Sprayable Biopolymer Hydrogel for the Prevention of Postoperative Adhesions

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Statement of Purpose: Abdominal surgery can induce post-operative adhesion formation when fibrous bands form between injured tissues during aberrant wound healing, resulting in small bowel obstruction, female infertility, and chronic pain. Current products for adhesion prevention are difficult to apply and fail to properly address this severe surgical complication. Luna therefore developed a unique sprayable hydrogel to act as a physical barrier between tissues and protect susceptible tissue surfaces from forming adhesions. The hydrogel is applied as a two-component system in which the biopolymers interact to form an easily-visualized gel that will enzymatically degrade once the adhesion-formation window has passed. Pre-clinical studies and pathways for transitioning this technology from a small business to the clinic are discussed.

Methods: Luna's sprayable hydrogel is comprised of two biopolymers that interact with one another upon mixing to form a polyelectrolyte complex. The inclusion of ionic crosslinkers within the two components serves to further enhance the stability of the resultant gel structure. The gel is applied using mixing tip SA-3652 (Nordson Medical) with 10 psi CO_2. *In vitro* characterization has confirmed sterility, cytocompatibility, degradation, and shelf life.

The functionality of the product was demonstrated in a rabbit sidewall adhesion model[1–3], conducted by DaVINCI Biomedical Research Products. Surgical defects were created on adjacent abdominal wall and cecum surfaces. The wounds aligned upon surgical closure such that adhesions would form between the injured cecum surface and the incision site, the abraded abdominal wall surface, or to surrounding sites on the injured cecum in untreated control animals. The two wounded surfaces were coated with Luna's hydrogel barrier prior to closure in the treated animals. Adhesion analysis was performed 7 and 28 days after the procedure.

The extent, severity, and strength of adhesions formed between the cecum and surrounding tissues were evaluated and assigned ordinal scores. Each animal received a score 0-4 for extent, and 0-3 for severity and strength, with 0 indicating the absence of an adhesion and the respective maximum value indicating significant adhesion formation. These scores were summed for a total adhesion score 0-10 for each animal. In addition to assessing the adhesion scores, DaVINCI also noted the incidence of formation of adhesions between the cecum surface and the incision site, the abdominal sidewall, or to surrounding sites on the injured cecum. For all score sets, the Wilcoxon signed-rank test was used to compare the extent, severity, and strength of adhesions between treated and control groups, with statistical significance defined as $p < 0.05$. The Fisher Test was used to calculate statistical differences between the incidences of adhesion formation for each tissue pair.

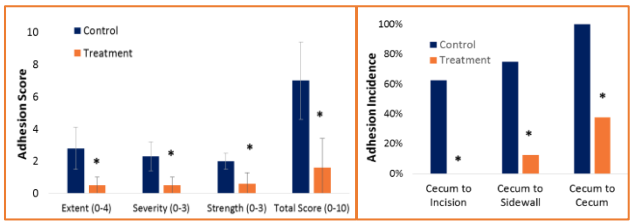


Figure 1. Demonstration of statistical reduction in adhesion score and incidence with application of Luna's product.

Results: The product was applied to the injured surfaces by the surgical staff at DaVINCI with minimal training, indicating clinical relevancy of the product. The resultant mean adhesion scores were significantly reduced in extent (2.8 to 0.5), severity (2.5 to 0.5) and strength (2 to 0.6) for all tissue pairs with the application of Luna's adhesion barrier product (Figure 1). The average total adhesion score was similarly reduced from 7.0 to 1.6. Luna also demonstrated a statistically significant decrease in the incidence of adhesion formation between the cecum and each of the surrounding injury sites associated with the application of this product.

Conclusions: Luna has demonstrated the efficacy for a sprayable hydrogel to prevent postoperative adhesions as a physical barrier between the injured surfaces. Design controls are being implemented to facilitate regulatory approvals, and a transition effort is being developed to determine pathways to clinical application. As a small business, Luna is identifying methods of funding first-in-human studies to better present this technology for licensing or acquisition by a larger medical device company.

References:

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