Volumetric CT: Quantifying Responses to Treatment

Quantitative Imaging Biomarkers Alliance — RSNA

Purpose and Aims

Long Term Goal

- Establish 3D Volumetric CT as Surrogate End-Point Biomarker for Tumor Response

Specific Aims

- Develop Methods and Processes for Accurate and Reproducible Measurements of Anatomic Structures and Masses

Stake Holders

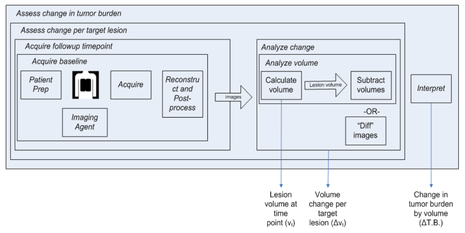
- FDA, NCI, NIST, ACRIN, imaging vendors, software companies, CROs, Extended PhRMA imaging group, and leading academic centers.

Approach

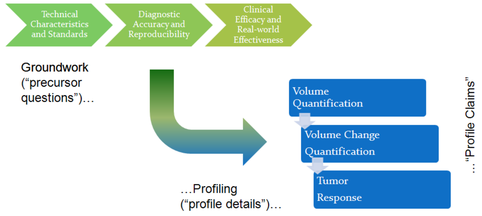
We formed our committee to be:

- Creators of roadmaps
- Stewards of objects and image sets
- Archivists of performance metrics

Formal Definition of the Marker, Identifying Activities and Read-outs



Roadmap of Experimental Activities and Analyses



Reader Study Evaluating Clinician Sizing of Synthetic Lung Nodules

Aim

To compare intra- and inter-reader bias & variability for the task of measuring synthetic lesion size among three lesion sizing techniques

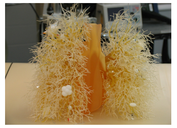
Sizing Technique

- Manual 1-D length
- Manual 2-D area
- Semi-automated 3-D volume

Anthropomorphic Phantom

Thorax phantom

Lung region air pathway insert



Phantom Nodules

- Densities: -10HU, +100HU
- Shapes:
  Spheres: 10, 20 mm diameters
  Lobulated: Vol. of 10 mm sphere
  Spiculated: Vol of 10 mm sphere
  Elliptical: Vol. of 20 mm sphere

CT Acquisitions

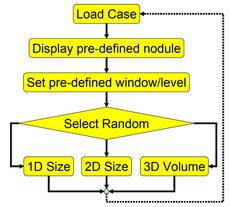
40 CT data sets

- Scanner: Philips, 16-slice
- Exposure: 120 kVp, 100 mAs
- Slice thick: 0.8 mm, 5.0 mm
- Recon kernel: Detailed filter
- Repeats: 2 for each nodule type

Reader Study Design

6 radiologists measured each of the 40 nodules using each sizing technique in each of 2 reading sessions

Reading Session 1



Reading Session 2

- Same reading process as Session 1
- Randomized case reading order
- Randomized sizing technique order

Preliminary Results

Bias and standard deviation of $Sz_{Relative}$ for 1D, 2D and 3D sizing methods across reader, nodules and CT slice thicknesses

$$Sz_{Relative} = \frac{Sz_{Est} - Sz_{True}}{Sz_{True}}$$

Sizing Method	Bias $Sz_{Relative}$	Std. Deviation $Sz_{Relative}$
1D (length)	-14.6%	20.4%
2D (area)	-18.8%	28.3%
3D (volume)	-1.3%	21.9%

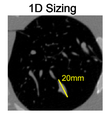
- Bias & standard deviation of $Sz_{Relative}$ for 1D, 2D and 3D sizing methods across reader and 0.8 mm slices for 10mm,+100HU spiculated nodule

Sizing Method	Bias $Sz_{Relative}$	Std. Deviation $Sz_{Relative}$
1D (length)	-14.9%	6.9%
2D (area)	-50.1%	7.2%
3D (volume)	+7.7%	15.8%

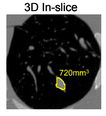
Sizing Example: Reader 1, 10mm,+100HU spiculated nodule

10 mm Spiculated Nodule
Truth: 22 mm, 343 mm², 529 mm³

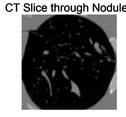
1D Sizing



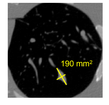
3D In-slice



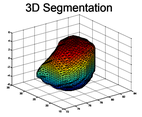
CT Slice through Nodule



2D Sizing



3D Segmentation



Patient Datasets for Comparing Nodule Sizing Methods

Aims

1. Investigate the minimum detectable level of change in patient datasets acquired under a "No Change" condition
2. Investigate variance of both readers and algorithm-assisted readers in measuring volumes, diameters and bi-directional diameters using patient datasets

Methods

Patient Datasets - MSKCC RIDER Coffee Break Experiment

- 32 NSCLC Patients
- Scanned twice over a period < 15 minutes (No Change)
- Same low dose acquisition for both scans, 1.25 mm slice thickness

Measurements (6 total)

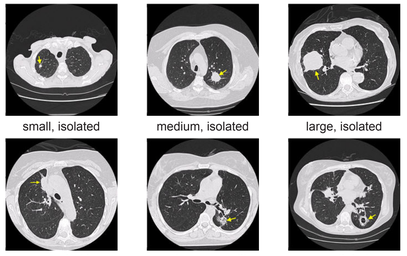
- Manual 1-D length
- Manual 2-D area (and derive 1-D length)
- Semi-automated 3-D volume (and derive 1-D length and 2-D area)
- Perform all measurements on both Scan 1 and Scan 2
- To obtain intra-reader variation, perform repeat measurements on Scan 1

Planned Analyses

- Variability between different measures (e.g. Volume vs. Diameter)
- Intra and inter-reader variation

Sample Images of Lesions to be Measured

- Size range is from 8 to 88 mm
- Shapes range from simple and isolated to complex and cavitated



small, isolated | medium, isolated | large, isolated
connected to mediastinum | complex composition | cavitated

Reader Study Design

- 5 radiologists measured each of the 32 lesions using each sizing technique in each of 3 reading sessions
- Each Reading Session followed reading study procedures similar to Reader Study Using Synthetic Nodules (See Diagram)

Reading Session 1

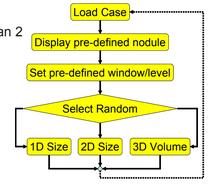
- Randomized case reading order
- For each case, assign either Scan 1 or Scan 2
- Randomized sizing technique order

Reading Session 2

- Randomized case reading order
- For each case, read remaining Scan
  - If Session 1 read Scan 1, then read Scan 2
  - Otherwise, read Scan 1
- Randomized sizing technique order

Reading Session 3

- Randomized case reading order
- For each case, read same scan assigned in Session 1
- Randomized sizing technique order



Current Status

- Reading Study Complete
- Currently in Data Analysis Phase
- Expected Completion 2nd Qtr 2011

Multi-scanner Imaging to Evaluate Sizing of Nodules in an Anthropomorphic Phantom

Aims

1. Develop and apply a CT imaging protocol based on quality measurement applicable to multiple CT imaging vendors.
2. Investigate the sources of error in reader measurements of volumes, diameters and bi-directional diameters of phantom nodules in the multi-scanner image set.

Method for image acquisition

1. **Develop and apply the Two Branches of the Imaging Protocol**
   - ACRIN Study (6678)
   - Develop quality-based protocol. Aim is constant image quality across scanners
2. **Image anthropomorphic phantom at five imaging sites**
   - 5 sites with 5 scanners from 4 manufacturers
   - Phantom to have 8 nodules with spherical, lobulated and spiculated shapes.
3. **CORE lab to Measure:** semi-automated 3-D volume & derived 1- & 2-D sizing
4. **Planned Analysis:** Variability between scanners, the different sizing measures and other factors. Intra and inter-reader variation.

Imaging Protocol

Branch 1: Current practice, based on ACRIN 6678

"FDG-PET/CT as Predictive Marker of Tumor Response and Patient"

Quality Control Parameters for CT Scan Tumor Volumetric Measurements

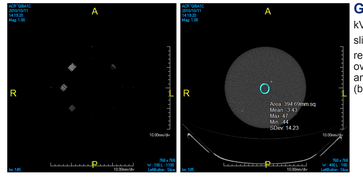
DICOM Tag#	Parameter	GE VCT 64	Philips Brilliance 16	Philips Brilliance 64	Siemens Sensation 64	Toshiba Aquilion
0018,0050	Slice Width	0.75 – 1.25 mm	0.75 – 1.25 mm	0.75 – 1.25 mm	0.75 – 1.25 mm	0.75 – 1.25 mm
0020,1041	Reconstruction Interval	0 – 20 % overlap	0 – 20 % overlap	0 – 20 % overlap	0 – 20 % overlap	0 – 20 % overlap
0028,0030	Voxel Size	0.55 – 0.75 mm	0.55 – 0.75 mm	0.55 – 0.75 mm	0.55 – 0.75 mm	0.55 – 0.75 mm
	Motion/Breathing Artifact	none	none	none	none	none
Scanner Dependent	mAs	X-ray Tube Current x Exposure time 95 - 245	Exposure 120-310	Exposure 120-310	Exposure 120-310	X-ray Tube Current x Exposure time 120-310
0018,0060	kVp	120	120	120	120	120
0018,1210	Reconstruction Algorithm	STD	B	B	B30	FC10

Branch 2: Image Quality/Performance-Based Branch Aim

Constant image quality across scanners, use ACR CT Accreditation Phantom

Required performance measured on ACR CT phantom

- Vary recon kernel to achieve target resolution of 6 lp/cm (and < 7 lp/cm) on the resolution section.
- Vary mAs to get noise = 17 +/- 1 HU (sd in center of water-equivalent section)



Guidance

kVp - 120 kVp
slice thickness - 1.0 mm
recon interval, 0% overlap, rotation time and pitch for 15 s scan (breath hold)

Markup

Adapt reading process of QIBA vCT 1-A/B.

- Determine volume with semi-automated tools, derive RECIST (1D), WHO (2D)
- 3 readers
- Repeat reads for each nodules
- Randomized case reading order

Current Status

- Currently defining quality imaging protocol with measurements of ACR phantom
- Scheduling imaging of anthropomorphic phantom
- Expected Completion 4th Qtr 2011

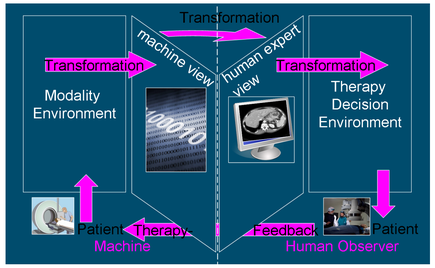
Tying Together the Meta-Analysis of Phantom Studies For Expanding to Multiple Algorithm Types

The Problem Statement

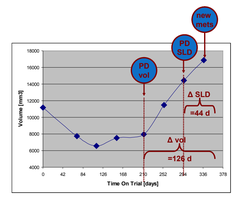
Although we have some knowledge gained of some phantom studies for the evaluation of image analysis algorithms

- We don't have a standard workflow or procedure for the evaluation of image analysis algorithms using phantom image data and
- We don't have metrics for the evaluation of volumetric image analysis algorithms using phantom image data for calculations of the
  - Absolute volume
  - Volume changes

Quantification in Imaging Applications The Solution Space – a loopBranch 1:



QIBA has started to show how volumetric image analysis can have an impact on individual patient care in some settings



Unique value is defined as difference between PD based on new lesions versus SLD versus VIA:

SLD = 44 d

vol = 82 d

Now we are working towards proving value in "real world" conditions

- We are extending prior quantitative imaging research to build statistical power across a fuller range of medical settings which better represent all of the major device manufacturers and many image analysis software companies.
- We are working on how to quantify early treatment-induced changes on medical images that predict long-term health outcomes.
- We are collaborating with patient advocates and regulatory authorities on processes for qualifying volumetric image analysis in specific contexts.
- We are forming alliances with image device manufacturers and instrumentation innovators to harmonize the output.
- We are engaging radiologists and clinical imaging scientists to create consensus around best practices.