Fistula Treatment - Preclinical Evaluation Of A Porous Adhesive Filler

TISSIUM

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Objective of the device

Sphincter-preserving technologies have been developed to treat perianal fistulas. However, their clinical performance remains limited. Device limitations include extrusion due to tract biomechanics and incomplete filling, both of which have been associated with tract re-epithelialization and treatment failure.

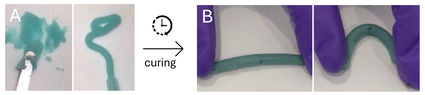
Description of the device

TISSIUM developed a filler composed of a biocompatible polymer with adhesive properties, poly(glycerol-co-sebacate)acrylate-based adhesive, and a porogen powder.

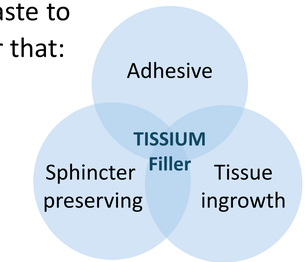


This filler is a viscous paste that can be injected and conforms to the fistula tract. The polymer was formulated to cure within minutes after injection, allowing the paste to become a solid but flexible porous filler that:

- adheres to the surrounding tissue
- enables fast tissue ingrowth.



Aspect of TISSIUM Filler (A) before and (B) after chemical curing.



Performance in porcine model

An *in vivo* study was conducted to evaluate its performance against a commercial plug for fistula treatment.

● **Method**: The porcine model, based on the work of Buchanan and colleagues, involves the creation of chronic fistulas lined with scar and granulation tissue. This allows for a representative surgical procedure, including curettage, flushing, and suturing of internal orifice.

36 fistulas

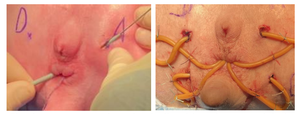


1m & **3m** timepoints

3 groups

Empty Control (sutured internal orifice)	TISSIUM Filler (product injected and sutured internal orifice)	Biodesign® Fistula Plug (applied per IFU)

1. Fistula creation



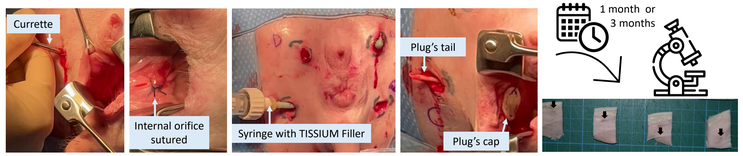
Fistulas were created mechanically with catheters and drains.

3 weeks



Drains were removed after 3 weeks. Resulting fistulas were ≥4 cm long and 3 mm wide.

2. Fistula treatment



Debridment Groups: All.

Suturing of internal orifice. Groups: Empty control + TISSIUM.

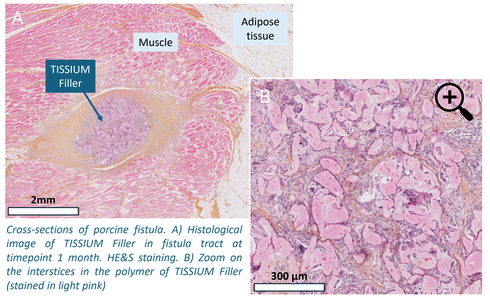
Filler injection in retrograde manner, from internal to external orifice. Group: TISSIUM.

Plug slid into tract and sutured to internal orifice. Group: Biodesign® Fistula Plug.

Cross-sections of porcine fistula. Arrows indicate the tract location, closer to the skin near the external orifice (left section).

● **Study results**: TISSIUM Filler was successfully injected and cured in fistulas. At both timepoints, all cutaneous and internal orifices were closed, demonstrating that the porcine model results in fast healing independent of the treatment group. TISSIUM Filler was not extruded from the tracts after 1m (n=16) or 3m (n=10), while Biodesign® Fistula Plug could not be identified on histology at 1m (n=4) nor 3m (n=1) thus indicating extrusion or premature degradation.

Importantly, TISSIUM Filler acted as a scaffold, with its interstices already filled with fibrous tissue at 1m. At both timepoints, the foreign body and local inflammatory responses were mild for TISSIUM Filler. Mononuclear inflammation was similar across all groups.



Cross-sections of porcine fistula. A) Histological image of TISSIUM Filler in fistula tract at timepoint 1 month. HE&S staining. B) Zoom on the interstices in the polymer of TISSIUM Filler (stained in light pink)

Conclusion

TISSIUM developed a porous and adhesive filler for fistula treatment to minimize the risk of extrusion observed with existing devices. Preclinical testing in a porcine model showed that TISSIUM Filler is not extruded from fistula tracts despite mechanical constraints in the perianal environment. The product performed as intended with cell ingrowth and low inflammatory response. Such animal model is however limited to assess healing rates due to spontaneous tract closure occurring after fistula debridement.

References

Buchanan, G. N. *et al.* Experimental model of fistula-in-ano. *Dis Colon Rectum* **48**, 353–358 (2005).

Buchanan, G. N. *et al.* Pilot study: Fibrin sealant in anal fistula model. *Dis Colon Rectum* **48**, 532–539 (2005).