

# Acute Effects of Postmastectomy Radiotherapy after Immediate TRAM Flap Reconstruction in Breast Cancer Patients

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**Objectives:** To study the acute effects of radiotherapy after mastectomy and immediate transverse rectus abdominis myocutaneous (TRAM) flap reconstruction in breast cancer patients treated at Ramathibodi Hospital.

**Material and Method:** Between January 2004 and March 2005, ten breast cancer patients (age 32-51 years) were treated with postoperative radiotherapy after mastectomy and immediate TRAM flap reconstruction. Medical records of these patients were retrospectively reviewed. Radiotherapy was delivered to the chest wall and reconstructed TRAM flap using 6-MV x-ray or Cobalt-60. The total dose was 45 to 50.4 Gy delivered in 25 to 28 fractions. Patients were evaluated weekly during the course of radiation and then at 1 and 2 months after treatment completion to determine acute effects or toxicities of radiation.

**Results:** During radiation, 3 patients developed erythema or mild hyperpigmentation of the skin, and 4 developed moderate hyperpigmentation. Three patients who were treated with Cobalt-60 and/or bolus to the chest wall developed skin desquamation (1 dry desquamation, 2 moist desquamation). No patient required a treatment break because of acute side effects. One patient who received chemotherapy after radiation developed recalled moist desquamation.

**Conclusion:** Radiotherapy after mastectomy and immediate TRAM flap reconstruction is well tolerated and is not associated with increased acute complication or radiation interruption. The authors have noticed that chemotherapy given after radiation was related to severe skin reaction, so it should be used with caution.

**Keywords:** TRAM flap, Reconstruction, Radiotherapy, Acute effect, Breast cancer

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Breast cancer is currently the most common female cancer in Ramathibodi Hospital<sup>(1)</sup>. A number of patients were treated with modified radical mastectomy (MRM) because they were not suitable for breast conservation. Breast reconstruction has become an integral part of the surgical treatment for women who underwent mastectomy. There are two major techniques

of breast reconstruction, including an autologous tissue reconstruction and the placement of a prosthetic expander or implant<sup>(2,3)</sup>. The techniques of autologous tissue reconstruction include transverse rectus abdominis myocutaneous flap (TRAM flap), latissimus dorsi myocutaneous flap, and rarely gluteal flap, and lateral transverse thigh flap, while TRAM flap is most commonly performed since it provides the best cosmesis and lowest complication<sup>(2,4)</sup>. Randomized trials have shown that adjuvant radiation after mastectomy can reduce locoregional recurrence and improve survival in women with high-risk breast cancer<sup>(5,6)</sup>. These find-

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ings result in an increasing number of patients being referred for postoperative radiation. While an immediate reconstruction with TRAM flap has become a popular choice for women undergoing MRM since it can be done in a single surgical procedure, there is very little information regarding acute and late effects of radiation on the reconstructed tissues. Additionally, controversies exist over both the type and timing of reconstruction that is most suitable in this setting. The present study was to evaluate the acute effects of radiotherapy after mastectomy and immediate TRAM flap reconstruction in breast cancer patients treated at Ramathibodi Hospital.

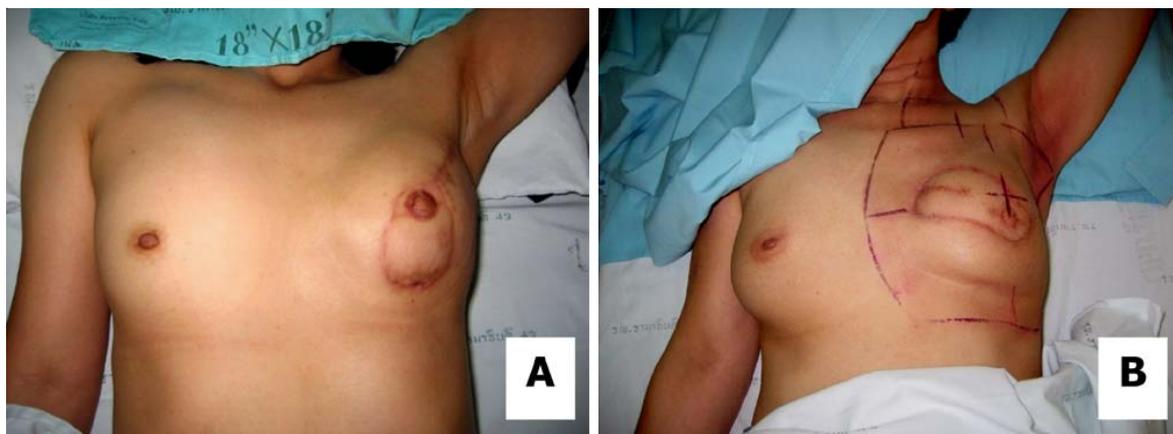
### Material and Method

Between January 2004 and March 2005, ten women with breast cancer (all had invasive ductal carcinoma) who underwent MRM and immediate pedicled TRAM flap reconstruction at Ramathibodi Hospital received adjuvant radiation to the chest wall and supraclavicular fossa after their reconstruction. The medical and radiotherapy records of these patients were retrospectively reviewed. Information regarding patient and disease characteristics, treatment approach, indications for adjuvant radiation, and radiation techniques were recorded and shown in Table 1. Patients' age ranged from 32 to 51 years (median 46 years). One patient had hypertension as a comorbid disease. All patients received adjuvant chemotherapy before starting radiation treatment. Intervals between surgical reconstruction and initiation of radiation ranged from 4 to 7 months (median 5 months). Radiotherapy was delivered by 6-MV x-ray from a linear accelerator in 8 patients, and by

Cobalt-60 teletherapy machine in 2 patients. Tangential fields with 30-degree wedges were used to treat the chest wall and reconstructed TRAM flap (Fig.1). During a part of radiation (3-25 fractions), a bolus material was applied onto the chest wall in 6 patients. Total radiation doses were 50 Gy in 6 patients, 50.4 Gy in 3 patients, and 45 Gy in one patient, delivered in 25-28 conventional fractions. No additional boost was given. Tamoxifen was given during radiation in 2 patients. Three patients received tamoxifen, and one patient received chemotherapy (docetaxel) after radiation completion. Patients were evaluated on a weekly basis during the course of radiation treatment and then were followed-up at 1 and 2 months after radiation completion to determine acute effects or toxicities of radiotherapy. The authors specifically looked at the degree of skin reaction and the need for treatment break.

### Results

During the course of radiation, skin reaction gradually occurred after 2 to 3 weeks of treatment initiation. No patient experienced adverse event to other organs and none required a break in the course of radiotherapy because of acute side effects. At the end of radiation treatment, only toxicities to the skin were found, including erythema in one patient, erythema to mild hyperpigmentation in 2, moderate hyperpigmentation in 4, dry desquamation in 1, and moist desquamation in 2 patients (Table 2). Dry desquamation was treated with skin moisturizer and topical steroid cream to relieve irritating symptoms. Moist desquamation was managed by daily dressing with normal saline solution, topical antiseptic, and silver sulfadiazine



**Fig. 1** A) A patient with immediate pedicled TRAM flap reconstruction before radiation therapy  
B) A different patient during radiation therapy using tangential fields covering the chest wall and TRAM flap

**Table 1.** Patient characteristics, systemic treatment, and indications for adjuvant radiation

Pt #	Age	Stage	Adj. CT	TAM	Indications for RT
1.	43	IIB	6FAC	No	Closed margin
2.	45	IIB	4EC	After RT	AN+, extracapsular extension
3.	51	IIA	4EC, 4Docetaxel	No	AN+
4.	48	I	4EC	During RT	Closed margin
5.	46	IIB*	3CEF	After RT	AN+, ALI
6.	45	IIB*	4Docetaxel	No	Initial T3, ALI
7.	32	IIB*	2CEF	During RT	Initial T3
8.	47	IIB	6FAC	No	AN+
9.	49	IIA	6CMF	No	Closed margin
10.	51	IIB	6FAC	After RT	T 5 cm, multifocal, ALI, AN+

American Joint Committee on Cancer (AJCC) staging system 2002

\* Clinical staging before receiving neoadjuvant chemotherapy

Pt # = patient number; Adj. CT = adjuvant chemotherapy; TAM = tamoxifen; RT = radiotherapy; C = Cyclophosphamide; E = Epirubicin; F = 5-fluorouracil; A = Adriamycin; M = Methotrexate; AN = axillary lymph node; ALI = angio-lymphatic invasion; T = primary tumor

**Table 2.** Acute skin reaction of each patient according to treatment

Pt #	Machine	Dose (Gy)	Separation (cm)	Bolus	Acute reaction	Grading*
1.	Co-60	45	20.30	1cm/25F	Moist desquamation	3
2.	6 MV	50	14.90	0.5cm/15F	Hyperpigment	1
3.	Co-60	50	18.80	No	Dry desquamation	2
4.	6 MV	50	18.00	1cm/5F	Erythema-hyperpigment	1
5.	6 MV	50	18.70	No	Hyperpigment	1
6.	6 MV	50.4	19.40	No	Erythema	1
7.	6 MV	50	20.40	No	Hyperpigment	1
8.	6 MV	50.4	17.80	1cm/11F	Hyperpigment	1
9.	6 MV	50.4	19.40	1cm/11F	Moist desquamation	3
10.	6 MV	50	19.20	1cm/3F	Erythema-hyperpigment	1

\* Grading of severity for acute skin reaction: 1= mild degree or minimal symptoms, 2= mild to moderate, 3= moderate to severe, 4= severe, life-threatening

Pt # = patient number; Gy = Gray; MV = megavolt; Co-60 = Cobalt-60; F = fraction

cream. Skin reactions resolved gradually after treatment completion. Moist desquamation was completely healed within 2 weeks. One patient (patient #2) received chemotherapy at one month after finishing radiation treatment. Initially, she had only hyperpigmentation of the skin, which was already resolved after radiation completion. She then developed severe recalled skin reaction, including moist desquamation and inflammation, in an irradiated area after receiving chemotherapy.

## Discussion

In spite of a widespread use of breast-conserving therapy for early breast cancer, a large propor-

tion of patients still undergo mastectomy and an increasing number of them will opt for breast reconstruction. As a result of studies demonstrating survival advantages of postmastectomy irradiation<sup>(5,6)</sup>, many patients undergoing mastectomy and breast reconstruction are being referred for radiotherapy. In these patients, there are many concerns regarding the reconstructed techniques, timing of reconstruction (immediate vs delay), effects of breast reconstruction on radiation dose distribution, effects of radiation on reconstructed tissues, and long-term outcomes, including local control, and cosmesis. The potential negative impact of breast reconstruction on the efficacy of

postmastectomy radiotherapy has never been directly addressed<sup>(7)</sup>. As some reconstruction techniques significantly distort the chest wall anatomy, radiotherapy portals need to be modified adequately. Additionally, a non-uniform thickness of the chest wall across the radiation fields may also cause significant dose inhomogeneities. These can make treatment more difficult and may increase normal tissue toxicities<sup>(7,8)</sup>. Radiation complications can be divided into acute and late (chronic) complications. The physiology of acute complication is inflammation and loss of rapidly dividing cells. In curative radiotherapy for breast cancer, when given as a sole treatment, the authors have found that most of the patients experienced acute toxicities only to the skin, which can range from erythema and hyperpigmentation (mild degree) to more severe dry and moist desquamation. The study from Hanks et al demonstrated that radiation after TRAM flap reconstruction was well tolerated and was not associated with increased acute side effects. Twenty percent of patients (5/25) developed dry desquamation and another 20 percent developed moist desquamation. The occurrence of acute toxicity could not be predicted based on any treatment-related factors. However, 60% of the patients who had bolus as a part of treatment developed moist desquamation. The authors recommended that using bolus should be avoided unless there is a specific indication requiring its use<sup>(9)</sup>. A review of radiotherapy for breast cancer in patients undergoing breast reconstruction from Senkus-Konefka et al found no obvious difference in type and intensity of acute radiation reaction after breast reconstruction compared to the intact breast<sup>(8)</sup>. Several other studies have evaluated effects of radiotherapy on autologous tissue reconstruction<sup>(10-19)</sup>. Most of them reported that radiotherapy following immediate TRAM flap reconstruction was well tolerated with manageable acute toxicity. Long-term complication rates and cosmetic outcome were also acceptable. Most importantly, breast reconstruction does not seem to affect locoregional control or survival. Autologous reconstruction is considered the procedure of choice rather than a prosthetic implant in patients undergoing radiotherapy, and TRAM flap technique generally gives the best results<sup>(8)</sup>. In the present series, the majority of patients experienced only mild to moderate skin reaction, only 3 patients developed skin desquamation. Two of them were treated with Co-60 and bolus (Table 2). Skin reaction was worst in patient number 1 who was treated with Co-60 and 1-cm bolus for the whole course of radiation. However, all of them recovered after a few weeks of conservative treatment.

Anderson et al reported low complication rates of radiotherapy following breast reconstruction and custom wax bolus could be used safely<sup>(10)</sup>. The present study has shown that adjuvant chemotherapy given before radiation and tamoxifen were not associated with increased acute skin complication but in one of presented patients, chemotherapy given after radiation resulted in severe recalled skin reaction and detrimental cosmetic outcome. Ways for improvement include the use of computed tomography-based treatment planning, custom wax bolus/tissue compensator, or intensity-modulated radiotherapy to increase dose homogeneity and reduce normal tissue complication.

### Conclusion

Radiotherapy after mastectomy and immediate TRAM flap reconstruction is well tolerated and is not associated with increased acute complication or radiation interruption. However, the authors have noticed that chemotherapy given after radiation was related to severe skin reaction, so it should be used with caution. Further follow-up is needed to determine late complication, cosmesis, and tumor control.

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**ผลข้างเคียงระยะเฉียบพลันของการฉายรังสีในผู้ป่วยมะเร็งเต้านมภายหลังการทำผ่าตัด modified radical mastectomy และ immediate TRAM flap reconstruction**

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**วัตถุประสงค์:** เพื่อศึกษาผลข้างเคียงระยะเฉียบพลันของการฉายรังสีในผู้ป่วยมะเร็งเต้านมภายหลังการทำผ่าตัด modified radical mastectomy และ immediate transverse rectus abdominis myocutaneous (TRAM) flap reconstruction ณ โรงพยาบาลรามาริบัติ

**วัสดุและวิธีการ:** ทำการศึกษาข้อมูลย้อนหลังของผู้ป่วยมะเร็งเต้านม 10 ราย (อายุ 32-51 ปี) ที่ได้รับการรักษาโดยการผ่าตัด modified radical mastectomy และ immediate TRAM flap reconstruction ตั้งแต่ มกราคม พ.ศ. 2547 ถึง มีนาคม พ.ศ. 2548 การฉายรังสีครอบคลุมบริเวณหน้าอกและ TRAM flap โดยใช้ เอกซเรย์ พลังงาน 6 เมกะโวลต์จากเครื่องเร่งอนุภาค หรือ เครื่องฉายรังสีโคบอลต์ 60 ปริมาณรังสีที่ใช้อยู่ในช่วง 45-50.4 Gy ให้ใน 25-28 ครั้ง ผู้ป่วยได้รับการตรวจเพื่อประเมินผลข้างเคียงระยะเฉียบพลันทุกสัปดาห์ระหว่างการฉายรังสีและเดือนที่ 1 และ 2 หลังฉายรังสีครบแล้ว

**ผลการศึกษา:** ผลข้างเคียงระยะเฉียบพลันที่พบระหว่างฉายรังสีคือการเปลี่ยนแปลงของผิวหนังบริเวณที่ได้รับรังสีตั้งนี้ การเกิด erythema หรือผิวหนังมีสีคล้ำขึ้นเล็กน้อยในผู้ป่วย 3 ราย ผิวหนังมีสีคล้ำขึ้นปานกลางในผู้ป่วย 4 ราย ผู้ป่วย 3 รายที่ได้รับการฉายรังสีด้วยเครื่องฉายรังสีโคบอลต์ 60 และ/หรือการใช้ bolus ที่หน้าอก เกิด desquamation ของผิวหนังคือ dry desquamation 1 รายและ moist desquamation 2 ราย ไม่มีผู้ป่วยรายใดต้องหยุดฉายรังสีเนื่องจากผลข้างเคียงดังกล่าว ผู้ป่วย 1 ราย ซึ่งจบการฉายรังสีแล้ว เกิด moist desquamation ของผิวหนังหลังจากได้รับยาเคมีบำบัด

**สรุป:** จากการศึกษา ไม่พบผลข้างเคียงระยะเฉียบพลันที่เพิ่มขึ้นจากการฉายรังสีในผู้ป่วยมะเร็งเต้านมที่ได้รับการทำ TRAM flap reconstruction อย่างไรก็ตามพบว่าการให้ยาเคมีบำบัดภายหลังการฉายรังสี อาจทำให้เกิดผลข้างเคียงต่อผิวหนังที่รุนแรงกลับซ้ำใหม่ได้ จึงควรใช้ด้วยความระมัดระวัง

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