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Scientific Article

Clinical Development and Evaluation of Megavoltage Topogram for Fast Patient Alignment on Helical Tomotherapy

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Abstract

Purpose: To develop and evaluate a fast patient localization tool using megavoltage (MV)-topogram on helical tomotherapy.

Methods and Materials: Eighty-one MV-topogram pairs for 18 pelvis patients undergoing radiation were acquired weekly under an institutional review board−approved clinical trial. The MV-topogram imaging protocol requires 2 orthogonal acquisitions at static gantry angles of 0 degrees and 90 degrees for a programed scan length. A MATLAB based in-house software was developed to reconstruct the MV-topograms offline. Reference images (digitally reconstructed topograms, digitally reconstructed topograms) were generated using the planning computed tomography and tomotherapy geometry. The MV-topogram based alignment was determined by registering the MV-topograms to the digitally reconstructed topogram using bony landmark on commercial MIM software. The daily shifts in 3 translational directions determined from MV-topograms were compared with the megavoltage computed tomography (MVCT) based patient shifts. Linear-regression and two one-sided tests equivalence tests were performed to investigate the relation and equivalence between the 2 techniques. Seventy-eight MV-topogram pairs for 19 head and neck patients were included to validate the finding.

Results: The magnitudes of alignment differences of (MVCT − MV-topogram) (and standard deviations) were -0.3 ± 2.1, -0.8 ± 2.4, and 1.6 ± 1.7 mm for pelvis and 0.6 ± 1.2, 0.8 ± 4.2, 1.6 ± 2.6 mm for head and neck; the linear-regression coefficients between 2 imaging techniques were 1.18, 1.10, 0.94, and 0.86, 0.63, 0.38 in the lateral, longitudinal, vertical directions for pelvis and head and neck, respectively. The acquisition time for a pair of MV-topograms was up to 12.7 times less than MVCT scans (coarse scan mode) while covering longer longitudinal length.

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Conclusions: MV-topograms showed equivalent clinical performance to the standard MVCT with significantly less acquisition time for pelvis and H&N patients. The MV-topogram can be used as an alternative or complimentary tool for bony landmark-based patient alignment on tomotherapy.

Introduction

Image guided radiation therapy techniques have been developed to ensure accurate patient setup, so that the planned dose can be precisely delivered to the target while sparing nearby healthy tissue.[1-3] Before treatment delivery, a daily image is usually taken for registration to the reference image to determinate correct patient shifts. The reference image is normally generated using CT simulation. Patient alignment is a quantitative assessment to determine whether the patient is correctly positioned (as planned).

The unique geometric design and integrated on-board imaging system[3] of the tomotherapy system (Accuray Inc, Sunnyvale, CA) allows for acquisition of megavoltage CT (MVCT) images but also MV-topographic images (MV-topogram). The volumetric MVCT methodology is currently the only option available for image guided patient localization. During normal treatments, up to 25% of the operational time on a tomotherapy unit is due to pretreatment imaging, realignment, and patient positioning verification.[4] The amount of time dedicated to these tasks depends on the longitudinal length of the target(s); for longer scans, the MVCT imaging and reconstruction time can be extensive, resulting in even longer overall time when the patient is on the treatment couch. Tomotherapy provides the ability to treat very long targets, up to 150 cm in length, and is used for treatment such as craniospinal irradiation, total bone morrow irradiation (TMI), and total body irradiation, and so on.[5,6] It was reported that patient alignment using current MVCT acquisition usually takes >600 seconds for TMI cases, even using a coarse mode.[7] Often, repeated scans are required if the initial MVCT scan shows the patient needs to be repositioned. Magome et al proposed a fast MVCT imaging modality, acquired with fast couch speeds, for total body irradiation and TMI on tomotherapy. The scan time and imaging dose were reduced up to 30% of those from a conventional MVCT scan using coarse mode.[8]

This study was designed to develop a practical clinical workflow incorporating an MV-topogram protocol as an alternative patient localization tool and evaluate the performance of MV-topogram in terms of registration accuracy compared against the standard MVCT protocol for patients undergoing radiation to the pelvis and head and neck (H&N) on a commercial tomotherapy system. The clinical benefit of adopting the new technique would be to achieve the similar patient setup accuracy using far less imaging dose and shorter imaging time for appropriate treatment sites on tomotherapy.

Method and Materials

Description of the MV-topogram clinical trial

A total of 18 pelvis and 19 H&N patients enrolled in a prospective clinical trial were included in this study. The clinical trial was approved by the institutional review board (IRB #15-001641) at the Department of Radiation Oncology of University of California Los Angeles. The patients who were considered as appropriate candidates for the trial were those who were suitable for treatment with tomotherapy and had at least some bony anatomy for alignment. Patients were included if they were ≥18 years of age, undergoing radiation therapy in the department, and able and willing to read and understand the written or oral consent form and fully consent to this study. Patients were identified as potential subjects by the principal investigator at either their consultation or "CT simulation" visit in the department. Subjects were introduced to the study and asked to provide consent before their first radiation treatment by the principal investigator, one of the co-investigators (clinicians), or a study coordinator. Each subject was scanned using the standard MVCT scan and the proposed MV-topogram scan on a weekly basis. Each patient was formally consented to undergo weekly MV-topogram scans on a commercial tomotherapy unit (Accuray Inc) in addition to their clinical MVCT scans. Up to 7 weekly MV-topogram scans were acquired for each patient, spread throughout their treatment course.

MV-topogram acquisition workflow

The MV-topogram imaging workflow was created and integrated into our clinical workflow. The online MV-topogram acquisition workflow involved the following major steps. First, we acquired an open beam air scan to calibrate the MVCT detector. This was performed before positioning the patient on the couch. The detector response was immediately exported from the tomotherapy data server. Second, we setup the patient by aligning the tattoos to the red lasers according to the treatment plan. Before the MV-topogram scan, 3 1/8-inch tungsten BBs

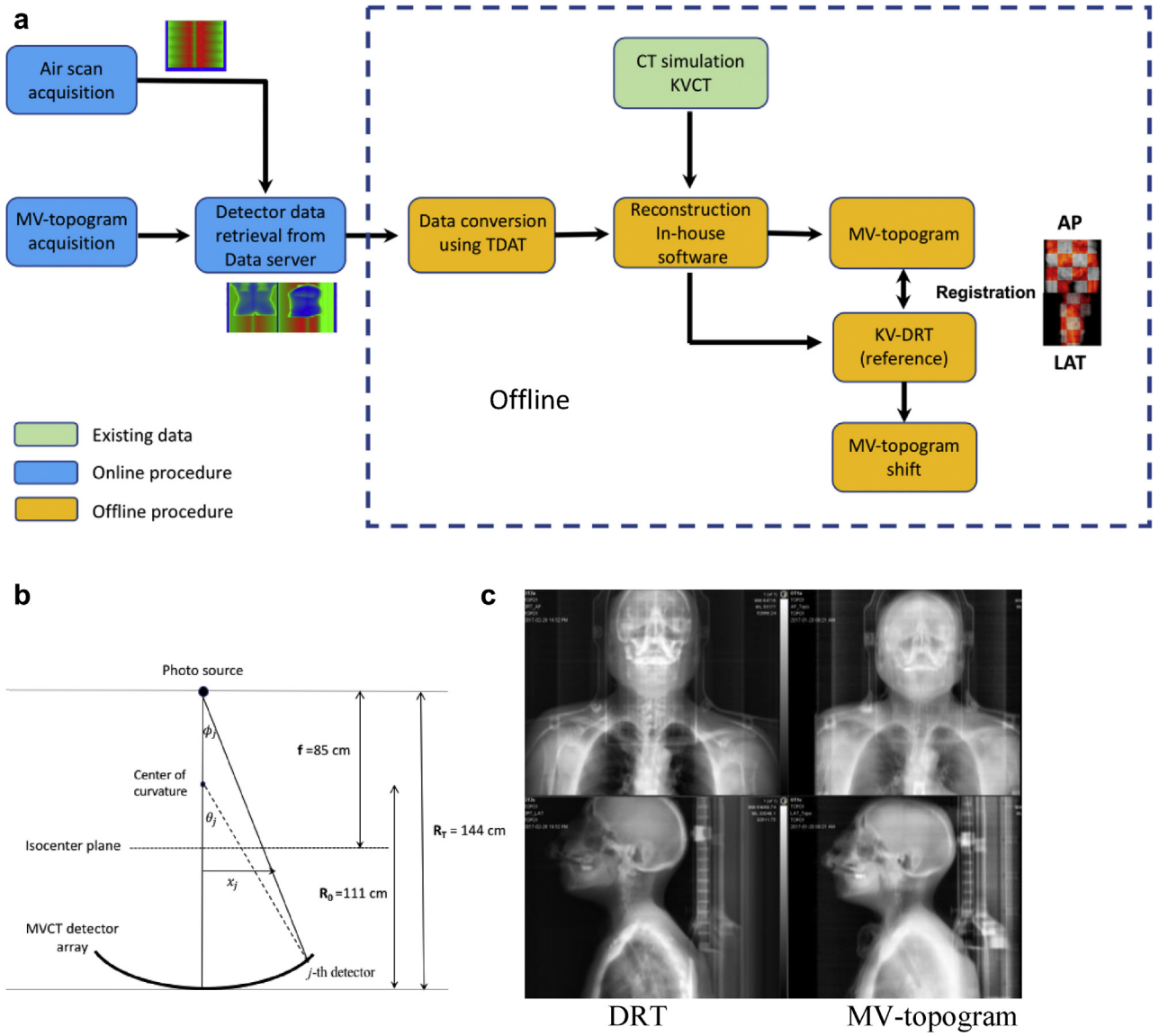

Figure 1 (a) Schematic diagram of the megavoltage (MV)-topogram imaging acquisition and reconstruction workflow used in this study. Blue boxes are the steps taken online, and orange boxes are the steps happened offline. (b) Tomotherapy MV computed tomography (MVCT) detector geometry and parameters. (c) The reconstructed digitally reconstructed topograms (DRT) and MV-topograms for a sample head and neck case was displayed. *Abbreviations*: AP = anterior-posterior; LAT = lateral; TDAT = TomoTherapy Display and Analysis Tool.

(setup BBs) were placed on the patient setup markers for visualization purposes. Third, we loaded a site–specific MV-topogram acquisition procedure created under calibration mode on tomotherapy treatment console. The MV-topogram protocol for pelvis cases requires 2 orthogonal acquisitions at static gantry angles of 0 degrees and 90 degrees for a programed 40 cm scan length of 10 seconds. All MLC leaves were open using a 1 mm collimator opening. The maximum couch speed of 4 cm/s was used to minimize the MV-topogram scan time and limit inadvertent patient motion. Although the default compression factor of 10 would be used for normal clinical operation, a compression factor of 1 (meaning no compression) was used to eliminate detector data averaging, acquiring images at the imaging pulse repetition rate of 80 Hz. These parameters were empirically selected based on previous publications[9-11] for the best tradeoffs between image quality metrics and scanning time. Lastly, we retrieved the detector data that had been saved on the tomotherapy data receiver server to a secure patient data server for offline MV-topogram reconstruction and analysis. After topogram scan acquisition, the standard clinical MVCT workflow resumed after realigning patient tattoos to the red lasers.

Figure 1 shows a schematic diagram of the MV-topogram imaging acquisition and reconstruction

workflow used in this study. The blue and orange boxes are the steps taken online and offline, respectively.

Offline MV-topogram reconstruction and registration

The offline MV-topogram workflow consists of the following steps: data conversion, data reconstruction, and image registration. The tomotherapy display and analysis tool (TDAT, Accuray Inc, Sunnyvale, CA) was used to convert raw detector data to comma-separated value (.csv) format. A MATLAB (R2019a, MathWorks Inc, MA) based in-house software was developed to reconstruct the MV-topograms and digitally reconstructed topogram (DRT, the reference image) using the planning CT and tomotherapy geometry. Contrast-limited adaptive histogram equalization[12] was used to enhance MV-topogram image contrast. The MV-topogram based alignment was determined by registering the MV-topograms to the DRTs in AP and LAT views using bony landmark on commercial MIM software (MIM 6.8.1, MIM Software Inc, OH). Finally, the shifts determined from MV-topograms in 3 translational directions were compared with the clinical MVCT based patient shifts. The offline MV-topogram reconstruction and registration workflow are displayed as the dashed box in Figure 1a. All offline procedures were performed on a 64-bit Windows 7 computer with 3.2 GHz Intel Core CPU and 32 GB RAM.

Figure 1b shows the geometric corrections of the MV-topogram. The reconstruction was detailed in a previous publication by Moore et al.[4] The on-board MVCT detector geometry and its specifications have been previously described.[13,14] To summarize, the lateral isocenteric position x_j of the j-th detector can be calculated as $x_j = f \times tan\theta_j$, $\delta x_j = \frac{f\delta\theta_j}{cos^2\theta_j}$, where f, θ_j and $\delta\theta_j$ are source-to-axis distance, the angular position of j-th detector, and the effective lateral width of the j-th detector, respectively. The angular resolution of the j-th detector $\delta\theta_j$ is defined as $\delta\theta_j = \frac{dector\ spacing}{R_D} \frac{\cos(\theta_j-\varphi_j)}{\sqrt{sin^2\varphi_j+\left[R_T/R_D-\left(1-cos\varphi_j\right)\right]^2}}$, where R_T, R_D and φ_j are the source-to-detector distance, the radius of detector array-to-focus point, and the angular position of the j-th detector from the geometric center of the detector, respectively. The lateral resolution can be calculated as: $Lateral\ resolution = \frac{\delta_{x_j}}{number\ of\ MVCT\ detectors}$. The longitudinal resolution is calculated by $l = \frac{v_{couch}}{I} \times C$, where v_{couch}, T, and C are couch speed, imaging repetition rate (hertz) and compression factor. The reference kV-DRT image was generated from planning kVCT images, and reconstructed using a fan beam projection (Mathworks, Natick, MA) consistent with the tomotherapy geometry. Reconstructed DRTs and MV-topograms for a representative H&N case are displayed in Figure 1c.

Standard clinical workflow using MVCT

After MV-topogram acquisition, the standard MVCT clinical workflow resumed by realigning the patient to the red lasers according to the original treatment plan. A routine MVCT scan was selected to cover the longitudinal range of the planning target volume. The MVCT image was fused to the corresponding planning CT on the treatment console using the auto-alignment tool first and, if necessary, followed by manual adjustments using anatomic landmarks. The translational shifts were generally applied to the patient, rotational corrections in yaw and pitch were reset to zero, and roll was corrected using software provided by the system.

Statistical analysis

We analyzed the patient mean shifts of their respective observations (numerical numbers) using two one-sided tests (TOST) equivalence procedures with paired design.[15] Details of TOST equivalence procedures are included in the supplement. The discrepancy was defined as the numerical distance between the initial patient setup position (according to patient tattoo made during CT simulation) to the actual patient position for radiation delivery. We considered these 2 techniques equivalent if the shifts between the MV-topogram and the standard MVCT were within ±2 mm.[15-17] Given each image was obtained independently, the relationship between MV-topogram and MVCT in a pair was assessed via simple linear regression model, with response variable as MVCT and independent predictor as MV-topogram. Significance level is set at 0.05. Analysis was completed using R version 3.6.0 with package TOSTER.[16,17]

Results

Patient characteristics

Eighteen pelvis patients who formally consented to the study were included in this analysis, including 8 anal cancer cases, 5 rectal cancer cases, 2 patients with sarcoma in the pelvis, and 3 endometrial cancer cases. All patients were immobilized using a commercial vacuum bag device (Vac-Lok). Nineteen H&N patients, immobilized with thermoplastic mask, were also included independently to validate the finding.

The average target length (and standard deviation) was 23.2 ± 4.5 cm with a mean MVCT acquisition time of 175.9 ± 31.2 seconds for pelvis site and 16.7 ± 6.3 cm

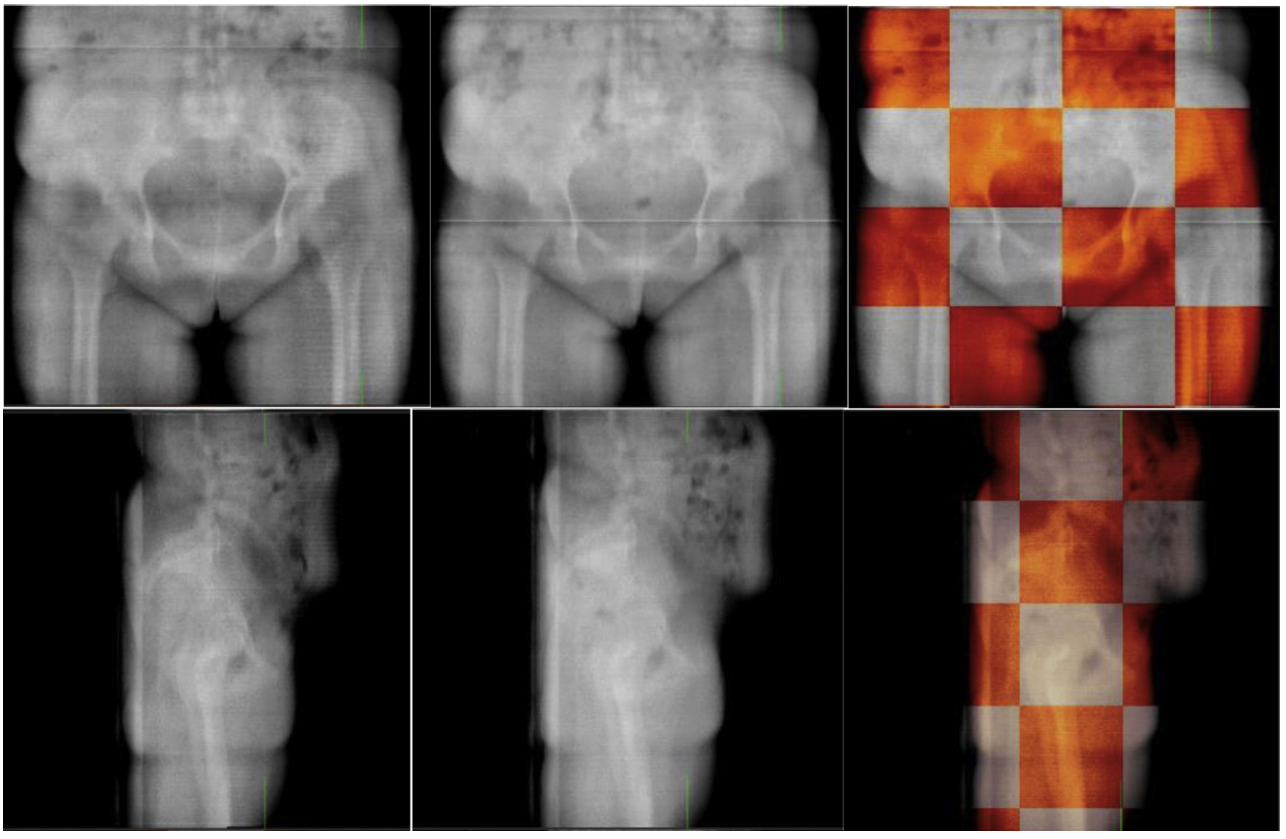

Figure 2 The reconstructed digitally reconstructed topograms (left), megavoltage topograms (middle), and the fused megavoltage topograms to the digitally reconstructed topograms using the rigid registration in anterior-posterior (top) and lateral (bottom) views for a representative pelvis case.

and 142.9 ± 32.0 seconds for H&N site. The average MVCT acquisition time was documented for treatment days when topograms were acquired using the MVCT scanning times displayed on the tomotherapy treatment console. The MVCT scans were acquired using coarse image acquisition mode (with interslice distance of 6 mm). The acquisition time for a pair of MV-topograms was 3.1 to 7.1 and 5.1 to 12.7 times less than that of MVCT scans, for pelvis and H&N respectively, in spite of covering the longer scan length of 40 cm.

Figure 2 displays the reconstructed DRT (left), MV-topograms (middle) and the fused MV-topograms to the DRTs using the rigid registration in AP (top) and LAT (bottom) views for a representative pelvis case. The MV-topograms had sufficient bony structure conspicuity to enable registration with the DRT images.

Figure 3 shows the correlations of patient translational shifts using bony landmark between the MV-topograms and MVCT imaging methods for pelvis patients. Considering all images were obtained independently, a simple linear regression model was carried out to assess the relation of MV-topogram and MVCT methods. With MV-topogram being the independent variable and MVCT method being the response variable, the coefficients (or the slopes) in this fitted linear model between 2 imaging techniques were 1.18, 1.10, and 0.94 and 0.86, 0.63, and 0.38 in the lateral, longitudinal, and vertical directions (X, Y, Z) for pelvis and H&N, respectively. The magnitudes of alignment differences of (MVCT − MV-topogram) (and standard deviations) were −0.3 ± 2.1, −0.8 ± 2.4, 1.6 ± 1.7 mm (for pelvis) and 0.6 ± 1.2, 0.8 ± 4.2, 1.6 ± 2.6 mm (for H&N) in 3 translational directions.

The boxplot (Fig 4) provides a graphic overview of the mean shifts of each patient in the X, Y, and Z directions using 2 imaging methods for pelvis and H&N patients, respectively. Overall, the mean shifts using the alignment methods were similar.

Equivalency tests

Using the TOST equivalence test for paired design,[15-17] with a significance level of 0.05, assuming equivalence bounds of −2 mm and 2 mm, the shifts, as the mean measure obtained from each subject, determined by MVCT and MV-topograms, were found to be equivalent for pelvis in lateral ($P < .001$ for both upper and lower bound), longitudinal ($P < .001$ for both upper and lower bound), and vertical direction ($P = .02$ for upper bound and $P < .001$ for lower bound). The equivalence of

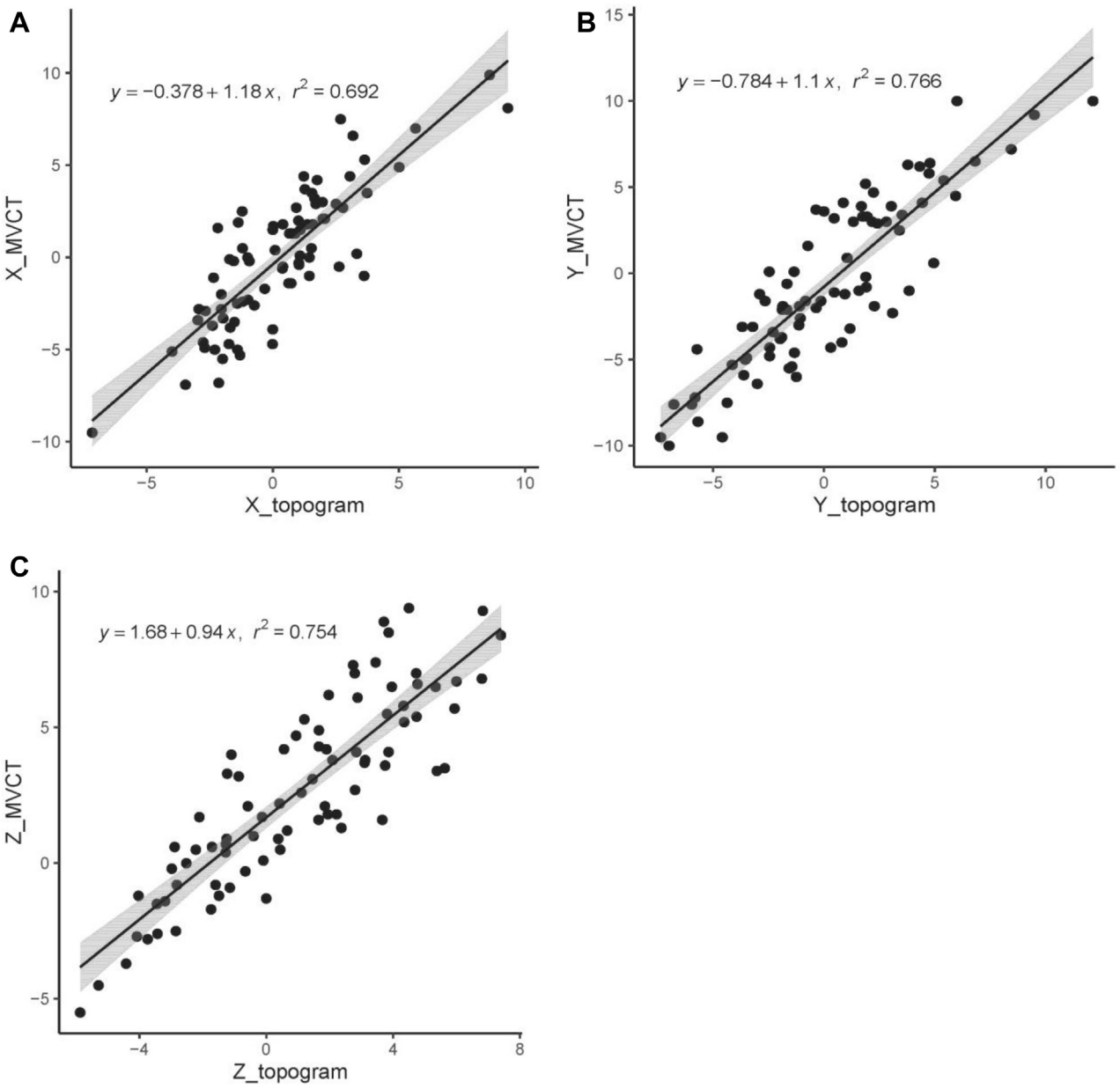

Figure 3 Correlations of patient translational shifts using a total of 81 pairs of megavoltage topograms and megavoltage computed tomography (MCVT) images for the cohort of 18 pelvis patients. Linear regression coefficients (or the slopes) between 2 imaging techniques were 1.18, 1.10, and 0.94 mm in the lateral, longitudinal, and vertical directions, respectively.

MVCT and MV-topogram was also found for H&N site ($P < .001$ for upper and lower bound of all 3 directions).

Discussion

The impletementation of the MV-topogram is not currently commercially available. To our best knowledge, this is the only IRB-approved clinical trial to evaluate the performance of MV-topogram based patient alignment. We integrated the MV-topogram as an alternative patient alignment workflow to our present MVCT based clinical workflow. The proposed MV-topogram offers the following advantages:

1. Fast and low dose bony anatomy alignment tool. The acquisition time of MVCT scan can be long depending on the target length, and MV-topogram can substantially shorten MVCT acquisition time while covering longer scan lengths
2. Although the daily MVCT localization dose is as low as 1 to 3 cGy, a MV-topogram based workflow could further reduce the imaging dose to hundredths of 1 cGy[4,9]

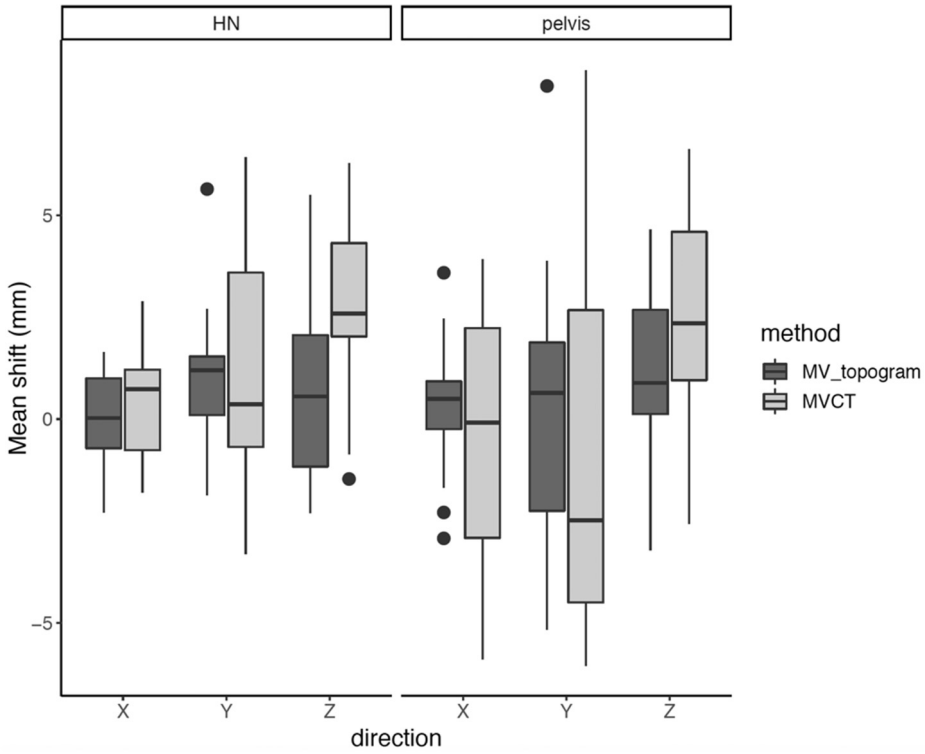

Figure 4 The mean shifts for each imaging modality in each patient in 3 translational directions using 2 imaging methods for head and neck and pelvis cases. *Abbreviation*: MVCT = megavoltage computed tomography.

3. For non-helical cases treated using TomoDirect, such as breast, a MV-topogram could be a beneficial alternative to the current MVCT workflow
4. Topograms could be used before conventional imaging to provide an efficient initial image for crude alignment for patients who are challenging to position. This would be more efficient than having to conduct MVCT scans and attempting to fix the incorrect positioning using shifts rather than straightening the patient
5. MV-topogram could also be used to select MVCT coverage based on anatomic landmarks. For example, the clinic could customize CT scan acquisition parameters, especially for long targets on a fraction-by-fraction basis. This could be easily accomplished using MV-topograms to allow the operator to anatomically select the scan ranges.

There would also be a few challenges of using MV-topograms in clinical practice. First, owing to the implementation of MV based x-ray imaging source on tomotherapy, similarly as MVCT, the MV-topogram technique would be limited to cases when bony landmark based patient alignment is suitable. Second, the residual rotational corrections were not fully accounted for owing to the limitation of the tomotherapy couch. Specifically, the yaw and roll rotations were set to zero, and the pitch rotations were accounted by gantry offset (from zero degree) for the standard MVCT based clinical workflow. Although other gantry angles of MV-topogram are possible, we used the MV-topogram protocol by consistently using AP and LAT views in the protocol. The discrepancies of patient alignments determined by the MVCT and MV-topograms can be partially explained by the uncorrected rotational shifts (less than 1 degree for most cases). Third, inter-observer variations could also account for the discrepancies of the shifts determined by MVCT versus MV-topograms. The mean (and standard deviations) of inter-observer variations for MV-topograms measured were −0.2 (1.2), −0.6 (1.7), and −1.0 (1.8) mm in the translational directions of X, Y, and Z, respectively, for a group of thorax patients.[10] The standard deviations of inter-observers were small (approximately 1 mm) determined by MVCT scans for both head and neck and pelvis patients.[18,19]

Depending on the target longitudinal length, the acquisition time of MVCT scans may be long and will vary for different anatomic sites. Although MVCT usually takes a few minutes to acquire, the acquisition of a pair of MV-topograms normally takes less than a minute to cover the same or longer extent in longitudinal directions. Currently, it takes an additional 2 to 3 minutes to accommodate the MV-topogram acquisition procedure into clinical workflow. The MV-topogram workflow includes the following steps, including MV-topogram acquisition on tomotherapy treatment console, navigate

to the data server and download raw detector data (online), data reformatting using tomotherapy display and analysis tool and MV-topogram reconstruction using the in-house software and imaging fusion in MIM (off-line). However, we believe that both the online and off-line MV-topogram processing times could be streamlined and significantly reduced if and when the MV-topogram became commercially available.

Conclusions

We conducted a pilot clinical trial by integrating the MV-topogram into our clinical workflow. For the studied pelvis and head and neck patients, MV-topograms showed equivalent clinical performance to the standard MVCT with significantly less acquisition time and dose. The MV-topogram could be used as an alternative or complimentary tool for bony landmark-based patient alignment treated on tomotherapy.

Supplementary Data

Supplementary material for this article can be found at https://doi.org/10.1016/j.adro.2020.05.014.

References

1. Jaffray DA, Siewerdsen JH. Cone beam computed tomography with a flat-panel imager: Initial performance characterization. *Med Phys*. 2000;27:1311-1323.
2. Pouliot J, Bani-Hashemi A, Chen J, et al. Low-dose megavoltage cone beam CT for radiation therapy. *Int J Radiat Oncol Biol Phys*. 2005;61:552-560.
3. Mackie TR, Holmes T, Swerdloff S, et al. Tomotherapy: A new concept for the delivery of dynamic conformal radiotherapy. *Med Phys*. 1993;20:1709-1719.
4. Moore KL, Palaniswaamy G, White B, Goddu SM, Low DA. Fast, low-dose patient localization on TomoTherapy via topogram registration. *Med Phys*. 2010;37:4068-4077.
5. Hui SK, Verneris MR, Higgins P, et al. Helical tomotherapy targeting total bone marrow: First clinical experience at the University of Minnesota. *Acta Oncologica*. 2007;46:250-255.
6. Schultheiss TE, Wong J, Liu A, Olivera G, Somlo G. Image-guided total marrow and total lymphatic irradiation using helical tomotherapy. *Int J Radiat Oncol Biol Phys*. 2007;67:1259-1267.
7. Takahashi Y, Vagge S, Agostinelli S, et al. Multi-institutional feasibility study of a fast patient localization method in total marrow irradiation with helical tomotherapy: A global health initiative by the international consortium of total marrow irradiation. *Int J Radiat Oncol Biol Phys*. 2015;91:30-38.
8. Magome T, Haga A, Takahashi Y, Nakagawa K, Dusenbery KE, Hui SK. Fast megavoltage computed tomography: A rapid imaging method for total body or marrow irradiation in helical tomotherapy. *Int J Radiat Oncol Biol Phys*. 2016;96:688-695.
9. Blanco Kiely JP, White BM, Low DA, Qi XS. Geometric validation of MV topograms for patient localization on TomoTherapy. *Phys Med Biol*. 2016;61:728-739.
10. Qi XS, Yang L, Lee P, et al. Fast, low-dose megavoltage-topogram localization on TomoTherapy: Initial clinical experience with mesothelioma patients. *Pract Radiat Oncol*. 2019;9:373-380.
11. Qi XS, White BM, Low DA. Development of a novel image guidance alternative for patient localization using topographic images for TomoTherapy. *J Phys Conf Ser*. 2014;489.
12. Zuiderveld K. *Contrast Limited Adaptive Histograph Equalization. Graphic Gems IV*. San Diego: Academic Press Professional; 1994:474-485.
13. Meeks SL, Harmon JF, Langen K. Performance characterization of megavoltage computed tomography imaging on a helical tomotherapy unit. *Med Phys*. 2005;32:2673-2681.
14. Keller H, Glass M, Hinderer R, Ruchala K, Jeraj R, Olivera G, Mackie TR. Monte Carlo study of a highly efficient gas ionization detector for megavoltage imaging and image-guided radiotherapy. *Med Phys*. 2002;29:165-175.
15. Schuirmann DJ. A comparison of the 2 one-sided tests procedure and the power approach for assessing the equivalence of average bioavailability. *J Pharmacokinet Biop*. 1987;15:657-680.
16. R Core Team. R: A Language and Environment for Statistical Computing [Internet]. Vienna, Austria: R Foundation for Statistical Computing; 2019.
17. Lakens D. *TOSTER: Two one-sided tests (TOST) equivalence testing. R package version 0.3.4*. 2018.
18. Qi XS, Hu AY, Lee SP, et al. Assessment of interfraction patient setup for head-and-neck cancer intensity modulated radiation therapy using multiple computed tomography-based image guidance. *Int J Radiat Oncol Biol Phys*. 2013;86:432-439.
19. Morrow NV, Lawton CA, Qi XS, Li XA. Impact of computed tomography image quality on image-guided radiation therapy based on soft tissue registration. *Int J Radiat Oncol Biol Phys*. 2012;82:e733-e738.