·临床研究·

鼻咽癌螺旋断层调强放疗图像引导策略

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摘 要:【目的】分析系统误差校正前后摆位误差的差异。为了确定在鼻咽癌治疗中最合适的影像引导策略，我们使用不同的扫描范围和影像引导频率对鼻咽癌(NPC)患者进行螺旋断层放疗(HT)。【方法】选择2019年10月至2020年02月在中山大学肿瘤防治中心接受HT治疗的NPC患者15例。每次治疗前均进行高压计算机断层扫描(MVCT)。放疗5次后，进行系统误差校正，调整摆位中心。采集了系统误差修正前后的摆位误差，以及不同扫描范围、不同扫描频率下的摆位误差进行了分析比较。【结果】系统误差校正前后摆位误差比较，左-右(LR)、上-下(SI)、前-后(AP)方向摆位误差差异有统计学意义(P<0.05)；“鼻咽+颈”、“鼻咽”不同扫描范围比较，偏航旋转误差差异有统计学意义(P<0.05)。经系统误差校正后的每日扫描频率与每周扫描频率比较，AP方向差异有统计学意义(P<0.05)。【结论】在鼻咽癌放射治疗中，根据前5次摆位误差可以纠正系统误差，然后选择小范围扫描进行每天的图像引导放射治疗。

关键词:鼻咽癌；螺旋断层放疗；影像引导放射治疗；摆位误差
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Image-guided Strategy of Intensity-modulated Radiotherapy in Helical Tomography for Nasopharyngeal Carcinoma

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Abstract:【Objective】This study aimed to analyze the difference in setup error before and after correction of systematic error. To determine the most appropriate image-guided strategy during HT treatment, we use different scanning ranges and image-guidance frequencies in patients with nasopharyngeal carcinoma (NPC) treated with helical tomotherapy (HT). 【Methods】Fifteen patients with NPC who received HT treatment in Sun Yat-sen University Cancer Center from October 2019 to February 2020 were selected. Megavoltage computed tomography (MVCT) scanning was performed before each treatment. After five times of radiotherapy, system-error correction was performed to adjust the setup center. The setup errors before and after the correction of systematic errors, as well as the setup errors of different scanning ranges and different scanning frequencies, were collected for analysis and comparison.【Results】When comparing the setup errors before and after the correction of systematic error, the differences in setup errors in the left - right (LR), superior - inferior

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(SI), and anterior - posterior (AP) directions were statistically significant (P<0.05).The different scanning ranges of "nasopharynx + neck" and "nasopharynx" were compared, and a statistically significant difference was found in yaw rotational errors ($P<0.05$). In the comparison of daily and weekly scan frequency after system-error correction, a significant difference was found in AP direction ($P<0.05$).【Conclusion】During radiotherapy for NPC, the systematic error can be corrected according to the first five setup errors, and then small-scale scanning was selected for image-guided radiotherapy every day.

Key words: nasopharyngeal carcinoma; HT; image-guided radiotherapy; setup error

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Radiation therapy is one of the three major treatment methods for malignant tumor treatment, among which the main treatment method for nasopharyngeal carcinoma (NPC) is radiation therapy [1]. Helical tomotherapy (HT) system is a widely used/ stable radiotherapy technology that integrates intensity-modulated radiation therapy (IMRT) and imaging-guided radiation therapy (IGRT). X-ray mode and film shooting use 3.5 MV computed tomography (CT) imaging mode [2]. The position of the target area can be tracked by the HT system in real time, and the patient position can be corrected online [3]. The HT system adopts a homologous double-beam structure, so the treatment space-coordinate system of the system completely coincides with the imaging space-coordinate system, which effectively reduces the systematic deviation of imaging. After megavoltage computed tomography (MVCT) image scanning, the image-registration system can automatically adjust the deviation of the patient's treatment position to improve treatment accuracy. However, HT treatment duration was reported very demanding for 25% of patients by a study of Aude Vaandering et al. It was determined that an average additional (10 ± 2) min (n = 30) was necessary for this procedure [4]. But reducing the scan frequency as the above study increases the risk of large setup errors. Hence, lengthy treatment times lead us to study the possibility of reducing the time or scanning range of pre-treatment MVCTs. This paper discusses the optimal imaging-guided strategy for the treatment of NPC patients based on the HT system.

1 Materials and Methods

1.1 Patient characteristics

A total of 15 patients with NPC who received radiotherapy at HT in our hospital from October 2019 to February 2020 were selected, including eight male and seven female patients, with ages ranging within 31~64 years (median age of 44 years).

1.2 Ethics approval and consent to participates

Our study was reviewed and approved by the Institutional Review Board of Sun Yat-Sen University Cancer Center, with the approval number of GYX2020-011. Informed consent for approval of the exemption by the committee.

1.3 Radiotherapy techniques

A patient was asked to lie supine with an alpha cradle back rest (Forrad, Guangzhou, China) supporting the head, neck, and shoulder and with a thermoplastic shell (*Civico*, *USA*) covering the head and neck down to upper chest (AC system). The planning CT imaged with 3 mm slice thickness was performed on a *Philips* Brilliance large-bore helical CT simulator, which is obtained for the planning purpose. MVCT was scanned and treated on Tomo Therapy Hi Art (CNNC Accuray, Tianjin, China), and daily MVCT is for the daily patient setup and image guidance.

1.4 IGRT procedure

The first five radiotherapy MVCT scans were performed to cover the "nasopharynx + neck". After first five, the system error correction was performed according to the average set-up error of the first five times and the set-up center was adjusted. After five treatment fractions, system-error correction was performed according to the average setup error of the first five times, and the setup center was adjusted. Five scans were then performed to cover the "nasopharynx + neck". The difference in setup error before and after system-error correction was compared. Daily MVCT scanning usually takes a long time, which increases the probability of adverse reactions in patients during radiotherapy, and is prone to random errors. To observe the difference in setup error in different scanning ranges, the next treatment was divided into "nasopharynx + neck" and "nasopharynx" for alternate scans. The schematic of the scanning range is shown in Fig. 1A and Fig. 1B. The scanning-slice and reconstruction-slice thicknesses were both 3 mm, and the automatic registration method of bone and soft tissue was used for image registration. A total of 450 MVCT scans were performed in 15 patients with NPC.

1.5 Statistical analysis

IBM SPSS 24.0 was used to analyze the data, and measurement data (setup error) were expressed as M (P_{25}~P_{75}). Data row Wilcoxon signed rank sum test and test level α=0.05 (two-tailed) were also used. (Each data table object is composed of date row and data column.)

2 Results

2.1 Comparison before and after system-error correction

When comparing the setup errors before and after the correction of systematic error, the differences in setup errors are on the six-dimensional orientation. They are six degrees-of-freedom rigid transformation, three for translation and three for rotation. Nonparametric rank sum test was performed on the six-dimensional orientation error data of 15 patients with NPC before and after system-error correction, as shown in Table 1. Fig. 2 more intuitively reflects the change of setup errors before and after adjusting the center point. It can be concluded from the table and the figure that after correcting the center point, setup errors is closer to 0 in the directions of LR, SI and AP.

2.2 Comparison of different scan ranges

The scanning ranges of "nasopharynx + neck" and "nasopharynx" were alternately used for MVCT scanning. Nonparametric rank sum test was performed on the obtained setup error data, as shown in Table 2. As can be seen from Table 2, using the different scanning ranges of "nasopharynx + neck" and "nasopharynx", a statistically significant difference was found in yaw rotational errors (P<0.05). Therefore, when we use the "nasopharynx" scanning range later, we must pay close atten-

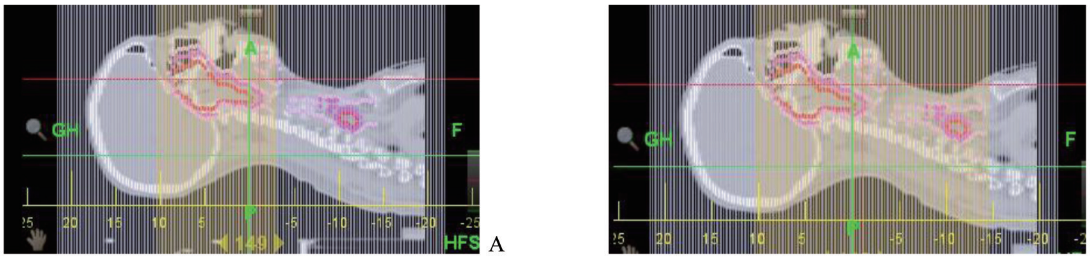
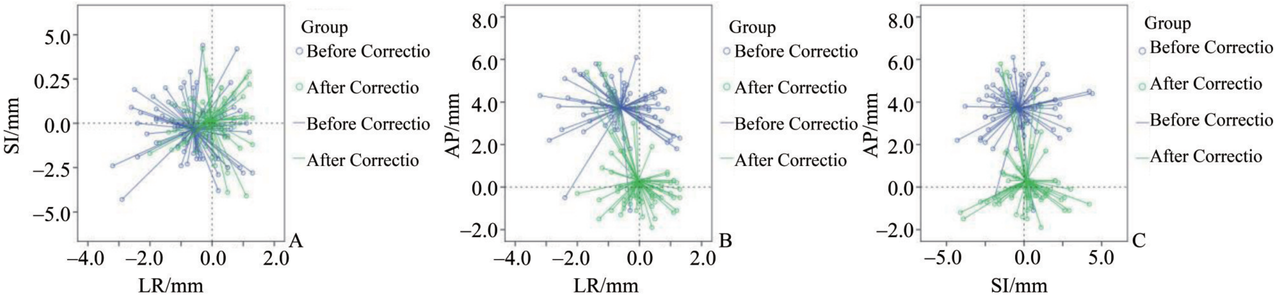


Fig. 1 The scanning range includes "nasopharynx" (A) and "nasopharynx + neck" (B)

Table 1 Comparison of setup errors before and after center-point adjustment

Items	LR/mm	SI/mm	AP/mm	Pitch/°	Roll/°	Yaw/°
Before correction	−0.7(−1.1~0.2)	−0.7(−1.5~0.6)	3.9(3.4~4.6)	−0.1(−0.4~0.0)	0.2(0.0~0.4)	0.0(−0.1~0.2)
After correction	0.0(−0.7~0.7)	0.5(−1.1~1.8)	−0.1(−0.6~0.8)	0.0(−0.4~0.0)	0.1(0.0~0.3)	0.0(−0.1~0.2)
n	75	75	75	75	75	75
z	1.633	1.796	5.226	0.735	0.980	0.653
P	0.010	0.003	0.000	0.653	0.292	0.787

"N" means sample capacity, "z" means z value, "P" means P value



A: The change of setup errors in the SI, LR direction; B: The change of setup errors in the AP, LR direction; C: The change of setup errors in the SI, AP direction.

Fig. 2 The change of setup errors after adjusting the center point

tion to the displacement value in yaw direction. When yaw rotational error is found to be large, we should use a long-range scan to avoid large deviations. In three directions of linearity, the error difference between the two scanning ranges was not statistically significant.

2.3 Comparison of different scan frequencies

The setup error data obtained by scanning every day and the positioning error data obtained every week were extracted for independent sample t test, as shown in Table 3. Fig. 3 more directly reflects the changes in setup errors of these two sets of data. Combining the Table 3 and Fig. 3, it can be clearly found that the difference of setup error in the AP direction is statistically significant, between the two groups of data scanned every day and every week, $P < 0.05$.

3 Discussion

HT is one of the most advanced radiotherapy systems in the world at present. The combination of IMRT technology and helical tomography technology can cause even deposition of the dose on the tumor target area, thereby improving the dose conformity of the tumor area. Sparing the surrounding normal tissues and organs significantly improves the treatment-gain ratio of tumor patients and achieves precise treatment effects comparable with surgery [5-6]. Precise dose projection places higher demands on the positional accuracy of the treatment owing to its steep-edge dose gradient [7]. IGRT technology uses various advanced imaging equipment to monitor tumors and normal organs in real time. Its application fully considers the movement of anatomical tissues during treatment and the displacement error between fractional treatments, which effectively improves the accuracy of radiotherapy. At the same time, it also better protects the organs at risk [8-9], which is an important guarantee for the accurate implementation of IMRT [10]. However, additional image verification increases the additional radiation dose of the patient and brings a certain economic burden to the patient, and the treatment time required for each patient also correspondingly increases. How to use the image guidance technol-

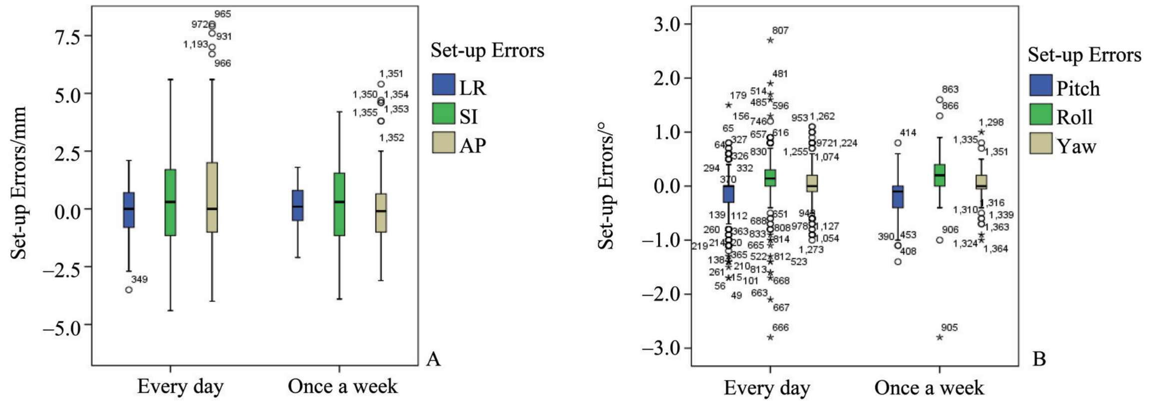
Table 2 Comparison of positioning errors in different scanning ranges [*M*/(*IQR*)]

Items	LR/mm	SI/mm	AP/mm	Pitch/°	Roll/°	Yaw/°
NP+ neck	0.0(−0.6~0.6)	0.4(−1.2~1.9)	−0.3(−1.1~0.7)	0.0(−0.4~0.0)	0.1(0.0~0.3)	0.0(−0.1~0.1)
NP	0.1(−0.6~0.8)	0.0(−0.5~1.7)	−0.5(−1.2~0.6)	0.0(−0.2~0.1)	0.2(0.0~0.4)	0.0(0.0~0.1)
n	150	150	150	150	150	150
z	1.040	0.942	0.630	1.309	0.564	1.654
P	0.230	0.338	0.823	0.065	0.908	0.008

"NP" means nasopharynx.

Table 3 Comparison of setup errors of different scanning frequencies [*M*/(*IQR*)]

Direction	Groups	*n*	Average	*z*	*P*
LR/mm	Every day	300	0.0(−0.8~0.7)	0.771	0.592
	Once a week	60	0.1(−0.5~0.8)		
SI/mm	Every day	300	0.3(−1.2~1.7)	0.449	0.988
	Once a week	60	0.3(−1.2~1.6)		
AP/mm	Every day	300	0.0(−1.0~2.1)	1.405	0.039
	Once a week	60	−0.1(−1.0~0.7)		
Pitch/°	Every day	300	0.0(−0.3~0.0)	0.689	0.729
	Once a week	60	−0.1(−0.4~0.0)		
Roll/°	Every day	300	0.14(0.0~0.3)	0.606	0.856
	Once a week	60	0.2(0.0~0.4)		
Yaw/°	Every day	300	0.0(−0.1~0.2)	0.433	0.992
	Once a week	60	0.0(−0.1~0.2)		



A: The comparison of setup errors obtained by scanning every day and every week in the three directions of LR, SI and AP; B: The comparison of setup errors obtained by scanning every day and every week in the pitch, roll, and yaw directions.

Fig. 3 The comparison of setup errors in the three directions

ogy reasonably requires targeted exploration to formulate the optimal imaging-guidance strategy. In the present study, we observed the differences in the positioning errors of patients with NPC before and after correcting the positioning system errors, different scanning ranges, and different scanning frequencies to identify a suitable method for helical tomographic image guidance for NPC.

Radiotherapy for patients with NPC in our hospital was performed with the alpha cradle system, which supports the head, neck, and shoulders, and an ideal fixation effect is achieved [11-12]. However, the accuracy of the position during radiotherapy implementation is related to the fixed device and to the systematic error of the radiotherapy equipment, the changes in the patient's own body contour, the movement of the organs, and the differences in placement methods of different radiotherapy technicians [13]. Thus, system-error correction is necessary to perform for each patient's radiotherapy setup. Herein, as shown in Table 1 and Fig. 2, the setup error was systematically corrected according to the median value of the patient's first five treatments. We observed that after adjusting the treatment center point, the linear setup error in the three-dimensional direction of the patient was significantly reduced, and the maximum median value was reduced from 3.9 mm to −0.1 mm, consistent with the conclusion of Huang et al.[14], i. e., errors in the three directions after the automatic correction of the HT machine are all less than 1 mm. Among them, the largest change in the positioning error of the treatment center point is AP direction error because of the relatively long time interval between the patient's position fixing device and treatment. The error is primarily affected by the change in the patient's body shape. For example, if the patient loses weight, the neck fat becomes thinner, and the thermoplastic omentum loosens, but the center of the field on the omentum does not sink [15]. Given that the treatment bed of the HT system is heavier, the bed board sinks as treatment progresses [6, 14]. Remeijer [16] and Fu [17] reported that the variation in target dose caused by the rotation error is very small and can be ignored, whereas the HT system itself can be corrected only by adjusting the errors in the linear and roll rotational directions [18]. The present study concluded that the differences in the LR, SI and AP directions were statistically significant before and after adjusting the treatment center point. Moreover, the placement errors in the pitch, roll, and yaw directions were small, and the median rotational swing before and after changing the treatment center point had bit errors all less than 0.3°.

Although the treatment of patients with the HT system can significantly improve treatment accuracy, the MVCT of the HT system still needs improvement [19]. The X-ray energy used in the CT scanning of the positioning CT and the HT system differs, and the contrast of the images differs, leading to a certain error in the image registration. The scanning range selected by HT system is smaller than the actual treatment length of nasopharyngeal carcinoma, which will also lead to errors. Guan et al.[20] showed that the positioning error of NPC patients with different scanning ranges differs. When the scanning range is too small, its accuracy cannot guarantee the accuracy of the entire target volume, and when the scanning range is too long (such as imaging-guided registration of the entire target volume), the patient receives additional radiation. If the entire target area is scanned in sections during treatment, although the matching degree of the images can be improved, it also increases the treatment time of the patient. In the present study, as shown in Table 2, by comparing the scanning errors of the nasopharynx and nasopharynx + neck, we found that the errors of small-scale scanning are only statistically significant in the yaw direction, with median values of 0.0(−0.1~0.1)mm and 0.0(0.0~0.1)mm, respectively. The mean does not considerably differ. In the three linear directions, the error difference between the two scanning ranges is not statistically significant. Thus, the scanning range of the nasopharynx for NPC radiotherapy image guidance is used to improve efficiency. When the yaw rotational error is found to be large, it should use a long-range scan to avoid large deviations.

Zhang [21] et al. conducted a study entitled "Avoiding Treatment Errors and Accidents," which recommends weekly image guidance. As shown in Table 3 and Figure 3, we compared and analysed the error data of daily scans and the error data of weekly scans after adjusting the center and found that the difference in error data in AP direction is statistically significant. If one considers scanning only once a week, attention should be paid to the difference in the results of comparing the AP axis direction. Yao[22] and others studied different frequency scans during HT system treatment. They found that the chest, abdomen, and pelvis can be used to guide the subsequent treatment according to the first five scans. Then, a weekly scan method can be used to ensure treatment accuracy. However, the target area of NPC is relatively irregular, and the important organs and tissues are distributed mostly in a small space. Based on the analysis results of this study, performing MVCT scan-guided radiotherapy is recommended every day for the treatment of patients with NPC.

Although we tried our best to analyze these cases from multiple angles, the number of cases in this study is still insufficient, which has a certain impact on the accuracy of the results. In the future, more cases should be collected in scientific research, and even multi-center sample collection should be carried out to improve the accuracy of the results. The incidence of cervical lymph node metastasis in nasopharyngeal carcinoma is high, and about 70% of patients have cervical lymph node metastasis upon diagnosis. Therefore, in the previous radiotherapy process, the treatment guidelines recommended that all patients with nasopharyngeal carcinoma in clinical stages should receive whole neck prophylactic irradiation, and the scanning range will be determined accordingly. In March 2022, a team from the Department of Radiotherapy of Sun Yat-sen University Cancer Center found that selective upper neck irradiation on the negative side of cervical lymph nodes in nasopharyngeal carcinoma could achieve a similar survival rate as standard whole neck irradiation. The results of this study have important implications for the updating of nasopharyngeal cancer treatment guidelines. If the guidelines are changed in the future, the optimal image-guided strategies for patients with different stages will be changed accordingly. At that time, the image-guided strategies will be discussed in more depth and detail.

4 Conclusions

Based on the above studies, when conducting spiral tomographic imaging-guided treatment of NPC patients, adjusting the treatment center point according to the error of the first five treatments is recommended. Small-scale scans are used every day to guide radiotherapy with MVCT scan images.

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