Lateral setup error analysis of dosimetric impact for nasopharynx carcinoma using intensity modulated radiotherapy treatment

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Abstract: Patients with nasopharyngeal carcinoma have been analyzed for lateral setup error. Systematic and randomized inter-fractional setup errors were evaluated in 48 patients with this case. Based on these errors, the margin was drawn from CTV to obtain the delineation of PTV structure, called PTV margin. MVCT system in tomotherapy has been used to get the number of error with four-degree direction setup. Moreover, the biggest error direction value was evaluated with in 6 patients and analyzed at D98 in each PTV and OARs. The result of PTV margin for the lateral, longitudinal, vertical, and rotation was 4.91 mm, 4.27 mm, 3.37 mm and 3.53 mm, respectively. According to the result of the PTV margin, a lateral direction showed the biggest value of error. So, achievable dose coverage of PTVs on the effect of the lateral shift were 87.04%, 60.19%, and 50% for 2, 4 and 6 mm, respectively. Furthermore, OAR dose in the right position is increasing with larger shift setup direction.

***Keywords**: dosimetric, laterally, MVCT, setup error*

1. Introduction

Nasopharyngeal carcinoma is one of the most common cancers in Southeast Asia, Nothern Africa, and Central Asia.[1,2] The target of the nasopharyngeal carcinoma is very close to the organ at risk (OAR) and the escalation doses of the different target in each area become a challenge for medical physics and oncologists to achieve a good treatment.[3] The effort to achieve a good conformity of the high dose on the tumor and also ensure that organs besides the target receive less radiation is done using an advanced technology. Intensity modulated radiation therapy (IMRT) as the mainstream advance radiation technology has been widely used in the clinic these recent years.[4] Moreover, IMRT can be employed to yield precise dose distributions that tightly conform to targets and reduce high doses to normal structures by generating steep dose gradients.

The clinical success at the delivered dose is also limited by the requirement of both motion management and reduction of inter-fractional setup error.[5] Because of these requirements, the dose difference between actual and planned dose of the target region and surrounding important normal tissues could differ significantly. As a result, setup error plays a key role in IMRT treatment.[6] The condition of the treatment setup such as sharp gradients, daily setup variations, and motion would increase the failure factor of radiotherapy purposes. The dosimetric effect of this condition has not been characterized yet.

The variation of setup error is important thing radiotherapy to get collection data during patient treatment. Systematic error and random error could be achieved from the variation of setup error.[7] In the practice, the full characterization of all geometrical uncertainties should lead to an objective determination of PTV margin.[8] The PTV margin is a geometric concept that accounts the intra-fraction motion, interfraction motion, and setup uncertainties.

Helical Tomotherapy is one of the advanced technologies to deliver the wanted radiation with IMRT technique.[9] This machine has a high energy photon which is designed not only for treatment but also for verification setup.[10] For the verification setup purpose, tomotherapy has four degrees of direction i.e. lateral, longitudinal, vertical, and rotational with megavoltage potential called Megavoltage Computed Tomography (MVCT) system. The MVCT can be used for visualization of tumoral or anatomical change during treatment and contraction of the actual dose received by the patient.[3] Although MVCT image has a lower contrast than Kilovoltage Computed Tomography (KVCT), their quality is sufficient for setup verification and tumor identification.[3,11]

In the real condition, the verification setup of patient treatment may generate the direction shift of laser from body landmark. This shift then becomes the data to create PTV margin of all direction. In this research, we analyzed the effect at PTV and OAR of the biggest value of direction shift to optimize tomotherapy treatment delivery. As a result, this study may generate the characterization of the specific dosimetric effect of tomotherapy machine.

2. Materials and methods

In this study, we analyzed systematic and random error calculation in the setup verification of 48 patients with nasopharyngeal carcinoma during 33 fractions. The random error (σ) is defined as the average of a standard deviation of the shift per patient along particular directions which can easily quantify systematic error (Σ) along those directions. The systematic component of the displacement represents the patient movement at the time during the entire course of treatment.[12] For each patient, dispersion around the systematic error was calculated to assess the random error. The relation formula of PTV margin between the systematic and random error is introduced by Stroom et al (2002), mathematically written as $M = 2\Sigma + 0.7\,\sigma$.[13] The setup variation was analyzed on four degrees of freedom (vertical, longitudinal, lateral, and rotation) direction of patients (Figure 1). ICRU 62 reported that PTV segment is divided into two distinct sub margins; the setup margin which accounts for uncertainties associated with patient setup and the internal margin which accounts for target motion.[14]

Simulation of nasopharyngeal carcinoma T2N0M0 stage was delineated on Rando phantom following the RTOG 0225 protocol.[15] IMRT plans for Rando and patients were generated using TomoPlan software. Each plan was evaluated by Dose Volume Histogram (DVH). Evaluation of DVH then followed ICRU 83 recommendation on the target and OARs.[16] Afterward, MVCT was performed to see the effect of setup error and then Plan Adaptive has been done to an evaluated dose of target PTV and OARs.

Pre-study in this research using Rando phantom with varied displacements such as 0.5, 0.8, 1, 1.5, 2, 3, 4, and 5 mm at the biggest setup error in Rando phantom. For real patient case, six patients were shifted 2, 4, and 6 mm on MVCT images to analyze the dosimetric effect because of the limitation of software which is the lateral movement of the patients can not under 2 mm. Moreover, the dosimetric impact due to the limited accuracy of the patient setup error was characterized. The lateral setup error was analyzed for dose coverage in the PTV and distribution of dose in the OAR, especially for serial organs. The achievable criteria for D98, D50, and D2 of PTV is 2% discrepancy and the OAR dose constraint used is from Emami.[17] The chosen OARs which are evaluated in this study are the right eye, left eye, right lens, left lens, right optic nerve, left optic nerve, brainstem, and spinal cord. The maximal dose constraint are 54 Gy for eye, optic nerve and chiasm, 10 Gy for lens, and 46 Gy for spinal cord.[18]

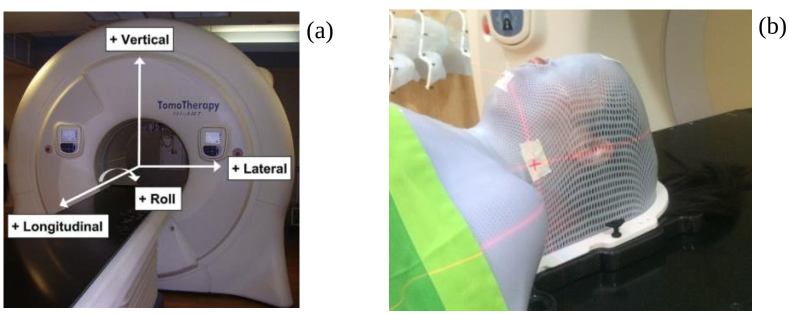

Figure 1. (a) Four degree of freedom of directions setup for patient treatment using tomotherapy and (b) immobilization devices (head and neck mask) that are used in our hospital

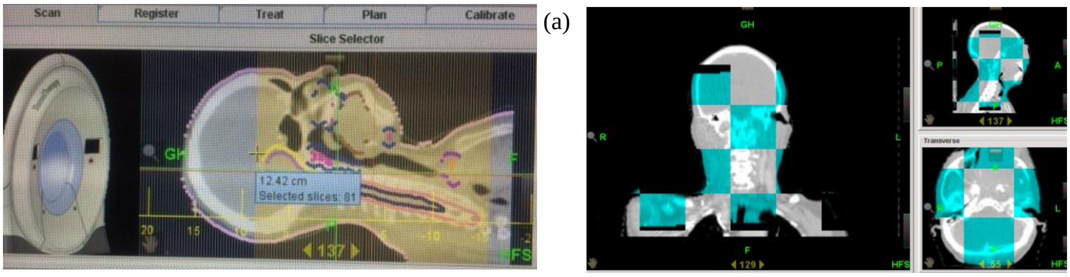

Figure 2. (a) scanning patient using MVCT, (b) verification setup for each patient

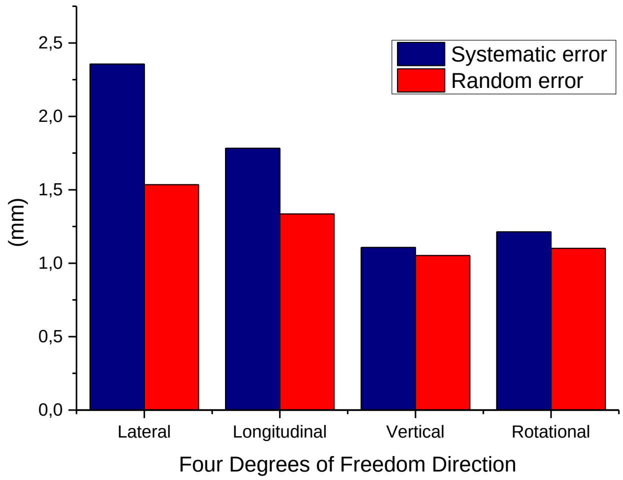

Figure 3. Systematic error and random error in each direction of 48 patients with nasopharyngeal carcinoma during 33 fractions

3. Results and discussion

The result of the systematic error and random error is shown in Figure 3, which resulted from highest and lowest value in the same directions for both errors. The highest value of the systematic and random error at lateral direction was 2.4 mm and 1.53 mm. Furthermore, the vertical direction had the lowest value of systematic and random error at 1.1 mm. Similar to the previous study by Kubicek (2012), we found that the lateral direction yielded the highest value of setup error.[19] Most probable patient movement occurred during treatment was in the lateral direction. Because of the result, characteristic dosimetry of lateral direction was evaluated.

Based on the result of Figure 3, PTV margin was shown in Table 1. This result can be used as the recommendation in our hospital, that the PTV margin has a different value for each direction, as the clinical application uses equal PTV margin value of each direction. It is expected to minimize the unwanted dose in normal tissue. The previous study by Thondykandy et al. (2012) recommended PTV margin of the Head and Neck case in the lateral, longitudinal, and vertical direction are 4.4 mm, 5 mm, and 3.5 mm, respectively, excluding the rotation direction.[12]

For the first evaluation, we used the Rando phantom. Figure 4 shows difference between the actual and planned dose of PTV. The lateral shift of more than 3 mm yields significant dose discrepancy, especially for D98. The dose coverage for each parameter of PTV mostly decreases with the larger shift of lateral direction. Even though, D98 on the PTV 60 Gy showed the highest discrepancy. This was due to the proximity of PTV60 to the normal tissue and had high dose gradient on the peripheral target.

Table 1. PTV Margins along four freedom directions in the tomotherapy

Directions	Four freedom direction (mm)			
	Lateral	Longitudinal	Vertical	Rotational
This study	4.91	4.27	3.37	3.53
Thondykandy et al (2015)	4.4	5	3.5	-

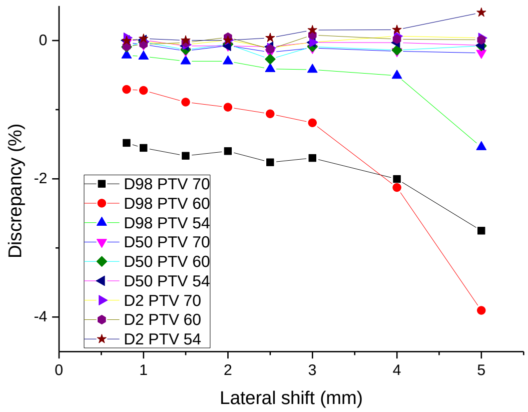

Figure 4. Deviation of volume coverage in the PTV using variation of lateral setup error in Rando phantom

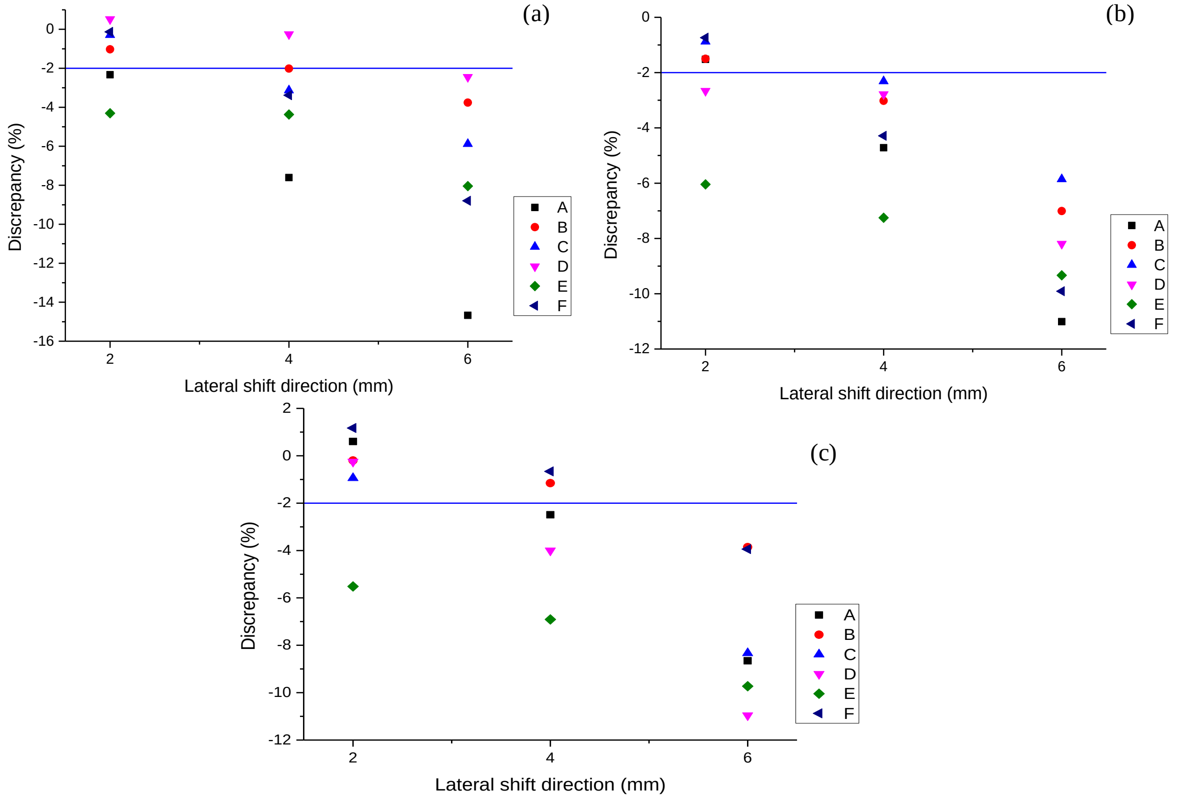

Figure 5. Dose discrepancies of D98 of (a) PTV 70, (b) PTV 60 and (c) PTV 54

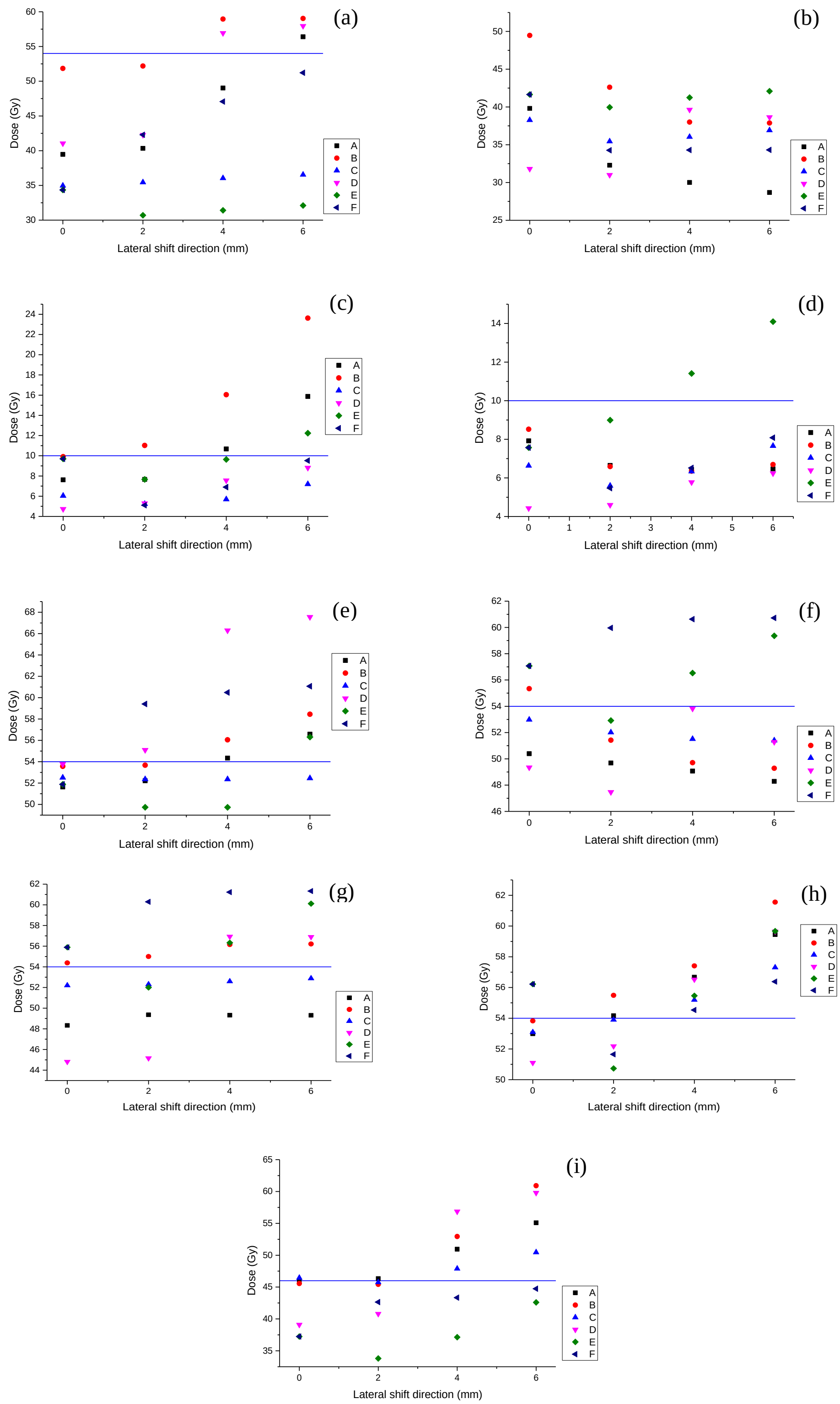

Figure 6. Value of maximal dose in the OARs effect shift lateral setup error of the (a) right eye, (b) left eye, (c) right lens, (d) left lens, (e) right optic nerve, (f) left optic nerve, (g) chiasm, (h) brainstem, and (i) spinal cord

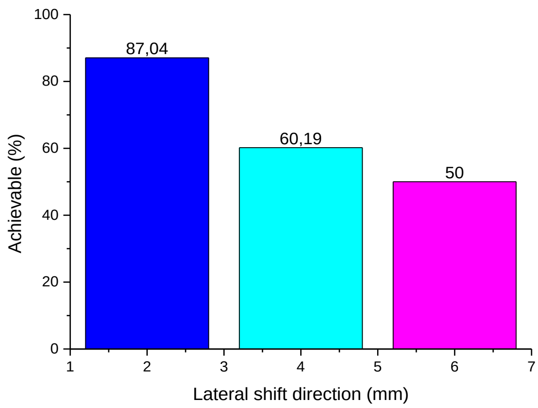

Figure 7. Achievable effect of lateral shift direction setup patients

Dose discrepancies for all PTVs D98 of patient treatment are shown in Figure 5. All of the PTVs obtain a decreased dose discrepancies of shift lateral direction. With lateral shift value 2 mm, resulting from the maximal dose discrepancies of 4%, 6%, 5%, of the PTV 70, 60 and 54, respectively. In 4 mm of the lateral shift, almost all dose discrepancies were not achieved with 2% parameter. However, in 6 mm lateral shift, the dose discrepancies where more than tolerance. It was up to 14.6%. So, the approximate achieved effect of the lateral shift direction until 2 mm.

Furthermore, we also analyzed the dose discrepancy of D50 and D2 in each PTV. Dose discrepancy at D50 had the highest value in PTV 70, 60 and 54, which were 0.79%, 1.4% and 1.84%, respectively. Then, each PTV had dose discrepancy at D2 from 0.14% - 4.3% at PTV 70, and 0.07% - 2.36% at PTV 60. Meanwhile, at PTV 54 it had 0.07% as the lowest value and 4.60% as the highest value. From these result, PTV 54 had the highest interval discrepancies due to the reason that the PTV 54 had the smallest volume compared to other PTV.

The result from dose difference of OAR from lateral shift direction effects is shown in Figure 6. For the right eye, the value of the safe boundary was 2 mm shift. However, the maximum dose value for a 6 mm shift of the eye was 59 Gy. For the left eye on all shifts, showed that the dose was still in the tolerance dose for eyes which is 54 Gy (Figure 6a,b). In the lens, the significant effect of the lateral shift can be seen from the dose difference. On the right and left lens, both had similar trend of dose results. For the right lens with 2 mm lateral shift, there was data above the tolerance of 10 Gy. Also for optic nerve, the lateral shift of 2 mm resulted in unsafe dose constraint with the maximum value of 59.4 Gy. For chiasm, brainstem and spinal cord, using lateral shift showed increasing dose with greater shifts. The average of 2 mm lateral shift yielded dose over the OAR's tolerance dose. The increase of lateral shift (+) direction in the OAR, increased the dose difference in OAR except for the left eye and left lens. The maximum dose of OAR still decreased along the increase of the lateral shift direction. Because the location of the left eye and left lens is further from the target PTV with the increase of the lateral shift. So, the dose of OAR will be lower than planning dose.Based on PTV and OARs, we evaluated the plan parameter evaluation which had 18 parameters for each patient. The evaluation of all patient treatment used IMRT technique in the tomotherapy. It resulted in a value of 87.04%, 60.19%, and 50% on evaluation for 2 mm, 4 mm, and 6 mm respectively. The increase of lateral shift on patient setup caused a decrease in the value of the achievable delivered dose. For IMRT technique, the peripheral PTV area has high dose gradient which becomes the reason that the effect of the shift is very important. This lateral shift can be used to minimize and evaluate dose delivery to the target and critical structures of the patient. That is why the lateral shift needs to be considered compared to the other direction. From this results, researchers suggest that patient setup should be accurate to decrease the uncertainty of the delivered dose and to ensure that the dose is not different with the planned dose.

4. Conclusion

In summary, the margin of PTV depends on the systematic and random error from the patient setup. The highest margin of the PTV in the nasopharyngeal carcinoma was the lateral setup with the value of 4.91 mm. The lateral shift direction of setup in patients affects the highest dose discrepancy at PTV D98. In addition, the position of OAR from the target is an important thing for plan evaluation parameter. The achievable value of plan evaluation parameter at lateral shift effects were 2, 4 and 6 mm with value 87.04 %, 60.19 %, and 50%, respectively.

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References

1. Adham, M. *et al.* Nasopharyngeal carcinoma in indonesia: Epidemiology, incidence, signs, and symptoms at presentation. *Chin. J. Cancer* **31,** 185–196 (2012).
2. Jemal, A., Bray, F. & Ferlay, J. Global Cancer Statistics: 2011. *CA Cancer J Clin* **49,** 1,33-64 (1999).
3. Gomez-Millan, J., Fernández, J. R. & Medina Carmona, J. A. Current status of IMRT in head and neck cancer. *Reports Pract. Oncol. Radiother.* **18,** 371–375 (2013).
4. Al., G. L. et. Effects of error on dose of target region and organs at risk in treating nasopharynx cancer with intensity modulated radiation therapy. *Pak J Med Sci* **32,** 95–100 (2016).
5. Deveau, M. a., GutiÉrrez, A. N., MacKie, T. R., TomÉ, W. a. & Forrest, L. J. Dosimetric impact of daily setup variations during treatment of canine nasal tumors using intensity-modulated radiation therapy. *Vet. Radiol. Ultrasound* **51,** 90–96 (2010).
6. Iebers, J. E. V. S., Eall, P. A. U. L. J. K., Iuwen, Q. W. U., Illiamson, J. E. F. W. & Llrich, R. U. K. S. C. Effect Of Patient Setup Errors On Simultaneously Integrated Boost Head And Neck IMRT Treatment Plans. *Int. J. Radiat. Oncol. Biol. Phys* **63,** 422–433 (2005).
7. Vaandering, A., Lee, J. A., Renard, L. & Grégoire, V. Evaluation of MVCT protocols for brain and head and neck tumor patients treated with helical tomotherapy. *Radiother. Oncol.* **93,** 50–56 (2009).
8. Erk, H., Emeijer, P. E. R., Asch, C. O. E. N. R. & Ebesque, J. O. O. S. V. L. The Probability Of Correct Target Dosage : Dose-Population Histograms For Deriving Treatment Margins In Radiotherapy. *Ini. J. Radiat. Oncol. Biol. Phys.* **47,** 1121–1135 (2000).
9. Welsh, J. S. *et al.* Helical tomotherapy: An innovative technology and approach to radiation therapy. *Technol. Cancer Res. Treat.* **1,** 311–316 (2002).
10. Sheng, K., Chow, J., Hunter, G., Larner, J. & Read, P. Is daily computed tomography image guidance necessary for nasal cavity and nasopharyngeal radiotherapy? An investigation based on helical tomotherapy. *J. Appl. Clin. Med. Phys.* **9,** 36–46 (2008).
11. Mackie, T. R. *et al.* Tomotherapy : A new concept for the delivery of dynamic conformal radiotherapy. **1709,** (2014).
12. Thondykandy, B. A. *et al.* Setup error analysis in helical tomotherapy based image ‑ guided radiation therapy treatments. 233–239 (2015). doi:10.4103/0971-6203.170796
13. Stroom, J. C. & Heijmen, B. J. M. Geometrical uncertainties, radiotherapy planning margins, and the ICRU-62 report. *Radiother. Oncol.* **64,** 75–83 (2002).
14. Ong, T. H. S. H. *et al.* The Impact Of Daily Setup Variations On Head-And-Neck Intensity-Modulated Radiation Therapy. *Ini. J. Radiat. Oncol. Biol. Phys.* **61,** 779–788 (2005).
15. Lee, N., Garden, A., Kramer, A. & Xia, P. A Phase II Study of Intensity Modulated Radiation Therapy (Imrt) +/- Chemotherapy for Nasopharyngeal Cancer. *Radiat. Ther. Oncol. Gr.* (2005).
16. DeLuca, P. M. & Seltzer, S. M. ICRU Report 83. *ICRU Rep. 83* **8,** 1–98 (2008).
17. B, D. E. Tolerance of Normal Tissue to Therapeutic Radiation. *Reports Radiother. Oncol.* **1,** (2013).
18. Gland, L. Normal Tissue Constraint Guidelines. 567–570
19. Ubicek, L. Y. N. K., Eo, S. O. S., Happell, R. I. J. C., Eraj, R. O. J. & Orrest, L. I. S. A. J. F. Helical Tomotherapy Setup Variations In Canine Nasal. *Vet Radio Ultrasound* **0,** 1–8 (2012).