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# Case Studies of Imaging Biomarkers - Description and requirements for standardized acquisition in multi-center trials: DCE-MRI, Volumetric CT, FDG-PET/CT

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# Organizations involved in Quantitative Imaging

- AAPM: American Assoc of Physicist in Medicine
- ACRIN: American College of Radiology Imaging Network
- ADNI: Alzheimer's Disease Neuroimaging Initiative
- CALGB: Cancer and Leukemia Group B
  - Imaging Committee and Imaging Core Lab
- CTSA: Clinical and Translational Science Award
- EORTC: European Organization for Research and Treatment of Cancer
- ISMRM: International Society for Magnetic Resonance in Medicine

# Organizations involved in Quantitative Imaging

- NCI CIP: National Cancer Institute Cancer Imaging Program
  - IRAT: Imaging Response Assessment Teams
  - RIDER: Reference Image Database to Evaluate Response
  - PAR-08-225: Quantitative Imaging for Evaluation of Responses to Cancer Therapies (U01)
  - OBQI: Oncology Biomarker Qualification Initiative
- NIST: National Institute of Standards and Technology
- RSNA QIBA: Radiological Society of North America - Quantitative Imaging Biomarker Alliance
- SNM CTN: Society of Nuclear Medicine Clinical Trials Network

# Requirements for CT Standardization

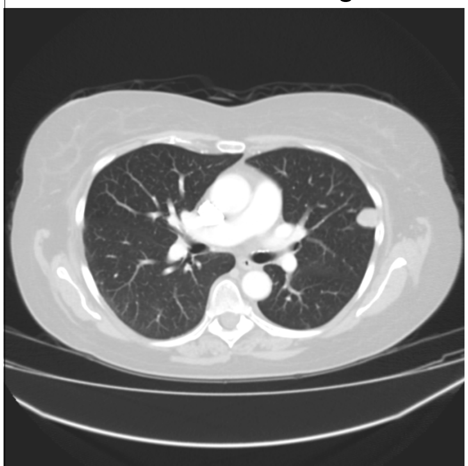
- Patient preparation (oral contrast, positioning, breathing protocol)
- IV Contrast (dose, rate, timing)
- Acquisition parameters (collimation, tube current, tube voltage, rotation speed, pitch)
- Reconstruction parameters (slice thickness/separation, window/filtering, FOV)

# CT automatic tube current modulation

- Benefit
  - Optimizes image quality for a given patient dose
  - Accounts for differences in patient size and shape
- Challenges
  - Proprietary modulation algorithms and parameter settings
  - Patient dose is difficult to predict before the scan
  - Intra-patient variability over time has not been studied
  - Difficult to standardize across sites

# Thin-slice CT Reconstruction

5 mm Axial Image

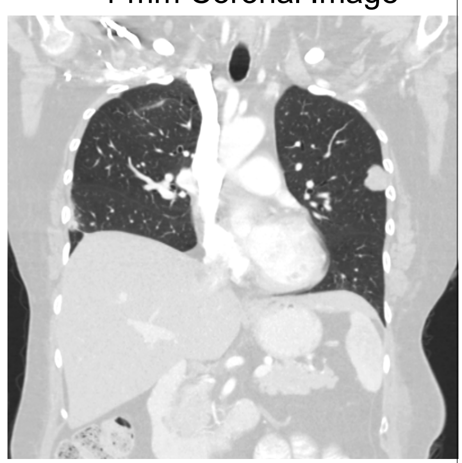


1 mm Axial Image

# Thin-slice CT Reconstruction

5 mm Coronal Image

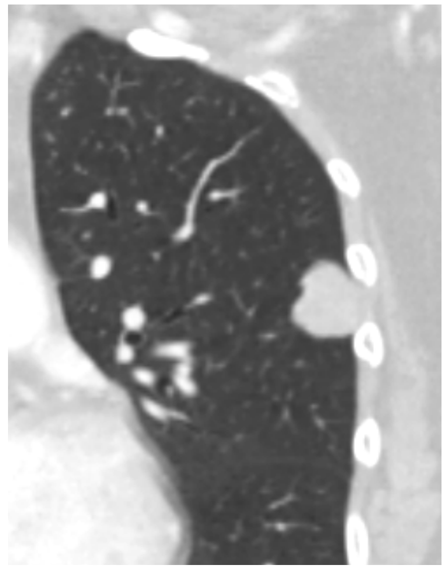
1 mm Coronal Image



# Thin-slice CT Reconstruction

5 mm Coronal Image

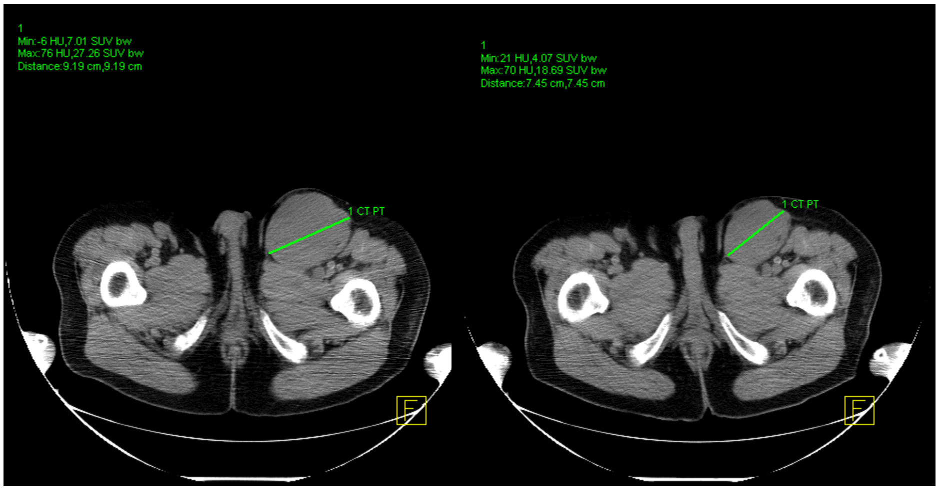
1 mm Coronal Image



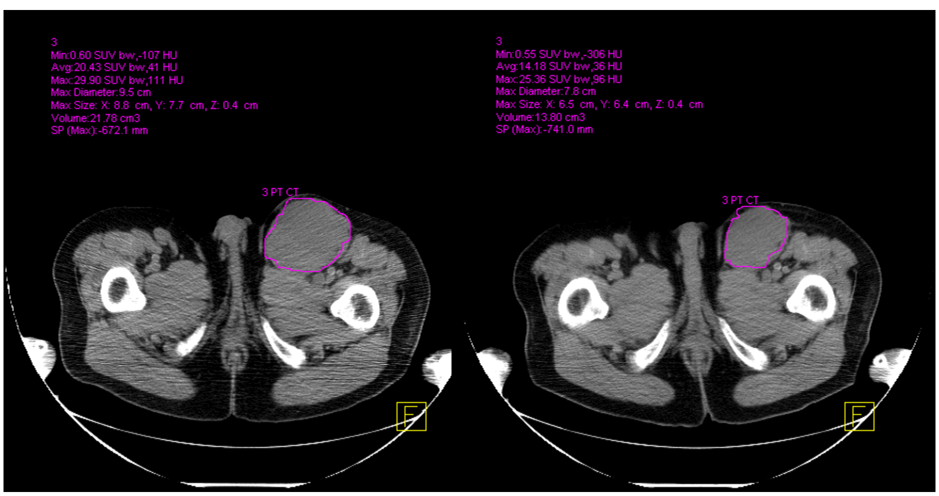
# Thin-Slice Reconstruction

- Advantages
  - Improves image quality (isotropic resolution)
  - Improves CAD, segmentation, volumetric quantification
- Challenges
  - May require greater dose
  - Larger data to archive
  - Overwhelming number of slices to review
  - Requirements for dictation
  - Use in clinical trials requires knowledge of potential subject prior to baseline scan

## Uni-dimensional Measurement
## Change in longest diameter = -19%




## Volumetric Measurement
## Change in volume = -37%

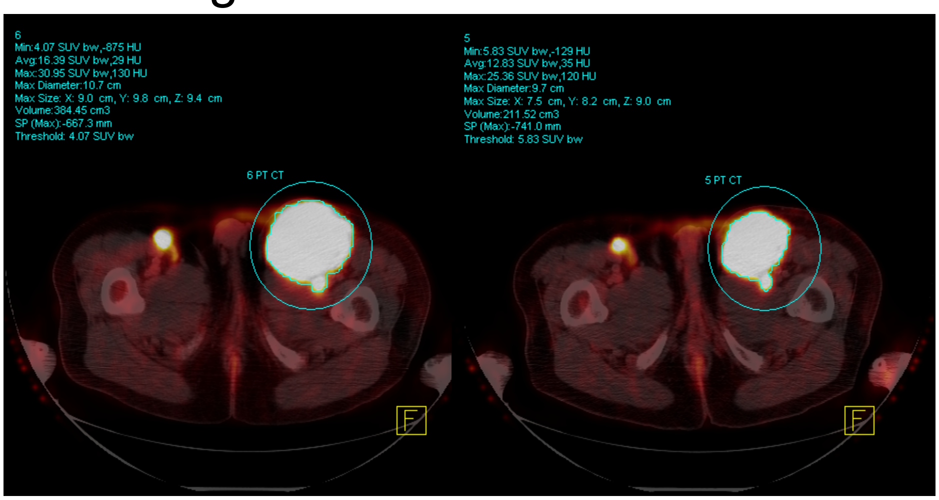


# PET SUV Quantification

$$\text{SUV (time)} = \frac{\text{Radioactive Concentration x Weight}}{\text{Injected Activity}}$$

- $^{18}$FDG SUV correlates with metabolic rate of glucose and/or the number of viable tumor cells
- Simplified semi-quantitative measure that can be routinely performed in clinical PET studies
- Adjusts for differences in patient size and injected activity

# Change in PET SUVmax = -18%



# $^{18}$FDG-PET Standardization

- EORTC (Young et al, EJNM 1999)
- NCI Consensus Recommendations (Shankar et al, JNM 2007)
- IRAT practice surveys and protocols
- Netherlands protocol (Boellard, JNM 2009)
- ACRIN: FDG-PET SOPs and biomarker qualification trial (6678)
- CTSA/UPICT: Protocol template
- VIEW Consortium: (ACRIN, CALGB)
- RNSA QIBA: FDG-PET sub-committees
- AAPM: FDG-PET in radiation oncology

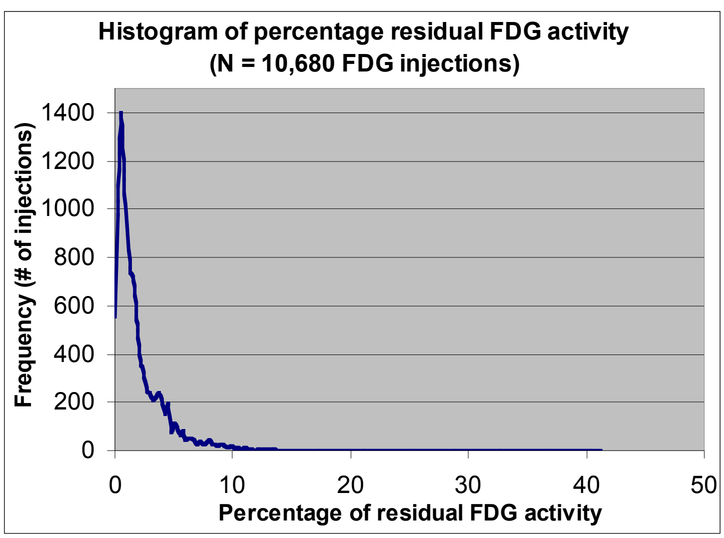
# Hardware/Software Requirements for Accurate SUV Quantification

- Dose calibrator accuracy – traceable standard
- Scanner normalization (detector efficiency)
- Scanner calibration
- PET corrections: attenuation, scatter, randoms, decay (images and doses)
- Partial volume correction for small objects
- Appropriate reconstruction algorithm
- Daily/weekly/monthly scanner QC

## Requirements for Reproducible SUV Quantification

- PET technique: $^{18}$FDG dose, $^{18}$FDG uptake period, emission scan length, scanning range, scanning direction (e.g. head to toe)
- Patient preparation: fasting, resting, medication
- Reconstruction parameters: slice thickness, filters
- Region-of-interest definition methods (mostly manual or semi-automated)
- Consistency is the most important factor!

## Potential error due to residual activity



# ADNI

- ADNI Imaging Goals:

1) Link all data at each time point and share data with public
2) Develop technical standards for imaging in longitudinal studies
3) Optimize acquisition and analysis
4) Validate imaging and biomarker data with psychometric and clinical assessments
5) Improve clinical trial methods

-from The Alzheimer's Disease Neuroimaging Initiative (ADNI): MRI Methods. Jack CR et al. JMRI 27:685-691 (2008).

# ADNI – Biomarkers for AD

- Alzheimer's Disease Neuroimaging Initiative

A longitudinal multisite study of elderly people with either mild cognitive impairment (MCI, N=400), Alzheimer's Disease (AD, N=200) or normal cognition (N=200).

Data was collected at 55 sites.

Half of the subjects were imaged using FDG positron emission tomography (PET). All were imaged using MRI on a 1.5T scanner with a structural imaging protocol.

# ADNI – Technical Issues

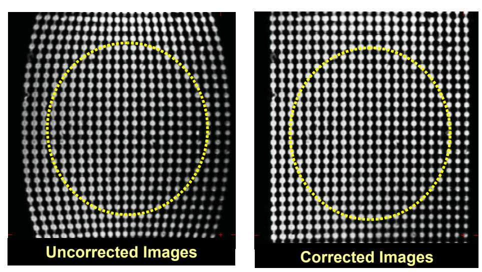
- While humans can make sense of images with minor artifacts, this is not usually true of automated processing pipelines.

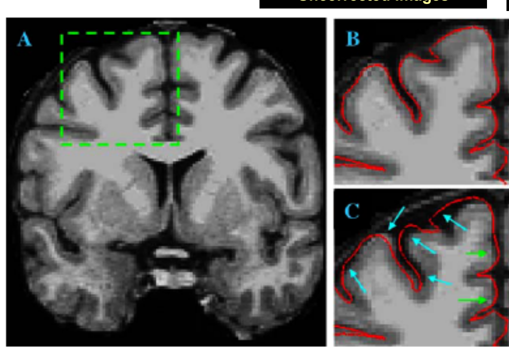
Therefore:

1. use larger fields-of view and many slices
2. no parallel imaging
3. no partial k-space imaging
4. correct for chemical shift artifacts
5. correct for intensity inhomogeneity

# Advances in Structural MRI

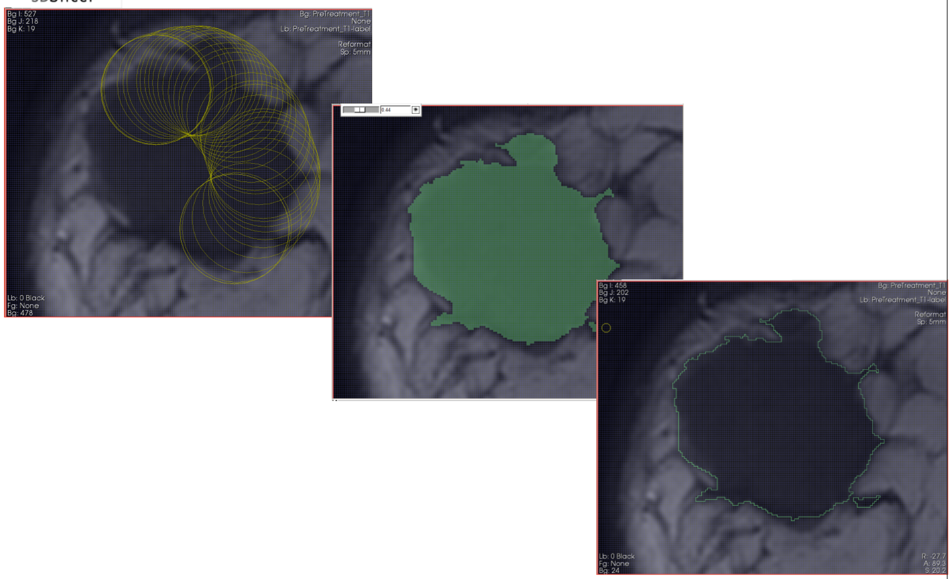
- Image calibration
  - Distortion correction (1.5T)



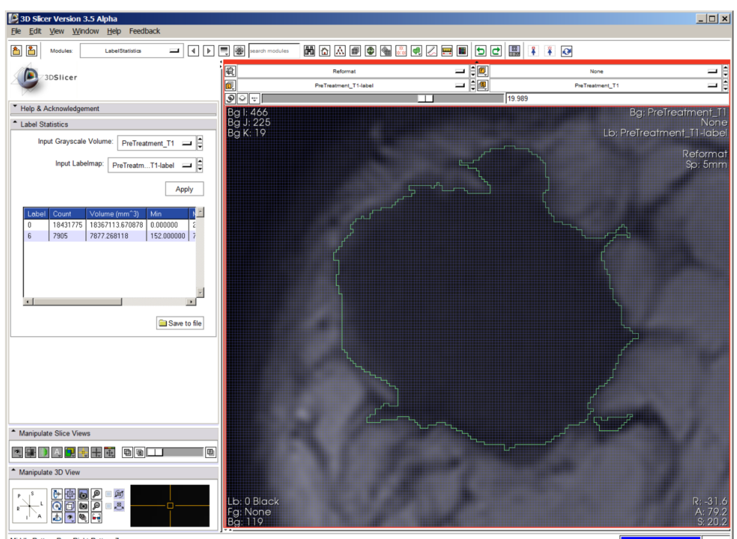

*Jovicich et al., 2006*

## Volumetric MRI Analysis using 3D Slicer: ROI Comparison



*Data courtesy of K. Macura, MD, PhD*

## Volumetric MRI Analysis using 3D Slicer: ROI Comparison




| Label | Count | Volume (mm^3) | Min |
|---|---|---|---|
| 0 | 18431775 | 18367113.670878 | 0.000000 |
| 6 | 7905 | 7877.268118 | 152.000000 |

3DSlicer

Volumetric MRI Analysis using 3D Slicer: ROI Comparison


3DSlicer

Volumetric Analysis using 3D Slicer: ROI Comparison

Pre- and Post-Treatment Comparisons:

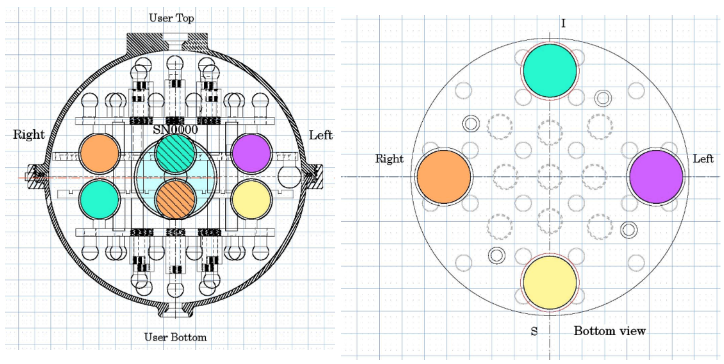
| | D1 (mm) | D2 (mm) | Volume ($mm^3$) |
|---|---|---|---|
| Pre-Tx | 48.7 | 48.7 | 7877.3 |
| Post-Tx | 26.1 | 17.9 | 38.2 |
| % Change | -46% | -63% | -99% |

# Requirements for DCE-MRI Standardization

- Patient preparation and positioning
- Gadolinium contrast (dose, rate, timing)
- Field strength
- Receiver coils
- Acquisition pulse sequence
- Distortion correction
- Reconstruction parameters (slice thickness/separation, filtering, FOV)
- Input function (normalized versus measured)
- Kinetic modeling and analysis

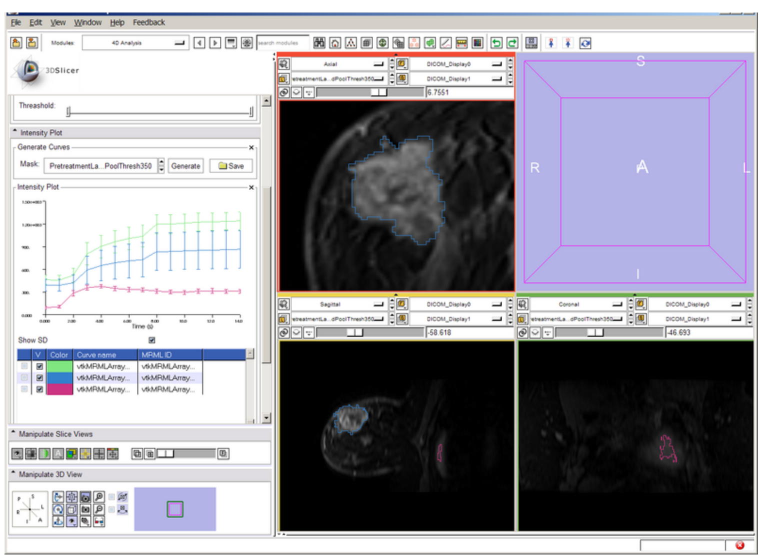
# RSNA QIBA DCE-MRI Technical Committee

- Jeffrey L. Evelhoch, PhD (Merck)
- M. Buonocore (UC Davis)
- E. Jackson (MDACC)
- G. Karczmar (Chicago)
- D. Barboriak (Duke)
- M. Rosen (Penn)
- M. Schnall (Penn)
- M. Knopp (OSU)
- G. Zahlmann (Siemens)
- D. Purdy (Siemens)
- S. Gupta (GE)
- L. Hilaire (GE)
- G. Slavin (Philips)
- E. Ashton (VirtualScopics)
- A. Schmid (Perceptive)




- Modified ADNI/IRAT phantom for DCE-MRI
- Defined generic DCE-MRI acquisition protocols
- Conduct multi-center phantom reproducibility study
- Define procedure for routine phantom use
- Develop simulated data set for algorithm testing

# DCE-MRI



# DCE-MRI Example

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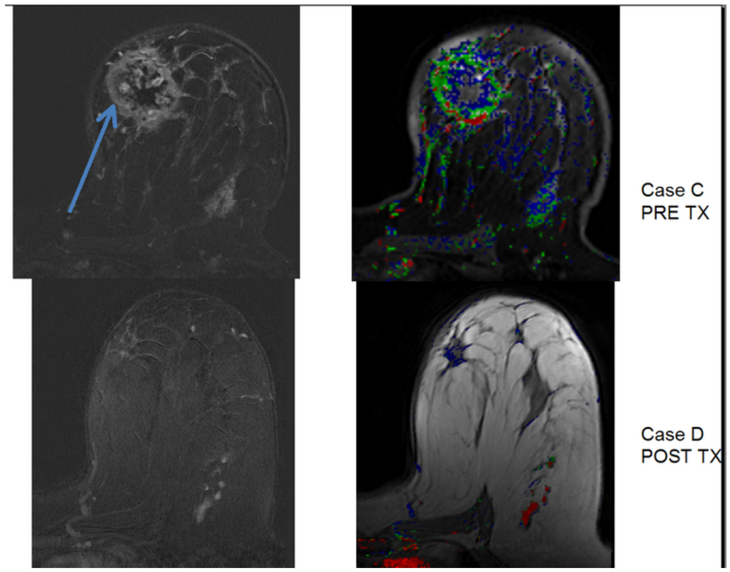


*Slide courtesy of K. Macura, MD, PhD*

# Acknowledgements

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# Acknowledgments - 3D Slicer

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