EVT24

Final Report: Medical Device for Gastrointestinal Leaks

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1. Executive Summary

Perforations causing leakage of pus in the gastrointestinal (GI) tract are common and negatively affect patient health. Endoscopic Vacuum Therapy (EVT) is a treatment developed to treat this condition. Current EVT procedures are complex, and current EVT devices require frequent replacement throughout the perforation's healing time. An updated EVT device should be inexpensive, simple to deploy, and capable of remaining in the body for extended periods of time without replacement.

The EVT device developed consists of a sponge which is compressed into a gelatin capsule and attached to a vacuum tube. Two potential sponges were developed. The first sponge contains a polyurethane core for compressibility and a bioabsorbable PLGA outer layer that serves as a buffer to tissue ingrowth (Fig.1). The second sponge is a polyurethane sponge coated in polyethylene glycol (PEG) (Fig.2). The PEG coating prevents tissue growth from attaching to the sponge, extending the lifetime of the sponge in the perforation. Once the sponge is deployed in the target region, the gelatin capsule dissolves, allowing the sponge to expand and fill the entire volume of the perforation while a vacuum drains infectious fluid (Fig. 3).

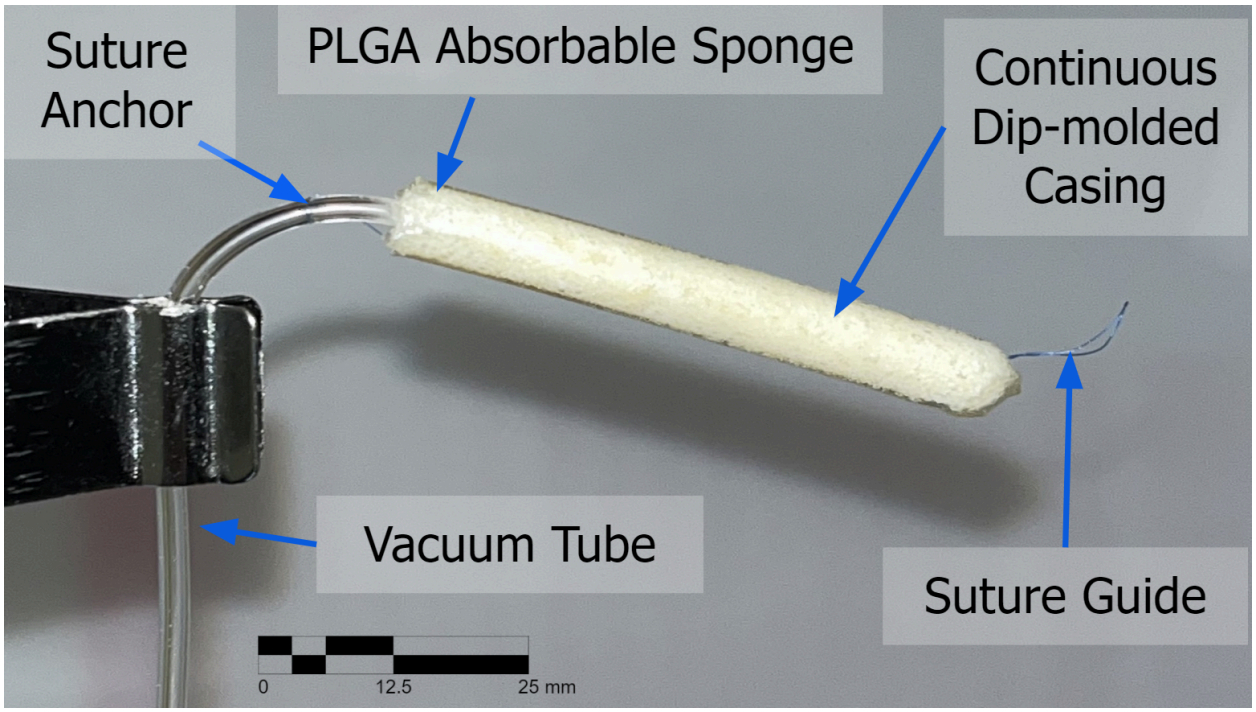


Figure 1: Final prototype with PLGA Absorbable Sponge

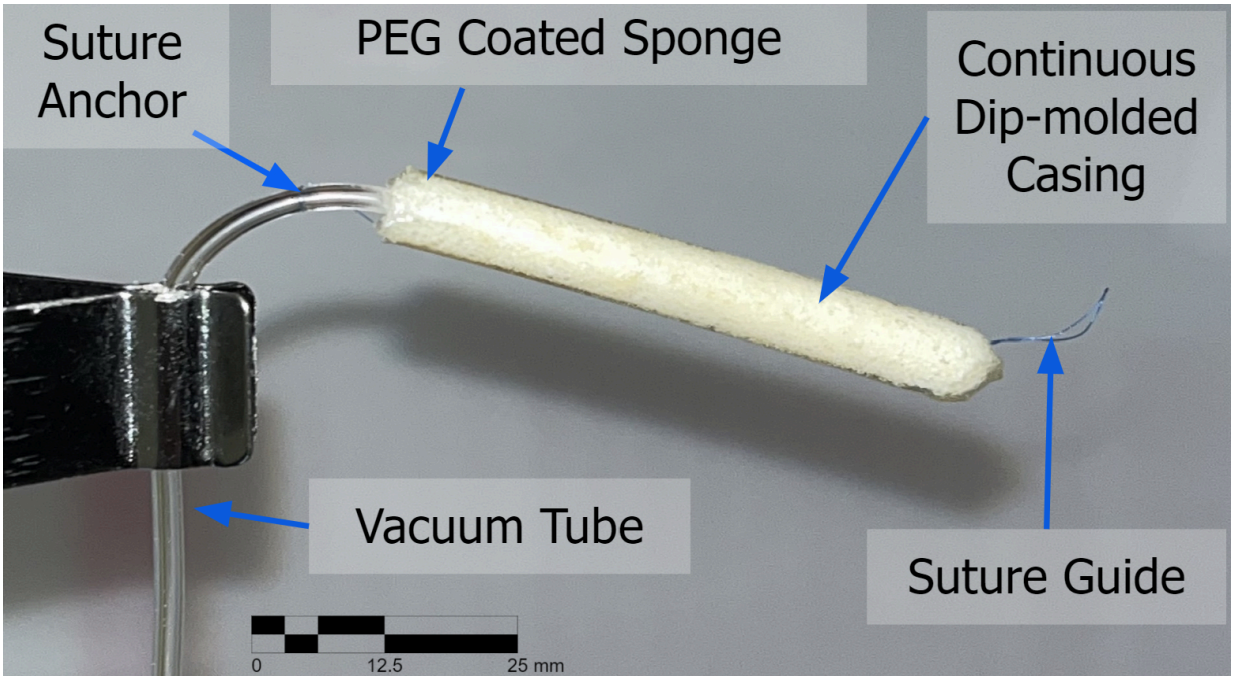


Figure 2: Final prototype with PEG Sponge

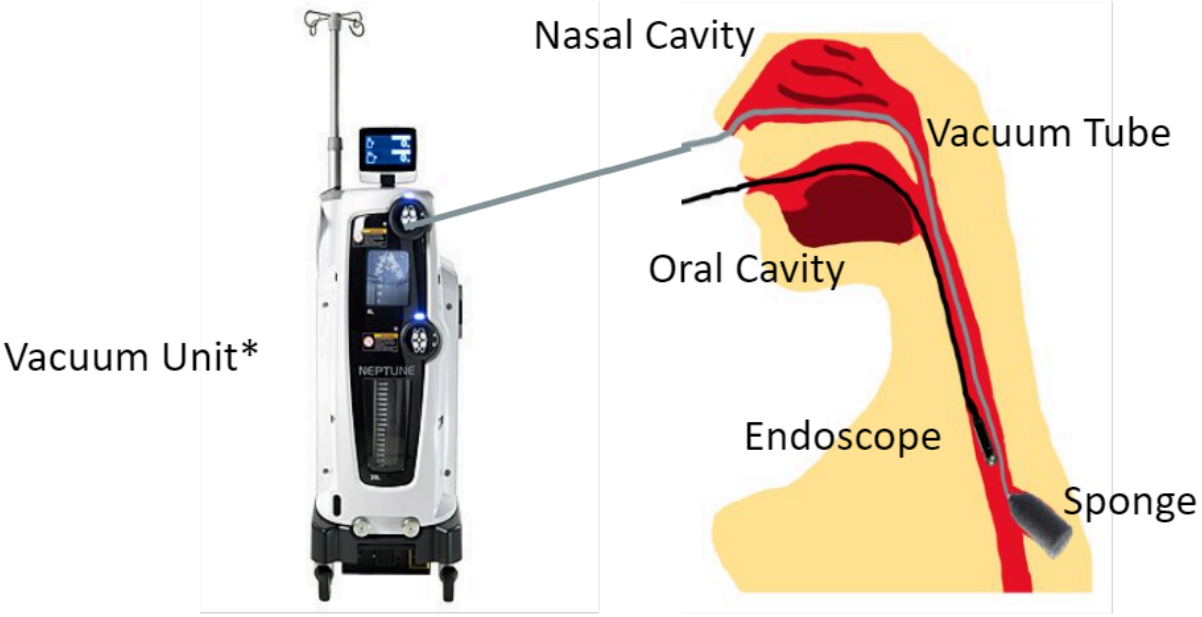


Figure 3: Diagram of fully expanded sponge deployed in a GI perforation

Several tests were performed to test the efficacy of this device. Absorbability tests were performed on open cell polyurethane foams varying in pores per inch (PPI). The final device featured a 45 PPI sponge which allowed for the optimal compression and absorbability characteristics. Dissolvability tests were performed on the gelatin dip molded casings as well as

the PLGA sponges. These tests showed that the gelatin casing would not dissolve prior to proper placement of the device in the perforation, and that the PLGA sponge slowly degraded over several days, as anticipated. A bacterial growth test was performed on the PEG sponges and yielded inconclusive results on whether the PEG coating would help negate tissue adhesion to the polyurethane sponge. A maneuverability test was performed using an endoscope and a pig stomach and determined that the device is readily navigable in the GI tract using the endoscope. Several sponge synthesis trials were performed using varying concentrations of PLGA, chloroform, and salt to achieve optimal mechanical properties.

Figure 4: Device being deployed in a simulated GI tract (pig stomach)

The final product significantly reduces the current device's deployment procedure complexity and time. The device is easily navigable in the gastrointestinal tract and compatible for use inside the human body. The device's life span in the body is theoretically significantly longer than the current device, however more comprehensive testing is required to confirm this hypothesis.

2. Project Brief

During many different gastrointestinal (GI) procedures, such as endoscopy, open surgeries, and laparoscopic surgeries, perforations can occur in the cavity wall or organ lining. These perforations allow non-sterile fluids to leak between the GI tract and the inside of the body, which can cause infections. The medical paradigm for this situation is to control the source of the infection in order to prevent infections, which in this case is to quickly and efficiently remove the non-sterile fluid and infectious material. Superficial perforations are easily treated with a drain, but for deeper perforations, limited treatments are available to control the infection.

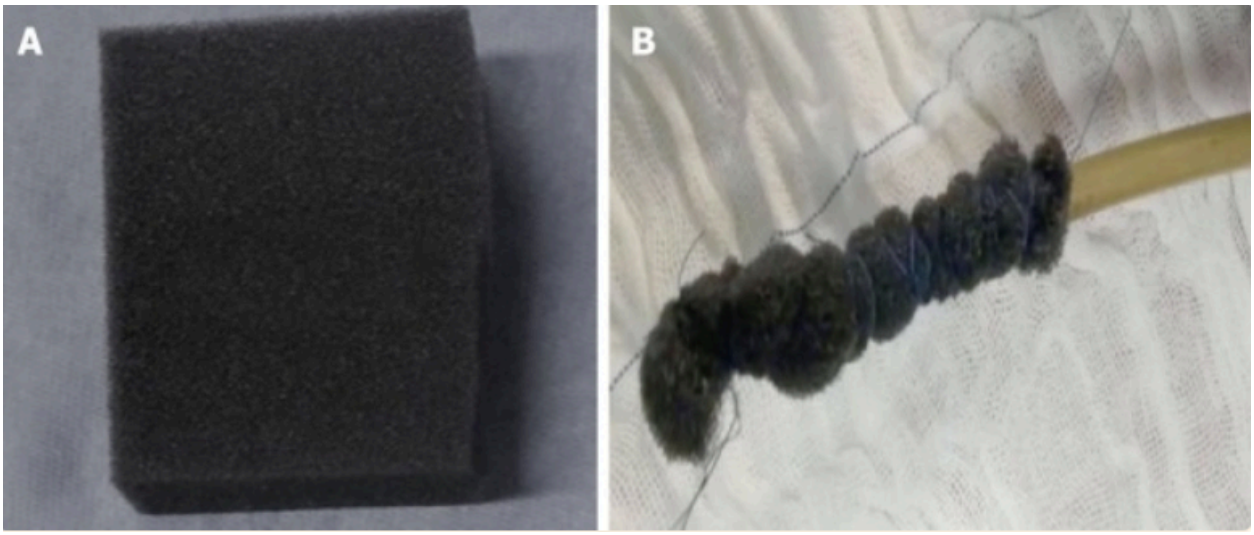


Figure 5. Improvised EVT device

One current method of removing infectious material is Endoscopic Vacuum Therapy (EVT). In EVT, a drain is placed near the infectious material and a vacuum continuously removes the material. The drain actively draws infectious material, or pus, out of the body. This procedure can be done in both the upper and lower GI tracts. Currently in the United States and in Brazil, EVT is used, but consists of crude, makeshift materials [1] (Fig.12). In Europe, a disposable EVT kit is commercially available (Fig.13).

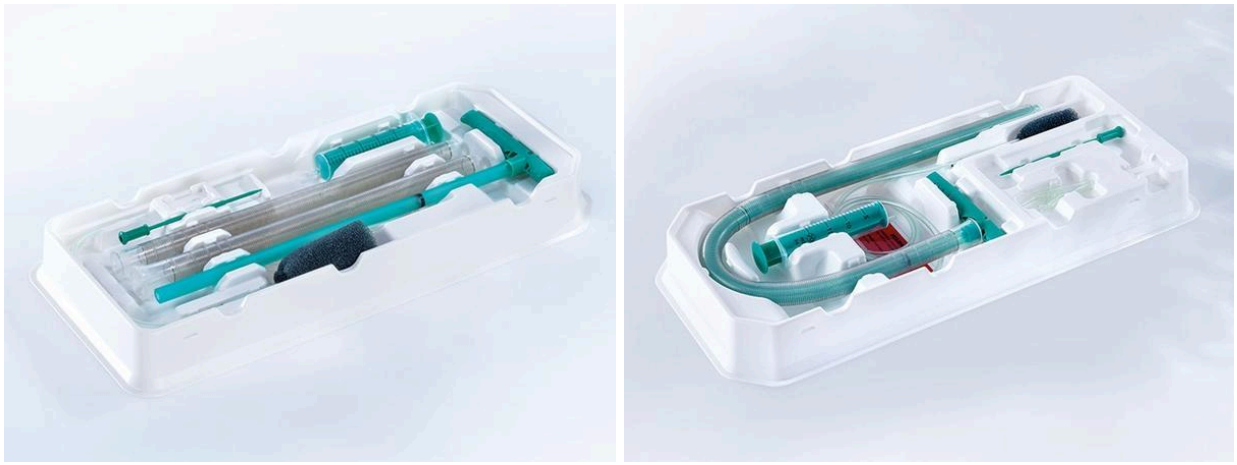


Figure 6. EVT kits commercially available in Europe. On the left is Endo Sponge which is primarily used in the colorectal area and on the right is Eso Sponge. [2]

Despite reported success overseas [3], EVT is not widely used in the US due to a lack of procedural knowledge and lack of FDA approval.

EVT supports the healing of perforations and cavities through various mechanisms (Fig.5). The sponge physically fills the cavity which blocks fluid from flowing out of the GI tract into the body. In addition, physical contact by the sponge with the cavity promotes vascularity in the region by irritating the wound. The vacuum tube allows draining infectious material out of the affected region and mechanically shrinks the cavity thanks to the negative pressure..

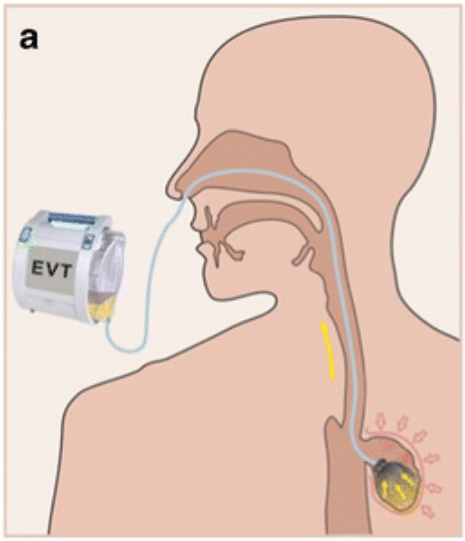


Figure 7. Example of EVT treatment with extraluminal placement of the sponge. The sponge is placed inside the cavity and fills it. A vacuum pump connected to the sponge by a vacuum tube and removes infectious material. The negative pressure from the vacuum also shrinks the cavity to assist the healing process.

There are several major issues with the current EVT device and procedures to improve upon. Firstly, the current EVT device needs to be replaced every 3-4 days. This is mainly due to tissue ingrowth in the sponge [4], which makes the sponge more difficult to remove and can lead to additional damage to the cavity upon removal. The frequent replacement of the device means that the procedure is required multiple times throughout the healing process. Small perforations require between 1-2 weeks to heal, but large perforations can take anywhere from 4-6 weeks. It would be ideal to extend the longevity of the current device so that the number of replacements can be reduced.

The second issue is the deployment of the device into the cavity. In the current procedure, an endoscope is first inserted through the mouth to find the location of the wound and determine its size (Fig.6). An over tube is placed over the endoscope, the endoscope is then removed before the sponge can finally be inserted. A clinician must then push the sponge through the tube using a “pusher” device, as the size of the sponge is much larger than the tube size. Once the sponge is inserted, the overtube is removed through the mouth. Another set of steps is then required to move the vacuum tube from the mouth to the nose.

In conclusion, a total of nine steps are required for deployment of the sponge into a cavity, including two for inserting and removing the overtube and three to move the vacuum tube from the mouth to the nose. Overall insertion of the sponge using Eso Sponge is not an easy task.

The goal of this project is to create an endoscopic vacuum therapy device which outperforms Eso sponge by reducing procedure time and complexity.

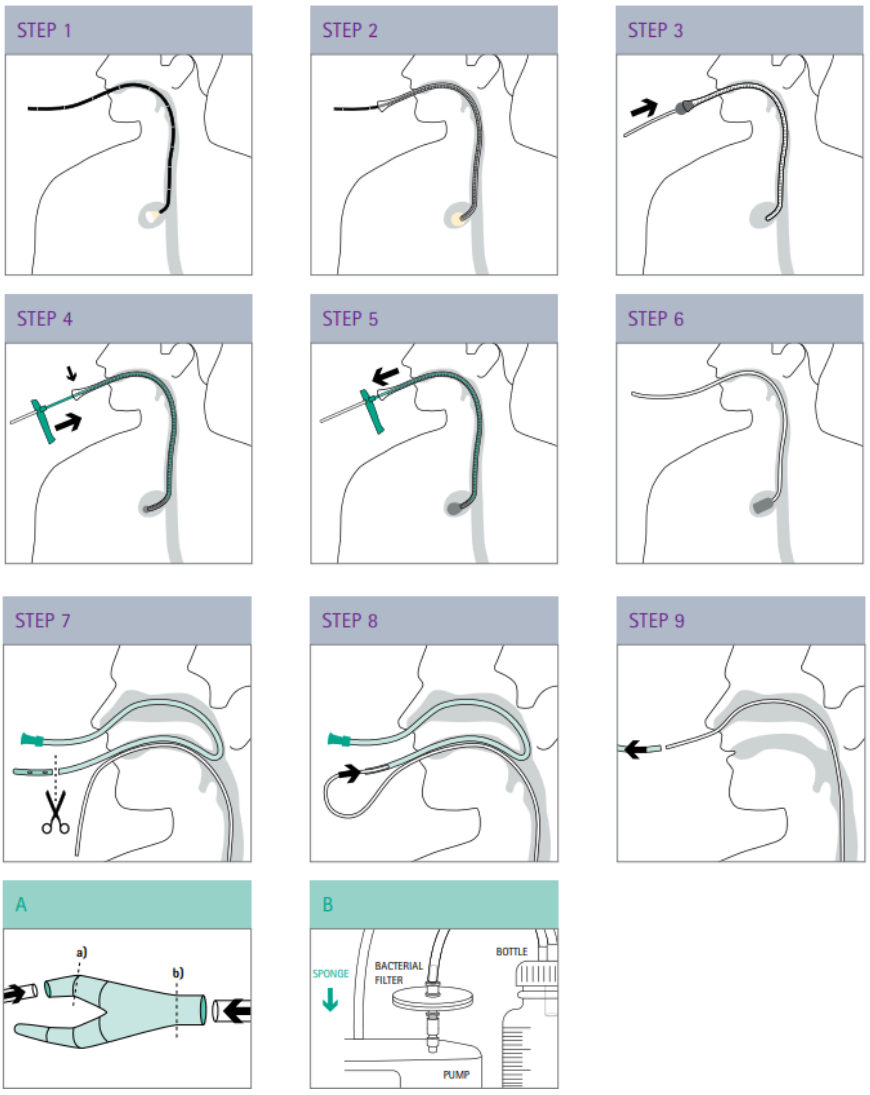


Figure 8. Eso Sponge deployment procedure. First, an endoscope is used to identify the location and size of the cavity. An overtube is placed over the endoscope as a guide. The endoscope is removed and the sponge is inserted into the cavity with a pusher. When the sponge is in the cavity, the pusher and overtube are removed. An additional tube is inserted through the nose and one end is pulled out of the mouth. The vacuum tube is inserted into the additional tube, which is used to pull the vacuum tube through the nose. [2]

3. Project Requirements and Achievements

Requirement	Test Method Name	Result Section	Requirements Met?
Effective Endoscopic Deployment	Gelatin Capsule Dissolvability Test (Sec. 6.1)	6.5 minutes (Sec. 7.1)	YES
	Prototype Procedure Test (Sec. 6.2)	7.5 minutes (Sec. 7.2)	
Reduced Procedure Time (One Hour Maximum)	Prototype Procedure Test (Sec. 6.2)	7.5 minutes (Sec. 7.2)	YES
Increased Sponge Longevity (Remain in Body for Minimum One Week)	Hybrid Sponge Longevity Test (Sec. 6.3)	Ongoing (Estimated 22 Weeks) (Sec. 7.3)	90%
Active Vacuum	Vacuum Test (Sec. 6.4)	250mL in 20.3 seconds (Sec. 7.4)	YES

4. Literature, Prior Art, and Background

The first major piece of literature that greatly influenced the design of the final device is a paper titled *Freeze-Drying Process for the Fabrication of Collagen-Based Sponges as Medical Devices in Biomedical Engineering* by a group of professors and graduate students at the Aristotle University of Thessaloniki. This paper describes “a systematic review of a key sector of the much promising and rapidly evolving field of biomedical engineering, specifically on the fabrication of three-dimensional open, porous collagen-based medical devices, using the prominent freeze-drying process.” [5] In this, it breaks down the composition of many different bioabsorbable scaffolds for use in many different areas of tissue engineering. This impacted our design giving way to a new avenue of tissue ingrowth mitigation along with detailed steps of how to make these scaffolds on our own. This breadth of knowledge even led to a meeting with the authors of the paper which assisted in getting the hard questions answered about collagen scaffold synthesis.

The second major source is a paper titled *Preparation of Cylinder-Shaped Porous Sponges of Poly(L-lactic acid), Poly(DL-lactic-co-glycolic acid), and Poly(ε-caprolactone)* by Xiaoming He, Naoki Kawazoe, and Guoping Chen. This paper describes a study in which "cylinder-shaped PLLA, PLGA, and PCL sponges were prepared by the porogen leaching method using a cylinder model" after which "the effects of polymer type, polymer fraction, cylinder height, pore size, and porosity on the mechanical properties of the cylinder-shape sponges were investigated." [6] The procedure described of the synthesis of the PLGA scaffold sample influenced the final PLGA scaffold synthesis procedure for the bioabsorbable layer. Using the data describing the effect of composition versus mechanical properties also informed next steps in terms of iterating on the procedure for our own use case.

The third major source is a paper titled *EndoPil: A Magnetically Actuated Swallowable Capsule for Weight Management: Development and Trials* by Phuoc T. P., Anthony M. H. T., Muneaki M., Lin C., Hung L. K., Khek Y. H, and Soo J. P. This paper describes "a novel tetherless, magnetically actuated capsule (EndoPil) which can deploy an IGB inside the stomach after being swallowed and being activated by an external magnet." [7] The paper also describes a procedure used to dip mold gelatin casings, which we iterated upon and used to mold own our gelatin casings to specified dimensions.

The fourth major source is a paper titled *A facile method to prepare PEG coatings on the fiber surface by the reconstruction of hydrogen bonds for enhancing the interfacial strength of fibers and resins* by Shaohu Zhanga, Mingzhuan Lia, Kan Chenga, and Shengjun Lu. This paper describes "a new method for functionalizing the surface of aramid fibers by hydrochloric acid is proposed, and new polyethylene glycol (PEG) coatings are prepared on the surface of the fibers by the reconstruction of hydrogen bonds for improving the bond strength with the resins." [0004] The method given for facilitating a PEG coating heavily influenced the final procedure used to coat the polyurethane sponge of the prototype.

The fifth major source is a paper titled *Preparation of Polyethyleneglycol (PEG) Coatings for Microencapsulation of Charcoal* by E. Piskin, K. Piskin, Akmaklk, V. Evren, M. Multu, and E. Arca. This paper explains how "Polyethyleneglycols (PEGs) with their high solubility in water cannot normally be used as a coating material in aqueous solutions such as blood." To solve this the authors propose "a ɣ-radiation procedure was … applied after coating charcoal granules with PEG in a non-aqueous phase." [8] The method proposed to achieve a PEG coating provides an alternate procedure in case the PEG coating on the polyurethane using our current procedure is too weak or does not adhere.

The sixth major source is a paper titled *Polyethylene glycol–coated biocompatible surfaces* by Norma A. Alcantar, Eray S. Aydil, and Jacob N. Israelachvili. In this paper, "efficacy of protein rejection on PEG-covered surfaces was studied through measurements of the fluorescence intensity of Texas red–labeled bovine serum albumin brought in contact with such surfaces in solution." [9] The results of the protein absorption tests done on PEG coated silica in this paper informed our confidence in PEG to mitigate tissue ingrowth in our own use case.

5. Project Output

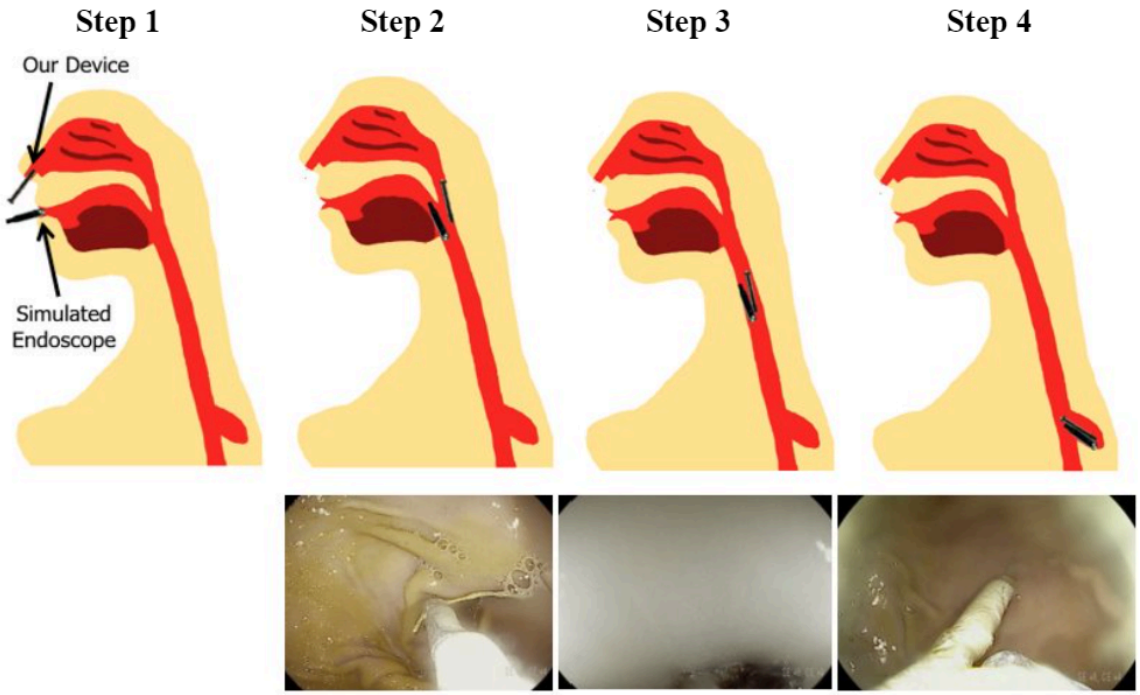


Figure 9: Location of device and endoscope during deployment (Top). View of device from endoscope (Bottom). ***Step 1:*** *Insert device into nasal cavity and endoscope into oral cavity.* ***Step 2:*** *Grab suture guide with endoscopic forceps.* ***Step 3:*** *Navigate the device down the esophagus using the endoscope.* ***Step 4:*** *Insert the device into the perforation.*

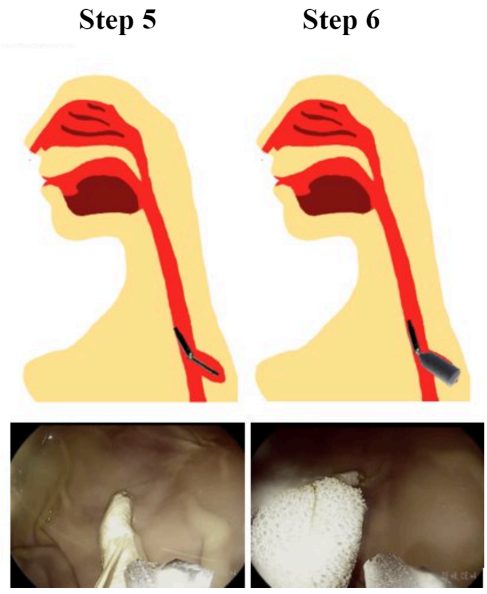


Figure 10: Location of device and endoscope during deployment (Top). View of device from endoscope (Bottom). ***Step 5:*** *Dissolve the gelatin casing with saline.* ***Step 6:*** *Monitor the devices expansion and positioning.*

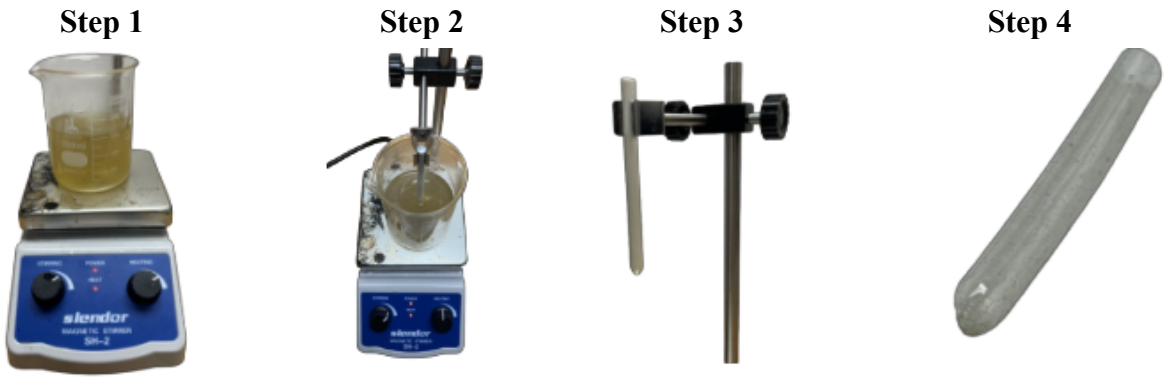


Figure 11: Gelatin dip molding procedure. ***Step 1:*** *Mix and heat the gelatin solution.* ***Step 2:*** *Dip the teflon molds into the heated gelatin solution.* ***Step 3:*** *Allow the casing to cure for at least 6 hours.* ***Step 4:*** *Remove the casing from the mold.*

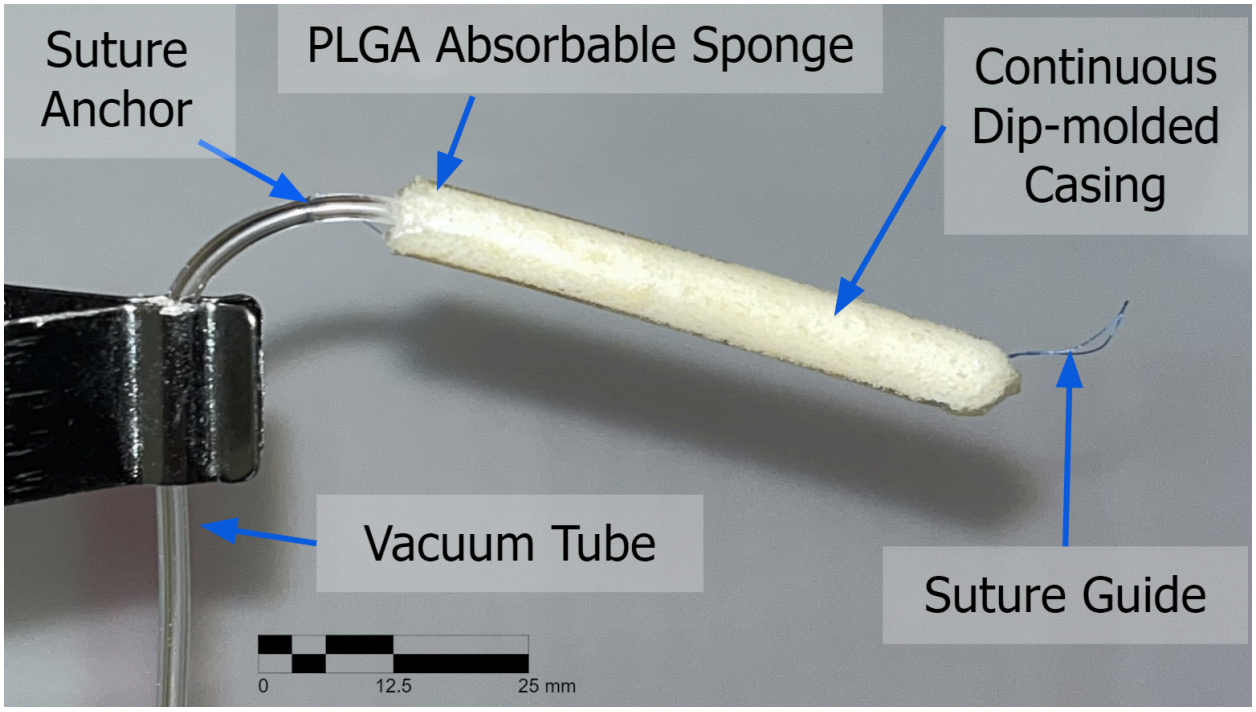


Figure 12: Final prototype with PLGA Absorbable Sponge

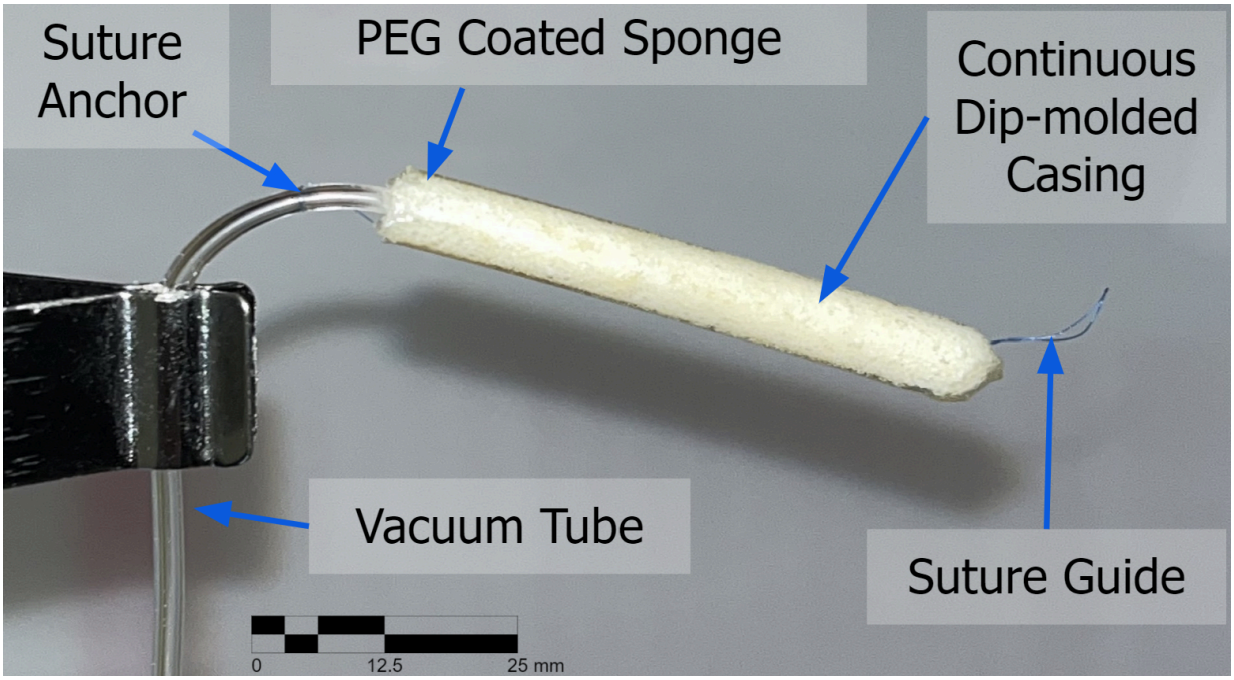


Figure 13: Final prototype with PEG Sponge

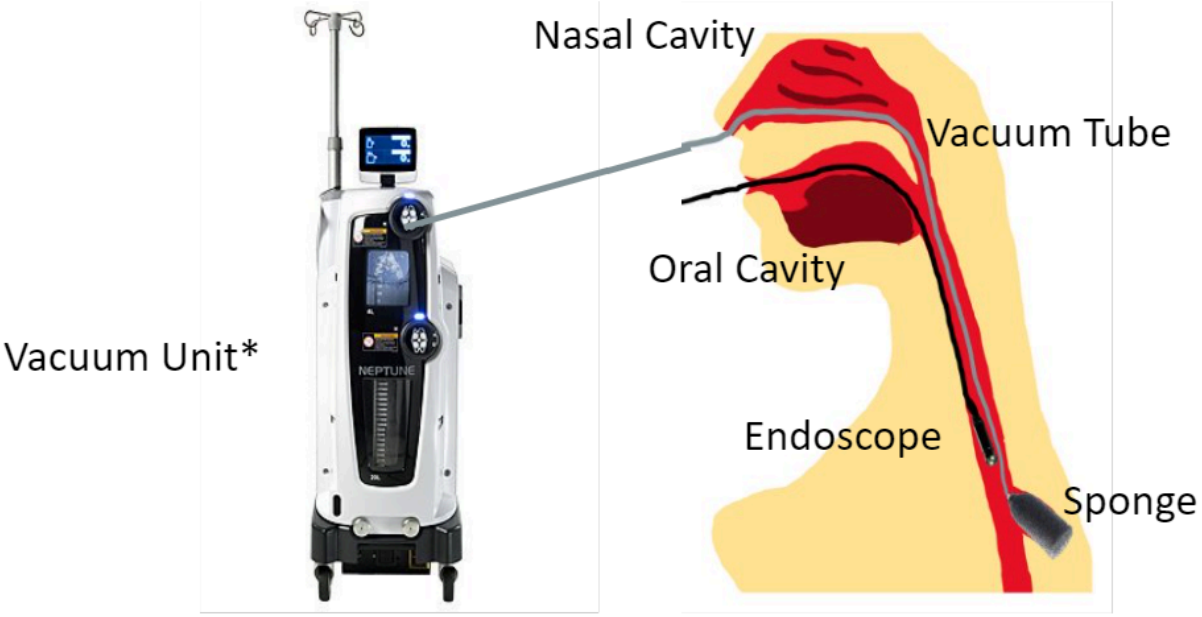


Figure 14: Diagram of fully expanded sponge deployed in a GI perforation

Figure 15: Various iterations of PLGA absorable spognes.

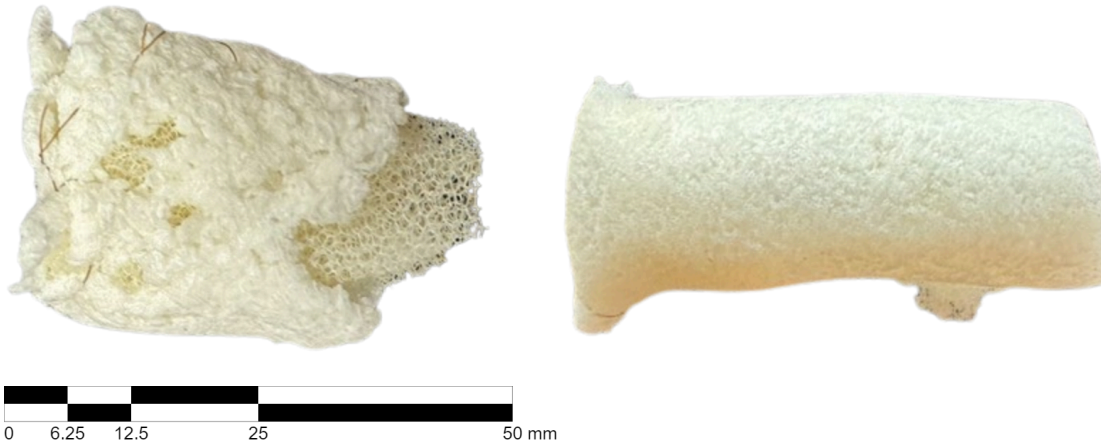


Figure 16: Two iterations of the hybrid sponge, polyurethane sponge core with PLGA absorbable outer layer.

6. Test Methods

6.1 Gelatin Capsule Dissolvability Test

Pill capsule dissolvability time is pivotal in the deployment of our prototype in the GI tract. The capsule must be able to maintain structural integrity long enough that it can keep the sponge compressed for the entirety of its journey to the cavity. In other words in must not dissolve for long enough that it allows the clinician a reasonable amount of time to maneuver the sponge to the cavity

In order to test the dissolving time of gelatin capsules three prototypes 6 mm in diameter and 50 mm in length were fabricated and inserted into an ex vivo pig stomach model. The model is composed of a pig stomach including the esophageal sphincter (the end of the esophagus which connects into the stomach) and a plastic bin with a hole cut into the side. The esophageal sphincter is fit around a pipe approximately 1 inch in inner diameter which is passed through the bin hole. This allows the user to access the inside of the stomach through the pipe. The pig stomach is an ideal testing method as it is the harshest environment that will be encountered by our prototype due to the gastric mucosa which breaks down gelatin.

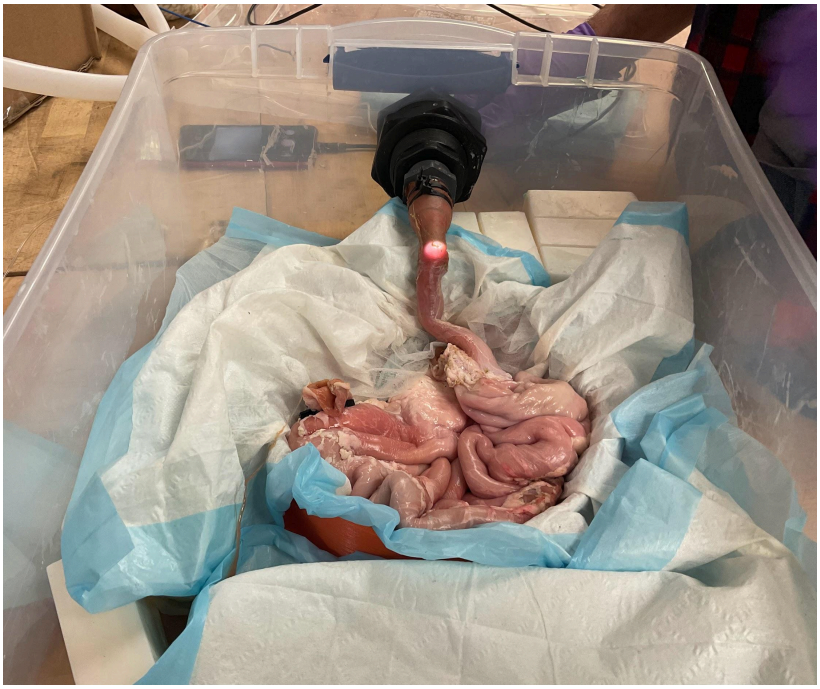


Figure 17: Ex Vivo pig stomach model.

Each prototype was inserted into the stomach past the esophageal sphincter followed by an endoscopic camera; at this point a stopwatch will be started. Time was marked once partial dissolution, meaning any piece of the sponge is visibly protruding past the initial 6 mm diameter in its compressed state, is observed. Likewise time was marked once the capsule is fully dissolved, i.e. no section of the sponge is being restricted by the gelatin capsule. At this point the

sponge was removed to confirm complete dissolution of the gelatin capsule and was disposed of with the pig stomach appropriately in a red biohazard bag. The modified bin can be reused for later testing.

This procedure will be repeated with prototypes which have a gelatin casing made using a dip molding process. These results serve as a good benchmark to compare to dip molded casings. A more efficient method may need to be developed to determine when the gelatin casing has been partially dissolved as it can occasionally be difficult to visualize the prototype with the current endoscopic camera. A higher performing endoscope has been acquired and will be used in future tests.

6.2 Prototype Procedure Test

The goal of this test is to ensure that it is possible to navigate the prototype down the esophagus to a cavity before testing it on a live pig. The procedure currently requires that the sponge be guided thanks to a forceps passed through the endoscope lumen which grabs on to a suture lead which sticks out the front of the prototype.

In order to test the efficiency of the EVT24 protocol the Ex Vivo Pig stomach model shown in Figure 8 was used once again. A lab assistant was asked to insert the prototype, using an endoscope, through the esophagus into the pig stomach, navigate it to a section of the stomach known as the Pyloric canal (the section of the stomach right before the beginning of the small intestine), and to then deploy the sponge by dissolving the casing using a water jet incorporated in the endoscope. The time from insertion of the prototype to complete dissolution of the gelatin casing was recorded. This procedure was performed twice: the first with an outer casing made from pill capsules and the second with an outer casing made using the dip molding method.

The lab assistant was also asked to give a qualitative description of the procedure explaining any difficulties they had and areas for improvement.

6.3 Hybrid Sponge Longevity Test

The longevity test serves to ensure that our final prototype is able to fulfill our goal of a time before replacement of 7 days. This test revolves around the amount of time the device will last within the body before tissue grows within the pores of the polyurethane sponge to the point at which removal becomes difficult and dangerous. The goal of this test was to characterize the degradation of the outer PLGA scaffold layer of the hybrid sponge and nail down an estimated time before replacement of the device.

The procedure required a 2 mm thick PLGA absorbable sponge, a clip, and 500 mL of lemon juice in a glass beaker at room temperature. Lemon juice has a pH in the range of 2 to 3 which is similar to that of gastric acid which is in the range of 1.5 to 3.5. The PLGA sponge was

immersed in the lemon juice completely. Following immersion, the thickness of the absorbable sponge was measured every 12 hours for a week.

For some context as to what this would mean for prototype longevity evaluation, polyurethane sponges used in EVT currently are replaced every 3-4 days due to tissue ingrowth. A couple assumptions are made from this fact: tissue ingrowth reaches a critical depth into the pores of the sponge at 5 days and this critical depth is estimated to be 1mm. The critical depth estimation is based on the geometry of the pores of the sponge, and at an ingrowth depth of 1mm, the tissue would be able to grow into and through 1-2 layers of pores. Using this assumption, our hybrid sponge with a 1mm thick layer of PLGA would encounter complete ingrowth of the outer scaffold at 5 days, at which the polyurethane sponge has the commonly used operational time of 3-4 days. This means that considering tissue ingrowth as the sole factor in replacement and degradation, the hybrid sponge would last 8-9 days before replacement is needed. This however is not the only factor in degradation. Another factor is the water solubility of PLGA, which degrades via hydrolysis, or exposure to water. Thus, this test will incorporate tests of PLGA degradation via hydrolysis to see if it dissolves prior to the rate of the tissue ingrowth, which was rated for 8-9 days. If the PLGA is degraded prior to this 8-9 day mark, then that dissolution time, plus the 3-4 days afforded for the polyurethane sponge, would be the estimated operational time before replacement. If the sponge lasts longer than 8-9 days, then this 8-9 day estimate stands and we can assume degradation due to hydrolysis is negligible.

6.4 Vacuum Test

This test aims to answer whether the sponge selected for this device is capable of pulling an active vacuum. A successful active vacuum allows infectious fluid to pass from the deployment site, through the sponge, and out of the body through the vacuum tube. An unsuccessful active vacuum would obstruct the vacuum tube and subsequently prevent the removal of infectious fluid from the deployment site. It is essential to select a sponge material that achieves an active vacuum, because an unsuccessful vacuum allows infectious fluid to continue to affect the deployment site, potentially worsening infection and preventing proper healing of the deployment site.

To perform this test, a 15.6 〖cm〗^3 cube sample (2.5 cm on each side) was cut of each sponge material being tested. A 2.5 mm diameter, 1.25 cm deep hole was cut into the center of one face of the cube. A 2.5 mm diameter, PVC (rubber) tube was inserted into the hole, such that the open tip of the tube was directly in the center of the sponge sample. The free end of the tube was connected to a vacuum pump with an adjustable and measurable negative pressure. The sponge was inserted into a beaker holding 250 ml of saline. The vacuum was turned on at a negative pressure of 125 mmHg. The time required for the vacuum to remove all 250 ml of the saline was recorded using a stopwatch.

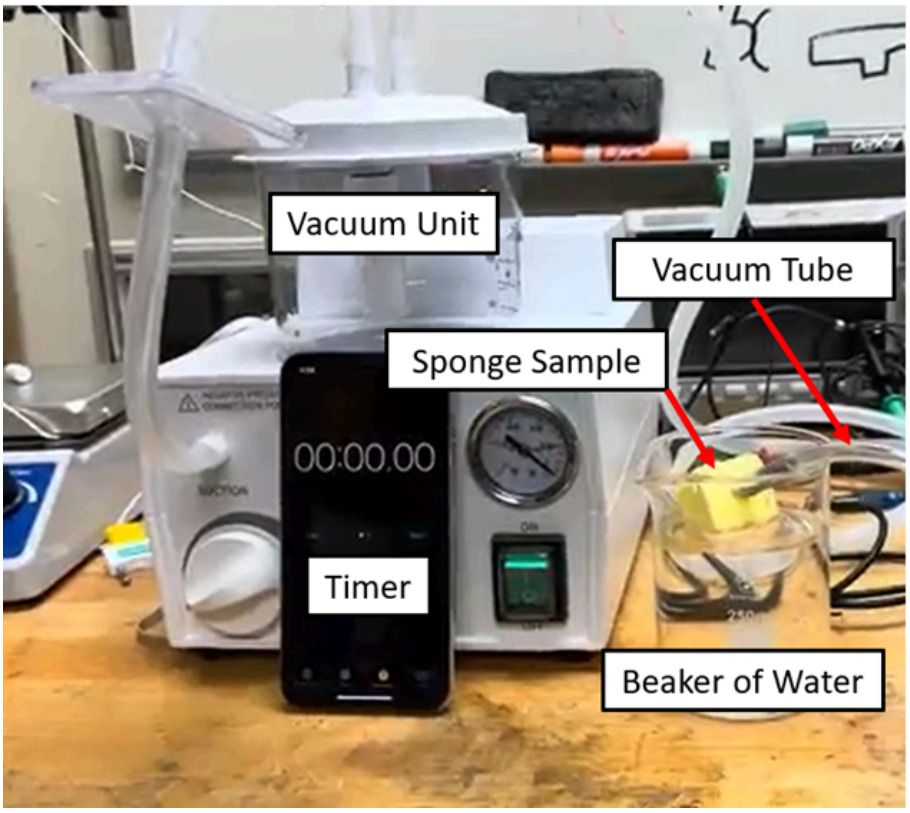


Figure 18: Labeled Diagram of Vacuum Test Apparatus

7. Results

7.1 Gelatin Capsule Dissolvability Results

Table 3: Partial and total dissolution times of three 6 mm diameter prototypes with gelatin casings made from pill capsules

	Partial Dissolution Time	Complete Dissolution time
Prototype #1	5:18	9:13
Prototype #2	6:03	7:42
Prototype #3	5:26	8:11
Averages	**5:35**	**8:22**

Table 4: Partial and total dissolution times of three 6 mm diameter prototypes with gelatin casings made using the dip molding method

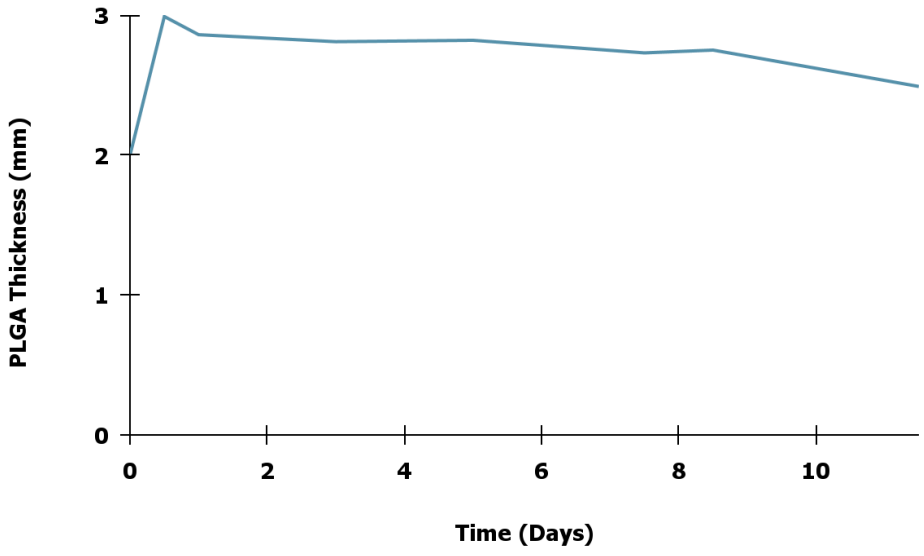
	Partial Dissolution Time	Complete Dissolution time
Prototype #1	7:04	9:45
Prototype #2	7:12	8:42
Prototype #3	6:13	8:11
Averages	**6:50**	**8:53**

On average 6 mm diameter prototypes with gelatin casings made from pill capsules reached partial dissolution after 5 minutes and 35 seconds.

7.2 Prototype Procedure Results

In the first procedure which used a prototype which had a casing made out of pill capsules the casing dissolved before the lab assistant was able to navigate the prototype to the desired location which was just under 5 minutes. In the second procedure which used a dip molded, continuous, gelatin casing the lab assistant was able to move the prototype to the Pyloric canal, dissolve the casing using the endoscope water jet and effectively "deploy the sponge.

7.3 Hybrid Sponge Longevity Results



The PLGA significantly increased in thickness in the first 12 hours and decreased slowly over time.

7.4 Vacuum Results

Table 5: Times for various sponge samples to collect 100mL of water when attached to a vacuum tube.

Sponge Sample	Time to Collect 100mL of Water [s]
Synthetic Rubber	3.2
45 PPI Open Cell Polyurethane	6.7
60 PPI Closed Cell Polyurethane	6.9
PLGA Hybrid Sponge	8.2
Polyvinyl Acetate	11.7
Surgifoam Hybrid Sponge	48.1

8. Discussion

8.1 Gelatin Capsule Dissolvability Discussion

Dip molded gelatin casings proved to take longer to dissolve in the stomach's acid environment than casings made from gelatin capsules. This is likely explained by a slightly thicker layer created by the dip molding process. This test indicates that time to dissolution can be modulated by increasing the gelatin thickness i.e. by dipping the mold in a gelatin solution more times.

8.2 Prototype Procedure Discussion

This test showed that initial procedure time estimates were far too optimistic. Although it is promising that the dip molded casings took longer to dissolve than the pill capsule casings, their thickness will have to be increased in future iterations such that they provide more time for the clinician to perform the procedure.

8.3 Hybrid Sponge Longevity Discussion

The thickness of the PLGA sponge increased in the first 12 hours, which was initially unexpected. This can be explained however by the sponge absorbing the lemon juice which would cause it to expand. The PLGA did decrease in thickness over time afterwards as expected. However, the dissolution rate is very slow. On the positive end, the PLGA shows that it will last longer than a week, which means that the limiting factor of the sponge is the tissue ingrowth into the polyurethane core and not the PLGA dissolving too quickly. By extrapolating the results, the PLGA sponge is expected to fully dissolve after about 22 weeks. While this is acceptable, it would be preferable for the PLGA layer to dissolve faster. One potential solution to this is to

decrease the thickness of the PLGA layer, but this should be done with caution so that new tissue does not grow through the PLGA sponge layer too quickly. New tissue should take at least 3 days to grow through the PLGA layer.

While this test sufficiently simulates the acidity of the gastrointestinal tract, it does not simulate the temperature. PLGA does dissolve more easily at higher temperatures. As such, this test should be reconducted at a temperature of about 40 degrees Celsius in order to replicate the internal body temperature of humans.

8.4 Vacuum Discussion

The vacuum tests showed that the open cell 45 PPI polyurethane sponge and closed cell (60-70 PPI) Mcmaster Carr polyurethane sponges had comparable times to suction 250 mL of water. This motivated the team to choose the open cell sponge for the prototype as it had similar performance while being more compressible and still a high enough PPI that it can filter out infectious material. Similarly these tests showed that the PLGA absorbable layer could be a promising solution to mitigating tissue ingrowth as it had a much shorter suction time than the hybrid sponge with a perforated surgifoam outer layer.

9. Conclusion and Next Steps

Our rigorous and ambitious overhaul and optimization of EVT has resulted in valuable contributions to the medical field. The design and test iterations reinforce this contribution and provide a pathway to bring the lifesaving procedure to the U.S. to treat people afflicted with GI tract perforations. Though prior solutions are available elsewhere and manufactured on a wide scale, we still improved upon this design with thorough documentation to prepare for preclinical trials.

The design was thoughtful and good, which is evident from our final design attributes and the data which reinforces these. This includes the gelatin dissolvability being suitable for estimated procedure time, the hybrid sponge longevity increasing operational time, and the changes to procedure eliminating critical patient and clinician time.

The test program to reinforce these conclusions was thorough, probing, and objective. Our conclusion on sufficient dissolution time stems from our extensive data on the dissolution of our gelatin capsules within a pig stomach, reaching accurate figures for dissolution during placement of the device. Our conclusion of increased operational time is backed up by our data on PLGA scaffold dissolution time via hydrolysis in a simulated acidic environment. This test data suggests dissolution via hydrolysis is not a limiting factor, meaning in vivo would be the only avenue left to come to a concise figure for operational time, despite knowing that it would last longer due to the nature of the physical barrier to tissue ingrowth. Our conclusion that our procedure saves time is reinforced by our test data on procedure time, having a procedure time of about 8 minutes from insertion, compared to the total procedure time of EsoSponge which ranges from 60 to 90 minutes.

Given our advancements in this field of EVT, now not only is there a pathway towards FDA approval for the first approved EVT device for the U.S., but there is now a pathway for improvement upon the prior art. This pushes the envelope on EVT research and development in the U.S., with the possibility of saving lives in the future.

There are many next steps for this project that the team has in mind. First we plan on finishing up our design iteration of our PLGA sponge synthesis to ensure we get the best version of this hybrid prototype. We also plan to improve upon the PEG coating procedure and PEG sponge testing procedure. Once both of these hybrid prototypes are at their best we will conduct a trade study to see which approach is the most effective in terms of tissue ingrowth mitigation or stalling. Once we have a clear idea of the best approach to improve operational time we will freeze the design and set forth on our mission for FDA approval, starting with preclinical trials.

9. Acknowledgements

The EVT24 team would like to thank the following contributors from JHMI: Dr. Venkata Akshintala, Dr. Mouen Khashab, Surya Evani; from ME Senior Design: Dr. Stephen Belkoff, Rich Bauernschub, Daren Ayres, Alan Yu; and additionally: Dr. Claire Hur, Dr. Xiomara Calderón-Colón, Dr. Leonard Bielory, Harrison Khoo, David Benavides, Chrysoula Katrilaka, Dr. Amalia Aggeli, Niki Karipidou.

10. Reflection

Due to the challenges of working on a project outside of the team's expertise, there were many things that the team learned. One of the things we learned was how to look for relevant research papers. Related to this is how to reach out to and prepare for meetings with experts in order to gain meaningful information to assist our project. Furthermore, we learned interdisciplinary team communication due to needing to communicate with people in different fields.

The team also learned a lot about the medical world. We learned how to use an endoscope and what endoscopy procedures were like. We also learned about many of the unique requirements and challenges of making devices inside the human body such as biocompatibility and tissue ingrowth. Additionally, we learned how to suture in order to create models for testing. Another critical part of the medical world we learned about was on the difficulties of navigating through the FDA approval process.

As a part of our project, the team also learned about sponges. We learned about the different types of sponges and how sponges are differentiated by pore size. Additionally, we learned how to make sponges of our own.

Finally, the team also gained a lot of experience in engineering skills. We learned how to create professional engineering drawings that were up to par for real world manufacturing. We also learned how to manufacture by dip molding. Additionally, we learned about using safety data sheets and developing procedures.

There are also some things that we would have done differently. First we would have reached out to the authors of relevant papers early on. We only started doing this in the spring and it led to connections with experts in the field which accelerated our progress and reinforced our background knowledge.

We also would have acquired approval to perform tests with biological matter on campus. This includes ensuring that our room is equipped to handle these experiments, including a sink. This would have helped with our testing timeline and iteration. Instead of commuting to test, we would have been able to conduct tests more times if the testing apparatus was hosted nearby.

One last thing we would have done differently is to reach out to our sponsors about preexisting testing apparatuses and models. We initially developed our own model of the GI tract using store bought materials, but after being informed of the ease of access to pig stomachs for testing we transitioned exclusively to that model. If we had asked earlier, we would have had better and more accurate test data sooner.

11. References

[1] de Moura DTH, de Moura BFBH, Manfredi MA, Hathorn KE, Bazarbashi AN, Ribeiro IB, de Moura EGH, Thompson CC. Role of endoscopic vacuum therapy in the management of gastrointestinal transmural defects. World J Gastrointest Endosc. 2019 May 16;11(5):329-344. doi: 10.4253/wjge.v11.i5.329. PMID: 31205594; PMCID: PMC6556487.

[2] https://www.bbraun.com/en/products-and-solutions/therapies/sutures-and-surgical-specialties/endoluminal-vacuum-therapy.html

[3] https://www.niddk.nih.gov/about-niddk/research-areas/obesity/longitudinal-assessment-bariatric-surgery

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10302432/pdf/materials-16-04425.pdf

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[6] https://www.researchgate.net/publication/347065912_EndoPil_A_Magnetically_Actuated_Swallowable_Capsule_for_Weight_Management_Development_and_Trials

[7] https://www.sciencedirect.com/science/article/abs/pii/S0927775720300182

[8] https://www.academia.edu/40131625/Preparation_of_polyethyleneglycol_PEG_coatings_for_microencapsulation_of_charcoal

[9] https://onlinelibrary.wiley.com/doi/10.1002/1097-4636(20000905)51:3%3C343::AID-JBM7%3E3.0.CO;2-D

Appendices

Appendix 1. Bill of Materials

Version: PLGA Outer Layer

Description	Source	Count	Unit cost	Subtotal
Unflavored Gelatin 4 pack	Giant	1	$2.99	$2.99
Polyurethane Sponge 45PPI	UFP Technologies (David Benavides)	1	$0	$0
PLGA 75-25 1G	Sigma Aldrich Fine Chemicals Biosciences	1	$133.74	$133.74
Clear Masterkleer Soft PVC Plastic Tubing	McMaster	6 ft	$0.51	$3.06
Dissolvable Suture	Amazon	1	$0.68	$0.68

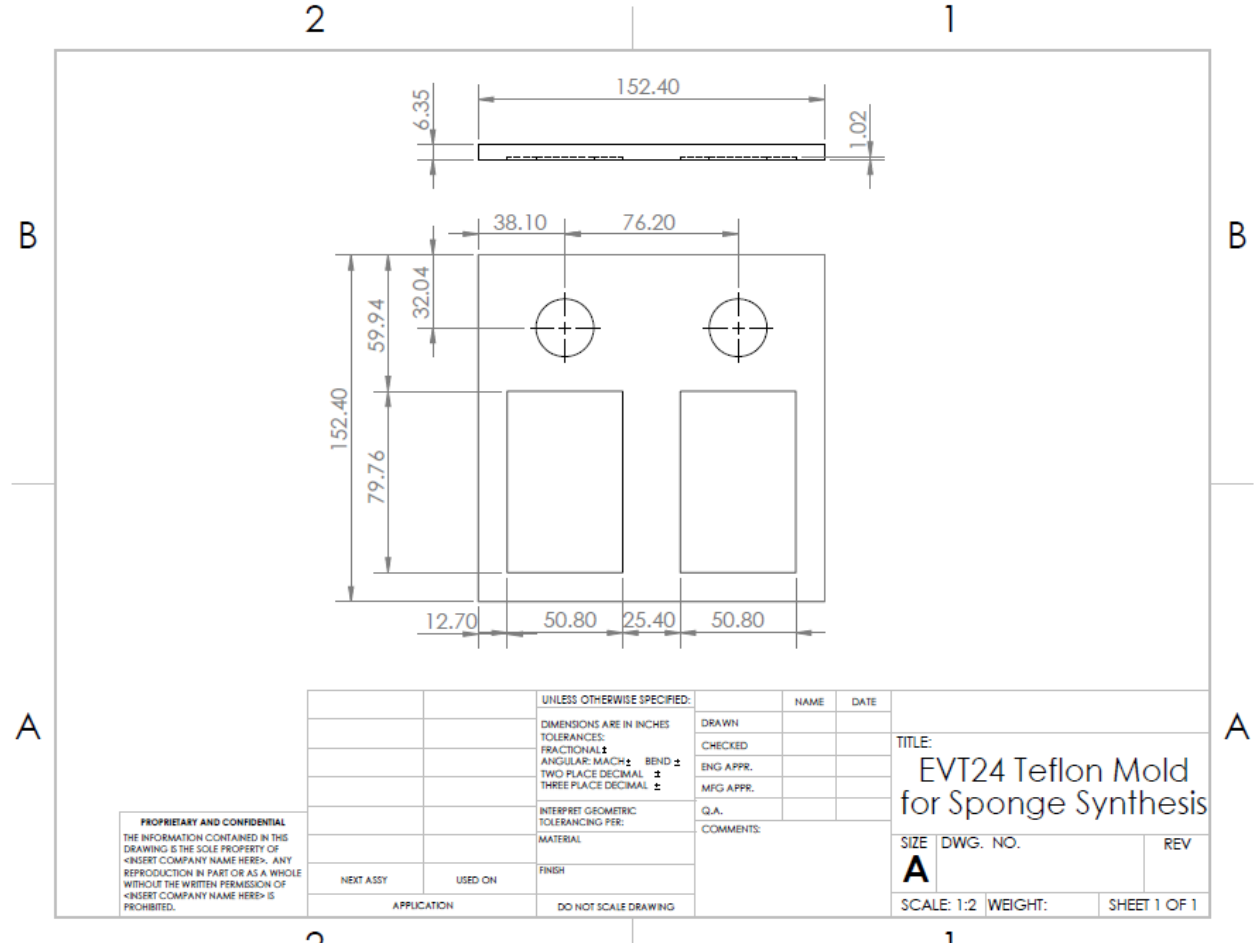
Total per Unit Cost: $140.47

Version: PEG Coating

Description	Source	Count	Unit cost	Subtotal
Unflavored Gelatin 4 pack	Giant	1	$2.99	$2.99
Polyurethane Sponge 45PPI	UFP Technologies (David Benavides)	1	$0	$0
PEG	CVS	15g	$0.10	$1.50
Clear Masterkleer Soft PVC Plastic Tubing	McMaster	6 ft	$0.51	$3.06
Dissolvable Suture	Amazon	1	$0.68	$0.68

Total Per Unit Cost: $8.23

Appendix 2. Manufacturing Drawing



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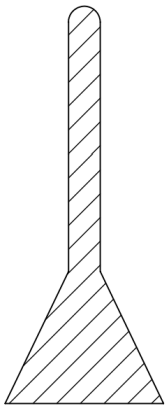
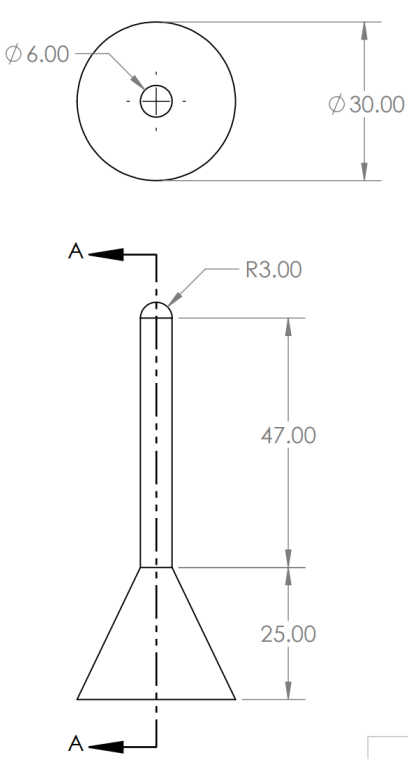
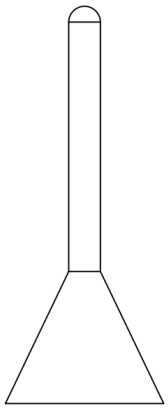
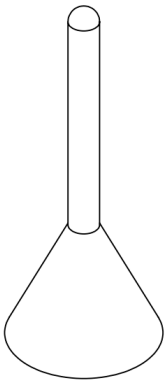


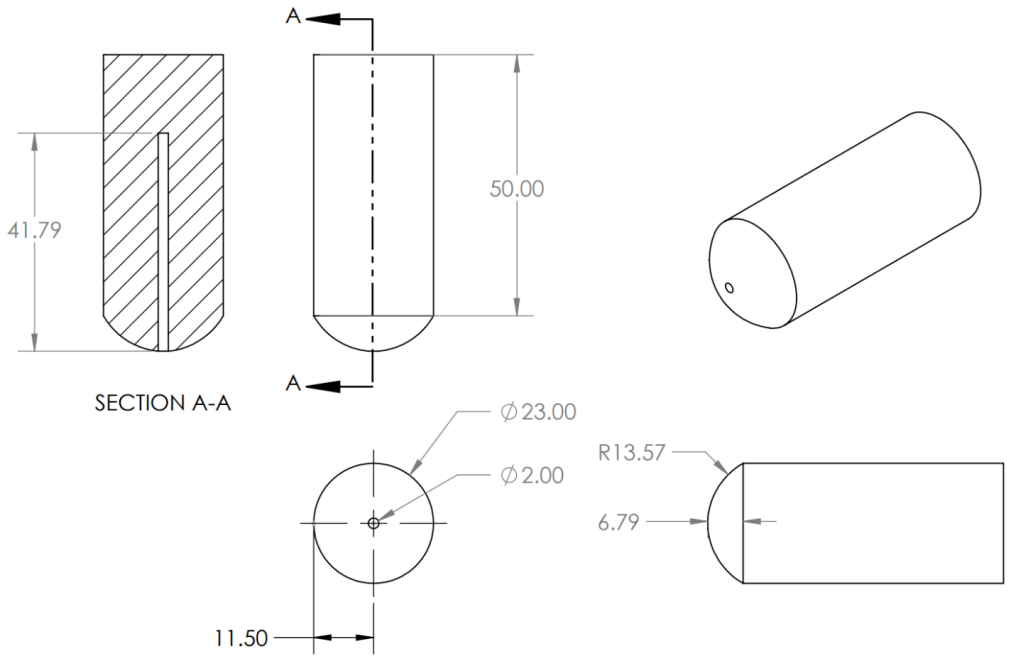
SECTION A-A







DIMENSIONS ARE IN MILLIMETERS TOLERANCES: ±1MM	TITLE: EVT24 Funnel Dip Mold
	MATERIAL ALUMINUM



PROPRIETARY AND CONFIDENTIAL THE INFORMATION CONTAINED IN THIS DRAWING IS THE SOLE PROPERTY OF EVT24. ANY REPRODUCTION IN PART OR AS A WHOLE WITHOUT THE WRITTEN PERMISSION OF EVT24 IS PROHIBITED.	UNLESS OTHERWISE SPECIFIED: DIMENSIONS ARE IN MILLIMETERS MATERIAL Polyurethane Foam	COMMENTS:	TITLE: EVT24 Sponge For UFP DWG. NO. 1 REV 1 SHEET 1 OF 1

Appendix 3. Finances

Project budget	$5,000.00		Committed	$2,931.96
Date	Description	Count	Unit cost	Subtotal
20230922	Super-Cushioning Polyurethane Foam Bar	1	$3.40	$3.40
20230922	1000 Sheets Candy and Chocolate Making Edible Rice Paper	1	$9.89	$9.89
20230922	100Pcs PVA Water Soluble Bag	1	$11.96	$11.96
20230922	Blate Papes Edible Film Squares, 200 Count	1	$19.99	$19.99
20230922	Shurhold 210 PVA Sponge	1	$17.13	$17.13
20230922	Primo Dental Products SECLBL Saliva Ejectors, Clear with Blue Tip (Pack of 100)	1	$6.64	$6.64
20231005	Mehron Sponge Stipple Carded	1	$6.95	$6.95
20231005	Empty Gelatin Capsules Size 000-120 Count	1	$9.99	$9.99
20231005	Size 000 Empty Capsules - Clear Vegan HPMC - 120 Count Jar	1	$11.99	$11.99
20231005	PH Meter	1	$11.99	$11.99
20231005	Karter Scientific, 3.3 Boro, Griffin Low Form, Glass Beaker Set	1	$16.99	$16.99
20231005	Acrylic Box Tray for 1" 25.4mm Element Cubes	1	$5.95	$5.95
20231005	FXTUL Manometer, Digital Differential Manometer	1	$45.87	$45.87
20231005	Slendor Magnetic Stirrer Hot Plate	1	$59.99	$59.99
20231005	Portable Veterinary Suction Machine 110V	1	$169.00	$169.00
20231005	KASHSURG Goodwill Hemosponges	1	$19.99	$19.99
20231019	Clear Plastic Tubing	1	$24.00	$24.00
20231023	Polyurethane Foam Bar	2	$3.40	$6.80
20231030	SURGIFOAM product code 1973	2	$140.53	$281.06
20231102	XPRS Nutra Size 2 (100 Count)	1	$7.89	$7.89
20231102	XPRS Nutra Size 3 (100 Count)	1	$7.89	$7.89
20231102	Mammography Skin Marker	1	$39.95	$39.95
20231105	Endoscope Camera	1	$27.99	$27.99
20231105	5 feet of 1 inch Inner Diameter Silicone tubing	1	$12.99	$12.99
20231105	5 feet of 5/8 inch Inner Diameter Silicone tubing	1	$12.99	$12.99
20231105	Assorted Medical Suture	1	$18.99	$18.99
20231109	Human Anatomical Nasal Cavity Throat Anatomy Medical Model	1	$42.99	$42.99
20231111	Clear Masterkleer Soft PVC Plastic Tubing	1	$15.50	$15.50
20231111	Assorted Medical Suture	1	$18.99	$18.99
20240213	NasoPore Fragmentable Nasal Dressing	1	$22.00	$22.00
20240214	Sodium Chloride (Salt), High Purity Crystals, 500 Grams (1.1	1	$18.95	$18.95

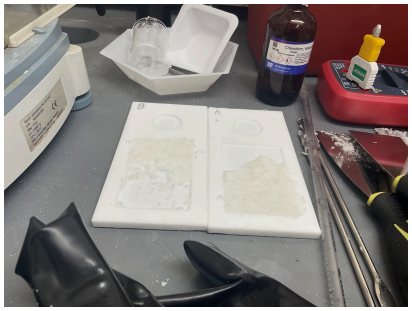
	lb.)			
20240214	3 Pcs 304 Stainless Lab Sieves	1	$22.99	$22.99
20240214	MAXTITE Type II Deionized Water	1	$15.95	$15.95
20240214	Chemical-Resistant Slippery PTFE Disc (6" Long, 2" Diameter)	1	$29.17	$29.17
20240220	BACOENG 1.5 Gallon 3.6 CFM Tempered Glass Lid Vacuum Degassing Chamer and Pump Kit	1	$159.99	$159.99
20240221	Oversized Chemical-Resistant Slippery PTFE Sheet 6”x6”x1/4”	1	$34.76	$34.76
20240222	Sigma Aldrich Fine Chemicals Biosciences POLY(D,L-LACTIDE-CO-GLYCO 1G	3	$133.74	$401.22
20240222	Chloroform Molecular Biology MP Biomedicals	1	$126.00	$126.00
20240223	Pack of 4 Lab Micro Double Ended Spatula Square/Round End (Flat Ends 50mm x 9mm), 9" Length, Stainless Steel	1	$14.99	$14.99
20240223	Lab Scale 2000g/0.01g High Precision Digital Scale Analytical Balance Electronic Scale for Kitchen Lab Weighing	1	$69.99	$69.99
20240223	5 Pack Putty Knife Scraper, 1" 2" 3" 4" 5" Putty Knife Set, Stainless Steel Putty Knife Scraper, Wallpaper Scraper Paint Scraper Tool for Spreading Drywall Spackle & Mud, Taping, Scraping Paint	1	$7.99	$7.99
20240223	Pure Ponta Weigh Boats Small - 125 Pack 7ml Plastic Disposable Trays for Scale, Square Weighing Dishes for Powder Weight, Crafts, Food Samples - Mini Pour Boat Tray, Anti-Static Lab Dish Container	1	$12.49	$12.49
20240223	Medical Action Infectious Waste Bag, Red, 3 Gallon, 14.5" x 19", 20/Roll	1	$6.50	$6.50
20240223	Showa Gloves 892-09 Showa Best Viton Glove, Size 9, Black	2	$103.99	$207.98
20240223	Glass-Filled Chemical-Resistant Slippery PTFE Rod 1/4” Diameter	1	$3.81	$3.81
20240312	Sigma Aldrich Fine Chemicals Biosciences POLY(D,L-LACTIDE-CO-GLYCO 1G	2	$133.74	$267.48
20240403	Sigma Aldrich Fine Chemicals Biosciences POLY(D,L-LACTIDE-CO-GLYCO 1G	4	$133.74	$534.96
20240403	DIYChemicals Polyethylene Glycol PEG 400 for Industrial Manufacturing, Fog Machines, DIY Beauty Products, Antifreeze, Solvent, Humectant – Non-Toxic, Odorless, Bulk - 8 fl oz	1	28.99	$28.99

Appendix 4. "How to"

Poly Lactic-co-Glycolic Acid (PLGA) Sponge Synthesis

1. Put on SHOWA 892 gloves and turn on the active fume extraction of the chemical fume hood. Ensure safety goggles are also worn.
2. Sieve NaCl through a 0.074 mm mesh into a plastic boat. Sieve the remaining NaCl within the sieve through a 0.18 mm mesh into a separate plastic boat. The particulates that fall through the 0.18 mm mesh shall be used and should have diameters between 0.074 mm and 0.18 mm.
3. Place magnetic stir bar inside of 50 mL beaker. Pour out 5 mL of chloroform in the 50 mL beaker under the fume hood.
4. Measure out 1g of PLGA and 9g of NaCl in separate plastic boats atop a scale.

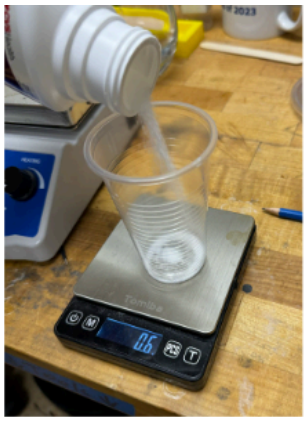
5. Still in the fume hood, add PLGA (1g) into the beaker of chloroform (5mL) heated to 40 degrees Celsius. Add sieved NaCl particulates (9g) and mix using a metal spatula until the PLGA pellets are dissolved and the mixture is homogenized.
6. Fill the Teflon mold with the polymer solution/NaCl mixture by pressing mixture into the space with a metal spatula and leveling the mixture with a putty knife. Record the mass of the filled mold atop the scale.



7. Air dry the filled Teflon mold under the fume hood for 24 hours. Also leave all equipment within the fume hood to dry.
8. Place filled mold in an vacuum chamber with a pressure of -29.92 inHg to vacuum dry in fume hood for another 72 hours to allow chloroform to evaporate completely. Again, leave all equipment within the fume hood.

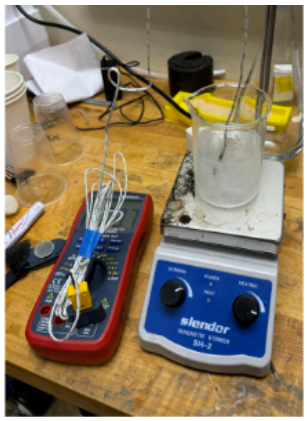
9. To ensure that the chloroform has completely evaporated, continue drying in the vacuum chamber in the fume hood, measuring the mass of the filled Teflon mold every hour until the mass stabilizes over three separate measurements and does not change anymore.
10. After mass stabilization and drying, loosen the molded PLGA/NaCl sheet using the metal spatula and rest atop the Teflon mold. All other equipment may also be removed from the fume hood.
11. Immerse the molded PLGA/NaCl mixture in a beaker of 500 mL of deionized water at room temperature to leach out the NaCl particulates, changing the water every hour.
12. Continue replacing the water for 4 hours.
13. Remove the scaffold from the DI Water and air dry the PLGA scaffold for 24 hours at room temperature, flipping it over after 12 hours atop the Teflon mold.
14. After use, if the final product is to be disposed, place it within a red biohazard bag and throw into the garbage.

Polyethylene Glycol Coating Method



Measure PEG

Measure Water



Mix at 40C for 20 minutes

Submerge Sponge for 12 hours

The ratio of PEG to deionized water is 15% by mass.

Gelatin Dip Molding

Mix Gelatin Solution

Dip Mold Into Solution

Allow Casing to Cure

Remove Casing From Mold

To make the gelatin solution, start by preheating an oven to 80 degrees Celsius. Measure out gelatin powder and water in a 1:5 ratio without mixing. Pour the water in a pot and bring it to a boil. Reduce to medium heat and slowly pour in the gelatin powder while stirring. After the gelatin is fully dissolved, stir the solution over medium heat for an additional 5 minutes. Place the pot in the oven for 15 minutes. Remove the pot from the oven and pour the gelatin solution into a beaker.

To prepare the molds, spray a mold release coating on the mold and let rest for 5 minutes before spraying a second coating.

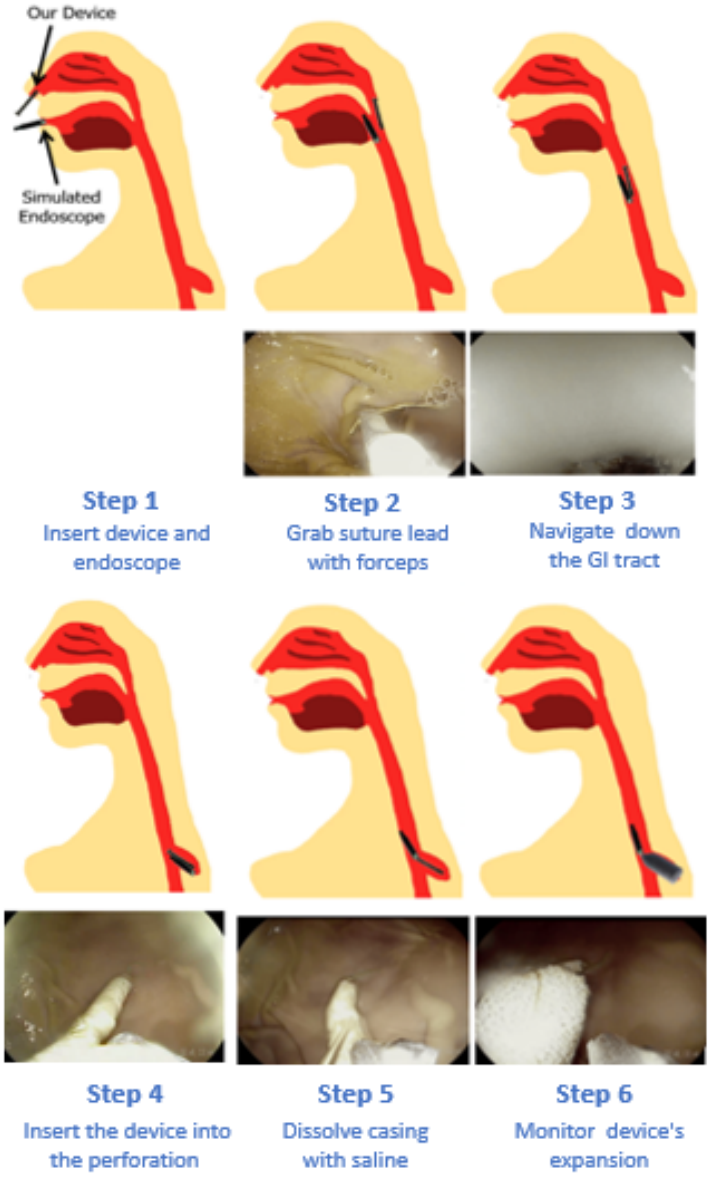
To create the gelatin casing, dip the mold into the gelatin solution 3 times in 2 minute intervals and allow to cure for 6 hours.

Appendix 5. Storage Boxes
Appendix 6. Design History File

Directory name	Contents
CAD	SolidWorks™ part files and assemblies for molds and product
Reports	All project reports & meeting minutes
Pictures	Photographs and video

Appendix 7. User Manual

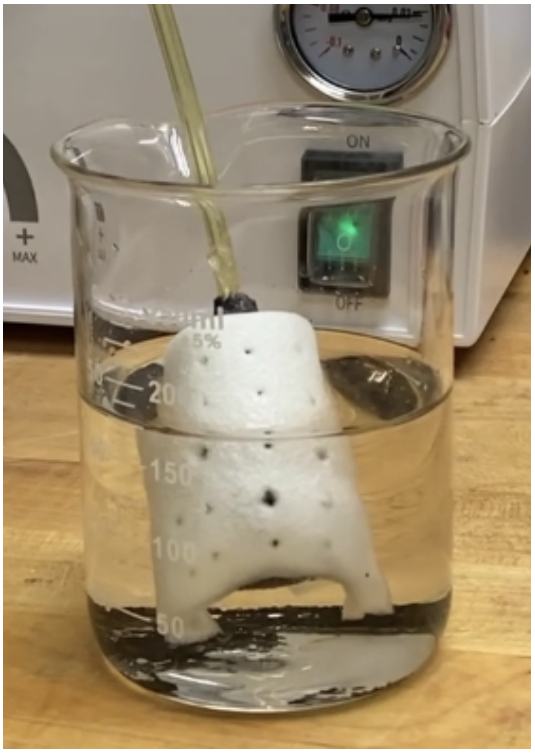
Users of this device should be trained and certified in the use of an endoscope. Standard safety and certification requirements for surgical procedures also apply.



Appendix 8. Prototypes and Side Branches

Bioabsorbable Film

Collagen Sponge



Fall Prototype