Preclinical Assessment of a Novel Bio-Spun™ Fistula Plug: An Acellular Treatment for Fistulas

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Objective of Technology

Anal fistulas remain a major source of morbidity in the United States and worldwide. Current management of complex fistulas involves extensive surgeries associated with prolonged recovery, complications and relatively low success rate. Previous attempts at less invasive techniques have been ineffective, creating a large void in treatment options for this disease. We present here a new version of the plug designed to close that gap.

Description of Technology

- A novel non-degradable, unibody, multi-armed fistula plug (Bio-Spun™ fistula plug) has been developed using proprietary electrospinning technology (Figure 1).
- The resulting structure of the Bio-Spun™ material closely resembles the structure of the body's own extracellular matrix (ECM), which helps native cells respond much more naturally as compared to other biomaterials.
- The plug design provides excellent handling and allows for fitting to different track sizes.

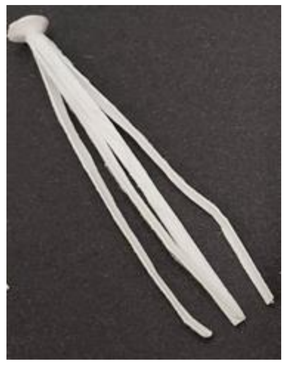


Figure 1: Picture of the Bio-Spun™ fistula plug (4mm size body diameter; 10cm length; 4 arms).

Methods

Bio-Spun™ fistula plugs were produced for both small and large animal studies, respectively.

Three models were used to assess fistula healing:

1. a rat dorsal subcutaneous tract model
2. a rat perianal fistula
3. a porcine perianal fistula model

In all experiments, Bio-Spun™ fistula plugs were compared to Cook Biodesign plug (control) and untreated track (non-implant control) after 30 days of implantation.

- The rat dorsal subcutaneous tract model allowed for two fistula tracts to be created without the issue of sphincter flexure.
- The rat perianal fistula plug mode was used to evaluate the control and test plugs in the target anatomic area (2mm size plugs; n = 2 plugs/test group evaluated).
- A porcine perianal fistula plug model was then developed based on the rat perianal model using the 4mm size Cook Biodesign and Bio-Spun™ fistula plugs (n = 3 plugs/test group evaluated).

Results

- The Bio-Spun™ fistula plugs had excellent handling and suture retention as compared to the Cook Biodesign plug.
- The rat dorsum subcutaneous tract and perianal fistula models showed that all Bio-Spun™ fistula plugs promoted tissue integration as compared to the Cook Biodesign plugs, which either had a fibrotic response or were ejected from the tract (Figure 2).

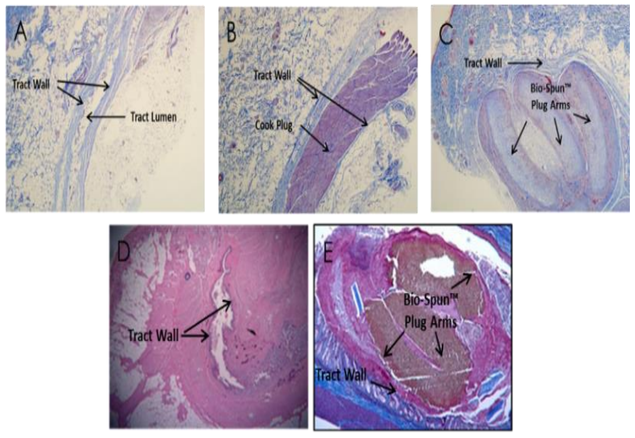


Figure 2: Histological assessment of no plug tract, Cook Biodesign (control) and Bio-Spun™ fistula plugs using a rat dorsal subcutaneous tract implantation model (Figures 2A-C) and a rat perianal fistula tract model (Figures 2D-E). Creation of the tracts was achieved via implantation of a catheter for 30 days followed by removal. For the no-plug control, the tract wall remained over the 30-day implantation period as indicated by thick collagen lining (Figure 2A). The Cook Biodesign plug remained in place in this model, with limited tissue ingrowth evident (Figure 2B) whereas the Bio-Spun™ fistula plug showed tissue infiltration into the tract and the plug wall (Figure 2C). Lack of tract healing was also evident using the rat perianal fistula model (Figure 2D). There were no Cook Biodesign plugs remaining in the tract after 30 days of implantation. In contract. the Bio-Spun™ fistula plug had excellent tissue infiltration into the tract and into the device wall (Figure 2E).

- In the porcine model, all Cook Biodesign plugs were ejected from the tract whereas one of the Bio-Spun™ plugs remained in place over the 30-day implantation period and had excellent tissue integration (Figure 3).

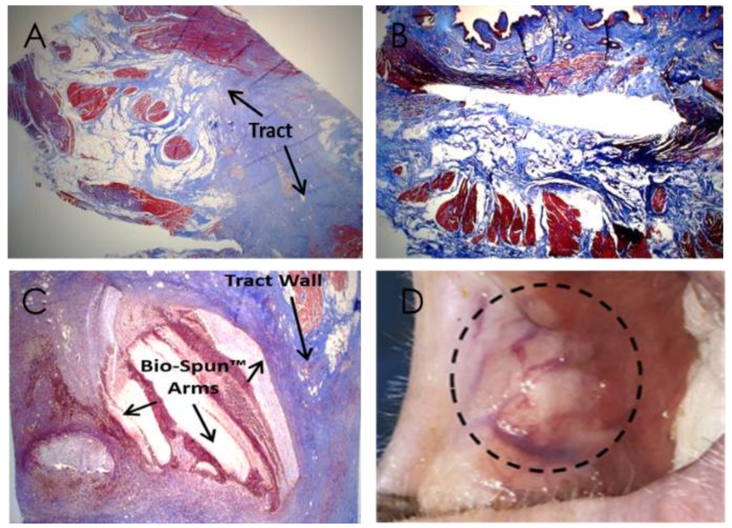


Figure 3: Histological assessment of no plug tract, Cook Biodesign (control) and Bio-Spun™ fistula plugs using a porcine perianal fistula model. For the no-plug control, the tract wall remained over the 30-day implantation period as indicated by thick collagen lining, with collagen deposition filling the complete tract (Figure 3A). The Cook Biodesign Plug histology section showing device being walled off with collagen (dark blue/purple), with most of the devices dislodged (Figure 3B). The Bio-Spun™ fistula plug histology showed full tissue integration of tissue into the arms of the device within the tract (Figure 3C). Gross image of the sphincter area shows complete tissue incorporation (healing) of the "head" portion of the device (Figure 3D).

Conclusions

The Bio-Spun™ fistula plug provides a viable, minimally-invasive solution that promotes healing of the tract. The nanofibrous scaffold of the Bio-Spun™ fistula plug induces cell migration and tissue ingrowth via mechanosensory contact.

Future Directions

The next step is to bring the Bio-Spun™ fistula plug through regulatory approval, which will require additional benchtop, biocompatibility and preclinical testing along with a first-in-human clinical trial.