

Authors' Response To Peer Reviews

Authors' Response to Peer Review of “Material-Driven Therapeutics to Establish a Penetrating Traumatic Brain Injury Rat Model and Implantation of a 3D-Printed Scaffold: Pre-Experimental Pilot Study”

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This is the authors' response to the peer-review report for “Material-Driven Therapeutics to Establish a Penetrating Traumatic Brain Injury Rat Model and Implantation of a 3D-Printed Scaffold: Pre-Experimental Pilot Study.”

Round 1 Review

Reviewer EW [1]

1. A key weakness of the study [2] is its very small sample size ($n=4$), which substantially limits the statistical power, generalizability, and reliability of the conclusions. With such a low n , it becomes difficult to determine whether the observed variability—particularly the severe inflammatory response in one animal—reflects true biological differences, procedural inconsistencies, or random outliers.

Response: We agree that this study has a very small sample size. That does impose limitations on statistical power, results, and conclusions. We however have stressed throughout the manuscript that this is a “pilot

study” to identify a technically feasible rat model. Since the aim of this study was to describe a model that could be used in future studies, only 4 animals were used, and results and conclusions based on those 4 animals are reported. After reporting this foundational study, we can now plan and initiate a study with control groups, a sufficient number of animals, and more detailed analyses. Some of these points are described in the Discussion section of the manuscript (lines 311-316).

2. The study lacks control groups—including a sham surgery group and a traumatic brain injury-only group—preventing clear attribution of histological changes to either the injury model or the implanted scaffold.

Response: As described above in the response to comment 1, we agree that this study lacks control groups, including well-defined sham surgery or traumatic brain injury-only groups. This will be taken into consideration in future studies, since we have established the feasibility of the technique in this manuscript. Some of these points are described in the Discussion section of the manuscript (lines 312-316).

3. *The behavioral assessment is limited to a modified neurological severity score, which is often insensitive to mild or focal injuries and may miss subtle cognitive or sensorimotor deficits.*

Response: Yes, we agree that the behavioral assessment reported in this study is limited. As described above in our responses to comments 1 and 2, this was a feasibility study. Since the number of animals was small, and there are a variety of behavioral assessments that are relevant and can be done, future studies will be planned accordingly. We will take into consideration

the animal groups and their evaluations. Some of the results relevant to this feasibility study are described in the Results section of the manuscript (lines 223-228).

4. *The study would be strengthened by incorporating additional validated behavioral tests.*

Response: We agree, and after completing this feasibility study, we are ready and motivated to carry out a detailed study with additional groups and evaluations. Some of the results relevant to this study are described in the Results section of the manuscript (lines 225-228).

References

1. Kobeissy F. Peer review of "Material-Driven Therapeutics to Establish a Penetrating Traumatic Brain Injury Rat Model and Implantation of a 3D-Printed Scaffold: Pre-Experimental Pilot Study". JMIRx Bio. 2026;4:e105277. [doi: [10.2196/105277](https://doi.org/10.2196/105277)]
2. Harley-Troxell ME, Dennis M, Dhar M. Material-driven therapeutics to establish a penetrating traumatic brain injury rat model and implantation of a 3d-printed scaffold: pre-experimental pilot study. JMIRx Bio. 2026;4:e75613. [doi: [10.1101/2025.03.20.644358](https://doi.org/10.1101/2025.03.20.644358)]

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