Clinical and Translational Radiation Oncology 13 (2018) 14–18

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.elsevier.com/locate/ctro

Short Communication

Axillary radiotherapy for nodal lymphoma: What CTV expansion is required to account for absence of pre-chemotherapy treatment position FDG PET-CT?

Robin Prestwich [a,*], Chirag Patel [b], Andrew Scarsbrook [b], Viv Cosgrove [c], Emma Thomas [a], Di Gilson [a], David Bird [c]

[a] Clinical Oncology, Bexley Wing, St. James's University Hospital, Leeds Teaching Hospitals Trust, Leeds LS9 7TF, England, UK
[b] Radiology and Nuclear Medicine, Bexley Wing, St. James's University Hospital, Leeds Teaching Hospitals Trust, Leeds LS9 7TF, England, UK
[c] Medical Physics and Engineering, Bexley Wing, St. James's University Hospital, Leeds Teaching Hospitals Trust, Leeds LS9 7TF, England, UK

ARTICLE INFO

Article history:
Received 15 August 2018
Accepted 3 September 2018
Available online 6 September 2018

Keywords:
Lymphoma
Radiotherapy
Axilla
Clinical target volume
PET-CT

ABSTRACT

Involved site lymphoma radiotherapy clinical target volumes (CTV) require expansion in the absence of treatment-position pre-chemotherapy PET-CT. This prospective imaging study evaluates CTV contouring for axillary lymphoma using diagnostic imaging compared with co-registered treatment-position PET-CT. Generous expansion axially and cranio-caudally is required to encompass pre-chemotherapy disease without treatment-position pre-chemotherapy PET-CT.

1. Introduction

There has been considerable progress in reducing radiotherapy target volumes in lymphoma patients to minimise late complications whilst maintaining local control [1–3]. The concept of involved node radiotherapy (INRT) was developed with the aim of treating only prior sites of lymph node involvement [1]. INRT requires the acquisition of a pre-chemotherapy Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography – computed tomography (PET-CT) scan in the radiotherapy treatment position with the use of the relevant radiotherapy immobilisation devices and subsequent co-registration to the post-chemotherapy radiotherapy planning CT scan. However, few centres routinely acquire a pre-chemotherapy FDG PET-CT in the potential radiotherapy treatment position [4]. The concept of involved site radiotherapy (ISRT) has been developed by the International Lymphoma Radiotherapy Oncology Group (ILROG) [2,3]. The ILROG guidelines provide guidance on delineating a clinical target volume (CTV) to encompass pre-chemotherapy disease, modified to anatomical boundaries, with an additional expansion to account for any uncertainty in defining pre-chemotherapy disease (including the quality and position of pre-chemotherapy imaging, response to chemotherapy, knowledge of potential subclinical extent, volume changes since imaging, proximity to critical structures) with modification to anatomical boundaries. This CTV expansion is essentially based upon clinical judgement [4]. The UK National Cancer Research Institute Lymphoma Radiotherapy Group [5] also developed ISRT guidelines and attempted to quantify the required CTV expansion specifying 1.5 cm craniocaudally in the direction of lymphatic spread with no axial expansion.

There is little data to guide the necessary CTV expansion to account for the absence of pre-chemotherapy imaging in the radiotherapy position. We have performed a prospective imaging study aiming to quantify the required CTV expansion, and have previously reported results for patients requiring head and neck radiotherapy [6]. Axillary radiotherapy is a less common scenario although CTV delineation is particularly challenging compared with the head and neck region, with differences in arm position between scans and less well defined anatomical landmarks. Here, we report data from patients in our imaging study with axillary nodal disease.

* Corresponding author at: Level 4, St. James's Institute of Oncology, St. James's University Hospital, Beckett St., Leeds LS9 7TF, UK.
E-mail address: Robin.Prestwich@nhs.net (R. Prestwich).

https://doi.org/10.1016/j.ctro.2018.09.003
2405-6308/

2. Methods

2.1. Study outline

This is a report on patients with axillary nodal disease included within a prospective single centre imaging study. Inclusion criteria were: age ≥18 years old, histologically proven Hodgkins Lymphoma (HL) or high grade non-Hodgkins Lymphoma (NHL), World Health Organization Performance status 0–2, Ann Arbor Stage I/II disease based upon clinical examination and any radiology investigations previously performed, residual disease in situ after biopsy, PET-CT staging not yet performed, clinical decision that sequential chemotherapy and radiotherapy will be the recommended treatment if stage I/II disease is confirmed on subsequent PET-CT staging. This study was approved by the Research Ethics Committee. Trial registration: ISRCTN Registry: ISRCTN46587767.

A total of 19 patients provided written informed consent and were recruited between October 2013 and January 2016; 3 of the patients who subsequently received chemotherapy and radiotherapy had axillary nodal disease.

2.2. PET-CT imaging

A 5-point thermoplastic immobilisation mask was fabricated prior to PET-CT acquisition, with arms by sides. FDG PET-CT imaging was performed as previously described [6]. A diagnostic half-body PET-CT with arms up on a soft head support was initially performed 60 min following a 400 MBq injection of FDG intravenously; if patients were not able to tolerate the arms up position an arms down position was used. A dedicated contrast-enhanced PET-CT of the axillary region was then acquired with the immobilization mask in place with a radiotherapy head rest, arms down (3–4 bed positions, 2 min per bed position).

2.3. Radiotherapy CT planning scan

The thermoplastic mask fabricated for the pre-chemotherapy PET-CT scan was fitted to assess whether the fit remained optimal. If this was not the case, a new thermoplastic mask was made attempting to maintain a similar neck position. The CT planning scan was acquired with intravenous contrast and 2 or 3 mm slice thickness (dependent upon institutional protocols at the time).

2.4. CTV contouring

Contouring was performed by an experienced radiation oncologist with access to clinical data and diagnostic imaging. To minimise recall, a minimum two week interval was mandated prior to contouring for each individual patient using different methods.

2.5. Contouring using side-by-side assessment of PET-CT acquired in diagnostic position ($CTV_{diagPET}$)

A post-chemotherapy CTV aiming to encompass initially involved lymphoma tissue was contoured using the pre-chemotherapy diagnostic position PET-CT by side-by-side assessment (blinded to treatment position PET-CT), taking into account changes in lymphoma volume and anatomical changes, whilst accounting for anatomical boundaries. To allow quantification of the 'errors' introduced by contouring without optimal co-registered imaging, no additional CTV expansion was undertaken ($CTV_{diagPET}$).

2.6. Contouring using co-registration of PET-CT acquired in radiotherapy position to planning CT scan (CTV_{INRT})

Contouring was performed according to the principles of the ILROG guidelines [2,3] and as previously described [6] (CTV_{INRT}). The contrast-enhanced pre-chemotherapy PET-CT acquired in the radiotherapy position was used to manually contour a gross tumour volume (GTV). Manual rigid registration was undertaken matching to the chest wall and local soft-tissue in the region of the delineated GTV using Mirada RTx v1.4 software (Mirada Medical, Oxford, UK).

3. Data analysis

3.1. Assessment of superior and inferior CTV extent

Distance between the superior slices of the CTV_{INRT} and $CTV_{diagPET}$ was recorded. Distance was similarly recorded for inferior slices.

3.2. Positional analysis

Positional metrics were used to compare CTVs in the axial plane as previously described [6,7]. The most superior and inferior overlapping slices of the CTVs (CTV_{INRT} and $CTV_{diagPET}$) were defined as the limits of the volume, excluding differences in the superior-inferior CTV length from influencing positional metrics. Positional metrics were calculated using ImSimQA software (v3.1.5, OSL, Shrewsbury, UK): Mean distance to conformity (MDC); Centre of gravity distance (CGD); DICE index; conformality index (CI); sensitivity index (Se. Idx). For the CTV_{INRT} and $CTV_{diagPET}$ axial plane comparison, the Se. Idx. calculated the overlap between $CTV_{diagPET}$ and CTV_{INRT} as a percentage of the volume of CTV_{INRT}.

3.3. Statistics

Linear mixed effects models were used to determine the significance of the differences between CTV_{INRT} and $CTV_{diagPET}$ [8]. A significant ρ-value was considered to be $\rho < 0.05$.

4. Results

3 patients who entered the study subsequently received axillary radiotherapy. Patients 1 and 3 had Hodgkin's lymphoma and patient 2 diffuse large B cell lymphoma; age range 21–70 years; mean pre-chemotherapy GTV 78 cm^3 (range 33–141). Each patient had received chemotherapy prior to planning for radiotherapy. Patient 1 had the diagnostic PET-CT scan arms down due to discomfort maintaining an arms-up position. (Fig. 1 provides an example of CTV_{INRT} and $CTV_{diagPET}$ in axial and coronal images.)

4.1. Intra-observer variation in CTV generation

Intra-observer variation in delineating CTV_{INRT} and $CTV_{diagPET}$ on 3 occasions for each patient are summarised in Table 1. Variation CTV extent was large for $CTV_{diagPET}$, with a mean of 7 mm superiorly and 13 mm inferiorly. By contrast, CTV_{INRT} varied by only a single CT slice (2–3 mm) superiorly and inferiorly. Similarly, CTV_{INRT} was significantly more reproducible in the axial plane compared with $CTV_{diagPET}$ for all positional metrics.

4.2. Comparison of CTV_{INRT} and $CTV_{diagPET}$: Superior and inferior extent

Table 2 summarises CTV volumes and differences in the superior and inferior boundaries of CTV_{INRT} and $CTV_{diagPET}$. Overall vol-