Clinical Oncology xxx (2016) 1–10

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Initial Results from the Royal College of Radiologists' UK National Audit of Anal Cancer Radiotherapy 2015

R. Muirhead [*], K. Drinkwater [†], S.M. O'Cathail [‡], R. Adams [§], R. Glynne-Jones [¶], M. Harrison [¶], M.A. Hawkins [*], D. Sebag-Montefiore [||], D.C. Gilbert [**]

[*] CRUK MRC Oxford Institute for Radiation Oncology, University of Oxford, Oxford, UK
[†] The Royal College of Radiologists, London, UK
[‡] Oxford University Hospitals NHS Trust, Department of Oncology, Churchill Hospital, Oxford, UK
[§] Cardiff University Department of Cancer and Genetics and Velindre Hospital, Cardiff, UK
[¶] Mount Vernon Centre for Cancer Treatment, Mount Vernon Hospital, Northwood, UK
[||] University of Leeds, Cancer Research UK Leeds Centre, St. James's University Hospital, Leeds, UK
[**] Sussex Cancer Centre, Royal Sussex County Hospital, Brighton, UK

Received 1 June 2016; received in revised form 8 August 2016; accepted 15 August 2016

Abstract

Aims: UK guidance was recently developed for the treatment of anal cancer using intensity-modulated radiotherapy (IMRT). We audited the current use of radiotherapy in UK cancer centres for the treatment of anal cancer against such guidance. We describe the acute toxicity of IMRT in comparison with patient population in the audit treated with two-phase conformal radiotherapy and the previous published data from two-phase conformal radiotherapy, in the UK ACT2 trial.

Materials and methods: A Royal College of Radiologists' prospective national audit of patients treated with radiotherapy in UK cancer centres was carried out over a 6 month period between February and July 2015.

Results: Two hundred and forty-two cases were received from 40/56 cancer centres (71%). In total, 231 (95%) underwent full dose radiotherapy with prophylactic nodal irradiation. Of these, 180 (78%) received IMRT or equivalent, 52 (22%) two-phase conformal (ACT2) technique. The number of interruptions in radiotherapy treatment in the ACT2 trial was 15%. Interruptions were noted in 7% (95% confidence interval 0–14%) of courses receiving two-phase conformal and 4% (95% confidence interval 1–7%) of those receiving IMRT. The percentage of patients completing the planned radiotherapy dose, irrelevant of gaps, was 90% (95% confidence interval 82–98%) and 96% (95% confidence interval 93–99%), in two-phase conformal and IMRT respectively. The toxicity reported in the ACT2 trial, in patients receiving two-phase conformal in the audit and in patients receiving IMRT in the audit was: any toxic effect 71%, 54%, 48%, non-haematological 62%, 49%, 40% and haematological 26%, 13%, 18%, respectively.

Conclusions: IMRT implementation for anal cancer is well underway in the UK with most patients receiving IMRT delivery, although its usage is not yet universal. This audit confirms that IMRT results in reduced acute toxicity and minimised treatment interruptions in comparison with previous two-phase conformal techniques.

Key words: Acute toxicity; anal cancer; audit; IMRT

Introduction

Anal cancer is a relatively rare tumour with an increasing incidence [1]. It is associated with infection with high-risk subtypes of human papilloma viruses [2]. The ACT2 study set the standard for radical chemoradiotherapy (CRT) in anal squamous cell carcinoma in the UK, with a 3 year disease-free survival of 73% [3]. However, the radiotherapy techniques available at the time of trial design, large anterior–posterior/posterior–anterior fields, were associated with significant acute toxicity, particularly in the skin and perineum. Although relatively modest total radiation doses were used, this toxicity often entailed long breaks in

Author for correspondence: R. Muirhead, Oxford University Hospitals NHS Trust, Department of Oncology, Churchill Hospital, Oxford, UK. Tel: +44-1865-235-209.
E-mail address: rebeccamuirhead@oncology.ox.ac.uk (R. Muirhead).

http://dx.doi.org/10.1016/j.clon.2016.10.005

Please cite this article in press as: Muirhead R, et al., Initial Results from the Royal College of Radiologists' UK National Audit of Anal Cancer Radiotherapy 2015, Clinical Oncology (2016), http://dx.doi.org/10.1016/j.clon.2016.10.005

treatment associated with worse oncological outcomes and considerable late pelvic radiation morbidity [4–8].

Intensity-modulated radiotherapy (IMRT) conforms doses around irregular volumes using multiple beams and varying dose rates. This minimises dose to normal organs with the aim of reducing toxicity. The Radiation Therapy Oncology Group (RTOG) 0529 single arm phase II study confirmed reduced acute toxicity with IMRT in radical anal CRT; when retrospectively compared with the previous RTOG 9811 trial, where radiotherapy was delivered conformally using a shrinking field technique [9]. RTOG 0529 delivered 54 Gy and 45 Gy in 30 fractions to primary tumour and prophylactic lymph nodes, respectively, in locally advanced disease and 50 Gy and 42 Gy in 28 fractions, respectively, to early disease.

In 2012, the UK Department of Health recommended that all patients who could benefit from reduced treatment toxicity through the use of IMRT should be offered this treatment [10]. However, the implementation of IMRT for any given indication brings a number of challenges. Converting ACT2 radiotherapy to an IMRT protocol required consideration of doses, volumes and technique [11]. Implementation without due care and quality control can result in geographical miss; potentially reducing cure rates and/or increasing toxicity. Some authors have questioned the uncritical adoption of IMRT, raising concerns regarding the steep and long learning curve required for the technique to be perfected and the lack of quality assurance [12]. Delhorme *et al.* [13] reported improved outcomes with the use of guidelines. However, in RTOG 0529, despite the stringent protocolised setting of a clinical trial, 81% of plans submitted for central review were rejected at first review and 46% required multiple revisions [9]. They also reported correlations between minor or major deviations from protocol and outcomes; patients who had a minor or major deviation in dose to small bowel had a increased rate of Grade 2+ toxicity. As such, it is vital in the multicentre implementation of IMRT to agree detailed homogeneous delivery guidelines, encourage education and mentoring; and incorporate adequate quality assurance.

To investigate the implementation of IMRT in anal cancer in the UK, the Royal College of Radiologists (RCR) surveyed 58 centres in November 2013, requesting information on current radiotherapy delivery techniques used for anal cancer and the ability and time frames for implementing IMRT [14]. The results showed that IMRT implementation had begun in a sporadic manner with different delineation, doses and constraints being used. The results of the survey are available as supplementary material. This highlighted the difficulties of implementing a new technique in a rare cancer with limited supporting evidence and few treating clinicians. As such, a working group of specialist clinicians in anal cancer was convened, supported by the Anorectal Clinical Studies Sub Group (CSG) of the National Cancer Research Institute (NCRI), to develop consensus guidance detailing standard radiotherapy volume delineation, dose and fractionation based on the volumes and doses used in the ACT2 study [15]. This was presented at the annual NCRI and other meetings [16] and highlighted in an editorial [14]. A national audit was initiated in order to assess the implementation of this challenging technique. Furthermore, future clinical trials will require an IMRT platform, and as such an IMRT solution was required, ideally with implementation and an audit of implementation before the development of further studies.

The audit presented here was carried out 2 years after the initial survey with the aims:

(i) To benchmark the national delivery of radiotherapy in anal cancer and identify potential for improvements.

(ii) To compare UK practice with National Comprehensive Cancer Network (NCCN) and ESMO-ESSO-ESTRO guidance.

(iii) To assess whether the number of patients receiving IMRT are in keeping with National Radiotherapy Implementation Group (NRIG) IMRT recommendations.

(iv) To document the compliance with suggested UK IMRT guidance.

(v) To describe the acute toxicity of IMRT as per UK guidance in comparison with previous ACT2 published toxicity.

(vi) To provide a UK-wide standard of care to optimise the opportunities for clinical research and improvements in this disease in the future at a national level.

Materials and Methods

We aimed to collect prospective data on all patients with a diagnosis of anal cancer, in all UK National Health Service cancer centres, starting radiotherapy over a 6 month period from 9 February to 27 July 2015. Patient demographic data included the age and gender of patient, whether or not they underwent a pre-treatment stoma, HIV and smoking status. Tumour demographic data included pathology, level of differentiation, stage and site of primary and lymph nodes. Details of chemotherapy and radiotherapy treatment and weekly CTC acute toxicity (v4.03, 2010) during treatment were collected. RTOG grading was used for skin toxicity. Finally patients were asked to complete a European Organization for Research and Treatment of Cancer (EORTC) questionnaire to document the baseline patient-reported outcomes of disease and treatment symptoms [17,18]. Data points collected are documented within supplementary material. A specifically developed web-based data collection form was constructed using Snap WebHost Professional survey software. The data form was reviewed by the RCR Clinical Oncology Audit Committee and, after revision, piloted in five centres. Clinical oncology audit leads acted as points of contact between the RCR and participating centres.

Data were reviewed by RM and DG. On review of the submitted data, grade 3 toxicity was noted if: it resulted in an admission, an interruption or discontinuation of

Please cite this article in press as: Muirhead R, et al., Initial Results from the Royal College of Radiologists' UK National Audit of Anal Cancer Radiotherapy 2015, Clinical Oncology (2016), http://dx.doi.org/10.1016/j.clon.2016.10.005