Evaluation of Screening Mammograms by Local Structural Mixture Models

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Outline

Breast Cancer and Mammographic Screening

Statistical Data of Breast Cancer:

- breast cancer happens to about 8% of women during their lifetime
- malignant findings are rare: about 1 to 3 in 1000 screening mammograms
- 5 to 10% of findings is proposed for surgical verification by biopsy
- expectably: about 60 to 80% of biopsies result in benign diagnoses
- retrospective examinations: about 10 to 20% false negative results

Meaning of Mammographic Screening:

- even hardly palpable breast tumors can make metastases
- $\Rightarrow$ early detection of malignant lesions is extremely important
- **mammographic screening** is the only effective tool to decrease the breast cancer mortality rates
- $\Rightarrow$ screening programs: millions of mammograms in one year
- $\Rightarrow$ strong motivation for computer-aided evaluation

Local Evaluation of Screening Mammograms

Idea of the log-likelihood image: ▸ LITERATURE

to emphasize mammographic lesions as “untypical” locations of high “novelty” and facilitate diagnostic evaluation of screening mammograms

local properties: inside pixels of a square window with trimmed corners
$\mathbf{x} = (x_1, x_2, \ldots, x_N) \in \mathcal{X}, \quad x_n \approx$ grey-levels of the window inside

local statistical model: multivariate probability density $P(\mathbf{x})$
$\log P(\mathbf{x}) \approx$ **to measure how unusual is the window inside** $\mathbf{x}$

METHOD: approximation of the density $P(\mathbf{x})$ by Gaussian mixture

- **data set:** by scanning the mammogram with the search window
- **EM algorithm:** to estimate the Gaussian mixture $P(\mathbf{x})$
- **log-likelihood image:** $\log P(\mathbf{x})$ displayed as grey-levels at window center
- **interpretation:** dark grey-levels indicate “suspect” locations

UTIA

Estimation of Local Statistical Model

Gaussian mixture of product components:

$$P(\mathbf{x}) = \sum_{m=1}^{M} w_m F(\mathbf{x}|\boldsymbol{\mu}_m, \boldsymbol{\sigma}_m) = \sum_{m=1}^{M} w_m \prod_{n=1}^{N} \left[\frac{1}{\sqrt{2\pi}\sigma_{mn}} \exp\{-\frac{(x_n - \mu_{mn})^2}{2\sigma_{mn}^2}\} \right]$$

log-likelihood function: (data set $\mathcal{S}$ by scanning the image)

$$L = \frac{1}{|\mathcal{S}|} \sum_{x \in \mathcal{S}} \log \left[\sum_{m=1}^{M} w_m F(\mathbf{x}|\boldsymbol{\mu}_m, \boldsymbol{\sigma}_m) \right]$$

EM iteration equations: (initial parameters chosen randomly)

$$q(m|\mathbf{x}) = \frac{w_m F(\mathbf{x}|\boldsymbol{\mu}_m, \boldsymbol{\sigma}_m)}{\sum_{j \in \mathcal{M}} w_j F(\mathbf{x}|\boldsymbol{\mu}_j, \boldsymbol{\sigma}_j)}, \quad w_m^{'} = \frac{1}{|\mathcal{S}|} \sum_{x \in \mathcal{S}} q(m|\mathbf{x})$$

$$\mu_{mn}^{'} = \frac{1}{w_m^{'}|\mathcal{S}|} \sum_{x \in \mathcal{S}} x_n q(m|\mathbf{x}), \quad (\sigma_{mn}^{'})^2 = \frac{1}{w_m^{'}|\mathcal{S}|} \sum_{x \in \mathcal{S}} (x_n - \mu_{mn}^{'})^2 q(m|\mathbf{x})$$

NOTATION: $w_m^{'}, \mu_{mn}^{'}, \sigma_{mn}^{'}$ $\approx$ new parameter values

Computational Experiments

- **local statistical model:** estimated from a single mammogram
- each mammogram is evaluated individually
- mirror transform is applied to right-hand-part of images to utilize the underlying symmetry
- $\Rightarrow$ the method need not be trained by other images
- $\Rightarrow$ it is not confronted with high natural variability of mammograms

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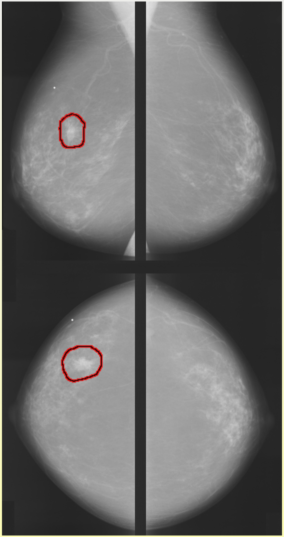
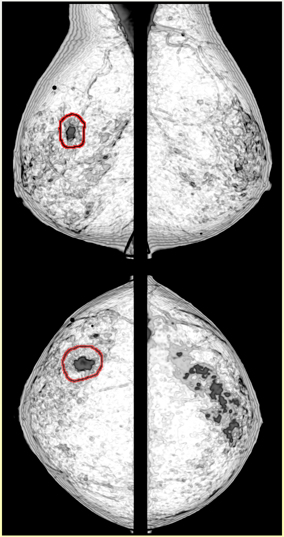
- **source database:** University of South Florida http://marathon.csee.usf.edu/Mammography/Database.html
- **chosen search window:** square window of 13 x 13 pixels with trimmed corners, dimension of $\mathbf{x}$ is $N = 145$ $(= 169 - 4 \times 6)$
- **model data set:** by scanning the four-view mammogram with the search window $(|\mathcal{S}| \approx 10^5 - 10^6)$
- **computing time:** cca 2 hours for 36 components but the computation can be parellelized

C-0016-1: segmentally distributed calcification

original image



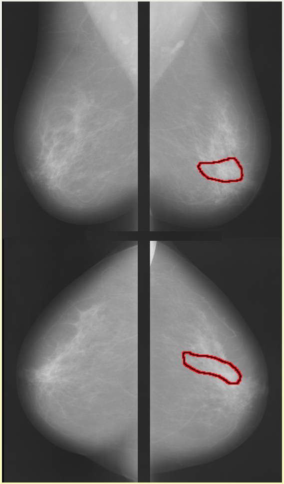
log-likelihood image



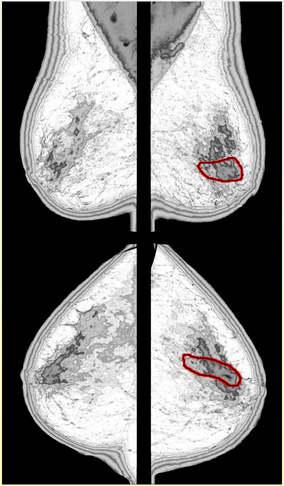
Remark: Pixel grey levels $\log P(\mathbf{x})$ defined by 145 neighboring pixels

C-0002-1: segmentally distributed calcification

original image



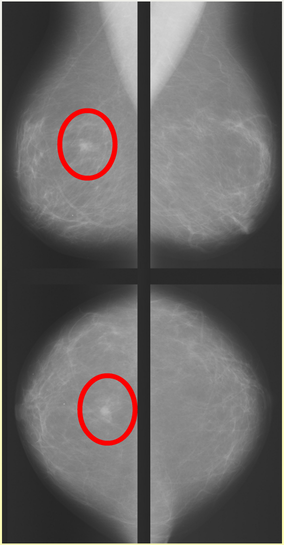
log-likelihood image



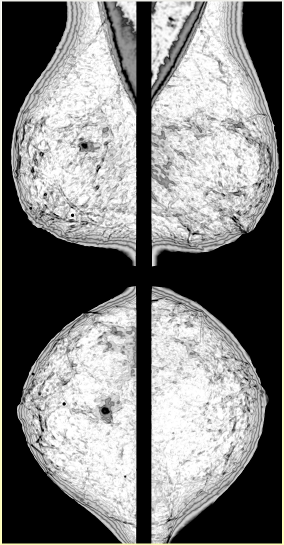
Remark: Large calcification emphasized by contour lines.

C-0143-1: mass, irregular shape, ill-defined margins

original image

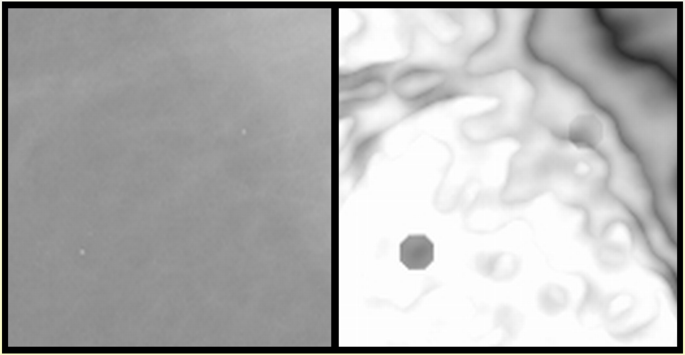


log-likelihood image



Identification of "Micro-Calcifications" by Spots

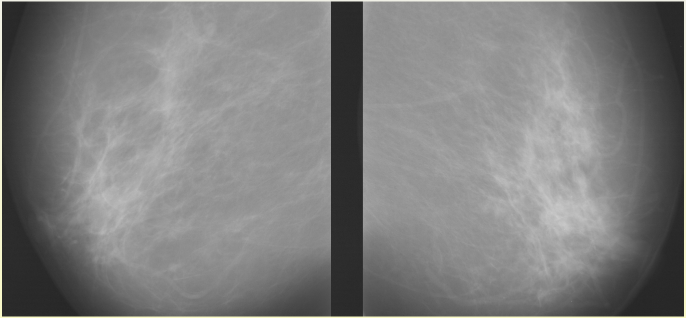
original micro-calcifications **corresponding dark spots**



Remark: window position containing a light pixel
$\Rightarrow$ implies decreased value of $\log P(\mathbf{x})$
$\Rightarrow$ light pixel is identified as a window-like dark spot

Identification of “Masses” by Contour-Lines

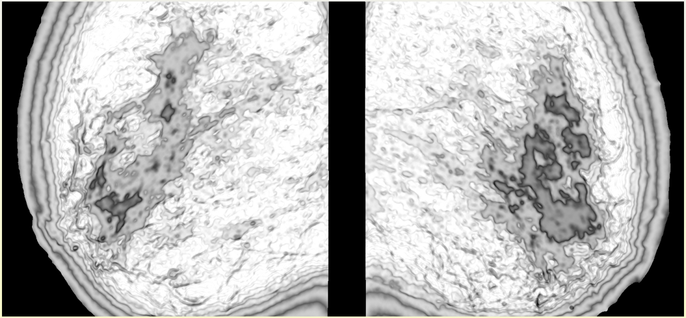
example of screening mammogram containing suspect masses



Remark: The masses may be quite subtle, may have smooth boundaries and different shapes. Detection and classification of masses is more difficult than detection of micro-calcifications.

Identification of “Masses” by Contour-Lines

contour lines around “masses” and at the mammogram boundaries



Remark: In high-dimensional spaces ($N \approx 10^2$) the log-likelihood values $\log P(\mathbf{x})$ are typically dominated by a single component of the mixture which is most adequate to the underlying region.
The “switching” of components at the boundaries of different regions is accompanied by decreased $\log P(\mathbf{x})$ values which produce contour lines.

Structural Mixture Model

IDEA: to exclude the less informative "noisy" variables in components

binary structural parameters: $\phi_m = (\phi_{m1}, \ldots, \phi_{mN}) \in \{0, 1\}^N$

$$F(\mathbf{x}|m) = \prod_{n \in \mathcal{N}} f_n(x_n|m)^{\phi_{mn}} f_n(x_n|0)^{1-\phi_{mn}}, \quad \sum_{m \in \mathcal{M}} \sum_{n \in \mathcal{N}} \phi_{mn} = s < MN$$

$\phi_{mn} = 0 \;\Rightarrow\;$ $f_n(x_n|m)$ replaced by common fixed density $f_n(x_n|0)$ $(\approx P_n(x_n))$

$$P(\mathbf{x}) = \sum_{m \in \mathcal{M}} F(\mathbf{x}|m) f(m) = F(\mathbf{x}|0) \sum_{m \in \mathcal{M}} G(\mathbf{x}|m, \phi_m) f(m)$$

$$G(\mathbf{x}|m, \phi_m) = \prod_{n \in \mathcal{N}} \left[\frac{f_n(x_n|m)}{f_n(x_n|0)} \right]^{\phi_{mn}}, \quad F(\mathbf{x}|0) = \prod_{n \in \mathcal{N}} f_n(x_n|0) \;\approx\; \textbf{background}$$

the fixed background density $F(\mathbf{x}|0)$ reduces in Bayes formula:

$$p(\omega|\mathbf{x}) = \frac{P(\mathbf{x}|\omega) p(\omega)}{P(\mathbf{x})} = \frac{\sum_{m \in \mathcal{M}_\omega} G(\mathbf{x}|m, \phi_m) f(m)}{\sum_{j \in \mathcal{M}} G(\mathbf{x}|j, \phi_j) f(j)} \approx \sum_{m \in \mathcal{M}_\omega} G(\mathbf{x}|m, \phi_m) f(m)$$

Remark: The model performs component specific feature selection

Structural Optimization - General EM Algorithm

structural optimization can be included into EM algorithm

$$L = \frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}} \log P(\mathbf{x}) = \frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}} \log \left[\sum_{m\in\mathcal{M}} F(\mathbf{x}|0)G(\mathbf{x}|m,\phi_m)f(m)\right]$$

E-step:

$$q(m|\mathbf{x}) = \frac{f(m)G(\mathbf{x}|m,\phi_m)}{\sum_{j=1}^{M} f(j)G(\mathbf{x}|j,\phi_j)}, \quad m = 1,2,\ldots,M$$

M-step:

$$f^{'}(m) = \frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}} q(m|\mathbf{x}), \quad m = 1,2,\ldots,M,\ \mathbf{x}\in\mathcal{S}$$

$$\mathrm{G}^{'}(.|m,\phi_m^{'}) = \arg\max_{G(.|m,\phi_m)} \left\{\frac{1}{|\mathcal{S}|}\sum_{x\in\mathcal{S}} q(m|\mathbf{x}) \log F(\mathbf{x}|0)G(\mathbf{x}|m,\phi_m)\right\}$$

$$\Rightarrow \quad G^{'}(.|m,\phi_m^{'}) = \arg\max_{G(.|m,\phi_m)} \left\{\frac{1}{|\mathcal{S}|}\sum_{x\in\mathcal{S}} q(m|\mathbf{x}) \log G(\mathbf{x}|m,\phi_m)\right\}$$

Remark. EM algorithm transforms the difficult problem of maximization of the mixture log-likelihood function L to the repeated maximization of the weighted log-likelihood functions of mixture components.

Proof of the Monotonic Property of EM Algorithm

sequence of log-likelihood values $\{L^{(t)}\}_{t=0}^{\infty}$ is nondecreasing:

$$L^{(t+1)} - L^{(t)} \geq 0, \quad t = 0, 1, 2, \ldots$$

In view of Kullback-Leibler information divergence we can write

$$\frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}} I(q(\cdot|\mathbf{x})||q^{'}(\cdot|\mathbf{x})) = \frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}}\left[\sum_{m=1}^{M} q(m|\mathbf{x})\log\frac{q(m|\mathbf{x})}{q^{'}(m|\mathbf{x})}\right] \geq 0$$

making substitution for $q(m|\mathbf{x}), q^{'}(m|\mathbf{x})$ in the logarithm we obtain:

$$\frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}}\sum_{m=1}^{M} q(m|\mathbf{x})\log\frac{P^{'}(\mathbf{x})}{P(\mathbf{x})} + \frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}}\sum_{m=1}^{M} q(m|\mathbf{x})\log\left[\frac{f(m)G(\mathbf{x}|m,\phi_m)}{f^{'}(m)G^{'}(\mathbf{x}|m,\phi_m^{'})}\right] \geq 0$$

whereby the first sum corresponds to the increment of L:

$$\frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}}\sum_{m=1}^{M} q(m|\mathbf{x})\log\frac{P^{'}(\mathbf{x})}{P(\mathbf{x})} = \frac{1}{|\mathcal{S}|}\sum_{\mathbf{x}\in\mathcal{S}}\log\frac{P^{'}(\mathbf{x})}{P(\mathbf{x})} = L^{'} - L.$$

Proof of the Monotonic Property of EM Algorithm

making substitution for the increment we obtain the inequality

$$L^{'} - L \geq \frac{1}{|\mathcal{S}|} \sum_{\mathbf{x} \in \mathcal{S}} \sum_{m=1}^{M} q(m|\mathbf{x}) \log \left[\frac{f^{'}(m) G^{'}(\mathbf{x}|m, \phi_m^{'})}{f(m) G(\mathbf{x}|m, \phi_m)} \right]$$

which can be rewritten in the form

$$L^{'} - L \geq \sum_{m=1}^{M} \left[\frac{1}{|\mathcal{S}|} \sum_{\mathbf{x} \in \mathcal{S}} q(m|\mathbf{x}) \right] \log \frac{f^{'}(m)}{f(m)} + \sum_{m=1}^{M} \frac{1}{|\mathcal{S}|} \sum_{\mathbf{x} \in \mathcal{S}} q(m|\mathbf{x}) \log \frac{G^{'}(\mathbf{x}|m, \phi_m^{'})}{G(\mathbf{x}|m, \phi_m)}$$

again, by using the substitution from the M-step, we can write

$$\sum_{m=1}^{M} \left[\frac{1}{|\mathcal{S}|} \sum_{\mathbf{x} \in \mathcal{S}} q(m|\mathbf{x}) \right] \log \frac{f^{'}(m)}{f(m)} = \sum_{m=1}^{M} f^{'}(m) \log \frac{f^{'}(m)}{f(m)} \geq 0.$$

since Kullback-Leibler information divergence is nonnegative

Proof of the Monotonic Property of EM Algorithm

in view of the M-step definition we can write the inequality

$$\sum_{m=1}^{M} \frac{1}{|\mathcal{S}|} \sum_{\mathbf{x}\in\mathcal{S}} q(m|\mathbf{x}) \log G^{'}(\mathbf{x}|m, \phi^{'}_m) \geq \sum_{m=1}^{M} \frac{1}{|\mathcal{S}|} \sum_{\mathbf{x}\in\mathcal{S}} q(m|\mathbf{x}) \log G(\mathbf{x}|m, \phi_m)$$

which can be rewritten in the form:

$$\sum_{m=1}^{M} \frac{1}{|\mathcal{S}|} \sum_{\mathbf{x}\in\mathcal{S}} q(m|\mathbf{x}) \log \frac{G^{'}(\mathbf{x}|m, \phi^{'}_m)}{G(\mathbf{x}|m, \phi_m)} \geq 0$$

therefore the increment of the log-likelihood criterion is nonnegative:

$$L^{'} - L \geq \sum_{m=1}^{M} f^{'}(m) \log \frac{f^{'}(m)}{f(m)} + \sum_{m=1}^{M} \frac{1}{|\mathcal{S}|} \sum_{\mathbf{x}\in\mathcal{S}} q(m|\mathbf{x}) \log \frac{G^{'}(\mathbf{x}|m, \phi^{'}_m)}{G(\mathbf{x}|m, \phi_m)} \geq 0$$

Remark. The proof is important for any new application of EM algorithm.

Structural Optimization Criterion

"structural" EM algorithm: explicit solution of the equation

$$G^{'}(.|m,\phi^{'}_m) = \arg \max_{G(.|m,\phi_m)} \left\{ \sum_{x \in \mathcal{S}} \frac{q(m|\mathbf{x})}{|\mathcal{S}|} \log G(\mathbf{x}|m,\phi_m) \right\}, \quad m \in \mathcal{M}$$

making substitution for $G(\mathbf{x}|m,\phi_m)$ we obtain:

$$\sum_{\mathbf{x} \in \mathcal{S}} \frac{q(m|\mathbf{x})}{|\mathcal{S}|} \log \prod_{n \in \mathcal{N}} \left[\frac{f_n(x_n|m)}{f_n(x_n|0)} \right]^{\phi_{mn}} = \sum_{n \in \mathcal{N}} \phi_{mn} \sum_{\mathbf{x} \in \mathcal{S}} \frac{q(m|\mathbf{x})}{|\mathcal{S}|} \log \left[\frac{f_n(x_n|m)}{f_n(x_n|0)} \right]$$

⇒ **the parameters $f^{'}_n(.|m)$ and $\phi^{'}_m$ can be optimized separately**

⇒ for any fixed structural parameters ϕ_{mn} we can write:

$$f^{'}_n(.|m) = \arg \max_{f_n(.|m)} \left\{ \sum_{\mathbf{x} \in \mathcal{S}} \frac{q(m|\mathbf{x})}{|\mathcal{S}|} \log f_n(x_n|m) \right\}$$

and given the new parameters of densities $f^{'}_n(x_n|m)$ we can write:

$$\phi^{'}_m = \arg \max_{\phi_m} \left\{ \phi_{mn} \gamma^{'}_{mn} \right\}; \qquad \gamma^{'}_{mn} = \sum_{\mathbf{x} \in \mathcal{S}} \frac{q(m|\mathbf{x})}{|\mathcal{S}|} \log \left[\frac{f^{'}_n(x_n|m)}{f_n(x_n|0)} \right]$$

Structural Optimization - Gaussian Mixture Model

Gaussian univariate densities: ▸ multivariate discrete mixture

$$f_n(x_n|m) = \frac{1}{\sqrt{2\pi}\sigma_{mn}} \exp\{-\frac{(x_n - \mu_{mn})^2}{2\sigma_{mn}^2}\}, \quad n \in \mathcal{N}, \ m = 0, 1, 2, \ldots, M$$

EM iteration equations: $(m \in \mathcal{M}, n \in \mathcal{N}, \mathbf{x} \in \mathcal{S})$

$$q(m|\mathbf{x}) = \frac{G(\mathbf{x}|m, \phi_m) f(m)}{\sum_{j \in \mathcal{M}} G(\mathbf{x}|j, \phi_j) f(j)}, \qquad w_m^{'} = \frac{1}{|\mathcal{S}|} \sum_{\mathbf{x} \in \mathcal{S}} q(m|\mathbf{x})$$

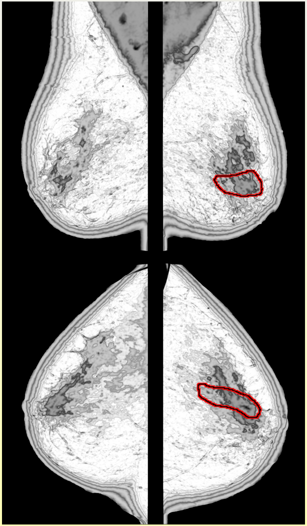
$$\mu_{mn}^{'} = \frac{1}{w_m^{'}|\mathcal{S}|} \sum_{x \in \mathcal{S}} x_n q(m|\mathbf{x}), \qquad (\sigma_{mn}^{'})^2 = \frac{1}{w_m^{'}|\mathcal{S}|} \sum_{x \in \mathcal{S}} (x_n - \mu_{mn}^{'})^2 q(m|\mathbf{x})$$

structural optimization: $\phi_{mn}^{'} = 1$ for the s highest values $\gamma_{mn}^{'}$

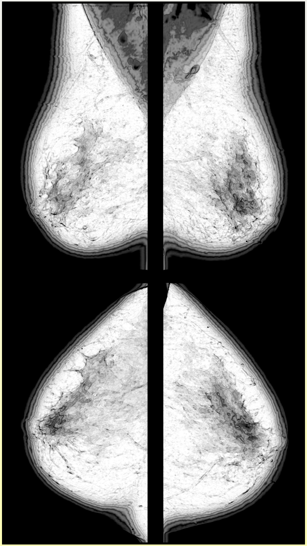
$$\gamma_{mn}^{'} = \frac{w_m^{'}}{2} \left[\frac{(\mu_n^{'(m)} - \mu_n^{(0)})^2 + (\sigma_n^{'(m)})^2}{(\sigma_n^{(0)})^2} - 1 - 2 \log \frac{\sigma_n^{'(m)}}{\sigma_n^{(0)}} \right]$$

C-0002-1: pleomorphic calcif., segmentally distributed

log-likelihood image

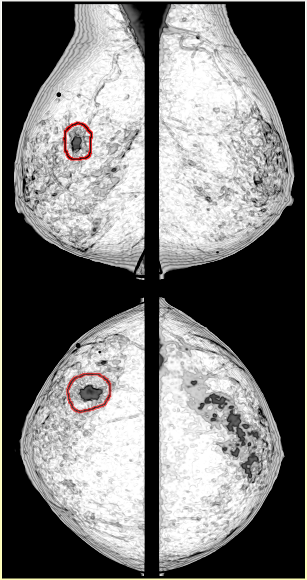


modified log-likelihood image

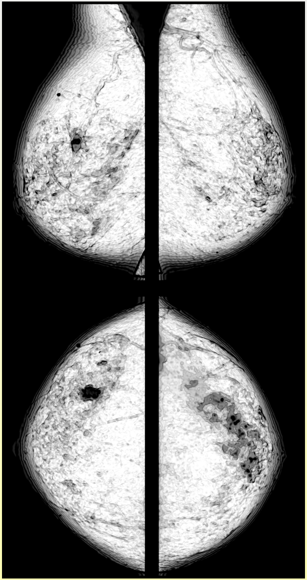


C-0016-1: segmentally distributed calcification

log-likelihood image

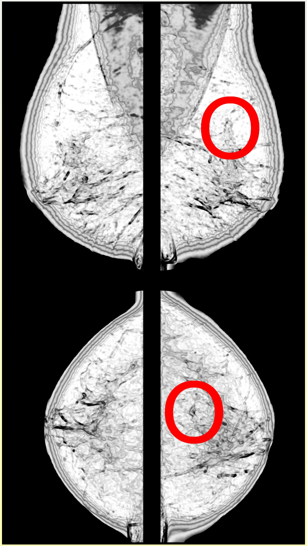


modified log-likelihood image

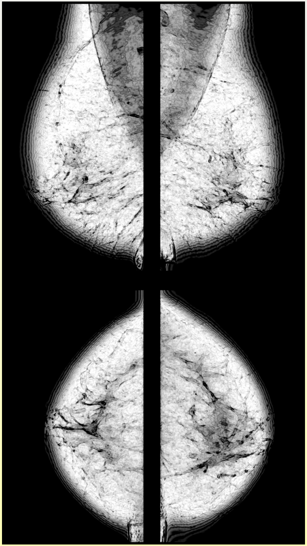


C-0188-1: malignant mass, oval margins

log-likelihood image

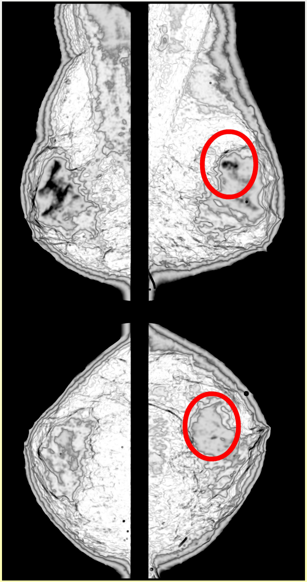


modified log-likelihood image

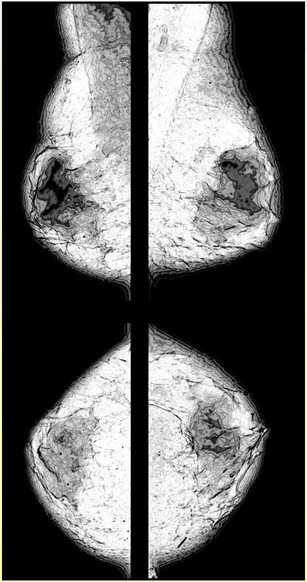


B-3056-1: mass, focal-asymmetric density, margins n/a

log-likelihood image

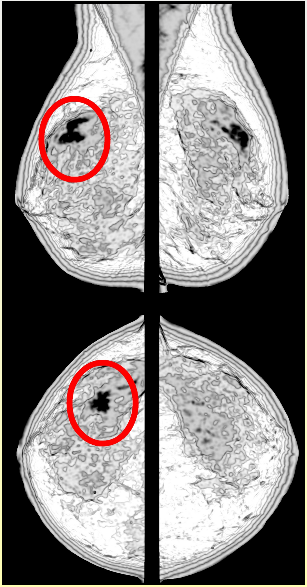


modified log-likelihood image

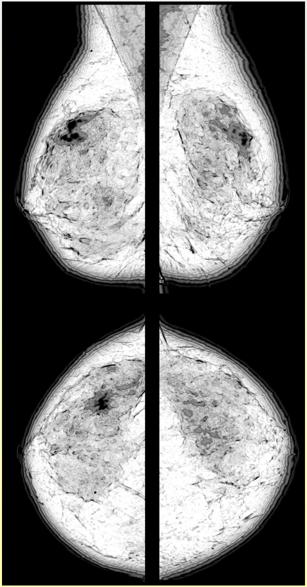


C-0001-1: : mass, irregular shape, spiculated margins

log-likelihood image

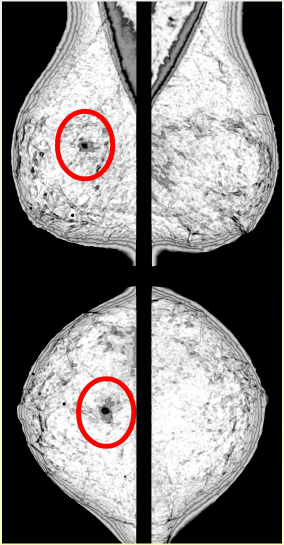


modified log-likelihood image

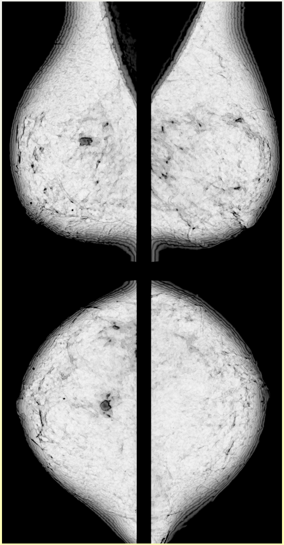


C-0143-1: mass, irregular shape, ill-defined margins

log-likelihood image

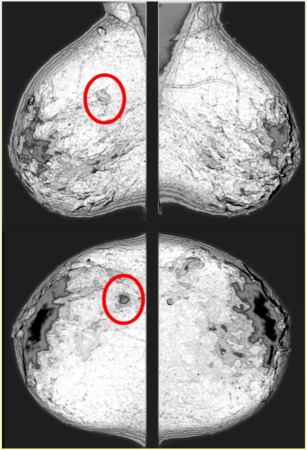


modified log-likelihood image

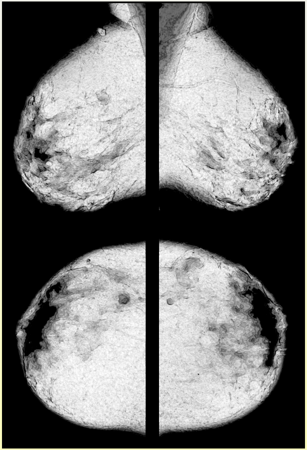


B-3020-1: mass, lobulated shape, ill defined margins

log-likelihood image

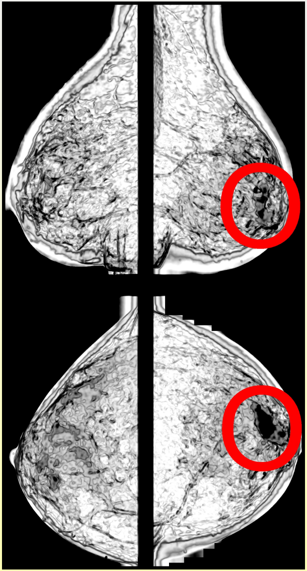


modified log-likelihood image

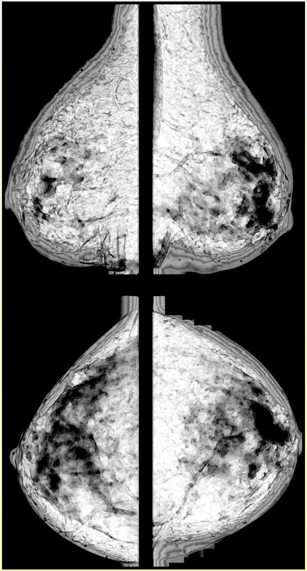


C-0206-1: malignant mass, lobulated margins

log-likelihood image

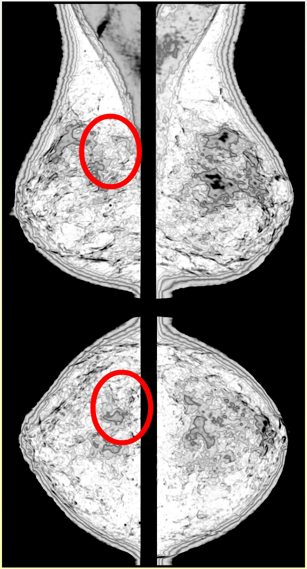


modified log-likelihood image

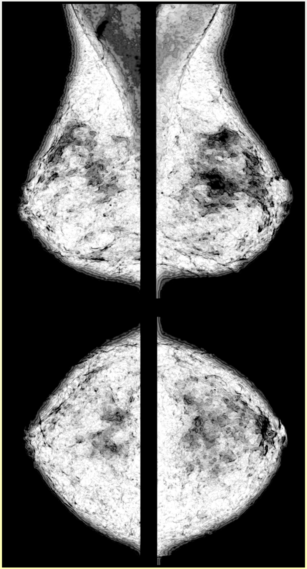


D-4163-1: punctate calcification, clustered distribution

log-likelihood image



modified log-likelihood image



Concluding Remarks

Log-Likelihood Image of Screening Mammogram:

- **purely statistical construct without any medical context**
- **aim:** to facilitate diagnostic evaluation
- **masses:** emphasized as dark regions with contour lines
- **micro-calcifications:** dark spots of the size and form of window
- **topological continuity:** image disintegrates for complex densities

APPLICATION in Monitoring Systems

- evaluation of multivariate time series by sliding window
- detection of unusual, suspect or unsafe states
- sequential optimization of mixture parameters (non-supervised training)
- clear statistical interpretation of the output
- invariant with respect to arbitrary linear transform of data Proof

Literatura 1/4

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◂ Back

Invariance with Respect to Grey-Level Transform

Invariance Property:

the statistical model is invariant with respect to arbitrary linear transform of variables

the transformed data and transformed mixture parameters

$$y_n = ax_n + b, \quad \tilde{\mu}_{mn} = a\mu_{mn} + b, \quad \tilde{\sigma}_{mn} = a\sigma_{mn}, \quad \mathbf{y} = T(\mathbf{x}), \; \mathbf{x} \in \mathcal{S}$$

can be shown to satisfy the EM iteration equations

$$F(\mathbf{y}|\tilde{\boldsymbol{\mu}}_m, \tilde{\boldsymbol{\sigma}}_m) = \frac{1}{a^N} F(\mathbf{x}|\boldsymbol{\mu}_m, \boldsymbol{\sigma}_m), \quad \tilde{P}(\mathbf{y}) = \frac{1}{a^N} P(\mathbf{x})$$

$$q(m|\mathbf{y}) = q(m|\mathbf{x}), \quad \mathbf{x} \in \mathcal{S}, \quad \tilde{w}_m = w_m, \quad m \in \mathcal{M}$$

and therefore the corresponding log-likelihood values differ only by a constant

$$\log \tilde{P}(\mathbf{y}) = -N \log a + \log P(\mathbf{x}), \quad \mathbf{x} \in \mathcal{S}$$

which can be removed by norming the output log-likelihood values Back

Structural Optimization - Multivariate Discrete Mixtures

univariate discrete distributions: $f_n(x_n|m), n \in \mathcal{N}, \; m = 0, 1, \ldots, M$

EM iteration equations: $(m \in \mathcal{M}, n \in \mathcal{N}, \mathbf{x} \in \mathcal{S})$

$$q(m|\mathbf{x}) = \frac{G(\mathbf{x}|m, \phi_m) f(m)}{\sum_{j \in \mathcal{M}} G(\mathbf{x}|j, \phi_j) f(j)}, \qquad w_m^{'} = \frac{1}{|\mathcal{S}|} \sum_{\mathbf{x} \in \mathcal{S}} q(m|\mathbf{x})$$

$$f_n^{'}(\xi|m) = \frac{1}{\sum_{\mathbf{x} \in \mathcal{S}} q(m|\mathbf{x})} \sum_{\mathbf{x} \in \mathcal{S}} \delta(\xi, x_n) q(m|\mathbf{x})$$

structural optimization: $\phi_{mn}^{'} = 1$ for the s highest values $\gamma_{mn}^{'}$

$$\gamma_{mn}^{'} = \sum_{\mathbf{x} \in \mathcal{S}} \frac{q(m|\mathbf{x})}{|\mathcal{S}|} \log \left[\frac{f_n^{'}(x_n|m)}{f_n(x_n|0)} \right] = f^{'}(m) \sum_{x_n \in \mathcal{X}_n} f_n^{'}(x_n|m) \log \frac{f_n^{'}(x_n|m)}{f_n(x_n|0)}$$

$\gamma_{mn}^{'} \approx$ Kullback-Leibler information divergence

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