Development of a 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 is therefore developing 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. We are working now to finalize pre-clinical studies, implement design controls, and develop pathways for transition to the clinic.

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 rat abdominal adhesion model[1–3]. Surgical defects were created on adjacent abdominal wall and cecum surfaces in Sprague-Dawley rats. The wounds aligned upon surgical closure such that adhesions would form between the two surfaces 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 days after the procedure.

The extent, tenacity, and type of adhesions formed between the cecum and abdominal wall were evaluated and assigned ordinal scores. Each animal received a score 0-4 for extent and type and 0-3 for tenacity, with 0 indicating the absence of an adhesion and the respective maximum value indicating significant adhesion formation. In a second method, a set of scaled scores was obtained by use of the extent percentages in combination with the ordinal scores for the tenacity. Briefly, these scaled tenacity scores were calculated as the product of the raw percentage of coverage and the ordinal tenacity score. For all score sets, the Wilcoxon signed-rank test was used to compare the extent, tenacity, and type of adhesions between treated and control groups, with statistical significance defined as $p < 0.05$.

Results: Luna demonstrated a statistically significant decrease in the incidence of adhesion formation between the abdominal and cecum injury sites from 90% (controls) to 20% with treatment, as the total primary adhesion score decreased from 6.6 to 1.1 in the treated animals. The mean scaled tenacity scores assigned to these adhesions also decreased from 1.50 to 0.25 (Figure 1). Luna also investigated secondary adhesions that formed between either of the injured surfaces and other surrounding tissues using a similar scoring system. These secondary adhesions are more difficult to prevent, and Luna was unable to achieve a significant reduction in their incidence as compared to control animals. However, these secondary adhesions are less likely to occur in control animals due to the formation of the primary adhesion, and analysis of the total score and scaled adhesion tenacity for these secondary adhesions demonstrated a trend of smaller, weaker adhesions in treated animals. Overall, Luna demonstrates a significant reduction in total adhesion incidence, and the resultant extent and tenacity of adhesions that did form, by the application of the biopolymer-based two-component hydrogel over the injured tissue surfaces prior to closure.

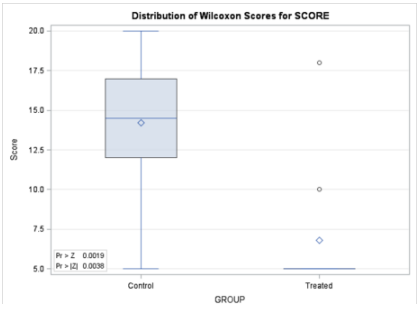


Figure 1. Wilcoxon rank sums for the scaled adhesion strength scores from the abdominal wall to the cecum surface.

Conclusions: Luna has demonstrated the efficacy for a sprayable hydrogel to prevent postoperative adhesions as a physical barrier between the injured surfaces. A uterine horn injury model in rabbits will next be utilized to establish definitive pre-clinical feasibility. Design controls are being implemented, and a transition effort is being developed to determine pathways to clinical application.

References:

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