QIBA 1A: Evaluation of nodule sizing by radiologists through CT phantom imaging of synthetic nodules

Nicholas Petrick, Hyun J. Grace Kim, David Clunie,
Kristin Borradaile, Robert Ford, Rongping Zeng,
Marios A. Gavrielides, Michael F. McNitt-Gray,
Charles Fenimore, Z. Q. John Lu, Binsheng Zhao
Andrew J. Buckler

Author Affiliations

Nicholas Petrick[a], Hyun J. Grace Kim[b], David Clunie[c], Kristin Borradaile[c], Robert Ford[d], Rongping Zeng[a], Marios A. Gavrielides[a], Michael F. McNitt-Gray[b], Charles Fenimore[e], Z. Q. John Lu[e], Binsheng Zhao[f] Andrew J. Buckler[g]

[a]Center for Devices and Radiological Health, U.S. Food and Drug Administration
[b]David Geffen School of Medicine at UCLA, Los Angeles, CA
[c]CoreLab Partners, Inc, Princeton, NJ
[d]Princeton Radiology, Princeton, NJ
[e]National Institute of Standards and Technology, Gaithersburg, MD
[f]Department of Radiology, Columbia University Medical Center, New York, NY
[g]Buckler Biomedical LLC, Wenham, MA, USA

Outline

- Objectives
- Study Design
  - Dataset
  - Reading protocol
  - Analysis method
- Results
- Summary
- Ongoing QIBA Projects

QIBA vCT Groundwork

- Quantitative Imaging Biomarker Alliance (QIBA)
  - To investigate the role of quantitative imaging methods as potential biomarkers in evaluating disease and responses to treatment
  - Current Technical Committees
    - Volumetric CT (vCT)
    - COPD CT
    - DCE-MRI
    - fMRI
    - FDG PET-CT

Objectives

- Overall Objected of QIBA vCT Effort
  - To develop groundwork data evaluating quantitative CT tumor sizing methods as imaging biomarkers
    - Clinical Trails
    - Clinical Practice

- Current study is the QIBA vCT Part 1A groundwork effort
  - Objective
    - To estimate bias/variance of radiologists estimating the size of synthetic nodules from CT scans of an anthropomorphic phantom
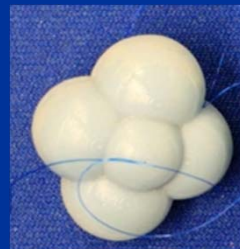
Dataset (Nodules)

- 10 synthetic nodules
  - 5 shapes X 2 densities

- Shape
  (Volume equivalent
  to sphere of given diameter)
  - 10 mm Sphere
  - 20 mm Sphere
  - 20 mm Ellipsoid
  - 10 mm Lobulated
  - 10 mm Spiculated

- Density
  - -10 HU
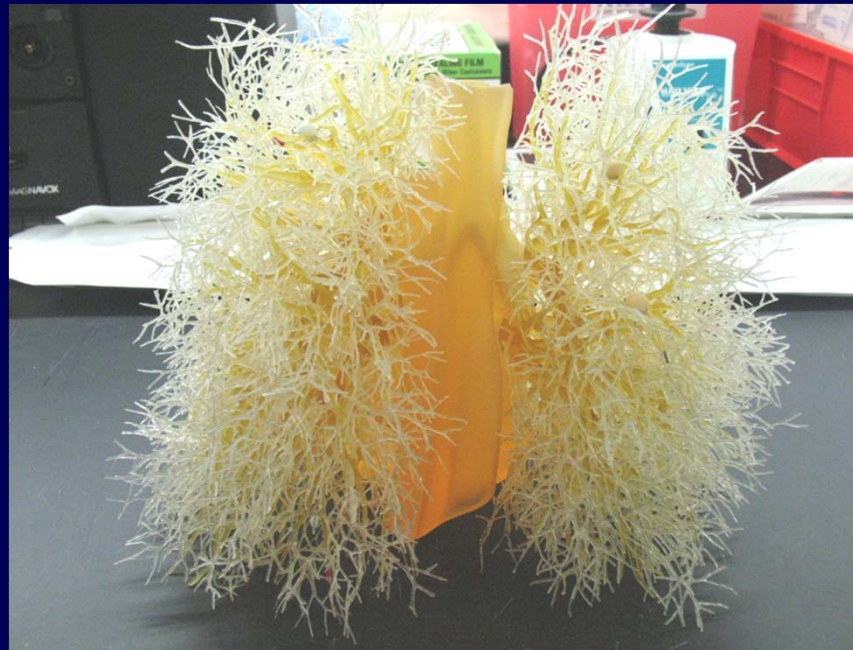 - +100HU

Spherical

Ellipsoid

Lobulated

Spiculated

Dataset (Thorax Phantom)

Anthropomorphic thorax phantom (Kyotokagaku Incorporated, Tokyo, Japan)

Dataset (Nodule Attachment)

- Nodules attached to synthetic vasculature

Dataset (CT Scanning)

- CT Scanner
  - Philips 16-slice MxIDT 8000 scanner

- Acquisition Parameters
  - Exposure (120 kVp): 100 mAs/slice
  - Pitch: 1.2
  - Recon kernel: B60 (Detailed)
  - Slice thickness (50% overlap):
    - 0.8 mm (16X0.75 collimation)
    - 5.0 mm (16X1.5 collimation)
  - Repeat Exposures: 2 scans for each nodule

Dataset

- 40 total dataset for segmentation
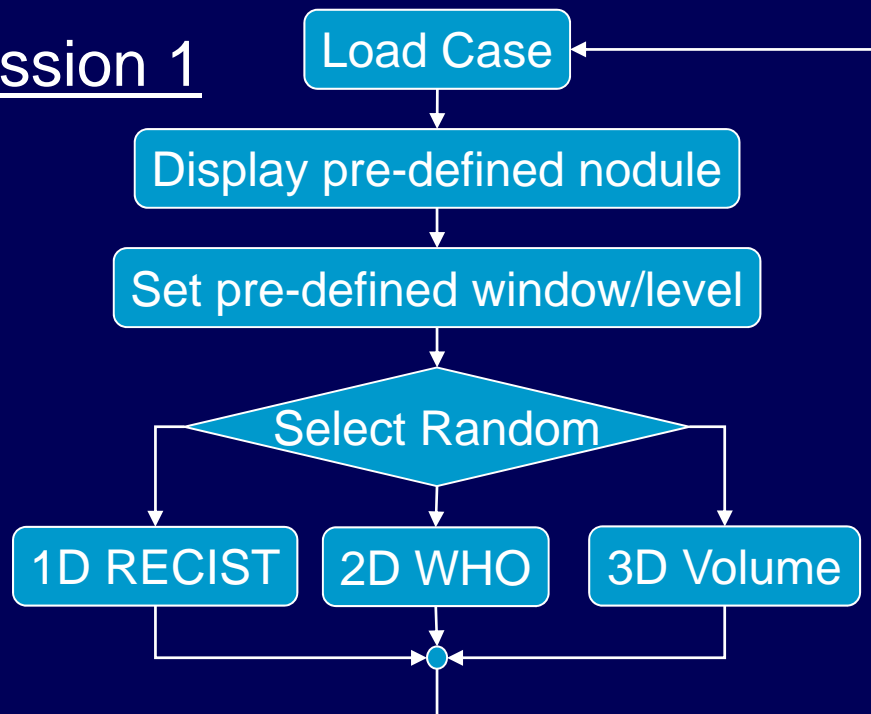 - 10 nodules X 2 slice thickness X 2 repeat scans

Reading Protocol

- Readers
  - 6 radiologists familiar with evaluating lesion response in drug trials

- Sizing Methods
  - 1D technique (linear distance)
    - Largest in-slice diameter for the lesion
    - Based on RECIST criteria
  - 2D technique (area)
    - Largest in-slice diameter for the lesion
    - Largest perpendicular diameter within same slice
    - Based on WHO criteria
  - 3D technique (volume)
    - Semi-automated volumetric measurement tool

Reading Protocol

- Semi-automated 3D lesion sizing
  - Define seed strokes
  - Apply segmentation tool
  - Evaluate quality of segmentation
  - Refine segmentation
    - Adding/subtracting seed strokes only
    - Repeat until satisfactory segmentation achieved

  - Software provided volume estimate

Reading Protocol

Session 1

Load Case

Display pre-defined nodule

Set pre-defined window/level

Select Random

1D RECIST   2D WHO   3D Volume

Session 2

- Same process
- Randomized reading order

Readers applied all 3 sizing techniques within each session

120 measurements per reader per session

Reading Protocol

- All readings session took place at CRO central facility
  - Proprietary software application
  - Consumer color LCD monitors
    - DICOM Grayscale Standard Display Function calibration
    - Lung window/level (1200 HU/-600 HU)

- Each measurement technique was independently applied (readers did not see their previous measurements concurrently)

Analysis

- Compared bias/variability among methods

$$Size_{Rel} = \frac{Size_{Est} - Size_{True}}{Size_{True}} \bullet 100\%$$

$$Bias_{Rel} = Bias(Size_{Rel})$$

$$Std_{Rel} = \frac{Std_{Est}}{Size_{True}}$$

Truth

- 1D
  - Longest diameter (calipers)
- 2D
  - Longest diameter (calipers)
  - Longest perpendicular diameter (calipers)
- 3D (weight-density method)
  - Measured weight (precision scale)
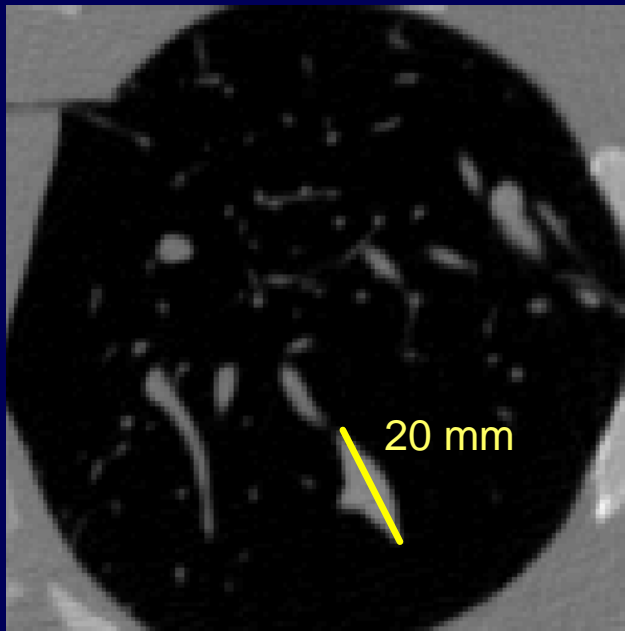 - Density (from manufacturer)

Regression Model

- Mixed-effect linear regression
  - Model relative bias
    - Fixed Effects
      - Nodule shape/size nodule density, slice thickness
    - Random Effect
      - Readers

- Comparison of biases
  - 1D vs. 2D
  - 1D vs. 3D
  - 2D vs. 3D

Example Case

- 10 mm spiculated
  - True longest diameter
    - 22 mm
  - True area
    - 343 mm^2
  - True volume
    - 529 mm^3
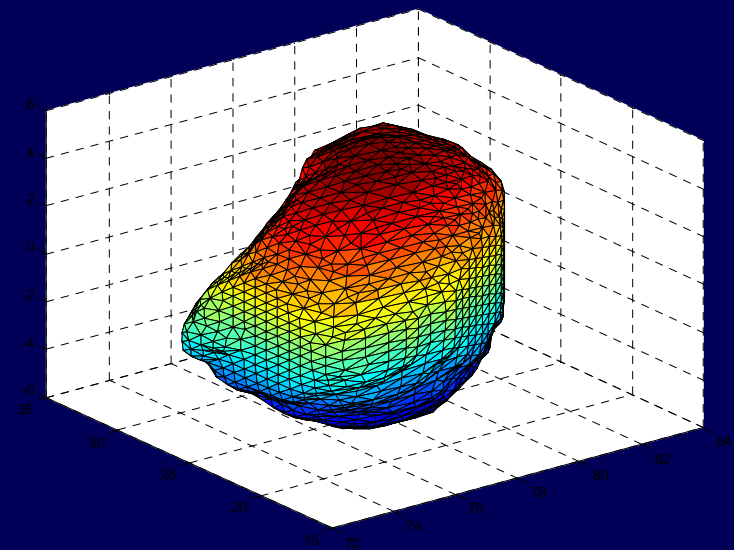
Example Case
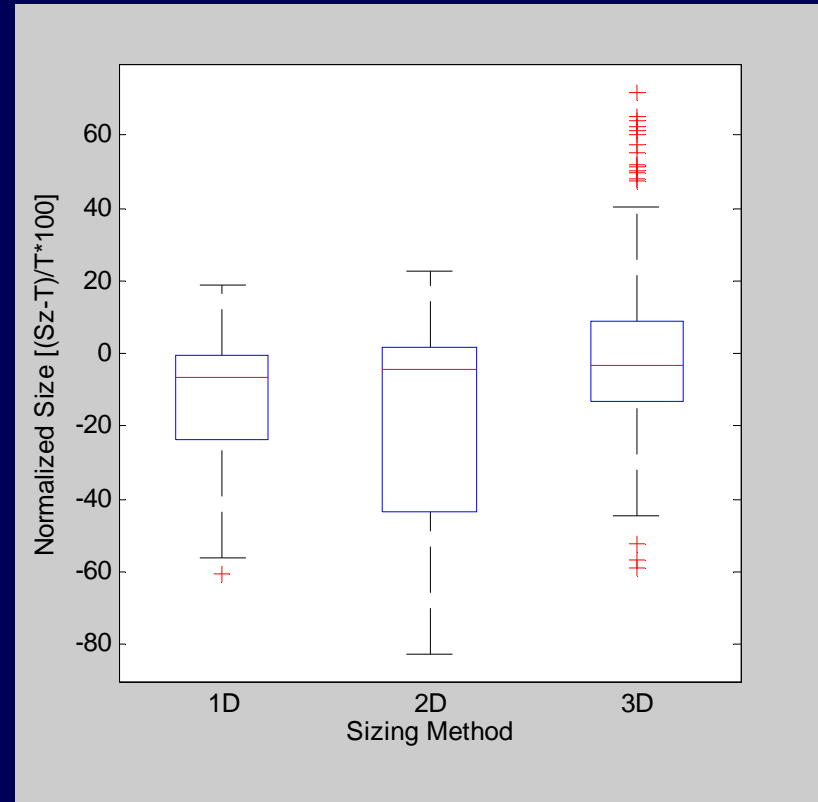

1D Size$_{Rel}$= -9.1%
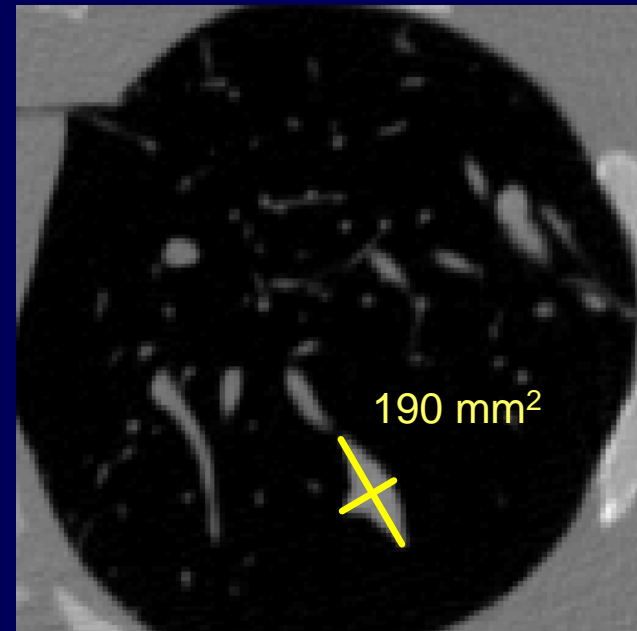
2D Size$_{Rel}$= -44.6%

Example Case

720 mm^3
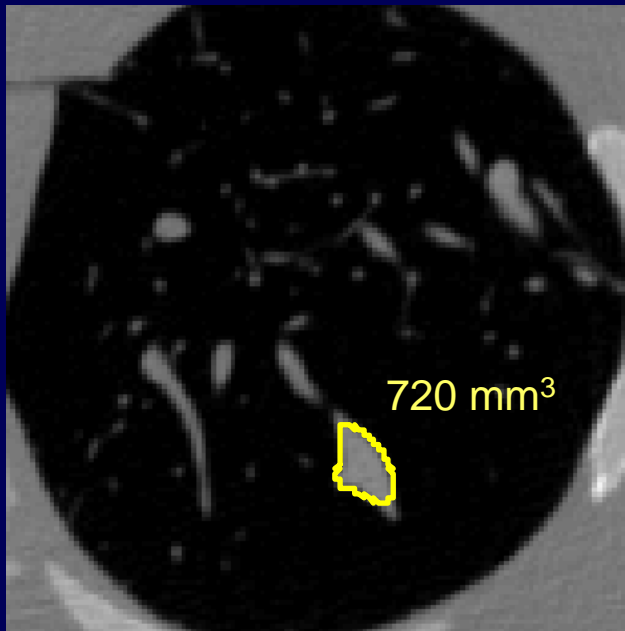
3D In-slice

3D Size$_{Rel}$= +36.1%

Combined Results

Size Method	Relative Bias	Relative Std. Deviation
1D	-14.6%	20.4%
2D	-18.8%	28.3%
3D	-1.3%	21.9%

Comparison of Biases

- 1D vs. 2D
  - -14.6% vs. -18.8%, p<0.001
- 3D vs. 1D
  - -1.3% vs. -14.6%, p<0.001
- 3D vs. 2D
  - -1.3% vs. -18.8%, p<0.001

- **By shape**
  - Spherical
  - Non-spherical
- **And slice thickness**
  - 0.8 mm
  - 5 mm
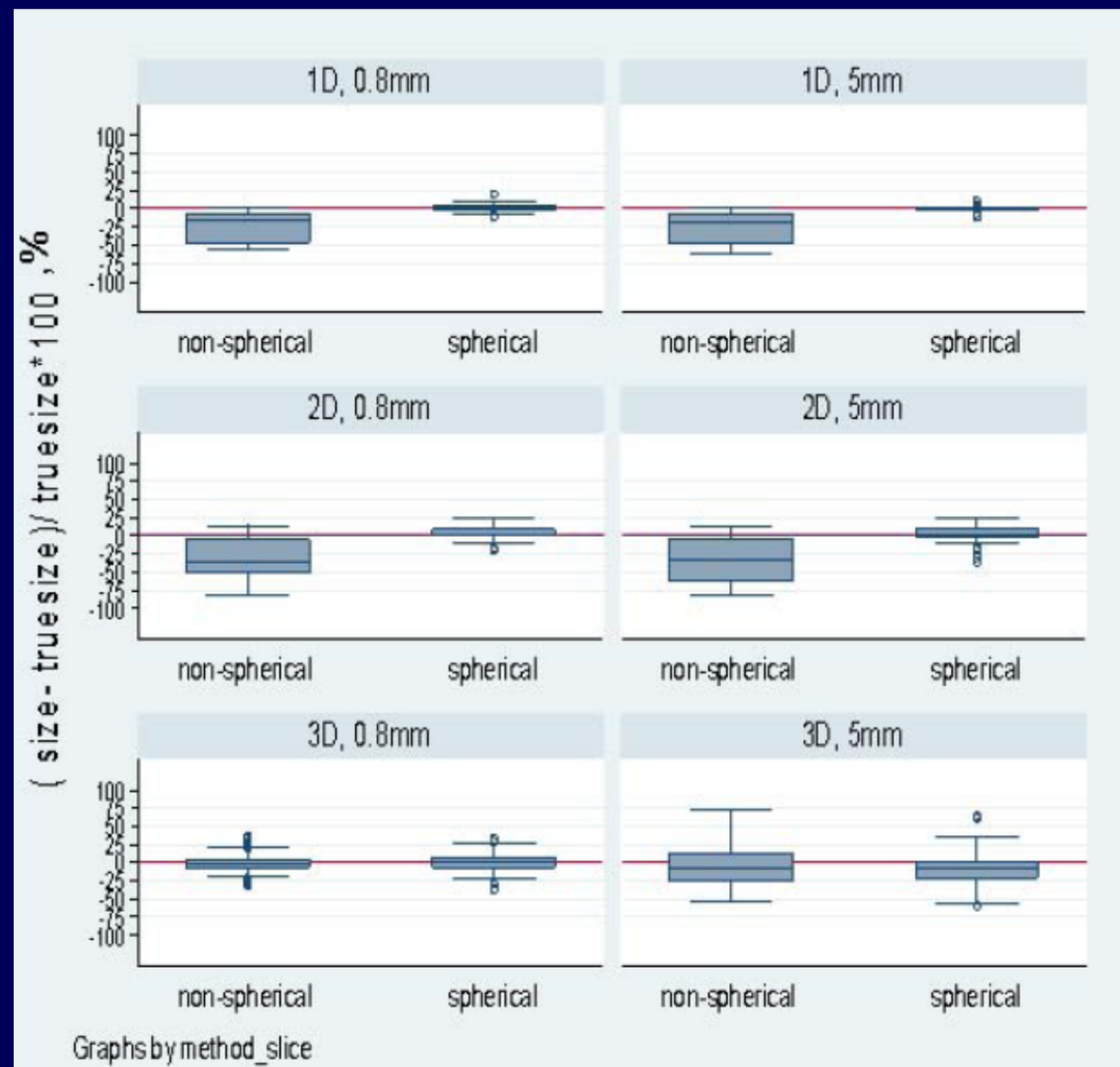
Bias and Variance

Size Method	Spherical Nodules		Non-spherical Nodules	
	0.8 mm	5.0 mm	0.8 mm	5.0 mm
1D	2% (±5)	0% (±4)	-23% (± 20)	-27% (±21)
2D	4% (±10)	0% (±11)	-33% (±26)	-33% (±29)
3D	1% (±12)	5% (±23)	0% (±14)	-2% (±30)

Summary

- 3D volume provides a low bias estimate of nodule volume
  - For spherical and non-spherical nodules

- 1D and 2D low bias only for spherical nodules

- Variance analysis similar relative precision between the 1D & 3D
  - 2D method larger relative standard deviation

- 3D volume at 0.8 mm slices, low bias and low variance
  - Independent of shape

Future Work

- Statistical analysis stratified by nodule and CT acquisition characteristics

- Statistical comparison of precision (variability)
  - Intra- and inter-reader

- Analysis of reader segmentation data
  - STAPLE or similar type of analysis

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