Peer Review File

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Reviewer A

« The paper is in my opinion overall suitable for publication, but I would suggest some minor revisions ».

We warmly thank the Reviewer A for this positive review.

Question 1 : Line 84: 'The use of IMPT significantly reduced radiation exposure to OAR and improved target coverage compared with IMRT' Although the paper is mainly focused on the shift from IMRT to IMPT, I suggest to provide a few clinical data from your Center (or at least data from a single patient as an example as a figure and/or table).

Reply 1 : We warmly thank the Reviewer for this question. We conducted a large scale dosimetric comparison between VMAT and IMPT to demonstrate this superiority on our patients (even though all patients did not receiver IMPT) and we added the relevant reference from our center.

Changes in the text : IMPT is expected to significantly reduce radiation exposure to OAR and to improve target coverage compared with IMRT. Based on a dosimetric comparison between IMRT and IMPT, we found that IMPT significantly reduced mean doses to the heart (2.36Gy vs 0.99Gy, $p<0.01$), to the left ventricle (0.67Gy vs 0.03Gy, $p<0.01$) and to the valves (1.29Gy vs 0.06, $p<0.01$) (6)

Question 2 : Line 86 'subject to a selection staff': please clarify this point.

Reply 2 : We warmly thank the reviewer for this suggestion. A dosimetric comparison is conducted to select the patients for IMPT. We added the relevant reference which describe our selection protocol.

Changes in the text : While IMPT treatments are still minoritary in our department and are systematically subject to a dosimetric selection process based on a comparison between optimal IMRT and IMPT plans (7,8)

Question 3 : Line 92: 'this single-center experience evidences how, once only used for highly-selected patients, proton therapy could become a reference technique in the treatment of mediastinal HL patients, surpassing IMRT'. I would rephrase as 'this single-center experience evidences how proton therapy, once only used for highly-selected patients, could become a reference technique in the treatment of mediastinal HL patients'. Moreover, I suggest to link this statement with the current limits of proton therapy (limited availability, high cost).

Reply 3 : We warmly thank the reviewer for this suggestion. we used the propose reformulation and added a statement about the availability and the cost.

Changes in the text : this single center experience evidences how proton therapy, once only used for highly selected patients, could become a reference technique in the treatment of mediastinal HL patients, despite multiple challenges including limited availability and financial cost.

Reviewer B

We warmly thank the Reviewer B for the positive review and the constructive comments.

Question 1 : « The use of IMPT significantly reduced radiation exposure to OAR and improved target coverage compared with IMRT » . This statement requires more details. Did the authors perform a dosimetric comparison between IMRT/VMAT and IMPT? If yes, details are required. If not, this statement is not appropriate.

Reply 1 : We warmly thank the Reviewer for this question. We conducted a large scale dosimetric comparison between VMAT and IMPT to demonstrate this superiority on our patients (even though all patients did not receiver IMPT) and we added the relevant reference from our center.

Changes in the text : IMPT is expected to significantly reduce radiation exposure to OAR and to improve target coverage compared with IMRT. Based on a dosimetric comparison between IMRT and IMPT, we found that IMPT significantly reduced mean doses to the heart (2.36Gy vs 0.99Gy, $p<0.01$), to the left ventricle (0.67Gy vs 0.03Gy, $p<0.01$) and to the valves (1.29Gy vs 0.06, $p<0.01$) (6)

Question 2 Last sentence: « proton therapy could become a reference technique in the treatment of mediastinal HL patients, surpassing IMRT »;. This statement is not in line with the actual literature data. The authors should provide a more balanced discussion on the comparison of IMRT and IMPT. Despite the preference of the authors for IMPT, it should be noted that several international institution with the possibility to offer both photons and protons, still use the firsts to treat most mediastinal lymphoma patients. Moreover, the NCCN guidelines still consider IMRT/VMAT the standard technique and the ILROG guidelines on the utilization of PT (Dabaja et al. Blood 2018, that I highly suggest to cite) suggest a careful adoption of IMPT (also taking into account all the physical limitations of PT in a delicate and anatomically complex district as it is the thorax) after a proper comparison with a competitive photon technique. A more balanced discussion is necessary with regard to this point.

Reply 2 : We warmly thank the reviewer for this suggestion. we added the proposed references and modifed the discussion accordingly

Changes in the text : In any case, the NCCN guidelines still consider IMRT/VMAT as a standard technique (9) and the ILROG guidelines on the utilization of IMPT suggest a careful adoption of this latter, taking into account all the physical limitations of IMPT in a delicate and anatomically complex district, as it is the thorax (10).

Question 3 : Line 83: « there were 12 grade II unfavorable HL, 2 grade II favorable HL »;: grade should be properly replaced by stage

Reply 3 : We warmly thank the reviewer for this correction ; this has been done

Change in the text : 12 stage II unfavorable HL, 2 stage II favorable HL