Progress Report

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QIBA Committee/Subgroup: Volumetric CT Technical Committee

Project Title: Validation of Volumetric CT as a Biomarker for Predicting Patient Survival

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The goal of this project is to validate volumetric CT as a better imaging biomarker for predicting patient survival using a retrospective dataset from a large, multicenter Phase II/III clinical trial in advanced colorectal cancer treated with a targeted therapy. About 450 patients enrolled to this clinical trial had measureable disease per RECIST definition and will be used in this study. Three in-house lesion segmentation algorithms developed for liver, lymph node and lung metastases will be applied to assist radiologists in obtaining tumor volumes on baseline and follow-up scans. The expected outcomes of this proposal include (1) obtaining the knowledge about the levels of intra-reader and inter-reader variability in measuring total tumor burdens and tumor burden changes (unidimensional and bidimensional measurements as well) and (2) evaluating the value of the volumetric CT in predicting patient survival.

We are currently exploring the intra-reader and inter-reader variability in measuring total tumor burdens and tumor burden changes.

When using RECIST to assess tumor response to therapy, there are several places where variations may occur. The sources include (but are not limited to) selection of target lesion, lesion size measurement, evaluation of non-measureable lesion and presence of new lesion. We have worked out a plan that allows us to study the variability caused by (1a) target lesion selection and lesion measurement, and (1b) lesion measurement only.

Study Design:

A subset of 30 patients who have baseline, 6-week (+/- 1 day) and 12-week (+/- 1 day) follow-up scans will be selected for this analysis. There will be three participating radiologists, one of them will interpret the data twice. RECIST 1.0 will be used, i.e., up to 5 lesions per organ and 10 lesions per patient will be measured. Computer generated lesion contours will be reviewed and edited if necessary by radiologists, in a side-by-side viewing fashion. Variability in total tumor burden and changes from 6-week and 12-week to baseline will be studied. The experiments designed for (1a) and (1b) are described below.

1a. For each patient data, one radiologist will blindly select the target lesions on baseline scan and measure the target lesions on each of the three scans twice in

two different sessions (> 2 weeks apart) and the other two radiologists will independently do the same, but only one time.

1b. The target lesions selected by one radiologist will be considered as the reference standard for the other two radiologists. After comparing the reference with their own selections, each of the two radiologists will blindly re-measure the missing lesions, i.e., the lesions that are in the reference but not in their original selections.

Project Status:

- We have completed all necessary preparation work including a research agreement with the pharmaceutical company who provides the trial data, IRB waiver, consensus reading, subset image data selection for the variability study, etc.
- Experiments for (1a) are just finished

We expect to complete (1b) by September and the statistical analysis of intra- and inter-reader variability by October 2011.