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Commentary: "Long-Term Outcomes and Prognostic Analysis of Computed Tomography-Guided Radioactive ^{125}I Seed Implantation for Locally Recurrent Rectal Cancer After External Beam Radiotherapy or Surgery": Letter to the Editor

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A Commentary on

Long-Term Outcomes and Prognostic Analysis of Computed Tomography-Guided Radioactive 125I Seed Implantation for Locally Recurrent Rectal Cancer After External Beam Radiotherapy or Surgery

By Wang H, Wang L, Jiang Y, Ji Z, Guo F, Jiang P, Li X, Chen Y, Sun H, Fan J, Du G and Wang J (2021). Front. Oncol. *10:540096. doi: 10.3389/fonc.2020.540096*

Because ^{125}I seeds can deliver a high dose of radiation to the tumor target while sparing surrounding normal tissues, it is increasingly used for the treatment of various cancer types and has already achieved promising efficacy. In a recent retrospective study, Wang et al. (1) investigated the long-term efficacy and normal tissue toxicities experienced by 101 patients with locally recurrent rectal cancer (LRRC) after external beam radiotherapy or surgery treated by interstitial implantation of ^{125}I seeds. The study is of great significance in the treatment of LRRC, which offers a highly effective treatment. However, there are still some issues that we expect to discuss with the authors.

First, when they applied the Chi-square test and Fisher's exact test to analyze factors correlated with adverse effects, they did not include the dose of the organ at risk (OAR) such as D2cc or D0.1cc of skin or mucosa. It is well known that the dose of OAR is closely related to the occurrence of radiation damage (2–4). Therefore, we recommend that the authors further analyze the detailed relationship between the dose of OAR and radiation damage. We also hope that the authors can explore the cutoff value of the dose of OAR (when the dose of OAR is greater than this calculated cutoff value, radiation damage is more likely to occur). Such results may be more favorable to the

formulation of a preoperative implantation plan to control post-implantation radiation damage. In addition, it is also necessary to include D100, V150, and V200, because D100 can reflect the dose in the peripheral area of the tumor, and V150 and V200 can reflect the volume of the high dose within the tumor target (5, 6). In our recent study (6), we found that the faster the tumor shrank, the more likely the ^{125}I seeds were to gather centrally, which might lead to the local ultra-high dose region, thereby causing radiation damage to surrounding normal tissues. If patients achieve complete remission over short periods, we believe that it is more likely to lead to radiation damage (6, 7). Thus, the short-term efficacy should also be included in the analysis of adverse effects.

Additionally, when they analyzed factors associated with local control (LC), they did not include all observed postoperative parameters such as D100, V150, homogeneity index (HI), conformal index (CI), and external index (EI), which we suppose are of paramount importance. We suggest that the authors include these missing parameters recorded. Another issue is how is the cutoff value calculated? For example, why is D90 grouped by 129 Gy? Why is GTV grouped by 50 cm^3? Unfortunately, we did not find the grouping basis in the *Method* section of the article. We hold that the most scientific approach is to use X-tile software to determine the cutoff value for all the continuous data (8). Furthermore, as the authors stated, treatment modalities used for LRRC patients after ^{125}I seed implantation were not consistent as well; some patients received postoperative chemotherapy, which, however, was poorly tolerated by other patients. It is well known that the combination of radiotherapy and chemotherapy can contribute to significant improvements in local tumor control and cure rates. Thus, it is recommended to include postoperative chemotherapy for covariate adjustment when the Cox proportional hazards regression model is used for multivariate analysis.

In conclusion, the authors left out some important variables in their analysis of adverse effects, and they failed to include postoperative chemotherapy for covariate adjustment in multivariate analysis of LC. In addition, they did not state the grouping basis of continuous data in the *Method* section of the article. We believe that the most scientific approach is to use X-tile software to determine the cutoff value for all the continuous data.

AUTHOR CONTRIBUTIONS

EC, FZ, and CJ wrote the letter. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Wang H, Wang L, Jiang Y, Ji Z, Guo F, Jiang P, et al. Long-Term Outcomes and Prognostic Analysis of Computed Tomography-Guided Radioactive ^{125}i Seed Implantation for Locally Recurrent Rectal Cancer After External Beam Radiotherapy or Surgery. *Front Oncol* (2021) 21(10):540096. doi: 10.3389/fonc.2020.540096
2. Jiang Y, Ji Z, Guo F, Peng R, Sun H, Fan J, et al. Side Effects of CT-Guided Implantation of 125I Seeds for Recurrent Malignant Tumors of the Head and Neck Assisted by 3D Printing Non-Co-Planar Template. *Radiat Oncol* (2018) 13(1):18. doi: 10.1186/s13014-018-0959-4
3. Mao MH, Zhang JG, Zheng L, Gao H, Zhang J, Liu SM, et al. The Incidence of Radioepidermitis and the Dose-Response Relationship in Parotid Gland Cancer Patients Treated With 125I Seed Brachytherapy: Incidence of Radioepidermitis and the Dose-Response Relationship. *Strahlenther Onkol* (2015) 191(1):26–33. doi: 10.1007/s00066-014-0738-6
4. Kuo HC, Mehta KJ, Yaparpalvi R, Shankar V, Bodner W, Garg M, et al. Model Assessment of Individual Tumor Control Rate and Adverse Effects in Comparing Locally Advanced Cervical Cancer Treatment Using Intracavitary With and Without Interstitial Brachytherapy. *J Contemp Brachytherapy* (2016) 8(6):525–32. doi: 10.5114/jcb.2016.64743
5. Okazaki E, Kuratsukuri K, Nishikawa T, Tanaka T, Sakagami M, Shibuya K. Comparison of Post-Implant Dosimetrics Between Intraoperatively Built Custom-Linked Seeds and Loose Seeds by Sector Analysis at 24 Hours and 1 Month for Localized Prostate Cancer. *J Contemp Brachytherarpy* (2020) 12 (4):317–26. doi: 10.5114/jcb.2020.98110
6. Chen E, Wang J, Zhao J, Liu Z, Xu K, Liang Y, et al. Dynamic Dose Study of 125I Seed Implantation in Treating Recurrent and Metastatic Squamous Cell Carcinoma at Two Months After Surgery. *J Intervent Radiol* (2020) 29(3):262–6. doi: 10.3969/j.issn.1008-794X.2020.03.009
7. Niu S, Di X, Du S, Shao Y, Zhang H, Wang J. The Effect of Tumor Volume Reduction on Duodenal Dose After 125I Seed Implantation. *Chin J Radiol Med Prot* (2017) 37(3):209–11. doi: 10.3760/cma.j.issn.0254-5098.2017.03.009
8. Camp RL, Dolled-Filhart M, Rimm DL. X-Tile: A New Bio-Informatics Tool for Biomarker Assessment and Outcome-Based Cut-Point Optimization. *Clin Cancer Res* (2004) 10(21):7252–9. doi: 10.1158/1078-0432.CCR-04-0713

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