Design of a Double-Dose Epinephrine Auto-injector Using 3D-Printing

By

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SHEEHAN, TIMOTHY Design of an epinephrine auto-injector, a device used in the treatment of anaphylaxis, capable of administering two separate doses. Department of Bioengineering, June 2015

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This project involved the design and prototyping of an epinephrine auto-injector capable of administering two separate doses. Epinephrine auto-injectors are used in the treatment of patients undergoing anaphylaxis, an allergic reaction causing the restriction of airways and a drop in blood pressure. The timely administration of epinephrine counteracts these symptoms and can be lifesaving. Currently the only devices available to consumers administer one unit dose of epinephrine and are then no longer usable. In 30% of cases where patients undergo these symptoms a second dose of epinephrine is required.

My design was based partially off the concept behind currently available auto-injectors featuring a compressed spring being released as a propulsion mechanism. The most challenging design concepts for me were to release and contain the springs, and to cover the needle after the first and second doses. The design process, as well as descriptions of the final design, are included in this report.

TABLE OF CONTENTS

Table of Figures

1. INTRODUCTION

In the United States, up to 40 million people are at risk for anaphylaxis, an allergic reaction causing the body to respond as if has been poisoned, constricting airways and dropping blood pressure. [1] This can cause death by asphyxiation if left untreated. Although the causes and reasons for allergic reactions are not fully understood, the symptoms of anaphylactic shock can be treated with the drug epinephrine. Also known as adrenaline, this hormone is released during the *fight or flight* response and works on pathways to constrict blood vessels (thus increasing blood pressure) and open airways. There are several devices available on the market today that allow a lay person to administer a single dose of life saving epinephrine in an emergency situation. Unfortunately, these devices are one size fits all and many times one unit dose is not sufficient and anaphylactic shock continues. In one 2005 study, of 105 patients who were given a dose of epinephrine, 36% required an additional dose when symptoms persisted.[2]

Epinephrine auto-injectors are designed to be used by people experiencing anaphylactic shock by administering a 0.3ml of 1:1000 epinephrine solution intramuscularly (IM). Currently available models work on similar principals from a consumer or patient standpoint: to be administered a safety cover is removed from either the proximal or distal end of the device and the proximal end is jabbed into the outer portion of the thigh at which point the dose is administered IM. Jabbing the proximal end into the hip of the patient releases a source of potential energy propelling the syringe and 1" needle forward into the patient and subsequently depressing a plunger to deliver the proper dose. Two distinct models exist with the Auvi-Q™ utilizing compressed air as the primary energy source and the EpiPen® which uses a compressed

[1] http://www.ncbi.nlm.nih.gov/pubmed/11146694
[2] http://www.sciencedirect.com/science/article/pii/S0091674905025716

spring. These models also differ in their method for protecting the needle in which the EpiPen® extends a cover over the needle (increasing the overall length of the device) rather than retracting the needle as the Auvi-Q™ does.

The goal of my design project is to design an epinephrine auto-injector that can administer two separate doses of medicine to protect patients in the case that one dose is insufficient. This report will first briefly discuss some existing devices that have performed similar functions to my goals before describing the design and functionality of the EpiPen® highlighting the injection and needle covering mechanisms. Next it will address how my proposed design will look and behave. Finally it will discuss the prototyping process, how it will be manufactured, and future improvements.

2. BACKGROUND

Previous devices have been made that address the 'double-dose' problem. The TwinJect, functions in a manner similar to the EpiPen® for the first dose but then can be disassembled to allow the removal of the syringe to inject a second dose.[3] This is a very novel and simple solution to the problem left unaddressed by single dose auto-injectors; besides being easy to disassemble it differs little in design from the EpiPen®. From a patient and parent standpoint, however, this device was not well received apparently due to discomfort with exposed needles and the complicated dose administration procedure involved.[4] The TwinJect was discontinued in 2012, possibly in part due to poor sales as a result to these fears. The TwinJect's design demonstrates there are designs that can implement a successful 'double-dose' but its failure

[3] Frew, A. J. "What are the 'ideal' features of an adrenaline auto-injector in the treatment of anaphylaxis
[4] http://www.peanutallergy.com/boards/new-epi-pen-twinject

suggest that an ideal model should maintain needle enclosure and a user procedure with as few and as simple steps as possible as exemplified by commercially successful models.

The pharmaceutical company Mylan, producer of the EpiPen® met the issue of the possible necessity of a double-dose by discontinuing single EpiPen® sales and only selling the EpiPen® 2-pack, requiring patients to own and presumably carry two auto-injectors at a time. While this approach, if users were to carry two EpiPen®'s at all times, would be effective it is very unlikely that most users would carry more than one device considering studies have shown that between 30-70% of users prescribed an epinephrine auto-injectors do not carry it consistently.[5] The additional EpiPen® adds additional bulk and can easily be separated from its sister meaning that most users will likely continue to carry at most one device. For reasons of convenience, and more importantly assuring that patients will have access to sufficient adrenaline in an anaphylactic emergency, it is important that two doses are available in a single device and that the resultant device be as compact and simple to use as possible.

My proposed design will attempt to emulate the compactness of the TwinJect auto-injector and the user simplicity and needle containment of the EpiPen. The user should be able to receive two separate doses of epinephrine without ever seeing the needle or performing complicated disassembly tasks.

EpiPen® Functionality

The EpiPen® is activated and the proper dose administered when 1) the safety (S) is removed from the distal end of the device and 2) the proximal end is depressed (A) (Figure 1). The depressive force needed to activate the EpiPen is approximately 25 N, a small force easily

[5] Frew, A. J. "What are the 'ideal' features of an adrenaline auto-injector in the treatment of anaphylaxis

administered by an able bodied person (Appendix 1). This action forces the element holding the compressed spring (D) backwards and forces its wings (B) into a compacting region (C) squeezing the wings inward and allowing them to move past the opening of the holder (H). The compressed spring is now allowed to expand pushing down on the plunger (E) which is attached to an ampoule (F). This propels the attached needle into the skin until the front of the ampoule (E) reaches the interior of the proximal end of the device stopping it and forcing the plunger to continue movement independent of the ampoule. This causes the breaking of the ampoule and the administration of the correct 0.3 mL dose over the next few seconds as the plunger continues to advance until a stopper on the plunger reaches the outer wall of the ampoule.

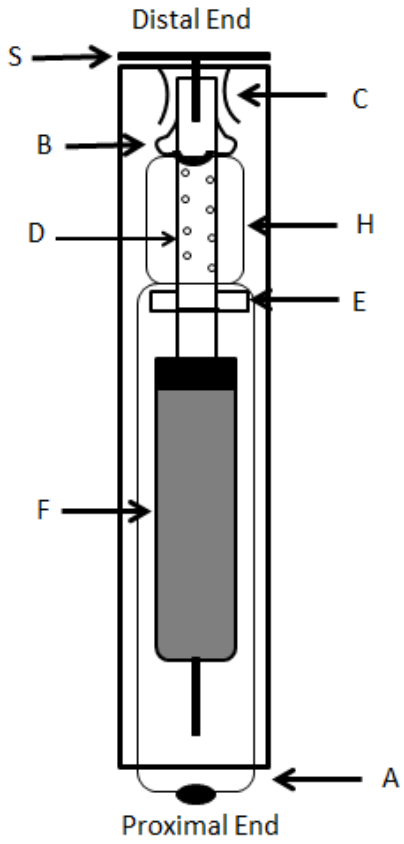


Figure 1: Schematic of functional aspects of the EpiPen® prior to activation: open circles represent x-section of helical spring. Upon removing safety (S) and pressing down on the proximal end (A) the needle will automatically be propelled through the opening and administer the correct dose of Epinephrine.

As a protective feature, the EpiPen® deploys a protective sheath after the unit dose of epinephrine is administered to prevent accidental needle stabs. When the ampoule (A) advances to the end of the inner casing (I) it rotates two wings (W) inward unlocking them from the tabs (T), freeing the inner casing from the outer casing (O) and allowing the compressed spring (S) to expand, extending the outer casing and covering the needle (Figures 2-4). The outer casing is now locked in place to prevent it from sliding back into the device and re-exposing the needle by a second locking mechanism (L).

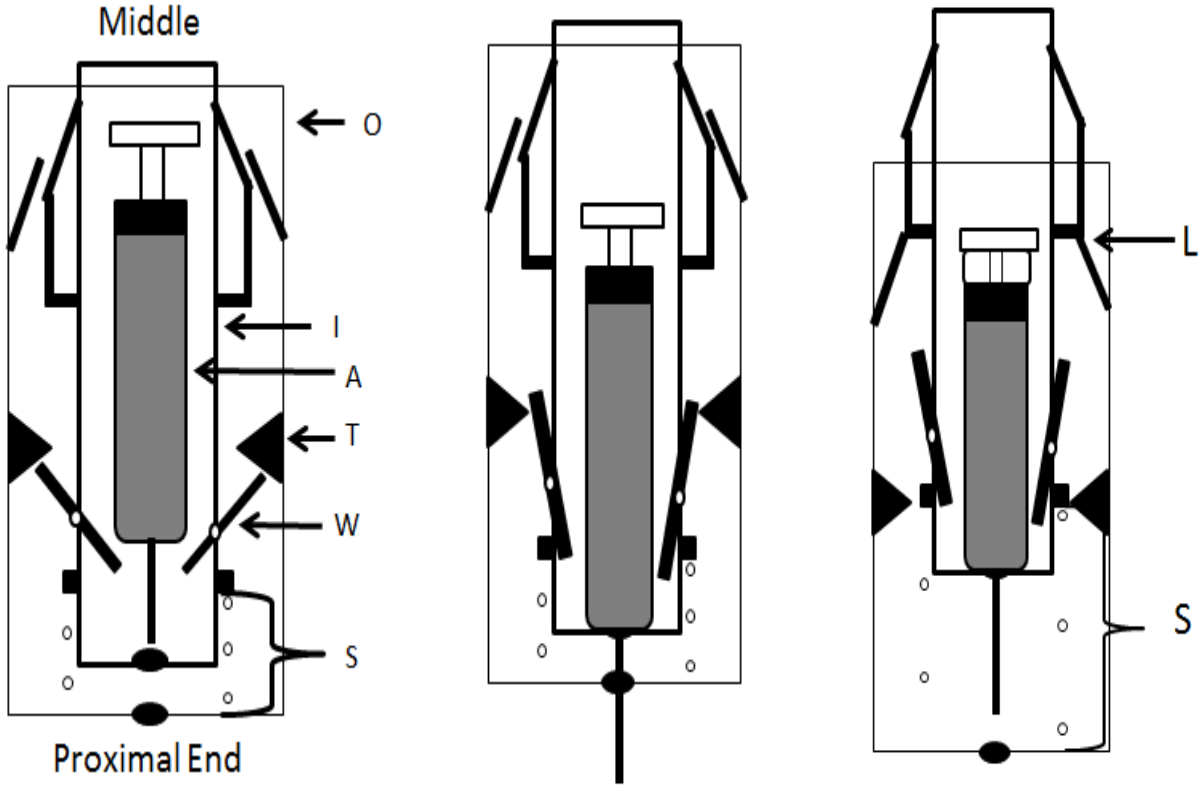


Figure 2-4: (L to R) 2. Schematic for needle covering mechanism prior to activation, open circles represent spring. Note that mechanism depicted involving the wings (W), ampoule (A) and tabs (T) is more discriptive of the concept and that the true interaction and is better seen in images presented on the next couple pages. **3.** The wings have been pushed in by the advancing ampoule. **4.** The unlocked outer casing slides forward and is locked in place by two locks (L).

Detailed images of the device and its components should help with the understanding of its functionality (Figures 5-10).

Figure 5: Fully assembled EpiPen® in carrying case, measuring about 6.5" long and 1.5" wide this device is intended to be carried in a backpack or carrying case with a second device close by.

Figure 6: EpiPen® reassembled after being activated, taken apart and reset to appear as it did prior to activation. The distal aspect of the device was torn open on either side to allow the spring holder to be removed from the outer casing. Note how the orange needle protrudes from the proximal end of the device prior to activation.

Figure 7: EpiPen®with outer casing removed and the blue safety still installed. The main compressive spring has been removed and not replaced in this image. The blue safety cap remains installed locking the spring from being released if it were present.

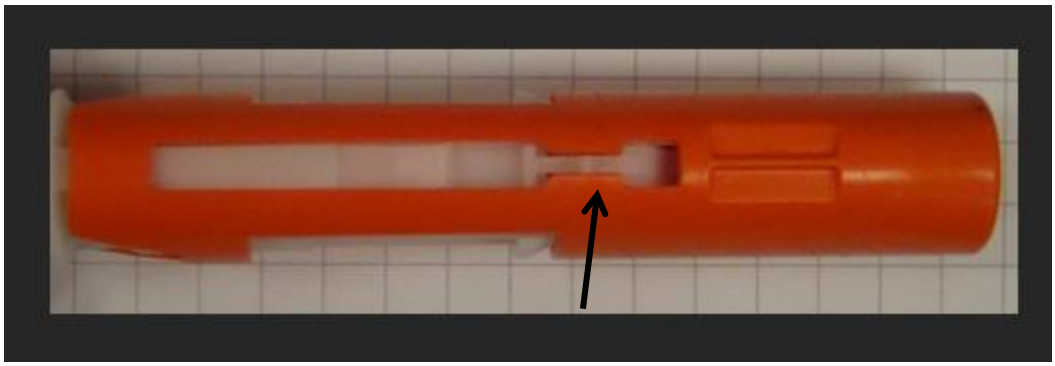


Figure 8: Side view of needle cover locking mechanism prior to activation. The arrow points to the lock point where the wings prevent the needle cover from sliding forward. These wings are pushed upward by the ampoule, causing them to flatten, when the device is activated.

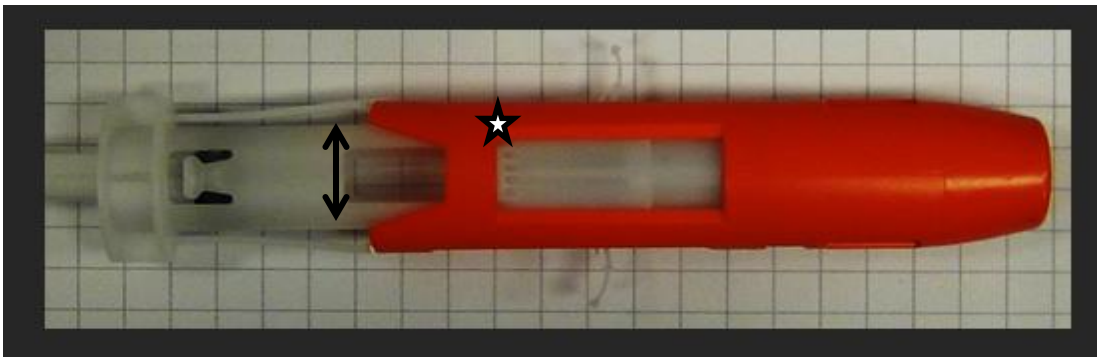


Figure 9: Top view of needle cover device after deployment, note how the wings are no longer pinned in place and have rotated outside. Further advancement in the proximal direction is prevented by the ledge located beneath the star while regressive movement in the distal is prevented by the leaf springs that have come out outside the arrows.

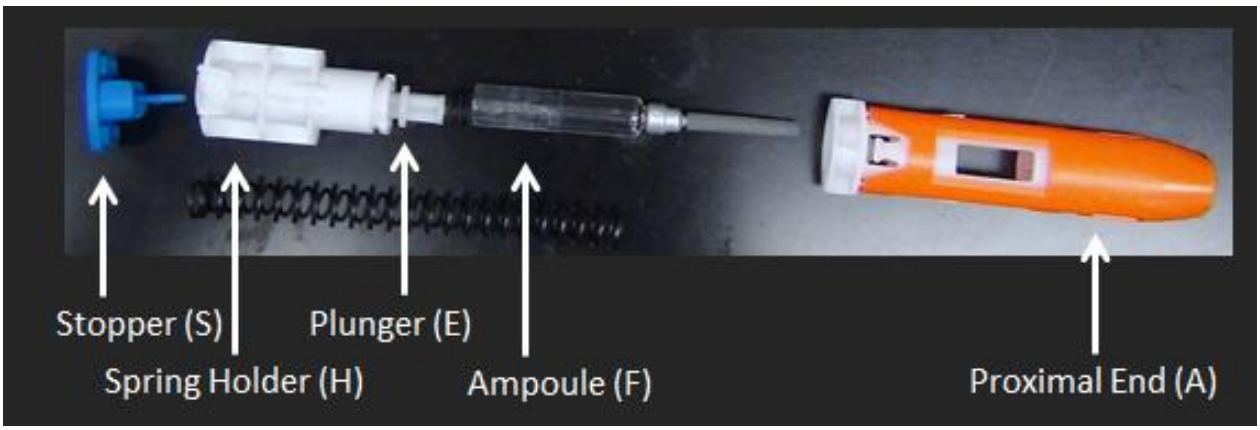


Figure 10: Exploded view of device including all parts except for the outer casing and the epinephrine solution. Notice the spring fully expanded is about twice as long as its compressed length corresponding to the distance from the distal end of the holder to the stopper visible just above the arrow for the plunger.

From a patient's perspective the procedure is relatively simple requiring only two motions (removing the cap and jabbing into the leg) once the device is removed from its protective carrying case. Since many people are squeamish around needles the fact that the needle is never actually seen by the patient when the device is used is a valuable feature. This is especially true since the EpiPen®'s needle needs to penetrate about 1" into the skin to perform the proper injection, significantly deeper than intravenous or subcutaneous injections.[6] Interestingly, requiring the device to be pressed firmly against the hip to fire causes the muscular tissue to be compressed beneath the device which helps ensure adequate penetration depth of the needle. The firing of the EpiPen® is irreversible and once administered the needle and internal components are inaccessible. After use, patients are encouraged to seek emergency medical attention immediately and dispose of the used EpiPen® at a pharmacy or hospital.

Surprisingly, there is still enough Epinephrine in the device to administer four additional doses, but at this point there is no way to access the needle or remaining epinephrine inside the ampoule without destroying the EpiPen®. In the event that symptoms persist, the user can use an additional EpiPen® if available, take an antihistamine like Benadryl, or seek emergency care where clinical doses of Epinephrine are available. Since a second dose or additional drugs are required in up to 36% of cases, it is clear that it would be beneficial if the EpiPen® or a similar device were capable of administering a second unit dose of Epinephrine if needed. In fact there are many guides online detailing how to hack an EpiPen®, in a situation where no more devices are available and an additional dose is needed, to extract the ampoule with the remaining doses inside.[7] [8] This is not an ideal course of action since doing so will take time, requires the proper

[6] Frew, A. J. "What are the 'ideal' features of an adrenaline auto-injector in the treatment of anaphylaxis
[7] http://www.academia.edu/5296446/Retrieval_of_Additional_Epinephrine_from_Auto-Injectors
[8] http://www.survivormedic.com/2014/05/12/how-to-take-apart-an-epipen/

tools, and involves releasing the main compressed spring which still contains a large amount of energy and can inflict injury.

3. DESIGN DESCRIPTION

Goals

The goals of my senior design project are to build a device that can administer two separate 0.3 mL doses with each dose delivered in a similar fashion as the EpiPen®. For an IM injection I will use a 1" 22 g needle with a covering to ensure sterility after assembly prior to the first dose. As my device is intended to be a proof of concept and will not be used on a person, I will not attempt to acquire real epinephrine, substituting water or saline solution, and will not ensure all syringes and needles remain sterile during manufacturing. This device is intended to fulfil a shortcoming of the EpiPen® of only administering one dose but is still considered a single event device. In the *likely* event that only one dose is needed the device should still be discarded of properly as the remaining solution has been exposed to air and will spoil and the needle is no longer sterile and can harbor bacteria.

In sequence, the following steps need to be performed by my device:

1. Pre-activation (Remove safety)
2. Activation by a downward pressing of the proximal end of the device
3. Forcefully stab a 22g needle 1" into a human thigh
4. Inject 0.3 mL of 1:1000 epinephrine solution
5. Cover the needle with a protective cover
6. Be activated a second time by rotating a cylinder
7. Repeat step 3
8. Repeat step 4
9. Repeat step 5

These steps correspond to the intended usage by a person suffering anaphylactic shock. The activation of first dose is similar to how most epinephrine auto-injectors work, by jabbing the device into the side of the thigh (3o'clock). This step is familiar to all users, is straightforward in an emergency situation, and compresses the tissue underneath the needle shortening the distance needed to reach the muscle. The device follows this activation with a logical sequence of events in which the right amount of epinephrine is administered to the correct location for maximal efficacy. It is important to cover the needle after injection to prevent accidental stabbings and to maintain the physical and biological integrity (sterility) of the needle.

In the case that a user continues to exhibit anaphylactic symptoms after the first dose of epinephrine, and they do not have access to medical personal, a second dose of epinephrine can be administered. This dose is administered in a different manner than the first dose. The pen is not stabbed into the leg, instead it is pressed firmly against the thigh (12 o'clock) and cylinder is manually rotated by the user. This action will again administer a unit dose of epinephrine in the same manner as the previous dose before again covering the needle.

These steps are accomplished using an assembly of 3D printed parts, two springs, elastic bands, and a modified 3cc syringe. A breakdown of these parts, how they interact, and how they have evolved is to follow.

Design Breakdown

The double dose epinephrine auto-injector consists of six independently moving pieces not including the syringe or springs. To aid in the description of these parts, Figure 11 will serve as a reference. The general description of the parts is as follows: 1, inner casing: contains all moving parts and protects contents; 2, spring container: contains main spring used drive needle

and inject contents as well as unlocks needle cover; 3-4, cylinders: lock spring container in place until rotated; and 5, needle cover: covers needle after injection. In addition, a sixth piece (not shown below for clarity), is designed to allow the push activation of the device and to act as a safety.

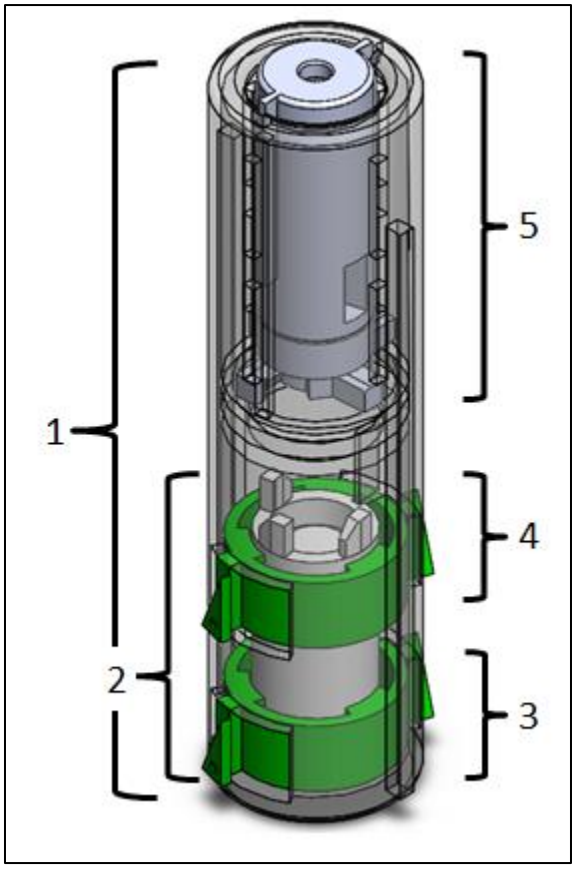


Figure 11: SolidWorks 3D depiction of all moving parts in device besides the outer casing. 1, inner casing; 2, spring container; 3-4, cylinders; and 5, needle cover. The top of this figure is where the needle would protrude from and is referred to at the 'proximal' end. The bottom is furthest from the body and is the 'distal' end.

Syringe Propulsion

The release mechanism of my device will act on a slightly different principle than the EpiPen® as demonstrated in Figure 1. In my design, a compressed spring is placed between the inner casing and the inside of a spring container; the container has a lip (L) which is held back by a cylinder (C) with corresponding ridges that prevent the forward advancement of the holder,

when the cylinder is rotated the holder is free to advance to the next cylinder propelling the syringe forward towards the proximal end of the outer casing and administering a unit dose of epinephrine (Figures 12-13).

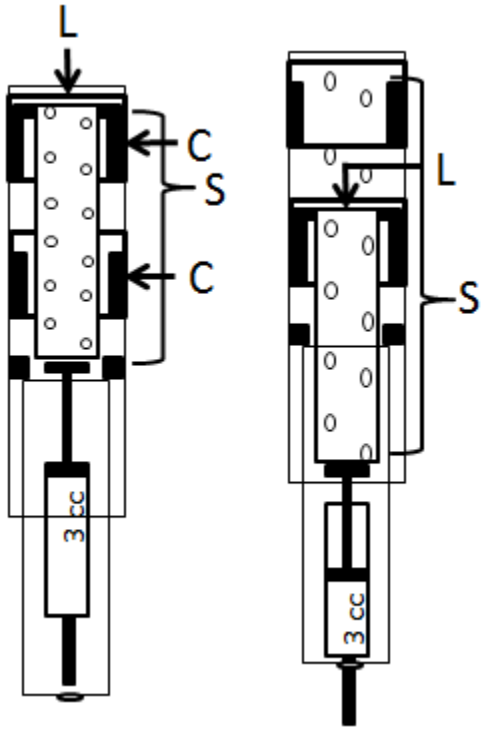
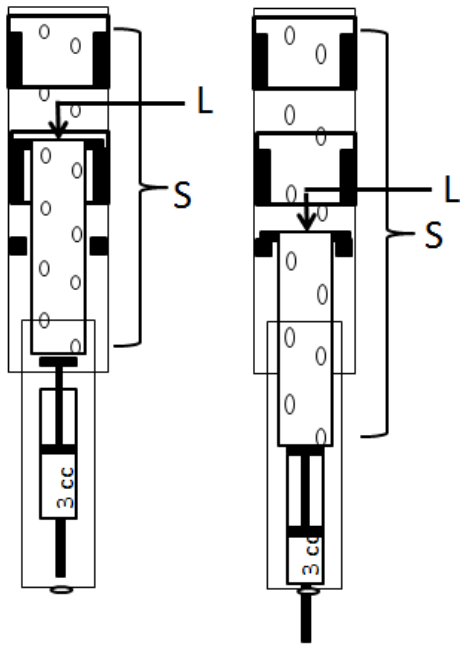


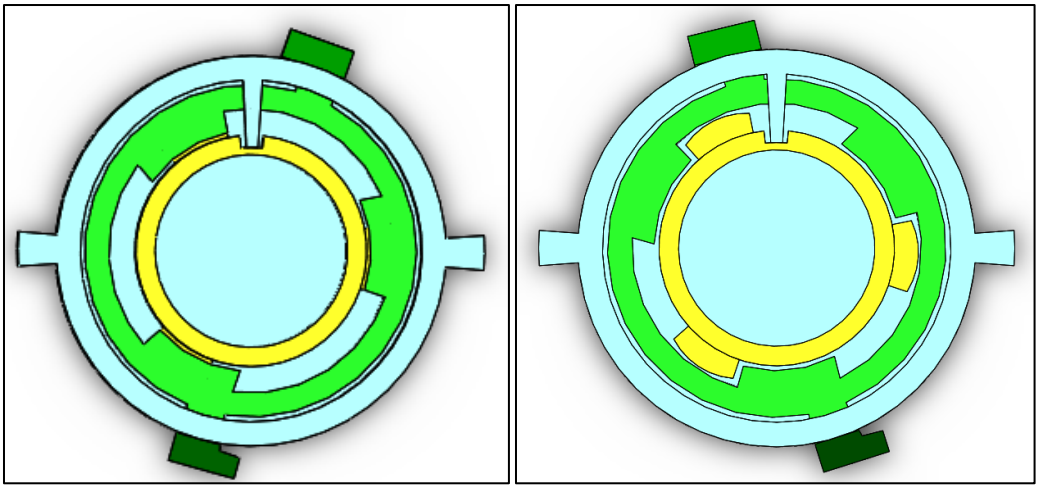
Figure 12-13: Proposed release mechanism for first epinephrine dose. The back lip (L) is held back by the first cylinder and is released when the cylinder is rotated. At this point the compressed spring (S) is allowed to expand propelling forward the plunger, syringe and needle injecting the dose. The back lip is stopped at the second cylinder (C).

At this point a needle cover is pushed over the needle and locked in place to protect the user and the needle (Figure 14). The main spring is still compressed enough to propel the syringe to administer a second dose but is held back by the second cylinder. (If needed) the second cylinder can be rotated and the back lip released allowing the spring to expand (Figure 15).

To ensure the spring container does not rotate with the cylinder, preventing it from advancing, a convex ridge was added to the inner casing to mate with a concave ridge on the spring container (Figure 16-18).



Figures 14-15: Needle covering mechanism automatically covers the needle after the first dose to protect needle and user. To administer a second dose the lower cylinder is rotated, allowing the lip to advance and the spring to expand to administer a second dose



Figures 16-17: SolidWorks depiction of spring containment: a ridge on the outer casing prevents the spring container from rotating with the cylinder, allowing it to advance proximally.

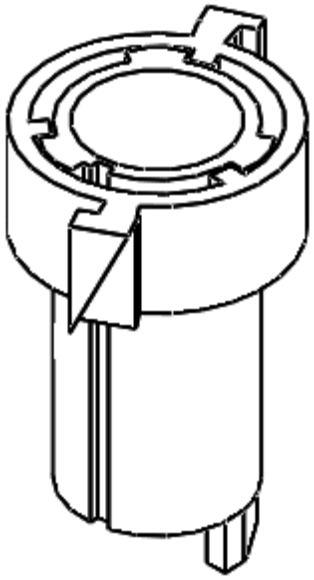


Figure 18: 3d perspective of final spring containment mechanism. Both are restricted by the inner casing so: spring container cannot rotate while the cylinder cannot move up or down.

Injection

A 1” 22g needle is used to perform intramuscular injections of 0.3mL. During these injections the plunger of the syringe is propelled by the spring container. It will travel through the path of least resistance, first pushing the syringe and needle to the device threshold, second pushing the needle into the target until the front of the syringe hits the inner casing, and third pushing the contents of the syringe out of the needle.

To accomplish the correct dosage, the plunger needs to advance the correct distance. First until it is at the threshold of the device (4mm), than one inch to reach the full depth of penetration (1in = 25.4 mm), and then far enough to inject 0.3mL from a 3cc syringe (measured 1.35cm/mL, so 0.3mL*1.35/mL=4.1mm). This means the plunger of the syringe must advance 33.5mm for both the first and second dose to deliver the correct amount of epinephrine. This distance is accomplished through the distance between and thickness of the cylinders for the first

dose, and the distance between the second cylinder and the ‘spring ledge’ on the inner casing (Figure 19).

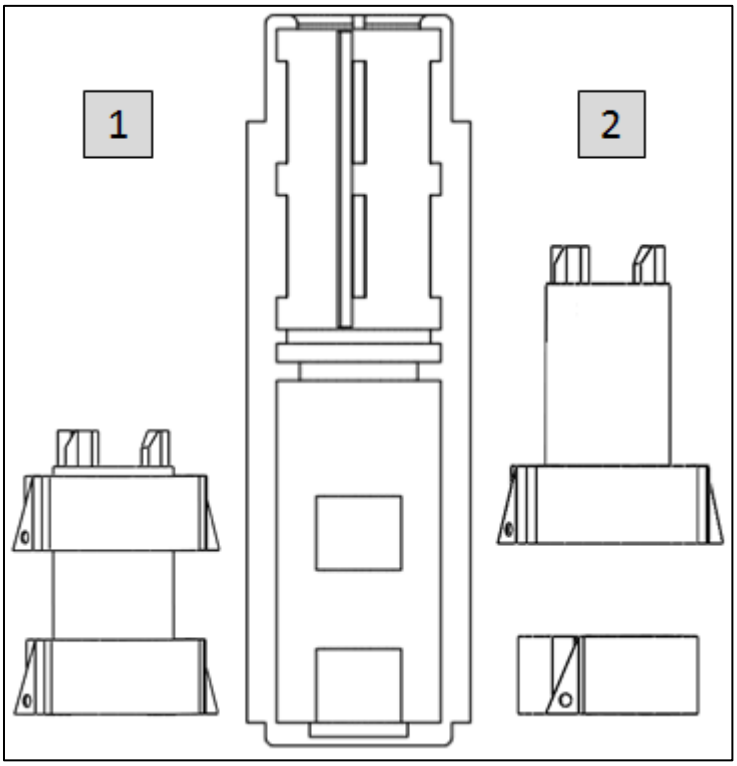


Figure 19: Injection Schematic. The spring container travels 33.5mm from the first cylinder to the second cylinder and an additional 33.5mm from the second cylinder to the first lip on the inner casing. This image illustrates the 1-2/3 possible positions of the spring container.

Needle Covering

After a dose of epinephrine is administered, the needle must be promptly covered to prevent accidental stabbings and protect the needle. This is accomplished through having a needle cover in which the distal end can rotate freely of the proximal end while they are locked together coincidentally. The proximal half, responsible for covering the needle, is rotationally locked to the inner casing via ridges (Figure 20). The distal half consists of four spokes which lock in place with the inner casing preventing any forward movement by the entire needle cover (Figure 21). When an injection takes place the spring container advances and has a geometry that

meshes with the needle cover causing the distal half to rotate and advance only as the plunger reaches its final position (Figure 22). The advancement is driven by a lower k spring than the main spring, located between the spring container and needle cover and fit around the syringe. As the cover advances, taut elastic bands rotate the needle cover into the locking position for the next position.

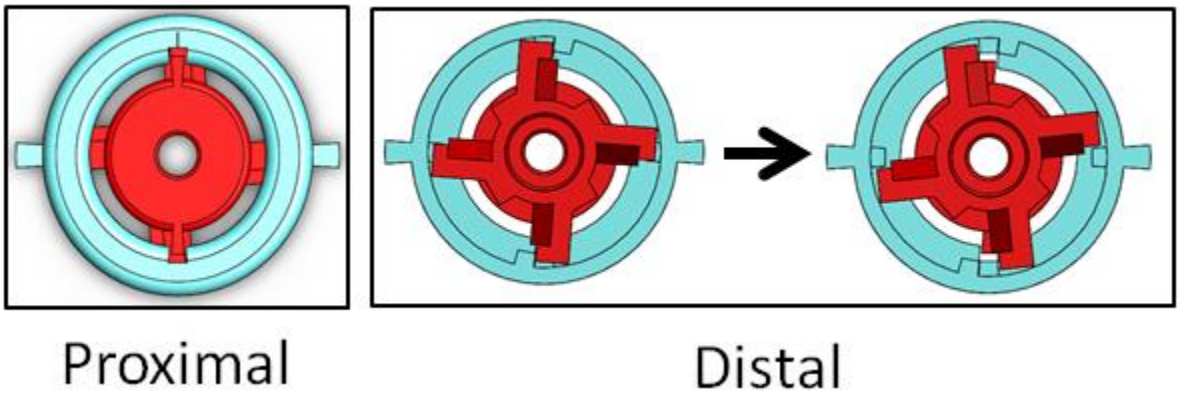


Figure 20-21: Design of Needle Cover. Proximal end of needle cover (red) locks inside of ridges of inner casing (blue). Distal end is impeded by lip on inside casing but is freed when rotated.

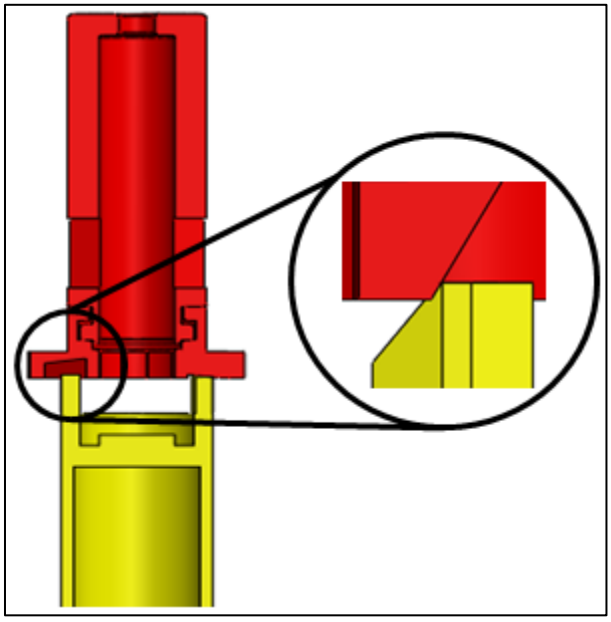


Figure 22: Exploded view of needle cover top. The top of the needle cover interacts with the distal end of the needle cover causing it to rotate counterclockwise and free it from lip on inner casing.

Push Action

Like the EpiPen®, this device is activated by jabbing the device into the outside of the thigh. This is accomplished by an outer casing that protrudes from the proximal end of the device (Figure 23). When the device is jabbed into the leg, the proximal end of the outer casing slides backwards towards the body of the device until it becomes flush with the proximal end of the inner casing. This causes two inclined planes to articulate with the planes of the first cylinder causing the cylinder to rotate CCW, release the spring container, and deliver the first dose (Figure 24). Since the outer casing must move independent of the inner casing, the user needs to be able to grip the inner casing while administering the dosage. This is accomplished by a cylindrical grip attached to the inner casing that attaches over the outer casing allowing it to slide freely underneath (Figure 25-26)

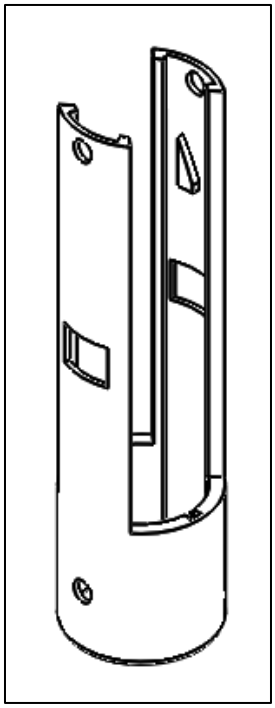


Figure 23: Push action cover featuring inclined planes that mate with the cylinders and holes for linchpins to lock in place. The top hole is necessary for manufacturing reasons so that end can be slid over the device initially, the second hole will act as a safety and must be removed prior to activation.

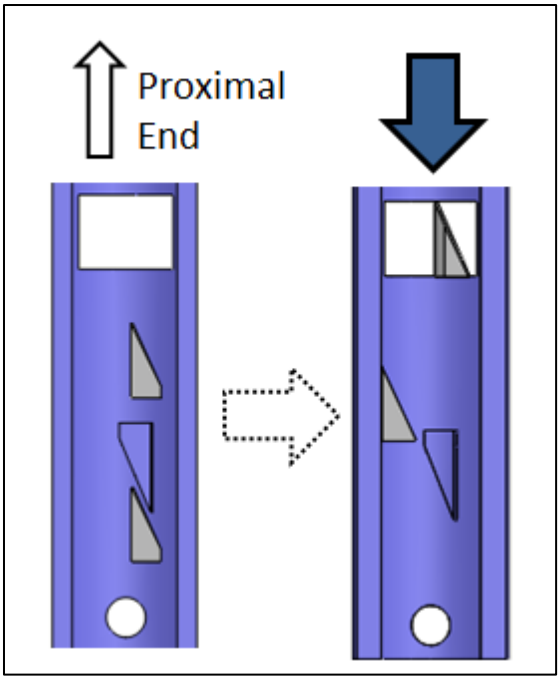


Figure 24: Cross section push action. When the proximal end of the outer casing is depressed, the first cylinder is rotated. Additionally, its advancement locates a cutout window directly above the second cylinder allowing it to be rotated by hand if the second dose becomes necessary.

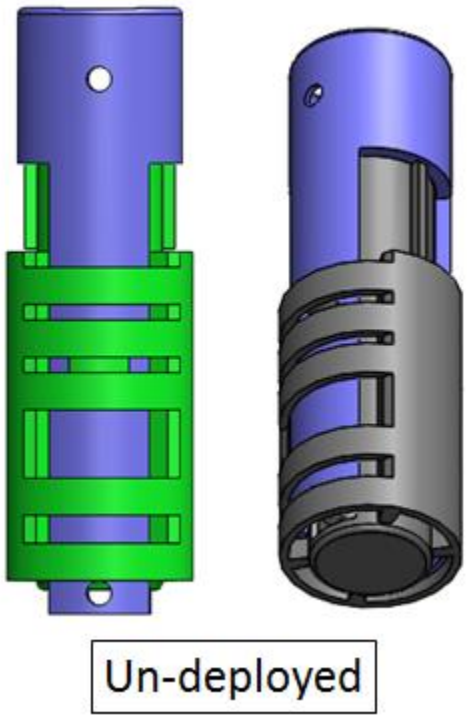


Figure 25: Push action un-deployed. When un-deployed, the inner casing can be gripped easily to allow push action deployment of epinephrine auto-injector.

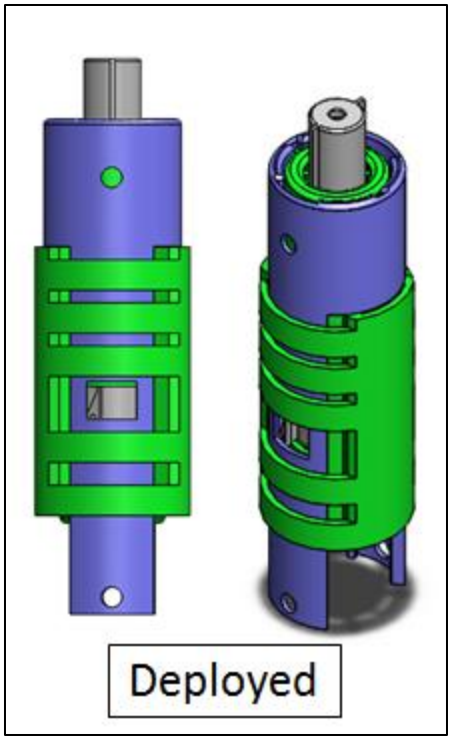


Figure 26: Push action post deployment. After deployment, a window allows access to the second cylinder. If necessary this can be rotated manually to administer second dose.

4. MANUFACTURING

3D Printing

This device has been successfully prototyped using 3D printing using standard extrusion techniques as well as UV curing. The primary machines used were the Stratasys OBJET CONNEX 500, the Stratasys Dimension, and the MakerBot Replicator. While these printers allow extremely fast prototyping with high resolution and low cost, this technique does introduce some limitations. First and most apparent is the inability to print parts inside of each other, this is significant primarily because the cylinders need to be nested inside of the inner casing and also because other parts need to be placed inside or around each other. The primary design response to this constraint was to print certain parts in half and then glue them together after placing the

interlocking parts in their correct location. This resulted in both the inner casing and part of needle cover to be printed in half and assembled post extrusion.

For prototyping purposes clear scotch tape was used to attach the halves of the casing as it allowed parts to be freely assembled and taken apart while providing adequate mechanical strength. For the needle cover however, a different technique was needed to ensure it could stand up to the mechanical stresses while also rotating freely. The primary challenges are that 1) the distal end needs to rotate freely from the proximal end, 2) the distal end experiences significant forces in the proximal and distal directions, and 3) the distal end experiences significant moments due the length of the spokes from the center axis. The first two challenges mean that the two parts need to interlock so that while they are able to freely rotate with minimal friction they also need to have a strong enough interlock to maintain their connection even under large forces.

The solution came somewhat experimentally through multiple rounds of prototyping. Since, in general, 3D extrusion produces prototypes that are as much as 1 layer larger than designed in all directions, significant tolerances had to be accounted for in the design. On top of this additional layer, often not all support material was readily removable further complicating the fit. Through trial and modification, eventually a dimension was found that allowed the two components to interlock well. At this point it was discovered that the current method, having a transverse cross-section of the entire distal component was not mechanically stable as when under proximal forces, the two sides tended to bend inward ruining the integrity of the joint. The solution found was to cut the distal end into three parts. The top most part with the spokes was left intact and separated from the interlocking pieces which were in turn cross sectioned to be

attached to the proximal end. The interlocking pieces were then glued to the spokes keeping the entire unit together. (Figure 27). This development is explored further in the prototyping section.

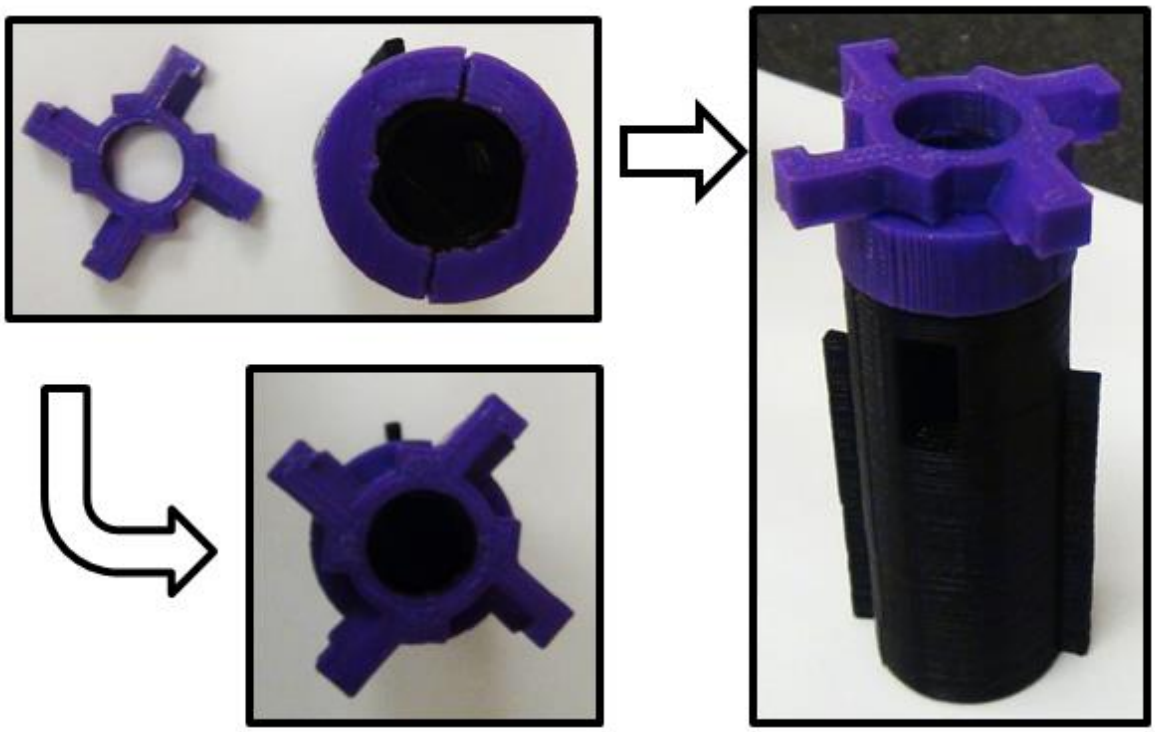


Figure 27: Needle cover assembly. The two rotating halves are placed around distal end of the needle cover and glued. Next the rotating wheel is glued on top of these, helping to hold them together.

Springs

The main spring (ref. McMaster 9657K449) used to drive the injection is a 3.5” steel compression spring with an outside diameter of 0.6” and a spring constant k=2.7lbs/in. Since our required length was closer to 5”, two springs were bound together using 28g bronze wire and one of the springs was trimmed using bolt cutters. The smaller spring (True Value Hardware) used to the drive the needle cover was cut to 1.5” with an outside diameter slightly wider than 0.6”. Importantly, this spring fit around the syringe and had a spring constant significantly lower than the main spring.

The spring constants used in this prototype are significantly lower than those used in the EpiPen with the main spring reported around 8.5lbs/in (K. Ghoreshi "Redesigning…EpiPen…" U. Conn.). The main reason for the use of such a less resistive spring comes down to assembly capabilities and safety. The forces required to compress such a spring would require the use of machinery and would slow the prototyping process. In a final design a more resistive spring would be used, and individual components would be tested to ensure they could withstand the additional mechanical stresses introduced by this.

Sterility

The sterility of the entire device, and especially the needle, the syringe, and its components are of the utmost importance. The EpiPen's needle is covered in a protective sheath to help it maintain its sterility. Furthermore, its epinephrine is sealed in an ampoule instead of a syringe protecting it from the elements. A sheath could easily be incorporated similar to the EpiPen® to maintain its biological integrity prior to injection. Problems, however, are introduced after the first injection as the needle has now been exposed to elements including skin and possibly soiled clothing.

However, this is likely not an issue. Since the majority of possible antigens entering the body will be from the path of the needle between the device and the muscle, there is little that can be done to eliminate this. This is a potential issue with all epinephrine auto-injectors and yet the ease of use and the extreme consequences of not using the device seem to greatly outweigh any possible risks of infection. The additional risks of infection by using the device twice within 30 minutes instead of just once would seem to be miniscule. A large increase in risk of infection however would occur if the device is not used as directed. Specifically, if it is used on two

separate occasions or on two different patients. The best way to combat this improper usage would be sufficient labeling and education.

Integrity

The majority of the device is quite robust and should not be damaged during normal use or wear and tear from carrying the device. However, the elastic band meant to keep the needle covering mechanism locked could lose its elasticity over time due to mechanical creep. The lifespan of the elastic bands would need to be tested to ensure there durability throughout the lifetime of the device.

Evaporation of the epinephrine solution is of significant concern as it could be quite significant given the time between the manufacturing and use of the device. Implementing a tight fitting rubber cap to the needle, similar to the EpiPen, could do a lot to minimize evaporation. Additionally an ampoule model that is only punctured on injection would prevent all evaporation prior to the first dose. As the model is currently designed with a syringe, testing would need to be performed to ensure evaporation is negligible over a relevant time period (>12 months).

5. PROTOTYPING

Spring Containment

The double dose epinephrine auto-injector has been through many prototyping stages. These prototypes have proved invaluable in testing the performance of parts and noting where certain parts may fail. The first part prototyped was the spring holder and its fit within the cylinder. The cylinder design has remained largely unchanged throughout the prototyping process while the spring container has seen some dramatic changes as the method for needle

covering has evolved. The two parts interlocking with the necessary tolerances can be seen below (Figure 28-29).

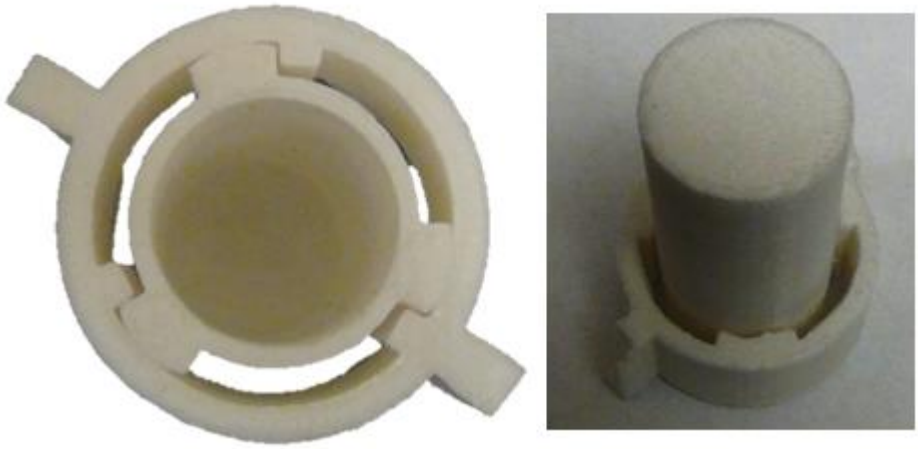


Figure 28: Spring Containment Prototype. The two parts interlock as expected; the spring casing can freely slide past when released.

Figure 29: Cylinder Prototype. Cylinder has remained primarily unchanged since the initial design. The dot is used for manufacturing ease due to this parts chirality. The dot belongs on the slot opposite the side of the inner casing with groove.

The spring container has seen several significant developments from its initial design. Firstly, a groove was engraved down its length designed to mate with the groove on the inner casing. This prevents rotation of the spring container, insuring it is released when the cylinder is

rotated. Next, when the method for covering the needle changed, the proximal end of the spring container was modified to allow for a smaller nested spring to propel the needle cover and to rotate the needle cover to unlock it. Three ridges were used instead of four so as to not interfere with the groove (Figure 30).

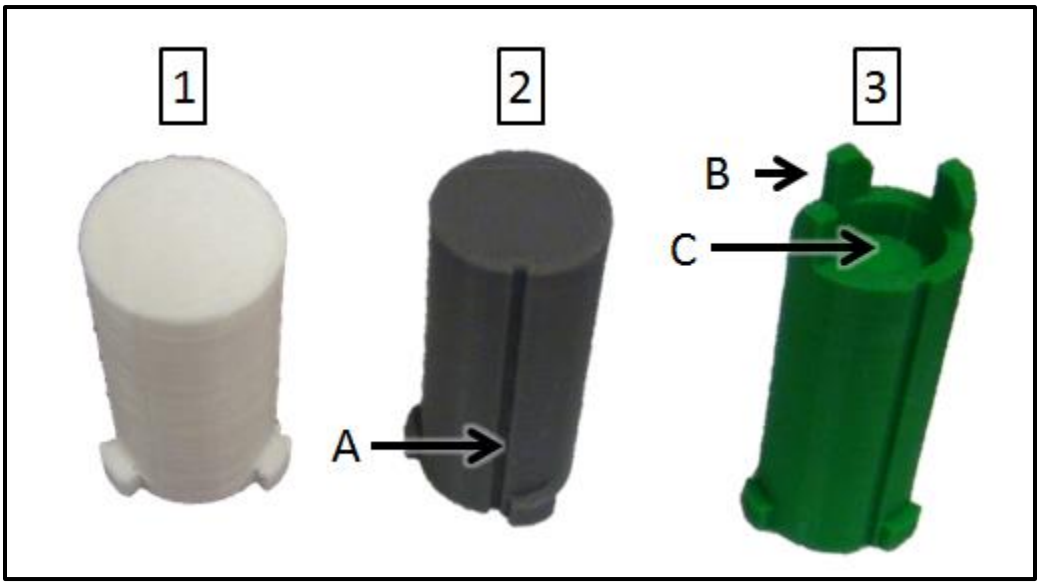


Figure 30: Three main prototypes of spring container. The first design was the most simple, meant to contain a spring and mate with the cylinder. The second design implemented a groove [A] to prevent rotation within the inner casing. The third design added ridges to rotate needle cover [B] as well as an indent to nest the smaller spring [C].

Inner Casing

The inner casing has evolved extensively to reflect changes in device function as well as the size and shape of all other parts. The first prototype for the inner casing featured slits for the cylinders and a bore hole at the proximal end meant for the most primitive needle cover. It also featured a ridge to stop the spring container during the administration of the second dose (Figure 31)

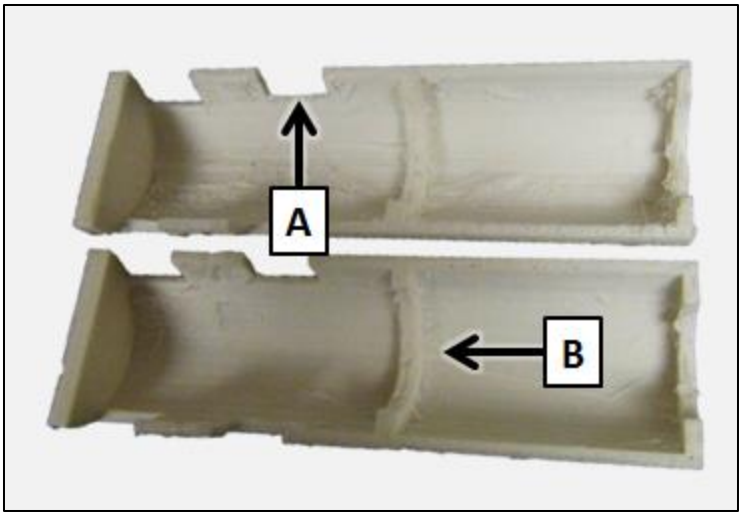


Figure 31: First Prototype Inner Casing. This prototype for the inner casing features slots for the cylinders [A] and a ridge to limit the advancement of the spring container during the second dose [B]. Visible in this prototype is physical noise and scaffolding material sometimes associated with 3D-printing.

The next prototype for the inner casing made some substantial changes. First, the cross-section axis was changed so the slots for the cylinders were complete in each piece. Additionally, geometry was added to the proximal end of the device to allow needle cover to advance but also to lock out. A groove was added at the injection end to prevent rotation of the needle cover and an indentation was added at the distal end to allow the main spring to nest partially. Finally a groove was added to prevent the needle cover from rotating independent of the inner casing (Figure 32).

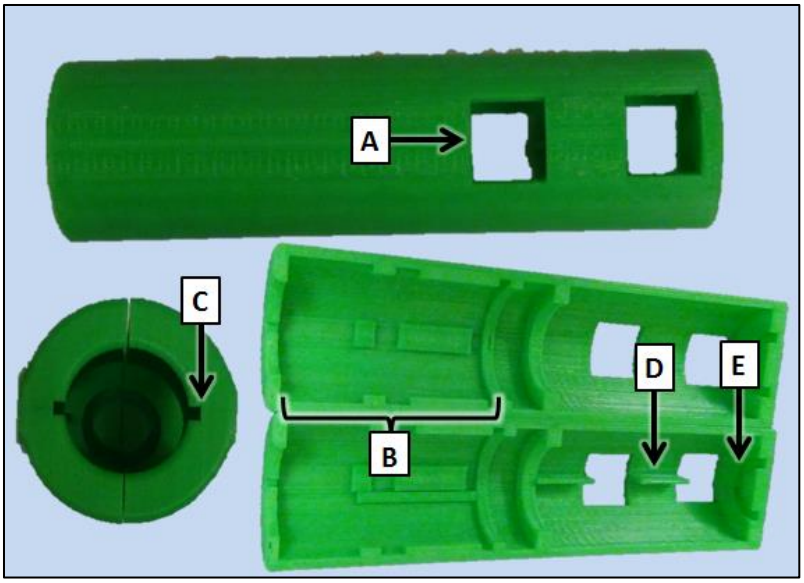


Figure 32: Inner Casing Updated Prototype. The cross section has been rotated 90° to allow cylinders to nest better [A]. Geometry has been added to allow spring holder to lock out [B], slits added to prevent rotation of spring holder [C], a groove to prevent needle container from rotating [D], and a notch engraved to nest the main spring [E]. Notice that this print appears with much less noise or scaffolding present than the previous prototype, print quality was often variable.

Needle Cover

By far the most complicated part of the design, the needle cover went through a continual evolution with its form changing dramatically. Initial designs tried to mimic the behavior of the EpiPen® with locking ridges that could be compressed by the syringes movement to allow the needle cover to advance and lock in place. It quickly became apparent however that this technique was not possible given the material properties of PLA which left parts strong but not flexible. After two prototypes in which the lip broke off, it was decided a different technique was needed (Figure 33).

Figure 33: Early prototype of needle cover. Lip indicates where the ridge intended to lock in place broke off.

Next it was considered that the needle cover could have a piece that rotated freely and lock on the inner casing similar to how the needle container does. Since the user will be able to touch the proximal end of the needle cover, the proximal part would have to be locked to prevent rotation with the distal part allowed to rotate independent of the proximal end. To get the two parts to lock concentrically but allow the distal part to rotate required a very precise fit, this was improved through several stages of prototyping. An example of an early prototype with poor fit and sequential prototype with an improved fit can be seen below (Figure 34).

Next a method for effecting the spokes to rotate when the dose is administered was installed. Large windows were cut into the sides of the needle cover and small nubs were added above these windows and onto the rotating end. The theory here is that a wire could be fixed to the syringe, run over the nub and attach to the rotating part. When the syringe is pulled down, thus pulling the wire, the nub will act like a pulley converting the downward movement into a sideways pull thus rotating the spokes. Early prototypes proved this method was plausible but that the nubs would not be sufficient for directing wire (Figure 35).

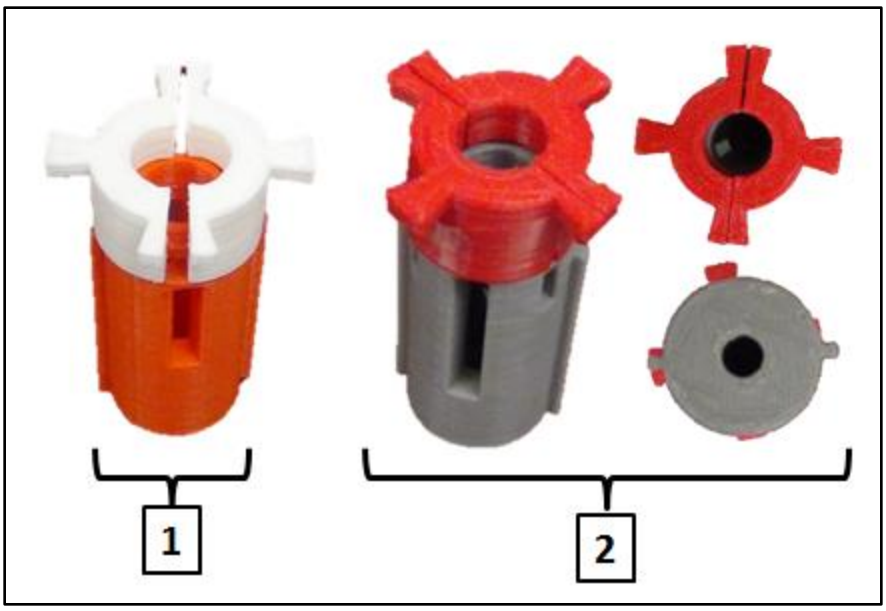


Figure 34: Needle Cover prototype with spokes. An example of the rotating spokes having a poor fit [1] and an improved fit [2]. At this point the two halves were glued together as shown.

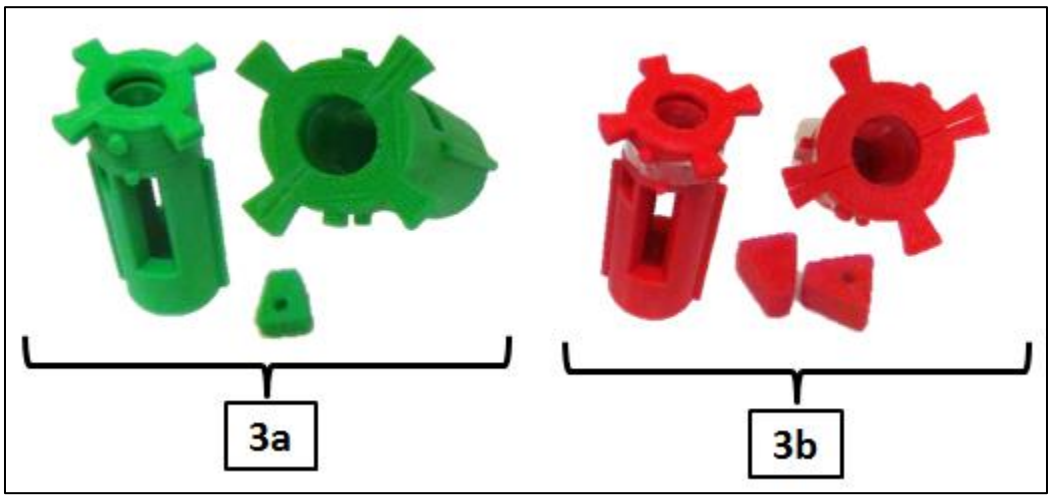


Figure 35: Needle Cover prototype with pulley system. The nubs found on both the body were meant to guide the wire while the nubs on the rotating parts are attachment points for the wire. The small cutouts seen below the needle covers were intended to be attached to the syringe to serve as a wire attachment point but that idea was abandoned.

The next prototype made three developments upon previous designs. First, instead of nubs, small loops were installed just above the window that proved to be much more effective at containing the wire. Additionally the cutouts were abandoned in favor of attaching the wire

directly to the syringe. Finally the rotating part was divided into three parts to be glued together during manufacturing instead of two to improve its strength and stability (Figure 36).

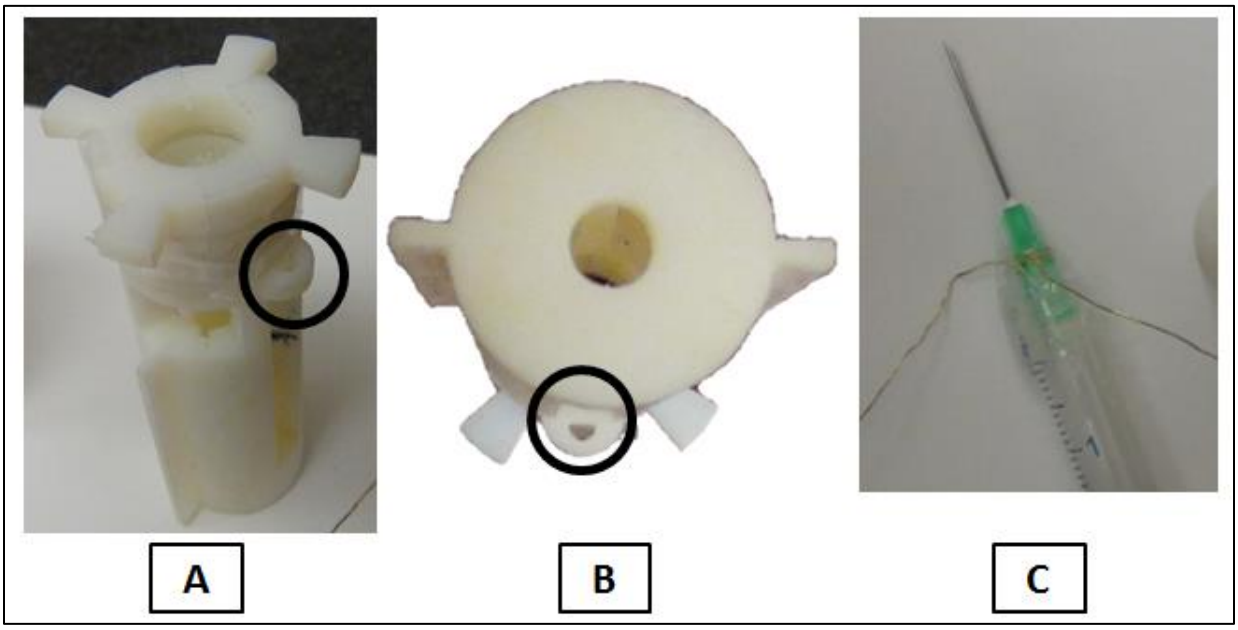


Figure 36: Needle Cover prototype with wire loop. The prototype for this needle cover introduced a loop for the wire to pass through [Circled]. Additionally, the rotating top was subdivided into three sections to improve structural integrity. Finally the wire was wrapped around the front of the syringe instead of being attached to the sides [C].

While early tests of the prototype shown in the figure above demonstrated the concept did work, it did have a few disadvantages. The primary disadvantage was that it required the needle to be very visible to the user due to the large slits along the sides. Additionally it introduced some logistical challenges as the wires had to be precisely the correct length otherwise they would either release the needle cover too early or not release it at all.

This was all amended with the final design for the needle cover release mechanism. This introduced spokes that featured inclined planes that are rotated when the needle container advances to its most forward position. This way the needle covering mechanism behaves

independent of the needle movement and can be tweaked by modifying the spring container. The design and how it mates with the spring container can be seen below (Figures 37-39).

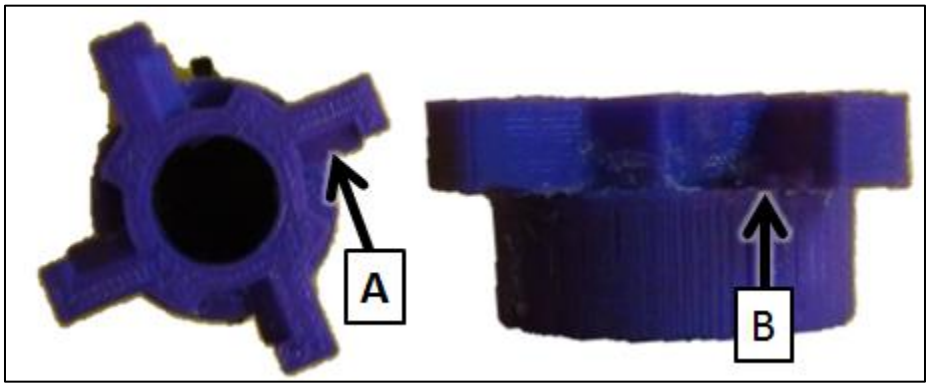


Figure 37: Rotating spoke attachment for needle cover. Inclined planes allow it to be rotated when spring container advances [A]. The top is glued to the bottom piece to hold everything together [B].

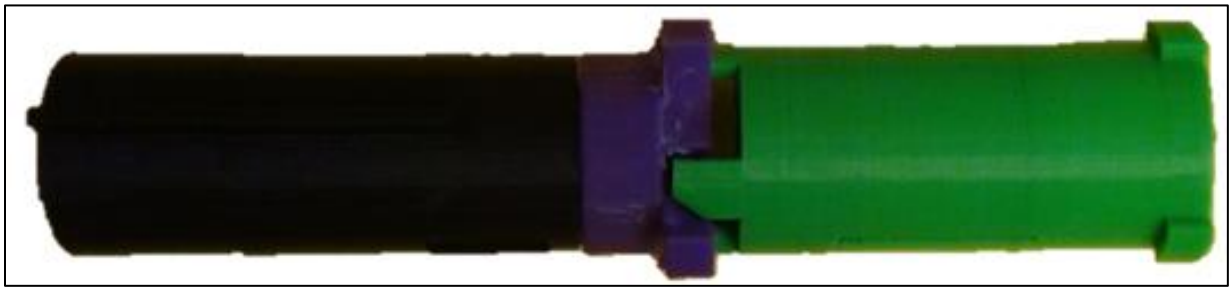


Figure 38: Spoke, spring container composite. Here the two pieces can be seen meshed together. As the spring container is rotationally locked, when it advances the spokes are forced to rotate.

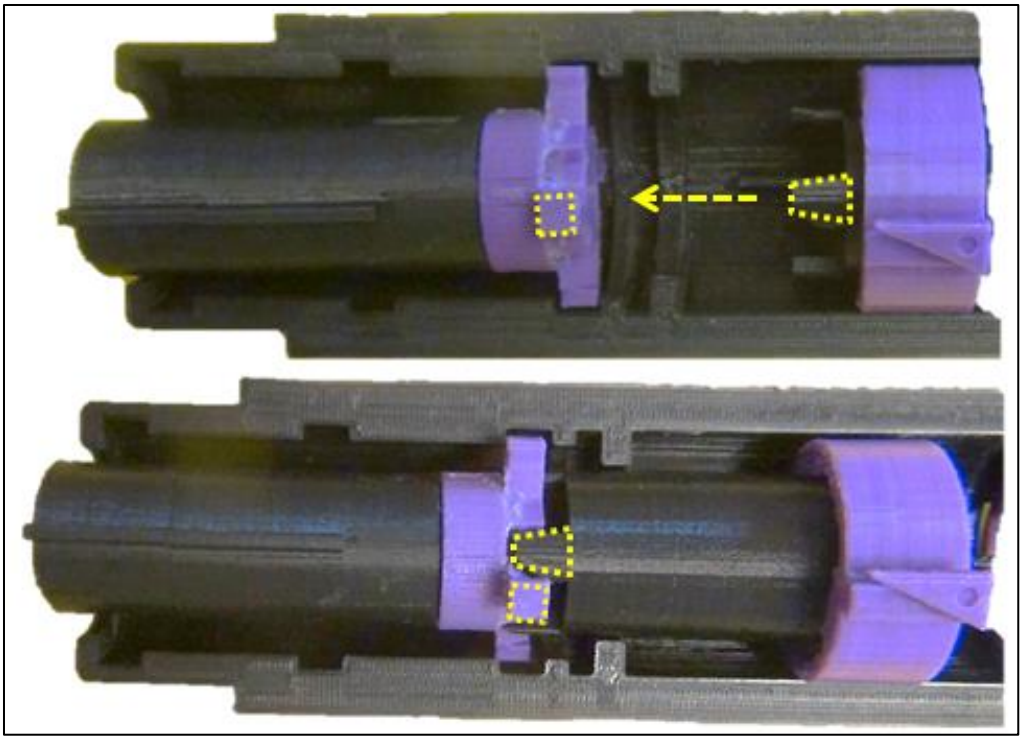


Figure 39: Movement of needle cover and spring container. Here the spring container advances to meet the needle cover and rotates it to unlock the needle cover from the inner casing.

Lock Out

To properly lock into place, the needle cover spokes need to have a strong tendency to rotate clockwise so they can mesh with the geometry of the inner casing. While initially torsion springs were intended going to be used. It was determined that elastic bands could be attached to both the straight and rotating part of the needle cover and perform the desired function. The bands were glued to windows inside the straight section and to the top side of the spokes (Figure 40). The bands were affective at forcing the spokes to stay locked in place, and locking them in play once they enter a region where they can after either the first or second dose (Figure 41).

Figure 40: Elastic band assembly. Rubber bands are stretched when needle cover is installed in inside casing, compelling it to stay in locked position.

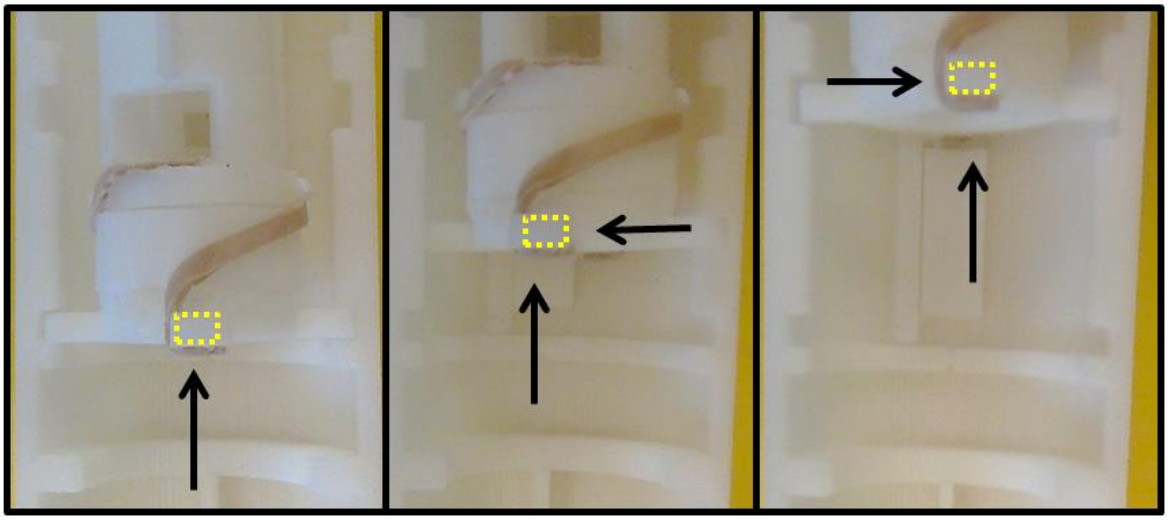


Figure 41: Rubber band assembly in situ. When the spokes are rotated and unlocked it is able to advance forward, once they reach the open window they snap into place.

Final Assembly

Below is an image of the all inner parts assembled inside half of the outer casing including the syringe, and small spring; followed by an image of the entire device assembled (Figure 42). The main spring is left out in these images as it would not be visible and would be difficult to keep in place. The final prototype at this time does not match the final planned design. The updated push action setup is in queue to be printed by the Stratasys Dimension.

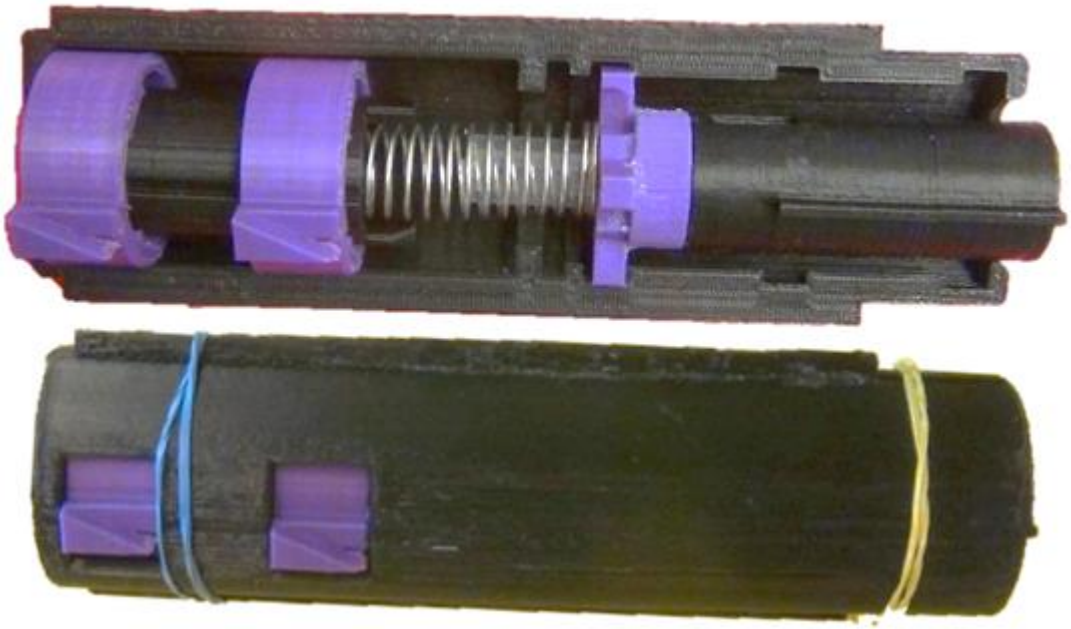


Figure 42: Final Prototype Assembled. Shown here as both a cross section and held together with rubber bands.

Future Work

The final design still needs to be printed and assembled. The needle cover will be glued together as will the inner casing once everything is placed correctly. A 3cc syringe will have its plunger trimmed so that when the syringe is in the proper position holding 1 mL of solution it will be flush with the front of the spring container. A piece of cellophane will be glued over the inside end of the needle cover to prevent dirt and bacteria from getting in contact with the needle. This will be easily punctured during injection.

Before increasing production substantial testing will be performed to ensure that the device can function in all conditions including after normal wear and tear and being held in any orientation. Testing will be performed to ensure the proper dose is administered at the correct depth by utilizing gelatin models. A working prototype is scheduled for demonstration on May 8th.

ACKNOWLEDGMENTS

This project would not have been possible without the help and support of the Union College collaborative design studio. Their equipment and helpful staff provided the backbone for prototyping this project in a rapid fashion. Special thanks to Josh Fields for taking primary oversight over this work. Likewise thanks to Stan Gorski for providing high quality prints on his equipment and for guidance throughout the project. Other thanks for this project go to Andrew Rapoff PhD. (force plate analysis), Steven Rice PhD. (scaffold removal), Jennifer Currey PhD. (Weights for spring analysis), the Boston Museum of Science (early prototyping), Lisa Galeo (fund management), and everyone else who has offered their equipment or advice throughout.

Special thanks to the Union College Bioengineering department and Union Student Research Grant (SRG) Committee for providing funding. This project would not have been possible without the wisdom and guidance of Takashi Buma PhD.

APPENDIX

Trigger Force Calculation

To determine the activation force needed to trigger the EpiPen a Passport 2-Axis Force Platform was coupled with an Xplorer GLX data acquisition module. A large nut (>1" length) and washer were placed on top of the force platform such that the needle could protrude without hitting anything when the EpiPen® is activated. The force platform was zeroed and set to acquire at 2 kHz. Two trials were conducted, in the first trial an arm swing meant to approximate the motion recommended to use the EpiPen® was performed to get an idea of how much force would be administered by the average person (Figure A1) and in the second trial the EpiPen had more and more force applied to it until it fired revealing the minimum activation force (Figure A2-A3) The activation force was determined by looking at the force data and identifying the highest force applied before the rapid spike indicating the firing of the EpiPen®.

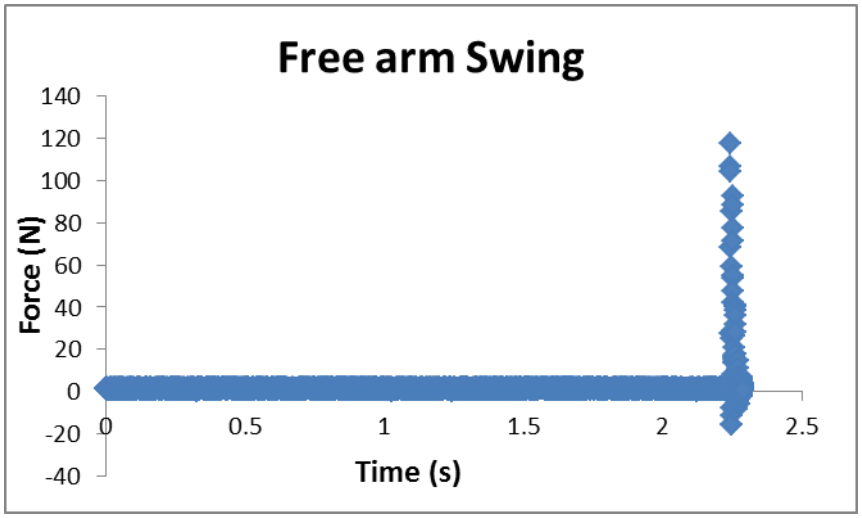


Figure A1: Force applied during EpiPen swing is around 120 N or around 27 lbs. captured using PASCO Capstone software.

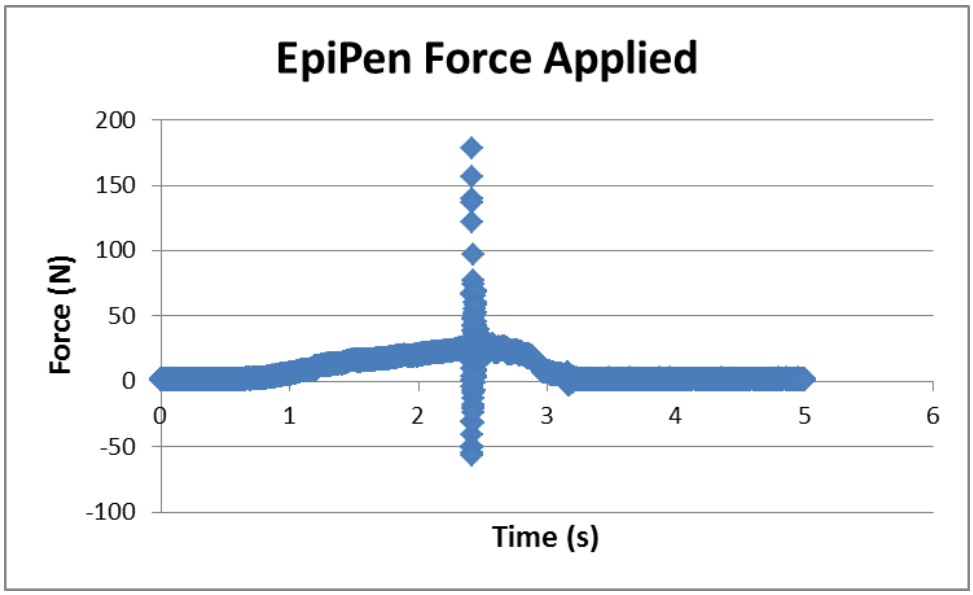


Figure A2: Force applied to activate EpiPen®, the large spike corresponds to the firing of the EpiPen.

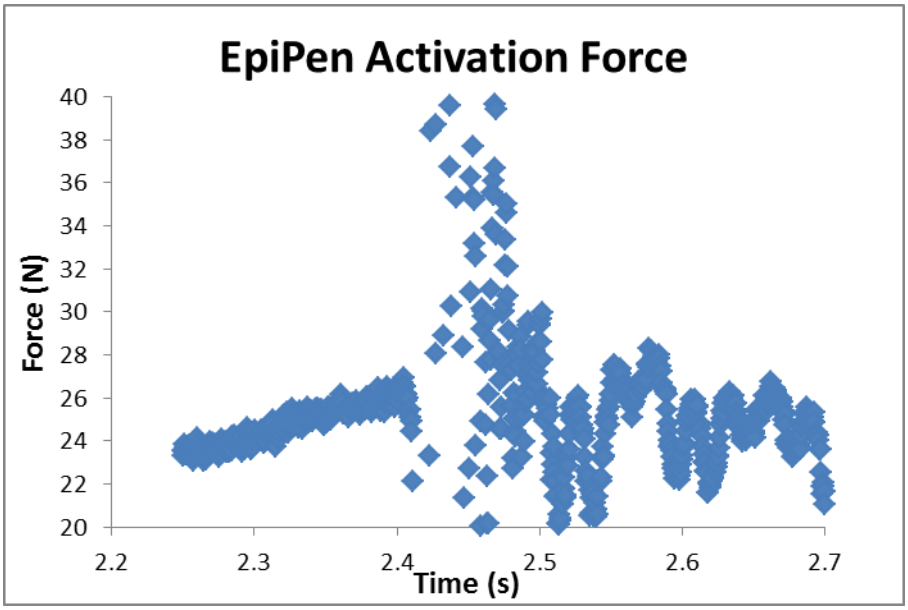
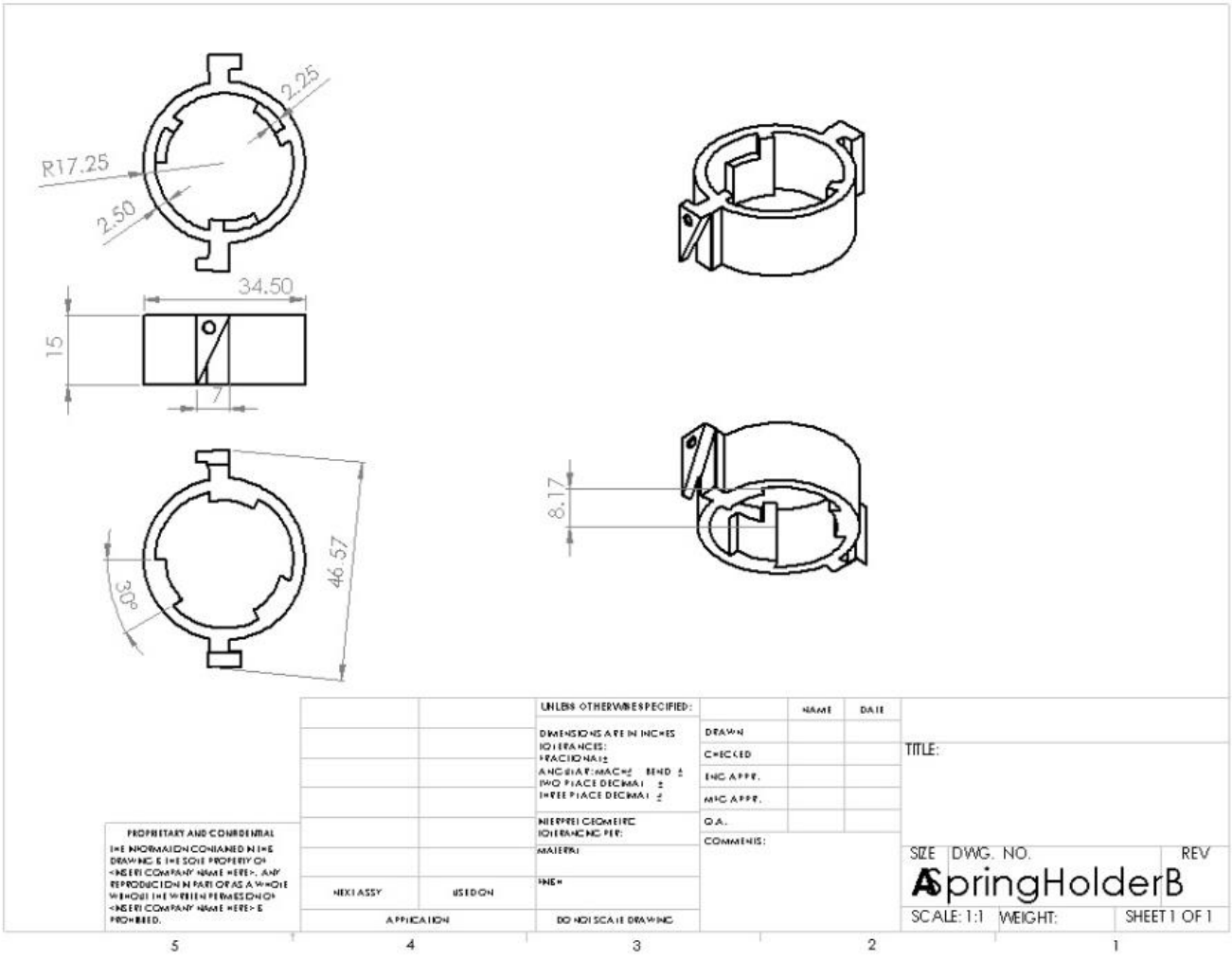


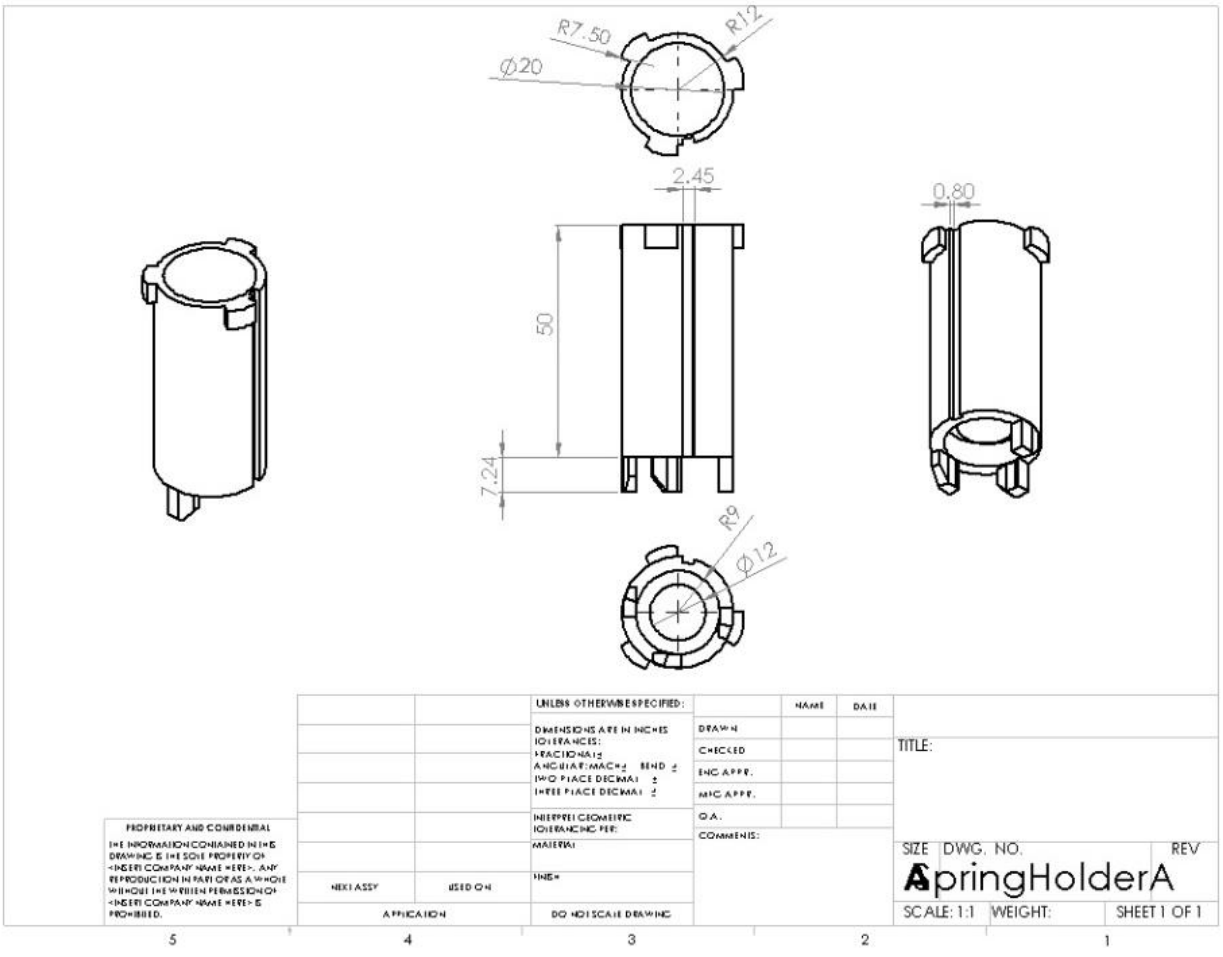
Figure A3: Force applied to the EpiPen® focused to the time around activation. The needed force applied for activation is 27N or 6 lbs.

Knowing this activation force is valuable in constructing a prototype as that force can be established as a baseline for what is appropriate in a typical epinephrine auto-injector.

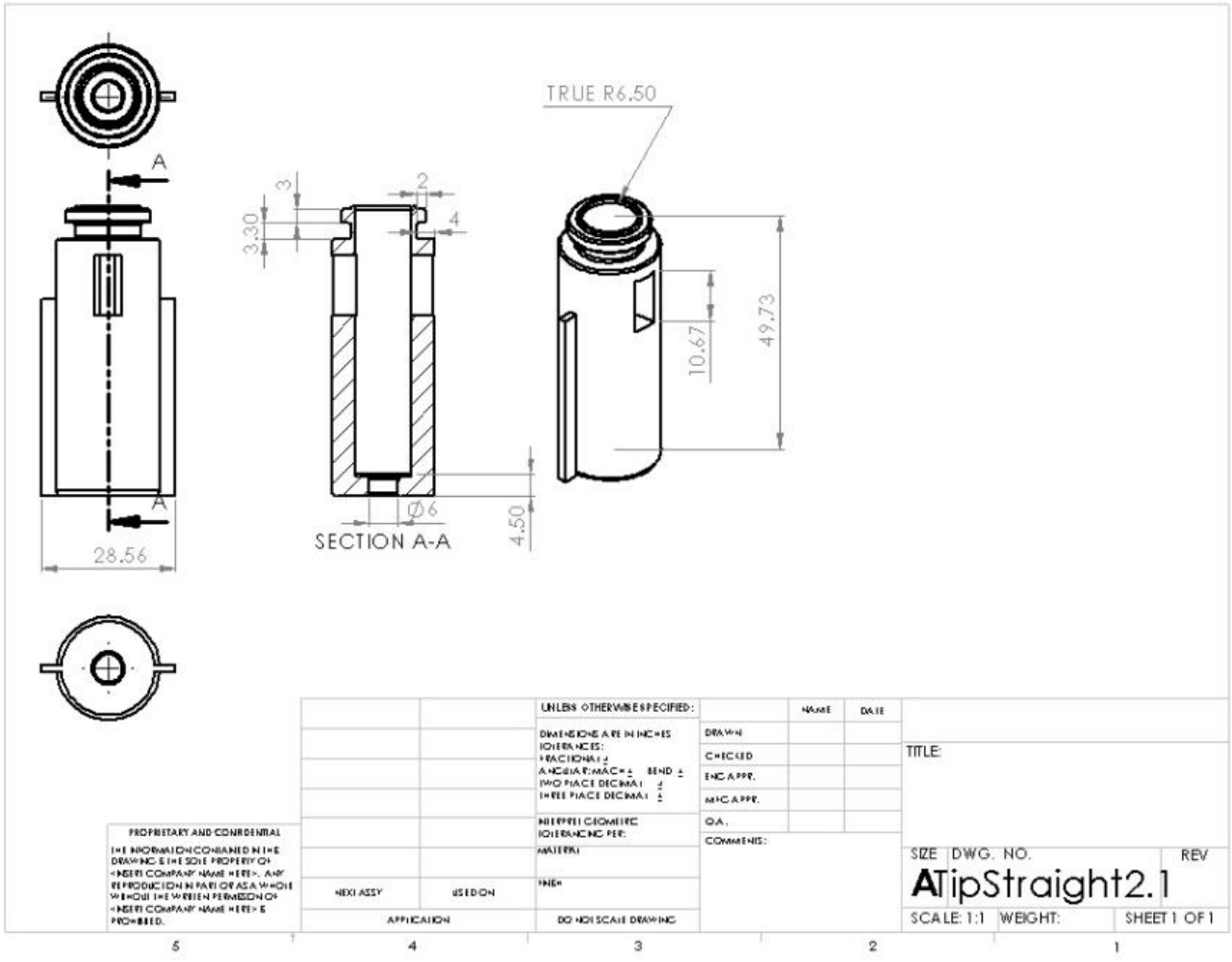
Drawing Cylinder



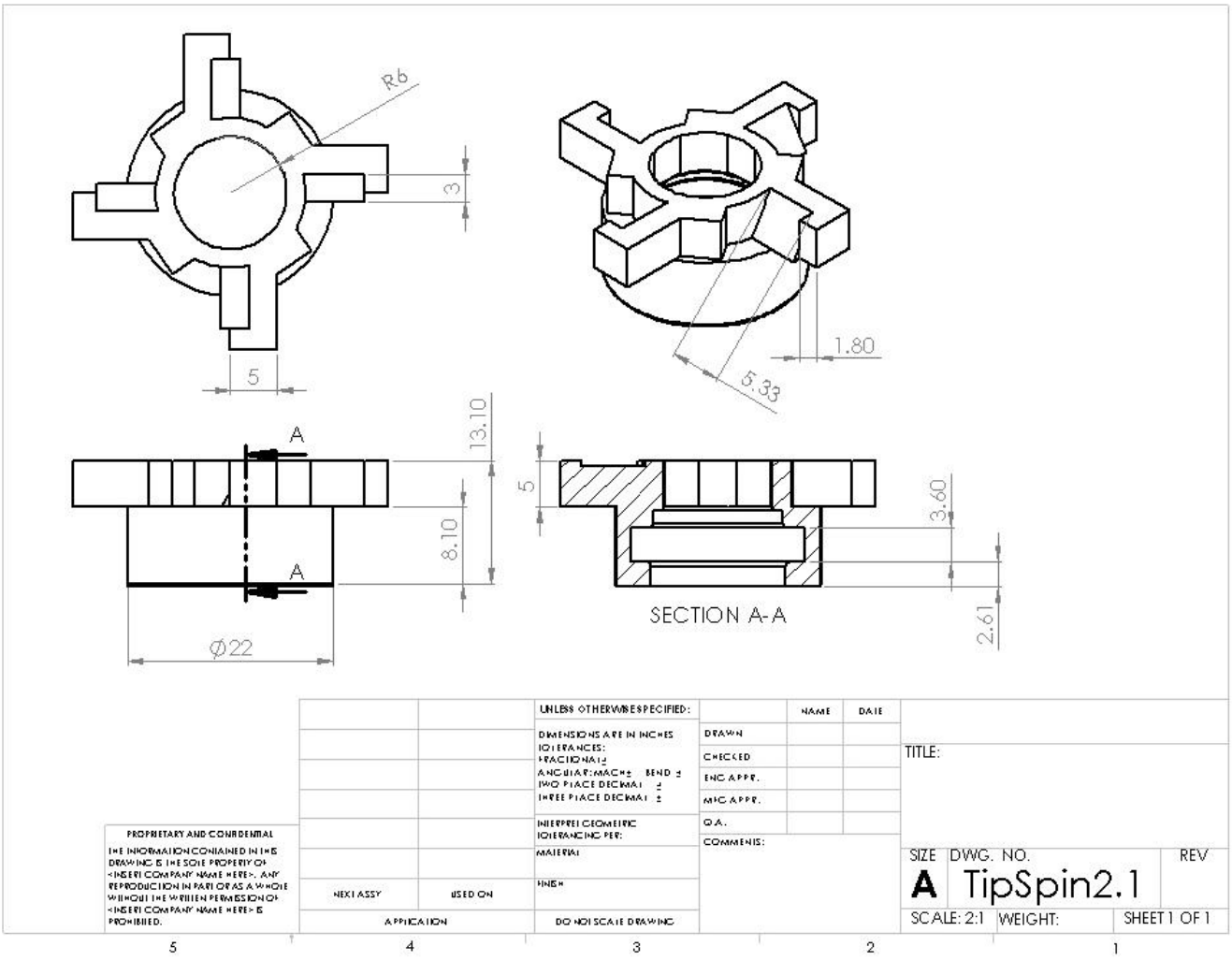
Drawing Needle Container



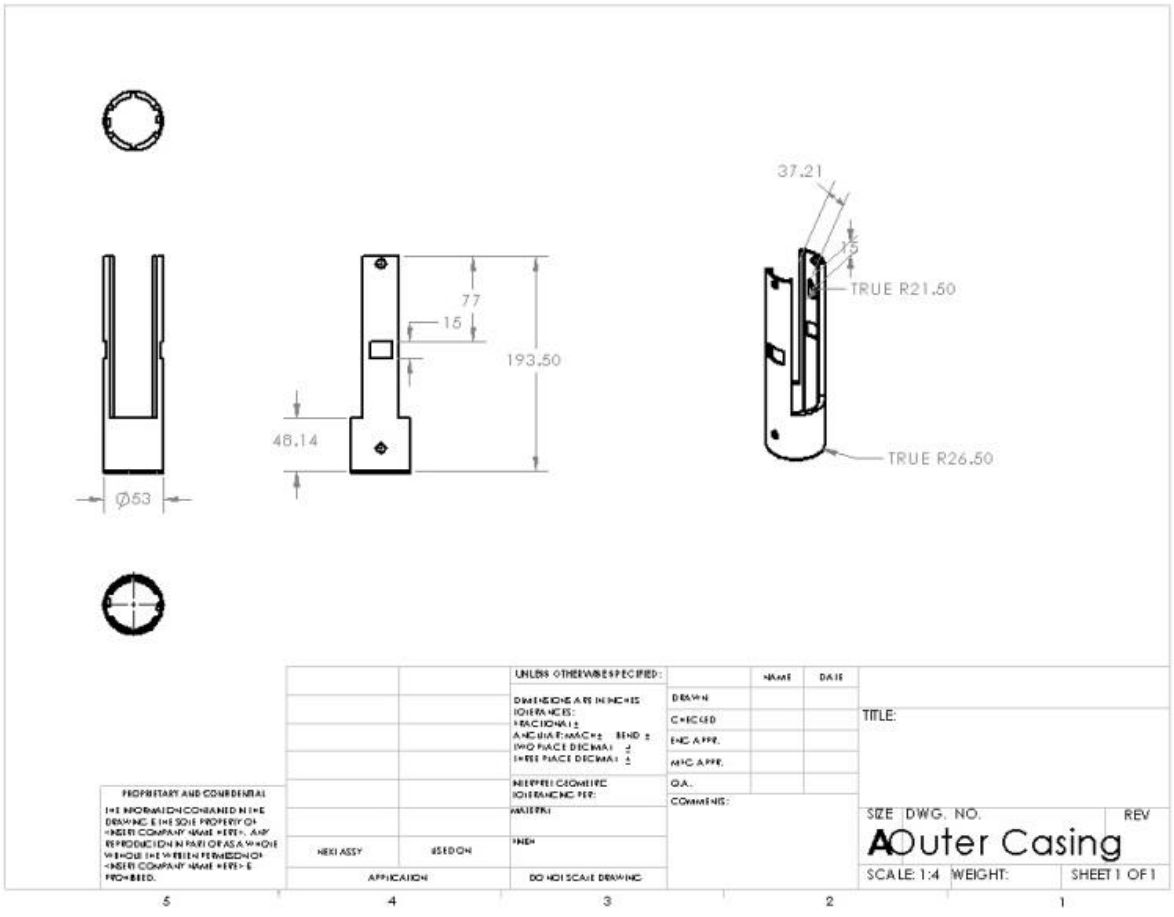
Drawing Needle Cover Straight



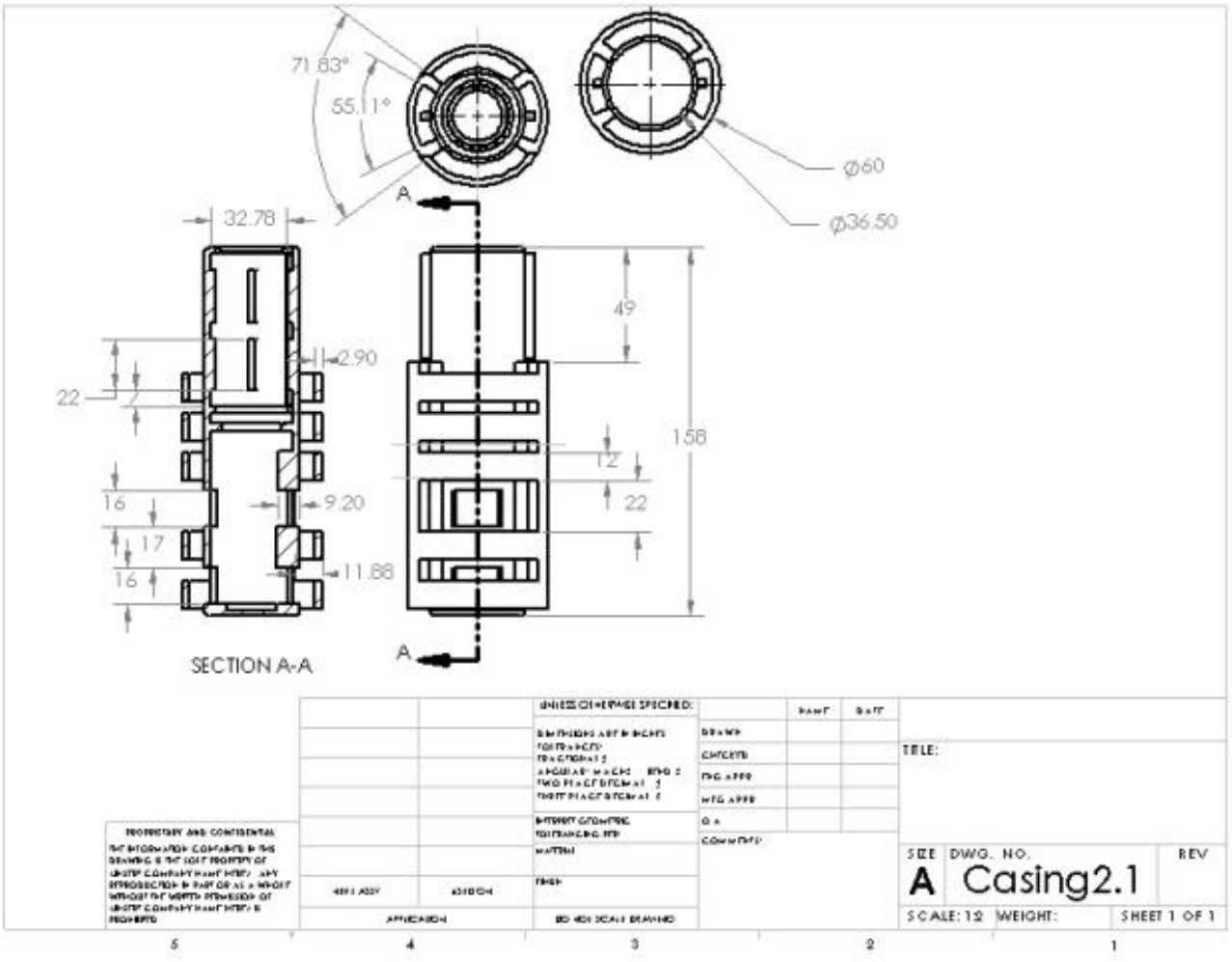
Drawing Needle Cover Spokes



Drawing Push Action



Drawing Inner Casing



Drawing Inner Casing Old