Reviewer 1.

This is an experimental study that compares the efficacy and safety of a MAR1 substance as a surgical adhesive to other 3 groups of mice relative to other commercially available "haemostatic glue" (Beriplast) and NaCl. It is a well-written and well-documented study in very good and appropriate language so; on my opinion the paper needs some minor necessary amendments:

1. Authors could comment and mention that the elevated levels of ALT observed with MAR 1 should attributed rather to surgery itself or anesthesia than to the use of substance by the patient.

We thank the reviewer for the valuable comments and suggestions.

The elevated levels of ALT were indeed due to the handling and manipulation of liver lobes during the surgical procedure rather than the use of MAR-1. This is further supported by the degradation rate of MAR-1, which showed no toxic effects during the degradation process. The glue gradually degraded and the animal behaviour and body weight gain were normal.

We have added the following sentence in our discussion: "The elevated ALT levels in the MAR-1 group was probably due to repeated manipulation of the liver lobe during the surgical procedure. Nevertheless, the values were within the physiological range and did not increase at a later time point."

2. Could authors provide a possible explanation why there was an increase in hemorrhage with NaCl only on 21st day and not on day 14th and 90th?

We thank the reviewer yet again for this valid question.
The study had 3 time points, 14, 21 and 90 days, each time point had a different set of animals. Therefore, the results obtained from these different time points showed variation.

Reviewer 2.

1. The authors reported MAR-1 showed similar hemostatic properties, no adverse effects on a liver resection model. The paper is of some scientific interest and clinical value. 2. The quality of work reported in the paper is average.

(1) The quality of Figure 4 is not good. The authors should add the μCT scans of MAR-1 rat on day 14, 21, and 90 post-operative days.

We thank the reviewer for this comment.
Since the picture was an embedded file in the word document, the quality of image was compromised. Therefore, we would like to provide the reviewer with a separate image file with a better quality. The μCT scans were performed only on day 1 and day 7. After this period, the animals gained weight and would not fit into the CT bed.

(2) In Figure 5 and Legends, the survival rate between the three groups should be explained in more detail, and if possible, add some statistical parameters (P value, e.g.).How about the results of Mantel-Cox test?

We thank the reviewer for the suggestion.

We have included the Mantel-Cox test results and the P value summary in the figure legend and the results as follows:

Figure 5. Survival proportions between the treatment groups were calculated during 14, 21 and 90 post-operative days. P=0.9906 as per Mantel-Cox test. (n=7)

As per Mantel-Cox test, the P value was 0.9906 and there was no statistical significance seen between MAR-1 and other the groups.

Reviewer 3.

The Authors show data in favour of a novel, polyurethane based, surgical adhesive on a liver resection rat model. This is a well written study. Methods are adequate and results clearly presented. The authors conclude that compared to fibrin, MAR-1 showed similar hemostatic properties, no adverse effects, and is biocompatible. MAJOR point I am concerned that the authors might have underestimated the importance of ALT elevation, which is not adequately addressed. They simply state that "Although the ALT levels were significantly higher in the MAR-1 group, the values were well within the physiological range." In my opinion, this aspect should be thoroughly addressed, considering the composition of MAR-1 and discussing the liver toxicity potential of each component. The authors should also provide more details (wherever possibile, because I understand confidentiality reasons) on the development of MAR-1.

We thank the reviewer for the suggestions.

Yes, the increase in ALT was noticed and this could be due to resection procedure and manipulation during the surgical process. We have added the following sentence in our discussion: “The elevated ALT levels in the MAR-1 group was probably due to repeated manipulation of the liver lobe during the surgical procedure. Nevertheless, the values were within the physiological range and did not increase at a later time point.”

Regarding the chemical composition of MAR-1, we added the following sentence in the materials and methods part:

MAR-1 consists of two different components: a isocyanate-functional polyester-ether pre-polymer and an amino-functional asparagine acid ester. This adhesive technology and its polyaddition reaction is well-known.

Moreover, MAR-1 was tested in-vitro for cytotoxicity in compliance with EN-ISO 10993-5:2009. The results showed that MAR-1 was non-cytotoxic.

Also up to 90 days after application of the adhesive on the liver resection surface, we could not detect any adverse events within the MAR-1 group. Body weight, behaviour, liver function test, haematological parameters were all in physiological range.

Reviewer 4.

The manuscript is well-written and the data shown in the manuscript was understandable. But several issues may be addressed.

1. Bleeding mass was higher at 21 days only in NaCl group. Why?

We thank the reviewer yet again for this valid question.
The study had 3 time points, 14, 21 and 90 days, each time point had a different set of animals. Therefore, the results obtained from these different time points showed variation.

2. Bleeding time was not different at 21 days only in each group. Why?

As mentioned previously, the animals were different at different time points and therefore, we noticed these variations in the groups.

3. ALT value was higher at 21 days inky in MAR-1 group. Why? I think these differences were due to the variety of surgical interventions. If more number of mice were included, these differences will be absent. Authors should discuss these points to show the safety of MAR-1.

The reason for increased ALT levels was due to repeated manipulation of the liver lobes during the surgical procedure. Therefore, we added this sentence in the discussion part: "The elevated ALT levels in the MAR-1 group was probably due to repeated manipulation of the liver lobe during the surgical procedure. Nevertheless, the values were within the physiological range and did not increase at a later time point."

4. Authors mentioned that liver resection is the only curative treatment options for hepatocellular cancer. But loco-regional therapy such as radio frequency ablation is also curative treatment option for small hepatocellular cancer.

Yes, that's true. Therefore, we changed the sentence as follows: "it is the one of the curative treatment options for hepatocellular cancer patients (4)."