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Edited by:
Keiichi Jingu, MD, PhD
Professor, Department of Radiation Oncology, Tohoku University Graduate School of Medicine, Japan

Review Article

Use of Deformable Image Registration for Radiotherapy Applications

Noriyuki Kadoya*

Departments of Radiation Oncology, Tohoku University School of Medicine, Japan

Abstract

Deformable Image Registration (DIR) has become commercially available in the field of radiotherapy. DIR is an exciting and interesting technology for multi-modality image fusion, anatomic image segmentation, Four-dimensional (4D) dose accumulation and lung functional (ventilation) imaging. Furthermore, DIR is playing an important role in modern radiotherapy included Image-Guided Radiotherapy (IGRT) and Adaptive Radiotherapy (ART). DIR is essential to link the anatomy at one time to another while maintaining the desirable one-to-one geographic mapping. The first part focused on the description of image registration process. Next, typical applications of DIR were reviewed on the four practical examples; dose accumulation, auto segmentation, 4D dose calculation and 4D-CT derived ventilation imaging. Finally, the methods of validation for DIR were reviewed and explained how to validate the accuracy of DIR.

***Corresponding author**
Noriyuki Kadoya, Department of Radiation Oncology, Tohoku University School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai, 980-8574, Japan, Tel: +81-22-717-7312; Fax: +81-22-717-7316; Email: kadoya.n@rad.med.tohoku.ac.jp

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INTRODUCTION

In recent year, Deformable Image Registration (DIR) has become commercially available in the field of radiotherapy. DIR is an exciting and interesting technology for multi-modality image fusion, anatomic image segmentation, Four-dimensional (4D) dose accumulation and lung functional (ventilation) imaging. Furthermore, DIR is playing an important role in modern radiotherapy included Image-Guided Radiotherapy (IGRT) and Adaptive Radiotherapy (ART). DIR is essential to link the anatomy at one time to another while maintaining the desirable one-to-one geographic mapping. We will discuss these applications of DIR in radiotherapy.

Deformable image registration

Image registration is a method of aligning two images into the same coordinate system, so that the aligned images can be directly compared, combined and analyzed. Image registration is classified into two groups; rigid registration and DIR. A rigid registration has six degrees of freedom: three rotational plus three translational variables. The deformation of the transformation matrix for DIR, however, is much more complicated because the matrix consists of a huge number of unknowns. The generalized registration process is shown in Figure 1. The fundamental framework for image registration generally requires four steps; namely, it requires an interpolator (which defines how voxels get

sampled during the registration process), a similarity metric (such as Mutual information), a transformation (which specifies how a volume can change during the various steps in the optimization process-such as rigidly, affinely, deformably), and lastly the optimizer. The optimizer strives to find the best possible solution that registers the two volumes by marching over a small subset of the solution space. It does this by comparing the answers given by the similarity metric for the evaluated transformed spaces.

Dose accumulation with deformable image registration

Basically, although we can add them with same planning CT image, it is impossible to add two dose distributions with different planning CT (or Cone-Beam CT (CBCT)) images due to difference in reference CT image between the two plans. DIR technique enables us to make dose accumulation with dose warping [1-6]. A schematic diagram of creating dose accumulation with dose warping is shown in Figure 2. First, DIR is performed between CT1 (moving image) and CT2 (reference image) to create a transformation, T1. Then, Resultant transformation was applied to dose 1 to create dose 1', which is warped dose distribution according to reference CT image. Finally, we added the two dose distributions (dose 1 and dose 1') to create dose accumulation. Figure 3 shows example difference CT images with rigid registration and DIR in head and neck patient between different time points. This figure indicated that the dose accumulation with rigid registration occurred large error of dose warping due to large difference between the two CT images. On the other hand, the difference between the two CT images using DIR could reduce the difference so that the dose warping with DIR could achieve high accuracy of dose accumulation. This dose warping technique is expected to be useful for evaluation of dose accumulation between previous plan and current plan for re-irradiated patient, and interfraction dose. Arai et al evaluated the differences between cumulative dose in the spinal cord using rigid registration and that using DIR for two-step adaptive IMRT for head and neck cancer and showed the difference between the two registrations was 1.6 Gy and demonstrated that the difference might depend on the accuracy of the registration [7].

Furthermore, Modern radiotherapy can use multimodality treatments, such as external beam radiotherapy and brachytherapy. To evaluate the irradiated dose for tumor and other organ at risks accurately, dose accumulation between different treatments is required.

Auto segmentation

Intensity Modulated Radiotherapy (IMRT) is a modern radiation therapy which enables delivery of the tumor with very high precision. When the patient's anatomy is changed and a new adaptive plan is to be developed, the biggest issue is to redefine all contours. This procedure is mostly carried out manually; it requires high concentration and is very time-consuming and tedious for the operator. Harari et al reported that the average physician's time to fully contour a single head and neck case is approximately 2.7 h [8]. Another disadvantage of manual contouring is potential errors arising from both inter-observer and intra-observer variability in delineation. Chao et al showed that the auto segmentation with DIR was able to reduce the variation among physicians with different experiences in Head and Neck IMRT while saving contouring time [9]. To solve this issue, auto segmentation with DIR is useful [10,11]. The process of auto segmentation consists of three steps; collecting the reference CT image and contours (atlas), performing deformable image registration between the reference CT and the new CT and applying deformable transformation to map the original contours on the reference CT to the new CT. Sample case in prostate patient is shown in Figure 4.

4D-dose accumulation

Respiration induces both rigid body translation/rotation and organ deformation. During this deformation, voxels may migrate and distort, making an assessment of the dose on a voxel-by-voxel basis problematic. DIR is a tool that can relate 4D-CT volumes at different respiratory phases to each other on voxel-by-voxel basis [3,6,12-17]. The sample procedure is shown in Figure 5. When the reference CT image is maximum expiration CT image, the other phase CTs were deformed to match the reference image to create transformations. Then, dose distributions at other phases were added to dose distribution at reference CT to make 4D dose accumulation. Velec et al investigated the effect of breathing motion and dose accumulation on the planned radiotherapy dose to liver tumors and normal tissues using DIR [18]. They showed that rigid accumulation caused discrepancies greater than 1Gy in 10 patients (48%) compared to DIR, resulting

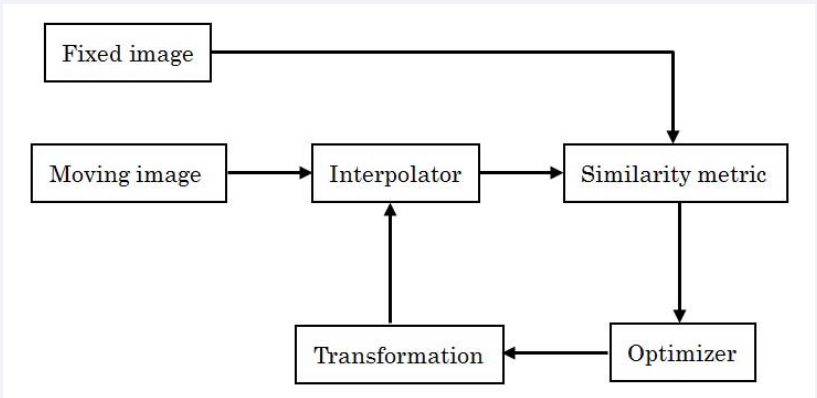

Figure 1 Flow chart of image registration process.

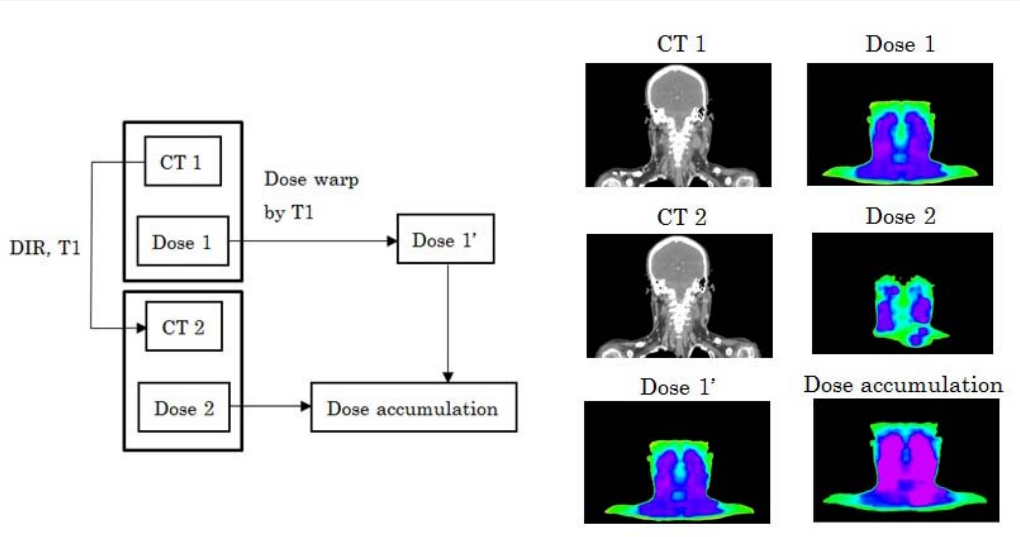

Figure 2 Schematic diagram for dose accumulation with deformable image registration (DIR). DIR was perfumed between CT1 and CT2 to create transformation, T1. Then, T1 was applied to Dose 1 to make Dose 1'. Finally, the Dose 1' added to Dose 2 to create dose accumulation.

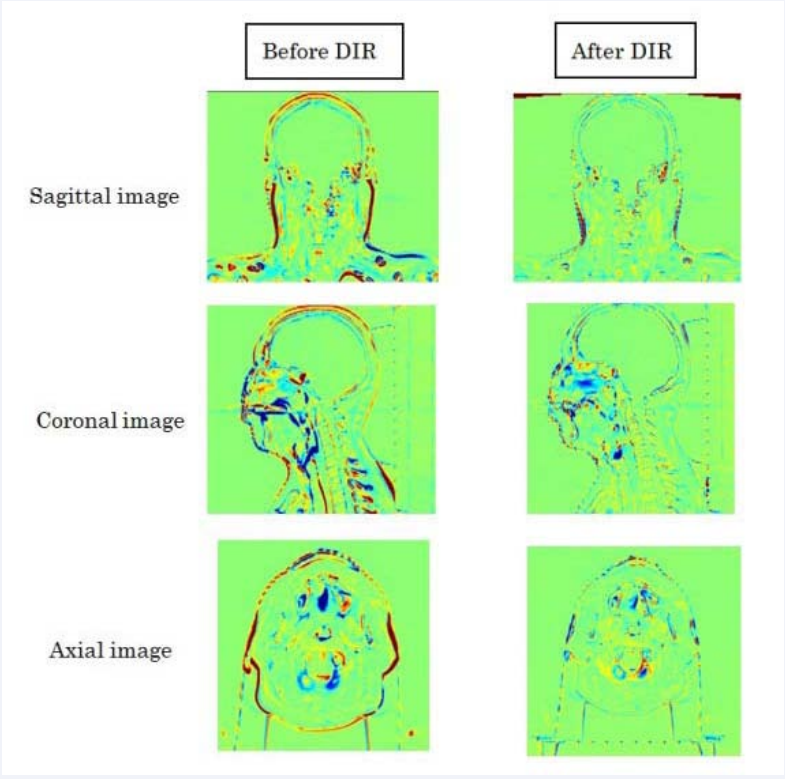

Figure 3 Example difference CT images with rigid registration and deformable image registration in head and neck patient between different time points.

in changes up to 8% in tumors and 7% in normal tissues. Thus, 4D dose accumulation using DIR is essential to assess the dose for tumor and normal tissues accurately.

4D-CT derived ventilation imaging

At present, the clinical standard for lung ventilation imaging is based on nuclear medicine (i.e., Single Positron Emission CT (SPECT)). 4D-CT images, developed for radiotherapy treatment planning, also contain CT characteristics that reflect the changes in air content of the lungs due to ventilation. Guerrero et al have developed a method for extracting ventilation images from 4D-CT which is potentially better suited and more broadly available for image guided radiotherapy than the current standard SPECT ventilation imaging. Because 4D-CT data is routinely acquired for

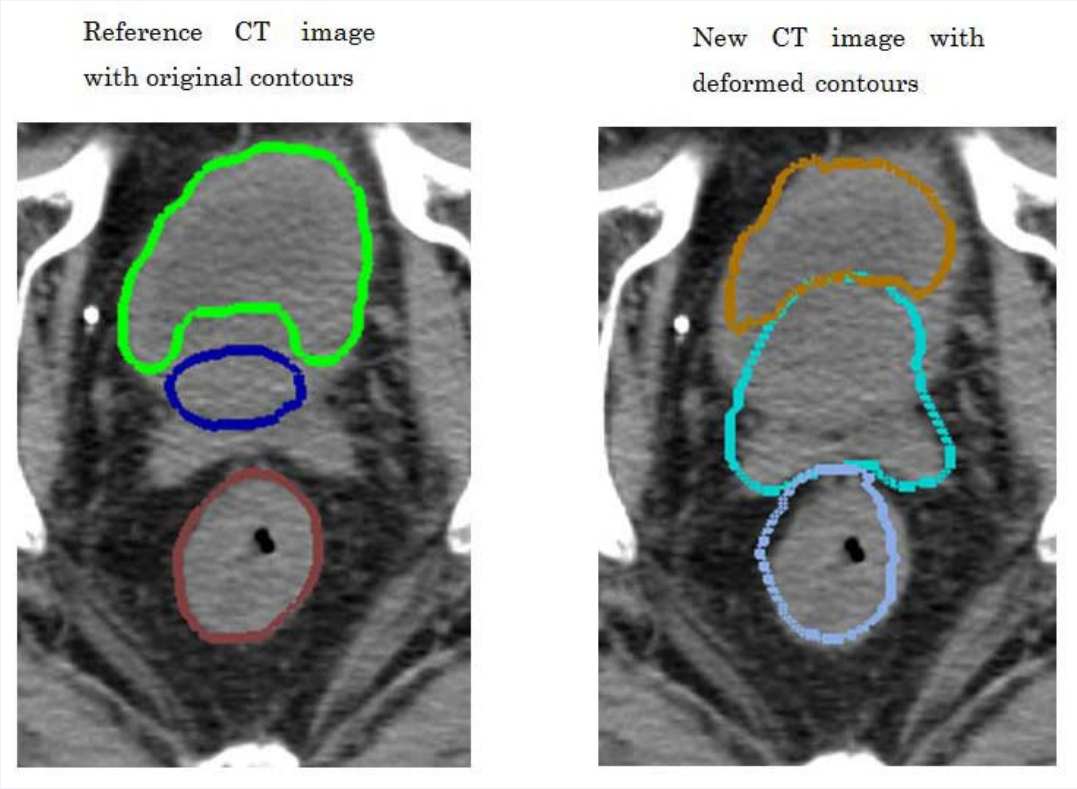

Figure 4 Example of auto segmentation by deformable image registration for prostate cancer patient. The left figure showed the reference CT image with original contours. The right figure showed the new CT image with deformed contours.

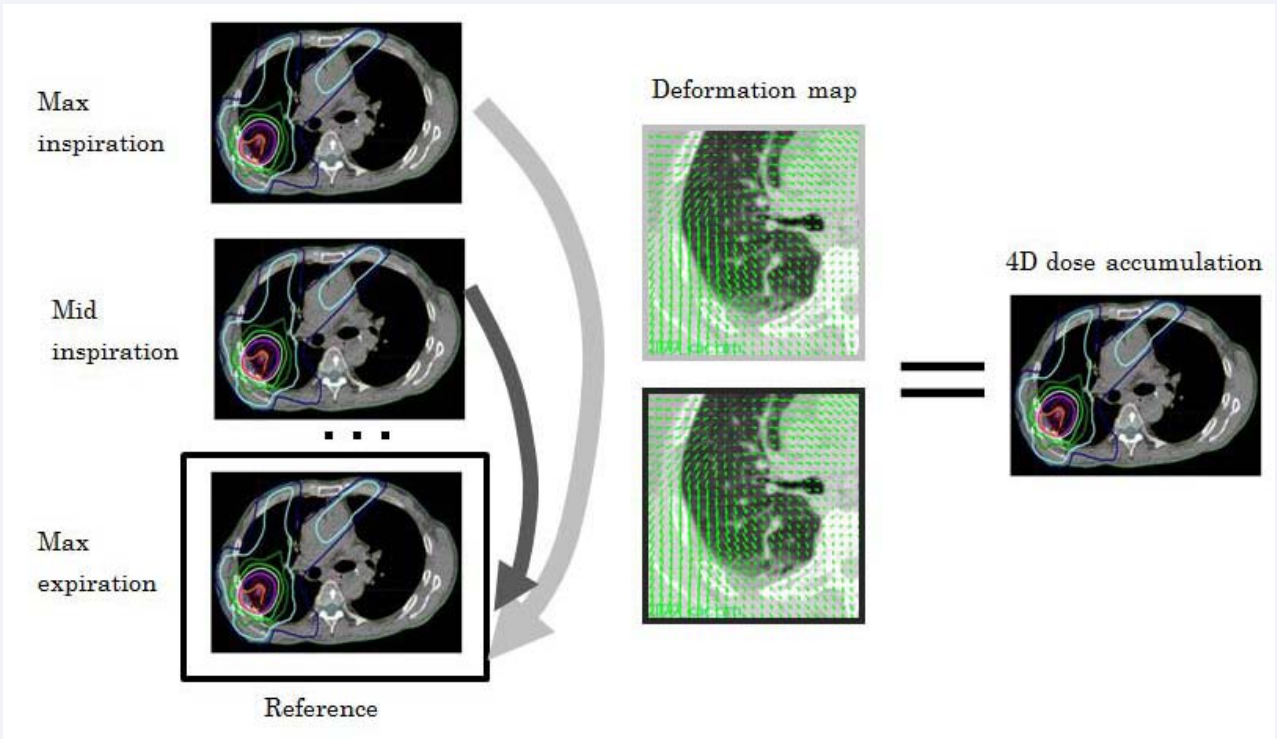

Figure 5 Schematic diagram for creating four-dimensional (4D) dose accumulation. When the reference CT image is maximum expiration CT image, the other phase CTs were deformed to match the reference image to create transformations. Then, dose distributions at other phases were added to dose distribution at reference CT to make 4D dose accumulation.

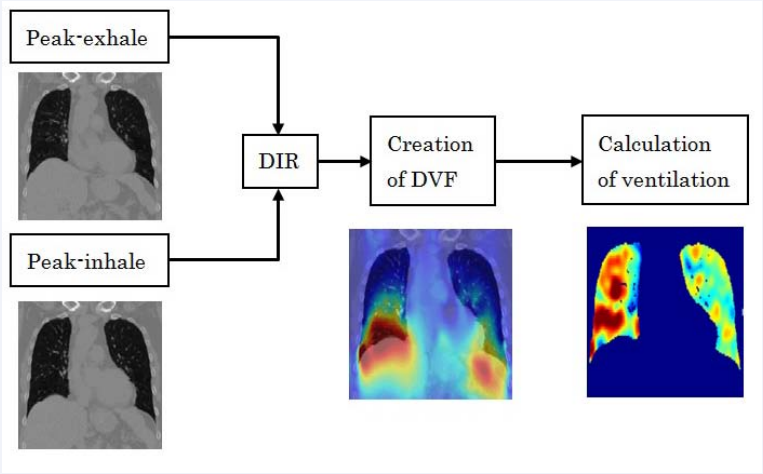

Figure 6 Schematic diagram for creating four-dimensional CT derived ventilation image.

lung cancer treatment planning, 4D-CT ventilation imaging dose not add any extra dosimetric and monetary cost to the patient. Furthermore, 4D-CT ventilation imaging has higher resolution, lower cost, shorter scan time, and/or greater availability compared to SPECT. Figure 6 shows a schematic diagram for creating 4D-CT ventilation imaging. First, we acquired 4D-CT scans and DIR for spatial mapping of the peak-exhale 4D-CT image to the peak-inhale image, deriving a Displacement Vector Field (DVF). Ventilation image was created throughout quantitative analysis (Jacobian or Hounsfield Unit (HU) change metric). For the Jacobian metric, regional volume change (i.e., surrogate for ventilation) is defined by

$$V_{jac}(x,y,z)=\left|\begin{array}{ccc} 1+\frac{\partial u_x(x,y,z)}{\partial x} & \frac{\partial u_x(x,y,z)}{\partial y} & \frac{\partial u_x(x,y,z)}{\partial z} \\ \frac{\partial u_y(x,y,z)}{\partial x} & 1+\frac{\partial u_y(x,y,z)}{\partial y} & \frac{\partial u_y(x,y,z)}{\partial z} \\ \frac{\partial u_z(x,y,z)}{\partial x} & \frac{\partial u_z(x,y,z)}{\partial y} & 1+\frac{\partial u_z(x,y,z)}{\partial z} \end{array}\right|-1, \quad (1)$$

where u (x,y,z) is the displacement vector mapping the voxel at location (x,y,z) of a peak-exhale image to the corresponding location of a peak-inhale image. For the HU change metric, regional volume change V_{HU} is defined by

$$V_{HU}(x,y,z)=\frac{HU_{ex}(x,y,z)-HU_{in}\{x+u_x(x,y,z),y+u_y(x,y,z),z+u_z(x,y,z)\}}{\left[HU_{in}\{x+u_x(x,y,z),y+u_y(x,y,z),z+u_z(x,y,z)\}+1000\right]}, \quad (2)$$

where HU is the HU value. Note that the air and tissue densities were assumed to be -1000 and 0 HU, respectively.

For planning study, Yamamoto et al quantified the impact of functional planning compared with anatomic planning [19]. They showed that the average reduction in the high-functional lung mean dose was 1.8 Gy for IMRT and 2.0 Gy for Volumetric Modulated Arc Therapy (VMAT), indicating the potential of functional planning in lung functional avoidance for both IMRT and VMAT. In terms of the clinical benefit of using 4D-CT ventilation image, Vinogradskiy et al tested the potential benefit by evaluating whether dose to highly ventilated regions of the lung resulted in increased incidence of clinical toxicity [20]. Their data suggested that incorporating ventilation-based functional imaging can improve prediction for radiation pneumonitis. In addition, Kadoya et al demonstrated the pulmonary function change measured by 4D-CT ventilation image, showing the validation of 4D-CT ventilation imaging [21].

Validation of deformable image registration

It is necessary to perform accuracy verification of available automatic DIR software for use in radiotherapy. For validation of DIR, a number of reference standards have been utilized, including synthetically deformed images, phantoms and expert-delineated control points [22,23]. DIR phantom made in our university is shown in Fig.7. The lung was simulated as a rubber latex balloon filled with slightly dampened yellow sponges. The balloon was mounted inside a Lucite cylinder that simulates the thoracic cavity. Lucite beads and nylon wires were inserted in lung to simulate vascular and bronchial bifurcations.

While synthetic images and phantoms might provide useful qualitative evaluation of DIR performance characteristics, they lack sufficient realism to provide credible validation of registration spatial accuracy for use in the clinical setting. Brock et al assessed the accuracy of DIR algorithms under development at multi institutions on common datasets [24]. Datasets from a lung patient (4D-CT), a liver patient (4D-CT and MRI at exhale) and a prostate patient (repeat MRI) were obtained. Radiation oncologists localized anatomic structures for accuracy assessment. The range of average absolute error for the lung 4D-CT was 0.6-1.2mm (left-right [LR]), 0.5-1.8mm (Anterior-Posterior [AP]), and 0.7-2.0mm (Superior-Inferior [SI]); the liver 4D-CT was 0.8-1.5mm (LR), 1.0-5.2mm (AP) and 1.0-5.9mm (SI); the liver MRI-CT was 1.1-2.6mm (LR), 2.0-5.0mm (AP), and 2.2-2.6mm (SI); and the repeat prostate datasets was 0.5-6.2mm (LR), 3.1-3.7mm (AP), and 0.4-2.0mm (SI). Their results indicated that majority of DIR algorithms performed at an accuracy equivalent

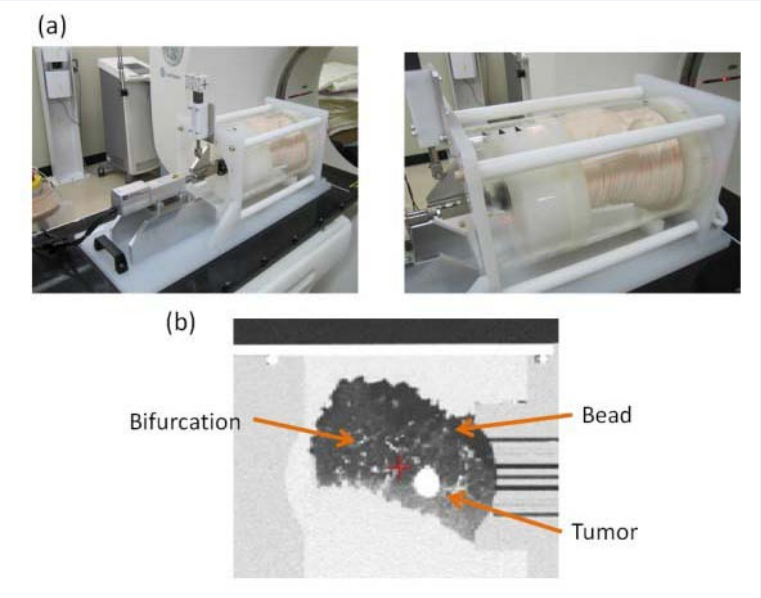

Figure 7 (a) Equipment of deformable lung phantom and (b) CT image of the phantom with bifurcation, beads and tumor.

to the voxel size. For commercial DIR software, DIR algorithms implemented commercial software has been evaluated by several researchers [24-27]. Kirby et al. evaluated eleven DIR algorithms including two commercial softwares MIM (Software Inc. Cleveland, OH, USA) and Velocity AI (Velocity Medical, Atlanta, GA, USA). Kadoya et al. evaluated four types of DIR algorithms including one commercial software (Velocity AI). These studies showed reasonable accuracy of DIR overall, but large DIR errors were observed in some patients. Thus, further improvement of DIR accuracy is still needed.

SUMMARY

DIR is an exciting and interesting technology for multi-modality image fusion, anatomic image segmentation, 4D dose accumulation and lung functional (ventilation) imaging. Furthermore, DIR is playing an important role in modern radiotherapy included IGRT and ART. In this paper, we described the typical applications for radiotherapy and showed the advantages of DIR. However, the accuracy of DIR is still being perfected and further improvement of DIR accuracy is still needed.

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