PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 69464

Title: Long-term clinical outcomes of lipiodol marking using standard gastroscopy for image-guided radiotherapy of upper gastrointestinal cancers

Reviewer's code: 03709972

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: Australia

Manuscript submission date: 2021-07-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-05 09:06

Reviewer performed review: 2021-07-06 15:13

Review time: 1 Day and 6 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes,   2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes   3 Key words. Do the key words reflect the focus of the manuscript? Yes   4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes   5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Yes 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Yes, the research objectives was achieved by the experiments.   7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently?   # discussion "the lack of a direct comparison with S-IGRT" >> Suggest to comment on CBCT fusion based on soft tissue [not bone] matching [for example, see ACR-ASTRO Practice Parameter for Image-guided Radiation Therapy (IGRT), Am J Clin Oncol . 2020 Jul;43(7):459-468] vs on fiducial markers in the current manuscript.   8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Figures and tables were sufficient and good.   9 Biostatistics. Does the manuscript meet the requirements of biostatistics? The manuscript meet the requirements of biostatistics.   10 Units. Does the manuscript meet the requirements of use of SI units? Yes   11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and

discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? # "there are conflicting data regarding the efficacy of increased radiation dose in treating oesophageal cancer.29" >> suggest to update ref-29 as its full paper "J Clin Oncol. 2021 Jun 8:JCO2003697. doi: 10.1200/JCO.20.03697. Online ahead of print.PMID: 34101496", may also cite another randomized controlled trial [Zhonghua Yi Xue Za Zhi. 2020 Jun 16;100(23):1783-1788., https://pubmed.ncbi.nlm.nih.gov/32536123/] 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? >> Appropriate 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? >> STROBE Statement was provided 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? >> Ethic approval was mentioned in the text "Austin Research Ethics Committee: H2013/04975"

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Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 69464

Title: Long-term clinical outcomes of lipiodol marking using standard gastroscopy for image-guided radiotherapy of upper gastrointestinal cancers

Reviewer's code: 05465713

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Attending Doctor, Doctor, Surgeon, Surgical Oncologist

Reviewer's Country/Territory: China

Author's Country/Territory: Australia

Manuscript submission date: 2021-07-05

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Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
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SPECIFIC COMMENTS TO AUTHORS

The authors reported the long-term outcomes of patients with upper gastrointestinal cancers after image-guided radiotherapy and comparable outcomes to literarure. This study was interesting and might provide some useful suggestions for clinical practice. This study was well written and structured. I support publication of this excellent study.

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 69464

Title: Long-term clinical outcomes of lipiodol marking using standard gastroscopy for image-guided radiotherapy of upper gastrointestinal cancers

Reviewer's code: 02537773

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Academic Research, Associate Professor, Doctor, Lecturer

Reviewer's Country/Territory: Germany

Author's Country/Territory: Australia

Manuscript submission date: 2021-07-05

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Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

The work deals with outcomes of lipiodol for image-guided radiotherapy. The authors have presented in 2016 the preliminary report on feasibility and aimed to study the clinical outcomes.   Little is known about the technique, therefore the information is very welcome in scientific community.   The title is clear. The abstract is quite extensive. The written language is very good. The infection technique description is very clear. Comments: 1. The authors use the wording fiducials. It is quite uncommon to apply this for fluid-based injection. Therefore, to keep the uniqueness of the method especially the difference to classical fiducial I personally would avoid the misleading wording and rather focus on marker (or lipiodol-marker etc). 2. The authors claim the method is less expensive, but do not provide the information/comparison. 3. Study flow chart is not complete: how many were screened? How many were excluded? What was the selection process for the patients for lipiodol-marking? 4. Why no historical cohort or subjects that havent received the lipiodol marker were included for comparison? 5. How long is the persistence of the marker in the tissue?   6. I have no concerns regarding the retrospective data analysis, but the use of a new tool may probably need the written agreement from the patients on the use of the medical product (at least off label use) while having approved alternatives? 7. More images from CT showing the correct placement would be very welcome. 8. What is the explanation of non-visibility of lipiodol-based markers? Why was IGRT not possible in 2 patients? 9. What is the histological view of the marker after surgery which was performed in some of the patients? 10. What is the time to treatment (table 2)? 11. The use of S-IGRT with 4 patients makes little sense to me, rather, historical or additional cohorts would be welcome. Why did the authors not used larger cohort including also the patient that were excluded for other issues. 12. Kaplan Meier Curves   would benefit from inclusion

of patient numbers at risk/follow up. 13. Figure 5 needs to be expanded by more images and probably also including the patients with S-IGRT. 14. What is the explanation for the low range of F-IGRT? 15. Table 1 would benefit from inclusion of additional columns related to the F-IGRT and S-IGRT, since it is part of the key analysis. 16.　　The conclusion on survival, PFS is speculative as have not been studied in this work (no comparison group)

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SPECIFIC COMMENTS TO AUTHORS

The authors have addressed my comments and where appropriate updated limitations section.