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The Relation of Radiation Dose to Acute Skin Reaction as Measured by Electrical Skin Conductivity

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ABSTRACT

Background : The external layer of healthy skin is the stratum corneum (SC) of the epidermis. The SC functions as a defensive sheet and has excellent water-holding capacity, which decreases with acute SC desquamation in response to ionizing radiation. By measuring the skin conductivity of a high-frequency alternating current, which correlates with the water-holding capacity of the SC, the relation of radiation dose to epidermal response can be investigated noninvasively.

Materials and Methods : The subjects were 38 women who receiving postoperative radiation as part of breast-conserving surgery or mastectomy for breast cancer. Until the end of radiotherapy, the ratio of the conductivity of a 3.5-MHz alternating current was calculated in irradiated chest areas and nonirradiated contralateral areas of the chest every week.

Results : Skin conductivity decreased exponentially with the increase in the absorbed dose of radiation.

Conclusion : Measuring skin conductivity of high-frequency alternating current is a useful method for examining the radiation effect of the skin noninvasively. This method can also be used to measure changes in the skin reaction after irradiation.

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Key words : acute radiation effect, skin, epidermis, conductance, water-holding capacity

INTRODUCTION

The external layer of healthy skin is the stratum corneum (SC) of the epidermis. Although the SC is a thin membrane about 20 μm thick, it is an efficient barrier to water and other substances[1]. Because the SC separates fully water-saturated viable tissue from the dry outer environment, a concentration gradient of water exists within the SC *in vivo*. Lipids and water-soluble amino acids play an important role in retaining water within the SC as extracellular fluid.

Exposure of the skin to ionizing radiation is followed by several acute responses, such as erythema and desquamation, whose severity depends on the conditions of exposure[2]. The desquamation of the SC in response to radiation may decrease its water-holding capacity. By measuring the water-holding capacity of the SC, the relation of the radiation dose to the epidermal response can be investigated noninvasively.

Electrical conductivity, *i.e.*, conductance, is the inverse of the impedance or resistance, and indicates how easily an electrical current passes through the skin[3]. Conductance in the skin increases with the amount of bound water between cells of the SC. In human skin, impedance decreases and conductivity increases as the frequency of an applied alternating current (AC) increases[4]. Studies with an *in vivo* model of SC has shown that skin conductance of a 3.5-

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MHz AC correlates well with the water content of the SC[5]. The purpose of the present study was to investigate the relation of the acute skin reaction to irradiation dose through quantitative measurements of water content of the SC as indicated by conductance of a 3.5-MHz AC.

Materials and Methods

To examine the acute skin reaction during irradiation, we studied women who had received postoperative radiation as part of breast-conserving surgery or after mastectomy for breast cancer from April 2001 through February 2002 at the Jikei University Hospital. Eighty-nine patients received postoperative radiation therapy for breast cancer during this period: 65 after breast-conversing surgery and 24 after mastectomy. Thirty-eight patients gave their informed consent and were enrolled in this study. The mean age was 53±11.8 years (SD), and the age range was 30 to 77 years. Four patients had received chemotherapy before irradiation.

In patients who were receiving breast-conserving therapy, the residual breast was conventionally treated (2 Gy/day, 5 fractions/week) with a tangential-field 4-MV photon beam to a dose of 50 Gy at a reference point. In patients who had undergone mastectomy, the chest wall was treated with an anterior 6-MeV electron beam with 5-mm-thick bolus to a dose of 50 Gy. The same dose specification and dose-fractionation schedule were used in all patients. Additional fractionated boost doses of 10 and 16 Gy, respectively, were given to patients receiving breast-conserving therapy and those who had undergone mastectomy.

The absorbed radiation dose of the skin in patients receiving breast-conserving therapy was estimated from measurements with thermoluminescence dosimeter in several patients. The skin-surface dose in patients who had undergone mastectomy was considered to be the same as the reference dose, because an appropriate bolus was used in the electron beam field.

To measure skin conductance, a skin-surface hygrometer (Skicon-200; IBS Ltd., Hamamatsu, Japan) was used. The probe of the hygrometer is composed of 2 concentrically arranged brass electrodes separated by a cylinder of synthetic resin. The 3.5-MHz current flows between these electrodes via skin tissue. The conductance ($Gx = 1/Rx$) of skin can be recorded automatically in terms of microsiemens (μS; μmho) after the probe has been applied for 3 seconds.

Conductance was measured at 4 points: the inner upper, inner lower, outer upper, and outer lower portions of the irradiated breast or chest wall. Conductance was also measured at the corresponding points on the contralateral nonirradiated side. Average conductance at these points was calculated on each side, and the ratio between irradiated and nonirradiated average values was calculated for normalization. Until the end of irradiation, the ratio of conductivity between the irradiated and nonirradiated sides was determined weekly in the air-conditioned outpatient clinic of our department.

Results

In 33 of the 38 patients, the conductance ratio gradually decreased during radiotherapy as the absorbed radiation dose increased (Fig. 1). The con-

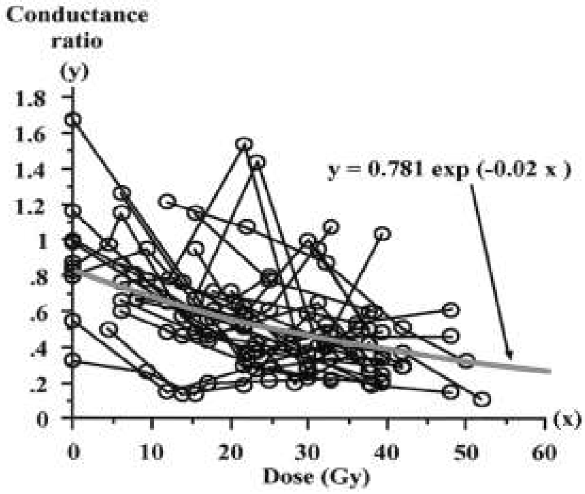

Fig. 1. Skin conductance ratio between irradiated skin and contralateral nonirradiated skin versus the estimated radiation dose of the skin. The regression curve obtained by the method of least-squares method shows the ratio decreasing exponentially as the radiation dose increases.

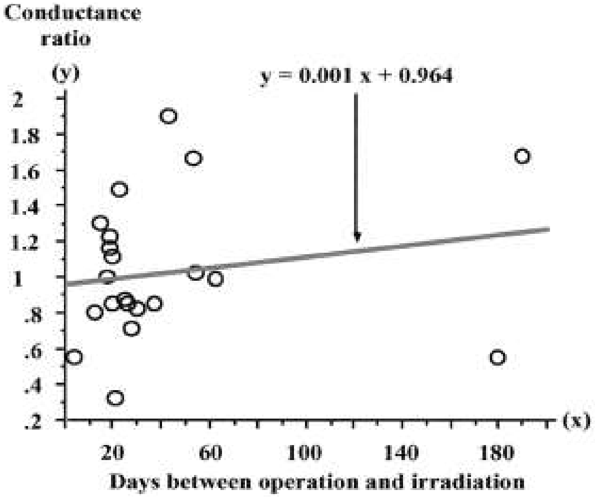

Fig. 2. Skin conductance ratio before irradiation versus the interval between surgery and the start of radiotherapy. The average skin conductance ratio of 27 patients before irradiation was 0.96± 0.405 (range, 0.154 to 1.899).

ductance ratio increased temporarily during the irradiation in 5 patients. These patients had applied a corticosteroid ointment during this period, because of increasing pruritus in the radiation field strengthens. Regression analysis with the least-squares method showed that the conductance ratio decreased monoexponentially as the radiation dose increased.

Before radiotherapy, the conductance ratio varied widely among the subjects (Fig. 1). In addition, the interval between surgery and the start of radiotherapy varied, because some patients received postoperative chemotherapy and others had delayed operative wound healing. However, the conductance ratio was not correlated with the interval between surgery and the start of radiotherapy (Fig. 2).

DISCUSSION

The radiosensitivity of mammalian cells differs with the degree of cellular differentiation and histologic type. Cells that are poorly differentiated or able to divide are believed to be radiosensitive, whereas cells that are highly differentiated or unable to divide are believed to be radioresistant. The skin can be roughly divided into the outermost layers, or the epidermis, and the deeper layers, or the dermis. Beneath the skin are the subcutaneous layers. The basal cells of epidermis divide, and by passing through the spinous-cell layer, the granular layer, and the SC, are shed from the skin surface. Although the dermis is composed largely of collagen fibers, it is highly vascular. Skin appendages include hair follicles, sebaceous glands, and eccrine (sweat) glands, and apocrine glands. Sebaceous glands open in the upper part of hair follicles, and the basal cells of sebaceous glands divide into daughter cells, which reach the lumen, the contents of which are finally secreted (holocrine). In contrast, sweat gland cells are well differentiated and do not divide. Therefore, to clarify the skin's radiosensitivity and its response to radiation *in vivo*, accurate analysis is necessary, because skin cells follow various pathways of development and differentiation.

In this study, we quantitatively measured the radiosensitivity of the epidermis, which morphologic studies have suggested is highly radiosensitive. Because the skin's reaction to irradiation may be modified by biopsy or other invasive investigative techniques, we used a noninvasive means to measure the response to radiation. Acute reactions to radiation include erythema and desquamation[6]. Because the SC thins with desquamation, physiologic changes of the SC with desquamation were investigated. Normally, lipids and amino acids between SC cells fix the water within the SC, so that the flexibility and water-holding capacity of the epidermis are maintained[7,8]. Therefore, the water content of SC would decrease with desquamation of the epidermis after exposure to radiation. For this reason, we used the change of water content within SC as an index for the acute skin reaction to irradiation.

Insensible perspiration and sweating from the skin are influenced by environmental factors, such as temperature, humidity, and atmospheric pressure, and by the body's general condition. Because this examination can be completed quickly and conveniently, this study was completed in our outpatient's clinic. Despite the use of air conditioning in the outpatient clinic, environmental condition were not uniform. However, seasonal variations are unlikely to have greatly affected the measurements, since they were carried out during 5 continuous weeks of radiotherapy. We examined the conductance ratio between irradiated and nonirradiated areas, because of the possibility of changes in conductance during radiotherapy in nonirradiated areas corresponding exactly to contralateral irradiated areas.

We found that the conductance ratio of the SC decreased exponentially as the absorbed radiation dose increased. This result indicates that the decrease in water content of the SC by means of increased insensible perspiration occurs earlier than visible desquamation. An earlier study found that the dielectric constant of the skin decreases as the absorbed radiation dose increases[9]. In our study, the conductance ratio increased rapidly but transiently in 5 patients. These 5 patients had temporarily used an ointment to relieve pruritus caused by irradiation, and the conductance ratio had increased during this time. We speculate that because the ointment suppressed insensible perspiration from the SC, both the water content and the conductance ratio of the SC increased.

Although the average conductance ratio before irradiation was 0.96, the SD was large (0.405). Because the interval between surgery and the start of radiotherapy varied, we also investigated the relation between this interval and the skin conductance ratio. We found no clear correlation. However, our finding that the conductance ratio varied before radiotherapy suggests that it is affected by endogeneous and exogeneous factors other than surgery. Therefore, further investigation of conductance ratio is warranted.

In this study, the relation between the acute skin reaction and radiation dosage was examined by means of the skin conductance ratio. However, the relation between recovery from the acute reaction and changes in the conductance ratio could not be examined in all patients, because the observation period was too short. Therefore, further observation is necessary to clarify this relation.

In addition to the skin conductance, tranepidermal water loss should be measured to help clarify SC function. However, only skin conductance was measured in the present study, because measurement can be made quickly and conveniently in our outpatient clinic.

Finally, because the skin is composed of various types of cell, functional effects, such as sweat expulsion[10,11], transepidermal water loss, and blood flow, should also be examined *in vivo* to gain a clearer understanding of the radiosensitivity of the skin.

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