A Novel Point-based Nonrigid Image Registration Scheme Based on Learning Optimal Landmark Configurations

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ABSTRACT

Image registration plays an increasingly important role in the field of medical image processing given the plurality of images often acquired from different sensors, time points, or viewpoints. Landmark-based registration schemes represent the most popular class of registration methods due to their simplicity and high accuracy. Previous studies have shown that these registration schemes are sensitive to the number and location of landmarks. Identifying important landmarks to perform an accurate registration remains a very challenging task. Current landmark selection methods, such as feature-based approaches, focus on optimization of global transformation and may have poor performance in recovering local deformation, e.g. subtle tissue changes caused by tumor resection, making them inappropriate for registering pre- and post-surgery images as a small cancerous region will be deformed after removing a tumor. In this work, a novel method is introduced to estimate optimal landmark configurations. An important landmark configuration that will be used as a training landmark set was learned for an image pair with a known deformation. This landmark configuration can be considered as a collection of discrete points. A generic transformation matrix between a pair of training landmark sets with different deformation locations was computed via an iterative close point (ICP) alignment technique. A new landmark configuration was determined by simply transforming the training landmarks to the current displacement location while preserving the topological structure of the configuration of landmarks. Two assumptions are made: 1) In a new pair of images the deformation is approximately the same size and has only been spatially relocated in the image, and that by a simple affine transformation one can identify the optimal configuration on this new pair of images; and 2) The deformation is of similar size and shape on the original pair of images. These are reasonable assumptions in many cases where one seeks to register tumor images at multiple time points following application of therapy and to evaluate changes in tumor size. The experiments were conducted on 286 pairs of synthetic MRI brain images. The training landmark configurations were obtained through 2000 iterations of registration where the points with consistently best registration performance were selected. The estimated landmarks greatly improved the quality metrics compared to a uniform grid placement scheme and a speeded-up robust features (SURF) based method as well as a generic free-form deformation (FFD) approach. The quantitative results showed that the new landmark configuration achieved 95\% improvement in recovering the local deformation compared to 89\% for the uniform grid placement, 79\% for the SURF-based approach, and 10\% for the generic FFD approach.

Keywords: Landmark-based image registration; Optimal landmark configuration; Iterative close point.

1. INTRODUCTION AND OBJECTIVE

Landmark-based nonrigid registration is a most popular method in medical image registration for its simplicity and high accuracy.\textsuperscript{1} A good landmark choice for registering medical images could result in an improved registration quality. Traditional ways to manually extracting landmarks involves manual selection of landmarks corresponding to anatomical structures, a task that usually involves engagement of medical experts. This procedure is also time-consuming and could allow for introduction of large errors,\textsuperscript{1} especially when there is large inter-observer variability between experts. Although many contributions have been made towards automatic feature-based landmark detection schemes,\textsuperscript{2} these methods mainly focus on optimization of global transformation schemes and may perform poorly when attempting to address local deformation. Alternatively, one can place the landmarks on a uniformly spaced grid.\textsuperscript{3} These landmarks may not represent informative landmarks (e.g.
landmark position on curvature) due to the uniformity and insufficient density of the sampling grid. Further, the optimal grid spacing is usually unknown to capture a local deformation (e.g. small tissue changes caused by tumor removal).

Identifying important landmarks to perform an accurate registration remains a challenging task. The objective of this work is to develop an effective approach to estimate an optimal landmark configuration to optimize image registration. The selected landmarks should not only be able to enhance registration performance, but also able to precisely capture local deformation, e.g. subtle tissue changes caused by tumor resection. For the approach presented in this work we make two assumptions: 1) by inducing a pre-defined synthetic deformation and attempting to recover the induced deformation we will be able to learn the optimal spatial configuration of landmarks, and 2) the induced deformation in the training phase is reasonably similar to the expected deformation in a new image. Therefore, this learned landmark configuration can be employed to better recover the deformation in the new image compared to an ad hoc landmark configuration (e.g. uniform) from a registration perspective.

The primary application of the algorithm developed in this paper is in the registration of pre- and post-treatment brain MRI acquired from patients suffering from aggressive brain tumors, e.g. glioblastoma multiforme (GBM). For such patients, the site of deformation (i.e. location of GBM) is known. In order to precisely evaluate changes in GBM as a function of radiation treatment, one needs to register the pre- and post-treatment MRI; hence different acquisitions may be with or without the tumor (i.e. with and without the deformation). Hence, identifying an optimal landmark configuration in the presence of different types of deformations (tumors) is not only able to enhance registration performance, but also able to precisely capture local deformation.

2. PREVIOUS WORK AND OVERVIEW OF NEW WORK

A typical landmark-based registration scheme consists of three main steps: (i) Placing landmarks on different images (either manually or automatically); (ii) establishing the correspondence between these landmarks; and (iii) computing the transformation between the images using the image correspondences obtained from (i) and (ii). Sun et al. revealed that such landmark driven schemes are sensitive to the numbers and locations of landmarks. A good landmark choice for registering medical images could result in an improved registration quality.

Traditional ways to manually extracting landmarks could allow for identification of the most important landmark points based on expert knowledge. For instance, Lombaert et al. introduced landmarks in the graph cut minimization framework where the point landmarks were placed on the blood vessels to perform a non-rigid registration on two arbitrary frames from a coronary cine-angiogram. Thus, manual selection involves identification of points corresponding to anatomical structures so that these methods are usually subject to intra- and inter-observer variability. Levis et al. have reported that inappropriate selection of landmarks on a pair of images could lead to a deteriorated registration performance by causing non-smooth interpolation artifacts between pixel intensities.

A number of automatic landmark selection methods have been previously published in the literature. Features or their combinations, such as intensities, anatomical structures (e.g. bones, organs or tissues), curvature, and shapes, have typically been used to guide fiducial placement. For example, Rechberg et al. presented an automatic approach for identifying landmark candidates by computing and choosing high distinctiveness values for the voxels within a region of interest. Gu and Qin proposed a global-to-local nonrigid brain image registration scheme in which the keypoints (i.e. landmarks) are selected based on a computed joint saliency map. The performance of such a scheme is dependent on a pre-defined criterion used, and therefore limited to specific types of applications. In addition, these methods mainly focus on optimization of global transformation and may be undesirable for registering images where the deformation is localized.

An alternative method is to apply a uniform grid to a region of interest in which landmarks might be placed uniformly on the grid knots. The extracted landmarks are considered to contribute equally in the registration process. Furthermore, each of these configurations can be employed with different levels of discretization. For example, Xie and Farin developed a hierarchical B-spline approximation model for multilevel nonlinear registration, in which a uniform knot spacing was used in conjunction with a cubic B-spline based approach. Tustison
et al.\textsuperscript{3} also adopted an equally spaced grid in their free-form deformation (FFD) image registration framework. The drawback of uniformly spaced placement is that these evenly distributed landmarks may not represent informative landmarks (e.g. landmark position on curvature) due to the insufficient sampling of points in certain regions in the grid, while a highly dense grid can result in over-fitting to the data as well as longer computation times for achieving an optimal registration.

In this work, we present a novel landmark-driven image registration scheme using a supervised learning method. The registration scheme consists of two modules. In the training module (shown in Figure 1), a collection of synthetic deformed images are generated under different aspects of the deformation, such as force direction, deformation location, and magnitude of displacement. The important landmarks are identified for recovering deformation between a target and a moving image via a thin-plate spline (TPS)\textsuperscript{14,15} based registration scheme. In the prediction module (shown in Figure 2), the learned landmark configurations are used as training sets to estimate the important landmark locations for an image pair with a known deformation. A new optimal landmark configuration is determined by simply transforming the training landmark set via an iterative close point (ICP) alignment method\textsuperscript{16} to the current deformation site meanwhile preserving the topological structure of the training landmark set.

The contributions of the work lie in the following: (1) A novel method is presented to estimate an optimal configuration of landmarks. Unlike existing landmark selection schemes to detect landmark candidates by computing certain features on image intensities or anatomical structures,\textsuperscript{1} critical landmarks are selected based on the prior knowledge of the training landmark configurations given the corresponding deformation locations; (2) The distribution of the predicted landmarks reveals high density within or in close proximity of the deformed region, allowing for one to accurately capture local deformation, e.g. brain tissue changes caused by tumor resection, making this a reasonable approach to consider for pre- and post-surgery image registration; and (3) Due to the fact that only spatial information is used in the estimation process rather than any image intensity related features, the new method can be potentially useful in registering two medical images for different domains and applications.
Table 1. Notation and symbols commonly used in this paper.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Symbol</th>
<th>Description</th>
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<tbody>
<tr>
<td>$\mathcal{C}$</td>
<td>2D image scene</td>
<td>$\tau$</td>
<td>TPS transformation</td>
</tr>
<tr>
<td>$C$</td>
<td>2D grid of pixels, $c \in C$</td>
<td>$\mathcal{G}$</td>
<td>TPS cost function</td>
</tr>
<tr>
<td>$c$</td>
<td>Spatial location of a pixel in $C$, where $c = (x, y)$</td>
<td>${S_k^c, S_k^{w_i}}$</td>
<td>Randomly chosen point sets for ${\mathcal{C}, \mathcal{W}_i}$ at simulation $k \in {1, \ldots, K}$</td>
</tr>
<tr>
<td>$f$</td>
<td>Intensity value associated with a pixel $c$</td>
<td>${S_o^c, S_o^{w_i}}$</td>
<td>Learned optimal landmark sets for ${\mathcal{C}, \mathcal{W}_i}$</td>
</tr>
<tr>
<td>$R$</td>
<td>A small circle-shaped region $R \subset C$</td>
<td>$u$</td>
<td>Displacement field</td>
</tr>
<tr>
<td>$\mathcal{D}$</td>
<td>Deformation field</td>
<td>$A$</td>
<td>Affine transformation</td>
</tr>
<tr>
<td>$\phi$</td>
<td>Deformation generation function</td>
<td>$\varphi$</td>
<td>Landmark selection criterion</td>
</tr>
<tr>
<td>$\mathcal{F}$</td>
<td>Factors to generate $\mathcal{D}$</td>
<td>$\xi$</td>
<td>Hausdorff distance</td>
</tr>
<tr>
<td>$\mathcal{W}_i$</td>
<td>Synthetic deformed image, where $i \in {1, \ldots, H}$</td>
<td>$T(R; t)$</td>
<td>ICP transformation, where $R$ is a rotation matrix, and $t$ is a translation vector</td>
</tr>
<tr>
<td>$\mathcal{L}$</td>
<td>Landmark distribution</td>
<td>${S_A, S_B, S_C}$</td>
<td>Optimal landmark configurations</td>
</tr>
<tr>
<td>${P, Q}$</td>
<td>Point bases for ${\mathcal{C}, \mathcal{W}_i}$</td>
<td>${C_A, C_B, C_C}$</td>
<td>Deformation center</td>
</tr>
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### 3. METHODS

#### 3.1 Learning Optimal Landmark Configurations

**3.1.1 Generating synthetic deformations**

We denote $C = (C, f)$ as an original image, where $C$ is a scene, $C$ is a grid of spatial locations $c \in C$, and $f$ is an intensity function associated with every spatial location $c \in C$. Notation and symbols commonly used in this paper are shown in Table 1. A circle-shaped artificial deformation field $\mathcal{D}$ is introduced on a small region $R \subset C$ to simulate the after-treatment deformation on a local region, which can be expressed as:

$$\mathcal{D}(C) = \phi(c; \mathcal{F}), \quad c \in R, \quad R \subset C,$$

where $\phi$ is a transformation function that can be computed by considering three factors ($\mathcal{F}$): (i) two forces $f_i, f_o$, pushing the points towards the target center or outwards to the target boundary, to simulate tissue changes after treatment; (ii) three locations $l_a, l_m, l_b$ representing three zones within the organ of interest which were employed to simulate different locations of the disease; and (iii) three deformation magnitudes $m_s, m_m, m_t$ reflecting small, medium, and large deformation, in turn aimed to simulate different size and extent of treatment-related changes. Figure 1 (left panel) shows an example of a synthetic deformation using $\mathcal{D}(f_i, l_a, m_s)$. A set of $H$ deformed images $\mathcal{W}_i$, $i \in \{1, 2, \ldots, H\}$, is generated by moving the pre-defined deformation field $\mathcal{D}$ to various locations on the original brain MRI. By deforming the original data, we could easily validate the registration results by knowing the ground-truth deformation. Moreover, it allows us to potentially identify the trend of landmark localizations associated with different deformation profiles.

**3.1.2 Identifying critical landmarks**

The optimal landmark distributions $\mathcal{L}$ are learned through three experiments: (1) Experiment 1: $\mathcal{L}$ in $\mathcal{D}(f_i, f_o)$; (2) Experiment 2: $\mathcal{L}$ in $\mathcal{D}(l_a, l_m, l_b)$; (3) Experiment 3: $\mathcal{L}$ in $\mathcal{D}(m_s, m_m, m_t)$.

For each experiment, we first compute a landmark point base $P = \{p_j\}_{j=1}^M$, $p_j \in G$ where $G$ is a $N_g \times N_g$ uniform grid of spatial locations on $C$, and a corresponding point base $Q = \{q_j\}_{j=1}^M$ on $\mathcal{W}_i$. Two MRI brain images $\{\mathcal{C}, \mathcal{W}_i\}$ are registered via a thin-plate spline transform $\tau(C; \mathcal{W}_i; S_k^c, S_k^{w_i}), k \in \{1, 2, \ldots, K\}$, where $S_k^c = \{s_j^c\}_{j=1}^N \subset P$ and $S_k^{w_i} = \{s_j^{w_i}\}_{j=1}^N \subset Q (N < M)$ are randomly chosen point sets containing $N$ points for $\mathcal{C}$ and $\mathcal{W}_i$, respectively, and $k$ denotes the index of simulation. Let $v_j, j \in \{1, 2, \ldots, M\}$, store the frequency of each point pair $\{p_j, q_j\}$ that participates in the registration. The TPS is a non-rigid transformation model that is widely used to interpolate the displacement field $u$ between the corresponding landmarks. Given two point sets $\{S_k^c, S_k^{w_i}\}$ for original and deformed brain images, we define a landmark-based image registration problem as finding a displacement $u$ that minimizes the following cost function:17,18

$$\mathcal{G} = \int_\Omega \| \zeta u(x; s_j^c) \|^2 \, dx,$$
two steps to accomplish this. The closest points can be obtained by minimizing:

\[ \sum_{j=1}^{N_o} \varphi(x; S_a; S_i^w) \]

\( \varphi \): Hausdorff Distance

\( A \): Affine transformation

Figure 2. The schematic diagram of the ICP-based landmark selection scheme. \( S_A^{w_i} \) is a transformed version of \( S_A^{w_i} \) on the deformation center \( C_B \) via an affine transformation before aligned with \( S_B^{w_i} \) to obtain a generic transformation matrix \( T \). \( S_C^{w_i} \) is an estimated landmark configuration generated by transforming the training landmark set \( S_A^{w_i} \) (a transformed version of \( S_A^{w_i} \) on \( C_C \)) via the transformation \( T \) to the current deformation center \( C_C \).

subject to the constraint that \( u(a_j^t; s_j^i) = s_j^{w_i} - s_j^i, j \in \{1, 2, ..., N\} \). The operator \( \zeta \) denotes a symmetric linear differential operator and is used to interpolate the displacement field \( u \) between the corresponding landmarks. In this work, the interpolation operator \( \zeta \) is solved by the TPS transformation, in which the displacement field \( u(x; s_j^i) \) is computed by:

\[ u(x; s_j^i) = Ax + \sum_{j=1}^{N_o} \omega_j \psi(\|x - s_j^i\|), \]  

(3)

where the kernel function \( \psi(x) \) is a \( 1 \times N \) vector for each point \( x \) that is defined as \( \psi(x) = \|x - s_j^i\|^2 \log(\|x - s_j^i\|) \). \( A \) represents a \( 2 \times 2 \) affine transformation matrix, and \( \omega_j \) is a \( 2 \times 1 \) warping coefficient matrix representing the non-affine deformation.

For each iterative simulation, sum of squared intensity difference (SSD)\(^{10} \) is utilized as a selection criterion to compute measure scores for these selected points. After \( K \) simulations, an average measure score is calculated for each point pair \( \{p_j, q_j\}, j \in \{1, 2, ..., M\} \). Two subsets \( S_A^t = \{a_j\}_{j=1}^{N_a} \) for \( C_A \) and \( S_B^{w_i} = \{o_j^{w_i}\}_{j=1}^{N_o} \) for \( W_i \) containing \( N_o \) (\( N_o \approx M \) ) landmarks with the best values of \( \frac{1}{N_o} \sum_{k=1}^{K} \varphi(\tau; S_A; S_B^{w_i}) \), where \( \varphi \) is a selection function defined as the SSD measure, will be selected to form an optimal configuration. The two sets \( \{S_A^t, S_B^{w_i}\} \) serve as training point sets to estimate the optimal landmark configuration for a new pair of images.

### 3.2 Predicting Optimal Landmarks for New Images

A schematic diagram of the presented method is shown in Figure 2. For simplicity, we denote \( S \) representing a pair of optimal landmark sets \( \{S_A^t, S_B^{w_i}\} \), which is obtained in Section 3.1. Assume that two representative pairs of training point sets \( S_A \) and \( S_B \) are given. Since \( S_A \) and \( S_B \) are identical, alignment of point sets \( S_A \) and \( S_B \) is the problem of aligning the point set \( S_A^{w_i} = \{a_i\}_{i=1}^{N_a} \) with the point set \( S_B^{w_i} = \{b_i\}_{i=1}^{N_o} \), where the corresponding deformation centers are \( C_A \) and \( C_B \), respectively. In order to align these two pairs of landmark sets with each other, a new point set \( S_A^{w_i} = \{a_i\}_{i=1}^{N_o} \) is generated by transforming \( S_A^{w_i} \) to the location \( C_B \) via:

\[ S_A^{w_i} = A(S_A^{w_i}; C_A; C_B), \]  

(4)

where \( A \) is an affine transform. The ICP alignment method\(^{16} \) is employed to align point set \( S_B^{w_i} \) and \( S_A^{w_i} \) to obtain a transformation matrix \( T(R; t) \), where \( R \) is a rotation matrix, and \( t \) is a translation vector. There are two steps to accomplish this. The closest points can be obtained by minimizing:

\[ \frac{1}{N_o} \sum_{i=1}^{N_o} \|a_i - \vartheta_{S_B}^{-1}(a_i)\|, \]  

(5)
Figure 3. The landmarks are selected by: (a)-(d) ICP-based method under the deformation profiles $D(f_i, m_i)$, $D(f_i, l_i, m_i)$, $D(f_i, l_i, m_i)$, and $D(f_i, l_i, m_i)$; (e) Uniform-grid; (f) FFD; (g) SURF. The yellow points represent landmarks, and the red circle indicates the deformed region. The landmark configurations generated by the ICP-based method exhibited a unique pattern where the points located within and near the deformed region were selected. Identifying the landmarks in the presence of the deformation could help more accurately drive the registration compared to the other three methods.

where $\parallel \cdot \parallel$ is the Euclidean distance, and $\vartheta_{S_{wa}^{m_i}}(a'_i)$ represents the point in $S_{wa}^{m_i}$ that is closest to point $a'_i \in S_{wa}^{m_i}$. The rotation matrix $R$ and translation vector $t$ can be computed using the following mathematical expression:

$$\min \left\{ \frac{1}{N_o} \sum_{i=1}^{N_o} \parallel \vartheta_{S_{wa}^{m_i}}(a'_i) - (R \times a'_i + t) \parallel \right\}, \quad (6)$$

The obtained transformation matrix $T$ is used to estimate optimal landmark locations of new pair of images by given the displacement site. Based on the point set similar measure $\xi$, we assume that a new point set $S_C = \{S_{wa}^{m_i} \}$ with deformation center $C_C$ is subject to $\xi(S_{wa}^{m_i}; S_{wa}^{m_i}; S_{wa}^{m_i}) < \theta$, where $\xi$ is the Hausdorff distance measure, and $\theta$ is a pre-defined threshold. $S_C = \{c_i\}_{i=1}^{N_o}$ can be predicted based on $S_{wa}^{m_i}$, $C_A$, and $C_C$ given by:

$$S_C^{wa} = RS_{wa}^{m_i} + t, \quad \text{where} \quad S_{wa}^{m_i} = \{a_i^{m_i}\}_{i=1}^{N_o} = A(S_{wa}^{m_i}; C_A; C_C), \quad (7)$$

4. EXPERIMENTAL RESULTS AND DISCUSSION

4.1 Data Description

A simulated brain database (SBD)\(^{20}\) containing a set of realistic MRI data volumes is utilized to verify this new method. The SBD dataset allows quantitative brain image analysis to be conducted in a controlled and systematic way. The $T_1$-weighted brain images are used in our experiments.
Figure 4. (a) The difference map between the original and deformed images. The difference map between the original and registered images for: (b) ICP-based; (c) Uniform-grid; (d) FFD; (e) SURF. The difference map is overlaid on the original brain image. The colorbar shows the difference range. The ICP-based method gained the best registration result with the smallest difference range compared to the other three methods.

Two GBM patient studies were acquired under the laser-induced interstitial thermal therapy (LITT) using an FDA-cleared Visualase Thermal Therapy System (Visualase, Inc., Houston, TX). Both patients were monitored post-LITT via MRI guidance after initial 3-Tesla MRI. The patients were reimaged after 24 hours post laser ablation.

4.2 Landmark Evaluation

Three popular quality metrics, including mutual information (MI), normalized cross-correlation (NCC), and sum of squared difference, are utilized to quantitatively evaluate the registration performance. Three methods are used for comparison. A uniform grid placement method is applied to entire brain region where the landmarks are placed on the grid knots. The landmarks are equally distributed inside the brain region. A speeded up robust features (SURF)-based landmark detection method employs the SURF features, which are robust local descriptors, to identify informative landmarks. These landmarks are used as control points to drive a TPS registration. A classic free-form deformation (FFD) approach is developed to minimize a SSD similarity metric by using B-spline control points to approximate the shape of the intended deformation.

A collection of \( H = 286 \) pairs of MRI brain images are generated by varying the deformation factors \( F \) defined in Section 3.1.1. Half of the image pairs are utilized in learning the optimal landmark configurations and the remaining pairs are used for the landmark prediction task. We run \( K = 2000 \) simulations for each experiment to achieve statistical power of landmark distribution. A \( 5 \times 5 \) grid spacing is used to compute the landmark point base \( P \). The TPS transform is estimated using Bookstein’s method with default parameter settings. The registration results are analyzed in both visual and quantitative evaluations.
Figure 5. The comparison results using four methods measured by: (a) SSD; (b) SSD; (c) MI; (d) NCC. In each figure, the first bar is the measure score computed between the original and deformed images. The ICP-based method outperformed the other three methods using these four metrics, especially in SSD that measures the accuracy of recovering the local deformation, the ICP-based method yielded 95% improvement on the original deformation, and 89% for the uniform grid, 79% for the SURF-based approach, and 10% for the FFD.

4.3 Qualitative Results on SBD Dataset

The important landmark distributions are tested under different forms of deformation by considering force directions $f_i, f_o$, deformation locations $l_a, l_m, l_b$, and magnitudes of displacement $m_a, m_m, m_l$. Figure 3(a)-(d) show the landmark configurations generated by the ICP-based method using different deformation profiles. Compared to the other three reference methods, the identified landmarks exhibited high density inside and near the deformed region. This unique pattern allows to capture subtle changes inside the deformation. For the purpose of fair comparison, 200 points were selected for all the methods.

Figure 4 illustrates the difference maps between the original and registered images overlaid on the original brain image compared to the difference map between the original and deformed brain images. The colorbar on the right side of each figure shows the range of difference values between the original and registered images. Figure 4(b)-(e) are generated via the four configurations of landmarks shown in Figure 3(a) and (e)-(g), respectively. These four sets of landmarks are obtained using the same deformed MRI brain image. The FFD performed poorly because of insufficient control points selected inside the deformation to fit the B-spline function. The SURF-based method was seen to work well on the deformed region but introduced large errors on the brain boundary due to the ambiguous points selected in this area, then resulting in an incorrect TPS transformation. The uniform grid method provided a comparable result but showed larger errors in the deformed region compared to the ICP-based method.

4.4 Quantitative Results on SBD Dataset

Registration performance using the selected landmarks was validated by three quality metrics, including MI, NCC, and SSD. Two versions of SSD are computed based on different regions of interest. The SSD is computed between the original and registered images on entire brain region, and SSD is computed between the deformed regions within the brain on these two images. SSD allows to measure the local registration performance inside the deformation region of MRI brain images.

The average measure scores and associated standard deviations are computed for these four landmark selection methods and compared to the scores between original and deformed brain images. The higher MI and NCC scores indicate better registration performance, while the lower SSD scores show better results. For a fair comparison, 200 landmarks were used for all the methods. Figure 5(a)(b) show that the ICP-based selection scheme significantly improved the SSD measure on both global nonrigid registration and local deformation with 86% and 95% improvement on the original deformation, respectively. The uniform grid method also demonstrated good registration performance with improvement of 76% and 89% on SSD and SSD, respectively. However, the SURF-based method was able to recover the local deformation, while introduced large distortion beyond the deformation site, which can be visually inspected on Figure 4(e). The MI and NCC metrics indicate that the ICP-based method yielded better results compared to the other three methods although the difference was less
distinguishable than the SSD metric shown in Figure 5(a)(b). Again, the SURF-based method yielded the worst MI and NCC scores compared to other three selection methods due to the registration distortion caused by TPS interpolation.

Figure 6 shows the comparison results using the ICP-based and uniform grid methods by varying the number of selected landmarks. The trend of curves illustrates improved registration performance (decreased SSD measure values) for the ICP-based and uniform grid methods as the number of selected landmarks was increased. Figures 6(a), (b) suggest that the uniform grid method requires higher dense grid sampling to yield the same level of registration performance as the ICP-based method. The quantitative results confirm that the ICP-based method is capable of accurately recovering the local deformation as well as providing a superior global registration. This makes our ICP-based method uniquely desirable to register pre- and post-treatment brain images where the deformation site is known and the deformation region is localized.

4.5 Registering Pre- and Post-LITT Brain MRI in GBM

The ICP-based landmark selection method was validated on two patient studies who were diagnosed with GBM and who have undergone LITT and has a pre- and post-LITT multi-parametric MRI exam done. In this study we looked at only registering the T1-weighted MRI for the multi-parametric MRI exam pre- and post-LITT for the two GBM patients. Tumor was localized to one side (as shown Figure 7(a)) and the bottom (as shown Figure 7(e)) of the brain. The pre- and post-LITT brain MRI were first aligned with the synthetic brain image pair \( \{ C, W_i \} \) by matching the binary masks of two images. The location of the tumor site was then used to predict the optimal landmark configuration. Finally, the identified landmarks were utilized to register the pre- and post-LITT MRI.

Figures 7(i)-(l) show the difference maps between the registered and pre-LITT MRI which were encoded via a color bar and overlaid on the original pre-LITT MRI. The large differences in image intensity are shown in red and small differences are shown in blue. The ICP-based method yielded superior registration results with \( \{ \text{SSD}_1, \text{SSD}_2 \} \) of \{8.94, 5.33\} for the first patient study, and \{16.78, 9.46\} for the second patient study, respectively, compared to \{12.75, 7.89\} and \{17.55, 12.32\} obtained from the uniform grid. The performance scores were consistent with the visual examination of the difference maps illustrated in Figures 7(i)-(l). The experimental results illustrated that the real localized deformation induced by LITT is better recovered by the ICP-based method than simply uniformly picking landmarks.
Figure 7. The first and second rows show two different registration experiments performed on MRI obtained for GBM. Figures 6(a),(b) and (e),(f) show pre- and post-LITT brain MR images. Figures 6(c),(d) and (g),(h) demonstrate the landmarks (yellow points) generated by the ICP-based method and uniform grid, respectively. The red circle indicates the deformation site. Figure 6(i),(j) and (k),(l) show the difference maps between the registered and pre-LITT images using the ICP-based and uniform grid for these two patient studies, respectively. Note that the optimal landmark configuration yielded a better registration quality compared to the uniform grid.

5. CONCLUDING REMARKS

A novel landmark selection scheme, employing supervised learning to identify the spatial fiducial configuration for optimizing a point based registration scheme was presented. The new landmarks are determined by simply transforming the training landmark set to the current deformation location while preserving the topological structure of the configuration of landmarks. The experimental results demonstrated that the ICP-based landmark selection method achieves superior registration performance in global-to-local nonrigid brain MR image registration with 86% improvement on the global registration and 95% improvement on the local deformation, respectively. The optimally identified landmark configuration confirmed that the landmarks either within or near the deformed region are more important to ensure an optimal registration result, compared to the points far away from the site of deformation. The trend was consistently seen across different deformation profiles.
In future work we intend to further evaluate our method by attempting to more realistically model the deformations included based off what is typically observable following radiation or laser therapy for treatment of brain tumors. Moreover, localized intensity-related features can be integrated into the registration process to improve the accuracy of landmark correspondence. We believe that the nature of local deformation can be more precisely learned and modeled via an intelligent landmark location detection method based on both spatial and intensity features.

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