Clinics in Oncology

Research Article
Published: 31 Aug, 2016

A Quantitative Assessment of Imaging Frequency on the Treatment Setup Accuracy in TomoTherapy

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Abstract

Image guided radiation therapy (IGRT) is becoming the standard of practice for many treatment sites and techniques, especially those involving high dose gradients such as stereotactic radiosurgery (SRS), stereotactic radiotherapy (SBRT) and intensity modulated radiotherapy (IMRT). The purpose of this study is to quantify the setup accuracy for various IGRT frequency protocols from tattoo-only setups with no imaging, to imaging every fifth, fourth, third, second fraction, as well as daily imaging prior to TomoTherapy IMRT treatment. Total vector shifts were calculated from the lateral, longitudinal and vertical (x,y,z) displacements and the mean shift error for the various protocols analyzed for five treatment sites: cranial, head and neck, prostate, prostate bed and lung. On a given non-imaging day the shift relative to tattoos was determined by using the most recent imaged shift values and applying these to the current setup. Imaging data from 260 patients was analyzed for a total of 8,379 treatment sessions with displacement in the lateral, longitudinal and vertical directions. Lung patients and prostate patients had the largest vector shifts with a mean daily displacement of 10.4 mm. Prostate bed patients had an average vector shift of 9.0 mm, while head and neck and cranial patients had an average shift of 6.9 mm and 5.6 mm respectively. Increasing the imaging frequency increased the accuracy of the setup. Even if imaged every second day there is still an average error of 3.8 mm in the setup of cranial patients and 11.5 mm for lung patients ten percent of the time. Our data demonstrates that for TomoTherapy treatments, daily imaging is advisable for the five treatment sites presented in this study.

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Received Date: *20 Jul 2016*
Accepted Date: *22 Aug 2016*
Published Date: *31 Aug 2016*

Citation:
Bichay TJ, Davis S, Mayville AH, Bichay NDT. A Quantitative Assessment of Imaging Frequency on the Treatment Setup Accuracy in TomoTherapy. Clin Oncol. 2016; 1: 1064.

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Introduction

One of the more common goals of modern radiation therapy has been to more accurately deliver dose to a target while minimizing unnecessary radiation dose to surrounding normal tissues [1]. Gaining the ability to visually locate the region of interest, and precisely align the radiation delivery to the target has greatly improved the accuracy and efficacy of treatments [2]. Image guided radiation therapy (IGRT) has become a common tool for daily patient alignment. Modern radiotherapy machines have adopted the ability to quickly acquire planar x-ray images for comparison to planning digitally reconstructed radiographs (DRR) and/or 3D volumetric images (cone beam or helical CT) for reference to the original CT [2].

Historically, aligning a patient for radiation therapy consisted of matching fixed in-room lasers to specific locations on the patient, often identified by tattoos placed during simulation. In order to accommodate daily variations in setup alignment according to tattoos; significant setup margin is added to the target contour to prevent missing the target during treatment delivery [3]. The sacrifice of additional dose to surrounding normal tissues is necessary in order to ensure adequate delivery of target dose [3]. In 3D therapy typical penumbra about a target is approximately 8-15 mm. In IMRT, however, the falloff may be only a few millimeters [4]. Small positional errors that were of little consequence in 3D planning may now have serious consequences in IMRT [5]. In head and neck treatments for example it is typical to have a 70 Gy target within a few millimeters of a much more sensitive parotid gland or spinal cord.

IGRT has dramatically changed the way patients are setup on a daily basis, and therefore changed the inherent accuracy of treatment delivery. The ability to fine-tune the initial tattoo setup, according to the exact location of the target and nearby normal tissues, reduces the error in daily dose delivery. The intent of this study is to evaluate this gain in accuracy of IGRT using megavoltage helical CT scans (MVCT) for TomoTherapy procedures over simple tattoo setups. The daily three-dimensional shifts necessary to bring a patient's anatomy into alignment, following initial tattoo setup, have been collected for several treatment sites including lung, prostate, prostate bed following prostatectomy, head and neck, and cranium. An analysis of several imaging frequency protocols summarizes the increase in treatment accuracy provided by IGRT over traditional alignment to tattoos only.

Materials and Methods

All Patients were set up on a TomoTherapy HiArt (Accuray, Sunnyvale CA) treatment couch and aligned to lasers using skin tattoos, or marks applied to the patient's mask at time of simulation. Prior to treatment, patients were imaged with a helical megavoltage CT (MVCT) with a pixel resolution of 512 x 512. The imaging system gives an initial automatic prediction of shifts necessary to align patients to the treatment plan reference conditions based on the protocol chosen by the therapists. Therapists choose between bony anatomy only, bony and soft tissue anatomy, or the full image technique, which compares high and low densities, as well as air data points over the entire image for alignment. Following automatic alignment, additional manual shifts may then be applied to fine tune the treatment position based on the target region of interest or the presence of fiducial markers.

Rotations were accounted for and corrected in all patients, however for this study only translational offsets were statistically analyzed. Rotations about the *x* and *z* axes, pitch and yaw respectively, were corrected for manually by the therapists through physical movements of the patient if necessary. TomoTherapy has the unique ability to correct for rotations about the *y* axis, or roll, by varying the starting gantry angle position [6]. Because the TomoTherapy system has only the ability to automatically correct for roll rotations, the registration procedure gives the operator the choice of computing translations only, translations with roll only, translations with yaw only, translations plus roll and yaw, or translations plus roll, yaw, and pitch. In all cases we used a protocol of translation with roll only applied to bony anatomy or bony and soft tissue. In the case of lung patients where the tumor could be readily seen the therapists shifted the patient to ensure best alignment was in the tumor region. Similarly, for prostate patients the setup position was optimized to place the fiducials at the reference position.

At first release TomoTherapy offered fine, normal, and coarse imaging protocols, of slice thickness 2 mm, 4 mm, and 6 mm respectively. We developed, along with TomoTherapy, an "ultra-fine" protocol of 1 mm slice thickness specifically for intracranial SRS treatments [7,8]. For all cranial cases the imaging protocol chosen was ultra-fine. For all other treatment sites the imaging protocol was typically fine, though normal or coarse may be chosen for patients with very large tumors and therefore long scan regions. Scan length was determined by the therapists in order to adequately visualize the treatment region and any anatomical landmarks critical for alignment.

The kilovoltage CT (KVCT) images to which daily MVCT datasets were compared were acquired on a Siemens Sensation Open 40-slice wide bore CT scanner (Siemens Medical Solutions, Malvern, PA). For planning purposes, the KVCT, acquired at 512 x 512 resolution, was resampled to 256 x 256, which is also the image set used for daily alignment.

Boswell et al investigated the accuracy of the TomoTherapy automatic registration procedure. They determined the accuracy, excluding outliers, to be within one half of the CT voxel size in all translational directions. They also determined that manual registration was at best as accurate as automatic registration, but typically inferior. The main benefit of manual evaluation is to detect outliers and fine-tune the automatic registration based on specific landmarks.

Table 1: The number of patients studied and total imaging sessions analyzed by treatment site.

Treatment Site	Number of Patients	Total MVCT
Cranial	43	1,055
Head and Neck	58	1,761
Prostate	65	2,630
Prostate Bed	47	1,746
Lung	47	1,187
Total	**260**	**8,379**

Treatment sites

There were five treatment sites studied. Table 1 summarizes the number of patients and the total number of treatments in each category.

Cranial and head and neck patients were setup on a custom-formed pillow fixed onto an S-frame support (Civco, Coralville, IA), and with their arms to their sides. A custom-molded reinforced aquaplast (Civco) mask ensured minimal patient movement during the treatment procedure. Registration was accomplished utilizing agreement in bony anatomy.

Because of the difficulty in visualizing the prostate under MVCT, prostate patients were implanted with three visicoil gold markers (IBA Dosimetry, Bartlett, TN) prior to simulation. Following initial automatic alignment to bony anatomy, the fiducials aid the therapists in determining accurate prostate position during treatment. Both prostate and prostate bed patients were positioned with their legs placed in a Vac Loc custom-molded immobilizer (Civco). Prostate bed patients were aligned based on bony anatomy.

Lung patients were setup on a combination of Vac Loc support under the thorax with arms up in a Wing board (Civco). Lung patient alignment was based on bony anatomy and soft tissue with manual emphasis on agreement of the tumor region.

Shift calculation

The final treatment position is reported as a net movement from the initial lateral, longitudinal and vertical position (x,y,z). Shifts in x,y and z directions were analyzed at each treatment fraction for a total of 8,379 treatments. For each imaging session the resultant vector shift (v) was calculated from the analysis of:

$$v = \sqrt{(x_0 - x_1)^2 + (y_0 - y_1)^2 + (z_0 - z_1)^2}$$

Imaging protocols

The resultant mean setup error for various imaging protocols was calculated using Stata analysis software (Stata/Mp 14, Statacorp College Station, TX). For all treatments all patients were imaged daily and shifted to the appropriate position prior to treatment. We simulated the error in setup that would result if various imaging frequency protocols were used. For example, to simulate the setup error if imaging was carried out once every five days, we used the

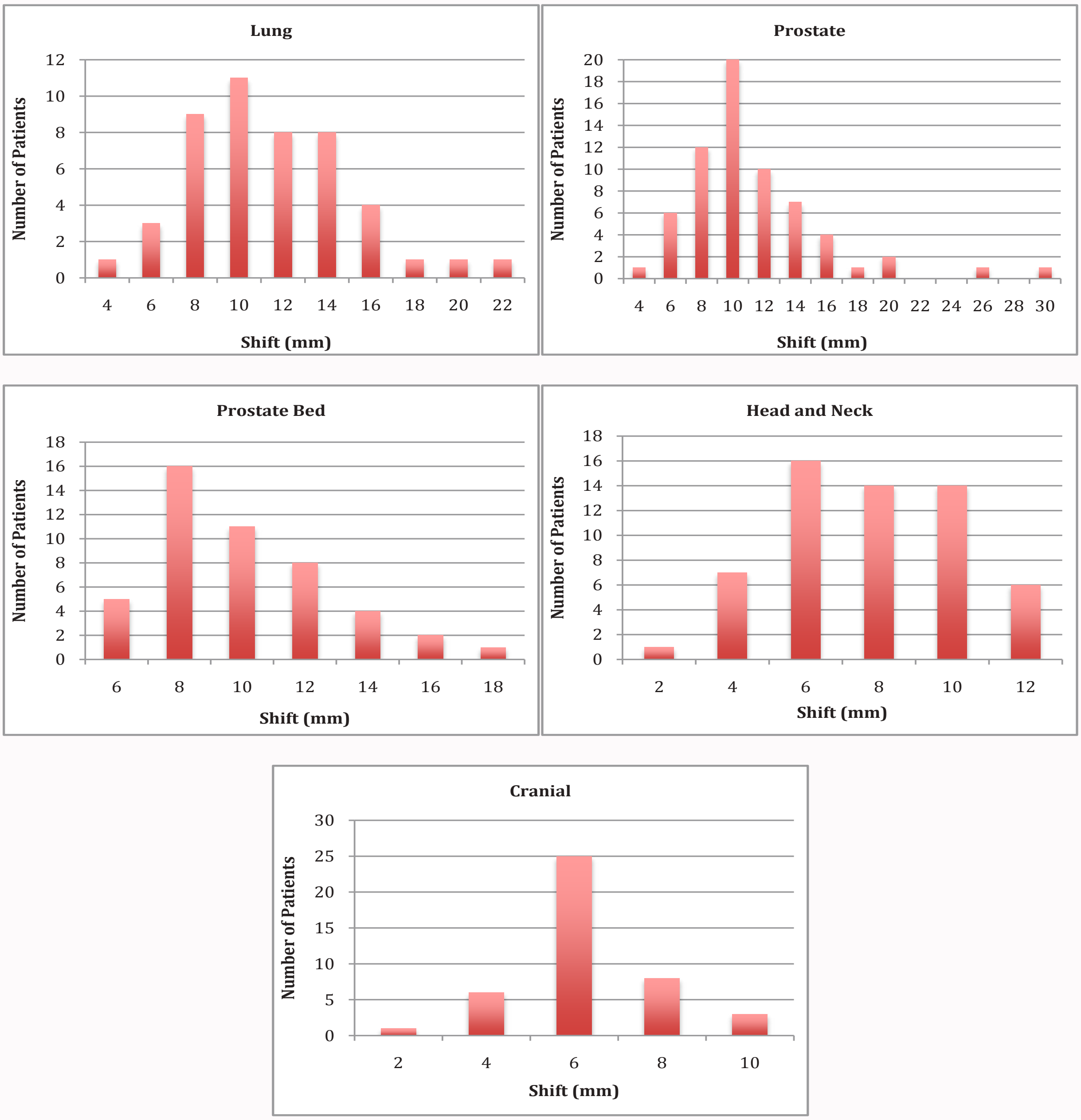

Figure 1: Frequency histogram of average per patient vector shifts. The values represent the mean vector position error for each patient for the total population of patients for each treatment site.

shift position carried out on the reference day for the four subsequent non-imaging days. The resultant error is the difference between the imaging day position and the actual position on the simulated non-imaging day. The following protocols were studied:

Daily imaging

Patients were imaged every day. The mean error in setup position is assumed to be zero since any offsets determined by imaging were applied prior to treatment.

Every second day

Patients imaged every second day. Patient initially set up based on tattoos and the reference position determined on the previous imaging day was applied. The difference between this position, and the actual shift determined at time of imaging on this day is the resultant error.

Every third day

Patients imaged on one day and this offset value was used for the next two days.

Every fourth day

Patients imaged on one day and this offset value was used for the next three days.

Every fifth day

Patients imaged every fifth fraction and this offset value was used for the next four days.

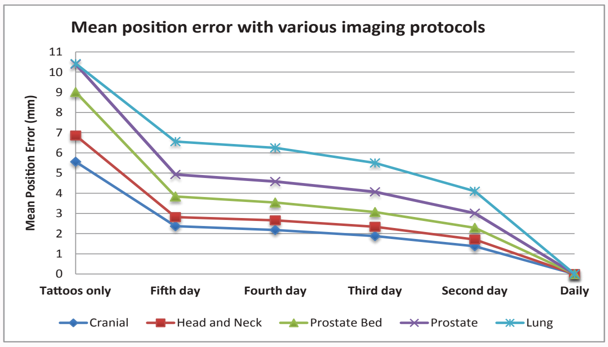

Figure 2: Mean position setup error with varying imaging frequency for the five treatment sites studied. The mean position error is the difference between the vector shift required based on IGRT and the tattoo position.

No imaging

If no imaging was ever carried out then the positional error would be equal to the calculated displacement for each treatment day.

Results

The daily MVCT is used to determine the extent of patient movement from the initial tattoo-laser based setup to an alignment matching patient anatomy in the treatment plan. If one assumes worst-case scenario where no imaging is done, the mean vector error over a course of treatment would be calculated from the shift error of each day. This data is presented in the series of histograms in Figure 1 for average patient shift required to correct for the setup error. The average displacement error for the total number of treatments for all patients for each imaging protocol is summarized in Table 2. The mean displacement error is least for cranial cases (5.6 mm) since these patients are fixed in a mask immobilizer which results in minimal movement relative to external marks. Similarly head and neck patients are also immobilized in a mask but show somewhat larger movements (6.9 mm). The greatest mean correction is that of prostate (10.4 mm) and lung (10.4 mm) patients where internal anatomy relative to external marks would be expected to be least stable of the sites studied. Prostate bed patients are setup day-to-day based on bony landmarks, which may be expected to have less variation (9.0 mm) compared to the soft tissue of prostate patients [9].

If imaging is carried out once per week, and the measured displacement is applied on the imaging day as well as to the next four fractions, there is improvement in setup accuracy compared to no imaging at all. For example the mean setup error in the prostate population decreases from 10.4 mm (Table 2) if never imaged to 4.9 mm for imaging once a week. Imaging every fourth day results in a further drop to 4.6 mm, then to 4.1 mm when imaged every third day and if imaged every second day the mean error drops to 3.0 mm. For the purpose of this study applying the shifts determined at daily imaging is assumed to result in no residual setup error. The data in Table 2 demonstrates a similar pattern for the other four sites studied in this paper. The prostate bed results demonstrate a reduction in setup error from 9.0 mm if never imaged to 3.8 mm if imaged once a week. Imaging every fourth day reduces the error to 3.5 mm, and every third day further reduces the error to 3.1 mm, and down to 2.3 mm if imaged every second day. The cranial results have a similar pattern but less magnitude where imaging once a week reduces the mean error from 5.6 mm to 2.4 mm, and for once every four days the error drops to 2.1. Every third day results in a further drop to 1.9 mm and every second day reduces it further to 1.4 mm. The head and neck

Table 2: Average error induced by varying the frequency of setup imaging, and the value which 10% of patients would experience errors in excess of.

Site	Frequency	Mean Error	SD	90th percentile
		(mm)	**(mm)**	(mm)
Prostate	Never	10.4	5.3	16.8
	Weekly	4.9	4.0	9.9
	Every-fourth	4.6	3.9	9.5
	Every-third	4.1	4.1	9.5
	Every-other	3.0	3.8	8.2
Prostate bed	Never	9.0	3.8	13.9
	Weekly	3.8	3.1	7.9
	Every-fourth	3.5	3.1	7.6
	Every-third	3.1	3.1	6.8
	Every-other	2.3	2.9	6.2
Lung	Never	10.4	5.4	17.7
	Weekly	6.6	5.8	14.6
	Every-fourth	6.2	6.1	14.2
	Every-third	5.5	5.9	13.4
	Every-other	4.1	5.7	11.5
Head and Neck	Never	6.9	3.0	10.8
	Weekly	2.8	2.2	5.8
	Every-fourth	2.7	2.3	5.7
	Every-third	2.3	2.3	5.4
	Every-other	1.7	2.1	4.9
Cranial	Never	5.6	1.9	8.0
	Weekly	2.4	2.1	4.9
	Every-fourth	2.1	2.0	4.7
	Every-third	1.9	2.0	4.4
	Eve ry-other	1.4	1.8	3.8

setup error was 6.9 mm if no imaging is carried out then drops to 2.8 mm for every fifth day, 2.7 mm for every fourth day 2.3 for every third day and 1.7 mm for every second day. Lung patient's setup error dropped from 10.4 mm with no imaging, to 6.6 mm with every fifth day imaging, to 6.2 mm with imaging every fourth day, 5.5 mm if imaged every third day, and 4.1 mm if imaging was carried out every second day. A graphical summary of the improvement in setup error is presented in Figure 2. The residual mean setup error for the various imaging protocols is demonstrated when moving from setup only on tattoos, to protocols involving various imaging frequencies.

The calculation of mean errors is useful in understanding the average magnitude of error involved in the various protocols. We were also interested in determining the amount of deviation that would occur in the worst case 10% of the treatment sessions for each one of these protocols. The data is presented in Table 2. For prostate patients if no imaging were carried out at all then ten percent of the time the mean error in displacement would be 16.8 mm. If imaging is carried out once per week then this error would drop to 9.9 mm then to 9.5 mm for imaging every fourth day or every third day and if imaged every second day it would be reduced to 8.2 mm. In the case of cranial patients if imaged every second day there would still be an average of 3.8 mm error in ten percent of the treatments. Lung patients had the greatest mean error where imaging once a week would result in a mean error of 14.6 mm ten percent of the time, and imaging every second day would still have an error of 11.5 mm ten percent of the treatments.

Discussion and Conclusion

The smallest mean patient shift was for cranial and head and neck patients. The result is expected as both anatomical regions are immobilized by a thermoplastic mask and relied largely on bony anatomy. The shift for head and neck is somewhat larger than cranial (6.9 mm vs. 5.6 mm) which is likely due to a longer region being treated. The longer region includes a flexible cervical spine, which can lead to some setup variation and may result in a registration bias from one therapist to another. The greatest shifts were for lung and prostate. In the case of prostate the shift was done to place the implanted fiducial markers back to the reference position at time of planning. Similarly in the case of lung the shift was to align the tumor with the reference position of the plan. Shifts were intermediate for prostatic bed where the alignment was based on bony anatomy as opposed to soft tissue.

Our results demonstrate that the error associated with various imaging protocols is seen to decrease with increased frequency of imaging. These results are similar to those of Kupelian et al. [10] who studied different imaging protocols for prostate patients. Treatment margins for IMRT will vary by treatment site and treatment modality being used. In the case of TomoTherapy for example with IGRT our center uses 3 mm setup uncertainty in all directions for cranial treatments. Even for frequent imaging of every second day there will still be a mean error greater than our margin in ten percent of the treatments. This effectively means that a geometric miss would occur in more than one in ten treatments. Similar results were found for the other four anatomical sites observed. We use a 5 mm margin for prostate except for the posterior aspect where 3 mm is used. Our data demonstrates that any imaging frequency other than daily would result in an error of greater that 8 mm in ten percent of treatments. Similarly a margin of 5-10mm PTV may be applied to lung protocols using IMRT. Our data demonstrates that for these lung patients the setup error would be 11.5 mm even if imaging was done every other day. This would suggest that with TomoTherapy, and perhaps other treatment systems where very conformal distributions are used, daily imaging is essential for acceptable target coverage without the addition of excessive margins. We have shown previously the error associated with setup on tattoos only for cranial [11] and for lung patients [12]. Previous publications have shown that setup position errors have both a random and a systematic component [13]. Our data agrees with this conclusion as the daily setup variation appears to have a random component since using a correction based on a previous day does not fully correct for the setup uncertainty. Schubert et al. [14] have taken an approach whereby the displacements for prostate patients over the first four days are used to generate a custom PTV. This approach appears effective at minimizing geometric miss with less frequent imaging; however it is at the cost of modifying each patient's PTV to account for the setup uncertainty. The present study limited the corrections in setup to translation and roll rotation only. Other rotation corrections for yaw and pitch could not be easily applied as the TomoTherapy couch is not readily amenable to allow this movement. This is discussed by Schubert el al. [13] who suggests that table sag would likely result in pitch variation and yaw may result in lateral displacement corrections.

The use of IGRT has allowed treatment margin reductions, which leads to a decrease in the volume of normal tissue treated. This reduction in normal tissue volume results in a decrease in the complication rate [15]. The use of IGRT ensures that this reduction in the complication rate is not at the cost of decreased tumor response. Several authors have demonstrated that with improved imaging both reductions in complication rates and increased tumor response can coexist [15]. Our data compares the improvement in setup accuracy with the frequency of imaging the patient prior to treatment. Intuitively one would predict that increased imaging frequency would result in increased treatment accuracy. Our data confirms this and assigns a numeric value to this increase in setup accuracy. The data for the five treatment sites studied is in agreement with a previous publication studying imaging frequency for prostate patients [10].

Given the results of this study daily imaging for TomoTherapy is advised for acceptable treatment accuracy for the five treatment sites studied.

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