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Evaluating the consistency of location of the most severe acute skin reaction and highest skin dose measured by thermoluminescent dosimeter during radiotherapy for breast cancer

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ABSTRACT

We conducted this prospective study to evaluate whether the location of the most severe acute skin reaction matches the highest skin dose measured by thermoluminescent dosimeter (TLD) during adjuvant radiotherapy (RT) for patients with breast cancer after breast conservative surgery. To determine whether TLD measurement can reflect the location of the most severe acute skin reaction, 80 consecutive patients were enrolled in this prospective study. We divided the irradiated field into breast, axillary, inframammary fold, and areola/nipple areas. In 1 treatment session when obvious skin reaction occurred, we placed the TLD chips onto the 4 areas and measured the skin dose. We determined whether the highest measured skin dose area is consistent with the location of the most severe skin reaction. The McNemar test revealed that the clinical skin reaction and TLD measurement are more consistent when the most severe skin reaction occurred at the axillary area, and the $p = 0.0108$. On the contrary, TLD measurement of skin dose is less likely consistent with clinical observation when the most severe skin reaction occurred at the inframammary fold, breast, and areola/nipple areas (all the $p > 0.05$). Considering the common site of severe skin reaction over the axillary area, TLD measurement may be an appropriate way to predict skin reaction during RT.

Introduction

Breast cancer is the most frequent cancer in women worldwide.[1] In Taiwan, it has also been the most common type of malignancy diagnosed among women since 1996. The statistics data from Department of Health, Executive Yuan, R.O.C., indicated that its incidence rate increased by 19.6 % from 2008 to 2011.[2] The age-adjusted incidence rate has increased gradually, reaching 74.63 new cases (including 64.28 invasive carcinoma and 10.35 carcinoma *in situ*) per 100,000 women in Taiwan in 2011.[3]

The prognosis for patients with breast cancer has improved considerably in recent years, with 5-year survival now approximately 90% in many countries.[4] This is partly due to widespread screening and partly due to greater use of adjuvant therapies.[5] Randomized clinical trials and meta-analyses have shown a benefit of adjuvant radiotherapy (RT) in breast cancer in reducing local recurrence and increasing overall and disease-free survival.[5-7] Nowadays, breast conservation therapy (BCT) is preferred for early stage breast cancer.[8,9] BCT involves the breast-conserving surgery (BCS), followed by 6 to 7 weeks of daily radiation treatments to the entire breast and possible regional lymph nodes (LNs).

The skin, however, is an inevitable organ that receives high radiation dose in the RT field of breast cancer. Skin is a relatively radiosensitive organ and vulnerable to different degrees of damage after certain dose of radiation,[10] and we can expect the radiation dermatitis to appear in the irradiated field during RT course.

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RT-induced acute skin reactions still remain a clinical concern. The total radiation dose, dose per fraction, overall treatment time, beam type and energy, and the surface area of the skin that is exposed to radiation all contribute to the skin reaction.[11] The thermoluminescent dosimeter (TLD) measurement has been documented as a suitable method for providing reliable dose data.[12] In this study, we used TLD to measure skin dose when obvious acute skin reaction occurred during RT course for breast cancer. We would like to see if the severity of skin reaction is corresponding to the measured surface dosage and evaluate the consistency of location of the most severe acute skin reaction and the highest skin dose measured by TLD.

Methods and Materials

Patients

Between January 2014 and December 2014, 80 consecutive women with breast cancer who were referred to our department for postoperative adjuvant RT after BCS were enrolled for this study. The eligibility criteria included those patients with pathologically proven primary breast carcinoma, curative intent for RT (no patient with stage IV disease) and not recurrence. There was no age limitation. This research proposal was approved by the Institutional Review Board of Kaohsiung Armed Forces General Hospital, and patient's written consent had been requested before study process.

Treatment planning

The thorax and lower neck areas of each patient were molded by a customized immobilization cast, followed by computed tomography (CT) simulation via the Philips ACQSim CT simulator. Treatment planning was conducted by the ADAC Pinnacle treatment planning system (TPS). The clinical target volume included the ipsilateral breast and possible axillary LNs. Internal mammary chain LNs or ipsilateral supraclavicular LNs (SCLNs) or both were included in the target only if a higher risk of tumor recurrence in those areas is expected. The planning target volume was clinical target volume with extension of 0.5 to 1 cm margins.

We used bilateral opposed tangential fields on megavoltage linear accelerators with intensity-modulated radiation therapy technique to cover the whole breast and possible axillary or ipsilateral internal mammary LNs or both. An anterior-posterior field with a tilt of 10° to 15° to spare more larynx, upper esophagus, and spinal cord was used to cover supraclavicular fossa when the ipsilateral SCLNs were included as the target. Treatment plans were designed to deliver the prescribed dose to the target volumes with consideration of normal tissue constraints. The prescribed dose for the planned target volume is 50.4 Gy in 28 fractions, and additional breast tumor bed boost for 10.8 Gy in 6 fractions via electron beam is reserved for patients with high risk factors.[13]

TLD measurement

We used standard 3.2 × 3.2 × 0.9-mm^3 LiF TLD-100H chips (Harshaw/Thermo Fisher Scientific Inc., MA) in this study. The absolute dose of TLD chips was calibrated by applying Varian LINAC iX, using a 6-MV beam. We then used calibrated Farmer-type ionization chamber to confirm the output of LINAC and to ensure that the outputs were within 0.5%. The TLD chips used in this study were irradiated and screened 3 times, and the required uncertainties were within ±3%. The qualified TLD chips were placed inside a solid water phantom at a depth of 5 cm, and the output from 55.25 to 222.75 cGy was applied to conduct the calibration experiment. The calibration equation was created and the linear-square correction curve was discovered to be highly linear (R^2 = 0.9934, Fig. 1).

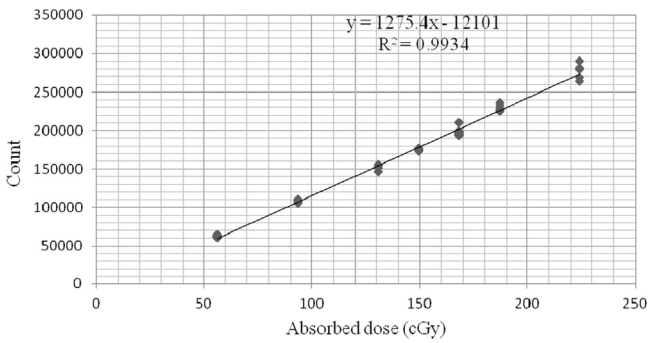

Fig. 1. Calibration curve and equation for the LiF TLD-100H chips.

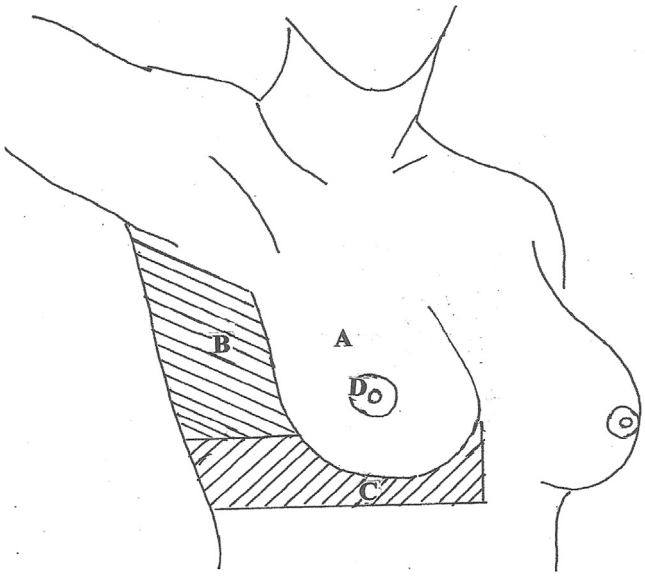

Fig. 2. The 4 parts of irradiated area are as follows: (A) main breast area, (B) axillary area, (C) inframammary area, and (D) areola/nipple area.

To minimize the statistical errors, all measurements were repeated at least 3 times. The readouts were obtained using a Harshaw TLD 5500 Automatic TLD reader (Bicron RMP, USA), after which the chips were annealed at 240°C for 15 minutes and cooled at ambient temperature. The chips were cooled to room temperature before irradiation.

To facilitate this clinical investigation, we divided the RT field into 4 areas. They are main breast area (A), axillary area (B), inframammary area (C), and areola/nipple area (D) (Fig. 2). Further, 3 qualified TLD chips were positioned onto the identified most severe skin reaction area of each part of patient's skin surface during 1 treatment of RT (Fig. 3). Totally 12 TLD chips were collected from each patient. The reading process consisted of a preheat at 100°C for 15 seconds, followed by the heating protocol with the temperature increasing linearly at 10°C per second to a maximal temperature of 260°C, at which the temperature was maintained constant. The photomultiplier signal was recorded during the linear-heating phase and at the maximal temperature, for a total acquisition time of 30 seconds. The mean skin dose of 3 chips in each area was calculated to determine the location of the highest skin dose.

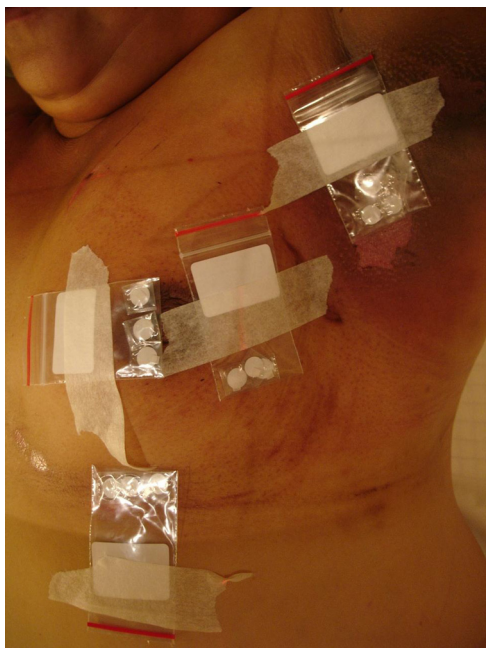

Fig. 3. LiF TLD-100H chips were placed onto a patient's skin in 4 parts. (Color version of figure is available online.)