Dual Energy Imaging

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DISCLOSURES

• Toshiba
• Philips

Outline

• Introduction
• Dual energy mammography
• Spectral mammography
• Dual energy breast CT
• Spectral breast CT
• Conclusion
Dual Energy Imaging

Dual Energy Mammography

Dual Energy Decomposition

\[ l = l(t_g, t_a) \quad h = h(t_g, t_a) \]

\[ t_g = t_g(l, h) \quad t_a = t_a(l, h) \]

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

Outline

- Introduction
- Dual energy mammography
- Spectral mammography
- Dual energy breast CT
- Spectral breast CT
- Conclusion

**Dual energy Mammography**

- Hologic Selenia Digital Mammography
- Tungsten anode x-ray tube.
- 28 kVp, 60 mAs, 50 µm rhodium filter.
- 49 kVp, 30 mAs, 300 µm copper filter.
- Scatter correction.

**Dual kVp Mammography**

![Graph showing intensity vs. tube voltage for 28 kVp with Rh and 49 kVp with Cu]
Mammographically dense breast has been shown to be strongly associated with breast cancer risk\(^1\).

\[ \text{Breast Density} = \frac{t_g}{t_g + t_a} \times 100 \]

**Breast Tissue Study**

- 20 postmortem breast pairs
- BI-RADS ranking by 3 radiologists
- Standard grey level thresholding
- Dual energy mammography
- Chemical analysis
Chemical Analysis

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

Fibroglandular Volume Fraction

\[%\text{FGV}\times100 = \frac{V_W + V_P}{V_W + V_L + V_P}\%

Right-left Breast Correlation from Chemical Analysis

\[Y = 0.99X - 1.0\%\]
\([R^2 \approx 0.964]\)
Visual estimation
Breast Imaging Reporting and Data System (BI-RADS)
BI-RADS 1-4 with increasing level of glandularity.

BI-RADS Rankings by Radiologists

Gray level thresholding
### Breast Density Variability

<table>
<thead>
<tr>
<th>Bi-RADS</th>
<th>Thresholding</th>
<th>Dual Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right - Left</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Chemical Analysis</td>
<td>2.1</td>
<td>1.8</td>
</tr>
</tbody>
</table>

### Outline

- **Introduction**
- **Dual energy mammography**
- **Spectral mammography**
- **Dual energy breast CT**
- **Spectral breast CT**
- **Conclusion**

### Spectral Mammography

- Philips MicroDose SI Digital Mammography
- Tungsten anode x-ray tube.
- Equivalent filtration 0.75 mm of Al.
- Noise floor 8.7 keV.
- No scatter correction.
Spectral mammography system

Spectral Mammography

Human Study

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

BI-RADS Rankings by Radiologists

Grey Level Thresholding
Spectral material decomposition

Breast density - Right (%) vs Breast density - Left (%)

$Y = 0.90X + 1.1\%$

(r ~ 0.96)

Breast Density Variability

<table>
<thead>
<tr>
<th></th>
<th>Bi-RADS</th>
<th>Thresholding</th>
<th>Spectral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right - Left</td>
<td>2.0</td>
<td>2.9</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Outline

- Introduction
- Dual energy mammography
- Spectral mammography
- Dual energy breast CT
- Spectral breast CT
- Conclusion
Dual energy breast CT

- 20 pairs of postmortem breasts
- Varian 4030CB on optical bench
- Scatter-glare and beam hardening Corrections

Dual Energy Decomposition

Dual energy CT

- Water
- Lipid (glycerol trioleate)
- Protein
- Polyoxymethylene
Calibration phantom

Water
Oil
Delrin plastic
(Polyoxymethylene)

Water
Lipid
Protein

Accuracy of Volumetric Water Fraction

Water fraction from Dual kVp CT
Water fraction from chemical analysis
Y = 1.08X - 0.025 (R^2 ~ 0.926)
RMS error: 4.7%
Outline

- Introduction
- Dual energy mammography
- Spectral mammography
- Dual energy breast CT
- Spectral breast CT
- Conclusion
Spectral breast CT

- 20 pairs of postmortem breasts
- eV 2500 CZT on optical bench
- Spectral distortion corrections

Rotation and translation stage

Spectral breast CT

![Graph showing photon energy and count rate](image)
Accuracy of Volumetric Water Fraction

\[ Y = 0.99X - 0.24\% \quad (r \sim 0.97) \]

Accuracy of Volumetric Lipid Fraction

\[ Y = 0.97X + 2.89\% \quad (r \sim 0.98) \]
Conclusions

- Dual energy imaging can be used to accurately quantify breast density or water, lipid, and protein contents in breast tissue.
- It can potentially improve breast cancer diagnosis.
ACKNOWLEDGMENTS

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X-ray Imaging Physics Laboratory

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Collaborators:
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Carlos Iribarren, M.D., MPH, Ph.D.

Right-left Breast Correlations

(a) Chemical analysis

\[ Y = 0.99 X - 1.0\% \]
\[ (R^2 = 0.964) \]

(b) Dual kVp CT

\[ Y = 1.03 X - 1.0\% \]
\[ (R^2 = 0.922) \]
Overall Accuracy of Volumetric Fraction

Average RMS error: 3.58%

RMS error (%) vs Sample mass (g)

Protein Simulated with Delrin

Percentage of known quantity and theoretical decomposition of pure water, lipid, and protein.

DE decomposition using all photons with spectral corrections:

- Water: $Y = 0.99X - 0.24\%$ ($r \approx 0.97$)
- Lipid: $Y = 0.97X + 2.89\%$ ($r \approx 0.98$)
- Protein: $Y = 0.99X - 0.36\%$ ($r \approx 0.97$)

Known Quantity vs Theoretical Decomposition
Introduction

- Breast tissue compositional information may improve breast cancer diagnosis.
- Water content of tissue is affected by pathology.
**Goal**
Validate dual energy CT for decomposition of breast tissue into water, lipid and protein using chemical analysis as the gold standard.

**Conclusions**
- The high correlation of Breast Density with respect to data from chemical analysis validates the use of dual energy mammography as an accurate measurement of breast tissue composition.

- Variability of breast density measurement is reduced by a factor of two as compared with BI-RADS ranking.
- Spectral mammography is expected to further enhance utility of breast density as a risk factor for breast cancer.
Goal
Develop a quantitative method to measure breast tissue composition in terms of water, lipid and protein using spectral CT.

Outline
- Introduction
- Simulation studies
- Physical phantom studies
- Postmortem breast studies

Introduction
Mammographically dense breast has been shown to be strongly associated with breast cancer risk.

Introduction
Assessing breast density using pattern classification and visual estimation

Breast density is defined as the percentage of glandular breast tissue:

\[
Breast\ Density = \frac{G}{G + A} \times 100
\]

Two-tissue assumption and three compartment model for breast.

- Adipose
- Glandular
- Water
  - Lipid
  - Protein
Introduction

Three compartmental model of breast

- Lesion characterization according to their composition
- Water content of tissue is affected by pathology


Outline

- Introduction
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- Physical phantom studies
- Postmortem breast studies
- Patient studies
Simulation Model

Analytical model to calculate optimal figure of merit (FOM)

\[ \text{FOM} = \frac{\text{SNR}}{\text{threshold energy (keV)}} \]

• Details
Theoretical Analysis I

WLP -> WLP (mean) energies of 50 kVp and 120 kVp

Chemical Analysis
Theoretical Decomp

Fractional composition

Lean Tissue

Water Lipid Protein
-0.2 0.0 0.2 0.4 0.6 0.8 1.0 1.2

Adipose Tissue

Water Lipid Protein
-0.2 0.0 0.2 0.4 0.6 0.8 1.0 1.2

Theoretical Analysis II

WLD Calibration -> ...

Chemical Analysis
Theoretical Decomp

Fractional composition

ICRU-44 WLD Decomp
RMSE = 0.03

Glandular Tissue

Water Lipid Protein
-0.2 0.0 0.2 0.4 0.6 0.8 1.0 1.2

RMSE = 0.04
Theoretical Analysis II
WLD Calibration

Water Lipid Protein
-0.4
-0.2
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4

Polyethylene
ICRU-44 (WLD)
Flat Panel
RMSE = 0.11

Fractional composition

Water Lipid Protein
-0.2
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4

PMMA
ICRU-44 (WLD)
Flat Panel
RMSE = 0.0001

Fractional composition

Water Lipid Protein
-0.2
0.0
0.2
0.4
0.6
0.8
1.0
1.2

RMSD = 0.13

Lean Tissue
Fractional composition
Chemical Analysis
Breast Composition (Hammerstein)

RMSD = 0.11

Adipose Tissue
Fractional composition
Chemical Analysis
Breast Composition (Hammerstein)

Outline

• Introduction
• Simulation studies
• Physical phantom studies
• Postmortem breast studies
• Patient studies
Photon counting and energy resolving detectors

- Photon counting
- Energy resolving
- Electronic noise rejection
- Examples: CdZnTe crystals

**eV 2500 – eV Microelectronics**

CdZnTe (CZT) crystals
4 crystals, 64 pixels
51.2 mm total length
0.8 mm pitch
5 energy bins

**Small field-of-view prototype**

- X-ray tube
- Object on rotation & translation stage
- Fore collimator
- All collimator
- CZT array
Experiment

Beam energy: 100 kVp
Threshold energy: 40 keV (meat), 42 keV (post-mortem breast samples)
Current: 1.0 mA
Scan time: 61.5 s/rotation
Scan mode: 2D (meat), 3D Helical (post-mortem breast samples)
Filtration: 1 mm Al (meat), 2 mm Al (post-mortem breast samples)
Dose: 3.74 mGy (meat), 1.75 mGy (post-mortem breast samples)

Phantom study

Bin1 (22 ~ 40 keV) Bin2 (40 ~ 100 keV)

Three material decomposition on phantom

<table>
<thead>
<tr>
<th>ROI</th>
<th>Water</th>
<th>Oil</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>measured</td>
<td>expected</td>
<td>measured</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
Outline

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- Physical phantom studies
- Postmortem breast studies
- Patient studies

Meat study

Bin 1 (22 ~ 40 keV)  Bin 2 (40 ~ 100 keV)

~ 30 mm

Post-mortem breast sample

Bin 1 (22 ~ 42 keV)  Bin 2 (42 ~ 100 keV)

~ 100 mm
Three material decomposition of post-mortem breast sample

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.

Conclusions

- Expected additional dose is low
- Proposed technique could be incorporated into existing screening mammography.
- Preliminary studies to date indicate the possibility of accurate breast density measurement in phantoms (within 3% error)
ACKNOWLEDGMENTS

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

Breast Density and Water Content

\[ BD = 2.15W - 0.49 \quad (R^2 = 0.98) \]

Breast Density and Lipid Content

\[ BD = -1.90L + 1.40 \quad (R^2 = 0.98) \]
**Breast Density and Protein Content**

- **Formula:** BD = 14.34 P – 0.45 (R² = 0.84)

**BI-RADS Reader Study**

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

**BI-RADS Ranking**

- Formula: Y = 0.89 X + 0.41 (Pearson's r ~ 0.921)
**BI-RADS Breast Density**

\[ Y = 0.89X + 8.91 \]

Pearson's \( r \approx 0.92 \)

**Observer Variability**

- **Histogram Thresholding**
  - Cumulus 4
  - Two thresholds
  - CC and MLO views in sequence
  - Right and left blinded
Fuzzy C-mean Clustering

- Automatic segmentation
- Total of 6 clusters
- First three clusters glandular tissue
Automatic Segmentation using Fuzzy C-mean

Dual Energy Decomposition

Fig 6: BD from DE right breast vs. left breast. BD from DE vs. %FGV from chemical analysis.
Breast density_MLO (%)

Y = 0.79 X + 3.4%
(Pearson’s r ~ 0.86)

Breast density_CC (%)

Y = 0.97 X + 7.6
(Pearson’s r ~ 0.96)

Breast Volume from Dual Energy

Breast Volume from Dual Energy

Breast Density from Dual Energy
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.

ACKNOWLEDGMENTS

This research was supported in part by Grant No. R01 CA136871 awarded by the NCI, DHHS.
Right-left Breast Correlations

(a) Chemical analysis

Y = 0.99 X - 1.0%  
(R^2 = 0.954)

(b) Dual kVp CT

Y = 1.03 X - 1.0%  
(R^2 ~ 0.922)

% FGV of right breast (%)
% FGV of left breast (%)

(b) Dual kVp CT

% FGV from right breast (%)
% FGV from left breast (%)

Y = 1.03 X - 1.0%  
(R^2 ~ 0.922)

Breast Tissue Composition

<table>
<thead>
<tr>
<th>Tissue</th>
<th>R (%)</th>
<th>C (%)</th>
<th>N (%)</th>
<th>O (%)</th>
<th>Cl (%)</th>
<th>Density (g/cc)</th>
<th>Ash (A.P.L.Ca)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glandular</td>
<td>10.2%</td>
<td>10.8%</td>
<td>3.2%</td>
<td>72.9%</td>
<td>-</td>
<td>1.66</td>
<td>9.5%</td>
</tr>
<tr>
<td>Connective (Sclerotic)</td>
<td>30.0%</td>
<td>3.2%</td>
<td>52.5%</td>
<td>-</td>
<td>-</td>
<td>1.85</td>
<td>-</td>
</tr>
<tr>
<td>Adipose</td>
<td>95.7%</td>
<td>1.7%</td>
<td>13.8%</td>
<td>-</td>
<td>-</td>
<td>0.65</td>
<td>-</td>
</tr>
<tr>
<td>Connective (Sclerotic)</td>
<td>65.3%</td>
<td>1.7%</td>
<td>19.5%</td>
<td>-</td>
<td>-</td>
<td>1.85</td>
<td>-</td>
</tr>
<tr>
<td>Glandular</td>
<td>10.2%</td>
<td>13.9%</td>
<td>3.7%</td>
<td>69.8%</td>
<td>-</td>
<td>1.90</td>
<td>-</td>
</tr>
<tr>
<td>Connective (Sclerotic)</td>
<td>50.0%</td>
<td>2.3%</td>
<td>35.8%</td>
<td>-</td>
<td>-</td>
<td>1.65</td>
<td>-</td>
</tr>
<tr>
<td>Adipose</td>
<td>11.2%</td>
<td>13.7%</td>
<td>1.7%</td>
<td>55.4%</td>
<td>-</td>
<td>0.95</td>
<td>-</td>
</tr>
<tr>
<td>Connective (Sclerotic)</td>
<td>50.0%</td>
<td>2.3%</td>
<td>35.8%</td>
<td>-</td>
<td>-</td>
<td>1.65</td>
<td>-</td>
</tr>
</tbody>
</table>

VLP Comparison

(a) Chemical analysis

Water, Light, Protein

(b) Dual kVp CT

Water, Light, Protein

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 bone and human skeletal muscle was 6.4% and 22.2% for bovine bone and human mammary gland tissues.
Spectral Mammography

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

Dual Energy Decomposition

$T_1 = \frac{a_n + a_p + a_{nh} + a_{nh}^2 + a_{np} + a_{np}^2}{\sqrt{1 + b_n + b_{np}}}$


VLP Comparison
Breast Tissue Composition

Table 1. Density and elemental composition of adipose tissue and glandular tissue used in theoretical investigations.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>H</th>
<th>C</th>
<th>N</th>
<th>O</th>
<th>Cl</th>
<th>Ca</th>
<th>Density (g/cc)</th>
<th>Ash (g/cc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glandular</td>
<td>10.2</td>
<td>18.8</td>
<td>6.9</td>
<td>67.5</td>
<td>0.7</td>
<td>-</td>
<td>1.65</td>
<td>0.85</td>
</tr>
<tr>
<td>(Resonance)²</td>
<td>10.7</td>
<td>18.8</td>
<td>6.9</td>
<td>67.5</td>
<td>0.7</td>
<td>-</td>
<td>1.65</td>
<td>0.85</td>
</tr>
<tr>
<td>Adipose</td>
<td>10.2</td>
<td>18.8</td>
<td>6.9</td>
<td>67.5</td>
<td>0.7</td>
<td>-</td>
<td>1.65</td>
<td>0.85</td>
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<tr>
<td>(Resonance)²</td>
<td>10.7</td>
<td>18.8</td>
<td>6.9</td>
<td>67.5</td>
<td>0.7</td>
<td>-</td>
<td>1.65</td>
<td>0.85</td>
</tr>
<tr>
<td>Glandular</td>
<td>11.2</td>
<td>61.1</td>
<td>1.7</td>
<td>18.9</td>
<td>-</td>
<td>-</td>
<td>0.81</td>
<td>0.85</td>
</tr>
<tr>
<td>(Resonance)²</td>
<td>10.9</td>
<td>61.1</td>
<td>1.7</td>
<td>18.9</td>
<td>-</td>
<td>-</td>
<td>0.81</td>
<td>0.85</td>
</tr>
</tbody>
</table>

Breast Tissue Composition

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

<table>
<thead>
<tr>
<th>Composition</th>
<th>Tissue Type</th>
<th>Known Density</th>
<th>Range in Apparent Density</th>
<th>Average Apparent Density</th>
<th>RMS Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hammerstein²</td>
<td>Adipose</td>
<td>0</td>
<td>[-11.3 - 226]</td>
<td>4.1</td>
<td>14.6</td>
</tr>
<tr>
<td></td>
<td>Glandular</td>
<td>100</td>
<td>[84.6 - 136.5]</td>
<td>112.3</td>
<td>24.6</td>
</tr>
<tr>
<td>Woodard and White²²²</td>
<td>Adipose</td>
<td>0</td>
<td>[7.6 - 26.4]</td>
<td>117</td>
<td>26.2</td>
</tr>
<tr>
<td></td>
<td>Glandular</td>
<td>100</td>
<td>[34.2 - 121]</td>
<td>74.6</td>
<td>43.8</td>
</tr>
<tr>
<td>Johns and Yaffe</td>
<td>Adipose</td>
<td>0</td>
<td>[-31.8 - 18.5]</td>
<td>25.7</td>
<td>26.2</td>
</tr>
<tr>
<td></td>
<td>Glandular</td>
<td>100</td>
<td>[109.6 - 115.8]</td>
<td>113.5</td>
<td>13.8</td>
</tr>
</tbody>
</table>

Breast Tissue Composition

Figure: Apparent density vs. known density for different studies.
Fig. 4 R&L