

We are grateful to Associate Editor and Reviewers for their relevant comments and the work they have invested to help us improving our manuscript. We believe that their positive remarks and questions allowed us to significantly increase the interest of our manuscript. Please find below the responses to reviewers' comments.

Reviewer #1:

Thank you for your valuable work.

1. Keywords: Surgical phrases may be added.

Reply: Thanks. We added a couple of them

2. Tables: You may consider adding recent literature comparison table for each therapeutic choice including survivals.

Reply: Thanks for Your constructive comment. Following your suggestion, we have extensively review the pertinent literature considered in the present review. Studies are extremely different concerning population, sample size, strategy of care. We believe that a comparative Table could be misinterpretable, this creating some confusion to the Readers. Moreover, most of series are surgical only, this representing an additional bias of interpretation itself.

3. 'Resection margin' data is added in your table, but surgical techniques and margins are not thoroughly discussed in the text.

Reply: Thanks for Your constructive comment. We perfectly agree with You. In the revised version of the manuscript, we have included in the discussion some paragraph on this issue.

4. At page 10, 3.2., first sentence; "about 70% of CRC metastases are un-resectable and radiotherapy represents a very promising and rapidly evolving non-invasive treatment modality,

particularly with stereotactic body radiation therapy (SBRT)” is suggested. Could you please add reference to that? Should the reader see this statement as a ‘take home’ message?

Reply: Thanks for Your observation. Actually, this is just the opinion of our Team. As you can see in the List of Authors, this review is the result of an Oncological Team dedicated on colo-rectal cancer disease.

5. Later in that section, page 12, last sentence of first paragraph; “in fact, SBRT is often offered to patients who are usually not eligible for other treatment modalities” sentence also needs a reference.

Reply: Thanks for Your constructive comment. we have included a reference in this sentence

6. Did you find any information about second primary lung cancer incidence in colorectal carcinoma patients who received SBRT for lung lesion without pathological diagnosis?

Reply: Very interesting suggestion. I have tried to explore the pertinent literature but no robust data on this incidence is available. This could be a topic for a specific project of research.

7. For mediastinal evaluation, should the patient undergo mediastinoscopy before metastasectomy if nodal disease is suspected? Should we change our approach as if treating a primary lung cancer?

What are your thoughts on this issue?

Reply: Thanks for your comment. Actually, the role of lymph node metastases during pulmonary metastasectomy is extremely debated and no clear evidence are available in the guide-lines, neither in those focused on colo-rectal cancers. In other malignancies (renal cancer with lung metastases) the presence of mediastinal lymph nodes seems to be a strong negative prognostic factors. In colo-rectal cancer some Authors believe that (at least) a sampling of the mediastinal lymph node should be done during pulmonary metastasectomy, while other do not routinely perform it. We usually

performed a mediastinal dissection only when lymph nodes are enlarged at CT-scan (in those cases where pulmonary metastasectomy is recommended by Tumor Board.)

However, this review is focused on solitary pulmonary metastases (that means only single lung lesion) and this discussion is, in our opinion, off topic. However, we are disposable to include it in the final version of the manuscript.

8. Is there a suggested cut-off level for high CEA, that was stated in literature, which we should avoid surgery? Could CEA levels give us a hint for recurrences after surgery, that the primary tumor may not be under control?

Reply: We wish to thank the reviewer for his/her kind comment. There is no CEA cut-off available at our best acknowledge. As reported in Table, CEA levels are predictors of survival after surgery in a large part of studies analysed in the present review. However, it's not clear if high levels of CEA are correlated with a neoplasm is not under control. Thus, surgery should not be excluded *a priori* in these cases.