

We would like to thank the reviewers for their advice and comments which helped us to improve the manuscript.

Please find below our answers to the reviewers' comments/questions point by point.

We have highlighted in yellow the parts of the manuscript that have been modified.

#### Reviewer #1

I suggest using subheadings and numbers to make the article more structured.

We added subheadings and numbers to make the article more structured.

#### Reviewer #2

Author may consider shortly elaborating about various aspects like patient preparation, simulation, target volume delineation etc.

We have added a paragraph dedicated to the radiotherapy treatment planification:

#### 2- Radiotherapy treatment planification

##### a- CT Simulation

Patients must be simulated and treated with an empty stomach after a fast of at least 4 hours or overnight.

Patients should be simulated supine with arms up using customized immobilization device.

A small volume (50 cc) of oral contrast medium should be used.

CT images should be acquired before and after oral contrast medium.

Intravenous contrast medium injection is recommended in case of lymph nodes involvement.

In order to reduce margins, respiratory motion should be assessed with 4D-CT.

##### b- Volume definition (ILROG recommendations)

The Gross Tumor Volume (GTV) corresponds to the gastric tumor and the macroscopically invaded lymph nodes as according to CT or PET-CT.

Because gastric MALT lymphoma is often associated with multifocal involvement of the stomach and may spread to regional lymph nodes, radiation volumes should include the entire stomach as well as the perigastric lymph nodes of the lesser and greater curvature.

The Clinical Target Volume (CTV) corresponds to the entire stomach from the oeso-gastric junction to the duodenal bulb; the whole gastric wall and the perigastric lymph nodes must be included.

The Internal Target Volume (ITV) needs to be determined by 4D CT in order to take into account stomach mobility during breathing.

In the absence of a 4D CT, 2 cm margins are added to the CTV to take into account of respiratory movement of the stomach.

For the planning target volume (PTV), an additional margin of 0.5 to 1 cm should be added, to take into account setup variation.

In order to reduce the margins to take into account the respiratory movements, modern irradiation techniques such as deep-inspiratory breath-hold (DIBH) and 4D-CBCT-IGRT (Cone Beam Computed Tomography-Image Guided Radiation Therapy), should be used. In a retrospective study of 10 patients treated for gastric non-Hodgkin lymphoma including 5 MALT and 5 DLBCL, Christopherson et al. have reported that DIBH led to reduced dose to the heart and the kidneys through improved spatial separation between the heart and stomach, while simultaneously allowing for reduced target volumes without compromising target coverage or increasing dose to other OARs [23].

Shimohigashi et al. reported that the use of 4D-CBCT reduced the PTV when applying 4D soft-tissue matching, compared to skin and bone matchings. Based on these results, authors recommended using the daily 4D-CBCT during RT treatment [24].

The following organs at risk (OAR) should be delineated: liver, kidneys, bowels, heart, lungs and spinal cord. 3D conformal RT, IMRT or VMAT (Figure 3), are recommended to reduce the dose delivered to the kidneys and liver.

### Reviewer #3

We added a paragraph dedicated to radiotherapy procedure (see reply to reviewer #2)

The figure came from screenprint with MS word error underline, this kind of amateur makes the reviewer lost all the patience

We have corrected the screenshot anomalies in Figure 1.

Radiation dosage , AEs , target delineate , movement management , radiation technologies need to be involved in the draft and be in a structured way.

See answers to reviewers #1 and #2

The authors need to discuss the role of radiotherapy in comprehensive therapy of MALT

See answer to reviewer #4

What's the novelty of this review ?

We conducted an extensive and up-to-date review of the literature. We confirmed that radiotherapy is an effective treatment for localized gastric MALT lymphoma after HP eradication failure.

Reviewer#4

Please mention reference for first paragraph on page 1

We added the following references:

- [1] Zucca, E, Bertoni, F. The spectrum of MALT lymphoma at different sites: biological and therapeutic relevance. *Blood* 2016;127:2082-2092.
- [2] Khalili, M, Sakhaee, E, Aflatoonian, MR, et al. Seroprevalence of bovine leptospiral antibodies by microscopic agglutination test in Southeast of Iran. *Asian Pac J Trop Biomed* 2014;4:354-357.
- [3] Thieblemont, C, Bastion, Y, Berger, F, et al. Mucosa-associated lymphoid tissue gastrointestinal and nongastrointestinal lymphoma behavior: analysis of 108 patients. *J Clin Oncol* 1997;15:1624-1630.

2. Please add staging and work up of gastric MALT lymphoma. It will give the introduction more depth.

We added a paragraph dedicated on staging and work up of gastric MALT lymphoma:

#### 1- Staging of MALT lymphoma

Previously, staging of MALT gastric lymphoma was based on the Lugano staging system [12] which is a modification of the Ann Arbor staging system. More recently, the Paris staging system [13] which corresponds to the TNM (tumor, node, metastasis) system for gastric cancer, has been proposed. The Paris system has the advantage, over the Lugano staging system, of better describing the depth of invasion into the gastric wall (Tables 2, 3).

According to ESMO guidelines, initial staging should include history and physical examination, full blood and differential counts, biochemistry including renal and liver function tests, protein electrophoresis, LDH and beta2-microglobulin, serum and urine immunofixation, serology for HBV, HCV and HIV and cryoglobulins and cryocrit if HCV-positive.

Staging should include:

- a) Gastroduodenal endoscopy, with systematic multiple biopsies and any abnormal lesion.

The following tumor analyses by an expert hematopathologist from biopsies are recommended:

- Immunohistochemistry panel analysis:

CD20, CD3, CD5, CD10, BCL2, kappa/lambda, CD21 or CD23, BCL6, cyclin D1 and IgD

- Helicobacter pylori testing

- Detection of t(11;18) (p21;p21) by FISH (Fluorescence in situ hybridization).

b) Endoscopic ultrasound is recommended to evaluate gastric wall infiltration and perigastric lymph node involvement.

c) Imaging should include chest and abdominal computed tomography.

3. There is no mention on prognostic index - MALT-IPI which will help classify the patients into different risk criteria

We added a paragraph on MALT-IPI:

The MALT-IPI Index was developed to identify patients with a poor prognosis and thus to allow for appropriate treatment of patients with extranodal marginal zone lymphoma of MALT. This index classified patients into 3 prognostic groups (low, intermediate, and high) that are predictive of event-free and overall survival. The 5-year event-free survival rates in the low-, intermediate-, and high-risk groups were 70%, 56%, and 29%, respectively. This index was based on: age  $\geq 70$  years, Ann Arbor stage III or IV and elevated LDH. The MALT-IPI has been developed from 401 patients treated with chlorambucil, rituximab, or both in the international randomized trial IELSG-19. The index was subsequently validated by merging three independent cohorts of MALT lymphoma patients (n=633 patients) [6].

4. The sub-heading perspectives should be modified on page 6

We changed the sub-heading

6. Various techniques of radiotherapy are mentioned below it and the sub-heading does not seem to match its content.

We changed the sub-heading

5. Please add a picture of radiotherapy planning.

We added a screenshot of a VMAT treatment planning

There has not been much focus on the techniques of radiotherapy, its description and target volume. Since the focus of the article is radiotherapy its important to stress on this aspect as well. For example, the authors should elaborate on ISRT, IFRT

We added a paragraph dedicated to radiotherapy procedure.

6. Do mention follow-up of patients after radiotherapy.

We mentioned the follow-up in a dedicated paragraph

7. In the conclusion, the authors should put in a flow chart summarizing the treatment options for gastric MALT

We put a flow chart summarizing treatment option for localized gastric MALT (Figure 2)