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Feasibility Study on Deformable Image Registration for Lung SBRT Patients for Dose-Driven Adaptive Therapy

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Abstract

The purpose of the study was to evaluate a treatment dose using planning computed tomography (pCT) that was deformed to pre-treatment cone beam computed tomography (CBCT) for lung stereotactic body radiation therapy (SBRT) treatment. Five lung SBRT patients were retrospectively selected, and their daily CBCTs were employed in this study. Dosimetric comparison was performed between the original and recalculated plans from the deformed pCT (dose per fraction) by comparing a target coverage and organs at risk. Dose summation of five fractions was computed and compared to the original plan. A phantom study was conducted to evaluate the dosimetric accuracy for the dose per fraction. In the phantom study, the difference between the mean Hounsfield Unit (HU) values of the original and deformed pCTs is less than 0.5%. In patient study, the mean HU deviation of the five deformed pCTs compared to that of the original pCT was within ±5%, which is dosimetrically insignificant. While the internal target volume (ITV) shrank by 17% on average among the five patients, mean lung dose (MLD) increased by up to 7%, and D95% of PTV decreased slightly but stayed within 5%. Results showed that MLD might be a better indicative metric of normal lung dose than V20Gy as the ITV volume decreases. This study showed a feasibility to use a deformed pCT for evaluation of the dose per fraction and for a possible plan adaptation in lung SBRT cases. Readers should be cautious in selecting patients before clinical application due to the image quality of CBCT.

Keywords

Lung SBRT, Adaptive Radiotherapy, CBCT, Deformable Image Registration

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1. Introduction

Radiation therapy plays a crucial role in the management of lung cancer. However, the efficacy of stereotactic body radiation therapy (SBRT) for lung cancer is limited by the variations in the anatomy of patients during treatment course. A large number of SBRT patients underwent significant gross tumor volume (GTV) changes. For instance, more than 20% GTV volume reductions were reported in the studies. Bhatt *et al*. found that there was a 32% the reduction of GTV volume from daily CBCTs among 24 lung SBRT patients and Qin *et al*. reported 21% of mean GTV volume reduction in 5th CBCT images among 40 lung SBRT patients [1]. Without the careful plan review, tumor volume changes will inevitably make the original GTV delineation inaccurate and consequently compromise a target dose coverage and organs at risk (OARs) dose reduction. Adapting tumor response in the treatment plan makes possible to reduce the amount of healthy lung in the irradiated volume. This in turn can translate in a reduction in the risk of radiation induced pneumonitis [2] [3]. Thus to accomplish a dose per fraction assuring minimizing a normal lung dose for the patient, the original plan will need to be adapted with updated anatomy acquired by the pretreatment imaging modality.

Recently kilovoltage cone beam computed tomography (CBCT) attached to a linear accelerator has been widely utilized in radiation therapy clinic for patient setup/positioning and also it can provide on-treatment patient anatomy [4]-[6]. Previous dosimetric studies have shown that the adaptive planning based on the CBCT images can potentially reduce dose to adjacent OARs when a large tumor volume shrinkage has occurred. Qin *et al*. studied the dosimetric benefits of adaptive planning based on the CBCT images of lung SBRT patients. His study showed that the adaptive planning can potentially reduce dose to adjacent OARs if a large tumor shrinkage occurs during treatment course [7]. The common strategy of adaptive planning is to start with the original plan that is often generated with a planning CT (pCT) and the plan is subsequently altered with an updated anatomy and segmented structures resultant from daily CBCT. The latter is normally achieved through the deformable image registration (DIR) [8]-[11]. Whereas there are many investigations of CBCT based adaptive planning, the inaccuracy of the Hounsfield Unit (HU) in CBCT is inherent and often leads to an uncertainty in dose calculation [5] [12]-[14]. Specially, CBCT has displayed a maximum HU difference in the lung region. It was reported that the HU was reduced by 200 HU in the lung CBCT compared to pCT which leads to a target dose reduction by 4% - 13% [12]. Thus, as an undesirable consequence, the adapted plan quality of lung SBRT patients could be compromised.

On the other hand, to take an advantage of the ideal anatomical information from CBCT while keeping the HU values from pCT, an alternative method of the adaptive planning is to utilize deformed pCT images. In this study we propose a practical strategy to employ the pCT that is deformed to daily CBCT for the lung SBRT treatment evaluation and demonstrate a feasibility of reconstructing a dose per fraction and possible plan adaptation. First, a phantom study was performed to evaluate a dosimetric variation such as a HU value change after the deformable image registration of pCT. Second, a dosimetric comparison including target coverage, OAR doses, HU difference was followed among the dose per fractions based on the deformed pCT comparing to the original plan from the five selected patients.

This paper is organized in the following fashion. Section 2 describes the methods including patients enrolled in this study. The results are presented in Section 3 and the discussion is in Section 4. The conclusion summarizes the significance of this work. This study may help physicians to make a decision about whether re-planning is necessary. In our clinic, the adaptive planning is required if there is more than 5% deviation from a PTV dose coverage and 10% increase of mean lung dose in lung SBRT cases.

2. Methods

Five lung SBRT patients were retrospectively selected and their daily CBCTs were employed in this study. We used a deformable image registration (DIR) algorithm provided by Mim software v 6.3 (MIM Software Inc., Cleveland, OH) to deform pCTs to match with daily CBCTs. Dosimetric comparison was performed between the original plan and the five doses per fraction of each patient. The plans were calculated using the Eclipse treatment planning system (v11, Varian Medical System, Palo Alto, CA). A phantom study was done to evaluate a dosimetric accuracy of the plan based on the deformed pCT.

2.1. Patient Population and CT Images

The pCTs of the patients were acquired with a 16 slice Philips scanner (Brilliance CT Big Bore, Philips, Cleve-

land, OH) with 3 mm slice thickness at 120 kVp and 350 mAs. All patients had a four dimensional (4D) CT scan with Varian RPM v 1.7.5 (Varian Medical System, Palo Alto, CA). From the 4DCT respiratory sorting, an image set of 25% respiratory phase and a maximum intensity projection (MIP) image using all respirational phases (0% - 90%) were created and exported to the Eclipse planning system. A physician draws an internal target volume (ITV) in the MIP image and a treatment plan is generated based on the image set of 25% respiratory phase (pCT).

CBCTs (On-board imaging, Varian Medical System, Palo Alto, CA) were acquired in the patient's treatment position with a field of view (FOV) of 46 cm and a scan length of 16 cm which is shorter than pCT including entire lungs and reconstructed with a slice thickness of 2 mm. Default thorax CBCT mode was selected for all patients with half fan mode, full trajectory, 125 kVp, 20 mA and 20 ms. Both pCT and CBCT imaging were performed while the patient was free-breathing.

A prescription of 60 Gy (5 fractions) to 95% of PTV was set for all patients. Each treatment was delivered every other day (MWF), and the CBCT was used for the patient setup prior to every treatment. For each plan, 7 to 9 static IMRT 6 MV beams from Varian TrueBeam STx v 1.6 were arranged near the ipsilateral side of the patient's thorax to minimize dose through the contralateral lung. It took about one to two weeks from the time of the pCT scan to the 1st day of CBCT as shown in **Table 1**, which also describes the patients' characteristics.

2.2. Treatment Planning Procedures

The general workflow of the suggested method is as follow: A pCT image set including structures and one of CBCT image set were exported to Mim software. The pCT images and associated contours were deformed to match the CBCT images in Mim software and the deformed pCT images and contours were exported back to Eclipse planning station. A physician redrew ITV on the CBCT images co-registered to the deformed pCT. This process is repeated for all five CBCTs and the same physician drew all ITVs on 5 CBCT sets consecutively. The same window level (W 800 L-600) was used. The PTV was expanded from the ITV by 5 mm as OAR structures were modified accordingly. The location of the treatment isocenter was manually transferred by an anatomic marker such as carina and verified by visual inspection using the offline review software (Aria v11, Varian, Palo Alto, CA. see **Figure 1**). The software records a treatment isocenter location after the daily patient positioning. Once the treatment isocenter was identified, a dose calculation was performed using the same MLC leaf motion as the original plan to reconstruct a delivered dose per fraction. The same prescription and plan normalization values were used as in the original plan. If there is more than 5% deviation from a PTV dose coverage and 10% increase of mean lung dose in the delivered dose per fraction comparing to the original plan, the adaptive planning is required, otherwise the original plan is continued.

As a result of image deformation, the pCT was automatically truncated due to a limited FOV of the CBCT. The pCT of the original plan were truncated in the same fashion as the deformed pCT for unbiased dose volume histogram (DVH) comparison and the plan was then recalculated. Target coverage and dose to healthy lung tissues (lungs minus ITV) were compared between the original plan and a dose per fraction recalculated from the deformed pCTs. As clinical DVH parameters, a mean lungs minus ITV dose (MLD, in Gy), a dose to 95% of PTV (D95%, Gy), and a volume of 20 Gy (V20Gy, cm^3) of the lungs minus ITV were selected. Mim Software was used to accumulate the individual doses per fraction registered to the dose of 1st day of treatment. In this study we chose the same dose grid as the original plan. A dose comparison between the dose summation and the

Table 1. The characteristics for the five patients used in this study. RUL = right upper lobe; LLL = left lower lobe; RLL = right lower lobe; LUL = left upper lobe. ITV = internal target volume; pCT = planning CT.

	Age (y)	Tumor Location	Tumor description	ITV volume (cm^3)	Equivalent ITV Diameter (cm)	Days from pCT to 1st CBCT
Patient 1	67	RUL	Small Cell Lung Ca.	8.2	2.5	7
Patient 2	84	LLL	Squamous cell Ca.	8.5	2.5	7
Patient 3	52	RUL	Lung metastasis	18.8	3.3	10
Patient 4	55	RLL	Non-Small Cell Lung Ca.	12.3	2.9	13
Patient 5	80	LUL	Adeno Ca.	49.2	4.5	7

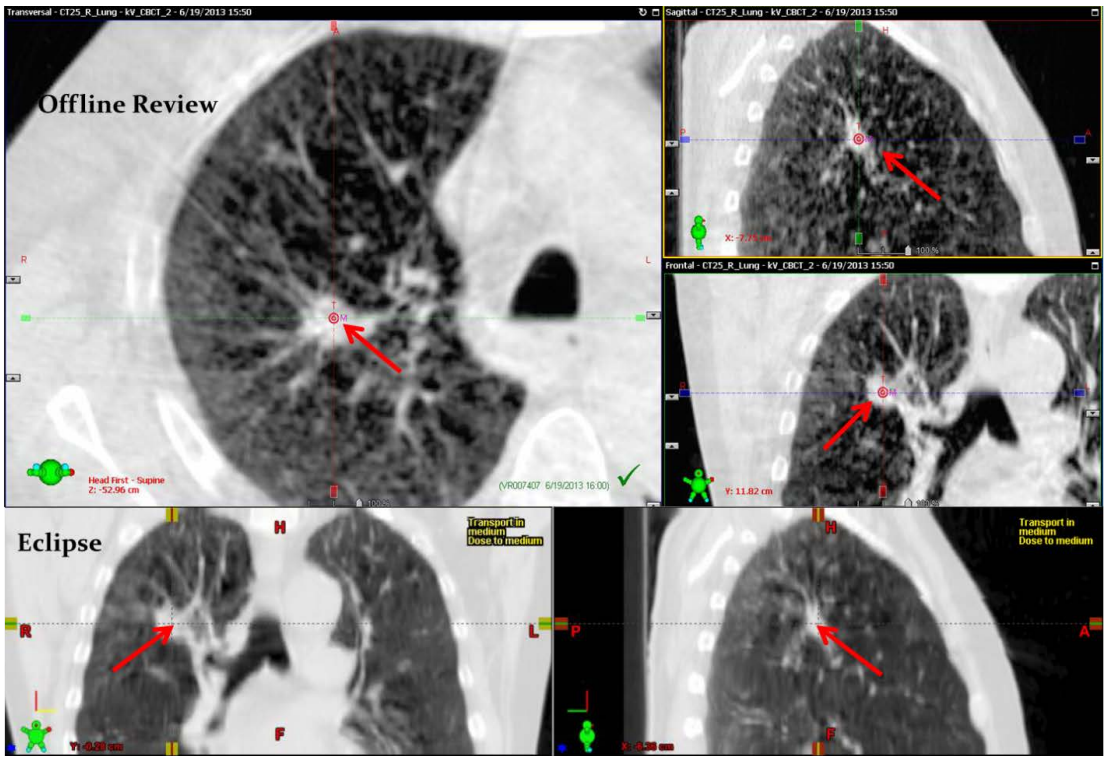

Figure 1. Treatment isocenter location (marked as a red arrow) after on-line match in the offline review (top) and manual isocenter transfer to the Eclipse treatment planning system (bottom).

original plan was carried out.

2.3. Deformable Image Registration by MIM Software V 6.3

To account for the anatomical variations revealed by on-treatment CBCT and incorporate them into the subsequent plan adaptation, a deformable image registration was carried out between pCT and CBCT using the MIM v 6.3 (MIM Software Inc., Cleveland, OH). MIM adopts a commonly used intensity based free form deformable registration algorithm. The primary goal of image registration is to find a transformation matrix $T(\vec{x})$ that maps an arbitrary point in one image set to the corresponding point on the other image (or vice versa) so that the best possible correspondence, as measured by the metric function, is achieved. $\vec{x}$ is the displacement vector that quantitatively parameterizes the deformation. The calculation often proceeds iteratively until the preset accuracy criterion is met. In order to avoid local maximum and enhance the calculation accuracy, MIM introduces a multiple resolution strategy that first down samples the image set and then gradually increases the resolution. The metric function is combined with a regularization term for the smoothness of deformation fields to form an energy function that is minimized by an optimizing algorithm. Upon the completion of the deformable registration, the displacement vector $\vec{x}$ can be utilized to warp the pCT image set and structures according to CBCT [6].

2.4. Phantom Study

To verify the dosimetric uncertainty of the deformed pCT, a Female Rando phantom (The Phantom Laboratory, Salem, NY) was scanned with a 3 mm thickness on our CT scanner after positioning it on the Vac Lock. The CT images were imported to the Eclipse planning station for planning. The lungs were contoured and an artificial PTV was generated in the right middle lobe with an equivalent diameter of 3.0 cm and a volume of 14.0 cm^3 as shown in **Figure 2**. The PTV density was overwritten as water (1 $g \cdot cm^{-3}$). A lung SBRT plan was created with 7 field static IMRT beams.

CBCT was performed with the phantom posed on the treatment couch in the same position as when it was

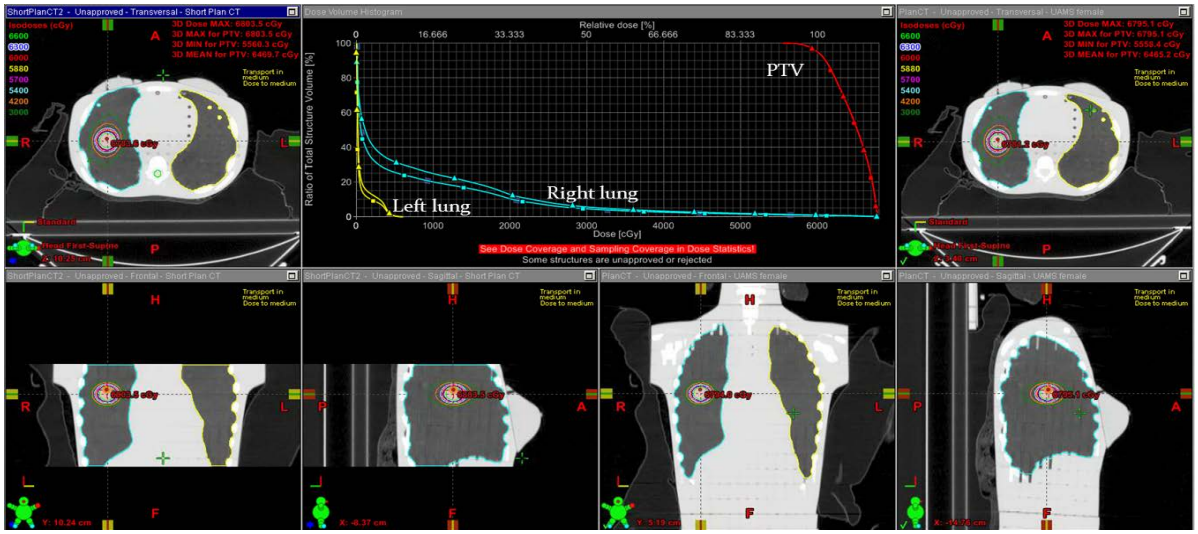

Figure 2. Phantom plan study 1-truncated original pCT (left, represented in DVH as a solid triangle) vs. non-truncated original pCT (right, represented in DVH by a solid square).

CT-scanned. The pCT images and structure set were deformed by the Mim software to fit the CBCT images. A plan using the deformed pCT was generated as described in section 2.2. The PTV and the location of the treatment isocenter were kept the same as in the original plan. The HU was used to compare between the original and the deformed pCTs. There was no artificial deformation introduced to compensate a breathing motion between pCT and CBCT.

3. Results

3.1. Phantom Study

First, the original plan with truncated pCT was compared to the original plan with non-truncated pCT. As seen in **Figure 2**, DVH showed both PTV coverages were identical but lung DVHs were not the same due to the difference of the lung volumes. Therefore the impact on the PTV dose by the truncated portion was not of dosimetric concern for the purpose of evaluating a dose per fraction.

Second, a plan with the deformed pCT was compared to the original plan with truncated pCT. As seen in **Figure 3**, DVH comparison showed the PTV and lungs were identical on both plans. Difference of the mean HU values between the original pCT and the deformed pCT was less than 0.5%. Dosimetric deviation caused by the deformed pCT became negligible as shown in **Figure 3**. This is an encouraging finding since other authors found 3% - 5% of dose differences in the CBCT based plan comparing to the pCT based plan due to HU variations [8] [15] [16].

3.2. Patient Study-Five Lung SBRT Cases

Target coverage and organ at risk (lung minus ITV) dose were compared between the original plan vs. a dose per fraction. **Figure 4** displays an overlay of DVHs between two plans at the 5th (last) day of treatment of the patient 1. It shows that daily PTV coverage was deviated from that of the original plan and a healthy lung dose (lungs minus ITV) also increased comparing to the original plan due to the target volume change. **Figure 5** shows an example of a mean HU value comparison between pCT and five deformed pCTs of patient 1 and patient 5. The deviation from all patients between the average of the five deformed pCTs and the original pCTs is within ±5%. This might be dosimetrically insignificant according to the study conducted by Zurl *et al.* [13].

Figure 6 shows the plan characteristics of all patients during the entire treatment course. It shows the trend of changes in ITV volume, mean lung dose, and V20Gy of lungs minus ITV. All parameters were normalized to each value from the original plan. On average, while the ITVs shrank by −17% ± 7.8% (range: +2.8% to −26%) from the pCT to the last treatment, MLD (average: 7.6 Gy ± 1.2 Gy) continuously increased up to ~7% from the 1st day of CBCT to the last CBCT, D95% of PTV slightly decreased but stayed within 5%, and V20Gy of lungs

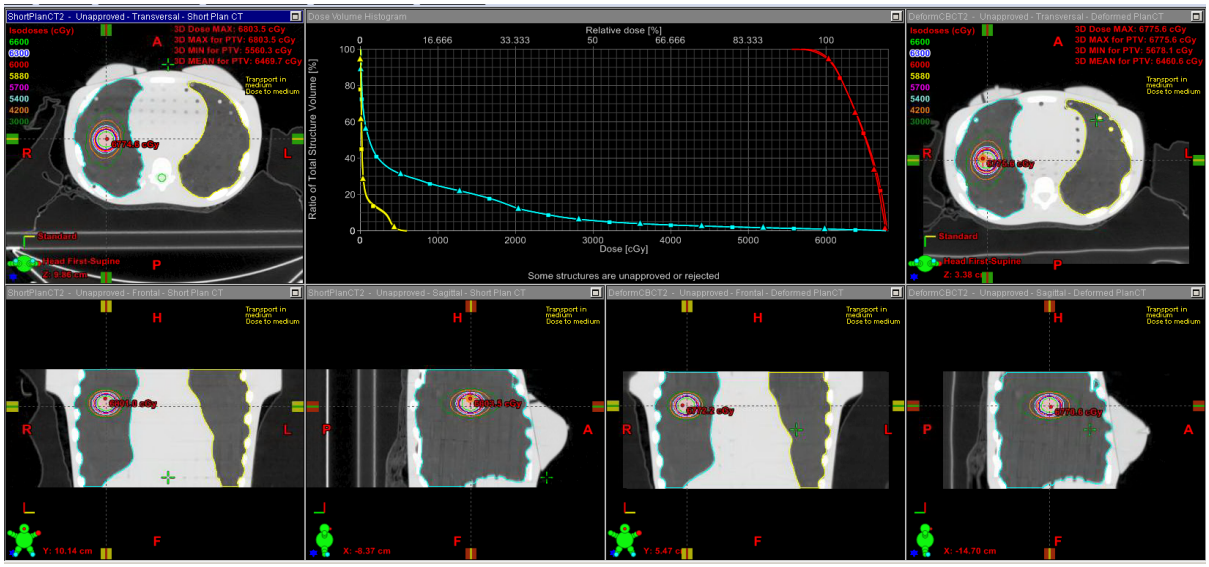

Figure 3. Phantom plan study 2-original pCT (left, represented in DVH by a solid square) vs. deformed pCT (right, represented in DVH by a solid triangle).

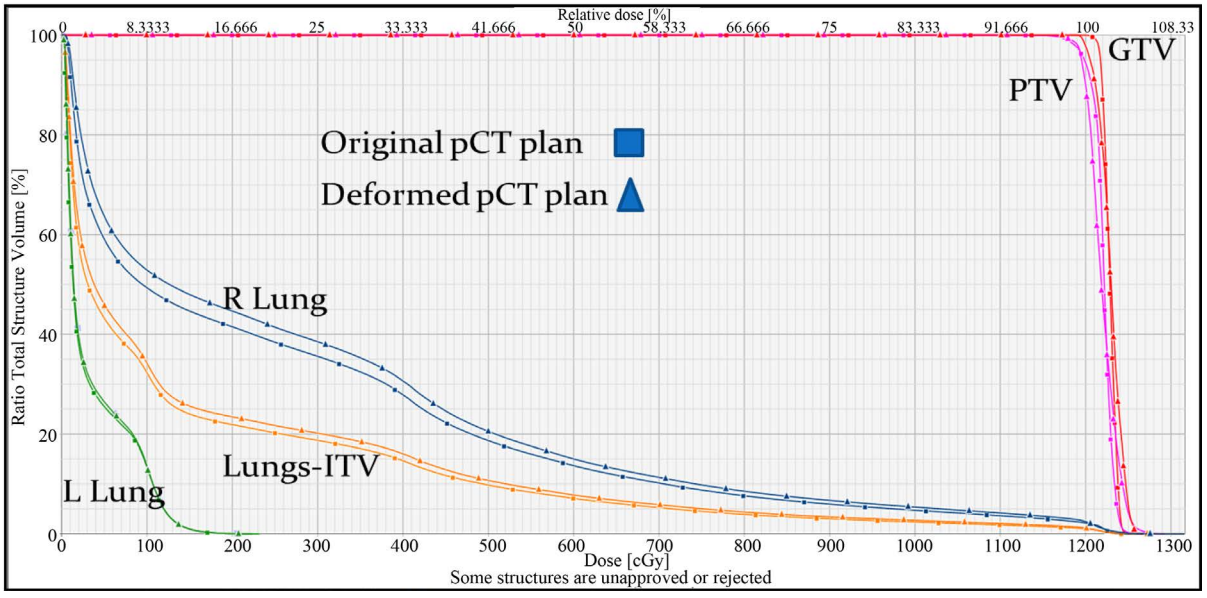

Figure 4. Dose comparison of the original plan and a dose per last fraction of the patient 1.

minus ITV (average: 389.7 cm^3 ± 91.0 cm^3) fluctuated within ±5% during the treatment course. MLD might be a better indicative metric of the lung dose than V20Gy as the ITV volume decreases. The same pattern was observed in the accumulated dose comparison. Specifically, D95% of PTV decreased by ~2.0%, and V20Gy of lung increased by ~3.0% when compared to the original plan. Therefore, according to the policy of our clinic, all doses per fraction were acceptable for treatment by our physician without requiring the adaptive planning. A GTV volume change (ranging from −14.1% to +2.4%) between the pCT scan and the CBCT of the 1st treatment, was found and this could possibly be caused by either physiological change during the 1 - 2 week or the difference on the ITV estimation between CT and CBCT.

4. Discussion

Daily CBCT can be used directly for the dose calculation for obvious reasons, *i.e.*, CBCT provides the updated

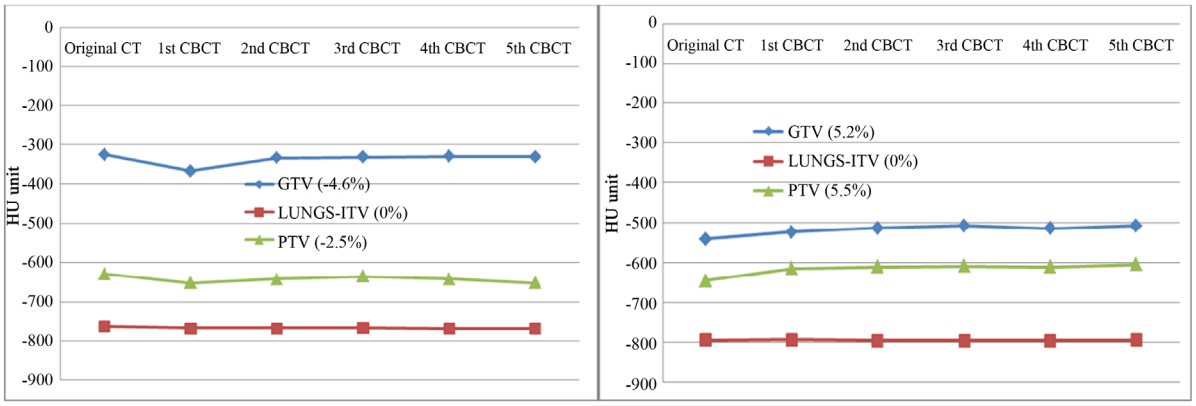

Figure 5. Mean Hounsfield Unit of patient 1 (left) and patient 5 (right) and parenthesis represents an averaged HU deviation of each organ from the original pCT.

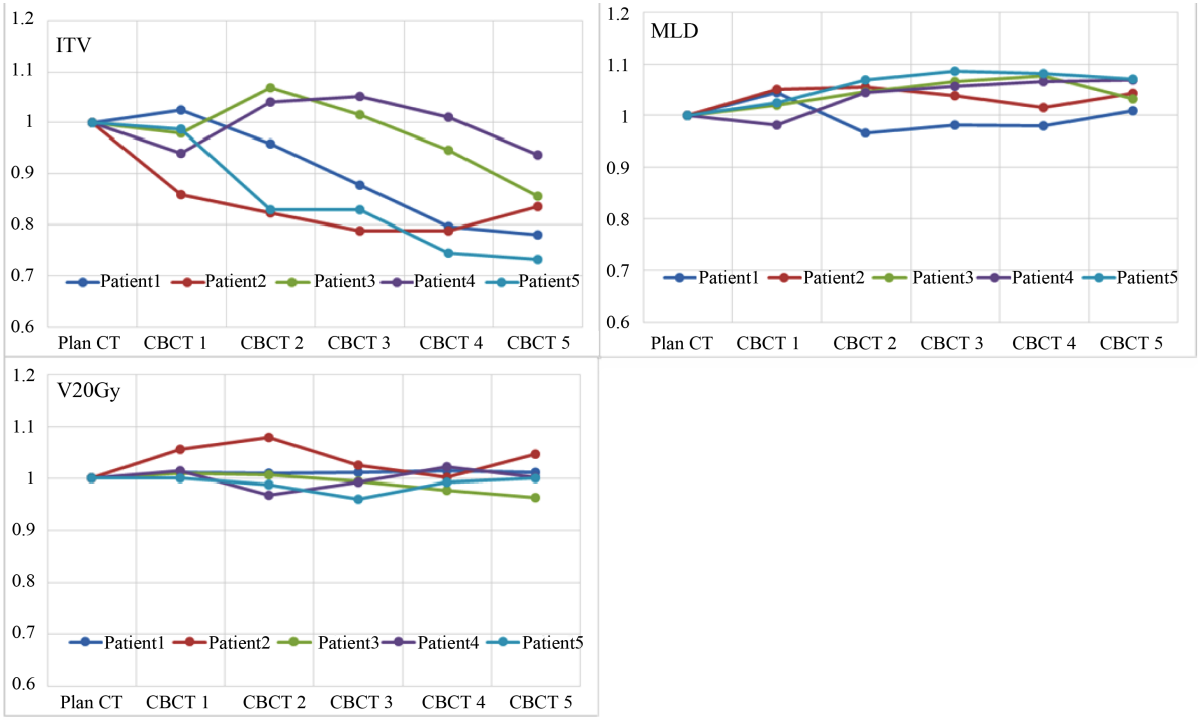

Figure 6. Plan characteristics of the five patients comparing to the respective original plan.

anatomy while a patient is in the treatment position. However, the downside of this strategy is that there are HU variations in CBCT that might cause large dosimetric uncertainties specially in the lung region. Some authors suggest HU correction on CBCT through pixel correction or relative electron density conversion. However, even after correction, dose calculation on CBCT could still vary by up to 5%. Veiga *et al*. mentioned HU to electron density conversion showed variations depending on the type of phantom used, thus an incorrect HU correction that could lead to large dosimetric deviations [8]. Therefore, in order to utilize the desirable anatomical information in CBCT while having as precise HU as possible, we proposed to use the deformed pCT image. Considering all the complications incurred by using CBCT, the proposed method in this study eliminates the dose uncertainty due to HU variation but still keeps the up-to-date patient anatomy from daily CBCT. In this study, we demonstrated a feasibility to reconstruct a dose per fraction with the pCT image set that was deformed to daily CBCT. Based on the difference between the reconstructed dose and the original plan, physicians can decide whether or not to adapt the plan. A phantom study was performed to evaluate a dosimetric uncertainty on the

deformable image registration. HU variation and its impact on the dosimetry were assessed through the patient study. Our computation results indicated that no plan adaptation was needed based on the data sample we included. However, the proposed method is still valuable to inform physicians about whether re-planning is necessary for the prospective lung SBRT patients.

We would like to point out that the limited field of view (*i.e*. 16 cm scan length) of CBCT could be a concern of the adaptive planning. Even though the dose difference was negligible as it was shown in the phantom study (Section 3.1), planners are recommended to truncate the original pCT according to the CBCT, otherwise DVHs of OARs will not be fairly compared as shown in **Figure 2**. If the outer body part is cropped in the CBCT images due to off-centered target location or the patient's thickness, the accuracy of the image registration will be degraded. In addition, the accuracy of the dose calculation with the limited FOV could be compromised with the non-coplanar beams. If the plan adaptation is needed, a physician can make a clinical judgment whether to use this deformed pCT or rescan the patient in a case-by case approach. It depends on how much the critical organ volume is encompassed in the CBCT scan. It is recommended that the same physician, who drew ITV on the original pCT, draws the ITV on the CBCT image to minimize potential inter-observer error. And there might be an uncertainty on the plan comparison between the original plans based the CT image set of 25% respiratory phase and the new plan based pCT deformed by respiration-averaged CBCT.

The image deformation was achieved with the MIM software as described earlier. Piper *et al*. reported that the pCT to CBCT image deformable registration algorithm using Mim software revealed that a correlation of deformed pCT to mid-treatment pCT is better than daily CBCT to the mid treatment pCT [17]. This result was comparable to self-correlation with 2 mm translational error applied. The impact of registration accuracy on the dose calculation could be significant since a large volume of deformation occurs in this study. In this work, no direct evaluation was performed and the phantom study have been done with a stationary Rando phantom, so the potential inaccuracies of the deformable registration with a patient-specific breathing motion was not studied, either. Nevertheless, it is worth mentioning that a well-known problem in image registration is the lack of quantitative validation. The most common evaluation technique is the visual inspection using checker board or spy glass. Another way of assessing the registration accuracy is to perform synthetic image experiments [18] [19]. The idea is to warp one of the input image sets with known deformation vector fields that serve as the "ground truth". Deformable image registration is then carried out between the synthetic image sets, and the calculation outcome is compared to the known "ground truth" so that a quantitative evaluation can be achieved. Regardless, it remains a challenging task to precisely evaluate the precision of deformable registration. CBCT artifacts might have an adverse impact on the deformable registration.

5. Conclusion

Whereas an adaptive planning was not required based on our internal protocol, the study still demonstrated a significant dosimetric deviation such as an increase of MLD by 7% due to ITV reduction through the doses per fraction reconstructed by the deformed pCTs. Suggested method in this study has an advantage over the direct dose calculation on CBCT for lung SBRT patients due to less HU variations. In conclusion, it is feasible to use a deformed pCT by CBCT for a calculation of the dose per fraction and for possible adaptive planning in lung SBRT cases. Readers should be cautious in the patient selection before clinical application of this method.

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