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A Diffeomorphic Demons based Deformable Thoracic CT Image Registration between Full Inhale and Full Exhale Frames

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Abstract

Deformable (elastic/non-rigid) image frames from sequences of the human thorax acquired for a subject during the process of breathing from three APs (Anatomical Positions) is registered. The images up for registration are modeled after tangible physically deformable objects. All the image elements are selected as Maxwell's 'demons'. The periphery of these images is considered to be deforming as an effect of the resultant forces of the demon elements. The paper presents an iterative non-parametric diffeomorphic demon registration process for thoracic CT (Computed Tomography) images. An alternate optimization approach concerning Thirion's demons algorithm to provide a fast non-linear registration algorithm has been proposed. The credibility and performance of the above proposed method is demonstrated by its exemplary experimental results.

Keywords: *deformable image registration, demons, diffeomorphism, convergence field, energy minimization.*

1. Introduction

Deformable images have been a constant focus of study and research in the field of image processing. There have been extensive intra and inter-patient studies resulting in staggering discoveries. In an intra-patient study finding correspondences between images taken at different timestamps has been a long standing issue.

Maxwell's demons have come a long way from a 'thought experiment' in thermodynamic concepts to medical image registration methods. They were conceptualized as 'finite beings' prejudicially mediating the to and fro motion of molecules in a bisected, closed and pressurized system. Thirion [1] proposed in 1998, an application of Maxwell's demons as image elements, each of which would have their own displacement and optical flow which would later be translated into image forces. The resultant of these forces would determine the deformation grid for the moving image and finally the deformed image.

The organization of the remainder of this document is as follows. Section 2 provides an insight into deformable image registration methods classifications and the state of the art techniques from the field as applied on medical images. Section 3 describes the proposed methodology with the help of appropriate illustrations. Section 4 informs about the experimental setup and the results obtained along with supportive statistical data. Section 5 concludes the article with a brief overview of the proposed.

2. Background

Image Registration is the alignment/overlaying of two or more images so that the best superimposition can be achieved. These images can be of the same subject at different points in time, from different viewpoints or by different sensors. This way the contents from both the images can be integrated to provide rich information. It helps in understanding and thus reducing the differences occurred due to variable imaging conditions. Most common applications of Image Registration include remote sensing (integrating information for GIS), combining data obtained from a variety of imaging modalities (combining a CT and an MRI view of the same patient) to get more information about the disease at once, cartography, image restoration etc. An image registration method targets to find the optimal transformation that aligns the images in the best way possible. If the underlying transformation model allows local deformations, i.e. nonlinear fields u(x), then it is called deformable image registration (DIR) [2].

An image registration algorithm can be divided into three main components, a deformation model, an objective function and an optimization method. A registration algorithm's result naturally depends on the deformation model and the objective function. The registration result's dependency on an optimization strategy follows from the fact that image registration is inherently an ill-posed problem according to Hadamard's definition of well-posed problems [3, 4].

Image registration has been categorized into two kinds based on the type of image it is being applied for. The two kinds of images are Rigid Images and Deformable Images. Rigid images are those of structures with rigid morphological properties e.g. bones, buildings, geographical structures etc. Deformable images are those of structures shape and size of which can be modeled after tangible physically deformable models [4]. Rigid image registration although is an important aspect of registration it is not the topic of discussion in this article. Since the discussion is about Medical Image Registration and almost all anatomical parts or organs of the human body are deformable structures, the concentration here is on DIR [5]. Only relevant and recent studies (Physical models) and state of the art techniques well within the scope are reviewed in this section. Currently used physical models can be further separated into five categories [6]:

2.1 Elastic Body Models:

These can be further subdivided into Linear and Non-linear models.

(a) Linear Models:
In the case of linear models, images under deformation are modeled as an elastic body. The image grid was modeled after an elastic membrane that is deformed under the influence of internal and external competing forces until a state of equilibrium is reached. The external force influences deformation in the image to achieve matching and the internal force exercises the elastic properties of the material [7]. This approach was extended in a hierarchical fashion by Bajcsy and Kovacic where the coarsest scale solution was up-sampled and was used to initialize the finer one when linear registration was used at lowest resolution [8]. Linear elastic models have also been found useful when registering brain images based on sparse correspondences. They were used for the first time by Davatzikos based on geometric characteristics to establish mapping between the cortical surfaces. Modeling the images as inhomogeneous elastic objects led to the estimation of a global transformation function. Spatially-varying elasticity parameters were used to emulate the fact that certain structures tend to deform more than others [9]. An important drawback of image registration in general is that if deformed image is used as input to an inverse process of the previously used transformation (forward), the output obtained will not be the same as original input image for the forward transformation. The idea of parallel estimation of both forward and backward transformations, while compensating for inconsistent transformations by adding a constraint to the objective function was introduced later. Linear elasticity was used as a regularization constraint and Fourier series' were used to parameterize the transformation [10]. A unidirectional approach was also introduced by Leow et al. that coupled the forward and backward transformations and provided an inverse consistent transformation by construction, thus diminishing the idea of a constraint addition to penalize the inconsistency error [11].

(b) Non-linear Models:
An important drawback of linear elastic models is their inability to cope with larger deformations. Nonlinear elastic models were proposed so as to account for large deformations. These models ensure the preservation of topology of deformable images emulating hyper-elastic materials and their properties. The use of the Finite Element method provided a solution for the nonlinear equations and local linearization [12]. Two of the modeling processes for deformation were proposed, they were based on the concept of St. Venant-Kirchhoff elasticity energy [13, 14].

2.2 Viscous Fluid flow models:

Image under deformation is modeled as a viscous fluid, these models do not assume small deformations hence can cope with the larger ones [15]. Christensen et al. extended their earlier work to recover transformations for brain anatomy; fluid transformation preceded by elastic registration step was used to refine the result obtained [16]. The processes in use till then had an important drawback in the form of computational inefficiency. To circumvent this shortcoming a new fast algorithm based on a convolution filter in scale space was proposed [17]. Fluid deformation models were used in an atlas-enhanced registration setting [18] while same models were used to tackle multi-modal registration [19]. More recently, an inverse consistent variant of fluid registration to register Diffusion Tensor images was proposed [20].

2.3 Diffusion models:

Thirion, inspired by Maxwell's Demons [21], proposed to perform image matching as a diffusion process, his work in turn inspired most of the work done in image registration using diffusion models [1]. The most suitable version for medical image analysis involved selecting all image elements as demons, calculating demon forces by considering the optical flow constraint, assuming a nonparametric deformation model that was regularized by applying a Gaussian filter after each iteration, and a tri-linear interpolation scheme. The use of Demons, was able to provide dense correspondences but lacked sound theoretical justification [4]. However, this did not stop it from being an immediate success and soon enough a fast algorithm based on demons [1] for image registration was proposed by Fischer and Modersitzki [22] which provided theoretical insights into its workings. Vercauteren et al. [23] adopted the alternate optimization framework that Cachier et al. proposed [24], to relate symmetric Demons forces with the efficient second-order minimization (ESM) [25]. In this methodology, an auxiliary variable was used to separate the matching and regularization terms. ESM optimization was used to perform matching by minimizing the data term whereas regularization was achieved by Gaussian smoothing.

A variation of Thirion's Demon Algorithm was proposed by Vercauteren et al. endowed with the diffeomorphic property [23]. In this approach, opposite to classical Demons approaches, an update field is estimated in all the iterations of the algorithm. A compositional rule is used between the previous estimate and the exponential map of the update field to estimate the running transformation. This exponential map is calculated by using the composition of displacement fields and the 'scaling and squaring' method [26, 27]. Diffeomorphism of the mapping is ensured by exponentiation of the displacement field. As an application of the model, Stefanescu et al. proposed a way of performing adaptive smoothing by taking into account the knowledge regarding the elasticity of tissues [28].

The Demons algorithm has found use not only in study of scalar images but its application has been extended to multi-channel images [29], diffusion tensor ones [30], as well as different geometries [31]. Peyrat et al. used multi-channel Demons to register time-series of cardiac images by enforcing trajectory constraints. Each time instance was considered as a different channel while the estimated transformation between successive channels was considered as constraint [29]. Yeo et al. [31] derived Demons forces from the squared difference between each element of the Log-Euclidean transformed tensors while taking into account the reorientation introduced by the transformation.

2.4 Curvature Registration:

These image registration methodologies don't necessarily need an extra affine linear pre-registration step, since the regularization scheme associated with it does not affect the affine linear transformations. This constraint has been used by Fischer and Modersitzki in [32, 33]. Despite several attempts to solve the underlying transformation function using the Gâteaux derivatives with Neumann boundary conditions, Henn [34] pointed out that the resulting underlying function space still penalized the affine linear displacements. Henn, further proposed including second-order terms as boundary conditions in the energy and applying a semi-implicit time discretization scheme to solve the full curvature registration problem. Beuthien et al. [35], proposed another way to solve the curvature based registration problem based on the approach presented in [36] for the viscous fluid registration scenario. Instead of devising a numerical scheme to solve the PDE that resulted from the curvature registration equilibrium equation, recursive convolutions with an appropriate Green's function were used.

2.5 Flows of Diffeomorphisms:

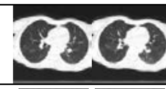
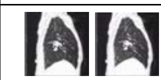
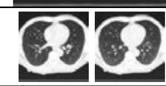
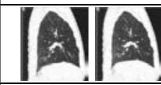
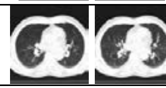
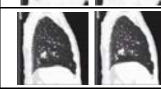
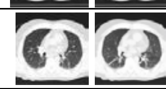
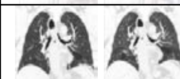
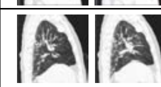
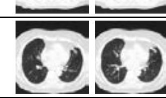
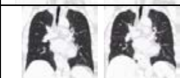
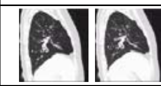
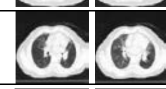
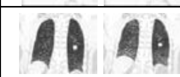
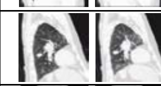
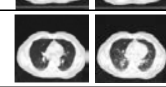
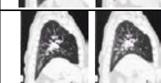
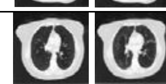
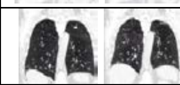
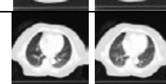
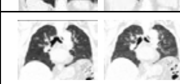
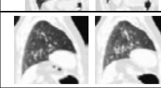
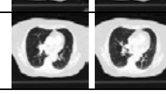
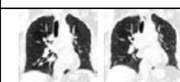
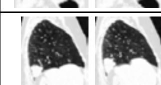
Flows of diffeomorphisms have also been one of the propositions for deformation modeling. In this case, the deformation is modeled by considering its velocity over time according to the Lagrange transport equation [15, 37, 38]. This framework is also known as large deformation diffeomorphic metric mapping (LDDMM). It allows for the definition of a distance between images or sets of points [39], [40]. The mathematical rigor of the LDDMM framework comes at an important cost. The fact that the velocity field has to be integrated over time results in high computational and memory demands. Moreover, the gradient descent scheme that is usually employed to solve the optimization problem of the geodesic path estimation converges slowly [41]. More efficient optimization techniques for the LDDMM have been investigated in [41], [42] & [43].

3. Materials and Methods

3.1 Preparation

The dataset used comprised of a total (3×2)×10 i.e. 60 thoracic CT images across 10 subjects. It was obtained from the publicly available database, http://www.dir-lab.com, with proper downloading permissions from the concerned administrator. All images were anonymized and all procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study. All patients or legal representatives signed informed consent. The image dimensions lie between 396×396 to 432×400 pixels. There were 6 frames from a temporal thoracic image sequence each for every Anatomical Plane (AP) i.e. Axial (supine), Coronal and Sagittal for all the 10 subjects acquired simultaneously with a gap of 0.1 second starting from time t= 0.1 to 0.6 seconds. All images were identified as $I_N^{AP}(x, y, t)$ where $\{N, t \in \Re^+ \mid 1 \le N \le 10; t = (0.1, 0.6)\}$, (x, y) are the x & y coordinates in the Cartesian plane and AP signifies the three anatomical planes of view i.e. Axial (a), Coronal (c) and Sagittal (s). Suppose the 3rd frame from coronal AP for subject 'case 7', would be notified as $I_7^C(x, y, 0.3)$. A view of the image database is shown in the table 1 for representational purposes.

Table 1: All three anatomical viewpoints for all the 10 subjects at time t=0.1 & 0.6 sec

	ANATOMICAL PLANES (T & M Images)		
	Axial	***Coronal***	***Sagittal***
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

3.2 Proposed Methodology

We had a temporal thoracic CT image sequence for the free-breathing process. First image frame of the sequence acquired at time t= 0.1 sec. is the full inhale frame. It is considered as the target (fixed) image. Similarly the frame acquired at t= 0.6 sec. is the full exhale frame and is considered as the moving (source/deformed) image. These both image frames are diametrically most deformed with respect to each other. A method has been proposed to register the moving image to the target image i.e. M→T as can be seen in figure 1.

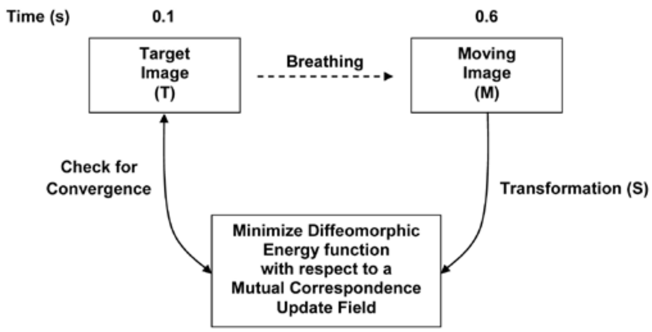


Figure 1: The proposed model

These images belong to the same domain and are related through a transformation T_R. The moving image M is transformed into M' such that a convergence is achieved between the M' and T image pair which would signify the closest moving image M can get to the target image T.

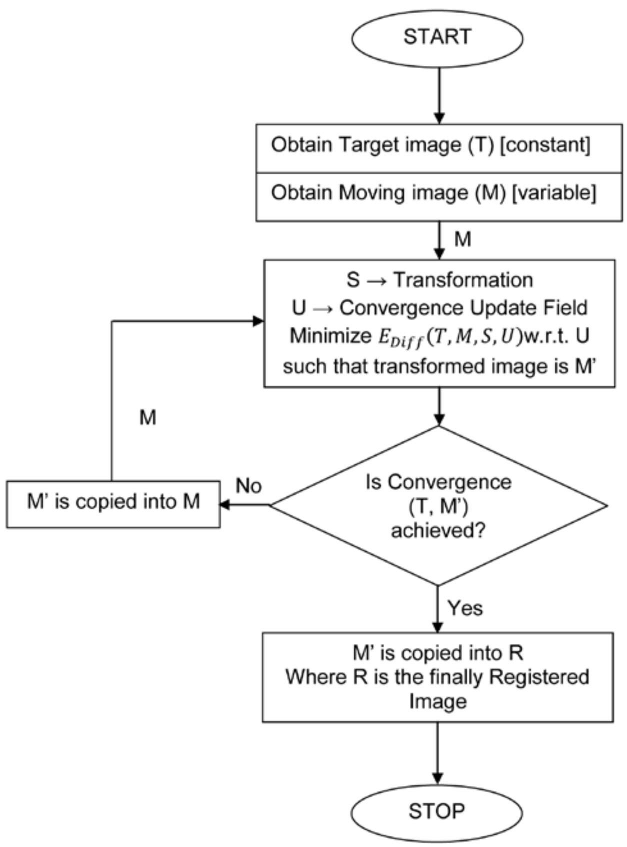


Figure 2: Flowchart of the iterative process in the registration procedure

A diffeomorphic energy function $E_{Diff}(T,M,S,U)$ is minimized with respect to the convergence update field 'U' in an iterative process over the image dimensions (as can be seen in figure 2). During the iteration, each time a transformed image M' is obtained, it is compared against the target image T using a Convergence() function. This function is checked at each step for a previously determined threshold. In case of a convergence achieved the iteration is stopped and the finally transformed image till that stage is considered as the required finally registered image R. In case of no progressive convergence in the consecutive iterations, the iteration is continued until the stopping factor eventually comes into play.

3. Results & Conclusion

Iterative diffeomorphic energy minimization using convergence factor across the image boundaries yield a transformed image (M') which was pitted against the actual target image (T) at different stages of the iteration to assess the level of transformation. Out of the ten subjects' data at hand, the coronal, sagittal and axial APs of subject 'case 7' has been chosen to elaborate and demonstrate the proposed technique with results. For coronal AP, the transformed image M' after the complete registration process showed an increase of 28.25% SNR (signal-to-noise ratio) value with respect to the target image (T) in comparison to the moving image with respect to target image; the change in PSNR (peak SNR) value was recorded at 23.37% increase in M'-T pair in comparison to M-T pair. A new metric called the SSIM (Structural Similarity) index has been used [44]. It has been used to estimate and measure the similarity between two images. It has been used as a deciding metric which would give a percentage similarity between the two images in question i.e. the fixed and the moving image and the fixed-transformed image pair. In case of coronal AP, the mean SSIM index for the M-T pair was calculated at 0.4371, the same index for the M'-T pair came at 0.4956. Along with similarity measures such as SNR, PSNR and m-SSIM, NCC (normalized cross-correlation) has been used to demonstrate as to how close the transformed image (M') has come to the target image (T) as a result of the registration process. The NCC value for M-T pair was estimated at 0.8282, for the M'-T pair it was calculated at a higher value of 0.9297 which further helps in establishing the closeness of the transformed image to the target source and hence, the proposed methodology as an efficient deformable image registration approach. Similarly for Axial AP case 7, the SNR increase was 3.39%, PSNR increase 2.36%, SSIM went from 0.7568 to 0.7484 and NCC increased from 0.955 to 0.959. For Sagittal AP case 7, the SNR increase was 35.4%, PSNR increase 27.29%, SSIM increased from 0.4677 to 0.5554 and NCC increased from 0.8853 to 0.9624.

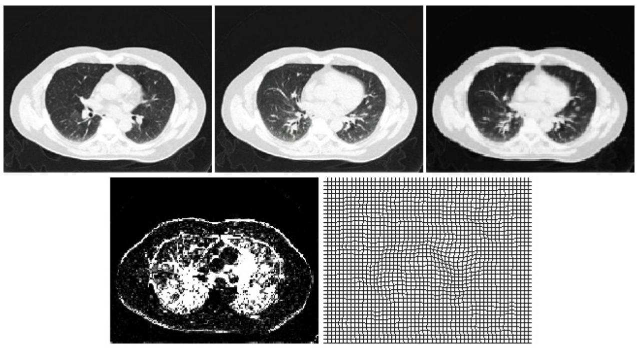


Figure 3: (in clockwise dir.) For case7 Axial, the Target-Moving image pair, Transformed moving image, the Transformation Grid and the Difference Image

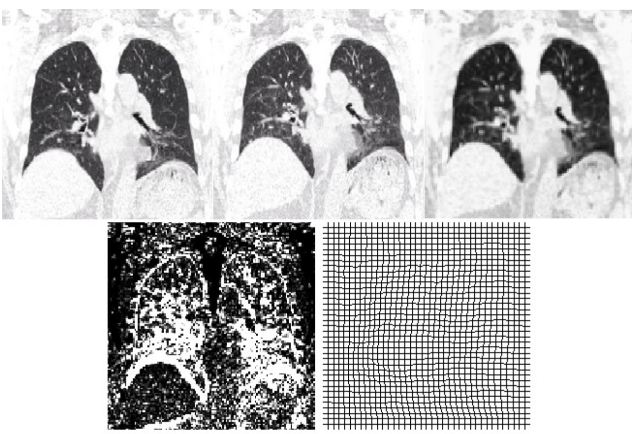


Figure 4: (in clockwise dir.) For case7 Coronal, the Target-Moving image pair, Transformed moving image, the Transformation Grid and the Difference Image

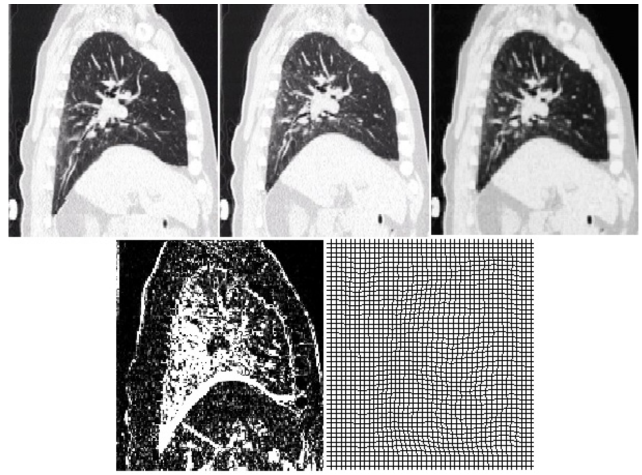


Figure 5: (in clockwise dir.) For case7 Sagittal, the Target-Moving image pair, Transformed moving image, the Transformation Grid and the Difference Image

The target-moving image pairs, the transformed moving image, transformation grid and the difference image have been shown for subject 'case 7' axial, coronal & sagittal APs in the figures 3, 4 and 5 respectively. These were results of the iterative process of diffeomorphic energy minimization of subject 'case 7' moving image frames from all APs.

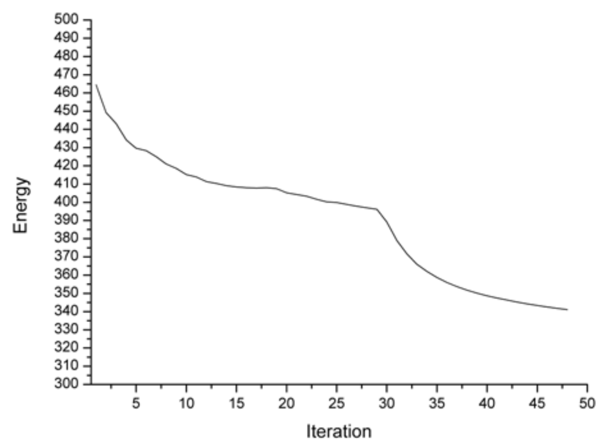


Figure 6: Energy minimization vs. Iterations for 'case 7' axial AP

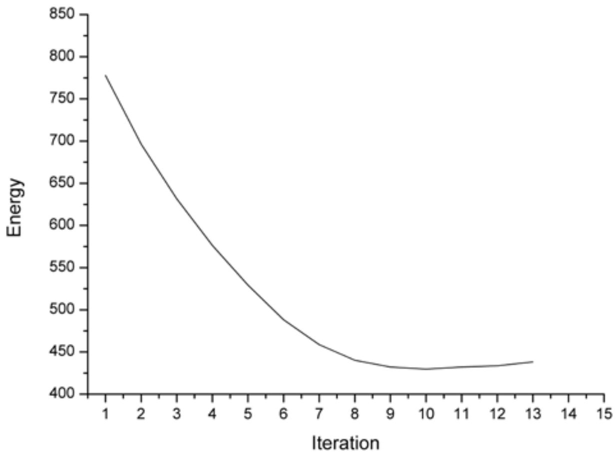


Figure 7: Energy minimization vs. Iterations for 'case 7' coronal AP

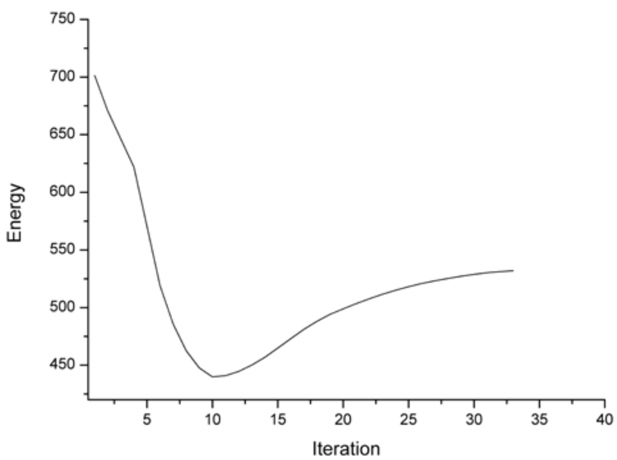


Figure 8: Energy minimization vs. Iterations for 'case 7' sagittal AP

The axial moving image frame took 48 iterations; the coronal image frame took 13 iterations and the sagittal image frame took 33 iterations for convergence of the update field. The proposed technique was practically implemented on all the subject data at hand i.e. three anatomical positions across ten subjects. After obtaining the finally registered images for complete dataset, they were pitted against the fixed images of their own sequence's respective sub-datasets. Similarity metrics such as SNR, pSNR, mean-SMIM index and NCC were calculated and compared for each M-T and M'-T pairs for improvements (if any) which might suggest closeness of the registered image towards the fixed image. All similarity metrics clearly seem to improve from S-T to M'-T image pair for all subjects. Where there are significant changes in the case of coronal and sagittal APs, respective changes are not as notable in axial AP's data, this can be explained by usually comparatively smaller deformations in the 'anterior-posterior' direction.

4. Future Direction

A novel, practically more feasible and accurate deformable image registration methodology for thoracic image sequences has been proposed. It could be a boon for real-life applications such as image acquisition for radiotherapy planning of thoracic lesions, dosimetric evaluation, tumour growth progression (with time) and determination of subject-specific deformable motion models.

This work can be looked upon as an automatic way of deformable image registration for high contrast medical images using demons as image elements. One way to improve this method is by improving and enhancing the quality as well as the quantity of the database used. Also, the aforementioned procedure can provide better results if applied for a different human anatomy altogether.

However diligently and accurately it may have been done, there might still be some scope of improvement and betterment in the methodology and also in its presentation. The search and pursuit of better methods for deformable medical image registration is still on.

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