Immobilisation precision in VMAT for oral cancer patients

M N Norfadilah1,2, R. Ahmad1, S P Heng3, K S Lam2, A B Ahmad Radzi2 and L S H John2

1Diagnostic and Radiotherapy Programme, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, 50300 Kuala Lumpur, Malaysia
2Radiotherapy Unit, Cancer Centre, Pantai Hospital Kuala Lumpur, 59100 Kuala Lumpur, Malaysia
3Cancer, Radiosurgery and Nuclear Medicine Centre, Sunway Medical Centre, 46150 Petaling Jaya, Selangor, Malaysia

E-mail: norfadilahmn@gmail.com

Abstract. A study was conducted to evaluate and quantify a precision of the interfraction setup with different immobilisation devices throughout the treatment time. Local setup accuracy was analysed for 8 oral cancer patients receiving radiotherapy; 4 with HeadFIX® mouthpiece moulded with wax (HFW) and 4 with 10 ml/cc syringe barrel (SYR). Each patients underwent Image Guided Radiotherapy (IGRT) with total of 209 cone-beam computed tomography (CBCT) data sets for position set up errors measurement. The setup variations in the mediolateral (ML), craniocaudal (CC), and anteroposterior (AP) dimensions were measured. Overall mean displacement (M), the population systematic (Σ) and random (σ) errors and the 3D vector length were calculated. Clinical target volume to planning target volume (CTV-PTV) margins were calculated according to the van Herk formula (2.5Σ+0.7σ). The M values for both group were < 1 mm and < 1° in all translational and rotational directions. This indicate there is no significant imprecision in the equipment (lasers) and during procedure. The interfraction translational 3 dimension vector for HFW and SYR were 1.93±0.66mm and 3.84±1.34mm, respectively. The interfraction average rotational error were 0.00°±0.65° and 0.34°±0.59°, respectively. CTV-PTV margins along the 3 translational axis (Right-Left, Superior-Inferior, Anterior-Posterior) calculated were 3.08, 2.22 and 0.81 mm for HFW and 3.76, 6.24 and 5.06 mm for SYR. The results of this study have demonstrated that HFW more precise in reproducing patient position compared to conventionally used SYR (p<0.001). All margin calculated did not exceed hospital protocol (5mm) except S-I and A-P axes using syringe. For this reason, a daily IGRT is highly recommended to improve the immobilisation precision.

1. Introduction

Novel radiotherapy technique Volumetric Modulated Arc Therapy (VMAT) allows superior conformal dose distribution to the treatment target volume within a short time interval. Thus, significant dose reduction to surrounding normal tissues can be achieved due to clinical target volume to planning target volume (CTV-PTV) margin was reduced for this advanced technique [1, 2]. However, this technique is frequently associated with a wide range of acute and chronic side effect complications causing local discomfort and pain.

The most common side effects of radiation therapy (RT) for oral cancer patients are dry mouth (xerostomia) and inflamed mucous membranes (mucositis) [3, 4]. Patients may have dental decay (caries) and death of bone tissue (osteoradionecrosis) resulting from poorly directed radiation during radiotherapy treatment due to setup uncertainties [5, 6]. Therefore, a study was conducted to identify and evaluate the ideal immobilisation device that can minimise setup uncertainties by maintaining the patient in the same position during the course of treatment. Thus, we comparing two immobilisation devices; syringe 10 ml (conventional approach) and customized HeadFIX® mouthpiece moulded with wax (a sub-device initially invented for stereotactic radiotherapy procedure).
2. Materials and methods

2.1 Patient selection
Ethical approval from research committee members of Universiti Kebangsaan Malaysia (JEPUKM) with ethic number NN-166-2014 and permission from management of Pantai Hospital Kuala Lumpur were granted for this study. Permission from patients and oncologists involved was consented after researcher explained risks and benefits of the research. Local setup accuracy was analysed for 8 oral cancer patients receiving radiotherapy. The patient that included in this study were consecutively assigned to one of the two immobilisation devices which were HeadFIX® mouthpiece moulded with wax (HFW) and 10 ml/cc syringe barrel (SYR). Inclusion criteria include patients with one type of oral cancer. Stages and types of the oral cancers are verified from histopathology and radiology reports. The patient was planned to receive radical radiotherapy treatment using VMAT technique and received a total dose of 60-70 Gy for 6-7 weeks. Patients who failed to finish the treatment as prescribed by the oncologist are excluded. Furthermore, patients who have excessive salivary secretion are also excluded as subjects because it will influence the immobilisation device setup. The characteristics of the patient are shown in Table 1.

| Characteristics               | No. of patients (%) |
|-------------------------------|---------------------|
| Patients (n)                  | 8                   |
| Men                           | 2 (25.0)            |
| Women                         | 6 (75.0)            |
| Age (y)                       |                     |
| Mean                          | 57                  |
| Range                         | 23-83               |
| Tumour location (n)           |                     |
| Hard Palate                   | 1 (12.5)            |
| Buccal Mucosa                 | 1 (12.5)            |
| Sublingual gland              | 1 (12.5)            |
| Submandibular gland           | 1 (12.5)            |
| Tongue                        | 4 (50.0)            |
| Medical History               |                     |
| Post-surgery                  | 2 (25.0)            |
| Concurrent chemotherapy       | 2 (25.0)            |
| Post-surgery & concurrent chemotherapy | 3 (37.5) |
| None                          | 1 (12.5)            |

2.2 Radiotherapy simulation
HFW was prepared and fabricated prior to simulation as shown in Figure 1. No special fabrication needed for SYR. Type-S thermoplastic mask of head-neck-shoulder was used to maintain head, neck and shoulder’s patient during treatment. Then, the immobilisation device HFW or SYR was threaded through a small hole as the mask was placed over the head as Figure 1 (iii). CT scans with contrast media were obtained in 2 mm slice thickness using 16 slice Brilliance™ CT Big Bore (Philips, Netherlands). Coverage of the scan was from frontal sinus to carina. The reconstructed CT images were imported to Monaco treatment planning system version 3.20.02 for planning purposes.

2.3 Radiotherapy treatment planning
Clinical oncologist contoured the tumour volume and medical physicist contoured organ-at-risk (OAR) e.g. spinal cord, parotid glands, and brain stem. Generally, CTV encompasses the entire gross tumour
volume (GTV) with an additional margin of 5 mm. PTV was created with addition of 5 mm margin on CTV. The secondary target was the metastatic cancer at high-risk lymph nodes group around the neck area. PTV to this lymph nodes group was the CTV plus 3 mm margin. A lower dose was given to low-risk lymph nodes. Next, the optimisation and dose calculation of CT images was performed with Monte Carlo algorithm. Treatments were planned by medical physicists with 6 megavolt (MV) photon with two arch VMAT technique. This followed by quality assurance routine to ensure that the dosage was as planned. The treatment planning was considered successful when the target volume dose of treatment exceeds 95% of the prescription dose.

2.4 Cone-Beam Computed Tomography (CBCT) volume acquisition
After radiotherapy planning has been approved, patients will be scheduled for radiotherapy treatment. On each treatment day, patients were positioned on the radiotherapy couch in supine position and instructed to lie motionless in their respective fixation. Prior to radiotherapy treatment, image guided radiotherapy (IGRT) was performed using CBCT scanner integrated with Eleka Synergy linear accelerator (Elekta, Crawley, UK). The parameters used were 100 kVp, 10 mA and 10 ms for nominal frame, collimator and filter F0 was S20. One full rotation of the head and neck cases was about 200 degrees starting from an angle of 100° to 250°. Approximately 361 projections been done. These projections were undergone reconstruction process to form a three-dimensional (3D) image in medium resolution. CBCT scanning was done by using a volumetric imaging system kV X-rays (XVI, Eleka Ltd., Crawley, UK). This process takes about two minutes. CBCT images were processed and displayed in coronal, sagittal and axial dimension.

2.5 Images registration
Registration of the images from treatment planning CT and acquired CBCT were processed by an automatic bone value algorithm. This was followed by manual adjustment based on target volume and bone near the PTV especially maxilla, mandible, and first until third cervical vertebrae [7]. Once the registration satisfied, the position of the treatment table was corrected based on the resulting position error. There were two categories of reading error; translational and rotational errors. Translational errors represent the position of the subject in three degrees of freedom (3 DoF); lateral (left-right), longitudinal (superior-inferior) and vertical (anterior-posterior). Whereas, rotational errors represent roll, yaw and pitch position. The ability of adjustment in translational and rotational errors in simultaneously means the system capable to correct errors in 6 DoF. The image registration process must be done carefully so that the radiation dose could be delivered as per prescribed.

2.6 Statistical analysis
Each position setup error measurement represents the total variation in patient positioning for the treatment session. The mean value (M), standard deviation, systematic (Σ) and random (σ) errors of all translational and rotational errors were calculated and compared for these 2 different immobilisation devices. CTV-PTV margin was calculated according to the formula PTV=2.5Σ+0.7σ [8]. A three-dimensional (3D) vector was calculated using the following formula: \( v = \sqrt{(x^2 + y^2 + z^2)} \). The hypothesis of a normal distribution was rejected for the majority of variables. Hence, the Mann-Whitney U test was used to determine if there was a significant difference between HFW and SYR results. All p-values were calculated with two-tailed tests, and statistical significance was defined as p< 0.001 with IBM SPSS statistic version 23.

3. Results
A total of 209 CBCT images were acquired and analysed from the 8 oral cancer patients; 120 for HFW and 89 for SYR.
3.1 Setup accuracy and reproductibility between immobilisation devices

Table 2 summarizes the isocentric setup variations for oral cancer patients HFM and SYR. The M values for both group were <1 mm and <1° in all translational and rotational directions. This indicate there is no significant imprecision in the equipment (lasers) and during procedure [9]. Figure 2 shows percentage distribution of setup errors in all 6DoF for HFW (represented in areas) and SYR (represented in line). All error toward zero value, referred as minimum error. If the number away from zero neither positive nor negative values, it means the error become bigger. Setup error in HFM was statistically significant lower than SYR for A-P, pitch and yaw directions with \( p<0.001 \). Meanwhile, SYR significantly \( (p<0.001) \) shows lower setup errors in R-L direction.

From Table 2, HFW has lower values (<1 mm) of systematic errors in all translational and in yaw directions (<1°) compared to SYR. In contrast, SYR only shows lower values (<1°) of systematic errors in all rotational directions. All random errors values in translational and rotational directions were lower in HFM compared to SYR.

In addition, comparative analysis for interfraction 3D vector and average rotational error reveal that there was a significant difference \( (p<0.001) \) in setup accuracy between the two immobilisation devices studied. By referring Table 3, the interfraction translational 3D vector for HFW and SYR were 1.93±0.66mm and 3.84±1.34mm, respectively. The interfraction average rotational errors were 0.00°±0.65° and 0.34°±0.59°, respectively.

### Table 2. Summary of the isocentric setup variations for oral cancer patients HFM and SYR.

| Immobilisation devices | HFW                      | SYR                      |
|------------------------|--------------------------|--------------------------|
| **Translational errors (mm)** | Min | Max | M | σ | Min | Max | M | σ |
| R-L                    | -2.10 | 3.20 | 0.53 | 0.99 | 0.87 | 3.08 | 2.22 | 1.12 |
| S-I                    | -2.30 | 3.40 | -0.12 | 0.64 | 0.87 | 2.22 | 0.87 | 1.09 |
| A-P                    | -3.00 | 2.00 | -0.76 | 0.09 | 0.85 | 1.47 | 0.85 | 1.47 |
| R-L                    | -4.50 | 2.70 | -0.48 | 1.09 | 1.47 | 3.76 | 2.87 | 2.87 |
| S-I                    | -5.20 | 8.90 | 0.31 | 1.70 | 2.87 | 6.24 | 5.06 | 5.06 |
| A-P                    | -6.20 | 4.50 | 0.18 | 1.52 | 2.86 | 5.06 | 5.06 | 5.06 |
| **CTV-PTV margin (mm)** | Pitch | Roll | Yaw | Pitch | Roll | Yaw |
| Min                    | -2.50 | -2.20 | -1.50 | -1.40 | -3.00 | -1.90 |
| Max                    | 2.90 | 2.80 | 1.40 | 3.30 | 2.70 | 3.00 |
| M                      | -0.13 | 0.12 | 0.01 | 0.32 | 0.10 | 0.41 |
| σ                      | 1.12 | 1.09 | 0.39 | 0.60 | 0.51 | 0.43 |
| σ                      | 0.51 | 0.64 | 0.49 | 0.62 | 0.89 | 0.75 |

**Abbreviations**: R-L=right-left; A-P=anterior-posterior; S-I=superior-inferior; Min=minimum, Max=maximum, M=mean setup errors, \( \Sigma \)=systematic error; \( \sigma \)=population random errors; CTV-PTV= clinical target volume-planning target volume.

### Table 3. 3D vector, and average rotational error for 2 different immobilisation device.

| Immobilisation device | Min | Max | Mean | SD | Min | Max | Mean | SD |
|-----------------------|-----|-----|------|----|-----|-----|------|----|
| HFM                   | 0.51 | 3.86 | 1.93 | 0.66 | -1.17 | 2.17 | 0.00 | 0.65 |
| SYR                   | 1.14 | 9.08 | 3.84 | 1.34 | -1.10 | 2.60 | 0.34 | 0.59 |

3.2 CTV-PTV margins

The margins calculated for each axis using the two immobilisation device were also shown in Table 2. For the HFW, the margin calculated in R-L axis was the largest (3.08 mm), while the A-P axis was the smallest (0.81 mm). However, for SYR, the margin calculated in R-L axis was the smallest (3.76 mm) and the S-I axis had the largest margin (6.24 mm).
4. Discussion

It has been widely observed that immobilisation devices are important in positioning reproducibility. In this study, the relative impact of HFW and SYR on the reproducibility during oral cancer radiotherapy was evaluated by using CBCT images. CBCT images provide an on-line 3D patient positioning assessments precision in sub-millimetre [9]. In order to evaluate the precision of the interfraction setup for immobilisation devices throughout the treatment time, population random and systematic errors must be determined. Systematic errors that occur in the same magnitude and direction each fraction throughout the treatment course was identified and minimised using image guided correction for every patient. During this study, systematic errors may be introduced during a patient’s treatment at the localisation, planning or treatment delivery phases. Meanwhile, random errors were influenced by patient compliance, department protocols and the immobilisation system itself [10].

HFW shows small values in overall of systematic and random errors described higher reproducibility of the treatment preparation performed compared to SYR. Thus, it improves setup accuracy and reduces PTV movement. With higher precision of customized immobilisation device, it could minimise the adverse effects of radiation especially oral mucositis [11,12,13]. It also increased the distance between the maxilla and mandible, focusing the radiation dose more precisely on the target volume (dosimetry) and immobilising the mandible [13,14,15].

Besides that, all margin calculated did not exceed hospital protocol (5mm) except S-I and A-P axes using SYR. However, since the VMAT treatment plans generated by steep dose gradients between PTV and OAR, the precise targeting and delivering of radiation therapy on a daily basis is imperative. Therefore, in some special situations, such as re-irradiation or the close proximity of OAR with high-dose regions and lower (i.e., 3 mm) margins could benefit from daily image guidance correction.

Figure 2. Percentage distribution of setup errors for HFW (120 CBCT images) and SYR patients (89 CBCT images) in right-left, superior-inferior, anterior-posterior, pitch, roll and yaw directions.
5. Conclusion
HFW shows smaller position setup errors in overall isocentric shift indicates higher reproducibility and thus more precise than the SYR. Even though the value were smaller, but this errors can be furthered minimised by careful attention to immobilisation and patient preparation techniques.

6. References
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