

Peer Review File

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Reviewer A

Comment 1: Veronesi U et al reported the treatment outcome about the IBRT compared to EBRT (Lancet Oncol. 2013 Dec;14(13):1269-1277.) This study is a randomized controlled equivalence trial. I think that the significance about IBRT is explained in this article. Please explain what the significance of this study.

Reply: We admit that we did not emphasize its significance when quoting this randomized controlled trial, and we revised it according to your opinion. We believe that despite the benefits of IORT, clinicians are most concerned about whether it will increase the recurrence rate, and the significance of this randomized controlled trial is to allay clinicians' concerns about the recurrence.

Changes in the text: We explained the significance of this study, see Page 12, line 7-17.

Comment 2: Recently, important article is reported. Brunt AM et al reported that 26Gy/5 fraction is superior to 40Gy/15 fraction and 27Gy/5 fraction in pT1-T3/pN0-pN1/M0 patients about the ipsilateral side recurrence rate (Lancet Onco.2020.21(5): 685-698. Quality of life after breast-conserving therapy and adjuvant radiotherapy for non-low-risk ductal carcinoma in situ (BIG 3-07/TROG 07.01): 2-year results of a randomized, controlled, phase 3 trial). In your article, patients received 50Gy and 39Gy-42.9Gy irradiation were enrolled. But I think that 26Gy/5 fraction may become standard therapy in EBRT. Please explain what the significance of this study.

Reply: We totally agree with you. After reading this article, we found this study is of great reference significance and quoted it in our manuscript to show the progress of the hypofractionation radiotherapy strategy.

Changes in the text: See Page 4, line 9-13.

Comment 3: Please write the boost irradiation dose (what is the information about the cut surface).

Reply: We would like to explain the boost irradiation dose and even include it in the statistical analysis, but the SEER database does not include information on irradiation doses, we can only get information about the mode of radiotherapy from it. We believe that it is important to design rigorous study with our own data and incorporate it into analyses in the future.

Changes in the text: We emphasize the importance of designing rigorous studies with our own data and incorporating irradiation dose into analyses in the future, see Page 14, line 4-7.

Comment 4: I think that relapse rate (irradiated breast) is important endpoints. If it is possible, please evaluate the rate (irradiated breast).

Reply: Although relapse rate is an important factor that merits analysis during the

comparison of two different radiotherapy modalities, we could not analyze recurrence data because information of recurrence is not recorded in the SEER registry. We sincerely believe that it's a good direction to evaluate relapse rate between IORT and EBRT in future well-designed longitudinal studies.

Changes in the text: We emphasize the importance of evaluating relapse rate between IORT and EBRT in future well-designed longitudinal studies, see Page 14, line 4-7.

Comment 5: In your article, there are next two results ①prognostic factor and ②IBRT/EBRT OS. I think that ②IBRT/EBRT OS is the most important result in this study. But this result is reported in another article. Veronesi U et al reported the treatment outcome about the IBRT compared to EBRT (Lancet Oncol. 2013 Dec;14(13):1269-1277). I think that ①prognostic factor is reported in some article. What is the news?

Reply: To the best of our knowledge, the number of patients in the IORT group of ELIOT trial by Veronesi U et al was only 651, and the primary endpoint was relapse rate, the overall survival was only a secondary outcome. Our study compared IORT and whole-breast EBRT in early stage breast cancer basing on a large, nationwide population-based registry, with a median follow-up period of 36 months, up to 1450 patients included in IORT group, and the baseline clinicopathological factors fully matched by PSM. The news in our study is that we have more patients, we take OS as the primary endpoint and we further compare the impact of beam radiation and radioactive implants on prognosis. In addition, in terms of study design, our study is more rigorous than general retrospective studies. Although there have been studies on IORT, the conclusions still need to be further verified, our study is a strong verification for these conclusions.

Reviewer B

Comment: This article is topical and of great interest to the radiation oncology community. The manuscript is logically organized and the scope is impactful. However, the manuscript requires significant proof reading and revision to improve the quality of English as there are many grammatical mistakes.

Reply: We proofread this paper repeatedly and corrected some grammatical errors.