J. Aichi Med. Univ. Assoc.
Vol. 45, No. 1/2/3, pp. 1–7 (September 15, 2017)

Breast Irradiation with Respiratory Gating Reduces Lung Dose: Assessment with a Phantom Simulating Respiratory Motion

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Purpose: In radiotherapy after breast-conserving surgery, a part of the lung is included in the irradiation field due to shifting of the thorax from respiratory motion, and radiation pneumonitis may be caused after therapy. To reduce the lung dose, using a breast phantom simulating respiratory motion, the dose was compared between the presence and absence of respiratory gating.

Materials and Methods: Phantoms resembling breast and lung tissues were prepared, and the phantom was assembled by placing the breast phantom on the lung phantom and moving it up and down to simulate respiratory motion. The phantom was divided into two from top to bottom, and a film to assess the radiation dose was interposed between them. Then, the irradiation field margin was set on the lung portion 5 mm from lower margin of the breast. Irradiation was administered with a 4-MV linear accelerator while the respiratory motion of the phantom was stopped at the expiratory phase (expiratory-phase breath holding), while the respiratory motion was continuous (spontaneous respiration) or only during the expiratory phase while the motion of the phantom was continuous (irradiation with respiratory gating). After irradiation, the films were scanned, and the respective lung doses were evaluated.

Results: Lung dose increased in the order of irradiation during expiratory-phase breath holding, irradiation with respiratory gating, and irradiation during spontaneous respiration. Lung dose during expiratory-phase breath holding and with respiratory gating were significantly lower than that of spontaneous respiration ($p<0.001$ and $p=0.018$, respectively). No significant difference was noted in lung dose between expiratory-phase breath holding and respiratory gating ($p=0.16$).

Conclusion: Irradiation with respiratory gating significantly reduced the lung dose as compared to irradiation during spontaneous respiration, and so may help to prevent the occurrence of radiation pneumonitis when clinically applied.

Key words: breast cancer, radiation therapy, radiation pneumonitis, breast-conserving surgery

INTRODUCTION

Breast cancer is the most common cancer in Japanese women, and it consists the fifth leading cause of cancer deaths following colon/rectum, lung, stomach and pancreatic cancers[1]. The number of breast cancers detected at early-

Received April 11, 2017; Accepted June 5, 2017
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stage has been increasing with the spread of screening program using mammography[2]. The standard treatment for early-stage breast cancer is consisted of breast-conserving surgery (BCS) followed by radiation therapy[3]. Radiation therapy after BCS is normally performed with tangential opposed portal irradiation for the whole remaining breast tissue as a target. During the irradiation, a part of the ipsilateral lung will be included in the field due to shifting of the thorax from respiratory motion, and the beam passing the lung tissue beneath the chest wall may cause radiation pneumonitis. Incidence of symptomatic radiation pneumonitis after breast irradiation has been reported as 1.1%, and some cases with serious symptoms has been reported[4)5)]. Collimation of the radiation field might be effective to reduce the lung dose, however, because the breast tissue moves with respiration, too much close collimation will make the dose for the base of breast insufficient associated with the risk of tumor recurrence.

Recently, respiratory gating technique in radiation therapy for lung tumors has been developed and being clinically applied to reduce the dose to the normal lung and to treat the tumor efficiently[6]. For the breast irradiation, however, there have been only a few research reports on respiratory gating[7)~9)]. The purpose of the present experimental study was to compare the dose to the lung with different respiratory-gating technique using a breast phantom simulating respiratory motion.

MATERIALS & METHODS

1. Dose-density curve

Gafchromic Film (EBT, R-TECH, Japan) was placed at the depth of 10 cm in the water-equivalent phantom with the thickness of 25 cm. The film was irradiated by 5, 10, 15, 20, 25, 50, 100, 150, 200, 250, 300 and 400 monitor unit (MU) using a linear accelerator (EXL-15DP, Mitsubishi, Tokyo) with 4-MV x-ray. The films were scanned with a flatbed scanner (GTX-970, Epson, Tokyo), and a dose-density curve was prepared using a density-analyzing software (DD-Analysis ver. 10.2.0, R-TECH, Japan). Measurements were performed 3 times each for the different doses and the mean values were used for analysis.

2. Phantom simulating respiratory motion

A hand-made phantom was prepared simulating the breast and lung tissues (Fig. 1). The breast part was made of 10 mm thick acryl boards with diameters of 3, 4, 6, 8, 10, 12 cm. The six disk boards were stacked to make a cone. The lung part was made of four 10 mm thick cork boards and was placed under the breast part. The phantom was cut at the midline to place the Gafchromic film in between. The phantom was positioned on a stand that moves up and down, using a motor to rotate an elliptic cam, simulating respiratory motion. The shape of the cam was designed so that the

Figure 1. A phantom simulating breast and lung tissues consisted of acrylic boards and cork boards.

expiratory phase (stand, down) was longer than the inspiratory phase (stand, up) as the physiological motion. Beneath the stand, a spring was attached as a switch that make a light turned on when the stand drops (Fig. 2).

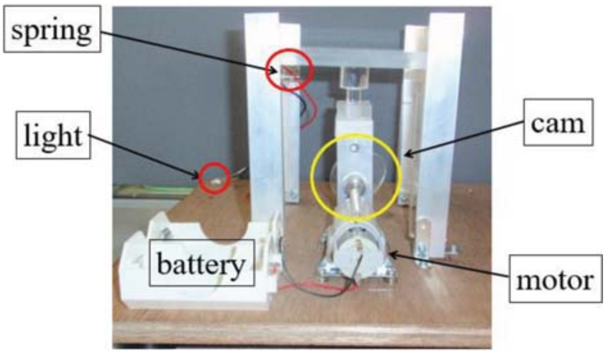

Figure 2. A stand of the phantom moves up and down by using a motor to rotate an elliptic cam. A spring is attached as the switch beneath the stand, and a light turns on when the stand drops.

3. Irradiation of phantom

The phantom with Gafchromic film at the midline was positioned on the patient table of the same linear accelerator that used for the preparation of dose-density curve (Fig. 3). The phantom was fixed so that the direction of Gafchromic film was vertical to the beam.

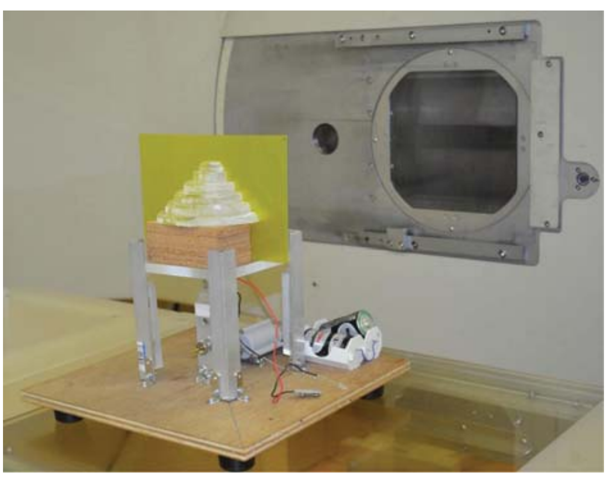

Figure 3. The phantom was divided, and a Gafchromic film was sandwiched in between. The phantom and the stand was positioned on the patient table of the linear accelerator.

First, the radiation field was set so that the upper margin of the beam is 2 cm above the top of the breast phantom and the lower margin of the beam is 0.5 cm below the breast phantom at the expiratory phase (stand, down). The radiation fields at the expiratory and the inspiratory phase (stand, up) are shown in Fig. 4.

The phantom was irradiated with 4-MV x-ray using a 30-degree wedge filter for a total of 600 MU with 300 MU from each side by the opposed portals.

Radiation was undergone with the 3 following conditions:

a

b

Figure 4. The radiation fields are indicated by the frame (arrows).
a. Expiratory phase. The field was set so that the upper margin is 2 cm above the top of the breast phantom and the lower margin is 0.5 cm below the phantom.
b. Inspiratory phase.

1) Irradiation during expiratory-phase breath holding: Irradiation was administered while the respiratory motion of the phantom was stopped at the expiratory phase (stand, down).
2) Irradiation during spontaneous respiration: Irradiation was administered while the respiratory motion of the phantom was continuous.
3) Irradiation with respiratory gating: Irradiation was administered only during the expiratory phase while the motion of the phantom was continuous, by manually switching the beam on during the light of the phantom was turned on (stand, down).

The film was exchanged each time between the sessions of irradiation, and the results of each irradiation method were measured 3 times each, for a total of 9 measurements.

4. Dose analysis

Each irradiated film was evaluated using the same scanner and the software as used for the preparation of dose-density curve. The dose distribution at the midline of the phantom was obtained, and the area under the curve was calculated for each condition of irradiation and compared. Statistical analysis was underwent using EZR ver. 1.27 (Saitama Medical Center, Jichi Medical University)[10]. Mann-Whitney *U* analysis and Bonferroni multiple comparison were used.

RESULTS

A dose-density curve is shown in Fig. 5. A linear correlation was confirmed between irradiated dose and the optical density of Gafchromic film. An example of Gafchromic film after irradiation of the breast phantom is shown in Fig. 6. Densitometry was made along the centerline of the phantom. Fig. 7 shows the graph of distributions of dose along the centerline of the phantom. The graph area with gray background corresponds to the lung part of the phantom. Table 1 shows values of the area

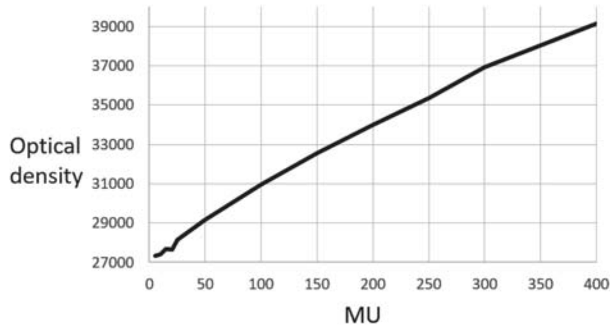

Figure 5. Dose-density curve.

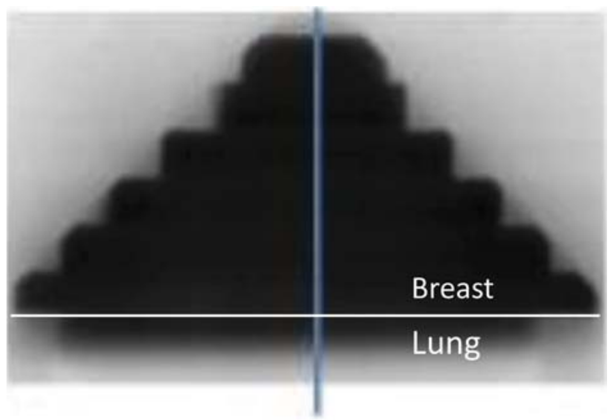

Figure 6. Gafchromic film after irradiation of the breast phantom. The area above the white line is the breast, and that below is the irradiated lung. Densitometry was made along the centerline of the phantom.

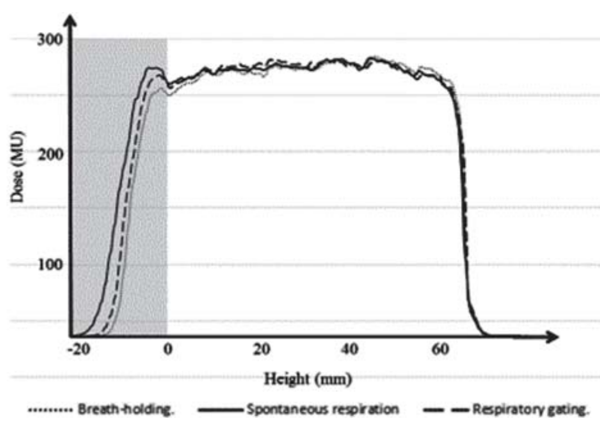

Figure 7. Graph showing distributions of dose along the centerline of the phantom. The area with gray background corresponds to the lung part.

Table 1. Comparison of lung does with three different modes of irradiation

Mode of irradiation	Area under the curve (MU)		
Breath holding	20750.9	$p < 0.001$ (Breath holding vs. Spontaneous respiration)	$p = 0.16$ (Breath holding vs. Respiratory gating)
Spontaneous respiration	26097.0	$p = 0.018$ (Spontaneous respiration vs. Respiratory gating)	
Respiratory gating	22389.0		

p values were based on Bonferroni multiple comparison.

under the curve corresponding to the lung part of the phantom comparing three different modes of irradiation.

Lung dose (the area under the curve) increased in the order of irradiation during expiratory-phase breath holding, irradiation with respiratory gating, and irradiation during spontaneous respiration. Lung dose during expiratory-phase breath holding and respiratory gating were significantly lower than that of spontaneous respiration (Bonferroni $p < 0.001$ and $p = 0.018$, respectively). No significant difference was noted in lung dose between expiratory-phase breath holding and respiratory gating (Bonferroni $p = 0.16$).

DISCUSSION

A recent report on Breast Cancer Registry by the Japanese Breast Cancer Society (JBCS) describes that the number of cases with BCS overtook those with modified or total mastectomy in 2003, and BCS continued to increase thereafter. In the standard procedure of BCS, radiation therapy after surgery is mandatory. In the JBCS registry data, an increase of the standard BCS with radiation therapy has been observed from 2004 to 2008, and at present, almost 80% patients are estimated to have radiation therapy after BCS[3].

Risk of radiation pneumonitis will increase depending on the radiation dose to the lung. A previous study reported that incidence and grade of radiation pneumonitis were significantly related to the percentage of pulmonary volume irradiated more than 20 Gy (V20)[11]. They suggested V20 of 25% or more appeared to be a factor predicting complication of radiation pneumonitis. Another report also suggests the mean lung dose of 20 Gy as a predictor of radiation pneumonitis[12].

Our present experimental study using a phantom simulating respiratory motion demonstrated that lung doses during expiratory-phase breath holding and with respiratory gating were significantly lower than that during spontaneous respiration. From the result, application of respiratory-gated irradiation for post-BCS breast radiation therapy is considered to be useful in preventing radiation pneumonitis.

Clinical application of breast cancer irradiation under active breath control or respiratory gating have been reported in only a few researches. Vikstroem and Hjelstuen reported that respiratory gating with deep-inspiration breath hold (DIBH) utilizing audio-visual guidance reduced cardiac and pulmonary doses for tangentially treated 17 left sided breast cancer patients without compromising the target coverage even when internal-mammary-chain lymph nodes were included[7)8)]. Verhoeven[9] compared 3 different treatment positions in their dosimetric planning of 34 patients with breast cancer: supine position in free-breathing, supine position with gating in DIBH, and prone position. They showed the lowest doses to the lungs were achieved in prone position while the coverage of the planning target volume breast was equal for the 3 treatment positions. It is considered that respiratory motion was restricted under prone position similarly to expiratory-phase breath holding in our study. All results from these previous reports show advantage of active breath control or respiratory gating irradiation as demonstrated in our experimental study.

Our results showed lung dose during expiratory-phase breath holding and with respiratory gating were significantly lower than that during spontaneous respiration, and no significant difference was noted between expiratory-phase breath holding and respiratory gating. We did not include DIBH and inspiratory gating in the experimental study. Under free breathing, time of inspiration is shorter than expiration so that inspiratory-gated irradiation would be associated with longer treatment time than expiratory gating. Furthermore, expiratory phase is the most stable and reproducible phase of the breathing cycle[13]. In the stereotactic irradiation therapy for lung tumors and liver tumors, respiratory gating during expiratory phase has been clinically applied[6)14)]. We suggest that radiation during expiratory-phase gating would be preferable in the clinical practice.

Our study has some limitations. First, the simulated respiratory movement of the phantom is not exactly the same as physiological respiration. A recent study on the chest wall movement by respiration showed that median chest wall movement was wider in anteroposterior (4.2〜5.4 mm) than superoinferior (2.5〜2.6 mm) and mediolateral (0.6〜1.1 mm) dimension[15]. Our phantom moved only in anteroposterior dimension. Movement in other dimensions should be considered. Second, the cycle of movement of the phantom was 8 seconds (7.5 cycles per minutes), which was slower than normal respiration. Finally, the shape of the thoracic cage was not considered.

In conclusion, irradiation with respiratory gating significantly reduced the lung dose as compared to irradiation during spontaneous respiration, and so may help to prevent the occurrence of radiation pneumonitis when clinically applied.

Acknowledgement:

We thank Dr. Kenta Murotani, Associate Professor, Clinical Research Support Center, Aichi Medical University Hospital for his advice on statistics.

Declaration of interest:

The authors have no conflict of interest to disclose.

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