SIMULTANEOUS REGISTRATION OF ICTAL SPECT, INTERICTAL SPECT AND MR IMAGES FOR EPILEPSY STUDIES: METHOD AND SIMULATIONS

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ABSTRACT
Subtraction of ictal and interictal single-photon emission computed tomography (SPECT) images is known to be successful in localizing the seizure focus in presurgical evaluation of patients with partial epilepsy. The subtracted images are also aligned with a patient’s high-resolution magnetic resonance image (MRI) and fused to identify the anatomical regions involved in the seizure. Computer-aided methods for producing subtraction ictal SPECT coregistered to MRI (SISCOM) have been developed. There are two registrations involved in SISCOM: between the ictal-interictal SPECT images and between the ictal image and MRI. Registration error of the first one has been shown to be more crucial. This article introduces a new method of registering all three images (ictal, interictal SPECT images and MRI) simultaneously in order to improve the registration accuracy of ictal-interictal SPECT images. Accuracy of this method is analyzed by Monte-Carlo simulation studies.

KEY WORDS
Image registration, ictal SPECT, SISCOM, Epilepsy

1. Introduction
SISCOM has been shown to improve the sensitivity and specificity of SPECT in identifying the seizure focus in presurgical evaluation of patients with partial epilepsy [1,2]. It was shown to outperform side-by-side visual interpretation and manual registration approaches. SISCOM steps include [4]: registering the ictal-interictal images; normalizing and subtracting them; registering the ictal image with MRI; displaying subtracted image on MRI. The registrations in SISCOM are either done by surface-based or voxel-based rigid-registration methods [4].

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 [3]. Registration errors (even subvoxel) at this step produce false-positive activation areas and obscured true-positive activation areas [3]. Therefore, the recommended approach is to register the two SPECT images, rather than registering each to MRI [4].

To improve the registration accuracy of SPECT registration, use of additional information such as simultaneously acquired (hence registered) transmission data, use of second radionuclide or use of scatter window data has been proposed and investigated. A recent paper by Hutton et.al. lists the related papers [5]. In order to incorporate such additional data, Pluim et.al. explains and references various mutual-information-based registration techniques [6].

Also in [6], another type of registration of multiple images has been explained when no knowledge about the transformation between individual images is available. Hence multiple transformations are to be found to transform the images to a common coordinate system. This approach has already been taken in [7] to register dynamic sequence of SPECT study frames to each other by using principle component analysis. It has been demonstrated by simulation and patient studies that simultaneous registration of multiple dynamic image sequence results in better performance than pair wise image registration techniques[7].

The above summarized studies motivated us to test whether registering ictal, interictal SPECT and MR images simultaneously can potentially improve the registration accuracy of ictal-interictal SPECT images.

This article shows our investigation results we have conducted so far using Monte-Carlo simulations. Section 2 summarizes SISCOM, 2.1 reviews surface-based registration techniques, 2.2 reviews voxel-based registration techniques, 2.3 introduces our new approach, 2.4 explains the simulations conducted, 2.5 gives the results.

2. SISCOM and Registration
Computer-aided methods for SISCOM are commonly used. SISCOM algorithm in Analyze software consists as the following steps [4]:

- Image masking: By thresholding and morphological image processing, masks of cerebral volumes of ictal and interictal SPECT images are obtained.
• Ictal and interictal image registration: Brain surface contours from mask images are used in surface-based registering. Voxel-based algorithm can also be used.
• Normalization: Mean brain pixel intensities of the ictal and interictal SPECT brain images are normalized to a constant value (to account for the differences in tracer uptake and decay).
• Subtraction: The normalized interictal image is subtracted from normalized ictal image. 2 std and above are chosen only as significant activation pixels.
• MRI coregistration: The extracerebral pixels on MRI are removed and the ictal image is coregistered to the extracted MRI brain using surface matching. A fused display of color-mapped SPECT activation areas are shown on extracted brain MRI.

SISCOM has been shown to improve the sensitivity and specificity SPECT in identifying the seizure focus in presurgical evaluation of patients with partial epilepsy [1,2]. Recent studies suggest that the sensitivity and specificity of SISCOM may surpass those of MRI, PET, scalp-recorded EEG, interictal SPECT, and visual analysis of ictal SPECT [1,2].

2.1 Surface Based Registration

In SISCOM, brain surface registration techniques [8,9] have traditionally been used to produce subtraction SPECT images [10,11]. 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 of accuracy [10]. Interpolated closest point transform that is recently introduced for medical images [13] claims that it can lead to registration accuracy that is comparable to that of voxel-based methods. Iterative closest point transform algorithm [12] is a widely used algorithm in arbitrary surface matching problems. Finally, [14] is a recent survey paper that overviews surface registration methods for medical imaging.

2.2. Voxel Based Registration

Several voxel-based registration algorithms have been developed that have been shown to provide increased registration accuracy in many cases [15-17]. However, because of the significant image contrast changes between ictal and interictal images (due to the difference in rCBF patterns), voxel-intensity based algorithm must be robust to these changes. A survey of other algorithms for coregistering SPECT or PET images are listed in [4]. A few studies that have specifically addressed ictal-interictal SPECT registration accuracy suggest that voxel-based registration is more accurate than surface matching [3], and Woods’ AIR algorithm [18] may be more robust than mutual information based algorithms [19-21] to ictal-interictal blood flow changes [3].

2.3 Proposed Registration Method

In our initial investigation for three-image-registration, a surface-based approach is taken. Registration problem is defined as optimization of a cost function:

\[
C(T_1, T_2) = \sum_i || T_1(y_i)-x_i ||^2 + \sum_i || T_2(z_i)-x_i ||^2 + \alpha \sum_i || T_1(y_i)- T_2(z_i) ||^2
\]

In (1), \(\alpha\) is a constant term to adjust the proportional weight of the ictal-interictal registration error versus SPECT-MR registration errors. Optimum \(\alpha\) is determined by a search mechanism. The optimization of the cost function (1) with respect to 12-parameters is done using Powell algorithm with standard parameters [24]. Initialization of \(T_1\) and \(T_2\) are computed by ICP algorithm [12].

2.4 Simulations

A realistic Monte-Carlo simulation study is conducted to compare the accuracy of ictal-interictal registration by using (i) ictal-interictal-MR registration method and (ii) direct ictal-interictal registration.

Monte-Carlo code developed in [25,26] is adapted for brain SPECT geometry. Photoelectric and single-scatter attenuation within head and photoelectric interactions within the detector are modeled. Energy resolution of detectors are modeled as a Gaussian function with 25% std. System geometry is as follows: parallel-hole collimator aperture size 2.2mm, aperture length 4.0cm, septal thickness 0.5mm. Detector array is a 60*60 array with 0.35*0.35 elements (detector total imaging area of 21*21cm). Detector and collimator rotates around maximum fov diameter of 22cm.

A patient brain mprage T1-weighted MRI set is used (Figure 1a) with 170*218*149 voxels of size 1*1*1mm. It is segmented using probabilistic SPM 2 (2003) [27] software. Voting is then applied so as to identify non-overlapping gray matter (GM), white matter (WM), CSF and extracerebral regions (ECR) (see Figure 1b) where
the class having maximum probability by SPM segmentation is chosen. The image intensities in each region is modified so that the activity rates of 10:3.3:1:0.01 are assigned to GM, WM, CSF, ECR respectively (Figure 1c). This template image is in perfect registration with MRI. It is then translated and rotated ($t_x=10\text{mm}, t_y=-3\text{mm}, t_z=5\text{mm}, r_x=1\text{deg}, r_y=-3\text{deg}, r_z=5\text{deg}$) to represent ictal SPECT template.

In order to create the interictal template, the original ictal template is modified significantly to represent contrast changes between ictal-interictal images. This modification is done by adding and subtracting volumetric regions of various sizes and amplitudes to the template (Figure 1d). This template is then translated and rotated to 15 different positions listed in Table 1 to represent interictal templates.

![Figure 1: A slice from the volume of (a) MRI, (b) segmented MRI into gray matter, white matter, CSF and extracerebral regions, (c) ictal template with activity rates of 10:3.3:1:0.01 for GM, WM, CSF, ECR before translation/rotation, (d) interictal template by contrast altering interictal template before translation/rotation, (e) FBP reconstructed ictal image, (f) FBP reconstructed interictal image.](image)

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 360\text{deg} (count rate of approx. 100K/slice).

The sinogram data of opposing angles are geometrically summed and 2D smoothing is applied by convolving with a $9\times9$ Gaussian filter of std=0.6. Then, image is reconstructed by using FBP algorithm at a pixel size of 2\text{mm} for all image planes. Filter in FBP is implemented using a frequency domain filter: $\sin(n\pi/r)$, where $r$ is roll-off factor as a fraction of Nyquist frequency “1.0”, and $n=\{0,...,0.5\}$ is frequency index vector. When $r<0.5$, filter coefficients are set to zero for $n>r$ ($r$ is chosen as 0.4 for this data).

Attenuation correction is implemented in a post-processing step using a correction matrix based on Chang’s technique [28].

Reconstructed images are thresholded to obtain the boundary points in each set. ~25,000 points in MRI and ~10,000 points in SPECT images are chosen to represent surfaces.

Next, the registration algorithms are run using MR and reconstructed SPECT images.

The evaluation of accuracy is performed by computing the average Euclidean distance error of 8-bounding box corner points around the brain. For each of the reoriented images, the position of the points transformed using the true transformation is compared with the position of points transformed using the transformation recovered from the registration. The displacement of the points due to difference between the recovered and true transformation is considered to be the error of registration. This is the same error measure used in [29]. It gives a much higher per-voxel registration error for brain, since the points considered are very far from the brain center.

2.5 Simulation Results

The registration results are shown in Table 2 for 15 image sets as the average displacement of 8-bounding box corner points of ictal-interictal images in units of mm. The second column displays the results for the direct ictal-interictal (2-image) registration method, and the other columns display results for inter-ictal-MR (3-image) registration method.

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Table 1: Translation (mm) and rotation (deg) values of interictal templates.
The results show that all of the 3-image surface registration results gave a smaller registration error than direct SPECT-SPECT surface registration. The results also reveal that the registration error reaches minimum at $\alpha=0$, in which case the cost minimization problem becomes two independent SPECT-MR registration problems.

ICP algorithm takes $\sim$1min to run on 2.0Ghz Pentium processor PC. The additional registration time required for three-image registration is $\sim$2min. Memory requirement of three-image registration is not significantly more than that of ICP algorithm.

### 3. Conclusion

The results indicate that ictal/interictal SPECT-MR surface registration method results in better SPECT-SPECT registration error than SPECT-SPECT surface registration method by 30%. The potential benefit of simultaneous three-image registration technique to improve the registration accuracy of SPECT-SPECT registration in voxel based registration remains to be seen.

As a future work, we are planning to look at the following issues:

- Incorporating voxel-based registration criteria, such as AIR [18] and mutual-information in (1).
- Incorporating hybrid (surface and voxel based) cost function in (1).
- Doing phantom and/or patient studies for validation.
- Looking at generalization of the technique to N-data volumes, for $N>3$.

### Acknowledgements

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### References:


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**Table 2: Registration error of 15 image sets as the average displacement of 8-bounding box points of ictal-interictal images in units of mm. The second column displays the errors for direct ictal-interictal registration method, and the other columns display the error for ictal-interictal-MR registration method.**