Design of a new breast vacuum bag to reduce the global and local setup errors and to reduce PTV margin in post-mastectomy radiation therapy

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ABSTRACT

To design a new breast vacuum bag to reduce global and local setup errors in post-mastectomy radiation therapy (PMRT). A total of 24 PMRT patients were immobilized with an old vacuum bag and 26 PMRT patients were immobilized with a new vacuum bag. The registration results were analysed using four regions of interest (ROI): the global ROI (including the whole region of the planning target volume (PTV), G ROI), the supraventricular area (S ROI), the ipsilateral chest wall region (C ROI) and the ipsilateral arm region (A ROI). The global and local setup errors of the two groups were compared. The global setup errors of the new vacuum group were significantly smaller than those in the old vacuum group with the exception of yaw axes (P < 0.05). The systematic error (Σ) and random error (σ) ranged from 1.21 to 2.13 mm. In the new vacuum group, the local setup errors in the mediolateral (ML) direction and roll axes for C ROI (the Σ and σ ranged from 0.65 to 1.35 mm), and the local setup errors in ML and superior-inferior (SI) directions for S ROI were significantly smaller than those in the old vacuum group. The total required PTV margins for the chest wall in ML, SI, and anterior-posterior (AP) were 4.40, 3.12 and 3.77 mm respectively. The new vacuum bag can significantly reduce the global setup errors and local setup errors in PMRT. The respiratory motion of the chest wall was negligible, and the 5 mm PTV margin could cover the local setup errors in PMRT using the new vacuum bag with cone beam CT (CBCT) correction.

Keywords: breast vacuum bag; global and local setup errors; post-mastectomy radiation therapy

INTRODUCTION

Post-mastectomy radiation therapy (PMRT) can significantly reduce the local recurrence of breast cancer and improve the overall survival rate of patients. To further improve the uniformity and accuracy of the target dose and reduce the dose to organs at risk (OAR), intensity modulation radiation therapy (IMRT), field in field (FIF) and other technologies are widely used [1]. However, the target area of PMRT is large, and there is a large setup error [2], which causes uncertainty regarding the target dose. Currently, reported breast immobilization methods include breast cradles, Alpha Cradle (foam), vacuum bag and arm support. There are a large number of setup errors associated with each of these different immobilisation methods, with system errors ranging from 0.7 to 5.7 mm, and random errors ranging from 1.0 to 4.1 mm [2, 3].

What we have found in clinical practice is that the size of the vacuum bag is relatively small, making it difficult to fix it well to the body and arm. Therefore, we hypothesised that changing the size and shape of the vacuum bag and strengthening the support of the body and arm can improve the fixation effect. At present, all reports about the setup errors have analysed the global setup errors [the errors of the whole...
region of planning target volume (PTV)], and do not involve the local setup errors [the difference errors between the whole region and sub-region of interest] [2, 4]. However, in our previous study, we found that there were large global setup errors and local setup errors in the use of vacuum bags [5]. Therefore, evaluation of the effect of the immobilization device should include the global setup errors and the local setup errors. Secondly, the patient’s breathing motion can cause chest wall motion. Computed tomography (CT) simulation positioning is only a snapshot image and does not include the patient’s breathing motion information. Therefore, the residual local setup errors and respiratory motion movement are the main factors when setting the PTV margin in PMRT treatment using image-guided radiation therapy (IGRT).

The purpose of this study was to design a new breast vacuum bag to strengthen the support of the arm, and to compare the global and local setup errors with the traditional vacuum bag. The study also aimed to quantify the respiratory motion amplitude of the chest wall, to analyse the correlation between the motion amplitude of the chest wall and the amplitude of the diaphragm and to determine the corresponding PTV margin based on the local setup errors and the motion amplitude of the chest wall.

**MATERIALS AND METHODS**

**Patients**

From March 2019 to December 2019, a total of 50 patients with PMRT were included in this study, and they were randomly divided into two groups. The old vacuum group was immobilised with an old vacuum bag (CIVCO Radiotherapy, Orange City, IA, USA) (24 patients), while the new vacuum group was immobilised with a new vacuum bag (Klarity Medical, Shenzhen, China) (26 patients). Each patient signed an informed consent form before treatment, and this study was approved by the Ethics Committee on Biomedical Research, West China Hospital of Sichuan University (No.2020180). There were 26 patients with breast cancer on the left and 24 patients with breast cancer on the right, with a median age of 48 years.

**Immobilization**

Based on the recommendations of the multidisciplinary team (including the radiation oncologists, the physicists and the radiotherapists), we designed and determined the shape and size of the new vacuum bag, which is 130 cm long and 100 cm wide. Then the manufacturer produced it (Klarity Medical, Shenzhen, China) (Fig. 1 A and C). Meanwhile, we measured the dimensions of the old vacuum bag (Fig. 1 B and D), which is 100 cm long and 70 cm wide (inner size 90 × 55 cm). The two types of vacuum bags were placed on a 15° wedge plate, and the upper side of the bag was formed to fit the shape of the patient’s head and to limit the longitudinal movement of the head. The abduction of the upper limb on the involved side was greater than 90°. Pressing on both sides of the upper part of the vacuum bag forms an arm shape to prevent the movement of the arm from causing deformation and motion of the adjacent chest wall. In the new vacuum bag group, the arms were fixed for more than half the length of the arm, and more than one-third of lower limbs were fixed on the lower side. In the old vacuum bag group, only one-third of the arms were fixed, and the buttocks were fixed on the lower side.

**Simulation and planning**

Free-breathing patients were simulated using Siemens 64-slice CT with a 3-mm slice thickness from the chin to the lower edge of the liver with intravascular contrast. The treatment plan was generated using the RayStation 4.7 (RaySearch, Stockholm, Sweden) treatment-planning system.

**Setup errors analysis**

The global and the local setup errors were analyzed using cone beam CT (CBCT) registration to the planning CT. A total of 945 CBCT images were obtained by XVI Release 5.0.3 for 40 patients (Synergy, Elekta, Crawley, UK). The number of frames per CBCT acquisition was ~400. The scanning parameters were tube voltage of 100 kV, tube current of 36.1 mA, S20 F1 filter plate, acquisition speed of 5.5 frames/s and acquisition angle of 50–210°.

The whole region of PTV was defined as a single region of interest (GROI) in planning CT to registration with CBCT image online. The other three sub-regions of interest were defined and analysed offline (including the supraclavicular area (SROI), the ipsilateral chest wall region (CROI) and the ipsilateral arm region (AROI)). The registration results between CBCT and the planning CT using the GROI were defined as the global setup errors. The difference between the registration results of GROI and the registration results of the other three sub-regions was defined as the local setup errors. The automatic registration gray value (translation errors and rotation errors, T + R) was used to obtain the coarse registration first, and then manual fine adjusting followed. The systematic errors (Σ) and random errors (σ) were computed along the medial–lateral (ML), superior–inferior (SI) and anterior–posterior (AP) axes, and the rotation errors along the pitch, roll and yaw axes were also recorded. A radiotherapist with 10 years of experience performed all the image registration. Two experience radiation oncologist audited the registration results for 40 CBCT images. The clinical target volume (CTV) CBCT PTV margin recipe by Van Herk [6]: 2.5 Σ + 0.7σ, was used, in which Σ is the standard deviation (SD) of the individual means for each ROI registration result per patient, and σ is the root mean square of the individual SD for each ROI registration result per patient.

**Evaluation of motion amplitude of the chest wall and diaphragm**

Six opaque lead markers with a diameter of 1 mm were put on the chest wall, arranged from the second rib to the sixth rib (Fig. 2). The motion amplitude of the chest wall and diaphragm were quantified by fluoroscopy (XVI motion view function) in the AP and ML directions. The correlation between the amplitude of the chest wall and diaphragm was analysed. The 95th percentile motion amplitude (A) of the chest wall was evaluated, then 0.45A [6] was added linearly to the CTV–PTV margin of the chest wall when the motion amplitude of respiration exceeded 1 cm.

**Statistical analysis**

SPSS 22.0 (IBM, Chicago, IL, USA) was used for all statistical analyses, with a significance level of P < 0.05. Differences were assessed for significance using the t-test (ANOVA). Pearson’s correlation coefficient was used to analyse the correlation between the amplitude of the chest wall and diaphragm.
RESULTS

Comparison of means between the two groups

The comparison of the global setup errors and local setup errors is shown in Table 1. In the global setup errors, except that there was no statistical difference in the yaw axis, the errors of the new vacuum group in other directions were significantly smaller than that of the old vacuum group ($P<0.05$). In the new vacuum group, the local errors in ML and yaw directions for chest wall ($P<0.05$) and the local setup errors in the ML and SI directions for the supraclavicular were statistically different than those in the old vacuum group ($P<0.05$). In terms of the local setup errors of the arm, except that there was no statistical difference in the pitch axis, the errors of the new vacuum group in other directions were significantly smaller than those in the old vacuum group ($P<0.05$).

Global setup errors and the local setup errors between the two groups

The global setup errors and the local setup errors for the new vacuum group and the old vacuum group are shown in Table 2 (translational results) and Table 3 (rotational results). The global setup errors of the old vacuum group ranged from 2.35 to 3.92 mm, and the corresponding PTV margins range from 9.79 to 12.18 mm. The global setup errors of the new vacuum group ranged from 1.21 to 2.13 mm, and the corresponding PTV margins ranged from 4.33 to 4.55 mm.

The local setup errors of the chest wall in the old vacuum group ranged from 0.9 to 1.44 mm, and the corresponding PTV margin ranged from 3.08 to 3.98 mm. In the new vacuum group, the local setup errors of the chest wall ranged from 0.65 to 1.35 mm, and the corresponding PTV margins ranged from 2.22 to 3.95 mm. In the old

Fig. 1. The shape and size of the new vacuum bag (A) and the old vacuum bag (B). The same patient immobilised with the new vacuum bag (C) and the old vacuum bag (D).
Motion amplitude of the chest wall and diaphragm

The motion amplitude of the chest wall and diaphragm were evaluated randomly for 34 patients (20 patients in the new vacuum group and 14 patients in the old vacuum group) (Table 4). Eleven patients received respiration motion evaluation once and 23 patients received respiration motion evaluation twice according to patients’ agreements. A total of 57 measurements in the ML and AP directions were obtained. Since the SI direction can be measured in both the AP and ML directions, there were 114 measurements in the SI direction. The motion of markers located in different ribs in the same direction was similar. The motion (mean ± SD) of all markers was 0.50 ± 0.50 mm in the ML direction, 0.84 ± 0.54 mm in the SI direction and 0.89 ± 0.58 mm in the AP direction. The motion amplitude of the diaphragm in the SI direction was 15.7 ± 3.60 mm, which was not statistically related to any direction of the markers on the chest wall. Meanwhile, there was no statistical difference in the chest wall motion between the new vacuum group and the old vacuum group. The motion amplitude of the 95th percentile in the ML, SI and AP directions was 1.0, 2.0 and 2.0 mm, respectively. If added linearly to the calculated chest wall PTV with 0.45A [6], the total required PTV margins for chest wall were 4.40 mm, 3.12 mm, and 3.77 mm for the ML, SI and AP directions respectively.

DISCUSSION

In this study, the global setup errors (systematic errors and random errors) of the old vacuum group were 3.26/2.35 mm in the ML direction, 3.92/3.41 mm in the SI direction and 3.79/3.32 in the AP direction. We summarised these errors reported by different authors [3, 7–11] in Table 5. These results are similar to the results of the old vacuum group in this study, indicating that there are large global setup errors in breast cancer radiation therapy, and we need to improve the current immobilisation device.

To simplify comparison with other studies, the local setup errors of the chest wall were used. The local setup errors in the old vacuum group in ML, SI and AP were 3.43/2.40 mm, 4.33/3.66 mm and 4.35/3.51 mm, respectively, which were slightly larger than the results reported in the above studies. However, the local setup errors in ML, SI and AP of the new vacuum group were 2.31/2.22 mm, 1.52/2.19 mm and 1.42/2.10 mm, respectively, which were smaller...
### Table 1. Comparison of means of the global and the local setup errors between the old vacuum group and the new vacuum group (mm). \( G_N \), the new vacuum group; \( G_O \), the old vacuum group. \( G\text{ROI-CROI}, G\text{ROI-SROI}, \text{and } G\text{ROI-AROI} \) represent the local setup errors for the supraclavicular area (\( S\text{ROI} \)), the ipsilateral chest wall region (\( C\text{ROI} \)) and the ipsilateral arm region (\( A\text{ROI} \)), respectively.

| Directions | \( G\text{ROI} \) | \( G\text{ROI-CROI} \) | \( G\text{ROI-SROI} \) | \( G\text{ROI-AROI} \) |
|------------|----------------|-----------------|----------------|----------------|
| Group      | \( G_N \)     | \( G_O \)        | \( G_N \)     | \( G_O \)        |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |
| \( \text{ML} \) | 500            | 446             | 500           | 446            |
| \( \text{SI} \) | 500            | 446             | 500           | 446            |
| \( \text{AP} \) | 500            | 446             | 500           | 446            |

| \( n \) | \( \text{Mean} \) | \( \text{SD} \) | \( P \text{ value} \) | \( \text{Mean} \) | \( \text{SD} \) | \( P \text{ value} \) |
|--------|----------------|---------------|----------------------|----------------|---------------|----------------------|
| \( \text{Pitch} \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) |
| \( \text{Roll} \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) |
| \( \text{Yaw} \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) | \( 0.0 \) |

The bold \( P \text{ value} \) indicates that this group of comparison is statistically significant.
Table 2. The global setup errors and the local setup errors of translational directions in the old vacuum group and the new vacuum group (mm). $G_{ROI}$ represents the global setup errors; $G_{ROI}$-CROI, $G_{ROI}$-SROI and $G_{ROI}$-AROI represent the local setup errors for the supraclavicular area (SROI), the ipsilateral chest wall region (CROI) and the ipsilateral arm region (AROI), respectively.

| Directions | The old vacuum group | The new vacuum group |
|------------|----------------------|----------------------|
|            | $\Sigma$  | $\sigma$  | Margin | $\Sigma$  | $\sigma$  | Margin |
| $G_{ROI}$  | ML        | 3.26      | 2.35   | 9.79     | 1.22      | 2.13   | 4.55   |
|           | SI        | 3.92      | 3.41   | 12.18    | 1.26      | 1.95   | 4.52   |
|           | AP        | 3.79      | 3.32   | 11.79    | 1.21      | 1.85   | 4.33   |
| $G_{ROI}$-CROI | ML       | 1.02      | 1.22   | 3.41     | 1.35      | 0.83   | 3.95   |
|           | SI        | 0.90      | 1.20   | 3.08     | 0.65      | 0.85   | 2.22   |
|           | AP        | 1.19      | 1.44   | 3.98     | 0.88      | 0.97   | 2.87   |
| $G_{ROI}$-SROI | ML       | 1.67      | 1.70   | 5.36     | 1.02      | 0.97   | 3.24   |
|           | SI        | 2.37      | 1.83   | 7.20     | 1.00      | 1.04   | 3.24   |
|           | AP        | 1.31      | 1.68   | 4.46     | 1.21      | 0.82   | 3.60   |
| $G_{ROI}$-AROI | ML       | 5.63      | 4.24   | 17.04    | 3.90      | 3.11   | 11.91  |
|           | SI        | 8.37      | 4.85   | 24.31    | 4.29      | 3.04   | 12.86  |
|           | AP        | 8.94      | 5.13   | 25.95    | 5.33      | 2.76   | 15.25  |

Table 3. The global setup errors and the local setup errors in rotational axis for the old vacuum group and the new vacuum group ($^\circ$)

| Directions | The old vacuum group | The new vacuum group |
|------------|----------------------|----------------------|
|            | $\Sigma$  | $\sigma$  |               | $\Sigma$  | $\sigma$  |               |
| $G_{ROI}$-CROI | Pitch   | 0.79      | 0.77   | 0.65     | 0.65  |
|            | Roll     | 0.67      | 0.85   | 0.97     | 0.83  |
|            | Yaw      | 0.68      | 0.62   | 0.61     | 0.54  |
| $G_{ROI}$-SROI | Pitch   | 1.44      | 1.58   | 1.04     | 0.64  |
|            | Roll     | 1.28      | 1.39   | 0.99     | 0.68  |
|            | Yaw      | 1.55      | 1.14   | 0.94     | 0.87  |
| $G_{ROI}$-AROI | Pitch   | 4.51      | 3.05   | 2.66     | 1.78  |
|            | Roll     | 7.52      | 3.75   | 2.63     | 1.78  |
|            | Yaw      | 4.4       | 3.12   | 2.55     | 1.82  |

Table 4. The motion amplitude of the chest wall (six markers) and PTV margins (mm)

|            | ML      | SI      | AP      |
|------------|---------|---------|---------|
|            | Average | SD      | Average | SD      | Average | SD      |
| Mark 1     | 0.54    | 0.50    | 1.05    | 0.23    | 0.93    | 0.57    |
| Mark 2     | 0.59    | 0.50    | 0.98    | 0.51    | 1.13    | 0.69    |
| Mark 3     | 0.39    | 0.49    | 0.99    | 0.46    | 1.09    | 0.66    |
| Mark 4     | 0.54    | 0.50    | 1.01    | 0.60    | 1.00    | 0.79    |
| Mark 5     | 0.47    | 0.50    | 0.99    | 0.51    | 1.00    | 0.71    |
| Mark 6     | 0.43    | 0.50    | 1.13    | 0.46    | 1.13    | 0.62    |
| Total      | 0.50    | 0.50    | 0.84    | 0.54    | 0.89    | 0.58    |
| Diaphragm  | /       | /       | 15.70   | 3.60    | /       | /       |
| 95th Percentile | 1.00 | 2.00 | 2.00 |
| 0.45A$^a$  | 0.45    | 0.90    | 0.90    |
| CROI margin| 3.95    | 2.22    | 2.87    |
| Total margin| 4.40  | 3.12    | 3.77    |

$^a$We used 0.45A linearly added to the calculated PTV margin according to the 95th percentile of amplitude (see [6]).
Reduce the global and local setup errors in PMRT with CBCT online correction.

This study mainly analysed the effects of a new vacuum bag and traditional vacuum bag for global setup errors, local setup errors and chest wall respiratory motion. However, there are some limitations of our study. First, there were differences between individual patients for these two groups because there were no data using both vacuum bags in the same patient. Furthermore, both the global setup errors and the local setup errors can be affected by different radiotherapist groups in immobilization, CT simulation and treatment. To ensure the accuracy of radiation therapy and reduce the patient’s additional radiation dose, optical surface imaging (OSI) systems \[17, 18\] play an increasingly important role in breast radiation therapy. Furthermore, to reduce the radiation dose to the lung and the heart, changing the patient’s position \[13,19,20\] and using deep inspiration breath-hold (DIBH) \[21,22\] technology were studied. Based on these studies, we will combine OSI and DIBH technology with the new vacuum bag in a further study.

**CONCLUSION**

The new vacuum bag can significantly reduce the global setup errors and local setup errors in PMRT. The respiratory motion of the chest wall is negligible. The 5 mm PTV margin could cover the local setup errors of the sub-regions in PMRT using the new vacuum bag with CBCT online correction.

**AUTHOR CONTRIBUTIONS**

Konglong Shen collected data and drafted the manuscript. Zhiguo Wang, Jie Xiong, An Li, Weifeng Wang, Wan Li, Jidan Zhou, Zhonghua Deng, and Bin Li helped to collect the data. Renming Zhong designed the study, and revised and approved the final manuscript. All authors read and confirmed the manuscript.

**CONFLICT OF INTEREST**

The authors declare that they have no competing interests.

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### Table 5. The systematic and random errors of PMRT reported by different authors (mm)

| Author              | Immobilization          | ROI                        | Systematic errors | Random errors |
|---------------------|-------------------------|----------------------------|-------------------|---------------|
|                     |                         |                            | ML    | SI  | AP  | ML    | SI  | AP  |
| Topolnjak et al. [3]| Double-arm support      | Chest wall                 | 3.10  | 3.80| 2.50| 2.20  | 2.80| 2.60|
| Batumalai et al. [7]| Vacuum bag              | Chest wall                 | 3.41  | 3.49| 2.24| 2.98  | 2.82| 2.74|
| Veldeman et al. [8] | Arm support             | Surgical clips             | -1.49 | 1.44| 2.80| 7.34  | 2.31| 3.21|
| Offerman et al. [9] | Vacuum bag              | Breast and the seroma cavity | 3.22  | 3.83| 5.72| 2.00  | 1.50| 2.60|
| Topolnjak et al. [10]| Supine                  | Excision cavity and clips  | 3.40  | 2.70| 3.40| 2.50  | 2.30| 2.40|
| Jain et al. [11]    | Breast board            | Skin contour and bony anatomy | 5.70  | 2.80| 2.30| 3.90  | 3.50| 3.20|

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