Published online: 2019-11-27

Review Article

Management of radiation wounds

Subramania Iyer[1,2], Deepak Balasubramanian[2]

[1]Department of Plastic and Reconstructive Surgery, [2]Head and Neck Surgery, Amrita Institute of Medical Sciences, Kochi, Kerala, India

Address for correspondence: Dr. Subramania Iyer, Department of Plastic - Reconstructive Surgery & Head- Neck Surgery, Amrita Institute of Medical Sciences, Kochi, Kerala, India. E-mail: subu@aims.amrita.edu

ABSTRACT

Radiotherapy forms an integral part in cancer treatment today. It is used alone or in combination with surgery and chemotherapy. Although radiotherapy is useful to effect tumour death, it also exerts a deleterious effect on surrounding normal tissues. These effects are either acute or can manifest months or years after the treatment. The chronic wounds are a result of impaired wound healing. This impairment results in fibrosis, nonhealing ulcers, lymphoedema and radionecrosis amongst others. This article will discuss the pathophysiology in brief, along with the manifestations of radiation-induced injury and the treatment available currently

KEY WORDS

Lymphoedema; osteoradionecrosis; plexopathy; radiotherapy; wounds

INTRODUCTION

Modern management of cancer involves using multiple modalities for treatment. One of the integral components of this treatment is the use of ionising radiation to effect tumour death. Such ionising radiation though required for tumour death, also causes damage to the surrounding normal tissue.[1,2] The deleterious effect of radiation on normal tissues is overcome to a great extent by the refinement of planning of radiation treatment and the use of focussed methods of radiation delivery like intensity-modulated radiation therapy (IMRT).[3] In spite of these technical advances, there is still damage to the surrounding normal tissues which is often manifested by delayed healing, chronic ulcers and bone necrosis. An understanding of the effects of radiation on the tissue is important to the surgeon as surgical management may become necessary for the removal of persistent or recurrent tumours in a radiated bed or for curing the complications of radiation like radiation-induced fistulas, strictures or necrosis of bone skin or cartilage. This article focusses on the pathophysiology of radiation-induced damage, the impact of radiation on tissue healing and the treatment for radiation-induced chronic wounds. The acute cutaneous and mucosal toxicity due to radiation therapy is usually managed by the radiation oncologist and does not come in the purview of this article.

Access this article online	
Quick Response Code:	Website: www.ijps.org
	DOI: 10.4103/0970-0358.101311

EFFECTS OF RADIATION ON NORMAL TISSUES AND IMPACT ON WOUND HEALING

Radiation therapy involves the use of ionising radiation given as daily fractions over a period of weeks to effect tumour death. The dose delivered is given to a field which includes the primary tumour and the surrounding nodal stations. So, an area of the adjacent tissues not directly involved by the tumour is also irradiated. This

effect of radiation causes two types of injuries to normal tissues, namely acute and chronic injuries. The acute effects are usually manifested in tissues which are rapidly proliferating such as mucosa and epithelium and this leads to painful ulcers, mucositis and desquamation.[4,5] These however resolve with supportive care. The chronic problems can manifest even years after treatment. Both these changes, that is, the acute and chronic have a significant impact on healing of wounds in these areas.

Normal wound healing occurs in three stages, namely, an inflammatory phase, a proliferative phase and a maturation phase.[6] The key components in wound healing include fibroblasts, collagen synthesis and chemotactic factors like the transforming growth factor (TGF) beta, platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF) beta. These cytokines are produced by the platelets and macrophages which enter the wound bed in the inflammatory phase of wound healing. In this context, radiation causes oedema of the vessel walls, stasis and occlusion of the vessels, thereby preventing the influx of platelets.[7] There is reduced angiogenesis and increased expression of matrix metalloproteinases. Due to the reduction of the cytokines, there is a reduced recruitment of fibroblasts in the wound bed. Radiation also causes direct damage to the fibroblasts and this in turn causes loss of tensile strength of the wound due to the reduced production of collagen and altered function of collagen. Recent findings attribute the pathophysiology of the radiation-induced fibrosis to reactive oxygen species which leads to the dysregulated production of abnormal myofibroblasts.[8] The tissues have an abnormal production of collagen and are paucicellular. There is a loss of normal tissue architecture with diminished healing capacity. Trauma to this compromised tissue results in poor healing because of the absence of blood vessels and inflammatory cells.

COMMON CLINICAL PROBLEMS RELATED TO WOUND HEALING IN THE PRESENCE OF RADIATION-INDUCED CHANGES

Operating in a freshly radiated area

Wounding of the irradiated area becomes a surgical necessity either for curing residual or recurrent cancers or for treating the radiation-induced complications. Inflammation is a major component of acute radiation injury to the skin and subcutaneous tissue. Wounding in the inflamed tissue laden with tissue oedema leads to unfavourable results in the healing. But the surgeon is forced to operate in this area for residual tumours immediately after radiotherapy or chemoradiotherapy. These tumours are sometimes the result of poor response of the tumour to a well-planned treatment protocol or due to its inappropriate use in advanced cases. In some instances, the surgical arm would have been an integral part of the treatment protocol especially in the cases of large lymph nodes where a neck dissection has been planned after the completion of radiation. Surgical procedures performed on previously irradiated tissue are associated with an increased morbidity in terms of delayed wound healing and breakdowns.[9-11] The timing of these procedures has been ideally kept as four to six weeks after the completion of radiation and before the lapse of 8–10 weeks. The former is to prevent the ill effects of intense inflammation and inflammatory mediators on tissue healing and to allow the wound to achieve tensile strength. Unnecessary delay in surgery beyond eight weeks is also detrimental to healing as the early process of fibrosis sets in after this period. In certain instances, planned surgery in a radiated area is better performed after a lapse of a six-month period to help the tissues overcome the detrimental effects to wound healing. This applies to clinical situations like reconstruction of the breast after mastectomy where postoperative radiation has been used[12] and creating a secondary tracheoesophageal fistula after laryngectomy.[13]

Management of acute healing complications

Wound breakdown as well as pharyngocutaneous fistula are not so uncommon complications occurring after surgery for cancers of the oral cavity or pharynx previously treated with radiation.[14] The wounds look quite clean during the first week, but breakdown occurs in the second week due to the inflammatory reaction at the edges and also secondary infections. The optimum time for intervention is unclear but is dependent on the clinical situation. Most of the fistulas are given a trial of conservative management.[15] Ideally, repair of the wounds or fistulae should be delayed till 12–18 weeks when the catabolic phase is over and use of vascularised tissue for cover should be considered. Exceptions to this would be exposure of the great vessels and their impending rupture where early use of vascular tissue cover should be considered. Both free and pedicled flaps are a good option to repair these defects.[16]

CHRONIC MANIFESTATIONS OF RADIATION-INDUCED INJURY

- Radiation-induced fibrosis of the skin
- Nonhealing ulcers
- Osteoradionecrosis
- Lymphoedema
- Plexopathy

Radiation-induced fibrosis

Radiation-induced fibrosis is a chronic progressive change seen in irradiated skin and subcutaneous tissue. The presence of reactive oxygen species leads to the dysregulated production of abnormal myofibroblasts. The tissues have an abnormal production of collagen and are paucicellular.[8] Trauma to this compromised tissue results in poor healing because of the absence of blood vessels and inflammatory cells. Clinically, the patients manifest with thickened fibrotic skin in the irradiated site and restriction of movement. Recent studies have shown partial reversibility of the fibrosis with the use of pentoxyphilline, which is a methyl xanthine derivative, and alpha tocopherol. The combination of these two drugs given for a long duration has been shown to cause regression of the fibrotic areas.[17]

The sequelae of the fibrosis can lead to severe functional problems to patients especially those treated with radiation or chemoradiation for head and neck cancers. There is intense fibrosis in the soft tissues of the neck and stricture formation in the pharynx leading to dysphagia.[18] This may necessitate reconstruction of the alimentary tract using a tubed pectoralis major or free flaps like radial forearm or anterolateral thigh (ALT) flaps [Figure 1]. Along with it, due to the poor quality of the skin and subcutaneous tissues in the neck, provision for skin cover also may be necessary which may be achieved by using a split-thickness skin graft or additional skin flap. Also, the fibrosis in the subcutaneous tissues may lead to a decrease in range of movements in the neck. The appearance of the neck becomes progressively unsightly.

Nonhealing ulcers/soft tissue necrosis

Nonhealing ulcers could be a problem in the irradiated area in the trunk and breast after therapeutic radiation of these areas [Figures 2-5]. Initial conservative measures include the use of hyperbaric oxygen (HBO) therapy and of pentoxyphylline.[19] But majority of these cases may fail to heal and will require radical debridement and cover with a vascular tissue. Great difficulty may be encountered in

Figure 1: A 40-year-old female patient post laryngectomy who received postoperative chemoradiation. There is intense fibrosis of the neck and remnant pharynx resulting in a stricture. The patient is being prepared for correction of the fibrosis and stricture with a tubed anterolateral thigh flap

Figure 2: Nonhealing chest wound in a patient who had a mastectomy followed by radiotherapy

Figure 3: A latissimus dorsi free flap was used to cover the defect, but the healing was impaired because of the postradiotherapy status

Figure 4: The wound was debrided and a pectoralis major muscle flap from the opposite chest was used to cover the deficient area

Figure 5: A split skin graft was placed over the pectoralis major muscle

Figure 6: Osteoradionecrosis in a 50-year-old male patient

cases of radical excision in the areas where great vessels are in proximity like the femoral vessels in an irradiated area of the inguinal region. But they are seldom seen in current practice due to the advancements in planning and delivery of radiation.

Osteoradionecrosis/chondronecrosis

Osteoradiaonecrosis (ORN) affects the irradiated facial bones especially the mandible [Figure 6]. Its incidence has been reported to be between 2 and 22%.[20] There are various factors which predispose for the development of ORN, namely, dentoalveolar infections, general nutritional states and abuse of tobacco and alcohol. The timing of development of ORN can vary. It could manifest early within the first year following radiotherapy but the risk of developing ORN exists lifelong. The usual manifestation of ORN includes pain, exposed bone, fistulae and pathological fracture. Care should be taken to rule out malignancy before a diagnosis of ORN can be made as there is a likelihood of recurrence of the tumour in the mandible or adjacent structures. Dental infections and dental extractions in previously irradiated patients can predispose to the development of ORN. Dental extractions prior to radiotherapy[21,22] can minimise the incidence of the development of ORN. For patients requiring dental extractions after radiotherapy, prophylactic pentoxyphilline (400 mg twice daily) and vitamin E (1000 IU once daily) are given one week before the planned extraction and continued for eight weeks. Alternatively, HBO (20 dives before and 10 dives after extraction; each dive is 2.4 atmospheres absolute for 90 minutes) can be tried.[8]

There are also no clear guidelines with regard to the management of ORN. Early ORN which is manifested by pain and exposed bone can be treated with pentoxyphilline and vitamin E for up to six months.[23] The role of HBO therapy has been controversial in established ORN. If there is sequestrum present, gentle saline irrigation or sequestrectomy can be done under the cover of the above drugs. However for established ORN, radical surgical management may be necessary and the key to successful treatment in these is radical excision followed by covering the wound with vascularised tissue preferably containing muscle.[24,25] This not only provides relief from the pain and fistula, but the vascular tissue will also provide the metabolic factors for wound healing.

Chondronecrosis is much rarer compared to ORN. It usually affects the laryngeal cartilaginous framework following irradiation to the neck for laryngeal or hypopharyngeal tumours. It presents as painful discharging wounds as well as tenderness over the cartilages.[26] With the current

radiation techniques, this is seldom seen. Ruling out a recurrence becomes extremely difficult in these cases, but suspicion of a recurrent cancer should always be kept in mind. However, this dilemma does not influence the treatment much, as a total laryngectomy with or without reconstruction of the alimentary tract is necessary in both the situations. Another unusual situation for chondronecrosis is after heavy irradiation for breast or chest wall tumours. The treatment may necessitate removal of the affected ribs and reconstruction of the chest wall.[27]

Radiation-induced plexopathy

This condition is particularly seen in patients who have been treated with chest radiation for breast carcinoma.[28,29] Progressive fibrosis of the brachial plexus roots develops and the risk for development of this plexopathy is lifelong.[30] It has been reported to be more common when hypofractionated radiotherapy is given especially in doses of excess of 2.5 Gy per fraction.[31] It is a difficult problem to treat and no consensus exists for the management of plexopathy. HBO[32] and the pentoxyphilline-tocopherol-clodronate combination[33] have been tried to treat plexopathy. There are no large-scale studies available detailing surgical management of this plexopathy; isolated reports exist about the use of nerve transfers.[34,35]

Radiation-induced lymphoedema

Lymphatic dysfunction is common after radiotherapy. The proposed mechanism is the loss of capillary lymphatics and increase in apoptosis of lymphatic endothelial cells.[36] TGF beta 1 is the common chemical modulator which interferes with the lymphatic regeneration. It is proposed that blocking of TGF beta 1 would promote lymphatic regeneration.[37,38] Selenium supplementation has been tried to reduce lymphoedema.[39] But systematic reviews have failed to find any benefit from taking selenium.[40] HBO has been tried with mixed results.[41,42] The lymphoedema may affect the head and neck or the extremities. Postradiation lymphoedema of the head and neck may present as acute respiratory distress due to the laryngeal component of the oedema. Immediate measures include intensive systemic steroids, but if they fail, tracheostomy, often of a permanent nature, may become necessary.

USE OF FREE TISSUE TRANSFER IN IRRADIATED AREAS

Microvascular free tissue transfer has been extensively used in the reconstruction of the irradiated areas with good rates of success. Several studies have failed to report any difference in outcomes between patients who have been irradiated and those who have not received radiation,[43-45] barring a recent prospective study published which reported that there was an increased rate of wound infection and flap failure in patients who have had prior radiotherapy.[46] The main difficulty in using free flaps in heavily irradiated areas is to find the recipient vessels in a densely fibrotic background. Various techniques have been described.[47,48] The success may depend on using flaps with long pedicles and using recipient vessels away from the field, for example, transverse cervical vessels in the neck, using end-to-side anastamosis to the main blood vessels or using vein grafts. In head and neck reconstruction, the use of the opposite side of the neck is often an easier alternative to use for the ipsilateral vessels. Care should be taken to avoid tension over the skin closure on these sites. This should be taken into account while planning the flaps by providing some muscle at the neck to be covered with skin grafts or by designing the cutaneous portion of the flaps to cover the neck also. The effect of radiation on wound healing has implications in the timing of the surgery. The timing of reconstructive surgery after recent radiation is unclear. A recent study published suggests that the optimal time to perform reconstructive free flap surgery is within six weeks of prior radiotherapy so as to perform surgery before fibrosis sets in.[49]

ROLE OF PROPHYLACTIC MUSCLE FLAPS

The incidence of wound breakdown leading to pharyngocutaneous fistulae has been considerably increased in salvage surgery following organ-preserving protocols for laryngeal and laryngo-pharyngeal cancers using chemoradiation.[14] Using the pectoralis major muscle routinely to reinforce the pharyngeal suture site as a prophylactic measure has been suggested to reduce the fistula rate.[50] Even when there is sufficient mucosa available to close the pharynx primarily, the additional use of free tissue for pharyngeal closure reduces the rate of complication.[51]

CONCLUSION

With all the recent advances in techniques of radiation delivery, an attempt is being made to reduce the incidence of complications of radiation. However, significant problems exist with the treatment of the skin, soft tissue

and bony complications. Nonsurgical modalities have shown promise in retarding progressive fibrosis that affects patients who have undergone radiation. Their role, however, is limited to established disease. Chronic wounds with exposed devitalised bone and fistulae need surgical intervention and vascularised flap reconstruction for closure. Further studies are required to identify adjunctive treatments for treatment of radiation wounds.

REFERENCES

1. Dormand EL, Banwell PE, Goodacre TE. Radiotherapy and wound healing. Int Wound J 2005;2:112-27.
2. Gieringer M, Gosepath J, Naim R. Radiotherapy and wound healing: Principles, management and prospects. Oncol Rep 2011;26:299-307.
3. O'Sullivan B, Rumble RB, Warde P; Members of the IMRT Indications Expert Panel. Intensity-modulated Radiotherapy in the Treatment of Head and Neck Cancer. Clin Oncol (R Coll Radiol) 2012;24:474-87.
4. Sciubba JJ, Goldenberg D. Oral complications of radiotherapy. Lancet Oncol 2006;7:175-83. Review.
5. Basu T, Laskar SG, Gupta T, Budrukkar A, Murthy V, Agarwal JP. Toxicity with radiotherapy for oral cancers and its management: A practical approach. J Cancer Res Ther 2012;8(Suppl 1):S72-84.
6. Reinke JM, Sorg H. Wound Repair and Regeneration. Eur Surg Res 2012;49:35-43.
7. Tibbs MK. Wound healing following radiation therapy: A review. Radiother Oncol 1997;42:99-106.
8. Lyons A, Ghazali N. Osteoradionecrosis of the jaws: Current understanding of its pathophysiology and treatment. Br J Oral Maxillofac Surg 2008;46:653-60.
9. Wang J, Boerma M, Fu Q, Hauer-Jensen M. Radiation responses in skin and connective tissues: Effect on wound healing and surgical outcome. Hernia 2006;10:502-6.
10. Sullivan MC, Roman SA, Sosa JA. Emergency surgery in patients who have undergone recent radiotherapy is associated with increased complications and mortality: Review of 536 patients. World J Surg 2012; 36:31-8.
11. Kunisada T, Ngan SY, Powell G, Choong PF. Wound complications following pre-operative radiotherapy for soft tissue sarcoma**.** Eur J Surg Oncol 2002;28:75-9.
12. Javaid M, Song F, Leinster S, Dickson MG, James NK. Radiation effects on the cosmetic outcomes of immediate and delayed autologous breast reconstruction: An argument about timing. J Plast Reconstr Aesthet Surg 2006;59:16-26.
13. Emerick KS, Tomycz L, Bradford CR, Lyden TH, Chepeha DB, Wolf GT, *et al*. Primary versus secondary tracheoesophageal puncture in salvage total laryngectomy following chemoradiation. Otolaryngol Head Neck Surg 2009;140:386-90.
14. Ganly I, Patel S, Matsuo J, Singh B, Kraus D, Boyle J, *et al*. Postoperative complications of salvage total laryngectomy. Cancer 2005;103:2073-81.
15. Redaelli de Zinis LO, Ferrari L, Tomenzoli D, Premoli G, Parrinello G, Nicolai P. Postlaryngectomy pharyngocutaneous fistula: Incidence, predisposing factors, and therapy. Head Neck 1999;21:131-8.
16. Magdy EA. Surgical closure of postlaryngectomy pharyngocutaneous fistula: A defect based approach. Eur Arch Otorhinolaryngol 2008;265:97-104.
17. Delanian S, Porcher R, Balla-Mekias S, Lefaix JL. Randomized, placebo-controlled trial of combined pentoxifylline and tocopherol for regression of superficial radiation-induced fibrosis. J Clin Oncol 2003;21:2545-50.
18. Hutcheson KA, Lewin JS. Functional outcomes after chemoradiotherapy of laryngeal and pharyngeal cancers. Curr Oncol Rep 2012;14:158-65.
19. Aygenc E, Celikkanat S, Kaymakci M, Aksaray F, Ozdem C. Prophylactic effect of pentoxifylline on radiotherapy complications: A clinical study. Otolaryngol Head Neck Surg 2004;130:351-6.
20. Støre G, Boysen M. Mandibular osteoradionecrosis: Clinical behaviour and diagnostic aspects. Clin Otolaryngol Allied Sci 2000;25:378-84.
21. Beumer J, Harrison R, Sanders B, Kurrasch M. Osteoradionecrosis: Predisposing factors and outcomes of therapy. Head Neck Surg 1984;6:819-27.
22. Epstein JB, Rea G, Wong FL, Spinelli J, Stevenson-Moore P. Osteonecrosis: Study of the relationship of dental extractions in patients receiving radiotherapy. Head Neck Surg 1987;10:48-54.
23. Delanian S, Depondt J, Lefaix JL. Major healing of refractory mandible osteoradionecrosis after treatment combining pentoxifylline and tocopherol: A phase II trial. Head Neck 2005;27:114-23.
24. Chang EI, Leon P, Hoffman WY, Schmidt BL. Quality of life for patients requiring surgical resection and reconstruction for mandibular osteoradionecrosis: 10-year experience at the University of California San Francisco. Head Neck 2012;34:207-12.
25. Baumann DP, Yu P, Hanasono MM, Skoracki RJ. Free flap reconstruction of osteoradionecrosis of the mandible: A 10-year review and defect classification. Head Neck 2011;33:800-7.
26. McGuirt WF. Laryngeal radionecrosis versus recurrent cancer. Otolaryngol Clin North Am 1997;30:243-50.
27. Skoracki RJ, Chang DW. Reconstruction of the chest wall and thorax. J Surg Oncol 2006;94:455-65.
28. Schierle C, Winograd JM. Radiation-induced brachial plexopathy: Review. Complication without a cure. J Reconstr Microsurg 2004;20:149-52.
29. Gosk J, Rutowski R, Reichert P, Rabczyński J. Radiation-induced brachial plexus neuropathy - aetiopathogenesis, risk factors, differential diagnostics, symptoms and treatment. Folia Neuropathol 2007;45:26-30.
30. Bajrovic A, Rades D, Fehlauer F, Tribius S, Hoeller U, Rudat V, *et al*. Is there a life-long risk of brachial plexopathy after radiotherapy of supraclavicular lymph nodes in breast cancer patients? Radiother Oncol 2004;71:297-301.
31. Gałecki J, Hicer-Grzenkowicz J, Grudzień-Kowalska M, Michalska T, Załucki W. Radiation-induced brachial plexopathy and hypofractionated regimens in adjuvant irradiation of patients with breast cancer--a review. Acta Oncol 2006;45:280-4.
32. Pritchard J, Anand P, Broome J, Davis C, Gothard L, Hall E, *et al*. Double-blind randomized phase II study of hyperbaric oxygen in patients with radiation-induced brachial plexopathy. Radiother Oncol 2001;58:279-86.
33. Delanian S, Lefaix JL, Maisonobe T, Salachas F, Pradat PF. Significant clinical improvement in radiation-induced lumbosacral polyradiculopathy by a treatment combining pentoxifylline, tocopherol, and clodronate (Pentoclo). J Neurol Sci 2008;275:164-6.
34. Wong M, Tang AL, Umapathi T. Partial ulnar nerve transfer to the nerve to the biceps for the treatment of brachial plexopathy in metastatic breast carcinoma: Case report. J Hand Surg Am 2009;34:79-82.
35. Tung TH, Liu DZ, Mackinnon SE. Nerve transfer for elbow flexion in radiation-induced brachial plexopathy: A case report. Hand (N Y) 2009;4:123-8.

36. Avraham T, Yan A, Zampell JC, Daluvoy SV, Haimovitz-Friedman A, Cordeiro AP, *et al*. Radiation therapy causes loss of dermal lymphatic vessels and interferes with lymphatic function by TGF-beta1-mediated tissue fibrosis. Am J Physiol Cell Physiol 2010;299:C589-605.
37. Avraham T, Daluvoy S, Zampell J, Yan A, Haviv YS, Rockson SG, *et al*. Blockade of transforming growth factor-beta1 accelerates lymphatic regeneration during wound repair. Am J Pathol 2010;177:3202-14.
38. Anscher MS. Targeting the TGF-beta1 pathway to prevent normal tissue injury after cancer therapy. Oncologist 2010;15:350-9.
39. Bruns F, Micke O, Bremer M Current status of selenium and other treatments for secondary lymphedema. J Support Oncol 2003;1:121-30.
40. Dennert G, Horneber M. Selenium for alleviating the side effects of chemotherapy, radiotherapy and surgery in cancer patients. Cochrane Database Syst Rev 2006;19;:CD005037.
41. Gothard L, Stanton A, MacLaren J, Lawrence D, Hall E, Mortimer P, *et al*. Non-randomised phase II trial of hyperbaric oxygen therapy in patients with chronic arm lymphoedema and tissue fibrosis after radiotherapy for early breast cancer. Radiother Oncol 2004;70:217-24.
42. Gothard L, Haviland J, Bryson P, Laden G, Glover M, Harrison S, *et al*. Randomised phase II trial of hyperbaric oxygen therapy in patients with chronic arm lymphoedema after radiotherapy for cancer. Radiother Oncol 2010;97:101-7.
43. Bengtson BP, Schusterman MA, Baldwin BJ, Miller MJ, Reece GP, Kroll SS, *et al*. Influence of prior radiotherapy on the development of postoperative complications and success of free tissue transfers in head and neck cancer reconstruction. Am J Surg 1993;166:326-30.
44. Choi S, Schwartz DL, Farwell DG, Austin-Seymour M, Futran N. Radiation therapy does not impact local complication rates after free flap reconstruction for head and neck cancer. Arch Otolaryngol Head Neck Surg 2004;130:1308-12.
45. Thankappan K. Microvascular free tissue transfer after prior radiotherapy in head and neck reconstruction - a review. Surg Oncol 2010;19:227-34.
46. Mücke T, Rau A, Weitz J, Ljubic A, Rohleder N, Wolff KD, *et al*. Influence of irradiation and oncologic surgery on head and neck microsurgical reconstructions. Oral Oncol 2012;48:367-71.
47. Jacobson AS, Eloy JA, Park E, Roman B, Genden EM. Vessel-depleted neck: Techniques for achieving microvascular reconstruction. Head Neck 2008;30:201-7.
48. Hanasono MM, Barnea Y, Skoracki RJ. Microvascular surgery in the previously operated and irradiated neck. Microsurgery 2009;29:1-7.
49. Halle M, Bodin I, Tornvall P, Wickman M, Farnebo F, Arnander C. Timing of radiotherapy in head and neck free flap reconstruction--a study of postoperative complications J Plast Reconstr Aesthet Surg 2009;62:889-95.
50. Patel UA, Keni SP. Pectoralis myofascial flap during salvage laryngectomy prevents pharyngocutaneous fistula. Otolaryngol Head Neck Surg 2009;141:190-5.
51. Withrow KP, Rosenthal EL, Gourin CG, Peters GE, Magnuson JS, Terris DJ, *et al*. Free tissue transfer to manage salvage laryngectomy defects after organ preservation failure. Laryngoscope 2007;117:781-4.

How to cite this article: Iyer S, Balasubramanian D. Management of radiation wounds. Indian J Plast Surg 2012;45:325-31.

Source of Support: Nil, **Conflict of Interest:** None declared.