Image Processing

5

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KEY POINTS

Image processing is a crucial element of modern digital mammography. Optimizing mammogram presentation may lead to more efficient reading and improved diagnostic performance. Despite that the effects of image processing are often much larger than those of acquisition parameter settings, little is known about how image processing can be optimized. Experts agree that comparison of features in various mammographic views is very important. This issue must be addressed by processing. Variation of image presentation across views and subsequent mammograms should be minimized. The dynamic range of electronic displays is limited. Therefore, processing techniques should be designed to limit the dynamic range of mammograms. This can effectively be done by applying peripheral enhancement in the uncompressed tissue region near the projected skin–air interface. Adaptive contrast enhancement can be applied to enhance microcalcifications and dense tissue in the interior of the mammogram. Mammogram processing should be aimed at displaying all relevant information in good contrast simultaneously, as human interaction to manipulate contrast during reading is too time-consuming to be applied on a regular basis.

5.1 Introduction

The goal of mammography is to detect and diagnose breast cancer, a task which is generally performed by experienced and skilled radiologists. For optimal reader performance, mammograms have to be matched to the human visual system when they are

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presented. In other words, characteristic features of cancer have to be displayed with optimal contrast to avoid being missed or misinterpreted. Within the limited possibilities of conventional screen-film mammography, this matching problem has received much attention in the past. Many innovations have been made in mammography to enhance visibility of cancers. Most notable in this respect is the gradual increase of contrast in the interior region of the breast at the cost of contrast in the periphery, where cancer seldom occurs. This change was only possible due to development of more accurate automatic exposure control (AEC) devices. With the latest generation of mammography films, the skinline and large parts of the periphery are hardly visible on mammography film alternators. With the introduction of digital mammography, a wide range of new possibilities has become available to enhance mammograms. An overview of digital mammogram processing techniques will be presented here.

Digital image processing is only one part of the mammographic imaging chain. Ideally, the design of a medical image processing method should be independent of image acquisition and display. For image display, this ideal can be achieved by ensuring that display devices conform to the DICOM display standard. Therefore, it is important that one is aware of the mechanisms used in the definition of this standard. Mappings to convert pixel values to luminance in display devices depend on parameter settings in the processed images, like window/level settings and values of interest lookup table (VOI LUT). Selection of appropriate values of these parameters is an issue that should be addressed by processing algorithms. On the other end of the chain is the acquisition device. Digital detectors in mammography devices differ and these differences have to be taken into account when processing algorithms are designed. Examples are variation in image resolution, gain, modulation transfer function, and noise characteristics. Fortunately, important acquisition parameters such as anode material, ltration, and kVp are provided in the DICOM header and can thus be used in processing algorithms. Despite many differences, there is a major advantage in the use of digital detectors: in the range of interest, pixel values are more or less proportional to X-ray exposure at the detector. This allows design of robust processing algorithms which can be applied to a variety of systems.

Digital mammography manufacturers have only just begun to explore the enormous benefit that digital processing and display may provide. An interesting pictorial essay of some mammographic processing techniques was given by Pisano et al. (2000a). Here, we will discuss some of the basic methods currently employed and more advanced methods that will likely become available in the next generations. Basic processing methods include grayscale transforms and adaptive contrast enhancement. A common dedicated mammogram processing method is peripheral enhancement, which has been adopted widely by manufacturers to overcome shortcomings of the dynamic range of digital displays.

5.2 Grayscale Transforms

Application of lookup tables (LUT) to change the grayscale of an image can be considered as the most elementary form of image processing, as it operates on individual pixels. Almost all digital imaging systems apply such transforms. Obviously, parts of the image with the highest diagnostic information content should be displayed with optimal contrast, while contrast may be reduced in parts which are less relevant. To achieve this, usually a nonlinear mapping of pixel values is required. The design of appropriate mappings has been facilitated by the DICOM standardization of displays. According to this standard, medical displays should be perceptually linear, which can be achieved by adhering to the DICOM Grayscale Standard Display Function. When a display is calibrated properly, similar differences in pixel values should be perceived as similar differences in luminance, regardless of the luminance level. This ensures that images in a clinical environment are presented in a predictable way, allowing optimization of image processing algorithms for a given diagnostic task.

Mammogram presentation has been perfected over the years in conventional mammography. Therefore, as a strategy to define a good grayscale transform for digital mammograms, one could aim at creating a film-like presentation. The transitions of signals in conventional mammography are well known. First, the response of a film-screen system to X-ray exposure E is determined by a characteristic curve, which expresses the relation between the logarithm of exposure and optical density D of the exposed film. Second, when viewed on a lightbox, the intensity of the transmitted light through the film is expressed by $I = I_0 \log_{10}(-D)$, with I_0 being the luminance of the lightbox. Using Weber's law a relation with perceptually linearized digital displays can be made. Within a wide range of intensities, just noticeable differences in the intensity correspond to equal differences in the optical density. Thus, by applying a characteristic curve with a shape similar to that of modern screen-film systems, the exposure representation of raw digital mammograms can be converted to a processed image which looks like a conventional mammogram when displayed on a DICOM calibrated display device. However, because higher optical densities represent lower intensity, after application of the characteristic curve, the image has to be inverted.

Examples of characteristic curves of mammographic screen-film systems are shown in Fig. 5.1. These curves can be well-modeled by

$$\begin{aligned} D(E) &= D_{bf} + D_{max}\left[\frac{1}{1+\mathrm{e}^{-g(\ln E-s)}}\right]^{q} \\ &= D_{bf} + D_{max}\left[1+(E/s)^{-g}\right]^{-q} \end{aligned} \tag{5.1}$$

with X-ray exposure denoted by E, $D(E)$ being the optical density, D_{bf} being the base plus fog optical density of the unexposed film, and D_{max} being the optical density of the fully exposed film. The parameters g and s represent the gradient and speed of the film, respectively. The parameter q can be used to model an asymmetric shape of the curve. An example of a symmetric model ($q = 1$) fitted to the characteristic curve of a Kodak Min-R 2000 film is shown in Fig. 5.1.

To compute a proper grayscale transform for a mammogram using the model mentioned earlier, the parameter s has to be determined. This parameter has to be chosen, such that relevant information in the exposure domain maps to the steepest part of the characteristic curve. In conventional mammography systems, this parameter is fixed, while exposure is adjusted to the proper range by means of the AEC unit of the mammography system. The AEC shuts off the exposure when a limiting value is reached in a measurement field, which is located in a central location in the breast projection. In digital mammography, exposure may vary over a wide range, as restrictions to proper film exposure no longer exist. The issue of mapping the exposure values in a proper range of contrast can be addressed in a similar fashion though, by computing the parameter s from exposure values in the interior part of the breast. When the breast is segmented, s can be chosen proportional to the average pixel value in the interior part of the breast. To avoid segmentation, a sliding window can be used to scan the central part of the image. The location where the average pixel value in the sliding window has the highest value represents the densest part of the breast. This value can be used to adjusts. For robustness, the window should not be too small, in the order of several square cm. An example of prior and current digital mammograms of a patient acquired with a Lorad Selenia processed with this method is shown in Fig. 5.2. It can be seen that all images have excellent contrast and have a very similar appearance.

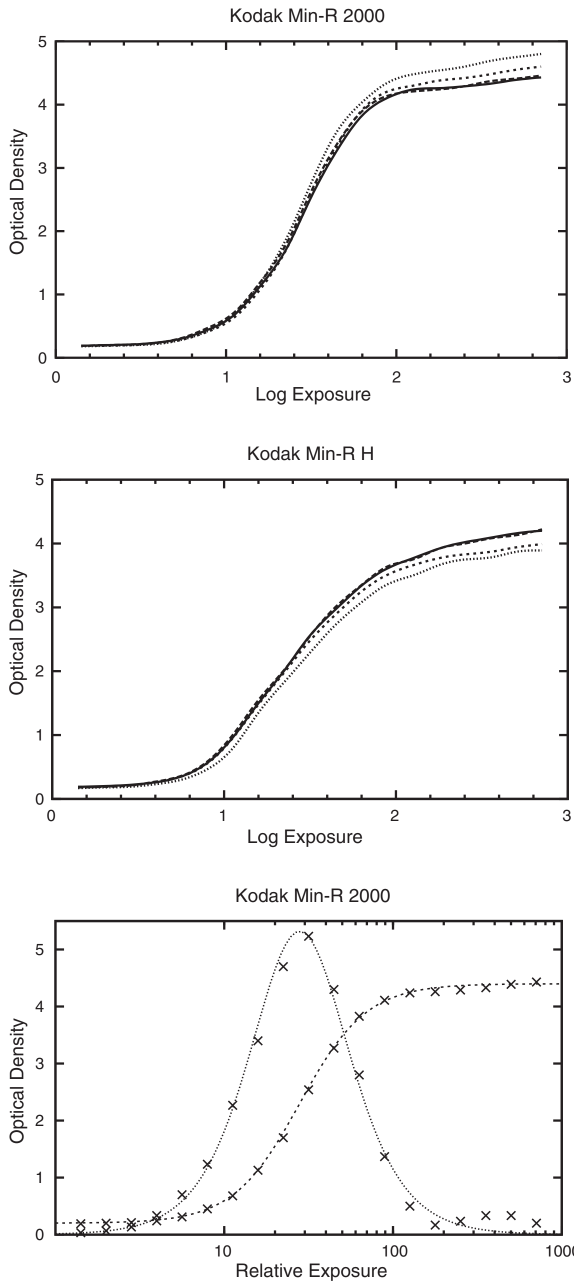

Fig. 5.1. Characteristic curves of a Kodak Min-R 2000 film and a Kodak Min-R H film. The *right figure* shows a model fit

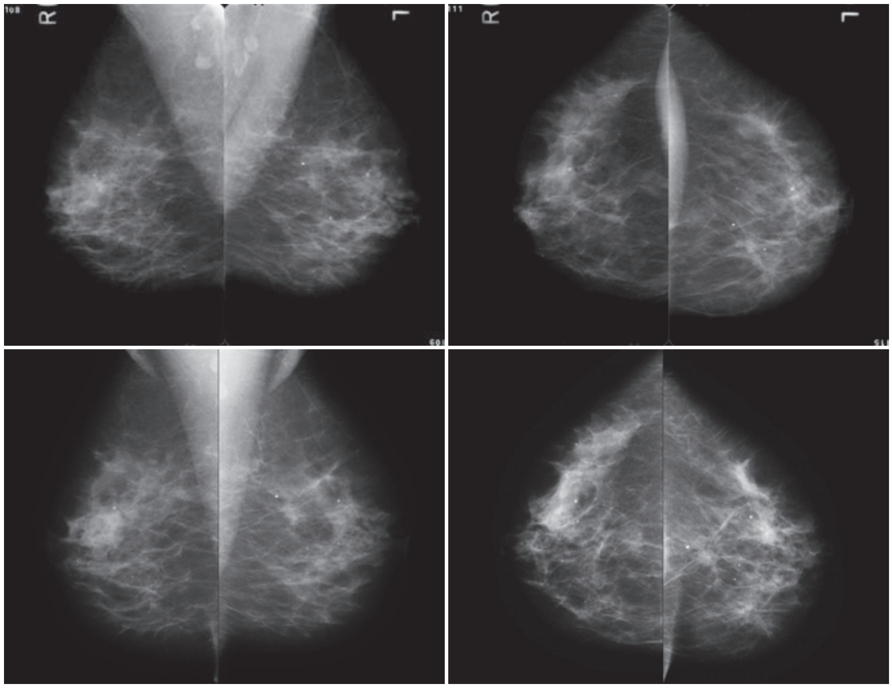

Fig. 5.2. Full field digital mammograms (Hologic Selenia) processed with a characteristic curve of a Kodak Min-R 2000 system to give them a film-like appearance. The two mammograms are prior (*top*) and current (*bottom*) mammograms of the same patient

Grayscale transforms are also be applied by the display system. DICOM has implemented several mechanisms for scale conversion of mammograms. Conversions are determined by values of tags in the DICOM header. Normally, a linear rescaling of pixel values within a range of interest is carried out based on the window and level settings. However, a nonlinear rescaling is also possible by defining a VOI LUT. Furthermore, a sigmoid function can be defined parametrically. Using these mechanisms, manufacturers may choose to maintain exposure-related pixel values and use DICOM functionality to define image presentation.

5.3 Spatial Enhancement

With digital imaging, a wide variety of methods have become available for spatial enhancement of images. In contrast to grayscale transforms, spatial enhancement techniques change pixel values based on spatial context. They can be used to sharpen edges, reduce noise, or to increase contrast of faint dense tissue regions. In this section, several general enhancement techniques are discussed, while more specific enhancement methods developed for mammography are discussed in the following sections. Image enhancement does not increase the information content in mammograms. Its aim is to increase contrast of relevant features in a mammogram, so that they can be detected and interpreted more easily. Because of the reduced dynamic range of softcopy display in comparison to film viewers, spatial contrast enhancement is seen by many as a requirement for proper presentation of digital mammograms.

5.3.1 Unsharp Masking

Unsharp masking is a technique for sharpening images by using a blurred mask of the original image. The technique was already in use in photographic processing and became very popular with digital imaging. Mathematically, the filter is expressed by

$$y_i' = y_i + f(y_i - s_i(\sigma)) \qquad (5.2)$$

where y_i and y_i' are the original and processed pixel value at location i, the smoothed image value at i is $s_i(\sigma)$, and f is a function determining the amount of enhancement. The results are strongly dependent on f and on the scale of the smoothing kernel. Blurring is often performed by Gaussian smoothing. The scale of the smoothing function determines the frequency range in which contrast enhancement occurs. Use of a small scale limits the enhancement to smaller structures. The function f determines the amount of

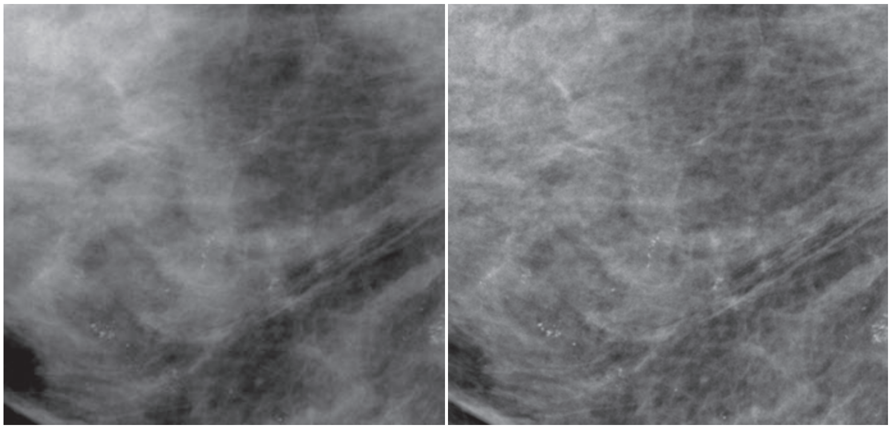

Fig. 5.3. Effect of unsharp masking on a mammogram with microcalcifications. On the *left*, the original image is shown. The right figure shows the processing result obtained with $\sigma = 1$ mm and f a sigmoid function with slope 1

enhancement. In the simplest case, a constant is used, causing a percentage of the difference image to be added to the original. However, this may render structures that already have high contrast too sharp or outside the pixel value range. To prevent this, a sigmoid function can be used to limit contrast enhancement to a fixed maximum value.

Unsharp masking is most often used to enhance high frequencies in an image. In digital mammography, the technique can be used to enhance microcalcifications. Figure 5.3 shows an example in which the visibility of microcalcification is clearly improved by processing. Blurring was performed by Gaussian smoothing with $\sigma = 1$ mm. When CRT displays are used, enhancement of high frequencies can compensate for unsharpness of the display device. A similar effect may be obtained by deconvolution, but in that case, characteristics of the display device have to be known. As most mammographic workstations are nowadays equipped with LCD displays, there is less need for compensating display unsharpness. Unsharp masking may also be advantageous to enhance digitized films, which often have reduced sharpness due to the digitizer characteristics. A disadvantage of unsharp masking is that it increases visibility of noise.

One can also use unsharp masking to enhance contrast of larger structures by using a larger scale for blurring. This may be advantageous if the dynamic range of images is large. Without processing, mapping of the full dynamic range to the available gray levels results in low contrast of image structures. This is shown in Fig. 5.4, where the same image is processed with different parameter settings. Contrast in the original image is low, while in the processed images with larger values, contrast is enhanced. Note that unsharp masking also gives rise to artifacts. These may especially be observed at sharp boundaries of bright structures. Enhancement causes darker and brighter rims at both sides of the boundary. This "ringing" effect is often visible when adaptive contrast enhancement techniques are applied.

5.3.2 Adaptive Histogram Equalization

Histogram equalization is a technique to compute a grayscale transform in such a way that in the processed image all gray values occur at equal frequency. The method is easy to implement and fast. However, in general, it does not produce an acceptable image, as it does not take into account that the information content in an image may depend on the signal level. When histogram equalization is applied to a mammogram, it redistributes gray levels in a way that expands contrast of the background at the cost of contrast in the tissue area. This can be easily understood: If we take a typical mammogram with one-third of the image representing the projected breast, the breast tissue maps to only one-third of the gray value range after processing. To overcome this limitation, improvements have been proposed (Pizer et al. 1987).

In adaptive histogram equalization, a different grayscale transform is computed at each location in the image, based on a local neighborhood, and the pixel value at that location is mapped accordingly. The local neighborhood is usually chosen as a square tile centered at the pixel to be processed. The diameter of the tile is an important parameter in the algorithm. When it is too small, the method becomes too sensitive to local variations, and when it is too large, limitations of the nonadaptive technique start to play a role. A typical

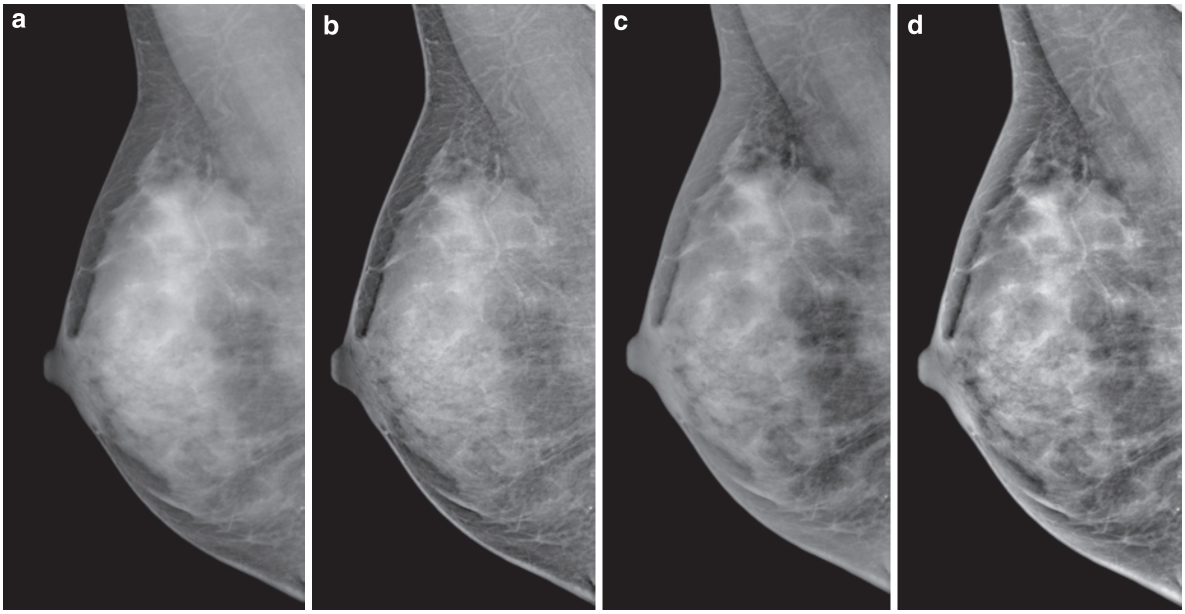

Fig. 5.4. Unsharp masking of a mammogram obtained with a GE SENOGRAPHE 2000D. The original image (**a**) is processed using the following settings: σ = 1 mm, slope = 1 (**b**) σ = 1 cm, slope = 1 (**c**) σ = 5 mm, slope = 4 (**d**)

value for the diameter is 1/16 of the original size of the image. Obviously, computing the transform at every pixel is computationally intensive. Optimizations have been proposed in which the transform is computed in a limited number of overlapping tiles, whereby processing of pixels not centered in tiles is performed by interpolation of the neighboring mappings.

By changing the slope of the transform that converts pixel values from the original to the processed image, contrast is increased. In this way, both signal and noise are enhanced proportionally. This may not be desirable, because when the enhancement of noise becomes too strong it may affect performance of the radiologists. With adaptive histogram equalization, there is a risk of increasing noise to an unacceptable level in image regions that have little signal variation, e.g., homogeneously dense tissue areas or background. To reduce contrast amplification in such areas, contrast limited adaptive histogram equalization (CLAHE) has been proposed. It can be easily shown that the slope of the transform computed by histogram equalization is proportional to the height of the histogram. Thus, by clipping and renormalizing the histogram before computing the transform, the slope can be limited. This is what CLAHE does. An additional parameter is introduced with which the maximum contrast enhancement can be adjusted. An example of CLAHE processing of a mammogram is shown in Fig. 5.5.

5.3.3 Multiscale Image Enhancement

With multiscale image processing techniques, it is possible to tune contrast enhancement to certain frequency bands. In this way, features occurring at different scales can be enhanced in a different way. For instance, one could aim at enhancing microcalcifications and masses in a range of scales, while suppressing other structures. A common multiscale processing technique is wavelet processing. Application in mammography was proposed by LAINE et al. (1994). In this method, multiscale edges identified within distinct levels of transform space provide local support for image enhancement. Mammograms are reconstructed from wavelet coefficients modified at one or more levels by local and global nonlinear operators. In each case, edges and gain parameters are identified adaptively by a measure of energy within each level of scale-space. The authors demonstrate that wavelet processing can reveal features that are barely seen in unprocessed traditional mammograms. However, the clinical benefit of displaying such features has not been demonstrated. It may be confusing for the readers to be presented with images that deviate strongly from the images they are trained with. More recently, HEINLEIN et al. (2003) also developed a mammogram processing method based on wavelets. The main novelty is the

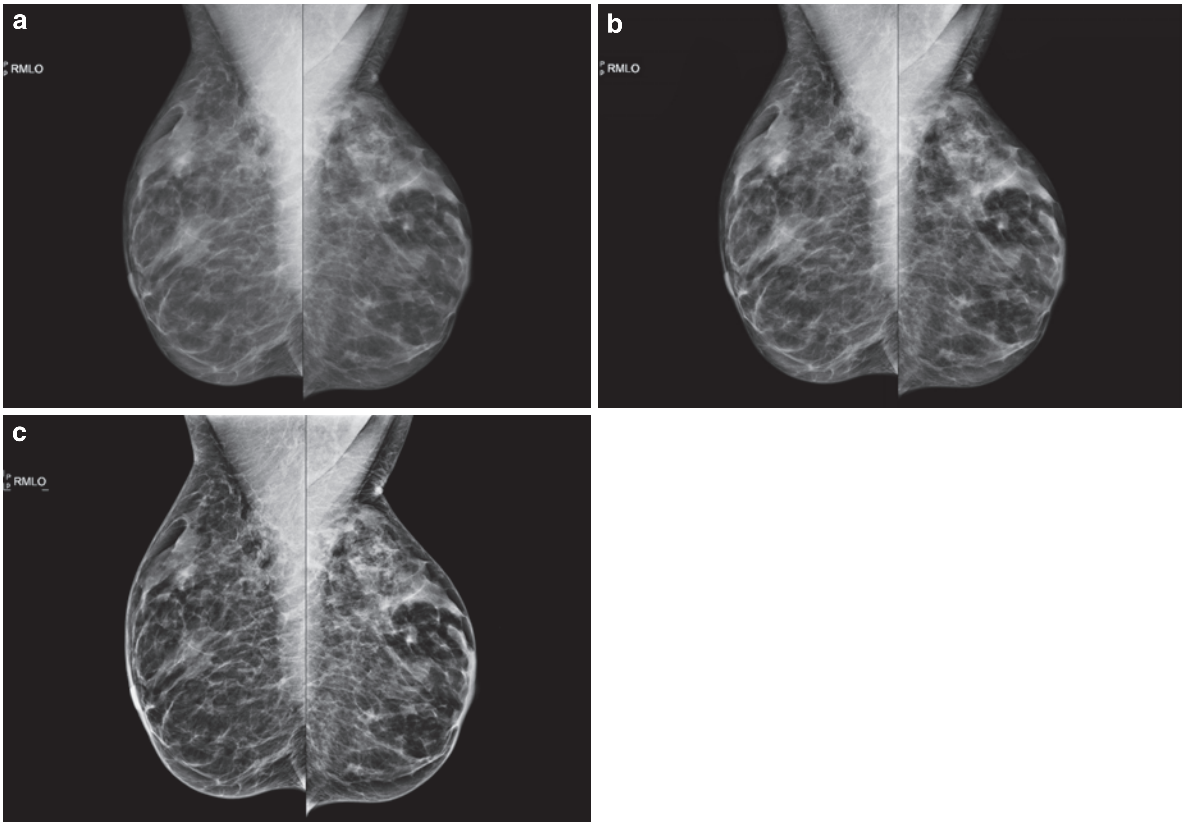

Fig. 5.5. A raw digital mammogram from a Lorad Selenia processed using nonspatial processing and peripheral enhancement (**a**). Figure (**b**) shows results obtained by applying contrast-limited adaptive histogram, equalization (CLAHE). The clinical image processed by the manufacturer, using a proprietary algorithm, is shown in (**c**)

application of a continuous wavelet transform. Furthermore, a model-based approach is used to make the method more specific for microcalcifications.

5.3.4 Peripheral Enhancement

Peripheral enhancement is a dedicated image processing technique developed for mammograms. It is used to improve the visibility of the peripheral uncompressed region of the projected breast, where tissue thickness is smaller than in the interior part of the mammogram. The technique is also referred to as peripheral equalization or thickness correction. In peripheral enhancement methods, the darkening due to decreased tissue thickness in the peripheral region is estimated from the mammogram and thereafter compensated for by a smoothly varying correction function. After correction, fatty tissues in the interior and peripheral regions have similar gray values. With peripheral enhancement, the dynamic range of the mammogram greatly reduces, and as a consequence, less manual adjustments of contrast settings are required to view details close to the skinline. This benefits workflow. In the following paragraph, we will discuss filter-based peripheral enhancement techniques and a parametric method in which the three-dimensional breast outline is modeled.

Peripheral enhancement was first developed as a preprocessing stage in computer aided detection (CAD) systems. Byng et al. (1997) were the first to propose the use of this technique for enhancement of mammogram display. The method that they describe is a nonparametric filter-based method. Filtering is used to obtain a blurred version of the mammogram representing tissue thickness. This approach can be used because breast thickness variations are smoother than tissue density variations. Thickness equalization is only applied in the periphery of the breast, which is simply determined by a threshold T representing gray values at the border of compressed and uncompressed part of the breast. Denoting s_i as the pixel in the

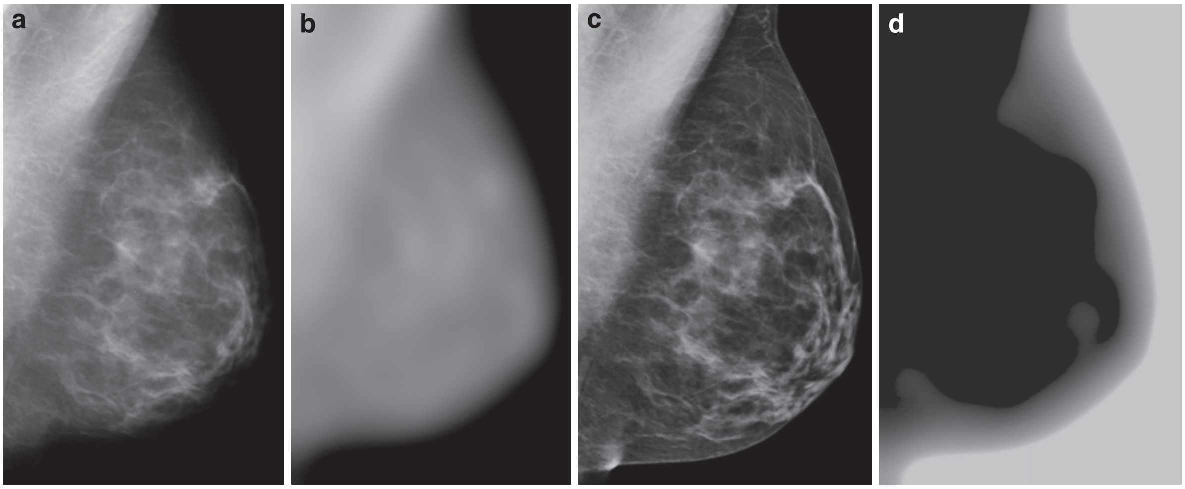

Fig. 5.6. Example of thickness correction with anisotropic smoothing and dense tissue interpolation. The original mammogram (GE FFDM) without enhancement is shown in (**a**). After segmentation and removal of dense tissue regions, the image is blurred by anisotropic diffusion (**b**). The corrected image (**c**) is obtained by adding an image representing the tissue thickness difference derived from the blurred image (**d**)

blurred image at location i, the equalized image is obtained by multiplying the pixel values in the periphery by a correction factor T/s_i. Only pixels for which $s_i < T$ are processed, which ensures continuity. In the method by Byng, a new threshold is determined in each image row by taking the average of a small region around the border point. Their method was evaluated with digitized screen-film mammograms, but is also applicable to full field digital mammograms.

Snoeren and Karssemeijer (2005) also used a blurred version of the mammogram to correct for thickness differences, but instead of using isotropic smoothing of the original mammogram, they used an anisotropic smoothing.

The processed image revealed details in the region behind the nipple which were not perceivable in the original. The bright area near the skin in the lower part is a skinfold. The interior part of the mammogram remained unchanged, but can be displayed in higher contrast after the correction.

Before smoothing, dense tissue areas are removed and interpolated using surrounding fatty tissue values (see Fig. 5.6). The idea is that by removing dense tissue, the image better reflects thickness differences in the mammogram. Linear interpolation was performed along the lines running equidistant to the skin edge. The reason is that thickness variations are much stronger in the direction perpendicular to the skin line. Gray values of fatty tissue on lines parallel to the skin are usually small. The segmentation of fatty and dense tissue itself is obtained in an iterative process in which a current equalized image is automatically thresholded by Otsu's thresholding method. Hence, when the thickness correction becomes better in subsequent iterations, the segmentation becomes better too. Anisotropic diffusion is used to smooth the mammogram in the direction parallel to the skin edge. This leads to more accurate estimates of the thickness profile and reduces artifacts. The correction is performed by adding a correction term to pixel values in the peripheral zone. Using a threshold T again on the blurred image, pixels yi representing higher exposure are replaced by $y'_i = y_i - s_i + T$, with s_i being the pixel value in the blurred image. The method is modality independent. With full field digital mammograms, it should be applied after a logarithmic transform of the pixel values, to avoid alteration of contrast. An example is shown in Fig. 5.6.

As a last technique, we describe a parametric method by Snoeren and Karssemeijer (2004) which is only suitable for unprocessed digital mammograms with a linear relationship between exposure and gray value. Instead of using a filtered image for correction, as in the previous two examples, a geometric model of the three-dimensional shape of the breast is used (see Fig. 5.7). The interior region is modeled by two nonparallel planes, requiring three degrees of freedom, one for the onset and two for the slopes. The exterior region is modeled by a band of semi-circles. This requires no additional degrees of freedom: The semi-circles are completely determined by the breast outline and the interior model. Given the parameters of the

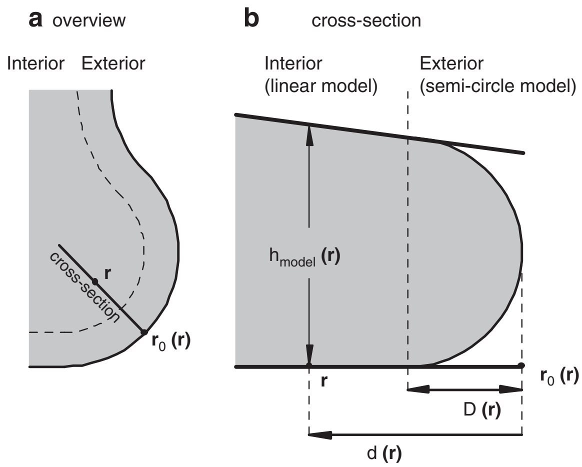

Fig. 5.7. Schematic representation of the interior and exterior part of the model for tissue thickness. The interior model (valid for $d(\mathbf{r}) \geq D(\mathbf{r})$): $h_{model}(\mathbf{r}) = a + \mathbf{a}\cdot\mathbf{r}$. The exterior model (valid for $d(\mathbf{r}) \leq D(\mathbf{r})$): $h_{model}(\mathbf{r}) = 2\sqrt{D^2(\mathbf{r}) - (D(\mathbf{r}) - d(\mathbf{r}))^2}$. Hereby, $\mathbf{r}_0(\mathbf{r})$ is the point on the skin line closest to $\mathbf{r}$; $D(\mathbf{r})$ is the distance of $\mathbf{r}_0$ to the interior/exterior border; $d(\mathbf{r})$ is the distance of $\mathbf{r}_0$ to $\mathbf{r}$. From Snoeren and Karssemeijer 2004 (©2004 IEEE)

geometric model and assuming a linear relationship between tissue thickness and log-exposure (Beer's law of attenuation), one can model the gray values of a breast that only consists of fatty tissue. Therefore, after fat/dense segmentation of the mammogram the model can be fitted to the "fatty" pixels in the unprocessed mammogram. The corrected image is obtained by adding a fatty tissue component in the periphery which fills in the air gap between the fitted planes and the breast. An example is given in Fig. 5.8. The case is challenging because the large cysts in the periphery may easily be distorted. The example shows that excellent results can be obtained using parametric model-based methods. It is noted that the method critically depends on accurate segmentation of the breast.

5.4 Matching Current and Prior Mammograms

In mammography, the comparison of images obtained in subsequent examinations of a patient is an important element in diagnostic and screening procedures. These comparisons are made to detect interval changes, to monitor progression of a disease, or to estimate the effect of treatment. Studies have shown that the use of prior mammograms in breast cancer screening effectively reduces the number of false-positive referrals (Thurfjell et al. 2000; Burnside et al. 2002; Roelofs et al. 2007). This is due to the fact that the use of priors allows radiologists to distinguish lesions that grow from normal dense structures in the breast that somehow look suspicious.

To make it easier for the radiologists to detect and interpret mammographic changes, mammograms in temporal image pairs should be presented in a similar way. Unfortunately, this is not always possible, because there are many sources of variability that are hard to control. Some already existed in conventional mammography, like variation in positioning and compression. However, variations related to exposure and film-screen differences were limited in conventional mammography. With digital mammography, a major new source of variation has been introduced: the variability in image processing methods. As image processing is usually performed on acquisition systems of modality manufacturers, using proprietary software, there is currently no way to make images look comparable on mammographic workstations if they are generated by systems from different vendors. This is a serious drawback of digital mammography which should be resolved.

Problems with display of priors are often striking when priors are digitized films. Digitization of prior screening mammograms is currently practiced on a large scale to bridge the transition period when screening transforms to a digital workflow. A typical example from a digital screening program is shown in Fig. 5.9. It is noted that the display problem will not disappear as soon as the transition to digital is completed. Similar problems occur when mammograms from different vendors have to be compared, and digitized priors will remain archived for use in future screening rounds, as radiologists in screening often like to look back several screenings when judging a potential abnormality. Therefore, proper display of digitized priors will remain a highly relevant issue. There is no need to say that display as shown in Fig. 5.9 is far from ideal.

Excellent matching of the presentation of prior and current mammograms is possible as long as no spatial enhancement algorithms have been applied by the manufacturer. The fact that pixel values in unprocessed mammograms are proportional to exposure provides an ideal setting for processing mammograms in a similar way, even if they are acquired with very different detector systems. Case-based mammogram processing based on raw data has been studied by Snoeren and Karssemeijer (2007). The approach suggested is

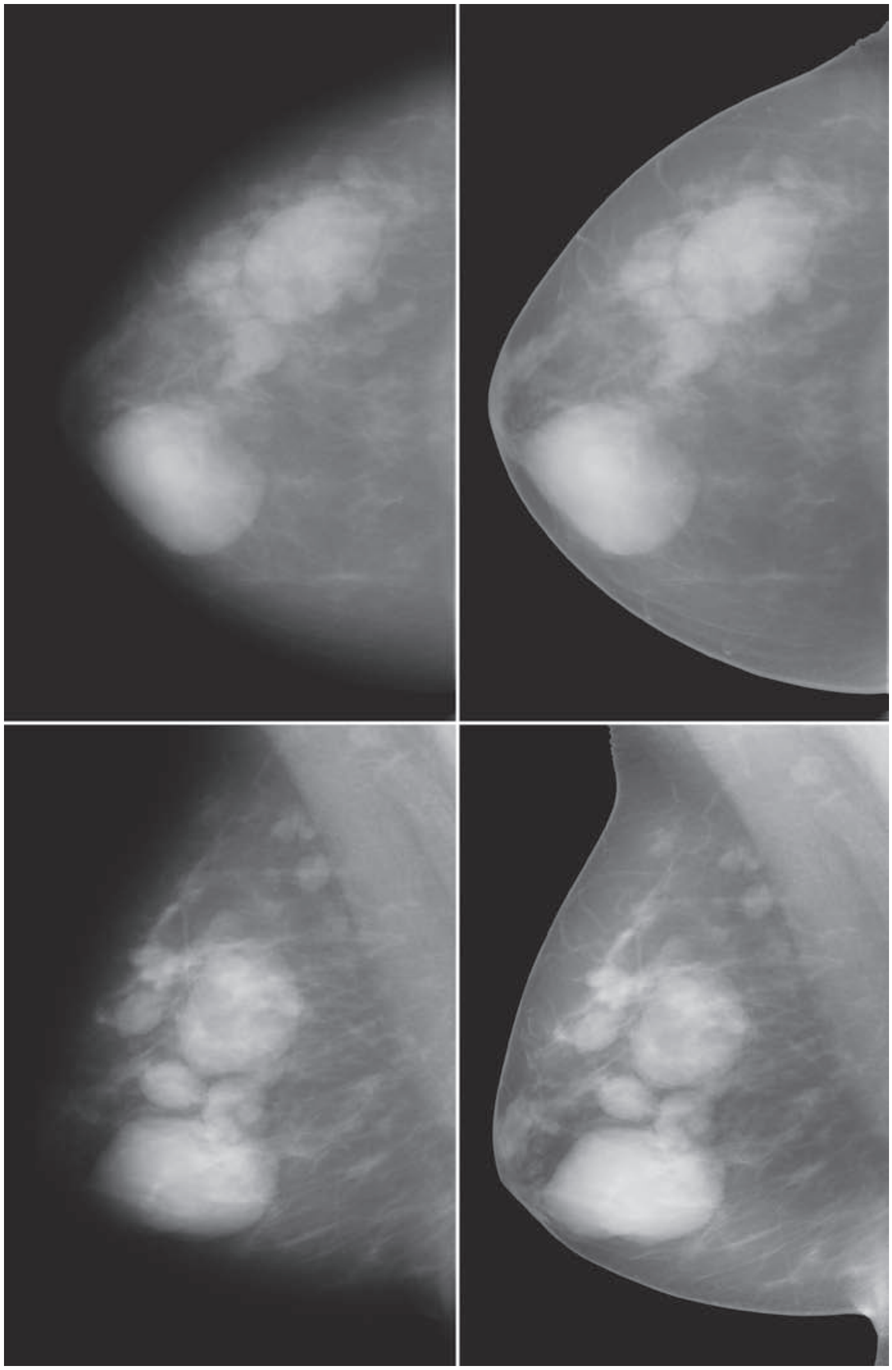

Fig. 5.8. Example of thickness correction with a geometric model. On the *left side*, cranio-caudal and medio-lateral views of the original mammogram are shown. On the *right side*, the thickness corrected images are depicted. The original mammogram was acquired with a GE Senograph 2000D. From Snoeren and Karssemeijer 2004 (© 2004 IEEE)

based on geometric image registration and subsequent derivation of a proper grayscale transform of all individual images. This transform is based on parametric histogram matching of overlapping regions in the registered images. Only transforms are allowed that are physically possible, given a model of the acquisition process. When digitized films are matched with full field digital mammograms, this model includes the characteristic curve of the film. Once images are transformed to the same domain, adaptive contrast enhancement can be applied. In this way, similarity in presentation of all views is maintained, as all images are processed by the same algorithm. An example is shown in Fig. 5.10. Also, the geometric registration has

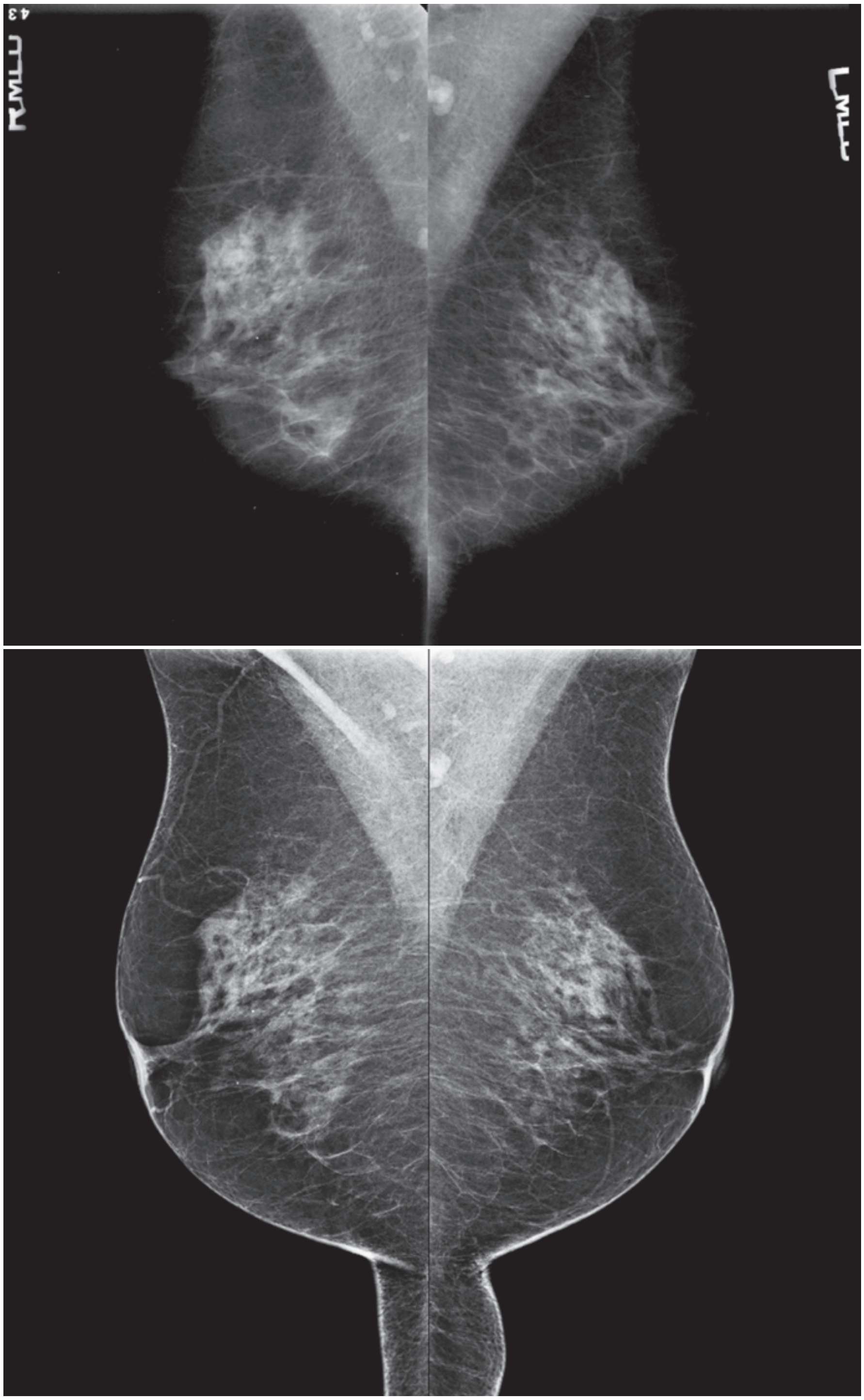

Fig. 5.9. A digital screening mammogram (*bottom*) compared with the previous screening mammogram which is digitized from l m. The FFDM image is acquired and processed by a Selenia system (Hologic)

advantages, as this ensures that corresponding mammographic structures are roughly located in the same space in the image matrix. When displaying mammograms electronically, toggling between current and prior mammograms on the same screen is a common technique. After registration structures appear in the same location on the screen, which makes comparison easier (Van Engeland et al. 2003).

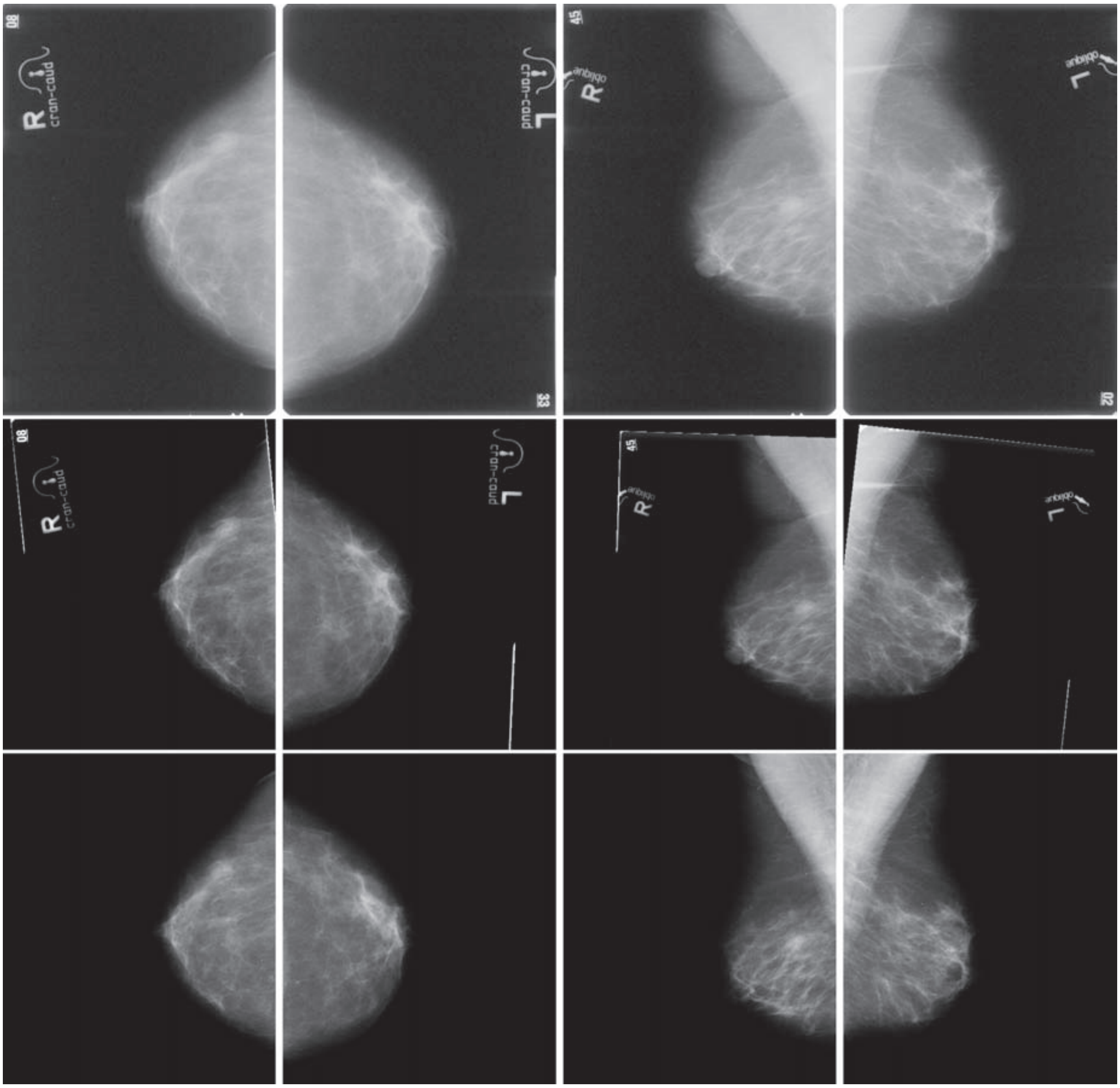

Fig. 5.10. A digitized prior screening mammogram (*top row*) is matched to a digital screening mammogram (*bottom*). The digitized prior views have first been registered geometrically to the unprocessed FFDM images. Subsequently, a model-based transform was computed for each view, which converts the digitized prior to the representation in which pixel values are proportional to exposure. After bringing them in the same space, any processing of the images will yield similarity in the presentation. Here, we applied only a lookup table as outlined in Sect. 5.2, without peripheral enhancement. The matched display of the prior is shown in the middle row

5.5 Physics-Based Methods

The physical processes involved in mammographic imaging are well understood. By modeling these, corrections methods may be designed to reduce variation of mammograms related to acquisition differences. An example is the scatter correction methods. The effect of scatter reduction in digital mammographic images was studied by Baydush et al. (2000). An iterative Bayesian estimation algorithm was formulated and used to process images of the American College of Radiologists (ACR) breast phantom acquired without a grid. The authors concluded that the technique can reduce scatter content effectively without introducing any adverse effects, such as grid line aliasing. Results suggest that the processing can increase contrast-to-noise ratio to values greater than that provided by a standard grid, which may potentially increase the visualization of subtle masses. This confirms the results of phantom measurements performed by Veldkamp et al. (2003).

Physical modeling of the mammographic imaging chain was extensively studied by Highnam and Brady (1999). They came up with the idea of converting mammograms to a representation in which pixels represents the amount of so called "interesting" tissue (fibro-glandular tissue and cancerous tissue) projected in the pixel. Their normalization method is based on the assumption that the X-ray attenuation coefficients of fibro-glandular and cancerous tissue are nearly equal, but are quite different from that of fatty tissue. After normalization, a mammogram is corrected for scattered radiation and the dependency of image formation parameters like tube voltage, spectrum, and exposure time. In a later work by the authors, this representation is referred to as Standard Mammogram Form (SMF).

Conversion of mammograms to a standardized format has many advantages. It allows development of uniform image presentation methods that remove variation due to use of different image detectors and acquisition settings. In particular, temporal comparison of mammograms could be greatly improved by application of image normalization. Also, quantitative image analysis methods aimed at automated detection of lesions or measurement of breast density would benefit from standardization. Unfortunately, manufacturers do not embrace the idea and tend to move away from standardization by developing proprietary algorithms for image processing. As most clinics do not archive raw images, the relation between digital mammograms and the quantitative potential of exposure values in the raw data is lost.

In screen-film mammography, application of SMF was hampered by uncertainties in the image acquisition process. The method only became feasible when digital mammography was introduced. An effective procedure for standardization of digital mammograms was developed and validated by Van Engeland et al. (2006). Assuming that pixel values are proportional to exposure, which is true for most digital detector systems, it can be derived that in good approximation, the thickness of dense tissue at a given location h_i can be written as

$$h_i = -\frac{1}{\mu_{d,eff} - \mu_{f,eff}} \ln \frac{\overline{y}_i}{\overline{y}_f}. \tag{5.3}$$

with $\mu_{f,\,eff}$ and $\mu_{d,\,eff}$ being the effective attenuation coefficients for fatty and dense tissue, respectively, $\bar{y}_i$ being the pixel value at i after thickness equalization, and $\bar{y}_f$ being a reference pixel value taken at a location with only fatty tissue. Note that there is no explicit dependency on breast thickness. The effect of breast thickness is included in the computation of the effective attenuation the coefficients, which also depends on other acquisition parameters. The method was validated for a series of cases by comparing it with MRI. By integrating dense tissue thickness over the breast, dense tissue volumes were obtained. These agreed well with dense tissue volumes measured in MRI data.

5.6 Evaluation of Mammogram Processing

Improved display of mammograms may lead to more efficient workflow and to more accurate detection of abnormalities. To determine the potential effect of processing in clinical practice, the performance of radiologists utilizing the processing methods has to be studied. In the literature, only a few examples of such studies may be found. Pisano et al. attempted to determine whether intensity windowing improves detection of simulated calcification in dense mammograms. Film images with no windowing applied were compared with film images with nine different window widths and levels applied. Using twenty students as observers, it was found that there was a significant variation in detection performance for clusters of calcifications, when the processing was varied (Pisano et al. 1997). It can be noted that, in practice, readers may apply intensity windowing interactively when reading mammograms on workstations. However, in practice it is too time-consuming to perform such operations on every mammogram.

Of the spatial enhancement methods, contrast-limited adaptive histogram equalization (CLAHE) has frequently been used in observer experiments. Hemminger et al. studied whether detection of simulated masses in dense mammograms could be improved with the technique and compared the effects of this processing method with histogram-based intensity windowing (HIW). The key variables in the experiments included the contrast levels of the mass relative to the background and the selected parameter settings for the image-processing method. Performance depended on the parameter settings of the algorithms used. The best HIW setting performed better than the best fixed-intensity window setting and better than no processing. Performance with the best CLAHE settings was not different from that with no processing. The authors concluded that CLAHE processing will probably not improve the detection of masses on clinical mammograms (Hemminger et al. 2001).

In a study by Pisano et al. (2000b), radiologists' preferences for digital mammographic display were investigated. Eight different image processing algorithms were evaluated using a series of twenty-eight images representing histologically proved masses or calcifications obtained with three clinically available digital mammographic units. Processing methods included histogram and mixture model-based intensity windowing, peripheral equalization, multiscale image contrast amplification, CLAHE, and unsharp masking. Twelve radiologists compared the processed digital images with screen-film mammograms obtained in the same patient for breast cancer screening and breast lesion diagnosis. Surprisingly, screen-film mammograms were preferred to most digital presentations, and none of the methods lead to a clear preference for the processed digital images. It is noted that this may have been due to inexperience of the radiologists with digital processing. Moreover, the comparison not only involved processing, because the comparison was made with screen-film mammograms. Also, acquisition differences may have played a role. In a later study, performance with digital mammography using different processing techniques was again compared with screen-film mammograms of the same patients (Cole et al. 2005). A total of 201 digital mammograms were used in combination with three processing methods: The manufacturers used default, multiscale image contrast amplification and a version of CLAHE. Three radiologists were involved in the experiments. It was found that for one manufacturer, the performance with digital mass cases was worse than screen-film for all digital presentations. The authors suggest that specific image processing algorithms may be necessary based on machine and lesion type.

A wavelet technique for spatial enhancement of microcalcifications in mammograms was evaluated by Kallergi et al. (1996). Digitized mammograms were used. Differences were observed between screen-film and unprocessed digitized mammography displayed on monitors. These differences were not significant when wavelet enhancement was included in the monitor display. Interobserver variation in the digitized reading was greater than that in film reading, but the wavelet enhancement reduced the difference. In a more recent study, the effect of wavelet processing on a mixture of mammographic findings was investigated (Kallergi et al. 2004). The study was designed as a localization response operating characteristic (LROC) experiment with 500 negative, benign, and cancer cases with masses and calcification clusters. Three observers reviewed the original and wavelet-enhanced images on a 5-Mpixel monitor, using a custom-made workstation user interface. Performance indexes were estimated for four different case combinations. It was found that wavelet enhancement improved the performance of all observers in all case combinations. The difference between enhanced and original performances was statistically significant. The authors argue that optimization of the softcopy quality is expected to require more advanced processing techniques than standard grayscale adjustments. Wavelet-based algorithms offer better softcopy quality than the originals, and a better starting point for additional manual grayscale adjustments or automated postprocessing.

Results of the studies summarized earlier indicate that positive effects of mammogram processing on diagnostic performance have not yet been clearly established. This may partly be due to the fact that most studies were performed with readers who were not yet familiar with softcopy reading and processed mammogram display. More research is needed to investigate the effects of various processing techniques.

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