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Original research article

IMPACT OF THREE DIFFERENT MATCHING METHODS ON PATIENT SET-UP ERROR IN X-RAY VOLUMETRIC IMAGING FOR HEAD AND NECK CANCER

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Impact of three different matching methods for delivery of Volumetric Modulated Arc Therapy (VMAT) in Cone-beam computed tomography (CBCT) on patient set-up error. As per institutional imaging protocol, 300 CBCT scans of 20 VMAT head and neck cancer patients treated with 60 Gy/30 fractions were chosen for the present study. Approved CT images of the plan were registered as a reference with the CBCT images on board. Grey-scale matching (GM), manual matching (MM), and bone matching (BM) between on-board CBCT and reference CT images were used to assess patient translation errors. Patient positioning verification was evaluated using the Clip-box registration in all three matching methods. Using the GM approach as a reference point, two additional matchings were rendered in offline mode using BM and MM. For analysis, random error (σ), systematic error ($\sum$), maximum error (E) mean set-up error (M), mean displacement vector (R), matching time (Mt), and multiple comparisons using Post hoc Tukey's HSD test were performed. In MM, less random and systematic errors were found than in GM and BM with an insignificant difference ($p > 0.05$) Compared to BM and GM, the maximum error, mean set-up error, and displacement vector were marginally less in MM ($p > 0.05$). In MM, an increased Mt relative to BM and GM was observed ($p > 0.05$). Furthermore, an insignificant difference in set-up error was revealed in a multiple comparison test ($p > 0.05$). Any of the three matching methods can be used during CBCT to check patient translation errors for the delivery of the VMAT head and neck patients.

1. INTRODUCTION

Radiotherapy (RT) is the primary treatment either in combination with chemotherapy or surgery, given to most of the head and neck cancer patients. During conventional RT, the irradiation of healthy tissue around the tumor significantly impacts side effects and quality of life for long-term survivors. The advancement of volumetric modulated arc therapy (VMAT) has reduced patient's side effects, improved the dose to the target, and has also reduced the time of treatment delivery. However, the positioning of patient and beam placement is a crucial task for achieving the entire course of patient treatment. Moreover, the geometrical uncertainty during patient set-up should be minimized to achieve a successful delivery of VMAT treatment.[1] Many factors lead to uncertainty in the positioning during head and neck patient treatment. In the radiotherapy planning and delivery process, the geometrical uncertainties constrain dose escalation and cause typical tissue complications.[2] Therefore, Image-guided radiotherapy (IGRT) is necessary to ensure the accuracy of patient set-up uncertainties and target motion in advanced techniques.

In conventional radiotherapy, patient set-up verification has been performed with the acquisition of 2-dimensional (2D) images, either kV or MV portal images, and compared with planning CT based on bony anatomy landmark. However, 3-dimensional images (3D), such as cone-beam CT (CBCT) is capable of generating images of soft tissue with a better spatial resolution at acceptable imaging dose as compared to 2D images (Jaffray 2002).[3] This combination of this technology with the medical linear accelerator will provide an ideal platform for high precision IGRT.

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Set-up error is an essential source of uncertainty in head and neck radiotherapy. Dionisi et al. (2013) assessed the accuracy of the set-up error using 420 CBCT scans for head and neck cancer patients in order to determine a correct clinical target volume (CTV) for the use in planning target volume (PTV) to be adopted. The study results revealed that the CTV-PTV margin of 5 mm is safe for clinical practice to expect re-irradiation or proximity of organs at risk and high dose regions.[4] Similarly, Di Biase et al. (2016) evaluated both translation and rotational set-up errors on seven head and neck patients treated with intensity-modulated radiotherapy (IMRT) and VMAT using CBCT pre-treatment imaging. Their results found that CBCT weekly allows for effective control of set-up error and necessary margin from CTV to PTV.[5] The CBCT based IGRT supports the reducing of uncertainties to a large extent to ensure a precise delivery of treatment.

There are some factors such as algorithm, matching, and registration methods used in CBCT software to ensure the geometrical accuracy of patient positioning error during treatment delivery.[6–8] Many authors have evaluated patient's set-up errors using different matching methods. A study by Campbell (2015) compared patient positioning error between manual soft-tissue registration and dual registration (DR) for sixty CBCT images from ten post-prostatectomy patients. The study results revealed that both methods produced clinically acceptable results, except increased variance in the anteroposterior (AP) direction due to the involvement of the bladder and the rectal filling.[9] Similarly, Van Beek et al. (2010) study quantified global and local set-up errors by comparing multiple regions of interest (ROI) registration with single ROI for 50 head and neck radiotherapy patients. They found that multiple ROI registration methods are secure, provide additional information on set-up error and support to select for re-planning.[10]

Hawkins et al. (2011) study reported that optimizing clip box registration for set-up error using CBCT will increase the maximum outcome for esophagus cancer.[11] To the best of our knowledge, no precise data are available for the comparison of three different matching methods, namely, manual, bone (T + R), and grey value (T + R) used in Elekta 3D X-ray volumetric imaging (XVI) system. Therefore, this study aimed to compare the impact of three registration methods on patient set-up error for head and neck VMAT patients.

2. MATERIALS AND METHODS

2.1. Patient

For the present study, twenty head and neck patients were treated with 60 Gy in 30 fractions using 6 MV photon beam with the VMAT technique. An alternative day CBCT imaging protocol was followed for six weeks. A total of 300 CBCT scans were acquired by institutional image guidance protocol for patient set-up verification. The patient's set-up was performed on a carbon fiber flat tabletop (Qfix, PA, USA) attached with a base plate using an indexing bar. Besides, patients were immobilized using a 5-clamp head, and shoulder thermoplastic (Orfit Industries, Wijnegem, Belgium) mask in a supine position. Two fiducial markers were placed on both the lateral side of the neck and one in anterior with the support of a moving laser system for isocenter reference.

The CT simulation was performed using PET-CT (Biograph Truepoint®, HD, Siemens Medical Solution, PA, USA) and generated 3 mm CT slice thickness for delineation of tumor and critical structure. All the delineations were performed based on the International Commission on Radiation Units (ICRU) 62. Plans were generated using Monaco™ TPS, followed by senior radiation oncologist approval.

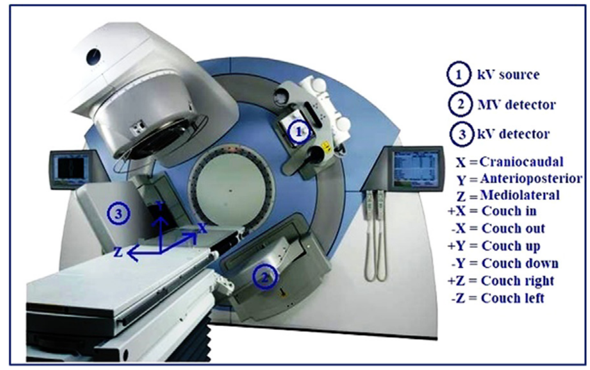


Fig. 1.

2.2. Image acquisition

Before image acquisition, the approved CT images, along with radiotherapy structures and plans, were transferred from Monaco™ TPS to the XVI system. Further, they were registered as a reference image data set. The XVI system, along with Elekta Synergy™ were mounted on the retractable arm at 90 degrees to the therapy beam direction. A flat panel detector, called the electronic portal imaging system, is mounted opposite to an X-ray tube for imaging, as shown in Fig. 1. The XVI system is capable of generating volumetric CT images with good contrast, low imaging dose, and submillimeter spatial resolution within the therapy room. Moreover, it offers a variety of image-guided options to suit the individual needs of the patient treatment. For head and neck patient image acquisition various parameters such as 100 kV, 18.3 mAs, gantry speed 360◦/min, fast scan, clockwise gantry rotation from 320◦ to 160◦, collimator M20, F1 filter, and 183 frames were used.[12]

2.3. Image matching

The acquired 3D reconstructed images during patient on-board were compared with reference CT images to calculate geometrical shift before treatment delivery. The image reconstruction was performed using Feldkamp's back-projection algorithms. The XVI version 5.0.2 has three different image matching methods, such as manual, bone (T + R), and grey value (T + R), where T and R represent the 3D translation and rotational set-up errors. Patient's translation error in the mediolateral (ML), craniocaudal (CC), and anteroposterior (AP) directions were observed as X, Y, and Z direction. Besides, the tolerance limits were fixed ≤ 3 mm and ≤ 1◦ for translation and rotation in any direction.

To perform different matching methods, except manual matching, suitable registration methods had to be used about CT images. There are three different registration methods, namely clip-box (CB), mask (MR), and dual (DR), used in XVI software.[12] However, for the present study, we used CB registration in bone and grey value matching method for patient set-up error. In the Clip box registration (CBR) method, a volume of interest is defined on the reference CT image around the anatomy of interest in the form of axial, coronal, and sagittal views. This image registration between image sets is limited only to the voxels within the CB, which contains the target volume, as shown in Fig. 2. The chamfer algorithm is used for image matching.

- **Manual matching (MM):** It is a method used for matching 3D images manually between reference and onboard based bony structures, as shown in Fig. 2. The criteria of this method are to

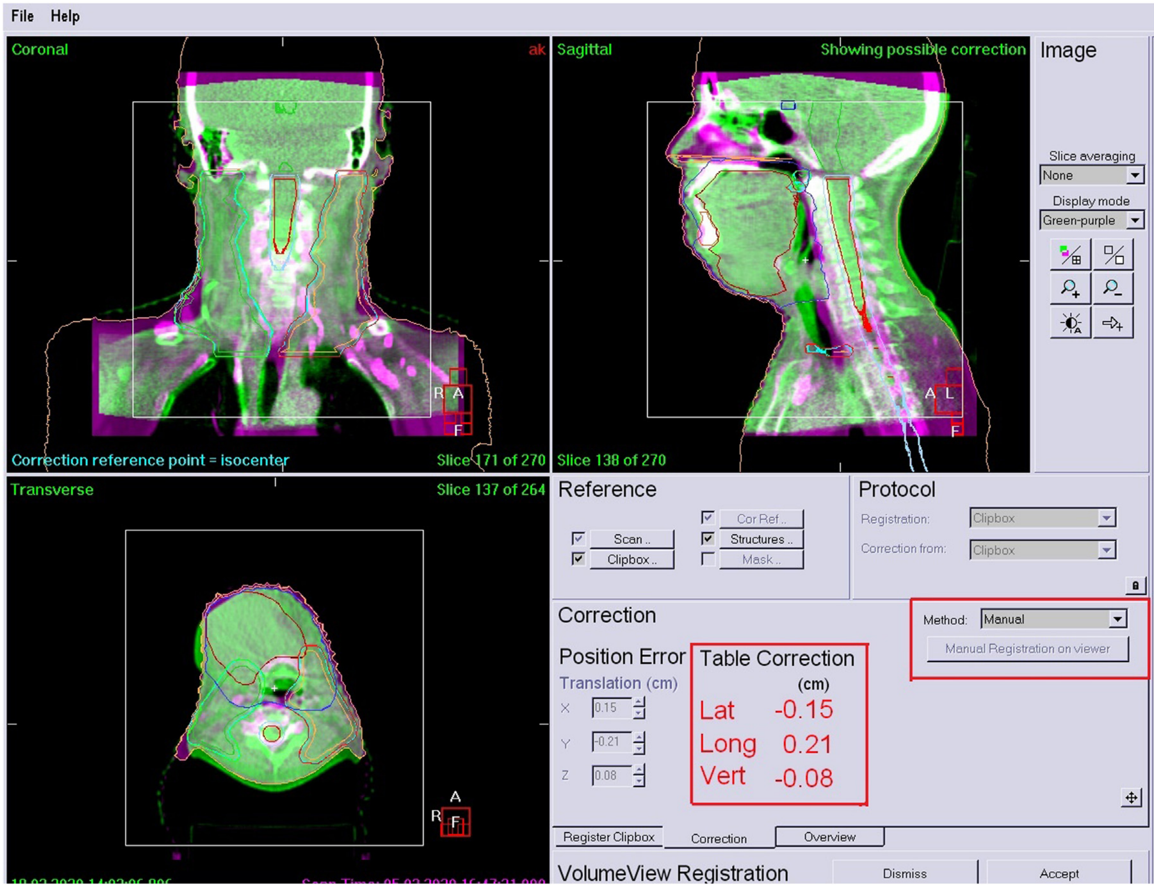


Fig. 2.

match the tumor and healthy critical organs perfectly matching after MM.

- **Bone (T + R) matching (BM):** It is a mode of automatic registration between reference and onboard CT images. The BM uses chamfer matching algorithms that calculate the translation and rotation with densities that are the same as bone densities, as shown in Fig. 3. However, the algorithm is not very sensitive to image noise so that it can calculate faster.
- **Grey value (T + R) matching (GM):** It is automatic matching performed between onboard and reference images based on the grey-scale intensity values of the voxels in the registration volume, as depicted in Fig. 4. The algorithm used is a gray level 'correction ratio' procedure.

In the present study, rotational errors were not used for the comparison of patient set-up errors. If the errors were > 1○, then a repeat CBCT followed by a repositioning of the patient set-up. Considering the GM method as a reference, the other MM and BM methods were performed in the offline mode for comparison.

2.4. Process of matching methods

As per ICRU 50, 62 and 83 protocols, gross tumor volume (GTV), clinical target volume (CTV), and organ at risk volume (OAR) were delineated by a radiation oncologist with radiologist support. To account for patient set-up uncertainty during treatment, the planned target volume (PTV) was defined around the CTV volume. As seen in Fig. 2, the CBR setting was performed around PTV along with bony structures such as the spine, mandible, maxilla, and nasal in the coronal, sagittal, and axial planes. The on-board CT images were compared with registered CT images by a radiation therapist for final set-up error followed by radiation oncologist approval. These corrections were applied through the patient couch parameter from XVI V5.0.2 software using the čonvert correctionöption.

2.5. Set-up errors

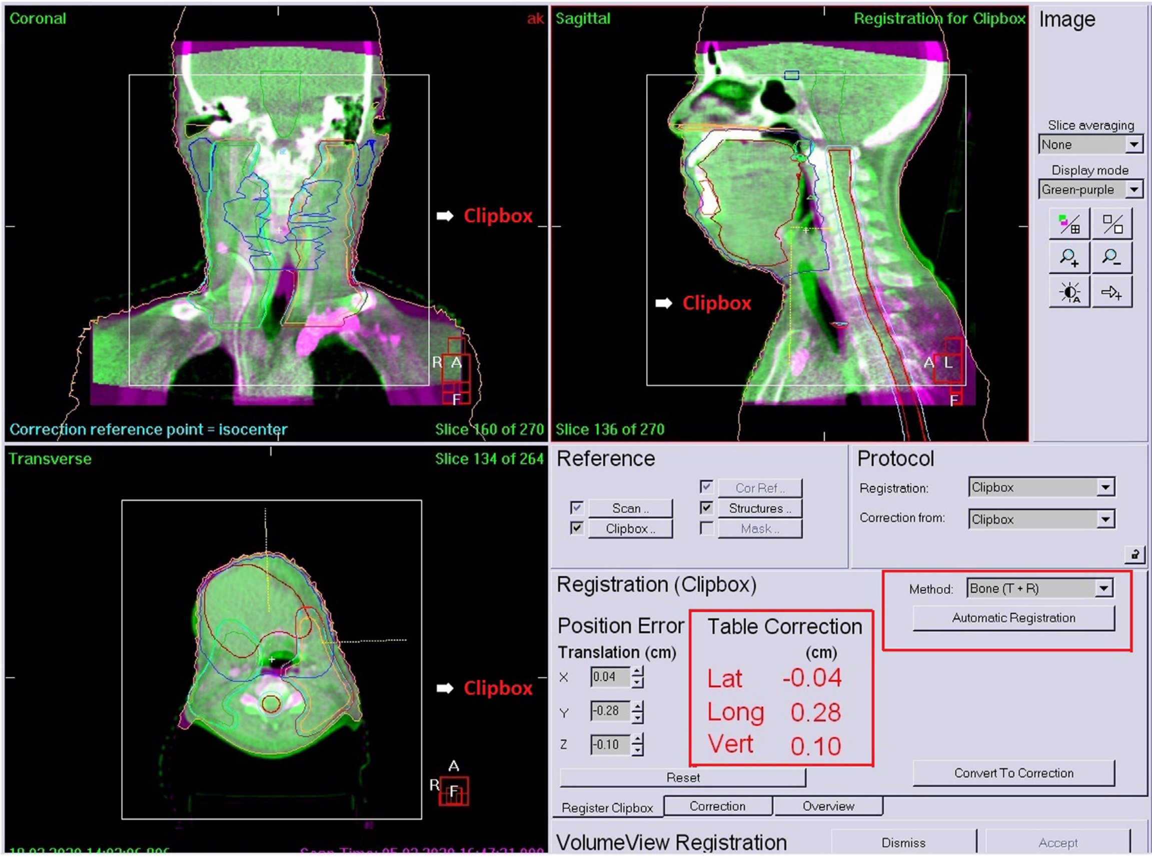
It is defined as the difference between the intended and actual treatment position of the patient. It is usually calculated as a patient set-up error in the treatment field position when an onboard treatment image is compared against the corresponding reference image. Further, it is classified into two categories, namely (1) Systematic error and (2) Random error. The systematic patient error ($\sum$) is estimated by calculating the mean of the measured set-up error for each imaged fraction in each direction using three different matching methods. The random error (σ) is calculated as the root mean square value of the standard deviation of errors recorded for each patient using three matching methods.

Mean set-up error (M) is calculated as the average value of set-up error in each direction. Maximum error (E) is computed based on maximum deviation in each direction using three matching methods. Mean displacement vector (R) is defined as a value combining set-up errors recorded in all three directions. It is quantified as both distance and direction using the mathematical formula, as mentioned below.[13]

$R = \sqrt{(d^2_{ML} + d^2_{CC} + d^2_{AP})}$ where, d_{ML}, d_{CC}, d_{AP} are deviations in ML, CC and AP directions.

The total time required for each matching method is called matching time (M_t). It is calculated from ŠTART TIMEänd ĚND TIMEöf each matching method to evaluate their efficiency.

$M_t = M_{ST} - M_{ET}$ where M_{ST} and M_{ET} represent the start and end time of the matching method.


Coronal
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Correction from:
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Registration (Clipbox)
Method:
Bone (T + R)
Automatic Registration
Clipbox
Position Error
Translation (cm)
X 0.04
Y -0.28
Z -0.10
Table Correction
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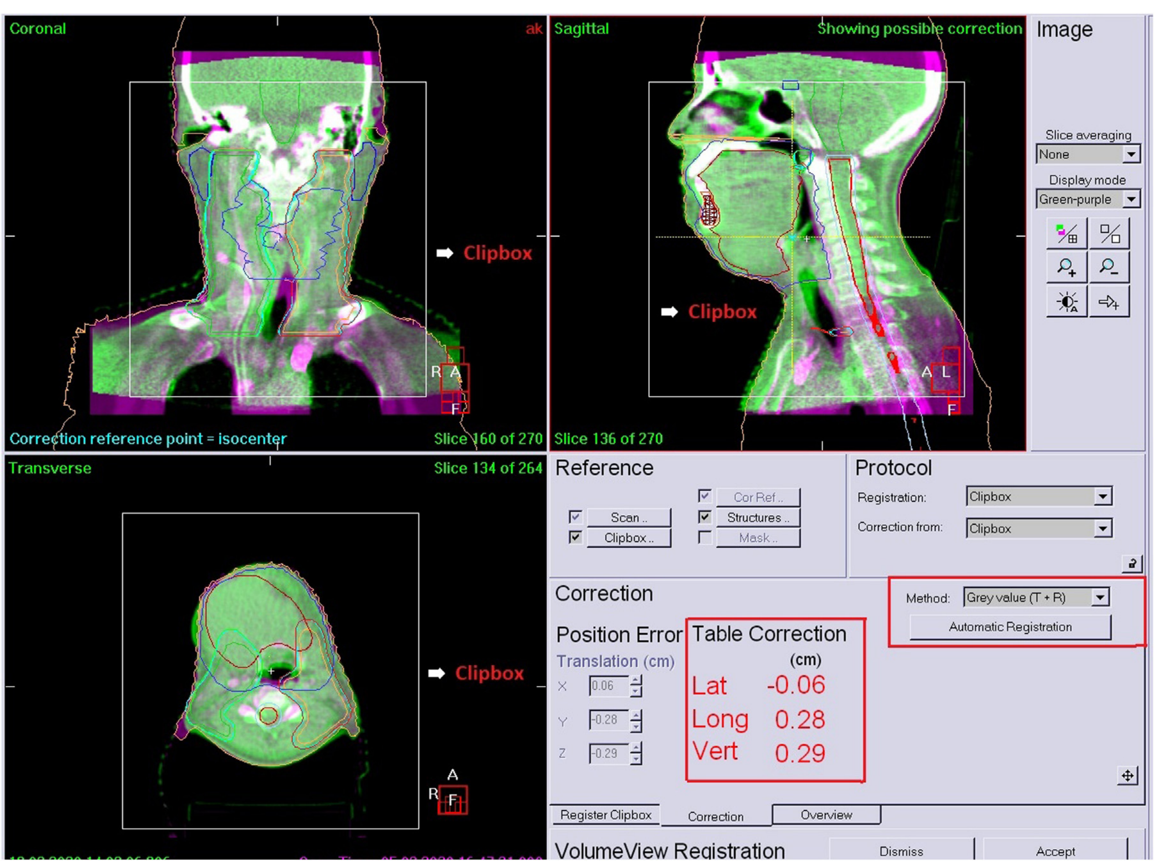
Fig. 3.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Cor Ref ..
Structures ..
Mask ..
Protocol
Registration:
Clipbox
Correction from:
Clipbox
Correction
Method:
Grey value (T + R)
Automatic Registration
Clipbox
Position Error
Translation (cm)
X 0.06
Y -0.28
Z -0.29
Table Correction
(cm)
Lat -0.06
Long 0.28
Vert 0.29
Register Clipbox
Correction
Overview
VolumeView Registration
Dismiss
Accept

Fig. 4.

Table 1
Comparison of systematic ($\sum$) and random (σ) errors between three matching methods

Techniques/Methods		Systematic error (in mm)			Random error (in mm)		
Matching method	Registration method	X	Y	Z	X	Y	Z
MM	CBR	0.26	0.22	0.04	0.69	0.93	0.98
BM	CBR	0.67	0.03	0.64	1.33	1.2	1.39
GM	CBR	0.36	0.28	0.64	1.52	1.36	1.76

X - Mediolateral (ML), Y - Craniocaudal (CC), Z - Anterioposterior (AP), MM - Manual matching, BM - Bone (T + R) matching, GM - Grey value (T + R), Systematic ($\sum$) error, random (σ) errors.

Table 2
Multiple comparison between three matching methods for head and neck cancer.

Setup error	Registration	(I) Technique	(J) Technique	Mean Difference (I-J)	Std. Error	Sig.
ML	CBR	MM	BM	-0.093	0.025	0.001*
			GM	0.010	0.025	0.915^{NS}
		BM	GM	0.104	0.025	0.000*
CC	CBR	MM	BM	0.025	0.025	0.567^{NS}
			GM	0.050	0.025	0.112^{NS}
		BM	GM	0.024	0.025	0.585^{NS}
AP	CBR	MM	BM	0.068	0.046	0.304^{NS}
			GM	-0.060	0.046	0.396^{NS}
		BM	GM	-0.128	0.046	0.016*

X - Medivolateral (ML), Y - Craniocaudal (CC), Z - Anterioposterior (AP), MM - Manual matching, BM - Bone (T + R) matching, GM - Grey value (T + R), Systematic ($\sum$) error, random (σ) errors*. The mean difference is significant at the 0.05 level, NS - Non significant.

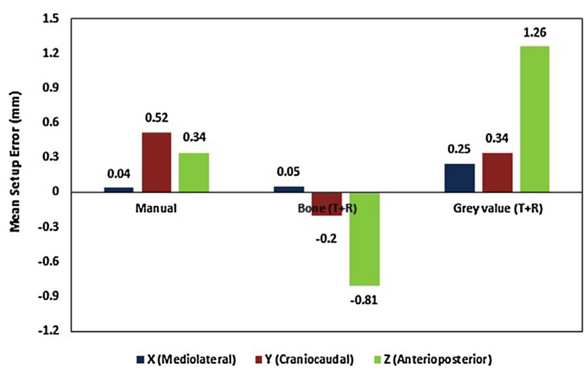

Fig. 5.

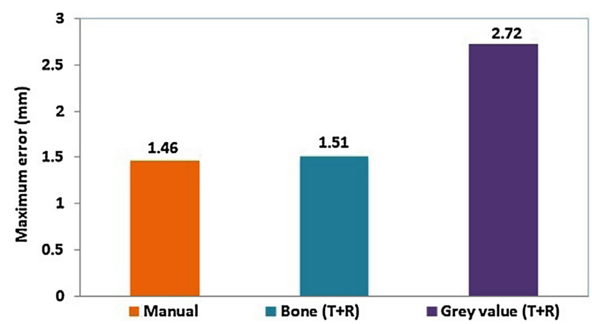

Fig. 6.

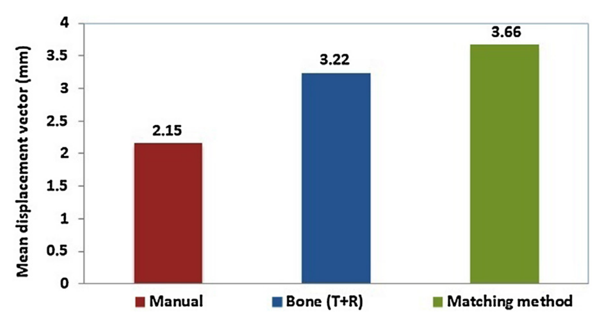

Fig. 7.

One-way ANOVA post hoc Tukey's HSD test was performed for multiple comparisons between MM, BM and, GM methods to evaluate the P value for measured results using SPSS Version 14.0 software.

3. RESULTS

The impact of different matching methods on patient set-up error showed some similarities and differences, and these results were represented using tables and graphs.

As shown in Table 1, the results of systematic and random error of patient setup in all three directions are as follows: In MM methods, ML direction, $\sum$ =0.26 mm and σ =0.69 mm; in CC direction, $\sum$ =0.22 mm and σ =0.93 mm; and in AP direction, $\sum$ =0.04 mm and σ =0.98 mm. Similarly, in BM method, ML direction, $\sum$ =0.67 mm and σ =1.3 mm; in CC direction, $\sum$ =0.03 mm and σ =1.2 mm; and in AP direction, $\sum$ =0.64 mm and σ =1.3 mm. In GM method, ML direction $\sum$ =0.36 mm and σ =1.5 mm; in CC direction, $\sum$ =0.28 mm and σ =1.3 mm; and in AP direction, $\sum$ =0.64 mm and σ =1.7 mm. The systematic and random errors were slightly less in MM as compared to BM and GM. However, no statistically significant difference was observed (P > 0.05). The results of mean setup errors for MM, BM and GM in the ML direction (0.04 mm, 0.05 mm, and 0.25 mm), in the CC direction (0.52 mm, -0.20 mm, and 0.34 mm), and in the AP direction (0.34 mm, -0.81 mm, and 1.26) were observed as shown in Fig. 5. Fig. 6 depicts that maximum errors were marginally less in MM as compared to BM and GM. However, statistically, no significant difference was observed (p > 0.05).

As seen in Fig. 7, the mean displacement vector results were less in MM as compared to BM and GM methods. Statistically, no significant difference was found among the three methods (P > 0.05). As visualized in Table 2, multiple comparisons were performed between MM-BM, MM-GM, and BM-GM in the ML, CC, and AP direction using post hoc Tukey's HSD statistical analysis. The intercomparison results reported that significant differences between MM-BM, BM-GM in ML, and BM-GM in the AP direction were observed (p < 0.05). However, no significant difference was observed in the CC direction.

Time taken by each matching method was calculated and compared between MM, BM, and GM. An increased Mt was observed in MM (1.75 ± 0.32 min) as compared to BM (0.45 ± 0.22 min) and GM (0.51 ± 0.23 min) with no significant difference ($p > 0.05$).

4. DISCUSSION

Advancement of new radiotherapy techniques such as VMAT requires greater accuracy in treatment planning due to reduced target delineation and set-up error. The process of precise dose delivery to a tumor volume is only possible with accurate positioning of patient during the treatment. Patients' rotational and translational errors were quantified by Guckenberger et al. (2006) who reported that a mean reduction of PTV minimal dose errors was 4.4% and 6% in translation and rotation, and 7% in combination.[13] A study by Prabhakar (2007) evaluated the impact of set-up error on the dose to target volume and critical organs for the treatment of 12 nasopharyngeal carcinomas with IMRT. He reported that the target volume decreased gradually with the increase of set-up error.[14] Similarly, Delishaj et al. (2018) investigated set-up error to evaluate the PTV margin for 60 head and neck cancer patients treated with IMRT using CBCT imaging for verification. They reported that based on the first three fractions and followed by weekly CBCT, 3-5 mm PTV margins appeared adequate to overcome set-up error issues.[15] Therefore, the routine use of IGRT resulted in reduced set-up error, critical organ dose, and increased dose escalation to the target volume. Nowadays, to ensure advanced radiotherapy techniques, many imaging modalities are used in delivery for patients to set up errors. However, 3D-CBCT verification can provide a better quality of images and improved accuracy, as compared to 2D images, as reported by Hawkins et al. (2011), We et al. (2010), and Li et al. (2008).[16–18]

Nakahara et al. (2018) investigated the dosimetric difference in target and OAR between bone matching (BM) and target matching (TM) using CBCT for 40 VMAT prostate cancer patients. They found that BM resulted in an increased rectal dose, and a high risk of CTV dose decrease.[19] Similarly, as reported by Rijkhorst et al. (2009), the dosimetric impact of different matching methods depends on the interfraction motion of the prostate in the AP direction.[20] Lorenzen et al. (2016) evaluated the use of EPID using both manual and automatic matching for patient set-up verification by comparison to CBCT in breast radiotherapy.[21] A study by Shi et al. (2011) investigated CBCT guided automatic alignment with gray-value based registration and manual matching using intraprostatic fiducial markers. Their results concluded that the manual matching to fiducials is one of the most reliable methods to maintain accuracy in prostate IGRT.[22] Similarly, Palombarini et al. (2012) evaluated by comparing two matching methods, i.e. automatic bone and manual soft-tissue for prostate cancer, and concluded that soft tissue matching allows for better localization of prostate during daily CBCT and may reduce the PTV margins.[23]

The study findings were supported by Jiao et al. (2013). They compared soft tissue matching (STM) with fiducial marker matching (FMM) in Elekta™ using 90 CBCT imaging data sets from 10 liver cancer patients. Their results revealed that STM is an equivalent method to FMM for set-up error. However, it is feasible to implement CBCT image guidance using the STM method clinically.[24] Therefore, the knowledge and understanding the importance of choosing a matching method according to the different clinical sites is an essential factor. However, the best way of selecting the matching method was not thoroughly investigated for each clinical site. Therefore, the present study compared patient set-up error between three matching methods to quantify set-up errors using CBCT imaging for head and neck cancer treated by VMAT technique. Also, the vendor recommends verifying the accuracy of each matching method before the implementation of any clinical use.[12]

The overall analysis of the results of the present study reveals no statistically significant difference in systematic error, random error, maximum error, mean displacement vector and mean set-up error when a comparison between three matching methods was made. However, marginally less set-up error was found in MM as compared to BM and GM methods. The multiple comparisons between the three methods did not show any statistically significant difference, except the ML and AP direction. However, overall results were well within the clinical tolerance limit. Zang et al. evaluated interfraction and intrafraction set-up errors and baseline shifts of golden fiducial markers using CBCT to calculate PTV margins for patients with liver cancer. They reported that margins of 5.5 mm, 14.6 mm, and 7.2 mm were needed to compensate baseline shifts when CBCT with the bone match is used for online correction of set-up error.[25] The total time taken for each matching method is very important in a busy clinic. Increased waiting time on treatment couch may increase intrafractional uncertainties before treatment delivery. In the present study results, the time taken by MM is slightly higher as compared to the other two methods: BM and GM.

5. CONCLUSION

The impact of three different matching methods showed an insignificant difference in patient set-up error. In all three directions, they are efficient enough to detect patient set-up errors using XVI software V5.0.2. So all three methods can be used without compromising accuracy in the head and neck VMAT delivery.

Conflictof interest

None.

Financial disclosure

None.

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