SIMULTANEOUS TRIPLE-REGISTRATION OF ICTAL SPECT, INTERICTAL SPECT AND MR IMAGES FOR EPILEPSY STUDIES: METHOD AND VALIDATION *

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ABSTRACT

Subtraction of ictal and interictal SPECT images is known to be successful in localizing the seizure focus in presurgical evaluation of patients with partial epilepsy. Computer-aided method for producing subtraction ictal SPECT coregistered to MRI (SISCOM method) is commonly used. There are two registrations involved in SISCOM: between the ictal-interictal SPECT images, which was shown to be more critical, and between the ictal image and MRI. The aim of this paper is to improve registration accuracy of ictal-interictal registration in SISCOM by registering all three images (ictal, interictal SPECT, MRI) simultaneously. The results of the simulation study demonstrates that, in surface-based registration, triple-registration method results in smaller ictal-interictal SPECT registration error than the pairwise registration method ($p<0.05$) for a range of cost-function parameter values.

1. INTRODUCTION

SISCOM has been shown to improve the sensitivity and specificity of Single-Photon Emission Computed Tomography (SPECT) in identifying the seizure focus in presurgical evaluation of patients with partial epilepsy [1, 2]. It has advantages over side-by-side visual interpretation and manual registration approaches. Recent studies suggest that sensitivity and specificity of SISCOM may surpass those MRI, PET, scalp-recorded EEG, interictal SPECT, and visual analysis of ictal SPECT [1, 2]. Computer-aided methods for SISCOM are commonly used. Among the two registrations involved in SISCOM, the registration error of ictal-interictal image registration is more crucial, and one of the major contributors to noise in SISCOM [4]. Registration errors (even subvoxel) at this step produce false-positive activation areas and obscured true-positive activation areas [4]. Therefore, the recommended approach is to register the two SPECT images, rather than registering each to MRI [3].

* Supported by Turkish Government Planning Agency (DPT) YUUP Grant: "Visual Archieval System for E-Government" and METU Grant: BAP-2002-07-04-03: "3D Brain Image Analysis".

1.1 Surface Based Registration

In SISCOM, brain surface registration techniques have traditionally been used to produce subtraction SPECT images [5-8]. Thresholding and morphological operations are generally used to extract the 3D brain surface. Surface-registration consistently matches SPECT images with better than 1 voxel dimension [7]. Iterative closest point (ICP) algorithm [9] and a multiresolution chamfer distance [6] are some of the techniques in the literature. Audette et al have presented a survey paper [10] that overviews surface registration methods.

1.2 Voxel Based Registration

Several voxel-based registration algorithms have been developed that were shown to provide increased registration accuracy in many cases [11-13]. A few studies that have specifically addressed ictal-interictal SPECT registration accuracy [4] suggest that voxel-based registration is more accurate than surface matching, and AIR algorithm [14] is more robust than (normalized) mutual information [15-18].

1.3 Using Additional Information in Registration

To improve the registration accuracy of SPECT registration, use of additional information such as a simultaneously acquired transmission data, injection of a second radionuclide or usage of a scatter window data have been proposed. Pluim et al [19] made a comprehensive survey of various mutual-information-based registration techniques of more than two images, where multiple images are simultaneously registered. Without acquiring additional data, MRI set is already available as additional information in SISCOM. This study investigates whether using MRI as additional information can improve the accuracy of ictal-interictal SPECT registration accuracy. The problem is formulated as simultaneous three-image-registration (ictal, interictal SPECT and MRI).

Our initial investigation results are presented in [20]. This article explains our methodology, and presents simulation, phantom and patient study results. More detailed analysis is given in [21].

2. METHODS

2.1 Proposed Registration Method

In our investigations for simultaneous three-image-registration, a surface-based approach is taken [20, 21], since formulation of the simultaneous voxel-based three-image-registration (SPECT-SPECT-MRI) is not trivial [19]. The approach taken in this section can be extended to a voxel-based cost function in future studies.

Registration problem is defined as simultaneous registration of ictal, interictal SPECT and MRI brain image surfaces. It is achieved as minimization of squared distance function below with respect to two rigid transformation functions T_1 and T_2 (each has 3 rotation, 3 translation parameters; a total of 12-parameters) between two SPECT and one MRI image sets:

$$D^2_{triple}(T_1(Y),T_2(Z),X)=\frac{1}{N_y}\sum_{i1}\|T_1(y_{i1})-x_{i1}\|^2 + \frac{1}{N_z}\sum_{i2}\|T_2(z_{i2})-\underline{x}_{i2}\|^2+\alpha\frac{1}{N_y}\sum_{i1}\|T_1(y_{i1})-\underline{z}_{i1}\|^2 \quad (1)$$

in which, $\{y_{i1}\}$ for $i1=1,\ldots,N_y$ is a set of points on the ictal brain surface Y, $x_{i1}=C(\ T_1(y_{i1}),\ X\ )$ is a point on the MRI brain surface X closest to $T_1(y_{i1})$; $\{z_{i2}\}$ for $i2=1,\ldots,N_z$ is a set of points on the interictal brain surface Z, $\underline{x}_{i2}=C(\ T_2(\mathbf{z}_{i2}),\ X\ )$ is a point on the MRI surface X closest to $T_2(z_{i2})$; and $\underline{z}_{i1}=C(\ T_1(y_{i1}),\ T_2(z_{i1})\ )$ is a point on the transformed interictal surface Z closest to $T_1(y_{i1})$, i.e. transformed ictal surface Y. In our implementation, $\underline{z}_{i1}=C(\ T_2^{-1}T_1(y_{i1}),\ z_{i1}\ )$, whose result is identical to the previous formula.

Note that in simultaneous three-image-registration, there are only two degrees of freedom (two transformations: T_1 and T_2) to be determined. We use MRI as "to" image volume in registration for both T_1 and T_2. Either transformation can be replaced by a transformation from ictal to interictal volumes (lets call it T_3), but this will not affect the methodology, since this transformation is a function of others.

The first term in (1) is the average squared distance between transformed (T_1) ictal surface and MRI surface. The second term is the average squared distance between transformed (T_2) interictal surface and MRI surface. The third term is the average squared distance between transformed (T_1) ictal and transformed (T_2) interictal surfaces. α is a constant to adjust the proportional weight of the squared distance between SPECT-SPECT surfaces versus that between SPECT-MRI surfaces. Such a term is considered appropriate in order to accommodate intra-modality and inter-modality distance terms together in the same cost function (1). Optimum α is determined by min. ictal-interictal SPECT registration error.

In order to evaluate the cost function (1), we need to compute the distance of a surface point in one data set to the other surface. To do this, the simplest approach is to determine the closest point among the points of the surface. In our implementation, k-d tree technique is used [22, 23] for fast computation (alternatively, chamfer distance based fast computation [6] may be used). To determine the optimum transformation parameters, the cost function (1) has to be minimized with respect to 12-parameters ($t1_x$, $t1_y$, $t1_z$, $r1_x$, $r1_y$, $r1_z$, $t2_x$, $t2_y$, $t2_z$, $r2_x$, $r2_y$, $r2_z$). We choose Powell algorithm [24] to this optimization (parameter is set to 10^{-4}).

Our investigations have revealed that, the cost function (1) has many local minima around the global minimum. But the cost function behaves as quite quadratic away from the global minimum. Therefore, after first Powell run, it converges to a local minimum within very close proximity of global minimum. Because of this behaviour, we decided to use randomly distributed initial configurations technique [15]: initializing Powell algorithm with 16 uniformly distributed random point set (within ±2 mm and ±2 degree of first Powell run solution), and then choosing the solution that achieves minimum cost function. Genetic algorithm [25], simulated annealing [24] and multiresolution approach [15, 26] are some of the other possible techniques.

2.2 Simulations

Validation of this study is difficult due to lack of appropriate (ictal, interictal SPECT and MRI) data set with external markers [13]. For these reasons, a realistic simulation study is conducted to compare the accuracy of ictal-interictal registration in: (i) simultaneous (triple) ictal-interictal-MRI registration and (ii) pairwise ictal-interictal registration.

The Monte-Carlo code developed in [27] is adapted for brain SPECT geometry. A high resolution patient brain MRI volume (T1-weighted, MPRAGE) is used (Fig. 1a) with voxel size 1x1x1mm. Cerebral and extracerebral regions are first segmented using "Brain Extraction Tool" [28]. Cerebral region is next segmented using probabilistic SPM2 (2003) [29] software. Voting is then applied to identify non-overlapping gray matter (GM), white matter (WM), cerebrospinal fluid (CSF) and extracerebral regions (ECR) where the class having maximum probability by SPM segmentation is chosen (Fig. 1b). The image intensities in each region is modified so that the radioactivity ratios of 24:10:1:1 are assigned to GM, WM, CSF, ECR respectively to form interictal SPECT template, as shown in Fig. 1c [30]. In order to create the ictal template, the interictal template is modified to represent contrast changes between ictal-interictal images: volumetric Gaussian activity spots of varied size (STD=10-20 mm) and amplitude (25-75% of the GM activity level) are added to form ictal SPECT templates (Fig. 1d). Next, the Monte-Carlo simulator is run using the ictal and interictal templates to generate projection data from a total of 120 angular views around 360deg to generate 5-pairs of ictal-interictal sinograms (count rates: 4.6 million counts for ictal and 7.0 million counts for interictal). Then, planes of images are reconstructed by using Filtered Back Projection (FBP) algorithm as shown in Fig. 1e-1f. Attenuation correction is implemented based on Chang method [31].

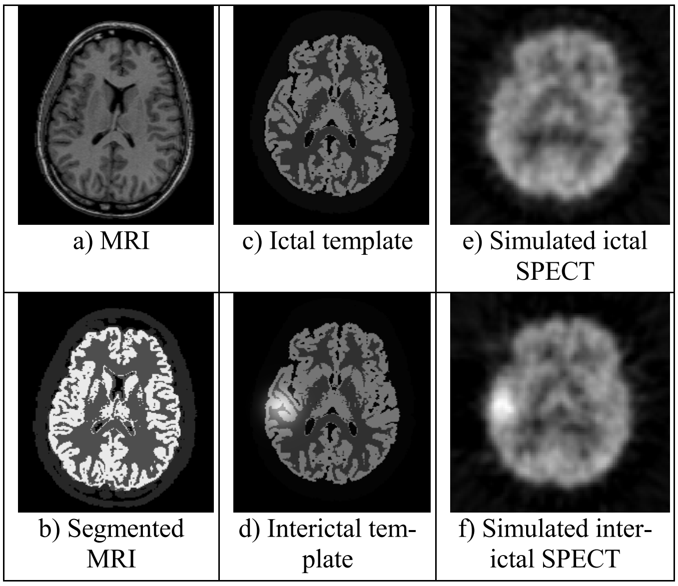

Figure 1: A slice from (a) MRI, (b) segmented MRI into GM, WM, CSF and ECR, (c) ictal template, (d) interictal template, reconstructed (e) ictal, (f) interictal image.

Next, 15 sets of Gaussian distributed random translation and rotation parameters are generated (STD=10 degrees for rotation and STD=10 mm for translation parameters). Using these parameters, 5-pairs of reconstructed ictal and interictal images are translated and rotated to obtain 15 image sets in random orientation for the registration algorithm in order to represent clinically unknown translation and rotated situation. Relative transformations between ictal and interictal SPECT is within ±35.85 mm and ±33.64 degrees.

After that, reconstructed SPECT images are thresholded to segment brain regions. A fill algorithm is used to segment all the voxels within the brain and boundary voxels in MRI and SPECT images are obtained. Next, pairwise- and triple- registrations are done by running Powell algorithm with randomly distributed initial configurations (to reach global minimum) to compute registration parameters.

Finally, the registration accuracy of each method is measured by computing the average Euclidean distance of 6 predetermined points which are on brain surface in orthogonal directions away from the center of mass of brain. We call this "registration error" in the results section.

2.3 Phantom and Patient studies

Since true registration parameters of phantom and patient images could not be known, an absolute measure of registration accuracy could not be obtained. Therefore, phantom and patient image registration tests are done by visual comparison method where physicians are made available all the views of registered images: colored/fused.

3. RESULTS

3.1 Simulation Results

The simulation data registration error results are shown in Table 1 for 15 image sets for different methods. Triple-registration method gives smaller ($p<0.05$) registration error than pairwise surface-registration method, only for the following α values: $\alpha=0.3$, $\alpha=0.5$, $\alpha=0.7$. However, for the cases: $\alpha=0.0$ and $\alpha\geq1.0$, statistically significant reduction in error is not obtained. Normalized mutual information (NMI) method (pairwise) results show that NMI error is smaller than all surface-based triple-registration errors ($p<0.001$).

	Surface-based triple registration						Surf.	Voxel
Set #	**α=0**	**0.3**	**0.5**	**0.7**	**1.0**	**2.0**	**pair**	**NMI**
1	0.90	0.79	0.76	0.73	0.71	0.71	0.69	0.26
2	1.89	1.75	1.72	1.77	1.79	1.85	1.88	0.33
3	0.72	0.83	0.84	0.85	0.90	1.14	1.69	0.38
4	1.55	1.63	1.68	1.70	1.73	1.84	1.88	0.46
5	0.96	0.73	0.75	0.77	0.78	0.82	0.85	0.37
6	0.65	1.27	1.33	1.39	1.42	1.52	1.58	0.50
7	1.44	1.42	1.50	1.46	1.55	1.60	1.66	0.56
8	1.08	1.54	1.59	1.64	1.66	1.67	1.72	0.55
9	1.12	0.69	0.67	0.70	0.72	0.88	0.88	0.93
10	0.96	1.11	1.18	1.22	1.25	1.32	1.41	0.30
11	1.20	1.14	1.17	1.18	1.19	1.21	1.28	0.67
12	1.72	1.58	1.56	1.54	1.55	1.53	1.54	0.54
13	1.39	1.32	1.31	1.30	1.33	1.35	1.26	0.98
14	2.01	1.95	1.88	1.86	1.86	1.85	1.88	0.53
15	1.22	1.29	1.31	1.31	1.33	1.26	1.15	0.76
Avg	**1.26**	**1.27**	**1.29**	**1.30**	**1.32**	**1.37**	**1.43**	**0.54**

Table 1: **Ictal-interictal registration error (mm) of 15 image sets using surface-based triple and pairwise registration and voxel-based pairwise normalized mutual information (NMI) methods. The last row displays the average error computed among 15 sets.**

If the cost-function (1) is examined carefully, the result of the optimization for $\alpha=0.0$ corresponds to individual SPECT-MRI registrations; on the other hand, for high α values, solution converges to pairwise (ictal-interictal) registration. Therefore, both limiting cases of α values are not expected to be the optimum working point of triple-registration, justifying the above statistical analysis results.

3.2 Phantom and Patient Study Results

Observer study results of phantom and patient data revealed no observable difference between the registration method results. We should point out that for the best performance of the method introduced in this paper, geometric and scale distortion in MRI should be corrected prior to application of the method [32]. In our phantom and patient studies, we were not able to do these corrections on MRI data, similar to many studies in the literature.

4. CONCLUSIONS

The results of the simulation study have demonstrated that, in surface-based registration, triple-registration method results in smaller ictal-interictal SPECT registration error than the pairwise registration method ($p<0.05$) for a range of cost-function parameter values. But, improved registration error is still higher than NMI error ($p<0.001$), which is a voxel-based registration algorithm. However, the results of this study can be used in the near future research to apply the triple-registration principle into improving the voxel-based registration results of ictal-interictal registration.

ACKNOWLEDGEMENTS

The authors thank Serap Saygı, Ayşenur Cila, Doğan Bor and Osman Saka for their assistance, helpful discussions and for providing MRI set.

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