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

FDA QI Initiatives

Nicholas Petrick
CDRH/OSEL/DIAM
U.S. Food and Drug Administration

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

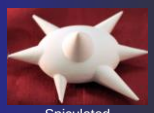
Phase 1: Lung Nodule Sizing

- Investigate sizing of lung nodules using an anthropomorphic thorax phantom
- Acquire CT data across a range of
  - Acquisition parameters
  - Nodule characteristics

Anthropomorphic Thorax Phantom

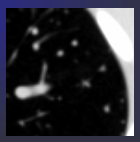
Synthetic Nodule Characteristics

Spherical

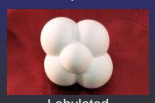


Spiculated

Elliptical



Mixed density



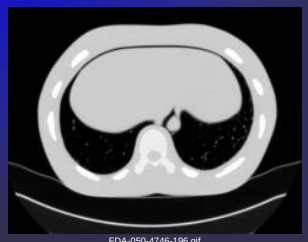
Lobulated

Synthetic Nodules

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

Inserting the Nodules

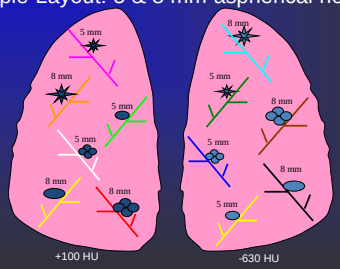
CT of phantom with embedded nodules



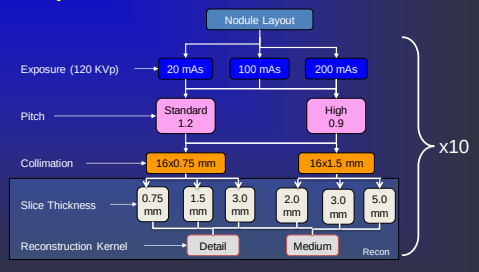
FDA-050-4746-196.gif

CT phantom data collection

- Example Layout: 5 & 8 mm aspherical nodules



CT phantom data collection



Public Release of FDA Phantom Data

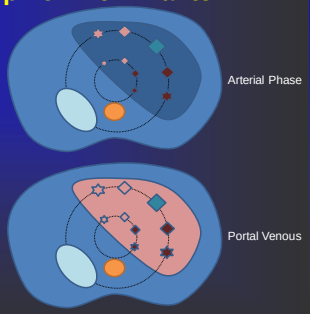
- The Cancer Imaging Archive (TCIA)
  - http://cancerimagingarchive.net/
  - >1900 series available, 720 additional series in process, more to come
    - Collection: Phantom FDA

Phase 2: Hepatic Lesion Sizing

- Joint QIBA/Columbia/FDA project
  - Lead by Binsheng Zhao, Colombia 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: 80HU;
    - 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

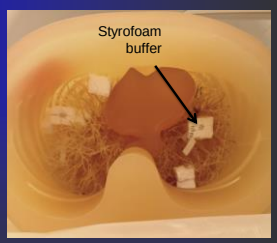
*Gavrielides et al., Academic Radiology, 20: 1364-1370, 2013

Study Design

- Synthetic nodules
  - 4 shapes
  - 4 sizes
    - 5, 8, 9, 10 mm

Study Design

- Nodules embedded within phantom vascular structure of lung
- Nodules don't directly touching vasculature



Study Design

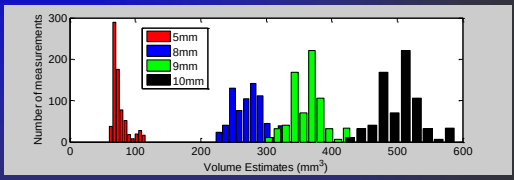
- Image collection protocols
  - Thin slice protocol
    - 0.75-3.0 mm reconstructions
  - Thick slice protocol
    - 2.0-5.0 mm reconstructions
- 10 repeats for each configuration

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

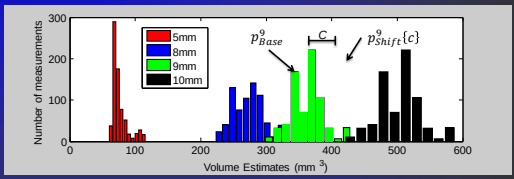
*Gavrielides et al., IEEE-TMI, 29:1795-1807, 2010

Histograms

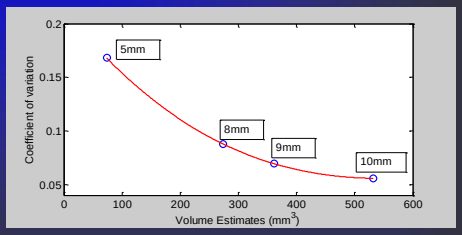


- 5→8 mm: Δ= 316%, $AUC_{5,8}$=1.0
- 8→9 mm: Δ= 42%, $AUC_{8,9}$=0.995
- 9→10 mm: Δ= 37%, $AUC_{9,10}$=0.999

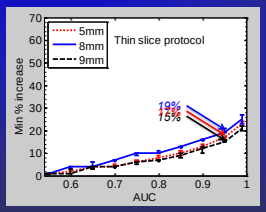
Histograms

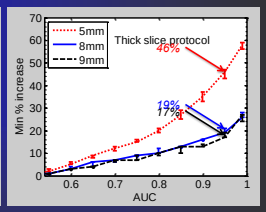


CV $\left(\frac{\sigma}{\mu}\right)$ as function of shifted volume



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

FDA QI studies

Sub-project 2
Volume estimation of low-contrast lesions with CT

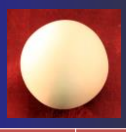
Purpose

- 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

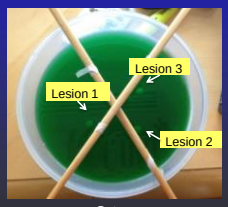
- Synthetic nodules
  - Spherical lesions



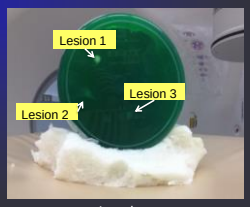
	Lesion 1	Lesion 2	Lesion 3
Diameter	8 mm	9 mm	9 mm
Density	104 HU	118 HU	27 HU
Contrast	31 HU	45 HU	-46 HU

Study Design

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



Setup



Imaging

Study Design

1: 8 mm, 31 HU

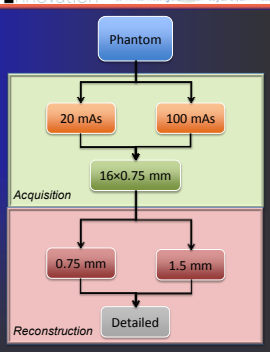
2: 9 mm, 45 HU

3: 9 mm, -46 HU

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

Study Design

- Image collection protocols
  - 10 repeats for each configuration
- Estimator
  - Improved matched-filter algorithm



Analysis

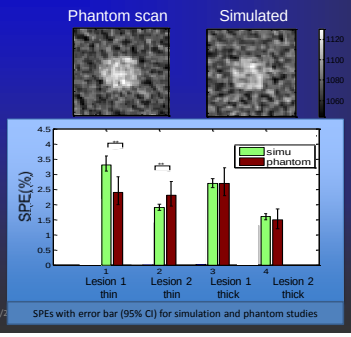
- Percentage error
  - $PE = \frac{Vol_{Est} - Vol_{True}}{Vol_{True}} \times 100\%$
- Percent Bias
  - $PB = \langle PE \rangle$
- Standard deviation of PE
  - $SPE = \mathrm{stdev}(PE)$

Results: Phantom

Exposure	0.8 mm slice protocol (PE ± SPE)			1.5 mm slice protocol (PE ± SPE)		
	Lesion 1	Lesion 2	Lesion 3	Lesion 1	Lesion 2	Lesion 3
20 mAs	3.6±5.6	-0.5±4.4	2.1±4.8	11.9±5.6	11.1±4.8	4.6±5.7
100 mAs	4.3±2.4	0.3±2.3	5.0±2.3	5.0±2.3	6.8±1.5	1.9±1.7

- 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



SPEs with error bar (95% CI) for simulation and phantom studies

- 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