A Hybrid Multimodal Non-Rigid Registration of MR Images Based on Diffeomorphic Demons

Huanxiang Lu, Philippe C. Cattin, and Mauricio Reyes

***Abstract*— In this paper we present a novel hybrid approach for multimodal medical image registration based on diffeomorphic demons. Diffeomorphic demons have proven to be a robust and efficient way for intensity-based image registration. A very recent extension even allows to use mutual information (MI) as a similarity measure to registration multimodal images. However, due to the intensity correspondence uncertainty existing in some anatomical parts, it is difficult for a purely intensity-based algorithm to solve the registration problem. Therefore, we propose to combine the resulting transformations from both intensity-based and landmark-based methods for multimodal non-rigid registration based on diffeomorphic demons. Several experiments on different types of MR images were conducted, for which we show that a better anatomical correspondence between the images can be obtained using the hybrid approach than using either intensity information or landmarks alone.**

I. INTRODUCTION

Magnetic resonance imaging (MRI) has become one of the most indispensable techniques to examine the human anatomy from anatomical and functional viewpoints. Since different imaging sequences are able to generate different information, we often need to fuse these images to have the necessary information in one single coordinate frame. For example, it is often required to register functional MRI images with T1/T2 images to remove the spatial distortion artifacts. Therefore, accurate multimodal registration methods play a crucial role in many clinical applications.

Among the wide variational image registration algorithms, two categories can be classified according to the used image information: intensity-based and landmark-based. The landmark-based methods define a unique smooth transformation from a source image to a target image based on corresponding landmarks. The correspondence of the points away from the landmarks is defined by a certain interpolation method, e.g. thin-plate spline (TPS) model [1], anisotropic landmark interaction [2], etc. More details can be referred to [3]. The main advantages of landmark-based approaches are the computational efficiency and the capacity of handling large geometrical deformations. Nevertheless, it does not guarantee the accuracy in terms of voxel to voxel correspondence, and the result can be significantly affected by the choice of the landmarks. Moreover, a pure landmark-based approach requires to select a considerably number of landmarks for 3D images, which is a tedious and error prone task. With intensity-based methods, the transformation is directly computed from the intensity information. Diffeomorphic demons [4][5] have proven to be a robust and efficient intensity-based method for monomodal image registration that uses the sum of squared intensity differences (SSD) as the similarity metric. As has been recently shown, it can be extended to cope with multimodal registration problem by adopting point-wise mutual information (PMI) [6]. However, with images of low resolution and quality, the intensity mapping for computing the PMI is not always reliable, especially in certain areas where intensity distribution is inhomogeneous (e.g. signal loss in echo planar imaging). This leads to inaccuracies in the final result.

In the last couple of years lots of research has been put into hybrid registration approaches which use both intensity and landmark information [7], [8], [9], [10], [11]. Most of these approaches use the spline deformation model to calculate the dense vector field . Besides, such parametric spline-based methods usually apply global optimization procedures which are computationally expensive.

In this work, we propose a novel hybrid approach based on diffeomorphic demons for multimodal MR image registration. The energy function is made up of point-wise mutual information, landmark information and a regularization term. The optimization of this energy results in a combination of a dense vector field and Gaussian basis functions for landmarks. In Section 2 the diffeomorphic demons algorithm using PMI for multimodal image registration is described. Then we show our hybrid scheme incorporating both landmarks and intensity information in Section 3. Experimental results on simulated brain T1/T2 images, functional MR images and brain tumor resection images are presented in Section 4.

II. MULTIMODAL DIFFEOMORPHIC DEMONS

The classic demons algorithm is based on a heuristic argument called "demons" that create forces according to local characteristics of the images in a similar way Maxwell did for solving the Gibbs paradox. The forces are inspired by the optical flow equations [4] and the method alternates between computation of the forces and regularization by Gaussian smoothing. The registration framework is treated as an optimization problem that aims at finding the displacement of each pixel so as to get a reasonable alignment of the images. This results in a computationally efficient algorithm compared to other non-rigid registration procedures such as those based on linear elasticity. To ensure the invertibility of the transformation, Vercauteren et al. [5] proposed a

This work was not supported by any organization

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diffeomorphic extension to the demons framework. The main idea was to adapt the optimization procedure to a space of diffeomorphic transformations. It is done by using an intrinsic update step which computes the vector field exponentials on the Lie group of diffeomorphisms.

The whole registration algorithm can be summarized by a model with an energy consisting of a similarity function, a transformation error function and a regularization term. Given the fixed image F, a moving image M, and a deformation field s, the energy function can be described as follows:

$$E(c,s) = Sim(F, M \circ c) + \sigma \left\| s - c \right\|^2 + \sigma\lambda Reg(s), \quad (1)$$

where Sim is the intensity similarity metric which will be described below, Reg is the regularization term which is typically a Gaussian kernel, c is the estimated transformation according to the metric. This energy function allows the whole optimization procedure to be decoupled into two simple steps. The first step solves for the correspondences by optimizing $Sim(F, M \circ c) + \sigma \left\| s - c \right\|^2$, with respect to c and with s being given. The second step solves for the regularization by optimizing $\sigma \left\| s - c \right\|^2 + \sigma\lambda Reg(s)$, with respect to s and with c being given.

In order to cope with images from different MR imaging techniques, one cannot simply use the intensity differences as similarity metric. Therefore, we replace the SSD in the classical demons with PMI which is able to cope with multimodal registrations. PMI calculates the contribution of the global MI from each voxel and is easy to plug in a dense field approach. The Sim term with respect to the update field at each iteration can be written in the following form:

$$E(\mathbf{u}) = -\log\left(\frac{p(i_F, i_{M\circ(s\circ\exp(u))})}{p(i_F)p(i_{M\circ(s\circ\exp(u))})}\right). \quad (2)$$

Nevertheless, in some fast MRI acquisition techniques, such as echo planar imaging technique (EPI), the intensity distribution is less homogeneous and much noisier, this usually gives false intensity mappings that makes the PMI estimation difficult. Besides, the optimization that we employ in our method searches greedily for the maximal MI value which does not necessarily lead to a better transformation [12]. Hence, some estimated vector fields calculated could point to a wrong position but with higher MI value. Thus, we apply a relatively strong regularization to smooth the vector fields at the cost of restraining large deformations. This can make the registration harder for difficult registration problems. Therefore, some prior anatomical information seems to be helpful to solve this kind of problem.

III. HYBRID REGISTRATION FRAMEWORK

In contrast to the segmentations used in [7], we choose to use a small number of point landmarks to minimize manual interaction. The point landmarks would generally be selected in the regions where the intensity-based approach could easily fail.

By incorporating the landmarks, we can reformulate the demons energy function as in [7]:

$$\begin{aligned} E(c,s) =& Sim(F, M \circ c) + \sigma \left\| s - c \right\|^2 \\ &+ \sigma\gamma \left\| s - l \right\|^2 + \sigma\lambda Reg(s), \end{aligned} \quad (3)$$

where l is the estimated transformation according to the landmark. Given n corresponding landmarks $\mathbf{p}_i$ and $\mathbf{q}_i$, $i = 1, \ldots, n$ that have been localized in F and M. The energy term respect to the landmarks can be written as:

$$\sigma\gamma \left\| s - l \right\|^2 = \sum_{i=1}^{n} (\mathbf{q}_i - \mathbf{p}_i \circ s)^2. \quad (4)$$

The optimization of this modified energy function with respect to c, l , s leads to the following steps:

1) Find the correspondence c of the dense field by minimizing $Sim(F, M \circ c) + \sigma \left\| s - c \right\|^2$ with respect to c.
2) Minimizing $\sigma\gamma \left\| s - l \right\|^2$ with respect to l. This is easily done by guiding the moving landmarks towards the reference landmarks.
3) Find the estimated transformation s by minimizing $\sigma \left\| s - c \right\|^2 + \sigma\gamma \left\| s - l \right\|^2 + \sigma\lambda Reg(s)$ with respect to s. s turns out to be a combination of convolution and splines:

$$s(x) = \alpha G * c(x) + \sum_{i=1}^{n} \alpha_i G(x - \mathbf{p}_i), \quad (5)$$

where G is the Gaussian kernel, α is a scalar value and α_i is a vector of weighting parameters.

One practical consideration of minimization on both c and l is that it may lead to difficulties and instability in converging towards a solution compared to the single energy formulation, because c and l could be pulling a same voxel in different directions. However, since we use a small number of landmarks, l can be minimized separately from the known information. With the guidance of the force from l, the transformation c could easily escape the local minima. In addition, this computation is straightforward, and is able to incorporate any registration algorithm in this hybrid framework with no modification to its implementation.

The final iterative hybrid registration algorithm can thus be written as follows:

- Given the current transformation s, compute a correspondence update field $\mathbf{u}$ by minimizing $E_{corr}(\mathbf{u})$ with respect to $\mathbf{u}$.
- For a fluid-like regularization let $\mathbf{u} \leftarrow K_{fluid} * \mathbf{u}$. The convolution kernel will typically be a Gaussian kernel.
- Compute update field $\mathbf{v}$ for landmark correspondence.
- Let $c \leftarrow s \circ \exp(\mathbf{u} + \mathbf{v})$.
- For a diffusion-like regularization let $s \leftarrow K_{diff} * c$ (else let $s \leftarrow c$). The convolution kernel will also typically be a Gaussian kernel.

IV. EXPERIMENTS AND RESULTS

A. Registration on Simulated Data

We first applied our method on artificially distorted images to evaluate the accuracy and robustness of the proposed hybrid approach.

Since a purely qualitative analysis is insufficient to validate multimodal non-rigid registration methods, our experiments base on recovering a synthetic deformation field. The synthetic deformation model we adopted consists of a regular grid with a random deformation at each node, interpolated by a thin plate spline [13].

To test our multimodal registration algorithm we need a set of perfectly aligned ground truth images from multiple modalities. For this reason we adopted the images from BrainWeb MRI Simulated Normal Brain Database [14]. This database can provide T1 and T2 images ($181 \times 217 \times 181$ voxels) with different noise and bias configuration. We generated five distorted T2 images with synthesized deformations. All the deformations are generated based on a grid size of $32 \times 32 \times 32$ and with maximum deviations of 8 mm. During the experiment, typically around 20 pairs of landmark were picked manually. We evaluated the registration result using root mean square (RMS) of the displacement field which can be computed as $e_{RMS} = \sqrt{\frac{1}{N_\Omega} \sum_{x \in \Omega} (\varphi_{syn}(x) - \varphi_{reg}(x))^2}$, where N_Ω denotes the number of voxels in the overlapping domain, φ_{syn} and φ_{reg} are the synthetic ground truth and the computed deformation field.

Table I shows the comparison of RMS between intensity-based approach and hybrid approach. One can see that globally the hybrid approach does not improve the result in terms of RMS. This is due to the fact that the radial Gaussian basis function utilized for the landmarks in the hybrid approach does not comply well with the synthetic deformation field generated by TPS. However, by observing certain anatomically important regions, we found that hybrid approach can recover some difficult distortions while the intensity-based approach fails (see Fig. 1).

TABLE I
RMS OF RESULTS ON SIMULATED MRI BRAIN IMAGES (MM)

Data	1	2	3	4	5
Intensity	2.05	2.08	1.83	1.94	2.01
Hybrid	2.23	2.01	1.82	1.88	1.98

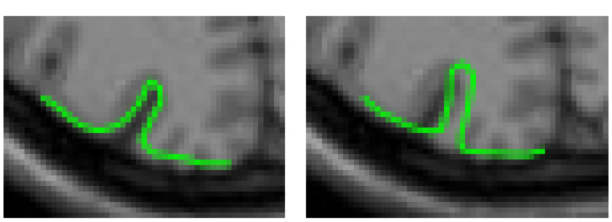

Fig. 1. Registration results overlaid on the occipital lobe of the simulated brain data. (a) hybrid approach. (b) intensity-based approach.

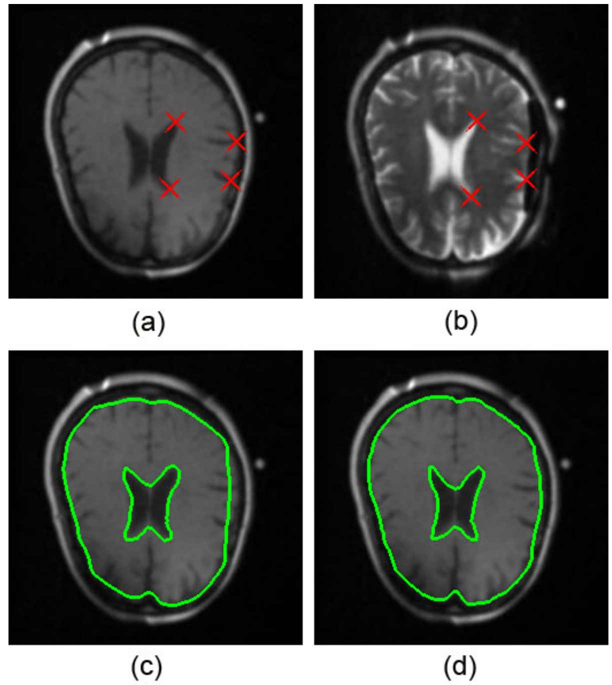

Fig. 2. Results on brain tumor resection data 1. Red crosses represent the picked landmarks in (a) T1 image, and (b) T2 image with tumor removed. Green lines in (c) and (d) indicate the result of intensity-based approach and hybrid approach.

B. Registration of Brain Tumor Resection Data

We also evaluated our proposed method using five real data sets from the National Center for Image Guided Therapy (NCIGT) in USA. The datasets ($256 \times 256 \times 20$) are functional MRI scans in T1 and T2 used for neurosurgery [15], shown in Fig. 2 (a) and (b). Depending on different levels of deformations, five to ten pairs of landmark were chosen for each data typically around the tumor resection area during the experiment.

Due to the lack of ground truth in real clinical data, we first performed a qualitative analysis by comparing the overlay of the extracted contour of the brain and the ventricle before and after the registration, shown in Fig. 2 (c) and (d). It can be seen that the contour extracted from our hybrid approach better overlays the edge of the target brain than the one from the intensity-based method, especially in the area where the tumor is removed. In order to allow quantitative analysis, we calculated the Hausdorff distance between the extracted contours. Hausdorff distance can be computed as:

$$d_H(X, Y) = \max\{\sup_{x \in X} \inf_{y \in Y} d(x, y), \sup_{y \in Y} \inf_{x \in X} d(x, y)\}, \quad (6)$$

where sup represents the supremum and inf the infimum. The comparison between the intensity-based approach and the hybrid approach is shown in Table II. We can see that in all cases the hybrid approach outperforms the intensity-based approach and improves the registration accuracy.

TABLE II

HAUSDORFF DISTANCE ON BRAIN TUMOR RESECTION DATA (MM)

Data	1	2	3	4	5
Unreg	13.01	12.59	11.67	14.98	12.39
Intensity	7.61	9.78	8.08	12.01	9.41
Hybrid	5.83	6.32	5.36	5.88	6.53

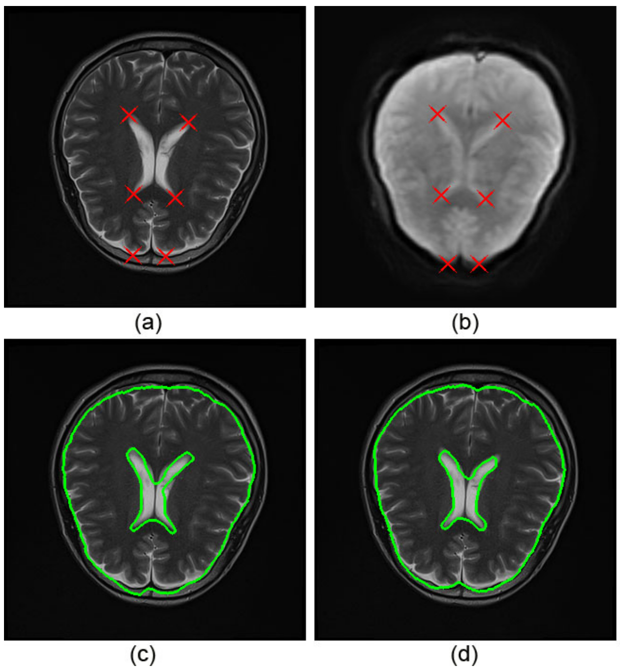

Fig. 3. Results on fMRI data 1. Red crosses represent the picked landmarks in (a) T2 anatomical image, and (b) fMRI image. Green lines in (c) and (d) indicate the result of intensity-based approach and hybrid approach.

C. Registration of fMRI Data

We also applied our approach to register fMRI images ($256 \times 256 \times 23$ voxels) to anatomical T1/T2 datasets in order to remove the EPI related spatial distortions. Five to ten landmark pairs were placed in the ventricle and the front lobe regions where EPI artifact are obvious. Figure 3 shows that the geometrical distortion in the frontal lobe in case 1 is better corrected with the hybrid approach than with intensity-based approach. We compared the Hausdorff distance between the two approaches as well. Table III indicates that the hybrid approach yields more accurate results with the guidance of only a few landmarks.

TABLE III

HAUSDORFF DISTANCE ON FMRI DATA (MM)

Data	1	2	3	4	5
Unreg	10.44	9.95	9.36	7.73	11.06
Intensity	8.54	7.29	8.96	6.37	10.39
Hybrid	7.07	6.62	6.50	5.54	7.74

V. CONCLUSION

In this paper we present a new hybrid approach based on diffeomorphic demons. Point-wise mutual information is employed as the similarity metric in order to cope with multimodal images. The energy functional combines both intensity and landmark information. From the experiment results on three different types of MRI datasets, we demonstrate that by incorporating human interaction, difficult registration problems that cannot be solved by pure intensity-based methods can be well registered by our hybrid approach. This can support accurate localization of lesions which is indispensable for many clinical application. Further work will be focused on improving the way that intensity and landmark information are combined by exploring more specific radial basis function.

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