ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 07, Issue, 10, pp.15773-15779, October, 2017

ORIGINAL RESEARCH ARTICLE OPEN ACCESS

CALCULATION OF OPTIMAL MARGINS BETWEEN CLINICAL TARGET VOLUME (CTV) AND PLANNING TARGET VOLUME (PTV)

***Dr. Chatharaju Swarna Kumari**

Basavatarakam Indo American Cancer Hospital And Research, Institute Banjarahills Road No 10 Hyderabad 500034

ARTICLE INFO

Article History:
Received 06th July, 2017
Received in revised form
25th August, 2017
Accepted 27th September, 2017
Published online 10th October, 2017

Keywords:
Clinical Target volume,
Planning Target volume,
Prostate cancer,
Radiotherapy, CBCT.

ABSTRACT

The purpose of this study was to estimate the CTV-PTV margin required for prostate cancer cases at the radiotherapy department of Basvatarakam Indo American Cancer Hospital and Research Institute, Hyderabad. Portal image data from patients treated at the radiotherapy departments during the period of 2013-2015 was used to estimate the set-up displacements for each prostate area. By using the acquired images the magnitude of the systematic, i.e. preparatory, and random, i.e. execution, error was determined in the anterior- posterior (AP), superior-inferior (SI) and right-left (RL) direction. The calculated PTV margin is based on the systematic and random errors of the entire patient populations. A total of 29 patients were used for the analysis of prostate treatments. The evaluation of the PTV margin was done for two different matching protocols; CBCT matching and DRR matching. Results show that there is no considerable difference in the margin values evaluated from DRR matching protocol and CBCT matching protocol. This happens due to the fact that both protocols depend on the bony anatomy matching. Larger shifts occurring in longitudinal direction can be attributed to immobilization. The immobilization used in the hospital does not have foot holder or indexer support. Based on ICRU suggestions and recommendations, the minimum PTV margin given to prostate cases in the institute is 0.5 cm in all directions. The observed table correction values pointed out that the PTV margins used in the institute is inadequate to provide sufficient coverage of tumour volume, setup uncertainties and internal organ motion in Prostate cancer cases.

****Corresponding author***

Citation: Dr. Chatharaju Swarna Kumari. 2017. "Calculation of optimal margins between clinical target volume (ctv) and planning target volume (PTV)", *International Journal of Development Research*, 7, (10), 15773-15779.

INTRODUCTION

When treating cancer patients with radiotherapy the ambition is to kill the tumour cells while sparing as much of the surrounding healthy tissue as possible. Before the start of a Radiotherapy treatment CT- images are acquired showing the anatomy of the body and tumour at the moment of acquisition, these images are used for designing a radiation treatment plan. The tumour volume is outlined in the CT-images forming the gross tumour volume, GTV. In order to account for subclinical disease a margin is added to the GTV called the clinical target volume, CTV.

The CTV still requires a further margin in order to account for daily setup error and internal organ motion. This volume is termed the planning target volume, PTV (ICRU report, 1993). The purpose of the PTV margin is to compensate for geometric uncertainties which will, if not corrected for, cause differences between the intended and actual delivered dose distribution to the CTV. The uncertainties can be divided into two parts, the interfractional and intrafractional error. The interfractional error describes the set-up displacement between treatment fractions while the intrafractional error is the displacement during the delivery of a treatment fraction mostly governed by the internal organ motion. The set-up displacement is the difference between the intended and actual treatment position. Both deviations

consist of a systematic and a random error component. The systematic errors are mainly introduced during the preparatory stages of radiotherapy and are considered to influence each treatment fraction in the same way and thereby causing a shift in the dose distribution while the random errors are day-to-day displacements that will cause a blur in the dose distribution (Marcel van Herk, 2000). By using image guided radiation therapy, IGRT, techniques including 2D-2D kilo voltage acquired x-ray images, the patient can be positioned before the delivery of every treatment fraction by online matching techniques. The table shifts required to place the patient in the correct treatment position is registered and has in this thesis been used for determining the magnitude of the interfractional systematic and random error in form of a patient population. The intrafractional error is mainly caused by the internal organ motion and its magnitude can be calculated by the root mean square value of the standard deviation of error occurring in patients.

Different treatments areas experience different amount of movement due to internal organ motion and immobilization techniques used. These factors in addition to the IGRT technique and matching protocol used will influence the amount of movement that needs to be taken into account. Using daily online matching protocols when positioning the patients has become more common in the last couple of years. By positioning the patient before the delivery of each treatment fraction the interfractional systematic and random error can be reduced and the PTV margin will need to account primarily for the intrafractional motion (Tony Greener, 2003). However, there are only a few treatments where daily online matching is used due to the large workload required during the course of treatment. In many situations different offline matching protocols are instead applied where only a number of fractions in the beginning of the treatment course are matched in order to correct for large interfractional systematic errors. The need to evaluate optimal PTV margins for each protocol is necessary since they each affect the positional accuracy differently.

The aim of the work is to evaluate what CTV-PTV margin is most suitable for prostate cancer treatments. The analysis will be done using stored portal image data from patients treated during the last couple of years at the department of radiotherapy treatment at Basvatarakam Indo American Cancer Hospital and Research Institute, Hyderabad where different online and offline matching protocols were used during the treatments.

Survey

Set-up displacements

Systematic error: The systematic error describes a constant deviation in the patient setup in a given direction during the entire treatment due to preparation errors that will cause a constant shift in the dose distribution (Marcel van Herk, 2000). This is illustrated in Figure 1.1. The systematic error is usually described and calculated in forms of a patient population and is considered to be composed of and summarized according to Equation 1 (Tony Greener, 2003).

$$\Sigma^2 = \Sigma^2_{motion} + \Sigma^2_{set-up} + \Sigma^2_{delineation} + \Sigma^2_{transfer} \quad (1)$$

The elements refer to the standard deviation, SD, of the individual errors of target motion and deformation, patient set-up, target delineation and image transfer. The target motion includes variations that occur in the position and shape during treatment that can be caused by bladder filling, weight loss and tumour regression. The set-up error includes all errors that are introduced during preparatory stages of treatment planning. Target delineation refers the errors caused by little knowledge of the actual extent of the CTV margin needed to account for microscopic spread. Image transfer error describes deviations that can arise when transporting images between different systems such as the treatment planning system and the linear accelerator. They are considered to be normally distributed and independent of each other allowing them to be summarised in quadrature (Marcel van Herk, 2000). The systematic error for a patient population can be determined according to Equation 2 (Marcel van Herk, 2004).

$$\Sigma^2_{pop} = \frac{\sum_n (\bar{x}_n)^2}{P-1} \quad (2)$$

In Equation 2, X_n is the mean value of the displacement in a given direction for patient in comparison to the initial position in the reference images acquired before the start of the treatment course and P is the number of patients in the population. The population systematic error is simply the standard deviation of all means.

Random error

The random errors describe the deviation between treatment fractions that can occur in any direction during the course of treatment and will give rise to a blur in the dose distribution.
The random error is defined according to Equation 3 (Tony Greener, 2003).

$$\sigma^2 = \sigma^2_{\text{motion}} + \sigma^2_{\text{set-up}} \quad (3)$$

In the equation the $(\sigma motion)^2$ is the SD of the random target motion and shape and $(\sigma set\text{-}up)^2$ is the SD of the random set-up error. For a population of patients the random error is defined as the root mean square of all standard deviations (Marcel van Herk, 2004). Random errors occur during the treatment and are therefore considered to be execution errors. Offline protocols cannot correct for random errors and the margin used must take that into account (Tony Greener, 2003). The random error for a population of patients can be calculated according to Equation 4 and 5 (Marcel van Herk, 2004).

$$\sigma^2_p = \frac{\sum_n (\Delta_n)^2}{N-1} \quad (4)$$

$$\sigma_{pop} = \sqrt{\frac{\sum_p \sigma^2_p}{P-1}} \quad (5)$$

In equation 4, Δ is the displacement of each fraction in a direction and N is the number of fractions for each patient and so σ_p is the individual SD of each patient in a direction. The equations can be used under the criteria that the number of analysed fractions is approximately the same for all patients.

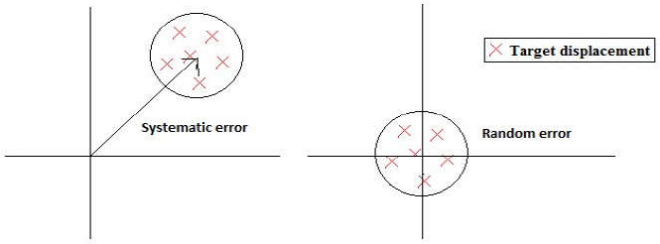

Figure 1. Illustration of the effect on the dose distribution due to systematic and random set-up displacements

Margin recipes

The relation in Equation 6 is one of the most known models for calculating PTV margins and it was derived by van Herk *et al*. (Marcel van Herk, 2000). With the prospect of giving a minimum cumulative CTV dose of at least 95% of the prescribed dose to 90% to the patient population they analytically derived a relation based on probability of dose distributions due to different geometrical deviations. No biological parameters were included and all parts of the CTV were considered equally important. The model has been developed with the set-up error, organ motion, penumbra effects and target delineation taken into consideration and it was derived using a spherical target with set-up deviations typical for prostate treatments. No rotational errors or shape deviations were considered.

$$PTV = 2.5\Sigma_{pop} + 0.7\sigma_{pop} \quad \text{.....(6)}$$

The recipe was later modified when a new study was conducted (Joep, 1990). The aim of the study was to develop a method for correct statistical evaluation of realistic treatment plans in terms of equivalent uniform dose, EUD, and tumour control probability, TCP, when different systematic and random errors are present. Based on the results from several simulations of a prostate plan with a variety of geometric errors a PTV margin was derived guaranteeing to give 90% of the patients a EUD of at least 98% but with no rotational errors taken into account. The recipe corresponds accurately with 1% TCP population loss for prostate plans with clinically reasonable values of Σ_{pop} and σ_{pop}. The recipe states that the PTV margin should be calculated according to Equation 7.

$$PTV = 2.5\Sigma_{pop} + 0.7\sigma_{pop} - 3mm \quad \text{.....(7)}$$

A similar model recipe was designed by Stroom *et al*. (Joep, 1999) where the PTV margin relation in Equation 8 was develoed. The relation was designed with the prospect of giving a 95% dose to 99% of the CTV, and lung, cervix and prostate deviation data was used for validation testing. The effect of random deviations was simulated by a convolution of the dose distribution with the distributions of movements in three dimensions while the consequences of the systematic errors on the dose distribution were calculated with the help of dose probability histograms, DPH. The DPH represents the average dose volume histogram for all systematic deviations in the patient group. The model does not include penumbra effects but it does include shape deviations and rotational effects.

$$PTV = 2\Sigma_{pop} + 0.7\sigma_{pop} \quad (8)$$

MATERIALS AND METHODS

Image acquisition and matching procedures

Before the start of a radiation treatment series of computed tomography, CT, images are acquired and used for tumour delineation and dose planning. Small tattoos are placed on the patient defining the position on the examination table during the CT acquisition. During the dose planning stage the isocenter coordinates relative to the tattoo is stated. Before the delivery of the first treatment fraction the patient is placed on the table by aligning the room lasers to the tattoos and the table is moved according to the coordinates that corresponds to the isocenter. New skin markers defining the position of the isocenter are outlined on the patient and in most treatments the patient is placed on the table top directly in that position for the remaining fractions. Thereafter, matching procedures using portal images are often used in order to more accurately place the patient in the correct treatment position.

The CT acquired image series are also used for creating the reference images needed for image matching. These reference images are created using the "external beam planning" application provided by Varian Medical Systems Incorporated. There are two types of reference images used at Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Digitally Reconstructed Radiographs (DRR) and Cone Beam Computed Tomography (CBCT) images.

The portal images used for matching are acquired using the onboard imaging system, OBI, provided by Varian Medical Systems. The OBI system is connected directly to the treatment unit by two extendable opposing arms, ExactArms, mounted orthogonally to the gantry. One of the arms contains the actual x-ray source and the opposing the digital amorphous silicon flat panel x- ray detector. The OBI system enables the use of 1D and 2D kilo voltage, kV, acquisition, 3D cone beam computed tomography, CBCT, and fluoroscopic imaging. The kV image and CBCT applications are used for correcting interfractional errors and intrafractional errors.

There are two types of matching procedures used, online and offline matching. Online matching is performed by the personnel at the treatment unit before the delivery of a treatment fraction and offline matching is performed post treatment using saved image data. The online matching is executed using the OBI application provided by Varian Medical Systems. The acquired image is automatically overlaid on the reference image with the isocenter of the acquired image placed on top of the isocenter of the DRR. The matching can be performed either manually or automatically. The manual matching is performed by dragging the reference image until the matching structures are correctly aligned with the matching structures of the acquired image.

Once the matching is executed the difference between the isocenter of the acquired image and reference image will be automatically registered in the software. Registrations are done in the vertical, longitudinal, lateral and rotational direction. The shift data will automatically be transferred to the linear accelerator and applied to the couch coordinates causing the table to move to the right treatment position. In order to enhance different structures in the images the OBI application enables the use of different window settings and filters. The automatic matching incorporate algorithms that automatically match different areas of the reference image to the acquired image. A region-of-interest, ROI, is placed around an anatomical landmark on the acquired image and the pixel values of the ROI are used for finding the corresponding structures on the reference images. After the matching is completed the shifts are registered and applied in the same way as for the manual matching. The image data used for the online matching is saved and can be used for offline matching and verification in the "Offline Review" application provided by Varian Medical Systems incorporated (Figure 3.1).

Matching structures

At Basavatarakam Indo American Hospital matching structures are usually drawn manually onto the DRR by an oncologist before the start of a treatment course, these help the RT technicians at the treatment units to more easily and efficiently execute the matching procedure (Figure 2).

Method of study

In order to evaluate the PTV margins needed for different matching protocols used in prostate treatments, data from patients treated for prostate cancer during the period of 2013-2015 at the department were used. The patients were all positioned with 2D-2D kV images and online matching was performed before the delivery of each fraction throughout the course of treatment and all table corrections were registered. All patients were treated in a supine position and fixated with an individual vacuum cushion.

Figure 1. Working environment of Offline Review

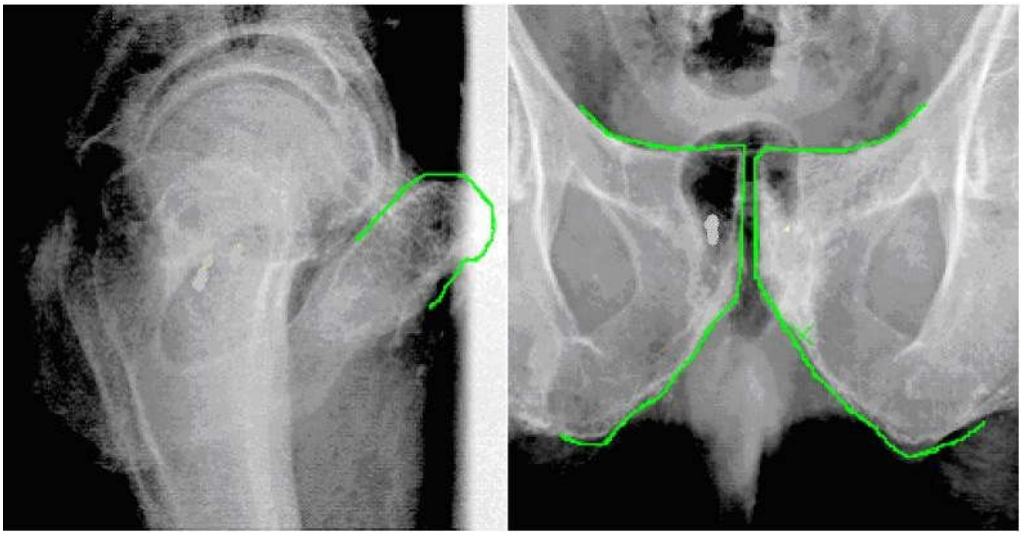

Figure 2. Typical matching structures for a prostate treatment

This study was performed on 29 patients in whom 15 patients analysed with CBCT and 14 patients with DRR verification. All patients were treated with IGRT or IMRT in Varian Novalis Tx with Rapid Arc linear accelerator. The data from the matching of the bony anatomy was used for estimating the systematic error and random error. Matching was done either CBCT or DRR image matching of bony anatomy. In this analysis, the delineation of the CTV was considered to be correct and transfer errors were considered to be negligible. Matching data of the Phase I plan only considered for study. The PTV margin was determined according to the van Herk model seen in Equation (6).

RESULTS

A total of 29 prostate cancer patients were used for the analysis and the number of imaged fractions vary from 15-20 per patient adding up to a total of 415 imaged fractions.

CBCT matching protocol

The range of table correction values forVertical, Longitudinal and Lateral directions are plotted. Daily table correction error in vertical direction varies from 0.8 cm to -1.0 cm (Figure1). Lateral table correction values ranged from 2.0 cm to -1.5 cm (Figure 4.2). Range of table correction in longitudinal direction was the highest among three directions. It ranges from +3.0cm to - 3.5cm (Figure 4.3). The data from shifts registered for the online matching of the CBCT images showed that the largest shifts occur in the lateral and longitudinal direction. In Table 4.1 the population mean shift, systematic and random error can be seen. The PTV margin is calculated in each case.

Table 4.1. Population mean systematic and random errors and corresponding PTV margins for the CBCT matching data from 15 patients adding up to 220 fractions

Cbct Matching Data In Cm			
	Vertical (AP)	Longitudinal (SI)	Lateral (RL)
Mean error	0.0637	-0.2781	0.1037
Systematic error,∑	0.1137	0.6135	0.2689
Random error, ϭ	0.2111	0.7011	0.2648
Margin	0.4321	2.0245	0.8577

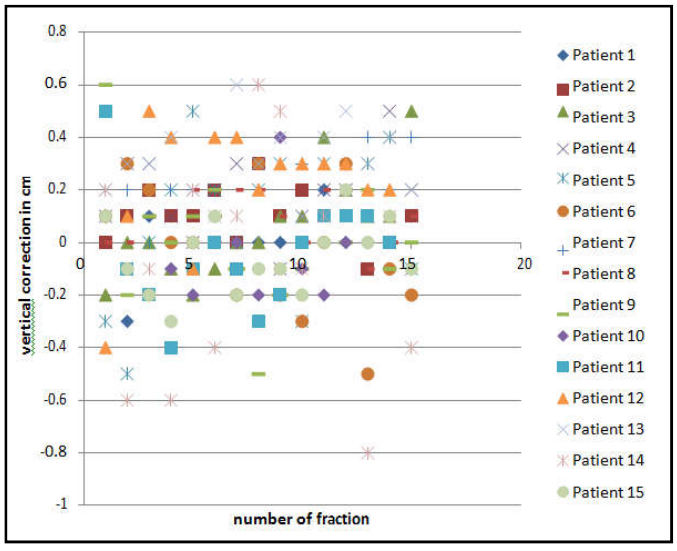

Figure 4.1 Plot of vertical table correction versus number of fraction

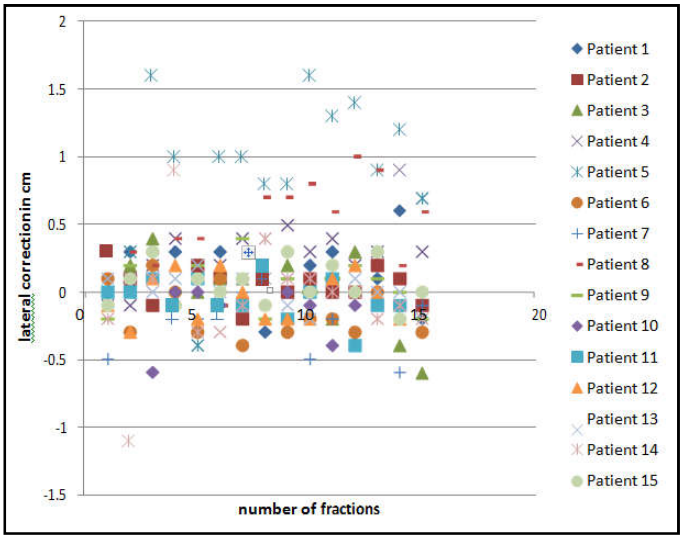

Figure 4.2 Plot of lateral table correction versus number of fraction

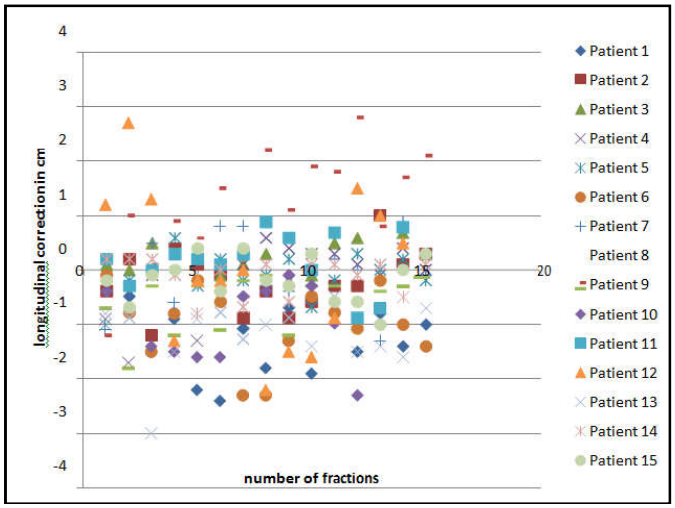

Figure 4.3 Plot of longitudinal table correction versus number of fraction

DRR matching protocol

The range of table correction values for vertical, longitudinal and lateral directions are plotted. Daily table correction error in vertical direction varies from 1.0 cm to -0.6 cm (Figure 4.4). Lateral table correction values ranged from 1.0 cm to -1.5 cm (Figure 4.5). Range of table correction in longitudinal direction was the highest among three directions. It ranges from +3.0cm to -2.3cm (Figure 4.6). The data from shifts registered for the online matching of the DRR images showed that the largest shifts occur in the lateral and longitudinal directions. In table 4.2 the population mean shift, systematic and random error can be seen. The PTV margin is calculated in each case.

Table 4. 2. Population mean systematic and random errors and corresponding PTV margins for the CBCT matching data from 14 patients adding up to 195 fractions

Drr Matching data in cm			
	Vertical (AP)	Longitudinal (SI)	Lateral (RL)
Mean error	0.141	-0.093	-0.0544
Systematic error,∑	0.1966	0.5832	0.2404
Random error, ϭ	0.1946	0.6191	0.2135
Margin	0.6277	1.8914	0.7505

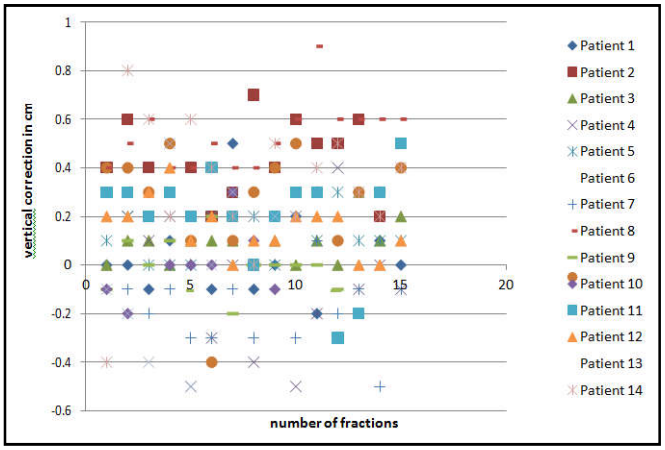

Figure 4.4. Plot of vertical table correction versus number of fraction

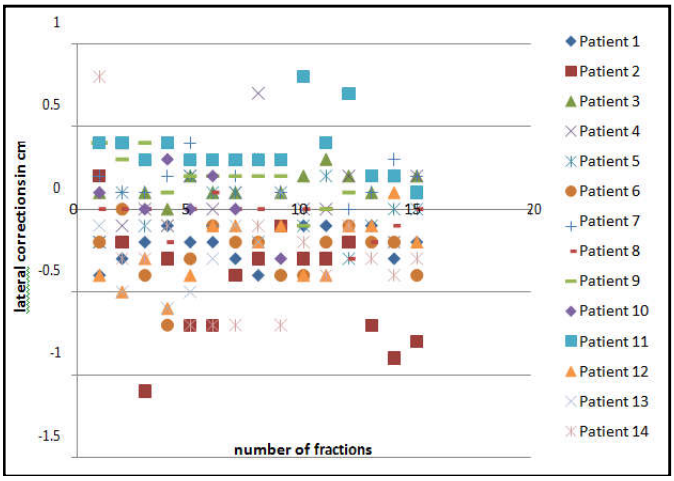

Figure 4.5. Plot of lateral table correction versus number of fractions

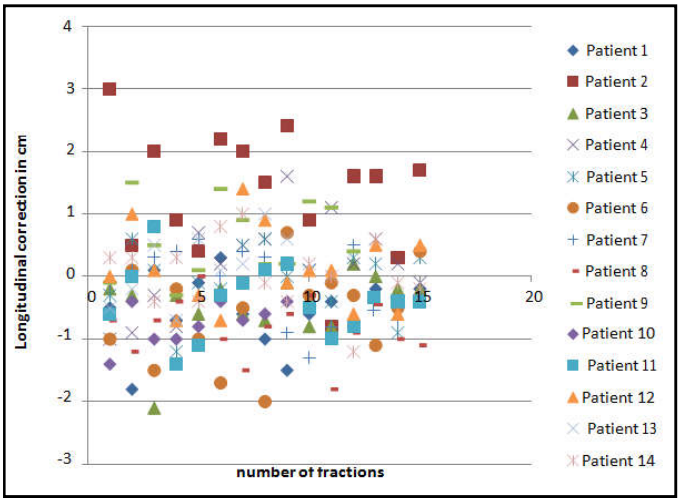

Figure 4.6. Plot of longitudinal table correction versus number of fraction

Optimal margins between CTV and PTV can be compared from different protocols (Table 4.3). In vertical direction margin required is 0.4321 cm from CBCT matching protocol and 0.6277 cm from DRR matching protocol. Margin required in longitudinal direction shows highest value in the both protocols. It is 2.0245 cm in CBCT matching protocol whereas 1.8914 cm in DRR matching protocol. Margin required in lateral direction is having an intermediate value of 0.8577 cm in CBCT matching and 0.7505 cm in DRR matching protocols. CBCT matching protocols shows slightly increased margin value in vertical direction than DRR matching protocol. But in longitudinal and lateral directions, DRR matching protocol shows a slightly increased value than in CBCT matching protocol.

Table 4.3. Comparison of PTV margins required in CBCT and DRR matching protocols

Margins Required for ptv in cm			
	Vertical (AP)	Longitudinal (SI)	Lateral (RL)
CBCT matching	0.4321	2.0245	0.8577
DRR matching	0.6277	1.8914	0.7505

Conclusion

Accurate tumour localization and verification is essential in IMRT and IGRT. CBCT and DRR image matching are the good tools for highly these highly conformal techniques. Because of low kV X-rays (40-150 kVp) are used in Kv-CBCT, the images shown reasonably good soft tissue contrast, with good quality bone matching which was helpful in verifying or delineating gross tumour volume. Results show that there is no considerable difference in the margin values evaluated from DRR matching protocol and CBCT matching protocol. This happens because both protocols depend on the matching of bony anatomy. Larger shifts occurring in longitudinal direction can be attributed to immobilization. The immobilization used in the hospital does not have foot holder or indexer support. In addition, no rotational or deformation error were taken into account since the image data was insufficient for executing such an analysis. Especially the rotational errors should be investigated since there might be considerable deviations due to rotation in the cases like prostate cancer.

Also, in the prostate evaluation no attention was paid to movement of the seminal vesicles. Studies have shown that they often move independently to the prostate and should perhaps therefore be included in the PTV margin evaluation since they often are included in the target, CTV. Based on ICRU suggestions and recommendations, the minimum PTV margin given to prostate cases in the institute is 0.5 cm in all directions. The observed table correction values pointed out that the PTV margins used in the institute is inadequate to provide sufficient coverage of tumour volume, setup uncertainties and internal organ motion in Prostate cancer cases.

REFERENCES

Dilshad Kottuparamban, L Nithya, Manish Bhushan Pandey. Comparison of different image mathching modalities using cone beam CT for head and neck, chest and pelvic cases. *Journal of Medical Physics* 2014, vol.39 389-390.

ICRU report 50. International Commission on Radiation Units and Measurements ICRU Report 50. Prescribing, recording, and reporting photon beam therapy. Bethesda, MD: ICRU; 1993.

James A Purdy, Jeff M. Michalski, Jeffrey Bradley, Srinivasan Vijayakumar, Carlos A. Perez, Seymour H. Lewitt. Technical basis of Radiation Therapy: Three

Dimensional Treatment Planning and Conformal Therapy. *Medical Radiology* 2006, 1: 179-202.

Joep C. Stroom, Hans C.J. Boer, Henk Huizenga, Andries G. Visser. Inclusion of geometrical uncertainties in radiotherapy treatment planning by means of coverage probability. *Int.J.Radiation Oncology Biol.Phys*. 1999, 43:905-919.

Marcel van Herk, Peter Remeijer, Joos V Lebesque, Inclusion of geometric uncertainties in treatment plan evaluation. *Int.J.Radiation Oncology Biol.Phys* 2002, 52:1407-1422.

Marcel van Herk, Peter Remeijer, Coen Rasch, Joos V. Lebesque. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. *Int.J.Radiation Oncology Biol.Phys*. 2000. 47:1121-1135.

Marcel van Herk. Errors and Margins in Radiotherapy. Seminars in Radiation Oncology 2004, 14:14:52-64.

Osama Dorgham, Mark Fisher. Performance of 2D/3D medical image registration using compressed volumetric data. *Medical Image Understanding and Analysis* 2008, July 2-3: pp. 261–265.

Tony Greener, Practical determination of systematic and random errors, Σset-up and σsetup using portal imaging. Geometric uncertainties in Radiotherapy. Prepared by a Working Party of The British Institute of Radiology 2003. Appendix 2c: 36-43.

****