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

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screentest ALBERTA PROGRAM FOR THE EARLY DETECTION OF BREAST CANCER

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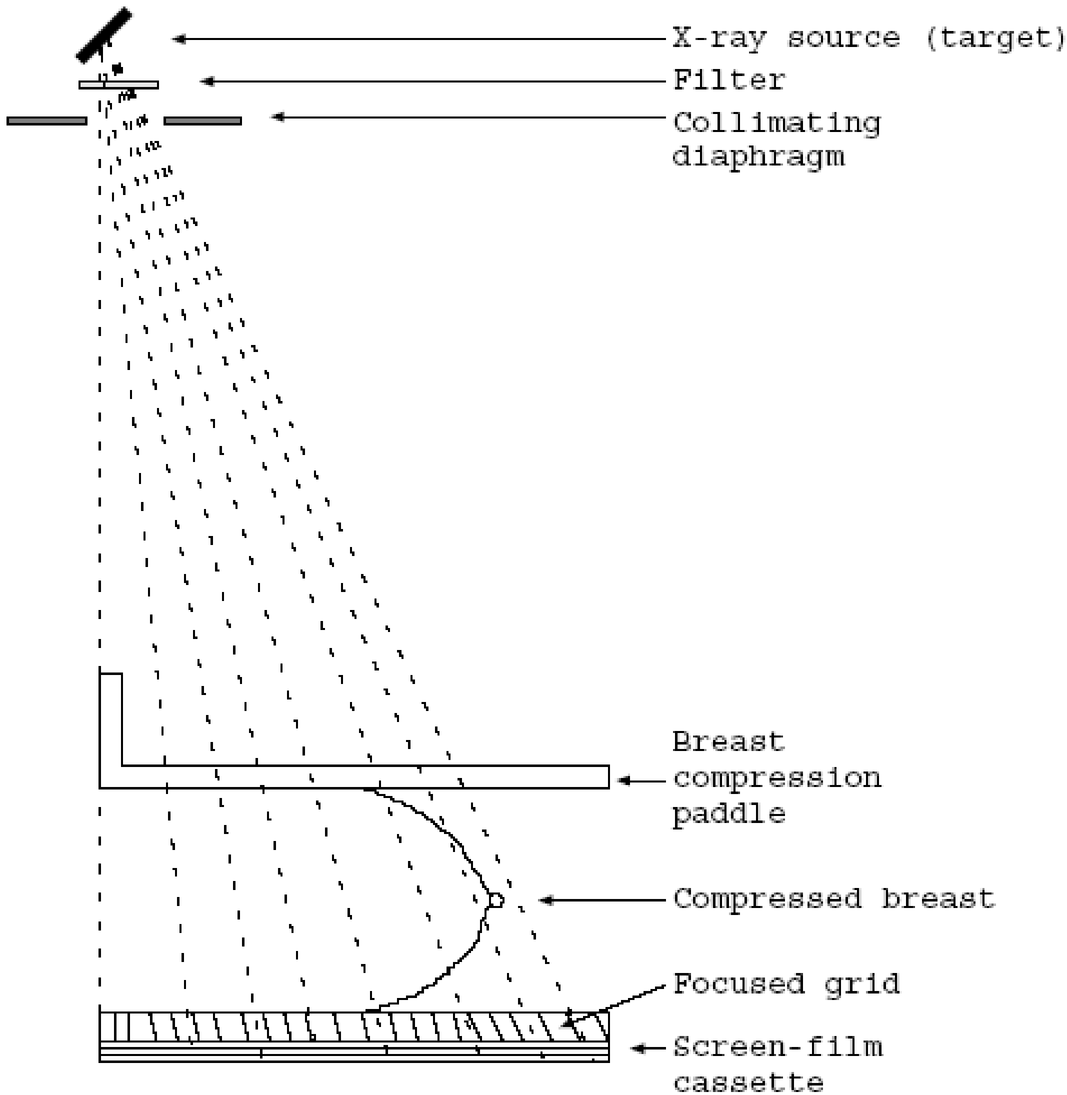
Alberta Cancer Board: Screen Test
Calgary, Alberta, CANADA

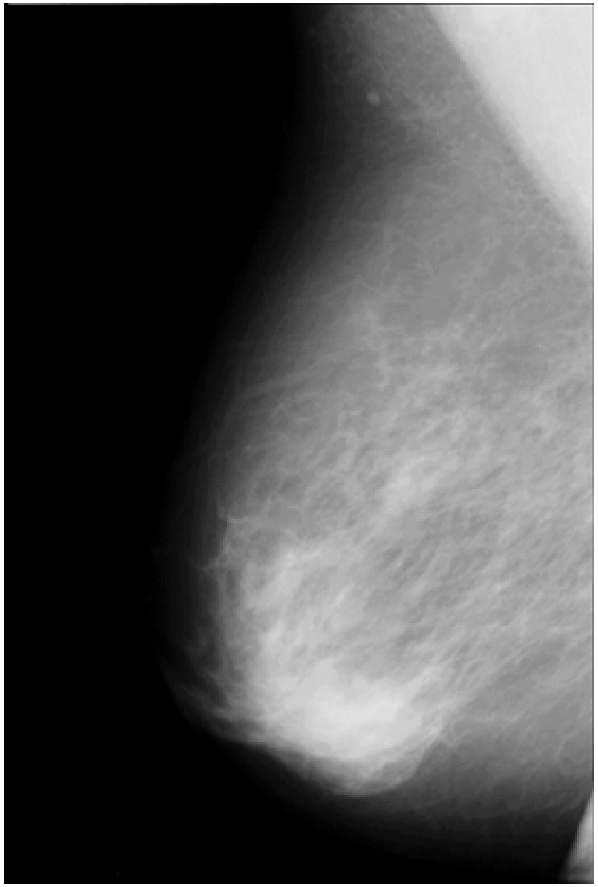
Breast cancer statistics

- 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:

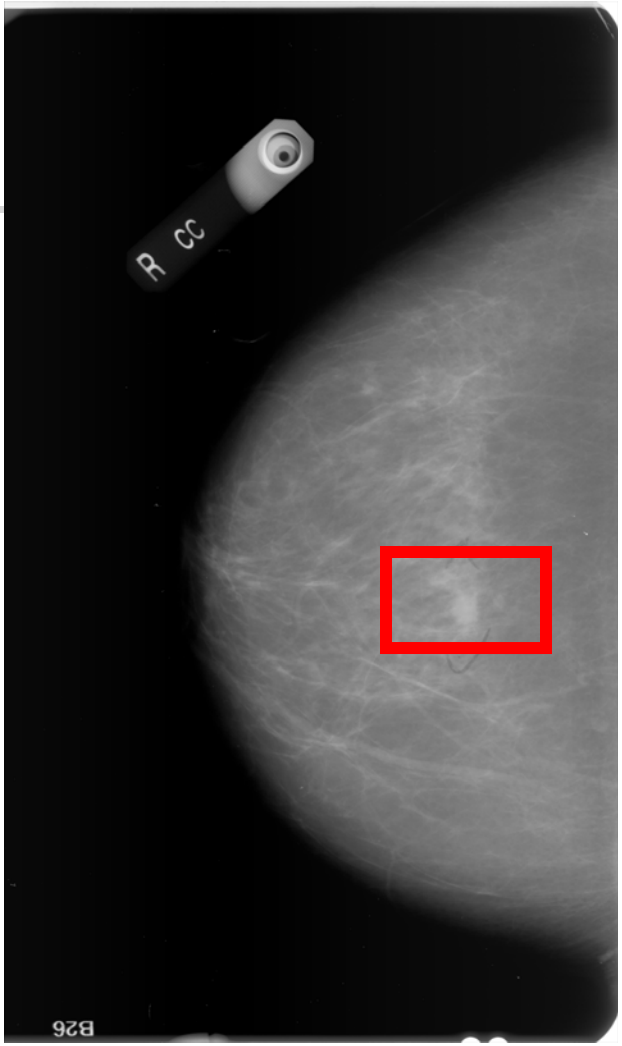
- Masses
- Calcifications
- Bilateral asymmetry
- Architectural distortion (subtle, often missed)

Two standard views per breast:

Cranio-caudal and Mediolateral oblique

Masses

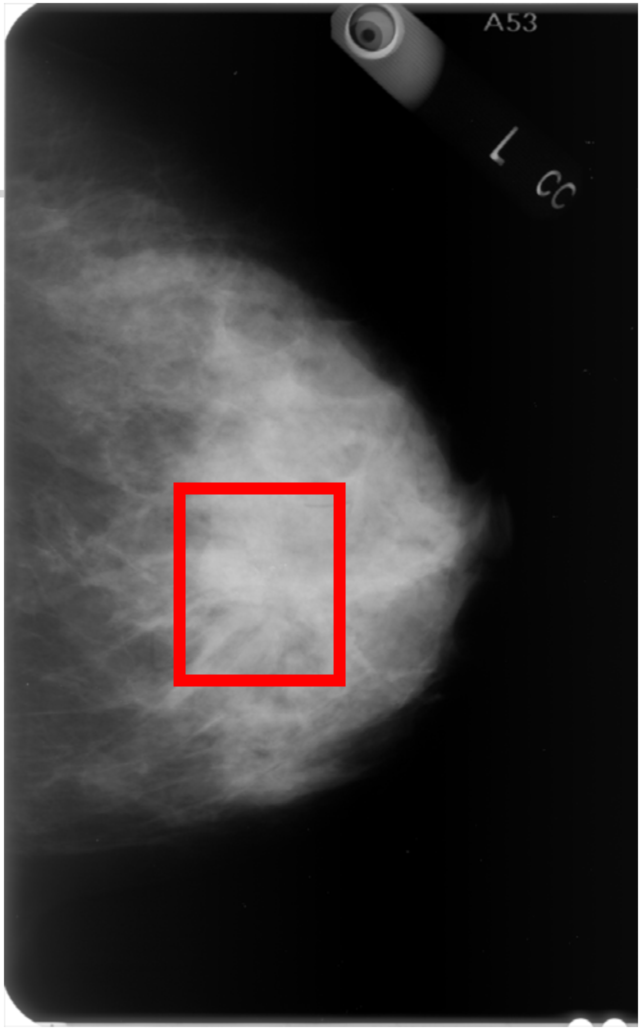
- Breast cancer causes a desmoplastic reaction in breast tissue
- A mass is observed as a bright, hyper-dense object



Mammogram with a mass

Calcification

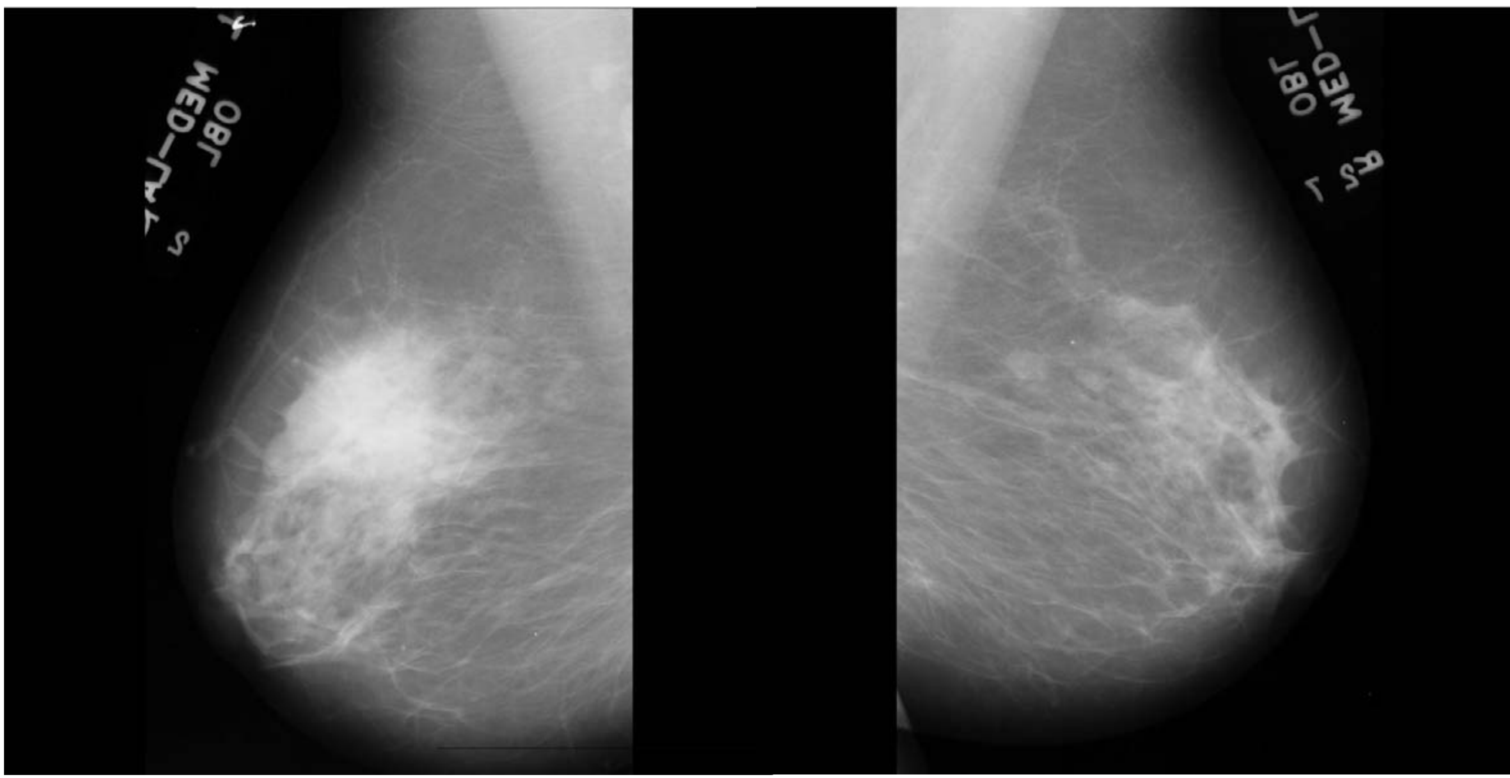
- Deposits of calcium in breast tissue



Mammogram with calcification

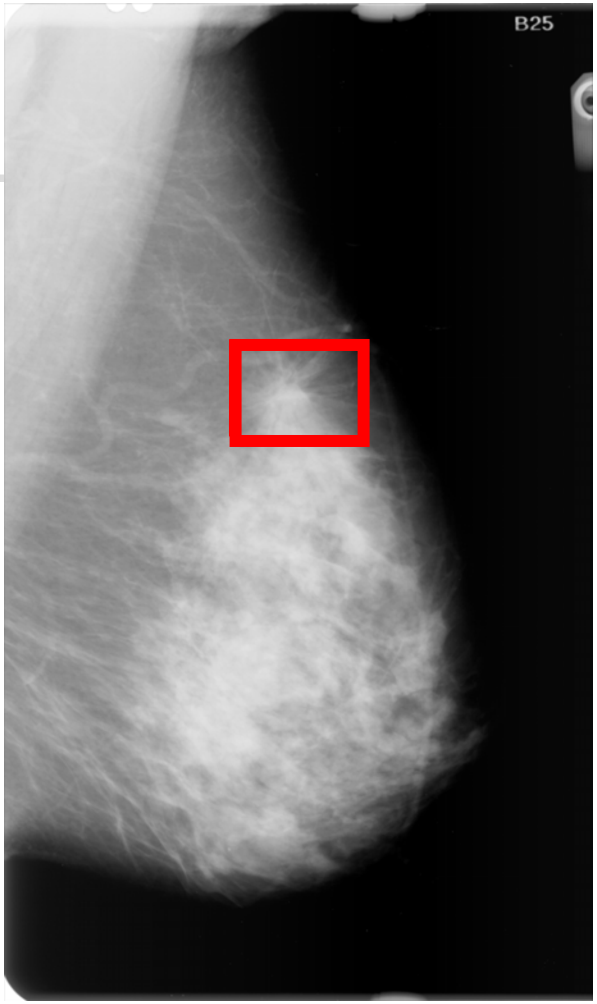
Bilateral Asymmetry

- 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]

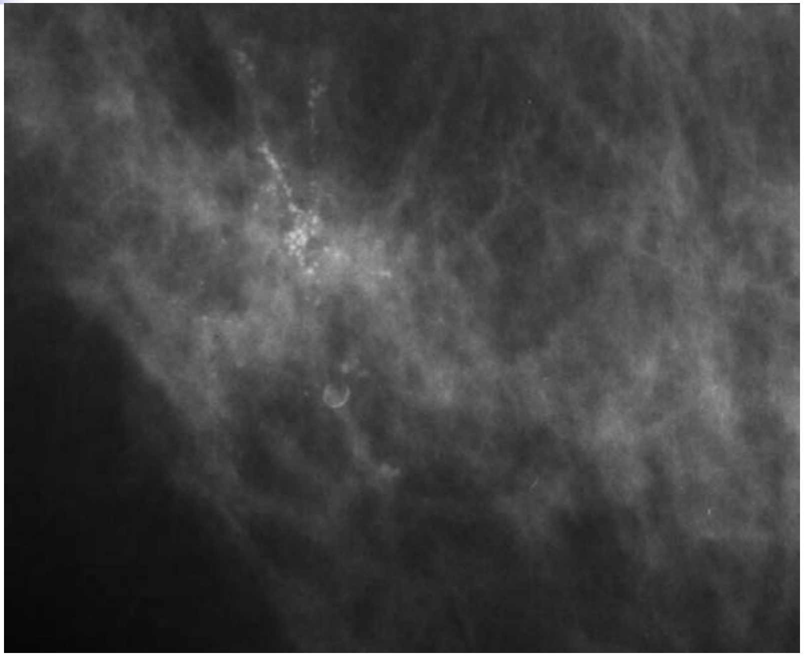
[1] *(Freer and Ulissey, 2001)* [2] *(Baker* et al.*, 2003)*

Simultaneous contrast

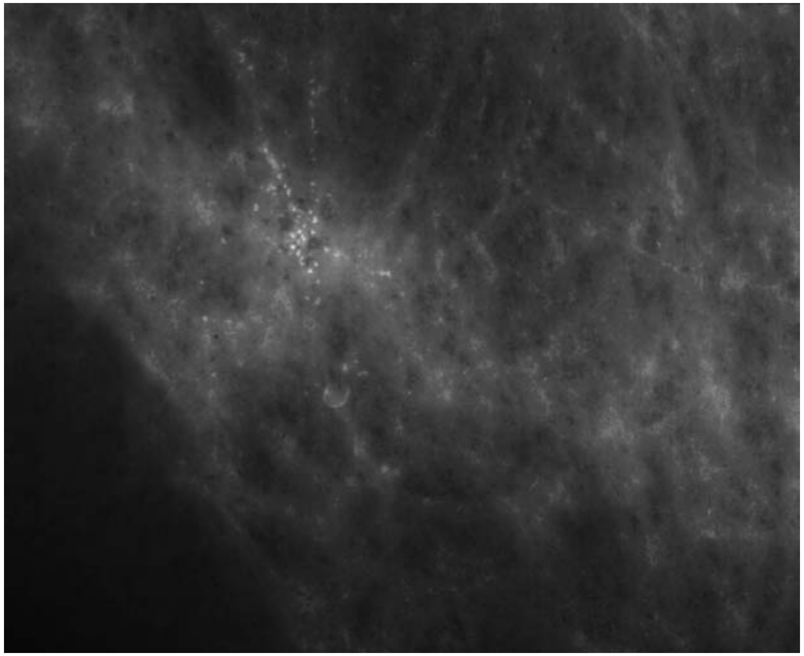
Simultaneous contrast

Just-noticeable difference

Contrast enhancement

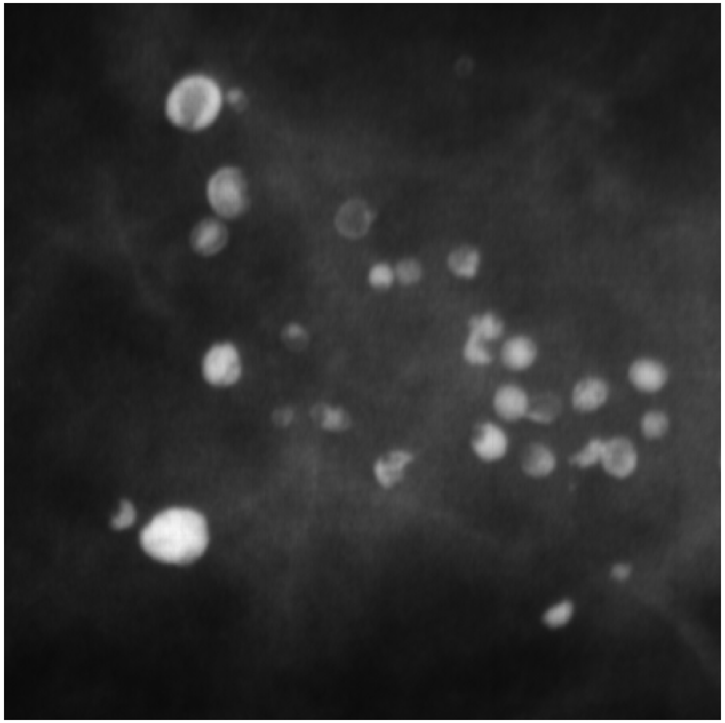


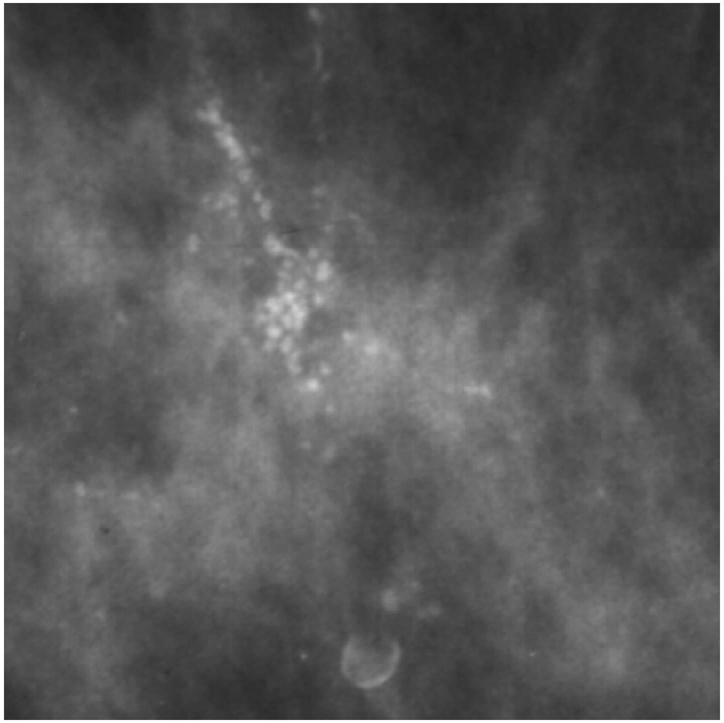
Original mammogram
with calcifications



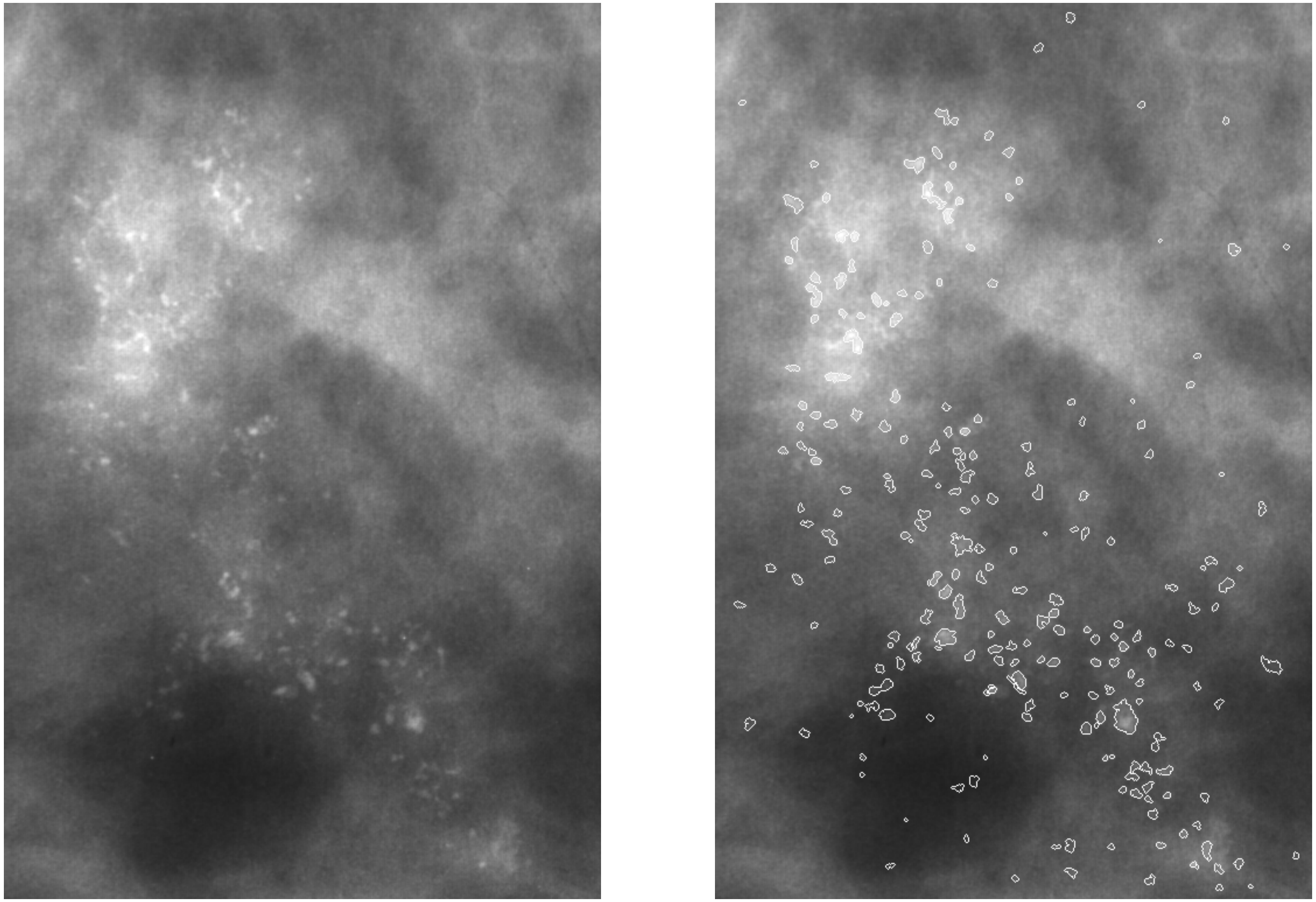
Enhanced image
using adaptive-neighborhood
contrast enhancement

Examples of benign and malignant calcifications

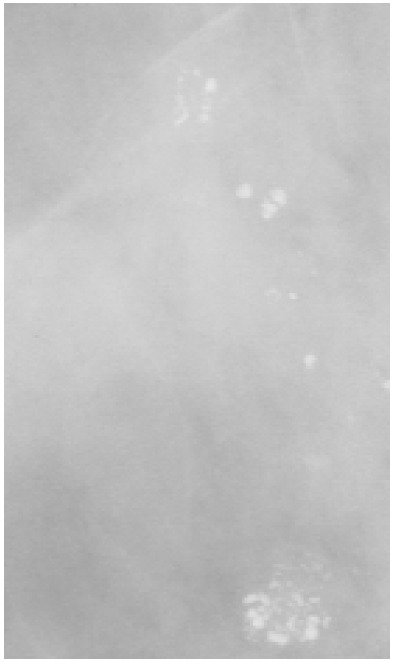




Detection of calcifications by region growing

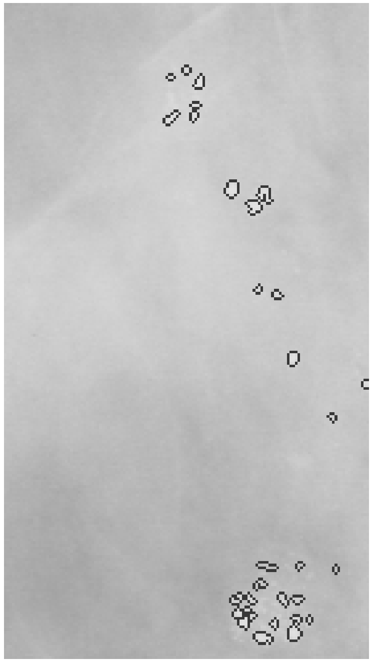


Detection of calcifications by error of prediction



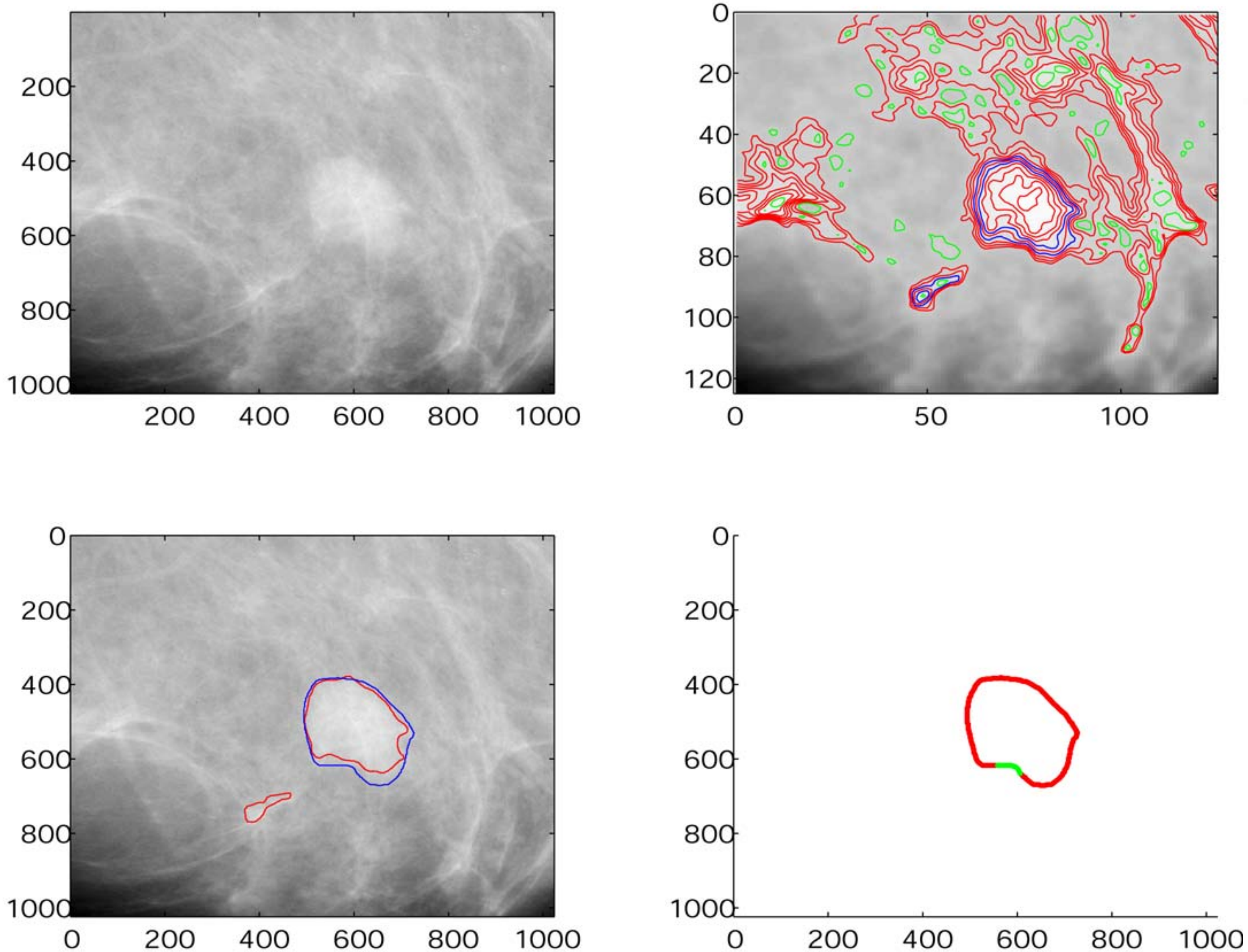
(a) Part of original mammogram

(b) Seeds detected using prediction error



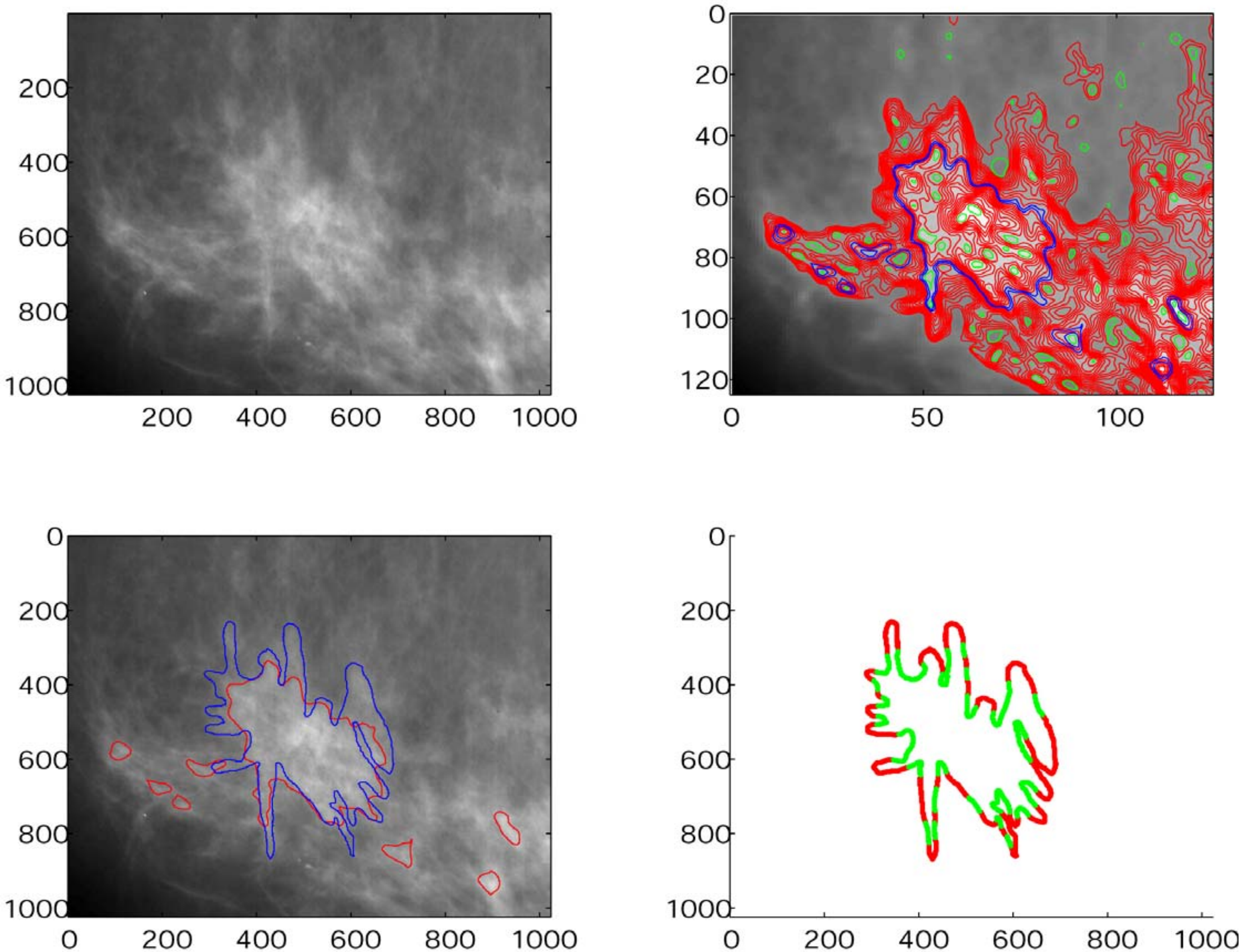
(c) Calcifications detected by region growing

Detection of masses by density slicing and texture flow-field analysis



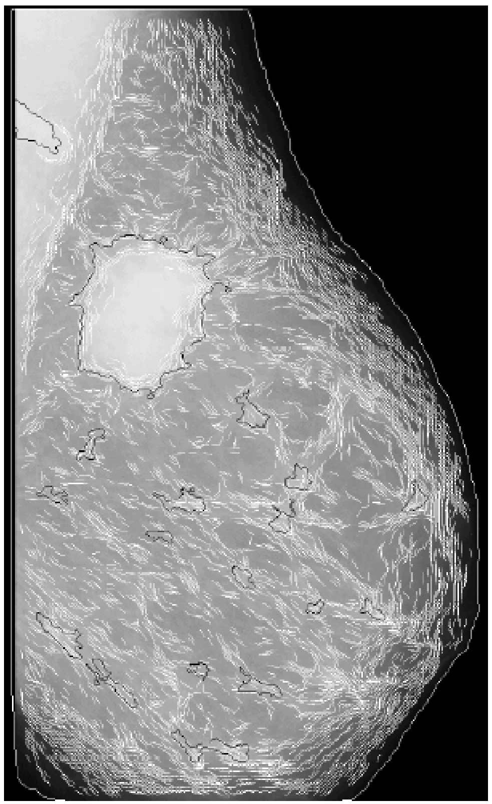
Most benign masses have smooth shapes with convex lobules.

Detection and analysis of tumors

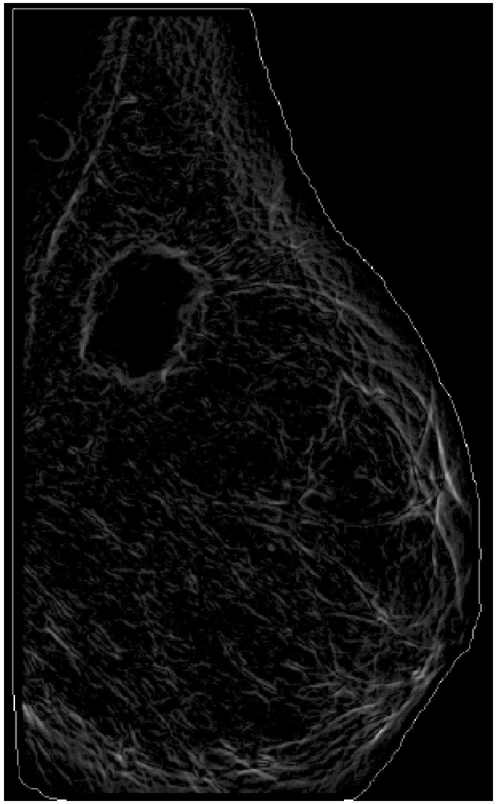


The green parts of the boundary represent concave segments, indicating malignancy.

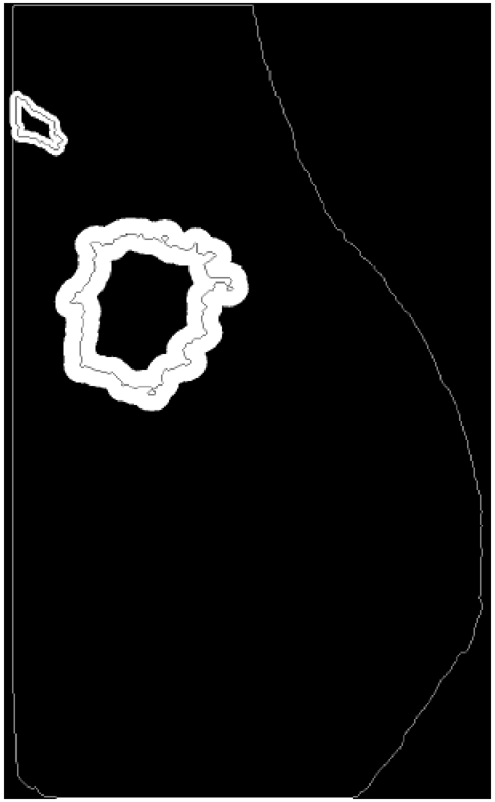
Detection and analysis of tumors



Orientation field

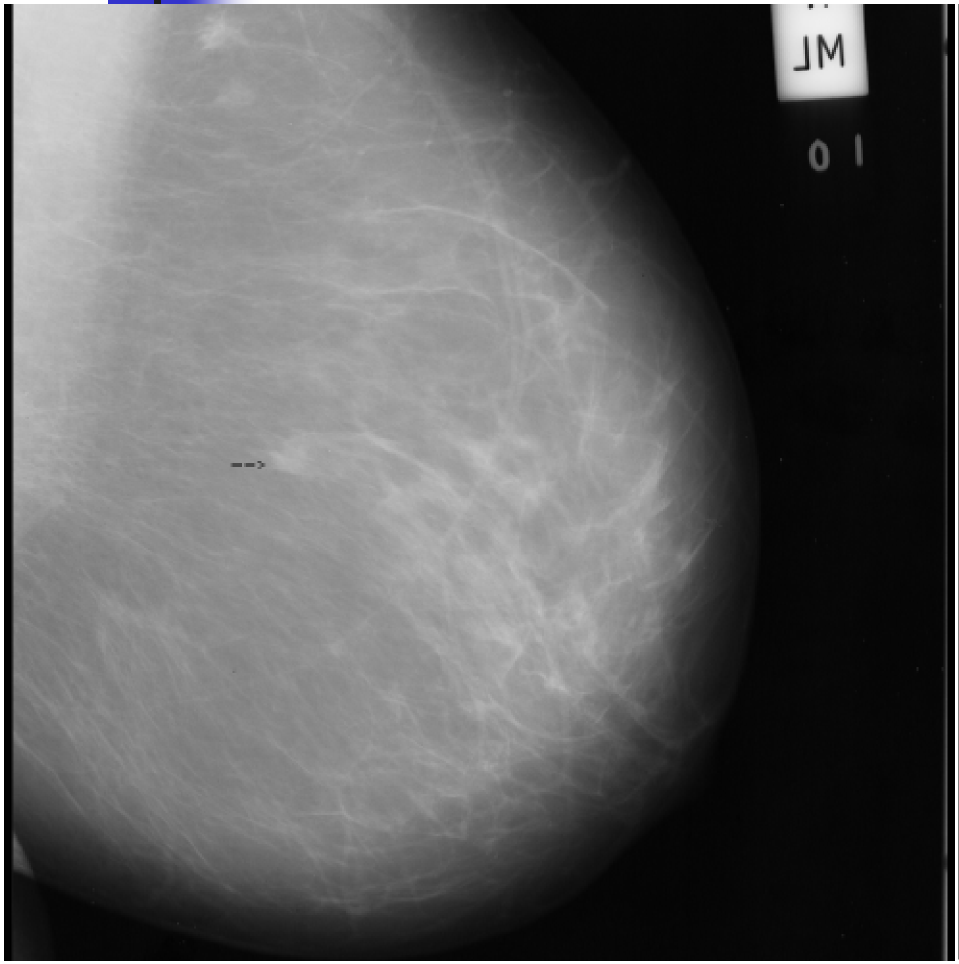


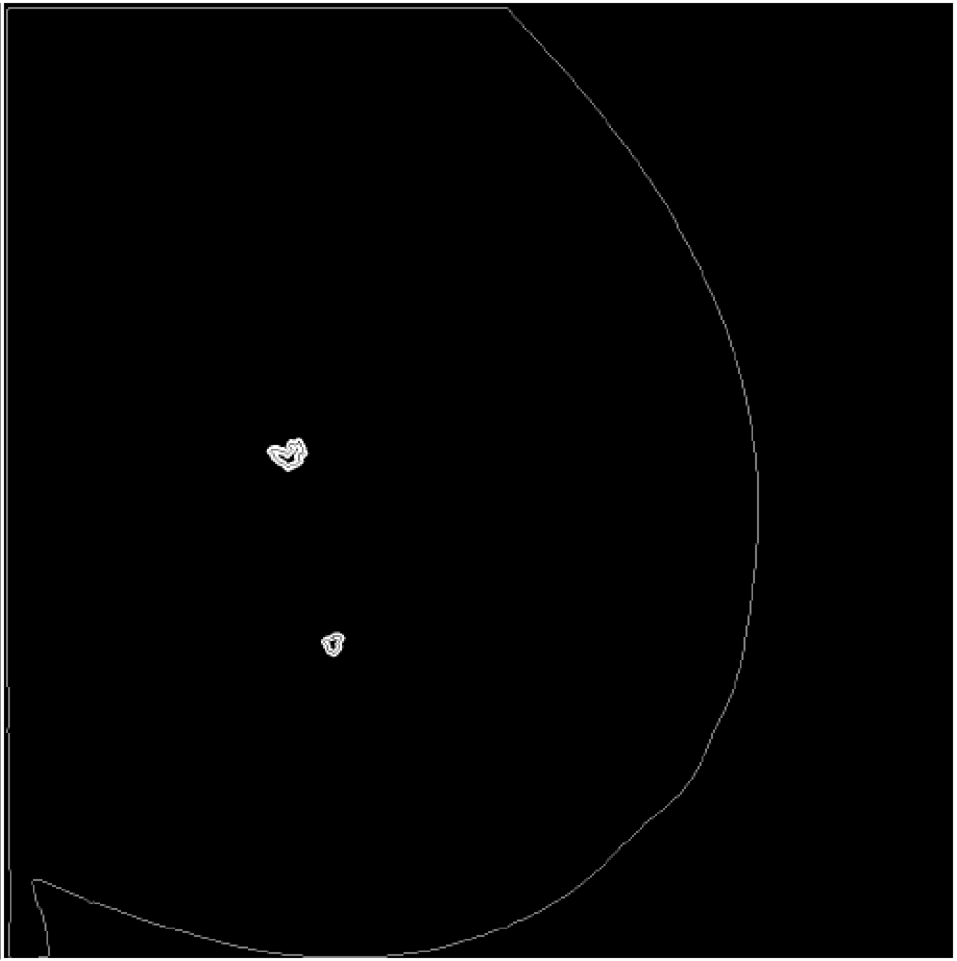
Coherence



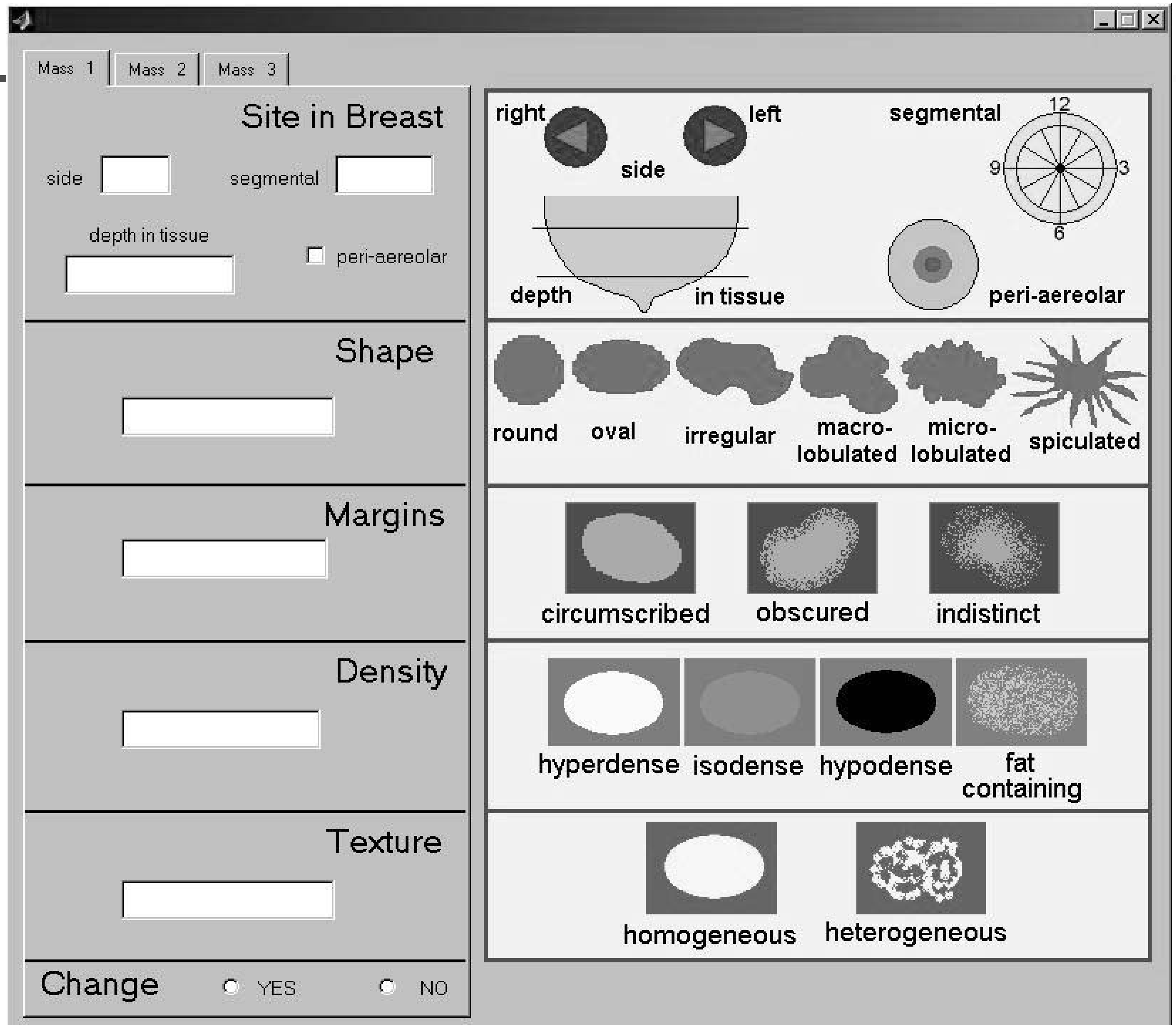
Tumor + FP detected

Detection of a subtle tumor





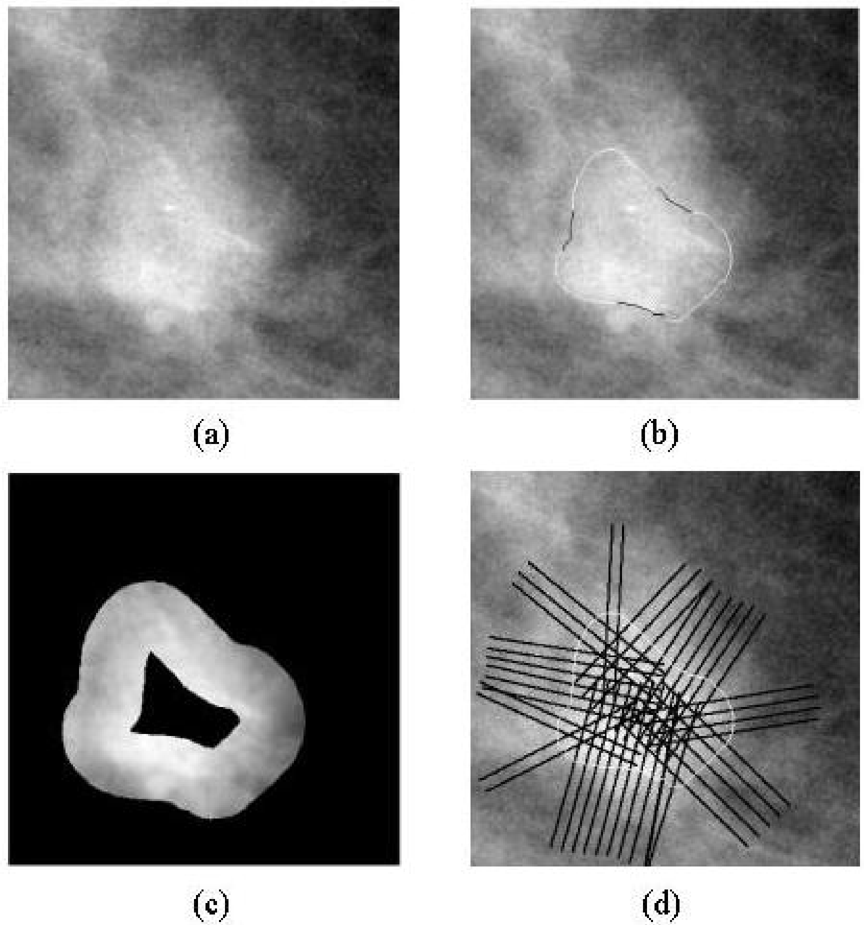
Radiological characterization of masses (BI-RADS)



Analysis of masses: feature extraction

Mass region

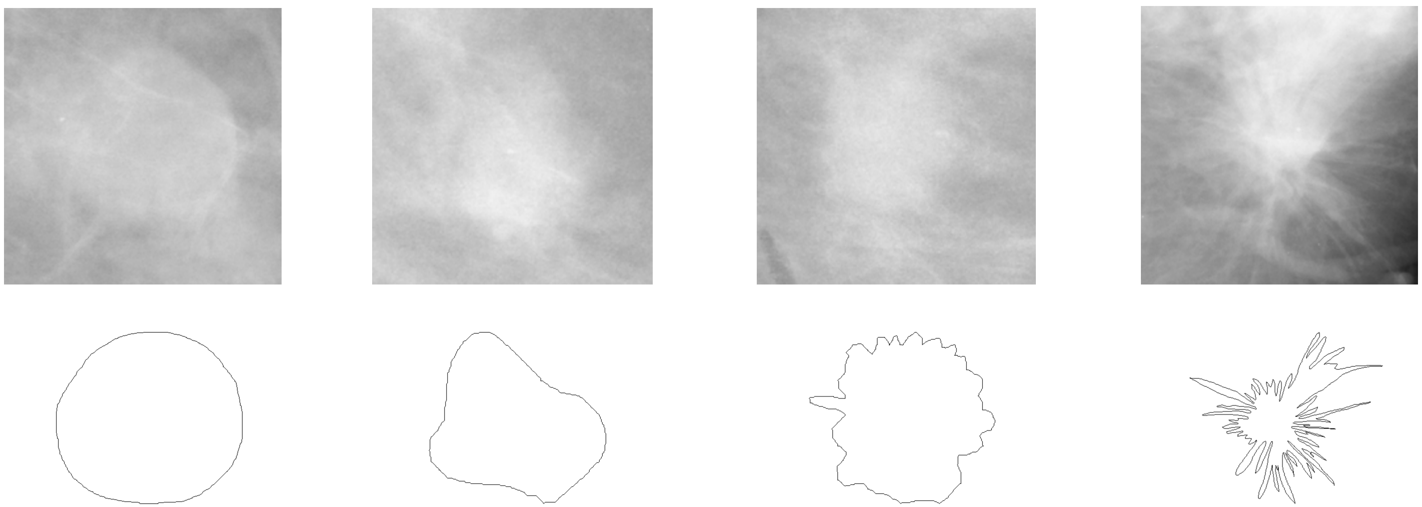
Ribbon for computation of texture features



Shape analysis: Fractional concavity

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

benign circumscribed

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

benign macrolobulated

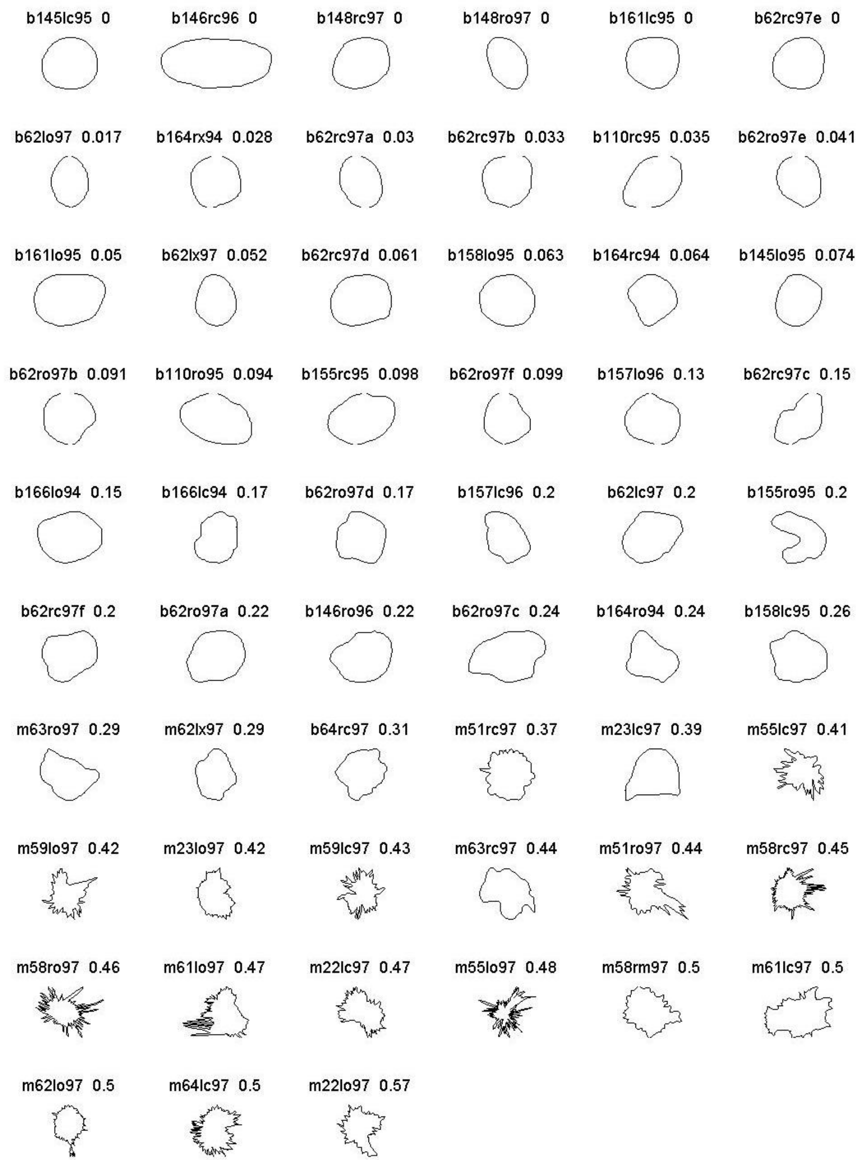
(c) m51rc97
F_{cc} = 0.64
A = 0.09
F_8 = 8.15

malignant microlobulated

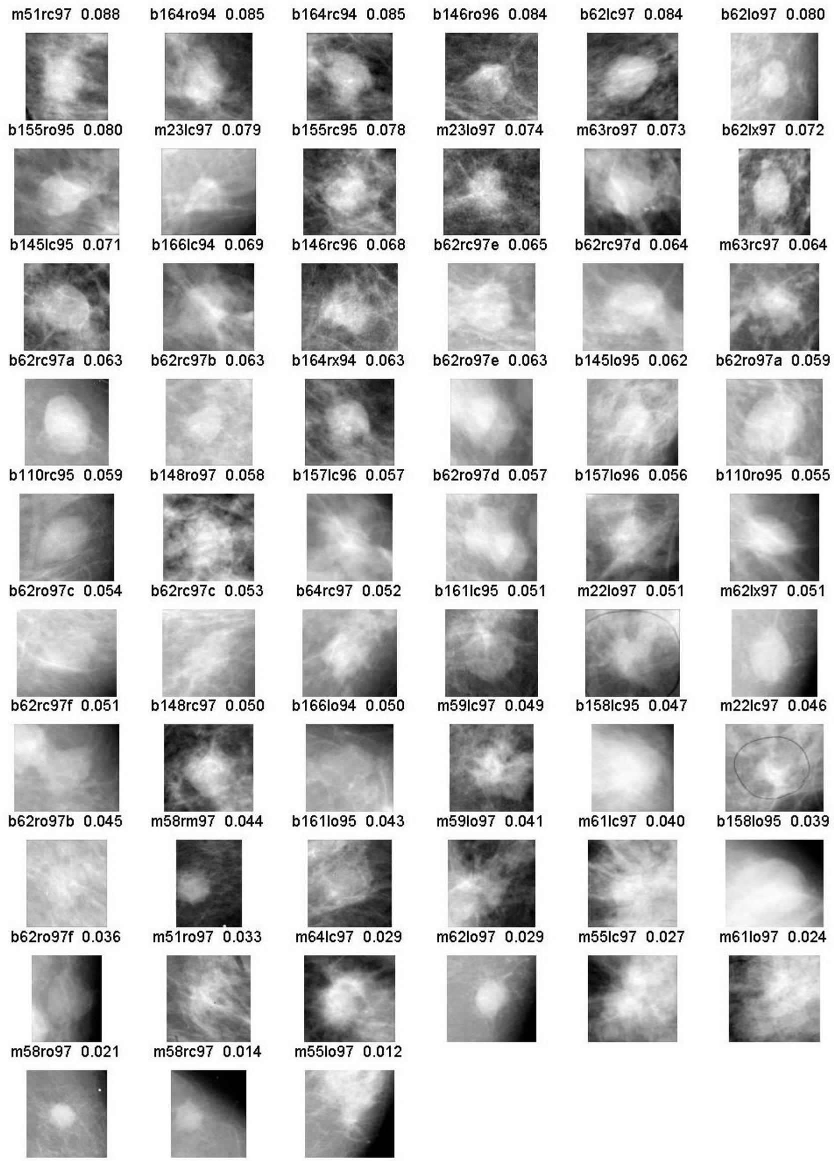
(d) m55lo97
F_{cc} = 0.83
A = 0.01
F_8 = 8.29

malignant spiculated

Rank-ordering using shape: F_{cc}



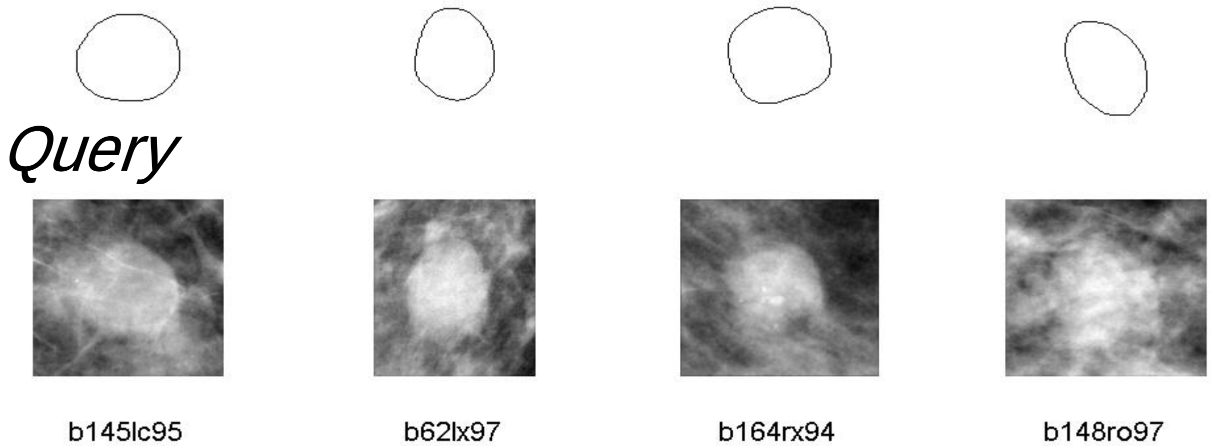
Rank-ordering using acutance



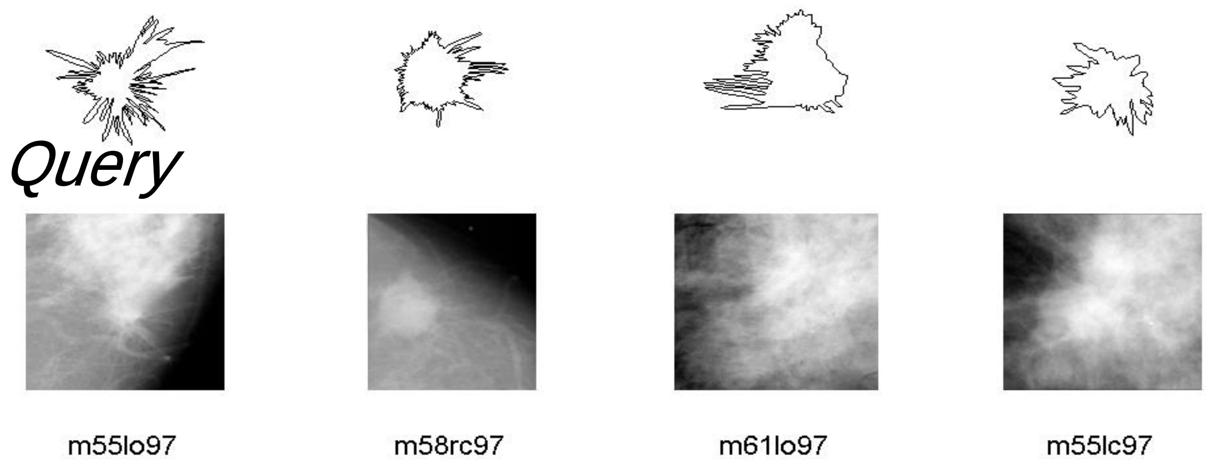
Classification of masses

	Logistic regression			Mahalanobis (pooled)			Linear discriminant analysis				KNN = 7			Recall
Features	**Sens**	**Spec**	**Avg**	**Sens**	**Spec**	**Avg**	**Sens**	**Spec**	**Avg**	A_z	**Sens**	**Spec**	**Avg**	**Avg**
F_{cc}	**90**	**97.3**	**94.7**	**90**	**97.3**	**94.7**	**100**	**97.3**	**98.2**	**0.99**	**90**	**97.3**	**94.7**	**90.4**
A	50	94.6	78.9	75	67.6	70.0	75.0	73.0	73.7	0.73	45	91.7	73.7	63.6
F_8	30	86.5	66.7	65	56.8	59.6	75.0	54.0	61.4	0.68	25	67.6	52.6	53.5
F_{cc}, A	90	97.3	94.7	90	97.3	94.7	100	97.3	98.2	0.98	90	100	96.5	84.6
F_{cc}, F_8	90	97.3	94.7	90	97.3	94.7	100	97.3	98.2	0.99	90	97.3	94.7	85.6
A, F_8	55	86.5	75.4	60	70.3	66.7	75.0	73.0	73.7	0.76	55	89.2	73.7	61.6
F_{cc}, A, F_8	**90**	**97.3**	**94.7**	**95**	**97.3**	**96.5**	**100**	**97.3**	**98.2**	**0.99**	**90**	**97.3**	**94.7**	**83.4**
14 texture	*	*	*	70	50.0	64.9	65.0	64.9	64.9	0.67	#	#	#	#

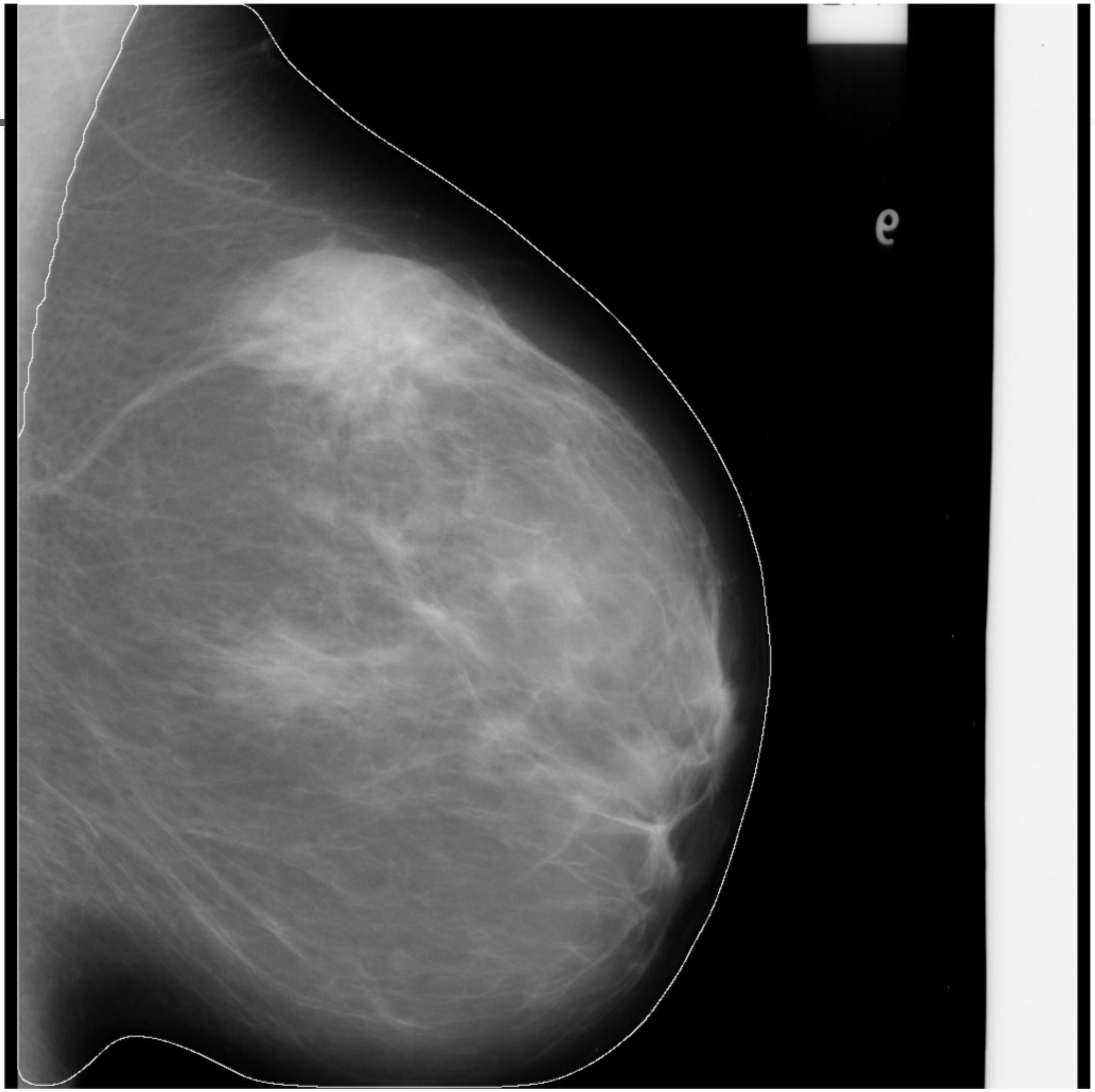
Content-based retrieval and analysis: benign mass



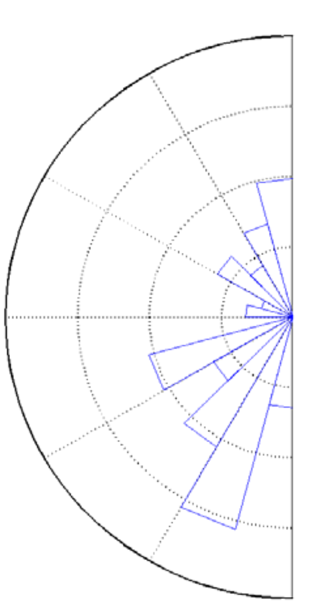
Content-based retrieval and analysis: malignant tumor

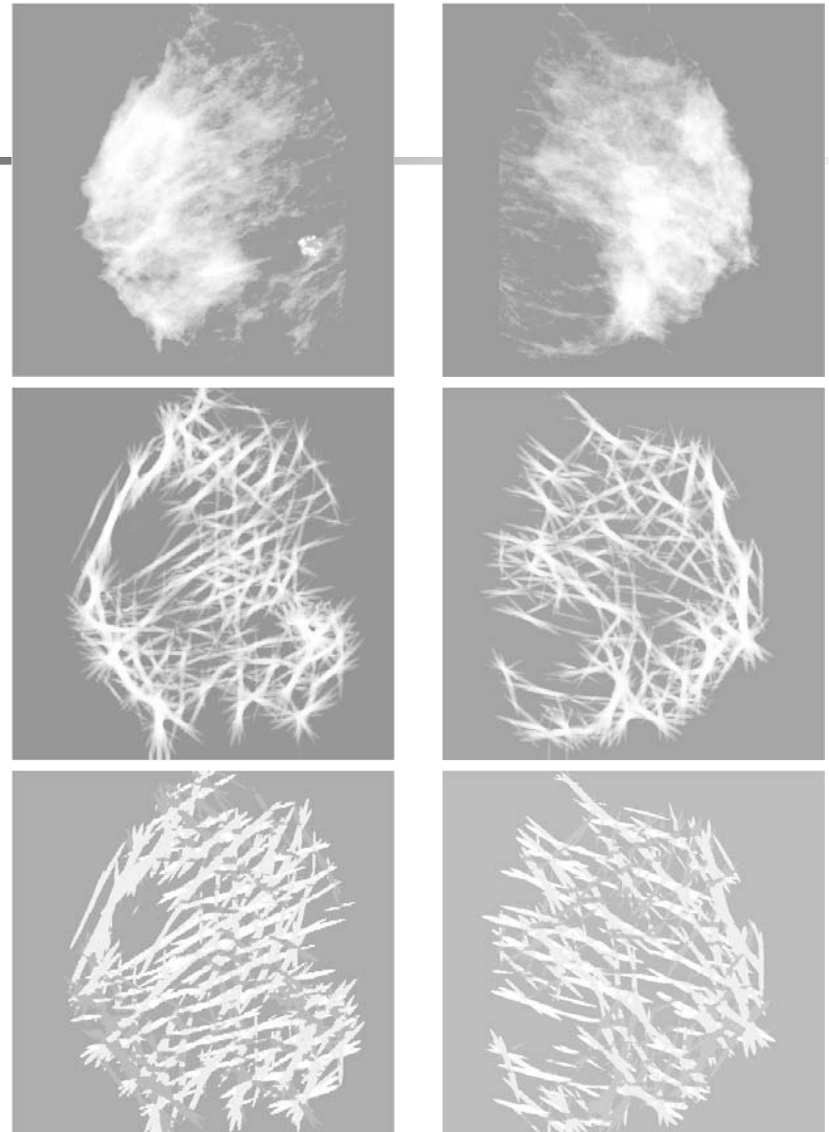


Detection of the pectoral muscle edge and the breast boundary using Gabor filters and active contour models

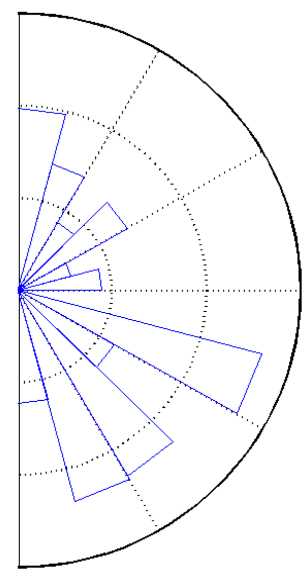


Analysis of bilateral asymmetry using Gabor filters

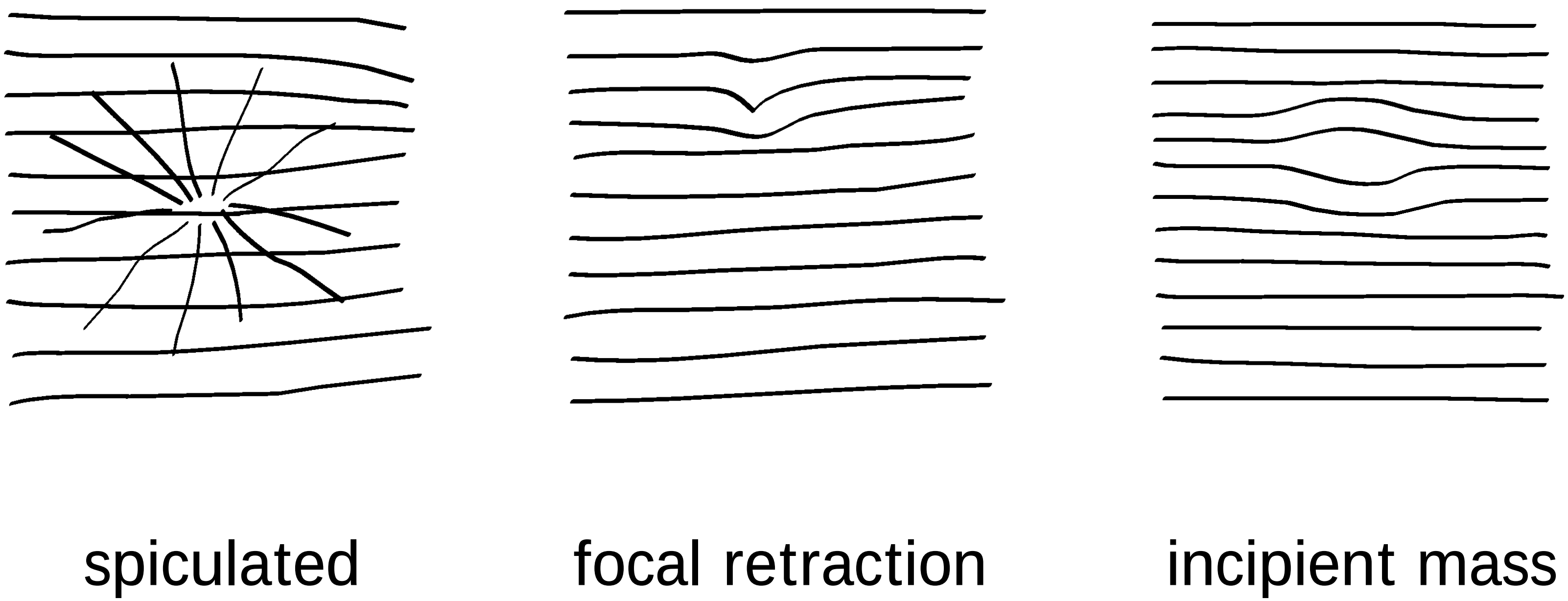




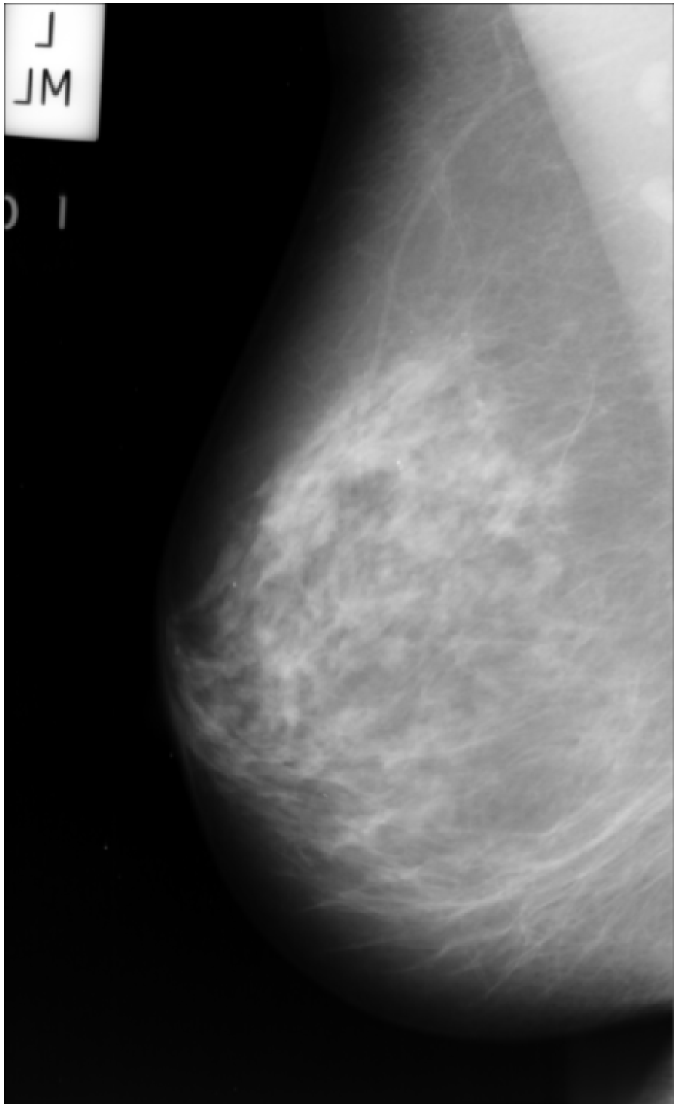
The directional distribution of fibroglandular tissue differs between the left and right breasts

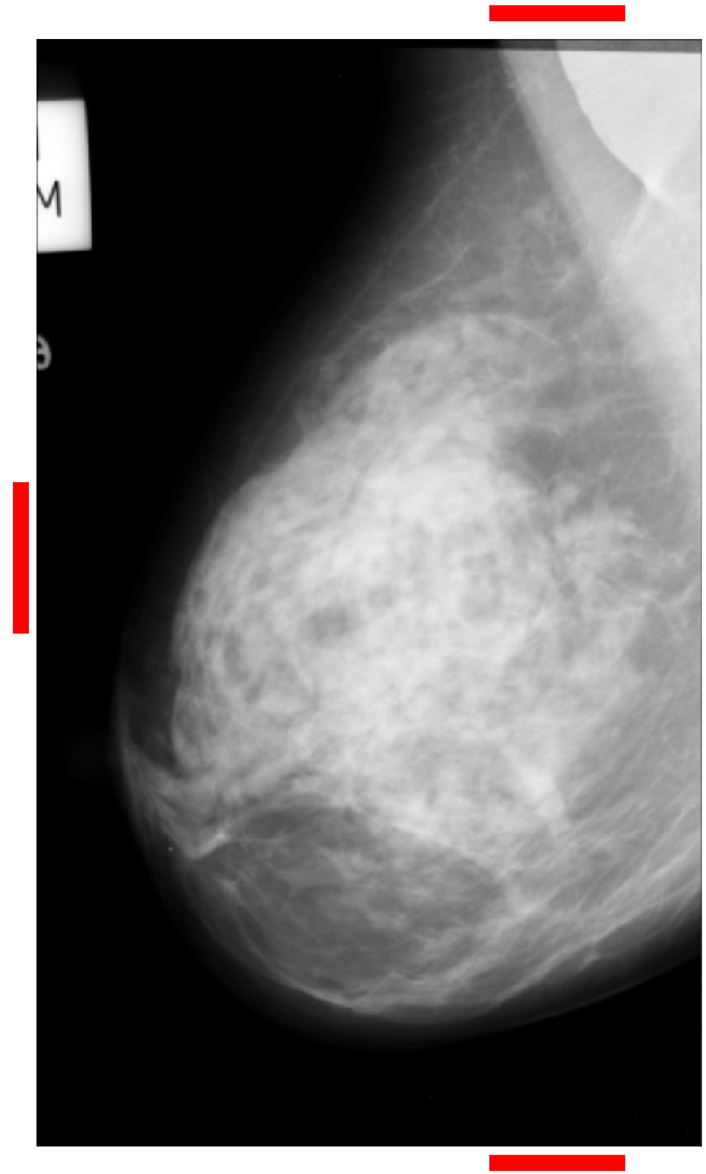


Architectural distortion

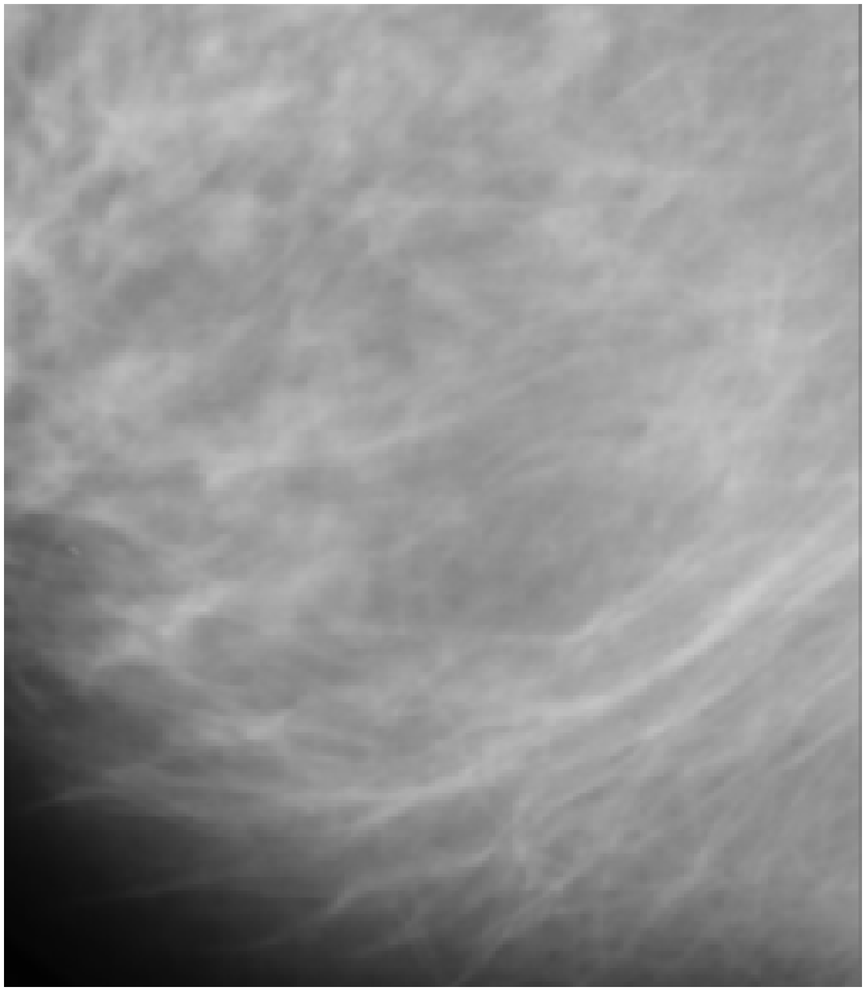


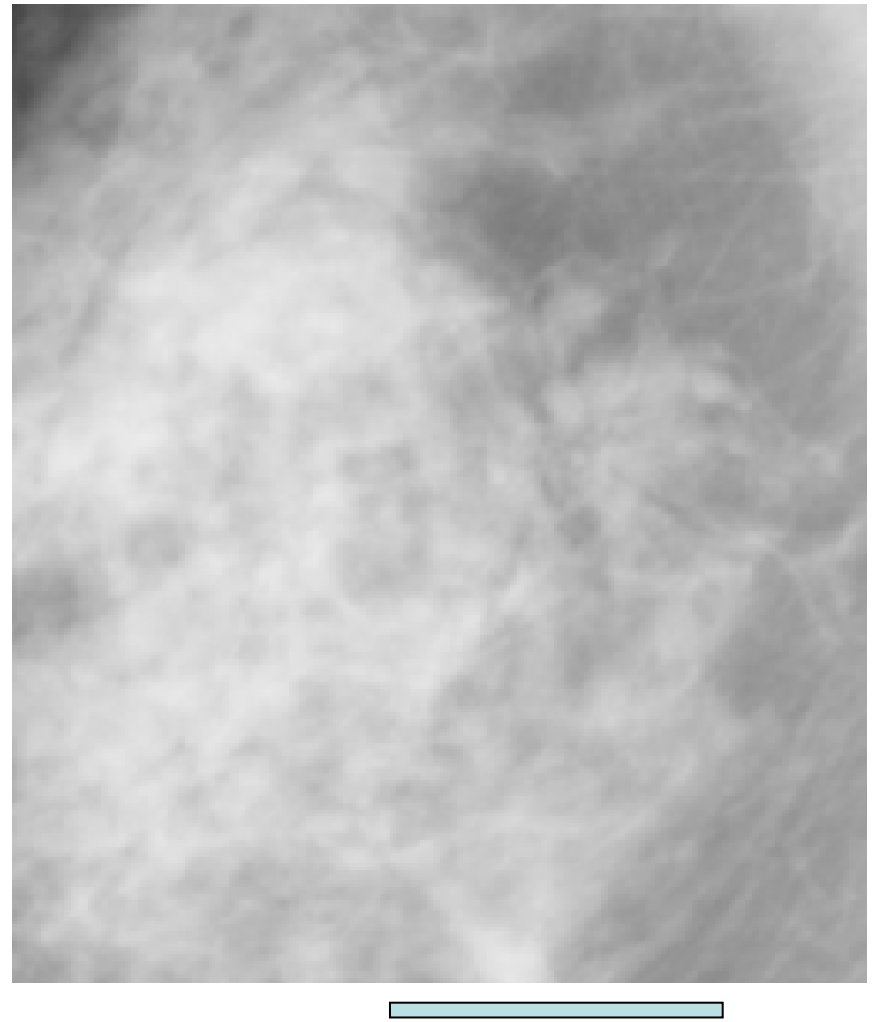
Normal vs. architectural distortion





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

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

<u>Design parameters</u>

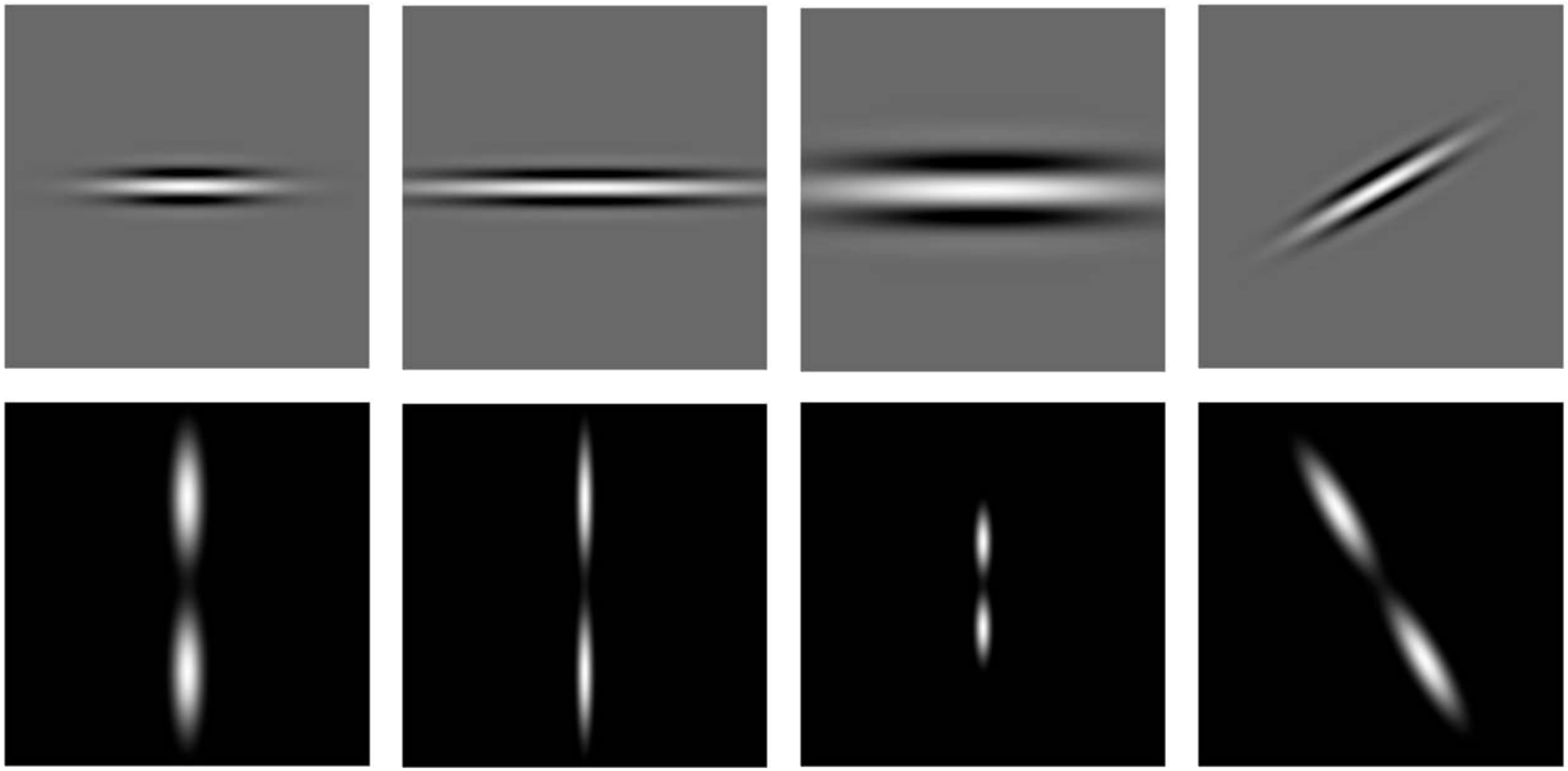
- line thickness τ
- elongation l
- orientation θ

<u>Gabor parameters</u>

$$f=\frac{1}{\tau};\qquad \sigma_x=\frac{\tau}{2\sqrt{2\ln 2}}$$

$$\sigma_y=l\sigma_x;\qquad \begin{bmatrix}x\\y\end{bmatrix}=\begin{bmatrix}\cos\theta & -\sin\theta\\ \sin\theta & \cos\theta\end{bmatrix}\begin{bmatrix}x'\\y'\end{bmatrix}$$

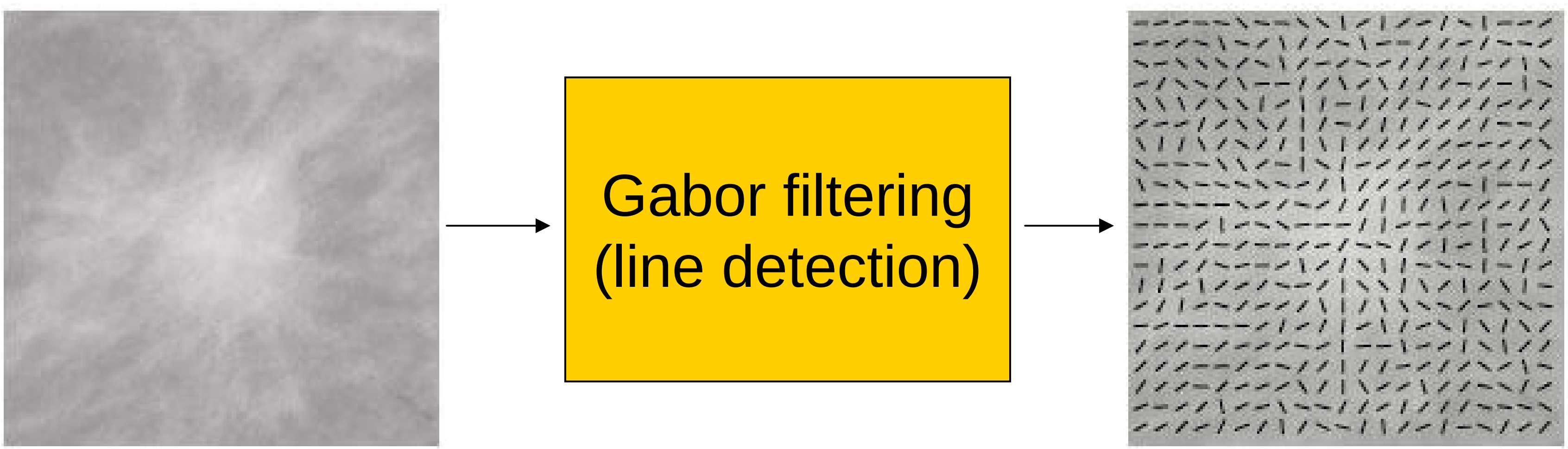
Design of Gabor filters



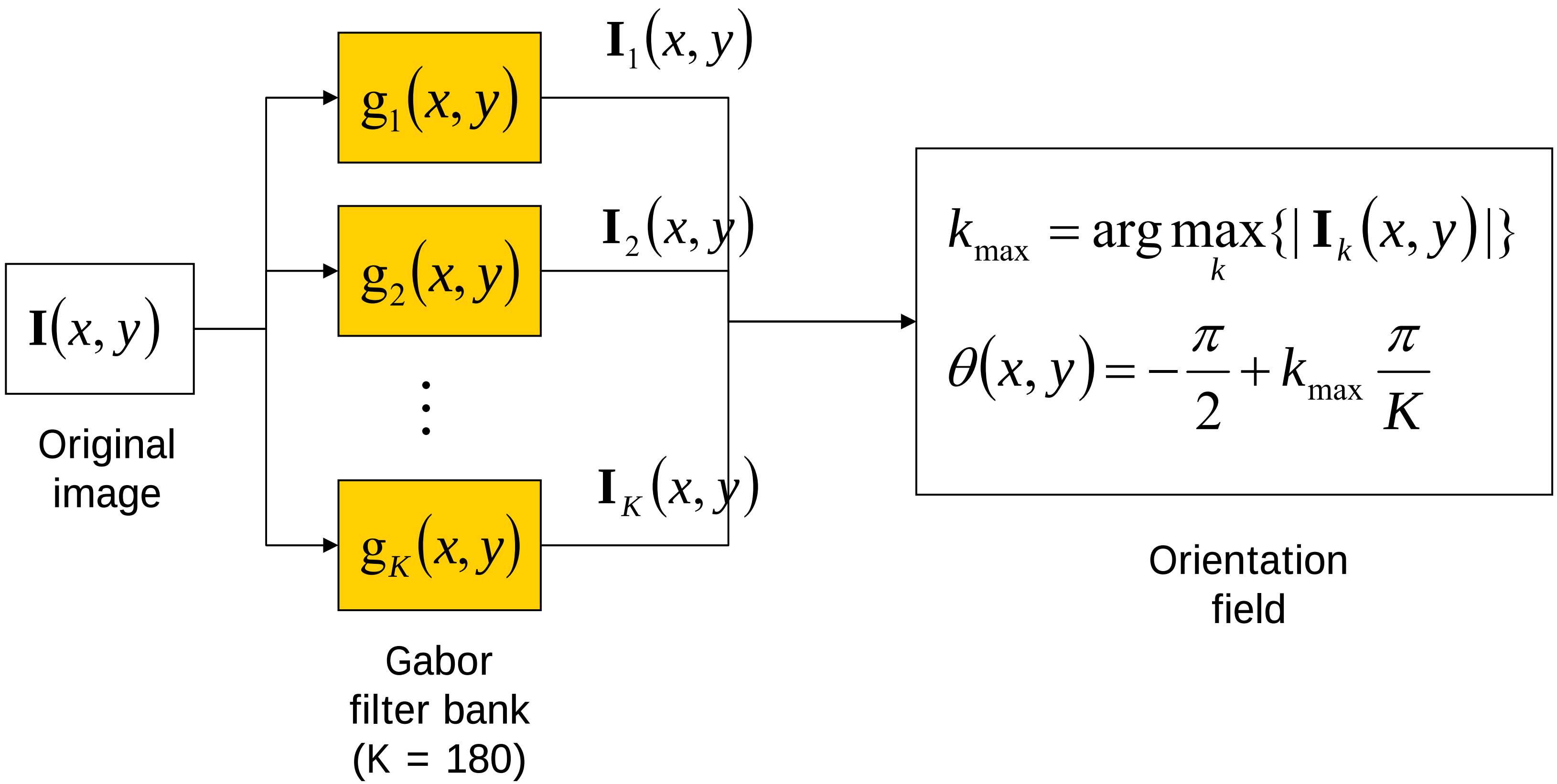
$l = l_0$	$l > l_0$	$l = l_0$	$l = l_0$
$\tau = \tau_0$	$\tau = \tau_0$	$\tau > \tau_0$	$\tau = \tau_0$
$\theta = \theta_0$	$\theta = \theta_0$	$\theta = \theta_0$	$\theta > \theta_0$

Extracting the orientation field

- Compute the texture orientation (angle) for each pixel

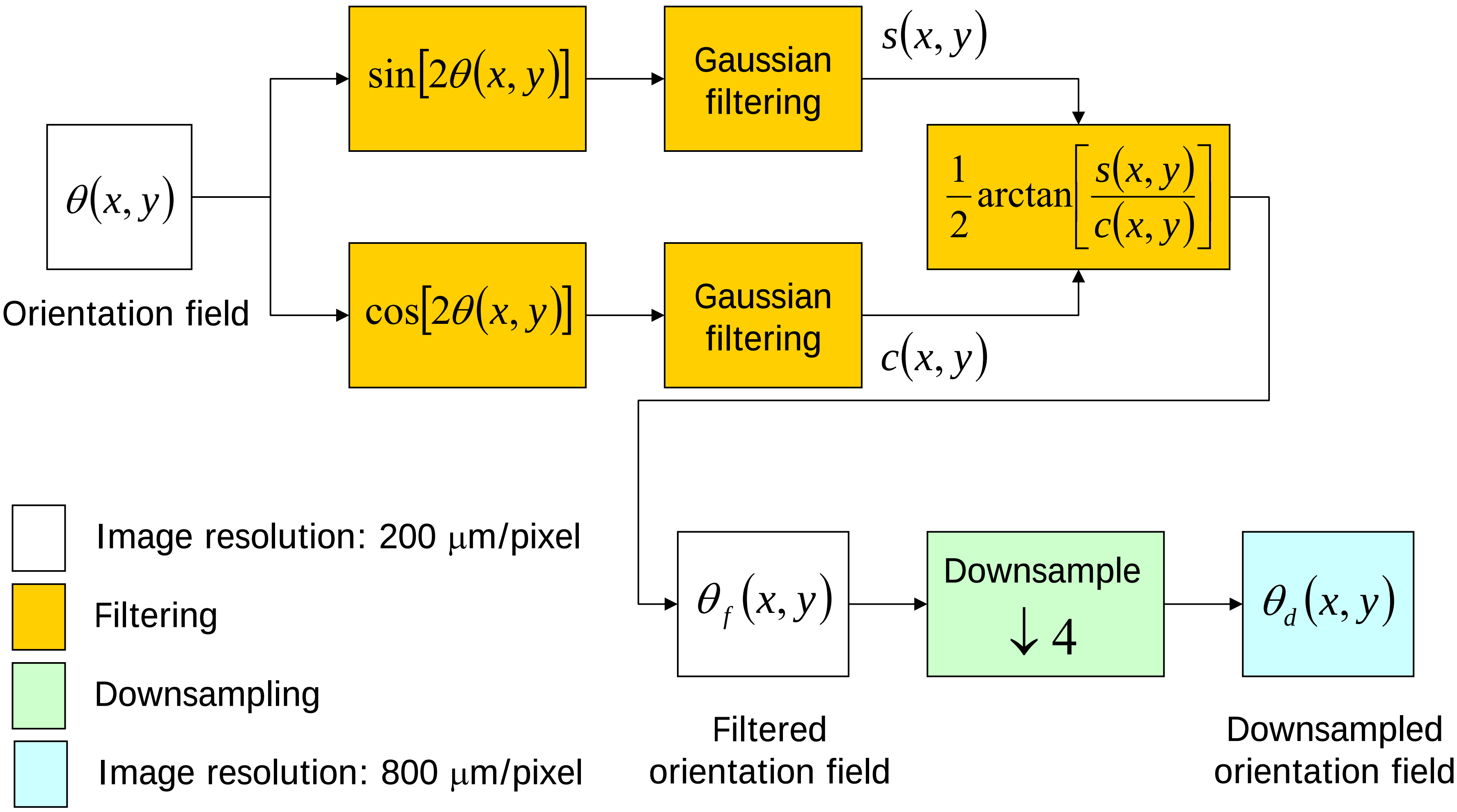


Extracting the orientation field

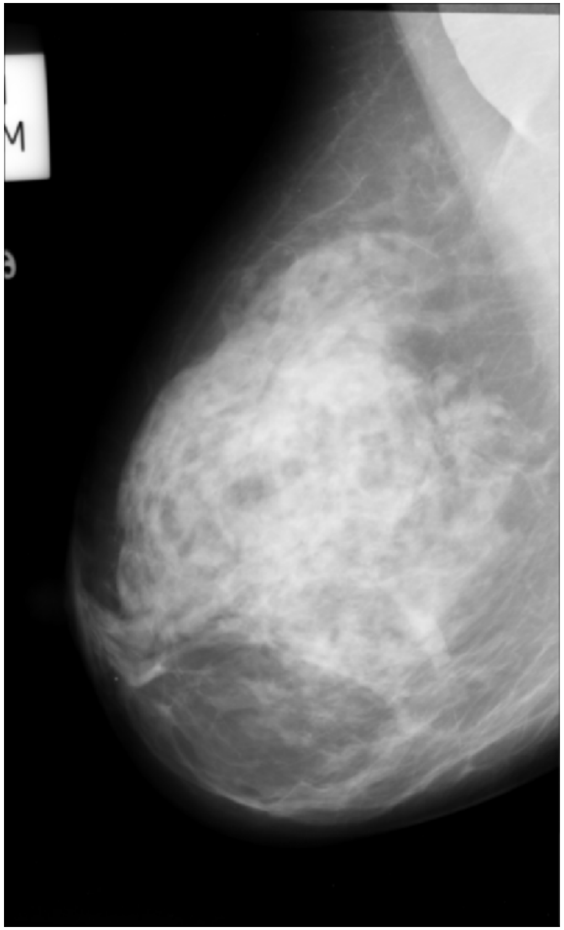


Filtering   Image resolution: 200 μm/pixel

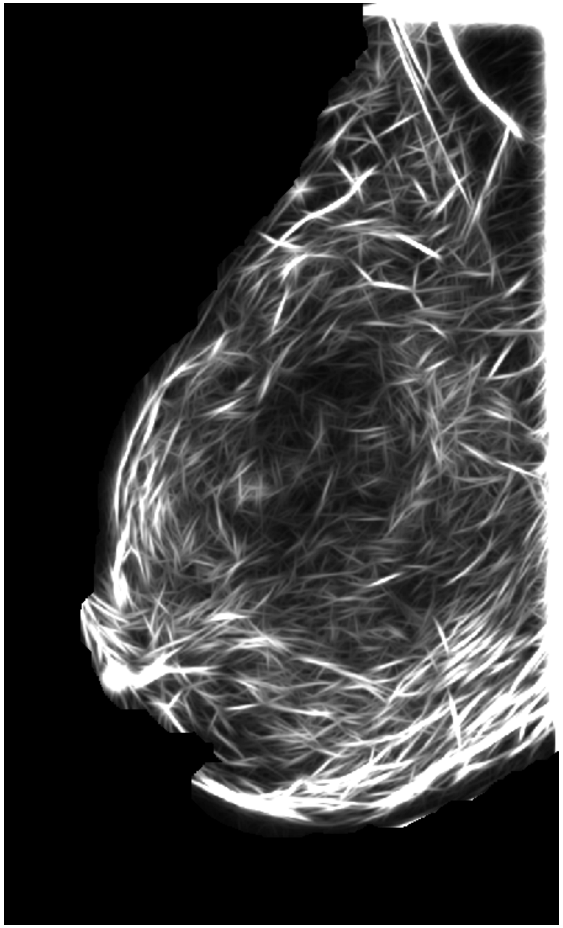
Filtering and downsampling the orientation field



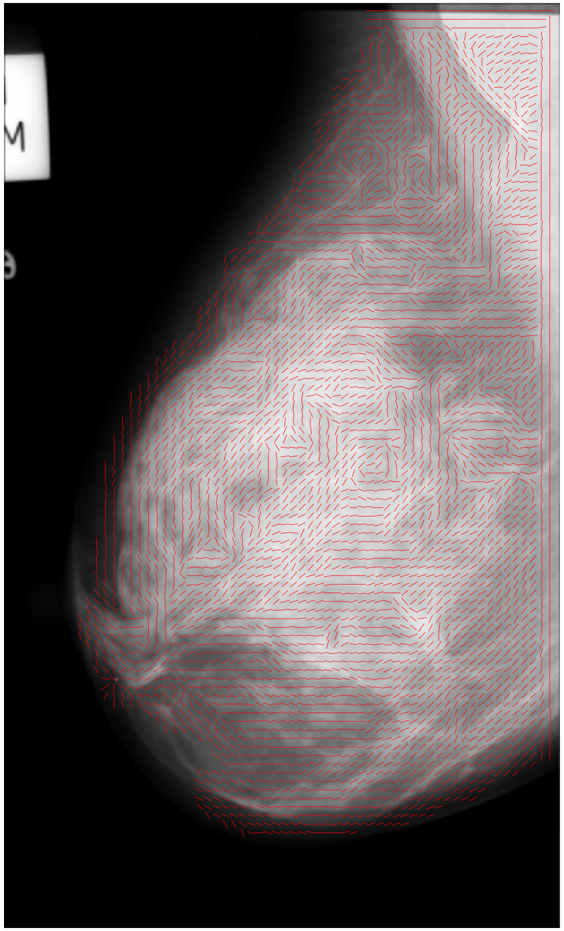
Orientation field: architectural distortion



Original image

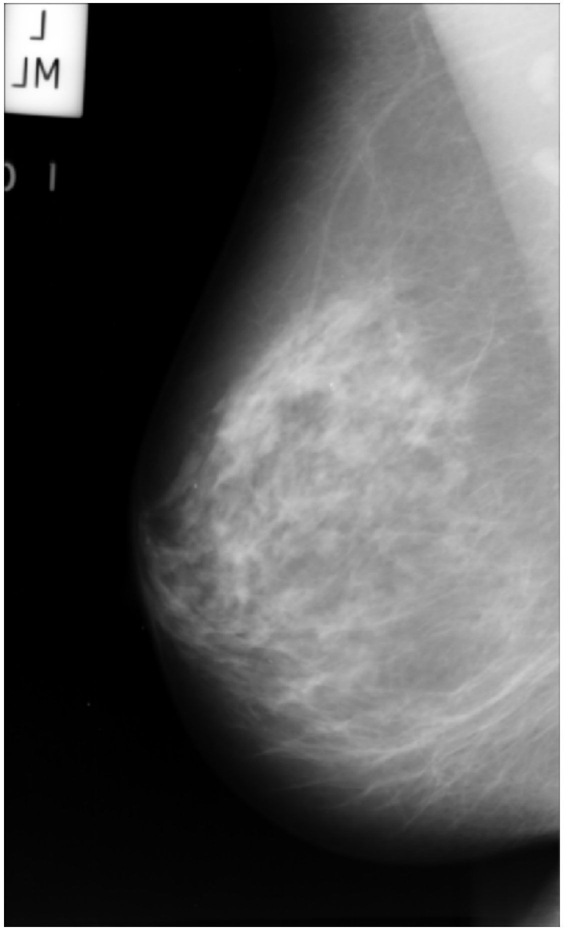


Gabor magnitude

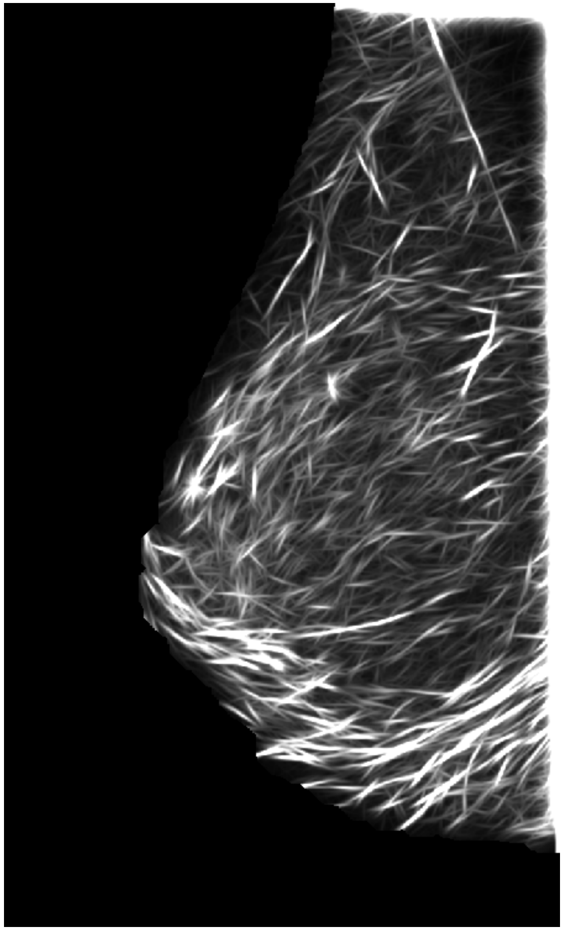


Filtered orientation field

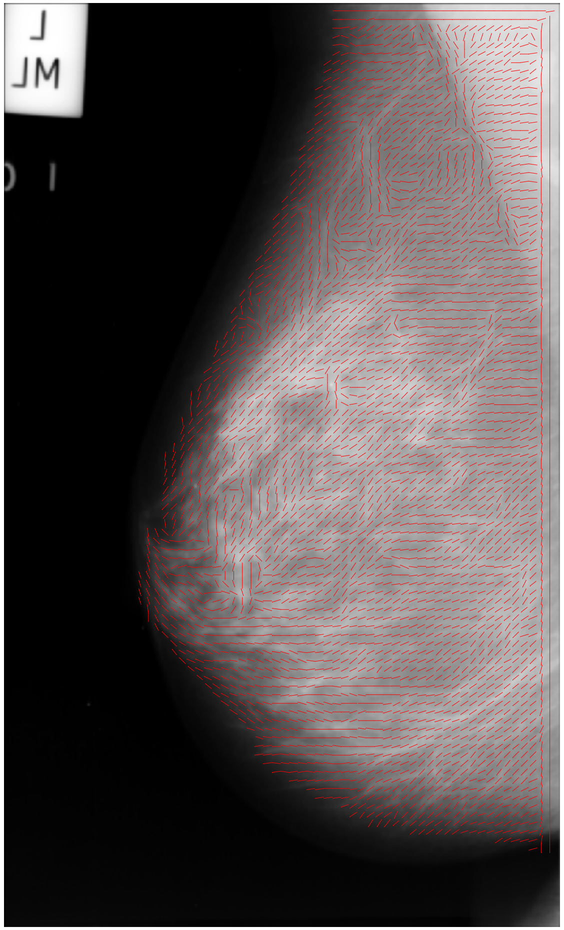
Orientation field: normal case



Original image



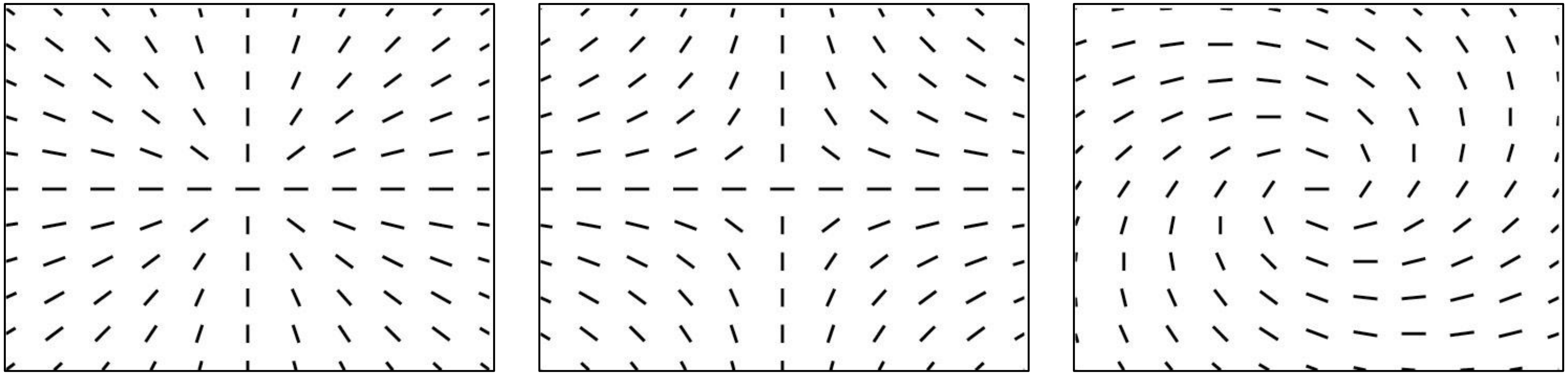
Gabor magnitude



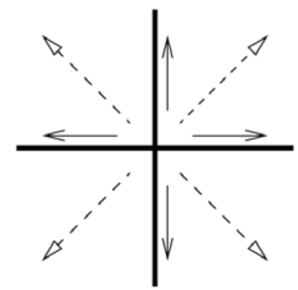
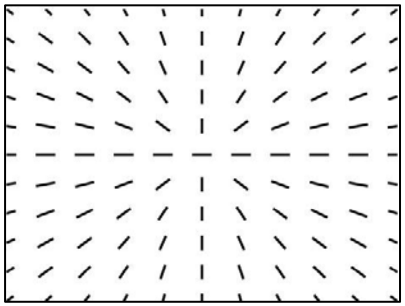
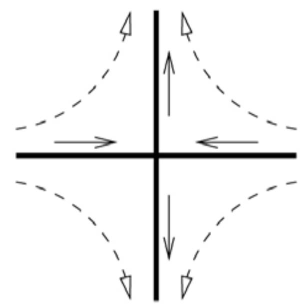
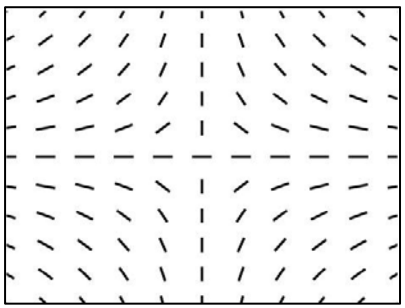
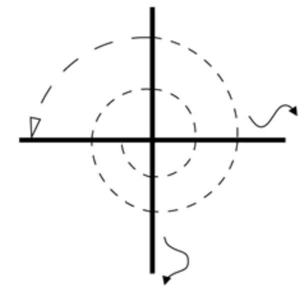
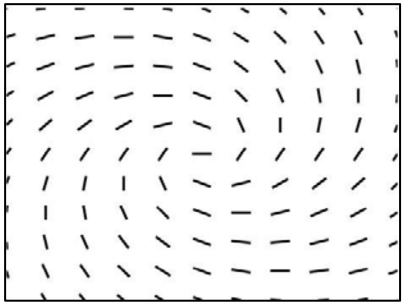
Filtered orientation field

Phase portraits

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



node saddle spiral

Phase portrait type	Eigenvalues of matrix A	Streamlines	Orientation field
Node	Real, same sign		
Saddle	Real, opposite sign		
Spiral	Complex conjugate		

Model error

Orientation field

$$\theta(x, y)$$

Model-generated field

$$\phi(x, y | \mathbf{A}, \mathbf{b})$$

$$\Delta(x, y) = \sin\left[\theta(x, y) - \phi(x, y | \mathbf{A}, \mathbf{b})\right]$$

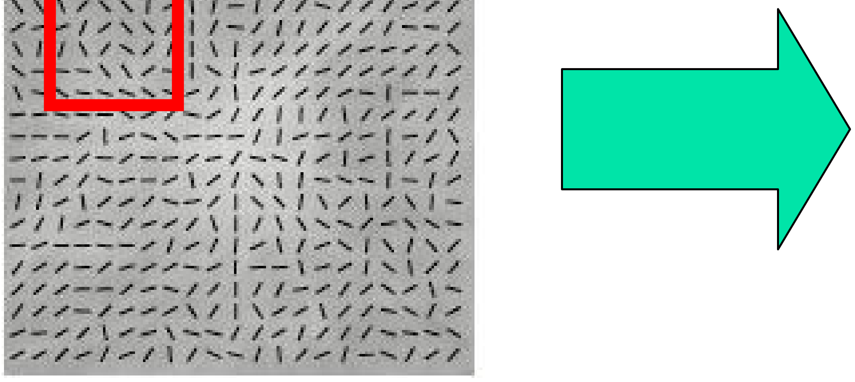
Local error measure

$$\varepsilon^2(\mathbf{A}, \mathbf{b}) = \sum_x \sum_y \Delta^2(x, y)$$

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



$$\mathbf{A} = \begin{bmatrix} 1.1 & 0.3 \\ -0.2 & 1.7 \end{bmatrix}$$

$$\mathbf{b} = \begin{bmatrix} -4.8 \\ -7.9 \end{bmatrix}$$

Texture analysis using phase portraits *(step 2 of 3)*

2. Find phase portrait type and location of fixed point

$$\mathbf{A} = \begin{bmatrix} 1.1 & 0.3 \\ -0.2 & 1.7 \end{bmatrix}$$

$$\mathbf{b} = \begin{bmatrix} -4.8 \\ -7.9 \end{bmatrix}$$

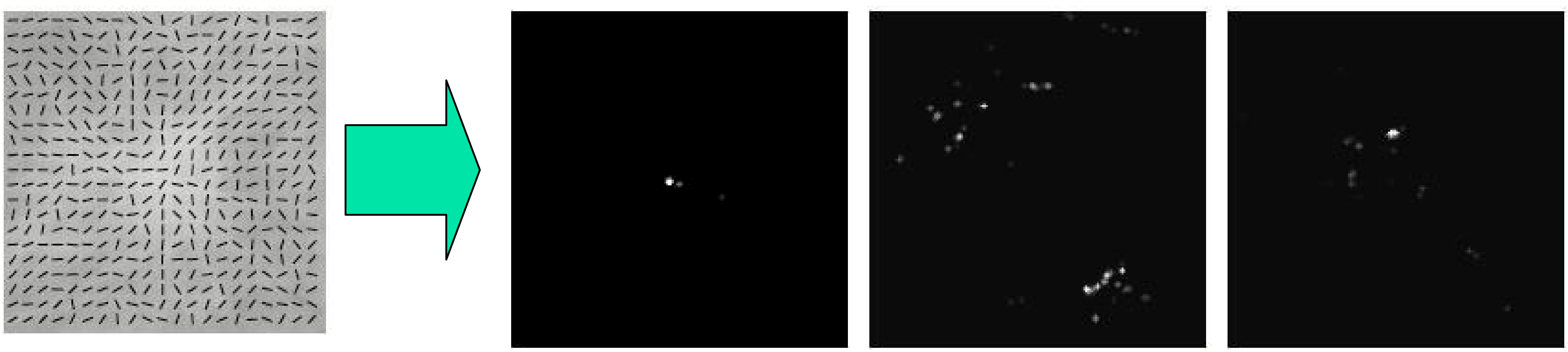
⇒

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

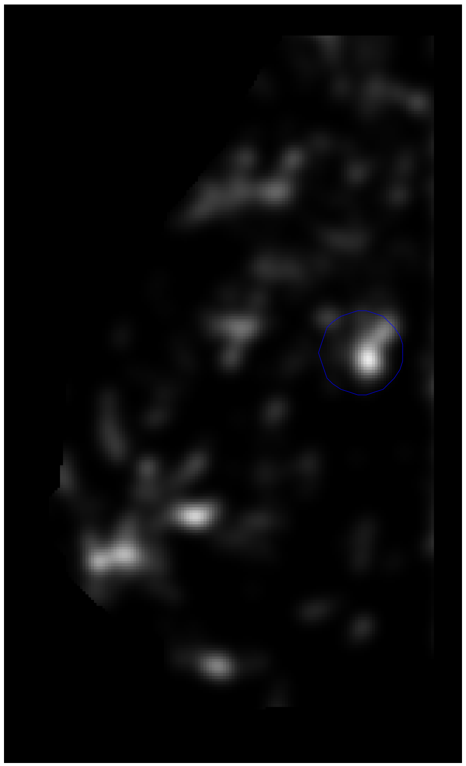


Orientation field — Node — Saddle — Spiral

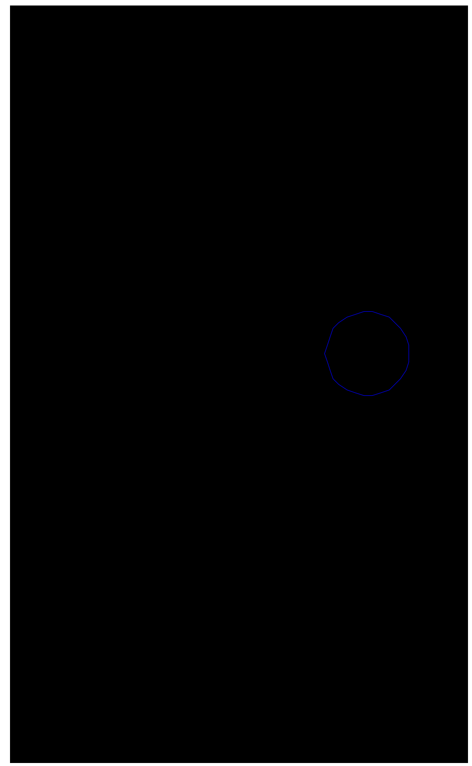
Post-processing and detection

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**

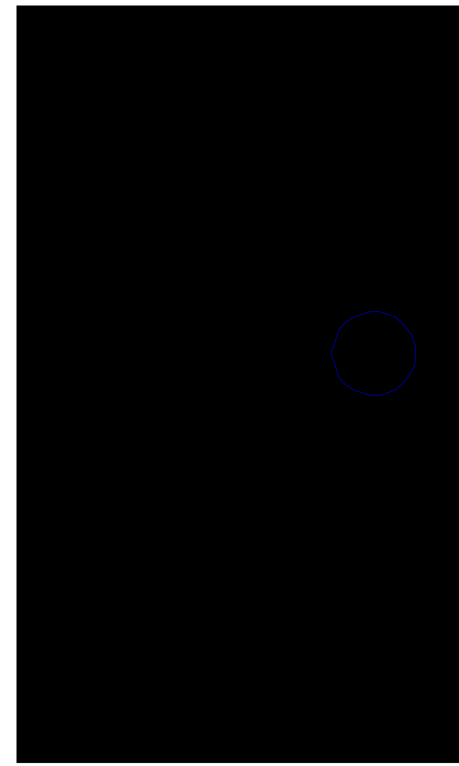
Phase portrait maps: architectural distortion case



node
[0, 1.1]

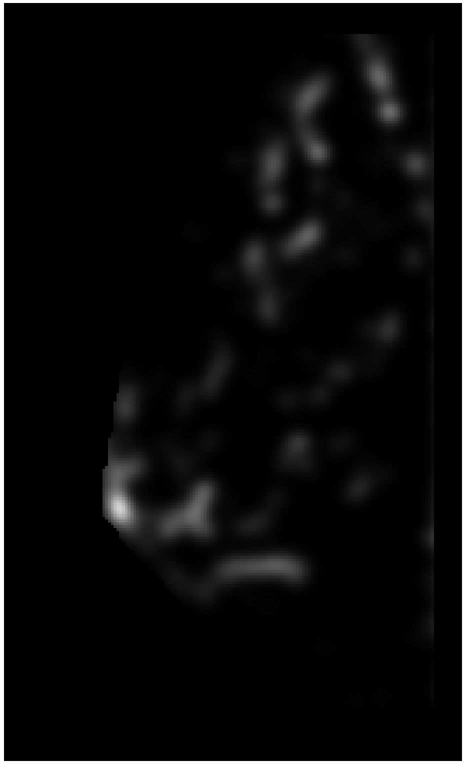


saddle
[0, 0.3×10^{-3}]

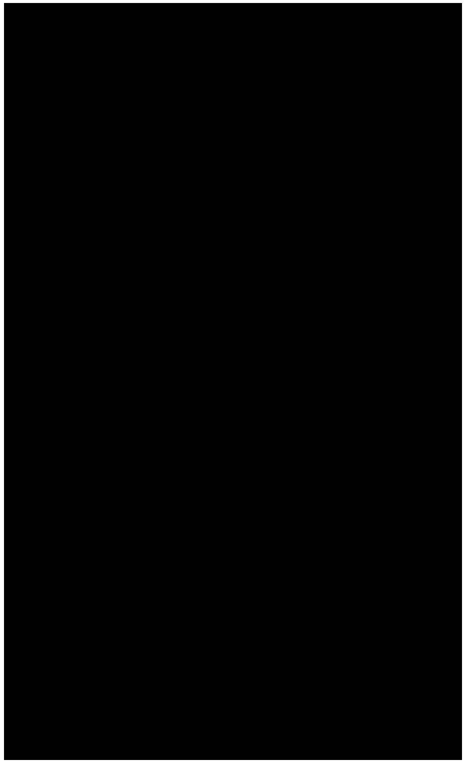


spiral
[0, 0]

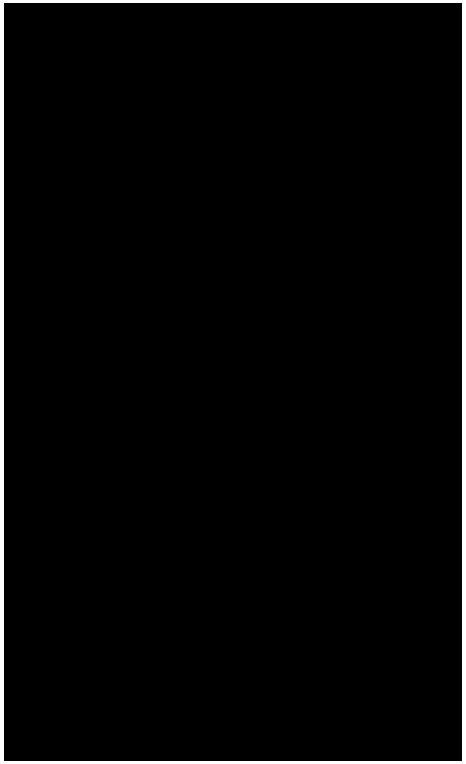
Phase portrait maps: normal case



node
[0, 0.98]

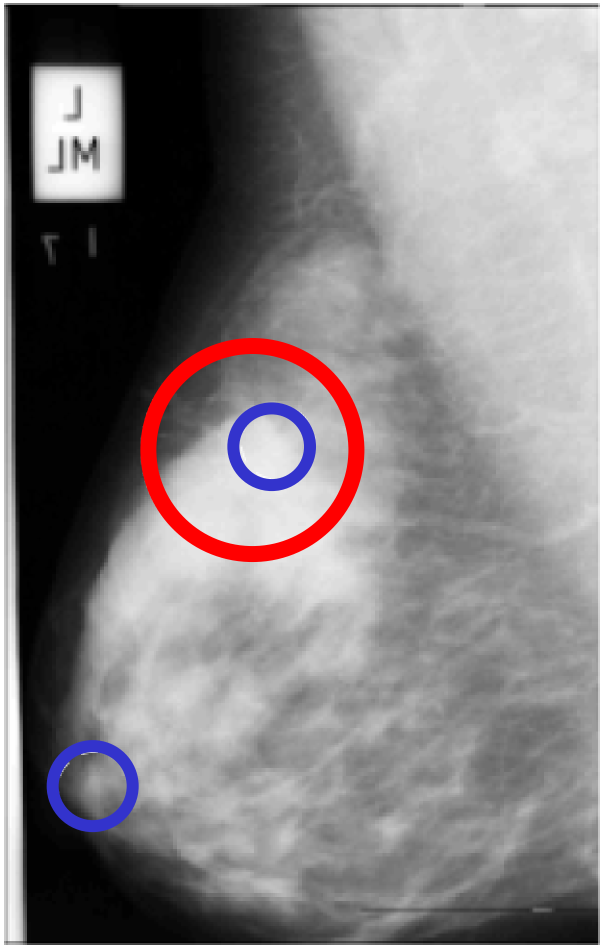


saddle
[0, 0.2×10^{-4}]



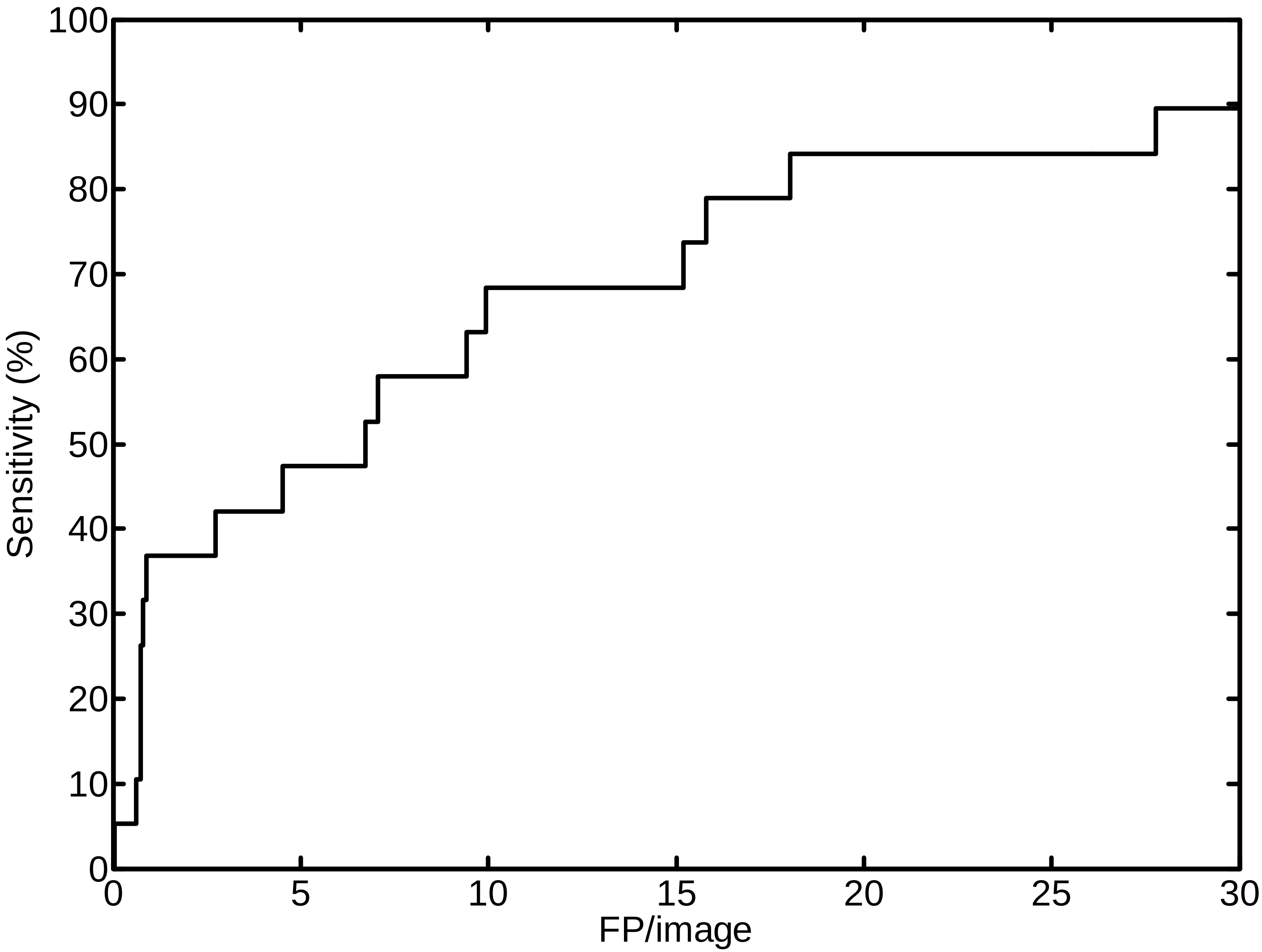
spiral
[0, 0]

Initial results of detection (2004)

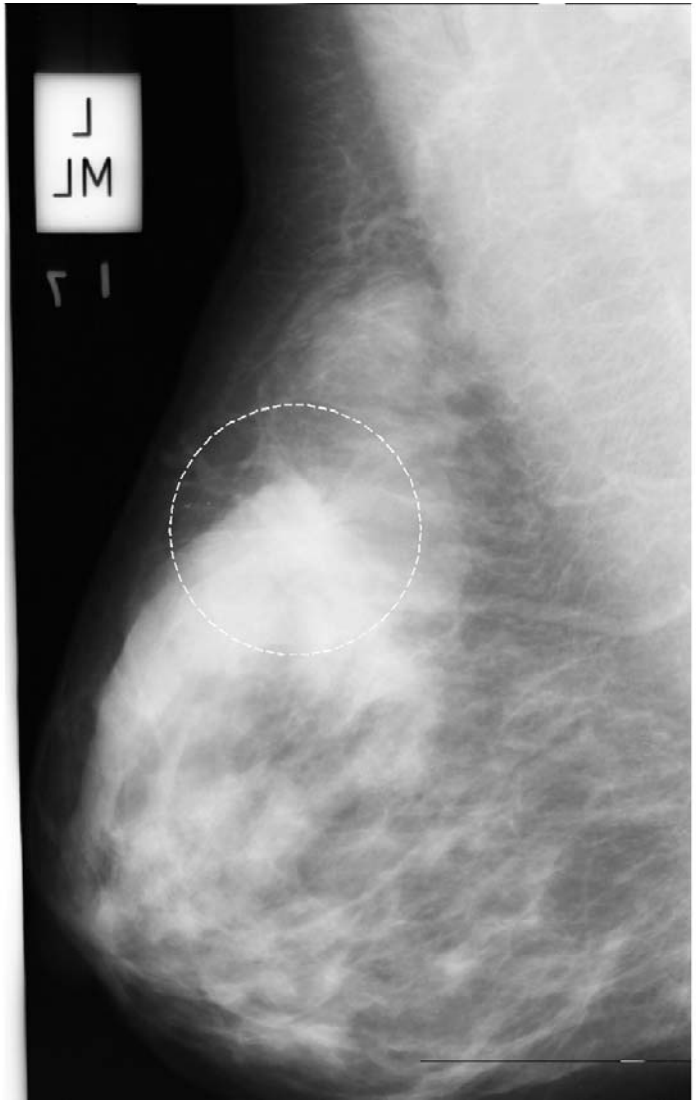


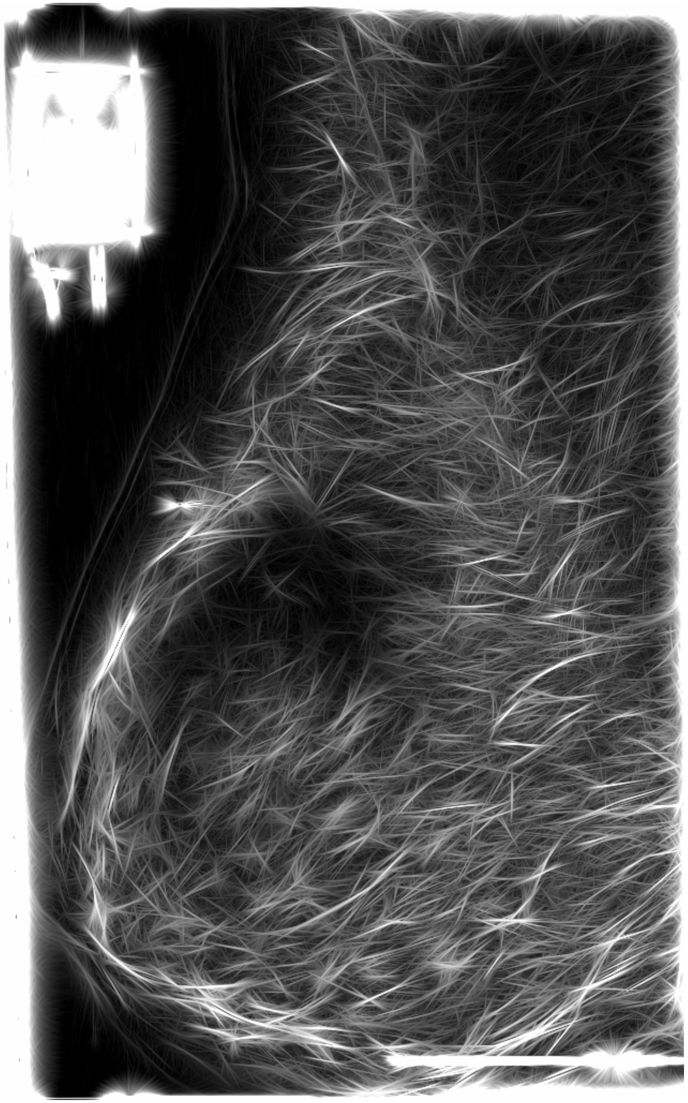
- Test dataset: 19 mammograms with architectural distortion (MIAS database)
- Sensitivity: 84%
- 18 false positives per image

FROC analysis



Reduction of false positives



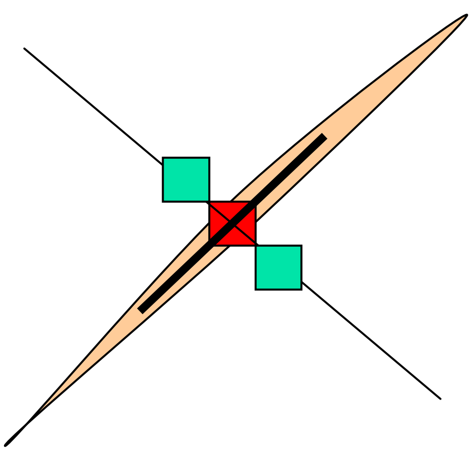


Rejection of confounding structures

- 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



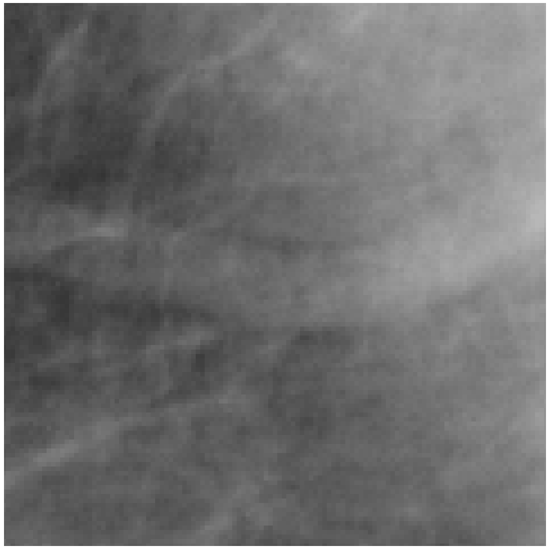
CLS

Gabor magnitude output

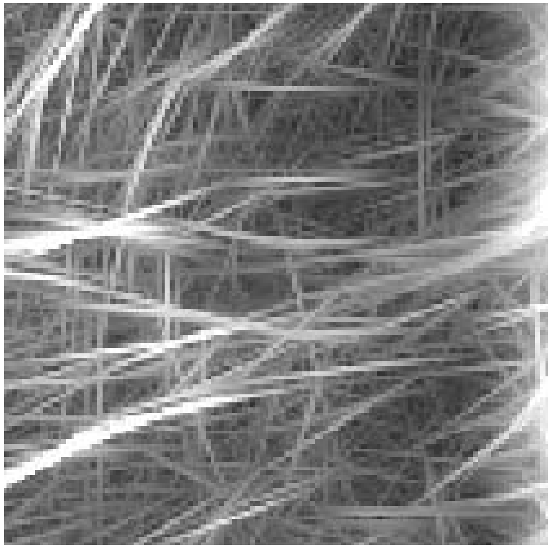
Core CLS pixel

Neighboring pixels along normal

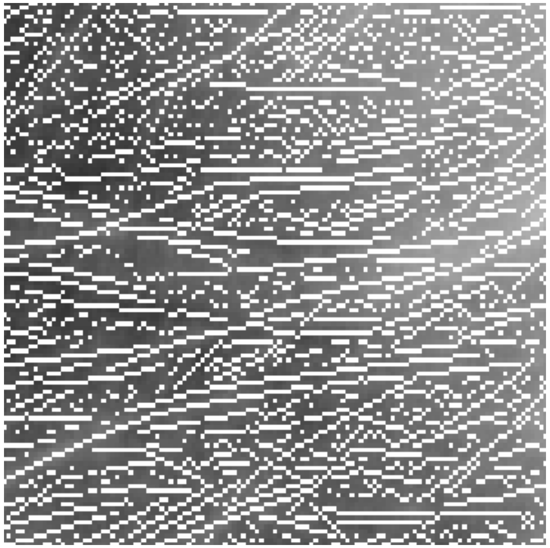
Nonmaximal suppression



ROI with a vessel



Gabor magnitude output



Output of nonmaximal suppression (NMS)

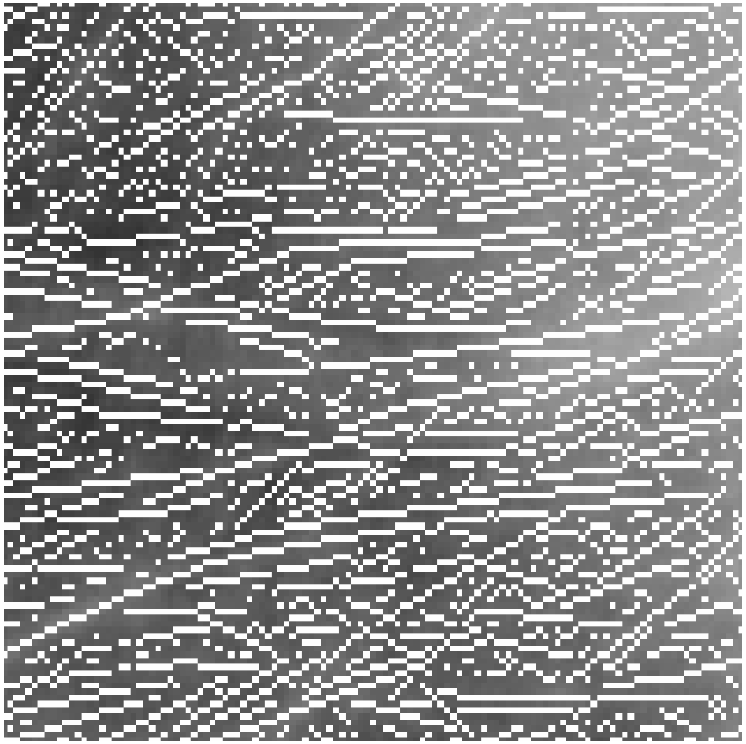
Rejection of confounding structures

- Main feature of confounding structures:

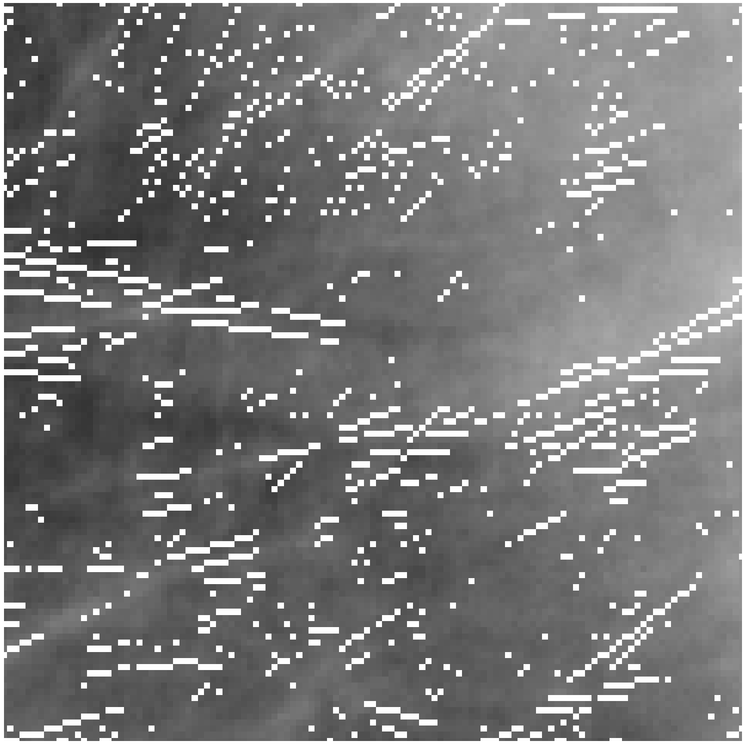
  Angle from the orientation field and direction perpendicular to the gradient vector differ by less than 30 degrees

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

Rejection of confounding CLS

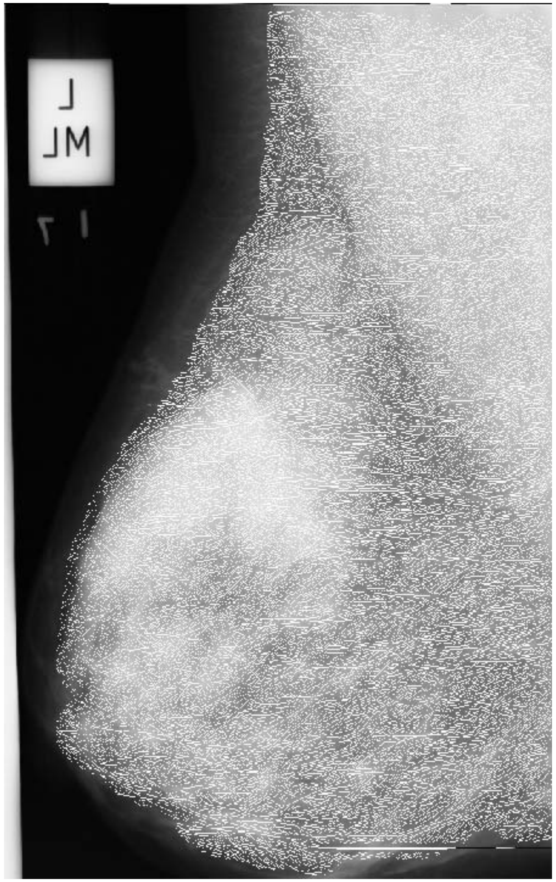


Core CLS pixels detected (Output of NMS)

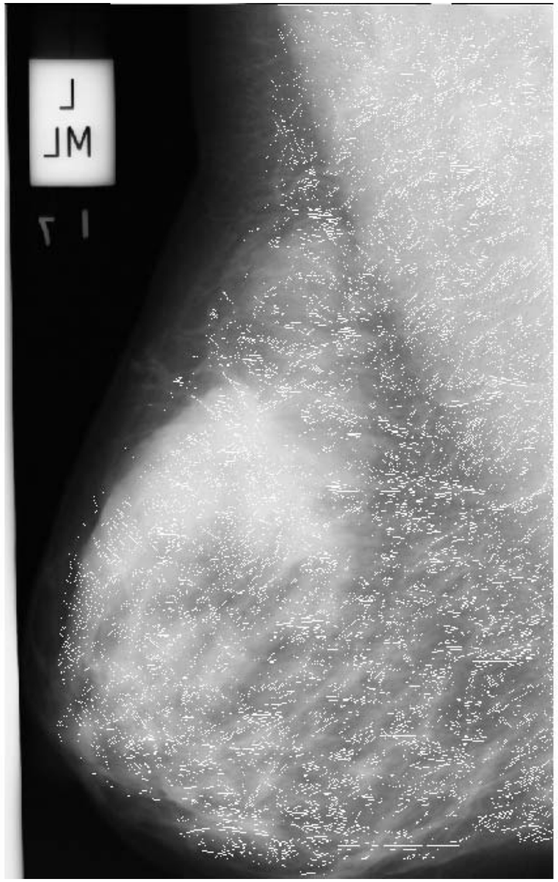


CLS pixels rejected from further analysis

Rejection of confounding CLS



Core CLS pixels detected (Output of NMS)

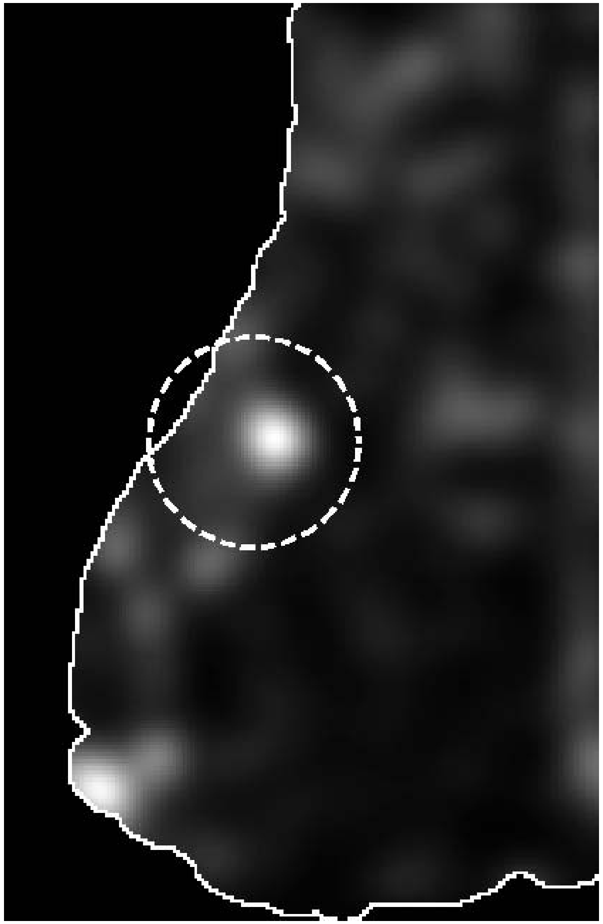


CLS pixels rejected from further analysis

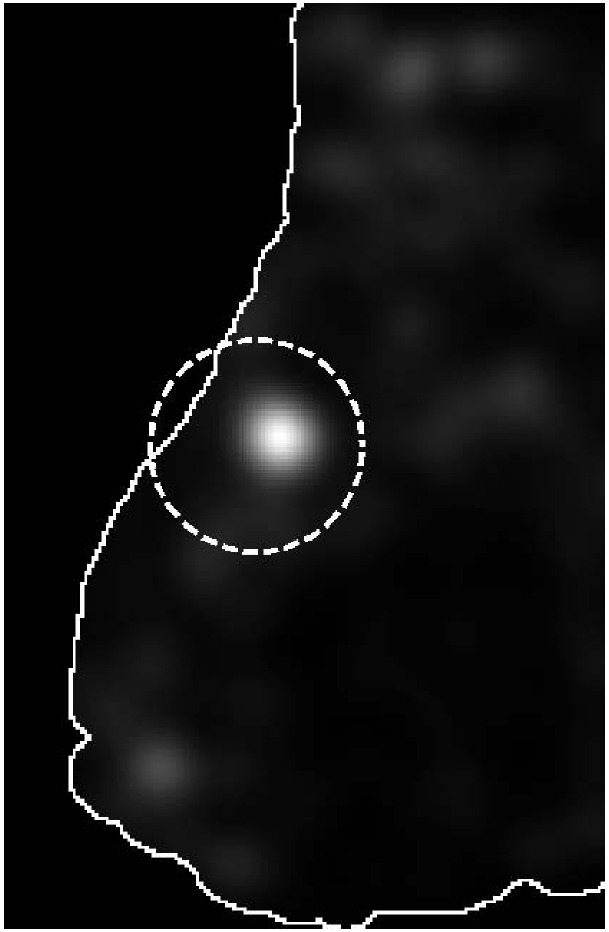
Improved phase portrait analysis

- 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

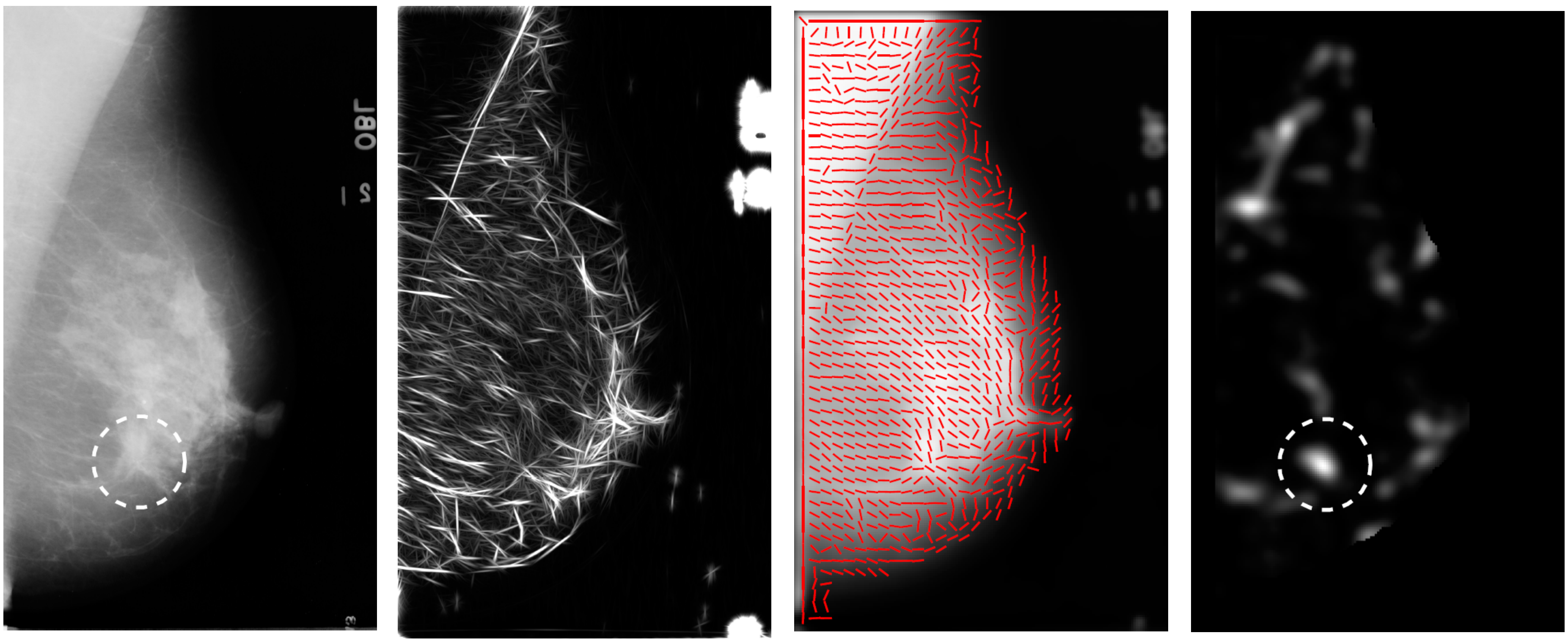


Node map
without CLS analysis

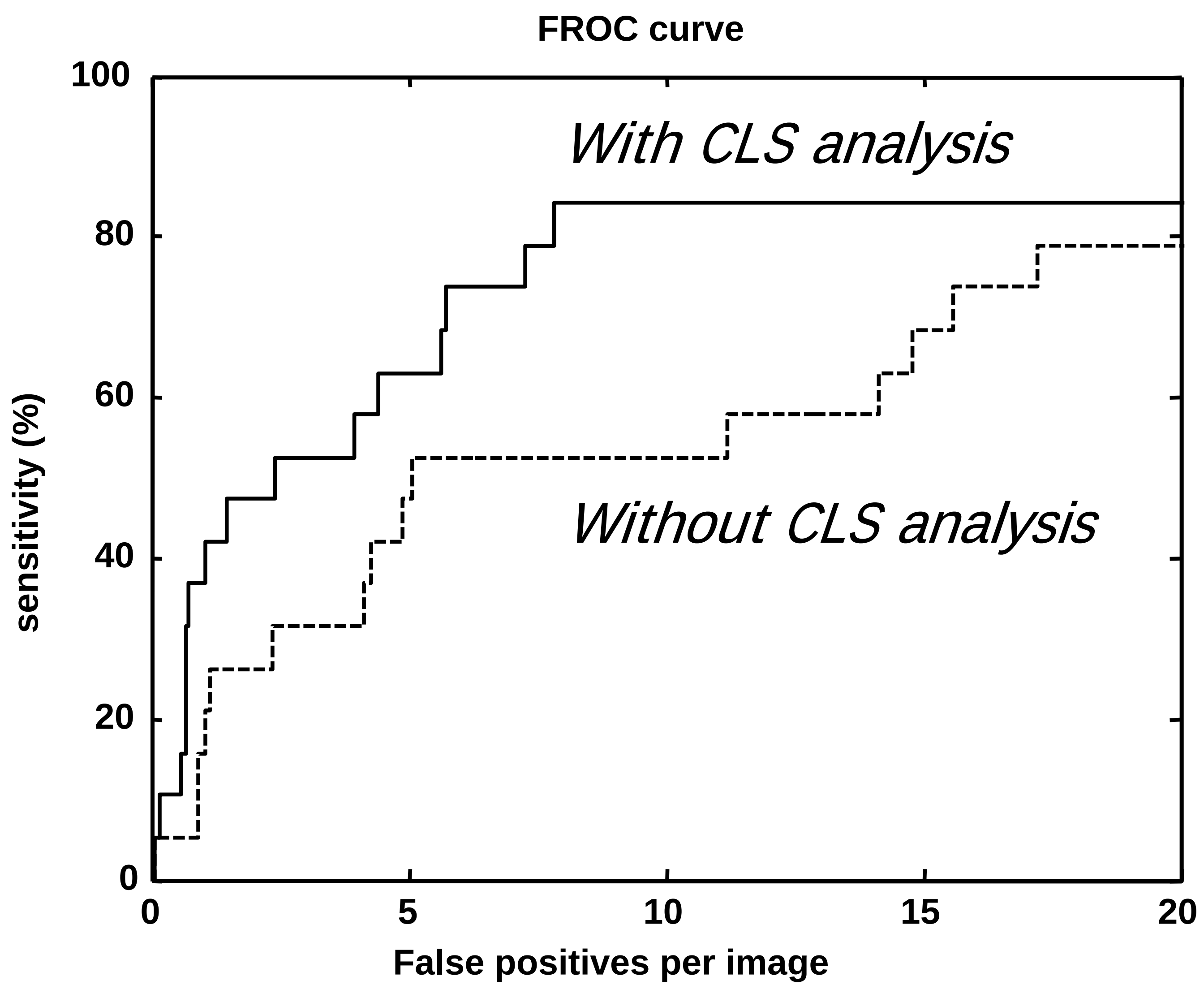


Node map
with CLS analysis

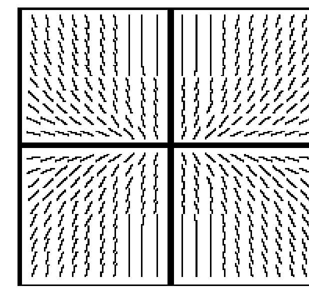
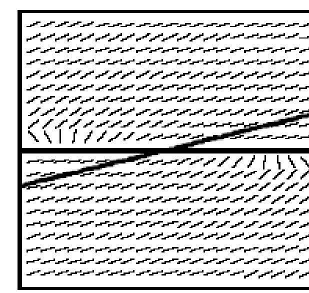
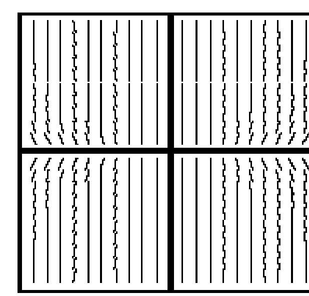
Result of detection of architectural distortion



FROC analysis (2005)



Effect of conditioning number of matrix *A* on the orientation field

Example	Matrix **A**	Eigenvalues	Angle between principal axes	Conditioning number	Orientation field
A	$\begin{bmatrix} 1 & 0 \\ 0 & 3 \end{bmatrix}$	$\lambda_1 = 1$ $\lambda_2 = 3$	90°	3	
B	$\begin{bmatrix} 1 & 7.46 \\ 0 & 3 \end{bmatrix}$	$\lambda_1 = 1$ $\lambda_2 = 3$	15°	21.85	
C	$\begin{bmatrix} 1 & 0 \\ 0 & 20 \end{bmatrix}$	$\lambda_1 = 1$ $\lambda_2 = 20$	90°	20	

Improved results (2006)

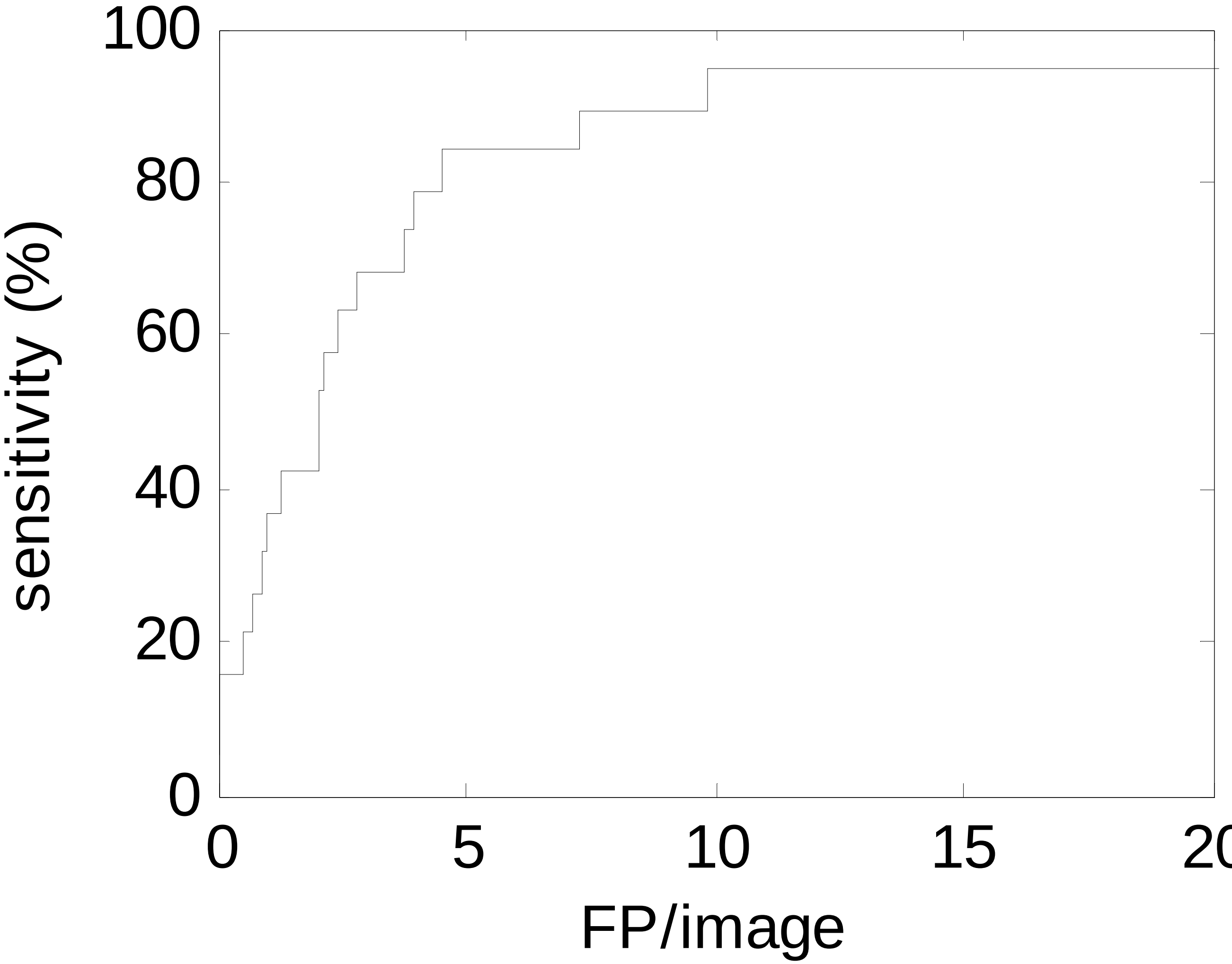
- 19 cases of architectural distortion
- 41 normal control mammograms (MIAS)

- 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

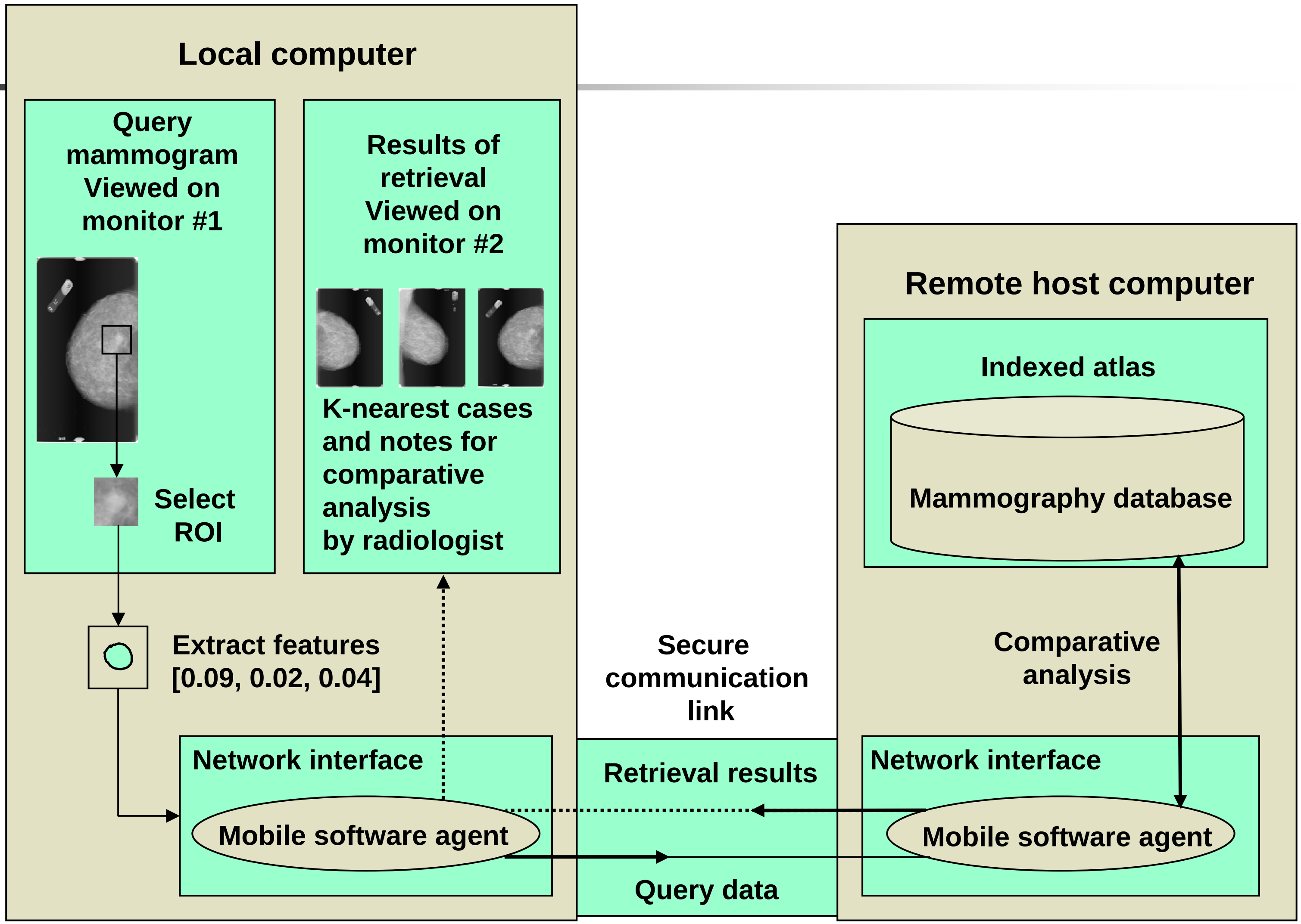
- Phase portraits can be used to detect architectural distortion
- Need to reduce false positives further
- Evaluate method with a large database
- Test method with screening mammograms taken prior to mass formation:

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



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- Natural Sciences and Engineering Research Council of Canada
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