# Skin Toxicity and Cosmesis after Hypofractionated Whole Breast Irradiation for Early Breast Cancer

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***Objective:*** *To assess and compare the impact on skin reactions and cosmesis between hypofractionated whole breast and conventional irradiation for early breast cancer.*

***Material and Method:*** *Seventy-three patients with operable breast cancer (pT1-3pN0-1M0) who underwent breast-conserving surgery were assigned for irradiation to either conventional arm (50 Gy in 25 fractions) with a sequential electron boost of 15-16 Gy over five weeks or hypofractionated arm (43.2 Gy in 16 fractions) with a concomitant electron boost of 0.6 Gy over three weeks.*

***Results:*** *At 3-week follow-up, skin toxicities in the hypofractionated arm were significantly worse than that seen in the conventional arm, while at 6-week follow-up, the percentages of skin toxicities in the conventional arm were higher. After a median follow-up of six months, there was no significant difference in skin toxicities between the two treatment groups. In addition, there were no significant differences in the mean scores of cosmetic outcome for patients between two regimens.*

***Conclusion:*** *This hypofractionated radiotherapy regimen of 43.2 Gy in 16 fractions with a concomitant electron boost showed good results in terms of normal tissue effects and cosmesis. A long-term follow-up is needed to confirm these favorable results.*

***Keywords:*** *Skin toxicity, Cosmesis, Hypofractionated radiotherapy, Whole breast irradiation, Breast cancer*

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Radiotherapy (RT) after breast-conserving surgery (BCS) in early breast cancer has demonstrated to be equivalent in terms of overall survival, local control, and disease-free survival rates when compared to mastectomy[1-9]. The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis has confirmed that breast irradiation after breast-conserving surgery substantially reduced the 5-year local recurrence rate from 26% to 7%[10]. Others studies also showed reduction in local recurrence comparing BCT with or without radiation[3,8,10-18]. The usually recommended radiation dose is 45 to 50 Gy to the whole breast in 25 daily fraction of 1.8 to 2 Gy over five weeks, with a boost of 10 to 16 Gy to the tumor bed[19,20]. This long radiotherapy schedule has many disadvantages such as patient inconvenience, higher costs of treatment, workload and machine utilization. These shortcomings, although not all, could be overcome by a shorter radiation schedule or accelerated hypofractionation, rending benefits to both patients and resources.

The Linear Quadratic (LQ) model[21], $E = nd(ad + bd^2)$, describes the relationship between total dose, fraction size and fractionation sensitivity expressed by the alpha/beta ratio[22,23]. It models the radiation effect. A utilization of the LQ model is to calculate the iso-effectiveness between two fractionation schedules by dividing both sides of the equation by alpha to obtain the Biological Effective Dose (BED). For acute reacting tissues and tumours, the alpha/beta ratio is in the range of 7 to 20 Gy. The late reacting tissues have the lower range of 0.5 to 6 Gy[21].

Yarnold J et al has shown that breast adenocarcinoma has an alpha/beta ratio of around 4 Gy, while the breast tissues have a lower value of

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3 Gy[24]. These findings imply that hypofractionation in breast cancer has a sound radiological basis[24,25]. Schedules used in studies of hypofractionated breast irradiation ranged from 40 to 44 Gy in 15 to 16 fractions over a three-week period, with daily fractions of 2.5 to 2.7 Gy[13,26-29]. Results from these studies showed low recurrence rates and good cosmesis[30-32]. Four large recent randomized trials have confirmed the equivalence of hypo-fractionationed whole-breast irradiation to conventional whole-breast irradiation in terms of local recurrence and cosmetic outcome[24,33-36].

To achieve equivalent turnover tumor and normal tissue effects, the LQ model is used to convert the conventional schedule to the hypofractionated one. The BED of the four randomized trials and the present study are comparable based on $\alpha/\beta = 4$ Gy.

The value of tumor bed boost had been shown to reduce the 10-year local recurrence from 10.2% to 6.2% by the European Organization for Research and Treatment of Cancer (EORTC 22881-10882)[20]. Furthermore, it is recommended by the study from Romestaing et al[37]. It is noteworthy that the afore-mentioned hypofraction studies did not deliver tumor bed boost. It is understandable that these studies had been initiated before the EORTC report[20]. For conventional breast irradiation, a sequential boost is used. Freedman GM et al demonstrated good cosmesis using hypofractionated whole breast Intensity Modulated Radiation Therapy (IMRT) with concomitant boost over four weeks[43]. The result, being consistent with some recently published results using various radiotherapy techniques, revealed low skin toxicity[44]. Culling evidence from Accelerated Partial Breast Irradiation (APBI) studies[38-42], the BED (alpha/beta 4 Gy) falls in the range of 75 to 98 Gy for the tumor bed with acceptable cosmesis and skin toxicity. Therefore, the authors apply a concomitant tumor bed boost with a BED not larger than 98 Gy expecting to obtain similar results and shorten the treatment duration.

The present study was undertaken to study the skin toxicity and cosmesis following hypo-fractionated whole breast irradiation with concomitant tumor bed boost.

## Material and Method

The present study was a non-randomized study. It was undertaken with the approval of the Research Ethics Committee of King Chulalongkorn Memorial Hospital. Informed consent was obtained after each patient had received both verbal and written information regarding the present study.

### *Patients*

Between October 2009 and June 2010, 76 patients with early breast cancer were referred to the Division of Radiotherapy, King Chulalongkorn Memorial Hospital for radiation treatment after breast conserving surgery. Inclusion criteria include women with operable breast cancer after breast conserving surgery (pT1-3pN0-1M0), aged at least 18 years, invasive or ductal carcinoma in situ, tumor margin $\geq$ 1 mm, no immediate reconstruction, requiring neoadjuvant or adjuvant chemotherapy. Excluded criteria include evidence of skin invasion by the tumor, bilateral breast cancer, history of connective tissue disease, previously treated with radiation therapy, post mastectomy, requiring concurrent chemoradiation. Patients were assigned to either the conventional or hypofractionated arm at their preferences.

### *Radiotherapy*

Patients in the conventional arm were given 50 Gy in 25 daily fractions of 2 Gy in five weeks to the whole breast. A sequential electron boost of 15 to 16 Gy in 5 to 8 fractions of 2 to 3 Gy was given subsequently to the tumor bed. In the hypofractionated arm, patients were given 43.2 Gy in 16 daily fractions to the whole breast concurrently with a boost of 0.6 Gy to the tumor bed, over three weeks. All patients were treated with opposing tangential fields in supine position, arms above the head. Photons 6 MV with a source-to-axis distance of 100 cm were used in all patients. Dose homogeneity of breast was achieved by using wedges. For tumor bed boost, an en-face electron beam with appropriate energy was used, prescribing at the 90% isodose line. For the whole breast irradiation, either conventional or three-dimensional (3D) planning were allowed, prescribing at the isocenter or the appropriate isodose line. The target volume of the whole breast was as follows, the medial border was located at the midsternal line, the lateral border at the mid axillary line, the superior border at the caudal end of the head of the clavicle, and the inferior border at about 2 cm below the inframammary fold. The volume of supraclavicular field includes the medial border at medial aspect of the sternocleidomastoid muscle, the lateral border at the coracoids process of the scapular, the superior border at the thyroid notch, and the inferior border at the superior border of the opposing tangent field.

***Assessment of endpoints***

The endpoints of skin toxicity were acute and late skin effects that occurred within 90 days and more than 90 days, respectively, after irradiation[45]. Skin toxicity was assessed clinically, using the Common Terminology Criteria for Adverse Event (CTCAE version 3) (Table 1)[46], by the principle investigator at three and six weeks and six months after starting irradiation. Cosmesis was evaluated using the 5-point scale (Table 2)[31]. Photographs in two positions, arms raised above the head and hands resting on hips, were taken before irradiation and at six months after starting radiation for comparison. Assessment was scored by a group of radiotherapists, blinded to patients' characteristics and treatment arm, at our department. The final agreed scores were reached by consensus. The length of follow-up time was calculated from the date of commencing radiotherapy to the date of the last follow-up.

Breast size was measured by calculating the difference between patients' chest at the fullest point and underneath their breasts around the rib cage. The difference of less than 1 inch defined as cup A, 2 inches as cup B, 3 inches as cup C, 4 inches as cup D and more than 5 inches as cup E. Measurement was done while standing straight with arms to the side and wearing a properly fitted bra[47].

***Statistical analysis***

The sample size of 74 patients was calculated using match pair method, from the following formula[48], with a 90% of power. Pearson Chi-square test was used for testing the difference between groups with an $\alpha$ value of 0.05. The Mann-Whitney U test was used for evaluating the significant difference of cosmetic outcome between the two groups. Binary logistic regression analysis was used to investigate correlation between skin toxicity and breast size volume.

**Results**

Between October 2009 and June 2010, 76 patients were included in the present study. During the present study, three patients in the conventional arm did not complete radiation treatment due to associate medical diseases. The authors did not include these three patients in their analysis. Of 73 patients, 34 were treated with conventional schedule and 39 were treated with hypofractionated regimen. Median follow-up was six months (range 6 to 9 months) in the conventional arm and 6 months (range 6 to 10 months) in the hypofractionated arm. Table 3 lists the patients and treatment characteristics of the two treatment groups. No significant baseline differences were observed in the distribution of age, tumor stage, stage grouping, breast size, menopausal status, histologic grade, hormonal receptor status and treatment characteristics. There were no significant differences between the two assigned groups when stratified by age, breast size, and type of radiation regimens. Three of the 73 patients were lost to follow-up after three and six weeks.

***Toxicity at three-week follow-up***

Table 4 shows the acute skin toxicity at three weeks after starting radiotherapy. Most patients experienced mild acute toxicity (none and grade 1 or 2). There was no grade 3 or greater toxicities. Hypofractionated arm were significantly resulted in higher cases of grade 1 and 2 erythema (58.1% vs. 30.8% for grade 1, 12.9% vs. 7.1% for grade 2, $p = 0.03$), grade 1 breast edema (48.4% vs. 28.2%, $p = 0.08$), grade 1 breast pain (48.4% vs. 25.6%, $p = 0.05$) and grade 1 and 2 hyperpigmentation (45.2% vs. 25.6% for grade 1, 38.7% vs. 30.8% for grade 2, $p = 0.04$). No cases of skin ulceration, fibrosis and telangiectasia were seen. Rib fracture was not evaluated due to short time of follow-up and it is not appropriate to have imaging at this time point.

The binary logistic regression analysis shows that erythematous skin and breast pain were significantly associated with both conventional and hypofractionated radiation techniques, while breast size did not result in differences in acute skin toxicity between the two arms. The correlations were medium size, OR 1.10 (95% CI 0.35 to 3.49) and large size, OR 0.99 (95% CI 0.2 to 5). There was no statistical differences between breast size and pain, medium size, OR 1.73 (95% CI 0.5 to 5.99) and large size, OR 3.3 (95% CI 0.6 to 17.3) (Table 5).

***Toxicity at six-week follow-up***

Table 6 demonstrates toxicity at six-week follow-up. There were no grade 3 or greater toxicities. Breast edema and breast pain were statistically higher in the conventional arm as grade 1 breast edema (69.2% vs. 29.4%, $p = 0.002$), grade 2 breast edema (5.1% vs. 2.9%, $p = 0.002$), grade 1 breast pain (64.1% vs. 38.2%, $p = 0.03$). No significant differences in other toxicities were observed between the groups. There were more patients with fibrosis, atrophic skin and telangiectasia when compared to those seen at three-week follow-up.

**Table 1.** Common terminology criteria for adverse events (CTCAE) version 3.0[46]

| Adverse events | Grade | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| Rash associated with radiation | Faint erythema or dry desquamation | Moderate to brisk erythema; patchy moist desquamation confined to skin folds and creases; moderate edema | Moist desquamation other than skin folds and creases; bleeding induced by minor trauma or abrasion | Skin necrosis or ulceration of full thickness dermis; spontaneous from involved site | Death |
| Ulceration | - | Superficial ulceration < 2 cm size; local wound care; medical intervention indicated | Ulceration ≥ 2 cm size; operative debridement; primary closure or other invasive intervention | Life-threatening consequences; major invasive intervention | Death |
| Breast edema | Swelling or obscuration of architecture on close inspection; pitting edema | Readily apparent obscuration of architecture; obliteration of skin folds | Lymphorrhea; interfering with ADL; gross deviation from normal contour | Progression to malignancy (eg. lymphangio sarcoma); disabling | Death |
| Breast pain | Mild pain not interfering with function | Moderate pain; pain intefering with function, but not ADL | Severe pain; pain intefering with ADL | Disabling | - |
| Hyper/hypopigment | Slight or localized | Marked or generalized | - | - | - |
| Atrophy (skin/subcutaneous fat) | Detectable | Marked | - | - | - |
| Induration/fibrosis | Increased density on palpation | Moderate impairment of function; marked density on palpation with or without minimal retraction | Dysfunction interfering with ADL;very marked density, retraction or fixation | - | - |
| Telangiectasia | Few | Moderate | Many and confluent | - | - |
| Rib fracture | Asymptomatic with only radiologic findings | Symptomatic but non-displaced; immobilization indicated | Symptomatic and displaced or open wound; operative intervention indicated | Disabling | Death |

**Table 2.** Cosmetic outcome assessment (5-point scale)[31]

| Category | Description |
|---|---|
| Very poor | Major functional and esthetic sequelae in treated breast<br>Very marked density, retraction and fixation<br>Breast asymmetry 40-75% |
| Poor | Obvious differences between treated and untreated breast<br>Marked distortion of nipple<br>Breast asymmetry 25-40%<br>Marked contour difference<br>Severe hyperpigmentation, severe edema<br>Marked mammillary deviation |
| Acceptable | Moderate differences between treated and untreated breast<br>Moderate distortion of nipple, absent nipple-areola complex<br>Moderate hyperpigmentation<br>Telangiectasia<br>Breast asymmetry 10-25%<br>Increased density and firmness<br>Slight edema<br>Prominent scar with surrounding retraction/ volume loss<br>Moderate contour difference<br>Moderate mammillary deviation |
| Good | Minimal difference between treated and untreated breast<br>Slight distortion of nipple<br>Mild hyperpigmentation<br>Breast asymmetry < 10%<br>Mild telangiectasia |
| Very good | Treated breast looks almost identical to untreated breast<br>Perfect symmetry<br>No visible distortion |

Assessment of correlation between skin toxicity and breast size, the binary logistic regression analysis showed that breast size had no effect on the incidence of breast edema and breast pain, breast edema for medium size, OR 1.22 (95% CI 0.39 to 3.89), large size: OR 2.41 (95% CI 0.42 to 13.88), breast pain for medium size, OR 0.83 (95% CI 0.28 to 2.45), large size, OR 9.8 (95% CI 1 to 95.6).

***Toxicity at six-month follow-up***

Although the late skin toxicity worsens over time, there was no any significant difference outcome between two treatment groups. The conventional arm revealed slightly higher patients with grade 1 atrophic skin but it was not statistically significance (15.4% vs. 2.9%, p = 0.07). Grade 3 or greater toxicities were not observed (Table 7).

***Cosmetic outcome assessment***

At six-month follow-up, photographic assessments of cosmesis were performed by our radiotherapists. The percentage of patients rated as very good, good, acceptable and poor were 7.7%, 69.2%, 20.5% and 2.6%, respectively, in the conventional arm. In the hypofractionated arm, the respective percentages were 11.8%, 73.5%, 14.7% and 0%. There were no patients categorized as very poor in both arms. The mean scores between the two arms were not statistically significant.

The percentages of the patient-self-reported scores of very good, good and acceptable were 48.7%, 46.2% and 5.1%, respectively, in the conventional arm as compared with 50%, 50% and 0% in the hypofractionated arm. There were no patients scored as poor in both arms. No statistical differences were observed between the two arms.

**Discussion**

The present study was undertaken to evaluate a hypofractionated radiation schedule using 43.2 Gy over 16 fractions (2.7 Gy per fraction) compared with conventional regimen 50 Gy over 25 fractions (2 Gy per fraction). Since breast cancer is the most common cancer seen in Chulalongkorn Hospital[49], a shorter radiation schedule would benefit both the patients and machine occupation. Moreover, the UK National Institute for Health and Clinical Excellence (NICE) has recently accepted fewer fractions as the standard of care for adjuvant radiotherapy in early breast cancer[50]. The authors' hypofractionated schedule is based on the equivalent BED to the conventional arm. The authors applied a concomitant boost to the tumor bed in order to shorten the treatment duration. With the BED of the tumor bed not higher than those reported in the accelerated partial breast irradiation studies[38-42], the authors would not expect worse complications from the present study.

In this preliminary result, the authors observed that skin toxicities in the hypofractionated arm at 3-week follow-up were significantly worse than that seen in the conventional arm, but were more in the conventional arm at 6-week follow-up. These phenomena could be the results of the higher rates of dose accumulation of acute reacting tissues in the hypofractionated arm[51], while the skin changes at

**Table 3.** Patients and treatment characteristics

| Characteristic | No. of patients in conventional (n = 39) | No. of patients in hypofraction (n = 34) | p-value |
|---|---|---|---|
| Age | | | |
| 18-49 | 16 (41%) | 15 (44.1%) | 0.79 |
| ≥ 50 | 23 (59%) | 19 (55.9%) | |
| Mean (SD) | 50 (10.4) | 49.8 (9.49) | |
| Menopausal status | | | |
| Premenopause | 20 (51.3%) | 20 (50%) | 0.91 |
| Postmenopause | 19 (48.7%) | 17 (50%) | |
| Breast size | | | |
| Size small (A) | 10 (25.6%) | 11 (32.4%) | 0.78 |
| Size medium (B, C) | 23 (59%) | 19 (55.9%) | |
| Size large (D, E) | 7 (15.4%) | 4 (11.8%) | |
| Tumor stage | | | |
| Tis | 3 (7.7%) | 3 (8.8%) | 0.83 |
| T1 | 20 (51.3%) | 15 (44.1%) | |
| T2 | 16 (41%) | 16 (47.1%) | |
| Nodal stage | | | |
| N0 | 31 (79.5%) | 33 (100%) | 0.006 |
| N1 | 8 (20.5%) | - | |
| Stage grouping | | | |
| Stage 0 | 3 (7.7%) | 3 (8.8%) | 0.25 |
| Stage I | 18 (46.2%) | 15 (44.1%) | |
| Stage IIA | 14 (35.9%) | 16 (47.1%) | |
| Stage IIB | 4 (10.3%) | - | |
| Histology | | | |
| IDC | 35 (89.7%) | 30 (88.2%) | 0.98 |
| ILC | - | - | |
| DCIS | 3 (7.7%) | 3 (8.8%) | |
| Other | 1 (2.6%) | 1 (2.9%) | |
| Margin | | | |
| < 1 mm | 9 (23.7%) | 2 (5.9%) | 0.04 |
| ≥ 1 mm | 29 (76.3%) | 32 (94.1%) | |
| Grade | | | |
| Grade I | 4 (14.8%) | 5 (17.9%) | 0.63 |
| Grade II | 7 (25.9%) | 10 (35.7%) | |
| Grade III | 16 (59.3%) | 13 (46.4%) | |
| Hormonal receptor | | | |
| ER- | 13 (36.1%) | 9 (28.1%) | 0.48 |
| ER+ | 23 (63.9%) | 23 (71.9%) | |
| PR- | 18 (50%) | 14 (43.8%) | 0.61 |
| PR+ | 18 (50%) | 18 (56.3%) | |
| Her 2- | 25 (69.4%) | 22 (68.8%) | 0.56 |
| Her 2+ | 8 (22.2%) | 5 (15.6%) | |
| Equivocal | 3 (8.3%) | 5 (15.6%) | |
| Treatment | | | |
| Surgery | - | 2 (5.9%) | 0.44 |
| Surgery and chemotherapy alone | 11 (28.2%) | 7 (20.6%) | |
| Surgery, chemotherapy and hormonal Tx | 18 (46.2%) | 16 (47.1) | |
| Surgery and hormonal Tx | 10 (25.6%) | 9 (26.5%) | |

IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; DCIS = ductal carcinoma in situ; ER = estrogen receptor; PR = progesterone receptor; HER 2 = human epidermal growth factor receptor 2

**Table 4.** Adverse effect (at 3-week time)

| Effect | RT technique | | p-value |
|---|---|---|---|
| | No. of patients in conventional (%) (n = 39) | No. of patients in hypofraction (%) (n = 31) | |
| Rash | | | |
| None | 24 (61.5) | 9 (29) | 0.03 |
| Gr. 1 | 12 (30.8) | 18 (58.1) | |
| Gr. 2 | 3 (7.1) | 4 (12.9) | |
| Ulceration | | | |
| Gr. 1 (none) | 39 (100) | 31 (100) | -[α] |
| Breast edema | | | |
| None | 28 (71.8) | 16 (51.6) | 0.08 |
| Gr. 1 | 11 (28.2) | 15 (48.4) | |
| Breast pain | | | |
| None | 29 (74.4) | 16 (51.6) | 0.05 |
| Gr. 1 | 10 (25.6) | 15 (48.4) | |
| Hyper/hypopigment | | | |
| None | 17 (43.6) | 5 (16.1) | 0.04 |
| Gr. 1 | 10 (25.6) | 14 (45.2) | |
| Gr. 2 | 12 (30.8) | 12 (38.7) | |
| Atrophy | | | |
| None | 38 (97.4) | 31 (100) | 0.37 |
| Gr. 1 | 1 (2.6) | - | |
| Fibrosis | | | |
| None | 39 (100) | 31 (100) | -[α] |
| Telangiectasia | | | |
| None | 39 (100) | 31 (100) | -[α] |

[α] No statistical intervention

**Table 5.** Results of binary logistic regression analysis correlation between skin toxicity at three weeks and breast size

| Effect and breast size | p-value | OR | 95% CI |
|---|---|---|---|
| Rash[+] | | | |
| RT[++] | 0.008 | 3.92 | 1.43-10.76 |
| Breast size | 0.98 | - | - |
| Small | - | 1.0 (reference) | - |
| Medium | 0.87 | 1.10 | 0.35-3.49 |
| Large | 0.99 | 0.99 | 0.20-5.01 |
| Breast edema | | | |
| RT[++] | 0.07 | 2.49 | 0.91-6.83 |
| Breast size | 0.47 | - | - |
| Small | - | 1.0 (reference) | - |
| Medium | 0.23 | 2.12 | 0.62-7.21 |
| Large | 0.39 | 2.06 | 0.39-10.95 |
| Breast pain | | | |
| RT[++] | 0.04 | 2.90 | 1.04-8.14 |
| Breast size | 0.38 | - | - |
| Small | - | 1.0 (reference) | - |
| Medium | 0.39 | 1.73 | 0.50-5.99 |
| Large | 0.17 | 3.26 | 0.61-17.31 |
| Hyper/hypopigment[+] | | | |
| RT[++] | 0.02 | 4.52 | 1.34-15.25 |
| Breast size | 0.06 | - | - |
| Small | - | 1.0 (reference) | - |
| Medium | 0.18 | 2.36 | 0.67-8.34 |
| Large | 0.26 | 0.38 | 0.07-2.06 |

[+] Comparison between none and mild toxicity (grade 1 & 2)
[++] Radiation techniques (conventional vs. hypofractionated schedule)

6-week follow-up were the typical sequences of skin changes of a conventional radiation schedule[52]. Worthy of note were the mild skin toxicities in both arms at 6-month follow-up and these changes were not different between the two arms. Cosmesis was also not significantly different between the two arms. Patients ratings of cosmesis showed no significant differences between the pre-irradiation baseline and the 6-month assessment. These results were in agreement with the scores rated by the radiotherapists. There were no differences in skin toxicities and cosmesis among patients with various cup sizes.

It is too early to compare the present results with the four large randomized studies[33-36]. However, the skin toxicity and cosmesis of the present study are not different from those reported at short follow-up[53-55]. The efficacy of boost irradiation has been demonstrated in two large randomized studies[20,37]. It is also recommended by the recent ASTRO, evidence based guideline that tumor bed boost in conjunction with hypofractionated whole breast irradiation should be used when it is indicated[56]. In present study, the authors employed a concomitant boost in order to shorten the treatment duration. Although studies of tumor bed boost, either concomitantly or sequentially, in hypofractionated breast irradiation are scarce[57-62], all these studies concluded that an incorporated boost is acceptable, safe and feasible.

Even the authors used such a high dose per fraction at the tumor bed in patients with hypofractionated radiation, the patients did not experience more skin toxicities as compared to the conventional arm. This should underscore the benefit of hypofractionation in reducing treatment time while keeping acceptable adverse events. Although the present follow-up is short and, undoubtedly, toxicity increases over time, the authors would not expect

worse outcomes using concomitant boost because the BED of the tumor bed in the hypofractionated arm is similar to that of the conventional arm.

The authors are aware of the limitations of the present study. Planning with 2D could result in inhomogeneity of dose distribution, cold and hot areas, severe late toxicities, and uncertain doses to the normal organs. The present study did not utilize 3D-planning in all of patients owing to the authors' limited resources. Recurrence in the breast and the tumor bed and survival are also the authors' grave concern. Long-term follow-up is needed to establish the efficacy of this regimen especially local control. Nevertheless, if the present hypofractionated schedule is at least equivalent to the conventional regimen after long-term follow-up in terms of toxicities, cosmesis, local control and survival, it is cost-effective for the patients and resource management.

**Table 6.** Adverse effects (at 6-week time)

| Effect | RT technique | | p-value |
|---|---|---|---|
| | No. of patients in conventional (%) (n = 39) | No. of patients in hypofraction (%) (n = 34) | |
| Rash | | | |
| None | 15 (38.5) | 20 (58.8) | 0.17 |
| Gr. 1 | 18 (46.2) | 12 (35.3) | |
| Gr. 2 | 6 (15.4) | 2 (5.9) | |
| Ulceration | | | |
| Gr. 1 (none) | 39 (100) | 33 (97.1) | 0.28 |
| Gr. 2 | - | 1 (2.9) | |
| Breast edema | | | |
| None | 10 (25.6) | 23 (67.6) | 0.002 |
| Gr. 1 | 27 (69.2) | 10 (29.4) | |
| Gr. 2 | 2 (5.1) | 1 (2.9) | |
| Breast pain | | | |
| None | 14 (35.9) | 21 (61.8) | 0.03 |
| Gr. 1 | 25 (64.1) | 13 (38.2) | |
| Hyper/hypopigment | | | |
| None | 1 (2.6) | - | 0.26 |
| Gr. 1 | 10 (25.6) | 14 (41.2) | |
| Gr. 2 | 28 (71.8) | 20 (58.8) | |
| Atrophy | | | |
| None | 38 (97.4) | 31 (91.2) | 0.24 |
| Gr. 1 | 1 (2.6) | 3 (8.8) | |
| Fibrosis | | | |
| None | 30 (76.9) | 26 (76.5) | 0.96 |
| Gr. 1 | 9 (23.1) | 8 (23.5) | |
| Telangiectasia | | | |
| None | 39 (100) | 33 (97.1) | 0.28 |
| Gr. 1 | - | 1 (2.9) | |

## Conclusion

The authors supported the use of hypofractionated whole breast irradiation 43.2 Gy over 16 fractions with concurrent tumor bed boost of 0.6 Gy daily in early breast cancer after breast-conserving surgery. Longer follow-up for further evaluation is needed.

## Potential conflicts of interest

None.

**Table 7.** Adverse effect (at 6-month time)

| Effect | RT technique | | p-value |
|---|---|---|---|
| | No. of patients in conventional (%) (n = 39) | No. of patients in hypofraction (%) (n = 34) | |
| Rash | | | |
| None | 37 (94.9) | 33 (97.1) | 0.64 |
| Gr. 1 | 1 (2.6) | 1 (2.9) | |
| Gr. 2 | 1 (2.6) | - | |
| Ulceration | | | |
| Gr. 1 (none) | 38 (97.4) | 34 (100) | 0.35 |
| Gr. 2 | 1 (2.6) | - | |
| Breast edema | | | |
| None | 32 (82.1) | 30 (88.2) | 0.57 |
| Gr. 1 | 6 (15.4) | 4 (11.8) | |
| Gr. 2 | 1 (2.6) | - | |
| Breast pain | | | |
| None | 34 (87.2) | 32 (94.1) | 0.32 |
| Gr. 1 | 5 (12.8) | 2 (5.9) | |
| Hyper/hypopigment | | | |
| None | 4 (10.3) | 4 (11.8) | 0.32 |
| Gr. 1 | 25 (64.1) | 26 (76.5) | |
| Gr. 2 | 10 (25.6) | 4 (11.8) | |
| Atrophy | | | |
| None | 33 (84.6) | 33 (97.1) | 0.07 |
| Gr. 1 | 6 (15.4) | 1 (2.9) | |
| Fibrosis | | | |
| None | 18 (46.2) | 15 (44.1) | 0.86 |
| Gr.1 | 21 (53.8) | 19 (55.9) | |
| Telangiectasia | | | |
| None | 39 (100) | 34 (100) | -[α] |
| Rib fracture | | | |
| None | 39 (100) | 34 (100) | -[α] |

[α]no statistical intervention

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## *การศึกษาผลข้างเคียงและความสวยงามของเต้านมภายหลังการฉายรังสีแบบเพิ่มปริมาณรังสีแต่ละครั้งแต่จำนวนน้อยลง ควบคู่กับฉายเพิ่มปริมาณที่ก้อนมะเร็งในผู้ป่วยมะเร็งเต้านมระยะเริ่มต้น*

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***วัตถุประสงค์:*** *เพื่อประเมินและเปรียบเทียบผลข้างเคียงและความสวยงามของเต้านมระหว่างการฉายรังสีแบบเพิ่มปริมาณรังสีแต่ละครั้งแต่จำนวนน้อยลงควบคู่กับการฉายเพิ่มปริมาณที่ก้อนมะเร็ง กับวิธีการฉายรังสีแบบปกติทั่วทั้งเต้านมควบคู่กับการฉายรังสีเพิ่มบริเวณก้อนมะเร็งอีก 5 วันในผู้ป่วยมะเร็งเต้านมระยะเริ่มต้น*

***วัสดุและวิธีการ:*** *ศึกษาผู้ป่วยโรคมะเร็งเต้านมระยะเริ่มต้น 73 คน ซึ่งต้องได้รับการฉายรังสีหลังจากได้รับการผ่าตัดแบบสงวนเต้านม โดยผู้ป่วยสามารถเลือกการฉายรังสีแบบปกติ คือปริมาณ 50 เกรย์ จำนวน 25 ครั้งร่วมกับการฉายเพิ่มที่ก้อนมะเร็ง 15-16 เกรย์ อีก 5-8 ครั้ง รวมเป็น 5 สัปดาห์ หรือ แบบเพิ่มปริมาณรังสีแต่ละครั้งแต่ลดจำนวนลงเป็นปริมาณ 43.2 เกรย์ จำนวน 16 ครั้งควบคู่ไปกับการฉายเพิ่มที่ก้อนมะเร็งอีก 0.6 เกรย์ในแต่ละครั้ง รวมเป็น 3 สัปดาห์*

***ผลการศึกษา:*** *เมื่อตรวจติดตาม 3 สัปดาห์พบว่าผลข้างเคียงของผิวหนังในกลุ่มฉายรังสีแบบเพิ่มปริมาณรังสีแ ต่ละครั้งแต่ลดจำนวนลงไม่ดีกว่าในกลุ่มฉายรังสีแบบปกติ ในขณะที่ผลข้างเคียงในกลุ่มฉายรังสีแบบปกติสูงกว่าอีกกลุ่มเมื่อตรวจติดตามที่ 6 สัปดาห์ และหลังจากเฝ้าติดตามเป็นเวลา 6 เดือน ไม่พบความแตกต่างของการเกิดผลข้างเคียงและความสวยงามของเต้านมในสองกลุ่ม*

***สรุป:*** *การฉายแสงแบบเพิ่มปริมาณรังสีแต่ละครั้งแต่ลดจำนวนลง 43.2 เกรย์ ใน 16 ครั้งควบคู่ไปกับการฉายเพิ่มที่ก้อนมะเร็งให้ผลดีทั้งในเรื่องผลกระทบต่อเนื้อเยื่อปกติและความสวยงามของเต้านม อย่างไรก็ตามยังต้องตรวจติดตามให้นาน เพื่อยืนยันผลการศึกษานี้*