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Technical solutions to reduce mediastinal irradiation in young patients undergoing treatment for lymphomas: Preliminary experience

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A B S T R A C T

This study aims at optimizing treatment planning in young patients affected by lymphoma (Stage II to III) by using an inclined board (IB) that allows reducing doses to the organs at risk. We evaluated 19 young patients affected by stage I to III lymphomas, referred to our Department for consolidation radiotherapy (RT) treatment on the mediastinum. Patients underwent 2 planning computed tomography (CT) scans performed in different positions: flat standard position and inclined position. A direct comparison between the different treatment plans was carried out analyzing dosimetric parameters obtained from dose-volume histograms generated for each plan. Comparison was performed to evaluate the sparing obtained on breast and heart. Dosimetric evaluation was performed for the following organs at risk (OARs): mammary glands, lungs, and heart. A statistically significant advantage was reported for V_5, V_{20}, and V_{30} for the breast when using the inclined board. A similar result was obtained for V_5 and V_{10} on the heart. No advantage was observed in lung doses. The use of a simple device, such as an inclined board, allows the optimization of treatment plan, especially in young female patients, by ensuring a significant reduction of the dose delivered to breast and heart.

Introduction

This study aims at optimizing treatment planning in young patients affected by lymphoma. We implemented the use of an inclined board (IB) (Fig. 1) to reduce doses to the organs at risk based on the experience of the MD Anderson Cancer Centre.[1] Lymphomas present a peak of incidence in young patients aged 15 to 30 years.[2] Patients affected by stage II to III Hodgkin lymphomas (HL) and non-HL (NHL) have, nowadays, a better prognosis, thanks to the constantly increasing knowledge about these pathologies. Last findings about the biological aspects, onset of symptoms, and pattern of spread led to a better application of different therapeutic strategies increasing long-term survival.[3-6] Radiotherapy (RT), itself, still plays an important role in the treatment of lymphomas by increasing the possibility of achieving a complete remission.[7-9]

The most frequently involved anatomic sites are supradiaphragmatic nodes such as mediastinal, supraclavicular, and axillary nodes. Young patients undergoing RT treatments on the mediastinum present with an increased risk of developing second malignancies, especially breast cancer and coronary artery disease.[10-13] Based on literature data, we decided to analyze dose distribution to mammary glands and heart, considered the most important organs at risk, by examining low-doses range (V_5 to V_{10}) and high-doses range (V_{20} to V_{30}).

A new positioning technique based on the use of an IB was implemented at our center to repeat and confirm dosimetric analysis performed by Dabaja *et al.*[1] This device allows the breast moving downward and outward, thus receiving lower doses especially to the internal quadrants. It also allows a remarkable heart sparing.

Methods and Materials

Between March 2011 and October 2012, 19 patients affected by stage II to III lymphomas were referred to our department for postchemotherapy (CHT) RT. All

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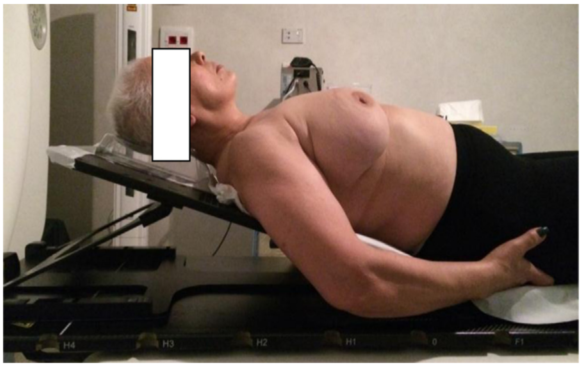

Fig. 1. Example of a CT planning scan performed with the inclined board. (Color version of figure is available online.)

patients were in complete remission on computed tomography-positron emission tomography (CT-PET). Patients' characteristics are summarized in Table 1. Patients underwent 2 different low-dose CT planning scans, the first performed in a standard positioning, the other on the IB (15° IB). The use of the IB has been previously investigated by Dabaja *et al.*[1] at MD Anderson.

Written informed consent was obtained from the patients for the purpose of this report as well as for any accompanying image. The ethics committee has approved this study.

We generated a plan for each acquired CT scan using Pinnacle treatment planning system (version 9.2) to compare different dosimetric parameters derived from dose-volume histograms. Patients were all treated in supine standard position. For each CT scan, we contoured the clinical target volume (CTV) comprising the involved nodes: craniocaudal limits were based on the images of pre-CHT CT-PET scan uptake, and lateral limits were arranged on post-CHT CT-PET scan images. Planning target volume (PTV) was defined as the CTV with a 15-mm expansion in all directions, based on International Commission on Radiation Units and Measurements 50 recommendations.[14] Organs at risk (OARs) were lungs (intended as the summa of the volumes of both lungs), heart, and right and left breast. The same physician contoured both treatment plans to reduce variability in organs and volume of interest delineation (Fig. 2). An isocentric technique was used; beam arrangements were anteroposterior and posteroanterior. Planning RT for both positioning allowed in evaluating differences in dose distribution to the target and OARs. Treatments with the IB were planned with 90° table position and 15° gantry angle rotation to compensate the beam divergence resulting from patients' positioning. When patients are placed on, the IB gravity allows breast moving downward and outward away from the radiation treatment field. The planning target volume receiving at least 95% of the prescription dose (V_{95}) and the dose covering at least 95% of the PTV (D_{95}) were used to approve the treatment plans. Volume of OARs receiving 5 Gy (V_5), 10 Gy (V_{10}), 20 Gy (V_{20}), 25 Gy (V_{25}), and 30 Gy (V_{30}) was evaluated in all of the patients in regard to lung and heart; breast doses were analyzed only in female patients (15 patients). Treatment was delivered with megavoltage (MV) photons (6/10 MV) produced by a linear accelerator (Elekta) using opposed fields (anteroposterior and posteroanterior fields).

Table 1
Patients' characteristics

Sex
Male (4)
Female (15)
Pathology
HL (14)
NHL (5)
Stage
II (15)
III (4)
Treated node area
Mediastinum (7)
Mediastinum + supraclavicular (12)
Total dose (2 Gy/Fr)
30 Gy (14)
36 Gy (5)
Breast volume (cc)
Mean right breast volume 572.97
Mean left breast volume 571.82

For each OARs considered, we assumed that the dose-volume parameters under investigation followed the Student's t distribution with $\nu = 19^\circ$ of freedom, both for the standard and the inclined plans. In addition, we considered that the differences between the average values of the 2 pairs of distributions are statistically significant if $p < 0.05$. Statistical calculations for the Student's t-test were performed using R version 2.15.1 (R CoreTeam, R Foundation for Statistical Computing, Vienna, Austria).

Results

Using the IB a considerable sparing of both breasts is evident, as reported in Table 2, and this effect is always statistically significant.

A greater sparing effect is obtained on the left breast (V_5 17.8% *vs* V_5 34%, V_{20} 26.6% *vs* 45%, and V_{30} 31.7% *vs* 44% for the right breast *vs* the left one, respectively). These differences are always statistically significant.

Heart sparing is obtained using the IB too in spite of the fact that it is less evident in comparison to breast reduction at the progressively increasing doses. Concerning low doses (V_5 to V_{10}), a statistically significant dose reduction has been observed (8% to 9.8%). For the higher dose range (V_{25}), we found a positive trend that did not reach the statistical significance (~8.5%).

No advantage at all seems to be possible in the case of lung. The use of the IB probably produces a slight increase in the amount of lung tissue receiving doses between 5 and 30 Gy.

As shown in Table 2, comparing dosimetric results obtained from both types of treatment plans, we observed that the use of the IB led to a percentage reduction of doses delivered both to mammary glands and to the heart.

Our results appear to be similar to those found by Dabaja *et al.* earlier.

Discussion

Standard therapeutic approaches for hematological malignancies include CHT, radiation therapy to the involved node or to the "bulky" disease, and hematopoietic cell transplantation in selected patients. Thanks to the introduction of new chemotherapeutic regimens, both complete remission and disease control rates increase in patients affected by HL and NHL. Newly introduced systemic therapies also led to an improvement in overall survival rates and reduction of side effects.

RT plays a crucial therapeutic role in the treatment of lymphoma by decreasing disease recurrence rates. Treatment plans are currently developed providing reduced field dimensions (from extended field to involved field and more recently to involved nodes). Despite this, efforts must be made aiming at further optimizing radiation treatment plans thus reducing related side effects.

Long-term side effects related to this complex treatment program include second malignancies and cardiovascular disease. Solid tumors are the major subtypes of second malignancies in patients treated for lymphomas, accounting for up to 75% to 80% of all cases. The latency period persists as long as 30 years, with a median onset interval of approximately 20 years. Mediastinal RT is associated with an increased relative risk of developing breast cancer of approximately threefold to fivefold compared to the general population. Breast cancer accounts for almost 40% of second cancer among female survivors. Data from literature suggested that doses of 20 Gy and lower than 5 Gy delivered to the breast could increase the risk of developing cancer.[15–18]

The sparing effect on the breast tissue is clearly demonstrated in Table 2 and has been already reported by Dabaja et al. in their previous experience.[1] The breasts move externally and downward, and their delineation on the planning CT clearly defines the advantage of the use of this simple technical device.