Development of a Semi-Laparoscopic Cecal Abrasion Model for Peritoneal Adhesions in a Rat

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Statement of Purpose: Laparoscopic procedures are quickly replacing their open counterparts[1], driving the refinement of devices to be laparoscopically deliverable. Mimicking laparoscopic delivery in preclinical models presents many challenges, including cost, timing, and usable peritoneal space in small animals. Often laparoscopic rabbit and porcine models replace open rodent models to meet working space requirements[2]. To overcome these challenges, we used laparoscopic tools in an open rat model, simulating device introduction. We successfully delivered both a membrane and a solution via trocar, with similar anti-adhesion efficacy as shown in an open model. The semi-laparoscopic model allows for the study of laparoscopic delivery, safety, and efficacy free of conventional positive pressure capnoperitoneum. This innovative model allows for faster device iteration, reduced preclinical costs, and a viable laparoscopic delivery option for smaller animals.

Methods: All rat peritoneal abrasion models were conducted in compliance with protocols approved by The University of Texas at Austin IACUC committee. Animals received no barrier or the Alafair membrane (HA/alginate) to separate injured tissues.[3-4] All animals were female Sprague-Dawley rats, 225-250g. The cecum was exposed via midline laparotomy incision of 4 cm, and held extracorporeal. The ventral cecum then was abraded with sterile gauze using a mechanical abrader. For semi-laparoscopic procedures, the cecum was then returned to the peritoneal cavity. Two 5 mm trocars (Applied Medical) were introduced to the left abdomen. A needlescopic MiniLap endo-grasper (Stryker) was introduced to the right abdomen. The Alafair membrane was delivered through one trocar using 5mm Epix laparoscopic padded graspers (Applied Medical), and placed onto the cecum. Both graspers were used to manipulate the membrane to cover the abraded ventral cecum surface. The Alafair Liquid Tissue Anchor (LTA) solution was then delivered onto the membrane surface via catheter down the 5mm trocar, followed by midline closure. All incisions were closed with 3.0 vicryl. Animals were sacrificed at 7 days and adhesions or lack of adhesions was observed. Statistical inferences were made using Mann-Whitney U tests, with a p-value < 0.05 considered statistically significant.

Results: The Alafair membrane and associated LTA can be delivered laparoscopically, as shown by success in the semi-laparoscopic model for peritoneal adhesions. Furthermore, the semi-laparoscopic model precludes the need for insufflation or laparoscope, reducing preclinical time and costs. Also, the semi-laparoscopic model allows for use of clinically available tools in a small animal model because the open midline provides a larger working space than the closed laparoscopic equivalent.

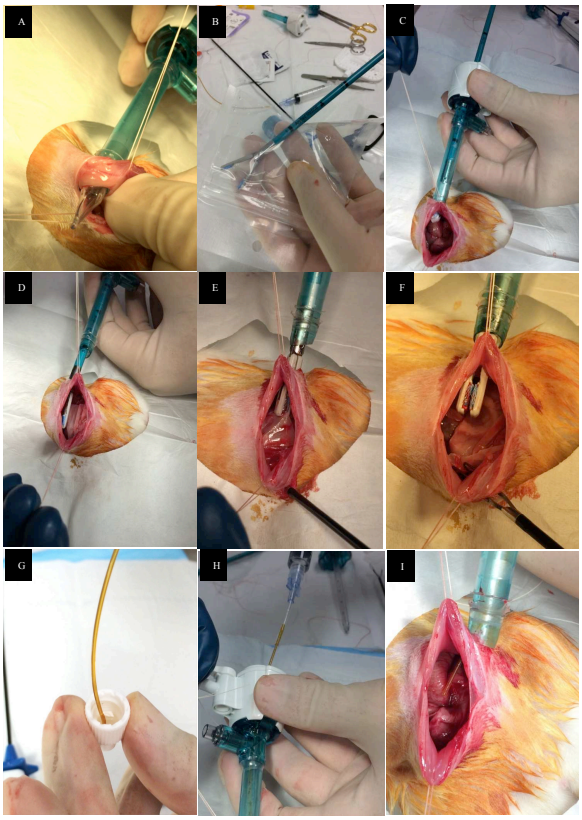

Figure 1. Semi-laparoscopic procedure in the cecal rat abrasion model. A) 5mm trocar inserted into left abdomen. B) Standard padded graspers remove Alafair membrane from sterile packaging. C) Alafair membrane travels easily down trocar and into peritoneal cavity. D) Alafair membrane is released from graspers and manipulation is easily visible. E) Needlescopic graspers are introduced to the right abdomen. F) Needlescopic graspers assist in positioning membrane onto cecum surface. G) LTA solution is drawn up into a 19 g. catheter via syringe. H) Catheter is easily fed down trocar. I) LTA is deployed onto membrane surface via syringe.

Conclusions:.A novel semi-laparoscopic method for preclinical testing, precluding the need for capnoperitoneum, has been established as a method for testing delivery and efficacy of a laparoscopically deliverable anti-adhesion device. By eliminating the need for insufflation or laparoscope, preclinical testing can be conducted faster and in smaller animals, providing a method for device iteration with fewer resources. These efforts may support faster decision-making for early-stage product development.

References: 1.Lingohr et al. European Journal of Medical Research 2014, 19:33. 2.Zimkowski et al. J Biomed Mater Res Part B 2014:102B:1093–1100. 3.Mayes S et al. BMES Annual Meeting, Oct 2013; Seattle, WA. 4.Mayes S & Zawko S. SFB Annual Meeting, April 2014; Denver, CO.