Bai *et al. Radiation Oncology* (2025) 20:35
https://doi.org/10.1186/s13014-025-02593-z

Radiation Oncology

RESEARCH

Open Access

Neck muscle training improving the setup of reproducibility in patient with head and neck cancer receiving radiotherapy - a prospective randomized controlled study

Fei Bai[1†], Lihua Zhang[1†], Xiaowei Yao[1], Bo Li[1], Jie Li[1], Qiuxia Hu[1], Yutian Yin[1], Changhao Liu[1], Zhaodi Xu[2], Linlin Xu[1], Jian Zang[1*] and Lina Zhao[1*]

Abstract

Background and purpose The aim of this study is to evaluate the effectiveness of a cervical muscle training intervention in decreasing setup errors in patients head and neck cancer (HNC) undergoing radiotherapy (RT).

Materials and methods HNC patients opting for RT at our center. The patients were randomly allocated to either the muscle training group or the control group in a 1:1 ratio. The magnitude of the setup error was measured at the levels of the clivus, C4 and C7 vertebrae respectively. The Van Herk formula was used to determine appropriate planning target volume (PTV) margins. (Trial Registration: ChiCTR2000041009, registration date: 12/16/2020)

Results A total of 221 patients were analyzed, with 109 assigned to the muscle training group and 112 enrolled in the control group. Compared with the control group, the setup errors in the X and Z direction of the clivus and the Z direction of C4 and C7 in the muscle training group were significantly lower ($p = 0.031$, < 0.001, < 0.001, < 0.001 respectively). The required PTV margins in the Z direction increased from 2.13 mm in the clivus to 3.63 mm in C7 in the muscle training group and from 2.89 mm in the clivus to 4.37 mm in C7 in the control group. Multivariate linear regression analysis demonstrated that the impact of neck muscle training, weight fluctuation, and cervical curvature on the setup error in the Z direction at C7 differed significantly ($p = 0.000$, 0.001, and 0.008, respectively).

Conclusion Neck muscle training can reduce setup errors and PTV margins in the anterior-posterior direction in patients undergoing RT for HNC.

Keywords Neck muscle training, Head and neck cancer, Radiotherapy, Setup error

†Fei Bai and Lihua Zhang contributed equally to this work.

*Correspondence:
Jian Zang
zj81327@qq.com
Lina Zhao
zhaolina@fmmu.edu.cn
[1]State Key Laboratory of Holistic Integrative Management of Gastrointestinal Cancers and Department of Radiation Oncology, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi 710032, China
[2]Department of Rehabilitative Physiotherapy, Xijing Hospital, Fourth Military Medical University, Xi'an, China

Introduction

Radiotherapy is a vital therapeutic modality used in the management of head and neck cancer (HNC). Recent advancements in technology, such as intensity-modulated radiotherapy (IMRT), volumetric-modulated arc therapy (VMAT), and image-guided radiotherapy (IGRT) devices, enable improved protection of critical organs in proximity to the tumor region (organs at risk, OARs), while ensuring optimal coverage of the tumor itself [1–3]. Consequently, they have become the standard approach for HNC treatment. However, the steep dose gradients inherent in these methods mean that even minor setup errors can significantly reduce the radiation dose delivered to the target site while simultaneously increasing exposure to OARs [4, 5]. Hence, it is imperative to mitigate setup errors to ensure the requisite treatment accuracy and quality for IMRT and VMAT.

Ensuring proper immobilization for head-and-neck radiotherapy (RT) is a complex undertaking due to the presence of 54° of freedom between the skull, mandible, and C7 vertebra [6]. Previous studies have demonstrated that despite adequate fixation measures, various sources of uncertainty can substantially influence IMRT accuracy [7]. These investigations have further revealed that random deformation errors in HNC can range from 0.5 mm to 3.6 mm, with differences of 2 mm to 6 mm observed between different matching regions and discrepancies of 4.7 ± 2.5 mm and 4.4 ± 2.5 mm observed between the skull/mandible and C4-C6, respectively [8–10]. As such, setup errors can vary considerably across different regions of the HNC anatomy, with the neck region experiencing the greatest discrepancy.

In our clinical experience, we have also observed that patients undergoing RT for HNC frequently demonstrate a reduction or straightening of their natural cervical curvature which contributes to increased neck setup error [11]. Furthermore, Ove et al. [12] noted an average anterior displacement of 3.08 ± 0.17 mm at the lower cervical spine, with no significant lateral or superior-inferior displacement. Similarly, Zhong et al. [13] found that the average anteroposterior error in nasopharyngeal carcinoma patients after RT ranged from 0.5 mm to -0.3 mm from C1 to C7, indicating a backward movement of the cervical spine. Consequently, preserving the natural cervical curvature poses a significant challenge in clinical practice. Research suggests that complementary interventions, such as acupuncture or tailored massage techniques, may help correct cervical straightening associated with cervical spondylosis [14]. Additionally, Zou L et al. [15] and Zhuang Q et al. [16] have proposed self-neck movements as a safe and cost-effective intervention for cervical spondylosis, offering simplicity and convenience. Regular neck muscle training/exercises have been shown to provide various benefits, including strengthening of the neck and back muscles, enhancing flexibility and stability of the neck and shoulders, and promoting cervical spine stability. Furthermore, these exercises can reduce muscle spasms, improve bone health, alleviate pain, prevent muscle loss, restore and improve neck mobility and function, and potentially prevent stiffness in the cervical joints. They may also improve blood circulation in the neck region and promote anti-inflammatory responses [15]. However, the role of neck muscle training improving the setup of reproducibility in patient with head and neck cancer receiving radiotherapy was not reported yet.

Hence, we conducted a prospective randomized controlled clinical study in order to examine the impact of neck muscle training on the reproducibility of setup in patients with head and neck cancer (HNC) receiving radiotherapy. Our objective was to assess the efficacy of a neck muscle training intervention in reducing setup errors, as well as to identify the potential variables that may influence such errors. This is, to the best of our knowledge, the first randomized controlled study to investigate whether neck muscle training intervention can improve the setup error in HNC patients receiving RT.

Materials and methods

Study design and patient inclusion

Patients with HNC who underwent RT were consecutively enrolled in this study, centre from February 2021 to October 2022. The inclusion criteria were as follows: patients who received RT for HNC; receiving Volumetric Modulated Arc Therapy(VMAT); between 18 and 65 years old; Karnofsky Performance Status (KPS) score ≥ 70; Patients should receive relevant examinations to exclude radiotherapy contraindications; patients must be informed of all aspects of the study and sign an informed consent form. The exclusion criteria were as follows: patients who had undergone previous cervical spine surgery with limited muscle movement in the neck; those with neck diseases affecting muscle movement; those with communication difficulty and unable to cooperate; those who were unable to effectively repeat neck muscle training. Patients were randomized into two groups: one with neck muscle training and the other with conventional treatment (control group). The study was a prospective, registry-based randomized controlled trial (Trial Registration: ChiCTR2000041009) and was approved by the institutional review board (approval No. KY20202071-F-1).

Neck muscle group training

The muscle training group began training one week before the start of planned CT. Subjects performed neck exercises three times a day and massage once a day [14]. Neck exercises were as follows: respectively turning the head down or up and to the left or the right, forward extension, retraction and neck rotation in the clockwise and counterclockwise directions, each for 5 min and three times a day. The massage was conducted for about 6 min and focused on (1) muscle relaxation: massaging along the neck bilateral transverse process and spinous process, relaxing the upper trapezius muscle, sternocleidomastoid muscle and other neck muscle groups. Notably, massage force should be moderate to avoid patients feeling pain and discomfort; (2) Seated retraction stretching exercise: Firstly, the mandible need to be retracted to its maximum extent, and slowly stretched backwards to a maximum stay of 3–5 S, followed by slowly returning to the starting position. Do 3 sets of 10 each in succession; (3) neck confrontation exercise: the patient's abdomen is then tightened, back straightened, and the hands crossed under the occipital bone behind the neck. The patient then inhales through the nose while extending the neck backwards. Pressure is applied with both hands forward and sustained for 3–5 s. This is followed by exhalation through the mouth and slow restoration. Three sets of 10 reps each are performed. The massage was first performed by a rehabilitation therapist. The control group received routine treatment without a neck muscle training intervention.

Position fixation and computed tomography (CT) simulation positioning

All patients were fixed with a head-shoulder thermoplastic mask and styrofoam. Simulated positioning was performed on a Philips Large Aperture Computed Tomography scanner (Big Bore Brilliance CT) to determine the approximate isocenter position and the initial isocenter with a red marker line on the thermoplastic film. The upper boundary of the scan was at the top of the skull and the lower boundary was 3 cm below the clavicle. The slice thickness was 3 mm and the slice distance was 3 mm. The scan was enhanced with an intravenous contrast agent.

Daily setup and image guidance

All patients received VMAT on a Varian Clinac iX linear accelerator (Varian, Delaware, USA). Before the first treatment, the treatment couch was moved to the accurate treatment position according to the treatment plan parameters and marked with a black treatment line on the mask. For daily radiation therapy, the patient was first immobilized with styrofoam and a head-shoulder thermoplastic mask, and then the treatment laser light was directed at the black treatment line. Cone-beam CT (CBCT) scans were performed weekly to verify the repeatability of the setup.

Image analysis

The clivus, C2-C4 and C6-T1 (or C5-C7) were selected as the three different regions of interest (ROIs) (Fig. 1A) for automatic image registration of planning CT and CBCT, to determine the setup error at the level of the clivus, C4 and C7 vertebral bodies [17] (C6 was used as a substitute if C7 was not captured by CBCT). C4 and C7 vertebral levels were chosen to represent the mid-neck and supraclavicular regions due to the correlation between the hyoid body and the anatomical structures below the cricoid cartilage [18]. Notably, previous clinical studies also divided the cervical nodes into II, III and IV levels [19]. For each setup verification, CBCT prioritized matching the clivus region because of its proximity to the primary tumor and vital organs such as the brainstem and optic chiasm.

For each patient, setup errors in four dimensions (left-right (x), head-foot (y), anterior-posterior (z) and the yaw (RTN) were recorded for each anatomical segment (clivus, C4 and C7) for all CBCTs during treatment. In this study, during data collection, we initially examined the setup error values of each CBCT online alignment. Subsequently, we identified various regions of interest for offline alignment. The resultant setup error values from offline alignment were then combined with those from online alignment to obtain the accurate setup error values of the regions of interest. For each patient and each anatomical segment, the setup errors in the four dimensions were analyzed separately to obtain the mean and standard deviation (SD). The mean of all individual patient means was calculated as the overall mean (M) as systematic error. The system setup error (Σ) was calculated as the SD of the individual means. The random setup error (σ) was calculated as the root mean square of the SD for all patients. The planning target volume (PTV) margin, expressed as $[2.5\Sigma + 0.7\sigma]$, was derived using Van Herk's formula, ensuring that 95% of the isodose lines covered 90% of the patients' clinical target volume (CTV) [20].

Observation items and time points

Weekly CBCT verification was conducted to assess setup errors at clivus, C4 and C7 levels; lateral cervical x-rays and PG-SGA nutritional status assessment were taken before treatment, at week 3 and at the end of treatment to assessmen*t* of cervical curvature (Fig. 1B) and nutritional status of patient; assessment of skin toxicity reactions (Common Terminology Criteria for Adverse Events version 3.0, CTCAE V3.0) and pain assessment (numerical rating scale, NRS) were conducted weekly.

Statistical analysis

Data were statistically analyzed using SPSS 25.0 statistical software. Count data were expressed as frequencies

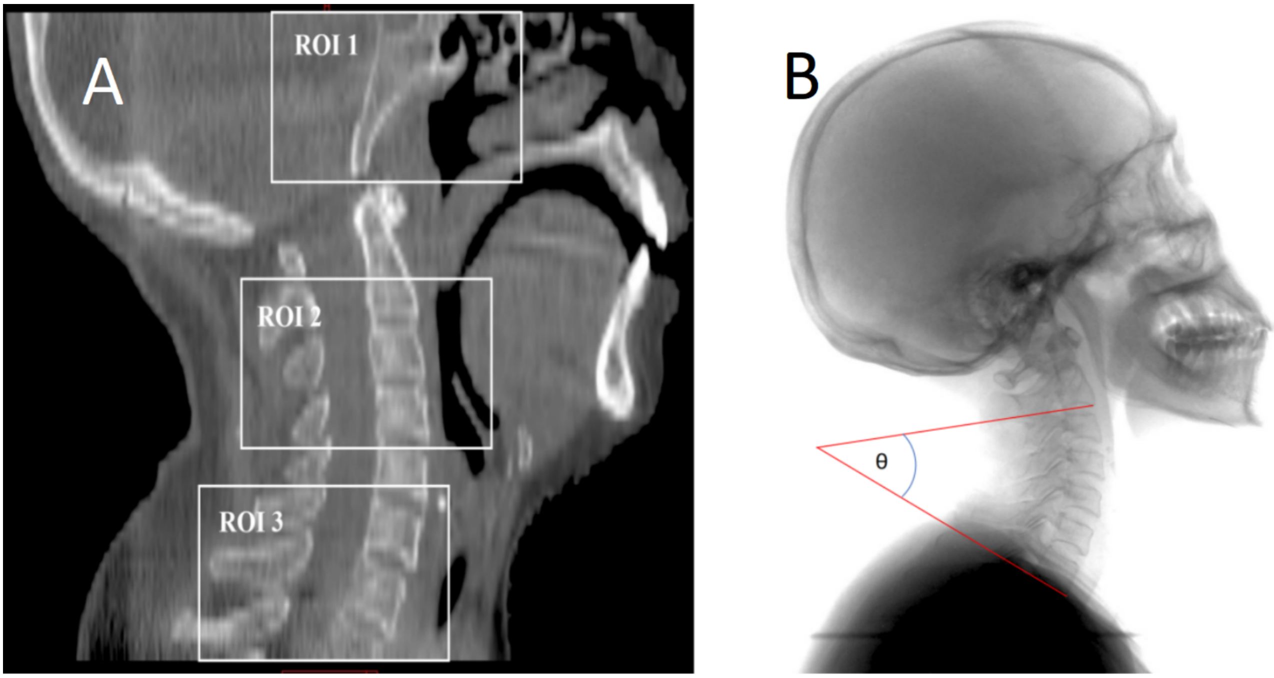

Fig. 1 **A** Three different regions of interest (ROIs) are used for automatic registration of planning CT and CBCT: (1) clivus area; (2) C2-C4; (3) C5-C7 or C6-T1. **B** is a schematic diagram of cervical curvature measurement. The angle between the lower edge of C2 and the line connecting the lower edge of C7 was used to represent the value of cervical curvature [30]

(n) and percentages (%), and the χ^2 test was used for comparing differences between groups. The measurement data were expressed as mean (M) ± SD, and the t-test was used for comparing differences between groups. Since the setup errors in all directions did not obey a normal distribution, they were expressed as median (25th percentile, 75th percentile), i.e. m (p25, p75). Comparisons between groups were made using the Mann-Whitney U test. Spearman correlation was used for analyses of correlations. Multivariate linear regression was used to analyzed the correlates affecting the setup error. $P < 0.05$ was considered statistically significant.

Results

A total of 230 patients were randomized between February 2021 and October 2022. Eight patients discontinued treatment due to financial constraints(Due to disparities in wealth and variations in health insurance reimbursement rates, some patients express that they cannot afford the substantial costs associated with combined treatments such as surgery, chemotherapy, and radiotherapy.), and one patient withdrew from the study after enrollment. Ultimately, 221 patients were included in the analysis, with 109 assigned to the muscle training group and 112 to the control group. The baseline characteristics of these patients are presented in Table 1. Of the 221 individuals, 154 (69.68%) were male and 67 (30.32%) were female. No significant differences in baseline characteristics were observed between the two groups ($p > 0.05$).

A total of 1,393 Cone Beam Computed Tomography (CBCT) scans were examined in a cohort of 221 patients. Among these, 686 CBCT scans were obtained from 109 patients assigned to the muscle training group, while the remaining 707 CBCT scans were acquired from 112 subjects in the control group.3 and 5 patients necessitated repeat CBCT scans before the first treatment in the muscle training and control group, respectively. The overall repeat CBCT scans were 32 (4.66%) and 37 (5.23%) in the muscle training and control group, respectively. Furthermore, among the patients in the muscle training group, 14 individuals (12.84%) exhibited a setup error of ≥3 mm from the clivus to C7. Notably, one of the three patients classified as "special cases" experienced a significant setup error during the initial treatment. Despite the attending physician's decision to re-perform an enhanced CT localization scan, the setup error remained substantial. As a result, a re-localization procedure was performed using the unenhanced scan, satisfying the treatment standard. It should be noted that the inability to fully match the enhanced scan image with the treatment image was attributed to the patients' trypanophobia and nervousness (Inadequate reproducibility in setup resulting from patient nervousness during CT planning can be addressed through re-planning of the CT scans; similarly, suboptimal reproducibility due to patient nervousness in the pre-treatment phase can be enhanced by repeating the procedure multiple times.). In the second case, the patient had a large setup error during treatment

Table 1 Baseline characteristics of patients

Characteristic		Muscle training group (*N* = 109)	Control group (*N* = 112)	*p*
Age(years)	mean (range)	51(20–66)	52.5(18–68)	0.068
Gender	Male	78	76	0.549
	Female	31	36	
BMI	mean (SD)	23.04(3.33)	23.23(3.33)	0.666
Tumor site	Nasopharynx	40(36.70)	43(38.39)	0.200
	Sinonasal carcinoma	3(2.75)	12(10.71)	
	Oral cavity	32(29.36)	23(20.53)	
	Salivary gland	14(12.84)	15(13.39)	
	Oropharynx	10(9.17)	12(10.71)	
	Hypopharynx	4(3.67)	4(3.57)	
	Others	6(5.5)	3(2.68)	
Oral stent	Yes	53	40	0.052
	No	56	72	
Surgery	Yes	61	61	0.823
	No	48	51	
Cervical curvature		21.60(11.15)	22.56(11.07)	0.524
Pre-treatment nutrition	mean (SD)	3.00(2.43)	2.84(2.00)	0.592
Education	Primary and below	13	24	0.066
	Secondary	55	59	
	Tertiary and above	41	29	
Treatment	RT	52	60	0.383
	CCRT	27	30	
	IC + CCRT	30	22	
RT Volume(cm^3)	mean (SD)	601.89(150.92)	592.98(147.32)	0.788
T stage	N(%)			0.596
	T1	11(10.1)	18(16.1)	
	T2	33(30.3)	27(24.1)	
	T3	26(23.9)	24(21.4)	
	T4	38(34.9)	41(36.6)	
	Tx	1(0.9)	2(1.8)	
N stage	N(%)			0.360
	N0	42(38.5)	35(31.3)	
	N1	26(23.9)	28(25.0)	
	N2	32(29.4)	42(37.5)	
	N3	8(7.3)	4(3.6)	
	Nx	1(0.9)	3(2.7)	
M stage	N(%)			0.834
	M0	103(94.5)	104(92.9)	
	M1	4(3.7)	6(5.4)	
	Mx	2(1.8)	2(1.8)	
Offline ART	N(%)	45(41.3)	50(44.6)	0.614

RT, radiotherapy; CCRT, Concurrent chemoradiotherapy; IC, induction chemotherapy; ART, adaptive radiotherapy;

Pre-treatment nutrition, nutritional status of patients was assessed using PG-SGA scores. PG-SGA: Patient-generated subjective nutrition assessment

because the patient laryngeal mucosa was scratched during laryngoscopy, causing the patient hesitance to lift his chin. In the third case, another substantial setup error occurred following a plan revision because the mask was overly tight. When a mask with significant constriction is employed to secure the patient, they may experience pressure, discomfort, and severe mask constriction, forcing their neck backward, particularly for head and neck tumors, resulting in significant setup errors. However, this error was rectified after adjusting the mold. In the control group, the setup error from clivus to C7 was ≥ 3 mm in 22 patients (19.64%). There was 1 special patient with a large error due to the mold being too tight.

The error range in X, Y and Z directions was − 7 to + 6 mm (Mean, -0.19 mm), -5 to + 5 mm (Mean, -0.15 mm) and − 7 to + 6 mm (Mean, 0.33 mm),

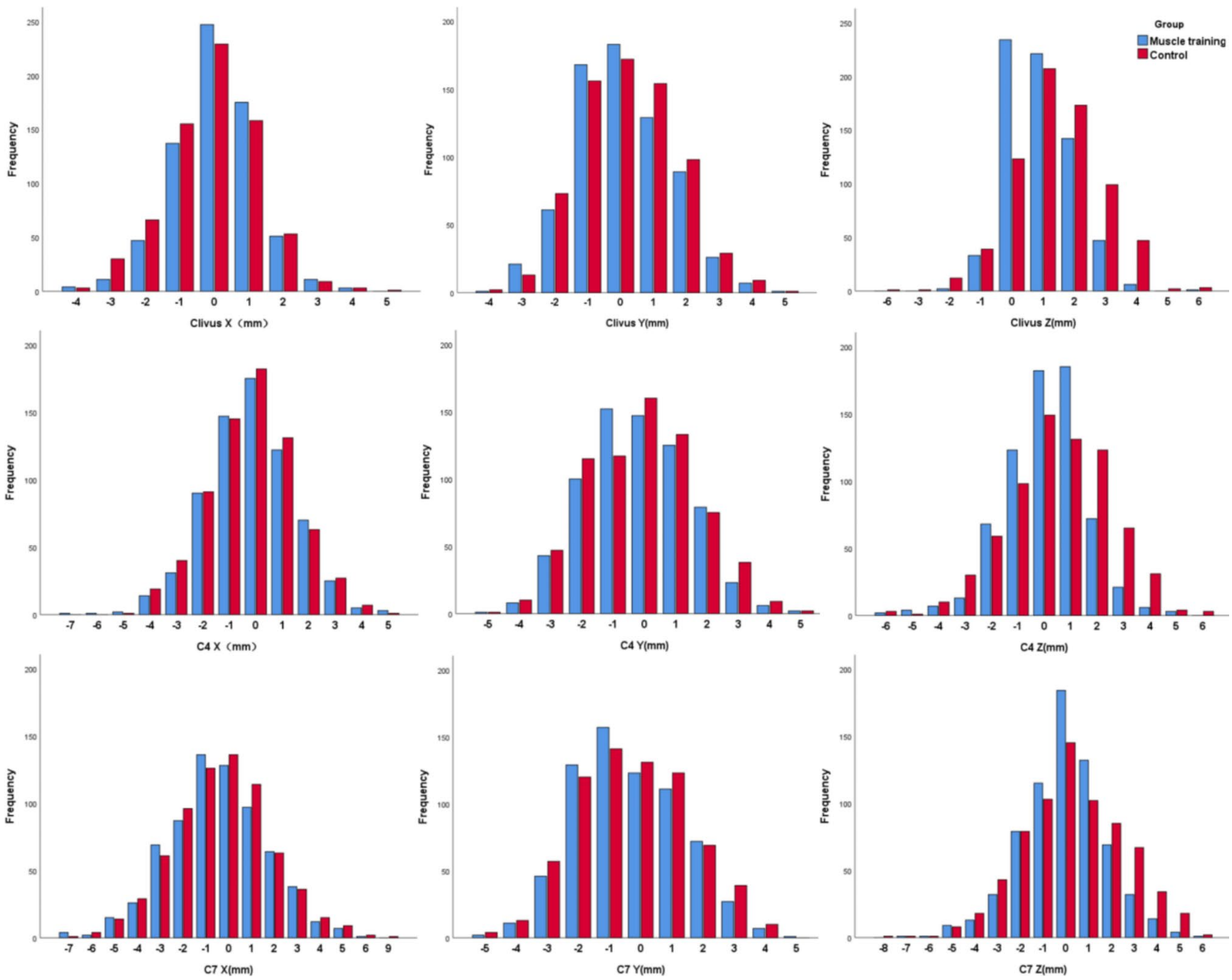

Fig. 2 Histogram of the range of setup error in three directions for the two groups of patients

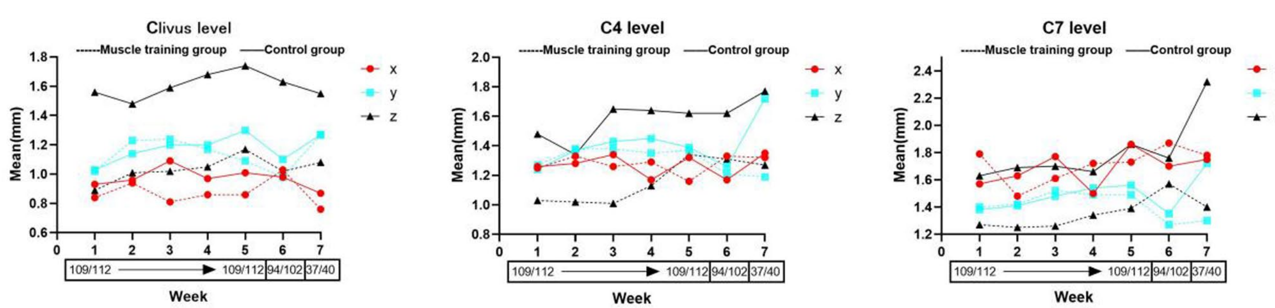

Fig. 3 Weekly positioning error line graph

respectively in the muscle training group and −7 to +9 mm(Mean, -0.23 mm), -5 to +4 mm (Mean, -0.08 mm) and −8 to +6 mm (Mean, 0.73 mm), respectively in the control group. The error range in the RTN rotation direction was −2.5–3.4 and −3.1-3.0° in the muscle training and control groups respectively. The setup errors greater than 3 mm in the X, Y and Z directions were 1.02, 1.31 and 1.02% at the clivus level, 3.79, 2.48 and 3.21% at the C4 level and 9.77, 3.06 and 6.27% at the C7 level respectively, in the muscle training group, and 1.02, 1.70 and 7.50% at the clivus level, 7.78, 3.11 and 7.35% at the C4 level and 10.61, 3.82 and 11.74% at the C7 level respectively, in the control group. In contrast to the muscle training group, the control group exhibited a two-fold higher incidence of setup errors exceeding 3 mm in the Z direction (refer to Fig. 2). In the line graph (Fig. 3) of weekly setup errors during the whole treatment process, it can also be found that the average weekly setup errors in the Z direction of the training group are smaller than those of the control group in all three regions of interest. It is also found that with the increase of the number of treatments, the setup error in the Z direction has a tendency to increase, and there is no obvious pattern of change in the other directions.

Table 2 Shows the overall setup errors for 221 patients in the muscle training and control groups (m (p25, p75)). Compared with the control group, the mean value of setup errors in the X and Z direction of the clivus and the Z direction of C4 and C7 in the muscle training group were lower (Mean comparison is 0.88 vs. 0.99 mm, 1.04 vs. 1.61 mm, 1.15 vs. 1.56 mm, 1.35 vs. 1.75 mm respectively). Notably, there were significant differences between the two groups in the above directions ($p = 0.031$, < 0.001, < 0.001, < 0.001 respectively).

The proportion of the difference between clivus and C4, clivus and C7 and C4 and C7 (C14, C17 and C47) > 3 mm was 1.02 vs. 0.24, 7.43 vs. 8.20 and 1.02 vs. 1.55% respectively in the X direction; 4.81 vs. 9.19, 8.45 vs. 19.09 and 0.29 vs. 0.43% in the Z direction; and 1.46 vs. 0.85, 1.89 vs. 1.98, and 1.6 vs. 0.85% respectively in RTN > 2°. The difference in the Y direction was almost within 3 mm in all comparison groups. A comparison of the difference between the two groups is shown in Fig. 4. C14 and C17 of the muscle training group in the Z direction were better than those of the control group ($p = 0.009$ and 0.033 respectively). C14 and C17 of the muscle training group in the RTN direction were better than those of the control group ($p = 0.004$ and 0.029 respectively). The control group was superior to the muscle training group in C17 in the X direction ($p = 0.014$), the other two groups had no statistical difference.

Table 3 shows systematic and random errors and the required PTV margins for each axis at the three anatomical levels for both groups. Comparative analysis at the anatomical level revealed that both systematic and random errors increase progressively along the craniocaudal direction. This was true for both the muscle training and control groups. The systematic error in the Z direction was 0.77, 1.05 and 1.30 mm from the clivus to C7 respectively, for the muscle training group, and 1.03, 1.37 and 1.59 mm respectively, for the control group. As the setup error increased, the required PTV margins in the Z direction also increased along the neck from 2.13 for the clivus to 3.63 mm for C7 in the muscle training group and from 2.89 in the clivus to 4.37 mm in C7 in the control group. The control group had larger errors in the X and Z directions, which were most pronounced in C7 and least in the clivus. The largest margin was in the Y direction rather than the X or Z direction at the clivus level. The muscle training group had a larger margin in

Table 2 Comparison of setup errors between the two groups of 221 patients (,m (p25, p75), unit: mm)

Group	N	Clivus				C4				C7			
		X	Y	Z	RTN	X	Y	Z	RTN	X	Y	Z	RTN
Muscle training	686	1(0,1)	1(0,2)	1(0,2)	3(1,7)	1(0,2)	1(1,2)	1(0,2)	4(2,6)	1(1,3)	1(1,2)	1(0,2)	1(1,3)
Control	707	1(0,1)	1(1,2)	1(1,2)	3(1,7)	1(0,2)	1(1,2)	1(1,2)	4(2,6.5)	1(1,2)	1(1,2)	2(1,3)	1(1,3)
z		2.163	0.923	9.156	0.294	0.092	0.997	6.457	0.519	0.271	0.679	5.369	0.688
p		**0.031**	0.356	**0.001**	0.769	0.927	0.319	**0.001**	0.604	0.786	0.497	**0.001**	0.492

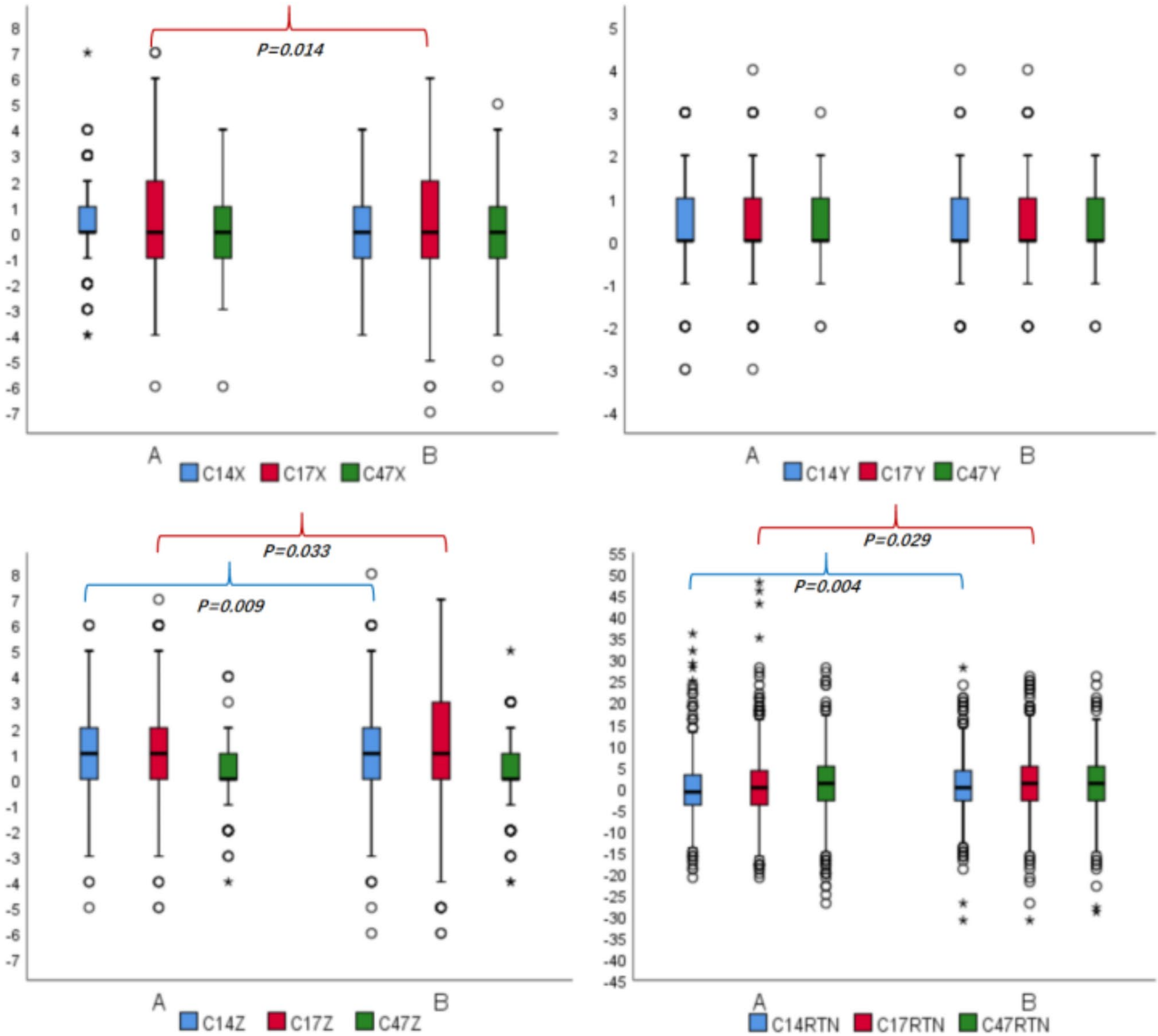

Fig. 4 Box plot of the differences between clivus and C4, clivus and C7, and C4 and C7 (C14, C17 and C47) of patients in the two groups, the muscle training group is **A**, and the control group is **B**, $P < 0.05$ between the two groups is statistically significant

Table 3 Summary data of systematic setup error and random setup error and PTV margin for 221 patients (bold requirement > 3 mm PTV margin)

		Muscle training group			Control group		
		X	Y	Z	X	Y	Z
Σ Systematic setup error	Clivus	0.87	1.04	0.77	0.98	1.06	1.03
	C4	1.21	1.18	1.05	1.19	1.35	1.37
	C7	1.51	1.25	1.30	1.57	1.39	1.59
σ Random setup error	Clivus	0.33	0.38	0.30	0.39	0.40	0.45
	C4	0.46	0.45	0.51	0.43	0.42	0.55
	C7	0.59	0.46	0.55	0.57	0.46	0.57
PTV margin	Clivus	2.41	2.87	2.13	2.72	2.93	2.89
	C4	**3.35**	**3.26**	2.98	**3.28**	**3.67**	**3.81**
	C7	**4.19**	**3.45**	**3.63**	**4.32**	**3.80**	**4.37**

the X direction, with the largest margin at C7 and the smallest at the clivus. The largest output was also in the Y direction at the clivus level. A comparison of the two PTV margins showed that the muscle training group had smaller margins than the control group, except at the C4 level where the muscle training group had larger margins than the control group in the X direction.

The Spearman correlation analysis of setup errors across different directions between the two groups revealed several noteworthy associations: In the muscle training group, the X direction was significantly negatively correlated with the RTN direction at both clivus and C4 levels (r = -0.502 and − 0.464, respectively). Similarly, the Y direction exhibited a moderate negative correlation with the Z direction at C4 and C7 levels (r = -0.248 and − 0.302, respectively). Other correlations, all with $p < 0.05$, exhibited weak associations ($r = 0.089$ and − 0.123, respectively). In the control group, the X direction was strongly negatively correlated with the RTN direction at clivus and C4 levels (r = -0.504 and − 0.451 respectively); the Y direction was weakly correlated with the Z direction at clivus, C4 and C7 levels ($r = 0.101$, -0.188 and − 0.226 respectively); and the Y direction was weakly correlated with the RTN direction at clivus and C7 levels ($r = 0.13$ and − 0.13 respectively). Detailed in see Fig. 5.

The mean change in cervical curvature was 1.91 degrees(Cervical curvature before treatment minus cervical curvature at end)in the muscle training group and 3.46 degrees in the control group, which was not statistically significant when the two groups were compared ($p = 0.143$). However, the change in cervical spine curvature in the control group was significantly greater than that in the muscle training group. The proportion of skin toxicity was 0% (0 cases) of grade 0, 26.6% (29 cases) of grade 1, 67.0% (73 cases) of grade 2 and 6.4% (7 cases) of grade 3 in the muscle training group and 0.9% (1 case) of grade 0, 20.5% (23 cases) of grade 1, 75.0% (84 cases) of grade 2 and 3.6% (4 cases) of grade 3 in the control group. The difference between the two groups was not statistically significant ($\chi^2 = 3.64$, $p = 0.303$). Mild, moderate and severe pain accounted for 20.1, 5.5 and 12.8% and 24.1, 6.3 and 11.6 in the muscle training and control groups respectively. The difference between the two groups was not statistically significant ($\chi^2 = 8.97$, $p = 0.345$). The pain reported by patients was due to more severe oral mucositis. Our analysis revealed no significant difference in body mass index (BMI) between the muscle training and

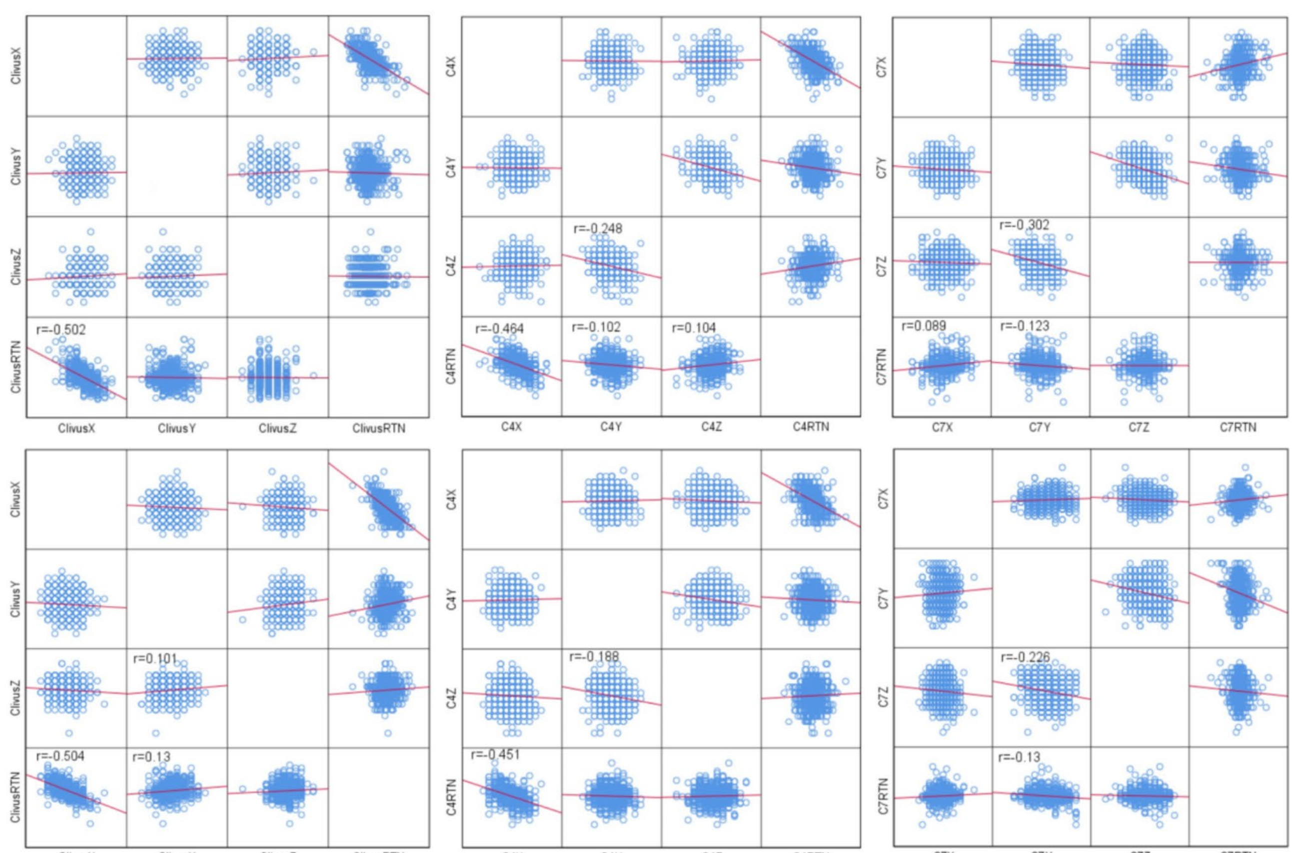

Fig. 5 Scatter plots of setup error in different directions for both groups. The three plots above are for the muscle training group and the three below are for the control group. The r-values for P-values < 0.05 are marked in the graphs

Table 4 Multi-factor linear regression results

	Variable	B	b-value standard error	Beta	t	*P*-Value	95%CI	
							Lower	Upper
Clivus Y	Oral stent(No*)	-0.128	0.053	-0.126	2.435	0.016	-0.232	-0.024
Clivus Z	Muscle group training(Yes*)	0.21	0.052	0.264	4.033	0.000	0.107	0.313
C4Z	Muscle group training(Yes*)	0.245	0.073	0.224	3.362	0.001	0.101	0.389
C7X	Sex(Females*)	-0.223	0.097	-0.177	2.291	0.023	-0.415	-0.031
C7Z	Cervical curvature	0.009	0.003	0.173	2.721	0.007	0.002	0.016
	Muscle group training(Yes*)	0.303	0.072	0.263	4.196	0.000	0.161	0.445
	Weight change	0.050	0.016	0.272	3.080	0.002	0.018	0.082

*Control group

control groups at either the third week (22.65 ± 3.17 vs. 22.80 ± 3.22, $p = 0.721$) or the treatment's end (22.08 ± 3.96 vs. 22.05 ± 3.23, $p = 0.943$). Similarly, no statistically significant differences were observed in body weight comparisons. Changes in weight and BMI between pre-treatment and the end of the treatment were also not significant (weight: 3.54 ± 3.30 vs. 3.38 ± 3.04, $p = 0.714$; BMI: 1.24 ± 1.16 vs. 1.19 ± 1.05, $p = 0.710$). Notably, the weight and BMI were decreased in both groups throughout the study, with no significant difference between them.

Multivariate linear regression equations were formulated by incorporating variables that had an effect on each level and direction as a result of univariate linear regression (see Table 1 in the Supplementary Information). The results revealed that there were statistical differences in the effects of the presence or absence of muscle group training, weight change (used absolute value of maximum weight difference from baseline, including either weight loss or gain) and cervical curvature on the C7 Z-directional setup error (b = 0.303, 0.050 and 0.009; t = 4.196, 3.080 and 2.721; $p = 0.000$, 0.002 and 0.007 respectively). There were statistical differences in the effects of the presence or absence of muscle group training on the C4 Z-directional setup error (b = 0.245, t = 3.362, $p = 0.001$). There was also a statistically significant difference in the effect of gender on the C7 X-directional setup error (b = -0.223, t = 2.291, $p = 0.023$). Moreover, the effect of the presence or absence of muscle group training on the clivus Z-directional setup error was statistically significantly different. There was a statistically significant difference in the effect of an oral stent on the clivus Y-directional setup error (b = -0.128, t = 2.43, $p = 0.016$). More information is detailed in see Table 4.

Discussion

In this study, we sought to reduce the setup error through a prospective randomized controlled trial by neck muscle training. Our findings indicate that such interventions may indeed lead to an improvement in the neck setup error among HNC patients, particularly with statistically significant improvement in the Z direction spanning from the clivus to the neck level. It was observed that the setup error exhibits a gradual increase from the clivus to the neck. Notably, PTV margins of 3 mm, 3.8 mm, and 4.4 mm were determined to be necessary at the clivus, C4, and C7 levels, respectively. In the muscle training group, PTV margins of 2.2 mm, 3.0 mm, and 3.6 mm were required, while in the control group, the corresponding margins were measured at 2.9 mm, 3.8 mm, and 4.4 mm in the Z direction at the clivus, C4, and C7 levels, respectively. Multivariate analysis identified neck muscle training, weight loss, cervical curvature, gender, and the use of an oral stent as factors influencing the setup error.

To our knowledge, this represents pioneering research exploring methods aimed specifically at mitigating neck deformation errors through a patient-centric lens while employing a multidisciplinary approach addressing clinical challenges encountered within this domain. The intervention incorporated an amalgamation of exercise therapy coupled with traditional massage techniques [14], which have garnered recognition within China due their efficacy preventing alterations associated with cervical curvature thereby reducing resultant deformations effectively. This approach boasts simplicity in its acquisition, as it can be readily grasped by patients' families under the guidance of a rehabilitation therapist, and is more likely to be sustained over the long term. It has been reported that effective massage and systematic neck exercises following RT can facilitate the dissipation of heat generated by radiation, enhance local tissue blood circulation, eliminate inflammatory byproducts, and impede the progression of fibrosis in the neck [21]. To ascertain whether the sustained adherence to this method can engender improvements in long-term toxic effects, further follow-up investigations are warranted.

Numerous studies have indicated that the presence of multiple bony landmarks that can move freely poses a significant challenge when it comes to accurately aligning skeletal structures in the treatment area [8]. Attaining an optimal match across the entire length of the neck is unlikely for head and neck cancer patients, and it may be possible to prioritize the matching of regions of interest (ROI) based on biological factors. However, this approach may result in a poorer overall alignment outside the ROI [12]. Our study confirmed this phenomenon by observing a gradual increase in setup errors between the clivus and C7, as well as an increased error range for all patients. Moreover, the frequency of errors larger than 3 mm, particularly in the X and Z directions, also demonstrated a notable increase. Interestingly, the muscle training group exhibited a significantly smaller proportion of errors larger than 3 mm in the X and Z directions compared to the control group. This finding indicates that the muscle training group achieved a more consistent and reproducible setup error.

Based on the error division diagram (Fig. 2), it can be observed that the error in the Z direction exhibits a positive skew at the clivus level and gradually decreases to negative values at the C4 and C7 levels. This pattern suggests the occurrence of deformations in the neck. These findings align with previous research conducted by Zhong et al. [13] and Kam et al. [7], who also reported setup-induced neck deformation errors. Ahn et al. [6] demonstrated that the movement of the skull is semi-independent compared to the neck. Additionally, the cervical curvature varies in an unpredictable manner, but it is somewhat related to the pitch and yaw of the skull. It was also found that with the increase in the number of treatments, there was a gradual increase in the Z-direction setup error in both groups. The probable reason for this is due to some combination of factors such as the occurrence of toxic side effects with the increase in the number of treatments and the deformation error of the neck. The errors in both groups approximated a maximum at about five weeks, and one possible reason for this is that some patients underwent offline ART at this time. The analysis showed that the mean setup error in the Z-direction in both groups was smaller after ART than before ART. This further suggests that ART may have had a role in reducing setup errors.

During the setup process for head and neck radiotherapy, mandibular and neck movements introduce notable uncertainties that can potentially result in rotational errors in the neck. These significant deformation errors necessitate careful consideration in clinical practice. To effectively mitigate issues arising requires prioritization two key strategies: enhancing postural fixation and improving the setup quality. Aiming to minimize rotation deformation errors, efforts should be concentrated on achieving robust postural fixation. In this particular study, our objective was to quantify the errors in setup at various positions, namely the clivus, C4, and C7, and subsequently analyze the differences in setup errors after implementing an intervention. Our findings revealed a progressive increase in setup error from the clivus to C7 in both the left-right and anterior-posterior directions, with C7 being the smallest at RTN. The group that underwent muscle training exhibited significantly less setup error in the anterior-posterior direction, from the clivus to C7, compared to the control group ($p < 0.001$). Additionally, it displayed less error than the control group in the left-right direction at the ramp level ($p = 0.031$). Lin et al. [22] also reported a gradual increase in setup error from the clivus to the neck. The decrease RTN may be attributed to the flexibility of the head relative to the neck, which aligns with clinical practice. Furthermore, further analysis demonstrated that regardless of whether surgery was performed or not, the muscle training group consistently exhibited less setup error in the anterior-posterior direction compared to the control group (refer to Tables 2 and 3 in the Supplementary Information). Additionally, we found that neck muscle training improved the positional repeatability of radiotherapy for head and neck tumors.

In a previous study [17], statistically significant differences in setup errors were observed across various regions of radiotherapy for nasopharyngeal carcinoma. Specifically, significant differences were noted between the clivus and C4 regions, as well as between the C4 and C7 regions. These findings highlight the importance of considering regional variations when assessing and addressing setup errors in nasopharyngeal carcinoma radiotherapy. We analyzed the difference between the two groups of patients in the different matched regions and found that the range of difference between the muscle training and control groups was (-6 to 7 vs. -7 to 6) mm in the X direction; (-3 to 4 vs. -2 to 4) mm in the Y direction; and (-5 to 7 vs. -6 to 8) mm in the Z direction, with both groups showing a large variation in error in the X and Z directions. Zhang, L et al. [9] and Polat, B et al. [10] obtained similar results. The statistical analysis comparing the percentage of differences exceeding 3 mm in different directions between the two groups yielded clear results. Specifically, in the Z direction, the control groups (C14 and C17) exhibited a percentage of differences that was more than twice as large as that of the muscle training group. Further analysis revealed no statistical difference between the two groups of operated patients in the Z-direction difference (see Fig. 1 in the Supplementary Information), but in the Y-direction and RTN the C14 muscle training group was smaller than the control group ($p = 0.031$, 0.004). A potential explanation for this observation could be attributed to the disparity in head and neck mobility between surgical and non-surgical patients. Surgical patients typically have reduced mobility due to the surgical procedure, resulting in less deformation in the neck region. Consequently, this limited neck deformation may contribute to the absence of a significant difference in the Z-direction error between the two groups. In non-operated patients, significant differences were observed between the muscle training group and the control group in the Z-direction for C14 and C17 ($p = 0.014$ and 0.005, respectively), with the muscle training group outperforming the control group. In addition, in the C47 muscle training group, although there was an improvement compared to the control group, the difference was not statistically significant ($p = 0.051$). No statistical differences were found in other directions (Fig. 2 in the Supplementary Information).This highlights the need to explore ways to reduce the neck deformation error in non-operated patients.

Currently, there is a certain deformation error in the neck region during radiotherapy of head and neck cancer, which increases gradually from top to bottom. Most scholars [9, 12, 17, 23] believe that different PTV margins should be used for head and neck tumors from top to bottom to solve the large error caused by position change and variability of different regions. Our results are consistent with this, demonstrating that a maximum of 3 mm PTV margins of extension is required at the clivus, 3.8 mm at C4, and 4.4 mm at C7 (Table 3). In the experimental group, 2.13–3.63 mm margins were needed from the clivus to C7 in the anteroposterior direction The control group required 2.89–4.37 mm of margins. Cheo T et al. [17] reported that nasopharyngeal carcinoma requires 2.33–6.52 mm of margins from clivus to C7, with the largest in X, followed by 4.7 mm in Z. After the necessary correction, the setup error was reduced to a range of 1.2–6.08 mm, with the maximum error observed in the X directions, and a magnitude of 4.01 mm in the Z directions. When comparing these results to the control group in our study, it is evident that the correction yielded similar improvements in the Z directions. However, notably, the correction was more effective in reducing errors in the X directions compared to the control group. Because we use a combination of styrofoam and 9-point head and neck shoulder membrane, it effectively immobilizes the neck and shoulder region, and provides optimal stability and fixation. This results in a significantly smaller margin requirement in the X direction. Further analysis revealed that a 3 mm margin was sufficient for muscle training in non-operative patients, with the exception of a 4 mm margin needed in the X direction of C7. In the control group, a margin of more than 3 mm or even 4 mm was required (Supplementary Data Table 5). Comparatively, there was no significant decrease in the required PTV margins in the muscle training group of surgical patients when compared to the control group (Supplementary Data Table 4). It appears that interventions are more effective for non-surgical patients, highlighting the need for new fixation methods or interventions to improve treatment accuracy in surgical patients. Considering the results of this study, the daily use of neck muscle training has the potential to reduce the frequency of necessary ART adaptations (patients with large setup errors in the routine method will need to be re-planned), However, the daily CBCT setting should not be reduced because setup errors in the neck region still vary widely.

It appears that different institutions in China do not currently utilize varying PTV margins from top to bottom, as the standard 3 mm margin is uniformly applied. The lack of consensus on the optimal matching of bone structures may contribute to the observed findings. Additionally, since the target volume and organs at risk in radiotherapy mainly consist of soft tissues, the deformation errors obtained may not completely reflect the overall accuracy of radiotherapy. Consequently, accurately calculating the impact on dose distribution becomes challenging due to various factors that go beyond the measured deformation errors [7]. Therefore, it is important for therapists to continuously innovate new fixation devices or interventions to reduce the setup error of head and neck tumors within the entire target area to less than 3 mm. In the future, a regression analysis of neck setup errors with regard to survival and recurrence will be conducted, provide new reliable evidence for different neck PTV margins.

In this study, we utilized Spearman correlation analysis to examine setup errors across all directions – an approach that is infrequently employed in prior research. Our objective was to determine whether variations in setup errors in one direction were correlated with changes in other directions. The results showed that there was a moderate negative correlation between Y and Z-direction setup errors at C4 and C7 level ($r = 0.209$, 0.258). At both the clivus and C4 level, a strong negative correlation was observed between X-direction errors and RTN ($r = 0.504$, 0.458). This was also the case in the analysis of the data for each of the two groups (Fig. 5). Additionally, these findings were consistent with observations made in clinical practice, which have demonstrated that increases in the Y-directional setup error, specifically towards either the head or foot side, are often correlated with specific anatomical changes in the neck region. Larger setup errors in the headward direction are associated with a forward bending of the neck, while larger errors in the footward direction are associated with a backward tilting of the neck. The muscle training group exhibited a higher correlation coefficient between the Y and Z directions compared to the control group. This suggests that, when influenced by errors in the Y direction, the Z direction error was smaller in the muscle training group than in the control group. This finding further demonstrates the efficacy of the intervention measures. At both the clivus and C4 level, an increase in X-direction error resulted in an increase in bed angle rotation error. This finding aligns with a study by Li et al. [24] on intracranial tumors, underscoring the importance of selecting a device with superior fixation capabilities and high repeatability for patients with head and neck tumors. Furthermore, it emphasizes the critical role of the therapist in meticulously adhering to the positioning process to minimize errors in any direction that may arise from the setu*p* procedure.

Several factors can influence the setup error, including the fixation device, the general characteristics of the patient (weight, gender, etc.), and the expertise of the therapist during the setup process. The fixation devices reported for head and neck tumor radiotherapy are mainly five-point and nine-point head-shoulder thermoplastic mask, the head is secured with a fixed headrest and a personalized vacuum pad, as well as the currently popular styrofoam [3, 22, 25]. Lin, CG et al. [22] reported that the combination of styrofoam and thermoplastic membrane for head, neck and shoulder fixation resulted in better effect and higher setup accuracy. This is consistent with the present study. This may be one of the reasons for the smaller setup error compared with other studies. The influence of general characteristics of patients on setup error has rarely been reported in head and neck tumors. Contesini, M et al. [3] showed that the increase in BMI correlated with a decrease in error for 29 patients. Pan CZ et al. [26] found that weight loss during treatment was an important factor affecting setup error in 30 patients with nasopharyngeal carcinoma. This study showed that women, weight loss, and cervical curvature increased the setup error. Neck muscle group training and oral stent were the factors influencing the reduction of setup error (Table 4). Previous studies have reported that the expertise of the therapist affect the setup error [27–29]. All therapists in this study had more than 10 years of working experience, hence the effect of different therapists on setup error can be ignored.

This study also has some limitations. First, this study is a single-center randomized controlled trial, hence its generalizability may be limited. However, it is worth highlighting that this trial represents the first prospective investigation to employ neck muscle training as a means to mitigate setup errors in HNC radiotherapy. Second, it is worth mentioning that in this study the implementation of neck muscle training was initially facilitated by rehabilitation physiotherapists, with subsequent involvement of patients' families. However, the sequential transfer of responsibility from healthcare professionals to families may have potential implications on patient compliance, potentially leading to an underestimation of the true effectiveness of the interventions. Third, the cervical curvature measurement method is relatively simple [30], but it may be influenced by various factors that could alter the accuracy of the measurement. Finally, a significant limitation of the study is the absence of daily volumetric imaging using CBCT, which affects the ability to accurately account for interfractional changes in soft tissue position, especially along the tongue, oropharynx, and larynx. This prevents us from clarifying the effectiveness of the intervention on soft tissues. In the future, we aim to enhance the image quality of CBCT using the dual-domain parallel deep learning network model with attention waning mechanism (AWM-PNet) proposed by our institution [31]. Moreover, we plan to investigate the impact of cervical deformation errors on cervical CTV and changes in soft tissue position and the effects of physical exercise on overall survival, late neck toxicities, and neck muscle mass change in both groups. We will also conduct multicenter randomized controlled trials to improve the level of evidence and validate the findings of this study.

Conclusion

In conclusion, the results obtained from this prospective study present compelling evidence to support the integration of neck muscle group training into the treatment protocol for head and neck cancer patients receiving radiotherapy. The study revealed a marked decrease in both the setup error in the anterior-posterior direction and the planning target volume (PTV) margin, indicating substantial benefits associated with this intervention.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13014-025-02593-z.

Supplementary Material 1

Acknowledgements
Not applicable.

Author contributions
(I) Conception and design: F Bai, L Zhang, X Yao, L Xu, J Zang; (II) Administrative support: F Bai, J Zang, L Zhao; (III) Provision of study materials or patients: F Bai, L Zhang, X Yao; (IV) Collection and assembly of data: B Li, J Li, Q Hu, Y Yin, C Liu, Z Xu; (V) Data analysis and interpretation: F Bai, Y Yin, L Zhang, L Zhao; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Funding
No funding was received for this study.

Data availability
Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

Declarations

Ethics approval and consent to participate
The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the First Affiliated Hospital of Air Force Medical University (ethical approval number: KY20202071-F-1). Written informed consent was obtained from participants to participate in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 29 May 2024 / Accepted: 23 January 2025
Published online: 12 March 2025

References

1. Rojo-Santiago J, Korevaar E, Perkó Z, et al. PTV-based VMAT vs. robust IMPT for Head-and-Neck Cancer: a probabilistic uncertainty analysis of clinical plan evaluation with the Dutch model-based selection. Radiother Oncol. 2023;109729. https://doi.org/10.1016/j.radonc.2023.109729.
2. Delaby N, Barateau A, Chiavassa S, et al. Practical and technical key challenges in head and neck adaptive radiotherapy: the GORTEC point of view. Phys Med. 2023;109:102568. https://doi.org/10.1016/j.ejmp.2023.102568.
3. Contesini M, Guberti M, Saccani R, et al. Setup errors in patients with head-neck cancer (HNC), treated using the intensity modulated Radiation Therapy (IMRT) technique: how it influences the customised immobilisation systems, patient's pain and anxiety. Radiat Oncol. 2017;12(1):72. https://doi.org/10.1186/s13014-017-0807-y.
4. Amro H, Hamstra DA, Mcshan DL, et al. The dosimetric impact of prostate rotations during electromagnetically guided external-beam radiation therapy. Int J Radiat Oncol. 2012;85(1):230–6. https://doi.org/10.1016/j.ijrobp.2012.03.020.
5. Jiang P, Zhang X, Wei S, et al. Set-up error and dosimetric analysis of HexaPOD Evo RT 6D couch combined with cone beam CT image-guided intensity-modulated radiotherapy for primary malignant tumor of the cervical spine. J Appl Clin Med Phys. 2020;21(4):22–30. https://doi.org/10.1002/acm2.12840.
6. Ahn PH, Ahn AI, Lee CJ, et al. Random positional variation among the skull, mandible, and cervical spine with treatment progression during head-and-neck radiotherapy. Int J Radiat Oncol. 2009;73(2):626–33. https://doi.org/10.1016/j.ijrobp.2008.10.007.
7. Kam MK, Chau RM, Suen J, et al. Intensity-modulated radiotherapy in nasopharyngeal carcinoma: dosimetric advantage over conventional plans and feasibility of dose escalation. Int J Radiat Oncol. 2003;56(1):145–57. https://doi.org/10.1016/s0360-3016(03)00075-0.
8. van Kranen S, van Beek S, Rasch C, et al. Setup uncertainties of anatomical sub-regions in head-and-neck cancer patients after offline CBCT guidance. Int J Radiat Oncol. 2009;73(5):1566–73. https://doi.org/10.1016/j.ijrobp.2008.11.035.
9. Zhang L, Garden AS, Lo J, et al. Multiple regions-of-interest analysis of setup uncertainties for head-and-neck cancer radiotherapy. Int J Radiat Oncol. 2006;64(5):1559–69. https://doi.org/10.1016/j.ijrobp.2005.12.023.
10. Polat B, Wilbert J, Baier K, et al. Nonrigid patient setup errors in the head-and-neck region. Strahlenther Onkol. 2007;183(9):506–11. https://doi.org/10.1007/s00066-007-1747-5.
11. Bai F, Zhang LH, Yao XW, et al. Feasibility of core cervical muscle group exercises and massage in the improvement of cervical spine curvature changes during radiotherapy for head and neck neoplasms. Cancer Res Clin. 2023;35(08):568–72. https://doi.org/10.3760/cma.j.cn115355-20230109-00019.
12. Ove R, Cavalieri R, Noble D, Russo SM. Variation of neck position with image-guided radiotherapy for head and neck cancer.Am. J Clin Oncol. 2012;35:1–5.
13. Zhong R, Song Y, Yan Y, et al. Analysis of which local set-up errors can be covered by a 5-mm margin for cone beam CT-guided radiotherapy for nasopharyngeal carcinoma. Brit J Radiol. 2018. https://doi.org/10.1259/bjr.20160849. 91 BRIT J RADIOL.
14. Wang G, Long X. Traditional Chinese medicine treatment selection for straightened cervical curvature and therapeutic observation. J Acupunct Tuina Sci. 2017;15(2):136–40. https://doi.org/10.1007/s11726-017-0990-2.
15. Zou L, Zhong C, Xu X, et al. Effect of Baduanjin exercise on cervical spondylosis: a protocol for the systematic review of randomized controlled trials. Medicine. 2021;100(12):e24813. https://doi.org/10.1097/MD.0000000000024813.
16. Zhuang Q, Feng H, Jing F, et al. Effect of Yijinjing exercise on cervical spondylosis: a protocol for systematic review. Medicine. 2020;99(27):e20764. https://doi.org/10.1097/MD.0000000000020764.
17. Cheo T, Loh Y, Chen D, et al. Measuring radiotherapy setup errors at multiple neck levels in nasopharyngeal cancer (NPC): a case for differential PTV expansion. Radiother Oncol. 2015;117(3):419–24. https://doi.org/10.1016/j.radonc.2015.09.032.
18. Mirjalili SA, McFadden SL, Buckenham T, et al. Vertebral levels of key landmarks in the neck. Clin Anat. 2012;25(7):851–7. https://doi.org/10.1002/ca.22124.
19. Grégoire V, Eisbruch A, Hamoir M, et al. Proposal for the delineation of the nodal CTV in the node-positive and the post-operative neck. Radiother Oncol. 2006;79(1):15–20. https://doi.org/10.1016/j.radonc.2006.03.009.
20. van Herk M, Remeijer P, Rasch C, et al. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. Int J Radiat Oncol. 2000;47(4):1121–35. https://doi.org/10.1016/s0360-3016(00)00518-6.
21. Lira FS, Dos Santos T, Caldeira RS, et al. Short-term high- and moderate-intensity training modifies inflammatory and metabolic factors in response to Acute Exercise. Front Physiol. 2017;8:856. https://doi.org/10.3389/fphys.2017.00856.
22. Lin CG, Xu SK, Yao WY, et al. Comparison of set up accuracy among three common immobilisation systems for intensity modulated radiotherapy of nasopharyngeal carcinoma patients. J Med Radiat Sci. 2016;64(2):106–13. https://doi.org/10.1002/jmrs.189.
23. Yang J, Garden AS, Zhang Y, et al. Variable planning margin approach to account for locoregional variations in setup uncertainties. Med Phys. 2012;39(8):5136–44. https://doi.org/10.1118/1.4737891.
24. Li B, Bai F, Yao X, Xu L, Zhao L. Clinical value of styrofoam fixation in intracranial tumor radiotherapy. Front Oncol. 2023;13:1131006. https://doi.org/10.3389/fonc.2023.1131006.
25. Delishaj D, Ursino S, Pasqualetti F, et al. Set-up errors in head and neck cancer treated with IMRT technique assessed by cone-beam computed tomography: a feasible protocol. Radiat Oncol J. 2018;36(1):54–62. https://doi.org/10.3857/roj.2017.00493.
26. Pan CZ, Pan JJ, Chen CB, et al. Electronic portal imaging device in the real-time correction of setup error in intensity modulated radiation therapy for nasopharyngeal carcinoma. Chin J Radiat Oncol. 2009;18(05):341–5. https://doi.org/10.3760/cma.j.issn.1004-4221.2009.05.341.
27. Wang HT, Yang JX, Shuai SS. Effect of different working experience of radiation therapist on intensity modulated radiation therapy in elderly patients with stage III non-small cell lung cancer. Chin Clin Oncol. 2018;23(5):449–52. https://doi.org/10.3969/j.issn.1009-0460.2018.05.013.
28. Prabhakar R, Laviraj MA, Haresh KP, et al. Impact of patient setup error in the treatment of head and neck cancer with intensity modulated radiation therapy. Phys Med. 2009;26(1):26–33. https://doi.org/10.1016/j.ejmp.2009.05.001.
29. Astreinidou E, Bel A, Raaijmakers CP, et al. Adequate margins for random setup uncertainties in head-and-neck IMRT. Int J Radiat Oncol. 2005;61(3):938–44. https://doi.org/10.1016/j.ijrobp.2004.11.016.
30. Li JP. The study on reliability of four methods of measurement for cervical lordosis. J Cervicodynia Lumbodynia. 2002;23(4):278–80. https://doi.org/10.3969/j.issn.1005-7234.2002.04.004.
31. Sun H, Yang Z, Zhu J, et al. Pseudo-Medical Image-Guided Technology Based on'CBCT-only'Mode in Esophageal Cancer Radiotherapy: A Novel IGRT Technique Based on the'CBCT-only'Mode[J]. Comput Methods Programs Biomed. 2024:108007.

Publisher's note