients (i.e., the first 50 patients who have more than 3 scans). Finally, correlations of tumor response and time-to-progression assessed unidimensionally, bidimensionally and volumetrically with clinical outcome (overall survival), tissue biomarkers and tumor genotype will be performed. By evaluating the magnitude of measurement variability and the optimal correlation, cut-off value or continuous change variables to identify tumor regression and progression can be established for unidimensional (ie. modified RECIST), bidimensional (ie. modified WHO) and volumetric response assessment methods. If proven successful and accepted by the oncology community and regulatory agencies, this research will aid the discoveries of cancer drugs and tissue biomarkers as well.

Primary goals and objectives

The primary goal and objective of this project is to validate the use of volumetric CT in predicting patient survival and correlating biological and genetic changes of tumors treated with target therapy using a retrospective dataset from a large, multicenter Phase II/III clinical trial in advanced colorectal cancer.

Deliverables

1. Knowledge about the levels of intra- and inter-reader variability in unidimensional, bidimensional and volumetric measurements of solid tumors obtained with computer-aided algorithms on single and multiple CT scans, involving the most common sites of metastases – lung, liver and lymph nodes
2. Validation result on the value of the volumetric response method in predicting patient survival and tumor biology using a large multicenter clinical trial data from advanced colorectal cancer patients.

The PI will regularly participate in QIBA VolCT Technical Committee TC meetings including VolCT 1C sub-group meetings, discussing and reporting project progresses with the committee members. It is anticipated that several clinically significant conference abstracts and peer-reviewed papers will be resulted from this study.

Timeline

In the first 7 months in year one, we will complete the intra- and inter-reader variability study using a subset of 50 patients, each having 5 scans on average. Intra-reader includes one radiologist's two readings in two separate sessions (at least one month apart) and inter-reader includes two independent radiologists' readings. "Reading" means computer-aided unidimensional bidimensional and volumetric measurements. These scans and the mark ups will be provided to other QIBA investigators.

Starting the 8th month in year one and throughout the rest of 18 months, one of the two radiologists will complete readings of target lesions on all scans in the rest of the total 451 patients. We will correlate the measurement changes with patient survival, tissue biomarkers and tumor genotype and their changes. The optimal cut-off values for tumor responses assessed by the three different measurement techniques will be investigated based on the levels of the measurement variability and the best clinical and biological correlations.