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Compare of Interfractional Setup Reproducibility Between Vacuum-Lock Bag and Thermoplastic Mask in Radiotherapy for Breast Cancer

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Abstract

Background: This study aimed to analyze the difference of setup reproducibility between Vacuum-lock bag and Thermoplastic mask in the radiotherapy for breast cancer. **Methods:** A total of 100 invasive breast carcinoma patients were collected, among whom 50 patients were immobilized with Vacuum-lock bag (VB group), and the other 50 patients were immobilized with Thermoplastic mask (TM group). Set up reproducibility in different axes and comfort levels between two groups at three treatment progress points during the radiation therapy were collected and analyzed. **Results:** The linear regression model showed that fixed device was an independent factor of radiotherapy setup error (SE). Further subgroup analysis based on different axes showed that the SE caused by the fixed device was obvious in all directions. The comfort level in the VB group was significantly larger than that in the TM group at the beginning of treatment, reduced as the treatment progress going on, and finally disappeared within three weeks. **Conclusions:** Thermoplastic mask could significantly reduce positioning errors in the radiotherapy of breast cancer. Although more discomfort was found in the TM group, it could be eliminated as the treatment progresses.

Keywords

Breast cancer, radiotherapy, positioning error, immobilization devices, vacuum-lock bag, thermoplastic mask

Abbreviations

BIS, Breast-Immobilizing System; CBCT, Cone-beam computed tomography; CTV, Clinical Target Volume; DPE, difference of positioning error; EPID, Electronic Portal Imaging Device; IMRT, intensity-modulated radiotherapy; ITV, internal target volume; LRM, linear regression model; OAR, Organ at risk; PE, positioning error; PTV, Planning Target Volume; TM, Thermoplastic mask; TPS, Treatment Planning System; VB, Vacuum-lock bag.

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Background

Breast cancer is the most common malignancy in the female in the world and China. According to the newest cancer statistics, breast cancer had the first incidence and the fourth mortality in Chinese female[1-3]. Postoperative radiotherapy is a very important treatment of breast cancer[4], which could improve patients' local-regional control and survival[5,6]. Precise immobilization devices play a very important role during radiation therapy as it can reduce geometrical uncertainties, raise the radiation accuracy, and improve the benefit of radiotherapy. In our institution, vacuum-lock bag (VB) and breast bracket with Thermoplastic mask (TM) are two main immobilization devices for radiotherapy in breast cancer in clinic. However, previous reports on breast positioning errors were mainly focused on breast board[7-9], vacuum bag[9-13], alpha cradle[14,15]. There was little research on the setup errors of thermoplastic mask (TM) in breast cancer. Therefore, it is of clinical value to explore the setup errors of TM fixed breast cancer radiotherapy and compare it with traditional VB.

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Methods

Patients

A total of 100 pT1 to 2N0 to 2M0 invasive breast carcinoma patients who received surgery followed by radiotherapy from January 2018 to January 2020 were enrolled in this study. Half of these patients were immobilized with Vacuum-lock bag (the VB group), and the other 50 ones were immobilized with Thermoplastic mask and arm grips (the TM group). Patients' clinical characters were listed in Table 1.

Immobilization Device

Vacuum-lock bag (R7504-35BC, Klarity Medical, Shenzhen, China)

Patients with Vacuum-lock bag remained supine in a Vacuum-lock bag with the head-turning to the contralateral side of the operative breast as much as possible. The ipsilateral upper limb extended along the Vacuum-lock bag and over the head, with the ipsilateral hand clinging to calvarium. The contralateral upper limb was downward along the body side.

Thermoplastic mask (RD305-3242C, Klarity Medical, Shenzhen, China)

Patients with thermoplastic mask supported on a body bracket (R605-12FCF & R605-2WCF, Klarity Medical, Shenzhen, China) were fixed with a thermoplastic mask wrapping closely to the body. Both upper limbs were extended above their head with two hands gripping the pole.

Radiation treatment Plan

Patients were fixed and scanned in a large aperture CT-simulation with 3 mm slice thicknesses. CT images were sent to the treatment planning system for the subsequent target delineate. Clinical target volume (CTV) is defined as the ipsilateral breast/chest wall and/or lymph nodes. Planning target volume (PTV) was defined as CTV expanded by 5 mm around and 10 mm in the superior and inferior direction, with 3 mm space under the skin surface. A simplified intensity-modulated radiotherapy (IMRT) plan was designed for everyone by Monaco (V5.11.03, Elekta) treatment planning software. The prescription dose was 50 Gy/25F to PTV. Dose limits of Organ at risk (OAR) were as follows: ipsilateral lung: $V20 < 25\%$, $V5 < 50\%$, Dmean < 12 Gy; contralateral lung $V5 < 10\%$; heart $V25 < 10\%$, Dmean < 6 Gy; spinal cord Dmax < 35 Gy.

Position Parameters

Position parameters contained patient positioning error (PE) in left-right (X), superior-inferior (Y), anterior-posterior (Z) directions, and 3D vector error (T) defined as root-sum square of X, Y, and Z. In this study, setup errors of all the axes were measured during radiotherapy with CBCT weekly, based on surgical clips present in the tumor bed and external breast contour. The beginning of the first, third, and fifth week during the radiotherapy were defined as T1, T2, and T3. The setup errors at these three time points were collected for analysis.

Comfort Levels

Comfort levels were classified into two levels according to the patient's choice to the question that what was your feeling about the immobilization during radiation therapy. The choice items included comfortable (A) and uncomfortable (B). Everyone was also queried about comfort levels at the beginning of the first (T1), third (T2), and fifth (T3) week during radiotherapy respectively.

Statistical Analysis

Continuous variables were presents as mean ± standard deviation and illustrated with the box plot. Mean of two continuous normally distributed variables were compared by paired samples Student's test. Mean of two continuous without normally distributed variables were compared by the Non-parametric rank-sum test. Relevant factors of continuous variables were explored with the Linear regression model and illustrated with forest plots. Categorical variable data were analyzed by Chi-square Test. $P < .05$ was considered statistically significant. All the data were analyzed by R version 3.5.3[16] (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patients' baseline and clinical characteristics of two groups (Table 1) have no significant difference ($P > .05$)

Position Parameters

Immobilization deviation of left-right (X), superior-inferior (Y), anterior-posterior (Z), and 3D vector error (T) of two groups were summarized in Table 2, and Figure 1. The data indicated that compared with the TM group, the VB group had higher PE in X, Y, Z axes, and 3D vector and at each time point (Figure 1) during radiotherapy.

Linear regression model and stepwise regression were performed to explore the association between the PE and different fixed devices, axes, and time points (Figure 2). The result showed that 1. The difference of positioning error (DPE) between the VB and TM group was significant. 2. The PE in

Table 1. Clinical Characteristics of Patients in Two Groups.

Characteristics		TM	VB	*P*-value
Patients		50	50	
Median age (years)		47.300 ± 8.906	50.640 ± 9.075	.067
BMI		25.116 ± 3.033	24.542 ± 2.338	.292
Treated side	Left	21	27	.317
	Right	29	23	

Table 2. Immobilization Deviation of Left-Right (X), Head-Foot (Y), Up-Down (Z) and 3D Vector Error (T) of Two Groups.

Time	Group	X (mm)	Y (mm)	Z (mm)	T (mm)
T1	TM	1.560 ± 2.375	1.480 ± 1.961	0.840 ± 1.462	2.949 ± 2.862
	VB	3.660 ± 2.967	4.340 ± 2.396	3.680 ± 2.691	7.643 ± 2.981
T2	TM	0.980 ± 1.778	1.460 ± 1.798	0.800 ± 0.990	2.484 ± 2.211
	VB	2.180 ± 2.413	2.780 ± 1.920	2.620 ± 1.602	5.114 ± 2.266
T3	TM	0.900 ± 1.581	1.020 ± 1.332	0.820 ± 0.896	2.162 ± 1.699
	VB	2.640 ± 2.529	2.600 ± 1.591	2.760 ± 1.572	5.268 ± 2.208

T2 and T3 were significantly smaller than in T1. 3. The PE in Y direction was larger than in X direction, but not significant.

Further subgroup analysis by different axes (Figure 3) demonstrated that 1. The DPE between the TM and VB group were significant in X, Y, Z and T axes. 2. DPE between T2 and T1 were significant in X-axis, Y-axis, Z-axis and 3D vector. 3. DPE between T3 and T1 were significant in X-axis, y-axis, z-axis and 3D vector. 4. DPE between the TM and VB group was significantly larger than that among different treatment progress points.

Comfort Levels

Table 3 presented the comfort levels of the two groups. It showed that the comfortable level of the VB group was significantly higher than those of the TM group at the beginning of radiotherapy ($P < .01$). But the difference became small as the treatment processing and eliminated within three weeks after the beginning of treatment (T3).

Discussion

Breast cancer is the most common cancer of female in the world and China[1-3]. The importance of breast radiotherapy is rising, with the increasing component rate of early-stage breast cancer[17]. The setup errors have always being a vexing problem during radiotherapy[18-21]. It plays an important role in the delineation and definition of PTV[21-24] or ITV[25], and therefore affects radiation effect[25-28] and toxicity[29,30] of the patients. A precise fixing device is beneficial to reduce the setup errors, improve radiation precision and efficacy. Nowadays, breast bracket with Vacuum-lock bag or Thermoplastic mask

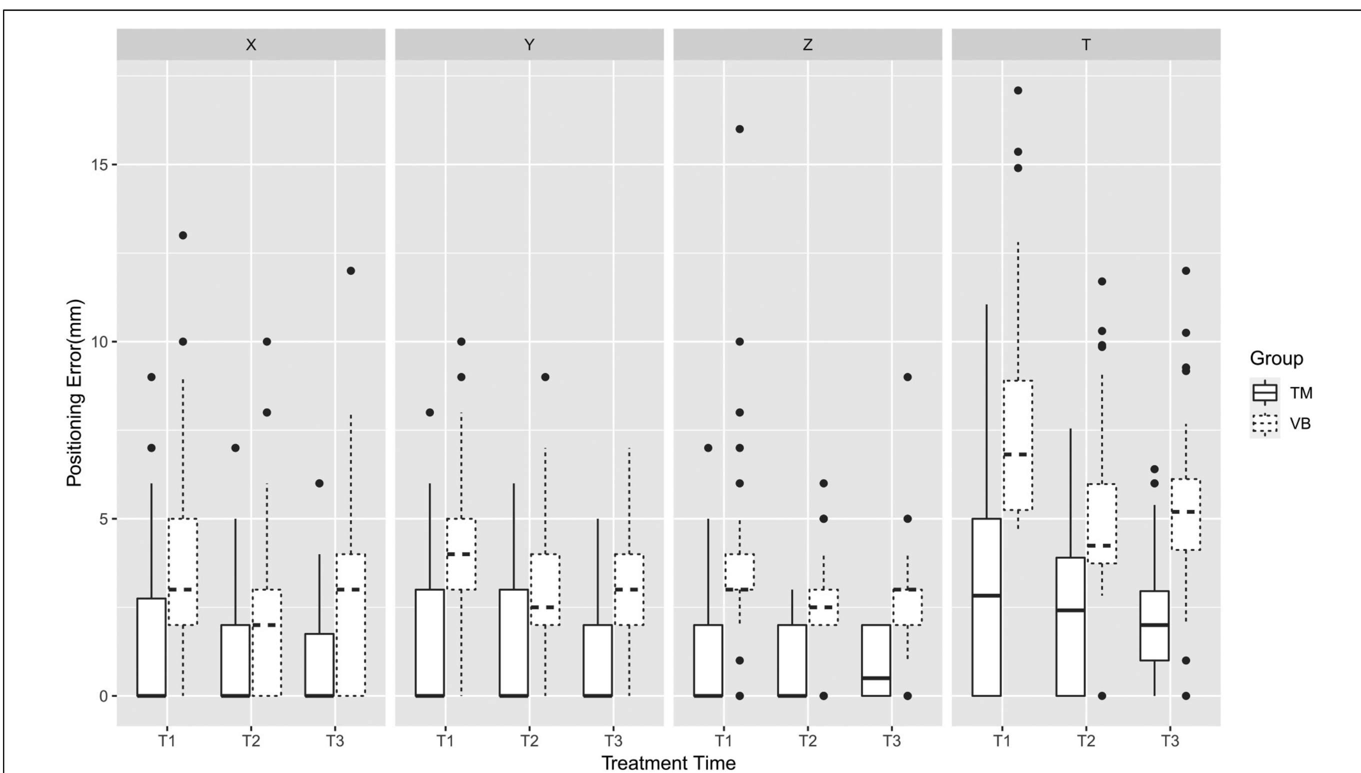

Figure 1. Box plot of treatment time to Positioning Error (PE) by two different fixed devices (TM vs VB) in X (X), Y (Y), Z (Z) axes and 3D vector (T).

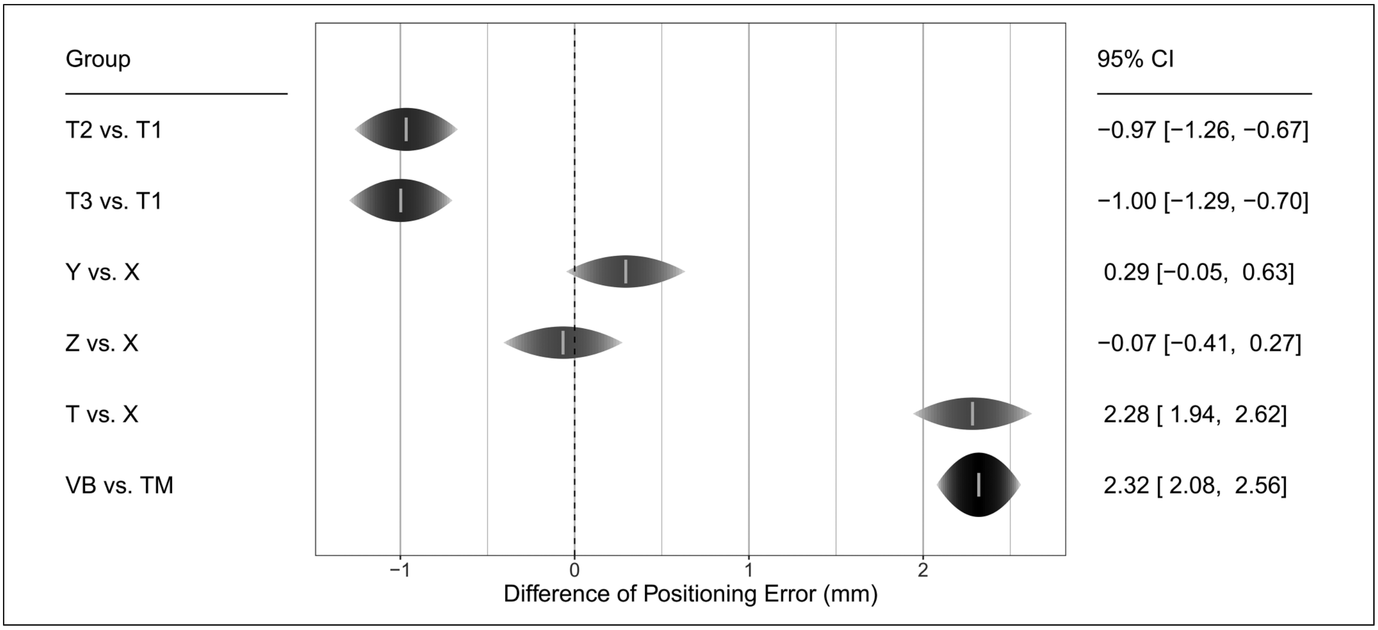

Figure 2. Forest plot of different factors to Positioning Error by linear regression analysis.

combined with respiratory gating technique, such as the optical surface management system, is believed to be more precise than other non-invasive breast-immobilizing system (BIS)[6], and be a benefit to patients' local control and overall survival. But because of the expensive cost and technical challenges, many hospitals, including our hospital, cannot perform this BIS. The major BIS in the irradiation department of this hospital is still the breast bracket, Vacuum-lock bag or thermoplastic mask[19]. Previous studies on the breast cancer radiotherapy fixation devices mainly focused on vacuum bag[9-13], breast board[7-9], and alpha cradle[14,15]. We found the PEs of vacuum bag[9-13] ranged from 2.7 to 5.1 mm around and 5.3 to 9.8 mm in superior-inferior axis in different studies, and study on thermoplastic mask combined with breast board were very few.

As a result of these, we design this study to explore the setup errors of TM and VB in our institution, and compare the setup errors and comfort levels of these two BISs. The result in Table 2 showed that PE of VB ranged from 4.1 to 6.7 mm, which was consistent with previous researches[9-13]. PE of TM ranged from 1.7 to 3.9 mm. The mean PE in the TM group was smaller than that in the VB group in each axis. The following analysis with the linear regression model (LRM) indicated that different fixed devices and radiation treatment progress points were both independent factors of PE, while the axis factor was not. PE affected by fixing devices was significantly higher than treatment progress and axis factors. These indicated different fixed devices were the most important independent factor of PE. Meanwhile, as the treatment processing, PE

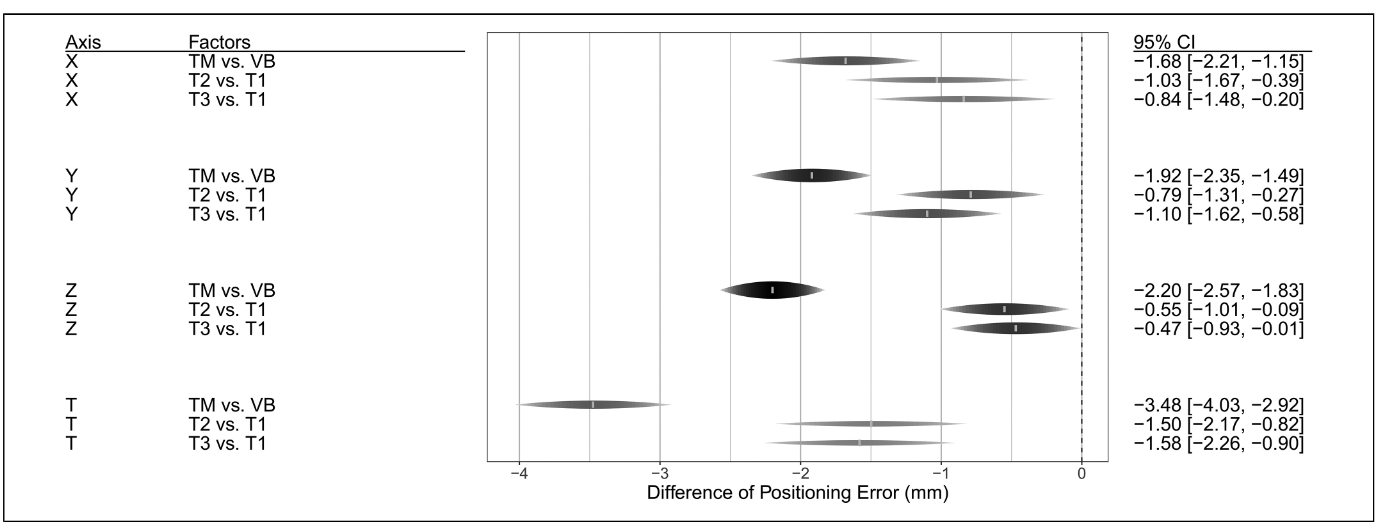

Figure 3. Forest plot of different factors to Positioning Error based on the axis by linear regression analysis.

Table 3. Comfortable Levels of Two Groups in Each Time Point.

Time	Group	Comfortable	Uncomfortable	X^2	P
T1	TM	25	25	6.178	.013[a]
	VB	38	12		
T2	TM	30	20	4.857	.028[a]
	VB	41	9		
T3	TM	38	12	1.040	.308
	VB	43	7		

[a]Chi-square test, $P < .05$.

could reduce nearly 1 mm, which might be attributed to the adaptation to immobilization position according to the repeated posture exercise during radiotherapy. While PE in X, Y, and Z-axis was similar, which revealed the effect of the axes to PE was very little.

The following subgroup analysis of PE based on different axes demonstrated that PE in the TM group was significantly smaller than in the VB group in all directions. And PE at T2 and T3 were also significantly smaller than that at T1 in all directions. All the above indicated both fixed with TM and going on of radiation treatment could significantly reduce PE in each axis. These two factors could shrink 2.5 - 3 mm PE in each axis and 5 mm PE in 3D vector. Of these, PE caused by the fixed device factor was twice as much as that caused by the treatment progress factor, indicated the fixed device factor was also the major independent factor of PE. Based on these data, we have reason to reduce the PTV margin of TM-fixed breast cancer patients by 1.68 - 2.2 mm in different axes, and therefore reduce the adverse reactions of OARs.

As for the comfort level difference between the two groups, the comfort level in the VB group was significantly higher than in the TM group in T1. While as radiotherapy progress went on, the comfort level difference between the two groups became small, and disappeared within three weeks. These indicated TM could increase the discomfort at the beginning of radiotherapy compared with VB, but this discomfort could be eliminated as the radiotherapy progress went on.

It is worth to note that we did not explore the real-time intra-fractional error of breast cancer radiotherapy in this study for the reasons of equipment, time and fee. Although previous studies[31-33] have confirmed that the intra-fraction setup error was much lower than the inter-fraction setup error, this still should not be ignored. But we will pay attention to this limit in the future.

Conclusions

In conclusion, Thermoplastic mask brought significantly less PE than with Vacuum-lock bag in all axes in the radiation therapy of the breast cancer. The extra discomfort caused by TM could be tolerated and disappeared as the treatment progressing.

Author Contributions

S.Y.Q and L.H.L conceived and designed the experiments and were responsible for writing the manuscript. S.Y.Q, P.J, and C.Q.F collected patients' position error and comfort levels. S.Y.Q and L.H.L were responsible for data analysis. All authors reviewed the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics Approval and Consent to Participate

The Institutional Review Board for human studies of The Affiliated Huaian No.1 People's Hospital of Nanjing Medical University, China (the approval number is YX-2021-027-01); approved the study protocol for this retrospective study, and informed written consent was obtained from all subjects. The study was performed following the approved guidelines.

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