Author's response to reviews

Title: Polyglycolic acid sheet with fibrin glue potentiates the effect of a fibrin-based haemostat in cardiac surgery

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Author's response to reviews: see over
Dear editor

This is in continuation of our previous correspondence. We would like to thank you and the reviewers for your suggestions and we feel that in answering the questions we have been able to improve our manuscript significantly. In the following pages, we provide answers to each question and we have revised the manuscript as was appropriate. We are sending you a “clean” version as it should appear, as well as a version where we have indicated the new text and the omitted parts.
To Reviewer: Dr Giovanni Cagnoni

Reviewer's report:
1) A more elevated number of cases for each experiment could give more statistical power but this in vitro demonstration of the effectiveness of Polyglycolic acid sheet is really far away any real intraoperative scenery with a wet field.

In response to the comment concerning low sample size, we think that the sample size is probably enough, because results from two experimental studies have reached statistically significant (p=0.03, and p=0.0004, respectively).

In response to the comment concerning far the effectiveness of PGA sheet being away real operative condition, we absolutely agree with reviewer’s comment. We have mentioned in discussion of the original manuscript that “it is probably impossible to achieve such high adhesive strength at a site of active bleeding with LV contraction in a critical situation”. It is probably the same meaning of reviewer’s comment. Our surgeon have to make the best effort to control catastrophic hemorrhage. We would just demonstrate that using a PGA sheet and fibrin glue for reinforcement of TachoComb could augment the adhesive strength in the present study, and it may be one option for such situation.

Finally, we thank you for your valuable comments that have improved our report.
**To Reviewer:** Dr Claudia Romagnoni

1. Have the authors checked the normality of the data with the Shapiro Wilk test?

   In response to the comment concerning the Shapiro Wilk test, we did not perform it.

2. The sample size is low, especially in consideration of the fact that this is an in vitro study, not an in vivo one. Are the authors sure that the small amount of data is sufficient to achieve a good statistical power?

   In response to the comment concerning low sample size in spite of in vitro study, we think that the sample size is probably enough, because results from two experimental studies have reached statistically significant (p=0.03, and p=0.0004, respectively).

3. The authors state that “one heart was used for each group” in the second experiment. Does it mean that a heart was always tested with TachoComb and one always with TachoComb, polyglycolic acid sheet and fibrin glue? If so, this may lead to a bias. It would be better if the tests were conducted on six different hearts, each one treated with both solutions.

   In response to the comment concerning how to use experimental hearts, we agree reviewer’s comment. In fact, we had used six different hearts for experimental 2. We would mean that one porcine heart was used for one TachoComb study and one TachoComb with a PGA sheet study. “One porcine heart was used for each group” in the original manuscript would mean what reviewer pointed out. We have also mentioned in the original manuscript, probably a similar matter of concern, that “The pericardium along the border of the left anterior descending artery, which was not rich in fatty tissue and not markedly curved (Figure 1B), was selected for attachment of the suture and the same site was not used again.” According to your comment, we revived our manuscript.
4. In the section “Results”, concerning the second experiment, the authors affirm that “the adhesive strength of the PGA sheet and fibrin glue combined with a TC sheet for porcine pericardium was significantly higher than that for rabbit skin”. Rabbit skin was used in the first experiment. Are the authors sure that these two informations are comparable? The test used was different. To enable this statement they should conduct the same kind of experiment (evaluation of the burst pressure with the circuit made with digital pressure gauge, syringe and pressure hardened plastic tank or evaluation of the peel-off pressure by means of the elevation of the suture loop) both on rabbit skin and porcine hearts.

In response to the comment concerning comparability between two experiments, we agree reviewer’s comment. Therefore, we omitted it in the revise manuscript.

5. In the discussion authors state that “one sheet may not have wide enough margins to be attached firmly to the ventricular surface and suppress active bleeding” so they add the PGA sheet. Being the contact surface with the healthy wall the key point for a good adhesion, they can affirm that we would not obtain the same results using, as already done in vivo by other colleagues, a pericardial patch (instead of the PGA) fixed with the glue?

Thank you for valuable comment. We cannot answer it exactly, and we did not affirm that we you would not obtain the same results using a pericardial patch instead of the PGA fixed with the glue. We agree with other published methods, such as an autologous pericardial patch with gelatin resorcin formaldehyde (GRF) glue or protein polymers (BioGlue®)(Cryolife, Inc.). We conjecture that their adhesive strength is probably greater than our methods. In Japan, the instruction of use of them is limited in aortic surgery, not cardiac surgery, so we do not any have clinical experience using them so far. We also suppose that after using a pericardial patch with GRF glue or BioGlue, regional cardiac wall motion becomes compromised, because such glues become heard solid, like a mold, although it is trivial concern in a patient with catastrophic situation such as LV rupture. Finally, we would just demonstrate that using a PGA sheet and fibrin glue for
reinforcement of TachoComb can augment the adhesive strength in the present study.

6. In the section “discussion” authors say “the study showed that TC alone might be adequate for patching the myocardium, since the burst pressure of 140mmHg”. Wasn’t the burst pressure 111.6?

In response to the comment concerning the burst pressure, the burst pressure was 111.6 ± 45 mmHg, and the peel-off pressure was 140.2 ± 28.8 mmHg. We are so sorry. According to reviewer’s comment we revised the manuscript.

Minor revisions:
1. In Figures 2 and 3 it would be better to show the whole standard deviation, not only the positive value.

In response to the comment concerning figure, we revised them.

Finally, we thank you for your valuable comments that have improved our report.