

## Split Course Superficial Radiotherapy in Scrotal Extramammary Paget's Disease Allows Course Completion With Minimal Side Effects: A Case Study

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### ABSTRACT

Symptomatic anogenital extramammary Paget's disease (EMPD) is a disease of the elderly that can be difficult to eradicate with topical therapies. Surgery with the recommended margins is effective, but the tissue loss may impact quality of life. Fractionated radiotherapy (RT) is recommended to 60 Gy at least, but continuous treatment may result in significant local acute effects making completion difficult. A fit, immune competent, 80-year old male of Chinese heritage was treated with definitive RT with curative intent for symptomatic recurrent multifocal EMPD of the scrotum and base of penis. Superficial RT was prescribed using a split course approach on

an Xstrahl® 300 machine with a generating energy of 100kV, HVL = 3.95 mm Al, delivered with 30 cm focus to source distance. Phase 1 was 20 Gy in 10 daily fractions at five per week given Monday to Friday. At least two weeks later, phase 2 was given using the same schedule. After another two weeks or more after completion of phase 2, an identical third phase of 20 Gy in 10 fractions, with no change in field size between the phases, was administered. The breaks between phases allowed for skin recovery. The highest toxicity was dry desquamation at the end of phase 1. The skin returned to normal four weeks after the final phase. The patient remained fully potent during and after therapy. With a planned split course approach, the full course to 60 Gy was completed according to schedule with minimal symptoms or impact on daily life.

**Key words:** Radiotherapy; Paget's disease; Extramammary; Scrotum; In-situ disease

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### Abbreviations

Al, aluminium; BoP, base of penis; cm, centimetre; CTV, clinical target volume; EMPD, extramammary Paget's disease; kV, kilovoltage; Gy, gray; HVL, half value layer; mm, millimetre; RT, radiotherapy; SCC, squamous cell carcinoma; SXRT, superficial radiotherapy

### INTRODUCTION

Extramammary Paget's disease (EMPD) is a relatively rare, in-situ cutaneous adenocarcinoma that mainly affects the anogenital region, particularly in the elderly. The earliest and most annoying symptom is pruritus, and this is associated on examination with the onset of erythematous-eczematous lesions<sup>[1]</sup>. Duration of response to topical

therapy, including steroid and antibiotic creams, imiquimod<sup>[2]</sup> and photodynamic therapy<sup>[3]</sup>, is disappointing. Surgical excision with wide margins of three centimetres (cm) is recommended, but this tissue sacrifice may result in unacceptable morbidity<sup>[4]</sup>.

Tissue conserving definitive radiotherapy (RT) has been employed with good effect, and 18 studies are summarised in an excellent review by Tagliaferri *et al*<sup>[5]</sup>. RT had been administered as definitive treatment for primary or macroscopic recurrent disease after surgery, with total doses ranging from 30 to 80.2 Gy delivered in 3 to 43 fractions. The authors recommended a definitive dose of at least 60 Gy for lasting complete response (CR). The problem with fractionated RT is that a continuous course can be associated with significant acute toxicities, especially in the sensitive anogenital area. New RT modalities have enabled treatment of extensive areas of in-

situ disease<sup>[6]</sup>. To date, experience has shown that a planned break in treatment of in-situ disease is associated with a reduction in acute toxicity, enabling course completion<sup>[7]</sup> without loss of oncological control.

We present a case of symptomatic recurrent multifocal EMPD of the scrotum and base of penis treated with split course RT. RT to a total of 60 Gy in 30 fractions was completed within the planned timeframe with minimal toxicity. To our knowledge, this is the first publication to approach EMPD with a planned split course approach.

## CASE STUDY

A cooperative, fit, immune competent 80-year old male of Chinese heritage presented for consideration of definitive RT for symptomatic



**Figure 1** Effect of treatment over time of the superior left scrotum and BoP. A: On presentation, symptomatic visible and palpable disease of the superior left scrotum and BoP. B: SXRT field is a 5 mm expansion on the clinical target volume (CTV)<sup>[8]</sup> of the visible and palpable EMPD disease. Field stability is achieved through adequate taping. C. Maximum toxicity of dry desquamation in normal skin surrounding tumor lysis of the EMPD. D. Complete response and complete skin healing four weeks after RT.

recurrent multifocal EMPD of the scrotum and base of penis (BoP). His disease had progressed through multiple courses of 5-fluorouracil 5% and imiquimod. He was using topical local anaesthetic cream to control the itch. He declined surgery, which may have required penectomy.

On examination, two large areas of EMPD were seen. The first area involved the left superior scrotum and BoP with a maximum dimension of 10 cm; the second involved the left inferior scrotum with a maximum dimension of 9 cm. Multiple punch biopsies carried out after failed topical treatment a few months earlier had again shown prominent pagetoid epidermal involvement by atypical cells with positive CK7 but negative SOX 10 staining, confirming adenocarcinoma in-situ. The spread was to a depth of 1.3 millimetres (mm) by involvement of the underlying eccrine ducts, but no dermal invasion was seen.

Given the changing and unpredictable profile of the treatment area, the only modality that would adequately cover the volume was superficial radiotherapy (SXRT). This treatment would require daily set up with visual placement of the treatment device for each fraction by an experienced radiation therapist (JS).

SXRT was prescribed with a split course approach. The patient was treated with an Xstrahl®300 machine (Xstrahl Ltd, Camberley, Surrey, UK) with a generating energy of 100 kV, HVL = 3.95 mm Al, delivered with a 30 cm focus to source distance with the prescription isodose of 100% to the surface and a rapid dose drop off with depth; dose measuring 40% at 3 cm depth. The first treatment phase consisted of 20 Gy in 10 daily fractions at five per week, given

Monday to Friday. At least two weeks later, the second phase was given also using 20 Gy in 10 daily fractions. At least another two weeks after completion of the second phase, an identical third phase of 20 Gy in 10 fractions was administered. There was no change in field size between the phases. The breaks between phases allowed for normal skin recovery. The highest toxicity in terms of symptoms, and on physical examination by an experienced physician (GBF), was dry desquamation observed at the end of the first phase. The skin returned to normal four weeks after the last phase and the itch was no longer present. The patient remained fully potent during and after therapy, which was an important quality of life end point for him.

## DISCUSSION

Symptomatic anogenital EMPD can be difficult to eradicate with the usual tissue conserving topical therapies. Effective surgery with three cm margins may impact quality of life and be declined by patients. RT to 60 Gy is tissue conserving, but a single continuous phase of RT may result in significant local acute effects making treatment completion difficult. With a planned split course approach, our patient was able to complete the full course to 60 Gy according to schedule



**Figure 2** Effect of treatment over time of the inferior left scrotum. A: On presentation, symptomatic visible and palpable disease. B: SXRT planning field is a 5 mm expansion on the CTV of the visible and palpable EMPD disease. C: Maximum toxicity of dry desquamation in normal skin surrounding tumor lysis of the EMPD. D: Complete response and complete skin healing four weeks after RT.

and with minimal symptoms or impact on daily life.

Split course RT is controversial. Randomised data has shown a detriment to local control in squamous cell carcinoma (SCC) of the head and neck<sup>[9]</sup> and anus<sup>[10]</sup>. In skin cancer, retrospective data shows no detriment<sup>[11]</sup>. In-situ skin cancer seems to have no loss of oncological control with a planned break, but data is of low evidence<sup>[12]</sup>. Split course RT may be an effective way of delivering effective tissue conserving treatment for anogenital EMPD with minimal toxicity.

The scrotum is a very mobile organ. As such, it does not lend itself to the usual immobilization and treatment set up which is essential for reproducibility with modern linear accelerator-based fractionated RT. Daily manual set up by an experienced radiation therapist working with a cooperative patient was essential to the favourable outcome in this case.

The Xstrahl<sup>®</sup> 300 machine was the treatment modality of choice in this scenario. It offers the flexibility to treat at any angle and a short delivery time. This avoids the patient being in the same position for long, thus decreasing errors due to involuntary organ movement. Organs, such as the upper penile shaft and testicles, are able to be manipulated out of the beam to reduce unnecessary side effects in normal tissues.

In conclusion, symptomatic anogenital EMPD of the scrotum can be treated to a complete response with minimal toxicity using an Xstrahl<sup>®</sup> 300 machine capable of SXRT with daily setup under the direct visual control of an experienced radiation therapist. SXRT to 60 Gy was delivered via a split course approach in three phases separated by at least two weeks. The highest toxicity was dry desquamation seen at the end of the first phase. The skin was back to normal four weeks after the last treatment phase. The patient remained fully potent during and after therapy. The combination of SXRT, an experienced radiation therapist and a split course approach were key to the success of this case.

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