Journal of Radiotherapy in Practice

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Dose accumulation with deformable image registration method using helical tomotherapy images for prostate cancer

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Original Article

Cite this article: Thongsuk W, Chitapanarux I, Wanwilairat S, and Nobnop W. (2020) Dose accumulation with deformable image registration method using helical tomotherapy images for prostate cancer. *Journal of Radiotherapy in Practice* **19**: 25–29.
doi: 10.1017/S1460396919000256

Received: 22 February 2019
Revised: 9 April 2019
Accepted: 10 April 2019
First published online: 6 June 2019

Key words:
deformable image registration; dose accumulation; helical tomotherapy; prostate cancer

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Abstract

Purpose: To evaluate changes of accumulated doses from an initial plan in each fraction by deformable image registration (DIR) with daily megavoltage computed tomography (MVCT) images from helical tomotherapy for prostate cancer patients.
Materials and methods: The MVCT images of five prostate cancer patients were acquired by using a helical tomotherapy unit before the daily treatment fraction began. All images data were exported to DIR procedures by MIM software, in which the planned kilovoltage computed tomography (kVCT) images were acting as the source images with the daily MVCT acquired as the target images for registration. The automatic deformed structure was used to access the volume variation and daily dose accumulation to each structure. All dose-volume parameters were compared to the initial planned dose.
Results: The actual median doses of the planning target volume (PTV) received 70 Gy and 50.4 Gy were decreased at the end of the treatment with an average 1·0 ± 0·67% and 2·1 ± 1·54%, respectively. As regards organs at risk (OARs), the bladder and rectum dose-volume parameters tended to increase from the initial plan. The high-dose regions of the bladder and rectum, however, were decreased from the initial plan at the end of the treatment.
Conclusions: The daily actual dose differs from the initial planned dose. The accumulated dose of target tends to be lower than the initial plan, but tends to be higher than the initial plan for the OARs. Therefore, inter-fractional anatomic changes should be considered by the DIR methods, which would be useful as clinically informative and beneficial for adaptive treatment strategies.

Introduction

Helical tomotherapy is a novel treatment approach that combines Intensity-Modulated Radiation Therapy (IMRT) delivery with built-in image guidance using megavoltage (MV) CT scans. The unit also allows the acquisition of MVCT images using the same radiation source detuned to reduce its effective energy to 3.5 MV.[1] The daily MVCT images are used in verifying daily setup before treatment to improve target localisation accuracy. Some patients, however, have significant daily anatomical changes, especially in prostate cancer, in which different filling conditions of the bladder and rectum can significantly influence the inter-fraction position of the prostate.[2–3] Consequently, the patient receives an actual dose different from the planned dose.

Deformable image registration (DIR) is the process which can be used to modify the structure according to anatomical changes for observing dosimetric effect. DIR attempts to register the different patient anatomy's image data sets into a reference image data set and determine the minimised differences between the two image sets by identifying the spatial correspondence.[4] The deformable images that were created can be used to recalculate actual target and OARs dose received. Therefore, this method can evaluate the difference in accumulated dose from the initial planned dose in each fraction. In this study, daily MVCT images from helical tomotherapy were used to generate a cumulative dose with a DIR method for prostate cancer. The daily cumulative doses were analysed to assess the variations from the initial plan.

Material and Methods

Patient characteristics

A retrospective randomised study of five prostate cancer patients who were treated with a helical tomotherapy unit (TomoTherapy, Inc., Madison, WI, USA) at the Radiation Oncology Division, Maharaj Nakorn Chiang Mai Hospital was carried out. All patients underwent IMRT with prescribed dose of 70 Gy in 28 fractions delivered to the planning target volume (PTV) following the RTOG 0415.[5] This study was granted an ethics exemption by the Institutional Review Board

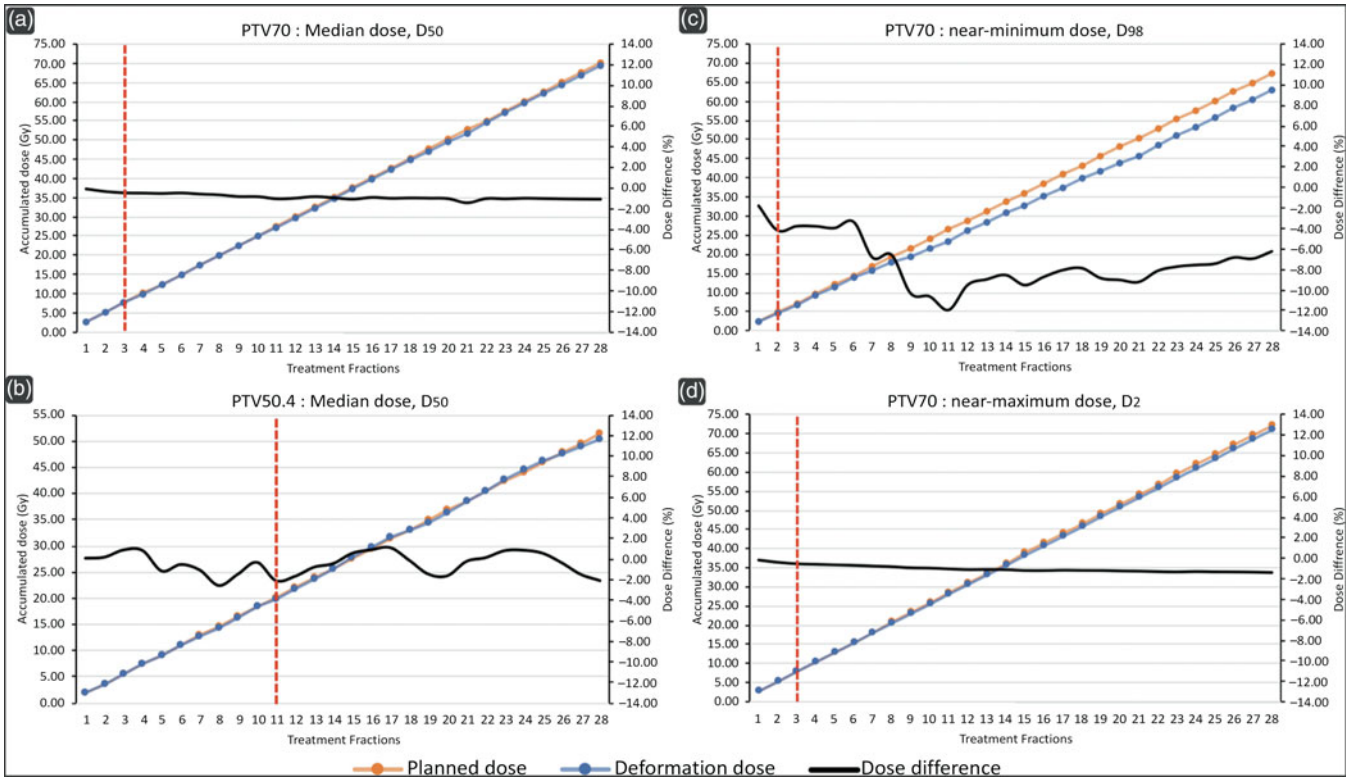

Figure 1. Daily accumulated dose and percentage of dose differences. Comparison between planned dose and deformable dose for median dose, $D_{50\%}$ of (A) the planning target volume prescribed of 70 Gy dose (PTV70) and (B) the planning target volume prescribed of 50.4 Gy dose (PTV50.4) including (C) near-minimum dose, $D_{98\%}$ and (D) near-maximum dose, $D_{2\%}$ of PTV70.

of Faculty of Medicine Chiang Mai University (study code RAD-2561-05828/Research ID: 5828)

Daily MVCT image acquisition

One hundred and forty MVCT images of the pelvis were acquired by using the helical tomotherapy unit. In an effort to ensure reproducible *bladder* filling, all patients received instructions to follow the bladder preparation protocol by empty their *bladder*, then drink 200 mL of water and *wait* for 25 *min* before the planning CT scan and prior to each day of treatment. Patient image alignment used a matrix of 512 x 512 with voxel dimension of 0.7634 mm^3 × 0.7634 mm^3 × 3 mm^3. The daily MVCT scan range must cover the entirety of the PTV, bladder and rectum. In cases where the image did not cover all of them, the data from the closest day were used.

Deformable image registration

MIM software (MIM Software Inc., Cleveland, OH, USA) was used to create the deformation vector field (DVF) with Free-Form Deformable Registration algorithm.[6] The planned kVCT images were acting as the source images and daily MVCT were acquired as the target images for registration. The automatic deformed structure was used to access the volume variation and daily dose accumulation to each structure.

Assessment of accumulated dose

The daily dose deformation values were summed to the accumulated dose and compared to the initial planned dose distribution. Regarding the PTV70, the median absorbed dose ($D_{50\%}$), the near-minimum ($D_{98\%}$) absorbed dose, and the near-maximum ($D_{2\%}$) absorbed dose values from each fraction were assessed. The PTV50.4 was assessed by $D_{50\%}$ absorbed dose. The rectum and bladder were evaluated by $D_{50\%}$, $D_{35\%}$, $D_{25\%}$ and $D_{15\%}$. The bilateral femoral head was assessed by $D_{10\%}$. All of these dose-volume parameters were compared to the initial planned dose.

The normality of the variable distribution was verified using the Shapiro–Wilks test. Paired sample *t*-test was performed for normal variable distributions, while the Wilcoxon signed-rank test was performed for non-parametric statistics using version 23 of the SPSS statistical program. Both test metrics were compared metrics to determine the statistical significance on each data set, with a threshold of $p < 0{\cdot}05$.

Results

ROI volume variations

The targets volume were decreased by an average of 2·8% ± 2·83 (PTV70) and 13·5% ± 6·96 (PTV50.4) at the end of the treatment course.

For the OAR, the average volume of rectum was decreased by 15·7% ± 5·76 at the end of the treatment course. However, the bladder volume increased by an average of 53·5% ± 12·58 from the initial plan.

Accumulated dose variation from initial planned dose

The accumulated dose of PTV70 decreased on with an average 1·0 ± 0·67% ($D_{50\%}$), 6·3 ± 3·95% ($D_{98\%}$) and 1·4 ± 0·42% ($D_{2\%}$) at the end of the treatment. The $D_{50\%}$ of PTV50.4 lower than the initial planned dose was 2·1 ± 1·54%. Figure 1 demonstrates the daily target dose variation of PTV70 and PTV50.4. The median

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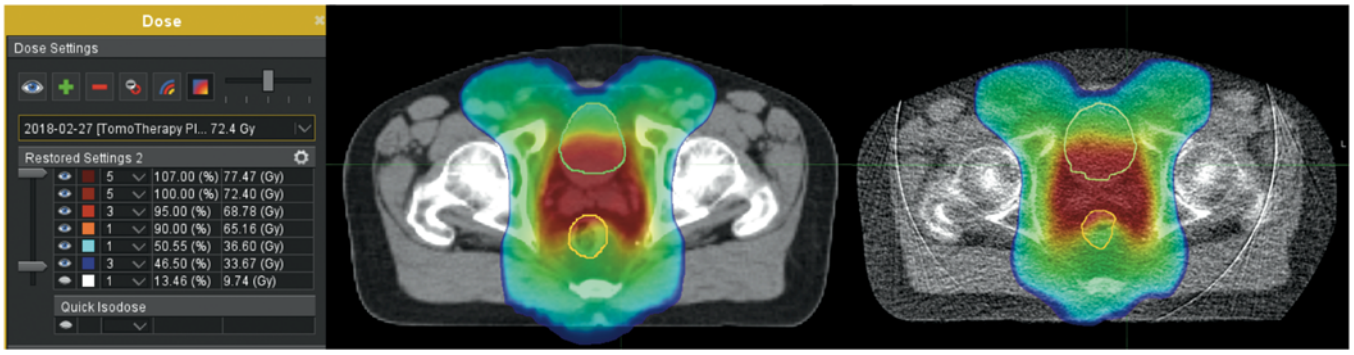

Figure 2. The dose distribution for bladder (green line contour) and rectum (yellow line contour) for the initial planned dose on kVCT image (left) and accumulated dose at the 28th fraction's MVCT image (right).

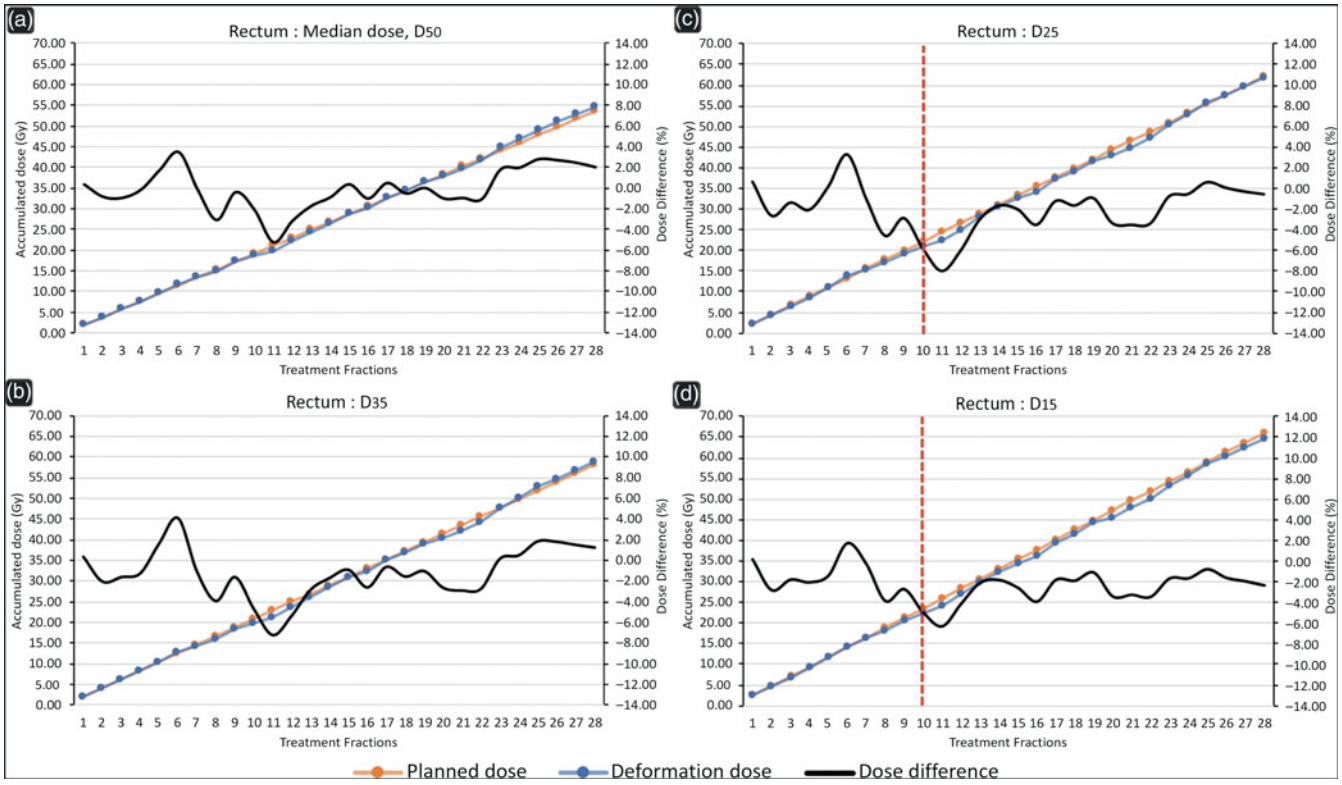

Figure 3. Daily accumulated dose and percentage of dose difference comparison between planned dose and deformable dose of the rectum for (A) $D_{50\%}$, (B) $D_{35\%}$, (C) $D_{25\%}$ and (D) $D_{15\%}$.

dose variation was significantly different from the initial planned dose after three fractions of treatment ($p = 0{\cdot}021$). However, the median dose of PTV50.4 was significantly different after 11 fractions of treatment ($p = 0{\cdot}027$).

Figure 2 illustrates the dose distribution for the rectum and bladder at the 28th treatment fraction compared with the initial plan. The rectum dose increased more than the initial planned dose by 2·1 ± 9·01% ($D_{50\%}$) and 1·2 ± 8·64% ($D_{35\%}$), However, $D_{25\%}$ and $D_{15\%}$ were decreased from the initial plan by 0·6 ± 7·18% and 2·4 ± 5·43%, respectively. Figure 3 illustrates that the dose variations were significantly different from the initial plan after ten fractions of treatment with $p = 0{\cdot}028$ and 0·033 for $D_{25\%}$ and $D_{15\%}$, respectively. $D_{50\%}$ and $D_{35\%}$ were not significantly different from the initial plan.

Figure 4 demonstrates $D_{50\%}$, $D_{35\%}$ and $D_{25\%}$ of the bladder were increased from the initial plan by 5·1 ± 7·68%, 3·2 ± 6·05% and 1·8 ± 4·35%, respectively. However, $D_{15\%}$ was lower than the initial plan by 0·3 ± 2·87% at the end of the treatment. This was significantly different from the initial plan after 11 fractions of treatment ($p = 0{\cdot}019$).

$D_{10\%}$ for the left head of the femur was significantly increasing from the initial plan after 21 fractions ($p = 0{\cdot}043$) by an average of 6·2 ± 5·87% at the end of treatment (Figure 5). However, the dose of right femoral head was decreased by an average of 0·2 ± 6·04% at the end of the treatment and not significant for throughout the treatment course.

Discussion

The variation of the bladder volume shows the highest increase of approximately 50% from the initial plan. This result was possibly

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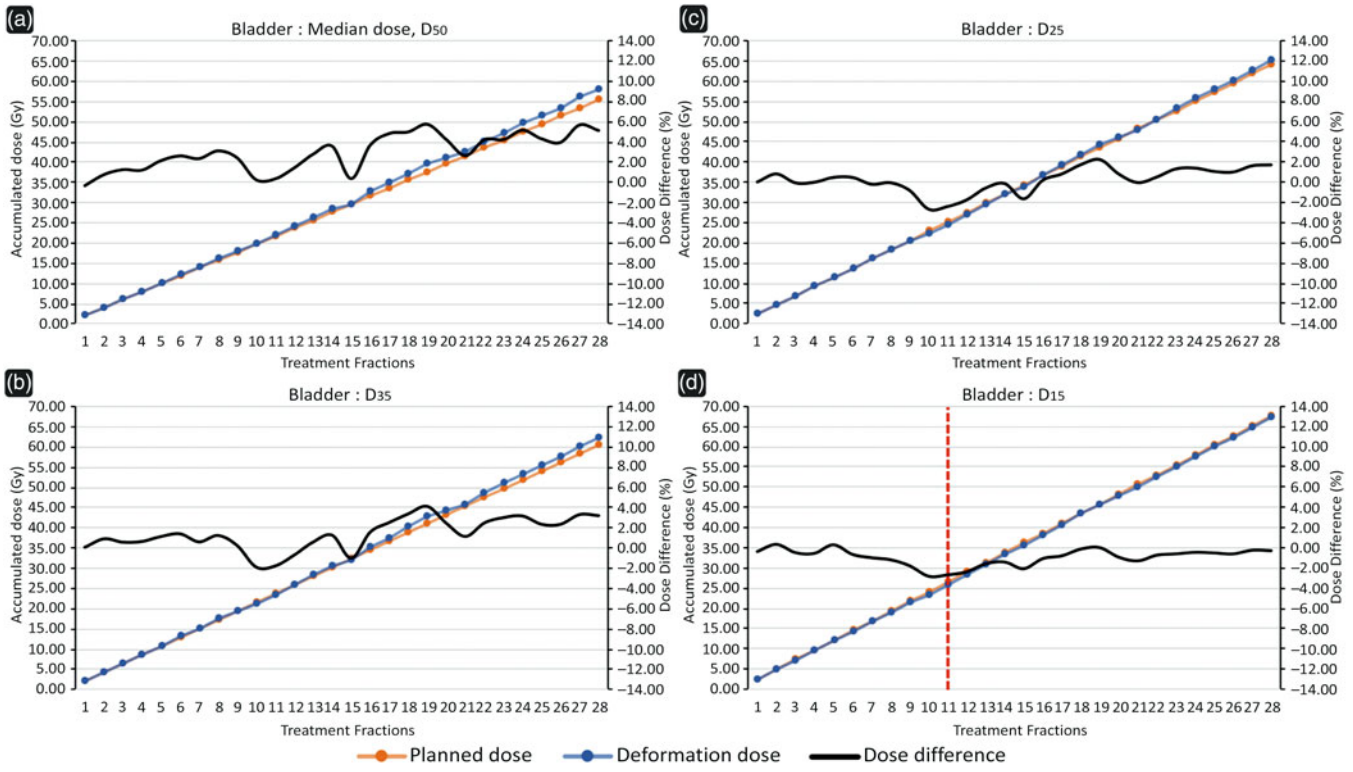

Figure 4. Daily accumulated dose and percentage of dose difference comparison between planned dose and deformable dose of the bladder for (A) $D_{50\%}$, (B) $D_{35\%}$, (C) $D_{25\%}$ and (D) $D_{15\%}$.

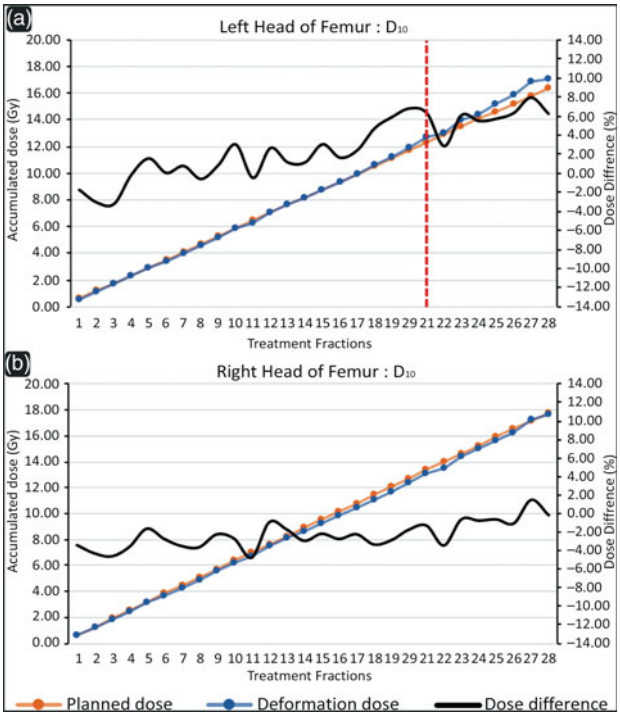

Figure 5. Daily accumulated dose and percentage of dose difference comparison between planned dose and deformable dose for $D_{10\%}$ of (A) left head of femur and (B) right head of femur.

caused by the physiologic processes or the different duration of patient preparation between pre-simulation and pre-radiation procedures. Moreover, the daily bladder volume had changed throughout the treatment course, as shown by standard deviation values that were as high as 12·6%. However, Pinkawa et al. [7] demonstrated the variability of bladder filling does not affect the prostate position with a full bladder when comparing with an empty bladder.

As regards the accumulated dose variation, the $D_{50\%}$ and the $D_{2\%}$ of the target varied from the initial by planned less than 2%. Nevertheless, $D_{98\%}$ was varied greater than 5%. These results were consistent with Godley et al.,[8] where $D_{95\%}$ and $D_{100\%}$ of the target were decreased from the initial plan by an average of 3·6% and 6%, respectively. In addition to the bladder and the rectum, the accumulated dose tended to increase from the initial plan, except the $D_{15\%}$ of the bladder and $D_{15\%}$, $D_{25\%}$ of the rectum. Our study showed a decrease from the initial plan at the end of treatment.

In each fraction of the treatment, the target and high-dose regions of OAR were significantly different between the dose from initial plan and deformable dose. The slight volume changes in the high-dose area, especially the target volume, can affect numerous dose variations, as seen from the deformable dose of the target, which was significantly different from the initial planned dose during the first period of treatment.

The results of this study demonstrate the difference between the actual dose and planned dose throughout the treatment. These effects result in the effectiveness of radiotherapy treatment in terms of decreased tumour control probability and increased normal tissue complication probability. Therefore, the DIR methods should be used for adaptive treatment strategies in clinical implementation to improve outcome.

The purpose of this study is to assess the daily cumulative doses. However, this study is a retrospective study. In some image sets, the MVCT scan range did not cover whole targets, bladder or rectum. The problem was resolved by selecting the image from the closest day for the cumulative dose summation. To decrease the effect to

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the study results, we allow to use only the image from the closet day. If the patient's image cannot be used more than two consecutive days, that patient will not be included in this study. In addition, another limitation of this study is the small number of patients, which is too small to draw any solid conclusions. Therefore, these limitations should be considered to define the daily image scan range and increase the sample size in a future prospective study.

Conclusion

The daily accumulated dose was evaluated with DIR software. Due to the patient's anatomical changes, the daily actual dose differed from the initial planned dose. The accumulated dose of target tends to be lower than the initial plan, while rectum, bladder and bilateral femoral head were higher than the initial plan. Therefore, The DIR methods on Helical tomotherapy MV images showed clinically useful information for observation as a result of interfractional anatomic changes and beneficial for adaptive treatment strategies.

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Acknowledgements. The author offers many thanks to TransMedics (Thailand) Co. Ltd. for supporting MIM software.

Financial Support. This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflicts of Interest. None.

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