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Original Article

Quality Assurance Peer Review for Radiotherapy for Haematological Malignancies

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Abstract

Aims: To assess the impact of weekly scheduled peer review of radiotherapy planning contours for definitive treatment of haematological malignancies based on rates of recommended changes.

Materials and methods: Analysis of a prospective database of contour-based peer review at weekly scheduled meetings for patients undergoing definitive radiotherapy for haematological malignancies at a single large cancer centre between January and December 2018. Recommended changes were prospectively classified as involving the gross tumour volume (GTV), clinical target volume (CTV), planning target volume (PTV), organs at risk or dose fractionation. A univariate analysis was carried out to explore the associations between recommended changes and disease, treatment characteristics and consultant experience.

Results: In total, 158/171 (92%) of all cases of haematological malignancy undergoing definitive radiotherapy were prospectively peer reviewed over a 12-month period. Overall, 26/158 (16.5%) changes were recommended within the peer review meetings. This included a total of 27 contour changes (GTV, CTV or PTV) in 25 patients. An increase in CTV was the most common change, occurring in 20/158 (12.7%) cases. One dose-fractionation change was recommended. Additional advice regarding planning technique/set-up was documented in 5/158 (3.2%) patients. There were no significant associations between rates of recommended change and disease type, stage, prior chemotherapy, first line versus refractory/relapse, anatomical site, radiotherapy technique or consultant experience.

Conclusions: Weekly contour-based peer review meetings resulted in a high rate of recommended changes. Compliance was high. Peer review was potentially beneficial for all disease and treatment characteristics and for any degree of clinician experience.

Key words: Lymphoma; peer review; plasmacytoma; quality assurance; radiotherapy

Introduction

Peer review is recommended as part of quality assurance in the radiotherapy process [1]. Peer review can be defined as re-evaluation of treatment planning decisions by at least one radiation oncologist who is not the prescribing physician [1]. Peer review guidance has been provided by the Royal College of Radiologists in the UK [2], in addition to the Canadian Partnership for Quality Radiotherapy [3], the American Society for Radiation Oncology [4] and the Royal Australian and New Zealand College of Radiologists [5]. There is no standardised protocol for how peer review should take place, and it can be based on an evaluation of contours and/or plan dosimetry [6]. Peer review is challenging to implement, particularly in tumour sites with fewer clinicians based in one centre. A significant potential downside to peer review is the time cost for all involved. Therefore, it is important to evaluate the process and potential benefits in each tumour site.

Radiotherapy is widely used in curative intent treatment for haematological malignancies, including lymphoma and solitary plasmacytoma. Radiotherapy planning for haematological malignancies is challenging, with clinicians encountering a wide range of differing diseases and multiple anatomical locations. In addition, treatment is delivered in a number of different settings, including radiotherapy alone, part of combined modality treatment following short-course chemotherapy for early stage disease, consolidation radiotherapy for bulk or extranodal disease after full-course chemotherapy and salvage treatment in the chemotherapy refractory/relapse setting.

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Modern radiotherapy delivery for lymphoma and solitary plasmacytoma is designed to achieve local control while minimising radiation dose to normal tissues. This aim has led to the development of the concept of involved site radiotherapy (ISRT) for lymphoma [7–11]. ISRT is based on the delineation of gross tumour volumes (GTV) and clinical target volumes (CTV). In the context of radiotherapy following chemotherapy, accurate reconstruction of the pre-chemotherapy GTV based on baseline pre-chemotherapy imaging can be particularly challenging. The concept of ISRT includes an expansion of the CTV to account for uncertainties in defining the pre-chemotherapy extent of disease, including the position and quality of pre-chemotherapy imaging [8,9], and is based on clinical judgement [12]. Most centres are unable to obtain pre-chemotherapy positron emission tomography-computed tomography scans in a radiotherapy treatment position to facilitate subsequent radiotherapy planning [12]. Only two studies have provided data to guide the extent of CTV expansion in the absence of this optimal treatment position pre-treatment imaging [13,14]. Multiple contouring studies have shown significant intra- and interobserver variability in generating ISRT CTVs [13–16].

Implementing peer review as part of the process of radiotherapy planning for haematological malignancies is particularly appealing in the context of the treatment of multiple anatomical sites and diseases, a prominent role for clinical judgement and intra- and interobserver contouring variability [13–16]. Reports of mixed tumour sites have included very limited numbers of patients with lymphoma (0.2–4.6% of patients reported) [3,17–19]. We are not aware of any dedicated reports providing a detailed evaluation of the peer review of radiotherapy for haematological diseases.

Here we detail our experience in a large UK centre of peer review of radiotherapy delivered with curative intent, either alone or as part of combined modality treatment, for haematological malignancies. Rates and types of recommended change, together with the influence of clinician seniority, are evaluated.

Materials and Methods

A weekly quality assurance meeting has taken place at Leeds Cancer Centre for a peer review of haematological malignancy radiotherapy contours since June 2017. Data have been prospectively collected since the inception of the meetings. The 12 months of data collection between January and December 2018 were retrospectively analysed for this report.

Case Review

During this time period, three consultant clinical oncologists were involved in treating haematological malignancies with radiotherapy and all had time allocated in job plans to attend the meeting (a minimum of two are required for the meeting to take place).

The weekly meeting is scheduled for 1 h. The meeting is routinely attended by clinical oncology trainees attached to the team and by a member of the dosimetry team. The role of the dosimetrist is to provide planning advice and to aid communication between clinicians and the radiotherapy planning team with regards to priorities/expectations for the plan. Case review takes place with access to two computers with large screen displays. One computer is used to display radiotherapy contours and diagnostic imaging, whereas the other is used to access electronic patient records and to document outcomes of peer review in electronic patient notes and in the prospective database.

The intention of the meeting is to peer review contours for all patients due to have radical treatment for haematological malignancy who have been contoured during the preceding week (excluding patients receiving electron treatment for whom there were no contours to review). Palliative cases are not reviewed within the meeting. Patients are identified by communication between treating consultants. Review is intended to take place regardless of attendance of the treating oncologist. For each case, a clinical synopsis is presented by the treating clinician or a trainee in the absence of the treating oncologist. Relevant radiology images are displayed. GTV and CTV contours are presented for each case. Organs at risk (OAR) are only reviewed if requested by the treating oncologist. Radiotherapy plans are not routinely reviewed but could be accessed if already completed. A period of 10 working days is routinely provided between a planning computed tomography scan and the start of treatment and consequently contours are usually reviewed before the production of a treatment plan. The meeting aims to reach a consensus on the radiotherapy treatment volumes.

Contouring and Treatment Approach

Patients receiving treatment to the neck region, axilla and upper mediastinum are routinely immobilised with a five-point thermoplastic mask. Intravenous contrast is routinely used for radical radiotherapy where this aids target volume delineation. Oral small bowel contrast is used at the clinician's discretion for abdominal treatment. Four-dimensional simulation is routinely used for stomach, spleen and lung radiotherapy. Planning computed tomography scans are carried out with 2 mm slice thickness. Diagnostic imaging is not carried out in the radiotherapy treatment position and co-registration of pre-chemotherapy diagnostic imaging to planning computed tomography is not available. Contouring is carried out according to institutional protocols, which are based around the principles of ISRT as per International Lymphoma Radiation Oncology Group guidelines for Hodgkin [8], nodal non-Hodgkin lymphoma [9], extranodal disease [10] and plasmacytomas [20]. Treatment is delivered with volumetric modulated arc therapy (VMAT) or three-dimensional planning for neck treatment, butterfly VMAT [21] or three-dimensional planning for mediastinal treatment and three-dimensional planning for other anatomical sites.

Outcomes

Outcomes of peer review, including whether changes are recommended, at the quality assurance meeting are prospectively documented in electronic patient records and the electronic database. Details of recommended changes to GTV, CTV, planning target volume (PTV), OAR, dose fractionation and if there are multiple changes on one case are recorded as free text. Additional comments and advice, e.g. regarding set-up, the type of planning, are also documented in electronic patient records and the database.

Statistical Analysis

The main end point of analysis was to determine the proportion of cases for which changes were recommended. Documented advice regarding set-up/type of planning (three-dimensional planning versus VMAT) was not considered in the overall 'rate of change' as it may have been implemented regardless of the meeting discussions. A comparison of the rate of change was made between the initial and the subsequent 6-month experience. The analysis was carried out using IBM SPSS Statistics, Version 21 (Armonk, NY, USA). Univariate logistic regression and Fisher's exact test were carried out for categorical/nominal and binary variables, respectively, to identify potential predictors of changes. Disease type, anatomical site, stage (analysed as ordinal data with stages I and IE grouped), previous short- or long-course chemotherapy, first-line treatment versus refractory/relapse, three-dimensional planning versus VMAT versus butterfly VMAT and consultant experience were included in the analysis. Statistical significance was declared at $P < 0.05$.

Results

In total, 158 patients were discussed within weekly haematology radiotherapy peer review quality assurance meetings between January and December 2018. Four of these patients were having two sites treated. In total, 48 meetings took place. Meetings did not take place in 3 weeks of the year due to the presence of only one consultant and one Bank Holiday. One hundred and seventy-six patients underwent 'radical' radiotherapy with curative intent at Leeds Cancer Centre during the 12-month period of 2018. Five received electron therapy and were not included in the peer review. The overall compliance rate was 158/171 (92%). The median number of cases discussed per meeting was three (range one to nine). The average time taken during the meeting each week to review radiotherapy contouring cases was 30 min (range 10–60 min), with an average time spent per case of 10 min (range 5–15 min).

Table 1 provides a breakdown of cases discussed by disease and stage; 81/158 (51.3%) cases were diffuse large B cell lymphoma and 26/158 (16.5%) cases were low grade B cell lymphoma (follicular lymphoma or marginal zone lymphoma); 103/158 (65.2%) patients had stage I/II disease and 55 (34.8%) had stage III/IV disease; 54/158 (34.2%) patients were receiving radiotherapy to extranodal sites; 22/158 (13.9%) patients were planned to receive radiotherapy as part of treatment for refractory/relapsed disease. Radiotherapy was planned as definitive treatment without chemotherapy in 45 (28.5%), after short-course chemotherapy for early stage high grade lymphoma in 26 (16.5%) and after the completion of full-course chemotherapy in 87 (55.1%) patients. Radiotherapy was planned to be delivered by a three-dimensional planned technique in 99 (62.7%), VMAT in 49 (31.0%) and butterfly VMAT in 10 (6.3%) patients.

Recommended Changes

Changes were recommended within the meeting for 26/158 cases (16.5%); details of the changes were prospectively recorded in each case on the electronic notes record. In total, 27 contour changes (GTV, CTV or PTV) were recommended in 25 patients. Two patients were recorded as having two changes (increase and decrease in different parts of the CTV in one patient and a decrease in the CTV and a PTV margin change in one patient). An increase in CTV was the most common change, occurring in 20/158 (12.7%) cases. By contrast, GTV changes were unusual, occurring in 2/158 (1.3%) patients. OARs were only altered in one case (heart contour in a butterfly VMAT case). Details of these changes are shown in Table 2. In addition to changes being recommended, advice was documented in 5/158 (3.2%) patients. This included set-up advice in three patients (relating to bladder/rectal filling) and in the type of radiotherapy delivery in two patients (suggestion of VMAT rather than three-dimensional planning).

The overall rate of change in the first 6 months versus the second 6 months of this period was 13/73 (18%) versus 13/85 (15%). All recommended changes were implemented. One patient who had already had a treatment plan generated required replanning before the start of treatment as a result of contour peer review. No delays in treatment start were identified as a result of the peer review process.

Table 3 provides the rates of recommended changes according to anatomical site, prior chemotherapy, diagnosis, stage, first line or part of refractory/relapse treatment, radiotherapy technique and consultant experience. The highest rates of changes were with treatment to the mediastinum (31%), although there were no significant differences in rates of change by anatomical site. The three consultant clinical oncologists involved had 6, 13 and 23 years of experience treating haematological malignancies at consultant level; there was no significant association between rates of change and consultant experience ($P = 0.09$). One consultant also treats head and neck cancer – the rate of change in the neck region for that consultant was 0/19. One consultant treats breast cancer (a rare anatomical site for radiotherapy for haematological malignancies) and the other solely haematological malignancies precluding acquisition of further data comparing rates of change as per anatomical site expertise.

Table 1
Details of peer reviewed cases by disease and stage

Disease	Stage					Total
	I	IE	II	III	IV	
DLBCL	14	11	10	10	36	81
Mediastinal B cell lymphoma	1	0	3	0	3	7
Central nervous system lymphoma	0	4	0	0	0	4
Hodgkin lymphoma	6	0	5	1	3	15
LP nodular Hodgkin lymphoma	4	0	3	0	0	7
Marginal zone lymphoma	3	6	3	0	0	12
Follicular lymphoma	8	2	4	0	0	14
Burkitt's lymphoma	2	0	0	0	0	2
Mantle cell lymphoma	1	0	0	0	0	1
Plasmacytoma	0	6	0	0	0	6
T cell lymphoma	2	1	4	0	2	9
Total	41	30	32	11	44	158

DLBCL, diffuse large B cell lymphoma; LP, lymphocyte predominant.

Table 2
Summary of changes recommended/treatment advice documented

Recommended changes	No. cases (%)
GTV change	2 (1.3)
CTV increased	20 (12.7)
CTV decreased	3 (1.9)
PTV change	2 (1.3)
OAR change	1 (0.6)
Dose-fractionation change	1 (0.6)
Other documented advice	
Set-up advice	3 (1.9)
Type of planning advice	2 (1.3)

CTV, clinical target volume; GTV, gross tumour volume; OAR, organ at risk; PTV, planning target volume.

Discussion

Variation in clinician contouring has been described as one of the 'weakest links' in the series of processes in radiotherapy treatment delivery [22,23]. There is strong evidence across multiple tumour sites that the quality of contouring [24,25] and clinician experience [26] affect clinical outcomes. In co-operative group trials, trial protocol violations have been shown to be associated with higher rates of treatment failure, inferior survival outcomes and increased toxicity [27]. The volume of radiotherapy delivered in a treating centre was shown to correlate with the quality of treatment plans (for head and neck cancer) [25]. Effective peer review is a potential method to address these issues. It has been suggested that rates of change >10% imply the value of peer review [28]. A systematic review in 2017 [1] identified 11 studies across multiple tumour sites and reported a mean modification rate of 10.8% of radiation treatment plans. Ballo *et al.* [17] found that tumour sites treated with intensity-modulated radiotherapy had higher rates of change from peer review. As expected, the rates of changes arising from peer review are related to the complexity of radiotherapy planning for the tumour site [29–31].

Although there is an increasing body of evidence evaluating peer review in multiple tumour sites, there are few data for radiotherapy for haematological malignancies. We are not aware of any dedicated reports providing a detailed evaluation of the peer review of radiotherapy for haematological diseases. Lymphoma radiotherapy peer review has been included in a small number of mixed tumour reports. These are summarised in Table 4, which serves to highlight the very limited numbers of patients with haematological malignancy reported and that these series largely predated the International Lymphoma Radiation Oncology Group guidelines [3,17–19]. One recent cross-sectional analysis of peer review across 14 Canadian centres found an overall 3.3% rate of change and provided analysis by anatomical site but did not separate haematological malignancies [32]. A non-concordance rate of 50% was reported for lymphoma but was based on only two patients in a study evaluating the quality of peer review in a cancer network in the USA by assessing non-concordance between community hospital-based peer review and peer review by an expert panel at an academic centre [33].

Our data report on our experience of a peer review programme that had been underway for 6 months before the reported data. The overall rate of recommended change of 16.5% is higher than the average found by the systematic review of multiple tumour sites [1]. This may reflect the complexity of radiotherapy for haematological malignancies, including the variability of anatomical sites and difficulties in contouring target volumes following chemotherapy (with which there are commonly significant anatomical changes and regression of tumour volumes). Most of the recommended changes were based on the CTV. In the treatment of lymphoma, the generation of the CTV according to International Lymphoma Radiation Oncology Group guidelines incorporates clinical judgement [8,9] and, hence, might be expected to be the step that would benefit most from peer review. The meeting additionally led to advice with regards to the set-up and planning technique for some patients. As it could not be determined whether these would have been implemented without the peer

Table 3
Summary of rates of recommended changes

	Total	No. changes	% Rate of change	*P* Value
Anatomical site				
Head and neck	44	9	20%	0.60
Mediastinum	13	4	31%	
Axilla	10	1	10%	
Abdomen (including spleen)	19	3	18%	
Pelvis	18	3	17%	
Extranodal	54	6	11%	
Chemotherapy				
None	45	7	16%	0.38
Short course	26	2	8%	
Full course	87	17	20%	
Diagnosis				
DLBCL	82	13	16%	0.61
Hodgkin's	15	5	33%	
LP nodular Hodgkin's	7	0	0%	
PTCL	8	0	0%	
Mediastinal B cell	7	1	14%	
Mantle cell	1	0	0%	
Marginal zone	12	0	0%	
Burkitt's	2	0	0%	
Follicular	14	3	21%	
Central nervous system lymphoma	4	0	0%	
Plasmacytoma	6	4	66%	
Stage				
1	48	7	15%	0.41
1E	24	2	8%	
2	32	6	19%	
3	11	4	36%	
4	43	7	16%	
Indication				
Part of first line	136	21	15%	0.37
Relapse/refractory	22	5	23%	
Radiotherapy technique				
3DP	99	14	14%	0.20
VMAT	48	8	17%	
Butterfly VMAT	11	4	36%	
Consultant				
1 (6 years' experience)	79	8	10%	0.09
2 (13 years' experience)	31	6	19%	
3 (23 years' experience)	48	12	25%	

3DP = 3 dimensional planning; DLBCL, diffuse large B cell lymphoma; LP = lymphocyte predominant; PTCL = peripheral T cell lymphoma; VMAT, volumetric modulated arc therapy.

review process they were not included in the overall rate of change, but represent a potential additional benefit of the peer review process.

From a time and resource point of view, it is appealing to focus peer review on complex/rare cases. However, the rates of recommended change arising from peer review were not significantly influenced by anatomical site, disease type, stage, first-line versus refractory/relapse indication, prior chemotherapy or radiotherapy technique. It is interesting to note that there were no changes recommended out of 19 patients receiving treatment to the head and neck region for the clinician who also specialises in the treatment of head and neck cancer. This suggests that anatomical site expertise may have a valuable role in the outlining and also a peer review meeting may benefit from the differing anatomical site expertise offered by the clinicians. We introduced butterfly VMAT [21] at the start of 2018 and it is notable that the rates of change were high for these patients (36%), although numbers were small. This probably reflects a learning curve and also the complexity of outlining for mediastinal treatments.

Across differing tumour sites, some [3] but not all [28,34] series have found that consultant experience may reduce the value of peer review. The data in our series are limited in ability to evaluate the influence of clinician experience as the most inexperienced clinician had 6 years at consultant level. Clearly clinician experience, skill and personality may all affect the peer review process. It has been suggested that more senior clinicians are less likely to have changes proposed due to a 'hierarchical bias' [29,30]. It is notable that in this report and in head and neck cancer from our institution [34], seniority did not lead to lower rates of changes. This

Table 4
Previous studies of peer review of mixed tumour types including haematological malignancies

Study	Setting	Location	Study period	Overall size of series (*n*)	Overall rate of change	No. haematological cases	Rate of change in haematological cases
Mitchell *et al.* [18]	Single institution	USA	2012–2014	442	9.5%	16 (0.2%)	25%
Lefresne *et al.* [3]	Single institution	Canada	2012	1247	7%	3% of total (exact number not stated)	8%
Ballo *et al.* [17]	Single institution	USA	2007–2011	2830	12.2%	105 (3.7%)	12.4%
Brundage *et al.* [19]	Single institution	Canada	1989–2096	3052	4.1%	140 (4.6%)	Not specified

type of experience relies upon an open and non-hierarchical approach to peer review.

Peer review can be based on contours or plan evaluation, although most programmes are based on contour rather than dosimetry assessment [29]. A downside of dosimetry assessment is that, if changes are recommended, full replanning is required, which is labour intensive. However, contour-based peer review should not lead to delays in treatment starting if changes are made. At our centre there is usually adequate time for peer review of contours to take place before the treatment start date to allow changes to be made without leading to delays. We do not always wait for peer review before putting contours through for plan generation, in order to avoid delays in treatment. This does carry the potential requirement for replanning, if contour changes are made; only one replan was required in this period due to contour changes.

Peer review can be based around an 'on-demand' model [28,35] or regular scheduled meetings [34]. The meeting approach with more than two clinicians has the advantage of providing more 'eyes' on the case, although it is potentially time-intensive. We have found that the scheduled meeting approach to peer review for haematological malignancies has additional potential benefits within our centre. Our service is set up based on three video-linked multidisciplinary meetings (MDT) with peripheral hospitals in addition to a central MDT. Our meeting is scheduled for 1 h and part of that time is regularly used for the consultants to discuss potential radiotherapy decisions arising from these MDT meetings. In addition, trainees are able to attend the meetings and can benefit from seeing/inputting into a wide range of cases.

One potential limitation of our series is that we had only implemented the peer review meeting 6 months before the start of the data reported. Some peer review reports suggest that rates of changes recommended may become less common with experience of peer review within a team [17,19,30,36]. However, similar to our experience in head and neck cancer [34], we found very similar rates of recommended change between the initial and the final 6 months of the time period, suggesting that this represents a stable process. A further limitation is that our reported experience is from a single large centre with three specialist clinicians. Other centres may not have more than one to two clinicians and this model of peer review may not be feasible. Alternatives could rely on electronic link ups between centres, as reported previously [37]. Although challenging to establish, peer review based on more than one centre has the advantage of minimising the risk of confirmation bias within an established peer review process.

In summary, a weekly meeting contour-based peer review of cases of definitive radiotherapy for haematological malignancies has led to a high rate (16.5%) of recommended changes, in addition to further treatment advice (e.g. set-up and planning advice). The value of peer review did not diminish with time.

Conflicts of Interest

The authors declare no conflicts of interest.

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