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Case Report

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Edema management with compression therapy during volumetric modulated arc therapy for extensive skin field cancerisation - a case study

Abstract

Non-melanoma skin cancer is the most frequently diagnosed cancer in Australia. Recent advances in radiation therapy (RT) allow large convex areas with extensive skin field cancerisation (ESFC) to be treated using volumetric modulated arc therapy (VMAT). RT doses and volumes are planned by radiation oncologists from pre-treatment computed tomography (CT) scans. Changes in limb volume due to the inflammatory response triggered by radiation can affect planned volumes and result in inaccuracies in dosimetry.

We present a case study comparing outcomes with and without compression therapy following wide field VMAT to bilateral lower limbs. As edema can affect dosimetry, we hypothesized that edema management using compression therapy would be beneficial in controlling acute edema during RT. In this case when compression was applied during RT, treatment was able to be completed as planned in comparison to RT without compression where additional breaks in treatment were required due to edema and pain. There has been little published research examining edema management during RT for wide field skin cancerisation, however this case suggests further investigation is warranted to examine the potential value of compression therapy and accurate objective measures during VMAT for ESFC.

Keywords: radiation, volumetric modulated arc therapy, non-melanoma skin cancer, extensive skin field cancerisation, edema, compression therapy, case study

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Abbreviations: RT, radiation therapy; ESFC, extensive skin field cancerisation; VMAT, volumetric modulated arc therapy; CT, computed tomography; UV, ultraviolet; NMSC, non-melanoma skin cancer; SCC, squamous cell carcinoma; Gy, Gray; SIB, simultaneous integrated boost; CBCT, cone beam computed tomography; BIS, bioimpedance spectroscopy; ECF, extra cellular fluid; L-Dex, lymphedema index; SIM, simulation; ICG, indocyanine green; MDACC, MD Anderson Cancer Center; CTV, clinical target volume

Introduction

Australia has the highest incidence of skin cancer in the world, with non-melanoma skin cancer (NMSC) including basal cell and squamous cell carcinomas being the most frequently diagnosed cancers.[1,2] Advances in radiation therapy (RT) such as volumetric modulated arc therapy (VMAT) allows for large areas of skin with extensive skin field cancerisation (ESFC) to be treated, providing a more homogenous dose whilst sparing normal tissue.[3] Volumes to be treated and areas to be avoided are planned by radiation oncologists from computed tomography (CT) planning scans taken in the treatment position, with RT doses prescribed for each volume.[4,5] ESFC commonly occurs in the lower limbs due to ultraviolet (UV) radiation from sun exposure.[6] Presumably due to the gravitational effect combined with the acute inflammatory reaction from RT, edema resulting in changes in leg volume has been observed when treating the lower limbs with VMAT.[3] It is important to monitor edema and volume changes during treatment as it can affect the fit of the bolus (individualised three dimensionally (3D) printed tissue density equivalent material designed to ensure dose to the skin as the target organ), which may result in inaccuracies in dose delivery with an increased dose to the dermis rather than the planned epidermis. As the dermis has higher vascularity than the epidermis, increased dose to this area may exacerbate acute toxicities, including edema.[3]

There are several ways to monitor edema, with manual circumferential measurements being widely used, due to its simplicity and the high inter/intra-rater reliability and reproducibility.[7,8] Extracellular fluid (ECF) levels can also be measured using bioimpedance spectroscopy (BIS). BIS technology monitors ECF by measuring the resistance (impedance) to an alternating electrical current when it is passed through body tissue.[9,10] Comparing ECF levels between limbs can be represented by the following ratio (unaffected: affected/at-risk) limb.[11] Alternatively, this ratio may be linearized and expressed as a Lymphedema Index (L-Dex) score.[11]

In the field of diagnostic imaging, indocyanine green (ICG) lymphography has been used to map the lymphatics and evaluate the severity of lymphedema since 2007.[12] Patterns of dermal backflow due to reflux of lymph fluid to the lymphatic capillaries in the dermis from the obstructed lymphatic vessels are used to determine severity of lymphatic congestion.

Compression therapy has been proven to be an effective treatment in reducing and controlling acute and chronic edema.[13] We hypothesised that compression therapy during VMAT for ESFC to the lower limbs would be beneficial in controlling acute edema. We report a case study where the VMAT technique was utilized to sequentially treat bilateral lower legs of a patient with ESFC over a 12-month period. Treatment to both legs was similar, however compression garments/wraps (for edema), were applied prior to, and throughout treatment to only the second leg. Subjective and objective outcomes were then investigated and compared following completion of RT.

Case study

An active, 83-year-old Caucasian male with a 50-year history of NMSC was referred for RT to multiple solar keratoses and NMSC on his arms and legs. He had undergone numerous treatments over the past 50 years including topical treatments, excisional surgeries, and skin grafts. Clinical examination revealed keratotic and pre-malignant changes over all sun exposed skin, and a 3cm malignant area on the postero-lateral region of the right calf. With the right leg having more extensive disease, this leg was treated first using wide field VMAT with a plan to subsequently treat the left leg.

VMAT to the right leg without compression therapy

RT to the right leg was planned with a prescription dose of 45 Gray (Gy) in 25 fractions to regions of skin cancerisation, simultaneous integrated boosts (SIBs) of 60Gy to the areas of invasive disease and a two-week planned RT treatment break (to commence between fractions 10 and 12), to allow toxicities such as edema and pain to settle. Acute edema was first documented after nine fractions (21.6Gy), with a nine-day break in treatment instigated after 12 (28.8Gy), a deviation from the standard practice of a 14-day break. An additional five-day break was required after 13 fractions (31.2Gy) due to increasing edema and pain. After 19 fractions (45.6Gy), cone beam computed tomography (CBCT) revealed edema present in the leg (Figure 4) likely resulting in significant dosimetry changes. This, along with increasing pain requiring Oxynorm®, resulted in a further two-week break from treatment. Three and a half months following completion of RT, the patient reported ongoing discomfort, and pitting edema was documented in the lateral aspect of the lower leg.

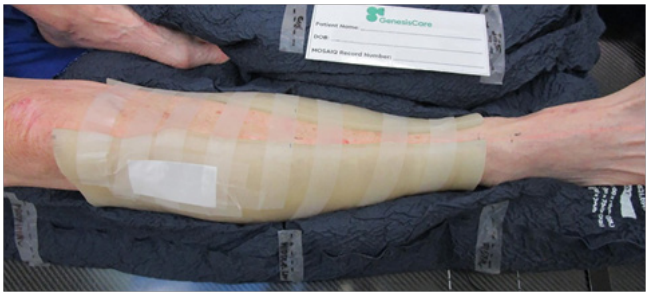

Figure 1 A photo of the right leg at CT planning simulation (SIM) with 3D bolus showing the skin preservation strip on the antero-medial aspect.

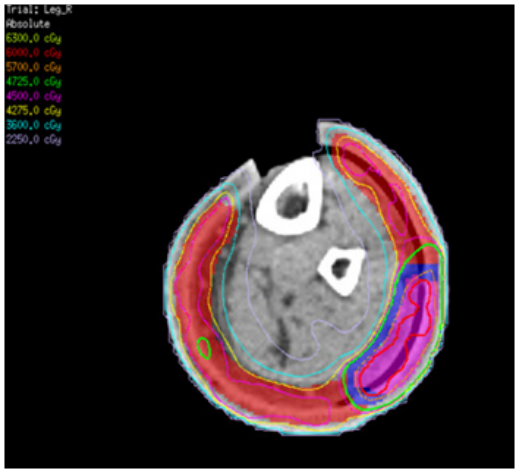

Figure 2 CT planning SIM right leg.

Figures 3 and 4 demonstrate the low dose CBCT (green) of the patient's right leg with 3D bolus in-situ fused with the planning CT (purple). Fraction 1 (figure 3) demonstrates good correlation between the CBCT and the planning CT. However, at fraction 19 (figure 4), the CBCT (green) demonstrates edema of the right leg with a region of soft tissue bulging through the gap in the bolus due to an increase in leg circumference.

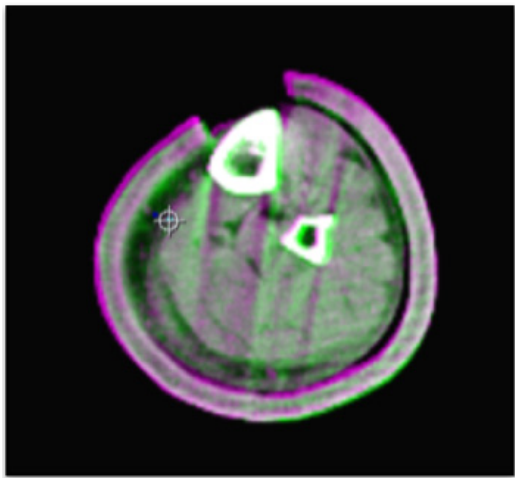

Figure 3 CBCT right leg fraction 1.

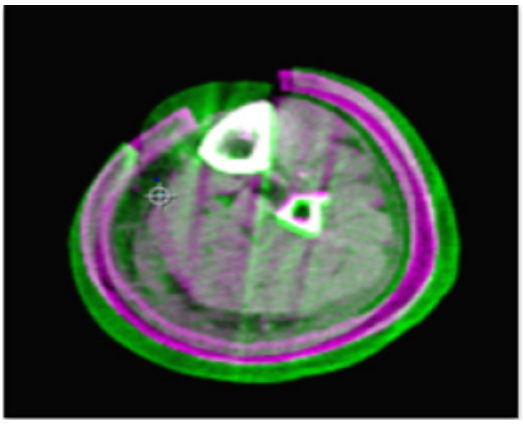

Figure 4 CBCT right leg fraction 19.

Edema assessment

Five months after completion of RT to his right leg and given the significant edema he experienced with treatment interruption and discomfort, the patient was referred to Macquarie Health Lymphedema Clinic for assessment and management of right leg edema, and work up prior to commencing RT to the second (left) leg. As edema was reported in both legs, possibly due to systemic causes (the patient had previously been diagnosed with mild to moderate renal failure), bilateral below knee compression stockings were trialled and subsequently prescribed. Additionally, diagnostic ICG lymphography imaging was recommended to evaluate the condition of the superficial lymphatic system.

ICG lymphography

ICG lymphography scans to both legs were performed prior to commencement of RT to the left leg. In the right leg (previous RT), lymphatic vessels were almost intact except for an obstructed vessel in the middle of the lower leg leading to congestion over the lateral aspect of the lower leg. Local congestion was also present around the medial malleolar region. As there were no control imaging scans

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before RT it was unclear whether this congestion was due to VMAT. This leg demonstrated original drainage patterns to the popliteal and ipsilateral groin regions and was diagnosed as MD Anderson Cancer Center (MDACC) Stage 2 (Stage 0 is normal and Stage 4 is advanced lymphedema), with moderate patent lymphatic vessels and segmental dermal backflow. [14]

ICG injection site (triangle), lymphatic vessel (blue), lymph node (round) and congestion red.

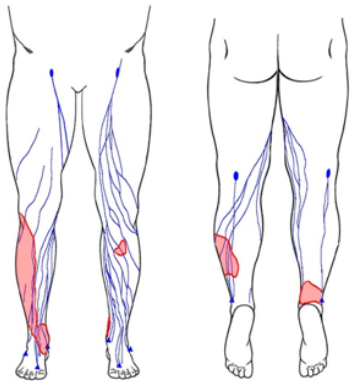

Figure 5 ICG schematic diagram.

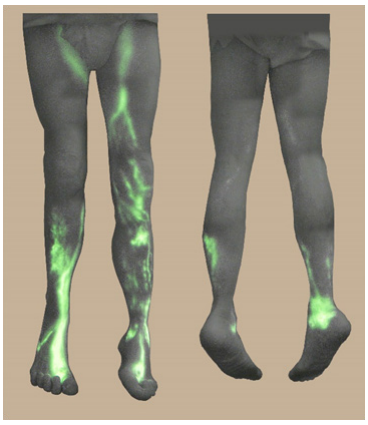

Figure 6 Montage of ICG images.

In the left leg (no previous RT), lymphatic vessels were almost intact. There were isolated areas of congestion in the anterior tibial region and on the lateral aspect of the lower leg. This leg also demonstrated original lymphatic drainage patterns to the popliteal and ipsilateral groin regions and was reported to be MDACC Stage 1, with many patent lymphatic vessels and minimal, patchy dermal backflow. [14] ICG findings suggest that the right leg was more congested than the left, with the congestion in the lateral aspect of the right lower leg confirmed by pitting edema identified on physical examination.

VMAT to the left leg with compression therapy

RT to the left leg was planned with a prescription dose of 45Gy in 25 fractions to regions of skin cancerisation, with a minimum two-week break after fraction 10. No SIBs were prescribed for this course of radiation. Prior to commencing treatment to his left leg, the patient had been wearing prescribed below knee, flat knit compression class one garments on both legs for three-months and compression therapy was maintained throughout RT treatment. During this course of RT regular circumferential and BIS measurements using the SOZO® device (ImpediMed®, Australia) were recorded for both lower limbs (Figure 11). After 10 fractions (18Gy), there was no change in leg volume however due to two areas of moist desquamation, the patient's left leg was fitted with a knee-high compression wrap leg piece (JOBST® FarrowWrap Lite® (20-30mmHg)), and a foot compression liner (JOBST® FarrowHybrid® ADI (20-30mmHg compression in the foot and ankle and a non-compressive liner above the ankle)) (Figure 12), allowing compression to be maintained without shearing forces to radiated skin when donning and doffing. After 19 fractions (45.6Gy) CBCT revealed minimal edema present in the leg (figure 10). Following the planned two-week break, RT treatment was completed without incident.

Six months following completion of VMAT to the left leg, the skin on both legs appeared smooth, with a good cosmetic result (Figure 13). No edema was evident, however the patient reported intermittent swelling in both ankles towards the end of the day if not wearing compression garments.

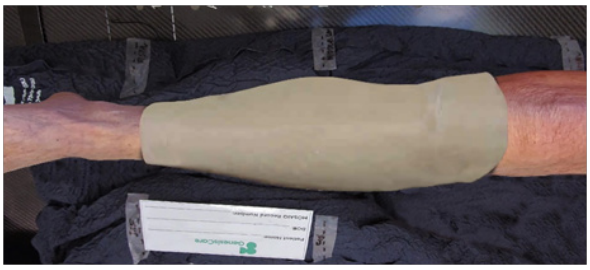

Figure 7 CT planning SIM left leg with 3D printed bolus; postero-medial skin preservation strip cannot be seen on this image.

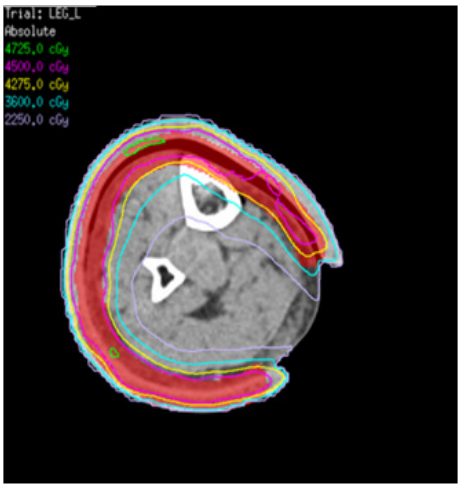

Figure 8 CT planning SIM left leg.

Figures 9 and 10 demonstrate the low dose CBCT (green) of the patient's left leg with 3D bolus in-situ fused with the planning CT (purple). The CBCT at fraction 1 (figure 9) and fraction 19 (figure 10) correlate well with the planning CT, demonstrating minimal swelling during RT to the left leg.

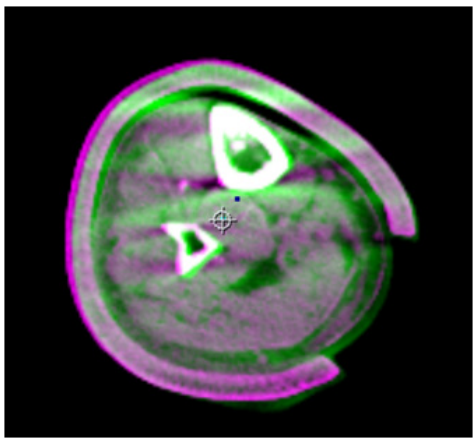

Figure 9 CBCT left leg Fraction 1.

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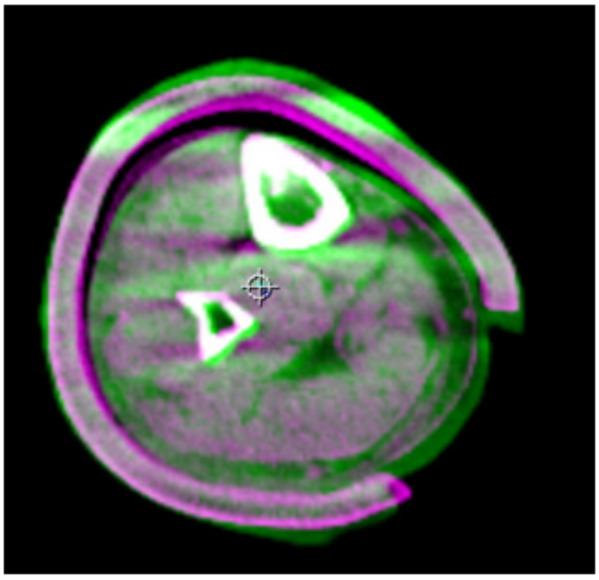

Figure 10 CBCT left leg Fraction 19.

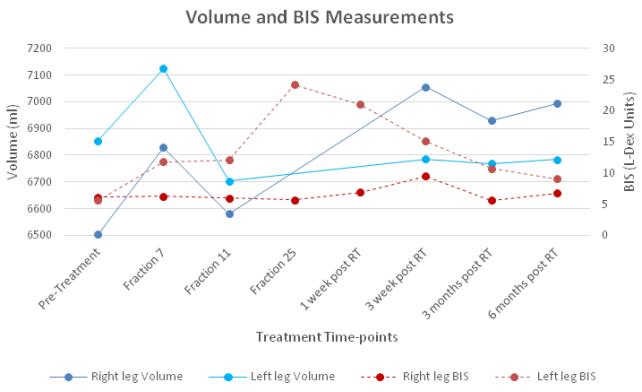

Figure 11 Bilateral volume and BIS measures during RT to the second leg.

*Note due to COVID-19 restrictions circumferential measurements were unable to be completed at fraction 25- and 1-week post completion of RT
BIS, Bioimpedance Spectroscopy; L-Dex, Lymphedema Index; RT, radiation therapy; ml, millilitres.

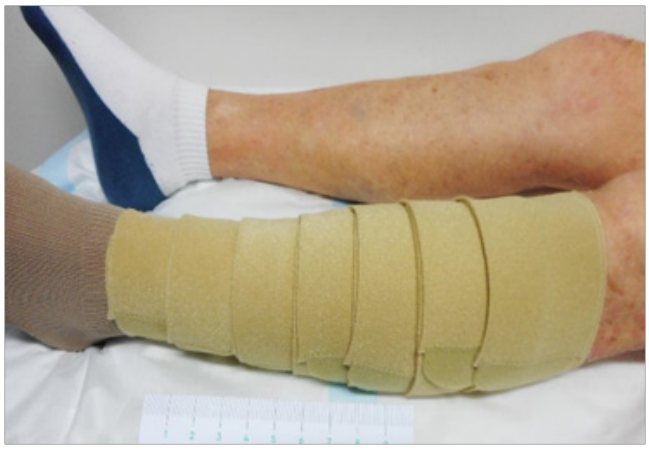

Figure 12 Left Leg JOBST® FarrowWrap lite® below knee compression wrap with JOBST® FarrowHybrid® liner.

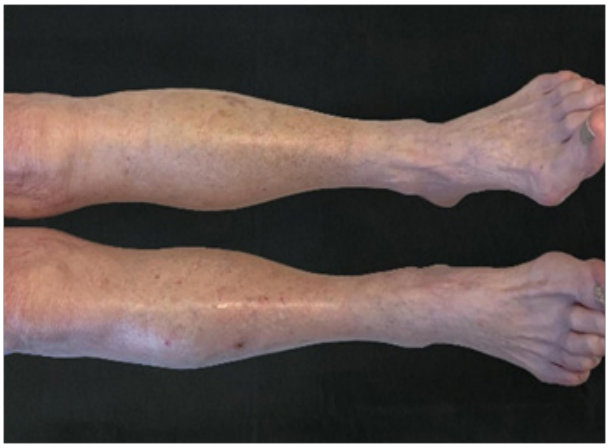

Figure 13 Photo 6-months post VMAT to the left leg.

Discussion

This case study examines the potential benefit of compression therapy and the value of objective measurements for monitoring edema during VMAT for ESFC of the lower limbs. RT was delivered to similar volumes and circumferences, with both legs being treated with a low dose of 45Gy to the larger volume. Additionally, the right leg had smaller 60Gy volumes to two areas of invasive disease (Figures 2&8). Overall, the treatment outcome for the skin of both legs was comparable, however toxicities during treatment differed considerably.

During treatment to the first (right) leg with no compression therapy, circumferential limb measurements were not taken, making the degree of edema difficult to assess. In conjunction with pain and poor fit of the 3D bolus it was significant enough for the patient to require an extra break from RT in addition to the planned break. In comparison, treatment to the second (left) leg (with compression therapy), was completed as planned with only the scheduled two-week break. During RT to the left leg limb volumes remained stable, allowing good fit of the 3D bolus throughout raising the question, can compression therapy during VMAT to the lower limbs assist with controlling acute edema during treatment? An issue with compression stockings for patients undergoing wide field VMAT to the lower limbs is shearing forces whilst donning and doffing garments causing damage to fragile, irradiated skin. In this case, a compression wrap was applied to allow continued, graduated compression to the left leg once areas of moist desquamation were identified, without shearing forces causing injury to the skin. As edema can affect the fit of the 3D bolus and alter dosimetry,[3] further investigations into compression therapy during VMAT for ESFC of the lower limbs may be justified. Additionally, compression therapy has been shown to benefit chronic wound healing such as venous ulcers, [15,16] therefore may theoretically assist with skin recovery post RT.

During VMAT for NMSC the planned target organ is the thin epidermal layer of the skin. A change in limb volume during RT can increase dose to the more vascular dermis which may exacerbate acute toxicities.[3] A break in RT after 10 fractions has been recommended to allow the normal skin time to repopulate and to decrease acute toxicities before starting the second phase of treatment.[3] Regular standardised volume measures (as were implemented in this case for the left leg) to monitor edema and changes in limb volume during treatment, may help to identify patients who require a longer break

in treatment to allow acute toxicities such as edema to settle. As standardised measures were not taken during treatment to the right leg, it is difficult to ascertain whether if monitored, this might have prompted a longer initial break in treatment, possibly negating the need for a subsequent break after 19 fractions.

Along with volume measures, extracellular fluid levels were monitored using BIS technology throughout treatment to the left leg and up to six months post treatment completion. The increased L-Dex score in the left leg during treatment was expected due to the acute soft tissue inflammation caused by RT, however the increased extracellular fluid did not appear to significantly affect leg volume when calculated by tape measurements or on CBCT scans (Figure 10). In the field of breast cancer increases in ECF indicative of sub-clinical lymphedema have been found to occur prior to a change in limb volume for at risk patients.[17] As BIS is a quick, non-invasive measure, further investigation may be warranted in patients undergoing wide field VMAT for NMSC, to assess whether BIS can predict toxicities such as edema to help identify patients who may require an increased break in treatment prior to a change in leg volume.[18]

Additionally, this patient completed ICG lymphography imaging prior to commencement of VMAT to his left leg to assess lymphatic drainage pathways, with ICG findings suggesting the right lower leg was more congested over the lateral aspect. Whether this was due to the previous RT or surgeries is unable to be determined as there were no prior scans for comparison, though interestingly good patent vessels were seen on the antero-medial aspect where the skin sparing strip was left. Literature from limb sarcoma studies found circumferential irradiation can result in fibrosis, pain and edema and recommends sparing a longitudinal strip of skin to reduce this risk.[19,20] During planning of the clinical target volume (CTV) by the radiation oncologist, a strip of skin of at least 2.0 cm is left to preserve the superficial lymphatics and allow for lymphatic drainage,[3,5] though it is unclear whether this is necessary in patients with circumferential disease undergoing VMAT for lower limb ESFC.[5] Future studies with repeat ICG lymphography imaging pre and post RT for comparison are warranted to provide further information about the potential effect of wide field VMAT on the superficial lymphatic system.

Conclusion

Modern RT treatment modalities such as VMAT allow large areas of skin affected by ESFC to be treated, however toxicities such as edema can be challenging, especially in the lower limbs. This case study suggests that regular monitoring, and intervention with compression therapy when indicated may feasibly help to control acute edema, allowing patients to better manage during treatment and highlights the benefits of a multidisciplinary team approach for comprehensive assessment and management of potential side effects.

Acknowledgments

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Conflicts of interest

All authors declare that there is no conflict of interest for the management or preparation of this case study.

References

1. Fransen M, Karahalios A, Sharma N, et al. Non–melanoma skin cancer in Australia. *Med J Aust.* 2012;197(10):565–568.
2. Staples MP, Elwood M, Burton RC, et al. Non–melanoma skin cancer in Australia: the 2002 national survey and trends since 1985. *Med J Aust.* 2006;184(1):6–10.
3. Fogarty G, Christie D, Potter A. Volumetric modulated arc therapy (VMAT) for extended skin field cancerisation (ESFC): Radiobiological learnings from unique patient cases. *Int J Radiol Radiat Ther.* 2019;6(5):156–162.
4. Fogarty G, Christie D, Spelman LJ, et al. Can modern radiotherapy be used for extensive skin field cancerisation: An update on current treatment options. *Biomed J.* 2018;2:8.
5. Potter A, Price M, Papworth D, et al. A technique for treating extended skin field cancerisation using volumetric modulated arc therapy. *Int J Radiol Radiat Ther.* 2019;6(4):111–119.
6. D'Orazio J, Jarrett S, Amaro–Ortiz A, et al. UV radiation and the skin. *Int J Mol Sci* 2013;14(6):12222–12248.
7. Bakar Y, Özdemir ÖC, Sevim S, et al. Intra–observer and inter–observer reliability of leg circumference measurement among six observers: a single blinded randomized trial. *J Med Life.* 2017;10(3):176–181.
8. Taylor R, Jayasinghe UW, Koelmeyer L, et al. Reliability and Validity of Arm Volume Measurements for Assessment of Lymphedema. *Phys Ther.* 2006;86(2):205–214.
9. Khalil SF, Mohktar MS, Ibrahim F. The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases. *Sensors(Basel).* 2014;14(6):10895–10928.
10. Ward L. Is BIS ready for prime time as the gold standard measure. *J Lymphedema.* 2009;4(2):52–56.
11. Ward LC. Bioelectrical Impedance Spectrometry for the Assessment of Lymphedema: Principles and Practice. In: Greene A, Slavin SA, Brorson H, editors.. *Lymphedema*. Cham: Springer International Publishing; 2015. P. 123–132.
12. Unno N, Inuzuka K, Suzuki M, et al. Preliminary experience with a novel fluorescence lymphography using indocyanine green in patients with secondary lymphedema. *J Vasc Surg* 2007;45(5):1016–1021.
13. Committee E. The diagnosis and treatment of peripheral lymphedema: 2016 consensus document of the International Society of Lymphology. *Lymphology.* 2016;49(4):170–184.
14. Nguyen AT, Suami H, Hanasono MM, et al. Long–term outcomes of the minimally invasive free vascularized omental lymphatic flap for the treatment of lymphedema. *J Surg Oncol.* 2017;115(1):84–89.
15. Lee N. An evaluation on the use of adjustable compression wrapping devices as an alternative to compression bandaging in lower leg wounds. *Wounds Int.* 2018;9(4):12–19.
16. Powers JG, Higham C, Broussard K, et al. Wound healing and treating wounds Chronic wound care and management. *Journal of the American Academy of Dermatology.* 2016;74(4):607–625.
17. DiSipio TD, Rye SM, Newman BP, et al. Incidence of unilateral arm lymphedema after breast cancer: a systematic review and meta–analysis. *The lancet oncol.* 2013;14(6):500–515.
18. Cornish BH, Bunce IH, Ward LC, et al. Bioelectrical impedance for monitoring the efficacy of lymphedema treatment programmes. *Breast cancer research and treatment.* 1996;38(2):169–176.
19. Tepper J, Rosenberg SA, Glatstein E. Radiation therapy technique in soft tissue sarcomas of the extremity—policies *of treatment at the National Cancer Institute. Int J Radiat Oncol Biol Phys. 1982*;8(2):263–273.
20. Stewart AJ, Lee YK, Saran FH. Comparison of conventional radiotherapy and intensity–modulated radiotherapy for post–operative radiotherapy for primary extremity soft tissue sarcoma. *Radiother Oncol.* 2009;93(1):125–130.