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

Yaqi Song, MD1, Jin Peng, BD1, Qianfeng Chen, MD1, and Honglei Luo, BD1

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.

Received: December 14, 2020; Revised: June 12, 2021; Accepted: July 8, 2021.

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 female1-3. Postoperative radiotherapy is a very important treatment of breast cancer4, which could improve patients’ local-regional control and survival5,6. 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 board7-9, vacuum bag9-13, alpha cradle14,15. 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.

1The Affiliated Huai'an No.1 People’s Hospital of Nanjing Medical University, Huai'an, Jiangsu, China

Corresponding Author:
Honglei Luo, Department of Radiation Oncology, The Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University, Jiangsu, Huai'an 223300, China. Email: lhlhayy@163.com

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access page (https://us.sagepub.com/en-us/nam/open-access-at-sage).
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 (R Foundation for Statistical Computing, Vienna, Austria).

Results

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

| 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 1. Clinical Characteristics of Patients in Two Groups.
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\(^1\text{-}^3\). 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\(^18\text{-}^21\). It plays an important role in the delineation and definition of PTV\(^21\text{-}^24\) or ITV\(^25\), and therefore affects radiation effect\(^25\text{-}^28\) and toxicity\(^29\text{-}^36\) 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

| 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|

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

**Figure 3.** Forest plot of different factors to Positioning Error based on the axis by linear regression analysis.
data, we have reason to reduce the PTV margin of TM -
was also the major independent factor of PE. Based on these
studies31-33 have con
reasons of equipment, time and fee. Although previous
fractional error of breast cancer radiotherapy in this study for the
as the radiotherapy progress went on.

apy compared with VB, but this discomfort could be eliminated
TM could increase the discomfort at the beginning of radiother-
small, and disappeared within three weeks. These indicated
therefore reduce the adverse reactions of OARs.

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

| Time | Group | Comfortable | Uncomfortable | X² | P |
|------|-------|-------------|---------------|----|---|
| T1   | TM    | 25          | 25            | 6.178 | .013<sup>a</sup> |
|      | VB    | 38          | 12            |     |   |
| T2   | TM    | 30          | 20            | 4.857 | .028<sup>a</sup> |
|      | VB    | 41          | 9             |     |   |
| T3   | TM    | 38          | 12            | 1.040 | .308  |
|      | VB    | 43          | 7             |     |   |

<sup>a</sup>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 radiother-
rapy 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
studies31-33 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.

Funding

The author(s) received no financial support for the research, authorship
and/or publication of this article.

Ethics Approval and Consent to Participate

The Institutional Review Board for human studies of The Affiliated
Huain 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 fol-
lowing the approved guidelines.

ORCID iDs

Yaqi Song <https://orcid.org/0000-0001-6868-6422>
Honglei Luo <https://orcid.org/0000-0003-0551-0651>

References

1. Feng RM, Zong YN, Cao SM, Xu RH. Current cancer situation
in China: good or bad news from the 2018 Global Cancer
Statistics? Cancer Commun. 2019;39(1):1-12. doi:10.1186/
s40880-019-0368-6
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA
Cancer J Clin. 2020;70(1):7-30. doi:10.3322/caac.21590
3. Chen W, Zheng R, Zhang S, et al. Cancer incidence and mortality
in China in 2013: an analysis based on urbanization level. Chin J
Cancer Res. 2017;29(1):1-10. doi:10.21147/j.issn.1000-9604.
2017.01.01
4. Kutcher GJ, Smith AR, Fowble BL, et al. Treatment planning for
primary breast cancer: a patterns of care study. Int J Radiat Oncol
Biol Phys. 1996;36(3):731-737. doi:10.1016/s0360-3016(96)
00368-9
5. Telli ML, Gradishar WJ, Ward JH. NCCN guidelines updates:
breast cancer. J Natl Compr Cancer Network. 2019;17(55):552-
555. doi:10.6004/jnccn.2019.5006
6. Macdonald S, Oncology R, General M. Breast cancer breast
radiotherapy (SuPr study): comparing set-up errors and respiratory
motion. Radiother Oncol. 2009;90(1):93-98. doi:10/djgfp
8. Kirby AM, Evans PM, Helyer SJ, Donovan EM, Convery HM,
Yarnold JR. A randomised trial of supine versus prone breast
radiotherapy (SuPr study): comparing set-up errors and respiratory
motion. Radiother Oncol. 2011;100(2):221-226. doi:10/bwxmk
9. Offerman S, Lamba M, Lavigne R. Effect of breast volume on
treatment reproducibility on a tomotherapy unit in the treatment of
breast cancer. Int J Radiat Oncol Biol Phys. 2011;80(2):417-
421. doi:10/c25p7r
10. White EA, Cho J, Vallis KA, et al. Cone beam computed tomography guidance for setup of patients receiving accelerated partial breast irradiation. Int J Radiat Oncol Biol Phys. 2007;68(2):547-554. doi:10.1016/j.ijrobp.2005.11.049
11. Batumalai V, Holloway L, Delaney GP. A review of setup error in supine breast radiotherapy using cone-beam computed tomography. Med Dosim. 2016;41(3):225-229. doi:10.1080/03015629.2015.1102138
12. Zhou J, Li S, Ye C, et al. Analysis of local setup errors of sub-regions in cone-beam CT-guided post-mastectomy radiation therapy. J Radiat Res. 2020;61(3):457-463. doi:10.1093/jrr/jst146
13. Shen K, Xiong J, Wang Z, et al. 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. J Radiat Res. 2020;61(6):985-992. doi:10.1093/jrr/jst095
14. Fatunase T, Wang Z, Yoo S, et al. Assessment of the residual error in soft tissue setup in patients undergoing partial breast irradiation: results of a prospective study using cone-beam computed tomography. Int J Radiat Oncol Biol Phys. 2008;70(4):1025-1034. doi:10.1016/j.ijrobp.2007.07.003
15. Feng CH, Gerry E, Chmura SJ, Hasan Y, Al-Hallaq HA. An image-guided study of setup reproducibility of postmastectomy breast cancer patients treated with inverse-planned intensity modulated radiation therapy. Int J Radiat Oncol Biol Phys. 2015;91(1):58-64. doi:10.1016/j.ijrobp.2014.09.039
16. R Core Team: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2020. URL https://www.R-project.org/.
17. Tian Y, Li X, Liu J, et al. Comparison of radiotherapeutic management of operated breast cancer in 1999 and in 2006: a sampling survey on the southeast coast of China. Tumori. 2010;96(2):254-259. doi:10.1177/030089161009600211
18. McCune K, Parsons L, Schoenfeld L, Maddeford A. A technique for evaluating cast foam positioning and immobilization devices used in breast cancer radiotherapy. Med Dosim. Off J Am Assoc Med Dosim. 1991;16(3):119-125. doi:10.1016/0958-3947(91)90121-h
19. Biston M-C, Jarril J, Dupuis P, et al. Comparison among four immobilization devices for whole breast irradiation with Helical Tomotherapy. Physica Med. 2020;69(2020):205-211. doi:10.1016/j.ejmp.2019.12.023
20. Mirimanoff RO, Franzetti-Pellanda A. Immobilization devices in conformal radiotherapy for non-small cell lung cancer TT - Systèmes d’immobilisation pour la radiothérapie conformationnelle du cancer bronchique non à petites cellules. Cancer Radiother: Journal de la SOCIETE FRANCAISE de Radiotherapie Oncologique. 2000;4(4):279-284. doi:10.1016/s1278-3218(00)80006-2
21. Park JI, Ye S-J, Kim HJ, Park JM. Dosimetric effects of immobilization devices on SABR for lung cancer using VMAT technique. J Appl Clin Med Phys. 2015;16(1):5217. doi:10.1120/jacmp.v16i1.5217
22. Takakura T, Nakata M, Yano S, et al. Evaluation of setup error and adequate setup margins in patients with prostate cancer treated by IMRT and fixed in the prone position using a set of immobilization devices. Nihon Hoshasen Gijutsu Gakkai Zasshi. 2006;62(1):130-135. doi:10.6009/jjrt.62.130
23. Bansal S, Bhattacharyya M, Kalita AK, et al. Determination of optimal clinical target volume to planning target volume margins for conformal radiotherapy planning using image guidance system in rectal cancer in prone position. J Med Phys. 2019;44(1):65-67. doi:10.4103/jmp.JMP_74_18
24. Cuijpers JP, Dahele M, Jonker M, et al. Analysis of components of variance determining probability of setup errors in CBCT-guided stereotactic radiotherapy of lung tumors. Med Phys. 2017;44(2):382-388. doi:10.1002/mp.12074
25. Lischalk JW, Woo SM, Kataria S, et al. Long-term outcomes of stereotactic body radiation therapy (SBRT) with fiducial tracking for inoperable stage I non-small cell lung cancer (NSCLC). J Radiat Oncol. 2016;5(4):379-387. doi:10.1007/s13566-016-0273-4
26. Cortes-Arroyo H, Rodriguez-Cuevas S, Labastida S. Quality control in planning and technique of radiotherapy with cobalt-60 for T1 glottic cancer increase local control and organ preservation. Am J Surg. 1997;174(5):477-480. doi:10.1016/S0002-9610(97)00159-1
27. Burkoň P, Slavik M, Kazda T, et al. Stereotactic body radiotherapy - current indications TT - extrakraniální stereotaktická radiotherapie - přehled současných indikací. Klinicka onkologie: casopis Ceske a Slovenske onkologicke spolecnosti. 2019;32(1):10-24. doi:10.14735/anko201910
28. Giraud P, Helfre S, Lavole A, Rosenwald JC, Cosset JM. Non-small-cell bronchial cancers: improvement of survival probability by conformal radiotherapy TT - cancers bronchiques non à petites cellules: amélioration des chances de survie par la radiothérapie conformationnelle? Cancer radiother: journal de la Societe francaise de radiotherapie oncologique. 2002;6(Suppl.1):125s-134s. doi:10.11177/030089161009600211
29. Hoppe BS, Laser B, Kowalski AV, et al. Acute skin toxicity following stereotactic body radiation therapy for stage I non-small-cell lung cancer: who’s at risk? Int J Radiat Oncol Biol Phys. 2008;72(5):1283-1286. doi:10.1016/j.ijrobp.2008.08.036
30. Casas F, Viňolas N, Sanchez-Reyes A, et al. Spanish patterns of care for 3D radiotherapy in non-small-cell lung cancer. Int J Radiat Oncol Biol Phys. 2006;65(1):138-142. doi:10.1016/j.ijrobp.2005.11.049
31. Michalski A, Atyeo J, Cox J, Rinks M. Inter- and intra-fraction motion during radiation therapy to the whole breast in the supine position: a systematic review: motion during breast radiotherapy. J Med Imaging Radiat Oncol. 2012;56(5):499-509. doi:10/gjhxnn
32. Thomsen MS, Harrov U, Fledelius W, Poulsen PR. Inter- and intra-fraction geometric errors in daily image-guided radiotherapy of free-breathing breast cancer patients measured with continuous portal imaging. Acta Oncol. 2014;53(6):802-808. doi:10.3109/0284186x.2014.905700
33. Reitz D, Carl G, Schönecker S, et al. Real-time intra-fraction motion management in breast cancer radiotherapy: analysis of 2028 treatment sessions. Radiat Oncol. 2018;13(1):128. doi:10/gdw6rv