Peer Review File

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Reviewer A

This is a well written narrative review considering the management of pulmonary metastases. I would recommend to improve the structure of this review.

In the results, you should rather focus on different methods, like local vs. local+systemic, or different cancers; not a mixture of topics considering only two specific cancers in specific sections and later in the text additionally other cancers. Results should focus on facts and the discussion on the discussion of these results.
Author's answer: Thank you for the comment. We re-formatted the discussion and results sections as you suggested. We decided not to include systemic treatments in detail because the systemic therapeutic approach is generally based on the specific tumor histotype and achieves different outcomes based on the original tumor; hence, covering all the possible systemic treatments would have been beyond the scope of this narrative review. We tried to rephrase and change some sections in order to improve clarity and to focus on local techniques, rather than different cancers. We added this aim also in the introduction.

If possible, some tables would improve the message that you found in various studies.
Author's answer: Thanks for the comment. Based on your suggestion, we included two tables.

Table 1 reports the main outcomes of surgical approaches to pulmonary metastases according to the most relevant studies.
Table 2 summarizes the outcomes of SBRT on lung metastases across different studies.
We believe the new tables make our work more easily understandable and provide additional data of the reported studies (including some information that, while useful, were just hinted at in the text).

Considering the definition of oligometastatic disease, Guckenberger et al., Lancet Oncol 2020 needs to be cited and discussed.
Author's answer: Thank you for your comment. We have rediscussed this topic including the suggested article, as part of a general re-phrasing of the whole paragraph describing the therapeutic approach to pulmonary metastases.

Reviewer B

The title includes the important words "narrative review" and "perspective" which reflects the content well. The OBJECTIVE as stated is to summarise the available data but it is a bit light on data so that is not really achieved. That might be an impossible task because the scope as presented is very wide.

The specific focus is colorectal cancer [L.50]. It may be that a judgement should be made about a more realistic scope and that should be reflected in the title. Consider confining this to colorectal cancer because there are special considerations for sarcoma and germ cell tumours and other special instances such as thyroid and renal cancers.

Author's answer: Thanks for the suggestion. Our aim was to show strategy and oncologic perspective with specific reference to oligometastatic disease. We decided to use colo-rectal cancer as a model which could be representative of approaches to limited pulmonary metastases, at least for solid and especially epithelial tumors; however, while describing all the possible tumors associated with pulmonary metastases was beyond our possibilities in this manuscript, at the same time we did not believe our review could be exclusively limited to colo-rectal cancer, as we used it as a proof of concept for our perspective. In order to correct the scope of our review, we increased the reference to colo-rectal cancer in the abstract and added the following sentence in the introduction: "Notably, since colo-rectal cancer represents one of the first solid tumors for which regional approaches to pulmonary metastases were applied, a significant proportion of the collected literature is based on this tumor. Furthermore, the mechanism of metastatization from colo-rectal cancer has been widely studied, and hence provides a good physiopathological model."

Specific points

[L.69/70] "… pulmonary metastases can still occasionally be managed with local treatments …". Occasionally here is important because. Fewer than one in 30 patients who have had a colorectal resection subsequently had a lung resection in an English big data analysis. (Fenton et al. 2021) This is in line with the few other studies providing a denominator, for example the prospective Spanish study. (Embun et al. 2013)

Author's answer: Thanks for the suggestion. We decided to add the suggested reference to reinforce the meaning of "occasionally" and included the following sentence to increase the concept: "While the management of pulmonary metastases with local treatments appears appealing, it must be considered that this approach is still uncommon; for instance, fewer than one in 30 patients who have had a colorectal resection subsequently underwent lung resection as it has been observed in big data analyses."

It should be remembered that the oligometastatic state was paradigm proposed by radiation oncologists (Hellman and Weichselbaum 1995) which drew little attention for 10 years (Treasure 2012) but the recent widespread availability of stereotactic radiotherapy was welcomed by radiation oncologists. (Lewis et al. 2017) In fact there is no sound statistical or biological basis for the oligometasatic state. It is the fewness of the metastases that makes the disease amenable to piecemeal ablation and that also identifies patients with the least aggressive disease at the thin end of a distribution curve. (Treasure, Farewell, Macbeth, Batchelor, Milosevic, King, Zheng, Leonard, Williams, Brew-Graves, Fallowfield, et al. 2021) When these are balanced in a randomised controlled trial no difference in survival was seen. (Milosevic et al. 2020)

Author's answer: Thank you for your comment; like you proposed we added a new section about the term ''oligometastatic'' in paragraph 5, with a more comprehensive description of the oligometastatic state and suitable references.

[L.148-150] "Patients with lung metastases can present localized symptoms like pleural effusion,

cough, dyspnea, hemoptysis or common, non-specific symptoms due to metastatic cancer as vomiting, low back pain or loss of appetite."
This is a critically important statement completely unsupported by data. The CRC lung metastases removed by surgeons as part of the multidisciplinary management of advanced colorectal cancer are asymptomatic.
Localised symptoms should be carefully assessed and if due to a metastasis, it is appropriate to consider the likelihood that the symptoms will be relieved by excision or ablation of the related metastasis. But most metastases, and those that are detected in course of surveillance are treated in the belief that this will improve survival, usually at five years.
Author's answer: Thanks for the observation. In order to correct this part, we modified the sentence to emphasize the fact that most pulmonary metastases are in fact asymptomatic.

[L.148] While there may be cases when lung metastases co-exist with an effusion, lung metastases do not cause pleural effusion. Colorectal cancer can seed to the pleura and cause pleural effusion but there is no physiological mechanism by which a few small volume metastases can alter the Starling pressures to produce an effusion.

Author's answer: Thanks for the observation. We decided not to remove the reference to pleural effusion because of lack evidence of the mechanisms of presentation and also because pleural effusion is typical of pleural metastases rather than lung metastases.

[L.148] Dyspnoea? I have seen this cited recently. "If patients do not receive timely and effective treatment, they may die as a result of respiratory failure." (Qi and Fan 2018) It is not true. A cough due to metastases might occur but it is not usual.
Author's answer: Thanks for the suggestion. Based on your comment, we decided to modify the sentence and emphasize the concept that pulmonary metastases are often asymptomatic and only occasionally present symptoms like dyspnea or hemoptysis.

[L.149] And haemoptysis? This was suggested as a justification for pre-emptive lung metastasectomy. I asked a hall full of thoracic surgeons if any of them had ever seen that as a clinical problem. None had. Vomiting, low back pain and loss of appetite may occur for all sorts of reasons but must rarely be due to lung metastasis — are they ever treated and relieved by metastasectomy?
Author's answer: Thanks for the suggestion. We approached the concept of hemoptysis by specifying its rarity in this setting while we fixed the previous comment.

Minor point: this manuscript needs a routine check for English grammar and syntax.
For example
[L90] "any solid tumor can virtually spread to the lungs" Consider the word order. Perhaps the intended sense is "virtually any solid tumor can spread to the lungs".
Author's answer: Thanks for the suggestion, we change the sentence as you suggest to make the concept more understandable

[L.125/6] "This is one of the main factors justifies the increasing distribution of lung rectum metastasis, compared to colon." Perhaps "determining the greater frequency"?

Author's answer: Thanks for the correction, we changed the sentence as you suggest.

[L.162-4] "However, when metastatic sites are represented by limited size and number of pulmonary lesions, more radical approaches might be considered, including surgery or radiotherapy." This needs rephrasing

Author's answer: Thank you for your advice. We have rephrased the sentence.

[L.175] "in the pursue for radical treatment" perhaps "in the pursuit of"?

Author's answer: Thank you for your advice. We have rephrased the sentence.

Your paper reads well and the intended meaning is usually clear and, as always, I respect that your English is infinitely better than my Italian and I apologise for any typing errors in my review.

Author's answer: Thank you for your comments. In our opinion, these observations significantly improve the global quality of our manuscript, both in terms of grammar and in terms of concepts. Furthermore, we made use of the following suggested references in order to improve the data of our narrative review.

Brew-Graves, C., V. Farewell, K. Monson, M. Milosevic, N. R. Williams, E. Morris, F. Macbeth, T. Treasure, and L. Fallowfield. 2021. "Pulmonary metastasectomy in colorectal cancer: health utility scores by EQ-5D-3L in a randomized controlled trial show no benefit from lung metastasectomy." Colorectal Dis 23 (1): 200-205. https://doi.org/10.1111/codi.15386. https://www.ncbi.nlm.nih.gov/pubmed/33002305

Embun, R., F. Fiorentino, T. Treasure, J.J. Rivas, and L. Molins. 2013. "Pulmonary metastasectomy in colorectal cancer: a prospective study of demography and clinical characteristics of 543 patients in the Spanish colorectal metastasectomy registry (GECMP-CCR)." BMJ Open 3 (5): 5 e002787 doi:10.1136/bmjopen-2013-002787. https://doi.org/bmjopen-2013-002787 [pii];10.1136/bmjopen-2013-002787 [doi]. http://www.ncbi.nlm.nih.gov/pubmed/23793698.

Fenton, H. M., P. J. Finan, R. Milton, M. Shackcloth, J. C. Taylor, T. Treasure, and E. J. A. Morris. 2021. "National variation in pulmonary metastasectomy for colorectal cancer." Colorectal Dis 23 (6): 1306-1316. https://doi.org/10.1111/codi.15506. https://www.ncbi.nlm.nih.gov/pubmed/33368958.

Hellman, S., and R.R. Weichselbaum. 1995. "Oligometastases." J Clin. Oncol 13 (1): 8-10. http://www.ncbi.nlm.nih.gov/pubmed/7799047.

Lewis, S.L., S. Porceddu, N. Nakamura, D.A. Palma, S.S. Lo, P. Hoskin, D. Moghanaki, S.J. Chmura, and J.K. Salama. 2017. "Definitive Stereotactic Body Radiotherapy (SBRT) for Extracranial Oligometastases: An International Survey of >1000 Radiation Oncologists." Am J Clin Oncol 40 (4): 418-422. https://doi.org/10.1097/COC.0000000000000169 [doi]. http://www.ncbi.nlm.nih.gov/pubmed/25647831.

Milosevic, M., J. Edwards, D. Tsang, J. Dunning, M. Shackcloth, T. Batchelor, A. Coonar, J. Hasan, B. Davidson, A. Marchbank, S. Grumett, N. R. Williams, F. Macbeth, V. Farewell, and T. Treasure. 2020. "Pulmonary Metastasectomy in Colorectal Cancer: updated analysis of 93 randomized patients - control survival is much better than previously assumed." Colorectal Dis 22 (10): 1314-1324. https://doi.org/10.1111/codi.15113. https://www.ncbi.nlm.nih.gov/pubmed/32388895.

Qi, H., and W. Fan. 2018. "Value of ablation therapy in the treatment of lung metastases." Thorac

Cancer 9 (2): 199-207. https://doi.org/10.1111/1759-7714.12567. https://www.ncbi.nlm.nih.gov/pubmed/29193688.
Treasure, T, V Farewell, F Macbeth, T Batchelor, M Milosevic, J King, Y Zheng, P Leonard, N. R Williams, C Brew-Graves, E Morris, and L Fallowfield. 2021. "The Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC) burden of care study: Analysis of local treatments for lung metastases and systemic chemotherapy in 220 patients in the PulMiCC cohort." Colorectal Dis. https://doi.org/10.1111/codi.15833. https://www.ncbi.nlm.nih.gov/pubmed/34310835.
Treasure, T, V Farewell, F Macbeth, K. Monson, N R Williams, C Brew-Graves, B Lees, O Grigg, and L Fallowfield. 2019. "Pulmonary Metastasectomy versus Continued Active Monitoring in Colorectal Cancer (PulMiCC): a multicentre randomised clinical trial." Trials 20 (1): 718. https://doi.org/10.1186/s13063-019-3837-y [doi];10.1186/s13063-019-3837-y [pii]. http://www.ncbi.nlm.nih.gov/pubmed/31831062.
Treasure, T. 2012. "Oligometastatic cancer: an entity, a useful concept, or a therapeutic opportunity?" J R. Soc. Med 105 (6): 242-246. http://www.ncbi.nlm.nih.gov/pubmed/22722968.
Treasure, T., V. Farewell, F. Macbeth, T. Batchelor, M. Milosevic, J. King, Y. Zheng, P. Leonard, N. R. Williams, C. Brew-Graves, L. Fallowfield, and PulMiCcinvestigators. 2021. "The Pulmonary Metastasectomy in Colorectal Cancer cohort study: Analysis of case selection, risk factors and survival in a prospective observational study of 512 patients." Colorectal Dis 23 (7): 1793-1803. https://doi.org/10.1111/codi.15651. https://www.ncbi.nlm.nih.gov/pubmed/33783109.

Reviewer C

The authors provide a comprehensive review of current management of pulmonary metastases. They include specific paragraphs on epidemiology, physiopathology, clinical presentation and diagnosis, therapeutic approaches including surgical resection and stereotactic radiotherapy, and lastly, combination therapies comprising locoregional and systemic therapies. This review is clinically relevant but several revisions and additions are necessary.

Comments:
- although the authors discuss surgical treatment in detail, there is no thoracic surgeon as co-author which I should recommend to refine the surgical paragraphs (some important references are missing; see further comments)

Author's answer: Thank you for this comment. Originally, the review was planned solely to report the perspective of medical oncologists, and hence no other specialists such as surgeons and radiation oncologists were originally involved. After seeing this comment, we asked the Editorial Team whether it was feasible to include other coauthors, and the Editorial Staff reported their preference not to involve additional authors in this phase of the submission. Based on this request, we still made our best to include as much data as possible based on your comments and discussions with surgeons and radiation oncologists at our Institution.

- line 152: the number of lesions could be underestimated on chest CT scan; in case of multiple lesions on CT scan, palpation of the lung might be important to detect small, additional lesions

Author's answer: Thanks for the question. We evaluated additional literature about intraoperative US and lung palpation. Subsequently, we added reference in the bibliography and a sentence specifying the use of bimanual palpation and intraoperative ultrasound.

- line 157: what do the authors mean by endoscopic biopsy: thoracoscopic or robotic approach?

Author's answer: Thanks for the specification. We mean bronchoscopy biopsy (we rephrased the sentence to make it clear).

- line 178: for lung metastases (wide) wedge excisions are preferred as most of these are hematogenous metastases in contrast to early primary lung cancer < 2 cm for which anatomical segmentectomies are indicated

Author's answer: Thank you for your comment. We agree with you and we rephrased our manuscript accordingly.

- line 183: the role of systematic nodal dissection should be addressed and discussed (and some

Author's answer: Thank you for your comment. We have discussed this topic in a whole new section and added the proper references

- line 187: what do the authors mean by R0 resection? This has only been fully defined for primary lung cancer. In case of

Author's answer: thanks for your advice, We modified the definition in the text.

- page 11: the authors should also mention radiofrequency ablation and cryotherapy (with some references) as possible local therapies and their current indications

Author's answer: Thank you for the observation. We have reviewed the literature and included in the manuscript evidence on the use of cryotherapy as a possible approach to the treatment of lung metastases, specifically with reference to ECLIPSE trial.

pages 12-13: although still experimental, isolated lung perfusion should also be mentioned as possible technique to combine surgical resection with high-dose locoregional chemotherapy (phase II study: Beckers P. Ann Thorac Surg 2019; 108: 167-174)

Author's answer: Thanks for the observation. We added a mention and reference for isolated lung perfusion.

- page 12: regarding oligometastatic disease the landmark, randomised phase II trial by Gomez D including some patients with lung metastases should be included (Gomez D. J Clin Oncol 2019; 37:1558-65)

Author's answer: Thanks for the reference. We added a section at the end of section 5.2 which includes the trial by Gomez et al.

- although the English language is generally good, the manuscript should be carefully checked by a native English speaker and several corrections are necessary; examples include:

line 104: PHYSIOPATHOLOGY
Author's answer: Thanks for the observation. We corrected as you suggested

line 106: determine (instead of determinate)
Author's answer: Thanks for the observation. We corrected as you suggested

line 128: venous (instead of veins) – determine (instead of determinate)
Author's answer: Thanks for the observation. We corrected as you suggested

line 211: what does "said" mean?
Author's answer: Thank you for your comment; in this context, the word "said" meant ''above mentioned''; We changed it to be clear.

lines 212-214: sentence to be rephrased (no verb)
Author's answer: Thank you for your comment. The sentence was rewritten adding the verb.

line 251: in patients (instead of inpatients) – high external dose radiation to mediastinum or chest
Author's answer: Thanks for the observation. We corrected as you suggested

line 315: Several
Author's answer: Thanks for the observation. We corrected as you suggested

lines 329-332 is the same sentence as lines 336-338
Author's answer: Thank for the observation. We removed the duplicate sentence as you noted.

Reviewer D

Thank you for submitting this manuscript dealing with contemporary management of oligometastatic pulmonary metastases from a number of different primary tumours. The topic is a worthy one and the literature has expanded considerably in this area in recent years. The manuscript attempts to cover the main histological types of malignancy and the main treatments for oligometastatic cancer. However, I have a few major concerns:

1. The use of PubMed for a literature search confuses the nature of the article. Usually, the use of PubMed in such a manner is associated with a formal systematic review of the literature. I think you need to be very clear that you used articles from PubMed, identified during an informal search, to support the article, but you are not writing an article which by definition (as a systematic review should) will include every important paper on the topic.

Author's answer: Thanks for the suggestion. We agree with you that the use of PubMed for an informal search should be specified in order to avoid confusion with a systematic review. In order to improve clarity, we specified in the introduction that our aim is to report the oncologist's perspective and that we used literature from PubMed to support our perspective, rather than doing

systematic searches.

2. Throughout the manuscript you talk about 'ablation treatment' and ablating lesions throughout the manuscript but do not specifically refer to radiofrequency ablation studies. It is not clear if by 'ablation' you mean any form of treatment to the lesions such as radiotherapy or SABR. This is not accepted nomenclature, as ablation should refer specifically to radiofrequency ablation.

Author's answer: Thank you for the comment. We have revised the manuscript focusing on correct nomenclature in relation to the different types of treatment.

3. Radiofrequency ablation treatment for pulmonary metastases should be discussed in this work as an alternative treatment for metastatic lung lesions.

Author's answer: Thank you for the suggestion. We included in the manuscript some data about the use of radiofrequency as an additional therapeutic approach for lung metastases.

4. Line 148: Pleural effusion is not a symptom
   Author's answer: Thanks for the observation. We decided not to remove the reference to pleural effusion because of lack evidence of the mechanisms of presentation and also because pleural effusion is typical of pleural metastases rather than lung metastases.

5. Lines 165-166: I think it is worth mentioning that the reason many researchers define oligometastatic disease as the presence of 5 or fewer metastases is because this is the original definition offered by Hellman et al in their landmark 1995 paper introducing the concept of oligometastatic disease. https://pubmed.ncbi.nlm.nih.gov/7799047/

Author's answer: Thank you for your comment. Based on your observation, we significantly modified the section describing oligo-metastases in order to be more comprehensive of available literature and definitions.

6. Lines 178-183: More detail and clarity is needed here. Whilst it is true that lobectomy does not need to be performed for oncological reasons, it is often performed for anatomical reasons (i.e. site/extent/number of lesions). Also, the resection most frequently performed is a non-anatomical sublobar wedge resection, although anatomical segmentectomy is performed in many cases.

Author's answer: Thank you for your observation. We modified the sentence in order to make it clear and more detailed, by adding the suggested information (along with similar observations by another reviewer). In our opinion, the current, renewed version of the sentence is now sufficiently clear.

7. Line 236: 'patients not fit for radical lung resection' is probably a better phrase than 'inoperable'.

Author's answer: Thank for the observation. We changed the sentence as suggested.

8. Lines 332-338 are a repetition of lines 325-332

Author's answer: Thank for the observation. We removed the same sentence as you note (we

apologize for the typo).

9. Line 357: need to clarify if by 'clinical trials' you mean prospective studies

Author's answer: Thanks for the question. With "clinical trial" we mean perspective clinical trials. In order to achieve clarity, we modified the sentence accordingly.

10. The work would benefit from further proofreading from someone with English as a first language. There are a number of sections where the grammar and syntax are incorrect, and in some places, this makes it difficult to fully grasp the message being conveyed.

Author's answer: Thanks for the observation. We modified significant parts of the manuscript during the revision, and at the same time we made our best to improve the syntax. Unfortunately, we could not get aid from anyone with English as first language, but we made our best to perform multiple proof readings and we hope this process will result in an improved manuscript.

11. Finally, I think the structure of the manuscript requires a major overhaul. A number of key results are introduced in the discussion rather than earlier in the manuscript. You either need to organize the manuscript by treatment or by histology. If by treatment, the results section should be broken down into subsections (surgery, radiotherapy, SABR, systemic therapy, RFA, multimodality therapy, immunotherapy etc) and within each subsection, systematically discuss the key papers for each important histological subtype (colorectal, lung, urological etc). The discussion then should summarise these findings but not present any new results not previously discussed. If you feel that organisation by histology is preferable, the layout will simply be the opposite: the results section is broken down into subsections according to histology, with each subsection then outlining the different treatment options for each different type of cancer.

Overall, I think a review article of this nature will be a welcome addition to the literature. However, based on my above comments, I think that the article currently submitted needs a complete overhaul to be suitable.

Author's answer: Thanks for the observation. We changed multiple parts of the structure during the whole revision, and we tried to keep the focus on different treatment approaches for manuscript organization, rather than histology, trying to include all the most relevant manuscripts for each treatment approach employed in the relevant solid tumors. Finally, we modified the discussion in order to summarize our findings without including new results which were absent from the other sections. Unfortunately, we were not able to include all the solid tumors given the limited space in the review and given the risk of reducing clarity. However, we hope the current form of the manuscript will be considered acceptable.

Reviewer E

The authors provide a narrative review on pulmonary metastases and try to provide a 360 degree view on the topic. Active management of non-lung cancer primary pulmonary metastases has gained momentum with the new-found interest in oligometastatic disease and such a publication may interest the reader. However, I have the following comments to make on the manuscript provided.

1. Among the key word combinations (MeSH terms) used by the authors, they have not selected the word 'lung' and have only used pulmonary metastases. This can considerably bias the output and impact the results of the review. We would therefore need the authors to address this. While it is not a systematic review, any narrative review also should provide a bare minimum of the number of articles returned with the MeSH terms used and the article repositories searched. This provides the reader with the understanding of how much background research has been done for the article and the credibility of the review. It appears that the authors have used only Pubmed for their research.

Author's answer: Thank you for the observation. We have checked the keyword combination by adding "lung" (initially we were afraid the term lung would have been too generic and produce too many and dispersive results); hence we checked the new articles and implemented our literature. Additionally, in the INTRODUCTION we included more details on our search, which was not actually meant to be systematic, but was used to support the oncologist's perspective. We specified keyword combinations, employed repositories, and research output, which included articles that were further selected by the coauthors.

2. It is unclear as to what the authors wish to convey in the paragraph between lines 95-102. Providing the conflicting nature of numbers or statistics in 2 papers may not be the ideal way of presenting data in a review. It is more appropriate if the authors can provide us with a range of % incidence of pulmonary metastases in non-pulmonary cancers that they have abstracted from various studies or a review article.

Author's answer: Thanks for the suggestion. We thought that it could be more detail to present two different types of data. However, as it seems to be unclear we decided to leave only the range of % of pulmonary metastases in non-pulmonary cancer obtained by biopsy in the text. Since the data from autoptic findings was still interesting, we decided to keep these data but limit their presence to a table (defined as table 1).

3. Please rephrase the line 125: This is one of the main factors justifies the increasing distribution of lung rectum metastasis, compared to colon.

Author's answer: Thank you for the suggestion. We rephased the sentence on the basis of your observation.

Lines 149-150 is just an example of grammatical error where prepositions have not been used. "Patients with lung metastases can present localized symptoms like pleural effusion, cough, dyspnea, hemoptysis or common, non-specific symptoms due to metastatic cancer as vomiting, low back pain or loss of appetite." Please get the manuscript reviewed by a native English speaker or an English language editor.

Author's answer: Thanks for the question. The current form of the manuscript underwent multiple proofreadings and we believe that its overall quality has significantly improved throughout the process.

Kindly rephrase the sentence from lines 174-176 "The surgical management of pulmonary metastases involves the radical resection of pulmonary secondary lesions, and it might be performed

in the pursue for radical treatment, disease prolongation, or symptom palliation."
Author's answer: Thank you for your comment. The sentence has been modified and significantly simplified for clarity, as the original sentence was exceedingly complex without providing useful information.

4. When dealing with a review on pulmonary metastases, differentials of a solitary pulmonary nodule and how to differentiate between them is essential and has been missed. I would recommend to include sensitivity and specificity of imaging modalities in differentiating between malignant and benign pulmonary nodule.

Author's answer: Thank you for your comment. We added the following sentences evaluating the performance of CT scan and PET scan with regards to solitary lung nodules. The following sentence was added: "The sensitivity and specificity of radiologic imaging represent a relevant issue for the management of pulmonary metastases, especially when solitary nodules are identified, and the malignity of these nodules needs to be determined. In a multicenter study enrolling 356 participants, the sensitivity and specificity of contrast-enhanced CT scan were 98% and 58%, respectively (14); in this context, dual time positron emission tomography with fluorodeoxyglucose achieved lower sensitivity (85%), while specificity was 77% (15)."

5. The authors describe the inconsistency of definition of oligometastases, while this is true that there exists inconsistency, the authors fail to provide the recently published literature on consensus of definition. I would encourage the authors to go through those and provide the readers with an abridged version of the definition to provide some clarity on the topic.
   Author's answer: Thank you for your comment. We significantly modified the paragraph describing the updated definition of oligometastases.

6. I would strongly suggest providing an explanation for elaborating on surgical metastasectomy from specific primary sites like CRC and RCC and not on other sites of solid tumors. Clearly, it is not lack of evidence and thus merits an explanation.

Author's answer: Thanks for the observation. We decided to use the colo-rectal cancer as an example, considering it a good model for physiopathology and management, as it has been extensively studied throughout years. Since we did not want to limit our data to colo-rectal cancer, we included also at least another solid tumor, we developed comments on RCC. However, as we are completing the revisions on the manuscript, we understand that just citing one additional tumor is not informative enough, while at the same time we cannot realistically think to include all the solid tumors with sufficient detail. Hence, we removed the paragraph involving renal cell carcinoma and left colo-rectal cancer as the only specific tumor with a dedicated section, for the above-mentioned reasons (longer "history" of metastasectomy and good physio-pathological explanations).

7. Line 231: sparing near tissues, please replace the word near with normal.

Author's answer: Thanks for the observation. We changed the sentence as suggested.

Line 241: 'radio-treated', please use appropriate scientific terminology.
Author's answer: Thank you for the observation. We have corrected this and other semantic mistakes

in the manuscript

8. While the authors have quoted recent literature of the SABR-COMET study, they failed to mention that nearly 50% of the study patients had lung metastases and this information is critical for a review on pulmonary metastases.

Author's answer: Thank you for your observation. We reported the percentage data of lung metastases within the study population and, in addition, we highlighted the outcome data on patients with lung metastases.

9. Line 318: I would encourage the authors to be more inclusive as metastatic disease is encountered in daily practice of a radiation oncologist as well.

Author's answer: Thank you for this comment. Originally, the review was planned solely to report the perspective of medical oncologists, and hence no other specialists such as surgeons and radiation oncologists were originally involved. After seeing this comment, we asked the Editorial Team whether it was feasible to include other coauthors, and the Editorial Staff reported their preference not to involve additional authors in this phase of the submission. Based on this request, we still made our best to include as much data as possible based on your comments and discussions with surgeons and radiation oncologists at our Institution.

10. Line 322: was previously considered as previously cured; please remove the repeated word.

Author's answer: Thank for the observation. We removed the same sentence as you suggested. We apologize for the typo.

11. This sentence is repeated verbatim 2 times in the discussion (327-329 and 334-336)

Author's answer: Thank for the observation. We removed the same sentence as you suggested. We apologize for the typo.