Tolerance of skin grafts to postoperative radiotherapy

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Abstract

Aim: The aim was to evaluate the integrity and functional outcomes of skin grafts following external beam radiotherapy (EBRT).

Materials and Methods: A prospective study of 15 patients, in whom EBRT was planned after their wound coverage with split-thickness skin graft (STSG). Parameters evaluated include defect size, time to postoperative radiotherapy, total radiotherapy dose, delays and interruptions in radiotherapy, wound complications, and the need for further surgical interventions.

Results: In all the 15 (6 men, 9 women) patients of STSG, radical doses of EBRT, that is, 50–70 Gy in 25–35 fractions are delivered over around 6 weeks. All STSGs were placed on healthy vascular tissue beds. Median time to initial radiotherapy after grafting was 3 weeks (range 3–6 weeks). There were no interruptions in radiotherapy treatment. In one patient, there was partial skin graft loss after radiotherapy that was adequately managed with conservative treatment. No patient requires further surgical intervention.

Conclusion: Adjuvant postoperative radiotherapy can be delivered to STSGs without significant complications. Postoperative radiotherapy can be started as early as 3–4 weeks after skin grafting. Skin grafts should be placed on well-vascularized healthy tissues. Minor skin graft loss resulting from postoperative radiotherapy can usually be treated conservatively.

Key words: External beam radiotherapy, split-thickness skin grafts, tolerance of skin graft

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Introduction

The treatment of malignant tumors requires a multimodality approach for complete eradication. This may include surgery, radiotherapy and chemotherapy. The surgical treatment of skin and soft-tissue malignancies frequently consist of wide local excision that preclude primary closure. This can present a challenge to the reconstructive surgeons when dealing with wounds that cannot be closed primarily, and also have to undergo postoperative radiotherapy. When a suitable bed is present, wound closure by skin grafting is reasonable and simple. Many surgeons and radiotherapists believe that skin grafts may not tolerate radiotherapy as well as normal skin as some of these skin grafts after radiotherapy undergo necrosis, resulting in chronic open wounds prone to infections. The objective of this study was to evaluate the integrity and functional outcome of patients whose skin grafts are subsequently irradiated.

Materials and Methods

A total of 15 patients were included in the study. In 11 cases, the wound coverage was done at the time of tumor excision. Four cases were referred for wound coverage following radical tumor excision either due to margin necrosis or wound infection. In these cases, optimal wound bed preparation was done and then skin grafts were applied secondarily. In one of the patients undergoing secondary coverage, negative pressure wound therapy was applied for the preparation of optimal wound bed before coverage. Tables 1 and 2 show tumor site and pathological diagnosis, respectively.

Radiotherapy was initiated on the patients after complete epithelial closure. The patients received radiotherapy with cobalt-60 teletherapy machine (gamma rays). Radiotherapy was delivered by three fields that is, one supraclavicular and anterior axillary field for treatment of draining lymph nodes and two tangential fields for treatment of chest wall with radical doses of 50–70 Gy in 25–35 fractions over a
period of 6 weeks. Patients were evaluated every week for any loss of skin graft or sign of local skin infection. Weekly blood tests were done during radiotherapy treatment. After completion of radiotherapy, weekly follow-up till 6 weeks was done.

In the study, various parameters noted included defect size, time to start external beam radiotherapy (EBRT), total dose, treatment delays, and interruptions during radiotherapy, wound complications in radiated areas, and need for additional surgery.

**Results**

Of 15 patients, 6 were men and 9 were women. The mean age was 52 years (range 32–77 years). The smallest grafted area was 5 cm², and largest was 360 cm². Eleven patients underwent radical excision of the tumor and primary wound coverage with split-thickness skin grafting (STSG). In four patients, wound coverage was done as a secondary procedure.

The median time to start of radiotherapy after skin grafting was 3 weeks (range 3–6 weeks). The mean dose of radiotherapy was 6000 ± 600 cGy. In the entire series, there was no graft breakdown during or at the completion of radiotherapy except in 1 (6.7%) patient. In this patient, wound healed with conservative management. No interruption in radiotherapy was required due to any local reasons. There were no interruptions with radiotherapy.

**Discussion**

Skin grafting is a simple method to resurface epithelial defects following wide local excision of malignancies. In cases where postoperative radiotherapy is required, many surgeons follow conventional belief of covering the wounds with flaps even when the area to be covered is otherwise suitable for skin grafting. Apprehensions of skin graft ulceration after postoperative radiation therapy for cancer have led many to question the suitability of this method of wound coverage.

Sumi et al.[1] studied the reaction of rat skin graft exposed to a single dose of 1000 or 1500 rads given at varying interval after skin grafting. They noted skin grafts irradiated in the early

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Table 1: Tumor site

| Tumor Site          | Number of cases (%) |
|---------------------|---------------------|
| Buccal mucosa       | 1 (6.7)             |
| Face                | 2 (13.3)            |
| Breast              | 6 (40)              |
| Upper limb          | 1 (6.7)             |
| Lower limb          | 3 (20)              |
| Back                | 2 (13.3)            |

Table 2: Pathological diagnosis

| Diagnosis                  | Number of cases (%) |
|----------------------------|---------------------|
| SCC                        | 4 (26.7)            |
| Invasive duct cell carcinoma | 5 (33.3)           |
| Cystosarcoma phyllodes     | 1 (6.7)             |
| Malignant fibrous hystiocytoma | 2 (13.3)         |
| Sarcoma                    | 2 (13.3)            |
| Malignant melanoma         | 1 (6.7)             |

SCC: Squamous cell carcinoma

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Figure 1: (a) Photograph of a patient with recurrent cystosarcoma phyllodes after tumor resection (b) Well-healed split-thickness skin graft 3 weeks postoperatively, at the time of initiation of radiotherapy (c) Split-thickness skin graft after 6 weeks of radiotherapy

Figure 2: (a) Photograph of a patient with squamous cell carcinoma of left foot after tumor ablation (b) Well-healed split-thickness skin graft 3 weeks postoperative at the initiation of Radiotherapy (c) Split-thickness skin graft after 6 weeks of radiotherapy
hypovascular stage (2 days) showed mild to moderate reaction, whereas those irradiated in hypervascular stage (2 days to 3 weeks) showed severe vascular reactions. Those irradiated in late hypovascular stage (3–4 weeks) reacted similar to normal skin. They suggested postoperative radiation could be started 3–4 weeks after grafting. In a similar study, Kulahci et al.[2] observed the effect of external beam irradiation timing on skin graft survival on rats. After full thickness skin graft 25 Gy unfractionated cobalt-60 irradiation was used on groups of rats on postoperative days 10, 20, 30, and 40, respectively. They stated that EBRT could be performed to skin graft areas as early as 10 days postoperatively.

There have been few clinical reports evaluating the effects of irradiation on skin grafts. Lawrence et al.[3] reported a series of 11 soft tissue sarcoma patients with skin grafts that received postoperative adjuvant radiotherapy, 4 of whom also received concurrent chemotherapy. Radiation therapy (5000–7000 rads over 5–6 weeks) was initiated from 3 to 20 weeks postoperatively. 10 of 12 irradiated skin grafts were intact after completion of radiotherapy. Bui et al.[4] in a retrospective study, reported 30 patients who underwent radiotherapy after skin graft. 27 patients had an intact skin graft after EBRT and only 1 required repeat skin grafting. They stated that radiation can begin as early as 6–8 weeks after grafting.

Sumi et al.[5] reported 7 patients who had received skin graft and postoperative radiotherapy (5000–5400 rads over 4 weeks) beginning from 3 to 27 weeks after grafting. All grafts were intact after radiation except for 1 that had partial necrosis. A study of 15 patients by Cram et al.[6] who underwent radiotherapy using cobalt-60 (4000–4400 rads over 3 weeks) beginning around 2 weeks after radical mastectomies and wound coverage with STSG. There was no necrosis after treatment. All the patients heal their wound, and there was no modification or interruption of radiotherapy. Rubin and Grise[7] studied effect of radiation on skin graft in a series of 7 patients. Six of seven grafts healed.

In our study, 14 of 15 patients had an intact skin graft after radiotherapy while 1 patient had partial graft loss after radiation, which eventually healed with conservative management. Thus, it shows that split-thickness grafts can tolerate postoperative radiotherapy without significant complications if the graft is allowed to heal adequately before initiating radiotherapy.

It is important to know about the optimal time for giving postoperative radiotherapy after skin graft surgery. There have been several experimental studies showing that skin graft radiation injury is related to the blood supply of skin graft during healing.[2,8] It was suggested by Sumi et al.[5] and Takahashi[9] that newly generated vessels showed high reactivity to irradiation, whereas old vessels in the grafts 3–6 weeks after grafting exhibited little reaction to irradiation. In the course of graft healing, invasion of newly generated vessels into the graft is indispensable for graft survival.[10,11]

In our series, the median time to initiate the radiation was 3 weeks after grafting when the graft had completely healed.

**Conclusion**

Patients with epithelial defects requiring subsequent radiotherapy can be surgically managed with STSG without expecting significant complications after irradiation. Radiotherapy application in these patients can safely be instituted after 3 weeks.

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