Generation of Digitally Reconstructed Radiographs in Therapeutic Geometry for Maker-less Localization of Lung Tumor in X-ray Image

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Abstract: Common clinical practice for tumor position management in respiratory gated radiotherapy is the use of fiducial markers embedded close to the tumor. However, as marker implantation is invasive to patients, tumor position management based on X-ray fluoroscopic images using deep neural network which is referred to as image-guided radiotherapy is intensively studied recently. This paper accordingly proposes the numerical generation of digitally reconstructed radiographs (DRRs) from the CT data of a patient to be used in training image-based localization system of lung tumor. We propose unified calculation algorithm that can cope with the cases when a nonzero couch angle is requested in the prescribed treatment plan. DRRs calculated by the proposed algorithm are verified by comparing them with physically obtained DRR of a patient taken during treatment, and the positional error metrics of the centroid of tumor show acceptable accuracy of numerically generated DRRs.

Key-Words: *Digitally Reconstructed Radiograph, lung tumor, tumor localization*

1. Introduction

Lung cancer has gradually become the leading cause of cancer deaths worldwide. There were above 1.6 million lung cancer deaths that amounted to about 19% of all types of cancer deaths, and about 1.8 million new lung cancer cases were confirmed in 2012 [1]. Radiotherapy is considered as one of the three major medical treatments of cancers. It aims to irradiate a tumor as precisely as possible to kill cancer cells while avoiding irradiation of healthy tissues. As lung tumors are known to exhibit respiratory-induced changes in their position and orientation inside the body, it is necessary to introduce a motion management system during treatment so as not to irradiate healthy tissues around the tumor.

Common clinical practice for the tracking of lung tumor motion in radiation therapy is to implant fiducial markers around a tumor to identify its position and orientation changes using X-ray fluoroscopic images [2]. Position management of tumors using fiducial markers is known to be robust not only to translation/rotational motions but also to deformation of the lung due to inhalation and exhalation [3]. However, implantation of fiducial markers is known to be invasive to patients and can be a cause of pneumothorax [4]. It might be more preferable if the location and the target volume of the tumor is identified directly by X-ray fluoroscopic image. The objective of the present study is closely related to the marker-less localization and dose delivery to tumors in radiation therapy that is referred to as image-guided radiotherapy (IGRT).

We need to construct an X-ray image processing system in the clinical implementation of IGRT. The system should be capable of recognizing tumor region inside the image in real-time. The use of deep neural network for marker-less pancreatic tumor target localization has been reported recently [5] in which a trained deep neural network was successfully used as the

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fluoroscopic image processor. The performance of a trained deep neural network that functions as the image processing block will be severely affected by the number of X-ray images of lung tumors available for training.

The deep neural network X-ray image processor should be trained with images of a specific patient to form a highly accurate personalized tumor identifier for treatment dose delivery. However, taking many X-ray kV images for this purpose cannot be put into practice as the cumulative amount of dose delivered to the patient might exceed the safety limit of the diagnostic use of X-ray. Adding lung tumor labels to X-ray images can also be a hard task when there are a large number of images to be processed, as the tumor labels are manually delineated by an experienced doctor that takes a long time to be completed.

The present paper accordingly proposes the automatic generation system of digitally reconstructed radiographs (DRRs) from a single 3D computer tomographic (CT) data of a target patient. The output of the system will be a DRR with automatically labeled lung tumor information. We propose a DRR generation system that can produce DRRs with non-zero couch angles at any known imaging direction. This function contributes to the increase of DRRs that can be used for training a deep neural network as a tumor locator of a specific target patient in their X-ray fluoroscopic images.

2. Ray-casting Algorithm for DRR Generation

As generation of DRR yields high computational cost if the resolution of original CT data is high. There is accordingly a trade-off between the computational time and image. Westover [6] proposed a splatting algorithm for fast DRR generation in which each voxel in the CT volume is projected to the detection plane separately. Although his algorithm reduces the complexity of the problem, the aliasing effect will cause image distortion.

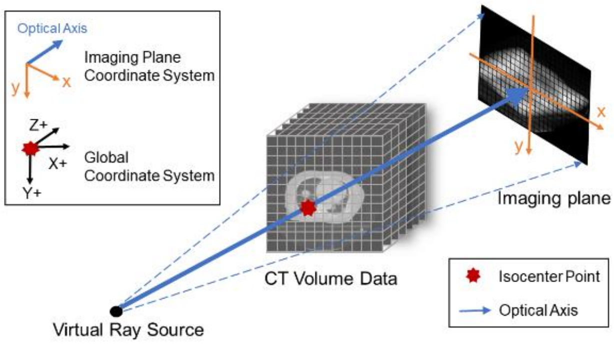

Fig.1 Calculation of DRR from 3D CT data

The light field algorithm [7] and the attenuation field algorithm [8] were proposed for fast DRR generation with acceptable quality whereas the range of projection angles that can be set for DRR generation is limited. If one wants to generate DRR for different projection setup, preprocessing step should be performed from scratch.

This study uses the classic ray projection method which is referred to as ray-casting. Fig.1 schematically explains the ray-casting algorithm. The intensity value of each pixel in the resulting DRR is determined by sampling of a CT volume and adding it along a line that connects the virtual ray source with a pixel in the image intensifier plane. While an X-ray was going through bones, organs and other human tissues, it was partly absorbed and attenuated before arriving at a point on the image plane that makes the difference of intensity value of a pixel in DRR.

We consider multiple X-ray lines that result in a DRR on an image plain in this algorithm. The number of rays assumed from the X-ray source point is the same as the number of pixels included in the resulting DRR. We note that the ray source and imaging plane here are virtual. Mutual positional relationship between the ray sources and an imaging plane is determined according to the geometry of the simulated imaging system. We performed equidistant sampling on each ray, and calculated the attenuation coefficient of a voxel in a CT volume by interpolation of its surrounding voxels.

The pixel intensity value of a DRR was strongly related to the associated CT voxel data. The attenuation of an X-ray intensity when it passes through an object is calculated according to the Beer-Lambert law

$$I_1 = I_0 \cdot e^{-\int \mu_x dx} \tag{1}$$

where I_0 is the initial intensity of the ray, μ_x is the linear attenuation coefficient of a point x on the ray line. It was known that the attenuation coefficient of an X-ray at a specific point x on the tissue can be calculated by the CT value of the voxel associated with a point x represented in Hounsfield unit:

$$\mu_x = \frac{CT_x(\mu_{water} - \mu_{air})}{1000} + \mu_{water} \tag{2}$$

where CT_x is the CT value of a voxel x, μ_{water} is the attenuation coefficient of X-ray in water, μ_{air} is the attenuation coefficient of X-ray in the air.

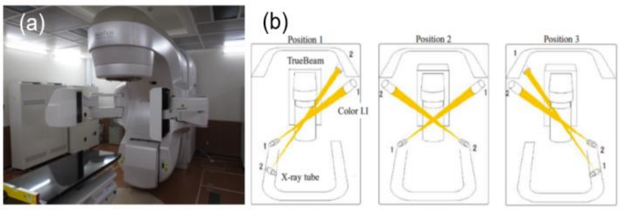

Fig.2 (a) medical linear accelerator (TrueBeam, Varian Medical Systems, USA) and
(b) real-time tumor tracking system installed in Yamaguchi University Hospital (SyncTraX, Shimadzu Co., Japan).

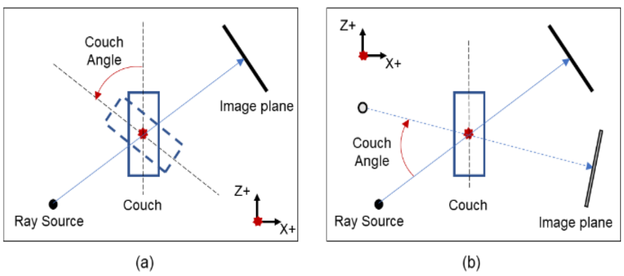

Fig.3 Couch Rotation on XZ plane.

3. Coordinate Transformation

DRR generation is equivalent to the process of X-ray penetration through CT voxels in a three-dimensional space. When a DRR is generated from an 3D CT data, the result of penetration can be calculated numerically. We use the geometric data of a real imaging system to set coordinate systems. When a DRR from different projection directions and angles was necessary, appropriate coordinate system transformations should be performed to calculate the change of direction.

Respiratory gated radiotherapy for lung tumor patients is performed in Yamaguchi University Hospital using a medical linear accelerator combined with a real-time tumor tracking system as depicted in Fig.2. The real-time tumor tracking system tracks the motion of a tumor based on stereo template matching technique on a stereo pair of images of a fiducial marker in the X-ray fluoroscopic image captured by the system, with the spatial geometry illustrated in Fig.2(b).

As the system takes stereo X-ray images at a frequency of 30 Hz for tumor motion tracking, a number of stereo X-ray image pairs can be obtained during treatment simulation and dose delivery. We would like to develop a deep neural network based fluoroscopic image processor that identifies the tumor region inside a captured X-ray image using the stereo X-ray images obtained with the system. To that end, we would like to generate DRRs calculated using the geometry of our clinical treatment system in Fig. 2 and the prescribed couch angle, using a CT data of the patient.

When an X-ray is emitted by a source to a human body, it passes through bones, organs including a lung and other tissues and is attenuated before arriving at the imaging plane. The intensity of an X-ray when arriving at the image intensifier of the imaging system depends on directional angle of an X-ray beam to the human body. If we artificially generate DRRs from the 3D CT data of to be used as training data in the deep neural network, we have to take the spatial location of the ray source and the corresponding image intensifiers shown in Fig.2(b) into account to determine the directional angles of an X-ray beam going through a CT volume, and the corresponding X-ray intensity on the image intensifier.

3.1 Global Coordinate System

The global coordinate system of a treatment room is a coordinate system of a medical linear accelerator. The origin of the global coordinate system is referred to as the isocenter. The X-ray optical axis is assumed to pass through the iso-center of the treatment system and is perpendicular to the imaging plane, as depicted in Fig. 1. The x, y and z axes are identical to the corresponding axial directions of the CT volume, that is, LR, SI and AP directions, respectively.

3.2 Coordinate System Conversion

We treat the number of pixels of an imaging plane as a variable when we establish a coordinate system of the imaging plane, as there might be cases when a different resolution of a DRR is requested. X-rays starting from the virtual ray source will reach the pixels on the imaging plane after they suffer from attenuation. A transformation between the global and the imaging-plane coordinate systems is introduced here to calculate coordinate values of pixels in the imaging plane in the global coordinate system, and the X-ray attenuation path. A rotation matrix R is determined according to coincide with a real imaging system geometry. $[x, y, z]^T_{plane}$ represents a coordinate value of a pixel of an imaging plane that is expressed in the imaging plane coordinate system depicted in Fig.1, and let $[x, y, z]^T_{global}$ be the corresponding coordinate value of the pixel expressed in the global coordinate system. Then

$$\begin{bmatrix} x \\ y \\ z \end{bmatrix}_{global} = \lambda \left(\begin{bmatrix} \Delta x \\ \Delta y \\ \Delta z \end{bmatrix} + R \begin{bmatrix} x \\ y \\ z \end{bmatrix}_{plane} \right) \tag{3}$$

applies, where $[\Delta x, \Delta y, \Delta z]^T$ is a translation vector which compensates for the displacement of the origins of the two coordinate systems, and λ is the scaling factor, $\lambda = 1$ in the subsequent calculations.

Let θ, ϕ and ψ denote the rotation angles around x, y and z axes, respectively. Then the rotation matrix R is defined by:

$$R = R_\theta R_\phi R_\psi \tag{4}$$

where R_θ, R_ϕ, R_ψ are given by

$$R_\theta = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\theta & -\sin\theta \\ 0 & \sin\theta & \cos\theta \end{bmatrix} \tag{5}$$

$$R_\phi = \begin{bmatrix} \cos\phi & 0 & \sin\phi \\ 0 & 1 & 0 \\ -\sin\phi & 0 & \cos\phi \end{bmatrix} \tag{6}$$

$$R_\psi = \begin{bmatrix} \cos\psi & -\sin\psi & 0 \\ \sin\psi & \cos\psi & 0 \\ 0 & 0 & 1 \end{bmatrix} \tag{7}$$

We note that θ, ϕ and ψ are determined from the geometric relationship between the real-time tumor tracking system and the global coordinate system.

3.3 Calculation with non-zero couch angle

The medical doctor sometimes prescribes a treatment plan with non-zero couch angle to maximally avoid irradiation of healthy tissues. One straightforward approach to generate a DRR from the CT data of the patient with non-zero couch angle requires a rotation of an entire CT volume to have a new coordinate value of a voxel in the global coordinate system before the ray-casting calculations were performed.

However, rotation of an entire CT volume would result in the significant increase of computational load, and the identification of CT voxel in which a ray line passes through becomes even more complicated. We accordingly propose to calculate a DRR corresponding to non-zero couch rotation angle by rotating the imaging system comprising the X-ray source and an imaging plane by the same amount of angle but in the reverse direction, as illustrated in Fig.3. When couch angle changes, only the ray source and an imaging plane should be rotated by the same angle but in the opposite direction. It reduces the amount of redundant calculations and the difficulty of voxel indexing in the ray-casting process.

4. Labeling lung tumor region in DRR

The medical doctor manually delineates the tumor region on the CT slices to determine the position and shape of the tumor. As we can generate DRRs from the CT data even when couch angle is non-zero, the region of the tumor in the CT data should be marked and the information should be transmitted to the generated DRR for future training of deep neural network. However, as delineation of a tumor is performed on 3D CT slices, the outline of delineated tumor volume might not be continuous in the three-dimensional space. This fact sometimes makes the identification of the tumor on the generated DRR very difficult or even impossible.

We accordingly propose a digital reconstruction method of a projected tumor in this paper. We first binarize every voxel included in a CT volume so that a voxel is made white if it constitutes the surface of a tumor, or otherwise is made black. Then, we perform maximum intensity projection on the binary CT volume with the same geometrical setup as the DRR projection. This procedure will produce a binary lung tumor image. Because of the discontinuity of the tumor contour in the 3D space, the binarized white voxels would result in jagged edges in the computed DRR. After smoothing the image by Gaussian filtering and using the binary image contour extraction method shown in [9], we can determine the edge of the region that correspond to white voxels in the CT data.

5. Results

We used a CT scan data of a lung tumor patient to validate the proposed algorithms for generation of DRR. It includes $512 \times 512 \times 115$ voxels and a single voxel whose size is $0{:}977 \times 0{:}977 \times 2$ mm. The patient was assumed to be aligned on a couch with Head First-Supine. The relation between the CT coordinate system and the body-assigned coordinate system are shown in Fig.4. The X, Y and Z axes correspond to RL (Right-to-Left), SI (Superior-to-Interior) and AP(Anterior-to-Posterior) directions, respectively.

We used the geometry labeled position 1 and 3 in Fig. 2(b) of the tumor tracking system for numerical generation of DRR. It includes four X-ray projection directions (position-1A, 1B, 3A, 3B). We assume three couch angles (0, 10 and -10 deg.) for the calculation and the DDR resolution is set to be 1024×1024 pixels. The result of our calculation is shown in Fig.5. Since the optical axis passes through the isocenter point and is perpendicular to the virtual imaging plane, the tumor target area is always located at the center of the obtained DRR as the centroid of a tumor volume in a CT data is located at the center of the global coordinate system. The DRRs generated in this study show good agreement to the X-ray images physically captured by the tumor tracking system.

In order to match the size of the fluoroscopic image captured during treatment, we next attempted to generate DRRs with 1000×1000 pixels that had tumor contours projected from a delineated CT data using the method presented in this paper. The results were shown in Fig. 6. Binary images show the outline and shape of the tumor on the generated DRR image with 1000×1000 pixels. Due to noise and jagged edges in the projection, the contours in the generated DRR seem to have slight deviation. To evaluate the projection quality of the tumor target area, the quantity

$$D = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2} \tag{8}$$

is used to calculate the distance between centroid of the lung tumor label and the isocenter point as the error of identified centroid, where (x_2, x_1) is the centroid of a lung tumor and (y_2, y_1) is the isocenter point of a DRR. The errors under four projection geometries and three couch angles were summarized in Table 1.

It was found from the table that errors corresponding to directions 1A and 3B was small, and the average positional error in position 1A and 3B were less than 0.15mm and 0.87mm, respectively. However, we had a larger error in the position 1B and 3A. Their average errors were 3.50mm and 3.40mm, respectively. The degradation was caused by the three-dimensional nature of tumor volume in the CT. The outline of tumor volume can be discontinuous in the projection direction, a lung tumor outlines on each CT slice might partially overlap while the other parts do not. When we projected all the outline voxels on the label , some voxels that do not belong to the target area are included, resulting in a deviation in the calculated centroid of a tumor.

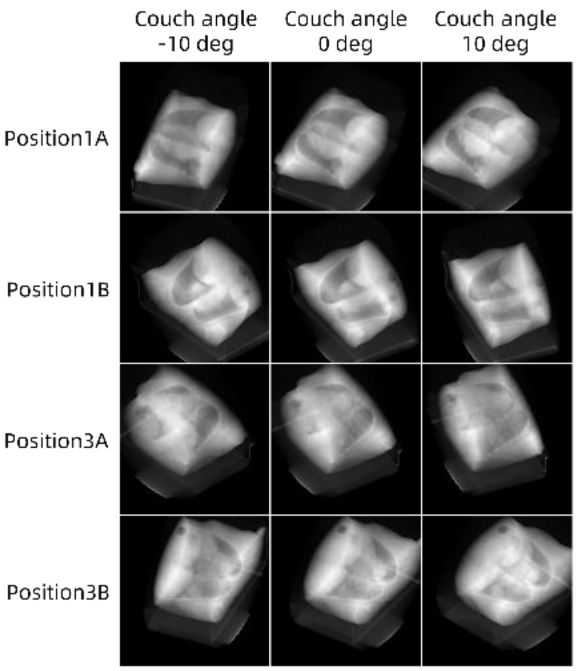

Fig.4 Result of the generated DRR with 3 different couch angles and 4 different geometries.

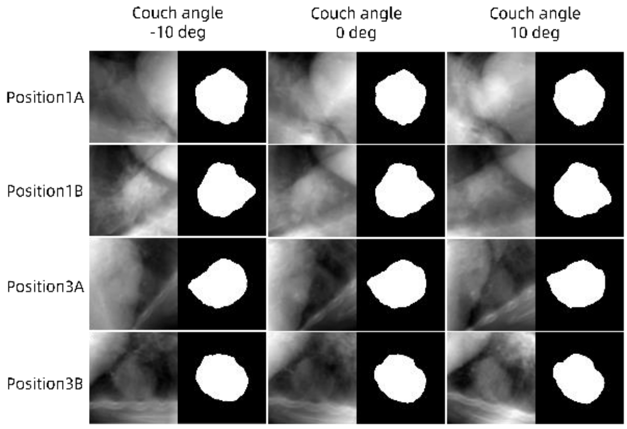

Fig.5 Results of tumor contour projection.

Table 1 Gravity Center Position Error Calculation

Gravity Center Position Errors [mm]	Couch Angle		
	-10 deg	0 deg	10 deg
Position 1A	0.141	0.141	0.141
Position 1B	3.765	3.178	3.570
Position 3A	3.912	3.513	2.789
Position 3B	0.860	1.581	0.141

6. Conclusion

This paper proposes a method to generate X-ray digital reconstructed radiographs that can generate a DRR from any requested direction of projection and non-zero couch angles. We also presented a method to generate a tumor contour in the DRR that was formed by the projection of the delineated tumor in the 3D CT slices. Experimental generation of DRR using a CT data of lung tumor patient reveals that the proposed method successfully generates a clear and complete projection contour close to the actual tumor contour. The errors caused by the projection were acceptable in some directions. To improve the accuracy of the method in all directions and angles and the efficiency of DRR generation, we are trying to improve the method and use GPU to accelerate calculation. This method will also be applied to the next phase of lung tumor detection study.

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