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Deep inspiration breath-hold for mediastinal lymphoma patients: Evaluation of a 5-year service

Katie S. Jones [a,*], Amanda Webster [a,b], Georgios Ntentas [c,d], Jessica L. Brady [e], N. George Mikhaeel [e]

[a] Department of Radiotherapy, Guy's & St Thomas' NHS Foundation Trust, London, UK
[b] Department of Radiotherapy, University College Hospital, London, UK
[c] Nuffield Department of Population Health, University of Oxford, Oxford UK
[d] Department of Medical Physics, Guy's & St Thomas' NHS Foundation Trust, London, UK
[e] Department of Clinical Oncology, Guy's & St Thomas' NHS Foundation Trust, London, UK

A B S T R A C T

Deep inspiration breath-hold (DIBH) is an advanced radiotherapy technique that has been shown to have dosimetric benefits in the treatment of patients with mediastinal lymphoma. Whilst there is much published data on the use of DIBH in breast radiotherapy, reports on the use of the technique in mediastinal lymphoma patients remain limited. As the first NHS centre in the UK to implement DIBH in this pt group, we have evaluated our experience and success in using this technique over a 5 year period.

Introduction

Over the past decades the optimal radiotherapy treatment for mediastinal lymphoma patients has changed significantly; from mantle field treatment in the 1990 s, to conformal radiotherapy and the introduction of Intensity Modulated Radiotherapy (IMRT) in the 2000 s [1]. Patients undergoing mediastinal radiotherapy for lymphoma have a risk of serious radiation-associated late toxicities such as cardiovascular disease and secondary cancers [2]. It was, hypothesised that this patient group could benefit from the use of a deep inspirational breath-hold (DIBH) technique, which has been previously implemented in breast cancer treatment, achieving heart sparing, as well as reduced lung toxicity [3].

Treatment for mediastinal lymphoma using DIBH has been investigated in several studies, first published in 2010. DIBH has shown to reduce radiation dose to organs at risk (OARs) such as heart and lungs [4] and allows a reduction in the clinical target volume (CTV) to planning target volume (PTV) margin. With optimal IMRT becoming more prevalent in recent years, different radiotherapy methods were examined, and it was found that IMRT techniques showed superior target coverage and OAR sparing, although creating a larger low dose bath when compared to conformal RT [5]. In 2018 Starke et al. assessed the volumetric modulated arc therapy (VMAT) on both patients in free-breathing (FB) and DIBH [6]. They compared full arc VMAT (F-VMAT) to Butterfly VMAT (B-VMAT) while establishing if DIBH had an additional benefit. They found a reduction in heart dose for patients treated with DIBH F-VMAT, while those treated with DIBH B-VMAT had reduced lung and breast dose.

Guy's cancer centre (GCC) is a national referral centre for lymphoma patients. Since 2016, all patients referred for mediastinal lymphoma radiotherapy at GCC have been considered for treatment in DIBH, using either B-VMAT or F-VMAT. We were the first NHS radiotherapy centre in the UK to implement this technique. The technique delivery and verification have changed over time in line with developments within the department. New immobilisation was introduced to deliver the B-VMAT technique. Additionally, there has been an increase in the level and complexity of Image-Guided Radiotherapy (IGRT) used in this patient group, from kV-kV orthogonal imaging in 2016 to daily CBCT with an online correction to 0 mm currently being utilised.

The aim of this work was to analyse the patients treated for mediastinal lymphoma in DIBH, with or without the butterfly technique, at GCC. Analysis was provided for patients treated between 2016 to the present day, to ensure that the service delivered has been optimal from the implementation phase. This study is supplemented by a short communication paper'Introduction of deep inspirational breath hold and Butterfly-VMAT techniques into clinical practice for the treatment of mediastinal lymphoma- lessons learned from an experienced centre' which details the implementation of the technique and how the B-VMAT

* Corresponding author.
E-mail address: katie.jones98@nhs.net (K.S. Jones).

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technique has impacted the service.

Methods

Data collection

Individual Patient data for this study was retrospectively collected from patients' attendances, referral documents, and patient entries in the ELEKTA MOSAIQ patient management system version 2.6. All data were anonymised and stored on a secure network drive with password protection. On-treatment imaging data was extracted from the patients' electronic imaging records, including annotations from treatment staff and CBCT images.

Patient Pathway

Clinical assessment: At the patient's initial clinic appointment, the clinical team review the patient's diagnostic imaging, based on the anatomical site of disease, decided whether the patient requires treatment with DIBH. Patients are then consented to radiotherapy and given an information sheet on DIBH which denotes background information including the rationale for treating in DIBH and some techniques to practice at home. All patients are referred for DIBH in the first instance.

Pre-treatment DIBH screening: Patients are screened for suitability at the pre-treatment scan. This screening excludes patients with breathing difficulties such as chronic obstructive pulmonary disease, patients unable to hold their breath for a minimum of 20 s at varying intervals, and patients unable to comply with the breath-hold terminology due to cognitive impairment. The breathing must be non-erratic and measured to the same repeat point on the patient's mediastinum, with the patient in the treatment position. Patients are informed that they will be coached to breathe in a specific way. RTTs are trained to encourage the patient to take a comfortable deep breath, ensuring their shoulders are relaxed and no arching of their back. The patient is then coached through two breaths using the specific terminology 'Take a breath in through the nose, and out through the mouth'. This is to allow assessment that the patient can take deep breaths without significantly changing their position, as well as accustoming the patient to the volume of breath required. At this point breathing instructions are repeated, and RTTs will inform the patient that they will be required to hold their breath on the next attempt. Patients are instructed to hold their breath using the terminology 'take a deep breath in and hold'; this terminology is consistent from this point throughout treatment. A timer is then used to ensure breathold is held for a minimum of 20 s, if this is not achieved the patient is not suitable for DIBH treatment.

RT planning CT: Scan limits are individualised depending on the extent of the disease; however, the whole lungs and heart should be included for any patient with DIBH. Both free-breathing and DIBH scans are taken, to ensure if patients are unable to tolerate breath-hold, switching to a free breathing plan is achieved efficiently. More recently this has enabled the development of permanent mark-free treatment, as the free breathe scan is utilised in patient set-up. Initially, contrast was given in the FB phase; however, following an exploratory internal study the optimal delay for patients to receive contrast in the DIBH phase has been calculated. These patient specific delays are calculated using patient weight, the area requiring contrast as well as the cannula flow rate. Patients are immobilised using a variety of equipment depending on the site of disease and sex of the patient. The most commonly used set-up is a thoracic board with arms above the head. A breast board can be used in female patients to displace the breast tissue away from the treatment volume. Similarly, some female patients may benefit from being treated with arms down. An SPSS head and neck board and 3–5-point thermoplastic shells are used for patients with disease above the larynx. A Q-fix board with a 3-point thermoplastic shell and separate shoulder immobilisation is further utilised for these patients with disease above the larynx, who also have additional axillary disease.

Treatment planning: The treatment planning techniques have been described previously [6]. All patients have a pre-chemotherapy PET scan with arms up which is fused with their RT planning scan, note this PET is not currently done in DIBH, but is the process is being developed as a service improvement. Either a F-VMAT or B-VMAT plan produced depending on disease location and ability to perform breath hold. If a patient could not perform breath-hold during the pre-treatment CT, a plan on the free-breathing scan was produced instead.

Treatment: Patients are treated on Varian Truebeam Linear accelerators and are set up and monitored during treatment using the AlignRT® surface guided system. Tolerances on AlignRT® are set to 5 mm and 3 degrees to represent the small CTV to PTV margin (0.5 cm)and the position is verified with imaging.

Verification: Treatment verification consists of daily cone-beam CT (CBCT) to an online correction of 0 mm from 2017. CBCT's are auto-matched to the bone, and this is then checked before adjustments are made to optimise soft tissue. Patients with treatment volumes over 17.0 cm have a weekly multi-scan, which involves two CBCT's taken at 15.0 cm succession to ensure the whole PTV volume is encompassed. Before 2017 the departmental protocol was in line with minimal IGRT guidelines [7], and patients were imaged using kV-kV orthogonal pair; the AlignRT® system has been used for DIBH lymphoma patients since 2014.

Review: Patients with visible contour change of $>$ 1.0 cm after three fractions are flagged to the planning team for dosimetric review to ensure the dose delivered in the patient's current plan is still optimal. Any internal anatomical changes are flagged immediately to a clinician. If PTV cannot be covered by a manual soft tissue adjustment, patients are not treated on this fraction until intervention from a clinician. Guidance is provided as to whether patients can continue treatment on the current plan, or if the PTV coverage requires a re-plan, or a full re-scan and re-plan.

Results

From October 2016 to September 2021, 110 patients were referred for mediastinal lymphoma radiotherapy. Of these patients, 105 (95%) were referred for treatment in DIBH. In the remaining 5 (5%) patients, DIBH was not indicated due to the location of their disease. Out of the 105 patients referred for lymphoma radiotherapy in DIBH, 96 (91%) patients were scanned in BH, with only 9 (9%) patients being scanned in FB after being unable to achieve breath-hold at their pre-treatment appointment. (Table 1).

Out of 110 patients, 86 (78%) were scanned using thoracic board immobilisation with arms up. Of the remaining 24 patients, 9 (8%) were treated on a Q-fix board, 11 (10%) were treated on an SPSS headboard with 5 point head and shoulder thermoplastic shell, and the remaining 4 (4%) were treated on a breast board.

A total of 96 patients commenced radiotherapy for mediastinal lymphoma in breath-hold. 59 (62%) of which were treated using B-VMAT in DIBH. The remaining 37 (38%) of patients were treated using conventional F-VMAT also in DIBH.

Of the 96 patients having radiotherapy in DIBH, 10 (13%) patients were re-planned, with 6 (6%) of these patients having a rescan during their treatment. The remaining 3 patients had a re- plan produced to further optimise their current plan, but a rescan was not required. For these patients it was a priority to start treatment, so newly optimised plans were delivered by fraction three. Of the 6 patients requiring a rescan, 1 was rescanned due to incorrect hand pole immobilisation at pre-treatment. 4 patients were re-planned and scanned after anatomical changes during treatment. Anatomical changes are defined as disease regression, progression or patient contour change. There were 2 patients who were rescanned during treatment due to being unable to achieve breath-hold consistently, this includes one of the patients with anatomical changes pertaining to disease progression. Both of these

Table 1
Summary of variable data collected for mediastinal lymphoma patients treated between October 2016 and September 2021.

	Patient Variable	n	Frequency (%)	Comments
	Referred DIBH	105	95	
Breathing technique	Referred for Free-breath	5	5	*Not applicable for disease location*
	Total scanned in DIBH	96	91	
	Total scanned in Free-breathe	9	8	*8% scanned in free-breath after being unable to achieve DIBH.*
Immobilisation	Thoracic board	86	78	
	Q-fix board	9	8	
	SPSS Head and neck board	11	10	
	Breast board	4	4	
Plan choice	B-VMAT	59	61	
	F-VMAT	37	39	
Re-scan & Re-plan	**Re-scan with re-plan**	7	9	
	Reasons for Re-scan & Re-plan			
	Anatomical changes	3	3	*Disease progression/ regression*
	Unable to achieve BH	2	3	*After 3 + fractions*
	Incorrect immobilisation/ procedure at pre-treatment	2	3	
Re-plan only	**Re-plan**	3	3	*To achieve dose constraints*
Image Verification for DIBH	Daily CBCT	93	85	
	Daily CBCT with weekly/daily Multi-scan	22	20	*Volumes > 17.0 cm*
	Weekly kV-kV pair	17	15	*Pre introduction of CBCT*

patients were re-scanned and treated in free breathe for the remainder of their RT course.

Ninety-three (85%) patients were imaged with daily CBCT, with 22 (20%) of these patients receiving a multi-scan either weekly or daily due to a total PTV volume length of > 17.0 cm. Of the 96 patients treated in breath-hold for a portion of their radiotherapy treatment, 8 (8%) patients had notes made on their imaging form about set-up related issues. These issues are categorised in terms of patient position, including shoulder position, pitch and roll issues, and the discrepancy between multi-scans. One (0.9%) patient required a rescan due to these issues. (Table 1).

Discussion

The results of this service evaluation indicate that DIBH for mediastinal lymphoma patients has been successfully implemented. The majority of patients (96 out of 110) managed DIBH and there was minimal to no disruption to their patient pathway to deliver this technique.

The pre-treatment screening process to produce reliable and achievable breath-hold for a variety of patients is sufficient. This is supported by Table 1 showing only two patients required a rescan on treatment after being unable to maintain breath-hold for the duration of their radiotherapy course. The screening process has been formalised to include the same terminology for patients throughout the pathway and is an integral part of the department's protocol. It is noted that formalising this terminology (pre-treatment and on-treatment), prevents ambiguity from being a factor in patients being unable to achieve DIBH consistently.

The patient pathway was not prolonged to deliver DIBH treatment. In the early stages of introducing the technique (up until 2018) there were limited delays to the patient pathway as both F-VMAT and B-VMAT plans were produced. Furthermore, this evaluation reports that only two patients were re-scanned during treatment due to the production of a free-breathing plan. Both free-breathing and DIBH plans were produced for patients who had difficulty meeting breath-hold requirements. Dose constraints were decided on a case-by-case basis dependending on optimal plan choice. This approach individualises the planning technique for each patient. Regardless of whether the patient's treatment was delivered using F-VMAT or B-VMAT, both plans were able to deliver a high standard of radiotherapy care ensuring optimal dose distribution.

10 (9%) patients required a re-plan. The low rate of re-scans in the results indicates that this technique is reproducible, with only 7 patients out of 96 treated in breath-hold requiring a rescan. From the two patients requiring a rescan due to pre-treatment error, this can be accounted for by incorrect immobilisation used in the first instance. This highlights the training required for staff to choose the correct immobilisation and ensure accurate set up at pre-treatment and shows the individualised service provided for the patient's set up. Due to the variable size and location of the disease in this group of patients, immobilisation cannot be standardised for all patients; therefore, staff have been specifically trained to select immobilisation based on these variables to best suit each patient. From the low number of re-scans from incorrect/insufficient immobilisation, we can infer that the staff training has enabled forward-thinking and problem-solving, therefore minimising delays in the patient pathway. We observed that the small CTV to PTV margins used with DIBH did not affect local tumour control [8], and only two patients were re-planned due to anatomical changes which, in both cases, was related to disease progression in patients with latter stage Non-Hodgkin's lymphoma, rather than treatment delivery.

Daily CBCTs enabled RTTs to assess soft tissue anatomy in the thorax and head and neck, as well as plan coverage for every patient. Disease progression was appropriately flagged by RTT's to the clinical team and action was taken, preventing target volume compromise and unnecessary gaps in radiotherapy treatment for intervention, further streamlining the pathway. This shows the importance of training to educate RTTs on soft tissue delineation on CBCT imaging, and the trigger points of escalation. From these results, the reliability of the patient set-up can be interpreted, with only five patients having annotations that indicated there were issues with reproducibility of patient position. This indicates that staff have shown the ability to problem solve the set-up within the limitations of the technique and recognise when a rescan is necessary, thereby improving the service for patients.

There are limitations with the evaluation as the data was retrospectively collated and the quality of the annotations by staff could be more articulate and thorough. This is to be addressed in the future as a service evaluation. It is also acknowledged that to continue to develop this service, this patient cohort should be regularly analysed to ensure the technique develops with the rate of radiotherapy and IGRT nationally.

Conclusion

Treatment using DIBH is the optimal option for most lymphoma patients undergoing mediastinal RT and based on this study, very achievable. The patient pathway does not have to be extended to deliver DIBH; however, consideration should be made to select and coach patients whilst also training and enabling staff to deliver this treatment, as described above. RTTs training is shown to be effective by the utilisation of staff skills when matching 3D images, as well as the skills shown by providing feedback to the MDT on soft tissue and anatomical changes. Few patients have had treatment interruptions and further interventions; thus it is acknowledged that the technique and training package provided is ensuring a high standard of treatment delivery in

these patients.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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