Quantitative Imaging Initiatives: Why, Who, What, and How?

FDA Qi Initiatives

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Outline of Talk
• Motivation
• Introduction
• FDA data collection
• FDA Qi studies
  – Estimating minimal detectable change
  – Volume estimation of low-contrast lesions
  – Impact of reconstruction slice overlap
  – QIBA Joint Projects:
    • Inter-comparison of lesion sizing techniques
    • Inter-comparison of volume estimation software tools
  – Material characterization using dual-energy CT
• Summary

The FDA Team
• Marios Gavrielides
• Qin Li
• Rongping Zeng
• Berkman Sahiner
• Kyle Myers
• Qi Gong

• Talk today focusing on their research efforts
Project Motivation

- Response to therapy is integral part of patient management
- Imaging is increasingly being used for assessing tumor response
  - Limited by uncertainty in the QI measurement

Why FDA?

- QIBs are growing area of interest
- Drugs (CDER)
  - Qualifying QIB for use in drug trials
- Devices (CDRH)
  - Potential for specific QIB device claims
  - Move towards having meaningful error bars on QI measurements

Project Goal

- Goal
  - Develop a paradigm for assessing specific QI tool and biomarker claims
    - Help facilitate transformation of radiology into a more quantitative science
- Methods
  - Well-controlled anthropomorphic phantom studies
    - Measure effect sizes
    - Identify influential imaging parameters
    - Determine smallest measurable change
Why Phantom studies?

- Allows the collection of large no. of CT scan & repeat CT scans with well-defined characteristics

- Practical
  - FDA doesn’t have direct access to clinical cases

Phase 1: Lung Nodule Sizing

- Investigate sizing of lung nodules using an anthropomorphic thorax phantom

- Acquire CT data across a range of
  - Acquisition parameters
  - Nodule characteristics

Anthropomorphic Thorax Phantom
Synthetic Nodule Characteristics

- Spherical
- Elliptical
- Lobulated
- Mixed density
- Spiculated

Synthetic Nodules

- Sizes: 5-40 mm
- Densities: -630 HU, -10 HU, +100 HU
- Locations:
  - Attached
  - Unattached

Inserting the Nodules
CT of phantom with embedded nodules

CT phantom data collection
- Example Layout: 5 & 8 mm aspherical nodules

CT phantom data collection

Nodule Layout
- Exposure (120 KVp)
- Pitch
- Collimation
- Slice Thickness
- Reconstruction Kernel

Exposure: 20 mAs, 100 mAs, 200 mAs
Pitch: Standard 1.2, High 0.9
Collimation: Med F, Low F
Slice Thickness: 0.75 mm, 1.5 mm, 3.0 mm, 6.0 mm, 10.0 mm, 12.0 mm
Reconstruction Kernel: Detail, Medium, Resin
Public Release of FDA Phantom Data

- The Cancer Imaging Archive (TCIA)
  - http://cancerimagingarchive.net/
  - >1900 series available, 720 additional series in process, more to come
    - Collection: Phantom FDA

Phase 2: Hepatic Lesion Sizing

- Joint QIBA/Columbia/FDA project
  - Lead by Binshehng Zhao, Columbia University

- Investigate sizing of soft tissue lesion using an anthropomorphic abdominal phantom
  - Acquire CT data across a range of
    - Acquisition parameters
    - Lesion characteristics

Semi-anthropomorphic Liver Phantom

- Two liver inserts
  - Arterial phase
    - Liver: 85HU
    - Lesions: up to 120HU
  - Portal venous phase
    - Liver: 110HU
    - Lesions: 45HU - 90HU

- Nodules
  - Spherical
  - Ellipsoid
  - Lobulated

- Data collection
  - Starting in Fall, 2014
**Phase 3: Cardiac Vessel Calcium Scoring**

- Joint FDA/NIH project
- Investigate material characterization using single- and dual-energy CT
  - Joint estimation of cardiac calcium size, density, texture
  - Phantom currently under development

**FDA QI studies**

Sub-project 1
Estimating minimal detectable change in lung nodules with CT

**Purpose**

- To determine the minimum detectable change in CT lung nodule volume
  - As a function of lesion size
- Clinical question
  - How early can true change in nodule volume be detected with CT

*Gavrielides et al., Academic Radiology, 20: 1364-1370, 2013*
Study Design

• Synthetic nodules
  – 4 shapes
  – 4 sizes
    • 5, 8, 9, 10 mm

• Nodules embedded within phantom vascular structure of lung

• Nodules don’t directly touching vasculature

• Image collection protocols
  – Thin slice protocol
    • 0.75-3.0 mm reconstructions
  – Thick slice protocol
    • 2.0-5.0 mm reconstructions
• 10 repeats for each configuration
Study Design

• Estimator
  - Matched-filter algorithm*
  - Minimizing cost between images of target and bank of 3D templates

• Cast determining minimum detectable change as a detection problem
  - Area under the ROC curve (AUC) used as detectability metric
  - Higher AUC => Higher Detectability

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*Gavrielides et al., IEEE-TMI, 29:1795-1807, 2010

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Histograms

- 5→8 mm: Δ = 316%, AUC_{5,8} = 1.0
- 8→9 mm: Δ = 42%, AUC_{8,9} = 0.995
- 9→10 mm: Δ = 37%, AUC_{9,10} = 0.999

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Histograms
CV ($\frac{\sigma}{\mu}$) as function of shifted volume

Results: Increase from baseline

- AUC = 0.95
  - 9 mm: 15%
  - 8 mm: 19%
  - 5 mm: 17%

- AUC = 0.95
  - 9 mm: 17%
  - 8 mm: 19%
  - 5 mm: 46%

Results

- CT imaging can detect small early changes in nodule volumes
  - Across a range of nodule shapes/size
    - Sub-centimeter nodules
    - Across a range of acquisition/recon parameters

- Potential lower bound on achievable performance
  - Expect increase in detectable change in clinical scans
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Sub-project 2
Volume estimation of low-contrast lesions with CT

Purpose

• To study the volume estimation performance for lesions with object-to-background contrast less than 50HU
  – Simulating soft tissue hepatic lesions

• To understand the relationship among performances obtained from phantom study, simulation and theoretical analyses
  – I’ll concentrate on phantom/simulation results

*Li et al., Physics in Medicine and Biology (Submitted), 2014.

Study Design

• Synthetic nodules
  – Spherical lesions

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Diameter</th>
<th>Density</th>
<th>Contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion 1</td>
<td>8 mm</td>
<td>104 HU</td>
<td>31 HU</td>
</tr>
<tr>
<td>Lesion 2</td>
<td>9 mm</td>
<td>118 HU</td>
<td>45 HU</td>
</tr>
<tr>
<td>Lesion 3</td>
<td>9 mm</td>
<td>27 HU</td>
<td>-46 HU</td>
</tr>
</tbody>
</table>
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Study Design

• Background
  – Gelatin-background ~73HU (~soft tissues) in a cylindrical container

• Central slice of Lesions 1-3
  – Air pocket found in Lesion 3 due to production flaw.

• Image collection protocols
  – 10 repeats for each configuration

• Estimator
  – Improved matched-filter algorithm
Analysis

- **Percentage error**
  \[ PE = \frac{|Vol_{Est} - Vol_{True}|}{Vol_{True}} \times 100\% \]

- **Percent Bias**
  \[ PB = PE \]

- **Standard deviation of PE**
  \[ SPE = \text{stddev}(PE) \]

Results: Phantom

<table>
<thead>
<tr>
<th>Exposure</th>
<th>0.8 mm slice protocol ( (PE \pm SPE) )</th>
<th>1.5 mm slice protocol ( (PE \pm SPE) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mAs</td>
<td>Lesion 1: 3.6±5.6 Lesion 2: -0.5±4.4 Lesion 3: 2.1±4.8</td>
<td>Lesion 1: 11.9±5.6 Lesion 2: 11.1±4.8 Lesion 3: 4.6±5.7</td>
</tr>
<tr>
<td>100 mAs</td>
<td>Lesion 1: 4.3±2.4 Lesion 2: 0.3±2.3 Lesion 3: 5.0±2.3</td>
<td>Lesion 1: 5.0±2.3 Lesion 2: 6.8±1.5 Lesion 3: 1.9±1.7</td>
</tr>
</tbody>
</table>

- **Bias:**
  - Generally higher bias for thicker slices
  - Exposure, contrast results, no clear trend

- **Variance**
  - **SPE** falls with increased exposure with a reduction factor of 1.9-3.0
  - **SPEs** falls as contrast increase
  - Slice thickness: no clear trend

Results: Phantom/Simulation Comparison

- Virtual helical CT developed to produce images with properties similar to real scans
- Good agreement found among performances in terms of **SPE**
Summary

- FDA anthropomorphic CT phantom data
  - Range of nodule, acquisition, reconstruction params
  - Useful for understanding source & magnitude of QIB measurement error

- FDA research expected to result in a viable assessment strategy
  - Support evaluation of technical performance of QIB claims
  - Support QIBA profile development and compliance procedures