2D-to-3D X-Ray Breast Image Registration

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Abstract. Digital breast tomosynthesis combines the advantages of digital mammography and 3D breast imaging. To facilitate the comparison of new tomosynthesis images with previous mammographic exams of the same woman, there is a need for a method to register a mammogram with tomosynthetic images of the same breast; this is the focus of our paper. We have chosen to approach this multimodality registration problem by registering a mammogram with individual tomosynthesis source projection images. In this paper, we analyzed the results of registering an MLO mammogram to nine tomosynthesis source projection images of the same breast. On average, we were able to compensate 90 percent of the per-pixel intensity differences that existed between the two images before registration.

1 Background

Early breast cancer detection requires identification of subtle pathological changes over time, and is often performed by comparing images from previous years. Projection mammography is considered the preferred screening modality for early breast cancer detection. However, diagnostic breast imaging is a multimodality task. Breast ultrasound is used for distinguishing cysts from solid lesions. Breast magnetic resonance imaging (MRI) offers functional information.

Recent research efforts have focused on developing 3D x-ray breast imaging modalities. Several modalities have been developed, including stereomammography, breast tomosynthesis, and breast computed tomography (CT) [1-3]. These modalities combine the advantages of mammography and 3D image visualization. The recent development of contrast-enhanced breast tomosynthesis may additionally provide functional information [4]. Of the proposed 3D x-ray modalities, breast tomosynthesis is the most likely to replace mammography as a screening procedure, chiefly because the acquisition geometry is nearly identical to mammography. In current implementations of tomosynthesis, between nine and 48 source projection images are acquired of the compressed breast as the position of the x-ray focus is altered. The total dose used is comparable to the dose needed for a mammographic exam. The projection images are used in a limited-angle CT reconstruction to form a tomographic image set. Several reconstruction algorithms have been proposed, ranging from filtered backprojection to sophisticated iterative reconstruction techniques [1,2]. Tomosynthesis produces tomographic images of the breast in which a given anatomical plane is in focus while

anatomical structures above and below the plane are blurred to such an extent as to be essentially removed from the image.

With the clinical introduction of tomosynthesis, it will be necessary for radiologists to compare tomosynthesis images with previous mammograms of the same women to detect subtle temporal changes in the breast. It will be also necessary to compare tomosynthesis data sets of the same patient taken at different times. The former comparison task, while of a limited lifespan, requires 2D-3D registration. The latter comparison could be approached by direct registration of the reconstructed data sets. Such a registration should take into account possible differences in reconstruction algorithms used for the two 3D data sets. Alternatively, this comparison can be approached as a 2D-3D problem, in which one registers the tomosynthesis source projection images from two exams. We can look at research in computer-aided diagnosis to support the choice of 2D-3D methods being used to process tomosynthesis images. Chan *et al.* [5] are using 3D processing methods for the detection of lesions in tomosynthesis data sets, while Nishikawa *et al.* [6] use separate processing of 2D source images.

Our current research focus is on the registration of a mammogram and individual tomosynthesis images of the same breast. In this paper we present preliminary results obtained by registering an MLO mammogram and nine individual tomosynthesis source projection images obtained from one patient.

2 Methods and Materials

The problem of registering mammograms and tomosynthesis images can be approached in two ways. *First*, one could try to address directly the registration of a mammogram and a set of reconstructed tomographic images. This is a true multimodality registration problem. Consider the problem of finding the position in a tomographic data set which corresponds to a lesion identified in a mammogram. In this registration schema, one would need to analyze all reconstructed tomographic planes, since each plane contains only a subset of the tissue structures which are visible in the mammogram.

Alternatively, one could initially perform the registration of a mammogram and one or more of the projection images; this is a 2D registration problem. Each projection image should contain basically the same tissue structures as the mammogram, with some variation in positioning, compression, and dose. This registration schema, applied in multiple projection images, would allow the lesion to be located in 3D from knowledge of the acquisition geometry.

In this paper, we focus on the registration of the medio-lateral oblique (MLO) mammogram and the tomosynthesis source projection images of the same breast. In a companion paper, we analyzed the registration of the central source projection and the MLO mammogram [7]. The central projection is acquired in essentially the same MLO breast position, but with a reduced dose. The non-central projections are acquired with the same breast positioning and compression, but with the x-ray focus in different locations.

At the Hospital of the University of Pennsylvania, tomosynthesis projection images are acquired on a Senographe 2000D (General Electric, Milwaukee, WI) which has been modified to allow independent motion of the x-ray tube head. The x-ray tube can be reproducibly positioned at nine locations, each separated by 6.25 degrees. In the current system the collimator variably occludes the detector (*see Fig. 1*). Each breast is compressed in an MLO position. The projections are acquired at a total dose equal to the dose of two-view mammography. Tomographic images are reconstructed, in planes parallel to detector, using a filtered backprojection algorithm.



Fig. 1. The clinical images used for the registration of an MLO mammogram (upper left) and the tomosynthesis source projection images (K=1,...,9) of the same breast. The images were acquired the same day by the same technologist, with nearly the same breast positioning. The mammogram and the central projection (K=5) were acquired with the same geometry, but with different dose. The non-central projections ($K\neq 5$) were acquired with different x-ray focus locations.

We use a non-rigid method to register the MLO mammogram and the tomosynthesis projection images of the same patient. The registration method combines intensity- and contour-based constraints to match regions of interest (ROIs) in the source and target images [8]. The registration task is formulated as the inverse problem of finding a geometric deformation that minimizes an energy function with free boundary conditions. The energy function includes three constraints designed (i) to prevent ill-posed solutions by regularization, (ii) to compensate for linear variations in image intensities, and (iii) to correct the initial mapping of the ROI in target image onto the corresponding ROI in source image. Before the registration, the ROIs in the source and target images were identified as the breast regions without the pectoral muscle. The pectoral muscle area was identified as the region above the line defined by two manually selected points on the muscle contour. In addition, the region occluded by the collimator were manually identified in each tomosynthesis projection image, and replaced by pixels of zero intensity; the same region in the mammogram was also replaced by pixels of zero intensity.

In this study, we registered the two images by deforming the mammogram to match the individual tomosynthesis projections of the same breast. The non-rigid registration method was performed in two steps. First, an initial registration was performed, based on the contour matching only. This initial step is followed by the corrections of the differences in the pixel intensity distribution between the target and source images. Detailed description of the registration method is given in our previous publications [8]. In an evaluation using synthetic images generated with a software breast model [9], an average displacement error of 1.6 mm was obtained for mammograms with compression differences of up to 3 cm. [10]. This is acceptable, as we have observed that the compression difference between mammography and tomosynthesis is approximately 1 cm.

To date, 51 clinical breast tomosynthesis exams have been performed as a part of an IRB approved clinical study in our institution. After providing informed consent, each patient in the study also received digital or film-screen mammography on the same day. As a result, there are only a few, specific variations that can exist between the images (*see Fig. 1*). This is of importance for initial testing of the registration methods because no temporal changes in the breast tissue will have occurred.

We evaluated the registration results by calculating the percentage of corrected differences, PCQD, defined as:

$$PCQD = \left[\Sigma_{ij}(\varDelta^2_{ij})^{PRE} - \Sigma_{ij}(\varDelta^2_{ij})^{POST}\right] / \Sigma_{ij}(\varDelta^2_{ij})^{PRE} \times 100\%$$
(1)

where $(\Delta_{ij}^2)^{PRE}$ and $(\Delta_{ij}^2)^{POST}$ represent the quadratic differences between the intensities of the pixels at position (i,j), before and after registration, respectively. $(\Delta_{ij}^2)^P = [M(i,j)^P \cdot T_K(i,j)]^2$, (K=1,...,9), where $M(i,j)^P$ represents the intensity of the pixel at position (i,j) in the mammogram, before (P=PRE) or after (P=POST) registration, and $T_K(i,j)$ represents the intensity of the pixel at position (i,j) in the Kth tomosynthesis projection. The higher PCQD values indicate the better registration performance. We also compared the root-mean-square (RMS) difference between the mammogram and the projection image, computed before and after registration:

RMS Image Difference =
$$[\Sigma_{ij}(\Delta^2_{ij})^P]^{1/2}$$
, (P=PRE, POST). (2)

3 Results

Fig. 1 shows the mammogram and the nine tomosynthesis source projection images acquired from the analyzed case. Fig. 2 focuses on the registration of the mammogram (upper left) to one of the tomosynthesis source projection images (upper right). The selected projection image is labeled K=2 in Fig. 1. The registration result (middle image) is shown in the form of a mammographic image non-rigidly deformed to match the tomosynthesis source projection. We have evaluated the registration performance using the difference images shown in the lower row of Fig. 2. The difference images were computed before (lower right) and after (lower left) registration.



Fig. 2. Illustration of the registration of a mammogram and tomosynthesis source projection image of the same breast. The upper row shows the registration image pair: a mammogram (left) to be registered onto a tomosynthesis projection image (right); projection K=2 (Fig. 1) was used. The registration result is shown in the middle row. The lower row shows the difference between the mammogram and the source projection, computed before (*left*) and after (*right*) registration.



Fig. 3. (a) RMS differences between the mammograms and individual tomosynthesis source projections of the same patient, computed before and after registration. The RMS image differences for each of the nine tomosynthesis projections are indicated by numbers 1-9; *solid* and *bold* numbers correspond to the differences computed after the initial and complete registration, respectively. The corresponding linear regressions are plotted by the dashed and bold lines, respectively. (b) RMS image differences as a function of x-ray focus location corresponding to different source projections.

We have registered the mammogram to all nine tomosynthesis source images. Using the difference images we computed the PCQD measure of the registration performance, defined in Eq. (1), after the initial registration and after the complete registration. The average values of PCQD \pm one standard deviation, were equal to $58\pm4\%$ and $90\pm4\%$, after the initial and complete registrations, respectively. Fig. 3(a) shows a plot of the RMS differences between the mammograms and central tomosynthesis projections, computed before and after non-rigid registration. The slope values of the linear regressions computed after the initial and the complete registration are equal to 0.13 and 0.10, respectively. Fig. 3(b) shows the RMS images differences values as function of the tomosynthesis source projection image label *K*.

4 Discussion

We have chosen to approach the registration of a mammogram and a tomosynthesis data set of the same breast, starting from the simpler problem of registering a mammogram and the individual tomosynthesis source projection images. The mammograms and tomosynthesis images were acquired on the same day by the same technologist, thus having minimal variations.

The computed average PCQD values are consistent with those computed in our study of non-rigid registration of mammograms and central tomosynthesis projections from 15 clinical breast image pairs [3]; in that study we computed the average PCQD values before and after registration of $52\pm 20\%$ and $94\pm 3\%$, respectively.

Fig. 3 suggests that the image differences computed after the registration show relatively low dependence on the differences computed before the registration; the slope of the linear regression corresponding to the complete registration, shown in Fig. 3(a), is equal to 0.10. This result is also comparable to that obtained in our analysis of the registration of mammograms and central tomosynthesis projections [3]; the slope of the linear regression in that study was equal to 0.20.

Fig. 3(b) shows a variation in the RMS image differences computed before registration as a function of the tomosynthesis source projections (i.e. different x-ray focus locations). Ideally, assuming no changes in breast positioning, the minimum RMS image difference between the mammogram and the tomosynthesis source projection image should correspond to the central source projection (labeled K=5). Tomosynthesis projection images acquired with a larger angle to the central projection should result in an increased image difference. In Fig. 3(b), the minimum image difference is observed for the source projection K=6. The observed variation is not significant. Small changes in breast positioning between the mammography and tomosynthesis exam could cause this observation. Another possibility is that the calculation of the RMS image difference is resolved in a new Senographe DS digital mammography machine (General Electric, Milwaukee, WI), optimized for the use in tomosynthesis, which is being installed in our department.

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5 Conclusions

We performed a non-rigid registration of a clinical MLO mammogram with nine tomosynthesis source projection images of the same woman. Individual tomosynthesis source projection images were acquired at different positions of the x-ray tube, each separated by 6.25 degrees. The mammograms and tomosynthesis images were acquired on the same day by the same technologist, thus having minimal variations. We evaluated the registration performance by computing the percent corrected quadratic differences between the mammogram and the central tomosynthesis projection. On average we were able to compensate 90 percent of the per-pixel intensity differences that existed between the two images before the registration. In this paper, we evaluated the registration performance based on the pixel intensity differences computed from clinical images of a single patient. We are currently expanding this work to include more patients and to evaluate the registration results based on the average displacements of manually or automatically extracted fiducial points.

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