Computers in Biology and Medicine 39 (2009) 961–977

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Robust and fast shell registration in PET and MR/CT brain images

Ho Lee[a], Jeongjin Lee[b], Namkug Kim[c], In Kyoon Lyoo[d], Yeong Gil Shin[a,*]

[a]School of Computer Science and Engineering, Seoul National University, 599 Gwanak-ro, Gwanak-gu, Seoul 151-742, Republic of Korea
[b]Department of Digital Media, The Catholic University of Korea, 43-1 Yeokgok 2-dong, Wonmi-gu, Gyeonggi-do 420-743, Republic of Korea
[c]Department of Radiology, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Poongnab 2-dong Songpa-gu, Seoul 138-736, Republic of Korea
[d]Department of Psychiatry, Seoul National University College of Medicine and Hospital, 101 Daehang-ro, Jongro-gu, Seoul 110-744, Republic of Korea

ARTICLE INFO

Article history:
Received 4 March 2008
Accepted 16 July 2009

Keywords:
MR–CT–PET registration
Multi-modality registration
Shell
Rigid registration
Brain segmentation
Normalized mutual information

ABSTRACT

A robust and fast hybrid method using a shell volume that consists of high contrast voxels with their neighbors is proposed for registering PET and MR/CT brain images. Whereas conventional hybrid methods find the best matched pairs from several manually selected or automatically extracted local regions, our method automatically selects a shell volume in the PET image, and finds the best matched corresponding volume using normalized mutual information (NMI) in overlapping volumes while transforming the shell volume into an MR or CT image. A shell volume not only can reduce irrelevant corresponding voxels between two images during optimization of transformation parameters, but also brings a more robust registration with less computational cost. Experimental results on clinical data sets showed that our method successfully aligned all PET and MR/CT image pairs without losing any diagnostic information, while the conventional registration methods failed in some cases.

1. Introduction

Image fusion [1,2] has been used to combine the information obtained from two or more images with different characteristics. In medical fields, image fusion is particularly useful for diagnosing abnormalities by simultaneously combining anatomical and functional information. For instance, images obtained from computed tomography (CT) and magnetic resonance (MR) imaging provide detailed information of anatomic structures with high spatial resolution, whereas they have low sensitivity and specificity for identifying tumors and defining their biological behavior. On the other hand, images obtained from positron emission tomography (PET) provide functional information for detecting changes in the metabolism caused by the growth of abnormal cells. However, these images have difficulties in achieving precise lesion size and shape as they are typically noisy and blurry because of the positron scattering, photon attenuation, the spatial resolution of detectors, and the head motion during lengthy acquisition. The fusion of PET and MR/CT images requires a preprocessing task for correcting differences between the images caused by patient movement, scanning location, and image resolution. Although a dual-modality PET–CT hardware fusion system has been introduced recently to minimize these potential misalignments between PET and CT images during the examination, patient movement is inevitable because of the different scanning times. Moreover, the high cost of PET–CT hardware fusion system limits its availability. Therefore we still need to develop a software-based image registration technique for aligning two images.

Existing image registration techniques [1,2] can be classified into three categories. *Feature-based methods* [3–8] extract corresponding features from two images and estimate the transformation between the images by using the features. These methods are appropriate for images that have a distinctive description. *Voxel-based methods* [9–17] attempt to measure the similarity between two images using all geometrically corresponding voxel-pairs of an overlapping area. These methods do not need segmentation or feature extraction, but they need more computational time to evaluate similarity between all corresponding voxels. For the similarity metrics used in *voxel-based methods*, mutual information (MI) [9–11,13,15] and normalized mutual information (NMI) [10,13–16] have been widely used. Since MI and NMI can estimate a statistical similarity between all intensity pairs taken from corresponding spatial locations in two images without assuming any affinity of intensity values, these metrics are efficient in the registration of multi-modal images. However, these metrics require the additional cost of generating a joint histogram during their iterative optimization process.

To take advantage of both *feature-* and *voxel-based methods*, *hybrid methods* [18–20] have been proposed. Most of these methods focus on finding the best matched pairs from several manually selected

* Corresponding author. Tel.: +82 2 880 6757; fax: +82 2 871 4912.
E-mail addresses: holee@cglab.snu.ac.kr (H. Lee), imagination@catholic.ac.kr (J. Lee), namkugkim@gmail.com (N. Kim), inklyoo@yahoo.com (I.K. Lyoo), yshin@snu.ac.kr (Y.G. Shin).

0010-4825/$ - see front matter © 2009 Published by Elsevier Ltd.
doi:10.1016/j.compbiomed.2009.07.009

[20] or automatically extracted local regions/volumes [18,19]. Using a simple gradient computation [18] or entropy-based detector [19], the automatic extraction of local regions/volumes is possible. Ding et al. [18] and Schreibmann et al. [20] select local volumes from one image and search the corresponding volumes from the other image using MI and normalized correlation coefficient or NMI. On the other hand, Huang et al. [19] select several local regions from two images and find the best matched pairs among them using the entropy correlation coefficient. These *hybrid methods* can achieve robust alignment when the corresponding local volumes of two images are of high quality. Conversely, they have difficulty in obtaining precise matching of PET and MR/CT brain images because of a low correspondence rate between the corresponding local volumes. The local volumes extracted from the PET image, which are typically blurry and noisy, may differ from the corresponding local volumes in the MR or CT image. Moreover, in brain images many mismatched local volumes are found because many anatomical features have analogous shapes, for instance, a head has a similar spherical shape to a brain.

To overcome the shortcomings of conventional methods, we propose a robust and fast hybrid method using a shell volume for the intra-subject registration of PET and MR/CT brain images. A shell volume that consists of voxels with high contrast and their neighbors is automatically selected from the PET image [21]. Using the shell volume, we attempt to find a corresponding volume in the MR/CT image. To find the best matched corresponding volume, we apply the similarity metric, NMI, to the overlapping volume between the shell and corresponding volumes. A shell volume is very effective in reducing irrelevant corresponding voxels between two images during the optimization process, which delivers a more robust and efficient registration method. The general approach of using a similarity metric on a specific volume with other areas removed by preprocessing steps was already introduced by Cizek et al. [22]. They demonstrated that the elimination of background or nonbrain voxels for the calculation of MI results in improving the accuracy and speed of multi-modal PET–MR registration of human brain images. Our shell volume-based registration algorithm belongs to this category, with the new contribution compared to Cizek's method that we use a shell volume consisting of high contrast voxels and their neighbors, instead of removing certain areas. We show that the use of a shell volume can greatly improve the accuracy of the rigid registration based on NMI and Cizek's method, without significantly compromising the speed of Cizek's method.

The organization of this paper is as follows: Section 2 presents the overall process of our method. In Section 3, the experimental results are summarized and a brief discussion is given with respect to accuracy, robustness, and computational time. Conclusions are presented in Section 4.

2. Methods

Fig. 1 shows the proposed algorithm of registration between images of different modalities. To separate the brain from nonbrain volumes in PET images, nonbrain volumes are first segmented by 3D region growing [23] with a proper threshold value. Subtraction of nonbrain volumes from the original volume retains subvolumes including the brain. Among these subvolumes, we select the largest one as a brain volume. The surface of the brain is then extracted by applying a conventional sharpening filter [24] on the segmented volume.

To select a shell volume, the extracted surface is converted to a 3D distance map [5]. A shell volume consists of voxels located at short distances from the surface of the brain. Using the shell volume, we attempt to find a corresponding volume in the MR/CT image by using NMI. To estimate the NMI in the overlapping volume between

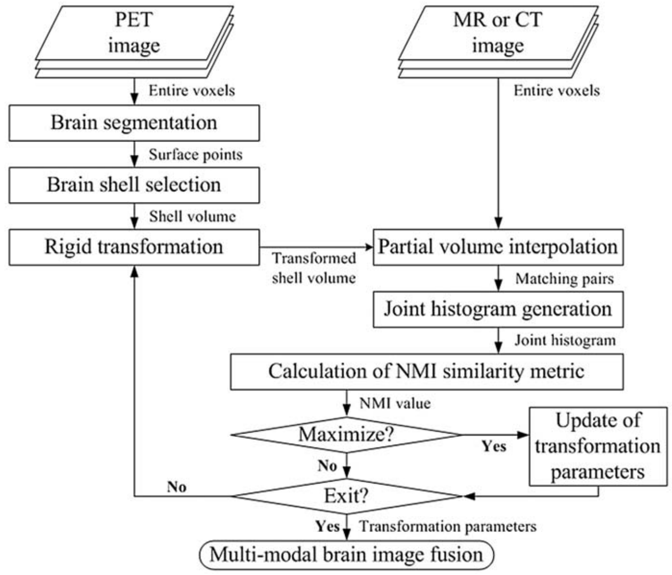

Fig. 1. Overview of the shell registration method.

a shell volume and corresponding volume while transforming a shell volume into an MR/CT image, a joint histogram is generated over corresponding voxel pairs. When the iterations of this optimization process are terminated, two images are fused by applying transformation parameters that give the best matched corresponding volume.

2.1. Automatic brain segmentation on PET image

Because PET brain images are blurry and noisy, it is difficult to find a threshold value that segments the brain area exactly. In our method, instead of segmenting the exact brain, we use an approximated brain volume that includes the brain. A proper threshold value makes it possible to get an approximate brain volume because the intensity of brain is higher than that of other structures in the image [25].

The intensity values in PET image are first normalized to a value between 0 and 255. Then, we segment the region by performing 3D region growing while increasing the threshold value from low to high, and calculate the difference in size between the segmented regions of the current and previous threshold values. The appropriate threshold value is determined by automatically finding the threshold value that maximizes this size difference.

To reduce the number of iterations of 3D region growing, we set the initial threshold value (T_1) to the average intensity value (I_{aver}) of the entire volume instead of the lowest intensity, because the intensity of the brain lies between the average intensity value and the maximum intensity value ($I_{\max}$). In addition, we can reduce the search space of 3D region growing by saving the maximum intensity of each plane. We use three max-tables to save the maximum along the x, y, and z directions. If the current threshold value is T_{i}, we can reduce the amount of 3D region growing in each direction by skipping image planes for which the values in the max-table in that direction are less than T_{i}. The reduced search space is a rectangular box.

By assigning the positions of eight corners of the rectangular box as seed points, 3D region growing is performed with the current threshold value, T_{i}. The size of the segmented region, $S(T_{\text{i}})$, whose intensity is less than the current threshold value, is the sum of the number of voxels within the newly included region and the number