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GROUPWISE REGISTRATION OF BREAST DCE-MR IMAGES FOR ACCURATE TUMOR MEASUREMENT

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Abstract

The registration of breast DCE-MR images can help correct possible motions during image acquisition, and is also important for diagnosis of breast cancer, i.e., discrimination between benign and malignant tumors. However, deformable registration of DCE-MR images is challenging due to drastic image contrast change over time (especially between pre- and post-contrast images). To improve the registration, we propose a novel hierarchical groupwise registration framework by specially considering the image characteristics of the breast DCE-MR images. Specifically, due to the similarity of post-contrast images, they are jointly registered by a groupwise registration method, and then registered together with the pre-contrast image by a robust correspondence detection technique based on local-steering-kernel features, instead of simple image intensities. Also, to accurately register the tumor region, we treat the motion in tumor area and other normal tissues differently by delineating rigid motion for tumor while non-rigid for other normal tissues. Our experimental results on both real and simulated images show that our method can achieve more consistent and accurate registration results than the conventional pairwise registration method.

Keywords

Dynamic contrast-enhanced breast MRI; Groupwise registration; Local steering kernel

1. INTRODUCTION

Breast DCE-MR image registration takes an important role in assisting diagnosis and quantification between benign and malignant tumors. The difficulties in registering breast DCE-MR images lie in the significant contrast changes from a pre-contrast image to post-contrast images, as well as the possible large motion during image acquisition.

Existing approaches [1, 2] typically register the post-contrast images to the pre-contrast image independently by optimizing the mutual information (MI) between the two images. However, these methods have several limitations. First, the independent registration of the post-contrast images to the pre-contrast image might result in inconsistent registration results when inspecting the warped post-contrast images over time. Second, although the intensity-based similarity measure is widely adopted in breast image registration, good anatomical correspondence between two images may be not easily established with this simple intensity feature. Third, it is noticeable that the motion of tumor (rigid) and normal tissues (non-rigid) have different patterns during MR scan.

To attack these limitations, we propose a novel feature based groupwise registration framework for the breast DCE-MR images. In our method, we first employ the unbiased groupwise registration algorithm [3] for registration of all post-contrast images. This is inspired from the observation that the contrast variation is much less among post-contrast images than that between any pre- and post-contrast images. Therefore, it becomes easier to

align all the post-contrast images to their group-mean image in the common space. After registration of post-contrast images, their group-mean image will be then registered to the pre-contrast image. In this way, we gain the consistent registration for all post-contrast images, since they are now registered together to the pre-contrast image. To better register group-mean image with the pre-contrast image, we also propose to use the contrast-invariant features, rather than original intensity, to establish the accurate anatomical correspondences. Furthermore, we require the tumor region to follow a rigid deformation during the registration, due to the generally rigid motion of (stiff) tumor in the breast.

We have evaluated our registration method on both real and simulated breast DCE-MR images. In all experiments, our method is able to achieve more accurate and consistent registration results, compared with a state-of-the-art pairwise feature-based registration algorithm [4].

2. METHOD

We will first present our groupwise registration framework in Section 2.1. As we will make it clear later, our framework needs to iteratively employ pairwise registrations in each round of groupwise registration. Based on our previous work [4], we describe a novel feature-based pairwise registration algorithm in Section 2.2.

2.1 The groupwise registration framework

The goal of the registration on a DCE-MR image sequence is to estimate the dense deformation fields $D_t = \{d_t(x) | d_t(x) = x + U_{S_t \to S_0}(X), X \in \Omega_{S_t}\}$ to warp each of N post-contrast images $S_t (t = 1, \ldots, N)$ to a pre-contrast image S_0, where $U_{S_t \to S_0}(x)$ denotes the displacement of a point x in the post-contrast image domain Ω_{S_t} to the post-contrast image S_t Fig. 1(a) shows the procedure of conventional registration methods, which independently estimate the deformation field D_t for each post-contrast image S_t to the pre-contrast S_0. Therefore, it needs N times of pairwise registration between pre-contrast image S_0 and each post-contrast image S_t, which is difficult to achieve consistent registration among all post-contrast images due to their independent registrations. It is notable that the intensity change of the tumor region among all post-contrast images is moderate in the post-contrast phase, compared to the fast change from the pre-contrast to the post-contrast (see the intensity histograms of images at different time points in Fig. 1(a)). Our proposed registration framework takes advantage of this observation, to first perform the groupwise registration of all post-contrast images to a group-mean image M , which is less challenging, followed by the pairwise registration between pre-contrast image S_0 and the group-mean image M.

Fig. 1(b) illustrates the proposed groupwise registration framework, which performs in two steps. In *first* step, we use the unbiased groupwise registration method [3] to simultaneously estimate all displacement fields D_{S_t} (with the same definition as D_t above, except the change from S_0 to M) towards the group-mean image M in the common space. This procedure is also completed by iteratively repeating 1) construction of the group-mean image by averaging the aligned post-contrast images, and 2) registration of each post-contrast image S_t to the latest group-mean image M . In the *second* step, the pairwise registration between pre-contrast image S_0 and group-mean image M will be employed to obtain the displacement field $D_{M \to S_0}$. Afterwards, the displacement field of each post-contrast image S_t toward the pre-contrast image S_0 can be calculated by the composition of $D_{S_t \to M}$ and $D_{M \to S_0}$.

The advantages of our registration method over the convention methods are: 1) we solve the registration problem in the divide-and-conquer way by first estimating the deformation fields for all post-contrast images and then register them together to the pre-contrast image via the group-mean image, rather than N times of independent registrations; 2) unbiased

groupwise registration increases the registration consistency by jointly considering all postcontrast images. Meanwhile, it is clear that the good pairwise registration algorithm is very important to achieve good registration results in both first and second steps. Therefore, we propose a feature-based registration algorithm next.

2.2. The robust feature-based registration method

We here describe our feature-based registration method in the application of DCE-MR breast images. Inspired by our previous work [4], we adopt the attribute vector and hierarchical deformation strategy in our breast image registration method. Largely, our method aims to minimize the difference of anatomical structures by robust feature matching while requiring the smooth deformation field. Therefore, our algorithm accomplishes good registration results by following two iterative steps. In the first step (feature matching step), we select a few driving points which have distinctive features to identify the correspondences. The non-driving points only follow the deformation of these driving points. In the second step (regularization step), the dense deformation field is interpolated according to the correspondences on the driving points, and Gaussian smoothing will be employed to make the deformation field as smooth as possible.

Contrast-invariant image descriptor—In our application, the image contrast varies dramatically over time. Therefore, the attribute vector based on intensity histogram [4] is not sufficient to find the reliable correspondence. We thus propose to use the local steering kernel (LSK) [5] as the morphological signature of the structure in the breast image, because it is robust to the contrast change. LSK on each point x is the gradient based image descriptor, calculated in the $P \times P$ local window, whose shape is adaptive to the local edge orientations. Therefore, the LSK on point x can be represented as $K(x) = \{K(x_i - x; C_i) | i = 1, \ldots P^2\}$, where x_i denotes one of P^2 neighboring point of x. The value of each element $K(x_i - x; C_i)$ in the particular LSK on each point x is given as:

$$K(x_i - x; C_i) = \frac{\sqrt{\det(C_i)}}{h^2} \exp\left(\frac{(x_i - x)^T C_i (x_i - x)}{-2h^2}\right), \quad (1)$$

where h denotes the kernel width, and the matrix C_i is a covariance matrix calculated from the gradients within the neighborhood of underlying point x_i. The examples of LSK on three pairs of correspondences (red boxes) between template (a) and subject image (b) are demonstrated in Fig. 2, with their LSK displayed in the color maps. It can be observed that the patterns of LSK are quite different in different locations of the image. Also, the LSK in one image is only similar to its correspondence in another image, which indicates its ability for correspondence detection in the registration.

To quantitatively measure the similarity between $K_T(x)$ on template point x and $K_S(x)$ on subject point Y, we use cosine similarity measure [5] to calculate the distance as:

$$\rho(K_T(x), K_S(y)) = \left\langle \frac{K_T(x)}{\| K_T(x) \|}, \frac{K_S(y)}{\| K_S(y) \|} \right\rangle = \frac{K_T(x) \cdot K_S(y)}{\| K_T(x) \| \| K_S(y) \|} \quad (2)$$

Adaptive motion—Considering the physical property of tumor, its shape is not non-rigidly changed during image acquisition, compared to the deformable normal tissues. Therefore, it is reasonable to consider the tumor area different from the normal tissue during the registration. To achieve this, we can first roughly extract the tumor region by inspecting the intensity change over time since the contrast change usually occurs within tumor. Particularly, we calculate the maximum intensity change of MR signal between the pre- and

all post-contrast images for each pixel. Then, the tumor area can be segmented by setting threshold on the value in the whole image, followed by some morphological operations.

During image registration, the estimated displacement of each point is the combination of global motion (guided by the shared affine transformation matrix of all image points) and the local deformation (guided by the correspondence detection) [4]. To enforce the motion rigidity of tumor, we increase the contribution of global motion for the points inside tumor. It is worth noting that the rigid transformation matrix for tumor is obtained by least-square fitting between the coordinates of template driving points inside the extracted tumor region and their correspondences in the subject image domain. Fig. 3 demonstrates the advantage of this strategy in registering a post-contrast image with a pre-contrast image (Fig. 3(a)). Fig. 3(b) and 3(c) display the deformation fields of tumor (the red box in (a)) without and with the rigidity constraint, respectively. It is observable that the deformation is more reasonable in the tumor area with the rigidity constraint.

In summary, we present a feature-based registration method for robust registration of breast DCE-MR images, with respect to the contrast changes. We adopt all the hierarchical deformation mechanism in [4] but using the local-steering-kernel features as a new attribute vector and enforcing rigidity constraint on tumor region. Second, we equip our groupwise registration framework (in Section 2.1) with this pairwise registration method to jointly align all post-contrast images and then finally register their group-mean image with the pre-contrast image.

3. EXPERIMENTAL RESULTS

Our proposed registration method has been evaluated on both real and simulated breast DCE-MR images, and its performance is compared with a state-of-the-art pairwise registration algorithm [1]. It is worth noting that we use the same set of parameters in all experiments below.

3.1 Experiments on real data

In this experiment, three subjects with more than 5 time-point scans are used. We evaluate the registration results of the pairwise registration and our proposed registration method by warping the multiple post-contrast images to its pre-contrast image. For each subject, we calculate the intensity entropy of all registered post-contrast images pixel by pixel. Note, lower entropy value indicates more consistent registration result over time. The overall averaged entropy value is 0.18 before non-rigid registration, 0.16 by pairwise registration method, and 0.14 by our proposed method. Especially, the entropy value is 2.33 in the tumor before registration. The entropy value reduces to 1.98 and 1.82 after pairwise registration method and our registration method, respectively. This experiment shows the advantage of our method over the pairwise one in terms of consistency of all aligned post-contrast images.

To visually inspect the registration accuracy, from left to right in Fig. 4(a) display the breast contours (in blue) of the two different post-contrast images overlaid on the contour (in red) of the pre-contrast image, before registration and after registration by pairwise method and our proposed method, respectively. In order to have a clear view, we further zoom-in the contour alignments within the green boxes. It is observable that the registered contours by our method are closer to the contour in pre-contrast image than that by pairwise method, which shows better performance in registration accuracy achieved by our method. It is worth noting that comparison of the difference images between the warped post-contrast images and pre-contrast image may be not applicable to evaluate the registration performance of breast DCE-MR images, because of the real intensity changes between pre- and post-contrast images during image acquisition.

Since the contrast agent takes effect to all tumor points homogeneously in pre- and post-contrast stage for the example we used, the intensity change of tumor points should be continuous and consistent over time. Therefore, Fig. 4(b) shows the evolution of intensity in the tumor region for all post-contrast images. From left to right are the intensity change curves before registration (in green) and after registration by pairwise method (in blue) and our proposed registration method (in red), respectively. It is clear that the longitudinal intensity changes of tumor points after registration is much more consistent by our method than by the pairwise method.

3.2 Experiments on simulated data

Due to the lack of ground truth in real data, we generate the simulated data to evaluate the registration accuracy. With a pre-contrast image and its manually labeled tumor, new post-contrast images can be simulated as follows. First, we enhance the intensity for each pixel in the pre-contrast image, to simulate contrast changes in tumor over time. In particular, the enhancement for each point is calculated by the multiplication of a spatially- and temporally-variable value and the Gaussian weight which is related with distance from underlying location to the center of tumor. Next, we simulate small motion for each contrast-enhanced image by warping it with the deformation field generated with random B-spline parameters.

We have applied the pairwise registration and our proposed registration methods to align the simulated post-contrast images to the pre-contrast image. Based on the ground-truth of deformation known in the simulation step, we can calculate the residual error between the ground-truth and the estimated deformation fields on each pixel. The average residual error is 0.71 pixel by the pairwise algorithm, compared with 0.46 pixel by our registration method. Moreover, it is worth noting that the maximum residual error is 3.05 pixel by pairwise registration method, while only 1.93 pixel by our registration method.

Similarly, we inspect the entropy value of all registered post-contrast images over time. Before registration, the overall entropy value is 0.23 for the whole image and 2.44 in tumor region. The overall entropy values by the pairwise registration method are 0.19 for the whole image and 2.09 in tumor area. By our proposed method, the overall entropy values are further decreased to 0.17 for the whole image and 1.9 in tumor region. Again, our method over-performs the pairwise registration method in terms of registration consistency.

4. CONCLUSION

In this paper, we have proposed a novel groupwise registration method to achieve accurate and consistent alignment for breast DCE-MR images. During registration, we use a local steering kernel as the morphological signature to establish the robust correspondence. Moreover, we adaptively treat tumor area different from normal tissues in the registration process, in order to better delineate the tumor motion. The registration performance of the proposed method has been evaluated in both real and simulated data, with comparison of a feature-based pairwise registration method, where our method gains more accurate and consistent registration results. In the future, we will further evaluate our proposed method on more images with various tumor patterns in the clinical study.

5. REFERENCES

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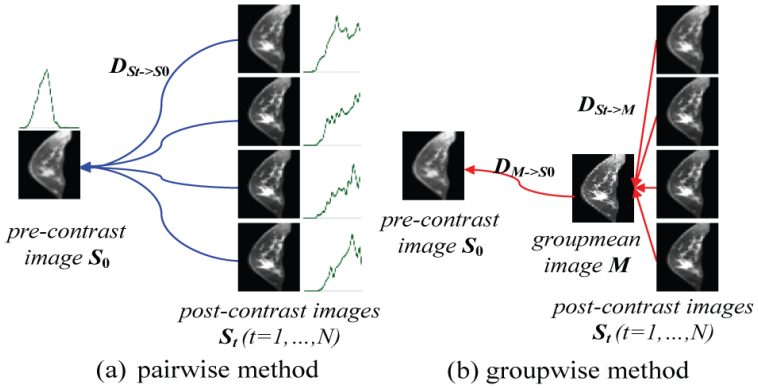

Fig. 1.

Illustration of the conventional pairwise registration approach (a) and the proposed groupwise registration framework (b).

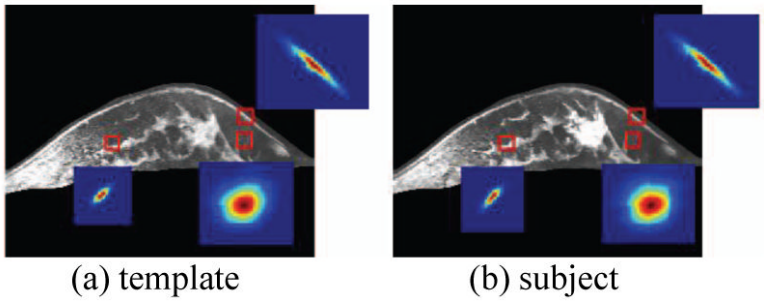

Fig. 2.
The LSK on three pairs of correspondences (red boxes) between template (a) and subject (b).

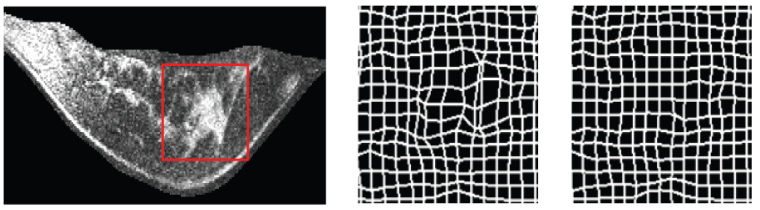

Fig. 3.
The advantage of rigid constraint on tumor region. (b) and (c) show the deformations inside the red box in (a), with and without rigidity constraint on tumor, respectively.

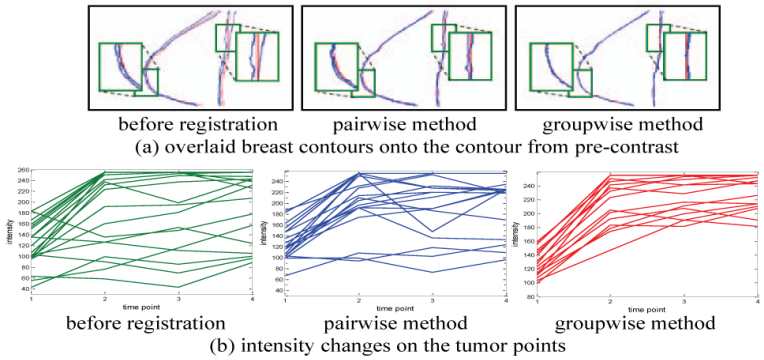

Fig. 4.

The demonstration of registration results by pairwise and our registration method. In (a), from left to right display the alignment of breast contours and the zoomed-in views in the green boxes, among all post-contrast images, before registration and after registration by pairwise and our registration method. (b) shows the evolution of intensity in tumor region before registration (in green), by pairwise registration (in blue) and by our registration method (in red). In all experiments, our method achieves more accurate and consistent registration result than pairwise method.