Deformable Registration of Planning CT and Daily Cone beam CT for Image Guided Adaptive Radiation Therapy System

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Abstract: Adequate medical image data analysis could provide improved disease understanding, diagnosis, staging, and measurement of the response to the treatment, especially for radiation therapy system modeling. In image guided radiation therapy systems, it is of great importance to register the planning images with the daily images for adaptive radiation therapy. Because there are various local and global deformations between the image pairs to register, we estimate the deformation in a coarse-to-fine manner using orthogonal wavelet basis. The wavelet coefficients are estimated by minimizing the energy function, where the internal forces are derived from the Navier partial differential equations (PDE) and the external forces are derived from the similarity measure between the registration pairs using normalized mutual information. The experimental results on head-neck and chest cancer studies with both intra- and inter-fraction registration are presented. And we validated the registration method quantitatively using synthetic, pre-defined deformations, and qualitatively using clinical images. The applications of proposed algorithm for image guided adaptive radiation therapy, including ‘automatic deformable re-contouring’ and ‘automatic deformable re-dosing’ throughout the course of radiotherapy were also studied.

Keywords: biomedical control system; image guided radiation therapy; deformable registration; wavelet; multi-resolution; cone beam CT; Planning CT; adaptive radiation therapy

I. INTRODUCTION

Medical imaging data analysis plays an important role in improving the clinical treatment, especially for radiation therapy system modeling. Radiation therapy has been proven as an effective treatment for many localized cancer types. Approximately 60% of cancer patients are treated with external beam radiotherapy during disease management (Khan and Stathakis, 2010). During the past 15 years, accuracy of delivered treatment doses has been greatly improved by the use of intensity modulated radiotherapy (IMRT). Although the dose can be accurately delivered to the planned location, intra and inter-fraction changes in patient geometry have required the use of motion-related margins in treatment plans (Stanton et al., 2010).

Recently, the advancement of volumetric imaging in the treatment room by using kilo-voltage cone beam computer tomography (CBCT), has provided the imaging data needed to perform image guided radiation therapy (IGRT) and adaptive radiation therapy (ART) (Sonke et al., 2009). The goals of both IGRT and ART are to increase the radiation dose to the tumor, while minimizing the amount of healthy tissue exposed to radiation (Paquin et al., 2009). Numerous clinical studies and simulations have demonstrated that such treatments can decrease both spreading of cancer in the patient and reducing healthy tissue complications (Lu et al., 2006).

In the adaptive radiation therapy treatment, to maximize radiation dose to the tumor and in the mean time to minimize radiation to healthy tissues, the patient alignment and the information on radiation beam angles are required to be updated continuously in the treatment room (Noel and et al., 2010). The image guided adaptive radiation therapy provides method to monitor and adjust the treatment plans to accommodate the changes introduced by patients or organs. The concepts require advanced image processing tools in order to be successful in clinical practice.

Deformable registration algorithms play an essential role in optimizing radiation dose delivery in both of ART and IGRT systems. For instance, registration of planning CT images with daily CBCT images can adjust the radiation planning. In addition, deformable registration is also important for treatment re-planning via re-contouring and re-dosing the daily CBCT when implementing radiation therapy planning (Lu et al., 2006).

Research has been done on deformable registration for planning CT and CBCT. For instance, B-spline based registration algorithms were used to estimate the deformation (Paquin et al., 2009), and in their work multi-scale deformable strategy was used to improve the registration efficiency. In the work by (Brock et al., 2006), finite element model (FEM) was used for the registration of planning CT and CBCT, which was aiming for obtaining a more accurate assessment of tumor response. In the head and neck cancer diagnosis, demons deformable registration algorithm was used for the CBCT...
guided procedures (Nithiananthan et al., 2009). Optical flow based registration was used for CBCT based IGRT (Ostergaard Noe et al., 2008) and the acceleration via graphics processing units (GPU) improved the registration efficiency for an online CBCT system.

In this work, for estimating deformation more efficiently, we use a multi-resolution wavelet representation to express the deformation field. Clinical applications in IGRT system demonstrate the efficiency of our proposed algorithm.

II. MATERIAL

Datasets were collected from 10 patients treated under the on-board imager (OBI cone beam CT, Varian Medical System) which has been in daily clinical use at Shandong Cancer Hospital. Before treatment planning, each patient underwent a series of imaging studies including an intravenous contrast planning CT imaging (Philips Brilliance Big Bore 16). Then the GTV (gross tumor volume) and PTV (planning target volume) were delineated on every section of the planning CT scans by the radiation oncologists. Radiation Physiast the organs such as liver, external surface, spinal cord, kidneys, spleen, and stomach on the planning CT. These contours were reviewed and edited by radiation oncologists. Finally, treatment planning is made with four components including radiotherapy structure (RTstruct), radiotherapy planning (RTplan), radiotherapy dosing (RTdose) and Dose Volume Histograms (DVH) analysis. At the time of each delivered treatment fraction, a KV CBCT was obtained during normal breathing. Of the 10 patients investigated, 5 cases had head-neck cancer and another 5 cases had chest cancer, where planning CT image size is 512x512x96 and CBCT image size is 384x384x64. The methods used for radiotherapy are IMRT for head-neck (H&N) and conformal radiation therapy (CRT) for chest.

III. DEFORMABLE REGISTRATION ALGORITHM

Firstly, we express deformable process using Navier partial differential equations (PDE), and then the deformation field is represented using the wavelet basis. The deformation energy function includes two components. The first one is internal force which is derived from the Navier PDE, and the second one is the external forces which are the normalized mutual information of image pairs to be registered.

A. Deformable registration problem

The equilibrium state for an isotropic homogeneous body can be described by Navier partial differential equation (PDE) (Holden, 2008). In contrast to classic thin-plate or B-spline based registration method, Navier PDE is a physical model based method for deformable registration. Navier PDE models movement of the organ tissues as an elastic object because that organs can be considered as elastic media that are exposed to external forces and are smoothly deformed.

As in (Bajcsy and Kovacic, 1989), elastic constants \( \mu \) and \( \lambda \) define the elastic properties of the body and \( u=(u_1, u_2, u_3)^T \) is the vector of external forces which are distributed across organ and tissues. As in (Bajcsy and Kovacic, 1989), elastic constants \( \mu \) and \( \lambda \) define the elastic properties of the body and \( u=(u_1, u_2, u_3)^T \) is the vector of external forces which are distributed across organ and tissues. As in (Bajcsy and Kovacic, 1989), elastic constants \( \mu \) and \( \lambda \) define the elastic properties of the body and \( u=(u_1, u_2, u_3)^T \) is the vector of external forces which are distributed across organ and tissues. As in (Bajcsy and Kovacic, 1989), elastic constants \( \mu \) and \( \lambda \) define the elastic properties of the body and \( u=(u_1, u_2, u_3)^T \) is the vector of external forces which are distributed across organ and tissues.

The use of warp complexity by a coarse-to-fine strategy to express the deformation field is effective to recover the deformation in the registration process. The wavelet basis, which is multi-resolution approximation of deformation field, is suitable for such a coarse-to-fine optimization process starting from the low resolution approximation of global deformation, through the details in its different orientations, and ending with finest details of local deformation. Furthermore, wavelet basis has the advantage over Navier-Cauchy eigen functions because they allow deformations with local support to be modeled from a finite set of basis functions (Holden, 2008). So we can do deformable registration by expressing the deformation field using wavelet representation. Here, we expand the elastic deformation field \( \mathbf{u} \) with wavelet transform and then estimate the wavelet parameter vector \( \mathbf{c} \), for 3D that yields:

\[
\mu \nabla^2 u_i + (\lambda + \mu) \frac{\partial^2 u_i}{\partial x_i^2} + F_i = 0 \quad (i=1,2,3),
\]

In (1), \( \theta \) is cubical dilation and has following expression,

\[
\theta = \frac{\partial u_1}{\partial x_1} + \frac{\partial u_2}{\partial x_2} + \frac{\partial u_3}{\partial x_3}
\]

In (1)-(2), \( X=(x_1, x_2, x_3)^T \) represents the coordinate system before deformation process and \( F=(F_1, F_2, F_3)^T \) is the vector of external forces which are distributed across organ and tissues. As in (Bajcsy and Kovacic, 1989), elastic constants \( \mu \) and \( \lambda \) define the elastic properties of the body and \( u=(u_1, u_2, u_3)^T \) is the vector of external forces which are distributed across organ and tissues. As in (Bajcsy and Kovacic, 1989), elastic constants \( \mu \) and \( \lambda \) define the elastic properties of the body and \( u=(u_1, u_2, u_3)^T \) is the vector of external forces which are distributed across organ and tissues. As in (Bajcsy and Kovacic, 1989), elastic constants \( \mu \) and \( \lambda \) define the elastic properties of the body and \( u=(u_1, u_2, u_3)^T \) is the vector of external forces which are distributed across organ and tissues. As in (Bajcsy and Kovacic, 1989), elastic constants \( \mu \) and \( \lambda \) define the elastic properties of the body and \( u=(u_1, u_2, u_3)^T \) is the vector of external forces which are distributed across organ and tissues.
\[ x' = x + u^1 (x, y, z; \mathbf{c}) \]
\[ y' = y + u^2 (x, y, z; \mathbf{c}) \]
\[ z' = z + u^3 (x, y, z; \mathbf{c}) \]  
(4)

where \((x, y, z)\) are coordinates in the floating image and \((x', y', z')\) are corresponding coordinates in the reference image. The registration algorithm estimates the wavelet coefficient \(c\) by minimizing the energy function in following sections. The 3D separable wavelet decomposition of deformation field, \(u(x)\), everywhere within a cubical support \(N=(N_x,N_y,N_z)\) can be presented:

\[
\left\{ \begin{array}{l}
    u(X) = \sum_{k=0}^{N_x-1} 2^{-j/2} c_{jk}^{i} \Phi_{s}^{j} \left( 2^{-j/2} X - K \right) + \\
    \sum_{j=R}^{J} \sum_{s=2}^{S} \sum_{k=0}^{K_{s}.-1} c_{jk}^{i} \Phi_{s}^{j} \left( 2^{-j/2} X - K \right)
\end{array} \right. \]

\[N_{j} = 2^{-j} N = 2^{-j} (N_x, N_y, N_z) \]
\[K = (k_s, k_j, k_z)\]
\[X = (x, y, z)\]
\[i = 1, 2, 3\]

In (5), as in normal wavelet transformation, \(i\) is an index denoting the three directions \(x, y\) and \(z\) of the vector function \(u(x)\), \(s\) is an index denoting the subband, \(j\) is an index denoting the resolution levels, and \(k=(k_x, k_y, k_z)\) is the translational index within \(N_{j} = 2^{-j} N = 2^{-j} (N_x, N_y, N_z)\) support. Each wavelet coefficient \(c_{jk}^{i}\) is indexed by the directions \(i\), the orientation \(s\), the resolution \(j\), and the spatial location \(k\) it stands for.

The basis functions are 3D functions that are translated across a cubical grid with intervals of 2 and within a support of \(N=(N_x,N_y,N_z)\). Each basis function is weighted by the corresponding wavelet coefficient \(c_{jk}^{i}\). The basis functions are a tensor product of one-dimensional scaling and wavelet functions. Substituting the deformation field, \(u\), in (3) as represented in (5) results in a linear combination of the integral (Gefen et al., 2003). It can be concluded that the result is linearly proportional to the Wavelet-Galerkin discretization matrix of the homogenous static Navier PDE (Gefen et al., 2004). This implies that minimizing the elastic energy is equivalent to solving Navier PDE.

C. Similarity measure as the Constraint

Once the internal force and expression of the deformation field are obtained, the most important part of the elastic matching model is where and how the external forces are applied in order to obtain consistent deformation. The solution to this problem depends on the forces and with the appropriate force modeling with which we can estimate the deformation locally as well as globally. There are many different ways to formulated the external forces, such as using information from the input data, from external knowledge (i.e., interactively or from a knowledge base) or from some other processes. In the registration process the task of external forces is to bring similar regions in patient images into correspondence. So the external force which we need then is the global and local similarity measure between the region at some particular position \(x = (x_1, x_2, x_3)\) in one object and corresponding regions in another object at position \(x + u, u = (u_x, u_y, u_z)\).

The similarity function at some particular position \(x\) is denoted as \(S(u)\). The best possible match is expected for the displacement vector \(u\) which maximizes \(S\). Provided that the similarity function has a maximum, a force proportional to the gradient vector of the similarity function \(S(u)\) can be applied to increase the similarity measure. The external forces are determined in such a way that an image-based similarity metric is maximized. Using image intensity as the similarity measure, for instance, normalized mutual information (NMI), has the advantage of directly exploiting the raw data without requiring segmentation or extensive user interaction. The external force is defined as a proportion to the NMI. Because the energy function should be minimized for estimating the wavelet coefficients, here we define external forces as the inverse of NMI:

\[ \text{external}(c) = 1 / \text{NMI}(X, X(u)) \]  
(6)

The energy function \(E(c)\) is composed of external forces, \(\text{external}(c)\), and internal forces, \(\text{internal}(c)\):

\[ E(c) = \text{internal}(c) + \text{external}(c) \]  
(7)

The deformation is determined by the registration parameters that are represented as the wavelet coefficients \(c_{jk}^{i}\). Firstly wavelet coefficients in the highest scales corresponding to the lowest resolution signal component are estimated and then the wavelet coefficients corresponding to higher resolution signal components are estimated.

Normally, the number of parameters \(c\) is identical to the number of grid points in the represented transformation cubical support, and the optimization algorithm needs to handle a large number of parameters. However, since the deformation of interest (the elastic deformation) is by its nature smooth, it can be estimated with only lower resolution levels and still can provide reasonable accuracy. In our work, we use the sixth resolution level.

In order to simplify expression for the elastic energy and to reduce computational complexity, it is assumed that the scaling and wavelet functions used satisfy a principle which is called threefold orthogonality. The consequence of satisfying this property of threefold orthogonality is that minimizing the elastic energy of the deformation is equivalent to minimizing separately the elastic energy of the different deformation components (Gefen et al., 2003). In our work, we only approximate threefold orthogonality using semi-orthogonal spline wavelet of order 3. The outputs of registration are deformation maps that are the voxel-to-voxel displacements between reference image and floating images.
IV. EXPERIMENT AND DISCUSSION

CBCT-CBCT, PCT-PCT and PCT-CBCT are registered respectively for both mono-modality and multi-modality experiments. We compare proposed method with traditional B-spline based free from deformation method. Both artificially deformed images and real clinical images are performed in our experiment for validation.

A. Validation of the algorithm with known deformation

Experiments on a set of reference and floating image pairs with known deformations were carried out to establish the ground truth for validating registration accuracy. In our experiment, floating images were obtained by deforming the reference images using known B-spline vector, and therefore the deformation between reference image and floating image was available as “ground truth”. The difference between known deformations and deformation vectors calculated by proposed algorithm can be served as a criterion for accuracy evaluation.

Ground truth data should be obtained for evaluating the efficiency of algorithm qualitatively. We applied three levels of known deformation fields on reference images. Both mono-modality and multi-modality image registrations were tested in the experiments. We repeated this procedure for all different image pairs, and PCT-CBCT image pairs were registered by oncologists using commercial software manually in Shandong cancer hospital before our experiment. PCT-PCT, CBCT-CBCT and PCT-CBCT were registered respectively. For each experiment, the floating images were deformed used known spline vectors as mentioned before, and then registered with the reference image.

We computed the deformation difference (DD) with the pixel-wise sum of mean absolute difference between the vector deformation worked out by proposed method and the known vector deformation for each pair of images. Table 1 is the DD comparison for the H&N patients between the proposed wavelet based method (WR) and the traditional B-spline based free form deformation method (FFD) (Mates et al., 2003), while Table 2 is for the chest cases. Each value in Table 1 and Table 2 is the mean value of all experiments using clinical data.

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<tr>
<th>Table 1. H&amp;N-Deformation difference between the WR and FFD</th>
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<td>FFD(D1)</td>
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<td>WR(D3)</td>
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<th>Table 2. Chest-Deformation difference between the WR and FFD</th>
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<td>FFD(D1)</td>
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From Table 1 and Table 2, DDs gained by WR are always smaller than the FFD, indicating that the WR is more accurate than the FFD for three level of deformation. The CBCT images contain noise and artifact which would reduce the registration accuracy and robustness. Furthermore, the registration accuracy is affected by the deformation between the reference image and the floating image. Larger deformation can decrease the accuracy. However, from the tables, WR is more robust than FFD method with more stable lower DD for three kinds of registration and three levels of deformation. Chest deformation is larger than H&N deformation, from tables (1) and (2) deformation in chest is more difficult to resume than the deformation in H&N. Accuracy of the WR registration was also demonstrated by better visualization of the checkboard images after registration from figure 1.

![Fig. 1. Checkboard after planning CT and CBCT deformable registration, the first row is using WR, the second row is using FFD (Chest patient)](image)

V. CLINICAL APPLICATION FOR ADAPTIVE RADIATION THERAPY

Deformable automatic re-contouring and re-dosing for improving the treatment processing are ART applications of deformable registration. We performed qualitative evaluation of the automatically generated contours for all cases by visual inspection of the contour matches with the underlying structures in CBCT images.

The deformable registration technique provides the voxel-to-voxel mapping between reference image and floating image. The vertices of the reference surface were displaced in accordance with the deformation map, forming the deformed surface. The new contours were reconstructed by cutting the deformed surface slice by slice along transversal, sagittal and coronal directions (Lu et al., 2006).

The contours and dose in planning CT image can be transferred to CBCT image by deformation maps. Figure 2 is one example of the chest patient, where contours in CBCT are generated automatically by the deformation map. Similarly, figure 3 shows corresponding dose distributing in CBCT is generated automatically by same deformation map.

After statistic analysis with the radiation oncologist, the overlap between the automatically generated contours and the contours delineated by the oncologist using the planning system is over 90%, while the dose distributing overlap is also over 90%. The WR deformable registration algorithm provides deformation maps to quickly create, transform, quantitative...
analysis, aiding adaptive therapy, transferring contours and dose to radiation therapy treatment planning systems, and archiving contours and dose for patient follow-up and management.

Fig. 2. Re-contouring in CBCT image using the deformation map for chest patient. The first row is the planning CT which is contoured by the oncologist manually. Contours in the second row are generated by the deformation map automatically using the wavelet based registration.

Fig. 3. Re-dosing in CBCT image using the deformation map for chest patient. The first row is dose distributing in the planning CT which is generated by the oncologist using planning system. The second row is automatically generated dose distributing by the deformation map.

VI. CONCLUSION

In this paper, we presented a deformable registration method for image guided adaptive radiation therapy based on multi-resolution wavelet. After obtaining the deformation maps with the registration method, adaptive re-contouring and re-dosing can be achieved for the image guided adaptive radiation therapy application.

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