

Dear Editor

Thank you for your kindness to consider our paper suitable for publication in your journal. We studied carefully the attached comments listed by the reviewers, made the requested revisions and coupled with the reviewers' requirements and we provide you a manuscript where the changes asked are highlighted in red.

Following you can find point by point explanations and details about the modifications we made according to the reviewers' remarks.

Reviewer 1:

We added figures regarding the surgery and pathology as requested. In adding the pathology figures with added Dr. Aggeliki Cheva to the authors who, as a pathologist provided the figures and the figure legends.

Reviewer 2:

We changed the statistics used. After performing a normality test we used ANOVA to compare all 4 groups and the least significant difference (LSD) as post hoc analysis to make comparisons between groups.

Regarding the collagenase analysis there seems to be a poor phrasing in the manuscript so we rephrased. Actually, we didn't perform analysis on the one side of the anastomosis with 1 cm of the adjacent colon, but on 0.5 cm of adjacent colon both proximal and distal. We rephrased for clarity: "the anastomosis was resected along with a 0.5 cm segment of the colon on either side and divided into two parts vertically". Regarding, the studies mentioned by Agren et al 2006, and by Krarup et al 2013, where the levels of MMP are very different in the anastomotic line and the adjacent tissue, the levels of MMP were measured to up to 0.15-0.2 cm from the anastomotic line and were found decreased. In our experiment, we measured collagenase in a segment of 0.5 cm on both sides of the anastomosis in each

animal, so while the levels of collagenase will vary at the anastomotic line and at 0.5 cm, as the technique used was the same in all animals we have measured the collagenase activity in 1 cm of large bowel with the anastomosis in the middle in all animals and compared these values. The findings of these studies have been discussed in the discussion section.

The column plots were rearranged in the order Control4, Bioglue4, Control8, Bioglue8 and comparison lines including p values were added.

Description of groups was shortened and simplified and added to the operative technique section.

Language editing has been performed

The paper, including discussion has been shortened.

Reviewer 3:

We agree that long term safety should also be investigated. Regarding the use of albumin / glutaraldehyde glue in other digestive anastomosis and the short and long term safety, there are no studies regarding the long term safety and only two regarding short term which have been added to the discussion section.

With warm personal regards

Dr. Orestis Ioannidis