Improving CT Lung Cancer Screening Through Calibration Phantom and Software Innovations

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Late-Stage Lung Cancer
(1.76 Million Deaths/Year)

~5% five year survival

Early Lung Cancer

5mm Squamous Cell Carcinoma

~85% five year survival

[R. Gottlieb, Roswell Park Cancer Institute]

[Dr. Javier Zulueta, University of Navarra]
Small Lung Nodule Measurement

For a 6.0 x 3.6 x 3.6 mm Lung Nodule:

We are working with axial CT images with a maximum nodule diameter of between 6 and 9 pixels.

<table>
<thead>
<tr>
<th>Nodule Diameter</th>
<th>Diameter Change %</th>
<th>Volume Change %</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.0</td>
<td>17%</td>
<td>59%</td>
</tr>
<tr>
<td>7.0</td>
<td>14%</td>
<td>49%</td>
</tr>
<tr>
<td>8.0</td>
<td>13%</td>
<td>42%</td>
</tr>
<tr>
<td>9.0</td>
<td>11%</td>
<td>37%</td>
</tr>
<tr>
<td>10.0</td>
<td>10%</td>
<td>33%</td>
</tr>
</tbody>
</table>

Numerous CT Image Quality Issues Can Bias This Measurement

Use of Precise and Quality Controlled Quantitative Image Measurement Tools Is Critical

If This Is TRULY a +1.0 mm Max Diameter Increase Over 6 Months, This Is a > 250% Volume Increase Over A Year (640% for 3m)
Slice Thickness In X, Y, and Z
Quality of Lung Nodule Measurements: What Have We Learned Over The Last 15 years?

- While studies have shown great results, major quality issues persist & impact small (6-10mm) lung nodule measurements:
  - CT Image quality can greatly degrade in the periphery
  - 3D spatial warping can give the appearance of +- 40% Δ
  - Some recon kernels can bias HU values by > 50 HU
  - Lowering dose can result in resolution losses of > 200%
  - Many institutions continue to use thick slices
  - Difficult to determine if a segmentation is “good enough”
  - ...

- CT imaging technology is constantly changing
  - Scanner geometries and detectors
  - “Standard” reconstruction kernels
  - Iterative reconstruction algorithms
  - New AI-based measurement methods
  - Measurement equipment is being replaced/repaired and protocols are changing across lung nodule follow-ups
  - ...

We need to constantly measure and monitor CT detection and measurement equipment
2010: Roche ABIGAIL Study

Model A
Site 1

Model A
Site 2

[Henschke, … Avila, J Med Imaging 2016]
Clinical Biopsy Case
Table Phantom Scanning On a 16 Slice

Step & Shoot Acquisition

Helical Acquisition
CT Scanner Spatial Warping

- CT spatial warping was 1st reported at meetings in 2011.
- It took > 3 years to publish spatial warping results observed on multiple scanners from a phase II clinical trial (JMI 2016).
- Numerous presentations by me and others every year from 2011 – 2021 have described this problem.
- Yet, even today in 2021:
  - FDA approves these CT scanners for lung screening.
  - AAPM provides screening protocols for these scanners.
  - No mention of these model scanners in numerous lung screening guidelines.
  - Numerous medical physicists continue to deny this is real.

- So after > 10 years of studying and reporting on this it is long past time for the community to accept that this major CT image quality problem happened and that global CT image quality monitoring needs to be updated and running continuously so image quality lapses of this magnitude never happen again.
CTLX1 Phantom
The 1st Phantom To Build A 3D Math Model Across The Full Scanner FOV

- **Fundamental CT Image Properties**
  - **3D Resolution:**
    - 3D PSF Ellipsoid Volume $\leq 1.5\text{mm}^3$
  - **3D Resolution Aspect:**
    - PSF $Z/X \leq 2.0$
  - **Linearity Bias:**
    - Air and Acrylic Bias $< 35\text{ HU}$
  - **Image Noise:**
    - Acrylic Noise $\leq 50\text{ HU SD}$
  - **Kernel Edge Enhancement:**
    - Air to Delrin Enhancement $\leq 5\%$
  - **3D Spatial Warping:**
    - Delrin Cylinder RMSE $\leq 0.3\text{ mm}$

- **Lung Nodule Volume Change Performance**
  - Verifies That Image Quality Meets or Exceeds The QIBA CT Lung Nodule Profile Volume Change Measurement Recommendations
CT Image Quality Verification
Using Cloud-Based Computing Services

- Upload
- Check Each Time Scanner or Protocol Changes and Once Per Year
- Guidance: Webpages & FAQs

http://accumetra.com

Optimize
We Build 3D Mathematical Models of CT Scanners With An Emphasis On 3D Resolution

3D Gaussian PSF along with 3D sampling rate represents the resolution of the system
### Ellipsoid Scanning Simulation

<table>
<thead>
<tr>
<th>Simulated Object</th>
<th>Object Contrast</th>
<th>Object Position</th>
<th>Object Orientation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>215 HU</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Object Size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.0 mm x</td>
<td>6.0 mm x</td>
<td>8.0 mm x</td>
<td>10.0 mm x</td>
</tr>
<tr>
<td>3.0 mm x</td>
<td>4.5 mm x</td>
<td>6.0 mm x</td>
<td>7.50 mm x</td>
</tr>
<tr>
<td>2.25 mm</td>
<td>3.375 mm</td>
<td>4.50 mm</td>
<td>5.625 mm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6.75 mm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Simulated Scanner</th>
<th>CT Linearity</th>
<th>Resolution (PSF $\sigma$)</th>
<th>Sampling Rate</th>
<th>Noise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Perfect</td>
<td>0.798 x 0.798 x 0.697</td>
<td>0.89 x 0.89 x 1.25</td>
<td>40 HU SD</td>
</tr>
</tbody>
</table>

| Simulated Images | |
|------------------| |
| ![Image 1]        | ![Image 2] |
| ![Image 3]        | ![Image 4] |
| ![Image 5]        | ![Image 6] |
CT Image Quality:
Where Do You Want To Operate When Tracking a Nodule?

<table>
<thead>
<tr>
<th>Next Gen Scanner</th>
<th>Best Global</th>
<th>Avg SLN Passing</th>
<th>Max SLN Limit</th>
</tr>
</thead>
</table>

![CT Images](image_url)
Supporting Studies

• Volumetric Performance in a Phase II Lung Cancer Clinical Trial (N=20 sites)

• Anthropomorphic Phantom Prediction Study, SPIE 2017

• Clinical Small Lung Nodule Prediction Results

• 2016-2017 International Performance Study (N=27+ CT scanners)

• 2018-2019 International Performance Study (N=85+ CT scanners)
Problem: There is NO Accepted Standard For Measuring CT Resolution
CT Image Quality Properties Over Time (1.5 Years)  
Fully Automated Analysis of Phantom Data: Scanner 1

- **3D Resolution**
- **3D Resolution Aspect Ratio**
- **Image Noise (Acrylic)**

- **Edge Enhancement %**
- **HU Bias (Air & Acrylic)**
- **3D Spatial Warping**
CTLX1 Phantom Distribution

115 New CTLX1/2 Phantoms Distributed As Of 10/26/2021
Many Thanks to The Prevent Cancer Foundation

Countries And Major Organizations Are Adopting The CTLX1/CTLX2 Phantom
CTLX1 In Use Throughout The World

Accumetra IQ Phantom

- Potential context of use
  - Image quality assessment of CT system for lung cancer screening

Curtesy Rick Avila, Accumetra

Accumetra CTLX1 phantom

- Three modules placed at 0mm, 102mm, and 204mm from isocentre
- Each module is hollow cylinder of Delrin
- Air region inside and outside cylinder
- Teflon cylinder and Acrylic cylinder above and below Delrin respectively

Leeds is first site in the world to use this phantom on a mobile CT scanner
The New CTLX2 Phantom

Better Supports Radiation Dose vs Image Quality Studies

The CTLX2 will have an access port to insert “manufactured” nodules.

This nodule module has 6 6.0 x 3.6 x 3.6 nodules and 6 10.0 x 6.0 x 6.0 nodules.

Phantom weighs around 9 Kg or 20 lbs when filled with water, providing guidance on image quality when scanning a large patient.

This helps sites better determine small lung nodule CT image quality when Auto mA is enabled and also when lowering dose.

With the CTLX2 we are now seeing a lot more CT image quality problems (e.g. HU biases).
Table 1: Recommended reconstruction kernels for quantitative CT COVID-19 applications.

<table>
<thead>
<tr>
<th>CT Scanner Manufacturer</th>
<th>Models</th>
<th>Recommended Reconstruction Kernels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canon/Toshiba</td>
<td>All</td>
<td>FC05</td>
</tr>
<tr>
<td>General Electric</td>
<td>All</td>
<td>STANDARD</td>
</tr>
<tr>
<td>Philips</td>
<td>All</td>
<td>F, L</td>
</tr>
<tr>
<td>Siemens</td>
<td>All</td>
<td>Br40</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td>B40, I40</td>
</tr>
</tbody>
</table>

We Are Preparing Similar Guidance For Combined CT Lung Screening and COPD Imaging
Nodule Diameter Growth

What can we say if we use great CT imaging of a ~6mm nodule at baseline and again after 90 days?
Optimizing Radiation Dose and Resolution

Scanner A: 3D Resolution vs Iso-Center Distance

Scanner A: Noise vs Iso-Center Distance

Scanner B: 3D Resolution vs Iso-Center Distance

Scanner B: Noise vs Iso-Center Distance
• The CTLX1S Contains 80 Acrylic Ellipsoids Ranging In Size From 6mm To 10mm
• Scanning And Measurement Using Two Software Systems Revealed High Bias
Using Different CT Scanners To Follow-up

- T1
- Δ
- T1 + 90 days

Resolution vs Iso-Center Distance

Noise vs Iso-Center Distance
Machine learning / deep learning will increasingly be used throughout the CT image acquisition pipeline.

View Data Acquisition -> Reconstruction -> Post processing Filters

Not every innovation change will be for the better.

The potential for major problems occurring is high. Particularly with challenging detection and measurement applications (e.g. assessing small lung nodule growth rates).

A Global Image Quality Safety Net Is As Important As Ever
Summary

• **Global Network**: A new low cost CT calibration phantom (CTLX1, CTLX2) is being used by a globally network (N=115) to quickly verify CT image quality. It monitors, optimizes, and shares crowd-sourced protocols for lung cancer screening (+COPD is next).

• **3D Mathematical Models**: We create 3D math models of the scanner/protocol image formation process across the full 3D scanner field of view. Global sites can now easily & accurately assess the 3D performance of a CT scanner (highly useful and disruptive).

• **Clinical Application Performance Prediction**: The 3D math models are used with simulation software to directly predict performance for a wide range of applications.

• **CT Image Quality Clinical Uses**: Potential clinical uses include:
  – Setting more precise lung cancer screening follow-up times
  – Nodule volume growth/doubling time estimation tools that consider volumetric error
  – Optimizing both radiation dose and CT image quality for nodule detection and measurement
  – Enabling sites to use different, but calibrated, CT scanners and protocols for follow-up scans
  – Establishing and updating image acquisition recommendations in real-time
  – Maintaining a global safety net for catching issues when deploying new CT innovations (AI)

• **CT Image Resolution**: Preliminary data analysis indicates that CTLX1 results are both accurate and reproducible. But NO accepted 3D CT resolution standards exist to compare against!!
Thank You