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CLINICAL INVESTIGATION **Lymphoma**

DOSIMETRIC BENEFITS OF INTENSITY-MODULATED RADIOTHERAPY COMBINED WITH THE DEEP-INSPIRATION BREATH-HOLD TECHNIQUE IN PATIENTS WITH MEDIASTINAL HODGKIN'S LYMPHOMA

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Purpose: **To assess the additional benefits of using the deep-inspiration breath-hold (DIBH) technique with intensity-modulated radiotherapy (IMRT) in terms of the protection of organs at risk for patients with mediastinal Hodgkin's disease.**

Methods and Materials: **Patients with early-stage Hodgkin's lymphoma with mediastinal involvement were entered into the study. Two simulation computed tomography scans were performed for each patient: one using the free-breathing (FB) technique and the other using the DIBH technique with a dedicated spirometer. The clinical target volume, planning target volume (PTV), and organs at risk were determined on both computed tomography scans according to the guidelines of the European Organization for Research and Treatment of Cancer. In both cases, 30 Gy in 15 fractions was prescribed. The dosimetric parameters retrieved for the statistical analysis were PTV coverage, mean heart dose, mean coronary artery dose, mean lung dose, and lung V20.**

Results: **There were no significant differences in PTV coverage between the two techniques (FB vs. DIBH). The mean doses delivered to the coronary arteries, heart, and lungs were significantly reduced by 15% to 20% using DIBH compared with FB, and the lung V20 was reduced by almost one third. The dose reduction to organs at risk was greater for masses in the upper part of the mediastinum. IMRT with DIBH was partially implemented in 1 patient. This combination will be extended to other patients in the near future.**

Conclusions: **Radiation exposure of the coronary arteries, heart, and lungs in patients with mediastinal Hodgkin's lymphoma was greatly reduced using DIBH with IMRT. The greatest benefit was obtained for tumors in the upper part of the mediastinum. The possibility of a wider use in clinical practice is currently under investigation in our department.** **© 2012 Elsevier Inc.**

Hodgkin's lymphoma, Radiation therapy, Intensity-modulated radiotherapy, Deep-inspiration breath-hold radiotherapy, Involved-node radiotherapy.

INTRODUCTION

Patients with early-stage Hodgkin's lymphoma who are treated with combined modality treatments, chemotherapy, and consolidation mediastinal radiotherapy have an excellent clinical outcome, with overall survival attaining approximately 90% (1–4). However, late complications can significantly affect the quality of life of the survivors (5). These late complications (cardiovascular and second malignancies) are due to both large radiation doses and fields (6) and also to chemotherapy (7, 8). Therefore, in an optimal combined modality treatment setting, patients should receive minimal chemotherapy and minimal radiotherapy to lower the risk of late complications without jeopardizing the excellent clinical outcome. The intensity of the treatment could be tailored through an early biologic evaluation with the 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) scanner after several chemotherapy cycles, but this remains to be demonstrated in randomized trials. Radiotherapy can be minimized by reducing doses, reducing the radiation field size using involved-node radiotherapy (INRT) (9–11) and optimizing the delivery of radiation with modern radiation techniques, such as intensity-modulated radiotherapy (IMRT) (12–16) or breathing-adapted irradiation (16).

Basically, respiratory motion can be managed with two different concepts: breathing-synchronized radiotherapy

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(commonly termed gating) (17) or deep-inspiration breath-hold (DIBH) radiotherapy (18). Breathing-synchronized radiotherapy requires external markers. However, it has been demonstrated that external markers are not always well correlated with the movement of the target within the thorax. Consequently, the implantation of radiopaque internal markers is mandatory to correlate the position of the external and internal markers (17, 19). In the case of mediastinal lymphoma, internal tumor radiomarkers would be difficult to place after chemotherapy because major responses have often occurred. DIBH with a spirometer is a reproducible technique and does not require internal markers (18). Furthermore, immobilization of the tumor reduces the blurring effect (internal organ motion leads to a blurry dose distribution) (20) and also offers an opportunity to reduce the margins. We recently reported our experience with 50 patients treated with INRT and either IMRT in free-breathing (FB) patients or DIBH with three-dimensional conformal radiotherapy (16). In this planning study, we assessed whether the dosimetric parameters of organs at risk (OARs) were improved by combining DIBH with IMRT, when compared with FB IMRT. The combination of IMRT and DIBH is in the process of being implemented in patients with Hodgkin's lymphoma in our department.

METHODS AND MATERIALS

Patients and simulation

All patients with early-stage (*i.e.*, Stage I or II) Hodgkin's lymphoma involving the mediastinum, and referred to our radiotherapy department, were studied. Included in this study were 28 consecutive patients. They were treated with either FB IMRT or DIBH conformal radiotherapy. Patients underwent simulation computed tomography (CT) (Sensation, Siemens, Erlangen, Germany) while immobilized in the supine position with a customized five-point immobilization mask. The CT images were obtained using 5-mm slices in two modalities for each patient: (*1*) the FB modality and (*2*) the DIBH modality, using the spiro Dyn'RX system (Spiro Dyn'RX system, Dyn'R, Muret, France). Image acquisition was performed during deep inspiration, measured with a spirometer. Patients wore video glasses that allowed them to visually monitor their breathing.

Volume definition

Contouring was performed on both CT scans (FB and DIBH) by the same physician (T.G.) using Imago (Dosisoft, Cachan, France). The clinical target volume was defined according to the INRT concept. The guidelines for this concept have been described by Girinsky *et al.* (9–11). The gross target volume length was that of the tumor mass before chemotherapy, and the width was that of the residual tumor after chemotherapy. When available, a prechemotherapy FDG-PET scan was used to increase the detection of involved lymph nodes (10, 15). A 10-mm isotropic margin was added for the planning target volume (PTV) for both the FB and the DIBH modalities. The contoured OARs were the lungs, the heart, and the origin of the coronary arteries (OCA), which constituted the first 3 cm of the aorta.

IMRT planning

The IMRT treatment plans were generated by Konrad V2.2.23 (Siemens, Erlangen, Germany) for a linear accelerator Oncor Impression (Siemens, Erlangen, Germany) with a multileaf collimator (82 leaves) and a 6-MV photon beam. Five equidistant coplanar beams were used. Normalization was done at the isocenter of the fields, which was the center of the PTV. For the PTV, 30 Gy in 15 fractions were prescribed. Dose constraints were assigned to the PTV, the OCA, and the heart. Concerning the PTV, the goal was to deliver >95% of the prescribed dose (*i.e.*, 28.5 Gy) to >95% of the PTV. The PTV undercoverage was defined as the percentage of the PTV not encompassed by the 95% isodose line and therefore should be <5%. The maximum tolerated dose was 115% of the prescribed dose (*i.e.*, 34.5 Gy) in one voxel. The dose constraints for the OARs included a mean lung dose <14 Gy, the lung V20 <35%, and a mean heart dose <20 Gy. In fact, the lowest dose possible was delivered to the heart and the coronary arteries. Two IMRT plans were calculated and compared for each patient: one for FB and one for DIBH.

Table 1. Comparison of clinical target volume (CTV) and planning target volume (PTV) between free-breathing and deep-inspiration breath-hold modalities

Volume	Free-breathing	Deep-inspiration breath–hold	Difference	p value
CTV (cc)	290 (240–350)	270 (220–320)	7%	0.0007
PTV (cc)	750 (640−850)	720 (620–820)	4%	NS

Nonparametric *t* test for matched observations: Wilcoxon test: mean. 95% confidence interval in parentheses.

Statistical analysis

The dosimetric parameters of each patient were compared (FB vs. DIBH) with a nonparametric *t* test for matched observations (Wilcoxon test). The threshold for statistical significance was $p < 0.05$. All statistical tests were two-sided and were performed using GraphPad Prism software (GraphPad Software, San Diego, CA).

RESULTS

The clinical target volumes were significantly smaller in the DIBH group, whereas the PTV volumes were not significantly different between the two modalities (Table 1 and Fig. 1).

Tumor coverage

The PTV undercoverage was not significantly different with either FB or DIBH IMRT.

Radiation doses to coronary arteries and heart

Concerning the OCA and heart, there was a significant reduction of 15–16% in radiation doses using the DIBH technique compared with FB IMRT (Table 2 and Fig. 2).

Lung radiation doses

Additionally, the DIBH technique allowed significant ($p <$ 000.1) sparing of the lungs: there was a 20% reduction in the mean lung dose and a 30% reduction in the lung V20 (Table 2 and Fig. 2).