Peer Review File

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Reviewer A

Comment 1: what data do the authors have to suggest that CGCRYODERM has "abundant molecules" for angiogenesis and recellularization? Which molecules are they referring to? Is there a reference?

Reply 1: We added the reference (number 20) on "abundant angiogenic growth factors" (e.g., activin A, angiopoietin-1, angiopoietin-2, CXCL16, DPPIV, EGF, endothelin-1, FGF isoforms, pentraxin 3, PD-ECGF, VEGF) of CGCRYODERM

Changes in the text: page 6 line 88

Comment 2: in the abstract, it sounds like all patients had both ADMs placed – one per breast – but in the Methods, it sounds like some study patients had both ADMs placed, depending on product availability – please clarify this very important point.

Reply 2: In our study, all patients included were reconstructed with two different ADMs (CGCRYODERM versus DermACELL per breast). Misleading sentences in the Methods section were removed from the manuscript.

Comment 3: how was sample size determined? What was the primary outcome that was being assessed? What was the expected effect size?

Reply 3: This is a retrospective cohort study. We have reviewed all ADM-implanted patients who were operated for breast reconstruction in our clinic and selected 45 patients who had undergone surgery with two different ADMs in each breast. Among the 45, eight patients who had previously undergone breast-conserving surgery were excluded. Five patients who under were treated with different reconstruction methods (one stage on one side and two stage on the other) were also excluded from this study. (page 9, line 156). We clarified the primary outcome as postoperative complications after implant-based breast reconstruction using two different ADMs per breast in the same patient. We found no significant differences between two ADMs in terms of any major outcomes.

Comment 4: the authors talk about "no statistical differences" between groups, but really this is an underpowered non-inferiority design study where there is no sample size calculation to truly enable them to make this statement.

Reply 4: We added this limitation with respect to the retrospective nature of our study and the small sample size in discussion part.

Changes in the text: page 12 line 235-236

Comment 5: given that only one patient was histologically assessed, and there is tremendous risk for sampling bias regardless, the value of the histological analysis is questionable at best.

Reply 5: We added the limitation of our study in terms of histologic analysis in discussion. We also added a brief description on the result.
Changes in the text: page 12 lines 231-234 and 241-243.

Comment 6: the manuscript needs to be edited for English grammar.
Reply 6: We requested the professional English editing.
Changes in the text: English proof is attached at the end of this script; *Acknowledgement,* page 13 line 260.

Reviewer B
Comment 1: Sizes of ADM's (8x16, 16x30), subpectoral vs. prepectoral implant placement, direct to implant vs. expander two stage, as well as extent of axillary node dissections are all critical variables required to elevate study tp publish status.
Reply 1: We added the information on sizes of ADMs used in our study as supplementary data 2. More information on axillary surgery (SLNB, ALND, plus number of lymph nodes examined), reconstruction method (one vs. two stage) and TE/implants (sizes, plus types) was added in Table 2. ADMs were placed in the subpectoral plane in all operations.
Changes in the text: Methods, page 7 line 128-129

Reviewer C: This is a retrospective study comparing two different ADMs in the same patients. However, the aim of the paper, some methodological aspects and the referencing of the paper could be improved. More information on differences between the breasts is needed.

Comment 1: Please include information on previous studies on breast reconstruction in which the two ADMs have been used, previously published complications and references!
Reply 1: We added more information and references on the previous studies comparing complications of different ADMs in both introduction and discussion.
Changes in the text: page 5 line 71-84, page 11 line 213-217.

Comment 2: Clinical outcomes is very diffuse – please be more specific regarding the outcomes of the study.
Reply 2: We changed the expressions from outcomes to postoperative complications in all sentences related to the aim of our study. We focused on inflammatory compilations such as seroma and infections. Details on these outcomes are described in the Discussion section.
Changes in the text: Page 10 line 176-186 and page 11 line 204-212.

Comment 3: This is not the first study to compare two different ADMs in the same patient:
https://pubmed.ncbi.nlm.nih.gov/33051871/

https://pubmed.ncbi.nlm.nih.gov/32515840/
https://pubmed.ncbi.nlm.nih.gov/31859575/
Reply 3: As the reviewer has pointed out, there are some articles that compared biological meshes (ADM) and synthetic meshes. We erased the expression that this is the first study to compare two different ADMs in the same patient and added those references in discussion.
Changes in the text: page 12, line 240-241.

Comment 4: Please clarify the ethics. Was the ethical permit obtained after the patients had been operated? Did the patients give informed consent to participate? Was the reason some patients obtained different ADMs availability of product in the operating room? (p. 7, lines 18-20). Where the patients informed about this? Were different implants used in the same patient as well??
Reply 4: We fully explained the possibilities that different products could be used depending on the availability of the products. All patients were aware of the information on ADMs they received. Same implants were used in all patients.

Comment 5: Some of the complications do not seem relevant for the follow-up time of 6 months (e.g., capsular contracture and prosthesis problems). Are they relevant to include?
Reply 5: Although we have previously stated that the follow-up period of our study was at least 6 months, the mean follow-up period was longer than 2 years (mean 925.78 ± 393.19 days, Table 2). We apologize for the confusion.
Changes in the text: Results, page 9 line 164.

Comment 6: Were the statistical analyses performed in Excel?
Reply 6: All data were queried using Excel and analyses were performed using SPSS. We added detailed information in statistical analysis.
Changes in the text: Methods, page 8 line 138-142

Comment 7: Histological analyses do not seem to be part of the aim of the study, as it isn't a 'clinical outcome'. Please modify.
Reply 7: We modified the primary aim of our study from (clinical) outcomes to postoperative complications.
Changes in the text: page 6 line 92.

Comment 8: There are factors, other than the ADM used, that are different between the two sides: e.g. previous breast-conserving surgery (BCS) on one side, unilateral breast cancer, please clarify. Perhaps these patients should be excluded?
Reply 8: We excluded 12 patients who had previously undergone BCS and received different reconstruction methods (one stage on one side and two stage on the other side). New 6 patients were added for analysis through additional chart review. All the changes in the period of chart review and number of

patients (excluded, included) in our study were described in *Results* (page 9 line 153-155). There were no patients with bilateral breast cancer who developed any complications in our study. We added the limitations of our study in terms of the laterality of cancer (*Discussion*, page 12 line 237-238).

Comment 9: More information on implants and TEs is needed. Were they different between the two sides?
Reply 9: We added more information on the types of implants (smooth round, anatomical textured) and TE (Siltex-textured Mentor TE, Biocell-textured Allergan TE) used in Table 2. Same types of implant/TEs were used for each patient.

Comment 10: Confounders still seem to exist at the two sides weren't identical.
Reply 10: We changed the expression from "subject-to-subject variability was removed" to "factors affecting complication risks were reduced" (page 11 line 201-202). We also added the limitation of our study in discussion (page 12 line 236-239).

Comment 11: A better discussion and comparison with previous findings in other studies are needed.
Reply 11: As suggested, we added discussion on comparison with previously reported findings.
Changes in the text: page 11 line 213-220

Comment 12: The meaning of the results from the histological analyses should be discussed.
Reply 12: We added the meaning of our results from the histological examination in *discussion.*
Changes in the text: page 12 line 230-233