

## Peer Review File

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### Reviewer A

The authors have done a retrospective study on 168 patients undergoing immediate expander reconstruction, and have collected demographic data, expansion data, timeline and complications.

Comment 1: However, there is no mention in text or tables in the results section concerning expansion data or time between operations, except their conclusion “Interestingly, a large final expansion volume and rapid expansion velocity of expander negatively influenced the occurrence of overall complications”. Please provide relevant data to support this.

Reply 1: We had already mentioned these points in the results, but for better understanding, a more explanation has been added to the text.

Changes in text: page 10, lines 18–20

Comment 2: The captions for figure 1 and 2 is the only mention of expansion velocity (230 cc / 58 days and 250 cc / 94 days, respectively). This seems extremely slow, as the standard expansion velocity in our clinic is (50-)100 cc /week.

Reply 2: Compared to Western patients, the target volume in Asian patients is smaller. When we calculated the biweekly speed, in figure 1, the patient's velocity was 55 cc/14 days, and in figure 2, the patient's velocity was 33 cc/14 days. This is not an extremely slow speed. We have added this point as a limitation of our study.

Changes in text: page 13, lines 17-24

Comment 3: So, since the title of this paper concerns expansion strategy and outcomes, please provide data and explanations:

- how do you choose expander size and fill volume compared to original breast size?
- implant size compared to original breast size (smaller/same/larger)
- initial fill volume
- intervals and volume for expansions
- interval from final expansion to second surgery

Reply 3: For a better understanding, we have added more details regarding expander/implant surgical strategy.

- Changes in text: page 6, lines 13-18

- Changes in text: page 6, lines 20-22

- Changes in text: page 7, lines 2-8

Comment 4: There are some contradictory statements in this paper: 2/19-21 and 7/27-29 on the size of mastectomy flaps and the risk of necrosis. Please revise.

Changes in text: page 11, lines 14 - page 12, 3

Comment 5: The statements that faster expansion would decrease the risk of seroma and biofilm formation seem speculative. Please provide references.

Reply 5: For improved clarity, I edited the sentence.

Changes in text: page 13, lines 2-3

Comment 6: The statement that obese patients use their upper body instead of core strength thereby causing seroma formation seems even more speculative.

Reply 6: I deleted the sentence, and added more details regarding this point.

Changes in text: page 12, lines 16-19

Comment 7: I don't understand the statement 7/29-8/2 about contact surface between implant and mastectomy flaps in different sized breasts (this statement makes no sense, unless your strategy is "one size fits all" for choice of expander). Please explain.

Reply 7: I apologize for the confusion. To make this point clearer, that entire paragraph has been revised.

Changes in text: page 11, lines 13-page 12, 3

Comment 8: In the conclusion, the authors discuss the expansion volume and velocity, and, again, there are no data in this paper to support these statements. In addition, they state that breast size can predict the risk of complications, but in their multivariate logistic regression analysis, this is not the case.

Reply 8: I have added a more detailed interpretation of the data to the results section.

Changes in text: page 10, lines 18-20

## **Reviewer B**

I am very grateful for your submission of this study to Gland Surgery journal as it is considered as a field of high interest and essential study for reconstructive breast surgeons. However, many aspects could improve based on the title and purpose of the study, so I would like to provide my comments on it.

Comment 1: The paper mentioned that as the first surgical procedure for the 2 stage operation, the tissue expander was inserted and the velocity was investigated. However, in this study, the group was classified as gram, which is the specimen weight. The weight and the volume varies depending on the density, so it is considered that this section requires supplementation.

Reply 1: Thank you for raising this pertinent point. Actually, we also thought about the possible relationship between gram and volume of breast. Intraoperatively, we measured both the mastectomy specimen volume and weight. However, too many variables can confuse readers, so we used specimen weight for our analysis, which makes it easier to understand. In this study, we have used Pearson's correlation factor between breast volume and weight (0.975). However, this can be a potential limitation; thus, we have added this point to our discussion section.

Changes in text: page 14, lines 9-13

Comment 2: Additionally, it is unclear how the breast volume was measured preoperatively as well as how the final breast volume was set up.

Reply 2: In the stage of expander insertion operation, intraoperatively, we noted the extent of initial expander inflation. The accumulated inflation volume after serial follow up was added to the initial inflation volume to calculate the final inflation volume. We have also added more details

regarding the assessment to the methods section.

Changes in text: page 7, lines 15-18

Comment 3: Moreover, it is written that the expansion velocity was researched, but the formula listed in the manuscript expressed a formula although it is definite even without having to clarify the formula, and the numerical values that should be included in the formula are unclear.

Reply 3: As per your suggestion, we have mentioned the units.

Changes in text: page 7, lines 22

Comment 4: If the first injection volume is eliminated from the final breast volume and divided by the date, then the daily cc expansion can certainly be calculated, but would treatment be available on days off and also on the weekends? Moreover, only the formula was clarified while there is a lack of explanation about how the initial volume and the final volume were decided, so this is pointed out as a problem.

Reply 4: No treatment was performed on weekends or days off. The inflation period was calculated as the difference between the first inflation date and the second surgery date. And how to determine the initial volume and the final volume was mentioned in the reconstructive technique part.

Changes in text: page 6, lines 13-18.

Comment 5: Patients' photos that were attached to support this reasoning were all patients with a very small breast volume, and these patients had surgical procedures with augmentation on the opposite side during the 2nd operation, so I have questions about how the final expansion volume was decided.

Reply 5: In our protocol, the final expansion volume limit was never over 120% of the designated expander volume. We have added more details regarding assessment in the methods section.

Changes in text: page 6, lines 13-18.

Comment 6: In addition, I would like to mention that the aesthetic outcome of both patient groups as attached are not satisfying. I am carefully presupposing that the result could have been better if the mastectomy had the equal incision as MLF.

Reply 6: We added your point regarding racial difference as a limitation. Actually, incision was decided upon by the breast surgeon, not the plastic surgeon.

Changes in text: page 13, lines 17-24.

Comment 7: Moreover, it is listed in the manuscript that there are more complications when the group is divided by the specimen weight and the size of the breast is larger, and it seems like skin sparing mastectomy and expansion performed on large breast patients is unnecessary.

In this case, should both breasts be reduced instead of the expander, and even give consideration to the aesthetic outcome? It is because I am aware that most patients want reduction because of discomfort when it gets bigger than 500cc, so do you mean to implement expansion fast, to a size that is 20~30% bigger?

Reply 7: We mentioned the racial difference in the discussion section. In Asian patients, breast reduction mammoplasty is not a common procedure, lesser than ten cases per year. Even for

size more than 500 cc, they need large breast volume, usually because of wide axillary dissection. To cover the depressed soft tissue, our surgeon had to insert a large volume expander/implant.

Changes in text: page 13, lines 17-24.

Comment 8: In addition, for patients who are likely to need radiotherapy after the surgical procedure, autologous breast reconstruction is usually performed and set up indication towards a direction that can minimize the complication from radiotherapy, and I am uncertain with which basis, surgical procedure of implant was performed on the patients that are enrolled in this study.

Reply 8: In the description of the demographics, we have provided more details about the pre- and post-adjuvant treatment, including chemotherapy and radiotherapy.

Comment 9: I assumed that expansion can be attempted since the skin flat is soft due to neoadjuvant radiation therapy, but unfortunately, very little patient group received neoadjuvant radiation therapy in this study. In addition, I would understand the use of the expander if most are cases in which radical mastectomy is performed and there is a lack of skin flap, but most in the patient pool are SSM and NSM.

Reply 9: In addition to the case of insufficient skin flap due to radical mastectomy, we decided to insert the expander when the skin flap was thin or not well perfused, and there was a possibility of radiation therapy after mastectomy.

Comment 10: Additionally, the prepectoral and subpectoral patient groups were researched without classification, and the area and part of the pocket that applies ADM are different, so it seems like different problems will occur during expansion, and nothing was mentioned about it, and there is not enough description about the two surgical procedures and it is considered that the indication that classifies the two surgical methods are deficient.

Reply 10: Thanks for raising this great point. We had completely excluded these points. According to your suggestion, we have added more details regarding the procedure employed.

Comment 11: Even in the complication section, there is a very low number of patients with statistical significance in table 2, where it was claimed that complications occur more in the large breast in terms of statistical significance, so it is considered that a review should be made first about whether the meaning is statistically valid. Based on these aspects, could it be stated that there is a negative relationship with the complication with greater expansion volume?

Reply 11: Yes, it is. For a better understanding of the statistics, we have added more details to the results section.

Changes in text: page 10, lines 18-20.

Comment 12: Furthermore, it seems that an explanation about the product for tissue expander insertion or photos should be added.

Reply 12: As per your suggestion, we have added a more extensive explanation for the figures. Changes in text: page 6, lines 2-5.

Comment 13: The information that only CGCryoderm was used as ADM is not enough. Moreover, in terms of the expansion velocity, are you trying to convey the meaning that it should be enlarged rapidly by 20-30% for 2-4 weeks? The difference between the 2-4 weeks gap is too big, and there is no data of volume measurement, so it does not seem reasonable to expand it largely by 20~30%.

Reply 13: We hope our previous answer addresses this comment as well.

Comment 14: Even in the discussion section, the explanation and reference about the risk factors like the large breasts and BMI in implant surgery seem very lengthy and this seems unnecessary. My question is, isn't this study intended to start with the expander to set up a directivity about expanding the speed of the expander during the process of connecting into the 2nd operation? It seems that explanation should be reduced for aspects that reconstructive breast surgeons would easily know about and also irrelevant to the study and speculative description for an explanation about the findings should also be condensed.

Reply 14: We totally agree with you. We have made many changes to the discussion section. Please go through them and consider our manuscript for publication.

- Changes in text: page 11, lines 14-page 12, lines 3

- Changes in text: page 12, lines 16-19

Comment 15: It is considered that there will be limits as a retrospective study instead of a prospective study, but the focus on the study should be set right to establish the method again and perform an analysis about the findings again.

Reply 15: We added this point to our discussion section as a study limitation.

Changes in text: page 14, lines 13-16

Thank you.

### **Reviewer C**

The authors present a retrospective study looking at outcomes after two-stage expander-implant breast reconstruction. There are several questions which may ask the authors to clarify:

Please comment on the following:

Comment 1: I could not find specific data about the average follow up period. The authors state a follow-up of at least 6 months. This is very short, as a lot of implant-based breast complications occur at a longer follow up. Please comment.

Reply 1: We added the follow up period range in the methods section. Six months was simply an inclusion criterion.

Changes in text: page 5, lines 3-4

Comment 2: The results of the study are limited by the Asian study population and therefore restricted applicability to women of different ethnicity. I might suggest a change of the title to reflect this study population.

Reply 2: We added more details regarding racial difference in the discussion section.

Changes in text: page 13, lines 17-24.

Comment 3: The authors show 2 patients in figures 1 & 2 - both with small cup sizes and mastectomy weight. I would rather appreciate 1 representative case from each of the 3 groups (small, medium and large breast).

Reply 3: We hope our previous answer addresses this point also.

Comment 4: In the patients presented in figures 1& 2 the reconstructed breast is much larger than before surgery. Additional breast augmentation was performed on the non-affected healthy side. Why was this approach chosen?

Reply 4: We have added more details to our discussion section.

Changes in text: page 13, lines 17-24.

Comment 5: In these cases, how was the final inflation volume determined?

Reply 5: We have added more details to our method section.

Changes in text: page 6, lines 13-18.

Comment 6: Were there differences in radiotherapy between the 3 groups?

Reply 6: In the demographics, we have explained the pre- and post-adjuvant treatment, including chemotherapy and radiotherapy, in greater detail. There was no significant differences between 3 groups

Comment 7: The authors investigated expansion velocity as a predictor of complications. However, I could not find any specific data on expansion velocity concerning the 3 different groups. Was there a difference in expansion velocity?

Reply 7: For a better understanding of the statistics, we have added more details to the results section. We apologize for this oversight. Although this is a very important point, it has caused quite a bit of confusion among the reviewers due to the way it is presented. Hence, for a better understanding, we have added a detailed explanation and hope that it can help clarify this aspect. Changes in text: page 10, lines 18-20.

Comment 8: The authors used submuscular and subcutaneous implant positioning. Was there a difference in complications between these 2 subgroups?

Reply 8: The implant insertion plane was also evaluated in this study and subcutaneous plane was used in only one case. However, it is determined by the operator through evaluating the thickness or perfusion of the skin flap. We mentioned this point in the methods section.

Changes in text: page 6, lines 8-9.

Comment 9: In the results section the parameters breast volume, -weight and -size are used. This is somewhat confusing – please use the measured parameters such as breast size / mastectomy weight / mastectomy volume.

Reply 9: For the density, both weight and volume of breast should be analyzed in the study.

#### **Reviewer D**

Comment 1: Unfortunately this paper does not convincingly make the connection between the

injection strategy and outcomes. There are simply too many other variables that impact outcome that were either ignored or glossed over. Finally, the pt images shown demonstrate a small breast expanded much more than original volume, a situation that can increase complications unrelated to breast weight, etc.

Reply 1: Thank you for the honest feedback. In order to better convince you regarding the validity and impact of this study, I have added sentences clarifying these aspects in the discussion section.

- Changes in text: page 11, lines 14-page 12, lines 3

- Changes in text: page 12, lines 16-19

#### **Reviewer E**

In the manuscript entitled “The investigation of the relation between expansion strategy and outcomes of two-stage expander-implant breast reconstruction”, Kim MJ and colleagues performed a retrospective study to identify the risk factors of complications in two stage breast reconstruction using tissue expanders. The manuscript itself did not contain new information and the study design was not rigid.

Comment 1: The complications can happen in different stage of the surgery and this requires documents.

Reply 1: We have defined the method employed to record complications in this study.

Changes in text: page 8, lines 2-5

Comment 2: Patient with neoadjuvant radiotherapy and adjuvant radiotherapy may present complications in different stage of the surgery.

Reply 2: We have defined the method employed to record complications in this study.

Changes in text: page 8, lines 2-5

Comment 3: The nipple-sparing mastectomy may increase the complications. However, the complications need to be determined because it inherently increases complications due to the inclusion of complications in nipple-areolar complex.

Reply 3: The type of mastectomy was one of the variables. This multifactorial risk assessment was also evaluated concurrently, and our results demonstrated that nipple sparing mastectomy increased the complication rate.

Page 10, lines 12-14

Comment 4: The authors included TE in different plane, which makes the data less reliable.

Reply 4: I apologize, but I am unaware what “TE” means here. I really appreciate your comments and I am willing to address this comprehensively. Please provide some clarification here.

Comment 5: The risk factors that been identified are all known factors.

Reply 5: In our study, we had multi-perspective of expansion protocols and its relationship with complications. We have emphasized this aspect as a novel feature of our study.