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3D Volumetric Visualization with Automatic Rigid and Deformable Hybrid Image Registration for Adaptive Radiotherapy

Chang-Yu Wang[1,2], Tsair-Fwu Lee [1,2]*, Chun-Hsiung Fang[1]

[1]National Kaohsiung University of Applied Sciences, Kaohsiung, Taiwan, ROC
[2]Department of Radiation Oncology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

Abstract

To provide more clinically convenient image fusions for adaptive radiotherapy (ART), an automatic rigid and deformable image registration framework (AIRF) is developed for multimodal visualization of multiple chronological images and multiple radiotherapy (RT) plans. Our hybrid image registration framework, AIRF, uses a faster but less accurate rigid registration method to provide an initial registration, followed by a slower but more accurate deformable registration method to fine tune the final registration. A multi-resolution approach is also employed in the image registration process to further improve the registration accuracy, robustness and efficiency. Volume visualization is provided to guide the automatic image registration process because it can reduce the global positioning error that results from a partial 3D visual presentation in the three conventional orthogonal planar views (axial, sagittal, and coronal). The AIRF can automatically align multiple volumetric images of patients taken over an extended period of time and can merge multiple radiotherapy plans based on different planning computed tomography (CT) images. It offers illustrative 3D volumetric visualization, hybrid rigid and deformable image registration, and automatic transfer of RT dose distribution and RT structure models such as treatment targets and organs at risk (OARs) onto chronological images. The AIRF can automatically register multiple volumetric image datasets of patients taken over an extended period of time and can merge multiple RT plans based on different planning CT images for 4D or adaptive radiotherapy.

Keywords: Volumetric visualization; Deformable; Automatic image registration; Adaptive radiotherapy

Introduction

Adaptive radiotherapy (ART) is a feedback treatment process that optimizes a patient's treatment according to patient-specific information measured during the course of treatment. It is because the location and orientation of the target volume can vary during a single treatment session due to normal biological processes, such as breathing or bowel peristalsis that it may result in treatment inaccuracy. (Han-Oh et al., 2009). ART intends to improve radiation treatment by systematically monitoring treatment variations and incorporating them to re-optimize the treatment plan early on in the course of treatment (Yan et al., 1997). However, the introduction of adaptive image-guided radiotherapy has contributed to a rapid accumulation of multi-modality imaging and radiotherapy planning data, making it difficult to consolidate information on a single patient (Verellen et al., 2008).

Radiotherapy planning data are a stack of image slices with segmentation data stored on a slice-by-slice basis. The segmentation data would consist of closed contours drawn around organs at risk (OARs) and target volumes. Each contour has a special tag identifying which structure it belongs to. Thus, the patient's anatomy information is stored in a file in the form of RT structure sets containing segmentation data which are also associated with the reference CT images (Ebert et al., 2004). The calculated RT dose distribution is another three-dimensional (3D) volume matrix co-registered with the associated CT image volume. Values in the RT dose matrix represent the dose delivered to tissue in the corresponding area in the CT image volume. In summary, a radiotherapy plan is the fusion of at least three volumetric data including RT dose, CT images and RT structure models (Figure 1).

There have been many kinds of volume visualization software for medical imaging which provide fantastic image processing and regions-of-interest (ROI) delineation functions to handle diagnostic images, such as from CT, MRI or PET. There are still many challenges in merging multiple radiotherapy plans by image registration. So far, most image fusion or contouring software cannot handle RT dose data. Proprietary radiotherapy treatment planning systems (TPS) can display RT dose and RT structure sets superimposed on fused images, but the fixed image for image registration in TPS is strictly limited to planning CT. Moreover, in TPS, RT dose or RT structure sets cannot be transformed and warped into later follow-up images.

In order to merge multiple radiotherapy plans based on different CT planning scans, an automatic rigid and deformable image registration framework (AIRF) is proposed and implemented for

***Corresponding author:** Tsair-Fwu Lee, Ph.D., National Kaohsiung University of Applied Sciences, Kaohsiung, Taiwan, ROC, Tel: 886-7-3814526; Fax: 886-7-3811182; E-mail: 1097404101@cc.kuas.edu.tw, tflee@cc.kuas.edu.tw.tw

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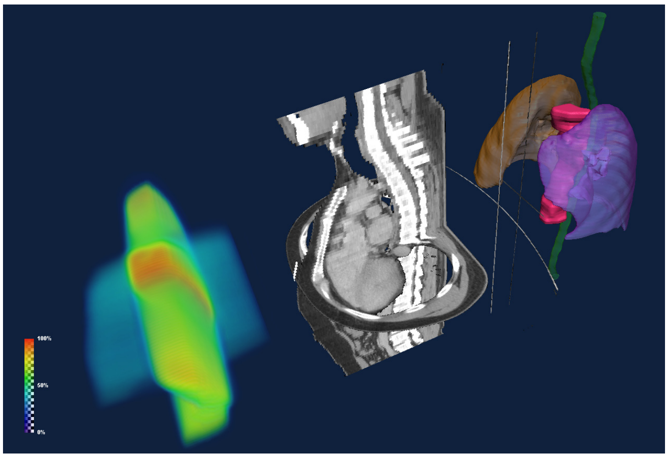

Figure 1: The volumetric visualization of a typical radiotherapy treatment plan consists of three volumetric datasets including, from left to right: RT dose, CT images and RT structure models.

volume visualization of radiotherapy plans, fused with longitudinal images or later radiotherapy plans. Aspects that require further development are identified and solutions to overcome limitations are examined.

Related Work

RT_Image, coded in the Interactive Data Language (IDL, ITT Visual Information Solutions), allows multiple imaging datasets and associated three-dimensional (3D) ROIs to be displayed at arbitrary viewing angles and fields of view. It also includes semi-automated image segmentation tools for defining metabolically-active tumor volumes that can help define target volumes for treatment planning (Graves et al., 2007).

CERR, based on the Matlab language (Mathworks Inc), provides a platform for the visualization and analysis of radiotherapy plans from a wide variety of commercial treatment planning systems (Deasy et al., 2003). It can support various types of research studies, including dose-volume analyses and radiotherapy planning comparisons.

These two software programs have helped significantly with the analysis and comparison of radiotherapy plans. However, slow speed is a major drawback due to the intrinsic limitation of a high-level computer language such as IDL or Matlab. As a result, the ability to render image volumes quickly and to display images fused from multiple volumetric image datasets together with RT dose and RT structure overlay is still lacking.

Design Overview

Retrieval of radiotherapy planning data

The CT image volume for radiotherapy planning is reconstructed from stacked DICOM CT slices. Raw data for radiotherapy planning such as RT dose data and ROI contours for treatment targets and organs at risk (OARs), together with the associated planning CT images, are exported from the Pinnacle TPS (Philips Medical) and then imported into our image registration framework for further processing.

Mesh generation from 2D contours

ROI contour sets are contoured by a physician or technician manually in a slice-by-slice manner on the transversal view of the planning CT image. Modern radiotherapy TPSs allow the user to grow a ROI by a specified 3D margin to simplify the process of manual segmentation (Pooler et al., 2008). Physicians can obtain a planning target volume (PTV) from a gross tumor volume (GTV) and a clinical target volume (CTV) where the user can specify the required margins in each of the six directions (right, left, anterior, posterior, superior and inferior). Therefore, the RT structures often overlap each other, and one voxel may represent more than one RT structure at the same time. Conventional label map technique of applying a single label to a voxel cannot be employed to represent the result of image segmentation in a RT scenario because a voxel may have two or more label indices.

3D surface models are necessary for volume rendering of treatment targets and OARs. Two common approaches are frequently used to generate a surface from sets of contour slices for each RT structure. One approach is to connect polygon contours between adjacent planes. Accuracy issues can arise from the connection algorithm and from contour or surface simplification methods. The second approach is to fill the polygon contours, stack these binary mask images to form a volume, and then to create an isosurface. Generally speaking, there is less interpolation in the second approach, and we use the latter approach to generate the surface mesh models from ROI contours for each RT structure.

Rigid and deformable image registration

An N-dimensional affine transformation is an (N+1)-dimensional linear transformation. Any affine transformation between 3D spaces can be represented by a 4 x 4 matrix. Hence, the set of transformation parameters can reduce to six for a rigid body registration: three parameters defining translation along the x, y, and z axes in millimeters; and three parameters defining rotation around the x, y, and z axes and representing Euler angles in radians. Thus, the aim of image registration is to find the translation matrix and the rotation matrices. Since the rotations around the three coordinate axes are not commutative, we define their order as rotation about the x, y, and then z-axis.

In fact, a 4 x 4 matrix can represent all types of affine transformation including translation, rotation around the origin, reflection, glide, scale, and shear. However, we use rotation and translation only for rigid-body registration in our framework. Multiple transformation matrices can be concatenated into a single matrix by multiplying them together, in the order in which they occur. To combine subsequent transformations we can easily multiply these 4 x 4 matrices together. The resulting affine transformation matrix which is the concatenation of multiple cascade transformations can then be applied to perform global warping between pairs of longitudinal image data or radiotherapy planning data. Accordingly, the transformed doses are added to obtain a spatially varying 3D cumulative dose.

This hybrid image registration framework uses a faster but less accurate rigid registration method to achieve an initial registration, followed by a slower but more accurate deformable registration method to fine tune the final registration. Deformable image registration is performed based on Demons algorithm (Guimond et al., 2001) to compensate for the change of external body contours and normal organ motion. A multi-resolution approach is also employed in the image registration process to further improve the registration accuracy, robustness, and efficiency. Initial RT structures are adapted to new CT images using a 3D deformation field generated from deformable image registration (Figure 2). ROIs could be automatically transferred onto the new CT images by extracting the boundaries of deformed 3D RT structures at each slice location in the new images.

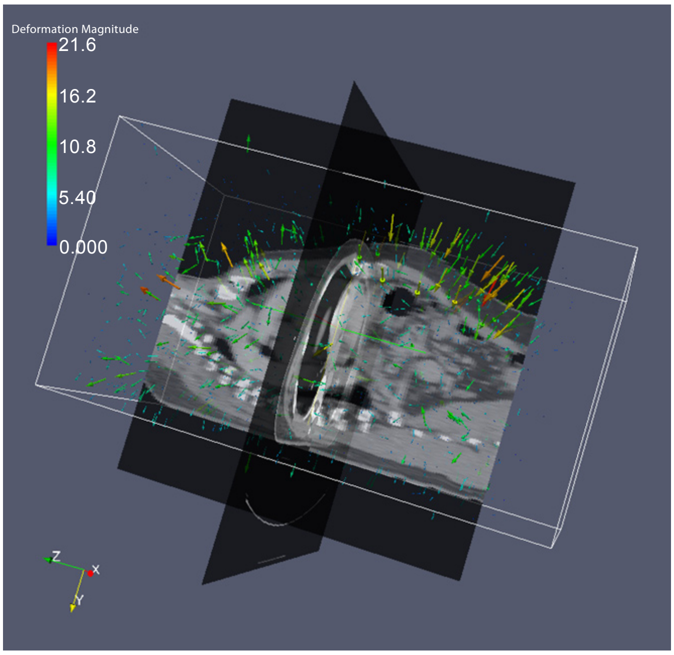

Figure 2: A 3D vector field shown in terms of color arrows represents the deformation field generated from the deformable image registration. The two orthogonal planar views represent the fixed and moving volumetric CT image data, respectively. The color scale legend indicates the displacement magnitude (in mm) of the 3D deformation field.

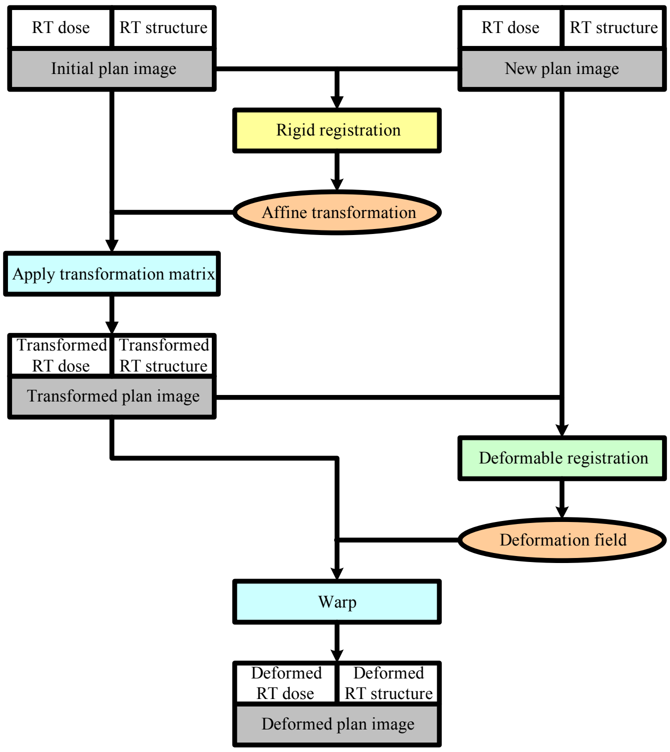

Figure 3: Flowchart of the Automatic Image Registration Framework (AIRF).

Framework implementation

The AIRF was implemented in the C++ language and was based on the Insight Toolkit (ITK) (Ibanez et al., 2005). 3D volume visualization was implemented using the Visualization Toolkit (VTK) (Schroeder et al., 2006). These open source toolkits will make it easy to extend the functionality of this framework in the future. To register multi-modal images, we use a mutual information maximization algorithm implemented in the ITK to compute the normalized mutual information (NMI) between fixed and moving images. The goal of automatic registration is to find the set of transformation parameters that result in the best value for an image similarity metric. The Demons algorithm implemented in the ITK was used in our framework for intra-modal deformable image registration. Figure 3 illustrates the flowchart of the AIRF. The entire image registration process is fully automated without manual intervention.

Results

Performance evaluation

The performance of the AIRF was compared to two well-established image registration methods, including a semi-automatic method and a fully automatic method. The semi-automatic image registration method implemented in GE image fusion software (GE Healthcare, Milwaukee, WI) is initialized with manually chosen landmarks (the LM method). The second method used for comparison is the Syntegra (GE Healthcare) NMI method which utilizes a normalized mutual information (NMI) algorithm for automatic image registration in the Syntegra image fusion software. In AIRF, the multi-resolution down-sampling strategy used for the test cases is based on the itk::MultiResolution-ImageRegistrationMethod and is defined for three computation levels. In the first (coarsest) level, the image is reduced by a factor of 8 in the column dimension, factor of 8 in the row dimension and factor of 2 in the slice dimension to alleviate the anisotropic voxel effect of most medical images (i.e. the slice spacing is 4-5 times larger than the row and column spacing) and to significantly reduce computation cost. In the second level, the image is reduce by a factor of 4 in the column dimension, 4 is the row dimension and 1 in the slice dimension. In the third (finest) level, the original images without sub-sampling are used for calculating the final optimized affine transformation matrix of the best alignment between the fixed and moving images. The test datasets consisted of ten pairs of radiotherapy plans for esophageal cancer. The average slice number of the 20 CT image datasets from the ten pairs of test radiotherapy plans was 106, and the CT image matrix size was 512 x 512 with a 5-mm slice thickness. The time for performing the entire image registration process for the AIRF method was compared to that for the semi-automatic method (LM method) and the fully automatic method (Syntegra NMI method), respectively, based on the paired t-test. The average times taken by an experienced radiation oncologist to perform image registrations using the LM method and Syntegra NMI method on esophageal cancer cases were 153.5 and 61.5 seconds, respectively. This was improved to 11.0 seconds using the AIRF method on an Intel Core Duo system running at 1.80 GHz with 6GB RAM under the Linux operating system. Using the AIRF method took only 1/14 and 1/6 of the time taken by the LM method and Syntegra NMI method, respectively. The time difference between each pair of these three methods was of statistical

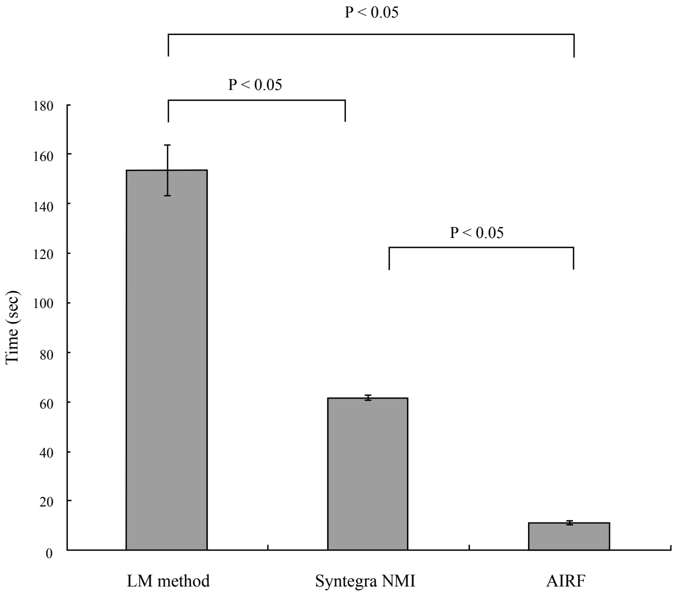

Figure 4: Performance comparison between different image registration methods.

significance ($p < 0.05$; paired t-test) (Figure 4).

To validate the registration accuracy of the AIRF, we evaluated several simulated CT image sets, which were intentionally misaligned by inducing pre-defined relative translations along the x, y, and z-axis directions, respectively. Given that an *a priori* knowledge of the translations was available, the accuracy of image registration could be verified. The results showed that the average error of image registration for the AIRF was only 0.0053 mm. With a pixel width of 0.938 mm in the simulated CT images, this implied that the AIRF could register images with sub-voxel precision.

Validation of image registration

In clinical practice, the accuracy of image registration is visually verified by physicians using anatomic bony landmarks as points of reference in 2D image slices. In addition to the three conventional orthogonal planar views (axial, sagittal, and coronal), 3D volume visualization is provided to guide the automated image registration process because it can better reflect global geometric information (Figure 5). The best achievable homogeneity of color distribution on a given anatomic voxel landmark can be distinguished visually. The skin and bone voxels could serve well as such anatomic landmarks as they are located on the surface of the image volume and are readily distinguishable from the surrounding air voxels.

Two radiotherapy plans can be merged based on the affine transformation matrix and the deformation file generated from the AIRF. Then the transformed doses can be added to obtain a spatially varying 3D cumulative dose. Visual examination of checkerboard images can be used to verify the image registration results. Figure 6 shows the final result after rigid and deformable image registration of two radiotherapy plans together with a checkerboard image illustrating how well the radiotherapy plan pair is registered. The checkerboard image contains white and red squares corresponding to intensity values taken from the moving images and the fixed images, respectively. The 3D cumulative dose in terms of isodose lines from these two radiotherapy plans is superimposed on the registered checkerboard image.

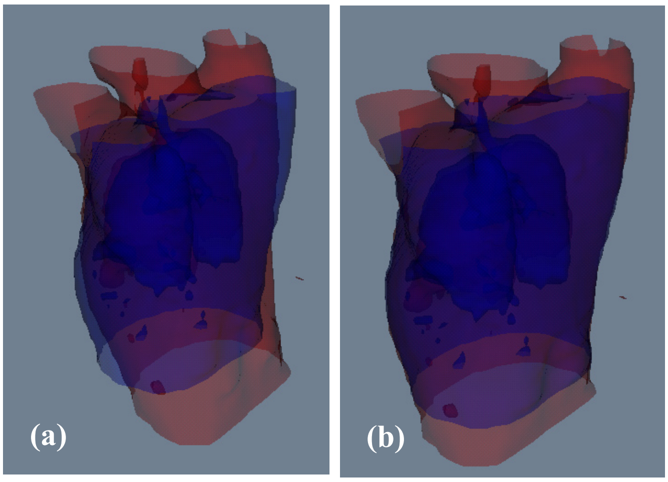

Figure 5: Monitoring the automatic registration process of two volumetric CT image datasets (red and blue) using volume visualization guidance. There is increased homogeneity of color distribution before registration (a) than after registration (b).

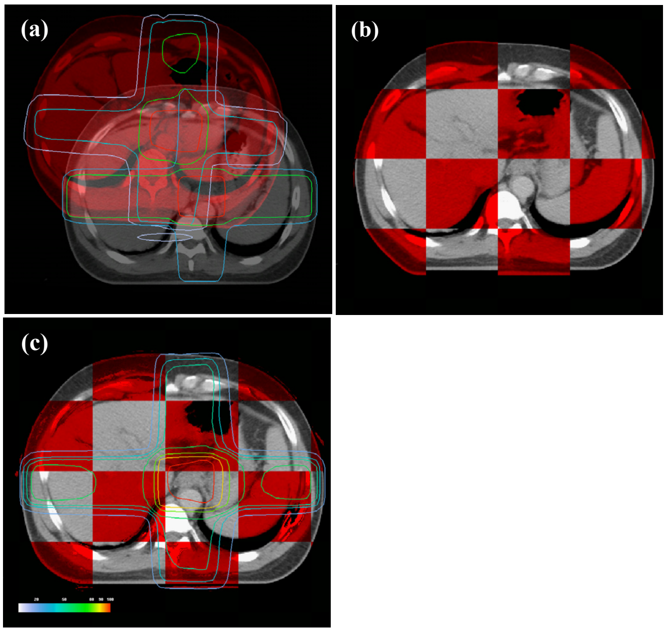

Figure 6: The merging of two radiotherapy plans based on two different planning CT images is shown in different color channels. (a) Two radiotherapy plans before registration has been superimposed with isodose lines ; (b) the alignment of the CT images of two radiotherapy plans improved after rigid registration, but the external body contours are not yet matched perfectly; (c) the external body contours and the positions of internal organs in the two radiotherapy plans match well after deformable registration. The radiation dose distribution is summed in 3D spatially and the total radiation dose is shown in terms of isodose lines. The color scale legend indicates the summed radiation dose levels.

Clinical applications

The AIRF has been demonstrated its clinical usefulness for automatic registration and volume visualization during the merging of multiple radiotherapy plans. The initial radiotherapy plan and new radiotherapy plan can be summed together into a single fusion plan for volume visualization. An illustrative 3D view of cumulative radiation dose distribution can be displayed, superimposed on volumetric images. The 3D cumulative radiation dose information is crucial to radiotherapy planning to avoid overdose damage to critical organs.

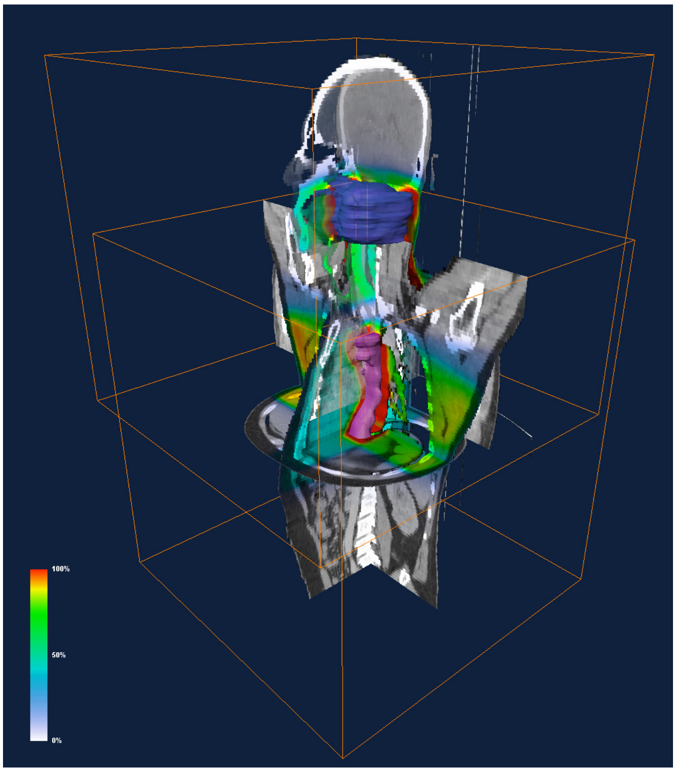

Figure 7: Volumetric visualization of a summed plan merged from an oropharyngeal cancer plan and an esophageal cancer plan superimposed with their respective volume sets of RT structure and RT dose. (The two bounding boxes represent two individual CT volume data.)

Furthermore, the application of the AIRF in merging radiotherapy plans is not limited to a single treatment site. It can be used in cases where the treatment target for the second course of radiotherapy is close to the previous target. For example, patients with metachronous cancers at different sites are not rare, and up to 20-25% of patients with esophageal cancer will develop a second cancer within two years (Parkin et al., 2005). In the past, it was difficult to evaluate the total dose from two individual radiotherapy plans, because no available TPS is capable of summing up plans based on CT images taken at different times. As a result, there is a risk that some area of the critical organs (e.g. spinal cord) is overdosed by irradiating it twice and this could potentially cause severe complications. With the AIRF, we can get a better 3D view of the cumulative radiation dose distribution. For example, the later oropharyngeal cancer radiotherapy plan and the earlier esophageal cancer radiotherapy plan could be summed together into a single fusion plan for volume visualization (Figure 7). The color scale legend shows the normalized summed dose from the two individual radiotherapy plans.

Discussion

Volumetric visualization of radiotherapy plans

Volume visualization techniques are commonly employed in the field of engineering and medical imaging and are powerful tools that can create impressive pictures (Patel et al., 2007). The AIRF offers illustrative volume visualizations of RT dose distributions, CT images, and surface mesh models of RT structures. We can easily align multiple volumetric images or radiotherapy plans of the same patient taken at different times, and the entire registration task can be done automatically. Then, we can produce a volume visualization of the merged radiotherapy plan. Visual comparison with the 3D volume visualization technique can improve registration accuracy and take less time, compared with conventional viewing techniques in three orthogonal planes (Li et al., 2005).

However, there needs to be awareness that volume visualization may add information not present in the original data by interpolating or otherwise representing missing data. Even a very coarse dose matrix can generate rather smooth isosurfaces by interpolation. Mapping dose data to a rainbow color could give the erroneous impression of values clustered in discrete bands and could hide significant detail within each color band.

Conventional image fusion software can only deal with diagnostic image data, such as CT, MRI or PET. None of these image fusion programs can handle or even project RT structure sets and RT dose distributions onto successive follow-up images. Furthermore, most image software has to re-slice and reformat the registered (moving image) volume in order to match it to the coordinate system of the reference (fixed image) volume. The reformatting process requires interpolation of pixels and adds some uncertainty. The voxels of most medical images are anisotropic instead of isotropic, because the image slice thickness is of the order of 3 to 5 mm which is significantly larger than the slice pixel spacing (<1 mm). The anisotropy of the image voxels adds additional uncertainty during interpolation.

In order to overcome these pitfalls, we extract the affine transformation matrix in each image registration pair and save the original image data without re-slicing it. We use the original image data, apply the transformation, and display the result of fusing the transformed images with RT dose and RT structure models. There may be some speed tradeoff, but information is not lost. Each image registration pair is linked by an affine transformation matrix. For RT dose and RT structure models, they can be transferred to the registered target images using the same calculated affine transformation matrix. Therefore, multiple image and RT plan pairs can be linked by affine transformations. The direction of the transformation mapping could be either chronological or anti-chronological depending on the purpose for the research.

Conclusions

The AIRF can automatically register multiple volumetric image datasets taken of patients over an extended period of time and can merge multiple RT plans based on different planning CT scans for 4D or adaptive radiotherapy. It offers illustrative volume visualization of RT dose distributions and RT structure models such as tumor targets or OARs superimposed on longitudinal follow-up images. It could be a useful tool in the research of cancer patient dosimetry and outcomes.

Conflict of Interest Notification

Partial presented at 3rd International Conference on Ubiquitous Information Management and Communication in Suwon, Korea, January 15-16, 2009.

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