

# Photon-counting detectors in mammographic imaging

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## Disclosures

Funding from:

- Philips
- Toshiba

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## Outline

- Introduction
- Breast density
- Lesion characterization
- Contrast-enhanced mammography
- Conclusions

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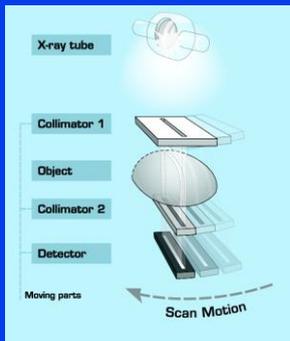
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## Scanning multi-slit geometry




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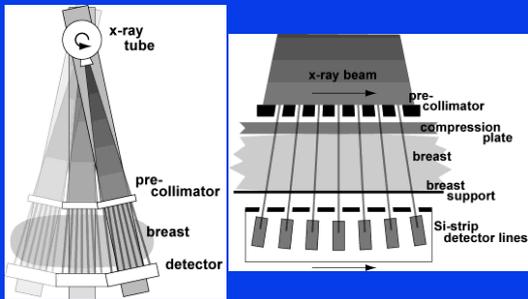
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## Scanning multi-slit geometry




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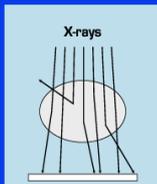
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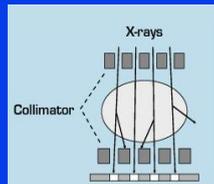
## Scatter rejection

Area detector



Scatter

Scanning multi-slit



No Scatter

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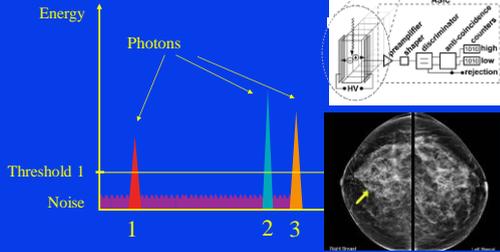
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# Eliminates Electronic Noise



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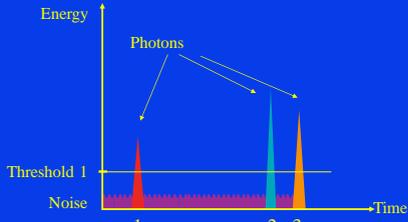
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# Photon counting mammography



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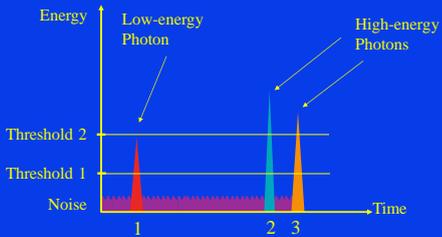
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# Spectral mammography



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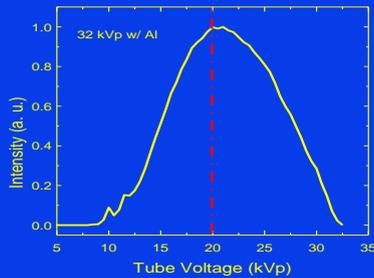
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## Spectral Mammography



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## Breast density

Mammographically dense breast has been shown to be strongly associated with breast cancer risk<sup>1</sup>

1. Boyd, et al. J National Cancer Inst, 87, p670-675, 1995.

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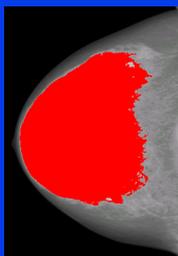
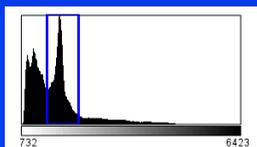
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## Breast density

- Breast Imaging Reporting and Data System (BI-RADS)
- Histogram Thresholding



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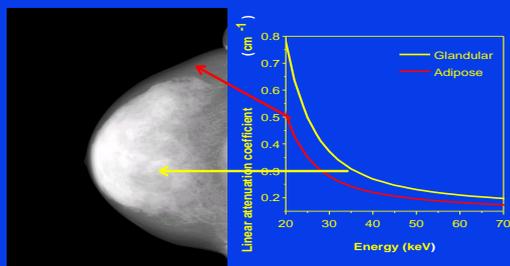
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## Dual Energy Mammography



H. Ding, *et al.*, Physics in Medicine and Biology 57, 4719-4738 (2012)  
Johnson, *et al.* Phys. Med. Biol. 58 (2013) 8573-8591

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## Human Studies

### Study 1

- 93 mammography patients
- BI-RADS ranking by 10 radiologists (5 US, 5 UK)
- Standard grey level thresholding (Cumulus)
- Dual-energy mammography

### Study 2

- 2034 mammography patients
- Breast density assessed by Quantra

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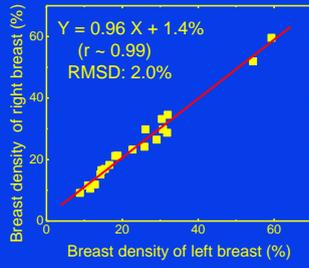
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## Bi-lateral correlation



$$(\text{RMSD})^2 = (\text{Biological Variation})^2 + (\text{Method error})^2$$

$$\text{Biological Variation} = 1.5\%$$

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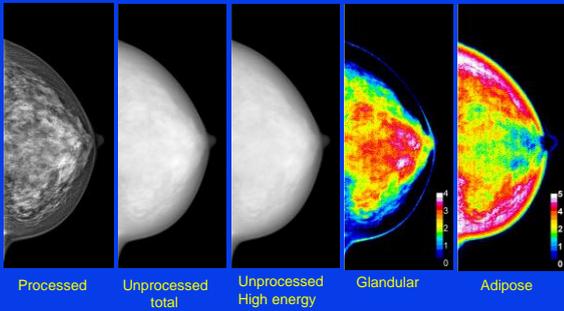
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## Spectral Mammography images



\* S. Molloy, et al. *Academic Radiology* 22, 1052-1059 (2015).

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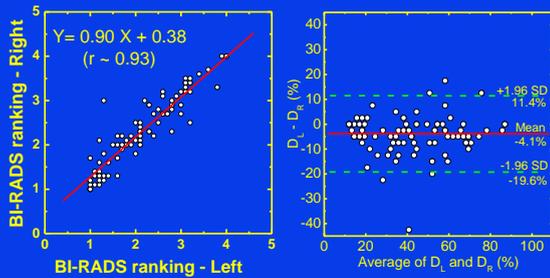
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## BI-RADS Rankings by Radiologists




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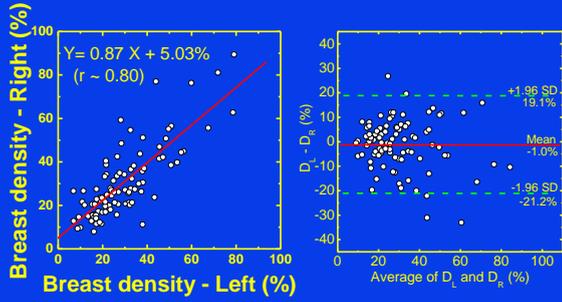
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## Histogram Thresholding




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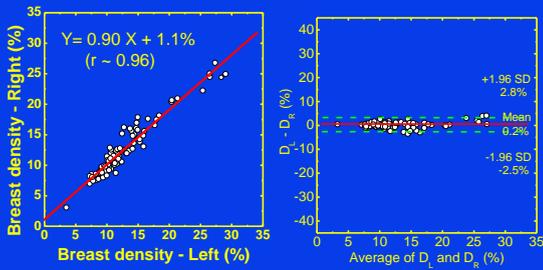
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## Dual Energy Decomposition




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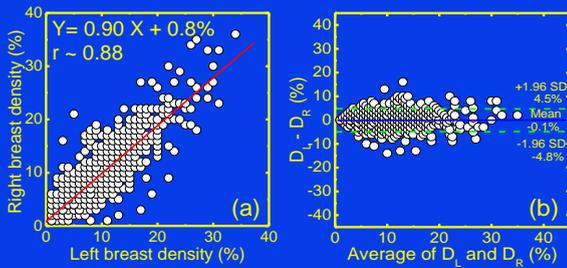
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## Quantra




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## Right and left breast density comparison

	SI-RADS	Cumulus	Quantra	Dual energy
Slope	0.90	0.87	0.90	0.90
Intercept	8.1%	5.0%	0.8%	1.1%
Pearson's r	0.93	0.80	0.88	0.96
SEE	4.3%	8.2%	8.0%	2.4%
Methodology Error	3.9%	7.9%	7.7%	1.9%

\* S. Molloy, et al. *Academic Radiology* 22, 1052-1059 (2015).

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## Reliability of breast density measurement

	No. of cases	Mean (%)	Standard Deviation (%)	Standard Error (%)	Median (%)	25 <sup>th</sup> Percentile (%)	75 <sup>th</sup> Percentile (%)	Minimum (%)	Maximum (%)
Quantra	30	-0.06	1.64	0.30	-0.25	-1.00	0.68	-4.20	4.00
Volpara	30	-0.33	1.39	0.25	-0.35	-0.90	0.58	-4.25	2.28
Dual-Energy	36	0.10	0.52	0.09	0.03	-0.16	0.2	-0.47	2.63

\* O. Alonzo-Proulx, et al. *Radiology* 275, 366-376 (2015)

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## Conclusions

- Breast density can be accurately quantified with spectral mammography.
- The precision of spectral mammography can be 3 to 4 folds higher than current clinical standard.

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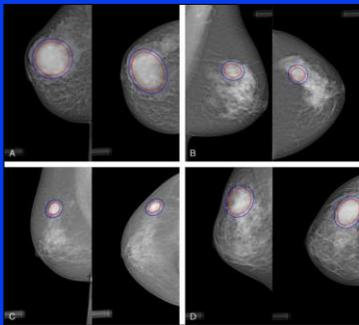
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## Lesion characterization



Erhard K1, Kilburn-Toppin F, Willsher P, Moa E, Fredenberg E, Wieberneit N, Buelow T, Wallis MG. Invest Radiol. 2016;51(5):340-7.

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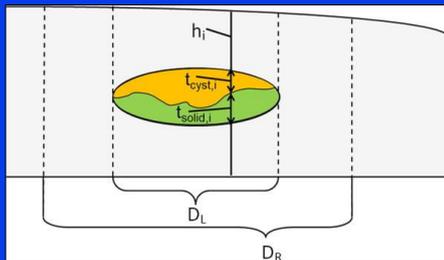
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## Lesion characterization



$$CVF = \frac{V_{cyst}}{V_{lesion}}, \text{ with } V_{lesion} = V_{cyst} + V_{solid}$$

Erhard K1, Kilburn-Toppin F, Willsher P, Moa E, Fredenberg E, Wieberneit N, Buelow T, Wallis MG. Invest Radiol. 2016;51(5):340-7.

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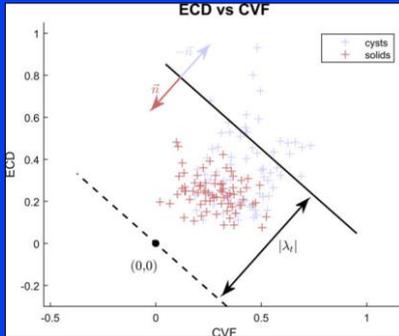
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## Lesion characterization



Erhard K1, Kilburn-Toppin F, Willsher P, Moa E, Fredenberg E, Wieberneit N, Buelow T, Wallis MG. Invest Radiol. 2016;51(5):340-7.

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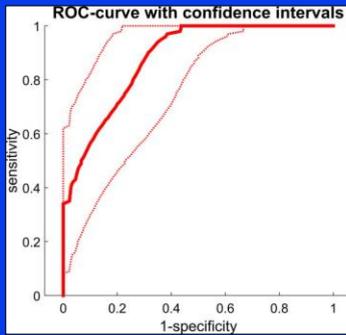
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## Lesion characterization



Erhard K1, Kilburn-Toppin F, Willsher P, Moa E, Fredenberg E, Wieberneit N, Buelow T, Wallis MG. Invest Radiol. 2016;51(5):340-7.

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## Conclusions

Discriminating cystic from solid lesions with spectral mammography demonstrates promising results with the potential to reduce mammographic recalls.

Erhard K1, Kilburn-Toppin F, Willsher P, Moa E, Fredenberg E, Wieberneit N, Buelow T, Wallis MG. Invest Radiol. 2016;51(5):340-7.

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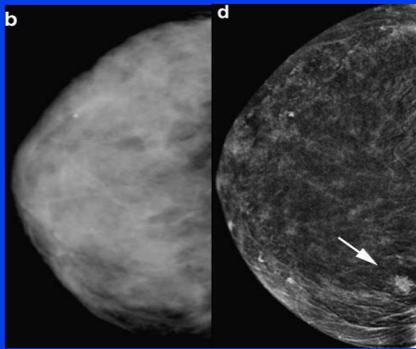
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## Contrast-enhanced mammography



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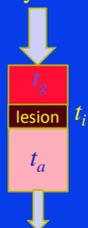
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## Quantitative contrast-enhanced mammography

- Malignant lesions are known to have higher vascular density.
- Iodine mass in a lesion is expected to be correlated with vascular density of a lesion.



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## Linear dual energy subtraction

Conventional CESM:

$$S_{DE} = \ln S_l - w \ln S_h \quad \left( w = \frac{\mu_g^l - \mu_a^l}{\mu_g^h - \mu_a^h} \right)$$



$$S_{DE} = T + \alpha t_i \quad \alpha = f(\mu_g^j, \mu_a^j, \mu_i^j)$$

- Total thickness ( $T$ ) is not evaluated;
- conversion slope ( $\alpha$ ) depends on local breast composition;

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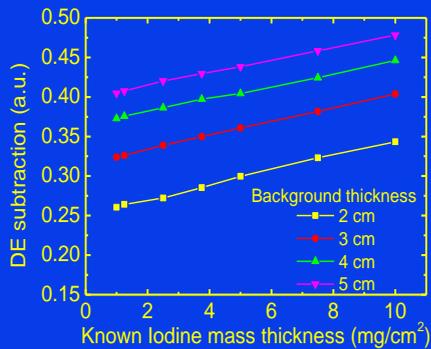
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## Linear dual energy subtraction




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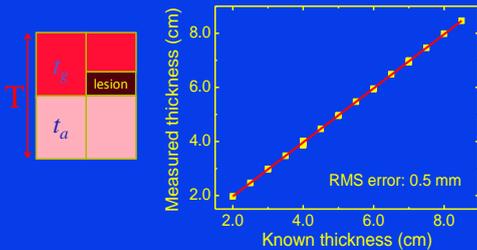
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## Dual energy material decomposition

Quantitative CESM:  $S_{DE} = T + \alpha t_i$



H. Ding, *et al.*, PMB 57, 4719 (2012).

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## Conclusions

➤ Phantom studies were performed to validate the feasibility of quantifying iodine mass thickness for breasts of various thicknesses and densities.

➤ The results show that the proposed quantification method offers high accuracy.

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## Conclusions

- Dual energy mammography can be used for accurate measurement of breast tissue composition and breast density.
- Dual energy mammography can potentially be used for characterization of cystic and solid lesions.

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## Conclusions

- Dual energy mammography can be used for accurate quantification of iodine in a lesion, which can potentially be used to estimate lesion vascular density.

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## Acknowledgements

### Cardiovascular Imaging Breast Imaging

- Benjamin Ziemer, PhD
- Bahman Sadeghi, MD
- Hanna Javan, MD
- Elliot Groves, MD
- Travis Johnson, MS
- Jerry Lipinski
- Shant Malkasian
- Brian Dertli
- Huanjun Ding, PhD
- Hyo Min Cho, PhD
- Nikita Kumar, MS
- Daniel Beidokhti

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## ACKNOWLEDGMENTS

This research was supported in part by Grant No. R01 CA136871 awarded by the NCI, DHHS. Momographic equipment was provided by Hologic and Philips Medical Systems.

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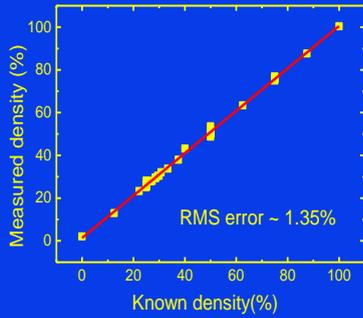
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# Phantom Study



H. Ding, et al., Physics in Medicine and Biology 57, 4719-4738 (2012)

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# Postmortem Study

- 40 postmortem breasts (20 pairs);
- 2 views (CC and MLO) for each breast;
- Dual-energy breast density quantification;
- Chemical analysis

Johnson, et al. Phys. Med. Biol. 58 (2013) 8573-8591

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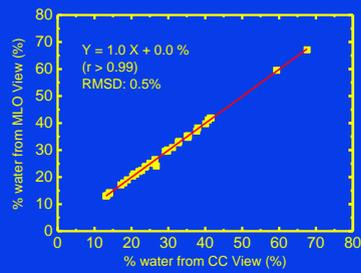
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# Reproducibility



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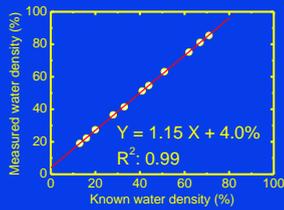
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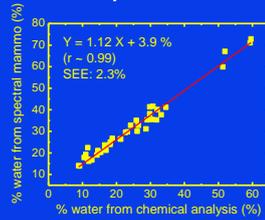
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# Accuracy

## Simulation



## Experiment




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# Lesion characterization

Lesion Type	Number	Size Range, mm
Solid lesions	62	10-60
Malignant solid lesions	47	10-60
Grade 1 (no special type)	6	13-27
Grade 2 (no special type)	13	10-35
Grade 3 (no special type)	20	13-60
Invasive lobular grade 2	5	14-50
Invasive mucinous grade 2	1	23
Micropapillary cancer grade 2	2	10-19
Benign solid lesions	15	10-25
Fibroadenoma	14	10-25
Intraductal papilloma	1	10
Cystic lesions	57	10-40

Erhard K1, Kilburn-Toppin F, Willsher P, Moa E, Fredenberg E, Wieberneit N, Buelow T, Wallis MG. Invest Radiol. 2016;51(5):340-7.

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# Lesion characterization

Cluster	1	2	3	4	5	6
Diameter	<10 mm	≥10 mm, ≤13.5 mm	>13.5 mm, ≤17.0 mm	>17.0 mm, ≤20.0 mm	>20.0 mm, ≤27.0 mm	>27.0 mm
No. lesions	31	24	22	25	24	24
Prevalence	0.57	0.67	0.64	0.56	0.38	0.38
AUC	0.60	0.75	0.73	0.82	0.98	0.99
Specificity (at 99% sensitivity)	0.64	0.25	0.33	0.55	0.80	0.93
NPV	0.74	0.93	0.95	0.98	0.99	0.99

For each cluster, the discriminator was trained first on all lesions outside the cluster and then evaluated only on the lesions in the cluster. Prevalence refers to the fraction of solid lesions among all lesions in a particular size cluster.  
AUC, indicates area under the receiver operating characteristic curve; NPV, negative predictive value.

Erhard K1, Kilburn-Toppin F, Willsher P, Moa E, Fredenberg E, Wieberneit N, Buelow T, Wallis MG. Invest Radiol. 2016;51(5):340-7.

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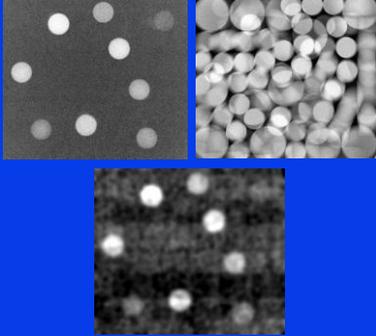
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## Phantom studies



Fredenberg et al.: Contrast-enhanced spectral mammography with a photon-counting detector, Med. Phys. 37,2010.

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## Breast Cancer Risk

- Women with the highest mammographic density have a factor of 4-5 increased risk of developing breast cancer compared with the lowest density.
- For every 1% increase in breast density the cancer risk is increased by 2%.\*

\* Boyd, et al. New England Journal Medicine, 2007. 356. p227-236

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## Goal

Develop a quantitative and accurate method to measure breast composition

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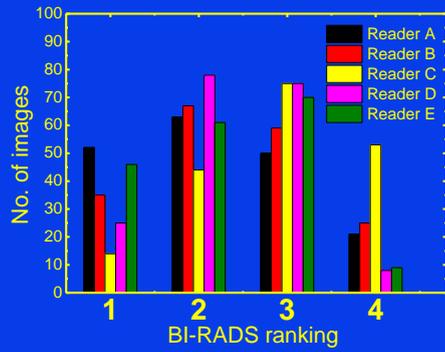
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## Observer variation -- BIRADS




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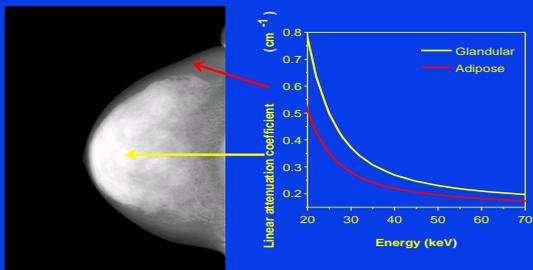
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## Dual Energy Mammography




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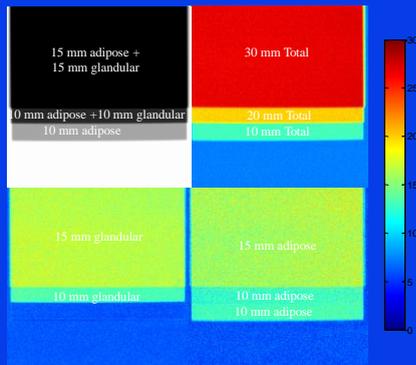
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## Spectral Mammography




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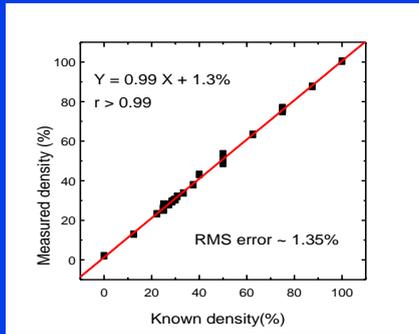
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# Phantom studies



H. Ding, *et al.*, *Physics in Medicine and Biology* 57, 4719-4738 (2012)

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# Breast Tissue Study

- 28 specimens from 14 breast pairs (right and left)
- Each sample imaged at two different orientations (view 1 and view 2)
- Dual energy decomposition (water and lipid basis)
- Chemical analysis (gold standard)



Philips MicroDose SI L50

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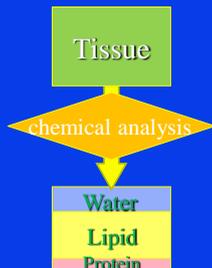
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# Chemical Analysis



1. Evaporate water in vacuum oven
2. Dissolve lipid in petroleum ether
3. Remove protein using vacuum filtration

T. Johnson, *et al.*, *Physics in Medicine and Biology* 58, 8573-8591 (2013)

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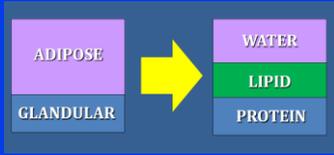
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# Fibrogladular Volume Fraction



$$\%FGV \times 100 = \frac{V_W + V_P}{V_W + V_L + V_P}$$

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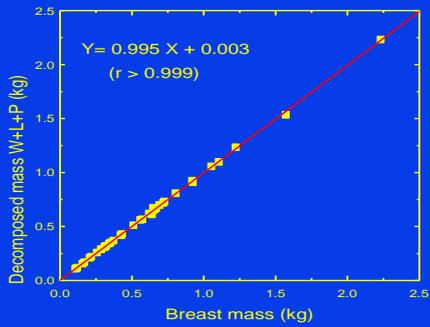
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## Chemical Analysis



T. Johnson, *et al.*, *Physics in Medicine and Biology* 58, 8573-8591 (2013)

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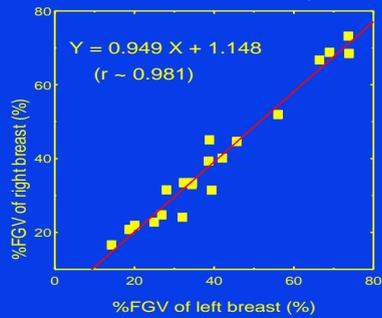
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## Chemical Analysis



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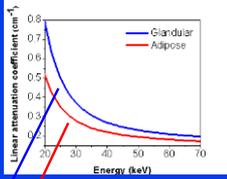
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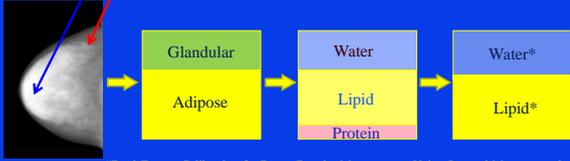
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# Dual Energy Decomposition



$$t_g = t_g(S_L, S_H)$$

$$t_a = t_a(S_L, S_H)$$



"Dual-Energy Calibration for Breast Density Measurement Using Spectral Mammography"  
57th AAPM Annual Meeting, SU-D-204-1

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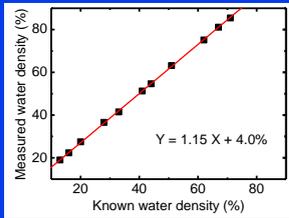
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# Simulation

Components	Median	Mean	Standard Deviation	Minimum	Maximum
Water	30.4%	34.2%	15.1%	12.3%	63.1%
Lipid	65.4%	59.9%	17.8%	26.0%	85.7%
Protein	4.7%	5.8%	2.7%	1.9%	11.4%



T. Johnson, et al., Physics in Medicine and Biology 58, 8573-8591 (2013)

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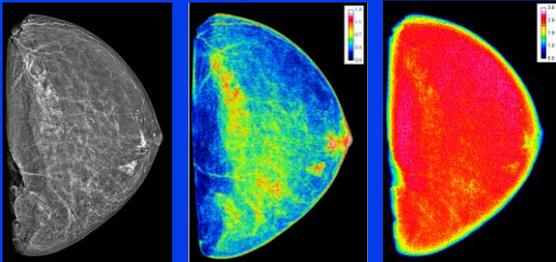
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# Examples of Spectral Mammography images



For Presentation

Water

Lipid

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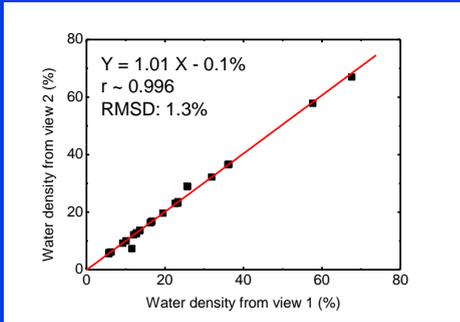
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## Comparison between views



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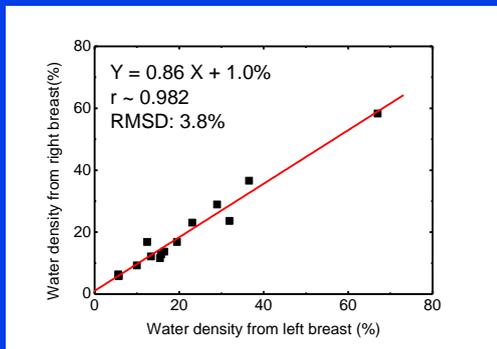
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## Comparison between right and left breasts



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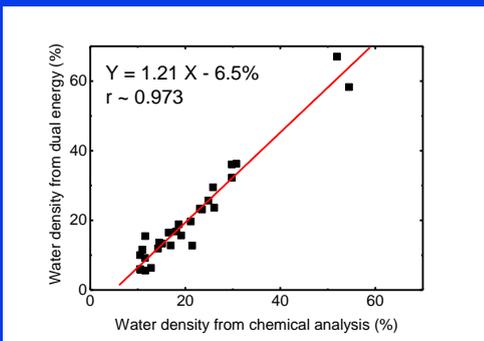
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## Comparison with chemical analysis



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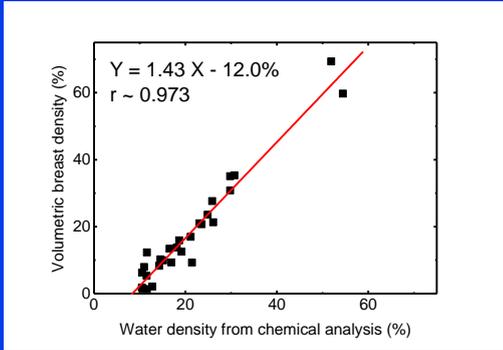
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## Comparison with chemical analysis



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## Human Study

- 93 mammography patients
- BI-RADS ranking by 10 radiologists (5 US, 5 UK)
- Standard grey level thresholding (Cumulus)
- Spectral mammography

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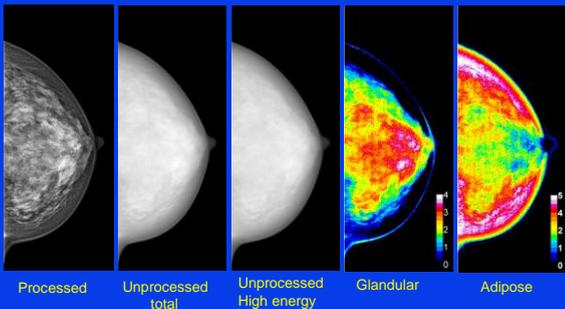
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## Spectral Mammography images



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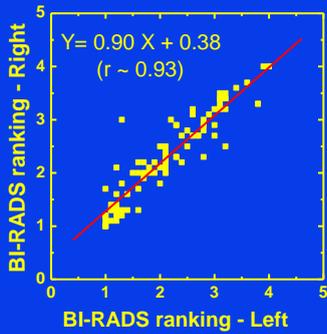
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## BI-RADS Rankings by Radiologists



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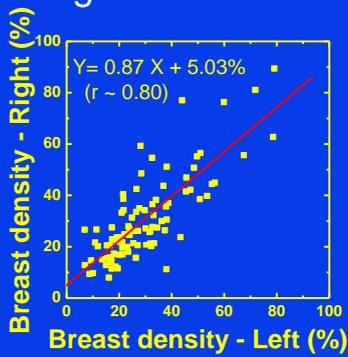
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## Histogram Thresholding



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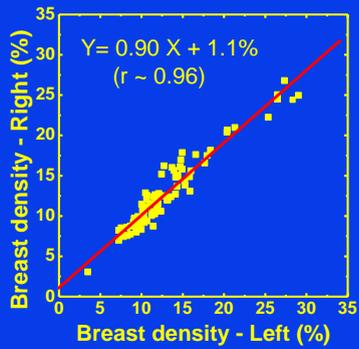
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## Spectral material decomposition



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# Breast Density Variability

	Bi-RADS	Histogram Thresholding	Spectral Decomposition
Right - Left	2.0	2.9	1.0

S. Molloy, et al., Academic Radiology S1076-6332(15)00201-9 (2015)

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# Breast density

Breast density is defined as the percentage of glandular breast tissue

$$\text{Breast Density} = \frac{G}{G + A} \times 100$$



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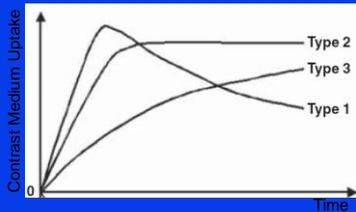
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# Dynamic contrast-enhanced spectral mammography



Generally, malignant lesions demonstrate a rapid uptake and washout of the contrast agent (type 1), whereas benign lesions are characterized by a more gradual uptake of contrast agent (type 2 and 3).

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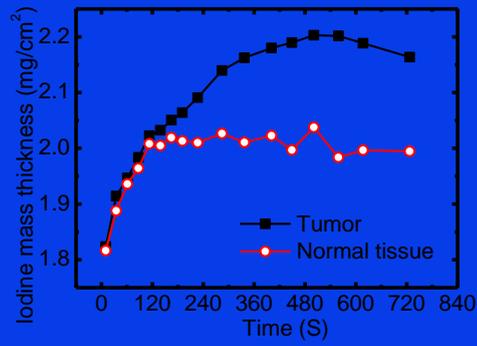
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## Phantom studies




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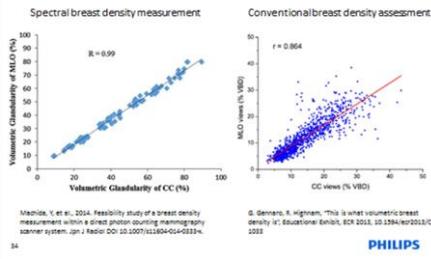
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## Clinical results




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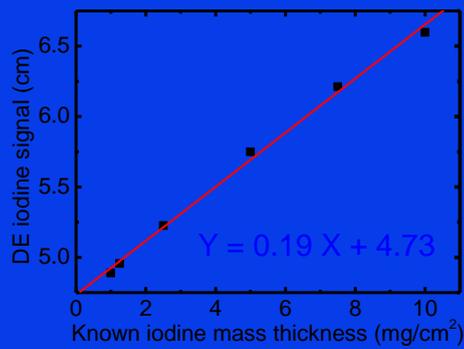
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## Phantom studies




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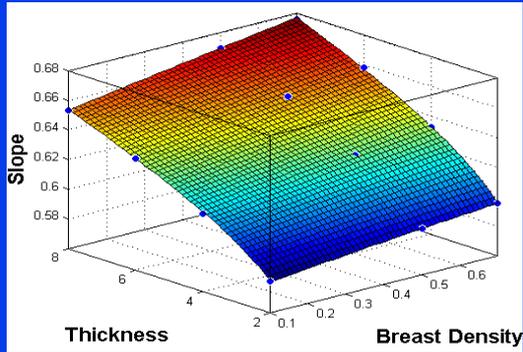
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## Phantom studies



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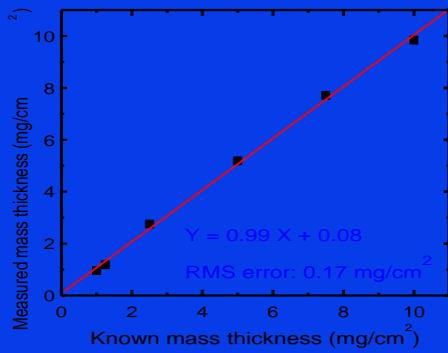
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## Phantom studies



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## Outline

- Breast density and cancer risk
- Current methods for breast density measurement
- Visual estimation (BIRADS classification)
- Grey level thresholding
- Fuzzy C-mean segmentation
- Techniques based on breast shape model
- Dual energy material decomposition
- Two material model for breast tissue (Glandular and adipose)
- Three material model for breast tissue (Water, lipid, protein)
- Problem of single measurement but 2-3 unknowns

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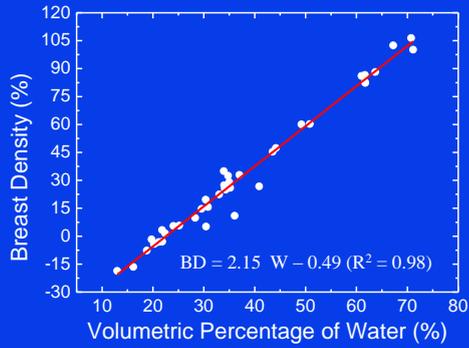
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### Breast Density and Water Content



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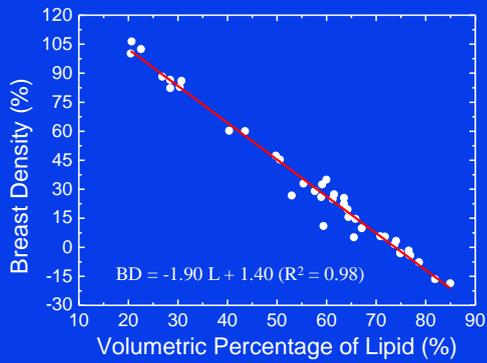
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### Breast Density and Lipid Content



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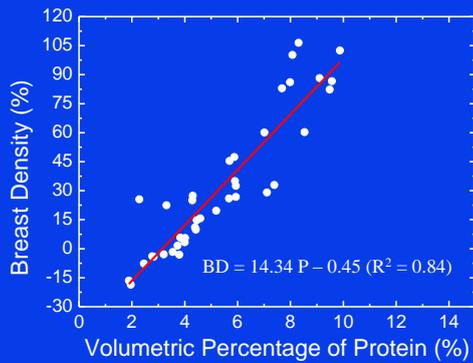
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### Breast Density and Protein Content



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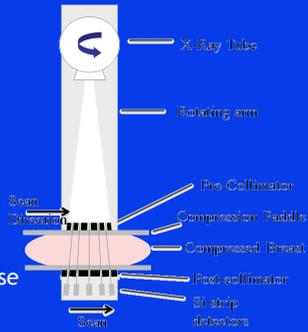
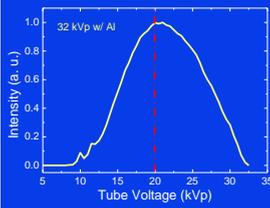
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# Spectral Mammography



Prototype Philips MicroDose Mammography SI

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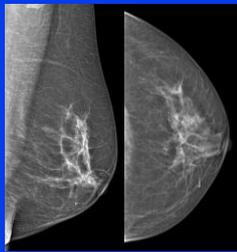
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# BI-RADS Reader Study

- IRB approval
- 93 patients
- 10 radiologists
- CC and MLO views
- Right and left breasts viewed in random order




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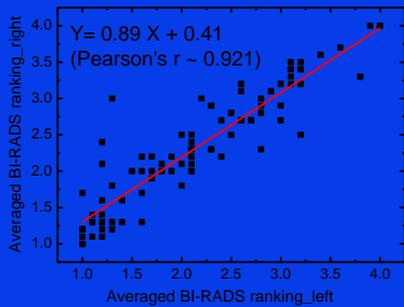
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# BI-RADS Ranking




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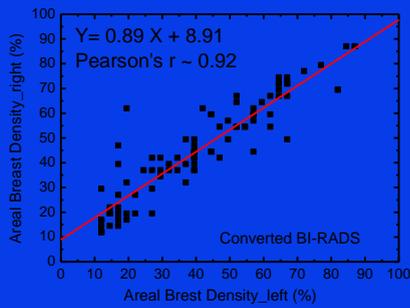
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## BI-RADS Breast Density



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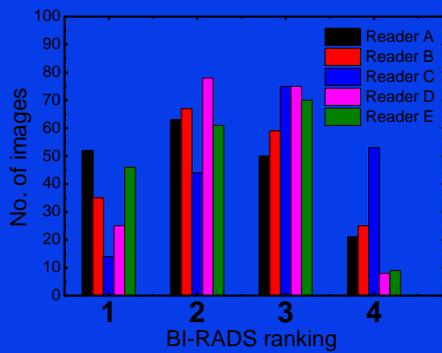
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## Observer Variability



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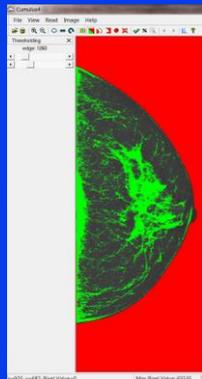
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## Histogram Thresholding

- Cumulus 4
- Two thresholds
- CC and MLO views in sequence
- Right and left blinded



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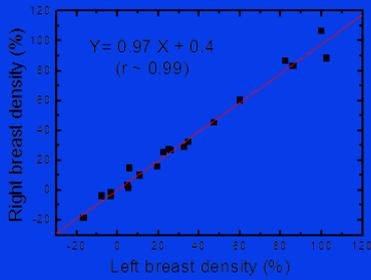
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## Automatic Segmentation using Fuzzy C-mean



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## Dual Energy Decomposition



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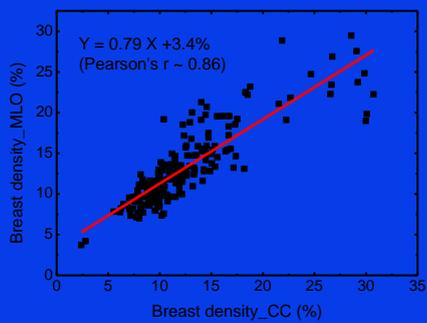
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## CC and MLO from dual energy



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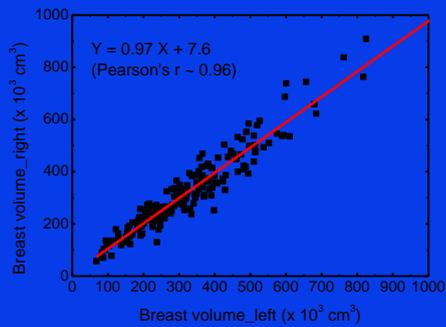
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## Breast Volume from Dual Energy



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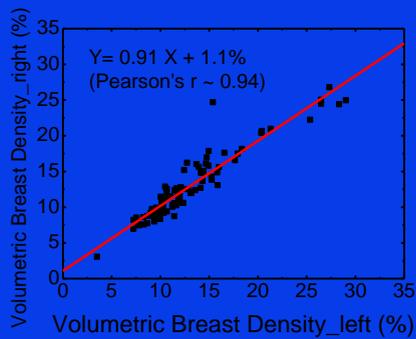
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## Breast Density from Dual Energy



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## Conclusions

- Spectral mammography offers quantification of volumetric breast density with excellent precision.
- It largely eliminates the inter- and intra-observer variability in breast density estimation.

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# ACKNOWLEDGMENTS

This research was supported in part by Grant No. R01 CA136871 awarded by the NCI, DHHS.

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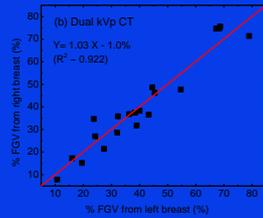
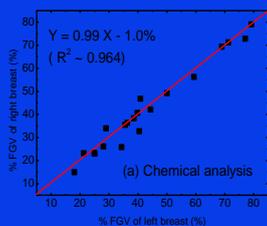
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## Right-left Breast Correlations



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# Dual Energy Decomposition



$$t_i = \frac{a_0 + a_1l + a_2h + a_3l^2 + a_4lh + a_5h^2}{\sqrt{1 + b_1l + b_2h}}$$

Ducote J L, Molloy S. Quantification of breast density with dual energy mammography: An experimental feasibility study, *Med. Phys.* 37: 793, 2010.

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# Breast Tissue Composition

Table 2. Density and elemental compositions of adipose tissue and glandular tissue used in theoretical investigations.

Tissue	H	C	N	O	Cl	Ca	Density (g/cc)	Ash (S,P,K,Ca)
Glandular Tissue (Hammerstein <sup>5</sup> )	10.2%	10.8%	3.2%	75.9%	-	-	1.04	0.5%
	18.4%	18.4%	3.2%	67.7%	-	-		
	30.5%	30.5%	3.2%	55.2%	-	-		
Adipose Tissue (Hammerstein <sup>5</sup> )	11.2%	49.1%	1.7%	35.7%	-	-	0.93	0.1%
	61.9%	61.9%	1.7%	25.1%	-	-		
	69.1%	69.1%	1.7%	18.9%	-	-		
Glandular Tissue (Woodard and White <sup>10</sup> )	10.2%	15.8%	3.7%	69.8%	-	-	1.06	-
	10.6%	33.2%	3.0%	52.7%	-	-	1.02	-
	10.9%	50.6%	2.3%	35.8%	-	-	0.99	-
Adipose Tissue (Woodard and White <sup>10</sup> )	11.2%	51.7%	1.3%	35.5%	-	-	0.97	-
	11.4%	59.8%	0.7%	27.8%	-	-	0.95	-
	11.6%	68.1%	0.2%	19.8%	-	-	0.93	-

Ducote J, Klopfer M and Molloy S. Volumetric lean percentage measurement using dual energy mammography, *Med Phys.* 2011 Aug;38(8):4498-504.

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# VLP Comparison

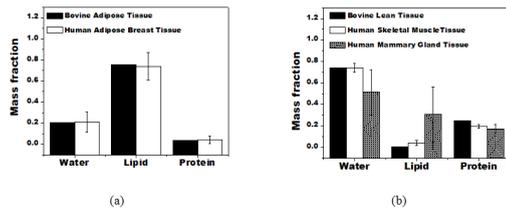


Fig. 5. The data in this study are shown next to the data of Woodard and White. Note for the data in this study, the error bars were too small to be seen. The RMS difference for bovine adipose and human adipose tissues was 1.2%. The RMS difference for bovine lean and human skeletal muscle tissue was 0.4% and 22.2% for bovine lean and human mammary gland tissues.

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## Spectral Mammography

- Philips MicroDose Digital Mammography System
- Tungsten anode x-ray tube.
- Appropriate energy bin selection.
- No Scatter correction necessary



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## Dual Energy Decomposition



$$t_i = \frac{a_0 + a_1 l + a_2 h + a_3 l^2 + a_4 l h + a_5 h^2}{\sqrt{1 + b_1 l + b_2 h}}$$

Ducote J.L., Molloy S. Quantification of breast density with dual energy mammography: An experimental feasibility study, Med. Phys. 37: 793, 2010.

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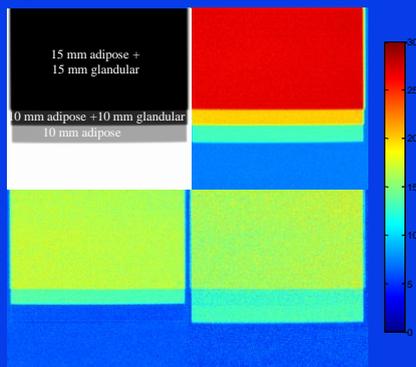
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## Spectral Mammography



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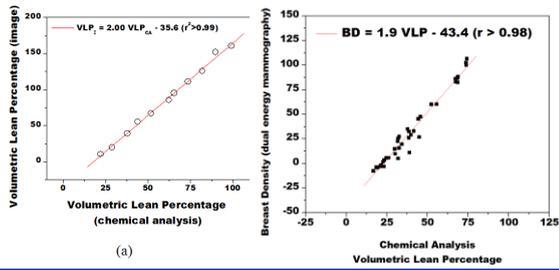
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## VLP Comparison



## Breast Tissue Composition

Table 2. Density and elemental compositions of adipose tissue and glandular tissue used in theoretical investigations.

Tissue	H	C	N	O	Cl	Ca	Density (g/cc)	Ash (S,P,K,Ca)
Glandular Tissue (Hammerstein <sup>9</sup> )	10.8%	10.8%	3.2%	75.9%	-	-	-	-
	10.2%	18.4%	3.2%	67.7%	-	-	1.04	0.5%
	30.5%	3.2%	55.2%	-	-	-	-	-
Adipose Tissue (Hammerstein <sup>9</sup> )	49.1%	1.7%	35.7%	-	-	-	-	-
	11.2%	61.9%	1.7%	25.1%	-	-	0.93	0.1%
	69.1%	1.7%	18.9%	-	-	-	-	-
Glandular Tissue (Woodard and White <sup>10</sup> )	10.2%	15.8%	3.7%	69.8%	-	-	1.06	-
	10.6%	33.2%	3.0%	52.7%	-	-	1.02	-
	10.9%	50.6%	2.3%	35.8%	-	-	0.99	-
Adipose Tissue (Woodard and White <sup>10</sup> )	11.2%	51.7%	1.3%	35.5%	-	-	0.97	-
	11.4%	59.8%	0.7%	27.8%	-	-	0.95	-
	11.6%	68.1%	0.2%	19.8%	-	-	0.93	-

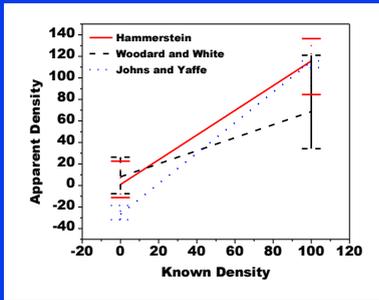
Ducote J, Klopfer M and Molloy S, Volumetric lean percentage measurement using dual energy mammography, *Med Phys*, 2011 Aug;38(8):4498-504.

## Breast Tissue Composition

Table 3. Summary of the apparent densities of breast tissue as compared to the composition determined from chemical analysis.

Composition Study Author	Tissue Type	Known Density	Range in Apparent Density	Average Apparent Density	RMS Error
Hammerstein <sup>9</sup>	Adipose	0	[-11.3 - 22.6]	4.1	14.6
	Glandular	100	[84.6 - 136.5]	112.3	24.6
Woodard and White <sup>10</sup>	Adipose	0	[-7.6 - 26.4]	9.0	16.5
	Glandular	100	[34.2 - 121]	74.6	43.8
Johns and Yaffe <sup>11</sup>	Adipose	0	[-31.8 - -18.5]	-25.7	26.2
	Glandular	100	[109.6 - 115.8]	113.5	13.8

# Breast Tissue Composition



Volumetric lean percentage measurement using dual energy mammography  
J Ducote, M Klopfer and S Molloi Med. Phys. (2011) AT-PRESS

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## System requirements for patient studies

- Minimal time interval (less than 1 sec) between low and high energy images.
- Ability to switch kVp between low and high energy images (i.e. 28 kVp to 49 kVp).
- Ability to switch beam filter between low and high energy images (i.e. Rh filter to Cu filter).
- Negligible lag and ghosting between low and high energy images.

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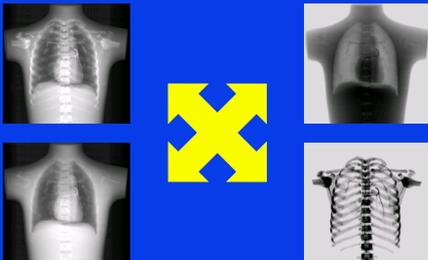
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## Dual Energy Imaging



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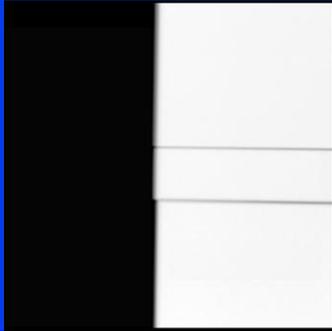
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# Dual Energy Imaging



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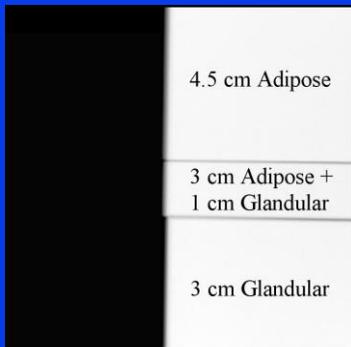
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# Dual Energy Imaging



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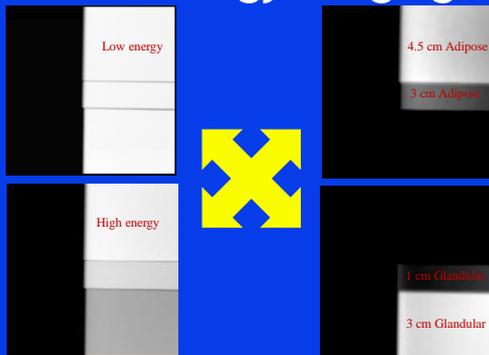
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# Dual Energy Imaging



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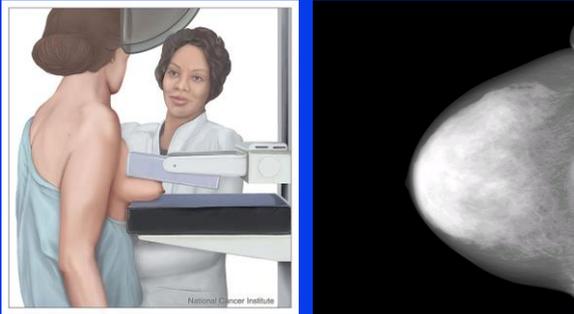
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## Screening Mammography



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## Visual estimation

Breast Imaging Reporting and  
Data System (BI-RADS)  
BI-RADS 1-4 with increasing  
level of glandularity.

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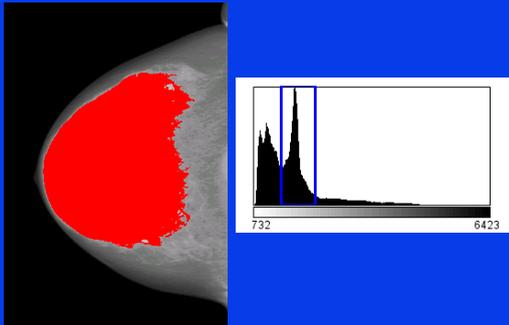
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## Histogram Thresholding



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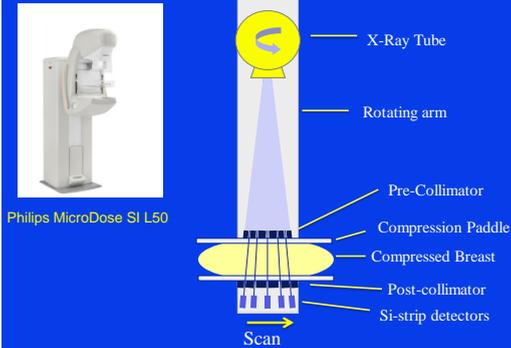
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## Spectral Mammography system



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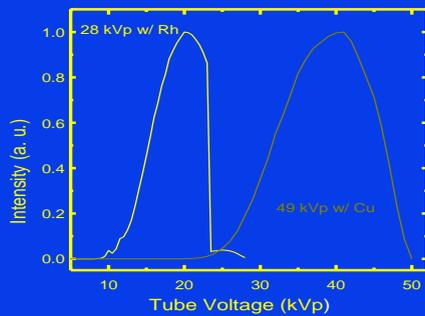
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## Dual kVp Mammography



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## Breast Tissue Study

- 40 breast tissue samples
- BI-RADS ranking by 3 radiologists
- Standard Histogram Thresholding
- Dual energy material decomposition
- Chemical analysis



Hologic Selenia Digital Mammography

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## Breast Tissue Composition

Two and three compartment models for breast composition.



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## Fibroglandular Volume Fraction



$$\%FGV \times 100 = \frac{V_W + V_P}{V_W + V_L + V_P}$$

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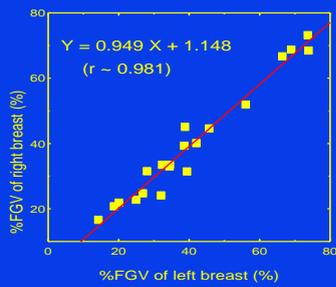
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## Chemical Analysis



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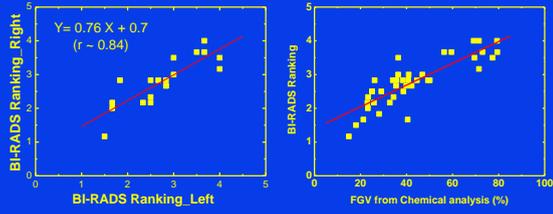
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# BI-RADS Rankings by Radiologists



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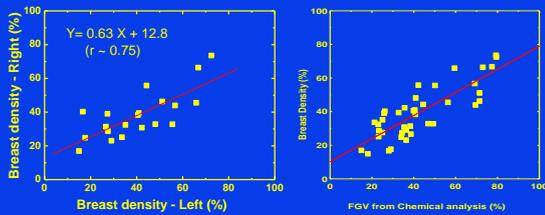
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# Histogram Thresholding



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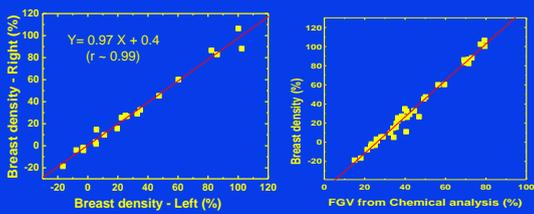
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# Dual energy material decomposition



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## Breast Density Variability

	Bi-RADS	Thresholding	Dual Energy
Right - Left	2.0	2.0	1.0
Chemical Analysis	2.1	1.8	1.0

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## Dual energy mammography requirements

- Minimize time interval between low and high energy images.
- Implement rapid kVp switching between low and high energy images.
- Implement rapid beam filter switching between low and high energy images (i.e. Rh filter to Cu filter).
- Minimize lag and ghosting between low and high energy images.
- Implement scatter correction.

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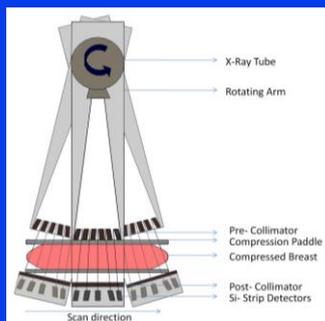
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## Spectral mammography system




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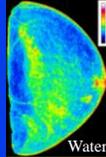
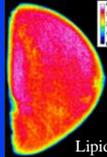
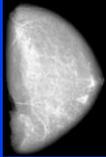
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## Post Mortem Study Details<sup>139</sup>

- 28 specimens from 14 breast pairs (right and left)
- Each sample imaged at two different orientations (view 1 and view 2)
- Dual energy decomposition (water and lipid basis)



- Chemical analysis (gold standard)

T. Johnson, *et al.*, *Physics in Medicine and Biology* 58, 8573-8591 (2013)

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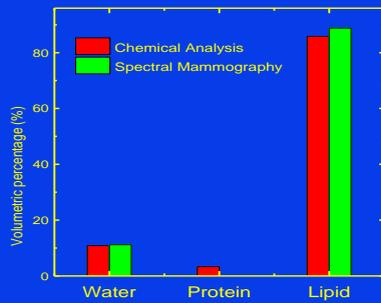
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## Spectral Material Decomposition



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## Breast Composition Variability

	Water Content (%)	Lipid Content (%)
Chemical Analysis	3.2	4.7

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