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Image Registration for Detection and Quantification of Change on Digital Tomosynthesis Mammographic Volumes

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Abstract

Objective—The purpose of this study was to achieve 3D registration of digital tomosynthesis mammographic volumes using mutual information.

Conclusion—Registration of digital breast digital tomosynthesis mammographic volumes was achieved with an average error of 1.8 +/- 1.4 mm.

Introduction

Digital tomosynthesis mammography [1,2] is a promising modality for routine breast cancer screening and diagnosis. Three-dimensional digital tomosynthesis mammography yields images of considerably better quality than does projection mammography, because anatomical features are displayed in greater detail. On mammograms, these features are often obfuscated by overlying tissue. Tomosynthesis yields substantial three-dimensional information that makes registration, subtraction, and detection of change a more realistic possibility. Precise spatial alignment of these image volumes would aid more rapid detection of changes in tumor appearance and growth over time, especially during neoadjuvant chemotherapy. However, the presence of artifacts caused by the highly asymmetric point spread function of digital tomosynthesis mammography suggests that spatial alignment of the two image sets might be difficult if there are large differences in the volumetric displacements of internal structures during compression. Our purpose was to achieve digital breast tomosynthesis image registration of whole breast image volumes acquired at different times in the same mammographic position and to assess the magnitude of residual error.

Subjects and Methods

A system combining automated whole breast ultrasound and digital tomosynthesis mammography [3] is under investigation for the detection and characterization of breast masses. With this system, 21 tomosynthesis projection images can be acquired over a 60° arc in 7.5 seconds. Each 3D tomosynthesis image volume is reconstructed from 21 projection images. To study whether registration was feasible, two such image volumes were acquired in each of our seven cases. Four of these cases consisted of images acquired within minutes of one another after the patient's breast was removed from the imaging unit, cleaned, repositioned

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and recompressed between the paddle and detector. In two of the other three cases, the image volume sets were acquired over a one-year period. In the third case, the acquisition interval was 6 months. All patients had clinical mammographic findings classified as negative (BI-RADS category 1) or benign (BI-RADS category 2). Institutional review board approval was obtained for this study and informed consent was obtained from every patient.

Special care was taken in stabilizing the breast during each examination. The breast was compressed between mammography-style plates and acoustic coupling was used for reproducible, large area scanning through the plates [4]. Registration was performed with mutual information for automatic multimodality image fusion (MIAMI Fuse™, University of Michigan) non-rigid 3D registration on the AVS platform (Advanced Visual Systems, Waltham, MA), based on the mutual information objective function and thin plate spline interpolation [5]. One image set was selected as the reference (usually the first of the two acquired image volumes; either can be selected). The other image set (called the target or homologous image) was spatially transformed to align with the reference frame. We registered the two 3D image sets by selecting 15 corresponding control points placed at key features, e.g. forks or sharp bends in blood vessels, ligaments and ducts. These points were employed as control points by the software and were moved to optimize the so-called mutual information (MI) of the two image volumes.

We estimated registration error was estimated by finding a different set of fifteen fiducial points in both image sets and measuring the Euclidean distance between the locations of each point on the reference and registered images. Three expert readers independently marked these points twice each, to provide a total of six measurements per case. The measurements were averaged to produce the final estimate of fiducial registration error.

Results

The mean registration error was 1.8 mm $\pm$ 1.4 mm. The minimum mean error of 1.2 mm was achieved for a dense breast over scans taken within the hour (Fig.1). One pair of image volumes acquired over a year-long interval was not be registered satisfactorily. This image set was registered only after down-sampling by a factor of 8, which greatly increased the residual error value. The registration error was only 1.6 mm, however, for an image volume pair on the contralateral breast of the same volunteer over a year-long interval (Fig. 2). The maximum mean error of 2.8 mm was observed for a pair of scans obtained with a 6-month gap. Of the four pairs acquired before and after repositioning, without a significant time lapse between the two acquisitions, registration was successful with an average registration error of 1.6 mm $\pm$ 1.2 mm. Table 1 shows the errors in every case. Vector plots (not shown) of the displacements of the ~15 or so control points throughout the image volumes showed in every case that the registration corrected both local tissue warping and global translation.

Discussion

We found for the first time to our knowledge that whole breast digital tomosynthesis mammography image volumes taken at different times can be spatially registered. The registration process was complicated by several factors; primarily, the compression of the breast at different times results in different mammographic appearances. Variable breast distortion during compression and actual physiologic changes (in case of a large time interval between scans) offer challenges. In some cases there can be high shear gradients at boundaries between tissues of differing composition. Digital tomosynthesis mammographic volumes also contain reconstruction artifacts that are dependent on the viewing angle. Furthermore, these digital tomosynthesis mammographic images have a slice thickness of 1 mm (this value can vary from 0.1 mm to half the lateral extent of the image), depending on the extent of target

object in the direction of x-ray tube motion. The axial resolution is clearly poorer than the 0.1 mm $\times$ 0.1 mm resolution in the image plane (voxel size was 0.1 $\times$ 0.1 $\times$ 1 mm³)

With care in selecting nearly identical locations in each of two same-modality image volumes of the breast, image based registration was quite successful. The exact manual identification of starter points is not always necessary, but we deemed it necessary for this limited study. It may be possible to develop feature recognition for automated selection of corresponding starter points.

Six out of seven tomosynthesis pairs acquired to date were registered with a residual error of 1-3 mm. Sickles et al [6] found that the mean and median sizes of cancers detected by mammography in a representative sample population of 332,926 patients were 20.2 and 15 mm respectively. Although an average registration error of 2 mm is relatively large compared to the tomosynthesis resolution of 0.1 mm, this error is small compared with the average size of mammographically detected breast cancers in a screening population. A tolerance of +/- 10% in tumor diameter change estimation in this first attempt at tomosynthesis registration is promising.

The subtraction technique shown in Fig. 2 may prove useful for highlighting change that is not due to registration error. Certain changes in the appearance of breast tissue over time can indicate the presence of malignancy, and comparison of the reference image and the registered image could help to identify such changes. Any improvement in the spatial registration of two 3D image volumes should aid in finding and comparing changes in breast tissue. When achieved, image registration should be relevant in interpretation of digital tomosynthesis mammographic volumes, particularly for less experienced readers and in computer-aided diagnosis.

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Fig. 1.
49-year-old woman with simple cyst in breast (case A1, Table 1). Tomographic images from image volumes that were acquired minutes apart and registered with mutual information for automatic multimodality image fusion.
(A) Reference Image.
(B) Checkerboard display with alternating squares from reference image and target image before registration.
(C) Checkerboard display with alternating squares from reference image and target image after registration showing better alignment of breast features than in B, especially in the top half of image.

Fig. 2. 50-year-old woman with normal breast (case B1, left craniocaudal, Table 1). Tomographic images from image volumes that were acquired 1 year apart and registered with mutual information for automatic multimodality image fusion.
(A) Reference image.
(B) Registered image from the most recently acquired image volume.
(C) Difference image shows changes in breast over 1 year.

Table 1**Registration Evaluation of Seven pairs of Breast Tomosynthesis Images**

Mean registration error (MRE) and standard deviation (SD) values for seven pairs of breast tomosynthesis images.

*B1: RCC was an unsuccessful registration because registration did not succeed until the images were down sampled by an unacceptably large factor (8).

Case	Time interval	MRE (mm)	SD (mm)
A1	<15 min	1.2	0.97
A2	<15 min	1.39	1.27
A3	<15 min	1.8	1.2
A4	<15 min	1.85	1.37
B1: LCC	12 mth	1.55	1.24
B2	6 mth	2.76	2.3
B1: RCC*	12 mth	-	-