Dosimetric Correction for a 4D-Computed Tomography Dataset using the Free-Form Deformation Algorithm

Daniel Markel, Hamideh Alasti and James C L Chow
Department of Radiation Oncology, University of Toronto and Radiation Medicine Program, Princess Margaret Hospital, Toronto, Ontario M5G 2M9, Canada.

james.chow@rmp.uhn.on.ca

Abstract. A Free-Form Deformable (FFD) image registration algorithm in conjunction with 4D Computed Tomography (CT) images was implemented within a graphical user interface, FFD4D, for dosimetric calculations. The algorithm was developed using the cubic-B-spline method with smoothness corrections and registration point assistance to mark fiducials. Validation of the algorithm was performed with manually measured geometric differences using a QUASAR Respiratory Motion Phantom. In this work, we used the FFD algorithm to demonstrate dosimetric corrections amongst 10 breathing phases of a lung cancer patient using the 4D-CT image datasets. Different methods to enhance the image processing speed for high-performance computing were also discussed.

1. Introduction

High-performance computing for medical imaging becomes popular as recent advances in medical imaging have enabled medical staff to create images of anatomy with unprecedented resolution and realism. The efficiency of high-performance computing in handling large image datasets makes the study of internal organ motion through image registration possible. In radiotherapy, interfraction and intrafraction organ motion can complicate treatment planning and execution. Localized lung motion in the order of 3 cm and prostate motion of up to 2.4 cm has been measured \cite{1,2}. Breathing motion with amplitude of 1.5 cm has been shown to reduce tumour control probability (TCP) values by 3\% \cite{3}. Common practice when treating lung tumours is to combine the gross target volume (GTV) from breathing phases containing the displacement maxima into one planning target volume (PTV) to ensure complete coverage \cite{4}. One drawback to this strategy is increased exposure to healthy tissue, which may cause higher toxicity and result in a higher risk of radiation pneumonitis \cite{5}. An alternative strategy that has been investigated is the use of a margin which only accounts for set-up error. Predictably this results in a decreased risk to healthy tissue but at the expense of tumor coverage \cite{6}. Precise and adaptive techniques appear to be the direction in which modern radiotherapy is headed. However, one of the shortcomings of most treatment planning systems such as Pinnacle\textsuperscript{3} (Philips Medical Systems, Andover, MA) is the lack of a proper image registration tool for dosimetric calculations of plans involving non-rigid targets. There are generally few reliable and freely available image registration programs that go beyond rotating and translating the image. Intrinsic image registration techniques generally fall into two categories, global and local. Global registrations involve the use of a single mathematical expression applied to the entire image. Such techniques include rotational, translational, affine, projective or conformal transformations. The parameters involved in global registrations are few and optimization of such parameters can be done quickly. Local registration techniques are used to account...
for non-uniform differences between images, which involve adopting different transformation parameters for each region of the source image.

Free-Form Deformation (FFD) registration methods involve the use of a control grid overlaid on the images. Figure 1 demonstrates the concept by deforming a cube, using a surrounding control lattice. Each control grid vertex is considered a parameter and optimized according to an error function. Performing more complex techniques such as the Finite Element Method (FEM) has been preferred for non-elastic deformation. However, one of the drawbacks of using the FEM is the difficulty in obtaining physical characteristics of the organs being deformed. The FFD algorithm requires no physical data other than the images. The software used in this study was created using a cubic-B-spline algorithm combined with smoothness, feature point, folding, maximum voxel displacement and volume change correction functions [9-11].

Figure 1. A hollow cube deformed using the FFD algorithm. Control grid is overlaid in black.

2. Methods

2.1. Theory

The in-house software developed for dose tracking relies on a cubic-B-spline FFD algorithm taken from Huang et al [11]. The algorithm makes use of a control grid overlaid on top of the image with control grid parameters (vertices) that are moved in order to warp the space, deforming the original data. The B-spline interpolation technique is defined by the following formula

$$L(\Theta; x) = \sum_{q=0}^{3} \sum_{l=0}^{3} B_q(u)B_l(v)B_r(w)(p_{eq,j+l+k+e}^0 + \delta P_{eq,j+l+k+e})$$  \(1\).

$L$ defines the new coordinates of the pixel $x$ representing the coordinates of the initial position of the pixel in question, and $p^0$ (unchanged control grid points) and $\delta P$ (change of the control grid points) define the final control grid parameters, $\Theta$. This formula is used to determine the three error functions used in the optimization routine. These include the data driven error as well as a smoothness correction and feature point error. They are as follows.

$$E_{data}(\Theta) = \int \int_{\Omega} \left| \Phi_j(x) - \Phi_j(L(\Theta; x)) \right|^2 \, dx$$  \(2\)

$$E_{smooth}(\Theta) = \int \int_{\Omega} \left( \frac{\partial}{\partial x} \Phi_j(x) \frac{\partial^2 L(\Theta; x)}{\partial x^2} + \frac{\partial}{\partial y} \Phi_j(x) \frac{\partial^2 L(\Theta; x)}{\partial y^2} + \frac{\partial}{\partial z} \Phi_j(x) \frac{\partial^2 L(\Theta; x)}{\partial z^2} \right) \, dx$$  \(3\)

$$E_{feature}(\Theta) = \sum_i (L(\Theta; x_i) - x_i)^2; i \in [1, n_c]$$  \(4\)

The three functions are combined using weighting factors $\alpha$ and $\beta$ in Eq. (5).

$$E(\Theta) = E_{data}(\Theta) + \alpha E_{smooth}(\Theta) + \beta E_{feature}(\Theta)$$  \(5\)

The optimization routine uses a gradient-based method according to Eq. (5).
2.2. Algorithm optimization and GUI

The goal of the deformation algorithm is to calculate the control grid parameters that will reproduce a source image to match a target image. The source and target images are assumed to be globally registered with coinciding resolutions at different phases of motion. Once calculated, the control grid is interpolated to the resolution of the source and target images to perform one-to-one voxel tracking and dose recalculation.

The image optimization process is summarized in Fig. 2. Initially, the selected anatomical structures on the DICOM images are contoured to outline the surfaces of target organs. This can be done automatically using edge detection functions in MATLAB or input through contours exported from Pinnacle³. It is these binary images that are run through the algorithm and optimized. Calculated control grids can be used afterwards to deform the original DICOM images. The first step in the optimization routine is to calculate the error function (Eq. (5)), which is based on three terms; least squares difference (calculated using the distance transforms of the binary contour images), a smoothness function (based on the gradient of the control grid) and error based on mismatching of feature points, which are manually designated by the user. The gradients of the control grid parameters are calculated analytically from the derivative of the error function and are subsequently used in a gradient-based optimization method to determine the correct control grid parameters that minimize the error function. After calculating an initial control grid, it is used to deform the original binary image of the source contour and calculate the next smoothness function. From the deformed source image and new position of the corresponding feature points, an adjustment to the control grid can be calculated and tested with varying step size, until it improves the value of the error function. Once this is done the process is repeated. After a preset number of iterations, the calculated control grid is outputted as the final deformation parameters. For registration of finer details of the images, the calculated control grid is interpolated to a higher resolution mesh and the optimization routine is repeated. Routines that are designed for creating physically realistic deformations and prevention of mesh folding were also implemented [11].

Figure 2. Flow chart of the cubic-B-spline FFD optimization routine used to register image sets. The routine was taken from Huang et al [11].

The main GUI of the FFD4D algorithm is designed using GUIDE on MATLAB as shown in Fig. 3. The big middle, top right-hand and bottom right-hand windows displayed the transverse, sagittal and coronal views of the lung patient’s CT images. The vertical scrollbar in the left-hand side was used to select the corresponding breathing phase (0 – 90%) for image processing. Image dataset of a breathing phase can be registered through deformation based on selected feature points on the CT images in the GUI (blue, green and purple buttons). Patient’s DICOM-RT and RTOG images are loaded into the software. Contours created in Pinnacle³ and exported inside RTOG files are viewed and included in the patient data for use with the registration routine.

Control grid corrections were implemented from Huang et al. in addition to the basic registration algorithm [11]. First, a mesh-folding correction was applied. Mesh folding is a common problem that prevents proper warping and reconstruction of an image and causes voxels of a CT image to disappear, which is physically incorrect when applied as a model for tissue deformation [12, 13]. A check is performed on each vertex of the control grid lattice to ensure that it falls within a boundary created by the nearest surrounding control points so that further folding is not created when interpolating the control grid to a finer mesh. A routine
was designed to check that all control points fall within the octahedron designated by the surrounding points. Points that fell outside this space were moved to the centre of the octahedron as opposed to their original position without motion as outlined in the literature, to preserve the general shape of the deformation [11].

Another correction is made to ensure that motion does not exceed the maximum voxel displacement [12]. The maximum voxel displacement was set to 4 cm per phase for all voxels, which is an acceptable upper limit for lung motion [1]. To implement it for the deformation vector of each vertex \( \mathbf{\delta}_{m,n,o} \) in the control grid lattice is multiplied by the factor,

\[
\alpha_{MVD} = -\exp\left(-0.1 \left( \frac{MVD(m,n,o)}{MVD}\right)^6 \right) \quad (6)
\]

This ensures that the deformation vector’s amplitude and subsequently voxel motion never exceeds 4 cm even if it avoids causing mesh folding. This forces a more anatomically correct deformation.

For validation purposes, a QUASAR respiratory motion phantom was chosen, as the changes due to motion are detectable and geometric features are easily identifiable. The phantom was moving 4 cm in the super-inferior directions to simulate the diaphragm motion of a patient due to free breathing motion [14]. The phantom has a cylindrical cedar insert (mimicking lung density), held within an acrylic oval body. One tissue-equivalent cubic (3 \( \times \) 3 \( \times \) 3 cm\(^3\)), and one spherical insert (1 cm diameter) are embedded in the cylindrical lung cedar insert. The “oscillation” mode of the phantom was used and a patient’s breathing profile was programmed into the motor to move the inserts according to the patient’s breathing pattern. The phantom was imaged in 10 phases using a GE light speed plus CT simulator (16 slices at 60 kVp), capable of 4D-CT imaging [15]. The 4D-CT images were binned into 10 phases along the breathing cycle, and each phase was registered to 30%. The inserts were then contoured using the Pinnacle\(^3\) treatment planning system, with a feature point designated at the center of the spherical insert. Geometric features of the inserts were compared using the GUI’s feature point sub-menu due to its ability to measure points in space from all transverse, sagittal and coronal planes. Images of the QUASAR respiratory phantom at all 10 phases were interpolated to 100 \( \times \) 100 \( \times \) 80 pixels prior to registration. The control grid lattice was first optimized at a resolution of 22 \( \times \) 22 \( \times \) 22 pixels at 5 iterations, then at a finer resolution of 42 \( \times \) 42 \( \times \) 42 pixels for another 5 iterations. All 10 phases were chosen for comparison using the corners of the cubic insert and the center of the spherical insert as points of comparison for a total of 81 points (9 points \( \times \) 9 comparisons).

For a 3D standard lung protocol at the Princess Margaret Hospital, the GTV at 0\% and 30\% phases are fused and a margin of 6 mm is added to define the PTV [4, 16]. This protocol does not incorporate image deformations in the dosimetry calculations. The in-house developed FFD algorithm was used to compare the
dosimetric data in our hospital versus all 10 phases of the breathing cycle after having been registered to the 30% phase. The tumor and lung were delineated at all 10 phases using Pinnacle® treatment planning system and then exported to the FFD4D program as shown in Fig. 3.

3. Results and discussion

Figure 4 demonstrates the accuracy of the registration software. Figure 4(a) shows the cubic insert at the 10% breathing phase, and Fig. 4(b) shows the same insert at 30% phase after a 4 cm motion in the superior direction. Figure 4(c) shows the image of the insert from the 10% phase after registration and deformation to the 30% phase. Table 1 summarizes the results of the 81-points of comparison taken from 10 phases in the respiratory motion phantom.

Dosimetry was calculated from a 6-beam intensity modulated radiotherapy (IMRT) plan treating a tumour in the right mid-section of the lung as shown in Fig. 5(a) [17]. The FFD4D software was used to determine the differences in a patient’s DVHs when deformation and motion are considered during 10 phases of breathing. The IMRT plan based on this standard protocol was copied to the other 9 phases image sets, and dosimetry was recalculated using the CT data of those phases [4, 16]. The dose data was then reconstructed using the transformation parameters calculated through registration of the contours of selected anatomical structures for each phase as shown in Fig. 5(b). The registered 10 sets of dose data were voxel-tracked and DVHs were calculated using the contours delineated in the 30% phase plan. DVH of these PTVs were compared with the voxel tracked one as shown in Fig. 6(a). The variability due to organ motion is clearly visible from phase to phase. Figure 6(b) compares a voxel-tracked DVH to that of the standard protocol demonstrating the reduction in the dose coverage of the PTV. Figure 6(b) shows a peak difference of 10 cm³ at 4400 cGy between the DVH based on the PTV as per the standard protocol and the DVH taken when motion of all 10 phases is accounted for [17].

It is generally difficult to comparatively validate registration software, as there are many methods of doing so and no gold standard [18]. The accuracy of FFD registrations has also been found to vary for different regions of the body, and is patient specific [18]. A trained physician or therapist is also necessary to properly identify the coordinates of anatomical features. For these reasons a phantom was chosen for validation. From geometric comparisons of the registered image sets, a total average error of 3.2 mm was found with a range of 1.7 – 4.3 mm (Table 1). This is comparable and on par with other registration programs. Other FFD algorithms have reported error ranges of 0 - 6 mm [18-22]. FEM software has reported error averages of 2.4 - 4.4 mm [7, 8]. Table 1 shows that errors in the x and y (left-right and anterior-posterior) directions are minimal and only exist because of the effect of image blur on the auto contouring filter used in Pinnacle® to draw the insert contours. Ideally they should not exist as the phantom motion was designated solely in the superior/inferior axis. The motion of the cedar inputs was also a purely rigid transformation, which is possible yet difficult for large amplitudes under FFD. Unfortunately no phantom yet exists that includes deformable inserts for this study, which is why the QUASAR phantom was chosen. Error in the z (superior-inferior) direction tends to increases with difference in starting positions, as larger deformations are necessary to register the two contours. At greater distances, registration points improve the deformation significantly.

The registration process required approximately 160 minutes per phase using a PC with a Pentium 4, 3.20 GHz processor, 1 GB RAM running MS-WINDOWS 2000 32-bit and MATLAB 2008a. When the process was run on the General Purpose Cluster at SciNet (University of Toronto), all registrations of 9 phases could be run in parallel. This greatly improved the computing time. However, to further increase the computing efficiency apart from parallel processing, the FFD algorithm was investigated to find out if high performance can be achieved by reduction of data space and reduction in solution search space. Control grids were optimized at two grid sizes of 22x22x22 and 42x42x42 for 5 iterations each. Application of deformations required approximately 1-5 minutes depending on the resolution of the deformed dataset. Calculations using FFD algorithms are well known to be computationally intensive. Changing the registration settings to reduce the iterations in the optimization routine, or using substantially less control grid parameters (e.g. using 12x12x12) can significantly reduce the calculation time to as little as 30 minutes in the case of FFD4D. However the detail of the registration is often sacrificed in this case. Other implementations of the cubic-B-spline algorithm have reported calculation times of around 70-100 minutes [20, 21]. One method of reducing calculation times is to use multi-resolution algorithms [21-23] which vary the resolution of the deformation parameters based on the magnitude of the displacement. This has proven to reduce calculation times significantly to as much as half an hour per phase depending on the parameters [20]. Using alternative error criteria and tailored hardware architecture have shown to reduce calculation times such that FFDs are appropriate for clinical implementation, with some registration times being as fast as 3 minutes [21, 24].
Figure 4. Coronal images of the QUASAR phantom at the (a) 10%, (b) 30% and (c) deformed image of (a) after registration. Red cross hairs designate points of comparison.

Table 1. Error from 9 phases after registration to the 30% phase.

| Phase | Δx (L-R) Average (mm) | Δy (A-P) Average (mm) | Δz (S-I) Average (mm) | Total Distance Average (mm) |
|-------|------------------------|------------------------|------------------------|-----------------------------|
| 0%    | 0.230                  | 0.034                  | 1.694                  | 1.737                       |
| 10%   | 0.656                  | 0.344                  | 2.252                  | 2.443                       |
| 20%   | 0.064                  | 0.000                  | 4.180                  | 4.185                       |
| 40%   | 0.000                  | 0.000                  | 2.717                  | 2.717                       |
| 50%   | 0.138                  | 0.000                  | 2.194                  | 2.236                       |
| 60%   | 0.061                  | 0.000                  | 4.082                  | 4.085                       |
| 70%   | 0.069                  | 0.000                  | 4.284                  | 4.287                       |
| 80%   | 0.206                  | 0.000                  | 3.344                  | 3.376                       |
| 90%   | 0.122                  | 0.000                  | 3.993                  | 4.001                       |
|       | **Final Average**      |                        | **3.229**              |                             |

Figure 5. (a) A transverse view of the patient displaying the 6-beam IMRT plan. (b) A coronal view of the patient showing the GTV contours of all 10 phases superimposed onto the 30% CT data as well as the PTV in orange colour.
4. Conclusions
A FFD algorithm was developed that includes smoothness correction, and feature point error. Maximum voxel and volume displacement prevention corrections along with checks for mesh folding have also been integrated into the software. This code was encapsulated into a GUI called FFD4D using MATLAB. Validation of the FFD algorithm was performed using a QUASAR Respiratory Motion Phantom due to the ease at which matching features at different phases in the motion cycle could be identified. It was found that the registrations performed on 10 phases of phantom yielded an average error of 3.2 mm, with a range of 1.7 – 4.3 mm. A demonstration of applying the software to patient dosimetry was also performed. It is concluded that performing the image registration of different breathing phases in parallel using high-performance computing cluster can enhance the image processing speed, and the FFD algorithm can produce a realistic dose-volume relationship of a lung patient due to the breathing motion in radiotherapy.

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