

## Evaluation of Setup Errors at the Skin Surface Position for Whole Breast Radiotherapy of Breast Cancer Patients

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We used image-processing software to analyze the setup errors at the skin surface position of breast cancer patients (n = 66) who underwent post-operative whole breast irradiation at our hospital in 2014-2015. The sixty-six digital reconstructed radiographs (DRR) were created at the treatment planning for each patient. The lineacographies (n = 377) were taken after the patients' setup during radiotherapy. The lineacographies and DRR were superimposed at the skin surface position for each patient with the image-processing software. We measured the deviations of the isocenters for the nipple-lung (X) direction and craniocaudal (Y) direction and the deviation of the rotation angle of the XY axes between the lineacography and DRR on the superimposed images. The systematic error ( $\mu$ ,  $\Sigma$ ) and random error ( $\sigma$ ) were calculated from the X and Y deviations and rotation angle deviation. The  $\mu$  of X, Y, and rotation angle were 0.01 mm, -1.2 mm, and 0.05°, respectively. The  $\Sigma$  of X, Y, and rotation angle were 1.8 mm, 1.5 mm, and 0.9°, respectively. The  $\sigma$  of X, Y, and rotation angle were 2.0 mm, 1.5 mm, and 1.0°, respectively. Our analyses thus revealed that evaluations using image-processing software at the skin surface position in routine breast radiotherapy result in sufficiently small setup errors.

**Key words:** breast cancer, radiotherapy, position verification, skin surface, image processing software

As part of the quality-assurance protocol in routine clinical treatments at Okayama University Hospital, the setup errors of the breast-conserving radiotherapy for breast cancer patients are examined. In the hospital's routine clinical radiotherapy, the position verification during radiotherapy is achieved by a visual comparison of the digital reconstructed radiograph (DRR) calculated at the treatment planning stage and the lineacography taken during the treatment [1-6]. For breast radiotherapy, the central lung distance

(CLD), cranio-caudal distance (CCD) [1,2] and inferior central margin (ICM) [3,4] have been used to evaluate the setup errors of the X and Y directions on two-dimensional images. However, the evaluation of the rotation of the XY axes is difficult with conventional verification methods, and there are few reports regarding the setup error of the rotation of XY axes on two-dimensional images [3].

In this study, we evaluated the setup errors by conducting a verification of the position at the skin surface instead of using the CLD, CCD and so on, since the

mammary glands are located directly under the skin. This verification method using the skin surface enabled us to evaluate the precise rotation error of the XY axes. The hitherto known verification method is usually done with a visual comparison, which leads to less-than-optimal objectivity. We therefore used image processing software for the verification to improve the accuracy of the evaluation.

Our aim is not to replace the usual verification methods with this new verification method using the skin surface for routine radiotherapy. The goal of the present study was simply to certify the accuracy of our daily clinical practice using this precise method, which is a burdensome and time-consuming research technique.

## Materials and Methods

**Patients and CT simulation.** At Okayama University Hospital from September 2014 to April 2015, 66 breast cancer patients were treated post-operatively with whole breast radiotherapy. Each patient was scanned in the supine treatment position, with both arms extended in a support above the head and with an immobilization wedge under the knees. Free-breathing computed tomography (CT) acquisition was performed with an Asteion Super4 Edition multi-slice CT scanner (Toshiba Medical Systems, Tochigi, Japan) and reconstructed with 2-mm-thick slices. To obtain reproducible patient positioning, prior to the CT scanning, three cross lines indicating the CT center were marked on the patient's skin with a marker pen and protective tape. The three cross lines were in a transverse plane at the height of the xiphoid process of the patient's sternal bone: one on the sternum and one on each lateral side at the middle axillary line.

**Treatment plans.** A single isocentric field setup was used for whole breast radiotherapy with two tangential non-parallel opposing beams. The treatments were delivered with the ONCR-K (Toshiba Medical Systems) equipped with an electronic portal image device (EPID).

**Position setting and verification.** The daily patient positioning consisted of the alignment of the three cross lines indicating the CT center with the treatment-room lasers, followed by an isocenter shift. The patient position was verified by a comparison of the megavoltage image of lineacgraphy and the DRR for the

beam from the medial side of 2 tangential non-parallel opposing beams. The lineacgraphies were taken after the patient's setup essentially at the first and second days of radiotherapy, and thereafter once a week. A total of 337 lineacgraphies were taken during radiotherapy.

**Correction of positioning errors.** When the positioning error of isocenter exceeded 1 cm based on a visual comparison of the lineacgraphy and the DRR, the patient was repeatedly re-positioned until the error became within 1 cm. After the re-positioning, lineacgraphy was performed and recorded to assess the setup error.

### Assessment of the setup errors.

#### 1. Superimposition of the lineacgraphy and DRR

Each DRR and lineacgraphy image was imported onto different layers using the image processing software Photoshop Elements (ver. 13.0, Adobe Systems, San Jose, CA, USA), and their scales were matched by scaling. The skin surface line was drawn manually on each layer of the DRR (Fig. 1A) and lineacgraphy (Fig. 1B) images for the range to cover the irradiation field. The superimposition of the lineacgraphy and DRR images (Fig. 1C) was done manually by rotating and shifting the images to match the three skin surface lines.

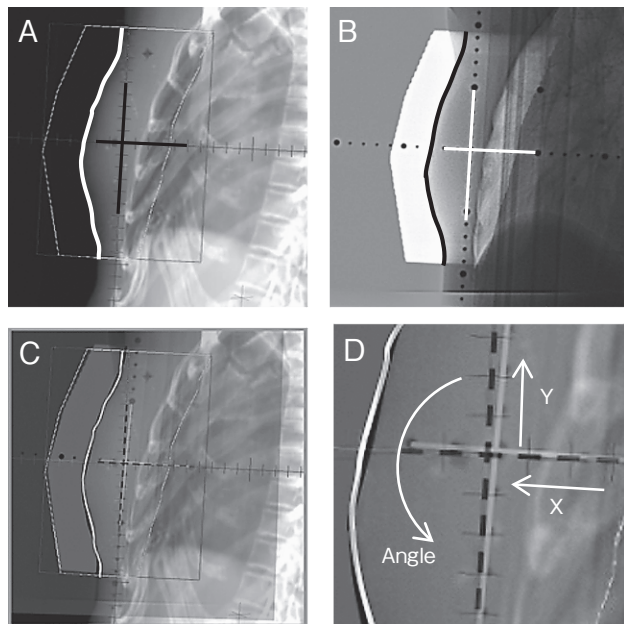
#### 2. Measurement of the setup errors

The superimposed images were imported to the image processing software ImageJ (ver. 1.44p, U.S. National Institutes of Health, Bethesda, MD, USA). The deviations of the isocenter of the lineacgraphy from that of the DRR was measured for the nipple-lung (X) direction and craniocaudal (Y) direction and the rotation angle of the XY axes (Fig. 1D). The 'plus' direction was defined as the nipple side of the X-axis, the head side of the Y-axis, and the forward-bending side of the rotation angle.

#### 3. Evaluation of the setup errors

We evaluated the systematic error, the random error, and the total vector error. 'Systematic error' is an error that is systematically generated in a certain direction due to several specific causes. This error can be corrected by measures such as image-guided radiotherapy. Generally, 2 types of systematic errors ( $\mu$ ,  $\Sigma$ ) have been used to evaluate setup errors. Systematic error ( $\Sigma$ ) is usually used for the analysis of many samples. 'Random error' is an accidental error that occurred due to an unknown cause. Although it can be made small to some extent by some measures, it is difficult to remove.

In the present patient series, the systematic error



**Fig. 1** The method of verifying the position of the skin surface and the assessment of setup errors. **A**, A digital reconstructed radiograph (DRR). A white line indicates the skin surface. A dotted cross line indicates the isocenter; **B**, A lineacgraphy. A black line indicates the skin surface. A white cross line indicates the isocenter; **C**, A superposition of DRR and lineacgraphy images for the same patient; **D**, The assessment of deviation of the isocenter for the nipple-lung direction (X) and craniocaudal direction (Y) and the deviation of the rotation angle of the XY axes between the DRR and lineacgraphy.

[7-9] was calculated as follows. First, the average value ( $m_1, m_2, \dots, m_n$ ) of the deviations between the DRR and lineacgraphy was calculated for the X-axis, Y-axis and angle, respectively, for each patient (1, 2, ..., n). The systematic error ( $\mu$ ) was defined as the average of each patient's deviation ( $m_1, m_2, \dots, m_n$ ) for the X-axis, Y-axis and angle, respectively, with the following equation:

$$\text{Systematic error } (\mu) = \text{mean } (m_1, m_2, \dots, m_n) \quad (1)$$

The systematic error ( $\Sigma$ ) was defined as the standard deviation (SD) of each patient's deviation ( $m_1, m_2, \dots, m_n$ ) for the X-axis, Y-axis and angle, respectively, as follows:

$$\text{Systematic error } (\Sigma) = \text{SD } (m_1, m_2, \dots, m_n) \quad (2)$$

Student's *t*-test was used to determine the signifi-

cance of differences in the systematic error ( $\mu$ ). F-test was used to determine the significance of differences in the systematic error ( $\Sigma$ ). The differences were considered significant when  $p \leq 0.05$ .

The random error [7-9] was calculated as follows. First, the standard deviation ( $\sigma_1, \sigma_2, \dots, \sigma_n$ ) of the deviations between the DRR and lineacgraphy was calculated for the X-axis, Y-axis and angle, respectively, for each patient (1, 2, ..., n). The random error was defined as the root mean square of each patient's deviation ( $\sigma_1, \sigma_2, \dots, \sigma_n$ ) for the X-axis, Y-axis and angle, respectively, as follows:

$$\text{Random error} = \sqrt{\frac{\sigma_1^2 + \sigma_2^2 + \dots + \sigma_n^2}{n}} \quad (3)$$

The total vector error was defined as the linear distance of the deviation of the isocenter between the DRR and lineacgraphy for each verification. The total vector error was calculated as the square root of the sum of square of X and Y deviations as follows:

$$\text{Total vector error} = \sqrt{X^2 + Y^2} \quad (4)$$

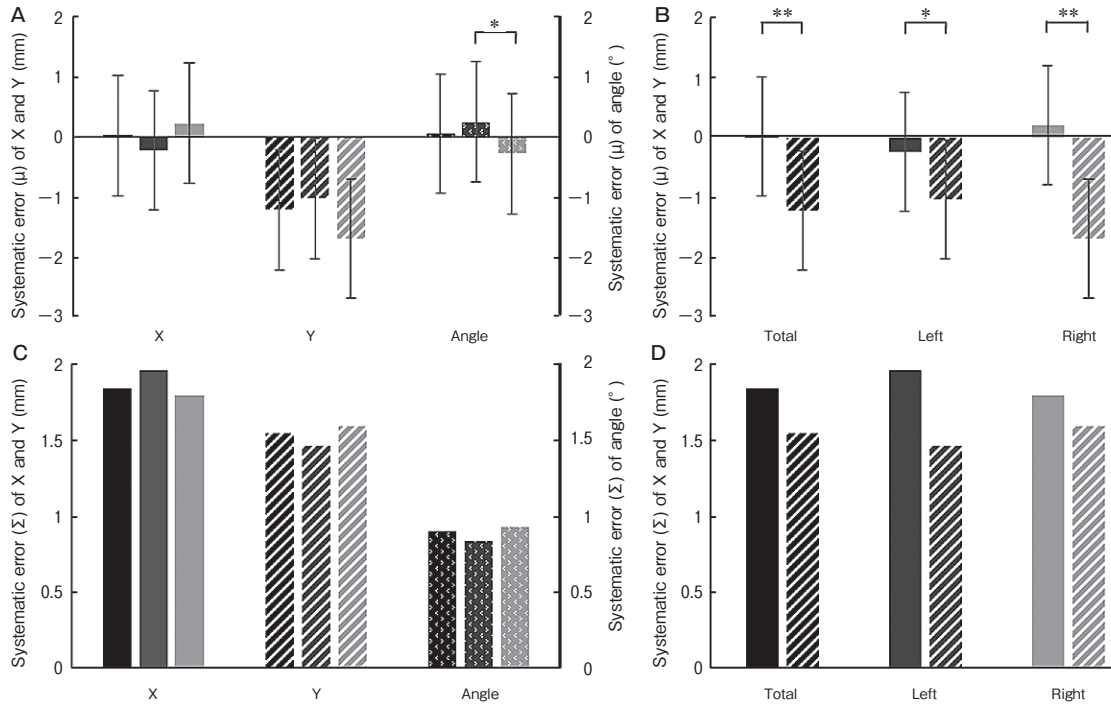
**Ethical approval.** This retrospective study was approved by the Ethics Committee of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences and Okayama University Hospital (approval no. 1506-036). The requirement for patient consent was waived for this retrospective study.

## Results

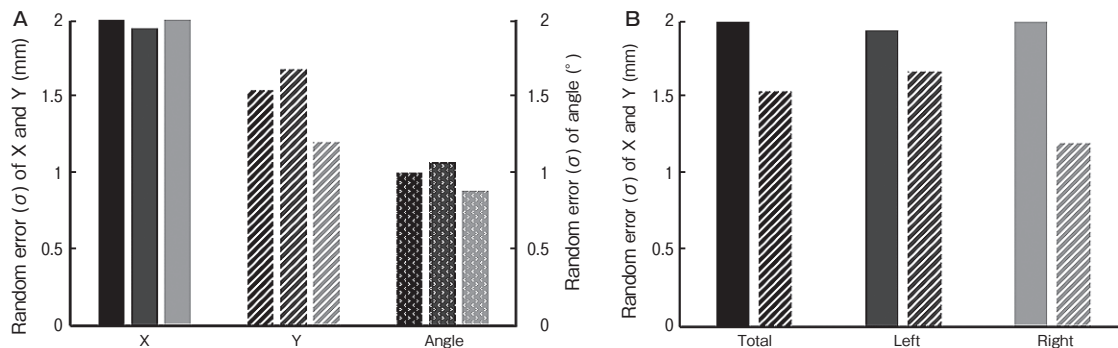
**Systematic error ( $\mu$ ) and systematic error ( $\Sigma$ ).** The systematic errors ( $\mu$ ) of the X, Y, and angle among the total of 66 breast cancer patients were 0.01 mm, -1.2 mm, and 0.05°, respectively (Fig.2A). The systematic errors ( $\Sigma$ ) of the X, Y, and angle among the total patients were 1.8 mm, 1.5 mm, and 0.9°, respectively (Fig.2C).

The examination by left breast and right breast indicated no obvious difference in the systematic error ( $\mu$  or  $\Sigma$ ) for the X-axis direction and the Y-axis direction (Fig.2A,C). The angle of the systematic error ( $\mu$ ) showed a significant difference between the left and right sides, but all of the  $\mu$  values of the angle were  $< 0.3^\circ$ , which is considered clinically insignificant.

We compared the systematic error ( $\mu$ , Fig.2B) and the systematic error ( $\Sigma$ , Fig.2D) of the X-axis and Y-axis directions. The magnitude of the systematic



**Fig. 2** The systematic errors. **A**, The systematic error ( $\mu$ ) of the X- and Y-axis directions and angle; **B**, The systematic error ( $\mu$ ) of the left- and right-side breast cancer patients (left 40 and right 26 patients); **C**, The systematic error ( $\Sigma$ ) of the X- and Y-axis directions and angle; **D**, The systematic error ( $\Sigma$ ) of the left- and right-side breast cancer patients. The black, dark gray, and light gray indicate the data for the whole patient series, left-side, and right-side breast cancer patients, respectively. The filled, shaded, and dotted columns indicate the data for X-axis, Y-axis directions and angle, respectively. \* $p < 0.05$ , \*\* $p < 0.005$ .



**Fig. 3** The random errors. **A**, The random error ( $\sigma$ ) of the X- and Y-axis directions and angle; **B**, The random error ( $\sigma$ ) of the left-side and right-side breast cancer patients. The black, dark gray, and light gray indicate the data for the whole patient series, left-side, and right-side breast cancer patients, respectively. The filled, shaded, and dotted columns indicate the data for the X-axis, Y-axis directions and angle, respectively.

error ( $\mu$ ) of the Y-axis direction was significantly larger than that of the X-axis direction among the total, left, and right patients. However, the maximum of the systematic error ( $\mu$ ) was  $< 2$  mm, which is considered clinically insignificant. No significant differences in the

systematic error ( $\Sigma$ ) were observed between X-axis and Y-axis directions among the total, left, and right patients.

**Random error.** The random errors of the X, Y, and angle among the total patients were 2.0 mm,

1.5 mm, and  $1.0^\circ$ , respectively, as shown in Fig. 3A. We compared the random error by the X- and Y-axis directions (Fig. 3B), and we observed that the magnitude of all of the random errors was  $< 2$  mm, which is considered clinically insignificant, among the total, left, and right patients.

**The total vector error.** Fig. 4 provides the histogram of the total vector error of each treatment. The means of the total vector error were 3.0 mm, 2.9 mm, and 3.2 mm in the total, left, and right patients, respectively. There were few total vector errors over 10 mm.

## Discussion

Our analyses of the cases of 66 breast cancer patients revealed that the systematic errors and random errors in breast cancer radiation therapy conducted at our hospital in daily practice were as small as  $\leq 2$  mm in both the X- and Y-axis directions, which seem clinically permissible. The setup errors identified in previous studies are summarized in the Table 1. Most of those studies used CCD [1, 2], ICM [3, 4], and CLD [1, 2] to evaluate the setup errors of the X and Y directions. The present study is the first to accurately evaluate setup errors by a verification of the position at the skin surface instead of using CCD, ICM or CLD. We used the skin surface because the mammary gland as the target is located directly under the skin. This verification method using the skin surface enabled us to evaluate the precise rotation error of the XY axes, which has rarely been reported [3]. We also used image processing software for the verification in order to improve the accuracy of the skin surface verification, which has been difficult to achieve by visual judgment. Our findings confirmed that the setup errors of the XY axes were either equal to or surpassing the previous studies' results.

The setup error of angle has also rarely been reported. Creutzberg [3] reported that the angle setup error was  $1.4 \pm 5.4^\circ$ . In the present study, the setup error of the angle was  $0.05 \pm 0.90^\circ$ , indicating that it was sufficiently permissible clinically.

The systematic error and random error are the world standards as evaluation parameters of accuracy for radiotherapy verification. However, in the calculation process of the systematic error for each patient, when the directions of the deviation of each treatment are opposite, the systematic error ( $\mu$ ) becomes less than the

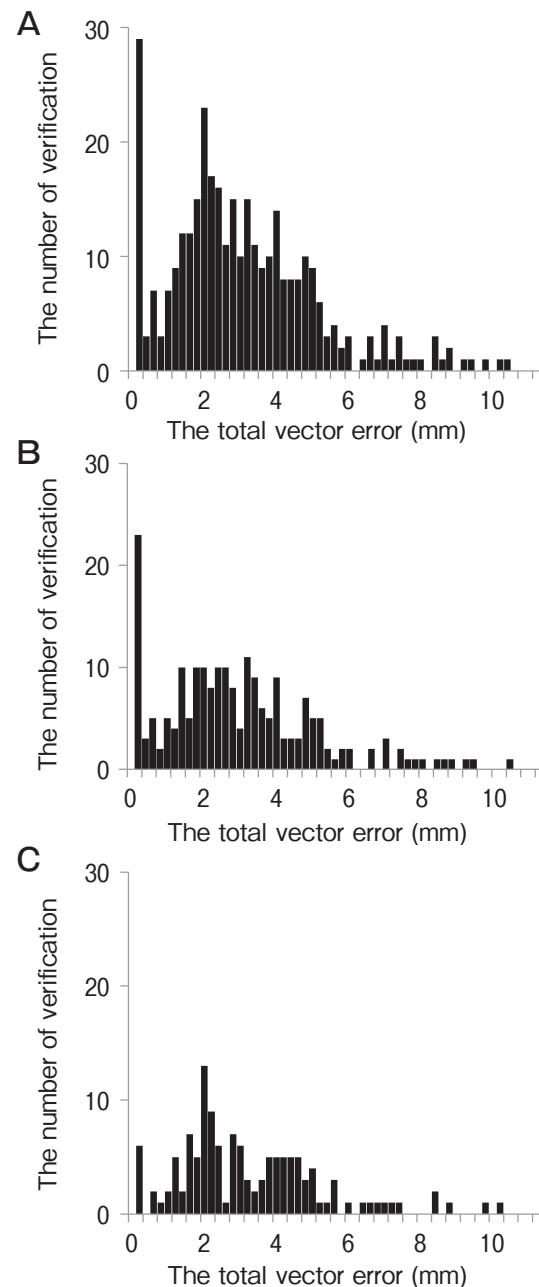


Fig. 4 The histogram of the total vector error of each treatment. **A**, The whole patient series; **B**, The left-side breast cancer patients; **C**, The right-side breast cancer patients. The means of the total vector error were 3.0 mm, 2.9 mm, and 3.2 mm for the whole series, left-side and right-side breast cancer patients, respectively.

**Table 1** Systematic errors ( $\mu$  and  $\Sigma$ ) and random error ( $\sigma$ ) in the relevant previous studies

	No. of patients	Systematic error ( $\mu$ ) (mm)		Systematic error ( $\Sigma$ ) (mm)		Random error ( $\sigma$ ) (mm)	
		X	Y	X	Y	X	Y
Van <i>et al.</i> (1991) [1]	12	-3.2	-1.3	2.7	4.7	1.7	1.8
Valdagni <i>et al.</i> (1991) [5]	20	2.7	1.8	-	-	-	-
		3.0	2.0	-	-	-	-
Creutzberg <i>et al.</i> (1993) [3]	31	2.8	-	4.6	-	-	-
Lirette <i>et al.</i> (1995) [2]	20	1.0	0.7	3.1	3.9	1.7	3.4
Fein <i>et al.</i> (1996) [4]	13	0.03	2.3	-	-	4.4	6.3
Petillion <i>et al.</i> (2015) [6]	20	-0.9	1.3	2.3	2.4	2.1	3.1
This study	66	0.01	-1.2	1.8	1.5	2.0	1.5

mean of the distance of the deviation. In this study, we evaluated the absolute value of the deviation at each treatment, *i.e.*, the total vector error. The average of the total vector error among all 66 patients was small at 3.0 mm, which is considered clinically insignificant.

As a limitation of this study, a change in the examined breast's shape during radiotherapy and a difference between the detection abilities of the MV and kV images might have affected the results. Either or both of these issues might have occurred in our patients and may thus have increased the setup errors. However, all of the setup error values observed herein were sufficiently small for routine breast radiotherapy.

In conclusion, the accurate verification using the patient's skin surface and image analysis software clarified that the setup errors of breast radiotherapy at our hospital were equal to or surpassed the setup errors reported previously.

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