AN EFFICIENT ALGORITHM FOR REGISTRATION OF PRE- AND INTRA- OPERATIVE BRAIN MRI IMAGES TO CORRECT INTENSITY INHOMOGENEITY

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ABSTRACT

Spatially-varying intensity inhomogeneity is a severe artifact, which occurs in intra-operative MR images of the brain. This artifact causes implications in the accuracy of image guided navigation systems being performed during neurosurgery procedures. Therefore, it is highly desirable to correct intensity inhomogeneity along with registration process to achieve an efficient and adaptive method to the image guided surgery constraints. In this paper, a modified Residual Complexity similarity measure is used to correct this artifact with the registration of pre- and intra-operative images. The results show that this similarity measure outperforms some well-known similarity measures such as NMI and SSD in registration of pre- and intra-operative images of the brain, by 31.5%.

KEYWORDS: intensity inhomogeneity; non-rigid image registration; similarity measure; residual complexity.

1. INTRODUCTION

Image intensity variation occurs in Magnetic Resonance Imaging (MRI) as a result of multiple factors such as radio-frequency (RF) coil non-uniformities, static field inhomogeneity and patient anatomy and position. The intensity inhomogeneity is a substantial artifact in real MR data and varies spatially in the image domain, due to inhomogeneities of B_0 and B_1 fields [1]. The inhomogeneity of the magnetic field is more significant in open-bore low field MRI systems with respect to conventional closed-bore systems [2]. In addition, by using surface coil detectors instead of head coils, the image intensity is brighter near the coils than deeper in the brain. As a result, surface coil detectors have inherently inhomogeneous reception profile, which leads to slowly varying intensity variations throughout the image [3]. The most commonly used intra-operative MRI systems during image guided neurosurgeries are low-field open-bore systems using surface coil detectors [4]. Therefore, this artifact may severely challenge intensity based image processing algorithms such as segmentation and registration used in image guided neurosurgeries.

One of the key steps in image guided neurosurgery with intra-operative MR imaging is the registration of pre- and intra-operative images. Several non-rigid registration methods have been proposed, including biomechanical models [5-6] or image-based methods [7-8], in which the focus has been on the type of transformation used. However, the selection of proper non-rigid registration technique requires considering the constraints of intra-operative imaging such as spatially-varying intensity distortions, which affects finding correspondences between images. In fact, one of the main components of image registration is the selection of an appropriate similarity measure, which is optimized in the correct alignment of the two images.

Regardless of the type of transformation used for registration of pre- and intra-operative MR images of the brain, there have been some similarity measures such as Sum of Squared Distances (SSD) [5], Normalized Mutual Information (NMI) [7] and Cross Correlation (CC) which are used extensively in literature. These similarity measures consider the correspondences between pixels regardless of their spatial dependencies, and are mainly based on the assumption that the intensity is spatially stationary over the image. However, this is not the case where the intensity distortions occur due to field inhomogeneity. The intra-operative constraints limit the application of time consuming pre-processing techniques for eliminating the effects of intensity distortions before image registration. Thus, it is highly desirable to use an embedded approach to solve both problems of intensity

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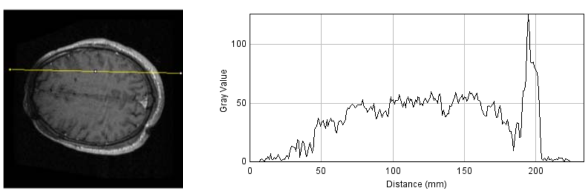
correction and precise registration in a unified framework.

Recently, Myronenko *et al* proposed a novel similarity measure called "Residual Complexity (RC)" for registration of images, which are corrupted by spatially-varying intensity distortions [9-10]. Their main idea was to minimize registration error in the Discrete Cosine Transform (DCT) domain rather than in pixel domain. Inherited from this idea, we utilized RC to perform registration procedure more locally and sparsely which is suited for real-time image guided neurosurgeries. In this paper, the performance of RC similarity measure to correct the intensity inhomogeneity occurring in intra-operative images is evaluated and compared with three conventional similarity measures.

In the next section, registration algorithm using RC is described. The algorithm is evaluated on synthetic data and then tested in registration of pre- and intra-operative images of the brain. The results are given in section 3, and finally, the discussion on the results is presented in section 4.

2. MATERIALS & METHODS

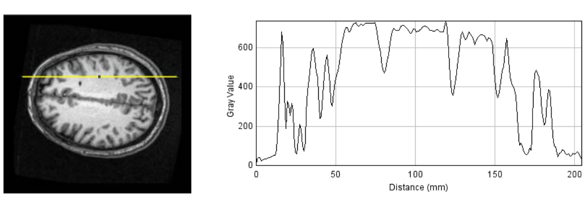
As explained before, intra-operative MR images are corrupted by spatially-varying intensity distortions as shown in Figure 1.



(a) (b)

Figure 1. (a) An example of intra-operative image with intensity distortion on its left side; (b) the profile of the same image.

As it can be inferred from Figure 1, the profile sketched for the brain image has a peak on its right side, which corresponds to an intensity peak of tissue signal. This peak is due to field inhomogeneity as it is missed out on the right side of the image. Figure 2, illustrates the same slice from pre-operative scan and its profile, which clearly shows both peaks. This image does not contain image intensity inhomogeneity throughout its profile. This example highlights the necessity of correcting this artifact along with registration procedure.



(a) (b)

Figure 2. (a) Pre-operative scans of the same slice in Figure 1; (b) the corresponding profile.

Image registration is composed of three main steps: similarity measure, transformation and optimization. This paper is focused on the role of the similarity measure to be adapted to the registration conditions. The optimum value of the similarity between two images can be obtained in the correct alignment of both images.

2.1. Definition of Residual Complexity

Residual Complexity is defined by eliminating the intensity inhomogeneity from the similarity measure formulation through solving the registration problem, analytically. The correct alignment is achieved where the residual of the images to be registered, reaches its minimum complexity. RC performs registration and intensity correction problems, simultaneously. This is done by introducing an intensity correction field that aligns the two images. An adaptive regularization term is defined for the intensity correction field. The registration problem is then solved analytically for intensity correction field and the regularization term. This procedure is fully explained in [10]. Due to the lack of space, only the final formulations are addressed here.

Consider two images *I* and *J*, which are to be aligned using the geometric transformation defined by *T*. The energy function of *RC* similarity measure is defined by:

$$E(T) = \sum \log\left(\left(q_n^T r\right)^2 / \alpha + 1\right) \tag{1}$$

$$r = \left(I - J(T)\right)$$

where α is a trade-off parameter and 'q_n' s are DCT basis functions. There are different choices for DCT basis functions, which are discriminated from one another regarding the choice of boundary conditions. In RC formulation, the commonly used form of DCT basis functions in image processing, i.e. DCT-II corresponding to Neumann midpoint boundary condition, is used for representation of 'q_n's. DCT-II is defined by the following formula in 1-D:

$$q_n(k) = \frac{w_n}{\sqrt{N}} \cos\left(\frac{\pi(2k-1)(n-1)}{2N}\right), \tag{2}$$

for $k = 1, 2\ldots$ N, $n = 1, 2\ldots$ N and

$$w_n = \begin{cases} 1, \ldots n = 1, \\ \sqrt{2}, \ldots n = 2 \ldots N. \end{cases} \tag{3}$$

where *N* is the size of the block on which the transform is performed.

As it can be seen in the above formulas, smaller DCT coefficients are more penalized with respect to the larger ones due to the existence of the term $log(x^2+1)$. The *log* function decreases rapidly to zero as the number of points is increased, causing the DCT coefficients to become sparse [9-10]. Therefore, the minimum value of RC similarity measure is achieved at the correct alignment of the two images, where the residual image can be represented using only a few DCT basis functions. This way, the images can be registered optimally even in the presence of spatially-varying intensity inhomogeneity.

2.2. The Algorithm

Here, the Free Form Deformation (FFD) Bspline transformation, which has been applied in registration of pre- and intra-operative MR images, is used for modeling the deformations of the brain [7]. In the transformation selection step of image registration, the goal is to find an optimal transformation **T**: $(x,y,z) \rightarrow (x',y',z')$ that corresponds each point in the source image to its corresponding point in the reference image. The FFD model based on Bsplines deforms the object (here the brain) by operating on a mesh of control points. In order to define the Bspline-based FFD, we consider the image domain as $\{(x,y) | 0 \le x \le N, 0 \le y \le M, 0 \le z \le M\}$. The $n_x \times n_y \times n_z$ mesh of control points $p_{i,j,k}$ with uniform spacing can be defined on the image domain. The FFD can be denoted as 3D tensor product of 1D cubic Bsplines:

$$T(x,y,z;p)= \sum_{n=0}^{3}\sum_{m=0}^{3}\sum_{l=0}^{3} B_n(u_x) B_m(v_y) B_l(w_z) p_{i+k,j+m,k+l} \quad (4)$$

where $i=\lfloor x/n_x \rfloor -1$, $j=\lfloor y/n_y \rfloor -1$, $k=\lfloor z/n_z \rfloor -1$, $u_x=x/n_x-\lfloor x/n_x \rfloor$, $v_y=y/n_y-\lfloor y/n_y \rfloor$, $w_z=z/n_z-\lfloor z/n_z \rfloor$; and B_n is the n-th basis function of B-spline [7]:

$$\begin{aligned} B_1(u) &= (1-u)^3/6 \\ B_2(u) &= \left(3u^3-6u^2+4\right)/6 \\ B_3(u) &= \left(-3u^3+3u^2+3u+1\right)/6 \\ B_4(u) &= u^3/6 \end{aligned} \quad (5)$$

For optimization of the RC cost function, the gradient descent method is applied.

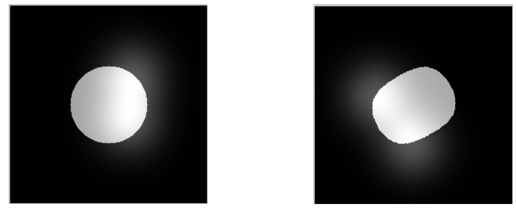
2.3. Dataset

In registration of pre- and intra- operative images, it is essential for the pre-operative (source) image to align the brain boundaries to those of the corresponding intra-operative (reference) image. In order to evaluate the performance of the algorithm in registering main features of images such as boundaries, which are the key point in our application, the algorithm is first applied to circle synthetic images. The synthetic reference image is a 256×256 circle image. This image is deformed using a sum of sinusoidal functions to construct the source image. The spatially-varying intensity inhomogeneity is simulated by adding a mixture of K Gaussian functions with standard deviation of *30* to the images as:

$$I_{after}(x,y) = I_{before}(x,y) + \frac{1}{K}\sum_{k=1}^{K} e^{-\frac{\|[x;y]-\mu_k\|^2}{2(30)^2}} \quad (6)$$

where $I_{before}(x,y)$ and $I_{after}(x,y)$ are the images before and after adding intensity inhomogeneity distortions, respectively, K is the number of Gaussians, x and y are the pixel locations, and μ_k defines the mean locations of the Gaussians.

Both the source and reference images are distorted using the abovementioned intensity distortion with different means of Gaussian functions. The corrupted reference and source images are illustrated in Figure 3.

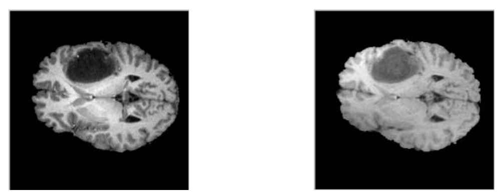


(a) (b)

Figure 3. The reference (a) and source (b) images to be registered.

The algorithm is then tested on the real pre- and intra-operative MR data. The dataset used for this work are adopted from Surgical Planning Laboratory at Harvard Medical School website (www.spl.harvard.edu/). The images are acquired from patients undergoing tumor resection surgeries, acquired on a 1.5T pre- and 0.5T intra-operative scanners. The resolutions of the images are either 256×256 or 286×286, with either 120 or 90 slices. The voxel resolution is 0.9×0.9×2.5 mm^3.

The brain tissue is segmented from the skull in the pre- and intra-operative images using *3D Slicer* software. An example of the pre- and intra-operative MRI images of the brain used is shown in Figure 4.



(a) (b)

Figure 4. An example of (a) pre- and (b) intra- operative MR images of the brain before and after opening dura. The brain tissue is segmented from skull in the images.

2.4. Implementation

The regularization term, which is used as the trade-off between the alignment of two images and the smoothness of FFD Bspline transformation is set to 0.01 and the value of α is selected to be 0.05. The algorithm is performed hierarchically in 3 different scales, with 70 iterations and grid spacing equal to 5.

2.5. Evaluation

2.5.1 *Synthetic data*

As noted before, it is essential to evaluate the performance of the registration algorithm in aligning main features like the edges of one image to those of the others. Therefore, a metric, which compares the edges, should be selected for evaluation. In order to quantify the results, the Baddeley's Delta image Metric (BDM) [11] is used. This metric is used successfully in evaluating binary images. Unlike the other metrics, it considers spatial information of the pixels and it provides a better visual result. This metric can be calculated using the following formula:

$$\Delta_w^p(A,B)=\left\{\frac{1}{N}\sum_{x\in X}\left|w[d(x,A)]-w[d(x,B)]\right|^p\right\}^{1/p} \qquad (7)$$

Where Δ indicates the delta metric, w is a convex continuous function, p is the value of the norm, and N is the total number of pixels in location 'x' in images **A** and **B**. In most applications, Baddeley suggests using the following function:

$$w(z)=\min\{z,c\}, \qquad (8)$$

where $c > 0$ is a constant [11].

If p=1, Δ is the mean of the difference of distances; by choosing p=2, Δ is the mean Euclidean distance. For $p\rightarrow 0$, Δ approaches its minimum and for $p\rightarrow\infty$, Δ approaches the maximum difference between the two sets. Here, we selected p=2 and c=1 [12]. The images are most similar when the value of Δ is small. This value ranges between *0* and *c*.

2.5.2 *Real data*

The registration is performed on real pre- and intra-operative MR images of the brain. The results are evaluated using "inverse consistency error" metric proposed by Christensen *et al* [13]. The inverse consistency metric evaluates registration performance based on desired transformation properties. This metric measures the inverse consistency error between a forward and reverse transformation between two images. Ideally the forward transformation should be equal the inverse of the reverse transformation implying a consistent definition of correspondence between two images. Thus, composing the forward and reverse transformations together produces the identity map when there is no inverse consistency error. The inverse consistency error is defined as the squared difference between the composition of the forward and reverse transformations and the identity mapping.

The voxel-wise cumulative inverse consistency error (CICE) with respect to template image j is computed as:

$$CICE_j(x)=\frac{1}{M}\sum_{i=1}^{M}\left\|h_{ji}\left(h_{ij}(x)\right)-x\right\| \qquad (9)$$

where $h_{ij}(x)$ is the transformation from image i to j, M is the number of images in the evaluation population and ||.|| is the standard Euclidean norm [13-14].

3. RESULTS

The evaluation of the performance of the algorithm with respect to other similarity measures, and in response to various amounts of Gaussian noise and intensity inhomogeneity, is presented in this section.

3.1. Synthetic Images

The first step in investigating the performance of RC measure is to apply it to synthetic images, as explained in the previous section.

3.1.1 *Comparison of RC with conventional similarity measures*

In order to evaluate the performance of RC measure, the registration result obtained by this similarity measure is compared with other common similarity measures including: Normalized Mutual Information (NMI), Cross Correlation (CC), and Sum of Squared Distances (SSD). The results are illustrated in Figure 5.

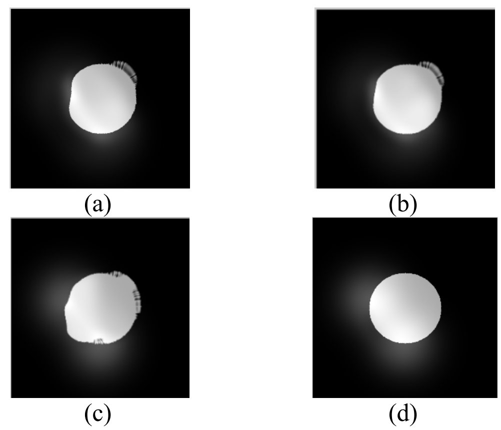


Figure 5. The comparison of the performance of conventional similarity measures: (a) SSD, (b) CC, (c) NMI with performance of (d) RC in registering images with spatially-varying intensity distortions.

As it can be observed, the RC measure has outperformed the other similarity measures in registering the two aforementioned images. The results can be better evaluated by considering the edge maps of the resulting images, as depicted in Figure 6.

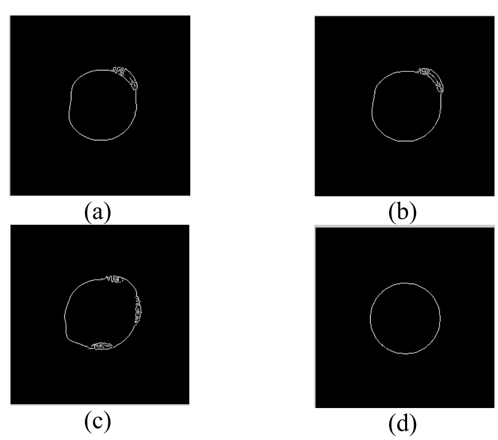


Figure 6. The edge maps of the registration results obtained from (a) SSD, (b) CC, (c) NMI, and (d) RC similarity measures.

The edge maps in Figure 6 are obtained by extracting the borders resulting from registration using various similarity measures. The edge maps are evaluated quantitatively using Baddeley's delta image metric as summarized in the following table:

Table 1. Evaluation of the performance of various similarity measures in comparison with RC using BDM

	Residual Complexity (RC)	Cross Correlation (CC)	Sum of Squared Distances (SSD)	Normalized mutual information (NMI)
Δ	0.059	0.173	0.179	0.2054

3.1.2 *The robustness of RC to Gaussian noise*

The MRI images are often corrupted by Gaussian noise, which decreases the image quality represented by Contrast-to-Noise Ratio (CNR), a commonly used term in MR image analysis [15]. CNR can be defined by the following formula:

$$CNR = \frac{|\mu_d - \mu_u|}{\sigma_u} \tag{10}$$

where μ_d and μ_u are the mean values of the desired region of interest (DROI) and the undesired region of interest (UROI), specified in Figure, respectively. σ_u is the standard deviation of the undesired region of interest.

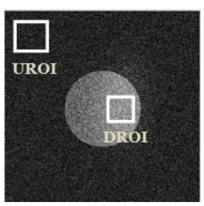


Figure 7. Definition of the desired region of interest (DROI) and the undesired region of interest (UROI).

It is essential to evaluate the robustness of RC in the presence of such noises. The images are distorted using additive Gaussian noise with various variances, which result in various CNR values. The results of registration using RC in comparison with CC, SSD, and NMI similarity measures in noisy images are evaluated in the Table 2:

Table 2. The evaluation of the robustness of RC in comparison with CC, SSD, and NMI in various image CNRs using BDM.

CNR	BDM of RC	BDM of CC	BDM of SSD	BDM of NMI
132.36	0.05	0.14	0.12	0.17
26.28	0.06	0.15	0.16	0.29
11.94	0.08	0.25	0.25	0.45
5.16	0.16	0.37	0.41	0.57
3.14	0.24	0.41	0.49	0.66

As it is apparent from Table 2, the RC similarity measure has an acceptable performance even in low CNRs about 11. This result is important in registration of pre- and intra-operative MRI images. Therefore, a registration algorithm which solves denoising problem within the same formulation is highly desirable.

3.1.3 *The robustness of RC to spatially-varying intensity distortions*

It is claimed that RC measure is an optimal similarity measure in response to the spatially-varying intensity distortions. Thus, it is applied to the problem of registering the images with various spatially-varying intensity distortions. This distortion is modeled by adding mixtures of Gaussian functions with different variances to the images. The robustness of RC in comparison with CC, SSD, and NMI is evaluated using BDM and the results are summarized in Table 3.

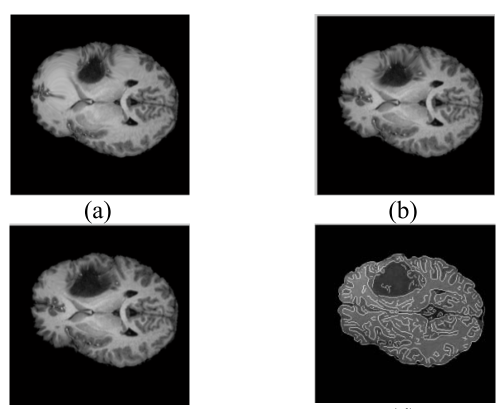
The results obtained in Table 3 imply that RC shows a degree of robustness in the presence of high spatially-varying intensity inhomogeneity values.

Table 3. Evaluation of the robustness of various similarity measures in registration of images with different values of intensity inhomogeneity.

Variance (pixels)	BDM of RC	BDM of CC	BDM of SSD	BDM of NMI
10	0.055	0.07	0.07	0.1
30	0.059	0.17	0.18	0.21
50	0.06	0.22	0.3	0.42
100	0.067	0.25	0.32	0.45
200	0.069	0.225	0.21	0.43

3.2. Real data

This procedure is then applied for registering the pre-operative MRI images of the brain to their corresponding intra-operative images. The results of evaluation using CICE measure are averaged over images of 3 patients, which are gathered in Table 4.



(a) (b) (c) (d)

Figure 8. The comparison of registering pre-operative images of the brain to their corresponding intra-operative

images using various similarity measures: (a) SSD; (b) CC; (c) NMI; (d) the overlay of edges of the registration result obtained by RC on the reference image.

Table 4. Evaluation of various similarity measures for registration of pre- and intra-operative MRI images using CICE

	SSD	CC	NMI	RC
CICE of case 1	63. 7	16.27	10.55	6.35
CICE of case 2	49.2	14.54	9.38	6.85
CICE of case 3	52.1	13.89	9.64	7.1
Mean ±Variance	55±7.6	14.9±1.5	9.86±0.38	6.76±0.146

As can be visually inspected from Figure 8(d), where the edge map of the resulting image is overlayed on the reference image, and can be quantitatively inferred from Table 4, RC provides the minimum error in registration of images, which are distorted by intensity inhomogeneity. Therefore, it has proved to outperform the other similarity measures in terms of preserving the overall topology and the borders of structures of registered images.

3.3. Modification of RC

The results can be further enhanced by thresholding the DCT coefficients. Human visual system is less sensitive to distortions around edges. Therefore, the coefficients contributing to higher frequencies can be discarded. The most frequent value of coefficients in the DCT matrix, occurring mostly in higher frequencies, is determined by taking the mode of the matrix. The coefficients, which hold this value, are set to zero, and the rest of the values remain intact. As the following table suggests, the registration is enhanced by 42% in comparison with the default RC mode.

Table 5. Thresholded RC vs. Default RC

	CICE
Thresholded RC	3.9
Default RC	6.75

4. CONCLUSION

The conventional similarity measures fail to perform well in the presence of slowly spatially-varying intensity distortions, which are common in MRI scans of the brain. This problem has been solved by using RC similarity measure, which was proved to be robust in the presence of various values of intensity inhomogeneity and Gaussian noises of different variances.

As shown throughout this paper, RC outperforms the NMI, as one of the most well-known similarity measures for image registration by 31.5%. In addition, the modified RC improves the results significantly by 42% with respect to the normal RC.

RC similarity measure provides desirable results, by focusing the optimality procedure around main anatomy of the brain from pre-operative scan along with the deformation of the tissue occurring in intra-operative images. This similarity measure can be used in image guided neurosurgery systems, to adapt the required analysis to the field of surgical operation. This enables the algorithm to compensate for the intensity inhomogeneity along with registration process, which cannot be solved during surgery using demanding processing methods, due to the limitations of operating room.

However, RC with the DCT basis functions only captures slowly varying intensity distortions. We are currently working on finding optimum basis functions to be able to adapt to the registration fields more locally and precisely.

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