

Dear editor:

Thank you very much for your letter and advice on our manuscript. We have revised our manuscript according to the comments raised by the reviewers and editorial office. The manuscript language was revised by the MedE Editing Service and the language evaluation has reached grade A. The amendments are highlighted in red in the revised version. It is noteworthy that the report of scientific research process is uploaded in the file of supplementary material. We hope that the revision is acceptable and look forward to hearing from you soon.

With best wishes,

Jianan Ren

Point by point replies to reviewers:

Reviewer #1 (ID: 00058573)

Comment 1: Nicely written and well conceived paper. I have only one query. Which part is being “stented”- is the fistula being stented or the fistula is being bypassed and the intestine with fistula connection is being stented. In case, it's the latter, which I think it is, then please change the title and manuscript accordingly.

Answer 1: Thank you very much for your careful review. In this study, it can be seen in Video 2 that the fistula was being “stented” directly, not being bypassed, to restore the integrity of GI tract.

Reviewer #2 (ID: 00070310)

Comment 1: Please summarize ‘Introduction’, because of repeated sentences.

Answer 1: Thank you very much for your careful review. The repeated statement “Several methods have been reported including biological dressings, fibrin glue, fistula patch, sump drainage, primary suturing and fistula VAC technique” has been deleted and now the “Introduction” is not wordy.

Comment 2: Please show the long-time outcome and safety of the stent.

Answer 2: The further follow-up demonstrated that no stent-associated complications occurred before ECF resection such as GI obstruction and dislocation of the stent. The nutrition status was improved continuously due to restoration of GI tract integrity. The related information “On September 20, the patient received ECF resection and was discharged 10 days later.” was added at the end of “CASE REPORT”.

TPU has been widely applied in clinical practice because of its good biocompatibility. The safety of the stent was measured using MTT assay as reported by literature [1]. This experiment was described as following: Generally, the leachate was obtained by immersion of stent in 10 mL DMEM with 10% FBS. 10×10^4 fibroblasts (L929) was seeded into 200 μ L fresh DMED or 200 μ L leachate in 96 well plate, followed by incubation at 37 °C for 24 hours, 48 hours and 72 hours. Then, MTT (5mg/mL) reagent was added to each well and further incubated for 4 hours.

Afterwards, the formazan salt was dissolved with 200 μ L DMSO. As soon as thoroughly dissolved, the solution was added to a new plate and measured with a microplate Spectrophotometer at 570nm (n = 3). As shown in Figure S3, the result indicated the leachate of stent did not influence the cell viability and exhibited a good biocompatibility.

Reference:

[1] Zhang S, Guo Y, Dong Y, Wu Y, Cheng L, Wang Y, Xing M, Yuan Q. A Novel Nanosilver/Nanosilica Hydrogel for Bone Regeneration in Infected Bone Defects. ACS Appl Mater Interfaces 2016 2016-06-01; 8(21): 13242-13250.

Comment 3: Please show in detail how to repair the fistula finally.

Answer 3: In clinical practice, many ECFs, especially with mucosal protrusion, are unlikely to achieve spontaneous closure. The consistent loss of enteric effluent will lead to lots of problems like water-electrolyte imbalance; surround tissue contamination and digestive tract bleeding. By application of 3D-printed fistula stent, the GI tract integrity will be restored to avoid these problems and make a good preparation of future ECF resection. Therefore, this study provides a new method to manage ECF.