Anastomosis Device for Small Lumen Structures

Executive Summary
1. Background

The Drexel Anastomosis Device (AD) is designed to be a rapid and efficient platform for anastomosis of small lumen structures. The AD is made of an FDA-approved biocompatible, bio-absorbable polymer (poly-lactic-co-glycolic acid, or PLGA) that delivers bioactive agents at a pre-programmed rate to improve healing. The device is expected to be especially beneficial in surgical procedures involving small lumen structures such as the common bile duct, ureters, and blood vessels, where a thin wall and reduced blood flow greatly increase the risk of poor healing, leaks, and strictures. The AD will have the potential to improve surgical outcomes, increase the ease of and reduce the time required for performing these procedures. Additionally, the device offers the potential of delivering therapeutic and bioactive agents locally at the anastomotic site to reduce the morbidity of targeted procedures. A custom AD applicator has also been designed, which will facilitate the use of the AD in all procedures and will be particularly useful in minimally invasive laparoscopic and endoscopic approaches to these advanced surgical procedures.

The AD technology is available for licensing from Drexel University. Please see Paragraph 9 for contact information.

2. Product

What unmet medical need does the product address?

Historically, surgical procedures requiring anastomosis of small lumen structures, such as the common bile duct, ureters, and blood vessels have not benefited from the reliability and ease of surgical stapling, which revolutionized abdominal surgery in the 1970s. Current barriers to the use of surgical staples in small structures include their size and susceptibility to ill effects from scarring at the tissue joint. When a structure is divided, its blood supply is divided as well making the end highly tenuous. This end is then joined to another structure with reduced vascularity. With a small lumen size and reduced blood flow, the risk of poor healing, leak or late stricture is very high. Absorbable staples have existed for over twenty years, but few surgeons use them since they have no proven advantage over stainless steel or titanium staples.

Bile duct anastomosis is the surgical reconnection of the bile duct to the small intestine. This procedure is performed in many situations, such as in surgery for pancreatic cancer and liver transplantation. Complications associated with bile duct anastomosis include leaks, fistulas, and infection, leading it to become known as the “technical Achilles’ heel” of liver transplantation. Current anastomosis techniques rely on manually suturing the bile duct to the duodenum or employing the use of staple clips to make the connection. However, when these two techniques were compared, complications such as leaks and strictures occurred 18% of the time with clips and 24% of the time with sutures. Newer techniques involving laparoscopic reconstruction have been applied to this procedure in recent years. However, a meticulous suturing technique is required for both open surgeries as well as laparoscopic assisted procedures and there is no treatment applied in situ to promote healing. Even with use of laparoscopy, the median operative time is around 300 minutes and bile leakage is common.

Product description

Drexel’s anastomosis device for small lumen structures is fabricated from an FDA-approved biocompatible, biodegradable polymer that will slowly degrade at a pre-programmed rate after sufficient healing is achieved. AD is comprised of a T-shaped Rivet (see Fig. 1), with threads on its outer wall of the Rivet’s foot, and the Ring, with matching threads on the inside, which provide for securing the Ring on the Rivet’s foot. The Rivet has a round hollow core traversing its entire to allow for the passage of fluids through it. The wall of the Rivet’s foot has two diametrically opposite longitudinal cuts that provide for mechanical flexibility facilitating snapping of the Ring on the Rivet’s foot. While Fig. 1 illustrates actual prototypes of the Rivet and the Ring as well as the head of the Applicator in comparison to a quarter, the sizes of the Rivet/Ring combination can vary depending on the lumen diameter of the structures to be connected.
To perform anastomosis, one would first secure the small lumen structure (such as bile duct) over the upper (T-shaped) end of the Rivet with a suture loop as shown on the drawing on the cover page of this summary. Then, the foot of the Rivet would be fed into an incision in the small intestine where it would mate with the Ring to connect the two tissues together. The Rivet is designed with multiple threads on its outer wall in order to lock it with the Ring. The Ring can be positioned within a range of distances from the upper end of the Rivet to allow for some variation in tightness between the bile duct and the small intestine. After time, the Rivet and Ring would slowly degrade in the body as the tissues heal. A simple biodegradable Ring can be replaced with a drug-eluting Ring loaded with wound healing agents, chemotherapeutic agents and/or radioactive therapy for local delivery of treatment to the site where it is needed most, the surgical margin. Alternatively, a separate drug-eluting washer can be placed on top of the regular Ring to be locked in between the inner wall of the small intestine and the Ring. This would allow controlling the drug release rate separately from the rate of degradation of the whole device, and ensure that mechanical properties of the Ring are not affected by adding the drug delivery capability. Adding drug delivery capability can reduce the procedure’s morbidity. Furthermore, eluted agents could be potentially personalized to meet a patient’s specific needs.

The device is initially targeted for use in small lumen structures, but is suitable to use in larger structures by increasing the physical size and configuration of the mechanical components. Due to the Rivet’s versatility, surgeons may perform side-to-end, side-to-side and, with minor product modifications, end-to-end anastomotic procedures. AD with a Ring without a drug makes the device a simple anastomosis device with a much shorter path to regulatory approval than its drug-eluting version.

The inventors have also developed an Applicator, the device that includes several unique features designed to facilitate the AD insertion during surgical procedure.

The AD realizes the convergence of four key technological and surgical advances:

- Biodegradable Polymer Technology
- Drug Eluting Capabilities
- AD And Their Delivery Devices
- Endoscopic / Laparoscopic Surgical Techniques

**Intellectual Property**

All patent applications for this technology are owned by Drexel University. Throughout the history of the AD’s development it was protected with 3 invention disclosures that resulted in 3 separate patent filings. The first PCT patent application was converted into National Phase applications in the U.S., EU, Canada, and Japan. The second is protected by a pending U.S. patent application. The latest improvements of AD and the Applicator are protected by a pending PCT patent application.

**3. Market Size and Potential**

According to Medtech Insight Report #A122, current and emerging wound closure products and techniques in Europe and the U.S. for 2003 were valued at approximately $3.4 billion. Of this, surgical sutures account for an estimated 50%, staplers and staples for 29% ($986 million), surgical sealants and glues for 9.5%, and wound closure strips for 3%. Frost and Sullivan estimates the in European markets, wound closure devices earned revenues of $217.0 million in 2005. Frost and Sullivan project this market to reach $543.0 million in 2012.
Bile duct procedures alone total 60,000 to 120,000 cases annually with morbidity rate of 40%. Liver transplantation, surgical resection for hepatocellular cancer, pancreatic cancer, and cholangio-carcinoma are just a few of the procedures that may require anastomosis of the common bile duct. The standard protocol is to hand-sew the common bile duct either to itself or its enteric counterpart, which is technically challenging, extremely time-consuming, and may lead to serious complications if it fails.

With current techniques, when resection can be attempted in early stage gallbladder and bile duct cancer, between 15% and 50% of patients survive 5 years or more. At late stage, fewer than 5% of patients survive 5 years or more. Pancreatic cancer is the 10th most common cancer in men and women, and 4th leading cause of cancer death. In 2006 33,730 new cases of pancreatic cancer were diagnosed. Moreover, peri-ampullary cancers, which include bile duct, ampulla and duodenum, add 10,000 more cases. Non-cancer related applications increase these numbers substantially. Benign bile duct obstruction, pancreatitis and inflammatory conditions represent 18,000 procedures annually; liver transplants 5,000-7,000 additional cases with mortality rate of around 2-5% for pancreas and liver major surgery.

4. Competitive Landscape and Advantage

The wound closure market encompasses major product categories like sutures, staples and glues. Two companies currently dominate the market. They are Johnson & Johnson and Covidien (formerly Tyco Healthcare). Johnson & Johnson markets products though Ethicon and Ethicon Endo and Covidien through Syneture and AutoSuture. Both companies’ offer synthetic absorbable products based on the same polymeric materials proposed for the AD.

Absorbable device technology is currently available for a variety of surgical applications from intestinal anastomosis to ligation. Nevertheless, there are no direct competitors utilizing similar technology for the AD’s intended clinical target (Bile Duct Surgery). Currently, bile duct surgical procedures rely on sutures as the only means of closure. A miniaturized AD that allows delicate structures to be joined safely while keeping vessels open will improve the speed, accuracy, and effectiveness of procedures, while lowering the morbidity and mortality rates of surgical interventions. This market represents an entry point to a broader anastomosis market: after demonstrating reductions of the high morbidity associated with this type of surgery, the product will gain acceptance as an alternative to metal surgical staples and other GI anastomotic devices in other anastomotic applications.

5. Reimbursement

A detailed reimbursement strategy was not developed yet. Current anticipated advantages for this device would be reduction in surgery time (device usage vs. time for suturing), improved outcomes and comparable costs. Substantial reduction in morbidity following bile duct surgery will result in obvious health care cost savings.

6. Regulatory

An initial 510(k) submission will focus on the AD as a mechanical anastomotic device without a drug delivery component. Competitive product analysis and preliminary review of potential substantially equivalent predicate devices show that the AD would make an excellent candidate for the 510(k) Class II approval process. The recommendation for this approval path is based on current FDA classification the following devices as Class II:

- Endoscopic tissue approximation device – Regulation Number 876.1500
- Stapler, surgical – Regulation Number 878.4800 (Class I)
- Staple, implantable – Regulation Number 878.4750
- Suture, absorbable, synthetic – Regulation Number 878.4830

The initial submission of the AD as a stand alone Medical Device would achieve fastest path to market since a 510(k) Class II classification for the Anastomotic Device would make significant clinical studies an
unlikely requirement. This approach would allow the initial 510(k) to focus on demonstrating to FDA that the Rivet device is at least as safe and effective as the predicate device selected.

A separate submission would be required for product claims regarding the device’s ability to deliver therapeutic and bioactive agents locally at the anastomotic site (both in combination with the rivet or as a stand alone drug delivery platform). This submission would be made to FDA as a Combination Product. FDA defines a combination product as a product comprised of two or more regulated components (drug/device or biologic/device) that are combined as a single entity or is a product labeled for use with a specified drug, device, or biologic where both are required to achieve the intended use, indication, or effect.

7. Development status

Development activities so far have centered on the fabrication technique for the Ring and on the drug eluting capabilities of the Ring. Initially Ring fabrication used solvent cast rings. Additional experimentation has led to the use of compression forming for the ring. This technique has yielded enhanced predictable drug release profiles based on varying the ratio of PLA and PGA polymers. Rapid prototypes of the Rivet, the Ring and the Applicator head have been manufactured for use in an animal model. Drawings exist for the manufacturing of a stainless steel applicator. Currently, the researchers are preparing CAD drawings of AD, and will work with an OEM to create clinical prototypes of the device to be used in animal experiments testing the ability of AD to achieve anastomosis.

In vivo testing data: To date we have completed 20 rat surgeries using prolene suture for an end to end anastomosis of the small bowel. Instron testing from days 2-21 revealed a rapid increase in wound strength from near 0 at day 2 to equal or stronger to the surrounding bowel by day 6. The prototype tests will be focused on days 3 to 5 to demonstrate increased strength in the early phase of anastomotic healing.

8. The Team

Margaret A. Wheatley, Ph.D. is a John M. Reid Chaired Professor of Biomedical Engineering in the Drexel School of Biomedical Engineering, Science and Health Systems and Department of Chemical Engineering. Her research focuses on ultrasound contrast agent development (tumor targeting and triggered drug delivery), controlled release technology (bioactive compounds), microencapsulated allografts (ex vivo gene therapy) for spinal cord repair.

Dr. Ari D. Brooks, M.D. is an Associate Professor, Department of Surgery, Drexel College of Medicine. In addition to being an active Oncologic Surgeon, he is the Vice Chair for Research in the Department, and is a co medical director of the Clinical Research Group for the University. He has a strong research program covering many areas including: Ultrasound Tissue Characterization, Tissue Turgidity, Prostate Brachytherapy, Zebrafish and Micromanipulation, Cholesterol Plaques, Urinary Iodine, Molecular Pathway of Iodine in Breast Tissue, Non thermal plasma use in Medicine, Magnetic Stents, Clinical outcomes research, and Data Mining.

Bradley E. Layton, Ph.D. is an Associate Professor in Mechanical Engineering and Mechanics of Drexel University and director of the Cell and Protein Mechanics Laboratory with a background in soft tissue mechanics, cell mechanics, protein evolution, and nanomanipulation.

9. Further information and licensing inquiries

Drexel University’s School of Biomedical Engineering, Science and Health Systems is an integral part and a driver of the regional economy. The focus of the School of Biomedical Engineering on translational research resulted in several ground breaking biomedical innovations. It is the goal of Drexel University to license those technologies either to established corporations or start-up companies to move those innovations from bench to bedside.
For licensing information please contact:

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