Note

Changes in Skin Surface Temperature and Erythema Intensity during and after Radiotherapy for Breast Cancer Patients

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The aim of this study was to measure two parameters concerning the severity of acute radiodermatitis and to investigate the clinical relevance of the measurement, considering the implication of preventive and protective skin-care for the radiodermatitis. The subjects were five patients with breast cancer who underwent postoperative radiotherapy after breast-conserving surgery. Skin surface temperature (SST) and erythema intensity (EI) within the irradiated fields were measured twice, during radiotherapy and one month after. The measurement during radiotherapy was performed in the last week of radiotherapy, and the irradiated dose ranged from 44 to 48 Gy. For the contralateral breast, measurement was also performed as a control. The SST during radiotherapy was 1.1 ± 0.7 (average ± standard deviation), and that after radiotherapy 1.0 ± 0.3. The EI during radiotherapy was 101 ± 44, and that after radiotherapy 85 ± 55. No significant difference in the values during and after radiotherapy was observed for each of the parameters. Inflammation of the irradiated skin tissues appeared to continue even one month after radiotherapy. Therefore it was suggested that skin-care is needed for a certain period following radiotherapy as well as during the therapy in order to prevent the condition of irradiated skin becoming worse.

Key words: breast cancer, postoperative radiotherapy, radiodermatitis, skin surface temperature, erythema intensity

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1. Introduction

The incidence of female breast cancer is increasing not only in Japan but also in overseas countries[1]. With regard to the treatment strategy of breast cancer, breast-conserving therapy has been a standard, and in order to enhance the curability, postoperative radiotherapy

Table 1. Background of the subjects (n = 5)

Factor	Number
Laterality of primary lesions	
Right	2
Left	3
Stage	
I A	3
II A	2
Combination therapy	
Hormone therapy	3
Chemotherapy	1
Hormone therapy & Chemotherapy	1

following breast-conserving surgery is carried out for the operated breast including latent cancer cells[2].

Because the primary lesions of breast cancer are located rather close to the skin, 4–6MV X-ray and tangential irradiation technique are employed to cover the entire affected breast. The dose of skin surface ranges from 50 to 60% of the prescribed one, usually 2.0 Gy daily at isocenter or the ICRU reference point[3]. Although there has been an advancement in irradiation technique recently, clinically-apparent acute radiodermatitis occurs in over 90% of patients and the severity varies among individuals[4, 5].

In most of the previous research, preventive care, cautions about life style so as not to worsen the signs and the symptoms, and treatment methods for the patients with acute radiodermatitis have been studied[6]. However, there have been few studies focusing on the serial changes of skin condition within radiation fields and the duration of acute radiodermatitis. In the current study, we measured two parameters in relation to the severity of acute radiodermatitis and investigated the clinical relevance of the measurement, considering the implication of preventive and protective skin-care for the radiodermatitis.

2. Materials and Methods

2.1. Subjects and Treatment
The subjects of this study were five patients presenting with breast cancer who underwent postoperative radiotherapy following breast-conserving surgery (Table 1). Age ranged from 38 to 71 years. For primary tumor lumpectomy was performed, and for regional lymph nodes axillary node dissection or sentinel node dissection. Radiotherapy was performed by a linear accelerator (Clinac iX, Varian Medical Systems, USA), employing 6 MV X-ray, at Hirosaki Central Hospital. Tangential irradiation technique with non-parallel 2 portals was used. Total target dose was 50 Gy in 25 fractions with a conventional schedule.

2.2. Measurement of skin condition
Measurement was performed using a Multi-skin instrument®, consisting of Maxameter MX18® and Skin-Thermometer ST500® (Courage + Khazaka Corporation, Gernmany), non-invasive devices employing the pen-type probes. The parameters were the skin surface temperature (SST) and the degree of erythema (erythema intensity: EI). For EI, measurement is based on absorption/reflection of light. The probe of the Mexameter MX18® emits 3 specific light wavelengths (568nm, 660nm, 870nm). The receiver measures the light reflected by the skin. As the quantity of emitted light is defined, the quantity of light absorbed by the skin can be calculated. The standard values of EI in Japanese female range from 100 to 200.

The room used for measurement was air-conditioned and the temperature was maintained around 25-26℃. Measuring point for the affected breast was chosen from the part of the skin within the irradiated fields but without the markings for radiotherapy. The operative wound was avoided. The corresponding point in the contralateral breast was selected as a control.

For SST, measurement was done twice, and it was obtained as an average. For EI, measurement was carried out five times. The highest and the lowest values were excluded, and EI was obtained from the residual three values as an average. The time-points of measurement were during radiotherapy (in the last week of treatment) and one month after completing radiotherapy. For the former, the irradiated target dose reached 40 to 50 Gy. In this period, peak reaction of acute radiodermatitis was usually observed. The difference in the two parameters, SST and EI, between the affected breast and the contralateral one was calculated at each time-point.

2.3. Clinical evaluation of acute radiodermatitis
At the time-points mentioned above, the severity or grade of acute radiodermatitis was clinically evaluated according to the common terminology criteria for adverse events (CTCAE) version 4[7].
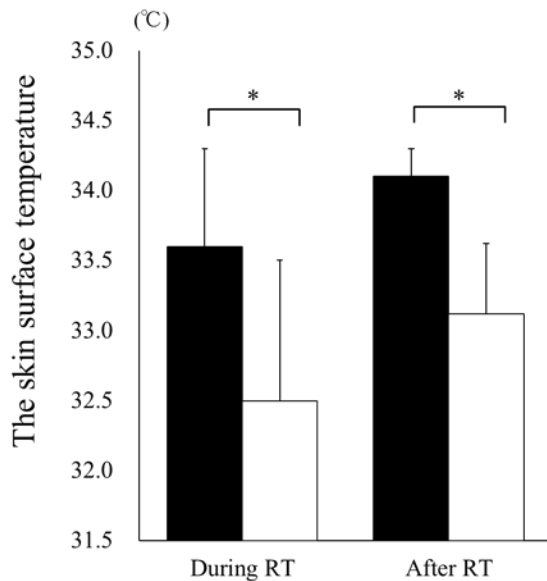
2.4. Data analysis
All data were analyzed using SPSS 16.0 Japanese for Windows and the difference in the values was analyzed using the Wilcoxon signed-rank test. $P < 0.05$ was considered to be statistically significant.

3. Results

3.1. Skin surface temperature
For all of the five patients, the average SST in the affected breasts during radiotherapy was 33.6 ± 0.7 (average ± standard deviation), and that for the contralateral breasts was 32.5 ± 1.0 ($P < 0.05$). The average SST in the affected

Fig. 1. Serial change in skin surface temperature (paired-t test, *P < 0.05, n = 5).
RT: Radiotherapy. Black column and white column indicate the skin surface temperature in the affected breast and the contralateral one, respectively.
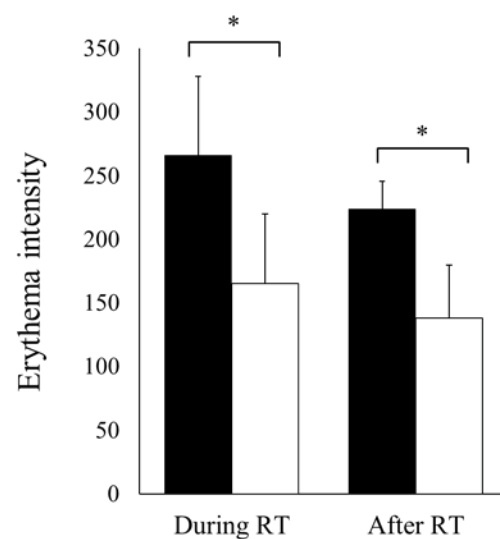

Fig. 2. Serial changes in erythema intensity (paired- t test, *P < 0.05, n = 5).
RT: Radiotherapy. Black column and white column indicate erythema intensity in the affected breast and the contralateral one, respectively.

breasts one month after radiotherapy was 34.1 ± 0.2, and that for the contralateral breasts was $33.1 \pm 0.5 (P < 0.05)$. There was no significant difference between the SST of the affected breast during radiotherapy and that after it. Also there was no significant difference between the SST of the contralateral breast during radiotherapy and that after it. The SST of the affected breast was significantly higher than that for the contralateral one not only during radiotherapy but also after radiotherapy (Fig. 1).

The difference in the SST between the affected breast and the contralateral one during radiotherapy was 1.1 ± 0.7, and that after radiotherapy 1.0 ± 0.3. There was no significant difference, which indicated no decrease of SST after the time-course of one month.

3.2. Erythema intensity
The average EI of the affected breasts for the five patients during radiotherapy was 267 ± 62, and that for contralateral breasts was 165 ± 55 ($P < 0.05$). The average EI of the affected breasts one month after radiotherapy was 224 ± 22, and that for contralateral breasts was 138 ± 42 ($P < 0.05$). There was no significant difference between the EI of the affected breast during radiotherapy and that after it. Also there was no significant difference between the EI of the contralateral breast during and that after it. The EI of the affected breast was significantly higher than that for the contralateral one not only during radiotherapy but also after radiotherapy (Fig. 2).

The difference in the EI between the affected breast and the contralateral one during radiotherapy was $101 \pm$

Table 2. The grade of acute radiodermatitis ($n = 5$)

	Grade 0	Grade 1	Grade 2
During RT	0	4	1
After RT	3	2	0

RT: Radiotherapy.
The grade of acute radiodermatitis was clinically decided according to the common terminology criteria for adverse events[7]. Grade 0: no change. Grade 1: faint erythema or dry desquamation. Grade 2: moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema.

44, and that one month after radiotherapy 85 ± 55. Some decrease of EI found one month after, although it was not significant.

3.3. Clinical evaluation of acute radiodermatitis
Table 2 shows the comparison between the grade of acute radiodermatitis during radiotherapy and that for one month after radiotherapy. For the former, a peak reaction of grade 1 (faint erythema or dry desquamation) to 2 (moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema) was observed[7]. For the latter, acute radiodermatitis was considered improved by clinical observation, resulting in grade 0 (none) to 1.

4. Discussion

Acute radiodermatitis is known to a induce feeling of warmth, itching, irritable feeling, pain, dryness,

erythema, pigmentation and mild and localized fever in the irradiated skin[8]. Our results also showed the occurrence of acute radiodermatitis, and some of the signs and symptoms were observed in all five of the patients.

As a mechanism for inducing acute radiodermatitis, the influence of radiation upon cell turnover of skin is regarded as important. In normal skin, stem cells in the stratum basal of the epidermis actively divide and reach the stratum corneum of skin surface over 2 weeks. After remaining as mature cells for 2 weeks in the stratum corneum, the cells gradually desquamate and exfoliate from the skin surface. Normal skin continuously repeats this system of cell turnover; however, in irradiated skin, it becomes difficult for stem cells to reproduce and maintain the skin structure for more than a short time, because of the damage to the stem cells and their depletion in number. As a result, the epidermis becomes thin and the barrier function of the skin is decreased[9].
In addition, various inflammatory processes occur not only in dermal tissues but also various neighboring tissues within irradiated fields. Acute radiodermatitis or skin toxicity is not a simple adverse event limited to the skin surface but a complex and interactive phenomenon caused by irradiation[5, 10].

So far it has been reported that acute radiodermatitis usually heals over one to two months after radiotherapy[11]. However, our study showed that no significant changes in the parameters, EI and SST, were found during and one month after radiotherapy. It was suggested that the inflammation still continued one month after radiotherapy. Furthermore, the parameter SST did not decrease, irrespective of the decreased grade according to the CTCAE criteria. In addition, the parameter EI did not significantly decrease, although some decrease was observed. These findings suggest that macroscopic inspection is not sufficient to evaluate the degree of inflammation in the irradiated breast. In particular, it should be noted that an apparent discrepancy was found between the values of the parameters, SST and EI, and the grade according to the CTCAE criteria one month after radiotherapy. Quantitative and objective analysis using the parameters revealed that there were certain continuous changes in the tissues due to irradiation, which could not be detected by the classical way, the grade according to CTCAE criteria.

Since the severity of radiodermatitis can be vary among individuals, it should be influenced by personal factors such as nutritional status, smoking and skin friction, genetic factors, and factors associated with radiotherapy[11, 12]. However, it is still difficult to predict individual radiosensitivity before treatment[13]. Therefore, quantitative and objective estimation of radiodermatitis is needed to carry out personalized and optimized care

during and following radiotherapy. For this purpose, the classical evaluation according to CTCAE criteria alone appears insufficient because the detectability is difficult.

It is generally said that typical supportive care for reducing and relieving acute radiodermatitis is to use mild soap for washing irradiated skin, to keep it dry and clean the skin within the radiation fields, to protect the irradiated skin from physical stimuli such as ultraviolet, and so on[14]. However, as mentioned above, the severity of radiodermatitis can vary depending on the factors of each individual. For personalized and optimized care to treat radiodermatitis, the quantitative and objective estimation of inflammation and informing the results to the patient are needed. Furthermore, inflammation of the irradiated skin tissues still continues even one month after radiotherapy.

The quality of life (QOL) of the patients undergoing radiotherapy depends upon the severity of adverse events[15]. Preventive and protective skin care for relieving acute radiodermatitis, on the basis of serial and accurate estimation by our methods, should play an important role to maintain the QOL of patients presenting with breast cancer who undergo postoperative radiotherapy after conservative surgery.

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