Title of Proposal: **Methodology and reference image set for lesion characterization in terms of texture and morphology**  
05/06/2016 (Revision)

QIBA Committee/Subgroup: 

NIBIB Task Number(s) which this project addresses:

Project Coordinator or Lead Investigator Information:

<table>
<thead>
<tr>
<th>Last Name: Samei</th>
<th>First Name: Ehsan</th>
<th>Degree(s): PhD</th>
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<tbody>
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Institution/Company: Duke University Medical Center

Amount Requested: **$68,267** for months 1-12

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
  - [x] 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

- [x] 2. Clinical Performance Groundwork
  - [ ] a. Assessment of intra-reader sensitivity and specificity
  - [ ] b. Assessment of inter-reader sensitivity and specificity

- [x] 3. Clinical Efficacy Groundwork
  - [x] a. Assessment of correlation between new biomarker and ‘accepted-as-standard’ method
  - [ ] b. Characterization of value in clinical trials
  - [x] c. Characterization of value in clinical practice
  - [x] d. Development/merger of databases from trials in support of qualification
  - [ ] e. Other

- [ ] 4. Resources (money and/or people) committed from other sources.
**Project Description**

Lesion characteristics offer a wealth of information about its phenotype and the progression of the disease or the treatment. Meaningful quantitative characterization of the lesion can thus be invaluable in disease classification and management. In the area of CT lesion characterization, most of the QIBA effort thus far has been focused on volume estimation. While volumetry is essential for effective lesion characterization, lesion volume is only one of several features that could be used to describe its radiological phenotype. Beside volume, there are three additional attributes that are considered as important, if not more important, in the phenotypical characterization of a lesion: morphology (including shape and boundary conditions), density, and internal heterogeneity (i.e., lesion texture). These attributes can be of significant clinical diagnostic and prognostic value.

One of the major challenges in lesion characterization is lack of access to the ground truth. The true nature of a clinical lesion is nearly impossible to ascertain. As such, most prior efforts to evaluate lesions have either focused on assessing change (e.g., change in the volume of a lesion), or relied on physical phantoms which can offer ground truth but fall short in accurately modeling real anatomical heterogeneities and diseased conditions.

Built upon a substantial track record of research in the development of virtual lesions, the objective of the present project is to develop hybrid clinical CT images containing virtual lesion models with known-exactly morphology and texture. This database will be used to investigate the accuracy of lesion quantification in terms of texture and morphology, thereby extending quantitative CT from volumetry to include additional features. This project is justified based on the well-established fact that lesion morphology and texture are clinically relevant to cancer characterization. However, due to lack of ground truth in traditional clinical databases, it has thus far been impossible to assess the accuracy with which morphological and textural phenotypic expressions can be accurately characterized. This project directly addresses this shortcoming by providing a database with ground truth. The work contributes to existing and emerging QIBA Profiles by assessing the impact of lesion morphology on volume quantification. It further advances the QIBA trajectory into new areas where quantitative imaging can meaningfully impact medical research and care, paving the way towards new Profile definitions.

Using a virtual insertion of realistic 3D lesions into clinical CT images, we will develop an image database that allows for comprehensive quantitative characterization of lesion features in CT. The dataset will provide anatomical variability as exists in actual clinical datasets, while at the same time the pre-defined lesion models with a priori known properties will offer the advantage of providing the ground truth. Furthermore, this platform will allow for a variety of datasets to be generated with multiple degrees of flexibility in key investigational areas including statistical variability of lesion models (size, shape, etc.) or repeated insertions of the same or different lesions at various insertion locations.

We will incorporate texture and morphology, two burgeoning areas of quantitative characterization in our lesion modeling and insertion framework. The framework will enable coupling statistical texture modeling with an analysis of lesion morphology to determine how measured lesions estimates (e.g., Haralick texture features or Hausdorff morphology deformations) are informed by the imaging system optics and reconstruction. The deliverables include 1) the development of virtual lesions with morphological and textural variability, 2) a database of hybrid clinical image sets with lung nodules and liver lesions for morphology and texture analysis, both data sets with confirmed and validated added lesions for gold-standard quantitative evaluation, and 3) a systematic analysis of the impact of CT image acquisition and reconstruction on lesion quantification in terms of volume, texture, and morphology. Developed for in the execution of this project, this will be established as a platform for multi-software analysis of lesion features.
Specific Aims

Aim 1. Generate a library of lesion texture features. Create textured lesion models to simulate the heterogeneous structures within lesions (mo. 1-5). Using low noise clinical CT images from the Lung Image Database Consortium (LIDC), the QIBA test-retest challenge, and Duke University Medical Center (DUMC), we will create a library of texture features by analyzing lesion images to extract lesion internal variances and structural inhomogeneities. This technique creates texture based on measured statistics such as Haralick features. This statistical feature model will be used to calculate the appropriate heterogeneity for each lesion’s internal structure. Additionally, we will employ the Clustered Lumpy Background (CLB) and wavelet texture modeling method as the basis for texture fabrication. The resultant image generated from the CLB is then blurred and noised reflective of the imaging system. The texture features of the image after blurring and noise addition are calculated and fed into a genetic algorithm to iteratively determine the texture model that most closely matches the reference images based on a statistical similarity measure, Mahalanobis distance. In this way, the modeled textured lesion would embody the true system related influence in terms of texture appearance. The analysis and modeling will be applied to cases with repeats to enable modeling lesions with test-retest variability. This provides for characterization of the utility of virtual lesions in terms of repeatability.

Aim 2. Create a framework for morphological analysis of vendor-specific lesion shape deformation and rendition (mo. 4-8). To assess the imaging system impact on lesion morphology and rendition, we will use the Hausdorff distance (HD) measurement. We develop a 3D quantification technique to measure differences between 3D lesion models and volumetric images of synthetic lesions corresponding to lesion models (Fig. 2). Lesion images from multiple imaging systems such as GE and Siemens will be segmented from the LIDC, DUMC, and QIBA databases, and modeled using a custom Duke lesion modeling tool. Virtual lesion models will be made using a technique from the Round 4 project. Using a HD based 3D quantification technique, comparisons between different imaging system lesion renditions will be made to assess higher-order deformation and local volume differences that are manufacturer dependent. The relevance of morphological definitions in the quality of volume estimation will also be investigated.

Aim 3. Generate a library of vendor-specific, realistic lesion simulations that incorporate texture and morphology based on a range of clinically relevant protocols (mo. 9-12). In this aim, we will extend our technique from a Round 4 project to include textures (internal structural variances and spatial heterogeneity) in lung and liver lesions. In this aim, we will use adjusted static reference clinical datasets with known truth (realistic lesions inserted). These datasets include 100 normal lung images with 100+ lung lesions and a corresponding 100 normal abdominal CT images inserted with 100+ liver lesions. Additionally, lesion models from ‘coffee break’ and LIDC datasets will be inserted using the adjusted and validated techniques developed in our Round 4 project to generate a library of lesions acquired from multiple CT scanner manufacturers. Inserted lesions will be assessed in the context of texture and morphology. For each case, the quality and location of the added lesions will be verified by experienced radiologists in terms of realism and suitability. This reference dataset will be used to conduct evaluation of quantitative performance across a select series of representative commercial and research software packages for nodule volumetry, texture and morphology analysis. The database will be made publicly available so other groups will be able to benchmark their volumetry, texture and morphology software using a validated reference clinical set without the need for additional image acquisition. We will also explore means to devise a resource to generate dynamic datasets based on a priori statistical definitions thus enabling formation of variable datasets for quantitative conformance and evaluation.
BUDGET (Preliminary)

Research assistant (100%): $32,465
A graduate student from the Duke Medical Physics Program will be recruited for this project.

Tuition remission (100%): $9,870
Required tuition remission per Duke University requirement.

Travel: $0
Funding for national/conference travel to report the results of the study will be provided by other sources.

Misc expenses: $600
Minimal coverage is requested to establish software platforms for Aim 3 (eg, Java-web access, etc)

Total Direct: $42,935

In-directs (59%): $25,332
In-direct costs are calculated based on standard rate at Duke University.

TOTAL FOR THE PROJECT: $68,267

COST SHARING
The Lung Image Database Consortium (LIDC) dataset and the QIBA test-retest cases are available at no cost. The DUMC cases are similarly available as they are captured through other research projects.

Duke will provide PI’s (Ehsan Samei’s) contribution to this project at no cost.

| Institutional Federal contract rates apply (please specify IDC %): | 59.00% |

BUDGET DETAIL
Budget categories might include the following: scanner time, materials, statistical support, data analysis, site visits (to oversee project-specific procedures), salary support: Project PI (minimal %), Research Staff, Graduate Student, Tech, etc.

<table>
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<tbody>
<tr>
<td>Research Assistant (100%)</td>
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<td>Software platform</td>
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Direct project cost: $42,935
Total indirect cost: $25,332

Total project cost, including indirects: $68,267