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:		
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Institution/Company: Columbia University Medical Center		

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.