Technical Note

Evaluation of the effect of random setup errors on dose delivery in Intensity Modulated Radiotherapy

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Abstract

Aim: To conduct a study on the effect of random setup errors inpatient for dose delivery in Intensity Modulated Radiotherapy plans using Octavius 4D phantom.

Materials and methods: 11 patients with cancer of H&N were selected for this study. An IMRT plan was created for each patient. The IMRT quality assurance plans were transferred to Mosaiq workstation in a linear accelerator. These plans were delivered at the reference treatment position. Subsequently, the QA plans were delivered on the Octavius 4D phantom after introducing errors in various translational and rotational directions. The setup inaccuracies introduced varied from 1 mm to 5 mm along X, Y. These setup uncertainties were then introduced along X and Y direction simultaneously in equal measures. Similarly, IMRT plans were delivered also after introducing roll and yaw rotation of 1, 2 and 3 degrees in phantom. The deviation of gamma indices at all these positions was analyzed with respect to the reference setup position.

Results: The percentage of points passing the gamma acceptance criterion decrease as we increase the setup error. The change is found to be very insignificant with setup error up to 2 mm along X, Y or XY direction. Similarly, the rotational error of up to 3 degrees is found to be acceptable.

Conclusions: Small setup (< 2 mm) correction in patients may not adversely affect the dose delivery. But an error of similar magnitude in 2 directions simultaneously has a much greater impact on IMRT dose delivery.

Key words: gamma indices; random setup error; IMRT; quality assurance; dose delivery.

Introduction

Setup error is used to describe the discrepancy between the intended and actual treatment position. It is determined relative to the isocentre, the field borders or both. It comprises of both systematic and random errors. Systematic errors can also be referred to as treatment preparation errors because once it enters the process, the systematic error will occur in each treatment fraction. Systematic errors may be introduced into patient treatment at localization, planning or treatment delivery phases. Its example can be patient movement during CT scan interobserver variability in contouring, jaw/MLCs in the wrong position or planning or treating the wrong site. The random component of any error is a deviation that can vary in direction and magnitude for each delivered treatment fraction. They occur at the treatment delivery stage and for that reason are often referred to as daily execution errors. Their examples can be internal or external daily variable movement, misinterpreting set up instructions, poor immobilization of patients, etc.

Intensity Modulated Radiotherapy (IMRT) is a radiation therapy technique that is used to avoid sensitive tissue close to a tumor site. Different techniques of IMRT like dynamic MLC method and segmented MLC method use a multi-leaf collimator to modulate the intensity of radiation. The segmented MLC method also called step and shoot uses segments. Volumetric-modulated arc therapy (VMAT) is another technique to deliver a conformal dose to the target in which a cone-beam continuously rotates around the patient. During each rotation, the cone beam is continuously shaped (or modulated) by a multi-leaf collimator. Besides, the dose rate or gantry speed is also optimized to generate highly conformal dose distribution.

The quality assurance (QA) of IMRT plans [1] is an essential part of medical physicist duty. One of the general metrics for evaluating calculation accuracy of a TPS is the gamma index which provides quantitative QA information. In gamma analysis, the essential component is dose differences (ΔD) and the distance to agreement (Δd). The dose differences are
the percent difference between the measured and calculated doses, point by point, which can be calculated subtraction of the two-dose distributions. This is shown as a percent deviation from the reference dose, which in this case is measured dose. To avoid erroneous results from the high dose gradient region, concept of DTA (distance-to-agreement) is used. DTA is the difference between the measured point and the nearest point in the calculated dose distribution with the same dose. Low et al. [2] suggested the gamma method which uses both dose difference criterion and the DTA.

Diego et al. [3] analyzed an individual segment of IMRT plans and found significant deviations in its absolute dosimetry. These discrepancies faded out when full treatment is considered and all segment doses are added together leading to overall deviations below a 5% action level. Various factors influence the result of IMRT quality assurance. Three treatment verification scenarios may lead to ionization chamber miss reporting namely, narrow beam irradiation, field penumbra location, and multileaf collimator transmission contribution. The analysis by using Monte Carlo (MC) simulation methods shows a relative contribution of each of the above 3 miss reporting scenarios. Kyeong Hyeon et al. [4] studied the influence of the IMRT set up error on 2D and 3D gamma evaluation method by using Monte Carlo simulation. The phantom alignment was found to be one of the factors which affect the outcome of IMRT quality assurance.

Christoph et al. [5] studied 6 patients to evaluate set up correction workflow. The patients included H&N, thorax and other cases. The maximum set up deviation was 3 mm for patients immobilized with body frame and 6 mm for patients positioned on a vacuum pillow. Su et al. [6] studied set up error in the treatment of nasopharyngeal carcinoma (NPC) using weekly CBCT. CBCT were obtained weekly for 30 patients undergoing IMRT. The pre-treatment kV CBCT scan was acquired using the Varian on-board imaging systems, a linear accelerator. This study suggested PTV margin of 3 mm, 1.2 ± 1.1) mm and (1.0 ± 0.9) mm respectively for H&N patients is acceptable when weekly CBCT was used. In Feng et al. [7] CBCT of 51 patients undergoing RT (H&N, thoracic and abdominal-pelvic tumors) were performed after initial set up, after repositioning and after treatment delivery. The interfraction setup errors on X, Y, and Z were (1.2 ± 0.9) mm, (1.2 ± 1.1) mm and (1.0 ± 0.9) mm respectively for H&N cases. Comparing with the post-correction position, the post-treatment setup errors in head and neck tumors increased significantly on all the axis (p < 0.05) whereas the difference was not significant in trunk tumors. After the online setup correction, the setup errors were reduced. Durin et al. [8] tried to investigate set up error and suggest an adequate PTV margin. 60 patients were included in the study. The mean set up error was < 2 mm in any direction. The range of translation shift was 0-9 mm in ML direction, 0-5 mm in SI direction and 0-10 mm in AP direction. After setup error correction, the adequate margin to overcome the problem of setup errors was found to be less than 3 mm.

Michael et al. [9] analyzed in detail the impact of daily setup variation on optimized IMRT canine nasal tumor treatment plan when variations are not accounted for lack of image verification or guidance. Due to setup variations, a loss of equivalent uniform dose (EUD) for target volumes of up to 5.6% was noted which corresponded to potential loss in TCP of 39.5%. Overdosing of brain and eyes were also reported. Xiang et al. [10] tried to investigate dosimetric changes of coverage when 6D setup errors were introduced. 6D set up errors were acquired with image registration tools for 10 patients of cervical cancer. Target coverage of PTV showed a significant decrease (3.3%) in set up errors introduced plans compared with original plans. This result indicated that CTV to PTV margin of 6 mm was sufficient to take into account 6D setup errors for most patients with cervical cancer. Theodore et al. [11] provided a detailed analysis of the potential impact of daily set up variations on the overall integrity of H&N IMRT. The errors of translational and angular setup for 10 H&N cancer patients obtained from high precision optically guided patient localization system, were applied to a distinct series of 10 H&N IMRT plans. The decrease in EUD for defined tumor volumes ranged from 21% when the largest offset histories were applied and 3-14% for plans when least and median offsets histories were applied. The adverse impact of daily set up variation was found to be considerably greater than recognized.

In this study, we have tried to determine the effect of setup uncertainties on the outcome of the IMRT plan. Setup errors can be translational as well as rotational. In the case of VMAT or IMRT delivery, a small error in patient positioning can cause a large difference in dose to the target and sparing of an oar. This study is a phantom study where the error introduced in phantom positioning were both rotational as well as translational. This study also analyses the difference in the effect of setup errors when it is along X or Y direction alone and also when it is along both X and Y simultaneously.
Materials and Methods

Eleven patients (Including 7 males and 4 females) who were supposed to undergo IMRT radiotherapy treatment were selected for this study. All 11 patients selected for this study were H&N cases. There was no age criterion for the randomly selected cases. All the 11 H&N patients were scanned with Siemens Somatom Definition Edge. These scanned images were transferred to the contouring station using DICOM. These images were then contoured by radiation oncologists delineating the target and normal structures. The CT images were then planned on Monaco TPS version 5.11.02. All the IMRT plans had 6 MV photon beams. The corresponding plans were delivered by Elekta Infinity LINAC. Elekta Infinity LINAC MLC comprises 40 pairs of leaves of 1 cm width at the isocentre. These plans were made as per the dose and OAR constraints are given by radiation oncologists.

QA plans were made for each plan. These QA plans were made for Octavius 729 phantom12. Octavius 4D system is an independent QA tool for pretreatment verification of radiotherapy treatment plans. The Octavius detector comprises of 729 detector air vented cubic ionization chambers uniformly arranged in 27 x 27 matrices with an active area of 27 cm x 27 cm. The ionization chamber is arranged in such a way that center-to-center distance is 1 cm and edge-to-edge distance is 0.5 cm. Detector volume is 0.5 cm x 0.5 cm x 0.5 cm with an effective point of measurement located at 0.75 cm below the surface of the array. It has dead time free readout and the arrays operate at chamber voltage of +1000 V. The gamma analysis was done with Octavius 4D system software Verisoft 4.2. IMRT plans were delivered to the Octavius 4D system. In the next step, the QA was performed with predefined errors in positioning of Octavius phantom on the couch. This study consist of 2 parts

1) The study on the effect of translational error and rotational error for dose delivery in patients using Octavius 4D phantom.

Translational Error

For the study of translational error in setup, three different errors were introduced and IMRT patient-specific quality assurance was performed. The correct position of the phantom was verified at the reference treatment position using CBCT image acquisition. The phantom was first displaced along positive X direction (Right-left) by 1 mm and then 1 mm more each time up to 5 mm. Similarly, the phantom was displaced along the positive Y direction (Cranio-caudal) by moving the couch in by 1 mm increment from 1 mm to 5 mm gradually. Subsequently, the error was introduced along X and Y direction simultaneously in equal amount i.e. error of (1,1) mm to (5,5) mm. These actions were then repeated for opposite direction i.e. negative X and negative Y. The directions concerning patient position are indicated in Figure 2.

At each of the 15 positions, we performed the QA by delivering the IMRT quality assurance plan generated in Monaco TPS. In addition to the QA performed at these 15 positions, it was also performed at the correct position of the phantom, to analyze the deviation with variation in setup error. By correct position we mean to imply that the phantom was placed at the isocentre without introducing any error.

Rotational Error

For the study on the effects of rotational setup error, the errors were introduced in the phantom positioning along two rotational axis one by one. One was by rotating the phantom along the axis of the cylinder and other by rotating the phantom perpendicular to the direction of the incident beam i.e. along Z-axis (Anterior-Posterior) with gantry at 0°. There is an inherent limitation in rotating phantom clockwise along Y-axis accurately by 1-degree increment and hence we tried to replicate the same scattering conditions by rotating the gantry in the counterclockwise direction by 1-degree increment from 1 to 3 degree while keeping the phantom at its original position. The IMRT QA plan was executed at all the 4 position which is G = 0°, 1°, 2° and 3° and analyzed. Next, the measurement was done by introducing the error in a rotational direction perpendicular to Z-axis. The IMRT QA plan is executed at these 3 positions i.e. at couch isocentre rotation of 1°, 2° and 3°. The obtained dose planes were compared to TPS generated dose planes using Verisoft 4.2.

The dose difference and distance to agreement criterion were 3%/3 mm in local mode with a cutoff value of pass rate equal to 95%. Each IMRT plan had 9 fields. The gamma evaluation was done for all the points and after the summation of all the fields. For dose values of less than 0.1 Gy increased tolerance of 5% dose difference was used. The doses below 5% of the maximum dose of the measured data set were suppressed. The CBCT correction data of these 11 patients were collected for further comparison with the results obtained from our analysis of the impact of a setup error. While our analysis of the impact of setup error comprised of rotational and translational errors the patient CBCT data were of translational error only.

Figure 2. Direction in which random Setup errors are introduced in Octavius Phantom. Y \(-\) Y is Cranio Caudal Direction, X \(-\) X is Left to Right Direction and Z \(-\) Z is Anterior to Posterior of the patient, when the patient is positioned in Feet first Supine position.
Results

Table 1 reports the average value and standard deviation of the gamma passing index for all the 11 VMAT QA plans at reference position as well as the values obtained by introducing error along translation direction X, Y and XY direction (Along both positive and negative X and Y direction). Table 2 reports the same after roll and yaw rotation. Table 3a and 3b tabulates the result of student t-test on gamma index obtained after introducing error in translational and rotational setup of the Octavius phantom. For student t-test, the hypothesis is that the two samples (sample here is referred to as gamma indices obtained with and without setup error) belong to the same population. The results are shown in Table 3. The critical value of t is $t > 2.042$ for $p < 0.05$ (for degrees of freedom 20). Hence the above hypothesis can be rejected with 95% confidence, i.e. in such cases, there is a significant change in the value of gamma indices.

The CBCT set up correction data of these 11 patients were collected. These data were translational. These data showed that the maximum set up error along X direction was 4 mm and along Y direction was 3.5 mm. The mean setup error was 0.31 mm and 0.16 mm along X and Y direction respectively.

Discussion

Several studies have been done to clinically implement kV CBCT for setup correction in RT. The shape and location of internal shift tissue structures at the time of treatment may deviate considerably for the CT scan acquired for treatment planning. A more rigid immobilization technique may not yield the desired results in such a case. Different approaches for 3D image acquisition like megavoltage CT and kilovoltage CT has been tested so far. This additional repositioning between CT scan and treatment adds more time to the overall problem. However, if the errors are up to a certain value it may have very little or no effect on IMRT dose delivery. These errors may be neglected or overlooked as they are dosimetrically irrelevant.

In this study, we have tried to evaluate the effect of random set up error introduced along with different directions. These errors included both rotational and translational errors. Cone-beam CT (CBCT) data of 11 patients showed that the maximum set up error along X direction was 4 mm and along Y direction was 3.5 mm. The mean setup error was 0.31 mm and 0.16 mm along X and Y direction respectively.

Table 1. Reading of gamma indices (average percentage & standard Deviation) for a shift in X, Y and XY averaged over all 11 patients.

| Shift in X direction (mm) | Average | Standard Deviation (d) |
|---------------------------|---------|-----------------------|
| 0                         | 97.46   | 1.22                  |
| 1                         | 96.96   | 1.56                  |
| 2                         | 95.99   | 1.61                  |
| 3                         | 94.65   | 2.21                  |
| 4                         | 92.97   | 2.82                  |
| 5                         | 89.82   | 3.01                  |

| Shift in Y direction (mm) | Average | Standard Deviation (d) |
|---------------------------|---------|-----------------------|
| 0                         | 97.63   | 1.05                  |
| 1                         | 97.34   | 0.96                  |
| 2                         | 96.78   | 1.61                  |
| 3                         | 95.98   | 2.78                  |
| 4                         | 94.32   | 5.03                  |
| 5                         | 92.12   | 7.26                  |

| Shift in XY direction (mm) | Average | Standard Deviation (d) |
|---------------------------|---------|-----------------------|
| 0                         | 97.63   | 1.05                  |
| 1                         | 96.75   | 1.57                  |
| 2                         | 96.01   | 1.44                  |
| 3                         | 90.89   | 4.97                  |
| 4                         | 85.56   | 9.26                  |
| 5                         | 79.96   | 9.15                  |

First column gives the value of shift. Second column gives the obtained value of gamma indices averaged over 11 patients for X, Y, XY direction. Third column gives the standard deviation of gamma indices for X, Y, XY direction.

Table 2. Reading of gamma indices (average percentage & standard Deviation) for roll and yaw rotation averaged over all 11 cases.

| Shift in mm | Average | Standard Deviation (d) |
|-------------|---------|-----------------------|
| 0           | 97.46   | 1.69                  |
| 1           | 96.90   | 2.15                  |
| 2           | 95.78   | 3.62                  |
| 3           | 94.65   | 4.99                  |

| Shift in mm | Average | Standard Deviation (d) |
|-------------|---------|-----------------------|
| 0           | 97.79   | 1.73                  |
| 1           | 96.49   | 3.62                  |
| 2           | 95.21   | 3.45                  |
| 3           | 93      | 5.32                  |

First column gives the value of rotational shift. Second column gives the value of gamma indices averaged over 11 patients for roll and yaw axis. Third column gives the standard deviation of gamma indices for roll and yaw axis.

Table 3a. Student t-test value for obtained gamma indices after translational shift of the phantom.

| Shift in mm | Student t Test value for shift along X direction | Y direction | XY direction |
|-------------|-----------------------------------------------|-------------|-------------|
| 1           | 0.54                                          | 0.76        | 0.98        |
| 2           | 1.54                                          | 0.75        | 1.72        |
| 3           | 2.36                                          | 1.18        | 2.82        |
| 4           | 3.10                                          | 1.37        | 2.75        |
| 5           | 5.00                                          | 1.59        | 4.09        |

Table 3b. Student t-test value for obtained gamma indices after rotational shift of the phantom.

| Rotation in degree | Student t Test value for shift along Roll Axis | Yaw Axis |
|-------------------|-----------------------------------------------|---------|
| 1                 | 0.44                                          | 0.69    |
| 2                 | 0.89                                          | 1.23    |
| 3                 | 1.13                                          | 1.82    |
From Table 1 we infer that the percentage of points above gamma passing rate decreases with an increase in shift of 1 mm along X, Y, and XY direction. However in most of the cases, for a shift of 1 mm these readings are not much different from reading at reference level and thus, pass the IMRT QA acceptance criterion which is 95%. The t-test value for the shift of 1 mm in X, Y and XY axis are 0.54, 0.76 and 0.98 respectively (Table 3a). This implies that the shift of 1 mm will not cause any significant change in the outcome of dose delivery. Similarly for a shift of 2 mm the value of student t-test coefficient is < 2.04 and well within acceptance criteria.

Thus we infer that the shift of 2 mm will not cause any significant change in dose delivery in a patient. But a shift of 3 mm along X-axis has an unacceptable consequence on dose delivery to the target as suggested by the Student t-test. The same may not be the case for Y-axis for a shift of 3 mm. A shift of 2 mm along XY direction has slightly more effect than shift along X-axis, but a shift of 3 mm in XY direction has an unacceptable impact on dose delivery.

In this study, we have tried to study the effect of rotation as well as translational error in setup. This study was done independently in each direction. These errors were also studied with setup errors along X and Y simultaneously. Several studies have been done in the past to measure the setup error through CBCT. But these studies [5-8] only measured the deviations in interfraction and intrafraction setup and the probability of their occurrence. Few literature positions [9-11] have also tried to analyze the effect of setup variation in various patient setup conditions. But the exact quantification of error i.e. its effect on delivery was not accounted separately along X, Y, and XY direction. This study also evaluates the effect of rotation on the delivery of IMRT plan.

Table 3b shows t values for gamma indices obtained after introducing rotational setup error. For a rotation of 1° along with roll and yaw direction readings recorded are not significantly different from reading measured at reference setup, as t value obtained is 0.43 and 0.66 respectively. Student t-value for rotation of 2° and 3° is < 2.04 and hence acceptable. Therefore rotational shift of 3° or less may not impact dose delivery to target drastically.

Studies have shown that variability in the setup has a role to play in the results of IMRT plan verification. Elizabeth et. al. [13] delivered six clinical patients IMRT QA plans to a variety of dosimeters, 3 times sequentially without changing set up and then delivered 2 more times after breaking down and rebuilding the set up between each. This allowed for the investigation of the reproducibility of both delivery and the physical set up. This study showed that variability introduced from the set up was generally higher than the variability from redelivering the plans. The radiographic film showed the poorest reproducibility of the dosimeters investigated. All dosimetric devices demonstrated the reproducibility of less than 4% in their QA results for all plans, with an average reproducibility of less than 2%. Hence the current study also has the inherent limitation of reproducibility of dosimeters. A large number of new methods, techniques, and detector systems have been designed for patient-specific IMRT verification purposes which do not rely on the use of ionization chambers for assessment of absolute dose in IMRT fields. This study has an inherent limitation as gamma indices are not a representation of PTV coverage. The gamma evaluation method has been criticized for being less clinically intuitive and being sensitive to dose grid resolution.

Conclusion

The results demonstrate that the errors of up to 2 mm are having a very small impact along X or Y direction. The impact of the errors up to 2 mm, if introduced along X and Y direction simultaneously was also acceptable but slightly more as compared to the condition when errors were introduced only in one direction. Similarly, it is found that the impact of roll or yaw rotation up to 3 degrees is very less if the rotational error is along the roll axis. However, the gamma indices deviation indicated that the rotational error along the yaw axis will have slightly more implication in dose delivery to the target. Hence, similar setup uncertainties along different directions may have a variable impact on dose delivery to the target.

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