

Peer Review File

Article Information: <https://dx.doi.org/10.21037/tcr-23-88>

Reviewer A

Comment 1: It would be interesting to know how many patients received 50 Gy/fraction of 2 Gy and how many 40 Gy/fraction of 2.67 Gy I suppose.

Reply 1: We thank the reviewer for the input. As only few patients received other daily fractionation than 2 Gy we initially did not show this in detail. As it seems to be of interest we expanded the information in table 1 to show given doses in detail.

Additionally, we added this explanation to the discussion session:

Still there is a lot of room for different interpretation of the results. The present analysis had a conservative interpretation. This means we rated any difference in comparison to the not operated breast as a worse cosmetic outcome. Regardless what lead to the difference (operation, chemotherapy, radiation or kind of radiation).

Total dose (Gy)	Single fraction (Gy)	Number of patients
40,05	2,67	1
45	1,8	1
46	2	40
50	2	27
WBI + EBRT	2	4

Changes in the text: Table 1 was supplemented with regard to those parameters.

Comment 2: Include how many patients had whole-breast irradiation without delay and how many after chemotherapy.

Reply 2: We thank the reviewer for the input. 4 patients had neoadjuvant chemotherapy and therefore no delay in WBI. In all other patients chemotherapy was given before starting whole-breast irradiation.

Changes in the text: Table 1 was supplemented with regard to this parameter.

Comment 3: Add the chapter title REFERENCES.

Reply 3: We thank the reviewer for pointing this out.

Changes in the text: We added the chapter title REFERENCES

Comment 4: And finally, I think it would be greatly appreciated if you could include a photo of a patient with a good cosmetic result and another with bad cosmetic results since the article is about cosmetics and this is a visual aspect.

Reply 4: We thank the reviewer for the input. We have added images of each severity according to the Harvard score in the respective positions (arms up, arms down and from the side).

Changes in the text: We added Figure 2.

Reviewer B

Comment 1: On table 1 you show the characteristics of the patients but

Comment:1.1 According to tumor size, in order to characterize better this series, it will be useful to know median size, range, or otherwise distribute the patients by groups, i.e. larger than 3.5, 2.0 to 3.5 and less than 2.0 cm.

Reply 1.1: We thank the reviewer for the input. The median tumor size (pT), which was determined by the pathologist, was 1.53 cm.

Changes in the text: Table 1 was supplemented with regard to this parameter.

Comment:1.2 Patients receiving chemotherapy: there were concomitant treatments?

Reply 1.2: 4 patients had neoadjuvant chemotherapy and no delay in WBI. In 42 patients chemotherapy was given before starting whole-breast irradiation. There were no concomitant applications of chemotherapy and WBI.

Changes in the text: None

Comment:1.3 Chemotherapy without anthracyclines, can you group them? i.e alkylating agents, antimetabolites...

Reply 1.3: We thank the reviewer for the input. Unfortunately, the exact treatment scheme was not recorded separately for the patients who received chemotherapy without anthracyclines, so that we are unable to make a more detailed subdivision. An error in table 1 regarding the number of patients who received chemotherapy with anthracyclines has been corrected.

Changes in the text: Table 1 was supplemented with regard to this parameter.

Comment:1.4 Can you explain the reason for re-resection in 8 cases? It seems that you had 5 cases of close margins. Please clarify.

Reply 1.4: We thank the reviewer for the input. Re-resection was performed due to close margins after resection in one person. No re-resection was performed due to toxicities. In all other cases re-resection was performed intraoperatively before starting IORT based on frozen sections.

Changes in the text: Table 1 was supplemented with regard to this parameter.

Comment: 2 Did you collect data on incidence of radiation dermatitis and grade?

Reply 2: Thank you for highlighting this important issue. We added the information as we collected the data.

Changes in the text: Wound healing disorders or seroma aspiration after operation appeared in 3 patients each. Six patients showed an erythema after WBI. Due to low event rate no further analysis was done to evaluate any influence of acute toxicity.

Comment:3 What was the incidence of seroma or hematoma in your patients? Any patient needed any drainage during follow-up? There were any other post-surgical complications like retraction or infection? If possible, please specify.

I consider that any incidence of complications can have some impact in final cosmesis results.

Reply 3: Thank you for highlighting this important issue. We added the information as we collected the data. A detailed analysis of toxicity data will be shown for the whole TARGIT BQR cohort in a separate analysis.

Changes in the text: Wound healing disorders or seroma aspiration after operation appeared in 3 patients each. Six patients showed an erythema after WBI. Due to low event rate no further analysis was done to evaluate any influence of acute toxicity.

Comment:4 Did you collect data on subjective cosmesis by patient, nurse or physician to make comparison with standardized images?

Reply 4: Thank you for this important question. In this analysis a lay person, a radiation oncologist and a gynecologist rated the photos. We do not have ratings from patients or nurses.

Changes in the text: none

Comment:5 Do you consider that software tools like BCCT-Core could be implemented in practice as a more robust objective evaluation? May be, you can make any mention in a short paragraph and individualize the reference 18 (Cardoso JS). If you consider that improved software should include more images (anterior and side) or different arms position, please consider to make any comment.

Reply 5: We share your opinion and have added a corresponding paragraph in the discussion part. Changes in the text: It has already been shown that the evaluation of the standardized photographs by software tools is comparable to the evaluation by experts.(18) By expanding the parameters included by the software tool (more images from different perspectives and more images with different positioning of the arms), even greater accuracy in the correct assessment of the cosmetic outcome could be achieved and thus represents a promising approach.

Comment:6 Reference 25 is incomplete. Please correct as follows : Clin Transl Oncol 2022 Sep;24(9):1732-1743.

Reply 6: The Reference has been corrected.

Changes in the text: 25. Laplana M, Garcia-Marqueta M, Sanchez-Fernandez JJ, Martinez-Perez E, Perez-Montero H, Martinez-Montesinos I, et al. Effectiveness and safety of intraoperative radiotherapy (IORT) with low-energy X-rays (INTRABEAM((R))) for accelerated partial breast irradiation (APBI). Clin Transl Oncol. 2022 Sep;24(9):1732-1743.