

GROUPWISE REGISTRATION FROM EXEMPLAR TO GROUP MEAN: EXTENDING HAMMER TO GROUPWISE REGISTRATION

Guorong Wu¹, Pew-Thian Yap², Qian Wang^{1,2}, and Dinggang Shen¹

¹Department of Radiology and BIRC, University of North Carolina at Chapel Hill, NC 27599, U. S. A

²Department of Computer Science, University of North Carolina at Chapel Hill, NC 27599, U. S. A

ABSTRACT

We extend the pairwise HAMMER registration algorithm to work in a groupwise manner for improving structural alignment of different individual brain images of a group. To achieve this, a tentative group mean is first generated from the previous aligned brain images (initially with affine registration), and all brain images are then registered onto the tentative group mean by HAMMER to obtain a refined group mean. Eventually, by repeating these two steps, a refined group mean image can be constructed. To obtain a better estimate of the group mean, we propose to average the aligned image according to anatomical shape, instead of intensity. Also, to alleviate possible large anatomical misalignment in the initial stages of the registration, a minimum risk estimator is employed for refining the correspondences before averaging, to prevent averaging across irrelevant anatomical structures, which, if not avoided, will render the group mean fuzzy. The performance of our groupwise registration method is evaluated by using real data (NIREP) in a ROI overlap analysis, and simulated data in an atrophy detection experiment. The results show that our groupwise registration algorithm yields better performance in both registration consistency and accuracy than the original pairwise HAMMER algorithm.

Index Terms— Groupwise registration, exemplar image,

1. INTRODUCTION

Due to the significant anatomical variation between individual brains, one of the focuses of recent research is to address the issue of finding a suitable frame of reference for unbiased analysis of brain images in certain population [1-3]. To this end, the virtue of groupwise registration is becoming increasingly apparent. Essentially, the ultimate goal of a groupwise registration algorithm is to find an image population center, commonly called an atlas, without resorting to the need of prior template selection, which, if not avoided, will inevitably lead to biasness.

A simple approach for groupwise registration is by applying exhaustively a pairwise registration algorithm to all possible pairs of images in the population [2, 4, 5].

However, an approach as such is computationally intensive and their applications are hence limited to only those with a small population of images. Recently, a more favorable approach for atlas construction is by considering the population statistics, which essentially jointly considers, at the same time, all images in the population in the course of registration. Joshi et al. [1] addresses the importance of diffeomorphisms in the case of large deformations, and cast the atlas construction problem as Fréchet mean estimation. The notion of congealing [6] is introduced in to bring images in a population into correspondence with each other jointly. It is based upon minimizing the summed pixel-wise entropies over at the corresponding location of different images. Balci et al. [3] further extends this method to a B-Splines based groupwise registration algorithm, which estimates the deformation field pertaining to each individual image simultaneously in each iteration. These methods, are basically intensity based methods. But in medical image analysis, it is important to build deformable anatomical models that take into account the underlying anatomy, and not simply the similarity of image intensities.

In this work, we present a method for extending the HAMMER algorithm [7], with software downloaded from <http://www.nitrc.org/projects/hammer/>, to work in a groupwise fashion by progressively warping every individual image in the group simultaneously towards the tentative group mean, and hierarchically evolve the group mean by averaging with respect to local anatomical shapes. In existing methods, anatomical details are often lost in the mean image, as a result of simplistic averaging of the images to form the atlas without proper consideration of local anatomical structures. However, few papers address the importance of keeping the anatomical structure clear during the groupwise registration. To our knowledge, fuzzy anatomical structure will lead to the ambiguity in correspondence detection when registering sharp individual images onto the blur reference, which will undermine the consequent evolution of the mean image.

To solve this problem, our groupwise registration algorithm is formulated to strictly retain structural details throughout the course of estimating the mean image. To achieve this, we employ geometrical features, i.e., 3D moment invariants, encapsulated in the form of attribute vectors, to describe the anatomical structure in the vicinity

of each voxel point. The mean image is then estimated in a voxel-by-voxel basis, where each voxel is contributed by all subjects, with their contribution weighted by the similarity of the attribute vectors, rather than simple intensity values. Particularly, only structural details, which are highly consistent in the population and highly similar to the current estimated group mean, is allowed to contribute to the further evolution of mean image, especially in the initial stages of the registration. This prevents unnecessary blurring of the mean image caused by naïve averaging of individual images which have large variability when still not aligned. As the registration progresses, and as we have a better estimate of the group mean, we relax some constraints to allow the acceptance of a wider range of shapes to participate as evolving forces to further refine the group mean. Using this scheme, structural information from all images in the population is progressively augmented to the group mean, making it increasingly representative of the whole population. Figuratively, this is equivalent to grouping the population information into bits of ‘digestible’ form and then feeding them to the group mean to help it evolve in a meaningful way. Our method yields two major advantages: a) the group mean has minimal anatomical structural difference in relation to all subjects in a group; b) the group mean retains population information and, at the same time, local anatomical structures.

2. METHOD

Given a group of N brain images $\{s_n | n = 1 \dots N\}$, the attribute vector $F_{s_n}(x)$ can be computed at each point x of a subject brain s_n . The overall goal of our groupwise registration algorithm is to simultaneously estimate a displacement field $\{d_{s_n}(x)\}$ for each subject s_n in relation to the tentative group mean \bar{s} , and more importantly, find the way to effectively estimate the group mean at each step of the iteration.

2.1. Groupwise Registration as Exemplar-to-Mean (EM) Evolution

Groupwise registration, as demonstrated in [1], can be achieved by iteratively aligning all subjects to the current tentative mean image, and based on the registration result, estimate a new refined mean image. However, in the initial stages of the registration, especially the affine registration stage, the alignment is often coarse and falls short in estimating accurate anatomical correspondences. This leads to a fuzzy mean image as Fig. 1(a). Therefore, if this mean image is further used as a template upon which individual subjects with clear structural details are registered, correspondence ambiguity will confound and limit further refinement of the mean image. *Supportive experiment results will be shown in the next section.*

To remedy this problem, we employ an exemplar-to-mean (EM) evolution approach described as follows. A

subject image closest (requiring the least amount of transformation) to the mean of the initial affine registered images is selected as the exemplar [8]. Using this exemplar as the template, we register all individual images in the population by HAMMER, and based on the results, generate a group mean. This is iterated until a satisfactory group mean is obtained. Our main contribution is on how this group mean should be estimated. The main idea of our approach is to evolve the current estimated group mean (initially the exemplar) to a more refined group mean, using a robust estimator, by progressively adding population and structurally consistent information to the current group mean. Initially, only a small amount of highly consistent structural information is allowed to be involved in the evolution of the mean. At later stages, this restriction is progressively relaxed to allow more information to further refine the mean so that it will eventually represent the whole population. We will describe in the upcoming section, how the criteria of population and structural consistency can be enforced.

Fig.1 illustrates the EM evolution process. It is clear from Fig. 1(a) that simplistic averaging of the aligned images cause fuzziness and loss of anatomical details when the registration accuracy is rough. In light of this, we have chosen to utilize the exemplar image, shown in Fig. 1(b), which will give us sufficient structural clarity, and hence a better head start, for correspondence identification. As we progressively have a better estimate of the group mean, we relax some constraints to allow the acceptance of a wider range of shapes to participate as evolving forces to further refine the group mean. From Fig. 1(b) to 1(d), we can see that the EM evolution generally progresses from the more ventricle to the cortex.

2.2. Mean Image Estimation

The mean image is estimated based on the similarity of local anatomical shapes. At each iteration t , after aligning all subject images to a previously estimated mean image $\bar{s}^{(t-1)}$ in the group, the new mean image $\bar{s}^{(t)}$ can be obtained by an anatomical shape similarity weighted averaging of each point x across population, which is realized as follows:

$$\bar{s}^t(x) = \frac{\sum_n e^{-\frac{1-sim\left(F_{\bar{s}^{(t-1)}}(x), F_{s_n}(x+d_{s_n}^{(t)}(x))\right)}{\sigma^2}} \cdot s_n(x+d_{s_n}^{(t)}(x))}{\sum_n e^{-\frac{1-sim\left(F_{\bar{s}^{(t-1)}}(x), F_{s_n}(x+d_{s_n}^{(t)}(x))\right)}{\sigma^2}}} \quad (1)$$

where $sim(\cdot, \cdot)$ measures the Euclidian distance between two attribute vectors and parameter σ determines the degree of acceptance of shape difference. It is worth noting that the value of $sim(\cdot, \cdot)$ is ranged from 0 to 1.

A smaller value of σ value indicates a higher requirement of structural shape similarity, and structural shapes with small similarity will be given very small weights. A bigger value of σ will give more allowance for dissimilar shapes. In this way, the value of σ should be

small in the beginning of evolution, since the correspondences are coarse and less reliable. Otherwise, the mean image will be trapped to become blurred and unable to serve as a template for further refinement. As the registration progresses, we increase the value of σ to encourage more information to be included to further refine the mean.

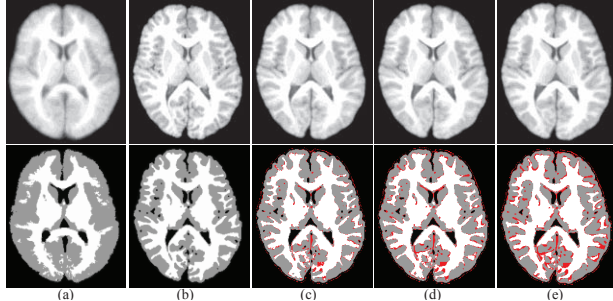


Fig. 1. The simple averaging mean image and its segmented image are shown in column (a). It can be observed that it is fuzzy and lacks structural details. (b)-(d) illustrate the evolution of the exemplar to the group mean. Throughout the process, more and more population structural variability information is added to the mean image, as indicated by the increasing fuzziness of some image region. Structural information which is consistent throughout the population is retained. The differences between the exemplar image and the successive group means are shown in red color in the bottom row of columns (c)-(e).

2.3. Robust Minimum Risk Estimator

To cater for possible misalignment, especially during the initial stages of the registration where correspondences are coarse, we use a local configuration based minimum risk estimator to reduce the influence of registration error on the group mean. In case of misalignment, the mean estimated by Eq. 2 is inaccurate because we might be averaging across different anatomical structures. A robust minimum risk estimator is used to help refine the structural correspondences and the respective similarity values for using Eq. 2. The core function of the minimum risk estimator is to gauge whether the correspondences between the current mean and a specific subject image is reasonable. If not, a new correspondence will be estimated to minimize the risk of erroneous averaging of irrelevant anatomical structures.

For each point x in the group mean $\bar{s}^{(t-1)}$ and its correspondence $x + d_{s_n}^{(t)}(x)$ in the subject s_n , the contribution of $s_n(x + d_{s_n}^{(t)}(x))$ to the group mean $\bar{s}^t(x)$ will be evaluated by the minimum risk estimator to check the consistency of their local anatomical shape. If the similarity between the current corresponding points $\text{sim}\left(F_{\bar{s}^{(t-1)}}(x), F_{s_n}\left(x + d_{s_n}^{(t)}(x)\right)\right)$ is beyond a threshold T , we will deem the correspondence as correct. Otherwise, we

will search the neighborhood of $x + d_{s_n}^{(t)}(x)$ in the subject s_n image to find a point which gives the highest similarity value with respect to $F_{\bar{s}^{(t-1)}}(x)$. The similarity is still required to be above the threshold T . Once such a point exists, we will update the similarity value to reflect the new correspondence.

Initially, it is necessary to use a larger T value to ensure the most reliable information gathered from the subjects and to minimize the risk of influence of misleading information from some possibly misaligned subjects. However, the value of T will be progressively decreased in the later stages of the registration when we have a better estimate of the group mean. The group mean $\bar{s}^{(t)}$ is finally constructed using Eq. 2, with the updated similarity values given by the minimum risk estimator.

3. EXPERIMENT RESULT

Two sets of experiments, based on real data and simulated data, are employed to evaluate the accuracy and consistency of the proposed registration algorithm in comparison with the original pairwise HAMMER algorithm.

3.1. Real Data

We use our proposed groupwise registration algorithm to align 16 brain images obtained from <http://www.nirep.org/> [9]. After registration, an overlap ratio can be calculated for each of the 32 manually delineated labels in each brain. We compare the overlap ratio values with those obtained using the pairwise HAMMER.

Considering the overlay ratios of all labels, our method achieves about nearly 2.0% improvement compared with pairwise HAMMER. We select a particular ROI, i.e., the right insula gyrus, to demonstrate how the overlap ratio changes at different iteration of the registration in Fig. 2, corresponding to the time spot shown in Fig. 1(a)-(e). In order to support our argument that fuzzy mean image will undermine the performance of groupwise registration, we also show the overlap ratio by the groupwise registration starting from the blurry mean image in Fig. 1(a). As a reference, we note that the overlap ratio obtained by pairwise HAMMER, selecting an arbitrary image as template, is 72.0% (see blue line in Fig. 2). For our method (red line in Fig. 2), it is clear that the overlap ratio is poor at the affine registration stage, which is around 58.6%. As the registration progresses, the overlap ratio increases from 72.0% at the stage where the exemplar is used as the template to a final 74.4% after several iterations. If we keep using the fuzzy group mean, instead of an exemplar, to perform groupwise registration, we can eventually achieve only 71.7% for the overlap ratio (see green line in Fig. 2). This result strongly supports our argument of using a clear group mean to effectively guide the groupwise registration during the whole registration procedure. For the same set of

data and the same ROIs, the result obtained by the B-splines based groupwise registration [3], using the free codes available in ITK, is 69.5%. All of these results are indicative of the improvement on registration accuracy gained by our method.

3.2. Simulated Data

In this experiment, a group of 12 subjects aged over 65 were selected, and simulated atrophy was introduced in both precentral gyrus and superior temporal gyrus on these subjects to generate another 12 atrophic subjects [10]. After aligning these 24 subjects by pairwise HAMMER and our groupwise registration method, the detectability of the simulated atrophy is evaluated by performing a paired t-test in SPM (<http://www.fil.ion.ucl.ac.uk/spm/software>) on the grey matter (GM) tissue density map. A smaller p value or a larger t value suggests the better separation between the two groups. We use equal $p=0.005$ as the threshold and the t-scores obtained by HAMMER and our groupwise registration method are shown in Table 1. It is observable that both p_{PWE} and p_{FDR} is no larger than HAMMER, but the t-values are larger by our groupwise method.

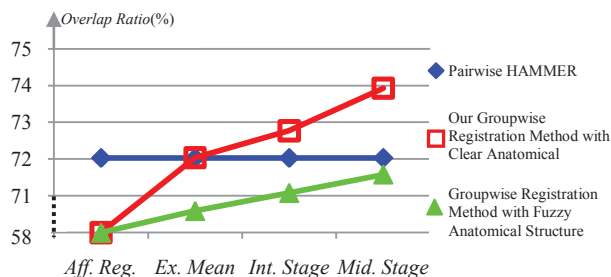


Fig. 2. Comparison of the labeling results on the right insula gyrus by pairwise HAMMER, our groupwise registration method, and the groupwise registration method using fuzzy group mean. The respective overlap ratios are shown in blue, red, and green, respectively. For groupwise registration, the results on different registration stages are also provided.

Table 1. Paired t-test results on simulated atrophy by pairwise HAMMER and our groupwise registration method.

	pairwise HAMMER			our groupwise registration		
	P_{PWE}	P_{FDR}	t-value	P_{PWE}	P_{FDR}	t-value
PCG	0.004	0.002	13.40	0.004	0.002	16.42
STG	0.076	0.005	9.95	0.027	0.005	13.67

4. CONCLUSION

In this paper, we extend the pairwise HAMMER registration algorithm for groupwise registration. The main idea is to evolve an exemplar image, closest to the mean of the affine aligned images, by progressively adding structural information derived from the population, finally ending in a

mean image which is representative of the whole population. Unlike many other groupwise registration methods which result in the loss of anatomical details, our method is designed to retain as much anatomical details as possible at each iteration of the registration. Experimental results validate the efficacy of our method in comparison with the original pairwise HAMMER algorithm and also the B-splines based groupwise registration algorithm [3].

5. REFERENCE

- [1] S. Joshi, B. Davis, M. Jomier, and G. Gerig, "Unbiased diffeomorphic atlas construction for computational anatomy," in *Neuroimage*, vol. 23 Suppl 1, 2004, pp. S151-160.
- [2] D. Seghers, D. E. Agostino, F. Maes, D. Vandermeulen, and P. Suetens, "Construction of a Brain Template from MR Images Using State-of-the-Art Registration and Segmentation Techniques," *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2004*, pp. 696-703, 2004.
- [3] S. K. Balci, P. Golland, M. Shenton, and W. M. Wells, "Free-Form B-spline Deformation Model for Groupwise Registration," *Med Image Comput Comput Assist Interv. MICCAI 2007*, 2007.
- [4] H. Park, P. H. Bland, A. O. H. III, and C. R. Meyer, "Least Biased Target Selection in Probabilistic Atlas Construction," *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2005*, pp. 419-426, 2005.
- [5] C. Studholme and V. Cardenas, "A template free approach to volumetric spatial normalization of brain anatomy," *Pattern Recognition Letters* vol. 25, pp. 1191-1202, 2004.
- [6] E. G. Miller, N. E. Matsakis, and P. A. Viola, "Learning from one example through shared densities on transforms " *In Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition 2000*.
- [7] D. Shen and C. Davatzikos, "HAMMER: Hierarchical attribute matching mechanism for elastic registration," *IEEE Transactions on Medical Imaging*, vol. 21, pp. 1421-1439, November 2002.
- [8] B. J. Frey and D. Dueck, "Clustering by Passing Messages Between Data Points," *Science*, vol. 315, pp. 972-976, 2007.
- [9] G. E. Christensen, X. Geng, J. G. Kuhl, J. Bruss, T. J. Grabowski, I. A. Pirwani, M. W. Vannier, J. S. Allen, and H. Damasio, "Introduction to the Non-rigid Image Registration Evaluation Project (NIREP) " *3rd International Workshop on Biomedical Image Registration*, vol. LCNS 4057, pp. 128-135, 2006.
- [10] Z. Xue, D. Shen, B. Karacali, J. Stern, D. Rottenberg, and C. Davatzikos, "Simulating deformations of MR brain images for validation of atlas-based segmentation and registration algorithms," *NeuroImage*, vol. 33, pp. 855-866, 2006/11/15 2006.