Development and Analysis of a Minimally Invasive Post-Infarction Epicardial Patch Delivery Device

by

Jonathan Tagoe

Submitted to the

Department of Mechanical Engineering

in Partial Fulfillment of the Requirements for the Degree of

Bachelor of Science in Mechanical Engineering

at the

Massachusetts Institute of Technology

June 2021

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ABSTRACT

After a myocardial infarct (heart attack), the heart develops scar tissue that can impede normal function and eventually result in heart failure. There are a number of methods currently employed in the field to slow this degeneration, but none focus on explicitly returning the heart to pre-heart attack levels of function. The Roche lab has developed an epicardial patch that can mechanically reinforce the heart back to prevent it from progressing into heart failure after a heart attack , but current implantation methods are too invasive. In this study, researchers designed and developed a delivery tool that would adhere the hydrogel and composite based epicardial patches on infarcted hearts in a minimally invasive operation. The device is a collapsible and inflatable sleeve prototyped using thermoplastic polymer films and casted silicone rubber components, designed for minimally invasive subxiphoid surgery. It utilizes vacuum for stabilization during application.

By characterizing the material properties with a universe mechanical tester, it was also found that the tool can reliably supply the necessary pressure to properly adhere the hydrogel patches. Through a series of ex vivo and in situ porcine experiments, it was found that the sleeve is effective at effectively positioning and adhering the patches to the epicardium. Such a tool would be helpful in applying therapeutics like the patch, presenting a low-cost, accessible solution for interventionalists. This delivery tool is still in development, as it is on its fourth iteration and in the future, would require extensive preclinical studies before moving into human trials..

Thesis Supervisor: Ellen Roche
Tile: Associate Professor

ACKNOWLEDGEMENTS

I would like to take Dr. Ellen Roche, Claudia Varela, and the Therapeutic Technology Design & Development Lab for providing invaluable guidance, support and advice throughout my year working on this device. I know for sure this project would not have progressed this far without your help!

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1. INTRODUCTION

After a myocardial infarction, a dense collagenous scar replaces ischemic tissue on the heart. This reduces cardiac function until the heart eventually deteriorates to failure which can only be resolved with a full heart transplant. Medical practitioners currently employ methods like medications such as beta blockers, lifestyle changes, and if severe enough, left ventricular assist device implantation. However, these methods do not seek to recover heart function to pre-infarction levels **early** after infarct to prevent adverse remodeling completely. A proposed solution that addresses this seemingly overlooked area comes in the form of patches that adhere to the outer surface of the heart, mechanically reinforcing the infarct region. However, the invasive nature of the implantation procedure has limited the patches' clinical translation since they would require open heart surgery.

The Roche group has developed an adhesive epicardial patch designed to mechanically reinforce an infarcted heart to achieve functional recovery. To apply this patch while circumventing the risks and efforts typically associated with open heart surgery, a minimally invasive delivery tool is necessary. According to the Mayo Clinic, minimally invasive heart surgery involves small incisions to reach the heart between the ribs, rather than cutting through the breastbone [1]. This significantly reduces surgical time, necessary risk to the patient and recovery time, potentially enabling more heart attack survivors to receive a patch implant.

The tool developed in this thesis consists of an air bladder made up of highly accessible, medical grade plastics (thermoplastic polyethylene and polyurethane) heat pressed together. Once folded, this creates a conical sleeve capable of wrapping around the heart and quickly inflating, providing enough compressive force to effectively adhere the patch to the epicardium. It is flexible enough to fold into a 25-millimeter diameter catheter and enters through a

subxiphoid incision, minimizing the incision size. To validate this approach, tool prototypes have undergone *ex vivo* and *in situ* testing with porcine hearts.

2. BACKGROUND

2.1 Epicardial Patches as Post Infarction Therapy

While current clinical methods typically restore blood flow to reduce the degree of tissue damage, there is not much focus on mechanically reducing the impact of scar tissue on heart remodeling. There have been attempts to use different types of epicardial patches to mechanically reinforce the heart to recover cardiac function. Fabric, extracellular matrix, and hydrogel patches have had varying levels of success but face barriers when it comes to clinical translation and further optimization through *in vivo* testing.

Firstly, most patches are attached to the epicardium through traumatic methods like sutures that can further damage heart tissue, limit the mechanical enhancement of the patch, and require an open-heart surgery for implantation. The Roche group has developed an epicardial patch that couples to the heart with an adhesive hydrogel, removing the need for sutures or other traumatic methods facilitating the conception of minimally invasive patch deployment strategies that clinically, may expand the patient population able to receive patch treatment and in preclinical animal models, can allow for researchers to study the optimal time of patch implantation after infarct generation without the need of an invasive surgery. This thesis aims to develop a tool that allows for patch deployment to the epicardium of a swine model of myocardial infarction.

2.2 Tools for minimally invasive implant delivery to the epicardium

A few minimally invasive surgery tools that deploy implants and therapeutics to the epicardium are in development. For instance, miniature robots from Carnegie Mellon, like the

HeartLander tool [2] and planar parallel wire robot [3] in Figure 1, respectively, attach to the surface of the heart with suction and can be remotely guided to apply therapies or execute injections. Such tools are small enough to enter through subxiphoid incisions, keeping the damage associated with accessing the heart at a minimum.

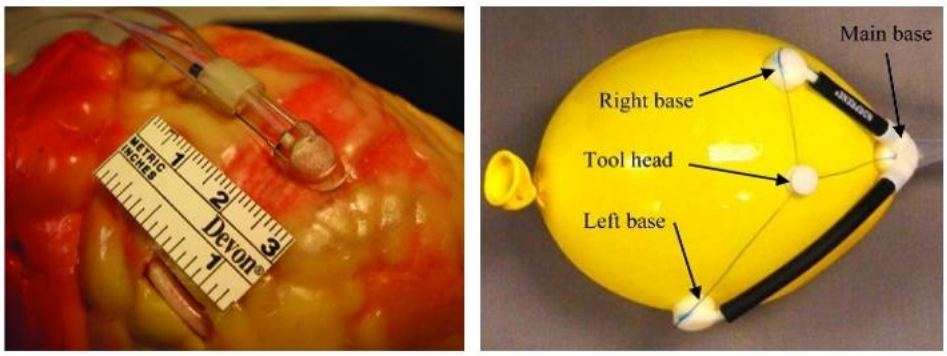


Figure 1*:*Left. *HeartLander tool in development at Carnegie Mellon university [2],* ***Right.*** *parallel wire robot for epicardial operations in development at Carnegie Mellon [3]*

Another existing tool was developed by Corinnova to deploy their minimally invasive cardiac assist device. As seen in Figure 2, the device is a thin bladder made of polymer and nitinol wire that is deployed from a tube that reaches the apex and surrounds the heart. By inflating and applying pressure at the same rhythm as the heart, the Corinnova device provides short term assistance for heart failure patients after hospitalization. Although the intent of the device is different from what we are proposing, in that an active cardiac assist device is deployed, this is still an effective form of minimally invasive tool.

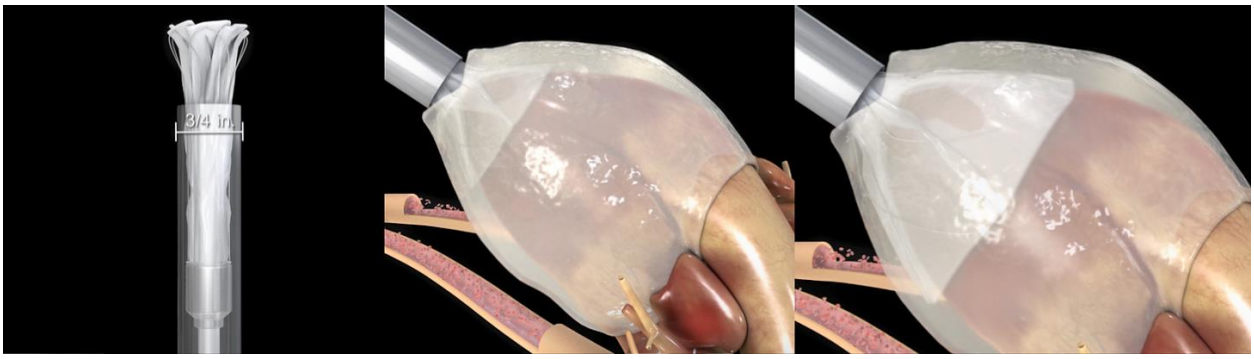


Figure 2: Virtual graphic of Corinnova heart assistance device deployment [4]

2.3. Requirements for an Epicardial Patch Delivery Tool

After identifying and analyzing the problems with epicardial patch implantation, the key requirements of the delivery tool were designated as follows:

1. Minimally invasive access and retrieval to intrapericardial space.
2. Stabilization of beating heart during operation
3. Rapid and reliable patch deployment and adhesion.
4. Be easy to manufacture and use, for both prototypes and final product.

The key requirement of the delivery tool is to enter the body through a subxiphoid incision of no more than 25 millimeters, keeping the operation minimally invasive to reduce damage to the patient's body. It will then access the heart itself through an incision in the pericardial sac and exit the body through the same incisions. The second requirement is to secure itself around the heart to ensure proper stabilization and minimize heart movement relative to the device, so the surgeon can accurately position the patch on the scarred region of the epicardium. The next requirement is to attach the patch quickly and reliably onto the epicardium, meaning the device should be able to supply enough pressure so the hydrogel adhesive on the patch can securely bond to the tissue. The final requirement is ease of access to materials and manufacturing methods, so the delivery tool can remain inexpensive for more surgeons to use on patients in of need surgery.

3. DELIVERY TOOL DEVELOPMENT

3.1 Vision

After researching current devices for epicardial implant delivery used in the field and brainstorming potential solutions, the key requirements were further divided into features that the optimal tool should include and weighted appropriately. The brainstormed ideas include: air pressure based sleeves (inflation and deflation); “RoboStamp”, a miniature robot that stamps the patch into place; “HeartRoller”, a tool that rolls the patch onto the surface like a paint roller; and Octo, a soft robotic, multi-armed device that functions like octopus tentacles. These were then compared based on which criteria they satisfied the most, and it was decided that a double layered, inflation based air bladder delivery tool satisfied the most design criteria effectively as seen in Table 1.

Soft components like polymer films were easy to access in lab and very flexible to prototype with, while also minimizing damage to tissue when in use. Applying pressure by inflation seemed to be the simplest, safest, and most convenient method of getting an epicardial patch to adhere to the heart, since hospitals already have access to air.

The Corinnova device mentioned previously also provided a foundation for a bladder-centric design and was simple enough to make the appropriate adjustments for this device’s purposes. The Corinnova device’s deployment procedure especially suited the envisioned method for the new delivery device, with a 25 mm subxiphoid incision to keep the operation minimally invasive and catheter-based retraction. In Figure 3, the envisioned deployment process is further detailed.

***Table 1**: Key criteria weighting sheet for brainstorming ideas*

Design Requirement	Priority Weight (1-3)	Vacuum Forming Sleeve	Inflation Pressure Sleeve	RoboStamp	Octo	Roller	HeartLander (Carnegie Mellon)
Access pericardial space	1	Separate tool is required					
Entry incision size (25mm)	2	Achievable but depends on tool size when collapsed		Achievable , Pre-assembled structure must be small	Achievable but depends on tool size when collapsed	Achievable, pre-assembled structure must be small	Achievable, Pre-assembled structure already small
Minimal heart movement during procedure/heart stabilization	1	1. apex stabilization can be achieved with suction cup 2. base stabilization with larger ring		Achievable, suction cups on surface of heart Separate tool for stabilization			
Manufacturability/ Assembly	2	Easy to access materials, chemically/thermally bond polymer films		Need to fabricate or buy parts, mechanically fasten together	Easy to access, Cast silicone rubber	Need to fabricate or buy parts, mechanically fasten together	wire system
Maneuverability	3	Medium, able to rotate while not deflated/inflated		Low, need precise position before placing on epicardium	Medium able to rotate while not inflated	Low, need precise position before placing on epicardium	High, remote control locomotion
Fast/on-demand patch deployment	3	Difficult, would require multiple steps to deflate sleeve and squeeze patch on to heart	Achievable, inflate sac and compress onto heart	Achievable, simple motion to apply patch	Complex, requires multiple degrees of motion to apply		Unsure of exact application for patch
Compatible with video assisted delivery	3	Yes, separate incision for endoscopic camera					

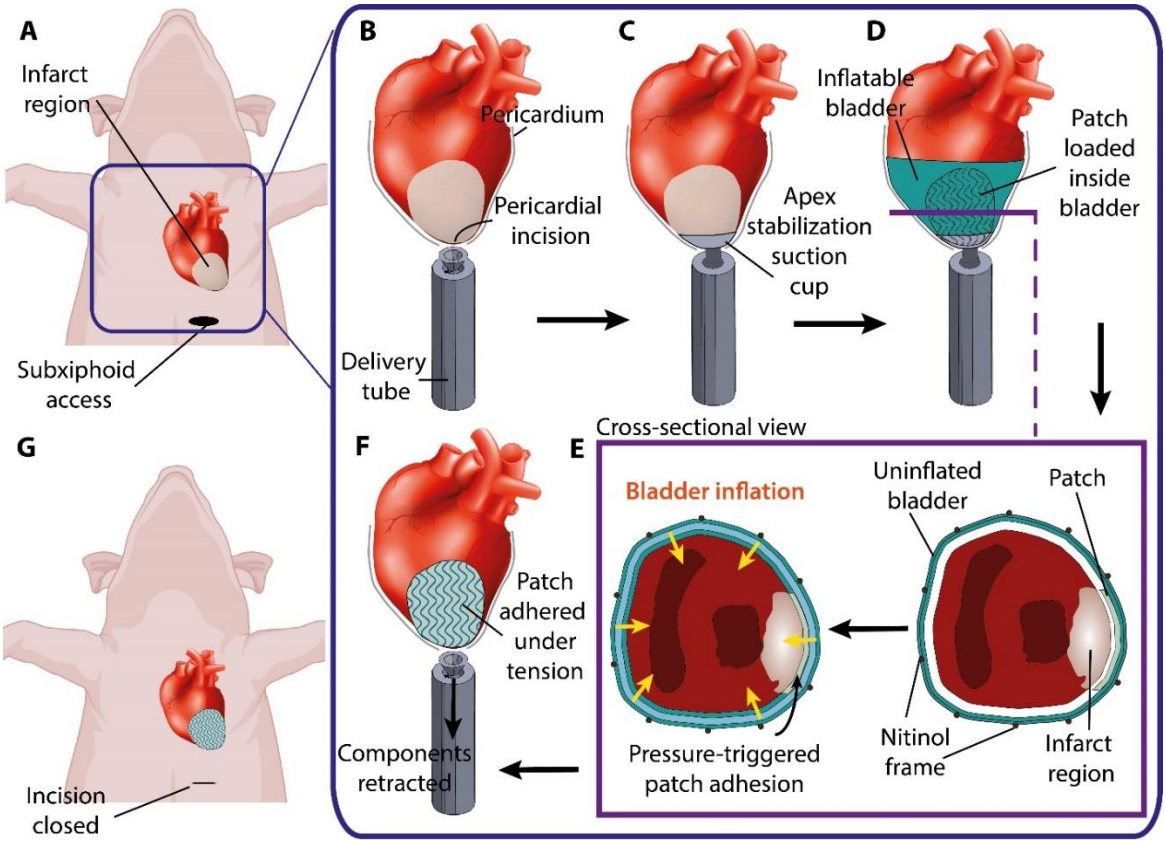


Figure 3: *Operation diagram for proposed inflation based delivery tool (courtesy of Roche Lab)* ***(A)*** *thoracoscopic camera and the delivery tool will be introduced to the thoracic cavity through a subxiphoid incision.* ***(B)*** *The tool will reach the heart at the apex. After performing a pericardial incision,* ***(C)*** *the apex stabilization suction cup will be deployed to anchor the tool to the heart apex.* ***(D)*** *The self-expandable, uninflated bladder will be advanced out of the delivery tube, sliding in between the epicardium and pericardium. The adhesive patch will be loaded in the surface of the inflatable bladder in contact with the heart surface.* ***(E)*** *After ensuring adequate patch positioning, the bladder will be inflated to trigger adhesion of the patch onto the infarct region.* ***(F)*** *The bladder and apex cup will be retracted back into the delivery tube and the components and thoracoscopic camera retrieved from the thoracic cavity.* ***(G)*** *The incision will be closed.*

3.2 Material selection: Sleeve

Prototyping began with determining the best materials to make the sleeve out of, mainly biocompatible polymers such as thermoplastic polyurethane (TPU) or thermoplastic polyether (TPE). The sleeves were designed with preferential inflation in mind. When the bladder inflates, the side with the thinner polymer film bulges out more than the thicker polymer rather than uniformly in a balloon. This ensures that the tool supplies enough pressure to remove any oil on

the adhesive side of the patch, allowing it to bond properly to the tissue, while preventing it from expanding too much and tearing the pericardium.

A wide range of polymer combinations were explored in this initial prototyping period conducted during the COVID-19 pandemic (Table 2) using common household items like clothing irons for manufacturing and 3D printed heart models for sizing. ImageJ, an image processing software, was used to measure the change in enclosed area when the sleeve was inflated to get a sense of how well the preferential inward inflation was working.

***Table 2**: Assessment table for inflatable air bladder prototypes*

Prototype ID	Layer 1 (contacts epicardium)	Layer 2	Layer 3 (contacts pericardium)	# of cavities	Qualitative assessment	Quantitative assessment
Green	2 mil Greem TPE, FibreGlast (Item #H811678)	8 mil TPU, American Polyfilm	11 mil TPU, American Polyfilm	1	- More elastic, better bonding with TPU	50% reduction in projected area
Pink	Durable pink TPE, (McMaster-Carr, 7889T28)	8 mil TPU (no change)	11 mil TPU (no change)	1	Pink TPE became brittle after heating	50% reduction in projected area
Green V2	2 mil Green TPE, FibreGlast (Item #H811678)	8 mil TPU (no change)	11 mil TPU (no change)	3	- Greater surface area contact	55% reduction in projected area

Using strips of Teflon paper, some prototypes included up to 3 individual pockets rather than a single large bladder, like in Figure 4. Upon inflation, these pockets tended to contract inwards, naturally closing the bladder into a triangular shape with 3 pockets. This would make folding the bladder into its conical shape much easier and prevented the bladder from coming undone when inflated.

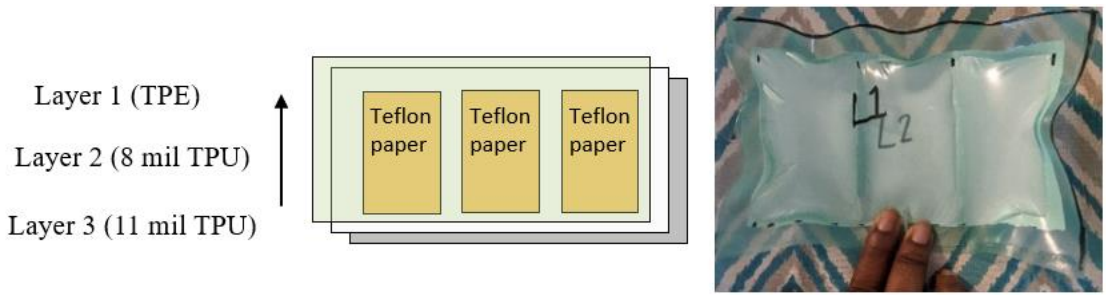


***Figure 4**: Schematic for Green V2 air bladder prototype, with sealed off pockets for better folding*

It was found that a combination of green 1mil TPE, 8mil polyester polyurethane and 11mil polyether polyurethane was the most effective version of the sleeve prototype, as shown I Figure 3.2.3. The green TPE bonded well with the TPU layer when heat pressed, maintaining secure seals for the air pockets even after multiple inflations. It was also thin enough for smooth deployment and retraction into the plastic tube.

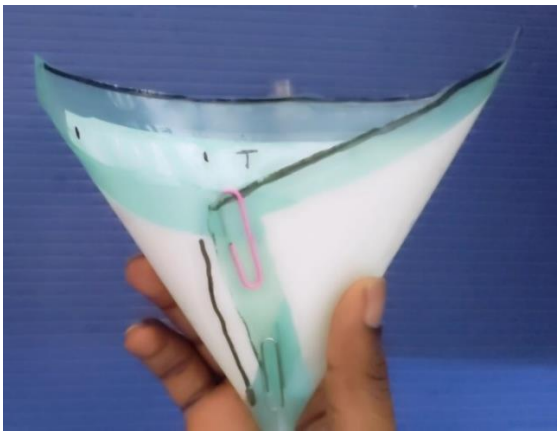


***Figure 5**: Folded Green V2 prototype*

3.2 Refining Sleeve Manufacturing

Upon arriving at the lab in person, prototyping began moving in a different direction due to access to more effective tools like vices, laser cutters and heat presses. More secure sleeves could be manufactured quicker, which resulted in more iterations of the prototype. Other plastic combinations were explored, ranging from a 3-layer variant to switching out the top layer for

different TPE or switching the bottom layer for nylon-backed TPU. A 2-layer version was eventually settled upon, due to its simplicity and similar inflation profile to the 3-layer iteration.

The layer facing outwards (towards the pericardium) is about 11 mil, while the layer contacting the epicardium is about 1 - 2 mil (1 mil = 0.0254 mm), resulting in a sleeve that is at most 11 - 12 mil thick. This ratio of thicknesses and stiffnesses of the polymers ensured preferential inward inflation.

***Figure 6**: **Left**. CAD model of laser printed mold for sleeve heat pressing, **Right.** iteration of laser cut mold made of 0.25" acrylic*

The sleeves are manufactured using laser cut molds designed in Solidworks (Figure 6) and a common heat press (Figure 7, left). The heat and pressure thermally bond the layers of plastic more effectively than a clothing iron, so the air pockets are kept sealed even at higher inflation pressures and large deformations. There is an indicator of temperature and press time on the heat press, enabling accurate adjustment of parameters. It also serves as a cheap rapid manufacturing method. With proper measurements, each sleeve can be custom made for every patient's needs (patch position, sleeve size, pocket shape, etc.). Extra channels were created for even distribution of air within the pockets (Figure 7, right), enabling uniform inflation and compression in all directions (Figure 8). At this point, prototypes were used to validate whether reliable inflation

could be achieved with sleeves manufactured with this method and whether it could provide the required amount of pressure.

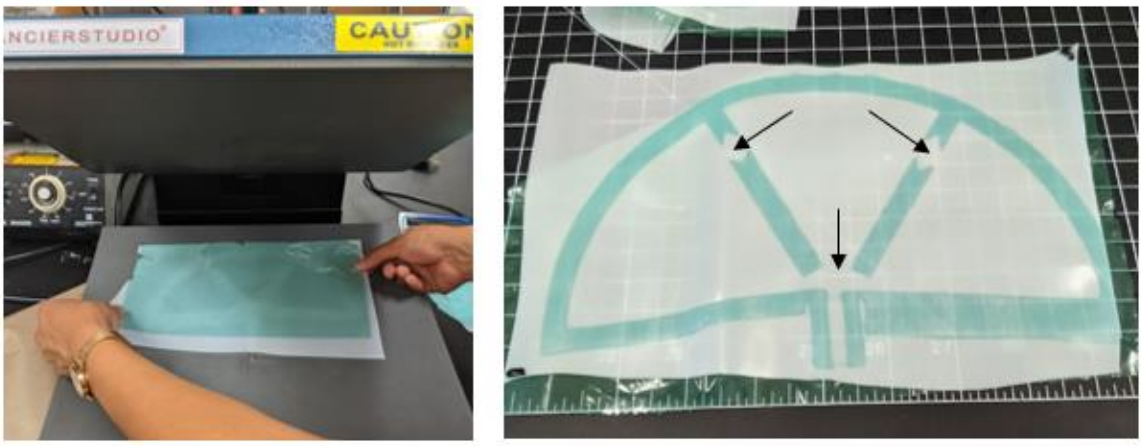


***Figure 7**: **Left**. layers of polymer film being prepped for heat press. Best results came from thinner layer on top, closer to the hot plate **Right**. recently heat pressed sleeve, with channels between sealed regions to allow air pockets to inflate evenly*

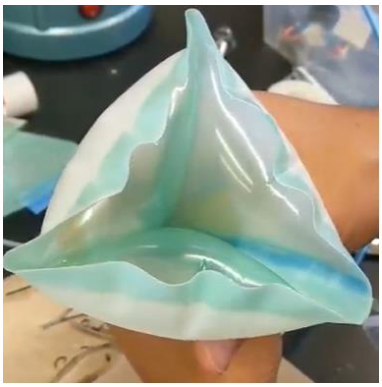


***Figure 8**: cut-out, folded and bonded delivery sleeve, central enclosed space completely occluded by inflated region*

The final protocol for sleeve manufacturing is as follows:

1. Set heat press to 305 degrees Celsius and 1 second press time (for this specific TPE-TPU combination)
2. Place layer of 2 mil TPE, Teflon paper square and strips of 11 mil TPU on surface.
3. Place large sheet of Teflon paper over all and heat press to bond.
4. Remove and place acrylic mold onto surface.

5. Place 11 mil TPU sheet on top of mold
6. Place previously pressed sheet of 2 mil TPE on top of TPU sheet
7. Lay down Teflon paper on top of films and mold, adjust heat press pressure to account for mold and press together.

3.3 Material Selection: Sleeve Frame

The other key component of the delivery tool is the framing, allowing it to take and maintain the desired conical shape to surround the heart in the pericardium. Initially, Nitinol wire was intended to be the framing material, but the wire available at the proved to be too elastic and difficult to attach to the polymer film delivery sleeve without bulky adhesives. The frame concept was initially prototyped in sketch model form using zip ties, tape, and string in lab (Figure 9). The zip ties provided enough structure for the sleeve to retain a conical shape when deployed and were not too difficult to reintroduce to the catheter when retracted. The heads of the zip ties even provided a bit of apex positioning assistance when introducing the device to the model heart. Pushing one of the heads against the apex acted as a guide for the rest of the sleeve to expand outwards radially and properly surround the heart.

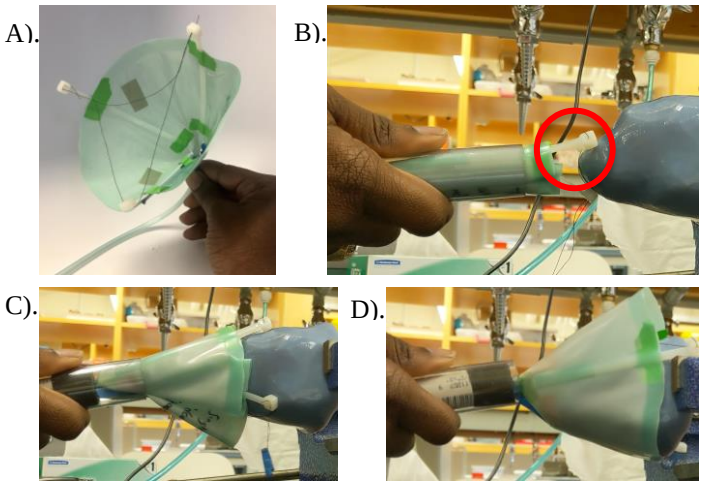


*Figure 9: **(A).** Initial frame prototyping with zip ties, **(B – D).**.deployment process with proposed frame concept. Note the red circile, highlighting how the bottom zip tie provides reference point for whole sleeve to deploy around heart model properly.*

Vacuum stabilization was another key requirement for the device, originally envisioned in the form of an apex suction cup. Effectively integrating such capabilities into the frame components allow them to serve a dual purpose, eliminating an additional part to the whole delivery tool. Moving away from the zip tie prototype, the next iteration was the vacuum-enable frame. The quickest way to create prototypes was to use cast silicone rubber. Casting opened a new dimension of design, since all it took was 3D printing a mold in whatever shape was necessary. The idea was to keep a similar shape to zip ties, but just add suction cups to the end of the frame for stabilization. There were many possibilities for the shape of the cup as well as the kind of silicone rubber to be casted (DragonSkin 20, 30, FX, SmoothSil 950,960), so a design study was conducted to find the most effective material/cup shape combination for the device (Figure 10). Using a silicone heart model, the grip strength of conical, cylindrical, and domed suction cup shapes as they were translated along the heart were characterized.

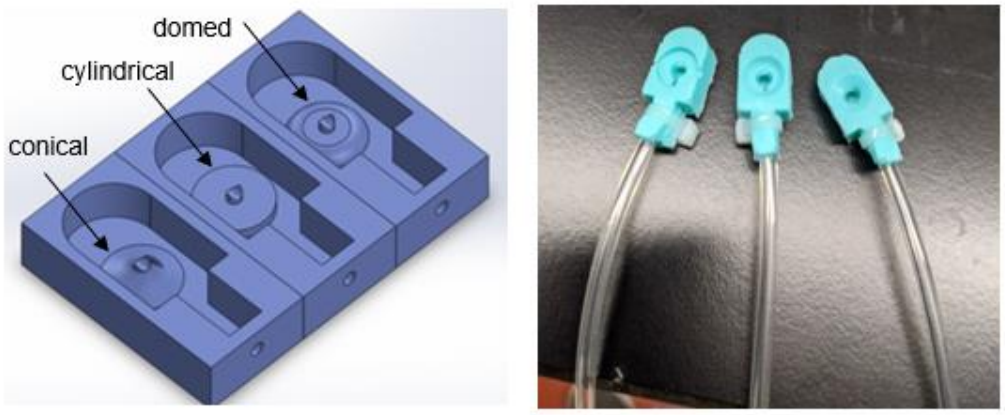


*Figure 10: **Left**. CAD model of mold for casting silicone rubber into test components of vacuum frame, **Right.** completed test components made of SmoothSil 960*

It was found that the conical suction cup provided the best grip over the 40 to 80 kPa range we tested with, and that Smooth-Sil 950 silicone rubber provided enough stiffness to the frame. This was important, since the softer rubbers tended to buckle when pushed along a flat

surface, which would impact tool deployment along the epicardium. It was also noted that the vacuum was strong enough to stay on the epicardium while being pushed along it, but weak enough such that the cups quickly disengaged during bladder inflation, as intended.

After testing the heads, longer molds were developed for a full silicone frame that enclosed the tubing for the vacuum line (Figure 11). The tubing itself provided more structure during deployment. 1/16” metal rods (McMaster-Carr, 9095K37) were inserted into the tubing to prevent silicone rubber from plugging them as well as keeping them straight within the molds as the rubber cured.

The frame is made of hard (Rockwell R93) 1/8” OD, 1/16” ID polypropylene tubing (McMaster-Carr, 5392K52) which provides a degree of springiness that makes deployment faster. The vacuum is run at pressure levels deemed allowable for medical gases by the Nation Fire Protection Association (NPFA99) [4].Tubing made of firm (Durometer 95A) polyurethane tubing (McMaster-Carr, 5648K67), of the same diameters was also explored but abandoned as deployment from the delivery tube proved more difficult.

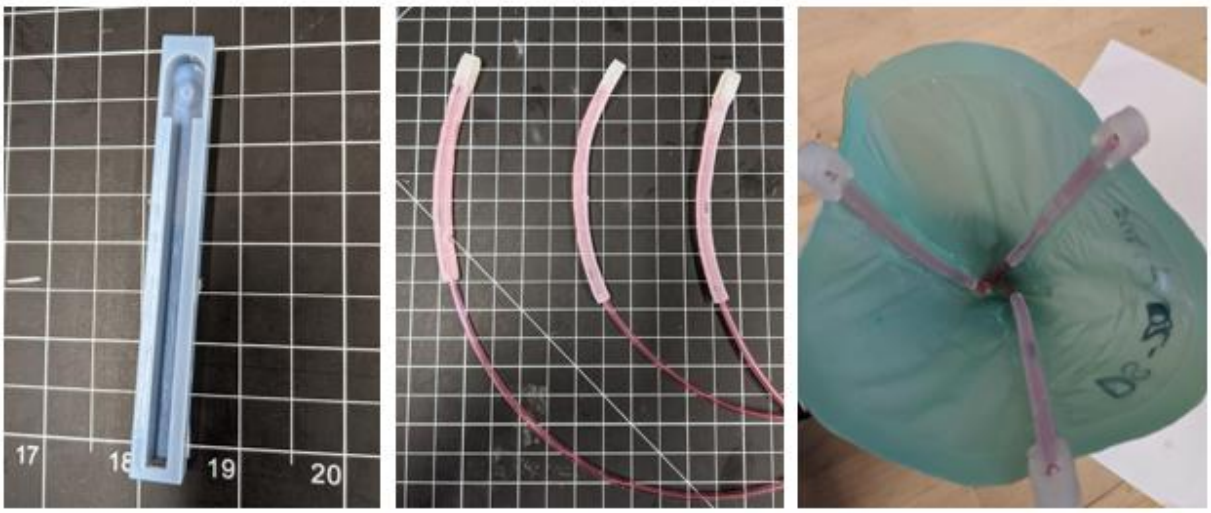


*Figure 11: **Left.** 3D printed mold for next iteration of vacuum frames, with conical suction cup, **Center**. Series of casted vacuum frames enclosing polyurethane tubing for vacuum line, **Right.** Vacuum frames attached to delivery sleeve*

Current silicone rubber frames are attached to the sleeve using Sil-poxy epoxy. The heads of the frames extend out about 2 centimeters from the edge of the sleeve to act as probes as they approach the apex. To prevent buckling inwards upon initial contact with the heart, the heads of the cast frame components were changed from semi-circular to wedged (Figure 12).

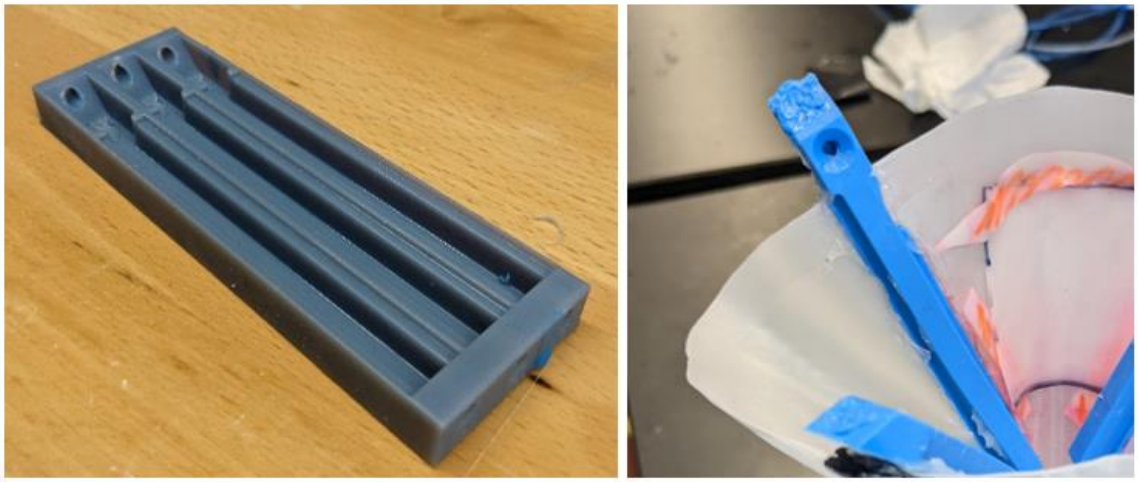


Figure 12: Left. *next iteration of 3D-printed mold for vacuum frames, with through-holes for inserting tubing and inclined face,* ***Right.*** *complete cast silicone rubber vacuum frame, made with SmoothSil 950*

The protocol for making vacuum frames cis as follows:

1. Insert tubing into 3D-printed mold (arms will be cast around them)
2. Prepare 2-component silicone
    a. Combine 20g of Smooth-Sil 950 Part A with 2g of Part B in a small cup
    b. Place in centrifuge and rotate at 200 rpm for 30 seconds, twice
3. Pour mixture into 3D-printed mold, making sure it is even on surface
4. Let cure overnight
5. Remove from mold and attach to sleeve with SmoothOn Inc. Sil-poxy adhesive

3.4 Assembly for patch deployment

To assemble the delivery tool for patch deployment, first the adhesive patch is attached to the internal surface of the delivery sleeve by introducing its corners in inlets made of strips of

TPU, as shown in Figure l3 (left).Then the tubing is inserted and pulled through holes in a custom 3D printed plunger that slides along a clear PVC tube of 25 mm outer diameter fabricated as a stand in for a medical grade syringe (Figure 13 center). When the sleeve is shaped like a cone, the heads of the frame are brought together in a radial pattern and the sleeve is rolled up. Then it is withdrawn into the tube. (Figure 13, right.)

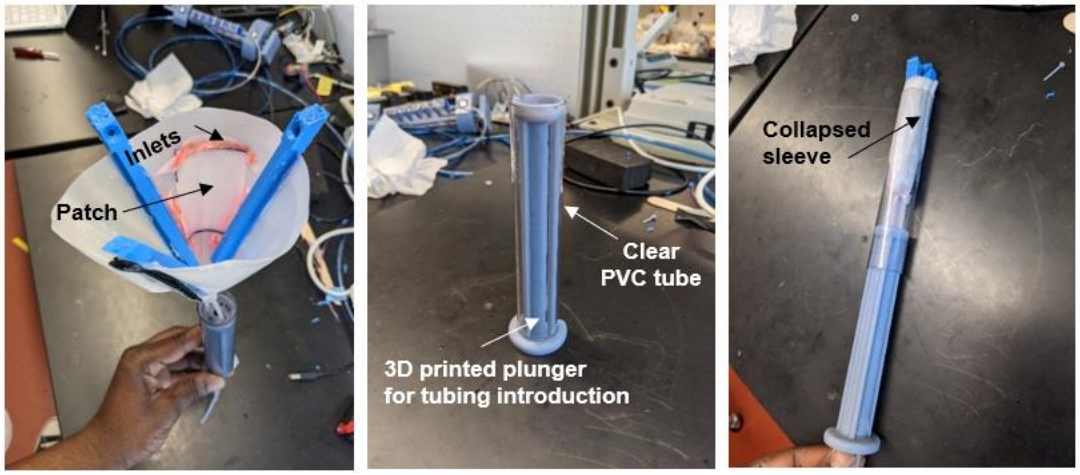


Figure 13: Left*. complete delivery tool prepped for pre-loading into catheter; TPU strips for holding epicardial patch in place are shaded red.* ***Center****. Prototype for syringe & catheter components of delivery tool.* ***Right.*** *Preloaded delivery tool*

4. DELIVERY TOOL VALIDATION

4.1. Sleeve Inflation Compression Testing

A hydrophobic layer is added to the adhesive side of the patch to prevent accidental adhesion during the patch deployment operation. Once the patch is in the correct location, pressure is required to push away any excess oil or blood on its surface so the hydrogel can effectively bond with the tissue. It has been shown that 77.5 kPa of pressure removes the 100 centistokes (unit for kinematic viscosity, cSt) oil layer [5] and that 5 seconds of pressure ensures hydrogel adhesion [6]. Using a mechanical testing (Instron 5944) machine, tests were conducted to calculate whether the sleeve design could provide the necessary amount of pressure to adhere

the patch to the epicardium when coated with silicone oil (10 cSt). The patch size was standardized to a 5 X 5 cm^2 surface area and the distance between the load cell and the deflated sleeve was varied from 0.25 cm- 1 cm to simulate the space between the pericardium and epicardium.

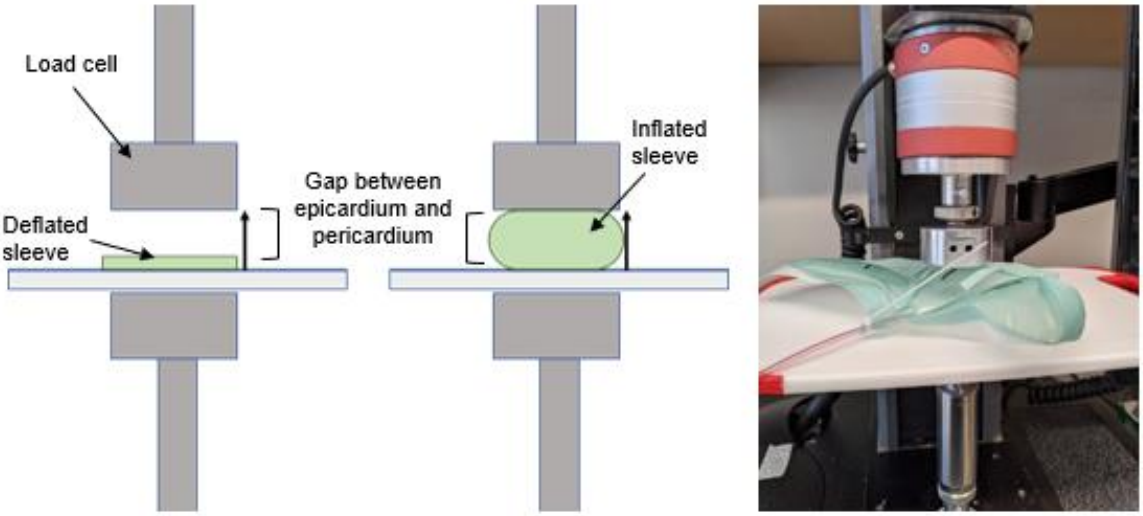


Figure 14: *Test setup for delivery sleeve compression pressure validation*

For the 0.25-centimeter gap (Figure 15), the measured force increases in a nearly linear manner as the inflation pressure increased. The time to reach maximum applied force also decreased as pressure increased, decreasing from 8.2 seconds at 35 kPa to 4.3 at 140 kPa.

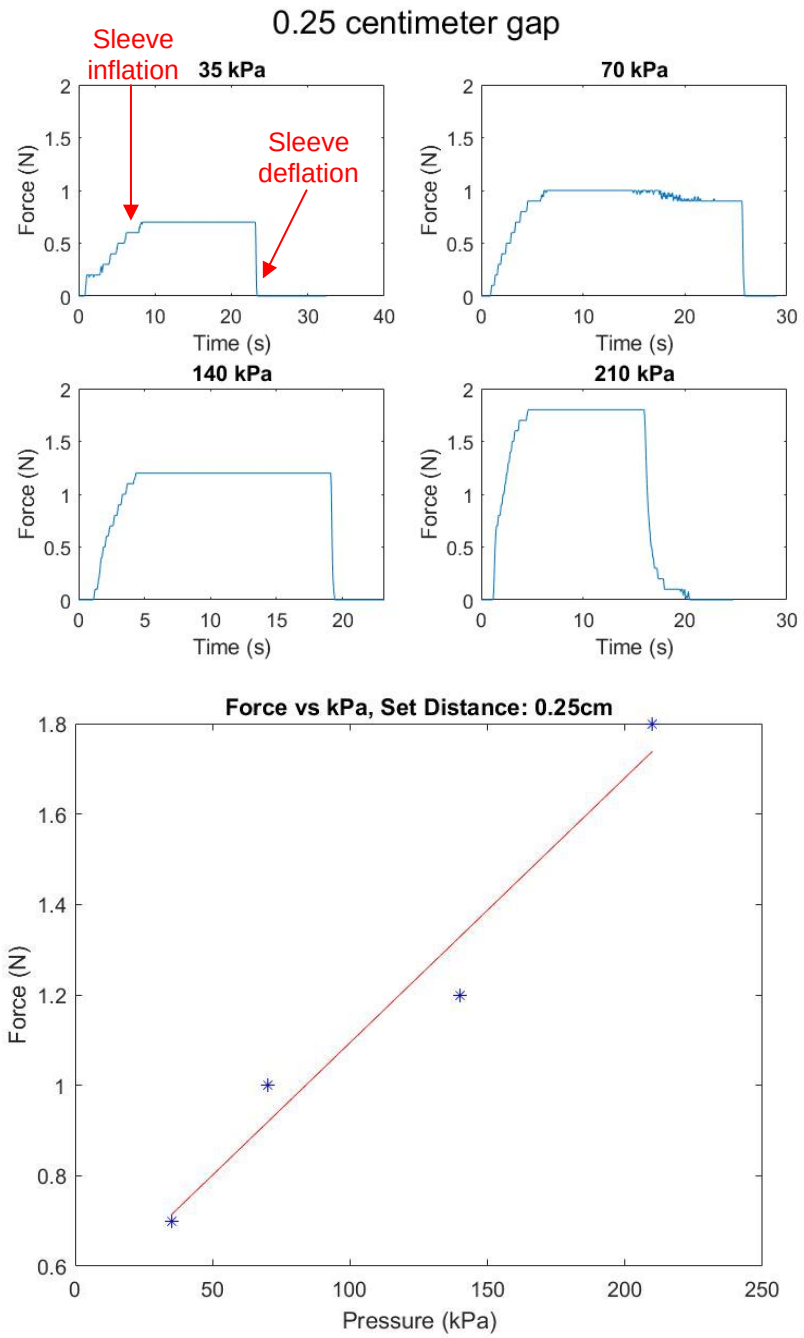


Figure 15: Top. *Force applied by air bladder after inflation, deflected 0.25cm, measured over time,* ***Bottom.*** *Trend line of maximum force measured by Instron testing machine at pre-determined pressures.*

For the 0.5-centimeter gap, the measured force follows the same general trend as the previous gap size and has similar maximums in force. The rise times also decrease as pressure increases but have overall increased from the previous gap size.

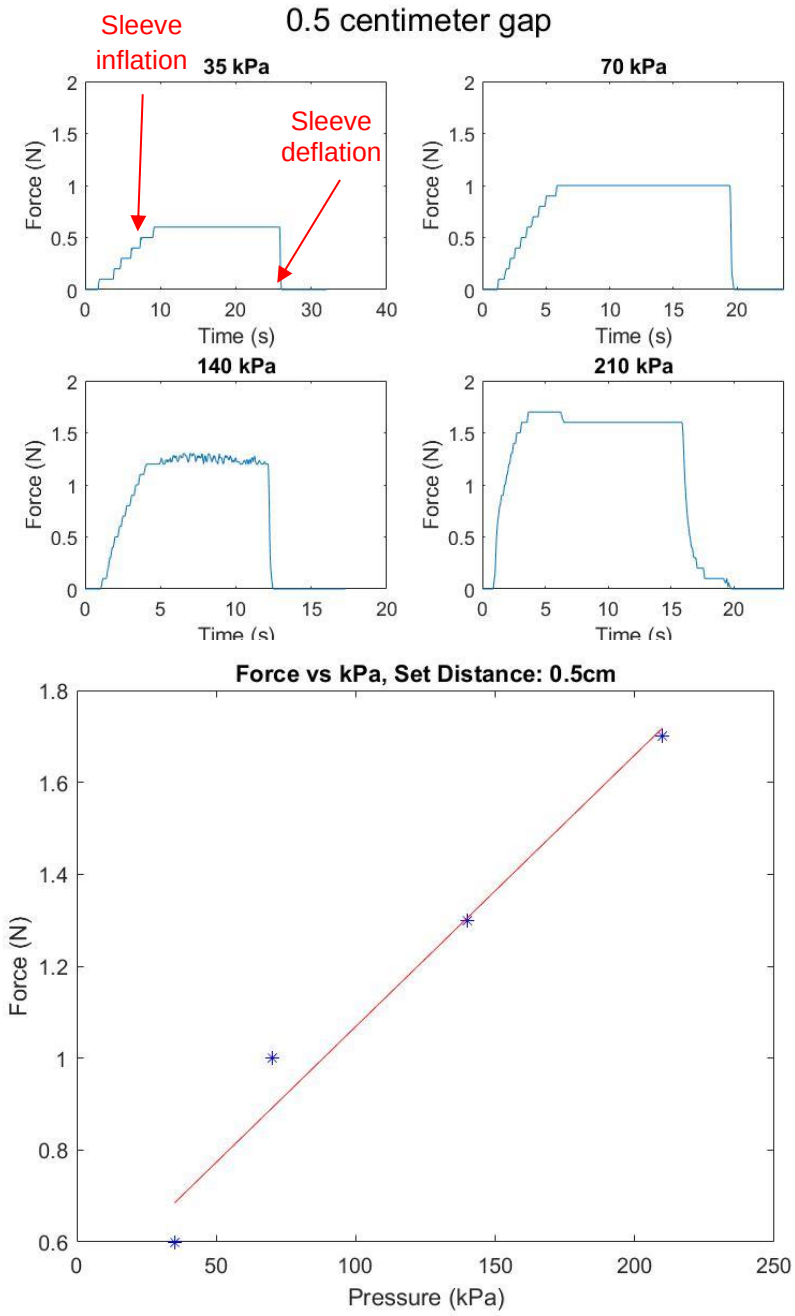


Figure 16: Top. *Force applied by air bladder after inflation, deflected 0.5cm, measured over time,* ***Bottom.*** *Trend line of maximum force measured by Instron testing machine at pre-determined pressures.*

For the 1-centimeter gap, the measured force, even at 210 kPa, was much less than the other gap sizes at the same inflation pressure. The trends remained the same for both maximum force and rise time, but these forces do seem like they would result in effective adhesion.

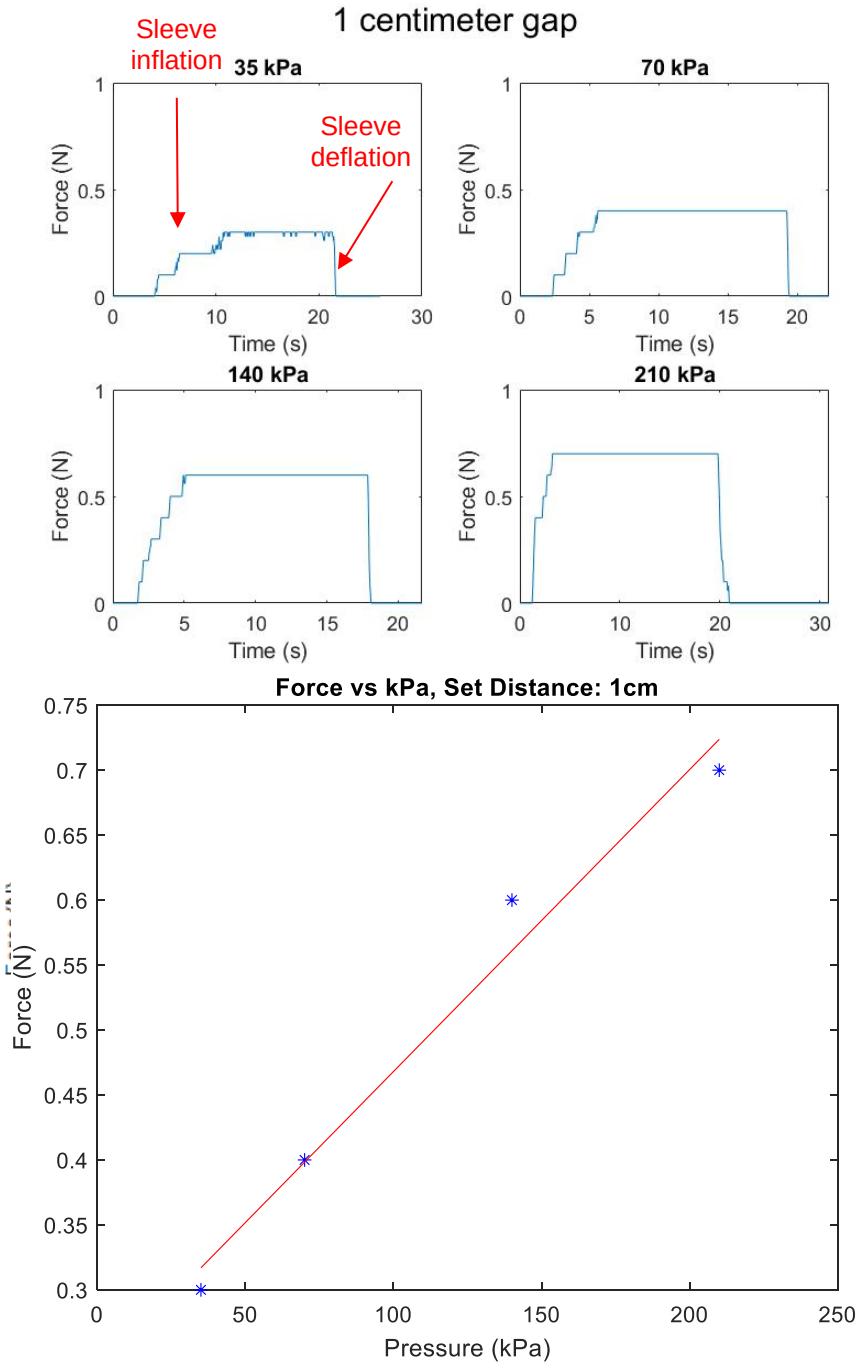


Figure 17: Top. *Force applied by air bladder after inflation, deflected 1 cm, measured over time,* ***Bottom****. Trend line of maximum force measured by Instron testing machine at pre-determined pressures.*

4.2. Ex Vivo & In Situ Testing

Initially, 3D printed models of a porcine heart in diastole and systole were used to test tool deployments (Figure 18, left). While close in approximate size to actual porcine heart, the hard plastic surfaces were not an accurate representation of cardiac tissue. Thus, an actual porcine heart was fixed in formaldehyde and used for *ex vivo* testing of subsequent iterations of the delivery tool (Figure 18, right). An aluminum and laser cut acrylic test frame (Figure 19) was constructed to standardize further testing and stabilize excised and fixed hearts. There were also attachments for a simulation pericardium made of silicone rubber.

As time went on, the fixed heart proved to be an effective test model but was noted to be too stiff compared to an actual heart beating through the surgery. In situ cadaveric testing was conducted in swine to improve device sizing and delivery route. This presented a real sense of what the deployment of the delivery tool would be like during a real surgery including the presence of pericardium and surrounding organs. On top of that, the heart was able to be excised, washed and frozen for future use in ex vivo prototype studies.

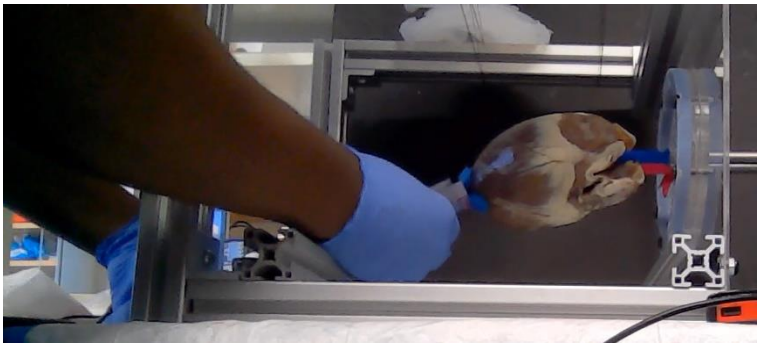
Figure 18: ***Left.*** *Delivery tool deployment using 3D printed systole heart model, with initial frame concept.* ***Right:*** *Deployment using fixed porcine heart with developed vacuum frame components*

***Figure 19**: Aluminum test frame for ex vivo experiments to standardize testing . Metal rods enter heart through gaps and aorta, allowing to remain upright during tool deployment*

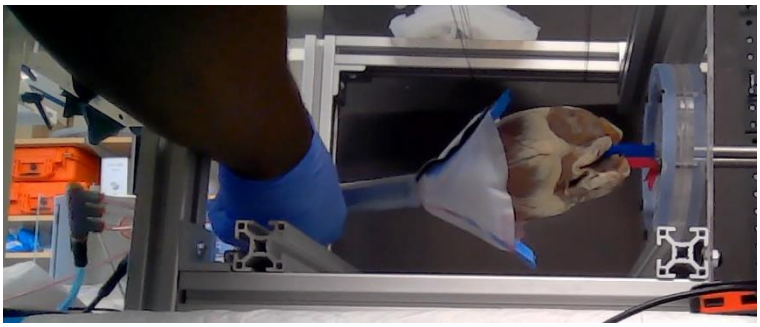
4.3 Ex Vivo & In Situ Results

Multiple deployment tests have been conducted at each step of the prototyping process. Figure 20 shows a successful ex vivo deployment procedure. The delivery tool reaches the apex of the heart and is deployed slowly to ensure vacuum probes are sealed. Once properly sealed, the tool is fully deployed surrounding the epicardium and inflated to apply pressure onto the patch for at least 5 seconds. The hydrogel adhesive force is stronger than the force restraining the patch to the sleeve via the inlets, so once the sleeve is deflated the patch is left behind and the tool is simply retracted and reinserted into the catheter (Figure 20).

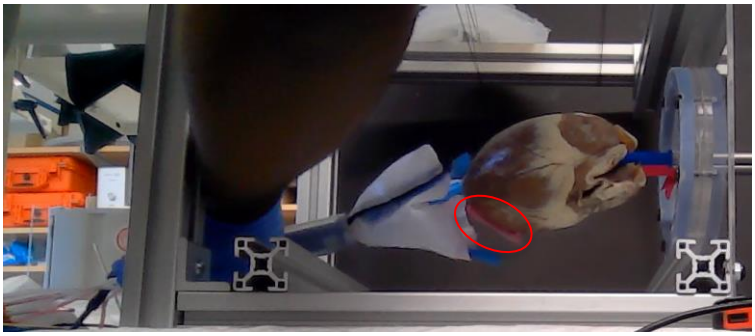
A).



B)



C)



D).

Figure 20: *Deployment process on fixed heart.* ***A).*** *Wedged vacuum frame design allows for easier apex approach.* ***B).*** *Once properly positioned and opened, sleeve is inflated.* ***C).*** *Patch is left behind on the heart as tool is retracted.* ***D).*** *Hydrogel effectively bonds with cardiac tissue.*

Figures 21 and 22 demonstrate that the deployment procedure can be replicated when part of the rib cage and pericardial tissue surrounds the heart.

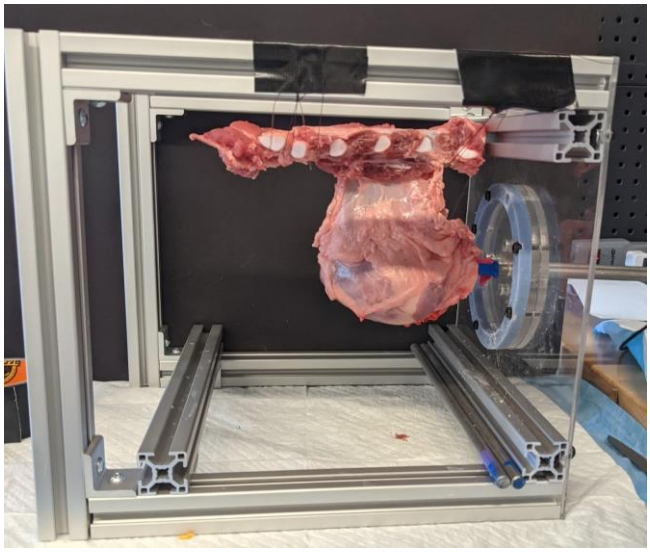


Figure 21: *Testing setup with recently excised heart with pericardium and ribs attached*

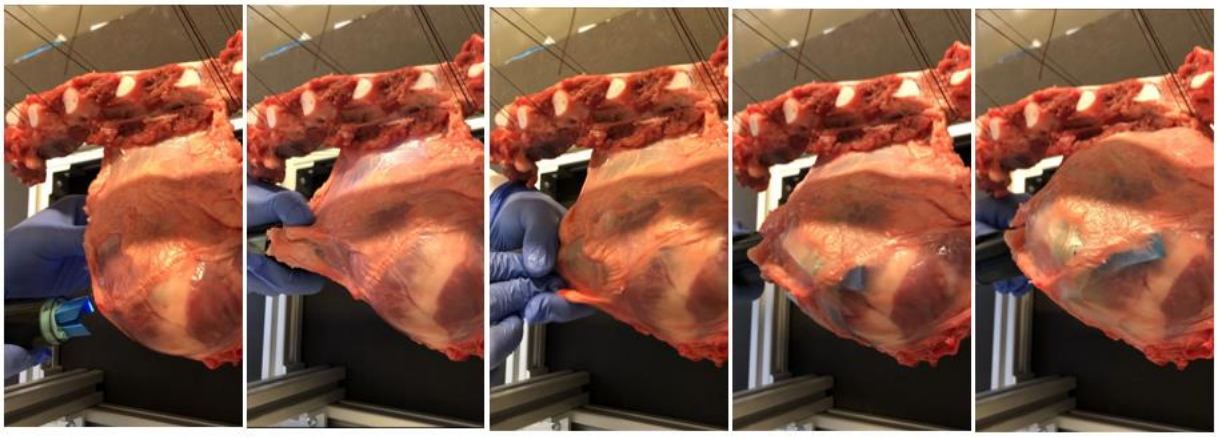


Figure 22: *Deployment process with natural pericardium. Once vacuum sealing is achieved with vacuum frames, delivery tool can effectively slide towards the base and inflate to adhere the patch*

Figure 23 displays an *in situ* deployment attempt at a porcine terminal study. The in situ attempts provided a good idea of sizing and how a surgeon would access the heart during an operation, but no patch was delivered. This was due to heart being depressurized in the cadaver, leaving it very flimsy and making it difficult for the vacuum frames to position themselves on the apex. Some kind of stiffening of the heart should take place to mirror true to life pressurization.

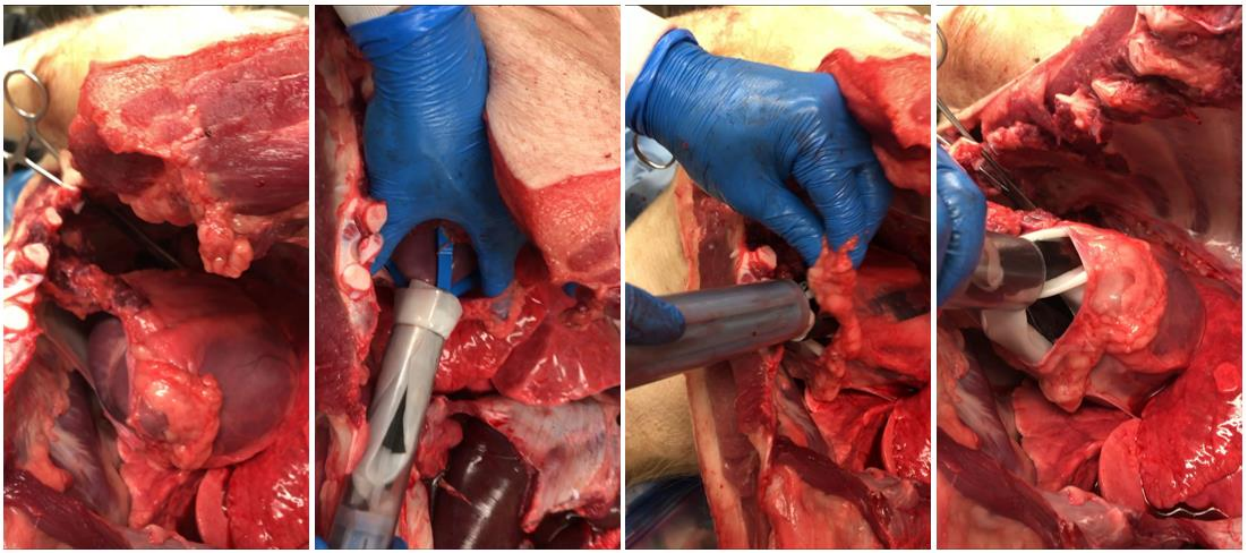


Figure 23: *In situ deployment attempt with recently euthanized pig cadaver.*

With each iteration, the device has become more effective at delivering the patch and satisfying the key requirements outlined above. The sleeve itself inflates rapidly and repeatedly, while remaining sealed in all 3 pockets. A slight issue is the TPU strips used to hold the sleeve in, as they become detached when under tension due to inflation. This could make the patch fold in on itself, reducing the area that contacts the epicardium and impeding proper adhesion.

The vacuum frames do not impede inflation, as they slip right in between the pockets because they are attached right over seals. They do make the sleeve thick when rolled up, making it difficult to deploy from or retract into the tube without grease or oil. The orientation and stiffness of the tubing has a big impact on the shape of the sleeve once deployed. The 3D-printed syringe allows the tool user to position each individual tube in the vacuum frame by twisting them. It has been found that positioning the tubing in a radial pattern with each tube curving outwards, tends to make the sleeve maintain the essential conical shape.

The vacuum also serves as an auditory indicator for deployment. When the hissing sound stops, that means all 3 vacuum frames are secured to the epicardium and proper deployment is more

likely to happen. This has been found to happen on hearts with and without a pericardium. In the future, there could be proximal sensors by the vacuum frame to ensure suction is reached and maintained during deployment.

6. CONCLUSION

The inflatable sleeve delivery tool is a cheap, accessible, and effective method for placing an epicardial patch on an infarcted region of the heart without invasive surgery.

Through the mechanical testing, it was found that the sleeve could provide the necessary amount of force over a 25 cm^2 area (standard epicardial patch size). This is adequate with a factor of safety of 2 to squeeze the hydrophobic layer out and allow the patch to adhere to the epicardium without significantly straining the pericardium, allowing for quick deflation and removal of the tool.

The porcine heart experiments exposed many of the slight idiosyncrasies that come with actually using the tool. Although patch deployment has been successful at multiple points, there are still many areas for improvement that would make this delivery device an attractive and effective tool for a surgeon to use. With more time and prototyping, the sleeve can be made more reliable and easier to access for initial patch placement, as well as customizable for different patch sizes.

7. FUTURE WORK

There are some limitations to the current work, with clear pathways to future enhancements. Consolidation of the framing, such that is integrated with the sleeve manufacturing rather than glued on top of it, is a clear next step. This would reduce overall size when rolled up facilitating

deployment and reduce the number of manufacturing steps. Another improvement would be finding a way to load patches consistently, pre-deployment. As stated previously, a reliable method to provide suction and routing for the tubing component would move the prototype even closer to a final iteration suitable for actual in vivo testing. With the experience from current in situ attempts, future work will include preserving in vivo properties in excised hearts by either artificial pressurization with a balloon inserted into the heart or filling the chambers them with gel or tissue. In the future, an enhancement of the device would be an attached endoscopic camera for visualization, and path-guiding features attached to the arms or sleeve for more accurate positioning during surgery.

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