ANASTOMOTIC LEAKAGE PREVENTION DEVICE
BUSINESS PLAN

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N.H. Diane Kim, Daniel B. Park, Sophie Wang, Timothy Weber
http://www.acunex.us

Executive Summary

Anastomosis is a surgical procedure which joins together two hollow tissues. It has many applications in gastrointestinal (GI) and colorectal surgeries. Typically, part of the gastrointestinal tract is excised, resected, or bypassed and the two tissues are rejoined. These procedures are performed to reduce digestive capacity (in the case of gastric bypass) or to resect cancerous portions of the GI tract. According to the CDC's National Center for Health Statistics (NCHS), more than 242,000 large intestinal excision surgeries[1] are performed each year in the United States.

Anastomotic leaks are a major problem in these procedures. Leaks can occur in anywhere between 2-20% of anastomotic procedures depending upon its localization within the GI tract. The development of anastomotic leaks can lead to other complications such as sepsis, stenosis, small bowel obstruction, and infection. Leaks substantially increase post-surgery mortality and morbidity risks, up to 6 fold as reported in some studies. Leaks develop as a result of improper healing of the joined tissue, where too much compression leads to ischemia in the tissue edges. Thus we identified a need to mitigate the effects of overcompression and keep subclinical leaks from developing into clinical leaks.

Surgical staplers are surgeons' method of choice for joining GI tissue. As a result, there are a variety of surgical staplers available on the U.S. market today which have many applications in both open and laparoscopic procedures. These are largely manufactured by two major companies. The current method of applying staples to tissue, however, is lacking in sensitivity to tissue thickness and the compressive force applied. Furthermore, high local stresses at the staples cause tissue failure at the staple line. Our solution will incorporate microneedles into an expandable stent, to seal tissues. The strength of the solution comes from the microneedles that will create tiny micro-punctures and become imbedded into the tissue. The self-expanding stent will conform to the contour and size of the gastrointestinal tract, and also engage the needles with the inside of the lumen, keeping it patent while the covered surface will prevent leakages that might compromise the anastomosis site.

Our device is capable of increasing maximum burst pressure of anastomosis, reducing stricture, and mitigating effects of overcompression that may result in clinical leaks.

Reimbursement will be similar to existing gastrointestinal stents because they are also single-use devices used as aids in various anastomosis procedures. The proposed design will also follow the same strategy.

Based on estimated costs of manufacture and the current price of competing staplers, we can expect in the long run to make a profit of at least 50$ per device sold. Despite a substantial initial outlay in capital to fund Food & Drug Administration (FDA) approval and clinical trials in the first 30 months, our projected timeline predicts that we will be able to break even in 4 years, and will see annual sales of $5-10 million in the years immediately following. It is expected that sales will increase as costs of production are decreased from mass production.

With strong backgrounds in biomedical imaging, cell and tissue engineering, biomechanics, academic research, and biomedical device regulation, combined with a set of knowledgeable engineering and clinical advisors, this team is skilled and motivated to design a function and successful device and a sustainable and profitable business model.

Problem Overview

Anastomosis refers to any techniques used to connect two hollow tubes or sections of tissues. It has many applications in gastrointestinal surgery, where part or gastrointestinal tract is excised, resected, or bypassed to reduce digestive capacity and/or throughput. Conventionally, suture or staples are used to create anastomosis although other tools, such as compression rings for colorectal regions and electrical welding for vascular structures, exist. However, the viscoelastic nature and properties of the tissue are complex to deal. For instance, staple biomechanics are highly dependent on tissue compression and stress relaxation. With too much compression and not enough time for stress relaxation to occur, tissue gets damaged, paving way for leaks. Surgeons attempt to detect leaks immediately after anastomosis by endoscopically insufflating the GI tract while the anastomosis site is laparoscopically submerged underwater. Despite these attempts to identify failure, failure with biological and mechanical causes can still occur days after operation. Leaks occur in 2-10% of GI anastomotic surgeries, the main factor affecting the rate being location of anastomosis. This jumps up to 30% in revisional surgeries. Anastomotic leaks often lead to major complications including sepsis, small bowel obstruction, stenosis, and surgical site infection. Leakages are also associated with higher rates of morbidity and mortality post surgery. Thus, our company identified a need for a reliable and effective method for preventing anastomotic leaks during and after gastrointestinal surgery.

The Market

The market is currently composed of two major companies (Ethicon and Covidien) that develop and manufacture a wide range of devices for many anastomotic needs. There are also a number

of smaller companies and startups that have been launched to address specific needs in anastomosis using novel technology. However, the market for a supplemental measure towards anastomotic procedures is a niche that remains largely unoccupied.

Two prominent competitors of Acustent are TISSEEL and Seamguard, which are products of TISSEEL and Gore, respectively. TISSEEL is a fibrin sealant indicated for use as an adjunct to hemostasis. The company website claims that TISSEEL can provide leakage prevention through reinforcement of the staple line. In addition, TISSEEL is bioabsorbable in 10-14 days. However, the main purpose of Tisseel is to reduce and prevent hemostasis, not prevent anastomotic leakage. Gore Seamguard is another bioabsorbable staple line reinforcement, composed of a 0.50mm polymer lining. Gore claims that the reinforcement can mechanically increase the strength of the resection line. In addition, it is claimed that the highly porous matrix that composes Seamguard can facilitate tissue generation, growth, and healing.

Significantly, both of existing devices do not directly address anastomotic leakage; TISSEEL is primarily intended for hemostasis, while Seamguard is focused on increasing the strength of the anastomosis, not preventing leaks. Additionally, both measures only span the approximate size of the anastomosis. Being liquid or very elastic materials, TISSEEL and Seamguard do not lend any structural support to the anastomosis site aside from the local patches.

As an alternative to stapler-based colorectal anastomosis, NovoGI has developed the anastomotic compression ring. The compression ring is inserted endoscopically and clamped on folded-in colon tissue on both sides of the anastomotic site. As the site anastomotic site heals, the compression ring is naturally passed through the remaining colon[1].
Additionally, Rocky Mountain biosystems appears to have received SBIR support to develop tissue fusion technology to buttress existing stapler-based approaches. They claim that their approach will eventually lead to anastomosis without the use of sutures or staples[2].

Business Model

After filing the initial patent, the company will proceed to manufacture working products. The initial manufacturing cost is expected to be $400 per unit, but this cost is projected to decline as basic machinery and processes for efficient creation of our device are established. The company will use investment funds and grants to pay for the associated costs to produce initial stock of our devices. Immediately following the patent's validation, the devices will be distributed among clinical collaborators for their use and to receive their feedback. At the same time, our sale staff will visit hospitals and surgical device forums to advocate and promote our device. The collaborator's feedback on direct use of our device and performance results will be used in

[1] Compression Anastomosis. Novogi Products. 2013.
[2] Colorectal Anastomosis Suture/Staple Line Sealing. SBIR/STTR. 2013.

this sale effort as well. We will send out samples to interested surgeons for them to experience the technology for themselves, and to spread the target market.

Following the trend of tools used in anastomotic procedures and basing on the mechanics of our product, our product will follow a disposable product model. Anastomotic surgery in gastrointestinal regions is a high-risk, high-cost field. Therefore, medical professionals prefer to dispose of instruments between surgeries and avoid the cost and risk of infection associated with reprocessing surgical tools. The high-cost of surgery lessens the burden in terms of reducing manufacturing costs and allows our model to be sustainable given the established financial clout of our competitors.

In the short term, we will partner with our clinical advisors at Columbia University Medical Center to test our product in clinical trials. Once FDA approval is obtained, a pilot program to sell and distribute our product will be established with select academic medical centers. This will ease the transition into the market and allow our product to be adopted more easily in operating rooms across the country.
As our product gains traction in the surgical device industry, we hope to expand to the national market. This disposable product model will allow our company to break even within 3 years, and our ultimate goal is to establish our company as a major player in the market, building a reputation for the reliability, safety, and efficiency of our product.

Reimbursement Strategy

The current design involves a microneedle array that will create micro-punctures and anchor within the two adjoining tissues to maintain a seal. Therefore, the proposed reimbursement strategy will be similar to those of existing gastrointestinal stents. Our microneedle arrays will come in packs and each deployment device and array will be intended for one-time use in each patient. Due to issues with sterility, this strategy offers the highest cost-effectiveness.

It has been suggested that these devices can be sterilized, but this is uncommon. The manufacturer likely sets the price point, such that it is not too expensive to require sterilization-reuse techniques. With one time use products, the reimbursement is stable and sustainable because hospitals must constantly be restocking their supply of the device.

In terms of reimbursements for the use of our device, we expect that current procedures will be extended to cover our device. As of today, a vast array of anastomotic procedures including bariatric surgery and colon resections are reimbursed by Medicare. These reimbursements include the cost of the use of current devices such as gastrointestinal endoscopic stents. One example is a colectomy done laparoscopically (CPT-44204) which has a national average

medicare reimbursement payment of $1,551. Furthermore, revisional surgeries are also reimbursed.[3]

Design & Development Plans

Current parameters of microneedles are: height of 1 mm, base diameter of 0.8 mm, material of plastic, which are placed on one side of a self-expanding stent. Our design is based on current needle adhesives that use a type of mechanical anchor in order to fasten to the tissue, as well as self-expanding stents

Deployment device, designed for one-time use and for exclusively use with the stent, is multiple components. First, a hollow tubular component with opening on one side encases the stent pre-deployment; a plunger end attached to the handle; and outer handle component that is secured to the aforementioned hollow encasing tube in order to allow for deployment of the stent by pulling the hollow case back. The microneedles are expected to be a permanent (possibly bioabsorbable) fixture in the body. Because the needles cannot be handled by the surgeons by themselves, a one time-use, disposable model will be employed to enable the application of the needles.

Initial Development Timeline
July 2014 - Begin Clinical testing
June 2014 - File provisional patent with Columbia Tech Venture
May - June 2014 - Complete final product design
May 2014 - Final prototype design

Financial Projections and Time-plan

Our design focuses upon the one-time use disposable model. Based on this design and estimated cost of components and labor, our device will initially cost $900 to manufacture. At this time, the device can be sold at $1600 to customers, creating a profit margin of $800. Although the price of the device does not allow for a high profit margin, as production becomes more streamlined, we expect costs to fall to at least $800, creating a profit margin of at least $800 per device.

There are a number of hurdles that must be overcome before our device can be brought to market and the profit margins can be used to fund the development and manufacturing of the device. The first hurdle is the current level of funding available for the design and development phase of this device. Therefore, the most critical step in the short term (next 6-8 months) would be to secure additional funding opportunities to allow this device to begin to be tested in clinical trials and be ultimately brought to market. The opportunity to secure funding from venture capital

[3] 2013 General Surgery Medicare Reimbursement Coding Guide. Covidien. 2013.

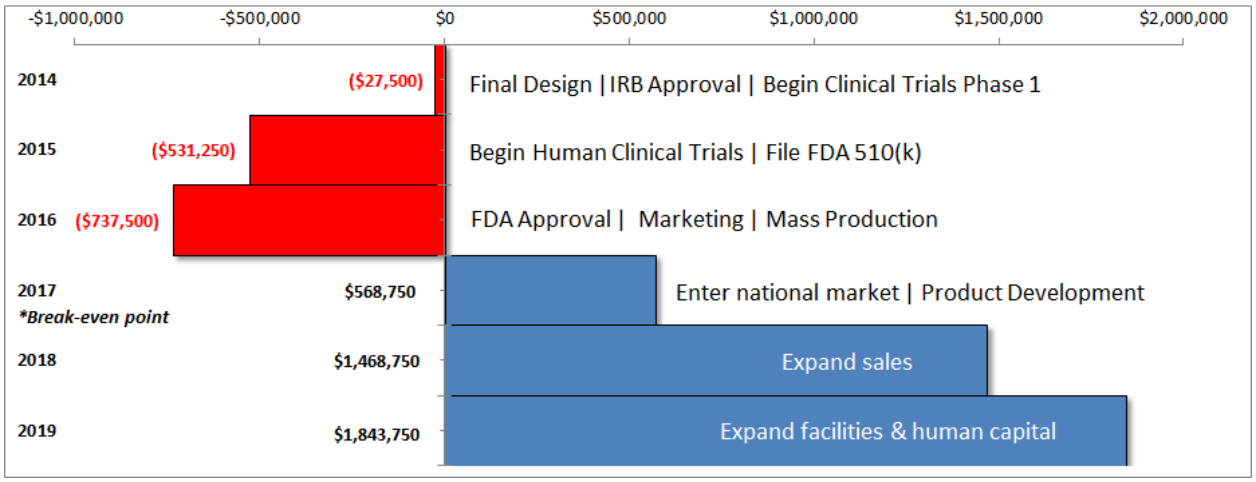
firms and biotechnology/biomedical engineering design competitions will be investigated.

Once funding has been secured, we will begin the long process of seeking FDA approval and proving that our device is safe and effective through clinical trials. Because our device will be used in surgeries - which are inherently high-risk procedures - the FDA approval process would classify our device as Class II, which involves the filing of a 510(k) application. Evidence in the form of data from testing and clinical trials are needed to support this application. We anticipate that this will be a large cost to contend with as we begin to establish our company. The chart below lays out both the timeline in terms of design, development, marketing, and expansion as well as tentative financial projections.

The timeline is outlined in the table below.

Time (months)	Stage of Process	Produced	Sold	Costs	Revenue	Profit
0.00 - 6.00	Seek grants for further development	5	0.00	$2,500	$0	($2,500)
(1/2014-6/2014)	Prototype design and test					
	Finalize design					
	Seek IRB approval for clinical trials					
7.00 - 12.00	Begin Clinical Trial 1 (animal model)	100.00	0	$12,500	$0	($25,000)
(7/2014 - 12/2014)	Begin to seek IRB approval for human trials					
	Begin intial filing of 510(k) for FDA approval			$10,000		
13.00-24.00	Run human Clinical Trials with clinical partners	50	0	$506,250	$0	($531,250)
1/2015-12/2015	File FDA 510(k) - wait for approval					

25.00-30.00	Gain FDA approval	500	500	$62,500	$87,500	($556,250)
1/2011-6/2016	Begin marketing			$50,000		
	Sell to a few select clinical partners					
31.00-36.00	Begin mass production	5000	5000	$500,000	$875,000	($181,250)
7/2016-12/2016	Sell product to national public market		(adjust based on sales in previous quarters)			
37.00-48.00	Continue sales to national market	10000	10000	$1,000,000	$1,750,000	$568,750
1/2017-12/2017	Continue development					
	Market					
49.00-60.00	Expand sales as market share increases	12000	12000	$1,200,000	$2,100,000	$1,468,750
1/2018-12/2018						
	Continue development					
1/2019-12/2019		15000	15000	$1,500,000	$2,625,000	$1,843,750
	Expand facilities, human capital (cost)	0		$750,000		



The above graph demonstrates the expected profit over the next five years. Our device would be sold at a price of $1600 over the long-term. Within this timeframe, we will be able to reach the projected break-even point in early 2017. However, due to the large share that Covidien and Ethicon hold in the market, an exit strategy will need to be engaged. The intellectual property rights will be sold to competitors so that the device will have the opportunity to be produced, backed by the financial clout of a larger, more well-established corporation.

If projections hold, however, our company would expect to be selling 40,000 units annually to the U.S. market within five years, which represents at most a market share of 16% or 15,000 procedures. This should result in an annual revenue in 2019 of $32,000,000 and a profit of $1,843,750 with expansion costs. Once a stable level of the market has been attained, however, we will look to expand our reach to both international markets as well as larger portions of the U.S. market. This venture will involved substantial investment in facilities, human capital, and research and further development of our product to better meet the needs of surgeons and patients worldwide.