Original Article Feasibility study of recalculation of the dose for lung cancer radiotherapy using cone beam computed tomography images from a linear accelerator: a heterogeneous phantom study

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Abstract: The goal of this study was to evaluate the feasibility of recalculating the dose based on cone beam computed tomography (CBCT) images using an end-to-end thorax heterogeneous phantom. A CT simulator (SIEMENS, Sensation Open, Germany) was used for calibrating the curve of HU-to-density. The CBCT system evaluated in this study was assembled on an Electron Linear Accelerator (Varian Medical System, EDGE, USA). Image acquisitions of electron density phantom for both computed tomography (CT) and CBCTs were performed, and then the CT number to relative electron density calibration curve was obtained. The end-to-end heterogeneous phantom was scanned by CT simulation and the target volume was contoured to design a dummy treatment plan. The CBCT image was scanned before the simulated treatment, and registration between the CBCT and CT images was performed. The dummy treatment plan was transplanted to the CBCT images to recalculate the dose of the treatment plan. Then, differences of the dose volume histogram and three-dimensional isodose distribution were evaluated between the recalculated plan and the original dummy treatment plan. The HU-to-density curves for CBCT of the EDGE accelerator showed in principle a single upward trend. The Darge of the clinical target volume and planning target volume for the recalculated plan based on the CBCT images were lower than the original dummy treatment plan based on the CT images by 1.69% and 2.62%, respectively. On the premise of the CT number-relative density curve calibration of the CBCT images, the recalculated dose based on the high-quality CBCT images can be used as an important basis for replanning in lung cancer irradiation.

Keywords: Cone beam computed tomography, heterogeneous phantom, dose calculation

Introduction

The goal of radiotherapy is to precisely deliver the therapeutic dose into a clearly defined target volume to achieve the goal of both treating tumors and sparing normal tissues. Technological advances, such as multileaf collimators [1], intensity-modulated radiation therapy [2], and volume-modulated radiation therapy [3], have enabled radiotherapy to conform highdose sculpting to the target volume and to spare normal tissue around the target volume. For most cases, although significant changes have taken place within a few days or weeks during the treatment course, the entire course of radiotherapy is performed as delivered in the first treatment. Although some cases may undergo planned modifications during the course of treatment, such modifications are not based on the mobility of tumor morphological changes. With the development of cone-beam computed tomography (CBCT) based on flat-panel detectors, image-guided radiation therapy (IG-RT) can be performed to correct the setup errors by obtaining the registration of CBCT setup images and planning images [4]. Adaptive radiotherapy considers the continuous changes of anatomy and/or physiology during the course of treatment and thus modifies the treatment plan at the appropriate time to adapt to the morphological changes of the target volume [5].

In this study, an electronic density phantom was used to calibrate the Hounsfield unit (HU)to-density curve of computed tomography (CT) and CBCT. An end-to-end heterogeneous phantom was used to validate the treatment plan, and the feasibility of recalculating the dose with CBCT images was evaluated to provide a reference for online replanning of the CBCT images.

Materials and methods

Image system and phantom

A CT simulator (SIEMENS, Sensation Open, Germany) was used for calibrating the curve of HU-to-density and designing the dummy plan. The CBCT system evaluated in this study was assembled on an Electron Linear Accelerator (Varian Medical System, EDGE, USA). To compare the image quality of the CBCT, this study also evaluated the image quality of a CBCT system assembled on another Electron Linear Accelerator. Because its image quality was relatively poor, the name "Model S" was used in this study instead of its real name, and the vendor's name and the place of production are also not given.

The electron density phantom (CIRS, Model 062, USA) and end-to-end heterogeneous thoracic phantom (CIRS, Model 036S, USA) were used for HU-to-density calibration and patient simulations, respectively.

Calibration of HU-to-density

The inhaled lung, exhaled lung, breast (50% gland/50% adipose), liver, muscle, adipose, solid trabecular bone (200 mg/cc) and solid dense bone (800 mg/cc) were inserted into the inner Head Insert and outer Body Ring of the 062 phantom in the appropriate locations. Distilled water was poured into the water equivalent insert, and then, it was inserted into the phantom [6]. The electron density phantom was placed on the CT or linear accelerator couch. Then, the lasers for patient positioning were aligned with the placement mark, and image acquisitions were performed. An offset scan was added for the CBCT of the linear accelerator EDGE to evaluate the effect of the cone beam: the offset distance was 7.5 cm. A thorax scan protocol was used for CT scanning with a voltage of 120 kV and a thickness of 3 mm. CBCT scans were performed in the thorax mode with a scanning angle of 360 degrees. CT images and the CBCT images for the electron density phantom were compared (Figure 1). Images were transferred to a treatment planning system (TPS) (Varian Medical system, Eclipse V13.6, USA). Under the contouring module, the inserts were delineated by using a "2D-brush" tool at the center plane of the electron density phantom. The maximum, minimum, average and standard deviation of the CT number were collected in the properties window. Relative density data were obtained from the manual of the vendor electron density phantom. The HU-to-density data was input into the TPS as the conversion from HU to the relative electron density for the CT images and CBCT images, respectively.

CT simulation and dummy treatment plan

The inserts for the lung, water equivalent material, soft tissue, spinal cord and bone were placed in the corresponding positions in phantom 036S. The phantom was aligned with the lasers of the CT simulator according to the marking lines, and the scanning protocol and condition were the same as that of electron density phantom calibration scanning. In the CT images, the dummy Clinical Target Volume (CTV) was contoured according to the "tumor of left lung" setting in a heterogeneous phantom, and the Planning Target Volume (PTV) comprised the CTV with a 3-mm margin in all directions. The dummy treatment plan was designed after delineating the organs at risk (OARs) (left lung, spinal cord, esophagus, heart and body outline). Then, 6-MV photon energy beams (gantry angles were 350, 20, 50, 80, 110, 140 and 170, respectively) were used in the dummy IMRT plan, using inverse optimization and sliding window techniques. The prescription dose to the PTV was 50 Gy in 25 fractions, and the plan was normalized to the 100% isodose line encompassing 95% of the PTV (V95% = 50 Gy).

CBCT scan and dose recalculation

The phantom 036S was aligned with the lasers of the linear accelerator according to the marking lines, then the couch was moved to the center of the "tumor". The CBCT images were acquired with the tumor at the isocenter, then the images were transmitted to the TPS. Automatic image registration was used to match the CBCT



Figure 1. Scanned image comparison for the electron density phantom at the same window width/level (400, -50). A: SIEMENS Sensation Open; B: Varian EDGE Linac CBCT (middle); C: Varian EDGE Linac CBCT (offset); D: Model S Linac CBCT (for comparison only).



Figure 2. Comparison of CT number profiles along the red dashed line as indicated on Figure 1.

images with the CT images. Target volumes and OARs in the CT images were copied to the CBCT images. The dummy treatment plan was transplanted to the CBCT images for dose recalculation. The dose-volume histogram (DVH) and 3D dose distribution between the plan based on CT images and the recalculated dose based on CBCT images were compared.



Figure 3. HU-to-density curves for CT and CBCTs.

Results

HU-to-density curve

CT number profiles were compared along the red dashed line (**Figure 2**). HU-to-density curves for CT and CBCTs are generated (**Figure 3**). The HU-to-density curve for CT showed a single upward trend. The HU-to-density curves for CBCT



Figure 4. Comparison between CT images and CBCT images for the end-to-end thorax heterogeneous phantom. A: CT/Mediastinal Window; B: CBCT/Mediastinal Window (red arrow indicates a lower CT number); C: CT/Lung windows; D: CBCT/Lung windows (red arrow indicates a ring artifact).



ter images of CBCT was slightly different from that of the offset images. The HUto-density curve of the Model S accelerator showed a nonsingle upward trend.

End-to-end heterogeneous phantom

CT images and the CBCT images were compared for the end-to-end thorax heterogeneous phantom (**Figure 4**). CT number profiles for CT images and CBCT images were also compared along the central axes of the beams for the dum-

Figure 5. Comparison of CT number profiles for CT images and CBCT images along the central axes of beams for the dummy treatment plan.

of the EDGE accelerator showed in principle a single upward trend. In the range where the relative density is similar to that of water, there was a small amount of oscillation in the HU-todensity curve. The HU-to-density curve for cenmy treatment plan (**Figure 5**). A distance zero represents the isocenter, and the direction of the source is given as negative. The water equivalent thicknesses (WET) [7] for each beam from the surface of the phantom to the isocen-



Figure 6. Percentage depth dose comparison for each beam between the original dummy plan based on CT images and the dose recalculation plan based on the CBCT images.



Figure 7. Comparison of DVH between the original dummy treatment plan based on the CT images and the recalculated plan based on the CBCT images.

ter based on the CT images were 4.67 cm, 3.59 cm, 4.19 cm, 4.27 cm, 4.50 cm, 4.74 cm, and 4.94 cm, respectively. The WET for each beam from the surface of the phantom to the isocenter based on the CBCT images were 4.41 cm, 3.39 cm, 4.21 cm, 4.41 cm, 4.69 cm, 4.95 cm, and 5.14 cm, respectively.

Dummy plan and recalculated dose

The relative depth dose for each of the beams was compared between the original dummy plan based on the CT images and the dosage recalculated plan based on the CBCT images (Figure 6). The DVH between the original du-

mmy treatment plan was compared based on the CT images and the dosage recalculated plan based on the CBCT images (Figure 7). The dose distributions between the original dummy treatment plans were compared based on the CT images and the dosage recalculated plan based on the CBCT images (Figure 8). The $\rm D_{_{95\%}}$ (the dose to 95% of the volume) of the CTV and PTV dosage recalculated plan based on the CBCT images were 1.69% and 2.62% lower than the original dummy treatment plan based on the CT images, respectively.

Discussion

Adaptive radiotherapy provides a potential solution in terms of radiation accuracy and adaptability to anatomical changes. It is a selfresponsive and self-correcting dynamic closed-loop system. Currently, the plan revision of adaptive radiotherapy usually adopts the online mode of CT-on-rails [8] or the offline mode based on CT resimulation [9]. In the online mode, patients have to reciprocate between the CT ring and the

treatment beam isocenter, and there is a position error between them. The errors have a great impact on the hypo-fraction or small target volume of stereotactic radiotherapy [10]. In the offline mode, it is generally through the subjective evaluation of tumor changes as determined by radiologists as to whether the treatment plan needs to be modified, and there is no objective index. In this study, CBCT images were used to recalculate the dose for the treatment plan, which could provide an objective index for modification of the offline treatment plan. With the continuous improvement of CB-CT image quality [11], it may even be possible to implement online adaptive modification tr-



Figure 8. Comparison of dose distributions between the original dummy treatment plans based on CT images and the recalculated plan based on CBCT images (the thinner lines are isodose lines of the original dummy plan based on CT images, the thicker lines are isodose lines of the dosage recalculated plan based on the CBCT images).

eatment plans based on CBCT images in the future.

Except for the linear accelerator of the ring gantry, such as in tomotherapy, the gantry of linear accelerators cannot rotate continuously. Therefore, CBCT scanning on a linear accelerator is a simple method to obtain volumetric threedimensional images [4]. Since the original design of CBCT assembled on an accelerator is only used to detect setup errors, image guidance based on CBCT can be achieved with high accuracy as long as the image quality can judge the interface with large density differences (such as tissue-air, tissue-lung, tissue-bone, etc.). CBCT images of the accelerator Model S used for reference in this study were worse than those of accelerator Model EDGE. However, various tissue interfaces (tissue-inhale lung, tissue-exhale lung, tissue-bone) can still be clearly distinguished and have the ability to correct the setup errors (Figure 2). In the dose calculation algorithm of the TPS, the electron density method is used to correct the effect of non-uniform tissue on the dose, so the CT number should be converted to the electron density for calculation. The HU-to-density curve of CB-CT assembled on the accelerator Model S is not a single upward trend, especially in tissues with densities greater than water (Figure 3). The non-unidirectionality of the calibration curve will result in two or more relative densities corresponding to one CT number. The TPS cannot determine their relative densities, so dose calculation cannot be carried out.

This study attempted to use CBCT images to recalculate the dose, which puts forward higher requirements for the image quality of CB-CT. Therefore, CBCT images with a high accuracy of CT number and a single trend of HU-to-density curve have a physical basis for recalculating the dose. The calibration curve of CBCT assembled on EDGE shows in principle an upward trend, but there was a small amount of oscillation in the tissues with similar water density

(Figure 3). This was due to the poor accuracy of the CT number for the CBCT images and the heterogeneity for different locations [12, 13]. In this study, by reducing the calibration points, these small fluctuations can be smoothed to obtain the overall upward trend calibration curve, which can be applied to dose recalculation for CBCT images. The image quality of CBCT is strongly related to the imaging dose. The cumulative dose of CBCT is 3-370 cGy [14], which is higher than the threshold dose of the second malignant tumor reported in the literature [14]. Therefore, the risk of increasing the imaging dose must be less than the benefit thus obtained, and at least a balance should be achieved. When CBCT is only used for patient setup, the image quality will be damaged more or less by realizing a rational low dose strategy on the premise that image quality can still be used for image registration. To achieve dose recalculation or even online adaptive radiotherapy, it can reduce the volume of the high dose and achieve high-precision treatment, such as stereotactic radiotherapy for lung cancer, which greatly exceeds the risk of increasing the imaging dose by improving the imaging quality.

The incidence of radiation pneumonia is highly correlated with the volume/dose of lung irradiation [15, 16]. In radiotherapy of lung cancer, the volume of primary tumors and lymph nodes

decreased significantly with increases in the irradiation fraction [17]. Especially for patients with atelectasis, the location of the atelectasis is difficult to distinguish from that of tumors. The treatment volume in the initial treatment plan is often large. During the progress of irradiation, a partial and complete response of the atelectasis may be achieved, so it is necessary to modify the treatment plan [18]. For stereotactic fractionated radiotherapy for lung cancer [19], because of the large dose per fraction, the retraction or progression of the tumor morphology between fractions will seriously affect the precise dose delivery of radiotherapy. The results of this study can provide some objective references as to whether to modify the treatment plan, and it has great clinical value.

In this study, the deviation between the recalculated dose based on the CBCT image and the dose based on the CT image comes from two aspects: First, although two series of images had been registered, there were still residual deviations (Figure 5). Galerani AP et al. [20] have found that there are still residual setup errors after image guidance correction. The CT number accuracy of CBCT images is lower than CT, which results in a difference of WET from the phantom surface to the isocenter on the axis of each of the beams. Among the seven beams, the WET of the five beams for the CBCT images is larger than that for CT images, and the total WET for the CBCT images is larger than that for the CT images.

Conclusion

In summary, on the premise of HU-to-density calibration of CBCT images, recalculating the dose of high-quality CBCT images can provide an important basis for the modification of lung cancer radiotherapy plans. This study is based on an end-to-end heterogeneous static phantom. Because lung tissue (tumor) is greatly affected by respiratory movement, more research support based on dynamic phantoms is needed before applying this research to clinical practice. With the development of technology, the online adaptive modification of treatment plans based on CBCT images can be realized after the process optimization of future TPS.

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Disclosure of conflict of interest

None.

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