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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

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Abstract

Purpose—To develop, characterize, and implement a fast patient localization method for total marrow irradiation.

Methods and Materials—Topographic images were acquired using megavoltage computed tomography (MVCT) detector data by delivering static orthogonal beams while the couch traversed through the gantry. Geometric and detector response corrections were performed to generate a megavoltage topogram (MVtopo). We also generated kilovoltage topograms (kVtopo) from the projection data of 3-dimensional CT images to reproduce the same geometry as helical

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tomotherapy. The MVtopo imaging dose and the optimal image acquisition parameters were investigated. A multi-institutional phantom study was performed to verify the image registration uncertainty. Forty-five MVtopo images were acquired and analyzed with in-house image registration software.

Results—The smallest jaw size (front and backup jaws of 0) provided the best image contrast and longitudinal resolution. Couch velocity did not affect the image quality or geometric accuracy. The MVtopo dose was less than the MVCT dose. The image registration uncertainty from the multi-institutional study was within 2.8 mm. In patient localization, the differences in calculated couch shift between the registration with MVtopo-kVtopo and MVCT-kVCT images in lateral, cranial–caudal, and vertical directions were 2.2 ± 1.7 mm, 2.6 ± 1.4 mm, and 2.7 ± 1.1 mm, respectively. The imaging time in MVtopo acquisition at the couch speed of 3 cm/s was <1 minute, compared with 15 minutes in MVCT for all patients.

Conclusion—Whole-body MVtopo imaging could be an effective alternative to time-consuming MVCT for total marrow irradiation patient localization.

Introduction

Total body irradiation (TBI) has been widely utilized as part of the conditioning regimen for hematopoietic stem cell transplantation. Dose escalation studies have shown a lower rate of leukemia relapse but also increased treatment-related toxicity (1–6). The introduction of total marrow irradiation (TMI) with helical tomotherapy (HT) or volumetric arc therapy using conventional linear accelerators has enabled dose escalation, leading to the success of bone marrow transplantation with acceptable toxicity (7–17).

Helical tomotherapy offers an intensity modulated beam with integrated megavoltage computed tomography (MVCT) imaging capability (18, 19). Megavoltage CT is suitable for regional tumor localizations as well as whole-body localization, which facilitates accurate dose delivery to long and complex-shaped targets such as TBI, TMI, and TLI (total lymphoid irradiation) (14, 20–22).

Unlike treatments of local and/or regional tumors, however, overall treatment time in TMI is very long (9, 11, 14) owing to the very long target size. Total marrow irradiation takes 600 seconds for MVCT acquisition, even in coarse mode, and 30 minutes for treatment delivery to targets that are longer than 90 cm. If a large degree of shift or a rotation was found after the initial MVCT scan, another set of MVCT scans would be necessary. Therefore TMI with HT may not be practical for routine clinical use without a significant reduction in treatment time.

In 2011, the International Consortium of TMI was formed with participants from 12 centers in 8 countries. Its initiative is to develop and support global health implementations for TMI. With support from multiple centers, we developed a method for a fast localization of TMI patients using a novel image registration method.

Here we report on the optimization of the image acquisition with geometric verification, followed by a multi-institutional image registration uncertainty test with use of a phantom. Finally, we show the feasibility of the fast localization for TMI and TLI patients.

Methods and Materials

Generation of megavoltage topogram and kilovoltage topogram images

Figure 1a shows an overview of the megavoltage topogram–kilovoltage topogram (MVtopo–kVtopo) image registration strategy. The 2-dimensional (2D) MVtopo images were acquired using the MVCT detector data by delivering static orthogonal beams in calibration procedures while the couch traversed through the gantry. The detector data were collected by software, T-DAT or TQA, from Accuray (Madison, WI), followed by the conversion to a binary file by the T-DAT software. Because the individual detector response varies (Fig. 1b), we corrected the detector response by using air scan data. Specifically, the detector response was normalized at 160th detectors, and an individual correction factor was calculated. Then the original detector response profile was divided by the normalized air scan data to get a flat detector response.

Generation of MVtopo and kVtopo images with geometric correction was performed as described by Moore et al (23). Briefly, lateral isocentric position x_j of the j_{th} detector was calculated as follows (Fig. 1c):

$$x_j = f \tan \theta_j \quad \delta x_j = \frac{f \delta \theta_j}{\cos^2 \theta_j}$$

where f , θ_j , and δx_j represent source-to-axis distance, the angular position of j_{th} detector, and the effective lateral width of the j_{th} detector, respectively. The angular separation of the j_{th} detector $\delta \theta_j$ is defined as follows:

$$\delta \theta_j = \frac{\text{detector spacing (cm)}}{R_D} \frac{\cos(\theta_j - \phi_j)}{\sqrt{\sin^2 \phi_j + [R_T/R_D - (1 - \cos \phi_j)]^2}}$$

where R_D , R_T , and ϕ_j represent the radius of detector array-to-focus point, the source-to-detector distance, and the angular position of the j_{th} detector from the geometric center of the detector, respectively.

The pixel size of the MVtopo image for lateral direction was determined by the following formula:

$$\text{Pixel size} = \frac{\delta x_j}{\text{Number of MVCT detector}}$$

The longitudinal length l was calculated by.

$$l = v_c \bullet C / \Gamma$$

where v_c , Γ , and C represent couch speed, system repetition rate in hertz, and compression factor that affects the image file size being proportional to the longitudinal pixel size,

respectively. For kVtopo images, we generated the sinograms from slice-by-slice kVCT images using a fan beam transform function (Fig. 1d). The MATLAB fanbeam function (Mathworks, Natick, MA) was used to generate the kVtopo image in the HT system and detector geometry by defining the parameters including source to image-center distance (D), detector spacing ($\delta\theta$), and detector geometry, which is in arc alignment, where D is defined using the following formula:

$$D = \frac{(f - \Delta l)}{\text{Pixel size}}$$

where l represents the distance from the green laser to the center of an object plane, as shown in Figure 1c.

Optimization of MVtopo image acquisition parameters and geometric verification of MVtopo and kVtopo images

We investigated the effect of couch speed (1.0 cm/s, 2.0 cm/s, and 3.0 cm/s), and jaw width on the geometric accuracy in MVtopo images using a cylindrical phantom with a nominal length and diameter of 18 cm and 30 cm, respectively. Generally, 3 jaw sizes (1 cm, 2.5 cm, and 5 cm) defined in Jaw Accelerator Machine (JAM) are commissioned for clinical use. However, acquisition of MVtopo images required for the calibration procedure allows for using noncommissioned jaw sizes. We used 1.0 cm, 2.5 cm, 5 cm, and a noncommissioned minimum jaw size (JAM = 0), which turned out to be 3 mm by radiographic films. On the other hand, the compression factor was kept at 1 and 4 for imaging Accelerator Output Mode (IM-AOM) with a nominal beam energy of 3.5 MV and treatment AOM (TX-AOM) with that of 6 MV, respectively (24).

The same cylindrical phantoms used in the MVtopo experiments were used for the geometric verification of kVtopo images. The kVCT scan was taken with a slice thickness of 5 mm and generated kVtopo image as described above. The dimensions of the phantom in MVtopo and kVtopo images were measured by ImageJ software (National Institutes of Health, Bethesda, MD).

Imaging quality was measured using a Las Vegas phantom provided with a Varian linear accelerator (Varian Medical Systems, Palo Alto, CA) and a RANDO phantom (The Phantom Laboratory, Salem, NY).

Imaging dose measurement

A cylindrical solid water phantom was used to measure the imaging dose. Topogram image doses from gantry 0 in IM-AOM and TX-AOM at various jaw sizes and couch speeds were measured using a 0.053 cc A1SL ion chamber (Standard Imaging, Madison, WI) at 2-cm depth, which is close, but beyond dmax, where dose gradient is not steep, and compared with those of MVCT.

Multi-institutional kVtopo-MVtopo image registration verification

We developed in-house image registration software using the MATLAB GUI platform. Figure 2 shows the scheme of the image registration in our in-house software. Helical tomotherapy machines have a fixed green laser, which is located at 70 cm from the machine isocenter. We used this green laser as a reference position for kVtopo-MVtopo image registration because it is easily identified in kVCT images in the treatment planning station. Specifically, 3 distances were measured to locate the reference position: (1) the top of patient's head to the green laser; (2) the tomo couch top to the green laser; and (3) the lateral shift from the top of the head to the green laser. In the patient MVtopo image acquisition, 2 metallic cross wires were placed on the green laser on coronal and sagittal patient skin surfaces before taking MVtopo images. We registered the green laser in the kVtopo image to the metallic marker position in the MVtopo image to set up the image registration origin. The software provides the capability to calculate the couch shift needed relative to the kVtopo image generated from simulation kVCT images.

Image registration uncertainty analysis was performed by 5 institutions using a solid water slab phantom (Accuray) with 15-cm width, 55-cm length, and 5-cm height with or without shifting predefined distances. The phantom setup is shown in Figure E1a (available online at www.redjournal.com). The predefined shifts were divided into 2 groups: the small (+10 mm for lateral and cranial-caudal directions, and +5 mm for vertical direction) and the large shift (+20 mm for lateral and cranial-caudal directions, and +10 mm for vertical direction) groups. First, the MVCT images were acquired and registered with kVCT images with transverse, coronal, and sagittal views. This was done by line matching using the phantom edge (Fig. E1b and d; available online at www.redjournal.com), with a confirmation that results by line matching closely agreed with that of marker matching. Then the orthogonal MVtopo images were acquired and registered with kVtopo images in the same way as MVCT-kVCT registration (Fig. E1c and e; available online at www.redjournal.com). The calculated couch shifts by MVCT and MVtopo images were compared. These experiments were repeated 3 to 5 times by 5 institutes. The image registration uncertainty was calculated as described in the Appendix (available online at www.redjournal.com).

Clinical use of MVtopo-kVtopo image registration for TMI and TLI patients

In clinical TMI or TLI cases, MVCT was first acquired with coarse mode and registered with the planning kVCT images. After localization with the MVCT, TMI or TLI treatment was done. After treatment, the couch was moved back to the initial patient setup coordinate with the aid of a digital readout of the couch position, which is the pre-MVCT registration position. Then MVtopo images were acquired with a minimum jaw size, all multileaf collimators open, and couch speed of 1 cm/s for the first 2 patients. The couch speed was increased to 3 cm/s for the following 4 patients owing to a newly installed tomotherapy couch. An IM-AOM with a compression factor of 1 or TX-AOM with a compression factor of 4 was used for G0 or G90 image acquisition, respectively. Forty-five MVtopo images from 2 institutes were registered with kVtopo images using the inhouse software. The discrepancies in couch shifts between MVCT-kVCT and MVtopo-kVtopo registrations were analyzed.

Results

Optimization of MVtopo image acquisition parameters and geometric verification of MVtopo and kVtopo images

Figure 3a shows the MVtopo images of a cylindrical phantom at gantry 0 at various couch speeds. The couch speeds from 1 to 3 cm/s affected neither the lateral nor the longitudinal dimensions, where the agreement with the nominal dimensions was within 1 mm (Fig. 3e and f). Figure 3b and c show the MVtopo images acquired using various jaw sizes and the longitudinal profile along the dashed red line, respectively. A reduction in distinct cranial–caudal edges of the phantom was observed when jaw size was decreased (Fig. 3c). Use of jaw size 1.0 cm increased the longitudinal dimension mismatch by up to 12 mm, owing to the lower longitudinal resolution (Fig. 3f).

Figure 3d shows a kVtopo image of the cylindrical phantom. The measured longitudinal and lateral dimensions were in agreement with the nominal dimensions to within 1.3 mm.

Three-millimeter jaw size provided the best image contrast, enabling the same visualization on electronic portal imaging device both at IM-AOM and TX-AOM, as shown in Figure E2 (available online at www.redjournal.com). The couch speed did not affect the image contrast in the 3-mm jaw size. This jaw size also provided better image quality for the RANDO phantom, as shown in Figure E3 (available online at www.redjournal.com).

Imaging dose

Table 1 shows the imaging dose at various couch speeds and jaw sizes. The MVCT doses were 1.2 cGy and 1.0 cGy in normal and coarse modes, respectively. On the other hand, MVtopo doses at 3-cm/s couch speed in IM-AOM at 2-cm depth were reduced by 71% and 97% for 1 cm and the minimum jaw size, respectively. Use of TX-AOM beam with 3-mm jaw size at 3-cm/s couch speed decreased the dose up to 0.7 cGy, which was still a 36% reduction of the MVCT dose.

Image registration accuracy with a slab phantom

The discrepancies in the calculated couch shift between MVCT-kVCT and MVtopo-kVtopo registrations in the no shift group for all centers were 1.2 ± 0.7 mm, 1.2 ± 0.9 mm, and 1.3 ± 0.8 mm for X, Y, and Z directions, respectively (Table 2). The image registration uncertainty by applying a coverage factor $k = 3$ (99% confidence level), in the no shift group was 2.8 mm, 2.8 mm, and 2.8 mm for X, Y, and Z directions, respectively. For small and large shift groups, the uncertainty ($k = 3$) was also within 2.8 mm.

Comparison between MVCT-kVCT and MVtopo-kVtopo image registrations in TMI or TLI patients

The MVCT imaging time was 600 seconds to acquire images from head to femur using coarse mode. The MVtopo imaging time, however, was only 90 seconds and 30 seconds for 1-cm/s or 3-cm/s couch speeds, respectively.

Figure 4 shows the discrepancies in calculated couch shift between MVtopo-kVtopo and MVCT-kVCT image registrations in TMI or TLI patients. The discrepancies in lateral, cranial–caudal, and vertical directions were 2.2 ± 1.7 mm, 2.6 ± 1.4 mm, and 2.7 ± 1.1 mm, respectively.

Discussion

Although HT can deliver elegant dose distributions for long and complex-shaped targets with MVCT localization, one major drawback is the prolonged overall treatment session for TMI patients. Megavoltage CT image acquisition contributes significantly to the time spent in the treatment vault.

Therefore, we developed, characterized, and implemented a fast patient localization method for TMI treatments using MVCT detector data to generate 2D orthogonal images (rather than MVCT images) using our in-house image registration software. Recently, Moore et al (23) reported a 2D image acquisition method using MVCT detectors in HT in an anthropomorphic phantom. However, their report did not explore image registration and clinical usage. Our phantom study from multiple institutes demonstrated that the registration uncertainty of MVtopo with kVtopo images was within 2.8mm ($k = 3$). The clinical use of the MVtopo image in TMI patients showed substantial reduction of imaging time, namely, 30 seconds for MVtopo images compared with 600 seconds for MVCT for a 90-cm target length. Furthermore, our analysis demonstrated that the couch shift calculated by MVCT registration closely agreed (within 3 mm on average) with that from MVtopo images. To the best of our knowledge, this is the first report that demonstrates the implementation and usefulness of a fast 2D topographic registration verified by multiple institutes for clinical TMI/TLI patient localization.

To perform accurate image registration, the geometric verification test was done for both kVtopo and MVtopo images. There are many parameters that can be set in MVtopo image acquisition. We found that the use of 1-cm jaw size caused inferior resolution of the cranial–caudal edges of the phantom. On the other hand, use of the smallest jaw size (JAM = 0) provides excellent longitudinal resolution, leading to the within 1-mm agreement in dimension with the nominal dimension. The benefit of the use of the smallest jaw size was also observed in image contrast. Our results with the Las Vegas phantom showed that the MVtopo image quality using minimum jaw size and couch speed of 3 cm/s was similar to an electronic portal imaging device image from a conventional linear accelerator (25, 26). The same tendency was observed in the RANDO phantom. These observations are likely due to less-scattered photons, resulting in more favorable imaging conditions. The couch speed did not affect the image contrast and the longitudinal resolution. Together, these data provided the optimal image acquisition parameters by using minimum jaw size (JAM = 0) and maximum couch speed of 3 cm/s.

These image acquisition conditions were also beneficial from the viewpoint of imaging dose. We found that a TX-AOM beam used in lateral MVtopo imaging provided good image contrast, owing to the presence of the patients' arms. However, even with the use of a TX-AOM beam, the imaging dose for MVtopo imaging was still less than MVCT doses.

The image registration accuracy using our in-house software was also verified by 5 institutes to minimize biases. Our results revealed that our image registration strategy provides <3 mm uncertainty with the systematic error of <1.5 mm. This uncertainty did not vary with the degree of couch shifts for all participating centers. These results suggest the robustness of application of MVtopo imaging for target localization in TMI patients.

Finally, we used these acquisition parameters to make MVtopo images for TMI or TLI patients. In the current version of the HT unit, there is no couch motion interlock observed even at the couch speed of 3.0 cm/s. This allows us to image a 90-cm target length in 30 seconds with MVtopo imaging, showing substantial reduction of imaging time (ie 600 seconds for 90-cm MVCT).

We also found that the couch shift calculated by MVCT and kVCT registration was close to MVtopo and kVtopo image registration. Six of 45 images in the registration data showed more than 4 mm but up to 5.5 mm discrepancies between MVCT-KVCT and MVtopo-kVtopo registrations. These relatively large discrepancies might have occurred as a result of the more complex anatomy of the patient versus the phantom and potentially the intrafractional patient movement due to the long treatment time (33 minutes on average). However, intrafractional motion should be very small because we used robust immobilization, such as whole-body Vac-Lok with a respiratory belt that can be fixed chest and abdomen, or whole-body thermoplastic masks as well as standard head-and-neck masks. To support this, our MVCT simulation results, in which MVtopo images were acquired soon after MVCT for 3 datasets, showed within 1-mm differences compared with TMI treatment (data not shown). Nevertheless, such discrepancies are still acceptable with the use of a 5-mm margin to generate the planning target volume from the clinical target volume (bones surrounding marrow) in TMI/TLI planning.

Although MVtopo image has less soft tissue sensitivity, target localization is not a problem in TMI owing to the use of bony landmarks around the marrow as the intended target. In TMI patients, rotations and body deformation are observed in localization. Clinical application of MVtopo may therefore be combined with MVCT (ie early fractions with MVCT, and later fraction with MVtopo). Nevertheless, the entire treatment time in TMI will be substantially decreased. Future work can be done to develop fast 3-dimensional imaging to solve the issues described above and expand the application for daily solid tumor localization.

In conclusion, whole-body MVtopo imaging may be an effective alternative to time-consuming MVCT for TMI target localization. It can reduce the overall duration of treatment session and provide for a significant reduction in the imaging dose. Because the TMI treatment efficiency is substantially improved, this will encourage collaborative clinical trials to study the feasibility and role of TMI as a better alternative to TBI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Schematic of topogram (topo) image acquisition. (a) Overview of the image registration strategy. (b) The way to correct detector response in MVtopo image. (c) Geometry of tomotherapy source-detector system. (d) The way to generate kVtopo image.

Fig. 2.
Schematic of in-house image registration software.

Fig. 3.

Optimization of image acquisition parameters and geometric verification. (a) Megavoltage topogram (MVtopo image) at various couch speeds in the minimum jaw size. (b) MVtopo image at various jaw sizes at a couch speed of 3.0 cm/s. (c) Longitudinal profiles along the dashed line. (d) Dimensional verification in a kilovoltage topogram (kVtopo) image. (e, f) Variations in dimensions at various jaw sizes and couch speeds compared with the nominal dimension in MVtopo image for (e) lateral direction and (f) longitudinal direction.

Fig. 4.

Image registration with megavoltage computed tomography (MVCT) and MV topogram (MVtopo) images in total marrow irradiation or total lymphoid irradiation patients. (a) Registered image at G0 angle. (b) Discrepancies in calculated couch shift between MVtopo and MVCT images. (c) Registered image at G90 angle. (d) Discrepancies in the calculated couch shift from G90 topo images. White and rainbow color images represent kilovoltage topo and MVtopo images, respectively. A color version of this figure is available at www.redjournal.org.

Table 1

Imaging dose (in cGy) at various jaw sizes, couch speeds, and Accelerated Output Mode Values represent mean $\pm$ SD.

Couch speed	IM-AOM				TX-AOM			
	Jaw 3 mm	Jaw 1 cm	Jaw 2.5 cm	Jaw 5 cm	Jaw 3 mm	Jaw 1 cm	Jaw 2.5 cm	Jaw 5 cm
1.0 cm/s	0.10 $\pm$ 0.01	0.87 $\pm$ 0.00	2.35 $\pm$ 0.01	4.78 $\pm$ 0.01	1.89 $\pm$ 0.01	16.20 $\pm$ 0.03	43.33 $\pm$ 0.04	88.31 $\pm$ 0.32
2.0 cm/s	0.06 $\pm$ 0.00	0.43 $\pm$ 0.00	1.17 $\pm$ 0.01	2.41 $\pm$ 0.01	0.94 $\pm$ 0.01	8.01 $\pm$ 0.02	21.65 $\pm$ 0.04	44.22 $\pm$ 0.04
3.0 cm/s	0.03 $\pm$ 0.01	0.29 $\pm$ 0.00	0.78 $\pm$ 0.00	1.60 $\pm$ 0.00	0.64 $\pm$ 0.00	5.46 $\pm$ 0.01	14.57 $\pm$ 0.03	29.43 $\pm$ 0.03
MVCT (normal)	1.24 $\pm$ 0.05							
MVCT (coarse)	1.00 $\pm$ 0.01							

Abbreviations: IM-AOM = Imaging Accelerated Output Mode; MVCT = megavoltage computed tomography; TX-AOM = Treatment Accelerated Output Mode. MVCT = megavoltage computed tomography.

Table 2

Differences in calculated couch shift (in mm) between MVCT-kVCT and MVtopo-kVtopo image registrations according to the data from 5 institutes

Directions	Group	All clinics	Clinic 1	Clinic 2	Clinic 3	Clinic 4	Clinic 5
X	No shift	1.2 ± 0.7	1.3 ± 0.8	1.3 ± 1.1	1.4 ± 0.6	0.8 ± 0.8	1.0 ± 0.4
	Small shift	1.0 ± 0.7	1.5 ± 0.7	0.3 ± 0.3	0.9 ± 0.6	1.0 ± 0.7	N/A
	Large shift	1.3 ± 0.8	1.1 ± 0.8	1.7 ± 1.1	1.3 ± 0.6	N/A	N/A
Y	No shift	1.2 ± 0.9	1.6 ± 1.0	1.4 ± 0.7	1.5 ± 0.8	1.0 ± 0.6	0.5 ± 0.8
	Small shift	1.3 ± 0.7	1.5 ± 0.9	1.0 ± 0.5	1.7 ± 0.6	1.1 ± 0.9	N/A
	Large shift	1.1 ± 0.8	0.8 ± 0.6	1.0 ± 1.2	1.5 ± 0.7	N/A	N/A
Z	No shift	1.3 ± 0.8	1.0 ± 1.0	1.9 ± 0.7	1.0 ± 1.0	1.6 ± 0.4	1.0 ± 0.4
	Small shift	1.2 ± 0.5	1.1 ± 0.7	1.5 ± 0.6	1.2 ± 0.6	1.3 ± 0.5	N/A
	Large shift	1.2 ± 0.7	1.1 ± 0.7	1.2 ± 0.8	1.3 ± 0.8	N/A	N/A

Abbreviations: kVCT = kilovoltage computed tomography; kVtopo = kilovoltage topogram; MVtopo = megavoltage topogram; N/A = not applicable. Other abbreviation as in Table 1.