Computer-Aided Diagnosis of Breast Cancer: Towards the Detection of Early and Subtle Signs

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Breast cancer statistics

- Lifetime probability of developing breast cancer is one in 8.8 (Canada)
- Lifetime probability of death due to breast cancer is one in 27 (Canada)
- Prevalence: 1% of all women living with the disease
- Screening mammography has been shown to reduce mortality rates by 30% to 70%
X-ray imaging of the breast
Mammography

Signs of Breast Cancer:

- Masses
- Calcifications
- Bilateral asymmetry
- Architectural distortion (subtle, often missed)
Two standard views per breast:
Cranio-caudal and Mediolateral oblique
Masses

- Breast cancer causes a desmoplastic reaction in breast tissue
- A mass is observed as a bright, hyper-dense object

Mammogram with a mass
Calcification

- Deposits of calcium in breast tissue

Mammogram with calcification
Bilateral Asymmetry

- Differences in the overall appearance of one breast with reference to the other
Architectural Distortion

- Third most common mammographic sign of nonpalpable breast cancer
- The normal architecture of the breast is distorted
- No definite mass visible
- Spiculations radiating from a point
- Focal retraction or distortion at the edge of the parenchyma

Mammogram with architectural distortion
Objectives of computer-aided processing of mammograms

- Enhancement of image quality
- Detection of subtle signs of cancer
- Quantitative analysis of features
- Objective aids to diagnostic decision
- Accurate and consistent analysis
- *Earlier detection of breast cancer!*
Some important problems

Detection of:

• Breast boundary (skin – air boundary)
• Pectoral muscle (in MLO views)
• Fibro-glandular disc
• Calcifications
• Masses and tumors
• Curvilinear structures
• Bilateral asymmetry (asymmetric densities)
• Architectural distortion
Computer-aided diagnosis (CAD)

- Increased number of cancers detected\(^1\) by 19.5%

- Increased early-stage malignancies detected\(^1\) from 73% to 78%

- Recall rate increased\(^1\) from 6.5% to 7.7%

- 50% of the cases of architectural distortion missed\(^2\)

\(^1\) (Freer and Ulissey, 2001) \(^2\) (Baker et al., 2003)
Simultaneous contrast
Simultaneous contrast
Just-noticeable difference
Contrast enhancement

Original mammogram with calcifications

Enhanced image using adaptive-neighborhood contrast enhancement
Examples of benign and malignant calcifications
Detection of calcifications by region growing
Detection of calcifications by error of prediction

(a) Part of original mammogram
(b) Seeds detected using prediction error
(c) Calcifications detected by region growing
Detection of masses by density slicing and texture flow-field analysis

Most benign masses have smooth shapes with convex lobules.
Detection and analysis of tumors

The green parts of the boundary represent concave segments, indicating malignancy.
Detection and analysis of tumors

Orientation field

Coherence

Tumor + FP detected
Detection of a subtle tumor
Radiological characterization of masses (BI-RADS)
Analysis of masses: feature extraction

Mass region

Shape analysis: Fractional concavity

Ribbon for computation of texture features

Normals to contour for computation of edge sharpness (acutance)
Objective representation of breast masses

(a) b145lc95
\[ F_{cc} = 0.00 \]
\[ A = 0.07 \]
\[ F_8 = 8.11 \]

(b) b164ro94
\[ F_{cc} = 0.42 \]
\[ A = 0.08 \]
\[ F_8 = 8.05 \]

(c) m51rc97
\[ F_{cc} = 0.64 \]
\[ A = 0.09 \]
\[ F_8 = 8.15 \]

(d) m55lo97
\[ F_{cc} = 0.83 \]
\[ A = 0.01 \]
\[ F_8 = 8.29 \]

benign circumscribed
benign macrolobulated
malignant microlobulated
malignant spiculated
Rank-ordering using shape: \( F_{cc} \)
Rank-ordering using acutance
## Classification of masses

<table>
<thead>
<tr>
<th>Features</th>
<th>Sens</th>
<th>Spec</th>
<th>Avg</th>
<th>Sens</th>
<th>Spec</th>
<th>Avg</th>
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<th>$A_z$</th>
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<td>97.3</td>
<td>94.7</td>
<td>90</td>
<td>97.3</td>
<td>94.7</td>
<td>100</td>
<td>97.3</td>
<td>98.2</td>
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<td>54.0</td>
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<td>94.7</td>
<td>85.6</td>
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<td>94.7</td>
<td>83.4</td>
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<td>14 texture</td>
<td>*</td>
<td>*</td>
<td>*</td>
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<td>64.9</td>
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<td>0.67</td>
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</tbody>
</table>
Content-based retrieval and analysis: benign mass

Query

b145lc95  b62lx97  b164rx94  b148ro97
Content-based retrieval and analysis: malignant tumor

Query

m55lo97  m58rc97  m61lo97  m55lc97
Detection of the pectoral muscle edge and the breast boundary using Gabor filters and active contour models
Analysis of bilateral asymmetry using Gabor filters

The directional distribution of fibroglandular tissue differs between the left and right breasts
Architectural distortion

spiculated  focal retraction  incipient mass
Normal vs. architectural distortion
Normal vs. architectural distortion
Detection of architectural distortion

1. Extract the orientation field
2. Filter and downsample the orientation field
3. Analyze orientation field using phase portraits
4. Post-process the phase portrait maps
5. Detect sites of architectural distortion
Gabor filter

\[ g(x, y) = \frac{1}{2\pi \sigma_x \sigma_y} \exp\left[ -\frac{1}{2} \left( \frac{x^2}{\sigma_x^2} + \frac{y^2}{\sigma_y^2} \right) \right] \cos(2\pi fx) \]

Design parameters

- line thickness \( \tau \)
- elongation \( l \)
- orientation \( \theta \)

Gabor parameters

\[ f = \frac{1}{\tau}; \quad \sigma_x = \frac{\tau}{2\sqrt{2\ln2}} \]

\[ \sigma_y = l\sigma_x; \quad \begin{bmatrix} x' \\ y' \end{bmatrix} = \begin{bmatrix} \cos\theta & -\sin\theta \\ \sin\theta & \cos\theta \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} \]
Design of Gabor filters

\[ l = l_0 \]
\[ \tau = \tau_0 \]
\[ \theta = \theta_0 \]

\[ l > l_0 \]
\[ \tau = \tau_0 \]
\[ \theta = \theta_0 \]

\[ l = l_0 \]
\[ \tau > \tau_0 \]
\[ \theta = \theta_0 \]

\[ l = l_0 \]
\[ \tau = \tau_0 \]
\[ \theta > \theta_0 \]
Extracting the orientation field

- Compute the texture orientation (angle) for each pixel

Gabor filtering (line detection)
Extracting the orientation field

\[ I(x, y) \]

Original image

\[ g_1(x, y) \]

\[ g_2(x, y) \]

\[ \vdots \]

\[ g_K(x, y) \]

Gabor filter bank (K = 180)

\[ I_1(x, y) \]

\[ I_2(x, y) \]

\[ I_K(x, y) \]

Filtering

Image resolution: 200 \( \mu \text{m/pixel} \)

\[ k_{\text{max}} = \arg \max_k \{ |I_k(x, y)| \} \]

\[ \theta(x, y) = -\frac{\pi}{2} + k_{\text{max}} \frac{\pi}{K} \]

Orientation field

Filtering

Image resolution: 200 \( \mu \text{m/pixel} \)
Filtering and downsampling the orientation field

\[ \theta(x, y) \]

\[ \sin[2\theta(x, y)] \]

\[ \cos[2\theta(x, y)] \]

Gaussian filtering

\[ s(x, y) \]

\[ \frac{1}{2} \arctan \left[ \frac{s(x, y)}{c(x, y)} \right] \]

Downsample

\[ \theta_f(x, y) \]

Filtered orientation field

\[ \theta_d(x, y) \]

Downsampled orientation field

Image resolution: 200 µm/pixel

Filtering

Downsampling

Image resolution: 800 µm/pixel
Orientation field: architectural distortion

Original image

Gabor magnitude

Filtered orientation field
Orientation field: normal case

Original image  Gabor magnitude  Filtered orientation field
Phase portraits

\[ \vec{v}(x, y) = \begin{pmatrix} v_x \\ v_y \end{pmatrix} = A \begin{pmatrix} x \\ y \end{pmatrix} + \mathbf{b} \]

node  saddle  spiral
<table>
<thead>
<tr>
<th>Phase portrait type</th>
<th>Eigenvalues of matrix A</th>
<th>Streamlines</th>
<th>Orientation field</th>
</tr>
</thead>
<tbody>
<tr>
<td>Node</td>
<td>Real, same sign</td>
<td><img src="image" alt="Node Streamlines" /></td>
<td><img src="image" alt="Node Orientation Field" /></td>
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<tr>
<td>Saddle</td>
<td>Real, opposite sign</td>
<td><img src="image" alt="Saddle Streamlines" /></td>
<td><img src="image" alt="Saddle Orientation Field" /></td>
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<tr>
<td>Spiral</td>
<td>Complex conjugate</td>
<td><img src="image" alt="Spiral Streamlines" /></td>
<td><img src="image" alt="Spiral Orientation Field" /></td>
</tr>
</tbody>
</table>
Model error

Orientation field \( \theta(x, y) \)

Model-generated field \( \phi(x, y|A, b) \)

\[ \Delta(x, y) = \sin[\theta(x, y) - \phi(x, y|A, b)] \] 
Local error measure

\[ \varepsilon^2(A, b) = \sum_x \sum_y \Delta^2(x, y) \] 
Sum of the squared error measure
Texture analysis using phase portraits (step 1 of 3)

1. Fit phase portrait model to the moving analysis window

\[
\begin{bmatrix}
-1.1 & 0.3 \\
-0.2 & 1.7
\end{bmatrix}
\]

\[
\begin{bmatrix}
-4.8 \\
-7.9
\end{bmatrix}
\]
Texture analysis using phase portraits (step 2 of 3)

2. Find phase portrait type and location of fixed point

\[
A = \begin{bmatrix}
1.1 & 0.3 \\
-0.2 & 1.7
\end{bmatrix}
\]

\[
b = \begin{bmatrix}
-4.8 \\
-7.9
\end{bmatrix}
\]

Type: node

Fixed point: \(x=3, y=5\)
Texture analysis using phase portraits (step 3 of 3)

3. Cast a vote in the corresponding phase portrait map

Orientation field  →  Node  →  Saddle  →  Spiral
Post-processing and detection

1. Filter the node map with a Gaussian mask
2. Detect peaks in the node map larger than the other peaks within a radius of 6.4 mm (8 pixels)
3. The peaks indicate the locations of architectural distortion
Phase portrait maps: architectural distortion case

node
[0, 1.1]
saddle
[0, 0.3 \times 10^{-3}]
spiral
[0, 0]
Phase portrait maps: normal case

- Node: [0, 0.98]
- Saddle: [0, 0.2x10^{-4}]
- Spiral: [0, 0]
Initial results of detection (2004)

- Test dataset: 19 mammograms with architectural distortion (MIAS database)
- Sensitivity: 84%
- 18 false positives per image
FROC analysis
Reduction of false positives
Rejection of confounding structures

- Confounding structures include
  - Edges of vessels
  - Intersections of vessels
  - Edge of the pectoral muscle
  - Edge of the fibro-glandular disk
Detection of curvilinear structures (CLS)

- Nonmaximal suppression

  If a pixel in the magnitude image is greater than its neighbors along the direction perpendicular to the local orientation field angle, the pixel is a core CLS pixel.
Nonmaximal suppression

ROI with a vessel

Gabor magnitude output

Output of nonmaximal suppression (NMS)
Rejection of confounding structures

Main feature of confounding structures:

Angle from the orientation field and direction perpendicular to the gradient vector differ by less than 30 degrees

(Adaptation of a method by Karssemeijer and te Brake: IEEE TMI 1996)
Rejection of confounding CLS

Core CLS pixels detected
(Output of NMS)

CLS pixels rejected from
further analysis
Rejection of confounding CLS

Core CLS pixels detected (Output of NMS)

CLS pixels rejected from further analysis
Improved phase portrait analysis

- Local error measure weighted by smoothed and downsampled map of CLS pixels

- Simulated annealing (SA) applied to obtain initial estimate of phase portrait parameters at every position of analysis window
  - Global optimization of weighted sum of squared error measure over 6-D space of $A$ and $b$

- Parameters further refined by nonlinear least squares
Improved detection of sites of architectural distortion

Node map without CLS analysis

Node map with CLS analysis
Result of detection of architectural distortion
FROC analysis (2005)

FROC curve

With CLS analysis

Without CLS analysis

sensitivity (%)

False positives per image
Effect of conditioning number of matrix $A$ on the orientation field

<table>
<thead>
<tr>
<th>Example</th>
<th>Matrix $A$</th>
<th>Eigenvalues</th>
<th>Angle between principal axes</th>
<th>Conditioning number</th>
<th>Orientation field</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>$\begin{bmatrix} 1 &amp; 0 \ 0 &amp; 3 \end{bmatrix}$</td>
<td>$\lambda_1 = 1$ [ \lambda_2 = 3 ]</td>
<td>$90^\circ$</td>
<td>$3$</td>
<td><img src="image" alt="Orientation field" /></td>
</tr>
<tr>
<td>B</td>
<td>$\begin{bmatrix} 1 &amp; 7.46 \ 0 &amp; 3 \end{bmatrix}$</td>
<td>$\lambda_1 = 1$ [ \lambda_2 = 3 ]</td>
<td>$15^\circ$</td>
<td>$21.85$</td>
<td><img src="image" alt="Orientation field" /></td>
</tr>
<tr>
<td>C</td>
<td>$\begin{bmatrix} 1 &amp; 0 \ 0 &amp; 20 \end{bmatrix}$</td>
<td>$\lambda_1 = 1$ [ \lambda_2 = 20 ]</td>
<td>$90^\circ$</td>
<td>$20$</td>
<td><img src="image" alt="Orientation field" /></td>
</tr>
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</table>
Improved results (2006)

- 19 cases of architectural distortion
- 41 normal control mammograms (MIAS)

- Symmetric matrix $A$: node and saddle only
- Conditioning number of $A > 3$ : reject result

- Sensitivity: 84% at 4.5 false positives / image

- Sensitivity: 95% at 9.9 false positives / image
FROC analysis with symmetric $A$ (2006)
Conclusion and future work

- Phase portraits can be used to detect architectural distortion
- Need to reduce false positives further
- Evaluate method with a large database
- Test method with screening mammograms taken prior to mass formation:

  *earlier detection of breast cancer*
Applications of computer-aided diagnosis

- Screening program or diagnostic clinic:
  - Consultation by radiologists
  - Decision support
    - Second opinion
    - Comparison with cases of known diagnosis
- Training:
  - Teaching, continuing medical education
- Teleradiology, telemedicine:
  - When local expertise is not available
Use of the University of Calgary indexed atlas with mobile agents

Local computer

Query mammogram Viewed on monitor #1

Select ROI

Extract features [0.09, 0.02, 0.04]

Remote host computer

Indexed atlas

Mammography database

Comparative analysis

Secure communication link

Retrieval results

Network interface

Mobile software agent

Query data

Mobile software agent

Results of retrieval Viewed on monitor #2

K-nearest cases and notes for comparative analysis by radiologist

Use of the University of Calgary indexed atlas with mobile agents
Acknowledgment

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