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## Peer Review File

**Article information:** <http://dx.doi.org/10.21037/ga-20-775>.

### Reviewer A

Comment 1: The subject is very important because we don't have the response of the safety of lipofilling. The follow up is good because it's almost 5 years but the number of patients is too limited (45 conservative surgery and 56 mastectomy)

Reply 1: The actual number of patients per group is, for the Lipofilling group: 45 breast conservative surgeries and 80 mastectomies). In the control group we have included: 43 breast conservative surgeries and 82 mastectomies. We cannot add new patients because as this is a retrospective study. Even though, I believe we have achieved interesting conclusions that worth to be share with the surgical community.

Changes in the text: N/A

Comment 2: it's also very difficult to compare the lipofilling between conservative surgery and mastectomy because the risk of recurrence is different for these 2 technics without lipofilling: is it possible to make comparison only for conservating surgery with or without lipofilling?

Reply 2: This comparison was described in table 2. The result was not statistically significant for locoregional recurrences ( $p=0.135$ ), distant metastases ( $p=0.388$ ) and total recurrences ( $p=0.333$ )

Changes in the text: We added some data in the text (see page 6, line 4-7).

Comment 3: It's the same for the smoker patient: the risk of recurrence is increasing without lipofilling

Reply 3: I agree with you. Consequently, we had already included smoking as one of the matching variables in order to avoid a possible bias.

Changes in the text: N/A

Comment 4: For the intra ductal carcinoma: some authors (Petit and al) showed on retrospective study that lipofilling on conserving surgery treatment increase the risk of local recurrence. Is it possible to make the comparison only for invasive carcinoma?

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Reply 4: This comparison is described in table 2. The result was not statistically significant for locoregional recurrences ( $p=0.220$ ), distant metastases ( $p=0.236$ ) and total recurrences ( $p=0.092$ ).

Changes in the text: N/A

Comment 5: The most important is to know if lipofilling on conserving surgery for invasive carcinoma increase the risk. You can't compare this risk with the risk for mastectomy.

Reply 5: We have added some data in the text, which analyzes the risk of locoregional recurrences in patients with intraepithelial neoplasia and breast conservative surgery.

Changes in the text: We added some data in the text (see page 11, line 3-8).

### **Reviewer B**

Comment 1: A well designed study. Nevertheless the major limitation of the study is the short follow up. I don't think that the impact of Adipose derived stem cells can be overlooked within 45 months, but the authors provide at least mid term results.

Reply 1: I agree with you, although our study is one of the studies with longest follow up after lipofilling. The follow up is a mean of 47.2 months with an interval from 6 months to 113 months.

Changes in the text: N/A

Comment 2: The literature discussion is very well done. Regarding the section: 'The only factor that is independently associated with an increased risk of TR is the size of the breast tumor (pT). Tumors less than 5 cm present with less risk of TR compared to those bigger than 5 cm (HR = 0.017, 95% CI 0.04-0.71)'. Can you please calculate and add the Relative risk (RR) for this fact? This is very interesting.

Reply 2: Thank you for your precise and valuable comment. It has clearly helped to improve the quality of the article.

Changes in the text: We added some data in the text (see page 9, line 20-22)

### **Reviewer C**

This is a study researching the safety of lipofilling in breast conservation. It is a retrospective cohort comparison study very much like past studies that they mention in

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their discussion and in Table 5. They find no differences in LRR. These are my comments:

Comment 1: The study does not add anything new to the literature. It is similar to the studies done in Table 5. It suffers from the absolute need for a prospective high level of evidence study that nullifies confounders found in a retrospective design. This is particularly true when injecting possible stem cells in a region of past cancer albeit oncologically stable for a period of time since the initial resection.

Reply 1: Our study might be similar to some other previous ones as this is a very relevant topic for the PS community. Nevertheless, its long follow-up period (mean= 47.2 months) is unique in the literature. We have also included several matching variables helping us to achieve a better comparison with the control group.

Changes in the text: N/A.

Comment 2: A strong limitation is that there is no defined regular time interval for the fat injection which is part of a limitation of a retrospective design. The authors can argue that he matches the time interval for the cohort comparison but by not injecting at a specific time interval for all breast reconstruction creates a possible confounder of lag time to track cancer recurrence since different patients get injected at variable times post op.

Reply 2: Thank you for your precise and valuable comment. It has clearly helped to improve the quality of the article.

Changes in the text: we have modified our text as advised (see Page 13, line 4-7)

Comment 3: Please cite the meta-analysis study from Cohen et al. (Lipofilling after breast conserving surgery: a comprehensive literature review investigating its oncologic safety, Stephanie Cohen<sup>1</sup>, Yurie Sekigami<sup>1</sup>, Theresa Schwartz<sup>2</sup>, Albert Losken<sup>3</sup>, Julie Margenthaler<sup>4</sup>, Abhishek Chatterjee<sup>1</sup>, Gland Surgery 2019) and specifically address in your discussion how your design meets their 7 measures of safety when studying lipofilling in breast conservation. This is important before having a conclusion statement supporting no difference in local regional recurrence.

Reply 3: Thank you for this key comment.

Changes in the text: Changes has been added to the text according to this comment (see

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page 12, line 15-24; page 13, line 1-2).

Comment 4: How much fat was injected for correction on average. Please also provide a range.

Reply 4: Thank you for pointing this mistake.

Changes in the text: We have added the range of fat was injected per session and total (see Page 7, line 24; page 8, line 1).