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Reviewer A

Comment 1: In the introduction of the manuscript, it is necessary to clearly indicate the knowledge gaps and limitations of prior study and the clinical significance of this study.

Reply 1: Thank you very much for your review and valuable feedback on our manuscript. We appreciate your suggestions to improve the introduction section, particularly regarding the clarification of knowledge gaps and limitations of prior studies, as well as the clinical significance of our study.

To address these concerns, we will make the following revisions to the introduction.

Changes in the text: We have modified our text as advised (see line 85,98)

Comment 2: The content of this study is too simplistic. Suggest increasing research on the pooled risk ratios for an overall response rate, disease control rate and complications.

Reply 2: Thank you for your review and valuable feedback on our manuscript. We appreciate your suggestion to enhance the complexity of our study by including research on pooled risk ratios for overall response rate, disease control rate, and complications.

We have analyzed the overall survival rate (line 198) and complications (line 190). Most patients have poor general conditions, making it difficult to accurately assess the disease control rate.

We sincerely appreciate your feedback and guidance. We will expand our study to include a more comprehensive analysis of pooled risk ratios for the overall response rate, disease control rate, and complications. This will provide a more in-depth understanding of the outcomes and potential risks associated with the intervention.

Changes in the text: No changes.

Comment 3: It is recommended to add advances in the application of percutaneous CT-guided 125I brachytherapy in tumors to the discussion.

Reply 3: Thank you for your thoughtful review and for recommending the addition of advances in the application of percutaneous CT-guided 125I brachytherapy in tumors to our discussion.

We agree that this is a valuable topic and would be a valuable addition to our manuscript. Therefore, added some data of it.

Changes in the text: we added some data of percutaneous CT-guided 125I brachytherapy in tumors (see line 85).

Comment 4: The number of patient samples in this study is too small, and a large sample study should be added for verification.

Reply 4: Thank you for your insightful comments regarding our study. We appreciate your feedback and agree that a larger sample size would strengthen the validity of our findings. We

do have relatively few samples, because this is a single-center study, and we really cannot increase the sample size; however, we plan to conduct further multi-center studies, continuously update follow-up and increase the sample size.

Changes in the text: We have modified our text as advised (see line 288)

Comment 5: The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “The efficacy and safety of biliary stenting alone versus stenting combined with iodine-125 seed strand implantation for the treatment of cholangiocarcinoma with malignant obstructive jaundice: a prospective, nonrandomized, controlled clinical study , PMID: 35927776”. It is recommended to quote the article.

Reply 5: Thank you for your valuable feedback on our manuscript. We appreciate your input regarding the comprehensiveness and the inclusion of relevant citations. We acknowledge the importance of this study in the context of our research. In our revised manuscript, we will ensure that this paper is appropriately cited in the introduction section.

Changes in the text: We have modified our text as advised (see line 98)

Comment 6: How can the results of this study help to develop therapeutic strategies against lung malignant nodule? It is recommended to add relevant content.

Reply 6: Thank you for your valuable feedback on our manuscript. In our revised manuscript, we will expand the discussion section to address the potential implications and applications of our findings in the context of lung malignant nodule treatment.

Changes in the text: we added some data (see line 281)

Reviewer B

Comment 1: First, the title needs to indicate the efficacy and safety of percutaneous CT-guided 125I brachytherapy + standard chemotherapy vs brachytherapy alone, and the clinical research design of this study, i.e., a retrospective comparative cohort study.

Reply 1: Thank you for your valuable feedback on our manuscript. We appreciate your suggestion to improve the title to be better. Based on your comments, we will revise the title to the following: "The efficacy and safety of percutaneous CT-guided iodine-125 brachytherapy combined with standard chemotherapy and brachytherapy alone for lung malignant nodule: a retrospective comparative cohort stud."

Changes in the text: We revise the title : **The efficacy and safety of percutaneous CT-guided iodine-125 brachytherapy combined with standard chemotherapy and brachytherapy alone for lung malignant nodule: a retrospective comparative cohort study**

Comment 2: Second, the abstract needs some revisions. The background did not describe the clinical significance of comparing percutaneous CT-guided 125I brachytherapy + standard chemotherapy vs brachytherapy alone and what the current knowledge gap is. The methods need to describe the inclusion criteria of patients, how the two groups were assigned, the

measurements of efficacy and safety outcomes, and follow up procedures. The Results need to briefly summarize the clinical characteristics of the two groups, in particular their baseline comparability. The current conclusion should be tone down since this is not a RCT.

Reply 2: Thank you for your valuable feedback on our manuscript. We appreciate your suggestions for improving the abstract. We will address each point raised and make the necessary revisions accordingly. 1. Background: We acknowledge that the current description of the background may not fully communicate the clinical significance of comparing percutaneous CT-guided 125I brachytherapy + standard chemotherapy vs brachytherapy alone, as well as the existing knowledge gap. In the revised abstract, we will expand on the clinical significance of this comparison and clearly state the research gap it aims to address. 2. Methods: We appreciate your comment on the need for additional details regarding the inclusion criteria, group assignment, measurements of efficacy and safety outcomes, and follow-up procedures. In the revised abstract, we will provide a concise yet comprehensive overview of these aspects, ensuring readers have a clear understanding of our study design and methodology. 3. Results: We understand the importance of summarizing the clinical characteristics of the two groups, particularly their baseline comparability. In the revised abstract, we will include a brief summary of the relevant clinical characteristics to highlight the comparability between the groups at the start of the study. 4. Conclusion: We acknowledge your point about toning down the current conclusion since our study is not an RCT. In the revised abstract, we will modify the conclusion to accurately reflect the findings of our retrospective comparative cohort study, avoiding any overstated claims. Thank you for your insightful comments, which will significantly enhance the clarity and quality of our manuscript.

Changes in the text: We have revised the Abstract (see line 34)

Comment 3: Third, in the introduction it remains unclear why the authors compared brachytherapy + standard chemotherapy vs brachytherapy alone, not brachytherapy + standard chemotherapy vs chemotherapy alone. The authors did not review the potential safety outcomes of brachytherapy + standard chemotherapy and what the current knowledge gaps are on the efficacy and safety of brachytherapy + standard chemotherapy.

Reply 3: Thank you for your additional comments regarding the introduction section of our manuscript. We appreciate your feedback, and we will address the points raised to provide a clearer rationale for our choice of comparison and to discuss the potential safety outcomes and knowledge gaps in more detail.

Changes in the text: We have modified our text as advised (see line 98).

Comment 4: Fourth, in the methodology of the main text, please describe the clinical research design, sample size estimation procedures, and assessment of baseline clinical factors. In statistics, please describe the test of the baseline comparability between the two groups and statistical methods for adjusting the potential confounders.

Reply 4: Thank you for your feedback regarding the methodology section of our manuscript. We appreciate your suggestions, and in the revised version, we will provide a more comprehensive description of the clinical research design, sample size estimation procedures, assessment of baseline clinical factors, and statistical methods used to assess baseline

comparability and adjust for potential confounders.

Changes in the text: we added some data (see line 116 125; 173).

Comment 5: Finally, please consider to cite several related papers: 1. Niu L, Zhou L, Xu K, Mu F. Combination of cryosurgery and Iodine-125 seeds brachytherapy for lung cancer. *J Thorac Dis* 2012;4(5):504-507. DOI: 10.3978/j.issn.2072-1439.2012.09.03. 2. Xu K, Niu L, Mu F, Hu Y. Cryosurgery in combination with brachytherapy of iodine-125 seeds for pancreatic cancer. *Gland Surg* 2013;2(2):91-99. doi: 10.3978/j.issn.2227-684X.2013.04.04. 3. Shi CZ, Zhao Q, Luo LP, He JX. Size of solitary pulmonary nodule was the risk factor of malignancy. *J Thorac Dis* 2014;6(6):668-676. doi: 10.3978/j.issn.2072-1439.2014.06.22.

Reply 5: Thank you for your valuable feedback on our manuscript. We appreciate your input regarding the comprehensiveness and the inclusion of relevant citations. We acknowledge the importance of this study in the context of our research. In our revised manuscript, we will ensure that this paper is appropriately cited in the introduction section.

Changes in the text: We have modified our text as advised (see line 85,98).