

## PHYSICS CONTRIBUTION

# UNCERTAINTY IN TREATMENT OF HEAD-AND-NECK TUMORS BY USE OF INTRAORAL MOUTHPIECE AND EMBEDDED FIDUCIALS

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**Purpose:** To reduce setup error and intrafractional movement in head-and-neck treatment, a real-time tumor tracking radiotherapy (RTRT) system was used with the aid of gold markers implanted in a mouthpiece.

**Methods and Materials:** Three 2-mm gold markers were implanted into a mouthpiece that had been custom made for each patient before the treatment planning process. Setup errors in the conventional immobilization system using the shell (manual setup) and in the RTRT system (RTRT setup) were compared. Eight patients with pharyngeal tumors were enrolled.

**Results:** The systematic setup errors were 1.8, 1.6, and 1.1 mm in the manual setup and 0.2, 0.3, and 0.3 mm in the RTRT setup in right–left, craniocaudal, and AP directions, respectively. Statistically significant differences were observed with respect to the variances in setup error ( $p < 0.001$ ). The systematic and random intrafractional errors were maintained within the ranges of 0.2–0.6 mm and 1.0–2.0 mm, respectively. The rotational systematic and random intrafractional errors were estimated to be 2.2–3.2° and 1.5–1.6°, respectively.

**Conclusions:** The setup error and planning target volume margin can be significantly reduced using an RTRT system with a mouthpiece and three gold markers. © 2006 Elsevier Inc.

Radiotherapy, Setup error, Head and neck, Intensity-modulated radiotherapy.

## INTRODUCTION

Intensity-modulated radiotherapy (IMRT) for head-and-neck tumors requires a precise setup for the treatment of patients. Immobilization of the patients' head, neck, and upper thorax with thermoplastic materials has been used in IMRT (1). Attempts to improve the setup error and reduce intrafractional uncertainty have been made using offline or online corrections instead of conventional megavoltage or orthovoltage imaging in the treatment room with simulation film or digitally reconstructed radiography (2–7). However, errors due to the intrafractional motion of the patient cannot be reduced simply by taking the image before irradiation. Unintended swallowing of the saliva and/or unintentional motion of the neck, chin, and shoulders can induce significant changes in the anatomic relationships, even with use of an individual face mask during irradiation. Frequent monitoring of the patient and a method for the rapid adjustment of the

patient couch are required to overcome such problems in fractionated RT.

Adjustment of the patient couch by remote control after online portal imaging of bony structures was reported to be useful in the early 1990s (8). However, a substantial amount of time is required to make corrections, and this approach is prone to error owing to uncertainties in the calculation of tumor location on the basis of the bony structure (9).

To overcome these issues, fiducial markers near the tumor may be useful for the setup of patients using fluoroscopy and a remotely controlled patient couch. van Asselen *et al.* (10) have proposed implanting gold markers into the deep muscular compartments in the parapharyngeal region of head-and-neck cancer patients. This technique is quite attractive but may be vulnerable to marker migration resulting from inflammatory changes in the anatomy, as well as eventual tumor shrinkage.

We have developed a procedure that involves the implantation of three gold markers into a mouthpiece used for the

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setup and monitoring of the positioning of patients with head-and-neck cancer. Remotely controlled patient couches have been developed for rapid adjustments to the couch position. Precise setup using fiducial markers near the tumor and two sets of fluoroscopic images in a real-time tumor-tracking RT (RTRT) system have been shown to be useful for the treatment of prostate (11–13), lung (14), liver (15), uterus (16), and esophageal (17) cancers. The remote-controlled patient couch in the present study was connected to the RTRT system online, to avoid irradiation without correction of the alignment of the patient couch.

In this study, the accuracy of an entire system used to adjust the positioning of a tumor into the correct alignment was investigated in patients with head-and-neck cancers treated with IMRT at our institution.

## METHODS AND MATERIALS

### *Setup using fiducial markers and RTRT system*

The details of the use of the RTRT system (previously Mitsubishi Electronics, since changed to Varian ME, Tokyo, Japan) and the associated algorithm have been described in previous studies (18–21). In brief, three gold markers were identified by fluoroscopic real-time tracking, and their positions relative to the coordinates set in the treatment system were calculated. The coordinates of the markers were detected with an accuracy of  $\pm 1$  mm during RT in a phantom experiment (18–20). The mean discrepancies between the actual and calculated rotational errors were  $-0.1 \pm 0.5^\circ$  (mean  $\pm$  SD) in static phantoms (21).

The calculated absolute vector displacement of the isocenter was then corrected using a remotely controlled couch, which was commercially available in Japan between 2001 and 2003 (Varian ME). The controlling bar of the couch is on the same console of the linear accelerator, which is in the control room of the linear accelerator, not in the treatment room. The couch itself is the same as the conventional couch and is made of carbon fiber. This system renders it possible to change the position of the table in the lateral, vertical, and longitudinal directions with an accuracy of  $\pm 0.1$  mm of the specifications. Two operators are sufficient to perform this procedure. In this context, one operator, usually a radiotherapist, pushes a bar on the console that is similar to the control bar of a helicopter; using this bar, the patient couch is pointed into the desired direction and placed at the desired distance. This type of control bar is commonly on the operating console of the linear accelerator, such that the radiotherapist who changes the position of the table can also deliver the therapeutic beam. The other radiotherapist operates the fluoroscopic portion of the RTRT system and initiates the fluoroscopic exposure before and after adjustment of the patient couch. The system does not allow the linear accelerator to deliver a therapeutic beam unless the couch coordinates are adjusted to the planned position.

For the treatment of head-and-neck cancers, three 2-mm gold markers were implanted into a mouthpiece that had been specifically made for each patient before CT as part of treatment planning (Fig. 1). To create the mouthpiece, a thin thermoplastic sheet (Imprelon; Scheu-Dental, Iserlohn, Germany) and a pressure-molding machine (mini-Star; Scheu-Dental) were used. The mouthpiece was 3–4 mm thick and was well fitted to the teeth and palate. The dental department required 2 days to develop the mouthpiece.

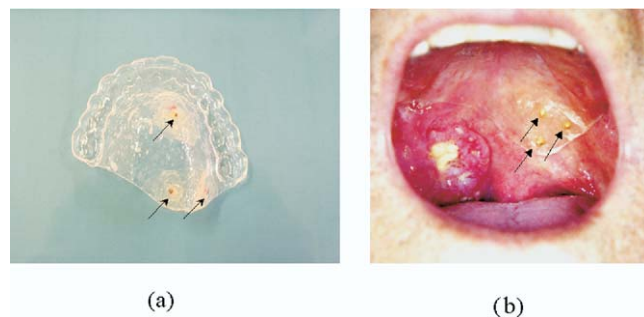


Fig. 1. (a) Mouthpiece containing three implanted markers in thermoplastic sheet. (b) Mouthpiece fixed in patient with oropharyngeal cancer.

Computed tomography (CT) was performed with the mouthpiece in the correct position with the patient immobilized using a thermoplastic shell (Thermoshell; Alcare, Tokyo, Japan) and an individualized neck rest (Moldcare; Alcare, Tokyo, Japan). The coordinates of the center of gravity of the three markers and their relationship to the center of gravity of the planning target volume (PTV) were transferred to the RTRT system before irradiation. The patient who wore the mouthpiece was positioned between room-mounted laser localizers. Next, two sets of orthogonal fluoroscopic images were taken (Fig. 2).

After the positions of the three markers were calculated, the translation and rotation of a rigid target volume in three-dimensional (3D) space were calculated, assuming no deformation of the target (Fig. 3). The resultant absolute vector displacement of the center of gravity of the PTV was then calculated. The position of the couch was adjusted to match the position of the actual center of gravity of the PTV at the planned position. For the present study, this approach was designated as the “RTRT setup.”

### *Estimation of interfractional and intrafractional setup error*

Eight patients (4 men and 4 women) with pharyngeal tumors were used for this analysis. All patients were treated with step-and-shoot IMRT using five ports and approximately 10–20 segments for each port between July 2002 and December 2004. The mean patient age was 60 years (range, 27–81 years). Six patients had oropharyngeal and 2 had nasopharyngeal cancers. The follow-up period was 10–30 months after treatment.

The patients were first positioned on the patient couch using the lines on a thermoplastic shell, and a room-mounted laser localizer was used for conventional RT (manual setup). In this study, setup errors in the manual setup procedure were estimated by measuring the discrepancy between the coordinates of the center of gravity of the PTV before and after RTRT setup.

Some residual error still occurs in the RTRT setup because of a number of factors, including intraobserver variation in the identification of the marker on the fluoroscopic images. In this study, after adjustment of the couch position according to the calculations made using the RTRT system, we took another fluoroscopic image and then measured the discrepancy from the initial measurement using the RTRT system. We considered the residual error as the setup error in the RTRT setup in the present study. Because the system accuracy with a phantom was  $\pm 1$  mm, corrections were only made when the discrepancy was  $>2$  mm in any direction.

We did not use a 3D conformal setup (20), in which the

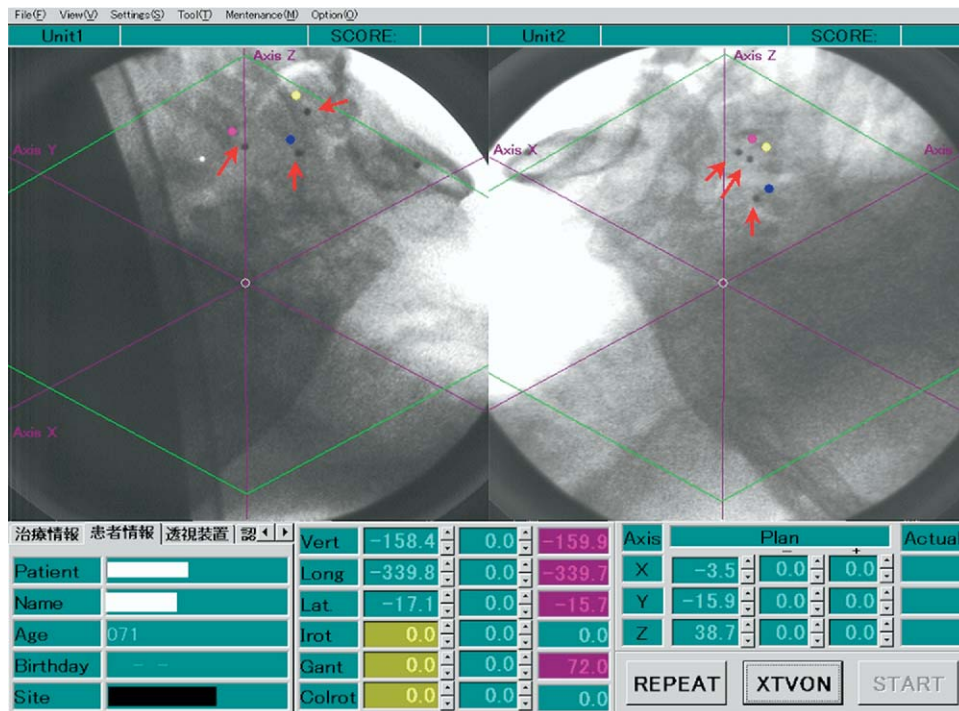


Fig. 2. Actual view of real-time tumor tracking radiotherapy system in patient wearing mouthpiece. Actual positions of three markers designated by arrows. Pink, yellow, and blue dots represent planned positions of markers determined during treatment planning computed tomography.

rotational error is corrected by rotating the patient couch, gantry, and collimator. In cases involving a rotational error of  $>3^\circ$ , the radiotherapists entered the treatment room and attempted to reposition the patient. No replanning was done to correct for rotational

error, and the patients were treated with the minimal rotational error achievable with repositioning.

The translational and rotational errors were measured 175 times in the case of the manual setup and 147 times in the case of the

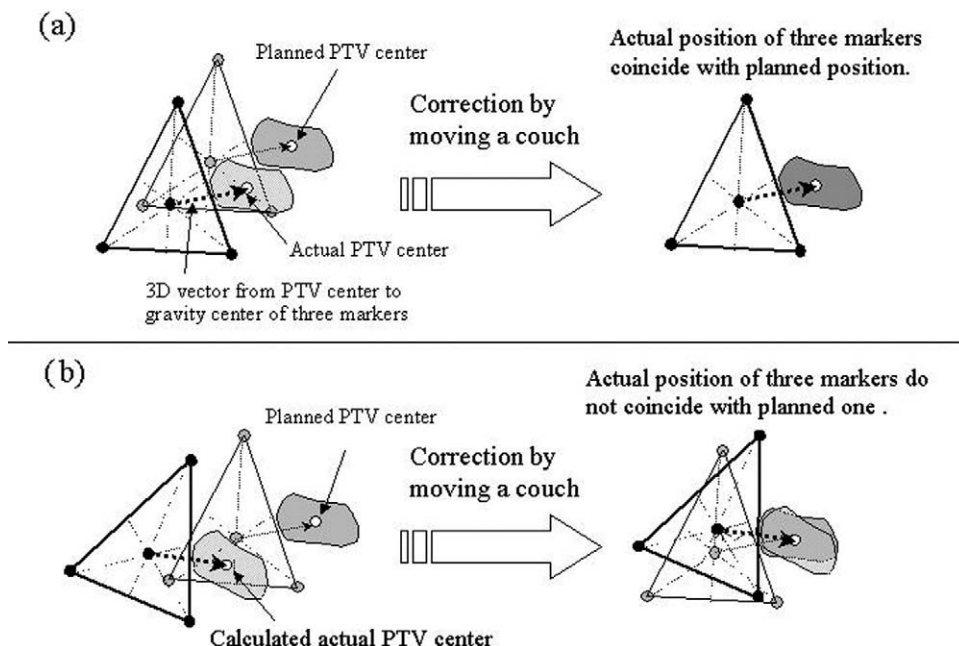


Fig. 3. Translational correction method of planning target volume (PTV) center for (a) PTV without rotation and (b) PTV with rotation. In cases involving rotation of PTV, actual positions of three markers did not coincide with planned positions after corrections were made to match coordinates of actual PTV center with those of planned PTV center.

Table 1. Patient characteristics

Characteristic	Patient							
	1	2	3	4	5	6	7	8
Gender	Female	Male	Male	Male	Male	Female	Female	Female
Clinical stage (TNM)	T3N0	T3N0	T3N0	T3N0	T4N1	T4N0	T4N0	T3N0
Tumor location	Oropharynx	Oropharynx	Oropharynx	Oropharynx	Nasopharynx	Oropharynx	Nasopharynx	Oropharynx
Subsite	Soft palate	Soft palate	Anterior pillar	Soft palate				Soft palate
Dose at 95% of PTV	65 Gy/26 Fr	65 Gy/26 Fr	65 Gy/26 Fr	65 Gy/26 Fr	40 Gy/16 Fr*	60 Gy/26 Fr	66 Gy/30 Fr†	65 Gy/26 Fr
Distance (mm) between								
Marker 1 and marker 2	14.5	8.1	15.3	30.8	32.3	23.1	18.9	22.8
Marker 3 and marker 1	12.6	8.3	19.1	24.7	27.8	26.7	21.3	22.5
Marker 2 and marker 3	11.4	6.8	16.6	24.0	30.5	11.5	23.1	26.7
Distance (mm) between tumor center and								
Marker 1	32.2	28.5	42.9	31.5	59.3	39.4	59.1	36.9
Marker 2	34.3	36.1	34.6	29.8	73.8	16.8	51.7	53.7
Marker 3	41.8	32.2	34.1	40.9	43.4	22.3	41.4	36.1
Center of gravity of 3 markers	35.6	32.1	36.1	30.8	57.5	25.0	49.8	40.7

Abbreviations: PTV = planning target volume; Fr = fractions; RTRT = real-time tumor tracking radiotherapy; IMRT = intensity-modulated radiotherapy.

\* Boost irradiation with RTRT.

† Boost IMRT with RTRT.

RTRT setup for the 8 patients. The rotational setup error was calculated a total of 186 times for the initial setup. The discrepancy between the number of measurements of rotation and translation resulted from repositioning the patient when major rotational setup errors occurred.

The position of the markers in the mouth was monitored during irradiation by frequent fluoroscopic measurements, usually once each beam orientation. To investigate the intrafractional movement, the difference from the planned position was measured during each fluoroscopic measurement. Intrafractional, systematic, and random setup errors were calculated for translational and rotational uncertainty. In total, the intrafractional movement was measured 1,019 times for translational errors and 1,059 times for rotational errors in the 8 patients.

Systematic setup error (the variation of the mean displacement of patients) was defined as the standard deviation ( $\Sigma$ ) of the mean displacement of all patients (22, 23). Random setup errors (day-to-day variation) were defined as the root mean square of the standard deviations for all patients ( $\sigma$ ). The Levene test was used to examine the difference in variance of setup errors for right-left (x, RL), craniocaudal (y, CC), and AP (z) directions between the manual and RTRT setups. The 3D discrepancy from the planned position between the manual and RTRT setups was compared using nonparametric, univariate analysis of variance methods with Dunnett's test. Values of  $p < 0.01$  were considered to indicate statistical significance using the software Statistical Package for Social Sciences, version 12.0 (SPSS, Inc., Chicago, IL).

## RESULTS

The patient characteristics are shown in Table 1. The coordinates of the center of gravity of the three markers were within 60 mm from the center of the PTV. The distance between each marker was distributed within a range of 6.8–32.3 mm. The distance between the center of the tumor and each marker was distributed within a range of 16.8–73.8 mm. The distance between the center of gravity of the three markers and the center of the PTV was distributed within a range of 25.0–57.5 mm.

All the patients wore the mouthpiece without symptomatic discomfort, except for a gag reflex in 1 patient. The mouthpiece fit efficiently into the upper jaw without any noticeable dislocation of the teeth. The time from the end of the manual setup of the patient to the start of RT was  $< 5$  min, except for on the initial day, when orthogonal megavoltage portal imaging was performed on all patients.

Scatter diagrams of the displacement of the center of gravity of the PTV from its planned position in the RL (x), CC (y), and AP (z) directions in the manual and RTRT setups were plotted (Fig. 4). It was apparent that the displacement was larger in the cases involving manual setup than in those with RTRT setup. The systematic and random errors in the translational direction in both setups are shown in Table 2. The systematic errors were 1.8, 1.6, 1.1, and 1.1 mm in the manual setup and 0.2, 0.3, 0.3, and 0.3 mm in the RTRT setup in the RL, CC, AP, and 3D directions, respectively ( $n = 8$ ). The corresponding random setup errors were 1.4, 1.4, 1.6, and 1.3 mm in the manual setup and 0.5, 0.6, 0.4, and 0.5 mm in the RTRT setup. Statistically significant



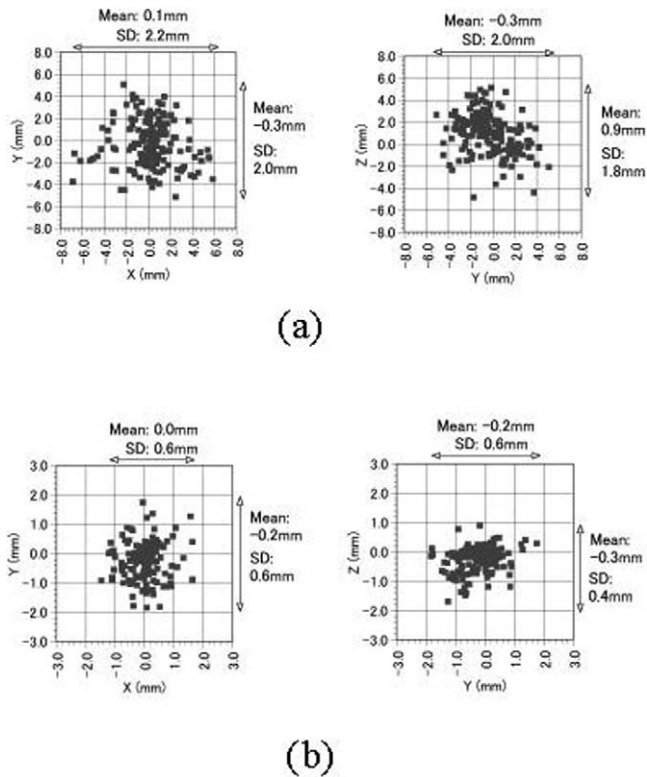


Fig. 4. Scatter diagrams were plotted to show displacement of center of gravity of planning target volume (PTV) from planned position for x, y, and z directions in (a) manual setup ( $n = 175$ ) and (b) real-time tumor tracking radiotherapy setup ( $n = 147$ ).

differences in the variances in the x, y, and z direction were seen between the manual and RTRT setups ( $p < 0.001$ ). A statistically significant difference was also observed for the 3D distance between manual and RTRT setups ( $p = 0.001$ ).

The systematic error in rotation was  $3.3^\circ$ ,  $2.2^\circ$ , and  $2.5^\circ$ , respectively, around the RL axis ( $\alpha$ ), CC axis ( $\beta$ ), and AP axis ( $\gamma$ ), and the random error was  $1.6^\circ$ ,  $1.5^\circ$ , and  $1.5^\circ$  around each axis, respectively.

The frequency of fluoroscopic monitoring was 2–10 times (mean, 5) in each fraction, depending on the intrafractional displacement of the patients. The mean frequency was 132 times (range, 36–246) during one treatment period.

Scatter diagrams of the temporal variation in the translational and rotational errors during the delivery of daily irradiation are shown in Fig. 5. Adjustment of the patient couch during irradiation according to the fluoroscopic examination was undertaken  $19 \pm 11$  times (range, 0–33) during a single daily irradiation. This procedure added approximately 1 min for one adjustment of the patient couch, 5 s for the exposure, 15 s for the calculation, and 40 s for correction of the couch. The average treatment delivery time in the 8 patients was approximately 30 min (range, 10–36 min).

The mean  $\pm$  standard deviation of the intrafractional translational error was  $-0.1 \pm 1.0$ ,  $-0.3 \pm 2.4$ ,  $-0.5 \pm 2.4$ , and  $1.6 \pm 3.1$  mm in the x, y, z, and 3D directions, respectively, with frequent modification of the patient couch

during delivery of the treatment beam. The systematic error and random error in the intrafractional, translational, and rotational uncertainty are shown in Table 3.

During the follow-up period, no apparent intensification of the mucosal radiation reaction was noted during or after administration of RT.

## DISCUSSION

We have adapted the use of a “safety margin” for tumor control in conventional RT. However, such a safety margin increases the risk of adverse effects in normal tissue. It is important to reduce the safety margin if it is purely a physical margin without any indicated pathologic necessity. A precise setup using a tight immobilization device may help realize the reduction of the physical safety margin. However, such a tight fixation system can often be uncomfortable for patients. The present study demonstrated that an RTRT setup, when applied together with gold markers implanted into a mouthpiece, can significantly reduce the systematic and random setup errors compared with those associated with the conventional manual setup protocol without the discomfort of tight fixation.

Several published results about setup uncertainty in head-and-neck treatments are summarized in Table 4. Hess *et al.*

Table 2. Interfractional translational and rotational, systematic, and random errors in manual setup and RTRT setup

Systematic and random translational setup error				
$\Sigma$ (mm)			$\sigma$ (mm)	
	RTRT (–)	RTRT (+)	RTRT (–)	RTRT (+)
x	1.8	0.2	1.4	0.5
y	1.6	0.3	1.4	0.6
z	1.1	0.3	1.6	0.4
3D	1.1	0.3	1.3	0.5
		RTRT (–) ( $n = 175$ )	RTRT (+) ( $n = 147$ )	$p$ (Levene test)
Setup error (mean $\pm$ SD)				
x		$0.1 \pm 2.2$	$0.0 \pm 0.6$	<0.001
y		$-0.3 \pm 2.0$	$-0.2 \pm 0.6$	<0.001
z		$0.9 \pm 1.8$	$-0.3 \pm 0.4$	<0.001
3D		$3.3 \pm 1.6$	$0.9 \pm 0.5$	0.001
Systemic and random rotational error				
	$n$	Mean°	f°	f–D°
f $\alpha$	186	–0.8	3.3	1.6
f $\beta$	186	0.2	2.2	1.5
f $\gamma$	186	0.6	2.5	1.5

Abbreviations:  $\Sigma$  = systematic error;  $\sigma$  = random error; RTRT = real-time tumor tracking radiotherapy; x = right–left direction; y = craniocaudal direction; z = AP direction; 3D = three dimensional;  $f \alpha$  = rotation around x axis;  $f \beta$  = rotation around y axis;  $f \gamma$  = rotation around z axis.

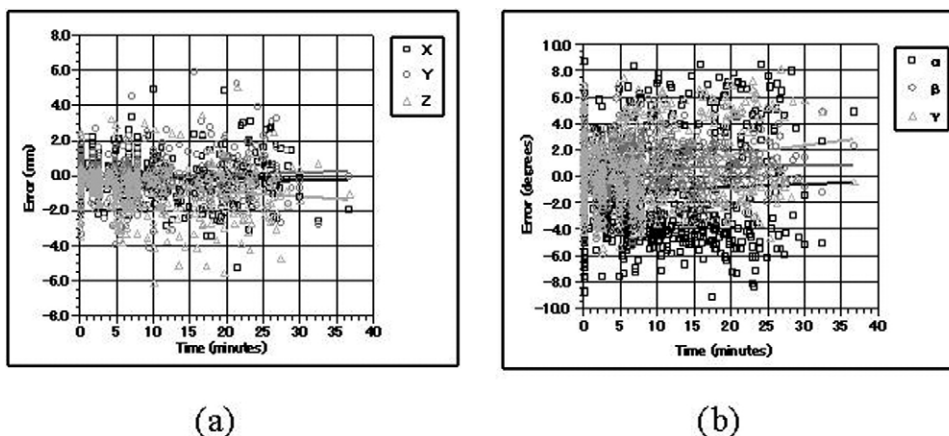


Fig. 5. Scatter diagrams of temporal variations of (a) translational ( $n = 1,019$ ) and (b) rotational errors ( $n = 1,059$ ) during delivery of daily irradiation. Each line represents regression line for corresponding direction and angle.

(3) reported that the mean and standard deviation of the setup error in the manual setup was 0–3 mm and 3–5 mm, respectively, in patients with head-and-neck cancer treated with individualized face-mask immobilization. Weltens *et al.* (2) also reported  $\pm 3.5$  mm as the standard deviation in this context. Gilbeau *et al.* (4) reported that the standard deviation in the setup errors (systematic errors) was 1.7, 1.3, and 0.9 mm for the RL, CC, and AP directions, respectively, at the head level and 1.0, 1.0, and 1.6 mm, respectively, at the neck level. The random setup error was 0.8–1.4 mm at the head level and 1.1–1.3 mm at the neck level. Fuss *et al.* (5) reported that the translational error at the isocenter was  $0.74 \pm 0.53$ ,  $0.75 \pm 0.60$ , and  $0.93 \pm 0.78$  mm in the RL, CC, and AP directions, respectively. Furthermore, Astreindou *et al.* (24) have shown that translational and rotational random setup uncertainties can significantly affect the dose distribution to patients with head-and-neck cancer treated by IMRT, in which the goal of treatment is that 95% of the clinical target volume receives  $\geq 99\%$  of the prescribed dose.

The above-mentioned analyses were based on comparisons of two-dimensional portal films with two-dimensional simulation films; thus, the measurement itself is limited with respect to three-dimensional accuracy. Using high-

precision optical measurements, Hong *et al.* (1) recently analyzed the accuracy of the current standard immobilization technique, including conventional thermoplastic masking, base-plate fixation to the patient couch, three-point laser alignment, and weekly portal film evaluation. In that study, Hong and colleagues (1) concluded that the mean setup error in any single dimension averaged 3.33 mm and the mean composite vector offset was 6.97 mm, with a standard deviation of 3.63 mm.

In our study, the interfractional systematic setup error was approximately 1.1–1.8 mm in the manual setup and 0.3 mm in the RTRT setup. The random setup error was approximately 1.5 mm in the manual setup and 0.5 mm in the RTRT setup. If we had adapted a formula for the PTV margin,  $2\Sigma + 0.7\sigma$  (22), the difference between the manual and RTRT setup would have been significant. Using  $\Sigma$  and  $\sigma$  in Table 2, the appropriate PTV margin was 4.7, 4.1, and 3.2 mm for the manual setup and 0.7, 1.0, and 0.8 for the RTRT setup in the x, y, and z directions, respectively.

However, the above assumptions did not include the intrafractional uncertainty. In the present study, the systematic error of intrafractional change of the marker position was  $< 1$  mm, with a random error of 1.0–2.0 mm. If we use  $2\Sigma + 0.7\sigma$  as the appropriate PTV margin, the margin for intrafractional uncertainty can be calculated at 1.1, 2.4, and 2.5 mm for the x, y, and z directions, respectively. In total, when the interfractional translational uncertainty and the intrafractional translational uncertainty are included, the appropriate PTV margin would be 5.8, 6.5, and 5.7 mm for the x, y, and z directions, respectively, in the manual setup. In the RTRT setup, the margins would be 1.8, 3.4, and 3.3 mm for the x, y, and z directions, respectively—approximately one-half of those of the manual setup. If frequent monitoring and adjustment during irradiation after manual setup are not used, the improvement in setup accuracy would be greater.

We did not include the uncertainty of the rotational error in this calculation of the PTV margin, but it will be included in our future studies using the calculation methods previ-

Table 3. Intrafractional translational and rotational systematic and random errors

Translational error	<i>n</i>	Mean (mm)	$\Sigma$ (mm)	$\sigma$ (mm)
x	1,019	−0.1	0.2	1.0
y	1,019	−0.3	0.5	2.0
z	1,019	−0.5	0.6	1.9
3D	1,019	1.6	0.7	2.5
Rotational error	<i>n</i>	Mean°	$\Sigma$	$\sigma$
f $\alpha$	1,059	−0.7	3.2	1.6
f $\beta$	1,059	−0.4	2.2	1.6
f $\gamma$	1,059	0.6	2.4	1.5

Abbreviations as in Table 2.

Table 4. Published results about setup uncertainty in head-and-neck radiotherapy

	Mean (mm)				SD (mm)			
	x	y	z	3D	x	y	z	3D
Hong <i>et al.</i> (1)	0.8	0.4	2.1	7.0	4.4	3.4	5.1	3.6
Weltens <i>et al.</i> (2)*				−0.4				3.5
Hess <i>et al.</i> (3)*				0–3				3–5
Gilbeau <i>et al.</i> (4) <sup>†</sup>	−0.7	−1.4	0.1		2.2	1.6	1.2	
Gilbeau <i>et al.</i> (4) <sup>‡</sup>	−0.5	−0.4	−0.5		1.5	1.5	2.1	
Fuss <i>et al.</i> (5)	0.7	0.8	0.9	1.6	0.5	0.6	0.8	0.8
Bel <i>et al.</i> (25)	−0.8	−0.6	−0.8		2.3	2.0	2.6	
This study								
RTRT−	0.1	−0.3	0.9	3.3	2.2	2.0	1.8	1.6
RTRT+	0.0	−0.2	−0.3	0.9	0.6	0.6	0.4	0.5

Abbreviations as in Table 2.

\* Estimated from lateral portals.

<sup>†</sup> Head level.

<sup>‡</sup> Neck level.

ously described (21). Astreinidou *et al.* (24) have suggested that a rotational error of 1° around the tumor center would not affect the size of the required margin for head-and-neck cancer. The rotational intrafractional uncertainty in our study may suggest an insufficiency in the immobilization capability of our fixation system. However, little data are available from other institutions regarding the intrafractional changes in the positioning of patients with head-and-neck cancers. The results of the present study strongly suggest the importance of intrafractional monitoring of the position of the target volume, even with the use of an individualized face mask.

More rigorous immobilization techniques may provide a solution for reducing this uncertainty. Nonetheless, the use of fiducial markers in patients with head-and-neck cancers has been reported by several investigators to improve the positioning of patients with head-and-neck cancers. Bel *et al.* (25) have used metal markers, which were placed on the fixation masks near the external acoustic meatus. The systematic error was 1.8, 1.7, and 2.0 mm and the random error was 1.5, 1.1, and 1.6 mm in the RL, CC, and AP directions, respectively, using these markers. van Asselen *et al.* (10) have demonstrated the feasibility of the implantation of fiducial markers in the musculature of patients with head-and-neck cancer. However, they also found migration or displacement in several cases (10). Such findings are consistent with our experience with the implantation of gold markers into the musculature in the treatment of patients with paraspinal diseases (19). It is likely that the muscular structure frequently contracts, which renders such markers unstable. In contrast, the use of three markers fixed into the mouthpiece exhibited stability during the entire treatment course of the present patients. No displacement of the markers occurred in this study, as determined by measurement of the distances among the three markers at each treatment session.

The possible pitfalls of the use of such a mouthpiece should be noted: namely, dislocation of the mouthpiece in the mouth, dissociation of the calculations for neck movements and head movements, metallic artifacts from dentures

at the CT planning stage, metallic artifacts from the gold markers, and an additional dose of irradiation to the mucosal surface from the gold markers. The fit of the mouthpiece may depend on the skill of the dentist and the material used for the mouthpiece. Willner *et al.* (26) investigated bite block immobilization in 1997. In our experience, a bite block was not so comfortable for the patients to reduce their motion during irradiation. The mouthpiece used in the present method was made of thin and hard material and fit well into the upper gum and was comfortable for the patients; however, these issues need to be investigated in future studies. The metallic artifacts from dentures render it difficult to delineate the gold markers on CT images. To resolve this problem, the pretreatment extraction of metallic dentures is required. Artifacts from the gold markers can also render the delineation of tumors difficult. MRI can be applied in such cases, using fusion software on a workstation, because gold markers do not create noticeable artifacts on MRI. Additional doses from scatter radiation from the gold markers may induce an increased mucosal reaction, such as can also occur in cases involving metallic dentures. The use of a plastic mouthpiece may reduce the irradiation dose resulting from the gold markers embedded in the mouthpiece; however, it will still be necessary to monitor mucosal reactions closely in the clinical setting.

## CONCLUSIONS

In this investigation, we examined the geometric accuracy of an RTRT system using a mouthpiece that had been implanted with three gold markers. The system was used on 8 patients who underwent IMRT for head-and-neck malignancies. Systematic and random setup errors were significantly reduced with the use of this RTRT system compared with the results obtained using the conventional manual setup protocol. The appropriate setup margin can be significantly reduced to approximately one-half that of the manual setup with the use of a mouthpiece and the present RTRT setup technique.

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