Study of the Precision of a 3-D Image Registration Technique Using 3-D PET Brain Simulated Images

Antoine Abche_
Dept. of Electrical Eng.
University of Balamand
P.O. 100, Tripoli, Lebanon

George Tzanakos
Department of Physics
University of Athens
Athens
Greece

E. Micheli-Tzanakou
Biomedical Eng. Dept.
Rutgers University
Piscataway, NJ, 08855
USA

Abstract - In this work, we present a method for evaluation of multimodal 3-D image registration techniques using Monte-Carlo 3-D PET brain simulated images as well as images of external markers in discrete image space characterized by the voxel size. This approach will offer an accurate and inexpensive way to evaluate the precision of any registration approach, in particular the methods that rely on extrinsic fiducial markers. The results show that the precision of the registration method is within a pixel of the modality with the poorest resolution.

Key-Words: - Registration, Multimodality, Alignment, Evaluation, Validation, Medical Imaging.

1 Introduction

The multimodal image registration has grown to a field of its own in the last few years because of its great value in a variety of applications. Referring to the literature, numerous techniques have been developed for medical applications to integrate images showing functional and metabolic activity (acquired by imaging modalities such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT)) with anatomical images (acquired by imaging modalities such as Computed Axial Tomography-CAT and Magnetic Resonance Imaging-MRI). Besides registering images obtained by two different modalities, they are used to integrate information acquired by the same modalities but at different times. Therefore, the integration of structural and functional information will be of great importance for improved diagnosis, better surgical planning, more accurate radiation therapy and better understanding and analysis of the functional images. For example, the continuous monitoring, treatment and investigation of a tumor over a period of time require that a particular region of interest to be identified in both functional and structural images and consequently the boundaries of the latter to be mapped on the corresponding images of the former.

Broadly, the image registration techniques can be classified in two main categories: featured based and intensity based methods. A feature-based approach requires the identification of the same feature in the two modalities involved. The features can be classified into external fiducial markers or internal markers. While in the first case, they are extrinsic devices attached to the head, the latter case requires the identification of the same internal or geometrical landmark (surfaces, points, edges,) in the same images. Since the latter are data dependent, it makes the corresponding algorithm dependent on the registration applications. On the other hand, the intensity-based approach depends on the similarity measure that is determined over the region that is overlapped in both sets of images. Various surveys about image registration methods can be found in the literature [1-4].

In this work, a method for the evaluation of a multimodal 3-D image registration technique using external markers is developed and presented. It is based on Monte-Carlo simulation techniques. Consequently, it will offer an approach that compares objectively the performance of different image registration techniques. This method provides an inexpensive and accurate way of studying the precision of the 3-D image registration using simulated images in two modalities as well as images of markers superposed on the simulated images. Furthermore, the effects of the various aspects of a 3-D image registration (such as the pixel resolution, thickness resolution, measurement errors,..) on the precision of the registration can be studied and evaluated. Finally, it will not be time consuming or unfriendly and hazardous. For example the patient will not be subjected to a repeated dose of x-rays (using x-ray imaging modalities) to evaluate the precision of the registration under different situations.

2 Method

In this work, the evaluation of a 3-D image registration technique is implemented using Monte-Carlo simulation techniques. Having generated the simulated 3-D PET Brain images (as well as images of the external markers) in both modalities according to a particular 3-D density distribution, we study how well these 3-D images can be brought into coincidence using a particular multimodal registration technique. It includes the isolation of the external markers from the rest of the image using an intensity based segmentation technique, the estimation of their 3-D positions and the corresponding measurement errors, the automatic correspondence between the external markers in the two modalities and the estimation of the registration parameters. The transformation is estimated minimizing a Chi-square function defined in terms of distances of corresponding markers in the two modalities weighted by the corresponding localization measurement errors using a sequence of nonlinear optimizing techniques: The simplex method followed by a gradient approach. Finally, the optimized registration parameters are used to accomplish the alignment of the two 3-D sets of images. That is accomplished by transforming the images of one modality to the coordinate system of the second modality and superposing the corresponding contours of the transformed images onto the images of the latter.

2.1 Image Generation

Both the markers and the images in the two modalities are generated using Monte-Carlo simulation techniques in continuous 3-D space and then discretized in such a way as to resemble a realistic experimental situation.

In our approach, 3-D images in one modality are generated according to a known distribution in continuous or discrete 3-D space. In this work, the Hoffman 3-D PET Phantom Brain images [11] represent the probability distribution images that are normalized to maximum voxel intensity. A large number of 3-D points are generated in one modality. Each image point is accepted or rejected as a part of the generated images according to the rejection method. The 3-D set of images is transformed to the coordinate system of the second modality according to a predefined transformation. The transformation is parameterized in terms of nine parameters: three translation (a_x , a_y , a_z), three magnification (Mx , My , Mz) and three rotation (Euler Angles α, β and γ) parameters. In each modality, the corresponding 3-D volume images are generated taking into consideration the characteristic features of the imaging modalities, namely, voxel size (pixel size and thickness) and noise or modality resolution (randomly and independently along each direction in each modality) to resemble a realistic experimental situation.

In a similar fashion, N external point markers in one modality are generated and transformed into the coordinate system of the second modality using the same predefined transformation. The external point markers are selected in such a way that their positions on the face of the simulated head do not favor a region more than another. They are assumed to have a spherical shape with a radius that is small and yet it can cover several consecutive slices. Then, each marker is randomly “smeared” from its 3-D original positions using Gaussian measurement errors simulating marker localization errors. The markers are independently perturbed in each modality and along each direction x, y and z. After the images of the external markers are discretized, they are superimposed on the corresponding images.

2.2 Extraction of External Markers

Since the external markers are assumed to be highly visible in the corresponding images with respect to the other objects that are pertaining to the same image, a threshold technique is applied to isolate the point markers from the rest of the image. The result of this process is the collection of all voxels that belong to the markers. Then, a classification algorithm based on connectivity is implemented to classify the collected voxels into different clusters. Each cluster defines an external point marker [5].

Having isolated a cluster of voxels, the position and the corresponding marker localization errors are determined from the statistic of the 3-D distribution of the counts in the various corresponding voxels. That is, histograms along x, y and z directions were obtained by projecting the 3-D distribution of each marker to the respective x, y and z-axes. Consequently, the centroid coordinates of each marker were estimated from the corresponding histograms. The coordinate of the centroid along the x direction of each marker can be determined as follows:

$$I_{ci} = \frac{\sum_{ijk} i \; f(i,j,k)}{\sum_{ijk} f(i,j,k)} \qquad (1)$$

Similar expressions can be derived for the coordinates of the centroid along the y and z directions. Consequently, the spatial coordinates are obtained by multiplying the pixels' coordinates by the corresponding voxel spatial resolution.

2.3 Pairing of Markers

The pairing of the corresponding markers in the two modalities is done as follows: Assuming that we have contiguous axial slices and have roughly the same orientation, they are stacked on top of each other to form a 3-D image. The markers in each modality are projected unto the yz plane. The markers with minimum and maximum z coordinates are identified in each modality and a line joining the two points is drawn. Then, each marker is assigned to the right or left of that line in the corresponding modality. The next step is to rearrange the points (on each side) in an ascending order based on the z coordinate. Thus, by starting at the fiducial marker with the minimum z-coordinate, the formation of a closed contour by moving in a clockwise direction becomes straightforward. In the other modality, the same procedure is repeated.

2.4 Image Registration

After the external markers are identified, matched and their 3-D spatial coordinates and their marker localization errors are estimated in each modality, the transformation from one coordinate system to another is estimated by finding [6,7]:

i) A magnification matrix M: it is defined as 3 by 3 matrix allowing different magnification along x, y, z directions. Correction of geometric distortion or warping along other directions such as xy and yz directions can be defined by filling the appropriate elements in the appropriate locations of the corresponding matrix.

ii) A translation vector $\vec{a} = (a_x, a_y, a_z)$,

iii) A 3 by 3 orthogonal rotation matrix defined in terms of three Euler angles α, β, γ [8].

Thus, each pair of corresponding spatial coordinates is related by nine parameters of the transformation, which could contain a maximum of 15 parameters if all elements of the magnification matrix are defined. To estimate the registration parameters, a Chi-square function is defined in terms of the squares of the residual in distances weighted by the corresponding combined marker localization errors ($\delta x_k, \delta y_k, \delta z_k$):

$$\chi^2 = \frac{1}{N} \sum_{k=1}^{N} \{ (\frac{\Delta x_k}{\delta x_k})^2 + (\frac{\Delta y_k}{\delta y_k})^2 + (\frac{\Delta z_k}{\delta z_k})^2 \} \quad (2)$$

$$\Delta x_k = x'_k - x_k \,,\ \Delta x_k = y'_k - y_k \,,\ \Delta z_k = z'_k - z_k \quad (3)$$

where (x'_k, y'_k, z'_k) and (x_k, y_k, z_k) are the position coordinates of the k corresponding pair of markers after transforming them to the same coordinate system and Δx_k , Δx_k , Δz_k are the residuals along x, y and z directions, respectively. The combined localization error involves the transformation of the measurement localization errors of the markers in one modality to the desired coordinate system (second modality) by error propagation methods. That is,

$$\delta x_k = \sqrt{\sigma_{1x}^2 + \sigma'^2_{2x}} \qquad (4)$$

Where σ_{1x} is the measurement localization error of the k'th marker in the first modality along the x direction and σ'_{2x} is the propagated error of the corresponding k'th marker from its coordinate system to the coordinate system of the first modality. Similar expressions to (4) can be defined for the measurement localization errors along the y and z directions.

Since the χ^2 function is dependent on the transformation parameters in a non-linear fashion, a sequence of two iterative non-linear optimisation techniques are implemented to estimate the nine registration parameters: a Simplex approach [9] followed by a Gradient approach [10]. Even though the simplex is stable, it is not very efficient. Thus it is used to obtain a rough approximation of the minimum and than it is switch to the variable metric method to zero in on the minimum with efficiency.

Then, the volumetric data of one modality are transformed to the coordinate system of the second modality to study how well the registration is. Usually, the resolution with better spatial resolution is transformed. The precision of the registration can be studied visually as well as quantitatively by studying the residuals of corresponding target points identified in images of both modalities.

2.5 Comparison

In the proposed registration approach, the optimization is accomplished by varying all the transformation parameters simultaneously (including the magnification parameters). That will provide the best registration parameters that will minimize the original corresponding 3-D set of points extracted from the imaging modalities involved. It is therefore the most general approach to estimate the transformation parameters. On the contrary, the Singular Value Decomposition (SVD)-based method decouples the magnification, rotation and translation parameters [12-15]. After estimating the magnification parameters (ratio of distances) and scaling the original data set, the rotation parameters are estimated using the closed form solution based on the SVD of a 3 by 3 cross-covariance matrix. Then, the translation parameters are determined using the centroids of the data sets. The overall process of SVD-based approach may not lead to the best estimate of all registration parameters that minimize the squares of distances of the two original matched data sets. This difference would lead to a better precision of the registration using the implemented approach [16]. Similar observations can be made about the registration techniques that are based on Fourier transform where the parameters are estimated separately [17, 18].

Using a Linear Based approach (LB) in which the rotation and magnification matrices are combined into one matrix A, the optimized parameters are estimated in the least square sense by computing the derivatives of a χ^2 function with respect to the 12 unknown parameters (9 for matrix A and 3 for the translation vector) whose values vanish at the minimum. Thus, a system of linear equations is formed and solved for the parameters. On the other hand, the rotation matrix of the proposed approach describing the orientation of the coordinate system in one modality with respect to the other modality is defined in terms of three parameters (Euler angles). Unlike the linear based approach, the proposed approach takes into account the correlation between the rotation parameters. Consequently, it would lead to a better precision and a smaller optimum number of fiducial markers to achieve the registration [16].

Furthermore, this approach takes into account the measurement errors (including propagated errors from one modality to the other) associated with the localization of the external point markers to weight the importance of a given marker position. This capability can not be easily accomplished with other registration techniques such as Singular Value Decomposition, Principal Axes and Correlation based methods.

3 Hoffman 3-D PET Brain Images

The simulated images in the two modalities are generated using the Hoffman 3-D PET phantom brain images [11]. They are created to simulate cerebral blood flow and metabolic images for PET. They are derived from a set of MRI scans taken over the whole brain, with the aid of standard anatomical atlases and expert personnel to provide boundaries when they are not clearly visible in the MRI images. In the phantom brain images, the gray structures, white structures and ventricles are assigned a relative activity level of 5, 1 and 0, respectively. The 18 slices of the 3-D PET brain images are illustrated in Figure 1. Each image is 256 by 256 pixels with a pixel resolution of 1 mm by 1mm. Two consecutive slices are paced at 6 mm intervals.

4 Results

The fiducial markers are assumed to be on the face of the head ($0° \le \phi \le 180°$) in various numbers and positions. The localization measurement errors of 3-D point in the two modalities $\sigma 1$ and $\sigma 2$ are distributed randomly and independently along x, y and z directions. For the purpose of presenting a quantitative measure in studying the precision of a 3-D image registration method, the spatial resolutions are selected to have a Full Width Half Maximum (FWHM) equals to 6 mm and 2 mm for the first and second modality, respectively. In this regard, the number of external markers was selected to be 14.

The parameters of the transformation were chosen to be the three Euler angles (α, β and γ), three translations along x, y and z directions and three magnifications corresponding to x, y and z. In he present study, the input values of the parameters of the predefined transformation were selected to be: α=5°, β=3°, γ= 2°, M_x=1.01, M_y= 0.98, M_z=1.05, a_x= 10mm, a_y=10mm and a_z=10mm.

Using the predefined transformation, the simulated images of the Hoffman 3-D PET brain images as well as the images of external markers were generated in both modalities as outlined earlier and assuming the above localization measurement errors.

The images in both modalities were generated having a pixel resolution of 2 mm by 2 mm and a slice thickness of 2 mm.

For estimating the spatial coordinates of the external markers and consequently to achieve the alignment of the two 3-D sets of volumetric data, the spatial coordinate system in each modality is chosen in such a way that the three orthogonal planes (xy, yz and xz planes) are parallel to image planes that subdivide the image into voxels. That is, the x, y and z-axes correspond to the indexes i, j and k of the voxels.

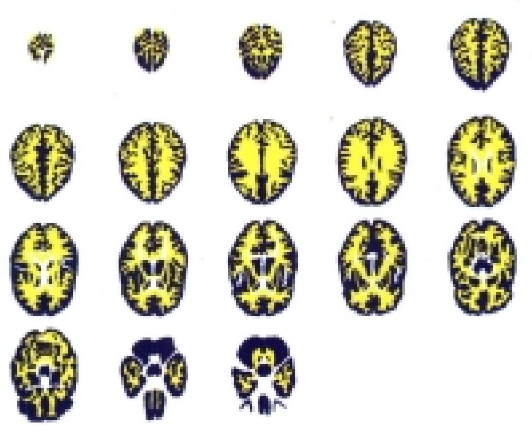

Figure 1: the 18 slices of the Hoffman 3-D PET Brain Images.

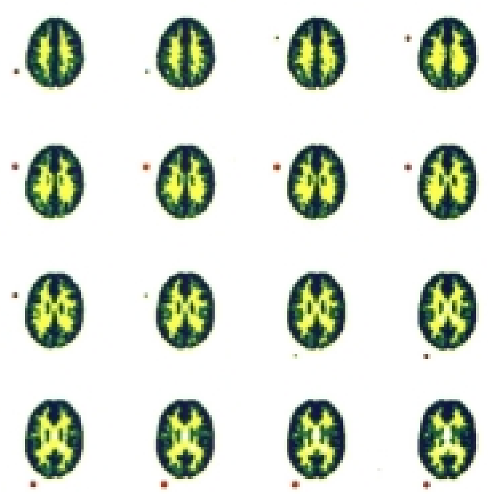

Figure 2: 16 consecutive slices in the coordinate system of the first modality.

Figure 2 shows a set of 16 consecutive generated images from the 3-D Hoffman images of the brain in the coordinate system of one modality. Figure 3 illustrates a set of 16 consecutive images in the coordinate system of the second modality. It is clear that one set of images is rotated and translated with respect of each other set. This fact is illustrated in Figure 4 in which the contours of two images in the coordinate system of the first modality are overlaid onto the images of the second modality before registration has been performed. After the recovery of the registration parameters according to the method described in section 2, the optimized parameters are used to transform one set of 3-D volume images to the coordinate system of the second modality. Figure 5 shows the superposition of 4 consecutives slices after registration. The contours of one modality are overlaid on the corresponding images of the second modality. These images clearly demonstrate the successful co-registration of two sets of 3-D volume images by bringing into coincidence the pairs of corresponding markers.

Figure 3 : 16 consecutive slices in the coordinate system of the second modality.

The precision of a 3-D multimodal image registration technique can be evaluated quantitatively by studying the residuals of the fiducial markers after registration. The positional residuals along x (Δx), y (Δy), z (Δz) directions as well as the residual of distances (ΔD), were estimated after the pairs of corresponding external markers were transformed to the same coordinate system. The centroid of each marker was estimated from the corresponding cluster of pixels (each cluster defines one marker) as outlined earlier. The residual of distance (ΔD) is obtained as follows:

$$\Delta D = \sqrt{\Delta x_k^2 + \Delta y_k^2 + \Delta z_k^2} \qquad (5)$$

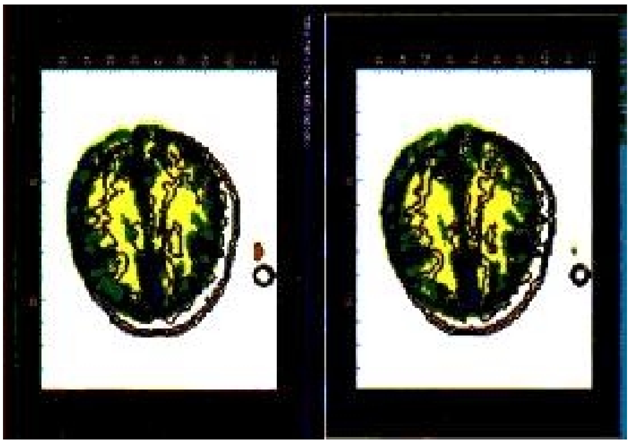

Figure 4: Superposition of two slices before registration.

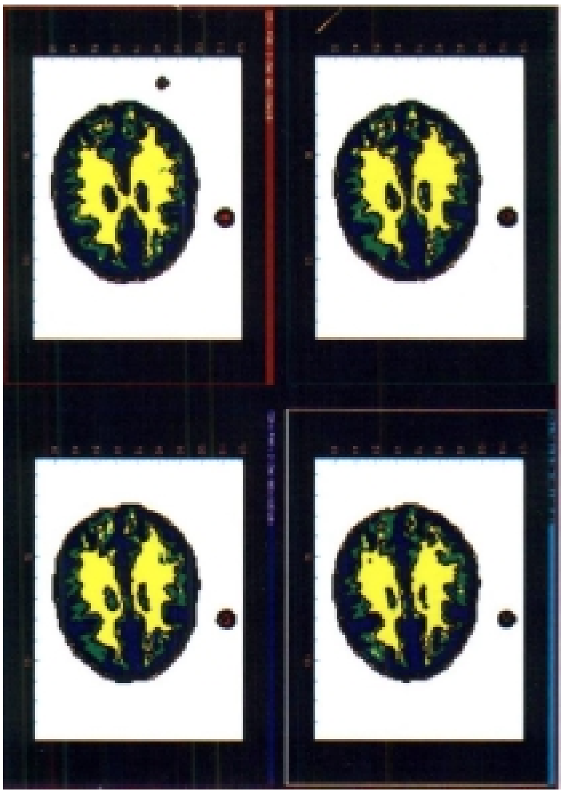

Figure 5: The composite image: The contours from one modality are overlaid on the images of the second modality.

Table 1 shows the residuals (or the errors) Δx, Δy, Δz as ΔD of corresponding fiducial markers after registration. The first eight markers are among the 14 markers used in the estimation of the registration parameters. It includes the residuals of the marker having the best (marker 1) and worst (marker 8) registration ΔD. Consequently, all the other markers used in the estimation of the registration parameters have an error ΔD that varies between these two values. The other four markers shown in the table were generated and not used in the optimization procedure. They are located in the front (markers 9 &10) and back (markers 11 & 12) of the assumed brain images. The results show the dependence of the precision of the registration on the position of the image point. The best registration, defined in terms of ΔD, is accomplished in the region where the external markers are located. On the other hand, the worst registration is achieved in the back of the phantom where no external markers exist. Also, it becomes clear that the residuals are within the pixel resolution of the modalities involved. Furthermore, the residual ΔD can be considered as a good quality for the precision of the registration.

Table 1: residuals Δx, Δy, Δz and ΔD of the markers after registration.

Marker	Δx (mm)	Δy (mm)	Δz (mm)	ΔD (mm)
1	-0.0468	0.0644	0.1968	0.2123
2	0.1369	0.4517	0.0391	0.4736
3	0.0772	0.0323	0.3857	0.3947
4	0.1323	0.2347	0.1245	0.2968
5	-0.0468	0.0644	0.1968	0.2123
6	0.4037	0.0699	0.0006	0.4097
7	0.0984	0.1638	0.2796	0.3387
8	0.3477	0.4387	0.2795	0.6245
9	0.2545	0.0708	-0.0316	0.2661
10	0.0439	0.2791	0.4034	0.4925
11	0.2953	0.7273	0.8746	1.1752
12	1.0304	0.4264	-0.6331	1.2823

5 Conclusions

A method that provides a quantitative evaluation of multimodal 3- image registration techniques using external markers was developed and presented. It is based on generating simulated images of Hoffman 3-D PET brain images as well as images of external point markers using Monte-Carlo simulation techniques. This approach can be extended to study the precision of registration techniques that are based on internal landmarks (surfaces, contours or points). For example, corresponding surfaces in the two modalities can be generated. Consequently, they can be extracted to recover the transformation parameters to accomplish the alignment of the two 3-D sets of images. In this work, the results show that 1) the precision of the registration is within a pixel of the poorest modality resolution 2) the precision is worst in the region of the back of the simulated brain images where the external markers are not used in the optimization process and 3) the alignment of the two 3-D sets is successful by inspecting visually the contours overlaid on the images of the second modality as well as the residuals.

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