CASE REPORT

Intensity-modulated radiation therapy to bilateral lower limb extremities concurrently: a planning case study

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Abstract
Non-melanomatous skin cancers represent 80% of all newly diagnosed cancers in Australia with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) being the most common. A previously healthy 71-year-old woman presented with widespread and tender superficial skin cancers on the lower bilateral limbs. External beam radiation therapy through the use of intensity-modulated radiation therapy (IMRT) was employed as the treatment modality of choice as this technique provides conformal dose distribution to a three-dimensional treatment volume while reducing toxicity to surrounding tissues. The patient was prescribed a dose of 60 Gy to the planning target volume (PTV) with 1.0 cm bolus over the ventral surface of each limb. The beam arrangement consisted of six treatment fields that avoided entry and exit through the contralateral limb. The treatment plans met the International Commission on Radiation Units and Measurements (ICRU) guidelines and produced highly conformal dosimetric results. Skin toxicity was measured against the National Cancer Institute: Common Terminology Criteria for Adverse Events (NCI: CTCAE) version 3. A well-tolerated treatment was delivered with excellent results given the initial extent of the disease. This case study has demonstrated the feasibility and effectiveness of IMRT for skin cancers as an alternative to surgery and traditional superficial radiation therapy, utilising a complex PTV of the extremities for patients with similar presentations.

Introduction
Skin cancers represent 80% of all newly diagnosed cancers in Australia and are classified into melanoma or non-melanoma. Non-melanomatous skin cancers are the most common with approximately 434,000 people treated annually and are further classified into either basal cell carcinoma (BCC) or squamous cell carcinoma (SCC). BCC is found within the basal cell layer or the lowest layer of the epidermis, is slow growing and rarely develops metastasis unless neglected. However, if left untreated BCC can invade locally, including spread to nearby bone. SCC develops within the outer layers of the skin and is commonly found on sun-exposed areas. SCC tends to grow and spread more rapidly than BCC and distant metastasis is possible through the lymph nodes or bloodstream. However, most of these patients present early and are managed with superficial radiation therapy or most frequently surgical excision; other treatment modalities can include deep radiation therapy and topical chemotherapy. Intensity-modulated radiation therapy (IMRT) when compared to traditional three-dimensional conformal radiation therapy (3DCRT) technique allows accurate treatment delivery to a three-dimensional planning target volume (PTV) while reducing toxicity to surrounding tissues through concave dose distributions. This technique has been employed for irregular targets in many instances, such as irradiation of head and neck mucosal SCCs or soft tissue sarcoma of the extremities, but there is a paucity of literature describing it for primary cutaneous skin cancers. This case study is an example, associated with an excellent clinical outcome, of where IMRT has been employed to treat a complex condition in the bilateral lower limbs.
Case Study

A previously healthy 71-year-old woman presented with widespread, diffuse and symptomatic hyperkeratoses and tender superficial, cutaneous skin cancers on both lower limbs. Upon examination the multiple lesions were found to be a mix of classic BCC and ulcerated dysplastic SCC. Her presentation was delayed due to social circumstances and previously the patient had been treated with surgeries, skin grafts and topical chemotherapy for Bowen's disease and multiple, biopsy proven superficial skin cancers. Despite prior therapies, the patient developed multiple, progressive lesions and recurrences on both lower limbs causing considerable discomfort which adversely affected her quality of life and mobility.

Surgery was precluded due to the disease extent, nature of the required surgery, likelihood of extensive skin grafting and lack of a suitable, unaffected donor site. Although topical chemotherapy was a genuine treatment option, the patient declined due to associated severe toxicity from previous treatments, resulting in radiation therapy as the recommended and selected treatment option. External beam radiation therapy and IMRT specifically was preferred over superficial radiation therapy due to the patient’s medical co-morbidities, the extent of disease, size of treatment fields and high risk of developing chronic non-healing ulcers as a late side effect with hypofractionated superficial radiation therapy treatment.

The patient was referred to Epworth Radiation Oncology for IMRT as this technique was considered the most effective option since both PTVs could be treated with homogenous coverage whilst optimising dose to the normal tissue structures.

Method

Ethics low-risk approval was obtained from Epworth HealthCare as well as patient consent for the use of any information or images pertaining to the development of this case study. All radiation therapy treatment plans were created on Varian Medical Systems (Palo Alto, CA) Eclipse™ planning system version 10 with the anisotropic analytical calculation algorithm (AAA) version 10.0.28.

The patient was prescribed a radical dose of 60 Gy in 2 Gy daily fractions over 6 weeks to both lower limbs. The chosen positioning and immobilisation method was feet-first supine in a personalised Vac-Lok Cushion (CIVCO Medical Solutions, Radiation Oncology, Orange City, IA, USA) with legs abducted so as to treat the limbs separately. The PTV excluded the posterior aspect of the limbs to allow for a strip of lymphatics to be spared and reduce the risk of gross oedema post radiation therapy. Figure 1 demonstrates the PTV and the IMRT dose-optimisation volumes that were utilised to achieve optimal target dose distribution and organ at risk dose-volume constraints. An IMRT PTV was created as a copy of the PTV with a 2-mm superior/inferior expansion so as to ensure optimal coverage of the entire PTV. A normal tissue volume (NTV) was also created by subtracting the IMRT PTV from the body of each limb with a 5-mm gap between the two structures so as to allow the optimisation programme to effectively reduce dose to healthy tissue without impacting on the homogenous distribution to the PTV. To reduce dose to healthy tissue through rapid dose fall off from the PTV, the NTV was optimised to receive less than 50% of the prescribed dose.

The treatment field arrangement comprised six fields that were positioned in angles, which neither enter nor exit the contralateral limb. Gantry angles of 10°, 62°, 125°, 180°, 230° and 310° were used for the left limb and gantry angles of 0°, 53°, 134°, 206°, 233° and 300° were used for the right limb. A 1.0-cm bolus was placed over the ventral surface of each limb to increase dose to the superficial, cutaneous lesions on the skin surface. Both limbs were planned according to the International Commission on Radiation Units and Measurements

Figure 1. IMRT optimisation and target volumes. Red contour – PTV and green contour – NTV (PTV minus leg by 5 mm). NTV, normal tissue volume; PTV, planning target volume; IMRT, intensity-modulated radiation therapy.
oncology nurses on a weekly basis (Table 1). Radiation-induced dermatitis associated with radiation by the radiation oncology nursing staff and graded weekly according to the National Cancer Institute: Common Terminology Criteria for Adverse Events (NCI: CTCAE) version 3 grading system for dermatitis associated with radiation by the onboard imaging system (including 1-mm shifts) was applied prior to treatment delivery. Events (NCI: CTCAE) were used to constrain the dose received by the healthy tissue and reduce the risk of developing gross oedema. The NTV mean value was observed to be the lowest in both of the IMRT treatment plans. In comparison, both the 3DCRT plans struggled to limit dose to this area and an increased mean dose of at least 14 Gy was observed.

Skin toxicity was measured against the National Cancer Institute: Common Terminology Criteria for Adverse Events (NCI: CTCAE) version 3 grading system for dermatitis associated with radiation by the radiation oncology nursing staff on a weekly basis (Table 1).

Table 1: NCI: CTCAE grading for dermatitis associated with radiation.

| Grade 0 | Normal |
|---------|--------|
| Grade 1 | Faint erythema or dry desquamation |
| Grade 2 | Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate oedema |
| Grade 3 | Moist desquamation other than skin folds and creases; bleeding induced by minor trauma or abrasion |
| Grade 4 | Skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site |
| Grade 5 | Death |

NCI: CTCAE, National Cancer Institute: Common Terminology Criteria for Adverse Events.

(ICRU) report 62 with a dose variation between +7% and −5%.

Retrospective 3DCRT plans were created for research comparison with the treated IMRT plans. The chosen 3DCRT method was anterior/posterior fields with multi-leaf collimation and sub-fields utilised to minimise the dose received by the posterior aspect of each limb.

Treatment verification was obtained with daily online kV/kV orthogonal (anterior obliques) imaging with a zero-action threshold. This meant that any move indicated by the onboard imaging system (including 1-mm shifts) was applied prior to treatment delivery.

Skin toxicity was measured against the National Cancer Institute: Common Terminology Criteria for Adverse Events (NCI: CTCAE) version 3 grading system for dermatitis associated with radiation by the radiation oncology nursing staff and graded weekly according to the NCI: CTCAE. The skin reaction reached a peak of Grade 3 at week 4 (30 Gy delivered) and the patient requested a hospital admission for pain management and assistance with continual skin care through the application of bi-daily silicon-based dressings. Figure 4A–D demonstrate the development of the skin reaction from CT simulation to the conclusion of the radiation therapy treatment at week 6 (60 Gy delivered). Pain was also present prior to and throughout radiation therapy and was adequately managed with analgesics.

Discussion

A well-tolerated treatment was planned and delivered through the use of IMRT. The results demonstrated that the 3DCRT plans were not capable of achieving the equivalent level of homogeneity and PTV coverage when compared with IMRT. Both IMRT and 3DCRT treatment plans met the required ICRU 62 recommendations of +7% and −5%, however, the images displayed in Figures 2A and B demonstrate that PTV coverage was compromised in both left and right lower limbs using the 3DCRT approach, in contrast to the highly conformal coverage achieved by IMRT (Fig. 2A). The dose to the posterior aspect of each limb was to be limited in an attempt to minimise the risk of developing gross oedema. This was quantified through measuring the mean dose to the NTV, which was observed to be at least 14 Gy higher when a 3DCRT approach was employed. Although the minimum and maximum doses to the PTV for both treatment approaches recorded similar results as shown in Table 2; the 3D dose distribution (Figs. 2A and B, 3A and B) demonstrated the superior conformity of PTV coverage and reduced dose to the NTV with the IMRT treatment plans.

One concern prior to the commencement of radiation therapy was the potential effect of IMRT and the use of...
Figure 2. (A) IMRT PTV coverage of 95%. (B) 3DCRT PTV coverage of 95%. NTV, normal tissue volume; PTV, planning target volume; IMRT, intensity-modulated radiation therapy; 3DCRT, three-dimensional conformal radiation therapy.

Figure 3. (A) IMRT PTV coverage of 50%. (B) 3DCRT PTV coverage of 50%. NTV, normal tissue volume; PTV, planning target volume; IMRT, intensity-modulated radiation therapy; 3DCRT, three-dimensional conformal radiation therapy.
bolus on the patient’s skin reaction. At week 4, the skin reaction reached a peak of Grade 3 (moist desquamation) as expected. Furthermore, the healing process was hampered by the patient’s co-morbidities of diffuse atheromatous and poor circulation affecting normal skin healing due to partial arterial blockages hindering blood flow. At the fourth week of treatment, the patient requested a hospital admission for pain management and assistance in receiving continual skin care with bi-daily silicon-based dressings.

Six weeks follow-up post radiation therapy demonstrated complete resolution of skin toxicity (Grade 0) as shown in Figure 5. A small cancerous nodule on the left limb persisted within the periphery of the treatment area that was subsequently surgically excised. It remains unclear why this single, well-circumscribed and differentiated SCC persisted while, literally, hundreds of other skin lesions resolved. This was regarded, overall, as an excellent result considering the initial extent of the disease.

|                | Left limb | Right limb |
|----------------|-----------|------------|
|                | IMRT (Gy) | 3DCRT (Gy) |
| PTV D 95% (min dose) | 57        | 57         | 57        | 58         |
| PTV D 2% (max dose) | 64        | 63         | 64        | 62         |
| NTV mean dose   | 34        | 48         | 32        | 54         |

NTV, normal tissue volume; PTV, planning target volume; IMRT, intensity-modulated radiation therapy; 3DCRT, three-dimensional conformal radiation therapy; D, dose.

Figure 4. Skin reaction from CT simulation to completion of radiation therapy. (A) Grade 0 (CT simulation). (B) Grade 1/2 (week 3). (C) Grade 3 (week 4 – hospitalised). (D) Grade 3 (week 6).
Conclusion

This case study presented a complex radiation therapy approach for treating skin cancer encompassing the lower limbs. For this patient, IMRT was the most advantageous option and resulted in improved dosimetric results when compared to 3DCRT. Furthermore, the acute skin toxicity from the treatment was short-lived, although moderately severe (Grade 3), well healing and resulting in an excellent curative, clinical, functional and cosmetic outcome. Further, long-term follow-up has shown no evidence of late radiation therapy side effects (data not shown).

This case study has demonstrated the feasibility and effectiveness of IMRT for skin cancers as an alternative to surgery or traditional superficial radiation therapy, utilising complex PTVs of the extremities for patients with similar presentation, poor peripheral vasculature or who are medically unfit for extensive surgeries and grafting procedures.

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Conflict of Interest

The authors declare no conflict of interest.

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Figure 5. Skin reaction (Grade 0) at the 6 weeks post radiation therapy follow-up.