Estimation of Breast Anatomical Descriptors from Mastectomy CT Images

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Outline

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  - Adipose compartment volume distributions in phantoms
  - Compartmental volume distribution in CT and in the phantoms
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- Discussion & Conclusions
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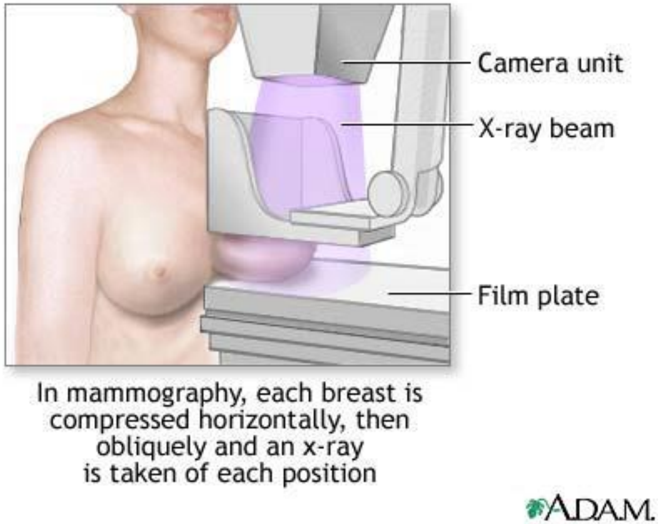
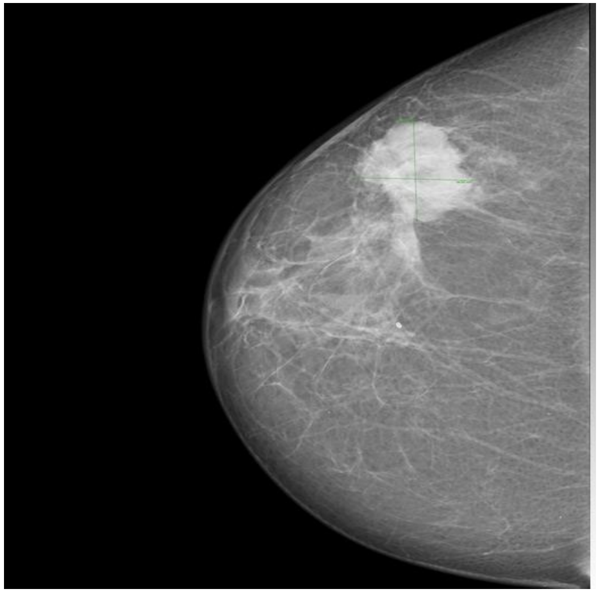
- References

Problem Statement

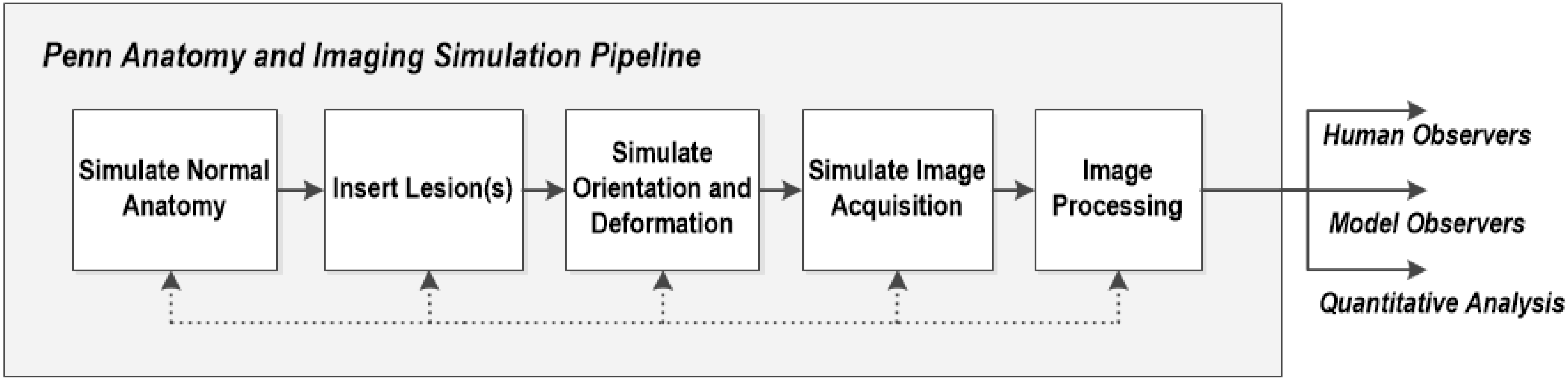




- Breast cancer is the second most prevalent cancer in the world
- Mammography is not enough to reduce the high mortality rate
- 20-26% cancers are missed and 70% biopsies turned out to be unnecessary
- Problem: mammogram image represents the 3D breast superimposed onto a 2D image plane
- 3D imaging modalities emerged for 3D visualization of breast and improved diagnosis

Problem Statement (Cont'd)

- Main Concern: Evaluation of image quality and radiation dose for new imaging modalities
- Limitation: A lot of clinical data, time-consuming, volunteer patients, and radiation dose
- Solution: Use of software phantoms, simulating the breast anatomical structures



Goal: Flexibility in the simulation and realistic generation of phantoms

- Flexibility: Mathematical modeling based on some geometric primitives
- Realism: Voxelization based on empirical data

Working Steps

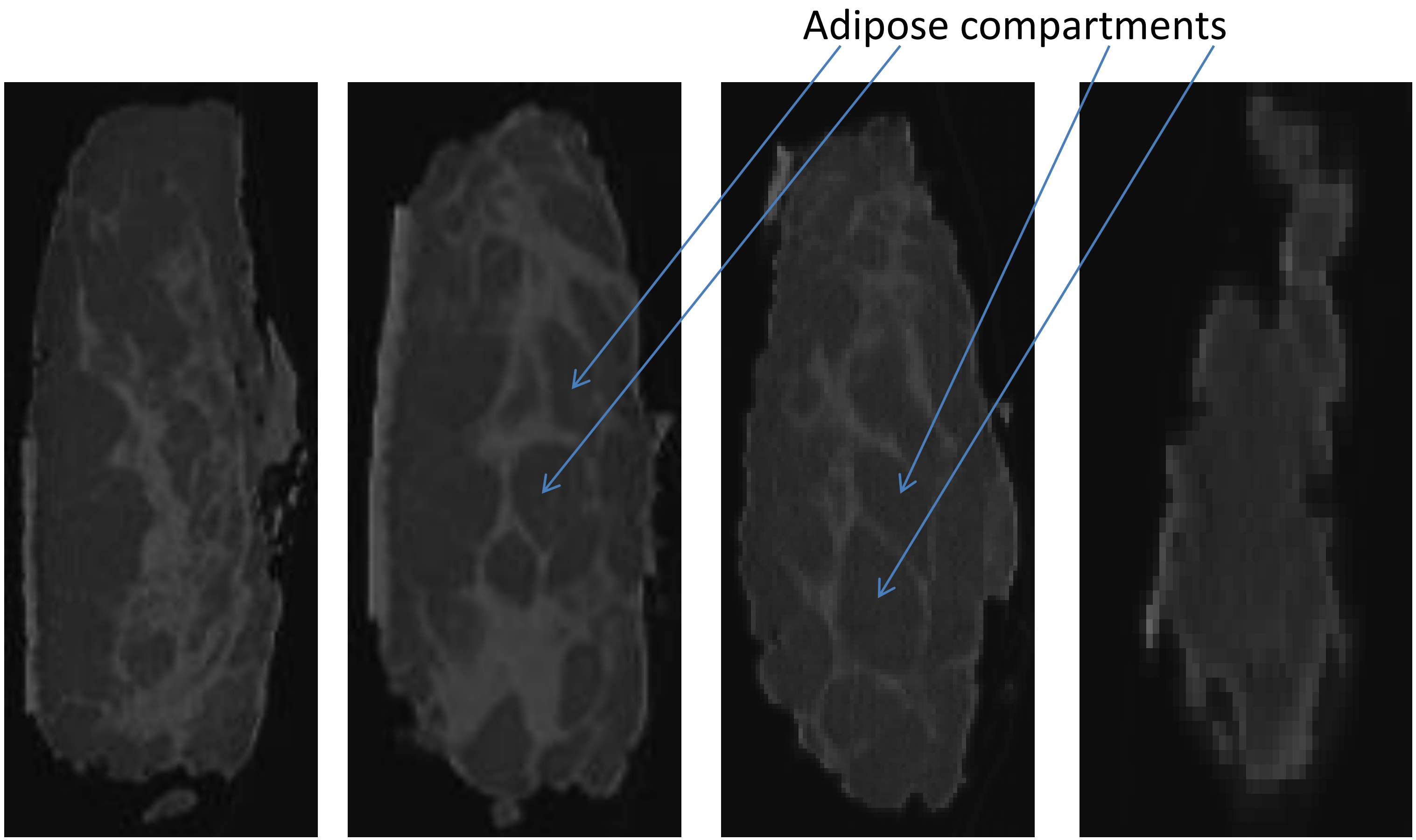
1. Estimation of adipose compartment volumes in mastectomy CT images through manual segmentation.
2. Validation of manual segmentation through automatic segmentation of tissue voxels.
3. Characterization of segmented adipose compartment volumes to determine their shapes, sizes, and orientation by ellipsoidal fitting.
4. Generation of anthropomorphic software breast phantoms through octree based recursive partitioning and partial volume computation.
5. Determination of adipose compartment volume distributions in the software-generated phantoms.
6. Distance measurement of adipose compartment volume distribution in mastectomy CT with each of the software-generated phantoms.
7. Determination of significant parameters or the combination of parameters by using multifactor ANOVA (ANOVAN)

Materials

- 3D CT Images of a mastectomy specimen
  - Acquired from University of Pennsylvania
  - 619 slices
  - Slice size and resolution: 512-by-512 pixels (0.72mm*0.72mm)
  - Slice thickness: 0.6 mm

- Phantoms
  - 1440 phantoms; controlling a set of simulation parameters
  - 642*1284 sized 2182 slices in each phantom
  - Each phantom occupied 1.7 GB space in the memory

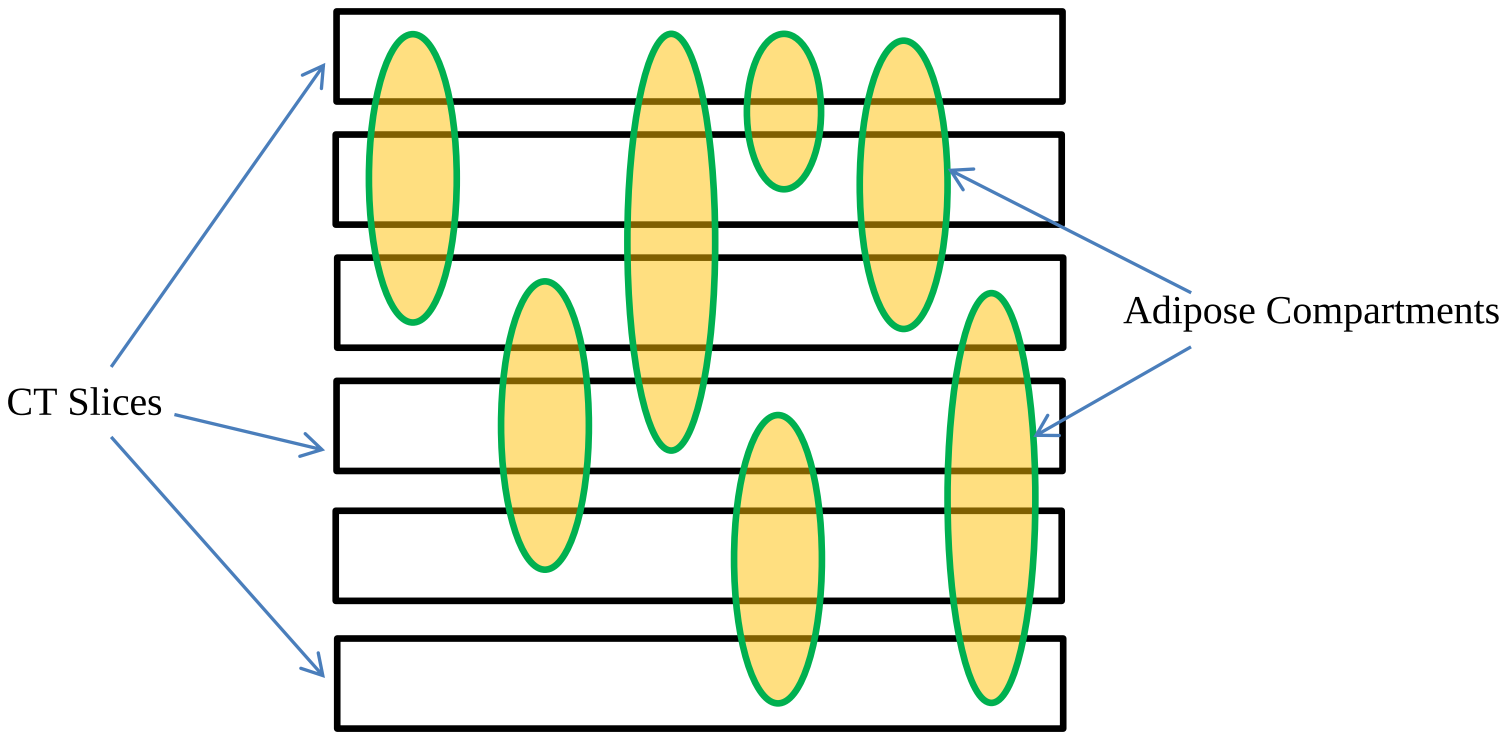
CT Image Slices



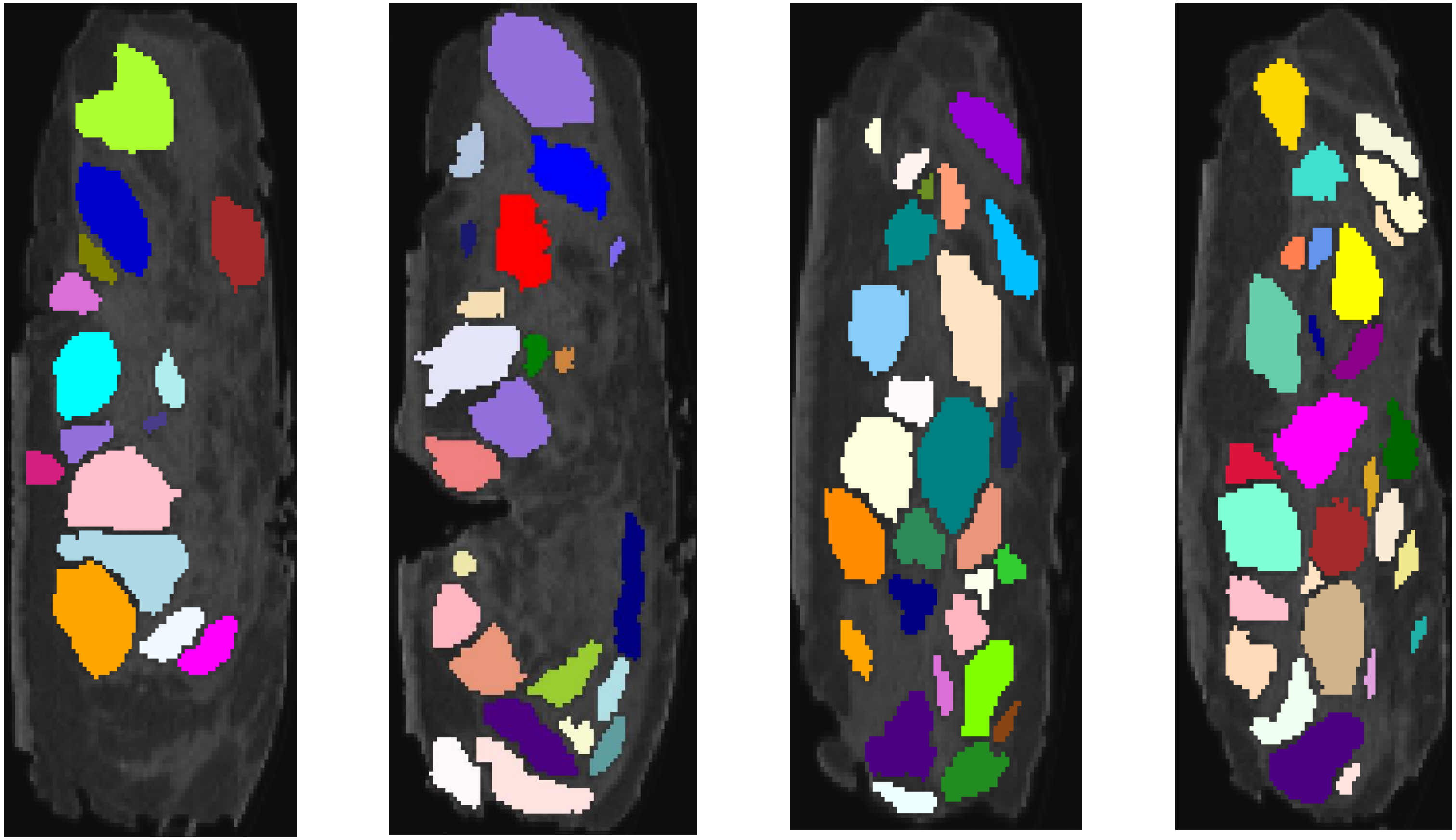
CT slices of the mastectomy specimen

Adipose Compartment Segmentation

- Each compartment spans in multiple slices
- 306 slices were found to contain adipose compartments
- The compartments were identified and segmented by manual boundary marking in ITK-SNAP



Segmented Compartments in CT Slices

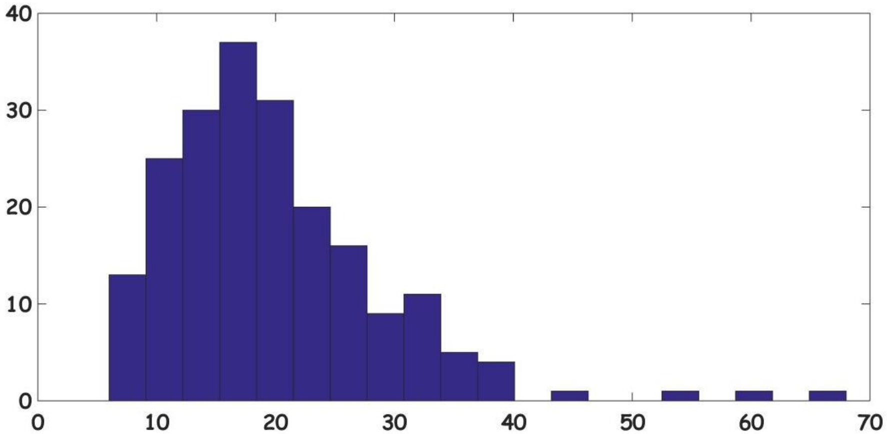


Segmentation marked slices

Segmented Adipose Compartments

3D visualization of 205 segmented adipose compartments in ITK-SNAP

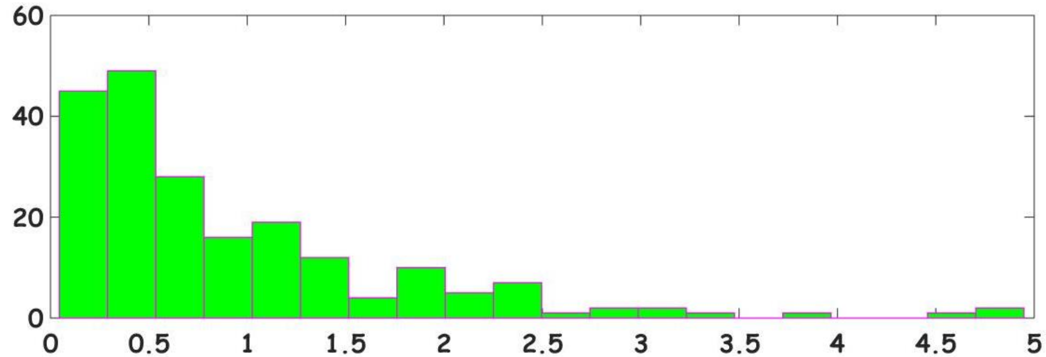
Adipose Compartments Volume Distribution



Histogram of #slices in segmented compartments

- ❑ Each segmented compartment spans approx. 20 slices on average

- ❑ The estimated volume is 0.91 cm^3 ± 0.87



Histogram of adipose compartment volumes (cm^3)

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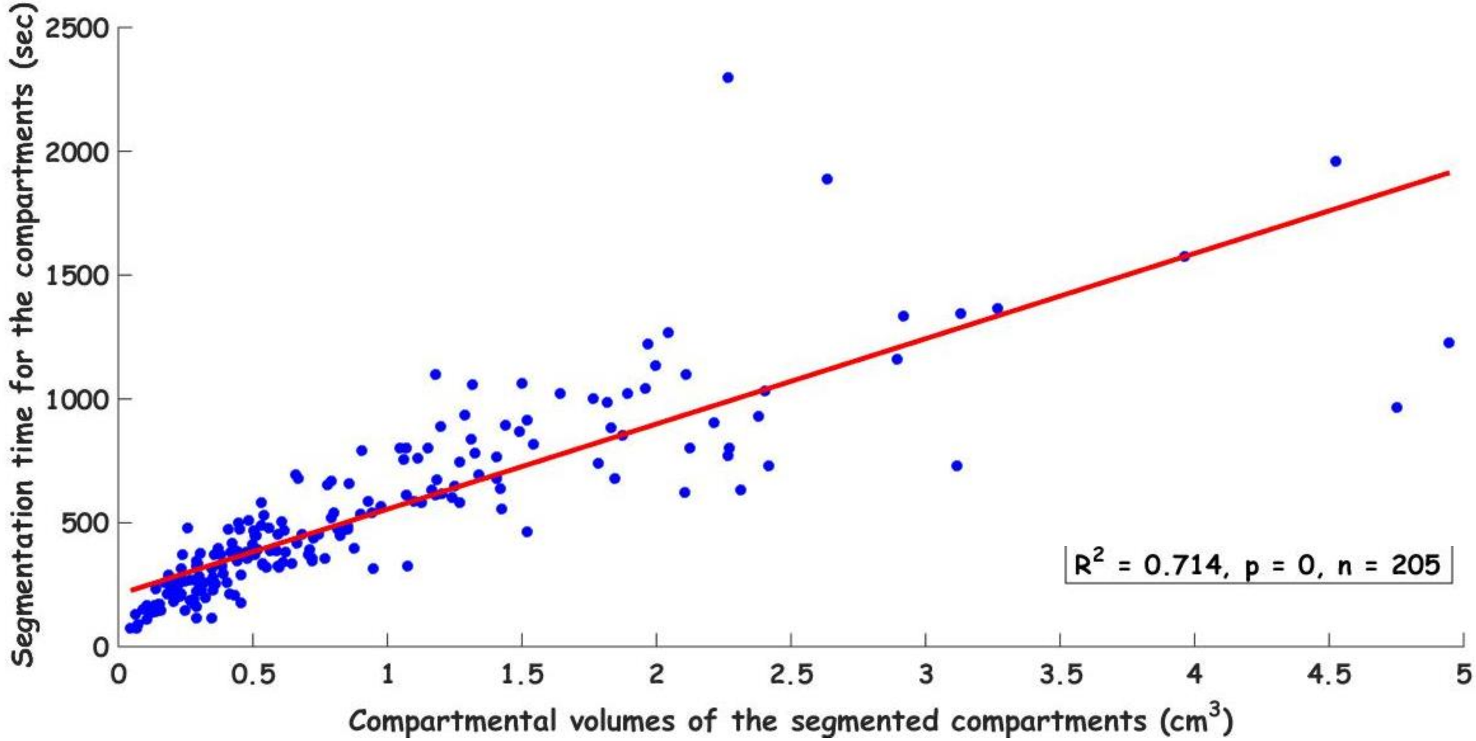
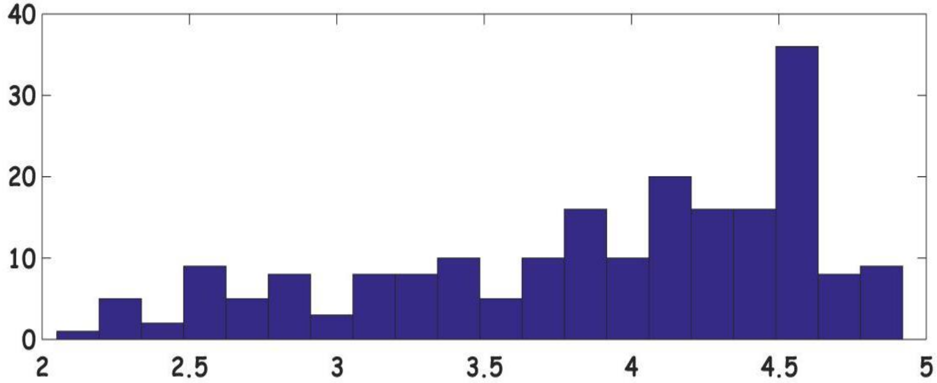
Time Vs. Volume

- Average time spent for segmenting each compartment is 8.75 minutes
- The estimated volume is correlated to the segmentation time ($p<0.0001$)



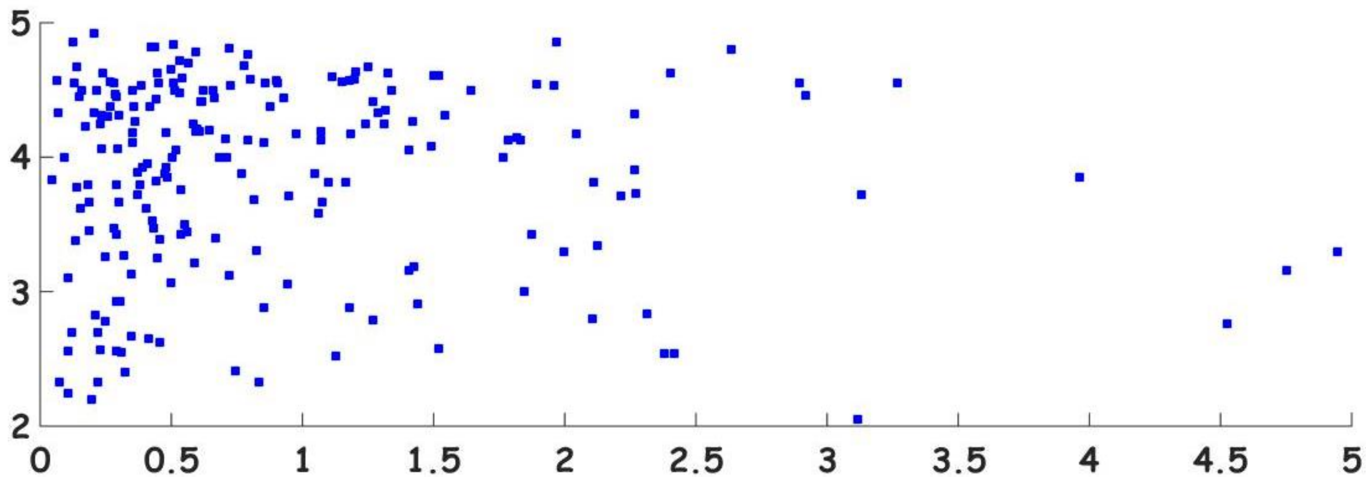
Segmentation time Vs. Compartmental volume

Confidence Vs. Volume



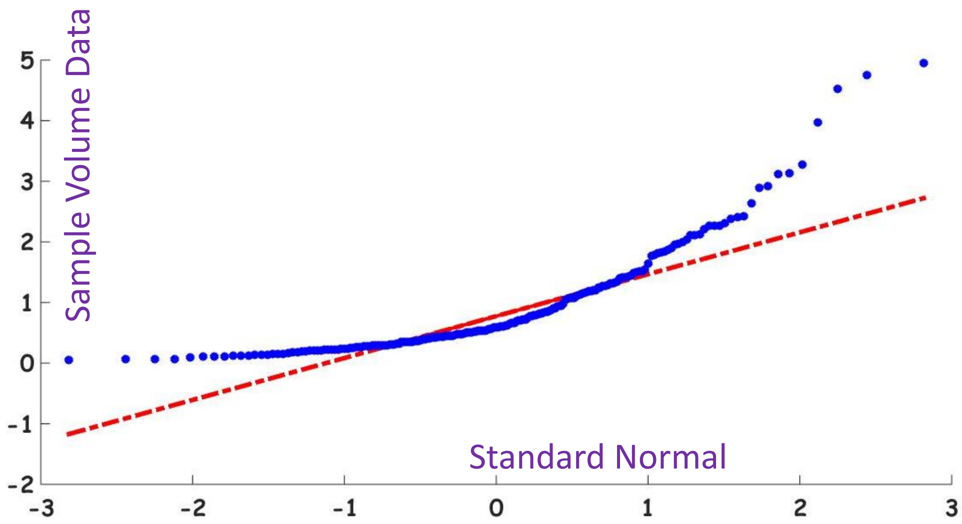
Histogram of average confidence level

- Confidence level was assigned in the scale of 5 (1-5) for every slice
- Volume is not correlated with confidence



Average confidence level (1-5) Vs. Compartmental volume (cm^3)

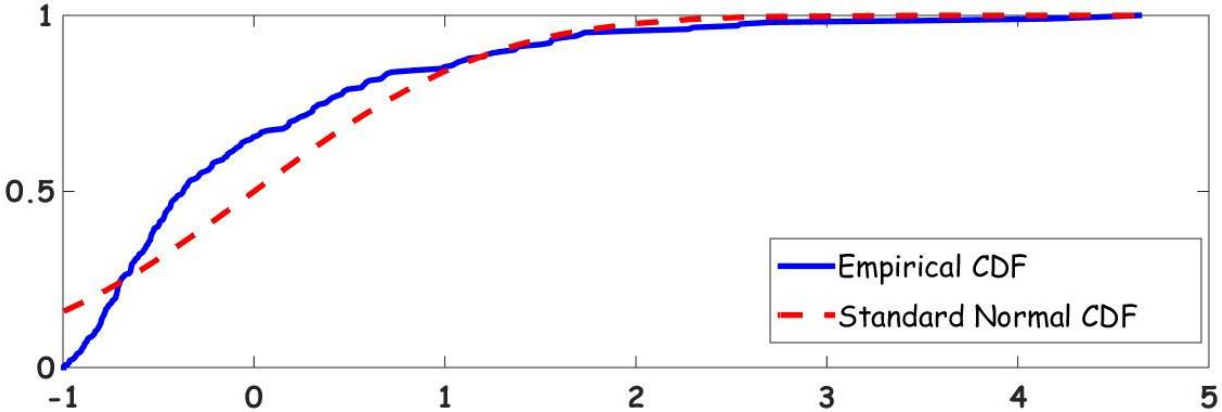
Distribution of Volume



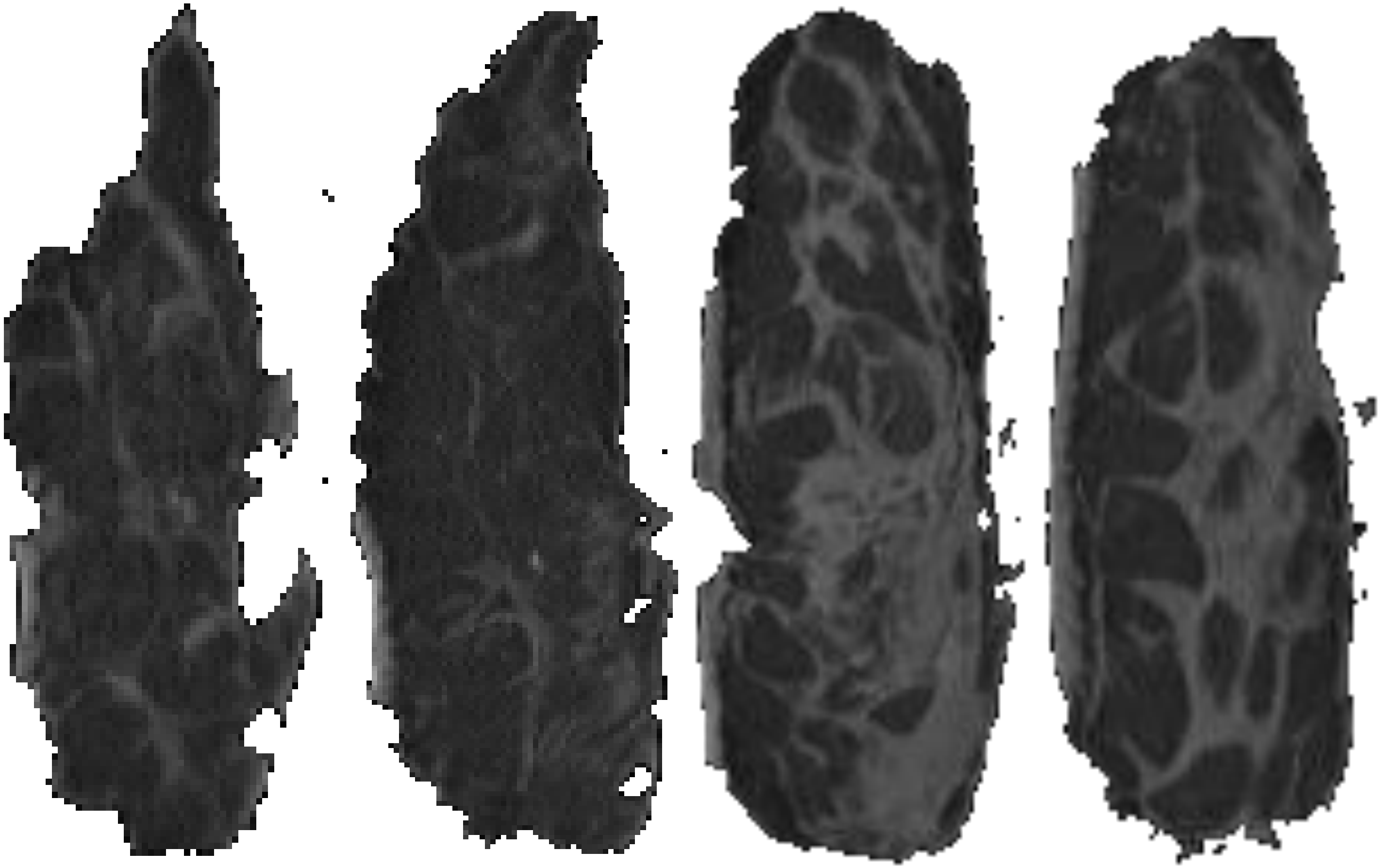
QQ plot of the sample volume data

- Kolmogorov-Smirnov test, Lilliefors test, Jarque-Bera test, and visual cdf comparison (between empirical and standard) rejected the normality of volume data.

- Distribution of volume was not normal, rather left-skewed

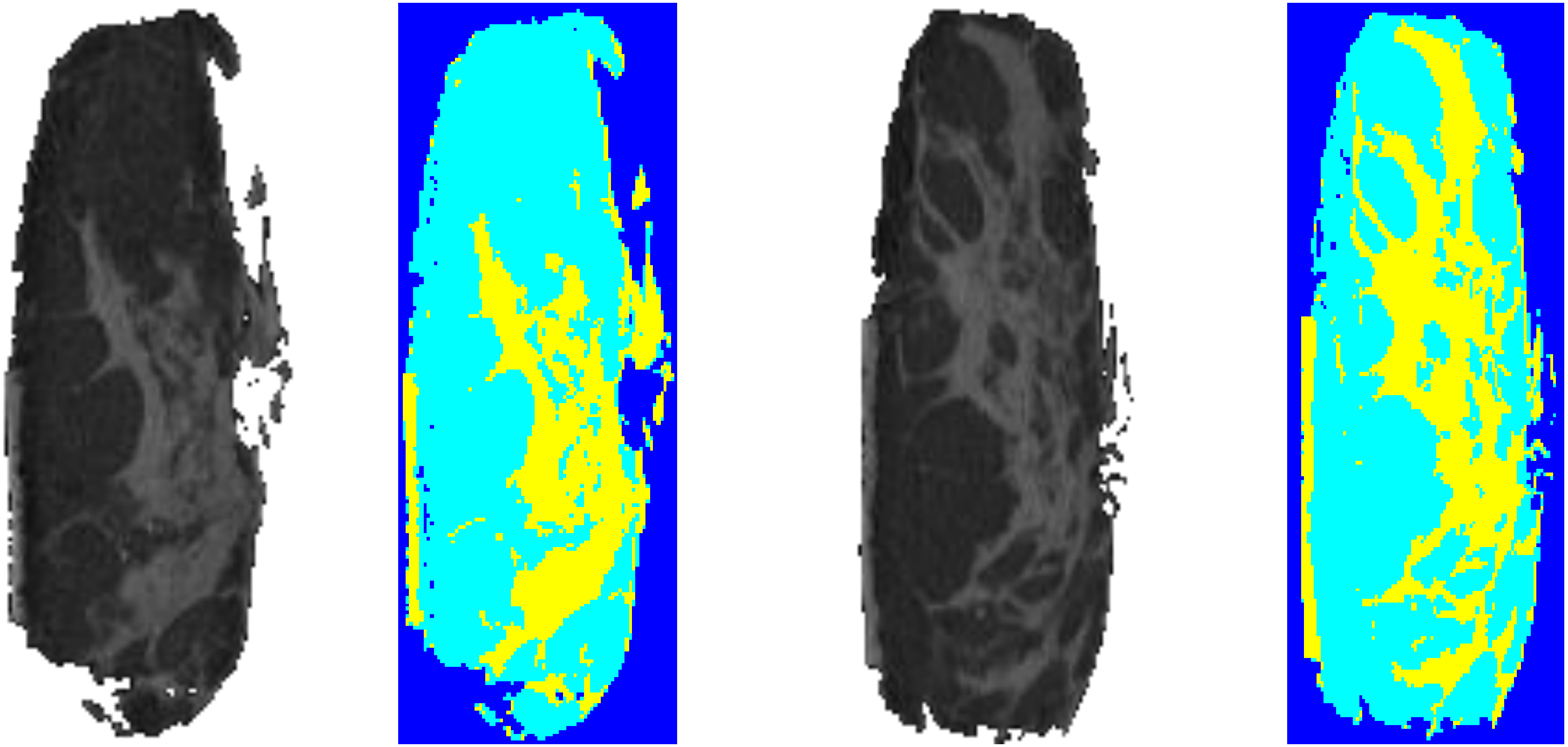


Contrast Adjustment of CT Image Slices

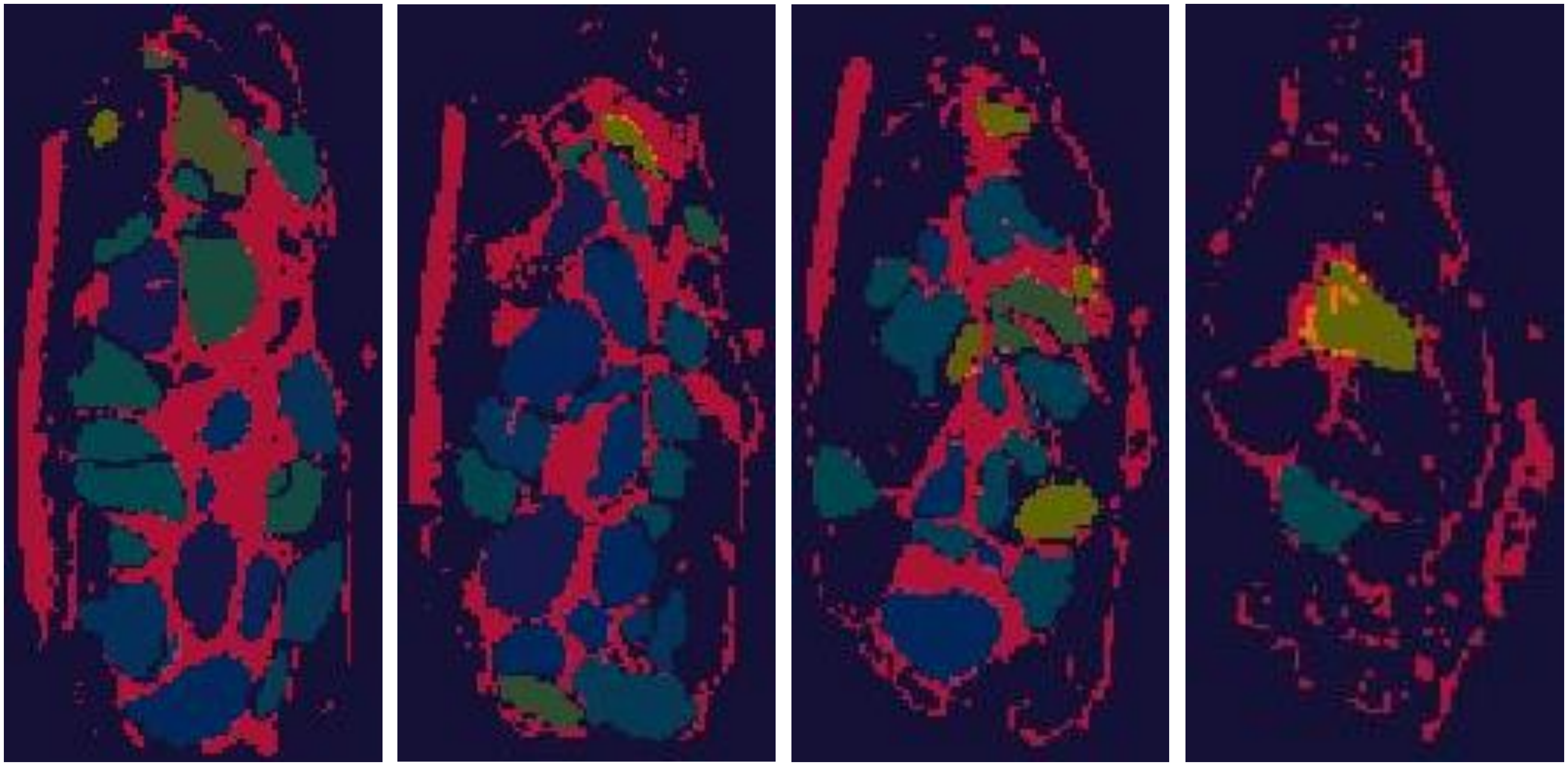


CT image slices of the mastectomy specimen after the contrast adjustment.

Segmentation through Multi-level Thresholding



Overlaid Manual and Automatic Segmentation Slices

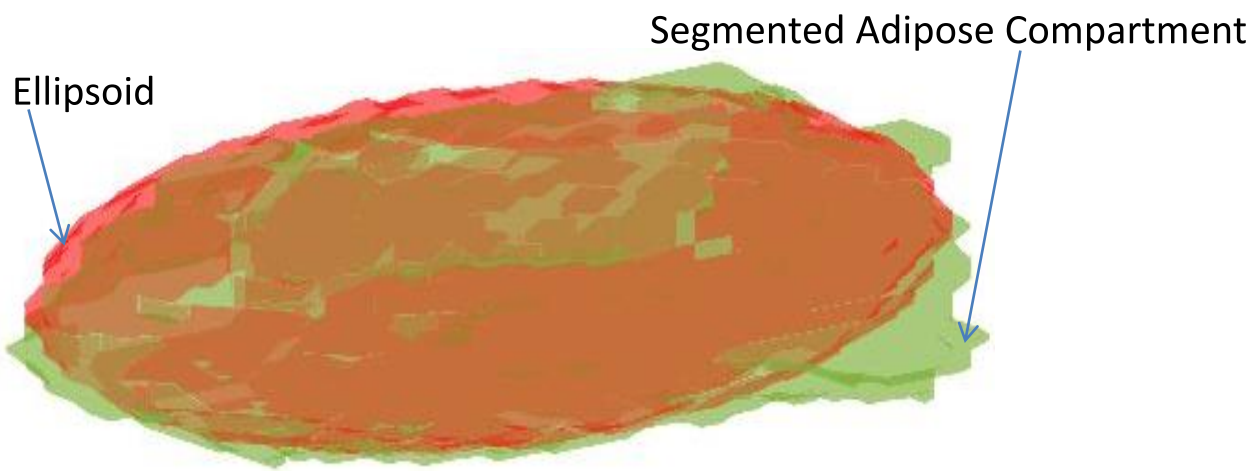


Characterization of Segmented Adipose Compartment Volumes

- The segmentation result was stored in VTK and fed to the ellipsoidal fitting algorithm
- The moment of inertia of an ellipsoid and each adipose compartment were matched for calculating the ellipsoidal semi-axes
- The moment of inertia was calculated relative to the barycenter of each adipose compartment

Fitting Accuracy

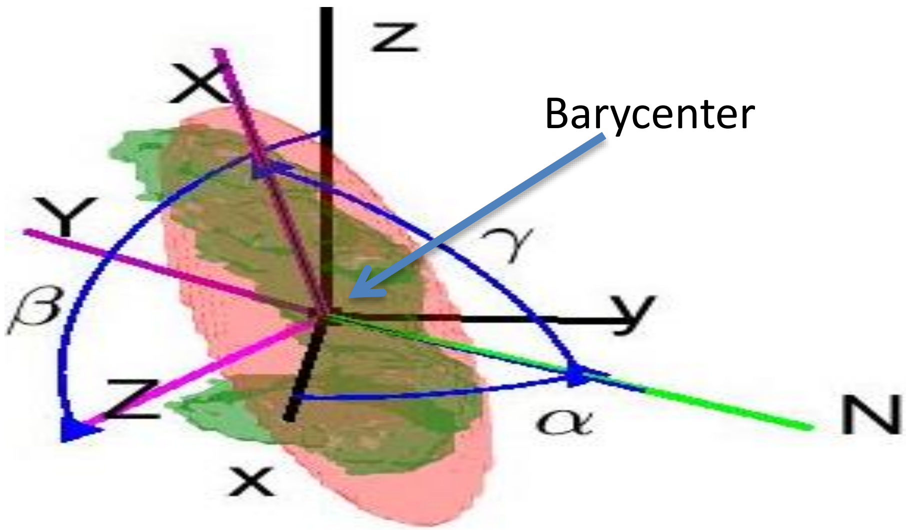
- The goodness of ellipsoidal fitting was determined for each of the non-ellipsoidal adipose compartments based on the overlapped volume of a compartment and the fitted ellipsoid
- Dice coefficient, $D = \frac{2|E \cap AC|}{|E|+|AC|}$, $0 \le D \le 1$
- D(average) = 0.79



Ellipsoidal Fitting of an adipose compartment (Dice coefficient = 0.88)

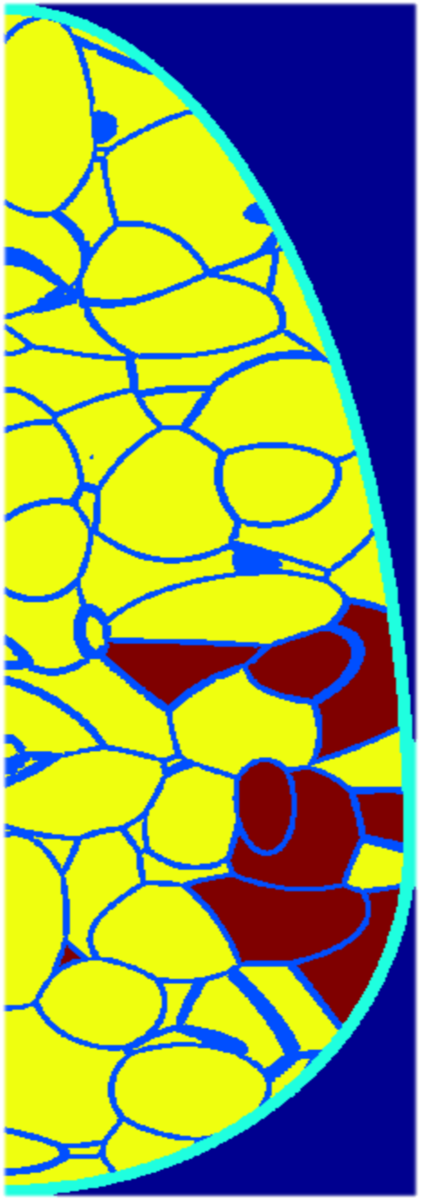
Characterization of Shape, Size and Orientation

- Size→ volume of each compartment in cm^3
- Shape ratio → the ratio of maximum and minimum sub-axes of the fitted ellipsoid
- Orientation→ Euler's angles for 3D rotation in Euclidean axes



The Euler angles are three angles used to describe the orientation of a rigid body.

Breast Phantom



The volume of breast bounded by skin

Breast split into tissue regions-compartments

- Fat
- Glandular

Boundaries of compartments correspond to Cooper's ligaments

Cooper's ligaments and glandular compartments are radiologically dense

Input Parameters in Breast Simulation

Parameter Types	Parameter Name	Parameters
Constant	Breast Size (cm^3)	930 cm^3
	Voxel size (cm)	0.01 cm
Variable	Skin Thickness (µm)	0.12, 0.15
	Ligament Thickness (µm)	0.02, 0.04, 0.06, 0.08
	#Compartments	167, 333, 500, 1000
	Combination of Speeds	(0.01, 100, 1, 1), (1, 1, 0.25, 4), (0.01, 100, 0.25, 4)
	Random Seed Generator	1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10000

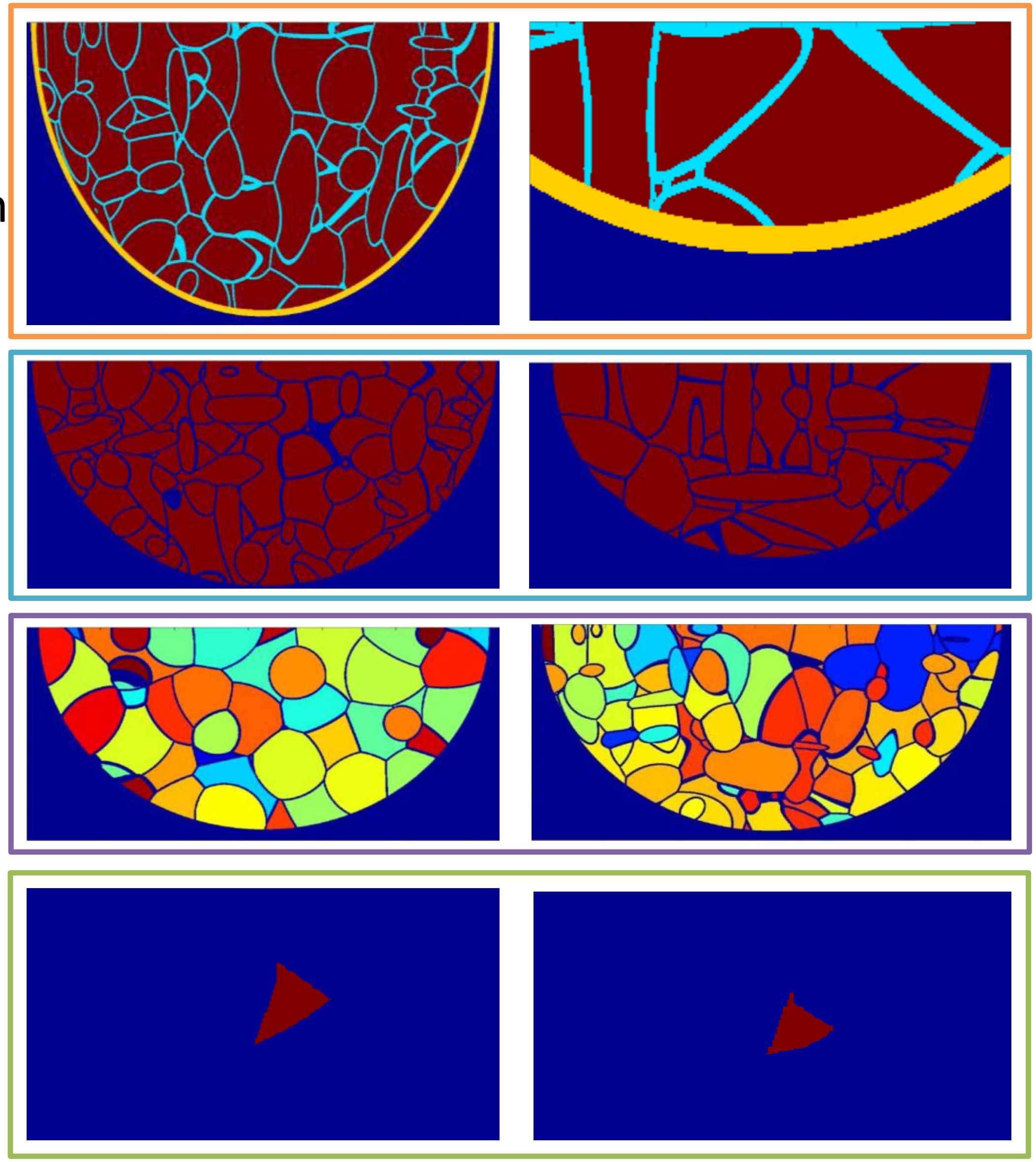
Distribution Determination in the Phantoms

Cross-sections of generated breast phantom

Adipose tissue Label

Adipose compartments

Individual compartment extracted



Volume = #voxels*voxel size

Distance Measurement of adipose Compartment Volume Distributions (CT Vs a Phantom)

- Distribution of adipose compartment volumes were compared between mastectomy CT and each of the 1440 software-generated phantoms

- Two approaches followed for distance measurement:

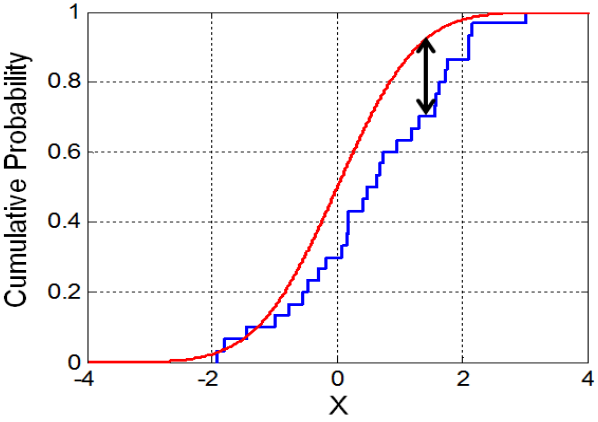
  - General approach-Kolmogrov-Smirnov distance (KSD) and Kullback-Leibler divergence (KLD)

  - Parameter based distribution distance (PDD)-linear combination of distribution parameter differences between CT and phantoms **(New Technique)!!!**

General Distance Measurements

- The KS distance was determined by testing two independent random samples input if they were drawn from the same underlying continuous population:

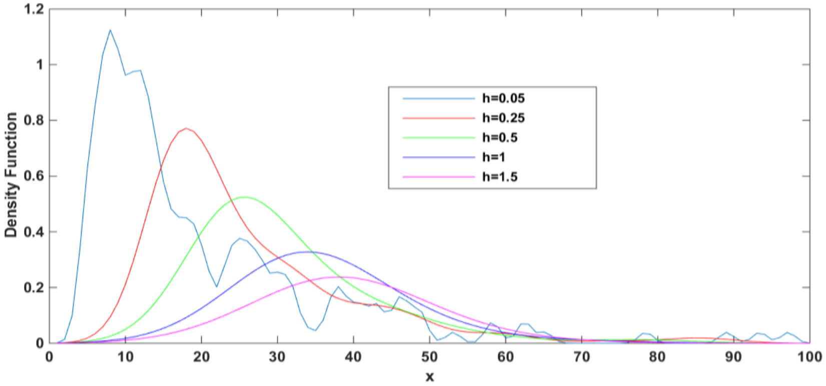
KSDist = max(|E(P)-E(Q)|)



- The KL divergence is the relative entropy between two probability distributions on a random variable, measures the distance between them

$$D(p||q) = \sum_i p(x) \log \frac{p(x)}{q(x)}$$

- The probability distributions kernel density estimation (KDE); based on normal Gaussian kernel, with a bandwidth parameter



Parameter-based Distribution Distance (PDD)

- Prioritized distribution parameters and corresponding assigned weights

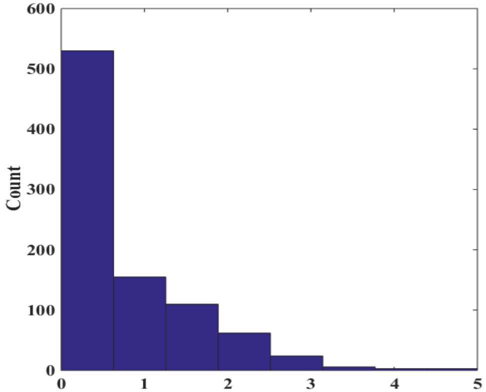
Parameters	Assigned Weights
Arithmetic mean	Wam
Standard deviation	Wsd
Skewness	Wsk
Kurtosis	Wkt
Median	Wmd
Maximum	Wmo
Minimum	Wmn
Mode	Wmx
Geometric mean	Wgm
Harmonic mean	Whm

- The measured absolute differences in the parameters were normalized in between 0 and 1 inclusive.
- Weighted sum of the normalized parameter differences was calculated as the distance: $D = \sum NP_i * W_i$

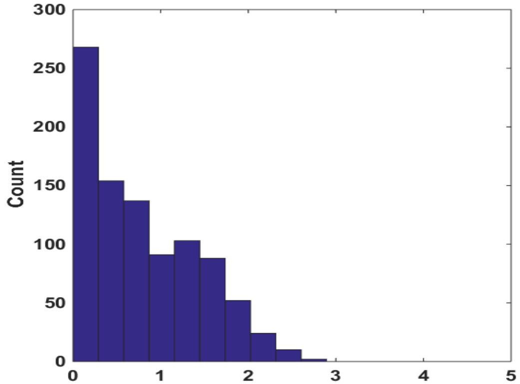
Minimum Distant Phantom Parameters

Parameters	Values for the minimum distant phantoms		
	PDD	KSD	KLD
Breast size	930	930	930
Voxel size	0.1	0.1	0.1
Skin thickness	0.12	0.12	0.15
Number of compartments	1000	1000	500
Ligament thickness	0.04	0.04	0.06
Percentage of dense tissue	10	5	0
Combination of Speeds	0.01 100 0.25 4	0.01 100 1 1	0.01 100 1 1

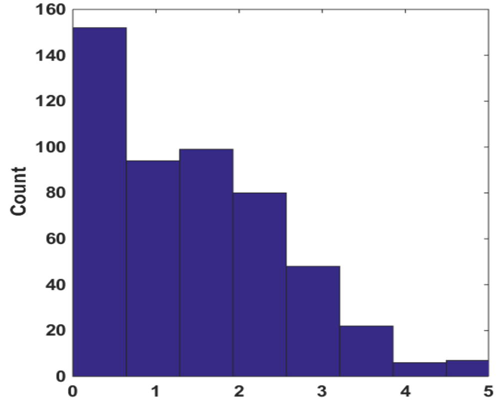
Minimum Distant Phantoms



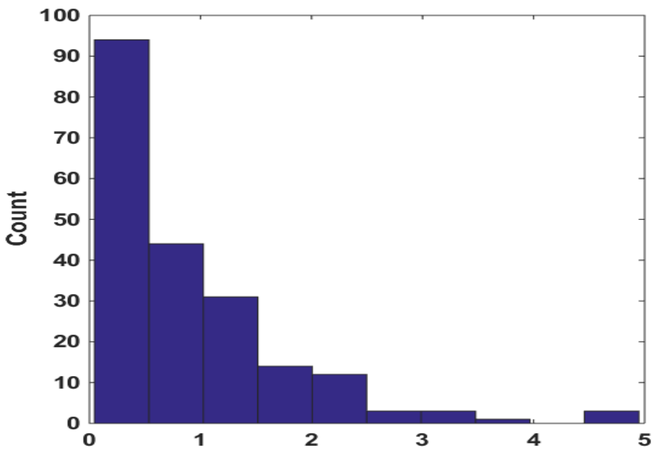
Min PDD distant phantom



Min KSD distant phantom



Min KLD distant phantom



Mastectomy CT

Determination of Influential Parameters

- The simulation parameters varied were used as the factors in the ANOVA

- Multifactor ANOVA groups:

  Skin Thickness

  Number of Compartments

  Ligament Thickness

  Percentage of Dense Tissue

  Combination of speeds

- 144 combinations for the groups with 10 repetitions made 1440 phantom generation parameters

- The significant parameters responsible for the variation of generated phantoms were determined comparing the ANOVA results with PDD, KSD, and KLD

Comparison of ANOVAN Results for PDD, KSD, and KLD Distance Measurements

Factors	PDD	KSD	KLD
Skin Thickness	Not significant	Not significant	Not significant
Number of Compartments	**Significant**	**Significant**	**Significant**
Ligament Thickness	**Significant**	**Significant**	Not significant
Percentage of Dense Tissue	Not significant	Not significant	Not significant
Shape parameters	**Significant**	**Significant**	**Significant**

Discussion & Conclusions

- A foundation of realistic phantom generation:

  determines the realistic breast phantom parameters

  combines mathematical modeling (flexibility) and empirical data (realism)
- Anatomical descriptors have been extracted from a mastectomy specimen by volumetric segmentation of adipose compartments
  - Adipose compartment sizes, shapes, barycenters, and orientations
- Validation of adipose compartment segmentation through the automatic tissue segmentation
- "Exhaustive" search to determine phantom with realistic distribution of adipose compartment sizes
- Determination of the phantom parameters that influence distribution of adipose compartment sizes; could be extended for other structures: ligaments, skins, etc.
- Limiting factors:

  Mastectomy specimen CT Image data (1 SPECIMEN!!)

  Manual segmentation of the adipose compartments

Future Work

- Future scope:
  - Use of other modality image data
  - Automatization of the adipose compartment segmentation
  - Validation of the realism for the phantoms closest to the mastectomy specimen

- Creation of an anthropomorphic 3D structured background in a test object

- Phantom based on 3D printed volumes representing adipose compartments

- Mammographic and tomosynthesis images were acquired for evaluation

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- Thesis committee
- INBRE III pilot project on Breast Cancer Research
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- Mr. Scott Cupp for the CT acquisition of the mastectomy specimen

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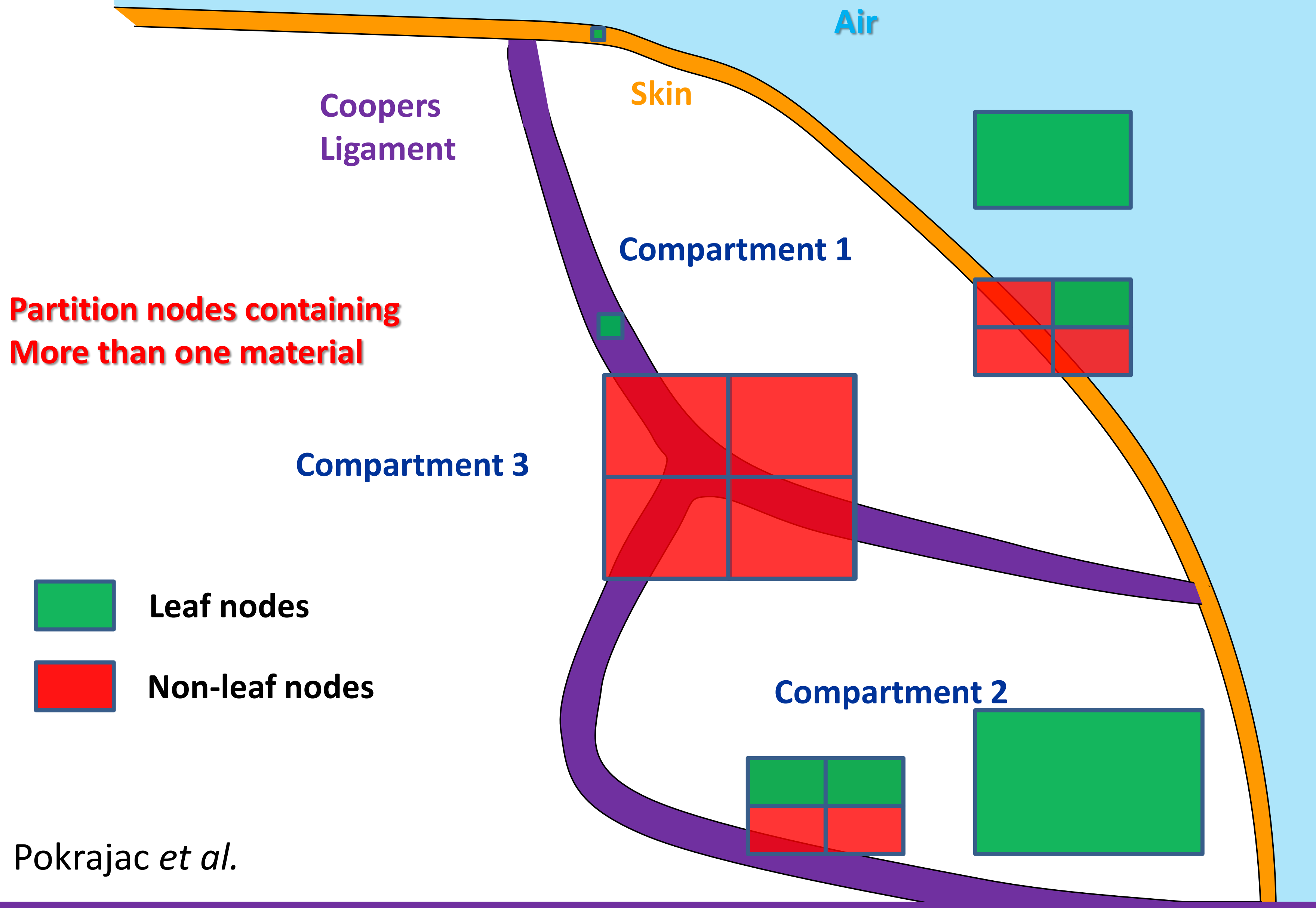
Thanks…..

Appendix

Moment of Inertia

- Our segmented adipose compartments were 3-D labeled by assigning unique intensity values.
- Each of the compartments contains a list of voxels of unique intensity values.
- $I_C = \begin{bmatrix} Ixx & Ixy & Ixz \\ Iyx & Iyy & Iyz \\ Izx & Izy & Izz \end{bmatrix}$; $I_{xx} = \sum_i m_i(y_i^2 + z_i^2)$, $I_{xy} = I_{yx} = -\sum_i m_i x_i y_i$
- $I_E = \begin{bmatrix} \frac{1}{5}m(b^2 + c^2) & 0 & 0 \\ 0 & \frac{1}{5}m(c^2 + a^2) & 0 \\ 0 & 0 & \frac{1}{5}m(a^2 + b^2) \end{bmatrix}$

Recursive Partitioning



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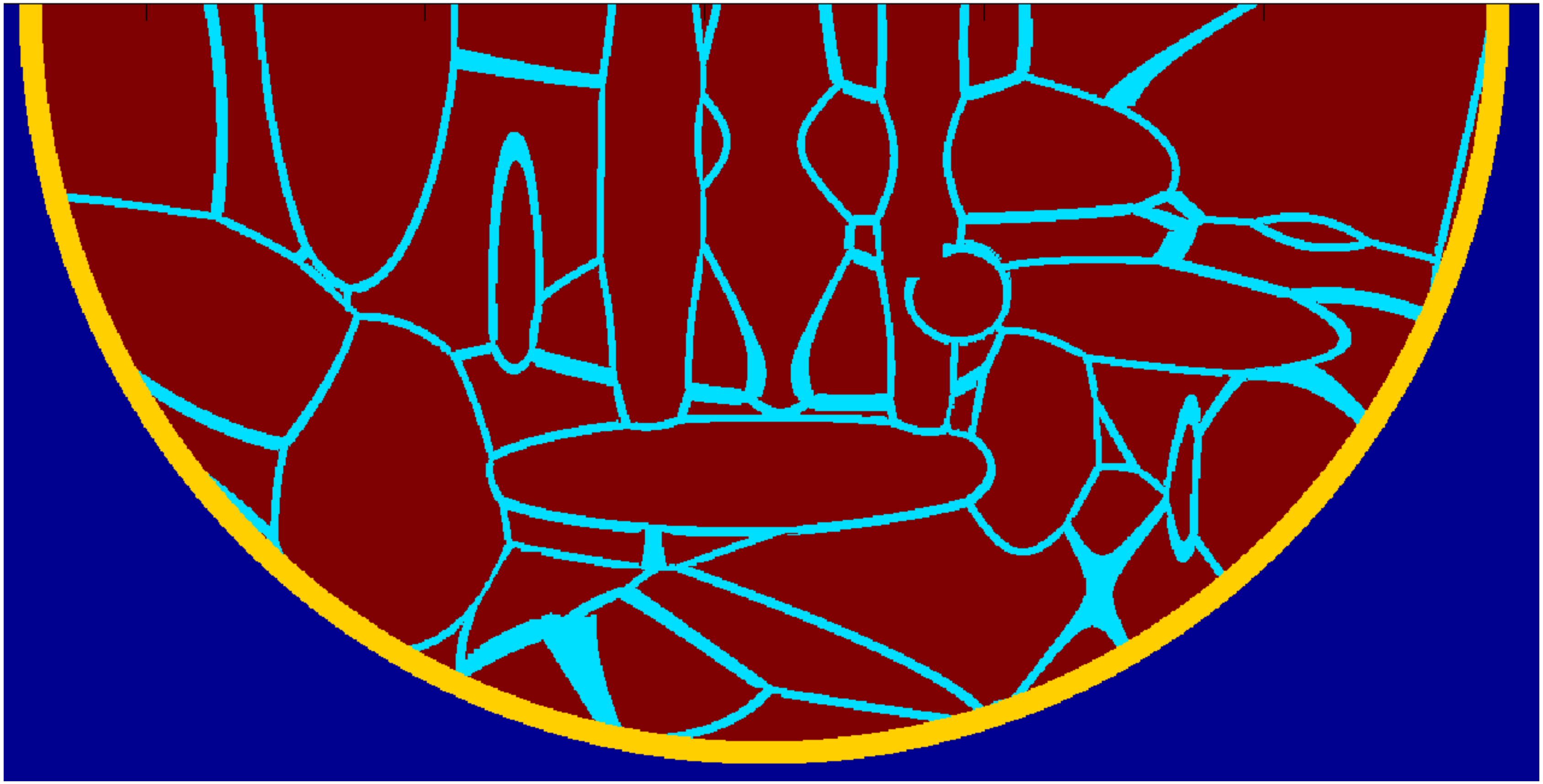
Generation of Breast Phantoms



Cross-section of a software-generated breast phantom

Parameter-based Distribution Distance (PDD)

$$am = VCT.Dam - VPH(i).Dam$$
$$gm = VCT.Dgm - VPH(i).Dgm$$
$$hm = VCT.Dhm - VPH(i).Dhm$$
$$sd = VCT.Dsd - VPH(i).Dsd$$
$$md = VCT.Dmd - VPH(i).Dmd$$
$$mo = VCT.Dmo - VPH(i).Dmo$$
$$mx = VCT.Dmx - VPH(i).Dmx$$
$$mn = VCT.Dmn - VPH(i).Dmn$$
$$sk = VCT.Dsk - VPH(i).Dsk$$
$$kt = VCT.Dkt - VPH(i).Dkt$$

$$Dst(i) = am*Nam+Wsd*Nsd+Wsk*Nsk+Wkt*Nkt+Wmd*md+Wmx*Nmx+Wmn*Nmn+ Wmd*Nmd\ Wgm*Ngm+Whm*Nhm$$

- Where Nam, Nsd, Nsk, Nkt, Nmx, Nmn, Nmd, Ngm, Nhm are normalized am, sk, kt, mx, mn, md, gm, and hm