COMPARISON AND EVALUATION OF MULTIMODALITY BRAIN IMAGE REGISTRATION METHODS

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ABSTRACT
Different types of medical images have their own unique characteristics and thus provide different information. Registration techniques integrate the information from various medical imaging from different modalities to align properly in the same coordinates. An efficient and affordable method to register three-dimensional (3D) image data from multiple imaging modalities is in great demand in clinical applications, especially in the evaluation of brain functional changes associated with structural abnormalities. Current auto-registration methods designed for 3D medical images can be divided into two categories: intensity-based and geometry-based methods. The mutual information (MI) algorithm is the most representative method in the first category. We used the previously developed registration method based on contour matching to represent the second category. This method contains two steps: coarse alignment using principal axes registration (PAR) and fine tuning through maximal cross-section matching. The aim of this study is to compare the performance between these methods. The results from seven sets of head volume acquired by computed tomography (CT), magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT) show that the proposed contour-matching method is better than the MI algorithm in terms of registration accuracy, especially when the contents between the pair of image volume for registration are inconsistent.

KEY WORDS
Image registration, mutual information, and brain image.

1. Introduction
Currently, the advent in medical imaging has provided the convenience in examining the inner structure of the human body. They are not only applied for diagnoses but also for image-guided treatment. However, owing to the different characteristics of medical imaging, a single type of medical image cannot provide the overall information for different needs. A high demand is present in combining the three-dimensional (3D) image data from different medical imaging modalities to provide physicians with complementary information. Because the scanning time and resolution of the images from different modalities are different, and the position of the patient may be inconsistent during image acquisition, image registrations are acquired to transfer the image sets from different modalities into common coordinates such that the position of the pathology and the associated normal anatomy from one modality coincide with those from another.

Many registration methods have been developed for 3D medical images from multiple imaging modalities. The multimodality image registration is commonly required by neurologist to evaluate the brain functional changes associated with structural abnormalities [1-2]. In general, they can be divided into two categories: intensity-based and geometry-based methods. The most representative method in the first category is the mutual information (MI) algorithm [3], which is commonly used in the medical image analysis package owing to the necessity of pre-segmentation; therefore, it can be easily and conveniently used by medical staff. The major limitation for the method, however, is that the registration process is time consuming because of the high cost of calculating the similarity function. In addition, the optimization procedure is susceptible to local optima, especially in 3D cases where the size of the solution space increases exponentially with the number of transformation parameters [4]. In addition to the limitations above, because the clinical images are typically truncated unevenly in different modalities and their mutual correspondence decreases, the registration accuracy can be limited when the MI method is applied to the pair of such image volumes with inconsistent content.

The advantage offered by methods belonging to the second category is their high efficiency owing to their low computational complexity. However, they typically require intensive user interaction to identify the corresponding features between two images. To avoid this inconvenience and to solve the problem of inconsistent content, we previously developed a hybrid registration scheme [5], including coarse registration using the principal axes alignment and then fine tuning the registration using a combination of maximal cross-section area detection and the general Hough transform (GHT).

In this study, the improvement in registration accuracy by adding the fine-tuning process in the hybrid registration scheme was verified, following a comparison with the MI registration.
2. Methods

2.1 Image Data

Seven sets of head images, including five consistent-contented and two inconsistent-contented sets, acquired by SPECT-CT and MRI scanning were used in this study. They were provided by the Kaohsiung Chang–Gung Memorial Hospital. The resolution of the original CT images is 0.59 mm × 0.59 mm × 3 mm, and that of the SPECT images is 2.34 mm × 2.34 mm × 3 mm. The resolution of the MR images varies in a wide range with the voxel size of 0.5 mm × 0.5 mm × 1 mm or 1 mm × 1 mm × 1 mm.

2.2 Preprocessing

Owing to the fact that the resolutions of the images from each of the three modalities were different, cubic spline was applied first to adjust the voxel size to fit a 1-mm³ cube. The process can reduce the number of transformation parameters from nine to six in a rigid transformation, thus enhancing the registration efficiency.

2.3 MI Registration

The process of the MI registration is described in brief as follows.

Define two input image sets as A and B. The entropy \( H(A) \) and \( H(B) \), joint entropy \( H(A, B) \), and conditional entropy \( H(A \mid B) \) of A given B, and \( H(B \mid A) \) of B given A, can be derived from (1)–(3), respectively.

\[
H(A) = -\sum_a P_a(a) \log P_a(a) \tag{1}
\]

\[
H(B) = -\sum_b P_b(b) \log P_b(b)
\]

\[
H(A, B) = -\sum_{a,b} P_{a,b}(a,b) \log P_{a,b}(a,b) \tag{2}
\]

\[
H(A \mid B) = -\sum_{a,b} P_{a,b}(a,b) \log P_{a,b}(a \mid b)
\]

\[
H(B \mid A) = -\sum_{a,b} P_{a,b}(b,a) \log P_{a,b}(b \mid a) \tag{3}
\]

where \( P_a(a) / P_b(b) \) denotes the probability function of the intensity \( a / b \) in image \( A / B \) and \( P_{a,b}(a,b) \) represents the joint probability. After the entropies are obtained, then the MI value can be calculated according to (4). The similarity in the mutual information (SMI) between the two sets of images is defined in (5).

\[
I(A, B) = H(A) + H(B) - H(A, B) = H(A) - H(A \mid B) = H(B) - H(B \mid A) \tag{4}
\]

\[
SMI = \frac{I(A, B)}{I(A, A)} \times 100\%
\]

The registration process is to iteratively search for the maximum SMI by increasing/decreasing the registration parameters. However, such search is exhausting and time consuming. In practice, we applied the imregister() function in MATLAB to execute the MI registration. The optimization of the searching process adopted in this function is the \((1+1)\)-evolution strategy, where the initialization of the searching path setting is required. The initial setting is explained and summarized in Table 1.

<table>
<thead>
<tr>
<th>Optimization parameters</th>
<th>Definition</th>
<th>Initial value</th>
</tr>
</thead>
<tbody>
<tr>
<td>InitialRadius</td>
<td>Initial step width</td>
<td>7.81 x 10⁻⁴</td>
</tr>
<tr>
<td>MaximumIterations</td>
<td>Maximal number of iterations</td>
<td>1000</td>
</tr>
<tr>
<td>GrowthFactor</td>
<td>Scaling factor of the step width</td>
<td>1.05</td>
</tr>
<tr>
<td>Epsilon(ε)</td>
<td>Minimal error between two iterations</td>
<td>1.05E-06</td>
</tr>
</tbody>
</table>

2.4 Hybrid Registration Method

This registration method includes two stages: principal axes registration was first applied to rotate the head into its neutral position followed by fine tuning via applying the GHT to the contour of the maximal cross-sectional area.

2.4.1 Rotate the head into its neutral position

The direction of the long axis of the head can be derived by finding its three principal axes. The original image was first segmented into a binary head, \( B(x, y, z) \); subsequently, the principal axes of the head can be calculated according to the theory of inertia matrix \( I \):

\[
I = \begin{bmatrix}
I_{xx} & -I_{xy} & -I_{xz} \\
-I_{xy} & I_{yy} & -I_{yz} \\
-I_{xz} & -I_{yz} & I_{zz}
\end{bmatrix}
\]

where \( I_{xx}, I_{yy}, \) and \( I_{zz} \) are the moments of inertia with respect to the x, y, and z axes, respectively.

\[
I_{xx} = \sum_{x,y,z} (y - y_g)^2 + (z - z_g)^2 B(x,y,z) \tag{7}
\]

\[
I_{yy} = \sum_{x,y,z} (x - x_g)^2 + (z - z_g)^2 B(x,y,z)
\]

\[
I_{zz} = \sum_{x,y,z} (x - x_g)^2 + (y - y_g)^2 B(x,y,z)
\]

where \( I_{xy}, I_{yz}, \) and \( I_{xz} \) are the products of inertia with respect to the centroid of the binary head, \( x_g, y_g, \) and \( z_g \) respectively.
\[ I_{x} = \sum_{x,y,z} (x-x_g)(y-y_g)B(x,y,z) \]
\[ I_{y} = \sum_{x,y,z} (y-y_g)(z-z_g)B(x,y,z) \]
\[ I_{z} = \sum_{x,y,z} (x-x_g)(z-z_g)B(x,y,z) \] (8)

The three eigenvectors of \( I \) represent the three principle axes that are orthogonal to each other. The eigenvector corresponding to the largest eigenvalue of \( E \) is the direction of the long axis of the head. Once the angle of the long axis is obtained, the tilted head can be rotated back to its neutral position with the axis aligning with the vertical world coordinate.

### 2.4.2 Maximal cross-section alignment

After the previous stage, the long axis from both head volumes coincided with each other, but the horizontal planes with the two short axes from the two volumes were still mismatched. In this stage, the maximal cross sections of the head were detected from both volumes. They were used as the feature to shift the slice level to the corresponding positions and to search for the registration parameters via the GHT.

The process of the GHT algorithm in this approach included two steps. First, an R-table was built by calculating the vector set \( \{v_i\} \) between each contour point \((x_i, y_i)\) and the center of the contour, \(P_c(x_c, y_c)\), in the CT image. Subsequently, the corresponding center point \(P'_c\) was derived by searching for the maximal intersection via remapping the vector information to each contour point in the MR image. In this study, as the voxel size had been adjusted to be the same, we adapted a robust search only for the rotation angle \( \beta \) in (9), when the optimal match between \(P_c\) and \(P'_c\) was achieved.

\[ x_c = x_i + r \cos(\theta + \beta) \]
\[ y_c = y_i + r \sin(\theta + \beta) \] (9)

where \( \theta \) is the angle between the directional vector \(v_i\) and the positive direction of the x-axis and \( r \) is the length of \(v_i\).

### 2.5 Registration Accuracy Evaluation

The accuracy of registration was evaluated by the non-overlapping errors that can be quantified by the sum of the distance error (SOD) and the Jaccard index \((JI)\). The calculation of the SOD and \(JI\) is according to (10) and (11), respectively.

\[ SOD = \sum_{i=1}^{n} \text{length}(S_i) \] (10)

\[ JI = \frac{|\Omega_1 \cap \Omega_2|}{|\Omega_1 \cup \Omega_2|} \times 100\% \] (11)

\( \Omega_1 \) and \( \Omega_2 \) represent the area inside the head contour in image 1 and image 2, respectively.

### 3. Results and Discussion

CT and MR images are categorized as structural medical images because they can reveal the structural information of the body. In contrast, SPECT images are classified as functional images because they provide functional information rather than structural information. Images from the aforementioned categories were used to compare the performance of the two registration methods. The experimental results are described in detail as follows.

#### 3.1 Qualitative Comparisons

A set of 2D cross-sections of the MR and CT volume data with consistent content from \textbf{case A2} is provided as an example to demonstrate the registration results of the two methods. When the same pair of 2D images (Fig. 1A–B) was used to compare the registration performance of the MI with that of the hybrid method, the registration accuracy of the MI is compatible to that of the hybrid method as shown in Fig. 1C–D. However, when the MI was applied to register the 3D volume data, the registration discrepancy increased more obviously in the MI than that yielded by the hybrid method. The evidence is demonstrated later in Table 3, where the \(JI\) (= 0.86) of the MI in \textbf{case A2} is far less than the \(JI\) (=0.95) of the hybrid method.

![Figure 1](image1.png)

Figure 1. A. One example of consistent volume pair (Case A4 in Table 3). The original CT image; B. The original MR image. C. Registration of AB by using MI method; D. Registration of AB by using the hybrid method.
Another set of the MR-CT section with inconsistent content is shown in Fig. 2, where Fig. 2B reveal the fragmented scanning contour as indicated inside the dashed-line boxes, rendering the MR image inconsistent to the CT image (Fig. 2A). As a result, the MI registration shows the distorted MR image overlapping with the CT image (Fig. 2C). In contrast, our hybrid registration still yields a good match without distortion (Fig. 2D). The superiority of the hybrid registration in solving the inconsistent volume problem is due to the tolerance of the GHT for the registration of the fragmented contours.

Serious distortions are associated with the MR image transformation after applying the MI registration in case A5, as shown in Fig. 3.

3.2 Quantitative Comparisons

3.2.1 Effect of fine-tuning

Two stacks containing equal slices from the CT and MR volumes were used to derive the \( J_I \) values before and after fine tuning. Table 2 summarizes the \( J_I \) values before and after fine tuning with the same number (=21) of slices in the stack.

![Figure 2](image1.png)

<table>
<thead>
<tr>
<th>Case</th>
<th>PAR</th>
<th>Hybrid</th>
<th>Improvement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.95</td>
<td>0.97</td>
<td>2.14%</td>
</tr>
<tr>
<td>2</td>
<td>0.87</td>
<td>0.96</td>
<td>9.58%</td>
</tr>
<tr>
<td>3</td>
<td>0.85</td>
<td>0.95</td>
<td>12.38%</td>
</tr>
<tr>
<td>4</td>
<td>0.76</td>
<td>0.85</td>
<td>12.25%</td>
</tr>
<tr>
<td>5</td>
<td>0.68</td>
<td>0.84</td>
<td>23.26%</td>
</tr>
</tbody>
</table>

3.2.2 Comparison between MI and the hybrid method

The \( J_I \) and SODE of the registration accuracy for the seven cases are listed in Table 3 and Table 4, respectively. The \( J_I \) value of the hybrid method is greater than that of the MI registration for all seven cases. In addition, the SOD of the MI is approximately twice that of the hybrid method. These results reveal that our hybrid registration surpasses the MI algorithm.

3.3 Functional and Structural Image Registration

Functional medical images, such as SPECT and positron emission tomography (PET) images, can provide the metabolic information of a specific region of the brain. However, such images cannot clearly reveal the brain structure. Hence, quantifying the metabolic level in a specific region of the brain is a great challenge to nuclear medicine physicians. In our previous study, we applied the hybrid registration method to MR and SPECT image fusion [6]. Subsequently, the dopamine tracer 99mTc-TRODAT-1 (revealed in the SPECT image) inside the basal ganglia (defined by the MR image) can be quantified. Such an index can help neurologists evaluate the stage of neurodegenerative diseases in patients.

In this study, we also compared the registration performance between MI and the hybrid methods using SPECT and MR images.

3.3.1 Direct 3D MI registration

To verify whether the distortion that occurred in MR and CT registration (shown in Fig. 2) can occur in this registration task, 3D MI registration was applied to register the MR and SPECT volume data from the same subject (case B1). Fig. 4 shows the distortion still existing after applying MI to register the inconsistent 3D volume pairs of the MR and SPECT images in the same case.
Table 3
Comparison of Jaccard index (JI) of the 7 volume sets

<table>
<thead>
<tr>
<th>Type</th>
<th>Case</th>
<th>MI</th>
<th>Hybrid</th>
</tr>
</thead>
<tbody>
<tr>
<td>consistent</td>
<td>A1</td>
<td>0.86 ± 0.14</td>
<td>0.95 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>0.86 ± 0.15</td>
<td>0.95 ± 0.01</td>
</tr>
<tr>
<td></td>
<td>A3</td>
<td>0.82 ± 0.09</td>
<td>0.92 ± 0.02</td>
</tr>
<tr>
<td></td>
<td>A4</td>
<td>0.88 ± 0.10</td>
<td>0.94 ± 0.02</td>
</tr>
<tr>
<td></td>
<td>A5</td>
<td>0.84 ± 0.13</td>
<td>0.93 ± 0.02</td>
</tr>
<tr>
<td>mean±std</td>
<td>C</td>
<td>0.85 ± 0.12</td>
<td>0.94 ± 0.02</td>
</tr>
<tr>
<td>inconsistent</td>
<td>B1</td>
<td>0.82 ± 0.05</td>
<td>0.88 ± 0.04</td>
</tr>
<tr>
<td></td>
<td>B2</td>
<td>0.74 ± 0.05</td>
<td>0.93 ± 0.01</td>
</tr>
<tr>
<td>mean±std</td>
<td>C</td>
<td>0.78 ± 0.06</td>
<td>0.90 ± 0.04</td>
</tr>
</tbody>
</table>

Table 4
Comparison of Sum of the distance error (SODE) of the 7 volume sets

<table>
<thead>
<tr>
<th>Type</th>
<th>Case</th>
<th>MI</th>
<th>Hybrid</th>
<th>Error Ratio of MI over Hybrid</th>
</tr>
</thead>
<tbody>
<tr>
<td>consistent</td>
<td>A1</td>
<td>445.38 ± 395.41</td>
<td>148.15 ± 37.83</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>411.43 ± 395.60</td>
<td>170.12 ± 32.21</td>
<td>2.41</td>
</tr>
<tr>
<td></td>
<td>A3</td>
<td>637.55 ± 322.69</td>
<td>250.94 ± 65.27</td>
<td>2.54</td>
</tr>
<tr>
<td></td>
<td>A4</td>
<td>379.12 ± 269.32</td>
<td>171.66 ± 34.08</td>
<td>2.21</td>
</tr>
<tr>
<td></td>
<td>A5</td>
<td>distorted</td>
<td>211.61 ± 70.30</td>
<td></td>
</tr>
<tr>
<td>inconsistent</td>
<td>B1</td>
<td>109.50 ± 90.14</td>
<td>54.36 ± 31.52</td>
<td>2.02</td>
</tr>
<tr>
<td></td>
<td>B2</td>
<td>209.90 ± 100.15</td>
<td>119.07 ± 42.85</td>
<td>1.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>101.12 ± 43.8</td>
<td>40.45 ± 22.45</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>91.81 ± 62.66</td>
<td>58.43 ± 14.47</td>
<td>1.57</td>
</tr>
</tbody>
</table>

3.3.2 Hybrid registration

The distortion caused by the MI registration in these cases could be due to the high degree of complexity in searching for the optimal solution in the direct 3D registration task. To explore the potential cause of the distortions, we attempted to decompose the registration in two steps as described in Sec. 2.4. The heads of the MR and SPECT were first rotated into their neutral positions. Following that, the maximal cross-sections of both volumes were determined and used to find the corresponding slice pair between the MR and SPECT volumes. In the second step, we applied the GHT algorithm as well as MI registration to find the optimal slice-by-slice matching. The results show that not only was there no distortion in the MI registration, but also that the registration accuracy of MI was comparable to that of the GHT as shown in Fig. 5. The results confirmed that direct application of MI to register 3D volumes is more likely to cause distortion than 2D image registration. In addition, the results also suggest that reducing the registration complexity from 3D to 2D by using the hybrid method can help in avoiding the distortion problems.

The registration accuracies of the 21-slice volume stack using these two methods are similar; however, the JI of GHT (0.84 ± 0.02) were still significantly higher (p<0.01 by student t-paired test) than that of MI (0.82 ± 0.02). The SOD was not used to evaluate the registration accuracy at this time. The reason for this is that the head contours in the SPECT images were too vague to define.

4. Conclusion

The registration and visualization of 3D head images obtained from multiple modalities can provide physicians with an integrated view and complementary information, thereby improving medical diagnosis and treatment. The MI algorithm is an intensity-based registration method without the need for prior segmentation or feature marking; thus, it is commonly adopted in the medical...
image analysis package. However, the registration accuracy of the MI must be carefully evaluated when the quantitative structural parameters are required to derive from the registration results for diagnostic purposes. This study compared the registration accuracy of the MI method with the hybrid registration scheme, a geometry-matching method. Our results revealed that the hybrid registration surpasses the MI. Nevertheless, the distortion caused by MI transformation is noteworthy when the anatomical quantification is concerned.

References


