Design and validation of a subdermal actuator for use in a dynamic arteriovenous shunt system

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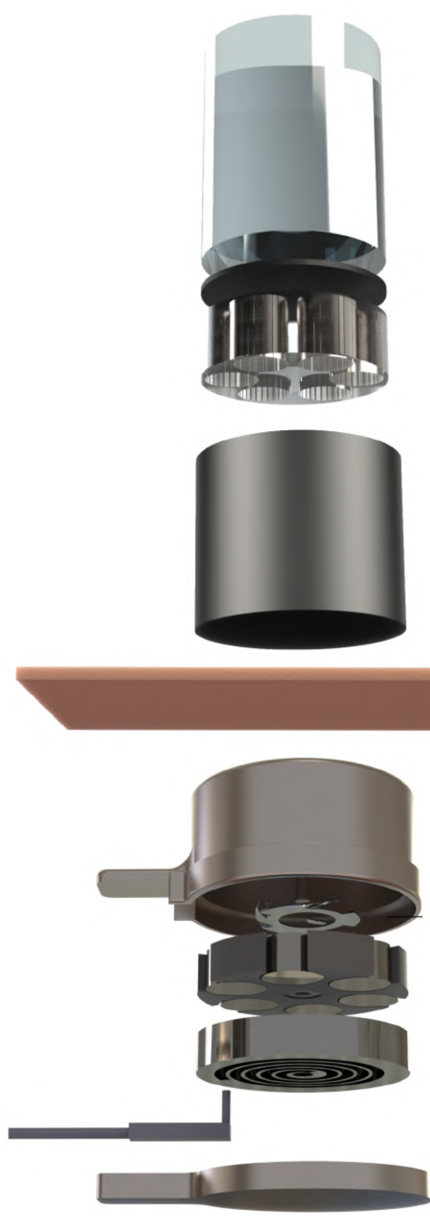
January 2020



Design and validation of an implantable actuator for use in a novel arteriovenous shunt system

by

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TU Delft

Preface

As I am finishing writing up my master thesis and therefore my time as a student, the world outside feels silent and empty. I started working on my master thesis just about when the COVID-19 pandemic hit our country. At times, this was an added challenge; waiting on the the research at the LUMC to continue and the labs to open, no access to the university library, digital meetings, etc. However, through perseverance and collaboration with all the great people involved, this thesis project still managed to turn out as a success.

I would like to thank my daily supervisor Tim Horeman for the opportunity to be a part of this interesting project, as well as his supervision and expertise. I would also like to thank my other daily supervisor, Joris Rotmans, for his clinical expertise, his enthousiasm and the time he could devote to our update meetings. From the LUMC, I would also like to thank Koen van der Bogt for his expertise during the cadaver studies.
The development department of the LUMC was essential in the success of this project. Thank you Joric for acting as an additional supervisor and all the advice and suggestions you could give. Thank you Jeroen for the amazing production work on the prototypes.

I would also like to thank my girlfriend for overcoming her fear and listening to all the gory details of my project, as well as the support and good times.
Thank you to my housemates, for allowing me to work in the living room everyday and all the fun breaks.

Lastly, I would like to thank my mom for all the support during my studies and giving me the freedom to make this period of my life as amazing as it was.

Leiden, January 2021

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Design and validation of a novel subdermal actuator for use in a dynamic arteriovenous shunt system

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1 Abstract

Introduction: Over 16,000 people in the Netherlands rely on kidney dialysis to stay alive. Good vascular access is needed to allow these patients to receive dialysis, however current vascular access methods like the ArterioVenous Fistula (AVF) are still lacking. Low patency rates, high reintervention rates and heart complications caused by a high flow in the shunt make the need for a better alternative high. As part of the LUMC vascular access group, a novel device is being developed that can close and open the shunt, therefore regulating the flow. The goal of this study is to validate the first prototype of an actuator used to actuate the valve regulating the flow, thereby giving a proof-of-concept.
Method: In this study, multiple design requirements of the actuator will be validated by performing four experiments: (1) a force test using a test setup with a load cell, (2) a reliability test, (3) a durability test using another test setup and a stepper motor and (4) a goat cadaver test.
Results: The force test revealed average peak force values between 15N and 67N, depending on skin thickness and actuator position. The reliability test resulted in a failed activation rate of 0%. The durability test showed that the actuator was still functional after 3500 cycles and the goat study gave two possible implantation locations for the actuator.
Discussion: This study successfully validated three design requirements for a subdermal implantable actuator. Hopefully it is the first step in providing dialysis patients with better outcomes and quality of life. This study however, did not research pushing forces and all experiments were performed ex-vivo. It was brought to light that resultant forces on the shunt could be dangerous. The next step in this research should be the selection of a transmission system and method for propagating forces so that the effect of the resultant forces on safety can be further investigated.

Keywords: dialysis, vascular access, implantable device, actuator, design, validation

2 Introduction

In the Netherlands, over 1 million people suffer from chronic kidney damage. Out of these 1 million, around 16000 need some kind of kidney function replacement therapy, like transplantation or dialysis. Out of these, 6500 undergo kidney dialysis in a dialysis center (ouderenzorg, 2020). When kidneys start failing, they fail to perform their important task, which is renal clearance of toxic small solutes and larger compounds in the blood. When this clearance does not happen or is impaired, multiple life threatening complications can develop, like volume overload, anemia, metabolic acidosis, hyperkalemia and encephalopathy (Rosner, 2005). Kidney dialysis essentially takes over the function of the kidney by running the blood through a kidney dialysis machine, resulting in renal clearance.
Ever since kidney dialysis was first used in 1945 by Willem Johan Kolff (Gottschalk & Fellner, 1997), getting reliable access to the circulation (vascular access) has been identified as one of the main challenges in kidney dialysis. To this day, vascular access is still seen as the Achilles' heel of dialysis.

Currently, the golden standard for vascular access is the ArterioVenous Fistula (AVF), see figure 1. An AVF is a surgically created anastomotic connection between an artery and a vein. AVFs for dialysis are usually placed between the radial artery and cephalic vein, the brachial artery and cephalic vein, or between the brachial artery and basilic vein (Shiu, Rotmans, Geelhoed, Pike, & Lee, 2019).

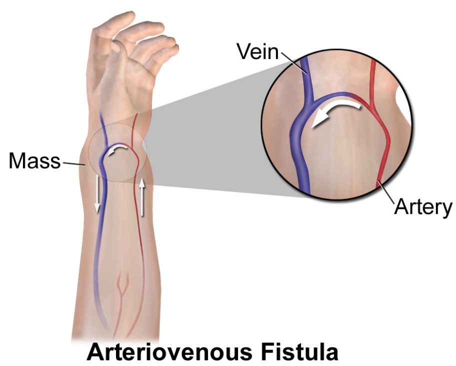

Figure 1: Graphic representation of an Arteriovenous Fistula (AVF), here placed between the radial artery and cephalic vein (Shiu et al, 2017).

Fistulas need time to mature before they can be used as a vascular access site and this maturation often fails. Out of these AVFs, 60% are not suitable for dialysis 4 to 5 months after surgery (Dember et al., 2008). When AVFs fail to mature, or when dialysis needs to start before AVF maturation, catheters inserted into the heart are often used for vascular access, which bring high risks of infection and thrombosis (Group, 2006).
The patency (time from functioning AVF until failure) rates of AVF's are also disappointing; from the AVF's that do mature, only 64% of AVF's are functioning after a year (Falk, 2006). The cause of these low maturation and failure rates is the increased flow in the shunt; for dialysis, a flow of at least 600ml/min is needed, but this can reach several liters per minute as well (Group, 2006). Compared to the flow of 28ml/min in the situation before the AVF, this is a large increase. Altered Wall Shear Stress (WSS) profiles and renal pathologies can cause outward remodeling and Intimal Hyperplasia (IH), which in turn results in stenosis and thrombosis (Krishnamoorthy et al., 2008). Additionally, the high flow means cardiac output is constantly elevated and the heart needs to work harder. Especially for the large group of patients that already suffer from congestive heart failure (35-40%) this causes an even worse prognosis (Alkhouli et al., 2015).
Not only from a medical standpoint a better solution is desperately needed; the costs per QALY for dialysis ($129,090/QALY) are in the top range of what is covered by most health insurers. In 2013, Medicare paid $2,8 billion for access related costs in the US.

The vascular access group of the nephrology department of the Leiden University Medical Center (LUMC) has been working on improving the quality of life and clinical outcomes of kidney dialysis patients through various research and development projects. The most recent project focuses on taking away the always-present high flow, that is only really needed during dialysis. By taking away this constant high flow, hopefully the strain on the heart and the other negative consequences of the current vascular access methods, like stenosis and the low patency rates, can be reduced.
In order to do this, the LUMC is working together with the Delft Technical University to develop a novel Dynamic Arteriovenous Shunt (DAS) system. This system could replace the current access method and be closed and opened at will, regulating the flow in the shunt. Now, the shunt could be opened during dialysis when high flow is needed, and closed in between dialysis sessions, when high flow is not needed and only results in complications.
The DAS will comprise two parts; a valve that regulates the flow and a remote actuator that serves as an interface that can actuate the valve. A transmission connects the two parts together. The focus of this study is on the development and validation of the actuator part of the DAS. The actuator needs to be able to generate a large enough force, and transmit it to the valve so that the shunt can be closed.
The aim of this study is to give a proof-of-concept for the actuator, proving that it could be used to actuate a valve.

3 Actuator design

The actuator was designed using a methodological design approach. First, design requirements were drawn up.

3.1 Design requirements

1. **Maximum dimensions:** Maximum dimensions were determined based on dimensions of other implantable devices and expert opinion; 3.5cm x 2.5cm x 1.3cm.
2. **Force output:** The theoretical needed force was determined in a mathematical model involving stiffness of the shunt and blood pressure and includes a safety factor; 6N
3. **States:** Each state is associated with a different output displacement. The shunt needs the ability to be opened halfway to regulate flow better, so at least three states are needed.
4. **Gradual output:** If the shunt were to open instantaneously, this could result in a sudden drop in blood pressure which could be dangerous. A gradual output spanning 15 seconds was determined to be adequate based on literature.
5. **Mechanical:** Based on bad experiences with a previous iteration, no electrical parts should be used.
6. **Durability:** The durability of the device was found by calculating the life expectancy of the 0.1 fraction of dialysis patients, assuming three dialysis sessions per week; 3500 cycles.
7. **Reliability:** When the actuator is activated it should always lead to actuation. The failed activation rate should be below 3%.
8. **Usability:** the usability features three sub-requirement, out of which at least two should be met:
   (a) Simple activation: only one movement or action is needed for operating the actuator.
   (b) No accidental activation: the actuator shouldn't be activated accidentally during everyday life.
   (c) The device gives tactile or auditory feedback on operation.
9. **Biological safety:** Similar to the usability requirement, the biological safety requirement features four sub-requirements, out of which at least three need to be met:
   (a) Biocompatibility: only biocompatible materials are used.

(b) Pressure ulcers: there are no sharp edges on the actuator that could result in pressure ulcers.

(c) Explantability: no ingrowth is possible so that explantability is easier.

(d) Reintervention & modularity: the connection to the transmission is modular, so that only the actuator has to be replaced during a reintervention in the case of malfunctioning.

Using the above requirements, various design functions were established that the device has to fulfill. These design functions and their respectable partial design solutions were incorporated in a morphological overview (see appendix), out of which multiple conceptual designs were generated.
These designs were graded against the design requirements in a Harris profile, so that a winning design could emerge.

3.2 Final design

The final design is shown in figure 2. An exploded view showing individual components and an activator can be seen in figure 3.

The actuator (implanted part) consists of a wheel with magnets that can rotate around an axis. This set of magnets is coupled to an identical set of magnets in the activator (external part). Due to the magnetic attraction between the sets of magnets, a rotation of the activator results in the same rotation of the magnetic wheel in the actuator.
When the wheel rotates, a magnetic backplate that is attached to the wheel also rotates. In this backplate is a spiral indent. A follower is inserted into this spiral, and is limited to only move axially by the housing of the actuator. Similar to an old turntable, rotation of the wheel will result in the axial movement of the follower. The transmission (most likely a Bowden cable) will be attached to the follower.

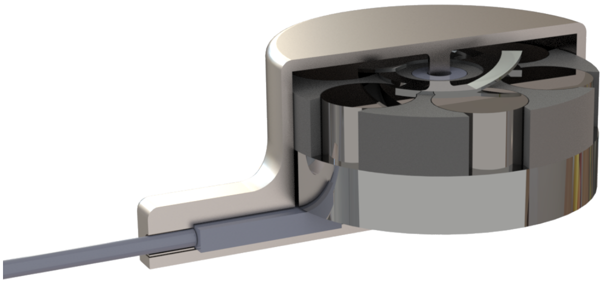

Figure 2: 3D render of the assembled actuator

In order to lock the actuator, a spring will push the wheel down when there is no magnetic coupling. This causes the follower to fall into a deeper recess at the end and beginning of the spiral, inhibiting rotation. When the activator is coupled to the actuator, the magnetic attraction will lift the magnetic wheel up against the spring, freeing the follower from the recess, allowing it to rotate again.

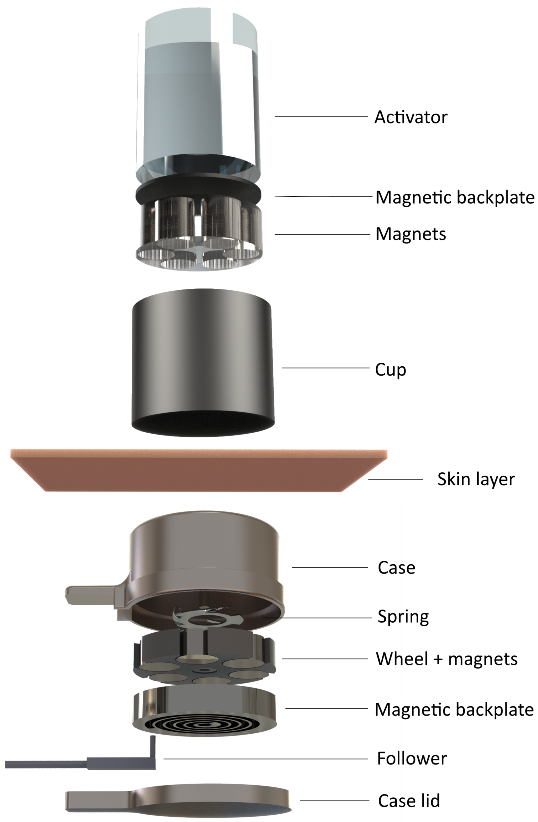

Figure 3: Exploded view of the developed actuator.

4 Method

In order for the current design to meet all the design requirements and provide a solid proof-of-concept, some experimentation is still needed for some of the requirements. In total, four different experiments are performed.

4.1 Force test

In order to validate the actuator, the first step is to validate the amount of force that it can output. To measure this, a test setup will be built using a load cell. This setup can be seen in figure 4.

In the test setup, the actuator (3) is fixated on a wooden base (1). Using an iron wire, the actuator is attached to a load cell (2). Voltage output from the load cell (Futek, Irvine, California, USA), is fed into a data acquisition system (Scaime, Juvigny, France) (5) powered by a power supply (National Instruments, Austin, Texas, USA) (7). The voltage data was imported into Labview (National Instruments, Austin, Texas, USA), in which the voltage data was converted into force data using a conversion factor obtained from

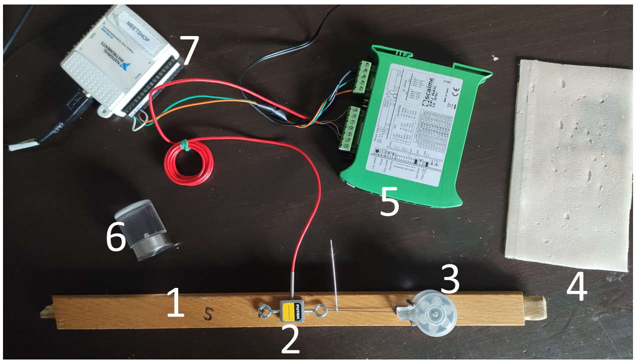

Figure 4: Test setup used to measure the output force of the actuator

a calibration test.

The force data was then imported into Matlab (MathWorks, Natick, Massachusetts, USA) in which the data was analyzed.
Two different wooden bases will be used with different distances between load cell and actuator. Additionally, three different pieces of silicone will be used to create distance between the sets of magnets with thicknesses of 3mm, 4mm and 5mm. This means that in total, 6 different measurements will be performed.

4.2 Reliability test

The next step is validating the reliability requirement. This is done by repeatedly activating and deactivating the actuator while it is placed in the test setup from section 4.1. Then, the amount of failed activations is counted. An activation was counted as failed when the force threshold of 6N was not reached, when the actuator failed mechanically, or for some other reason needed to be repeated for a successful actuation.

4.3 Durability test

Figure 5: Test setup used to measure the durability of the actuator

To validate the durability requirement, another test setup was built. In this setup, depicted in figure 5, a stepper motor was used to continually activate and deactivate the actuator. The same wooden base and load cell are used from the force test setup.

The activator is coupled to the actuator with a piece of silicone skin in between, and the stepper motor is attached to the activator. The stepper motor is instructed to rotate the activator back and forth continuously using the same rotation. The value for the rotation will be obtained by finding the rotation that corresponds with an output force of 15N in the force test setup.

Similar to the force test, force data was captured and analyzed in Matlab.

4.4 Goat cadaver study

As a last test, a functional test was done in a goat cadaver. This study was performed at the GDL (Gemeenschappelijk DierenLaboratorium) Utrecht. The other goal of this study was to explore the optimal implantation location in a goat, since this is the animal that will be used for the first implantation study. Goats are used due to their vascular similarities to humans.
The neck of the goat will be opened, exposing blood vessels. The actuator will be placed in the most optimal implantation location or locations and a functional test will be performed.

5 Results

5.1 Force tests

A total of six measurements were done, with at least 15 sub-measurements per combination of variables. Figure 6 shows the data of the test performed with a skin thickness of 3mm, at position 1 (outside of the spiral, with the follower fully extended out).

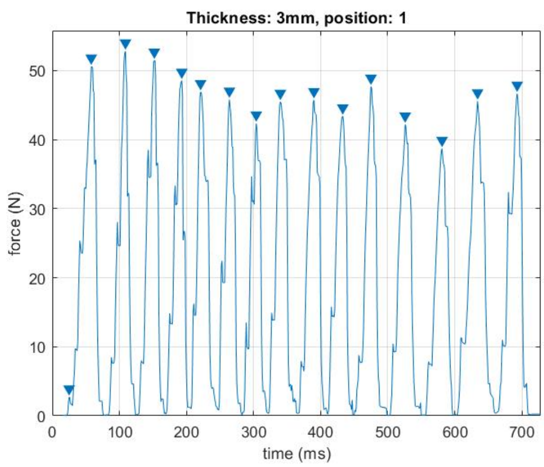

Figure 6: Force test results for a skin thickness of 3mm at position 1 (follower fully extended)

Table 1 summarizes the results of all six force tests.

Table 1: Table displaying the maximum and average peak force values for all measurements at different skin thicknesses

	Position 1		Position 2	
	Max peak value	Average peak value	Max peak value	Average peak value
3mm	53N	46N +-3.7N	74N	67N +- 3.7N
4mm	45N	34N +- 3.1N	70N	68N +- 3.4N
5mm	17N	15N +- 1.2N	23N	21N +- 1.2N

5.2 Reliability test

For the reliability test, the actuator was activated and deactivated a total of 450 times. Over all these activations, 0 failed activations were counted, resulting in a failed activation rate of 0%

5.3 Durability test

The actuator successfully completed all cycles in the test setup without breaking and was still functional after the test. Results from the test are shown in figure 7.

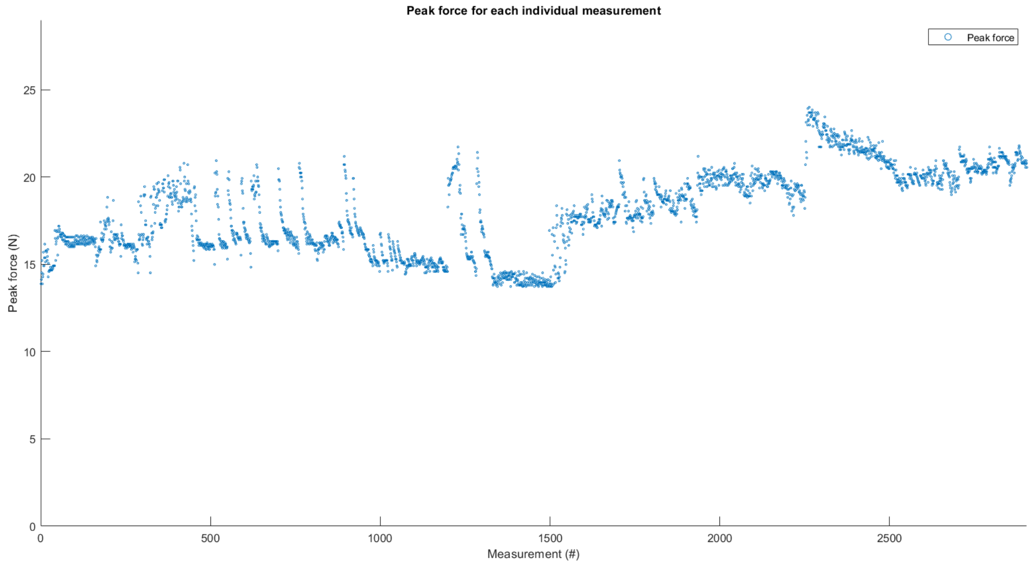

Figure 7: Results of the durability test. For each individual measurement, the peak force was taken.

5.4 Goat study

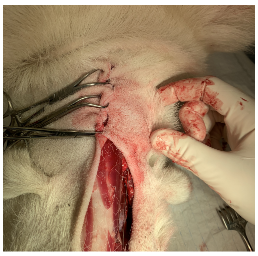

Figure 8: The actuator placed inside the neck of the goat with the skin covering up the actuator. The outline of the actuator can be seen between the fingers.

In the goat cadaver study, two different implantation locations were found; one at the most distal portion of the neck, and one at the most proximal portion of the neck. In both locations, the actuator was inserted (figure 9) and the skin closed back up (figure 8). The actuator was then coupled to the activator which was rotated. In both implantation locations actuation was possible and resulted in axial movement of the transmission.

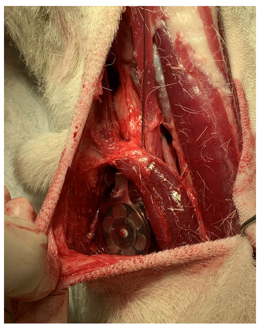

Figure 9: The actuator placed inside the neck of the goat

6 Discussion

From the force test, it can be concluded that the actuator can deliver enough force and fulfill the design requirement. This means that for a next prototype, some improvements could be made that increase durability or decrease size at the cost of force output.
The reliability test validated the reliability requirement with a failed activation rate of 0%.
The durability test showed that the actuator can still function after 3500 cycles with enough output force, thereby validating the durability requirement.
Lastly, the goat study gave a first functional test for the actuator in an implanted environment. Additionally, it gave two possible implantation locations. The distal implantation location was determined to be less optimal, since this location was close to the jaw bone of the animal and could cause problems when the goat is moving its neck or chewing food. Therefore, the proximal implantation location was picked as the best location for the goat study to be done in the future.

Although the overall results of this study were positive, there were a few shortcomings.
One thing that stands out with the durability tests, is the large fluctuations in the force output. A possible explanation for this could be the very small displacement that causes the forces. Only 1.66mm caused a force difference of 15N, meaning that small errors in the displacement could cause large force output fluctuations. During rotation of the stepper motor, the actuator could shift and rotate a bit on its wooden base, causing variations in the displacement. Additionally, a semi-stiff transmission was used, meaning that the stiffness of the transmission also played a role in the force output.
Even though the study could be improved on by fixating the actuator on the base better and introducing a spring in the transmission to eliminate fluctuations, the test still performed its function; it showed that the actuator is still functional after 3500 cycles and can still output adequate force.

Another shortcoming is that only the pulling force of the actuator was measured, even though it also needs to be able to push. The reason for this was that the requirement for the pulling force is much higher, since the pulling force closes the valve and therefore needs to compress the piece of graft against the blood pressure. The pushing force (and thus opening of the shunt) is assisted by the blood pressure. It would still be good however, to know how much pushing force is available and this should be tested as soon as a transmission system has been selected.

All experiments were performed ex-vivo or in a cadaver. While this is a good place to start for validation, the ex-vivo environment is very different from an environment as an implanted device in a living organism. Physiological responses like foreign body responses and and ingrowth of tissue could change the workings of the device.

Something that deserves more attention in the future stages of development is the rise of resultant forces on the shunt. When a pulling force is exerted on the actuator, either by hand during actuation, or by accident during everyday life, the pulling force could be propagated through the transmission to the shunt. This could cause large forces on the sutures that keep the shunt in place on the blood vessels. Large forces here could cause ruptures of blood vessels which could be fatal. Possible solutions include fixation of the actuator, or bending angles for the transmission.

6.1 Further research

For the actuator, the next step would be to select the best transmission system for connection to the valve. First, an overview should be made of all possible transmission system. Then, a couple promising transmission systems should be tested in conjunction with the actuator. This time, pushing and pulling tests should be performed. This would also be a good time to research bending angles and fixation methods for the actuator to better understand the risk of the resultant forces and how to limit them.

7 Conclusion

In this paper, a design for a novel subdermal actuator was presented as part of a dynamic arteriovenous shunt system. In order to provide a proof-of-concept of the device, three design requirements were validated using a force test, reliability test, durability test and goat cadaver study.
By validating the set design requirements, hopefully, the actuator and the DAS are one step closer to improving the life of kidney dialysis patients. Although there are still a lot of hurdles to pass before the device can be used in actual patients, the results from this study are positive and provide a proof-of-concept for the DAS as a device that can improve clinical outcomes like patency rates, reintervention rates and cardiac complications for patients relying on kidney dialysis.

7.1 Acknowledgement

The author would like to thank his daily supervisors, Tim Horeman and Joris Rotmans. Additionally, the people from the development department of the LUMC were of great help with the development of the prototype as well as with discussion on prototype design. The GDL Utrecht was very helpful with arranging the goat study, as well as Koen van der Bogt, for his expertise during the cadaver study.

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2. INTRODUCTION

2.1 Background

In the Netherlands, over 1 million people suffer from chronic kidney damage. Out of these 1 million, around 16000 need some kind of kidney function replacement therapy, like transplantation or dialysis. Out of these, 6500 undergo kidney dialysis in a dialysis center (ouderenzorg, 2020). When kidneys start failing, they fail to perform their important task, which is renal clearance of toxic small solutes and larger compounds in the blood. When this clearance does not happen or is impaired, multiple life threatening complications can develop, like volume overload, anemia, metabolic acidosis, hyperkalemia and encephalopathy (Rosner, 2005). Kidney dialysis essentially takes over the function of the kidney by running the blood through a kidney dialysis machine. In the machine, blood is exposed to a semipermeable membrane. On the other side of this membrane is a solution of dialysate. Three mechanisms make up the renal clearance:

- **Diffusion:** molecules move from the side with a higher concentration to the side with a lower concentration. This gets rid of small particles (limited by the size of the pores of the semipermeable membrane).
- **Ultrafiltration:** movement of a solvent (in this case plasma water) from the side with a higher pressure to the side with a lower pressure. This solves the volume overload caused by kidney failure.
- **Convection:** The blood moves down a pressure gradient, dragging molecules across the membrane. This gets rid of small and medium sized particles.

Ever since kidney dialysis was first used in 1945 by Willem Johan Kolff (Gottschalk & Fellner, 1997), getting reliable access to the circulation (vascular access) has been identified as one of the main challenges in kidney dialysis. To this day, vascular access is still seen as the Achilles' heel of dialysis.
There are three different methods of obtaining vascular access (see figure 1):

- **Fistulas**: an ateriovenous fistula (AVF) is an anastomotic connection between an artery and a vein. AVFs are usually placed between the radial artery and cephalic vein, the brachial artery and cephalic vein, or between the brachial artery and basilic vein (Shiu, Rotmans, Geelhoed, Pike, & Lee, 2019). The AVF is created surgically and needs to mature before being used as a vascular access site for hemodialysis. It needs to have a flow rate of at least 600mL/min, up from 28mL/min (for adequate dialysis speed), be located no less than 0.6 cm under the skin and have a diameter of at least 0.6 cm (for adequate puncturing) in order to be able to be used for sustained dialysis according to the guidelines set by the national kidney foundation (Group, 2006).
- **Grafts**: an arteriovenous graft (AVG) is a connection between an artery and a vein by use of an artificial piece of graft placed between them. AVG requirements are similar to requirements for AVF's.
- **Catheters**: catheters for kidney dialysis are usually placed in the neck (right internal jugular vain) and require a flow rate of at least 300mL/min for adequate dialysis speed (Group, 2006). Note that this is lower than for AVF's, resulting in a longer total dialysis time.

The main goal of the three access methods is to achieve a high flow rate, which is needed for maximum dialysis efficiency, and to prevent thrombosis in the shunt.
Out of these three, the preferred method is the fistula, since it has the lowest rate of thrombosis, and it requires the least amount of re-interventions (Allon, 2007).
Unfortunately, not all patients are eligible for a fistula at the moment that they need hemodialysis. Fistulas need time to mature before they can be used as a vascular access site and this maturation often fails. Out of these AVFs, 60% are not suitable for dialysis after 4 to 5 months after surgery (Dember et al., 2008). When AVFs fail to mature, or when dialysis needs to start before AVF maturation, catheters are often used for vascular access, which brings high risks of infection and thrombosis (Group, 2006). The exact reason for the low success rate of maturing fistulas is not known, however, there are probably multiple pathofysiological processes involved, such as outward remodeling and intimal hyperplasia (IH) (Rothuizen et al., 2013). These processes are influenced by renal pathologies present in dialysis patients and by altered Wall Shear Stress (WSS) profiles.
When AVFs do succeed in maturation and can be used as a vascular access point for hemodialysis, they still aren't without risks unfortunately. The change in WSS profiles caused by altered anatomy and blood flow patterns is

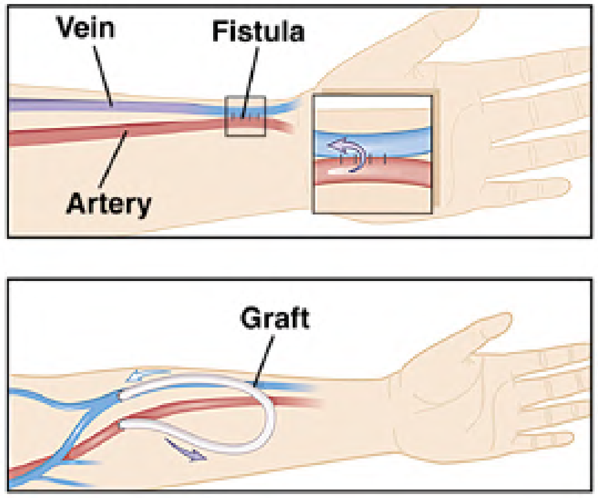


Figure 1: Graphic representation of an arteriovenous fistula and two different arteriovenous grafts (Fairview, 2020)

still present, which can cause stenosis of the AVF and thrombosis (Krishnamoorthy et al., 2008). This results in disappointing patency rates (% of usable AVFs after a certain time period), such as 64% after 1-year follow-up found by Falk et al. (Falk, 2006).

Additionally, the large diameter and flow rate in the fistula mean that the heart needs to work harder; the cardiac output of the heart increases proportional to the size of the shunt, requiring a rise in total blood volume and permanent activation of the sympathetic system, resulting in increased heart rate, contractility and blood pressure (Amerling, 2012).
The combination of this sympathetic activation with existing cardiovascular disease often present in patients with renal disease can be dangerous; it's quite hard to tell exactly what the added mortality of AVFs can be for these patients, since they already experience an increase in preload and cardiac output due to fluid retention, chronic anemia and other pre-existing cardiovascular pathologies, but the potentially deadly effects of AVFs should not be underestimated (Alkhouli et al., 2015).

It is clear that AVFs are still far from a perfect solution for vascular access for dialysis patients, with high failure rates, morbidity and mortality. Also from a financial standpoint, much can be improved for vascular access, with spendings for vascular access for end-stage renal disease payments of $2,8 billion paid by Medicare in the US in 2013 (Thamer et al., 2018).

The vascular access group of the nephrology department of the LUMC has been working to improve the quality of life and clinical outcomes of kidney dialysis patients through various research and development projects. The most recent project focuses on taking away the always-present high flow, that is only really needed during dialysis. By taking away this constant high flow, hopefully the strain on the heart and the other negative consequences of the current vascular access methods, like stenosis and the low patency rates, can be reduced.
In order to do this, the LUMC is working together with the TU Delft on a Dynamic Arteriovenous Shunt (DAS). This shunt would replace the current vascular access method and can be closed and opened at will, therefore regulating the flow in the shunt. This way, the negative effects of the high flow rate and altered anatomy are only present during the actual dialysis process, and the anastomosis can be closed when it is not needed in between dialysis sessions. This shunt will most likely be placed between the cephalic vein and the brachial artery in the upper arm. This is a common location to place AVF's as well and will be the first location to use for the DAS, with more locations being explored later. The actuator regulating the opening and closing of the shunt can be placed remote from the shunt itself, with a transmission connecting the two parts.

2.2 The arteriovenous shunt closure device

The device will consist of two main parts that can be distinguished:

- A valve-like system that can be closed and pushes down on the anastomotic region where the artery and vein are connected. By pushing down, it should fully close off the connection between the two vessels.

- An actuator that can actuate the opening and closing of the above mentioned valve system. The actuator needs to be able to me manipulated while it's implanted subcutaneously.

Two thesis projects will start to work on these main parts of the device. In the end, the two main parts need to be incorporated together into one device. The entire device should be able to be implanted subcutaneously.
The goal of these projects is to give a proof-of-concept of the DAS as a device, and prove the viability of further development into a fully developed product that can be validated in clinical studies and taken to market. The aim of this specific thesis project will be to provide the proof-of-concept for the actuator, while in a parallel project, the valve-like system will be worked on. The actuator needs to be able to be actuated distally from the valve, and transfer the force from the manual actuation to the valve, allowing it to open and close.
Showing a proof-of-concept is the first step in successful development of the DAS into a market-ready device, by not only checking the viability of the concept, but also for obtaining interest from potential investors or subsidies.

3. OVERVIEW

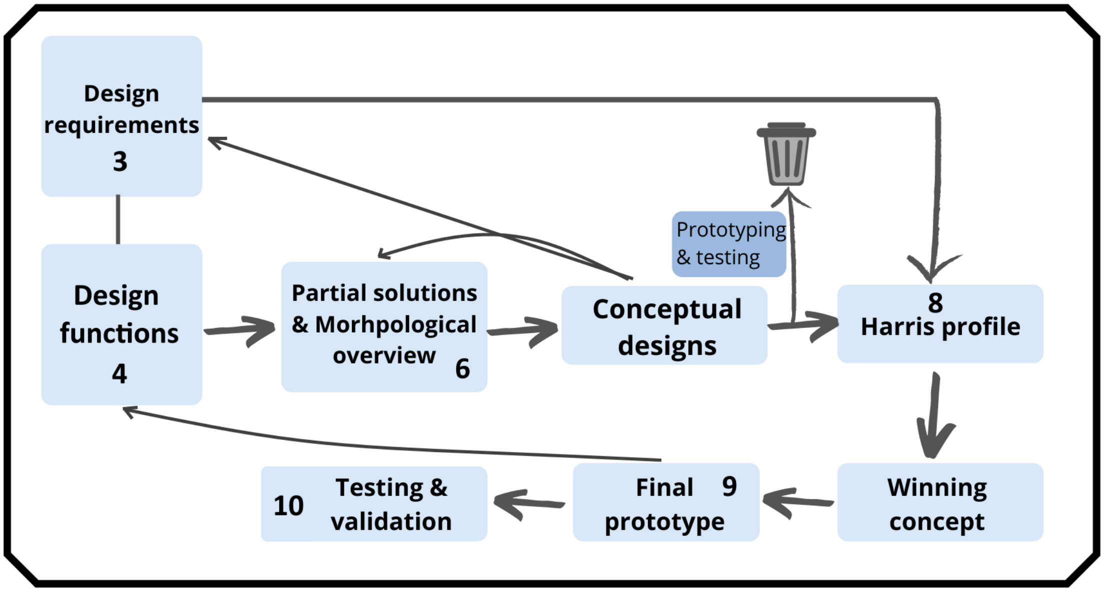


Figure 2: Flowchart of the structure of this design project

In this thesis project, a device will be designed and validated. The flowchart in figure 2 describes the general structure that this project will follow.
First, a set of design requirements will be drawn up in chapter 4 that the final device will have to meet. Then in chapter 5, a set of partial design functions will be identified that the design will need to fulfill in order to meet the identified requirements.
The next step, in chapter 7, will be to come up with different ways to meet these partial design challenges with partial design solutions. These solution will all be placed in a morphological overview.
Combining different partial solutions in the morphological overview, we can form multiple different conceptual designs. Using varying prototyping and testing methods, non-viable concepts will be discarded so that only the viable concepts remain.
In chapter 9 Harris profile will be formed in which the remaining concepts will be graded against the previously set design requirements in chapter 4 and out of this profile, a winning concept will be selected. This concept will then be further developed into a final prototype in chapter 10.
Lastly, this prototype will be used for testing and validation in chapter 11, ending up with our proof of concept.

4. DESIGN REQUIREMENTS

In this chapter, all the design requirements that the device will have to meet are drawn up. This will create a handhold for the further development of the device. Some of these requirements were added or updated later in the development cycle when new information came to light. Table 1 already gives an overview of all the requirements and their corresponding values. In the following sections, all individual requirements, and the reasoning behind their values, will be explained in more detail.

Table 1: Overview of the design requirements

	Requirement	**Value**	**Description**	**How to measure**
1	Dimensions	Height: 3.5cm, width: 2.5cm, length: 1.3cm	Max allowed dimensions	Calipers/ CAD
2	Force/energy	6.0N	Required output force of the actuator	Force sensor
3	States	>= 3	Amount of states that the actuator can be in	Force sensor & position
4	Gradual output	15s	Dampening time of the force	Timer, dampening needs to be adjustable & force sensor
5	Mechanical	n/a	No electrical parts used	n/a
6	Weight	n/a	Weight of the actuator	Scales
7	Durability	3500	Minimum amount of cycles before becoming inoperable	Test setup repeatedly activating actuator
8	Reliability	<=5%	Failed activation rate	test setup with force sensor
9	Usability	n/a	Device must meet sub-requirements	Various
10	Biological safety	n/a	Biological safety includes three sub-requirements that must be met	Various
11	Costs	< 500 euros	Production costs of the actuator	Cost assessment

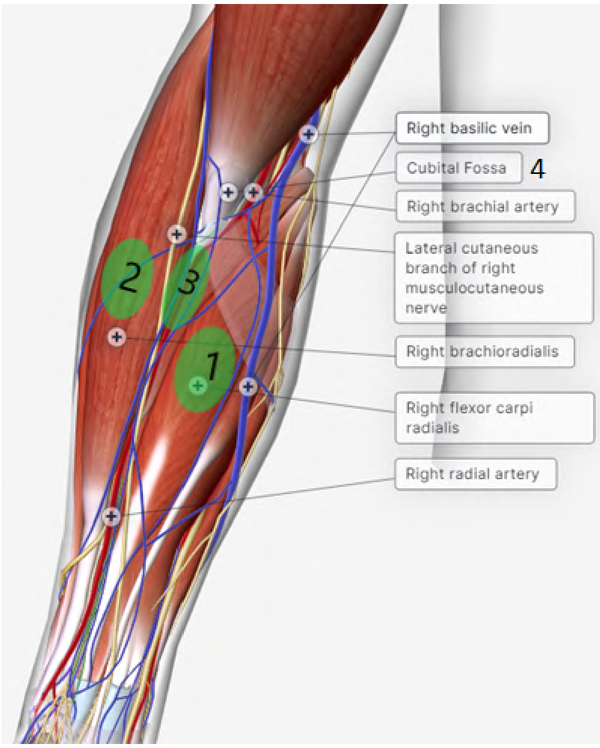
4.1 Dimensions

Determining the dimensions of the actuator is a crucial first step in the design process. These dimensions can greatly limit the design, or open up new possibilities. In general, the larger the allowed dimensions, the better, since it allows for more freedom in design.
In order to determine the dimensions, first the most suitable location for the actuator needs to be determined. A good location for the actuator would be a location where:

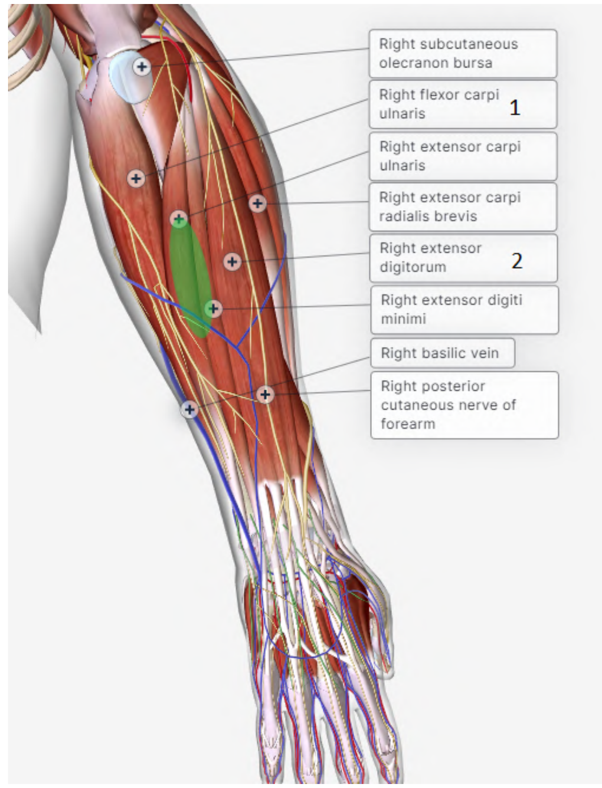
- There are no vital, sensitive structures that can be damaged by the actuator pushing down on them.
- The area is not being compressed or stretched when moving the arm. This could be by actual compression like in the cubital fossa, or could be by compression between a muscle and the skin when a muscle is contracted.
- There is enough room for the actuator. A subdermal pocket needs to be created. This should be easier in a wider area, and areas where some fat is stored; the fat can be removed and replaced by the subdermal pocket.
- The area is as close as possible to the anastomosis and valve.

4.1.1 Anatomy

We start by looking at the anatomy of the forearm.



(a) Anterior view of the right forearm.



(b) Posterior view of the forearm.

Figure 3: View of the anatomy of the upper arm, showing muscles, blood vessels and nerves. The green areas represent areas that could be interesting for implantation based on anatomy. Images generated using Biodigital Human (Biodigital, New York, NY, USA)

An anterior view of the forearm is given in figure 3a, showing the most prominent muscles, veins and nerves. As seen in the figure, the wrist area contains a lot of vital, sensitive structures. This is also an area where not a lot of fat is stored and where there is not a lot of room in general, so this will not be a good location for the actuator. The cubital fossa (4) is the 'armpit' of the elbow, the transition area between the upper and lower arm. Since this area gets compressed during flexion of the lower arm, it is not a good area either.
The area between the wrist and the cubital fossa is an area where the forearm is wider and there is generally more room. Also, some more fat is stored here. There are three main areas that could be interesting. The first one is on the flexor carpi radialis muscle (1). There are no sensitive structures located here and it runs past the widest area of the forearm. The brachioradialis has a similar area (2).
The problem with the flexor carpi radialis is that it is responsible for palmar flexion of the hand, which is a common movement with which the most torque can be generated out of all wrist movements (Vanswearingen, 1983) (followed by dorsal flexion, then radial deviation, and then ulnar deviation). This means that the muscle could also exert a large force on the actuator which is undesirable.
The brachioradialis muscle is a muscle that assists in elbow flexion, which makes it hard to determine whether it can exert more or less force on the actuator during contraction.
The third area is the area between the muscles described above, just distal of the cubital fossa (3). This area could be interesting because it is located between the muscles, which could reduce the stress on the actuator during movement of the arm. The problem is that there are some sensitive structures located here, which could potentially be damaged if there is not enough room for the implant.

The same thing can be done for the posterior side of the forearm, see figure 3b. The posterior side has much less veins and nerves running through it, which is advantageous. Like on the anterior side, less fat is stored and less space is available closer to the wrist. The strongest muscles are the flexor carpi ulnaris (1) and the extensor

digitorum (2); these can exert the highest force on the actuator. A good possible location for implantation could be the area between the extensor digitorum and the flexor carpi ulnaris, on the extensor carpi ulnaris and the extensor digiti minimi (green shaded area). These muscles lie a little deeper than the surrounding muscles, possibly making some room for a subdermal pocket to fit the actuator. Additionally, no sensitive structures run through here, and it is located on the widest part of the forearm.
A downside of areas on the anterior side of the forearm is that the actuator can get in the way and be uncomfortable when resting the arms on a desk or table.

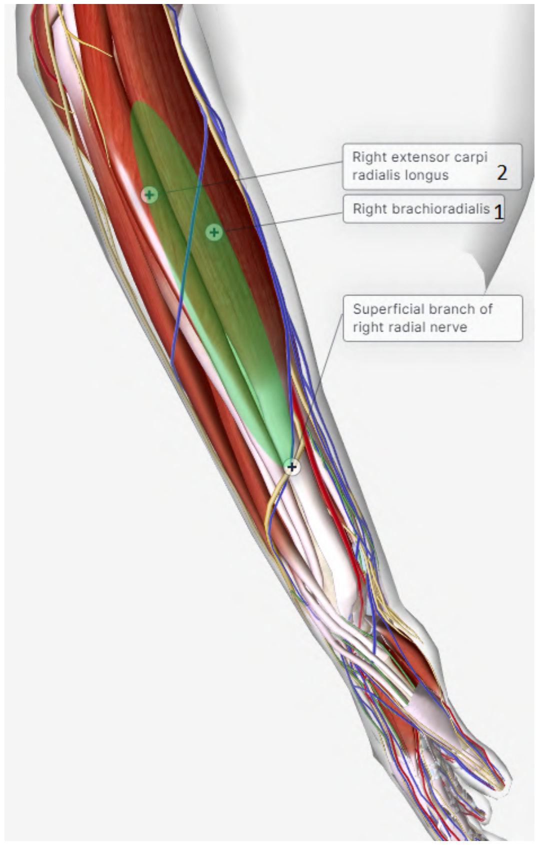
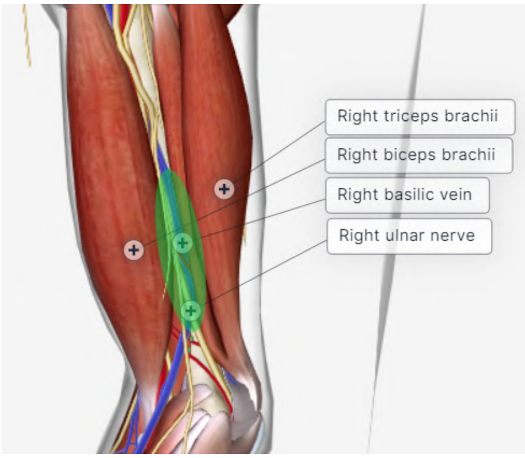


Figure 4: Radial view of the forearm, showing muscles, veins and nerves. Image generated using Biodigital Human (Biodigital, New York, NY, USA)

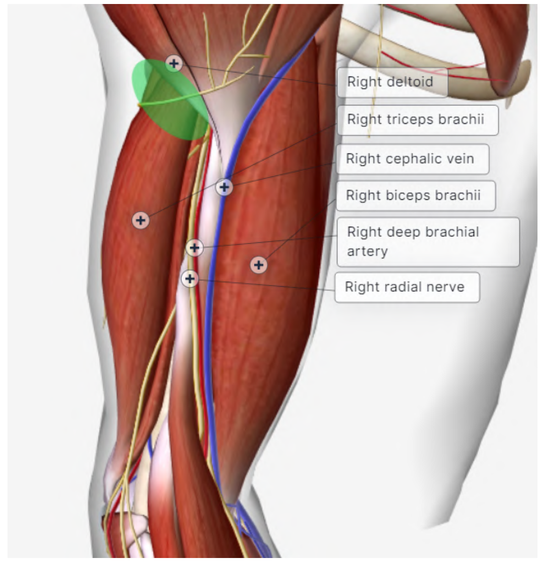
A radial view of the forearm is represented in figure 4. The radial side of the forearm consists mainly of the brachioradialis (1) and extensor carpi radialis longus (2). No main sensitive nerves or blood vessels run here. It is also an area that is relatively soft with some fat storage, possibly giving room for a subdermal pocket.

A view of the medial side of the upper arm is given in figure 5a. In the upper arm, the skin around the bicep is pretty tight, so there's not much room for implantation there. There is however quite some space in the crease under the bicep (green shaded area). This crease follows along the entire biceps muscle so there's quite some space length-wise. The only con is that there are some sensitive structures there, like the ulnar nerve and basilic vein.

The other side of the upper arm is shown in figure 5b. This side is quite similar to the medial side, with the difference being that the medal side has more space in the crease under the biceps than the lateral side does.
One potentially interesting area on the lateral side however, is the area under the posterior deltoid shown in green. There are no important sensitive structures here, and the skin is quite loose, especially in older patients, possibly giving enough space for a subdermal pocket for implantation. The problem with this area however, is that it is far away from the anastomosis and the valve.



(a) View of the medial side of the upper arm.



(b) View of the lateral side of the upper arm.

Figure 5: Medial and radial view of the upper arm. The green areas represent areas that could be interesting for implantation based on anatomy. Images generated using Biodigital Human (Biodigital,New York, NY, USA

4.1.2 Other considerations for the location

Aside from the above-mentioned considerations regarding the location of implantation, like available space and underlying sensitive structures, there are more considerations that can influence the decision for a suitable location.

- There is generally more space available in the upper arm. Especially in older patients that experience a lot of muscle atrophy, the lower arm can lack adequate space. This problem is less apparent in the upper arm.

- The valve will be implanted between the cephalic vein and the brachial artery in the upper arm. This means implantation in the upper arm might be easier, since the transmission of the force doesn't have to pass the elbow joint. Passing the elbow joint could prove troublesome because of the mobility in this joint; bending the elbow could cause high resulting forces on the actuator, valve and transmission which could in turn damage the blood vessels and graft.
  Similarly, the valve is implanted in the anterior or ventral side of the arm. This means it would be easier to place the actuator on the same side. This way, the transmission does not have to pass through, or around, the arm.

- The foreign body response against implantable devices is smaller around muscle tissue than around fat tissue. This can possibly make a location around muscle tissue more attractive.

- Comfort is another important factor to decide where to place the actuator. Most other considerations are from a clinical or technical perspective, but not from a patient perspective, even though the patient will eventually have to wear the device. In order to get more patient feedback, a survey was performed, see section 4.2.1.

- The implantation location may have an influence on the possible accidental activation of the actuator. The final design for the actuator may have a locking mechanism, in which case the location is not that influential. When the final design however does not have a locking mechanism, the location has a big influence on the accidental activation rate. In this case, implantation ventrally in the lower arm is suboptimal, since this area often rests on a surface, so the other (lateral) side of the lower arm may be better. The problem with the lateral side however, is that it is not shielded from any bumping or other touching from the environment. This means that the medial side of the upper arm is probably best with regards to accidental activation, since it never really rests on a surface, and is shielded from the environment. Additionally, while sleeping, this area is probably least disturbed by moving around.

4.2 Other devices

Looking at other implantable devices that have been implanted subdermally in the forearm, most common is the venous-access port system. This device is implanted for easy administration of chemotherapy, antibiotic therapy, or blood extraction.
In most studies, these devices are implanted in a subdermal pocket distal to the cubital fossa (Goltz et al., 2012)(Goltz et al., 2010), see figure 6. Another study describes the placement as "the upper portion of the forearm" which most likely indicates the same location (Foley, 1995). In another study, first the access vein was decided on, and then a subdermal pocket was created just distal to the access site (Akahane et al., 2011). Lersch et al. did something similar, where they placed the port adjacent to the vein entry side in a subdermal pocket. They also mention that the port was sutured to the underlying muscle fascia using resorbable sutures (Lersch et al., 1999). Unfortunately, the reasoning behind the placement of the ports in this location is not mentioned in the literature.

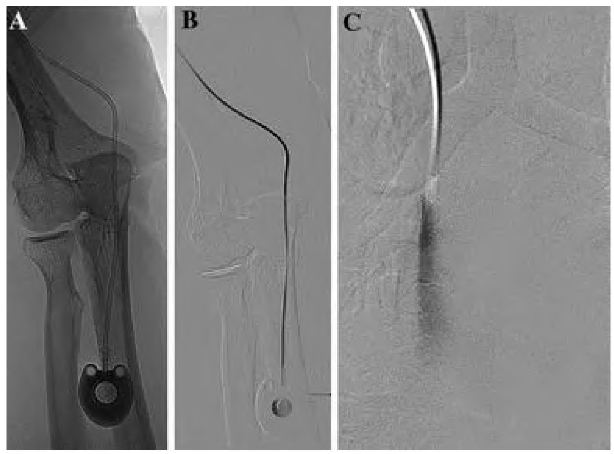


Figure 6: Radiographic images of placement of the access port distal to the cubital fossa (Goltz et al., 2012)

Looking at the dimensions of some of the devices mentioned in above articles, we can get an idea of what dimension should be possible in these areas.

- X-Port (Bard Access Systems, Salt Lake City, UT): 21.7mm x 24.7mm x 8.2mm. 6.7g.
- Titanium Vital Port Mini System (Cook, Bjaeverskov, Denmark): 19mm (diameter) x 7.2mm. 5g.
- P.A.S. PORTH T2 POWER P.A.C. (Smiths Medical, St Paul, MN): 24.5mm x 18.2mm x 11.5mm. 8.3g.
- Custom P.A.S. port (Foley, 1995): 26.7mm x 16.5mm x 7.4mm. 5.6g.
- Bard Titan Low Profile Port (March 1997; Bard, Karlsruhe, Germany): 24.8mm (diameter) x 9.4mm.

As seen above, most ports have roughly similar dimensions. The X-port and Bard Titan seem to be the biggest. Since all these devices are FDA cleared and have been in use for a while, we can say that an actuator that has a similar size could be implanted in a subdermal pocket distal to the cubital fossa. The problem with these dimensions however, is that we do not know whether these are the maximum allowed dimensions in this area, or the minimum dimensions that the manufacturers can make these devices (even though there might be room for larger devices).

4.2.1 Patient survey

Above, only clinical and technical considerations are discussed for the implantation location. Eventually however, patients will have to wear the implant, so their preference should definitely be taken into consideration as well. In order to do this, a patient survey was created and handed out physically to dialysis patients at the dialysis unit at the LUMC. In this survey, patients were asked for their preferred location to implant the actuator. For the survey, see appendix I, section 16.

4.2.2 Vascular surgeon

To discuss placement of the actuator and available dimensions, I had contact with a vascular surgeon at the LUMC. We concluded that the next step in determining the location and dimensions would be to actually look into an arm, and maybe 3D-print some differently shaped prototypes to test out different shapes. Unfortunately, due to the corona crisis that was not yet allowed at the time of the meeting. Until going into the lab is allowed, an estimate will be used. The surgeon agreed with taking dimensions that are similar to the venous access ports described above. Additionally, he suggested that an implantation site in the inner upper arm would be best for the actuator, between the biceps and the humerus. This location is where he usually implants venous access ports, because in his experience, this is where most room is available for implantation.

4.2.3 Value

As mentioned above, until experiments in the anatomy lab are possible again, estimated maximum dimensions will be used, as discussed with the surgeon. These will be 3.5cm x 2.5cm x 1.3cm.

4.2.4 How to measure

Dimensions can be measured in the CAD software where the actuator is designed, or physically with calipers.

4.3 Force/ energy

The force and energy that the actuator needs to output depends on the input force and energy needed by the valve. The maximum input of the valve is the energy that is needed to fully close the anastomosis by pushing down on two sides of a piece of graft.

4.3.1 Value

The value for the valve was determined in the parallel thesis project that is developing the valve. The calculated value to close the graft was determined to be 500N/m for a blood pressure of 200mm/Hg and a safety factor of 2 (so for a maximum blood pressure of 400mm/Hg). The length of the graft that is going to be needed for the valve system is estimated to be at least 3.0mm. Another safety factor of 2 will be used here in case the graft ends up longer than 3.0mm. This results in a needed input force for the valve of 500N/m x 0.0030m x 2 = 3.0N. Note that this rough calculation does not include the stiffness of the piece of graft. Until a better value can be given by testing in a test setup however, this rough estimate will do.
The valve will be designed in such a way that when no force is supplied, the valve is opened. This is done as a safety measure, so that when something breaks, the patient can still receive dialysis.
The valve system might use compliant mechanisms or other mechanisms that require some force to open, so just to be sure, another safety factor of 2 is used, resulting in a final value of 6.0N.
This force will be applied over a distance, since it needs to actually open the anastomosis, resulting in a certain amount of energy. This means that the actuator also should output a certain amount of energy, so the 6N force needs to be applied over a distance. The exact value for energy will need to be determined later. When the actuator can supply the 6N over at least 10mm, so 0.006J, that should be enough energy as an input for the valve. A transmission can then be used to end up with the exact needed force and energy for the valve that is to be determined later.

4.3.2 How to measure

The output force will be measured with load cell in a physical test setup.

4.4 States

The output of the actuator is a displacement with a minimum force of 6N, as shown in section 4.3. This output results in a certain amount of opening of the connected valve. The actuator needs multiple different output states, each outputting a different displacement, resulting in different levels of opening of the valve.

For adequate hemodialysis, a venous flow of at least 600ml/min is needed (Group, 2006). The venous flow is dependent on the connection between the cephalic vein and brachial artery; the larger the opening between the

two, the higher the resulting flow will be.
It is however preferable to get a flow that is not much higher than 600ml/min, since this high flow is associated with high Wall Shear Stress (WSS) profiles, which in turn is associated with restenosis and thrombosis, as explained earlier.
AVF's and AVG's often have a flow that is well over 600ml/min, often even reaching multiple liters per minute. The higher this flow is, the higher the strain is on the heart, and the higher the chance is for complications. This means that when the valve of the DAS is fully opened, this will result in a venous flow well over 600 ml/min as well. Keeping this in mind, it would be preferable to be able to regulate the flow in the shunt using different output states, so that the flow reaches at least 600ml/min but doesn't get too high. The possibility of a fully open valve should still be available however. This is because the flowrate in the cephalic vein increases about twofold in the first month after AVF placement (Lomonte et al., 2005). At the start of maturation, it could be desirable to fully open the valve in order to reach 600ml/min, while at a later stage this most likely will not need to be necessary.

4.4.1 Value

At this point in the development of the DAS, three 'states' should be possible; one which causes the valve to be fully closed, one which causes the valve to be fully open, and one which causes the valve to be in a state between opened and closed (preferably halfway). In a later stage of development, it could be desirable to have even more states (especially when a flow sensor is involved and the 600ml/min can be approached more accurately). At this point more research is needed to determine exactly how well the flowrate can be regulated and how many states are needed. For now however, three states is enough. A design that is capable of having more than two states (fully opened and fully closed) is likely to be able to be adapted in the future to suit more different states.

4.4.2 How to measure

Count the states, determine output forces by measuring with a force sensor, and measure actuation rod position.

4.5 Gradual output

The output of the actuator is a force that is required for the input of the valve. The valve will open the anastomosis between a vein and an artery. Once the valve is opened, the flow through the vein adjacent to the anastomosis is increased drastically from approximately 28ml/min (Rotman, Shav, Raz, Zaretsky, & Einav, 2013) to >600ml/min required for hemodialysis. Like mentioned before, this increase is postulated to be associated with an increase in cardiac output (CO). This assumption is supported by animal models using dogs with large AVF's (Guyton & Sagawa, 1961). This increase in CO is due to the fact that an AVF (or in this case an anastomosis facilitated by the DAS) lowers systemic vascular resistance. In response, the body increases cardiac output to maintain blood pressure (London, Guerin, & Marchais, 1999). Cardiac output is increased by a reduction in peripheral resistance, an increase in sympathetic nervous system activity and an increase in stroke volume and heart rate.

When the valve of the DAS opens (almost) instantly, the heart may not be able to match the required increase in cardiac output immediately and blood pressure could drop significantly, which is not desired. In order to prevent this, the valve will need to open gradually so that the body can adjust to the low resistance. This means that the force required to open the valve to the desired setting will need to be reached gradually as well; the force needs to be damped. In theory, this dampening could take place anywhere in the device (in the actuator, in the transmission, or in the valve itself), however, due to the fact that even less space is available for the valve and the transmission, it is desired to implement dampening in the actuator.

The exact required value for the dampening is hard to predict. No devices exist with a similar function, so no research is available on how fast an AVF can open without causing difficulties. However, in the study done by Guyton et al, dogs with impaired reflexes and regular dogs received an AVF. When opened, the cardiac output increased in two to three heartbeats. In the dogs with regular reflexes, the cardiac output increased even more in the following 15-30 seconds (Guyton & Sagawa, 1961). Guyton et al also looked at the change in right atrial pressure after opening of the AVF. Similarly to the cardiac output, it took about 15 seconds to increase the atrial pressure (in both reflex and non-reflex dogs), see figure 7.

Needless to say, this study was done in dogs, and not in humans. Additionally, the AVF's were opened during open-chest surgery and under anesthesia. Both are known to decrease reactivity of cardiovascular reflexes.

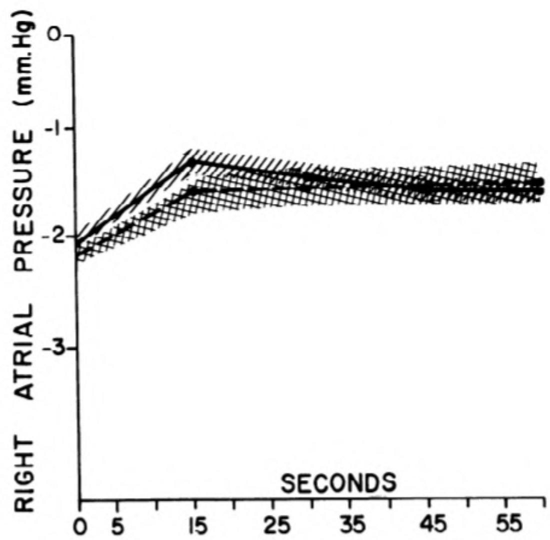


Figure 7: Increase in right atrial pressure after opening of an AVF in reflex (solid curve) and areflex (dashed curve) dogs (Guyton & Sagawa, 1961)

A more recent study investigated changes in CO after AVF placement in humans prospectively and found an increase in CO of 15% after three to fourteen days (Iwashima et al., 2002), which is significantly lower than what was found in the dog model by Guyton et al. This 15% however is an increase after days. For the sudden opening of the AVF, the immediate cardiovascular response is more important. Additionally, Iwashima et al did not measure any vascular resistance.

More insight can be gained on this subject by looking at a study done by Velez-Roa et al, in which the AVF of 18 renal transplant patients was occluded for 30 seconds (Velez-Roa et al., 2004). They found that the mean blood pressure increased and sympathetic muscle activation dropped within 5 seconds after occlusion. This suggests that it takes about 5 seconds for the body to react to the occlusion of the AVF. Unfortunately, the study did not mention how quickly they occluded the AVF, or how quickly they restored it after occlusion, and what happened then.

4.5.1 Value

For now, the value will be set at greater than or equal to 15 seconds, meaning it should take 15 seconds to gradually increase the required output force of the actuator from 0 to whatever is required to fully close the valve. Note that this value is heavily subject to change at this stage of development. This value will most likely have to be re-evaluated at a later stage, so to make this easier, the amount of dampening needs to be adjustable.

4.5.2 How to measure

The required time to reach the desired output force can be measured using a force sensor and a timer.

4.6 Mechanical

The actuator is to be implanted subdermally. For such an implanted device, it is desirable that it lasts for a long time, and is as small as possible. In order to achieve this, it is best to not use any electrical parts. Electrical parts are prone to breaking, and require batteries which will eventually run out, or take up a lot of space. In a previous iteration of the DAS, an electrical actuator was used in a goat model, but this proved to be too bulky, and the goat ended up removing it, causing it to bleed and die. To make sure the device can last a long time and not take up too much space, it would be best to purely use mechanical parts.
Aside from purely mechanical parts, there are some other material properties that could be interesting, like magnetic parts, or Shape Memory Alloys (SMA's).

4.6.1 Value

This requirement is not numerical, so a value can't be given. Instead, this requirement is met when the design uses no internally powered electrical parts.

4.7 Weight

Since the device is implanted into the patient for the long term, it will add weight to the arm that it is implanted in. This added weight may make it harder for the user to move their arm and be a hindrance. Depending on the weight of the device, and the implantation location, this could be a problem. When taking the maximum dimensions mentioned above; 3,5cm x 2,5cm x 1.3cm, we can calculate the maximum possible weight for the actuator. The maximum volume of the actuator is:

$$11m^3$$

If the actuator were made from pure titanium (which is a common material for implantable devices) with a density of:

$$4.506g/cm^3$$

the maximum weight for the actuator would be:

$$4.506g/cm^3 \times 11m^3 \approx 51g$$

A typical wrist watch weighs 100-150g, which is significantly more than that. Additionally, a watch is worn around the wrist which is further away from the shoulder joint, resulting in a higher moment around the shoulder (and elbow) than if it were placed at one of the possible implantation sites for the DAS. All this means that the weight of the device will not be a limiting factor in the design.

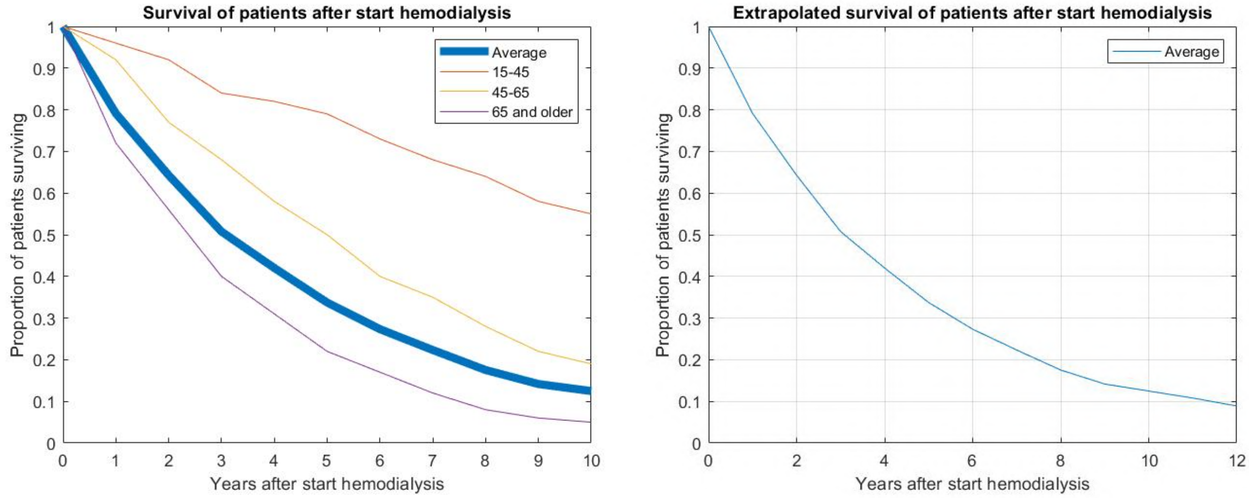
4.8 Durability

The actuator will be implanted subdermally into a human. This means that it won't be easy to replace or repair the device once it has been implanted. Because of this, durability is of great importance for implantable devices like this.
Simply put, this new device should have a better durability than the current methods. There are multiple ways however, to approach this requirement.

4.8.1 Cycles

One way to determine the needed durability of the actuator, is to look at the life expectancy of dialysis patients to see how long the device should be able to last. For this device, 90% of patients should outlive their implant. A study in 2011 found a mean life expectancy of a person on hemodialysis in the USA of only three years (Stokes, 2011). While this information is interesting, it doesn't give much insight into the distribution of the survival of dialysis patients. If the mean survival is three years, and the DAS is designed to last only three years, there could be many patients that survive longer than the average that outlive their implant, which is undesirable. So in order to determine a proper minimum lifetime for the DAS, the distribution of the survival data is needed. Unfortunately this information is hard to find in the literature, with most studies only reporting deaths per year, mean survival or percentage of survival after a certain time period (Robinson et al., 2014) (Saran et al., 2019). One study did report standard deviations, but this study only contains data from a single Colombian center (Enriquez et al., 2005), which isn't representative for the Netherlands as a country.

Luckily the Nierstichting, which is one of the funders of this project, has data that can be used (Nierstichting, 2018). The data from this factsheet was processed in Matlab (MathWorks, Natick, Massachusetts, USA). It contained survival curves for different age groups after the start of dialysis, and the amount of people in each age group. The data from the graphs was used to obtain one average survival curve for all age groups, see figure 8a. Note that this isn't perfect, since the data entries were read from the graphs supplied by the Nierstichting, but it gives a good estimate. Since the data from the Nierstichting stops after 10 years, and we're interested in the bottom 90% of patients (fraction 0.1), the data was extrapolated in Matlab using the cubic data fitting tool, see figure 8b.



(a) (b)

Figure 8: Survival curves of patients after starting hemodialysis. (a) shows individual curves for the age groups supplied by the Nierstichting, as well as an average survival for all ages. (b) shows an extrapolated average survival curve. Images generated in Matlab

We can find the desired value for the 0.1 fraction by reading the graph in figure 8b, which is around 11.4 years. Each year has 52.1429 weeks and hemodialysis patients receive treatment three times a week. Additionally, a safety factor of 2 is used. This means that the amount of times the actuator should be able to be activated and inactivated is:

$$11.4 \times 52.14 \times 3 \times 2 \approx 3500$$

4.8.2 Reintervention time

A different way of looking at the durability requirement, is to look at time to reintervention, also called primary patency. With current AVF's, the lifetime can be long, but it needs to be extended continuously, requiring many reinterventions.
Different studies found quite some different patency times, with some studies finding primary patency times of around 12 months (Brooke, Griffin, Kraiss, Kim, & Nelson, 2019)(Field et al., 2008), including a study performed on data in the Netherlands (Huijbregts et al., 2008). A meta-review done in 2014 however, found average primary patency times of twice as long (24 months) (Al-Jaishi et al., 2014). It mentions that primary patency times decreased in more recent years, but unfortunately did not try to explain why. Due to the large amount of studies included in the meta-review, 24 months will be taken as the average primary patency.

Reinterventions do not only cost a lot of money, but are also a big nuisance to patients and their quality of life. So when the durability of the actuator (and the DAS) has to be better than that of the AVF, it should last longer than 24 months until it requires a reintervention.

Looking at the secondary patency, which is the time from placement to abandonment of the AVF, it is hard to say what the average value is, since most studies don't follow-up long enough until they reach a patency rate of 50%. Generally speaking, it is possible to extend patency on an AVF quite far by doing reinterventions.

4.8.3 Costs

The durability requirement is interweaved with the cost requirement. When assuming that the costs for placing an AVF and the DAS are somewhat similar, the main factor influencing the costs is the amount of reinterventions needed. Reinterventions are needed when the AVF or DAS fails i.e. when the durability is lacking. This means that it could be possible to simply look at (long-term) costs per year for the durability of the DAS. When the long-term costs are lower than for AVF's, this probably means that durability is better as well, under the assumptions that:

- Initial costs for placement are similar
- Costs for reinterventions are similar

4.8.4 Value

Above, three different ways to determine durability were discussed. The first method looks at total lifetime of the device needed to survive the patient. The second method looks at time to reintervention (primary patency). The third method looks at a combination (costs per year).
Cycles may not be representative of actual durability, especially when tested ex-vivo. There are many factors that influence durability in-vivo that are not present ex-vivo related to being implanted into the body, like foreign body responses and clogging. It is likely that the actuator will need reintervention due to one of these factors before it mechanically fails. Reintervention time and long-term costs however, will be more representative for the actual durability, because they are measured when the device has actually been implanted. The problem with the last two methods is that they take years to measure, and require clinical trials. This is not within the scope of this thesis project, so these methods will not be used. Additionally, these methods include many more factors aside from simply mechanical functioning of the actuator that have to do with implantation. It would be good to first isolate mechanical functioning to make sure that durability is sufficient with regards to mechanical functioning before testing in vivo, so the cycle testing will be used.
The value for durability will be 3500 cycles. If the actuator can last for this many cycles and stay functioning, this is evidence that the actuator is less likely to fail due to a mechanical error when implanted.

4.8.5 How to measure

The amount of cycles can be tested in a test setup that repeatedly activates and inactivates the actuator.

4.9 Reliability

The valve of the DAS needs 6N in order to fully open, which is supplied by the actuator. This opening is needed to achieve a venous flow of 600ml/min for hemodialysis. Therefore it is important that everytime the actuator is activated, it actually supplies this force. Especially when multiple states are introduced in order to achieve a venous flow that is higher than 600ml/min but not too high, it is important that the opening and flow is consistent. Since there won't be any indicator in the valve to indicate that it has actually been opened or closed, it is important that the actuator always outputs the right force or displacement to be sure that the valve does what it is supposed to do i.e. it is reliable. If the force or displacement supplied by the actuator is too high, the resulting venous flow could be unnecessarily high (»600ml/min) resulting in stenosis and thrombosis, and if the force is too low, it can result in inadequate valve opening and a venous flow below 600ml/min, which is not enough for proper hemodialysis. A high reliability here means that the same input for the actuator always leads to the same output.

4.9.1 Value

An exact value that works for all types of actuators is hard to give here. Some actuators may have different states that correspond with a force; for example one state where the output force is 0N (fully opened), one where it is 3.0N (halfway open), and one where it is 6.0N (fully closed). Here, the opening of the valve is dependent on the supplied force. In this case it is important that each state outputs the correct force every time.
For this type of actuator, the error in the output force should not exceed 10% for the middle state where the shunt is opened half-way. For the state where the valve is supposed to be fully closed, the output force should never fall below the required force to fully close the valve. For the state where the valve is fully opened, the output force should be 0N.
Other actuators may have different states that correspond to different displacements as an output, independent of the input force. This would be the case for actuators with physical stops for example. Here, the opening of the valve is independent on the output force of the actuator, as long as the force is high enough to close the valve. In this case it is important that adequate force is supplied every time to overcome the physical stops and the pressure and resistance in the shunt.
For both types of actuators, an adequate input should always lead to an adequate output, meaning that the amount of failed activation attempts should be below 5%. Failed activation attempts could be due to inadequate

force being supplied by the actuator, due to a mechanism malfunctioning or due to other reasons, like the slipping of magnets. Note that failed activations could still be repeated until they become successful.

4.9.2 How to measure

The durability can be measured using the same force test setup used to measure the durability.

4.10 Usability

The DAS will be operated by nurses and patients, therefore it should be intuitive and easy to use. Operators should not have to worry about doing something wrong when activating the device. This requirement entails three sub-requirements:

- Ease of use: the activation should not be complicated, and preferably only require one movement (excluding a potential locking mechanism).
- No accidental activation: the point of the DAS is to close the connection between the vein and artery to prevent all the complications that come with an anastomosis that is always open. When the DAS keeps activating accidentally, that beats the point of the device. Preferably, the device should have a locking mechanism preventing accidental activation.
- The device gives some tactile or auditory feedback on activation. This is especially important, since (at least in the first version) no indicator will be implemented that can confirm that the valve had actually been opened of closed.

4.10.1 Value

This requirement is not numerical, so it can't have a value. Instead, it should meet at least two out of three sub-requirements.

4.10.2 How to measure

All sub-requirements have a binary measurement; they either have it or they don't, and thus don't require any testing or measuring.

4.11 Biological safety

The DAS, including the actuator, will be implanted into a human for a long duration. This will likely make it a class III medical device. Biological safety needs to be guaranteed in these devices.
This requirement entails multiple different sub-requirements:

- Biocompatibility: biocompatibility has to do with the inertness of materials in a physiological environment, causing minimal or no harm (Williams, 1998). The underlying material properties determining biocompatibility are very complex however, so for a proof of concept of the actuator, only materials that are already proven to be biocompatible should be used.
- Pressure ulcers: pressure ulcers or bedsores are a well known problem for people that have to lie in bed for a long time. The main contributor to these ulcers is pressure (Edlich et al., n.d.). This pressure usually comes from the outside, like a bed constantly pushing on the skin, but it can also come from the inside, caused by medical implants. The easiest way to prevent high concentrations of pressure is to avoid sharp edges.
- Explantability: even though the durability of the DAS is yet to be determined, it is likely that at some point, implants will have to be removed, either due to mechanical failure, or some biological influence. When this happens, the device needs to be able to be explanted without causing too much damage to surrounding tissue and structures. Therefor, it would be preferable if no ingrowth is possible in the device.
- Reintervention & modularity: like mentioned before, the DAS will consist of two separate parts connected with a transmission. This is done to prevent excessive forces on the anastomosis, and deal with the limited design space. These parts should be modular to allow replacement of a single part, as opposed to the whole device, in the case of malfunctioning to both reduce cost and severity of intervention.

4.11.1 Value

It is hard to determine a value for the biological safety requirement, since it and its sub-requirements are not numerical. Instead, to fulfill the biological safety requirement, at least three of its sub-requirements should be met.

4.11.2 How to measure

The biocompatibility sub-requirement is met when only known biocompatible materials are being used.
The pressure ulcer sub-requirement is met when there are no sharp edges on the outside of the device; all edges are filleted.
The explantability sub-requirement is met when no ingrowth is possible in the actuator.
The reintervention & modularity sub-requirement is met when the actuator and transmission can be replaced individually.

4.12 Costs

Needless to say, medical aid is expensive, and the same goes for vascular access for dialysis. In 2010 in the US, medicare paid 2.8 billion dollars for vascular access related services, which is 12% of the total budget for end-stage renal disease patients (Thamer et al., 2018). Thamer et al also indicated that a big contributor to these high costs is failing AVF's. While better clinical outcomes like improved patency rates or decreased complications could warrant a higher cost for the DAS, the actual advantages cannot be determined until later. This means that for now, it is best to aim for costs that are equal or less than the costs of current methods. This way, when the DAS has better clinical outcomes at the same (or lower) price, that immediately means that it is more cost-effective than alternatives, which makes reimbursement attractive for health insurance providers.

4.13 Value

AVF's use no materials (aside from some sutures), so there's no comparable costs there. AVG's however do have material costs. The costs for a piece of graft (the one used in the LUMC) are approximately 1000 euros. This means that the (retail) price for the DAS should also be 1000 euros or less. Note that this is for the entire device however, including the valve. Since the device is split in two, the costs are also split in two, resulting in a total of 500 euros retail cost for the actuator. Since a profit needs to be made, the actual production costs need to be lower. Later on, it might become apparent that the actuator will cost more than the valve, or vice versa, so this is subject to change.
While costs are important for the device in the long run, they shouldn't make that much of an impact at this point of development, since it is still in early stages and actual production costs are hard to predict.

4.14 How to measure

Production costs can be estimated by doing a cost assessment.

5. DESIGN FUNCTIONS

In order to fulfill the design requirements, certain partial design functions need to be fulfilled by the device. Additionally, some more design functions are identified that need to be fulfilled in order for the actuator to function. Multiple design solutions are formed for each design function. These solutions were formed during brainstorm sessions, where all ideas were welcome, and out-of-the-box thinking was encouraged. A short elaboration on each individual design functions and their solutions are given. All design functions and their respective solutions are given in a morphological overview, see figure 9, out of which concepts can be generated later.

5.1 Morphological overview

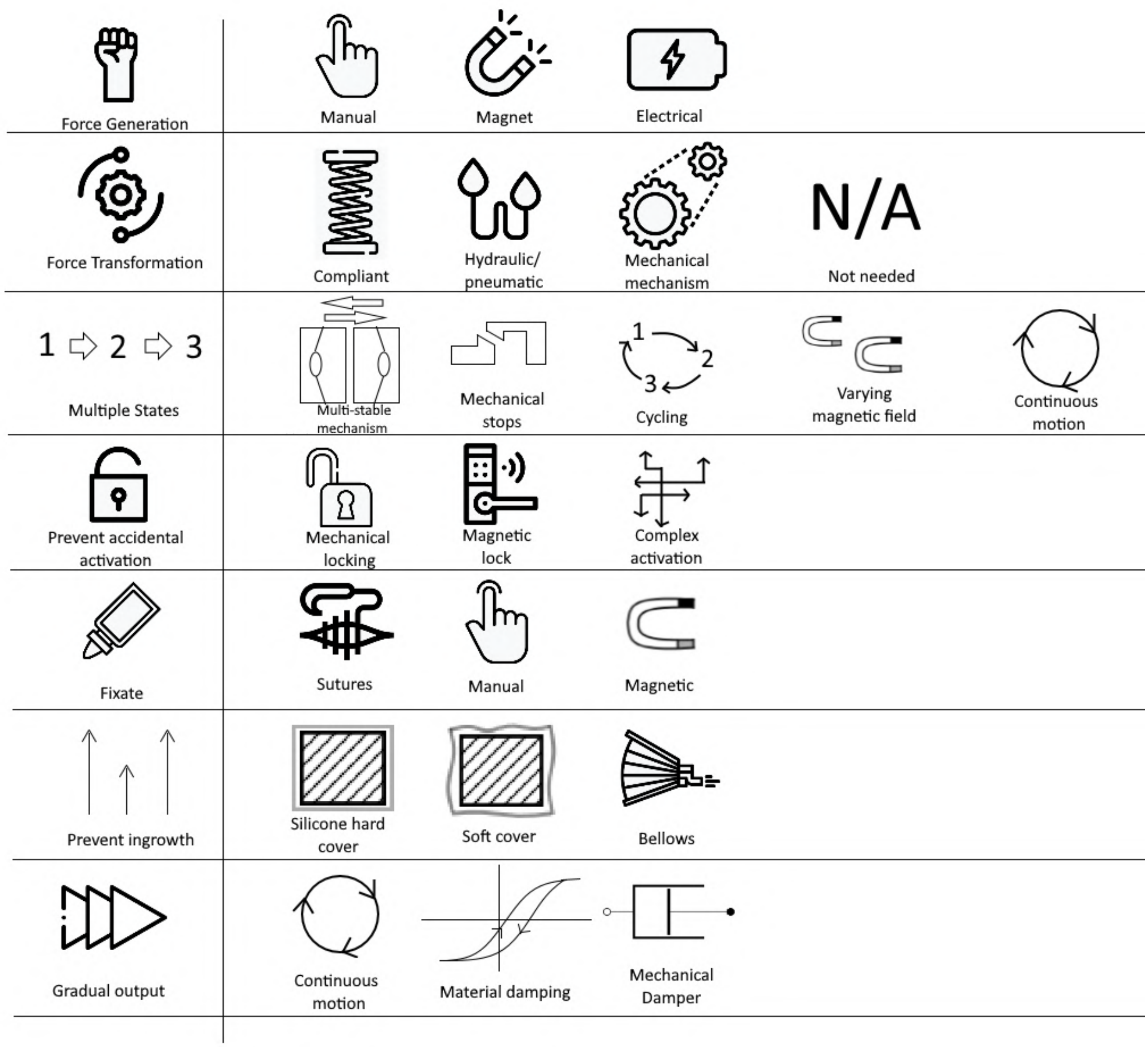


Figure 9: Morphological overview of the design challenges and their individual solutions

5.2 Force generation

The first design function is the generation of force. Following from the design requirements, we know that a certain force is needed as an input, to be transformed by the actuator into axial motion, which in turn is the input for the valve of the DAS. In order to come up with different ways of generating forces, a brainstorm session was held.

In the brainstorm session, six different mechanisms for generating force as an input for the actuator were identified. Below, these are mentioned and rated for how applicable they could be for use in the subdermal actuator.

Temperature: A change in temperature can result in expansion of a volume, which can in turn be used to push something back and forth. Another way in which temperature can be used is in the form of a Shape Memory Alloy (SMA), which can change its shape depending on the temperature.

Evaluation: Using temperature to achieve axial motion is interesting because it can be done without actually having to manipulate the skin. Additionally it could allow for a lot of different states of energy that the actuator can output, since there's basically an infinite amount of different temperatures resulting in different pressures and thus output energies. There are however multiple problems when using temperature. The first obvious problem is that you need to heat a fluid or gas, which means that the surroundings also get heated. This heating can be uncomfortable for patients or even damage surrounding tissue, depending on the temperature. The second problem is that, when a liquid or gas has is used, these are prone to leakage, which can cause the actuator to not function anymore, or even have toxic systemic or local effects on the body. In order to check the viability of using temperature to expand a gas or liquid and thus end up with a displacement, similar to in a piston, a quick calculation will be done. For this example, a liquid with a large thermal expansion coefficient will be taken, meaning that it will expand a lot when heated. Ethyl Alcohol has a high thermal expansion coefficient of $1100E^{-}6K^{-}1$ (lumen, 2020). When a cylinder with the maximum allowed dimensions is filled with ethyl alcohol, it has a volume of:

$$0.035m * \pi * (0.0075m)^2 = 6.19E^{-6}m^3$$

When this body of fluid is heated up by 5 Kelvin, it results in an expansion of

$$\Delta V = 1100E^{-6}K^{-}1 * 6.19E^{-6}m^3 * 5K = 6.81E^{-9}m^3$$

This ΔV relates to a change in height of the cylinder:

$$\Delta h = \frac{\Delta V}{0.035^2 * \pi} = 1.77E^{-6}m$$

This achieved change in height, a volume increase of 0.011%, of the cylinder is extremely small. To close the piece of graft, a force of 3.0N is needed (see design requirements). This means that a pressure of

$$P = F/A = 3.0N/\pi * 0.035^2 = 78 \times 10^1 Pa$$

is needed. The bulk modulus of ethyl alcohol is $K_b = 0.602GPa$ (efunda, 2020), meaning that a pressure of 779.5Pa results in a volumetric change of

$$\frac{78 \times 10^1 Pa}{K_b} = 8.6E^{-7}$$

or $8.6e^{-5}$%. This change is negligible, meaning that in theory, thermal expansion could be used to close the piece of graft. However, because the change in length of the actuator and thus the displacement is so low, this is not very practical.
Another problem with this method is that the environment will be heated, since the fluid needs to be heated during the entire duration of the dialysis, heating the environment as well.

Using temperature in combination with an SMA however, could be interesting. This time, no liquid or gas is used, which means no leakage. Additionally, SMA's can be heated remotely much more easily, using induction heating, without heating the environment as much.
Implementing a SMA however, can become quite complex. The goal of this thesis project is to provide a proof of concept for the actuator and the DAS as a whole, and, even though this could theoretically be achieved by using a SMA, it is a very complex solution, and won't be the easiest way to get to the goal of this project.
Additionally, using a SMA will make it very hard to make the DAS have three different states of opening, since there's no stable middle state between the martensitic and austenitic state of a SMA. Therefore, SMAs will not be explored further for this project.

Conclusion: not viable

Manual force: A physical force can be exerted by hand on a mechanism which translates the force into the desired axial movement.

Evaluation: The actuator could be placed just under the skin, so that it can still be handled. This means that a purely mechanical design that is activated, deactivated and locked by hand becomes viable. Such a design is preferable due to its simplicity in handling and lack of complex parts that would be prone to breaking. By using a manual input, quite a bit of force can be generated. This is however, dependent on how well something can be manipulated through the skin, which will be tested later.

Conclusion: viable

Gravity: Gravity could be used to achieve translational motion.

Evaluation: In theory, gravity could be used. However, this is highly impractical since it only works in one direction. If gravity were used, it would probably mean that a person would have to lift their arm during the entire dialysis process, or exert some kind of repetitive motion, slowly activating a mechanism. Additionally, the gravitational force on a very small mechanism probably won't be enough to close the valve. Accidental activation of the mechanism would also be a big problem.

Conclusion: not viable

Magnetism: Magnets can be used to attract and repel other magnets or magnetic materials to achieve translational motion.

Evaluation: Magnets are very interesting, since they can achieve translational motion remotely without physically having to manipulate the skin. Additionally, they don't require a battery or other electrical components. In a previous prototype, an attempt was made to use magnets to close a valve. However, not enough force could be achieved to actually close and open the valve. Another concern with magnets is that they can lose their magnetivity by means of high temperature, mechanical shock, demagnetizing fields or moisture (Hoadley, 2020), especially when implanted for a long duration like in case of the actuator. When these challenges can be overcome however, magnetism can be an elegant solution that doesn't add a lot of complexity and doesn't require manipulation through the skin.

Conclusion: viable

Muscle power: In theory, someone's own muscle power could be used to trigger a mechanism internally, which can result in axial motion.

Evaluation: Muscle power, for example from the close by biceps muscle, could provide enough energy to close a valve, however, it is far from practical. Muscle activation happens continually, and using this to trigger a mechanism would be really tricky; making it only occur when needed would be very hard. Additionally, introducing multiple states and tactile or auditory feedback would be over complicated.

Conclusion: not viable

Electrical energy: Electrical energy stored in for example a battery can be used to drive a motor or any other mechanism to achieve translational motion.

Evaluation: In theory, using electrical energy as a power source sounds attractive, since it can easily be used in a motor and doesn't require a manual input of energy and manipulation through the skin. A previous prototype of the DAS used an electrical actuator. However, this proved to not work well. The main reason was that quite some energy is needed to close and open the valve, much more than in for example a cardiac pacemaker. This means that if a battery were to be used, it would need to be too large to fit in the limited amount of available space. This in turn, means that wireless energy transfer would be needed, which adds a lot of complexity. Additionally, when large amounts of electrical energy are needed, this increases the risks involved and the dangerous effects when something ends up breaking. Because of these reasons, the decision was made to exclude any concepts using electrical energy. Additionally, similar to using a SMA, using electrical parts adds a lot of complexity, which defeats the purpose of an initial proof-of-concept prototype for this project.

Conclusion: not viable

5.3 Transform into axial force

The next design function is the transformation of the input force into an axial motion. The actuator needs to output an axial motion, which will act on a Bowden cable, which in turn is the input for the valve. The input force however, may not be axial or in the right direction, depending on the force generation mechanism and orientation. In another brainstorm session, methods of transforming forces were identified.

Compliant mechanism: Compliant mechanisms are flexible mechanisms allowing force and motion transmission through elastic deformation. A large benefit of compliant mechanisms is that they don't experience any friction and as a result, are less prone to wear than regular mechanisms. This is especially convenient for implanted mechanisms, since it isn't as easy to repair or replace them. A simple example is a compliant ring; if a pinching force is exerted on one side of the ring, this side will compress. As a result, the tangent sides of the ring will expand. This will effectively change the direction of the force.

Hydraulics/pneumatics: Hydraulics and pneumatics are widely used in engineering to transform motion. Due to fluids being (nearly) in-compressible, a force on one end of a tube will be fully propagated to the other side. The same principle applies to (high-pressure) gasses in pneumatics.
A problem with these methods is that they can leak fluid or gas. The fluids and gasses used for these types of systems are often toxic. Additionally, when they leak, functionality is lost, resulting in a different output energy and thus different levels of opening in the valve.

Mechanical mechanism: Many other mechanisms exist that can change the direction of a motion. Cranks can be used to transform rotational or other non-linear motion into axial motion. A screw mechanism can also transform rotational motion into axial motion.
Pulleys can be used to either transform a rotational input motion into axial motion, by winding a cable around it, or be used to change the direction of a motion. One thing to note is that they only work when pulling, since flexible cables are used. This means that some spring force will be needed to return the system to its original state. Aside from the examples given above, many more mechanical mechanisms exist that can convert the direction of a force.

Transformation not needed: Another option is that transformation is not needed. When the input force for the actuator is an axial force that can be supplied in the right direction, transformation of the force won't be needed. This could be the case if, for example, a slider is being used.

5.4 Output at least three states

The next design function is to have the actuator be able to output three (or more) different states. Like discussed in the design requirements, the actuator needs to be able to output three different states resulting in three different levels of opening in the shunt: fully closed, fully opened, and a state in between.

Multi-stable mechanism: multi-stable mechanisms are mechanisms that have more than one stable state. In our case, at least three states are needed. Such a mechanism would allow us to output three different states without any additional mechanisms. These multi-stable mechanisms are usually compliant mechanisms. An example of such a mechanism is represented in figure 10.
After a short literature search, unfortunately, no suitable tri-stable mechanisms were found to include for the actuator. By far, most multi-stable mechanisms are bi-stable, which is unacceptable for the actuator, since at least three output states are needed. Some tri-stable mechanisms were found, but these all had either very small displacements, required dimensions that were not available for the actuator, or were in some other way unable to

be implemented as an actuator.

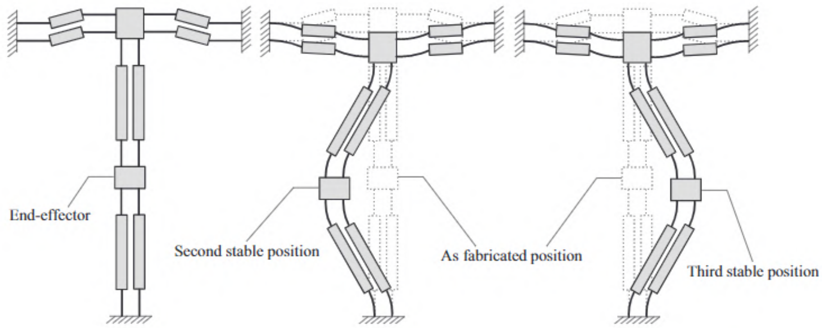


Figure 10: Illustration of a tri-stable mechanism in all its stable states (Chen et al., 2010)

Mechanical stops: Another way to have three distinct output states is to take a continuous motion, like a sliding motion, and introduce snap fit 'stops'. The motion will be stopped after it reaches one of the stops, and to overcome the stops, it requires a greater force. Alternatively, a second mechanism can be introduced that interacts with the stops, like a button or a magnetic mechanism, allowing the main element to surpass the stops.

Cycling: Another solution could be a cycling mechanism. In such a mechanism, the actuator is cycled between states every time it is activated. A benefit of such a system is that one consistent input can be used to control all the states of the system. An example of such a system is a click-pen mechanism in a pen. This mechanism allows the pen to cycle between two states with a simple pressing force on the back of the pen.

Varying magnetic fields: When a magnetic type of actuation is chosen, magnetic fields with varying strengths could be used. This is graphically represented in figure 11. A problem here however, is that the magnetic force itself most likely won't give enough force to close a valve, as was experienced in a previous prototype. It may be possible to overcome this problem using a statically balanced system to reduce the actuation energy, but these systems generally are only capable of outputting two states, where three or more are needed for the actuator. This means that, unless this problem can somehow be overcome, varying magnetic fields are not a viable solution for introducing at least three states into the system.

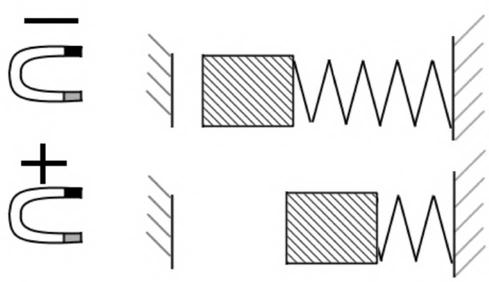


Figure 11: The concept of varying strength magnetic fields explained. In the upper case, a weaker magnet is used, pushing the object not that far. In the lower case, a stronger magnet is used, pushing the object further, resulting in a different state of actuation.

Continuous motion: When a continuous motion is used, in theory an infinite amount of states can be output. A prerequisite however, is that there has to be some feedback on the state, so that the operator knows how far open the shunt is. Another prerequisite is that the actuator stays in the induced position, and won't drift during dialysis.

5.5 Prevent accidental activation

The next design function is preventing accidental activation of the actuator. Since the actuator will be implanted in the upper arm, which moves a lot, and can bump into things, it will be prone to accidental activation, which can cause the actuator to open when not needed.

Mechanical locking: the most obvious solution is to have a mechanical locking mechanism in place. The mechanism will physically prevent the actuator from being activated. The lock could be interacted with in the form of a button, slider, knob, etc.

Magnetic locking: similar to a purely mechanical lock, a magnetic component could be added. Now, instead of needing another point of interaction on the actuator, which can make it harder to operate, a magnet could be used.

Complex activation: a locking mechanism might not always be needed. Because subdermal actuators are not commonly used yet in medicine, not much is known about their behavior, how well they can be operated, and how prone they are to accidental activation. It might turn out that this is not that big a problem for some designs. In any case, when a complex activation operation is needed for activation, accidental activation becomes much less likely, or impossible. When for example a pinching motion is needed for activation, locking will likely not be needed. Pinching is not a motion that really happens accidentally on the skin, unlike for example a simple pushing motion, which can happen when bumping into something, or while lying in bed.

5.6 Fixate

The next design function to tackle is the handling of the actuator. In order to activate the actuator using one of the proposed solutions, it needs to be held in place. If not, the actuator may just move, instead of activating it. Experimentation should point out how prone to slipping and moving the actuator is when it is implanted.

Sutures: one option is to use sutures to connect the actuator to the fascia around the biceps brachii and triceps muscles. This approach was discussed with a vascular surgeon who deemed it viable. The same approach is also used for similar implanted devices like port-a-caths, which sometimes remain implanted for multiple years. Exactly how well the actuator would be fixated is hard to say, and is highly dependent on the amount of sutures. Experimentation will need to be done in order to provide more insight into whether this is a viable solution for this device. Additionally, even when fixated well to the fascia, the fascia itself can also move, still possibly making it hard to operate the actuator. A possible danger of using sutures is that this will transmit forces on the actuator to the underlying fascia, which could be dangerous. Rodrigues et al found that tractive forces of up to 11.43N on a single suture on the fascia of a pig can be tolerated (Rodrigues, Horeman, Dankelman, Van Den Dobbelsteen, & Jansen, 2012). This should be kept in mind, as it is not unthinkable that such a force could be exerted. Using multiple sutures could make this less of a problem however, when forces are distributed over the individual sutures.

Manual: another option is to manually keep the actuator in place. This is the most obvious and simple solution, but is dependent on the activation method. If the activation method is a simple button requiring only one finger to press it, it could be possible to use the other fingers to keep the actuator in place. However, when the activation is a more complex movement like pinching (with the reason of not having to use a locking mechanism for example), it could be much harder to hold the actuator in place AND activate it, both due to not having enough dexterity in the hand, and having not enough space available on the actuator to both hold it and perform the required activation. Another limiting factor here is how well the actuator can be manipulated through the skin, which will be tested later on.

Magnets: when space is limited and keeping the actuator in place manually does not work out, another option is to keep the actuator in place using magnets. One or two magnets could be placed on the sides of the actuator. A band could be placed around the arm of the patient, also containing magnets. When placed around the arm, these magnets attract the magnets in the actuator, keeping it in place, and making it easier to operate it.

5.7 Prevent tissue ingrowth

The next challenge is to prevent the ingrowth of tissue when the actuator is implanted. Ingrowth from tissue could strongly impair the workings of the actuator due to clogging and blocking. Therefore, ingrowth should be prevented.

Rigid cover or housing: one option is to place a rigid cover all around the actuator. Any rigid biocompatible material could be used here. When there are any interactive buttons or sliders on the actuator, this might not be a good option however, because it makes operating the actuator impossible.

Flexible cover: the actuator can also be placed in a flexible satchel or container. This way, any ingrowth is prevented, and it can still be operated. A problem with this approach however, is that it can make fixating and operating the actuator harder. This is because there is yet another layer of material, aside from the skin, that can move.

Bellows: another option is to use a rigid layer around the non-moving parts of the actuator, and use a bellows-like structure around parts that need to be able to move, see figure 12.

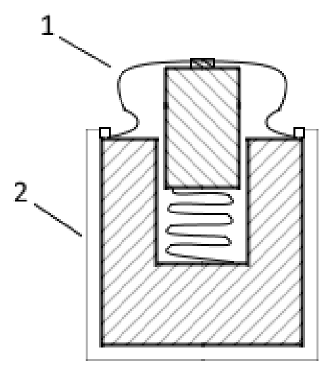


Figure 12: Example of the bellows solution (1) around a movable button, and a rigid layer (2) around non-movable parts.

5.8 Prevent immediate opening

Like discussed in the design requirements, if the force output by the actuator is not damped, this can result in immediate opening of the shunt, which can be uncomfortable or even dangerous for the patient. This means that the immediate opening of the shunt needs to be prevented.

Mechanical damper: one obvious solution for this function is to introduce a damper into the device. Generally, damping is a measure of dissipating vibration energy in a system. When damping is introduced into a system, it changes the response of a system. The response of a damped system to a step input is shown in figure 13. For our device, we want to slow down the response, meaning we need an overdamped system.

A damper controls and delays the movement by absorbing some of the energy. This causes the movement to occur in a delayed fashion.

With dampers, it should be taken into account that they dissipate energy, meaning energy that would otherwise go into the valve, would be lost. This increases the needed input and output energy for the actuator. Additionally, the valve should take 15 seconds to go from fully opened to fully closed, which is a long damping time. Testing will need to point out whether this is achievable, especially given the limited available space.

There are two different ways to implement a damper. One way is to use the damper to dampen the force input that can be given by the operator; for a slider, this would mean that the slider can't be moved from left to

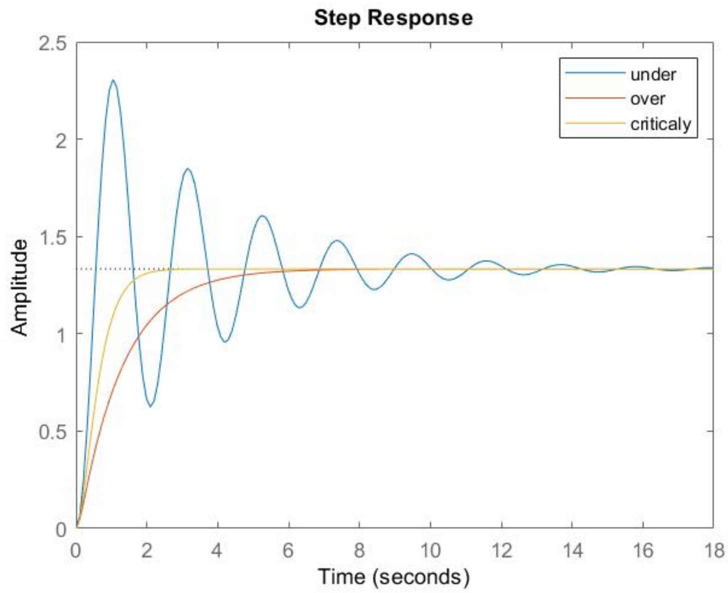
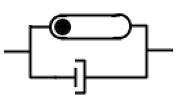
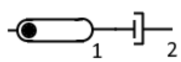


Figure 13: Step response of three different damped systems.

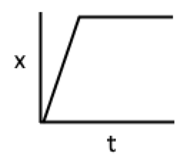
right too quickly, because of the opposing damping force, resulting in a gradual output. This is represented in figure 14a & 14d. Note that the output represented in figure 14d could still vary, depending on the force exerted on the actuator by the operator. A much larger force will still result in a steeper displacement graph.



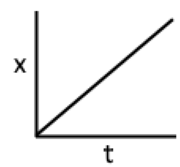
(a) First method of using a damper, limiting the input.



(b) Second method of using a damper, using the output of the actuator as an input, then making it gradual.



(c) Displacement output of the second actuator at point 1



(d) Final displacement output of both systems.

Figure 14: Systematic representations of the two methods of using a damper. Both result in the output seen in (b).

The other way is to dampen the energy *after* the input from the user (see figure 14b & 14c); for a slider, this would mean that the person operating the slider can slide from left to right as fast as they want, resulting in different outputs by the slider in figure 14c. The resulting energy is then stored (in a spring or other compliant mechanism). This energy is then released slowly by the damper, also resulting in a gradual output (figure 14d). This second method is preferable, since it is independent from the operator; no matter the user input, the output should always be (almost) the same. For the first method, it is still possible to vary the amount of force exerted on the slider, resulting in a different output.

There are multiple different types of mechanical dampers, all relying on different principles to dissipate energy and provide a damping force:

Fluid damper: Fluid dampers use a viscous fluid and shear stress to dissipate energy. They usually consist of a cylinder, filled with a viscous fluid, a piston rod and a piston head, see figure 15. When the piston head moves, fluid is forced through the microchannel(s) in the piston head, generating heat and thus dissipating energy.

These types of dampers use few components, making them simple in design and easy to scale down. The damping rate can be tweaked by altering the viscosity of the fluid and the diameter of the orifice or microchannel.

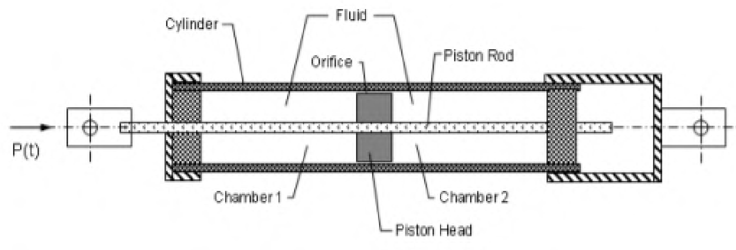


Figure 15: Example of a simple fluid damper (Comsol, n.d.)

There is a fluid inside that in theory could be prone to leakage. However, the damper can be placed in a sealed environment, since access to the damper is not needed once implanted, making leakage highly unlikely. Additionally, biocompatible liquids exist that could be suitable.

Air damper/ dashpot: similar to the fluid damper, air dampers or dashpots also use a cylinder and a piston. However, here, air can escape and enter the piston through a small air vent. A pressure difference between one side of the cylinder and the other side of the cylinder provides the damping force. Damping can work in both directions (pulling and pushing).

Friction damper: Used mostly as a means of energy dissipation in making buildings earthquake proof, friction dampers rely on friction to dissipate large amounts of energy.

5.8.1 Modular damper

It would be very helpful to have a modular damper that can be inserted into any design or concept, at any place (so right after the actuator, somewhere along the transmission, or just before the valve). The input for this damper could be any type of axial motion, and the output should be a gradual axial motion (preferably over +- 15 seconds). Such a damper could in theory be made quite easily by taking the simple fluid damper seen in figure 15 and introducing a spring to store energy. The concept for such a damper is shown in figure 16.

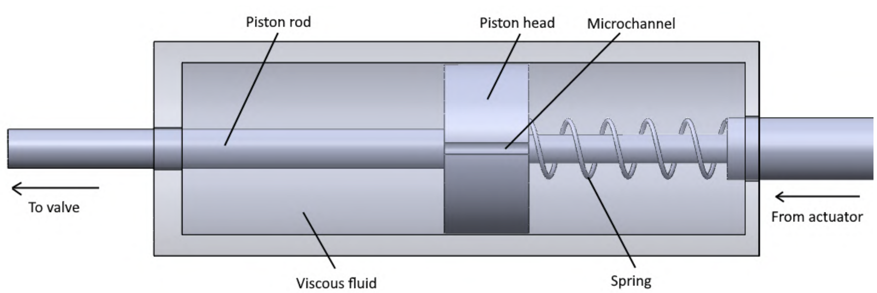


Figure 16: Design of a modular damper, transforming any input into a gradual output.

The input that comes from the actuator on the right side can be a near-instant axial movement. This movement compresses the spring, storing the energy. Then the spring exerts a force on the piston head, pushing it to the left. Due to the incompressibility of the viscous fluid in the damper however, the piston head can not move to the left as quickly as the input does. One or more microchannels in the piston head dissipates energy through viscous friction and allows the piston head to slowly move to the left, moving the piston rod as well. The time it takes the piston head to move can be tweaked by the viscosity of the fluid, and the size of the microchannels.

Continuous motion: not in all cases a damper is necessary. When the output of the actuator can be controlled well, a damper may not be needed. If, for example, a slider or rotating knob is used as an input, it can simply be activated in a slow and controlled manner over a larger time span. This way, the user itself has control over the speed at which the valve opens.
Note that this solution is not possible for some designs, since they do not allow for gradual activation.

Another thing to note, is that the output is dependent on the input given by the user. While the option exists to give a gradual output, for example with a slider, it would still be possible to move the slider quickly, resulting in an output that is too quick.
A way to (partially) prevent this, is to split up the motion into multiple smaller motions, with each submotion opening the valve a small amount. One way to do this would be to introduce multiple mechanical stops in the activation mechanism that have to be overcome.

Smart material choice: aside from using an additional mechanical damper for a gradual output, smart material choice can also result in damping of a motion. Especially of interest are viscoelastic materials. This group of materials exhibits both viscous and elastic material properties when undergoing deformation. As a result, they can dissipate energy during a loading cycle, seen as hysteresis in the stress strain curve (figure 17).
Another characteristic of viscoelastic materials is that they exhibit creep, which is the slow time dependent deformation of viscoelastic materials under a constant stress. This creep can be used to delay the motion of the actuator if used correctly.

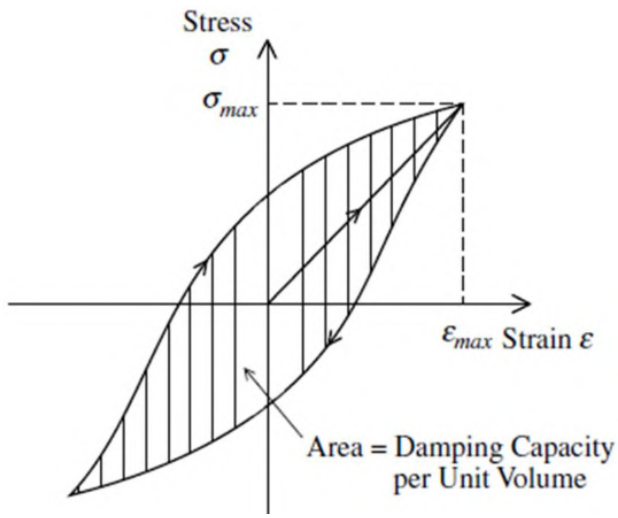


Figure 17: Hysteresis in a typical stress-strain curve for a viscoelastic material (Witoś & Stefaniuk, 2011)

The biggest challenge in using this approach would be to find a suitable material that is biocompatible and has the right viscoelastic properties. Another problem is that this approach can not be used with all mechanisms. It is most suitable for compliant mechanisms, since these rely on deformation, which can be slowed down using creep. Mechanisms of action that use a 'snapping' motion are less compatible with this sort of damping.

6. SIMULATING SKIN

Before a morphological overview and concepts are being generated, some thought is given to how to evaluate the generated concepts. In order to get a feeling for how well mechanisms can be handled through the skin, it is useful to have either actual skin to test on, or some sort of substance that can resemble human skin. This way, a couple different activation methods for the actuator can be tested to see how well they can be handled. This skin model can then be used as a simple, first evaluation of conceptual designs.
Actual human skin would be most optimal, since it is most representative of the eventual implantation. Actual human skin is however harder to come by, can only be used in an anatomy lab, and skin properties can change after death and preservation using formaldehyde. While some experimenting on actual human skin will be done in a cadaver study to determine the best location and dimensions of the actuator, initial handling will be tested using fake skin.

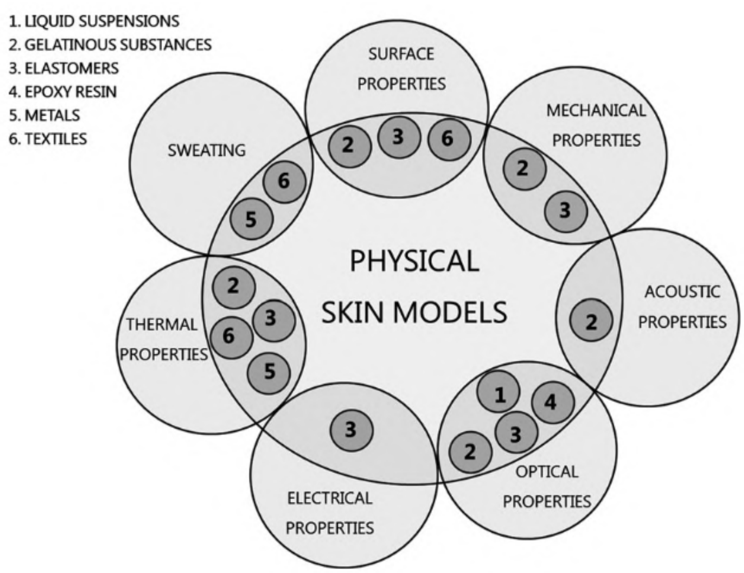


Figure 18: Overview of different properties of skin and the types of substrates that simulate them (Dąbrowska et al., 2016)

Multiple different substrates have been used to simulate fake skin, with different substrates simulating different properties like thermal, optical and mechanical properties. Dabrowska et al made an overview on the different kinds of substrates and what properties they simulate, see image 18 (Dąbrowska et al., 2016).

In this case, most interesting are surface properties and mechanical properties. Surface properties are interesting because they include the hardness of the skin, which influences how well you can feel and handle the implanted mechanism through it. Mechanical properties like the elastic modulus are interesting because they influence how easily the skin can be stretched when making a pinching movement for example. Looking at figure 18, we can conclude that gelatinous substances or elastomers are most suited for our needs.

In order to determine the needed 'hardness' of the skin, the shore hardness can be used (ASTM, 2017). Reports on skin shore hardness depend on some factors like temperature, humidity, and location of the skin that is measured, with reports generally ranging from 20A (Muthu, 2007) to 30A (Panduri, Dini, & Romanelli, 2017). The elastic, or Young's, modulus of human skin varies between 0.6MPa and 0.85MPa, dependent on age and gender.

Lastly, the thickness of the human skin is important. Thickness of skin depends on factors like the location of the skin on the body and the BMI of the person. Most studies on skin thickness focus on diabetes patients, since skin thickness is relevant for determining needle lengths. Two studies (Akkus & Kizilgul, 2012) (Jain, Pandey, Lahoti, & Rao, 2013) found skin thickness in this group of people in the arm region between 2.0-3.0mm.

From an old BSc graduation project on a skin model of the wrist area, multiple slabs of silicone replicated skin are available. These have differing mechanical properties, in the range of what could be found in real skin. They also come with a clamp to fixate the skin.

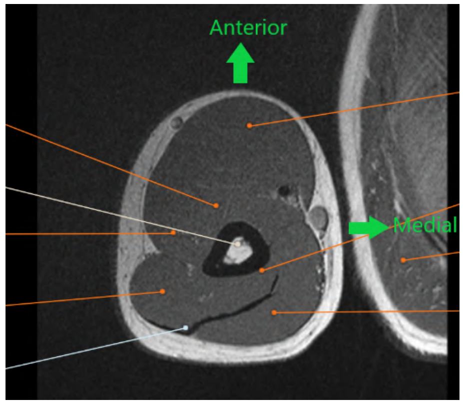


Figure 19: MRI image of the upper arm, acquired from Imaios.com

The actuator will be placed between the skin and the underlying tissue, mainly being muscle. The only thing that needs to be added to the existing model is some sort of underlying structure that resembles the biceps and triceps muscles in the upper arm. This muscle tissue will be simulated using a soft 3D printable resin called flexible resin (Formlabs, Somerville, MI, USA). The muscle structure including the crease in which the actuator is to be placed was modeled after MRI data obtained from Imaios (Micheau & Hoa, 2020), see images 19 20.

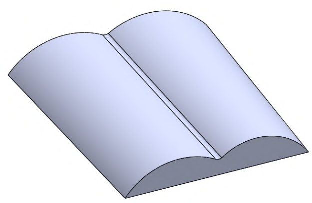


Figure 20: 3D model of the underlying muscle structure in the upper arm

The resulting model can be seen in figure 21.

(a) Skin model with the skin covering the underlying muscle structure

(b) Skin model shown with the underlying 3D-printed muscle structure exposed

Figure 21: The skin model for first evaluation of the function of conceptual designs

7. MORPHOLOGICAL OVERVIEW & CONCEPT SELECTION PROCESS

Now that the design requirements, design functions and partial design solutions are know, multiple design solutions can be combined into a conceptual design. This is done in a morphological overview, see figure 22. Multiple concepts will be generated from this morphological overview by combining partial design solutions, as indicated by the colored lines in figure 22. Using this method, a total of 13 different concepts were generated.

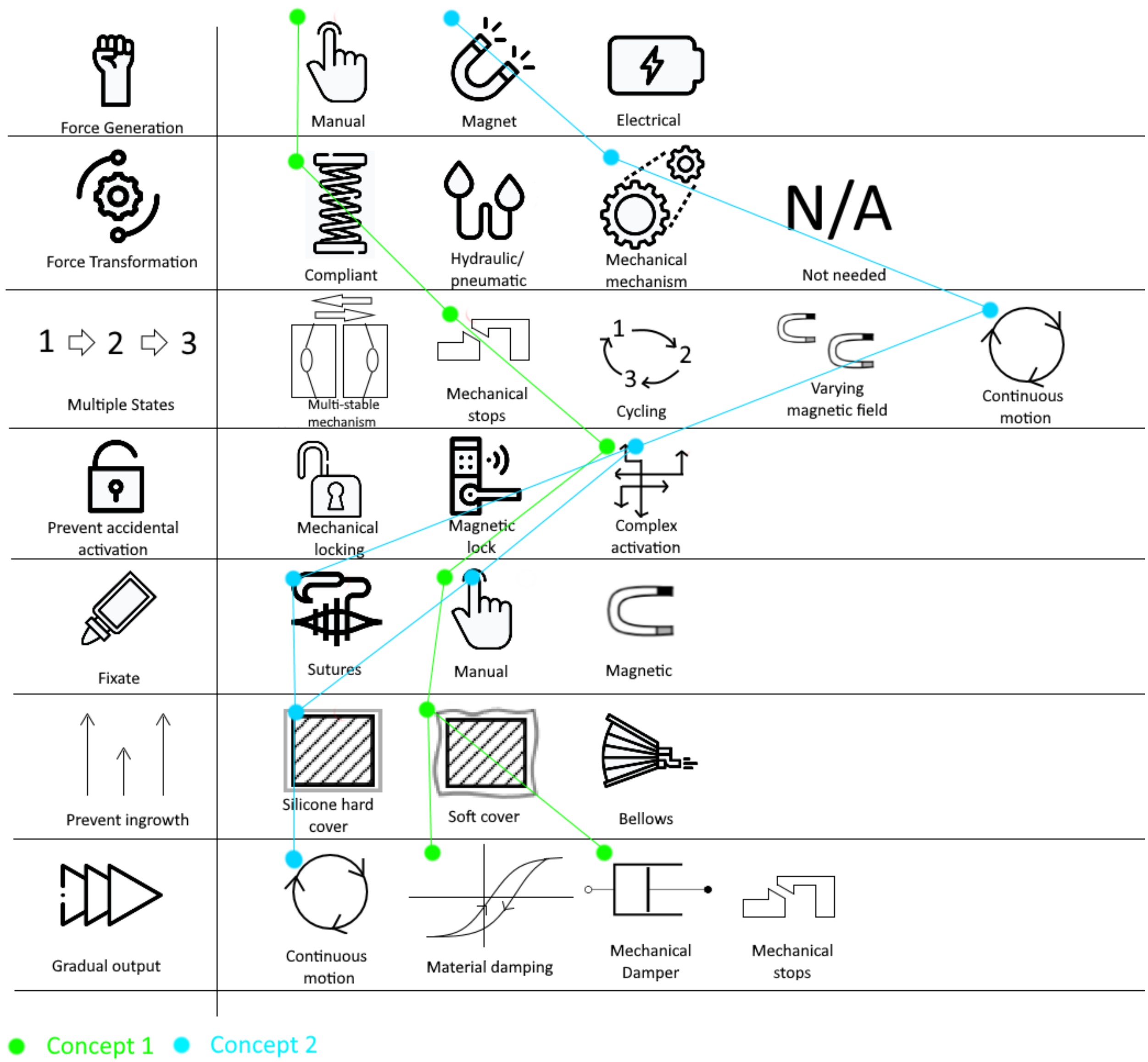


Figure 22: Morphological overview for the first two designs

For the concept selection, a funnel type process was used, see figure 23. The goal was to start broad with as many different concepts as possible, including out-of-the-box solutions. Then by means of elimination the pool of viable concepts was narrowed down.

Using the morphological overview and design solutions, a total of 13 different concepts were generated. For the sake of brevity, not all generated concepts were included in this report. Only the concepts that were thought to be viable after simple prototyping and testing in the skin model are described here. After testing and using them in the skin model to check viability, 4 concepts were left. After the human cadaver study, 2 more concepts were eliminated, leaving 2 concepts. These were graded in a Harris profile leaving 1 winning concept to be developed further into a prototype for testing and validation.

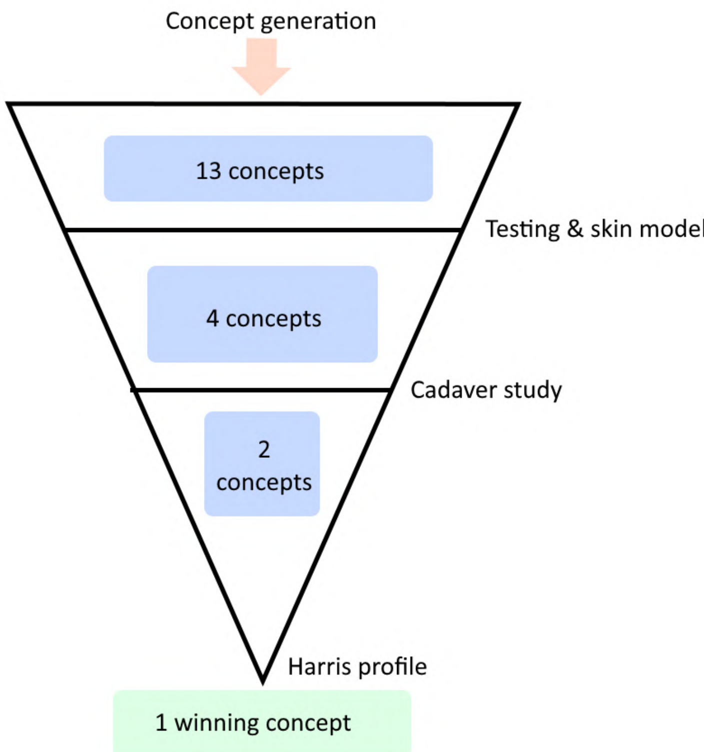


Figure 23: Overview of the concept selection process.

7.1 Concept 1 - compliant ring - theme: *minimalist*

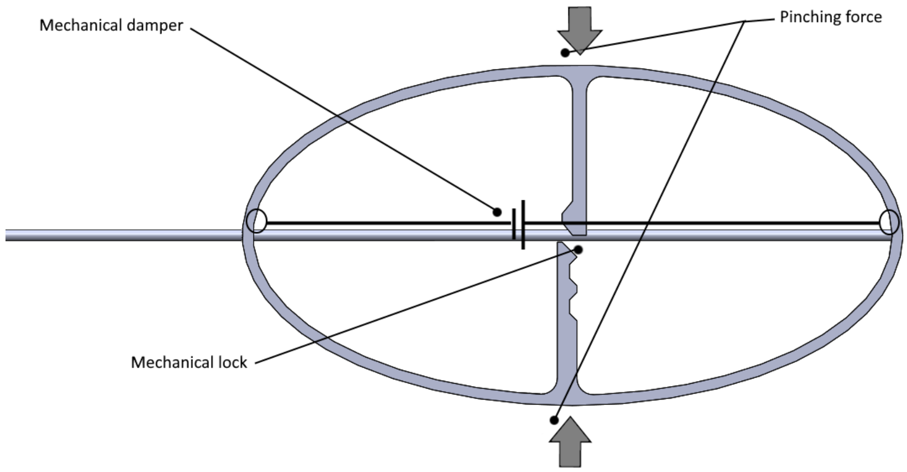


Figure 24: Schematic overview of the first concept

Figure 25: The first conceptual design, featuring a compliant ring, mechanical damper and mechanical locking mechanism.

The theme for this concept was *minimalist*. An attempt was made to combine design solutions to come up with a solution that is minimalist in design; little material used, no or few joints, simple mechanisms.

This concept uses a compliant mechanism. Compliant mechanisms are flexible mechanisms allowing force and motion transmission through elastic deformation. A large benefit of compliant mechanisms is that they don't experience any friction and as a result, are less prone to wear than regular mechanisms. This is especially convenient for implanted mechanisms, since it isn't as easy to repair or replace them. Such a mechanism fits well with the minimalist theme.
The concept uses two pawls that can slide past each other when the mechanism is compressed, and can lock in at least two places, resulting in at least three different output states. When the ring is compressed in one direction, it elongates in the other direction, effectively changing the length of the transmission, see figure 27.

Force generation: Force is generated manually through the skin by compressing the ring on two sides.

Force transformation: The compliant ring mechanism transforms the direction of the input force into the desired axial output force by means of mechanical deformation, as seen in figure 27.

Multiple states: Multiple states are introduced by the pawls in the middle of the ring that slide over each other. Additional nudges could be introduced to allow for more different output states.

Prevent accidental activation: Whether this concept is

Figure 26: 3D model of the first concept

prone to accidental activation is hard to predict. It does need a pinching motion to activate, which isn't very likely to happen accidentally. If, however, accidental activation turns out to be a problem, the two pawls can be placed directly in front of each other, so that pinching does not cause them to slide over each other. A third pawl can then be added that, when pressed, pushes one of the pawls to the side, allowing them to slide past each other again.

(a) Uncompressed state

(b) Compressed state

Figure 27: Illustration of the working principle behind the concept

Fixate: The actuator will be fixated manually by hand while operating it.

Prevent ingrowth: Preventing ingrowth for this concept is challenging, since the ring is open in the middle. Even when the actuator is placed in a pouch, tissue could still get in-between the ring. A solution could be to fill the ring with silicone, that can deform and still allow the actuator to function, but doesn't allow tissue to get in the way.

Gradual output: Two methods could be used to achieve a gradual output:

1. Material damping: viscoelastic materials could be used to introduce damping into the system. This causes the deformation to take place in a delayed manner. The ring itself could be made from such a material, or a viscoelastic material could be attached to the ring. Note that the silicone placed in the ring to prevent ingrowth could also introduce damping into the system.

2. A mechanical damper could be placed in the ring, attached on both the long ends. The input energy is now stored as deformation, and slowly released by the damper, resulting in a slow axial movement of the actuating rod.

7.1.1 Further testing & validation

To check the viability and function of this concept, it was 3D-printed. After a couple iterations, a functioning 3D-print was obtained and it was tested in the skin model, in which it was still operable.

7.2 Concept 2 - Rotating magnetic coupling - theme: *control*

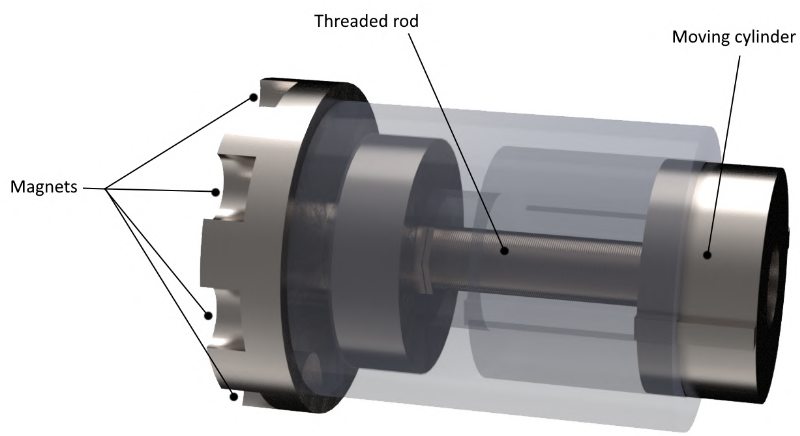


Figure 28: Overview of the second concept, which uses a rotational magnetic coupling and a threaded profile.

For this concept, the theme *control* was used. The goal for this concept was to have as much control as possible over the actuator. One way to achieve this is to take the control part of the device out of the body. When this is outside the body, the control is no longer limited due to not seeing what is going on in the body and due to having to actuate something through the skin. In order to achieve this, a magnetic coupling was used that can transmit any rotation through the skin, and then converting it into an axial displacement. This way, precise control is available over the speed of the displacement and the length of the displacement.

The concept is represented in figure 28. Inside a housing, a rotating wheel is placed with multiple magnets attached to the slots. Outside of the body, a similar magnetic arrangement is held, which is coupled to the magnets inside the body. Upon rotating the part outside the body, the implanted wheel will rotate with it. This will in turn rotate a threaded rod. The rotational movement is converted into an axial movement in the moving cylinder by means of another threaded surface coupled to the threaded rod. The cylinder is constrained to only be able to move axially, and not rotate.

Force generation: Force in the actuator is generated through the use of rotating magnets, coupled to another set of magnets outside the body. Since magnets are being used, and there is some distance between the coupled magnets, this design function is the hardest to meet. Sufficient magnetic force is needed to overcome the friction in the system and close the valve by spinning the wheel. The diameter of the wheel is made as large as possible, so that a larger moment arm can be created for rotating the wheel, but testing or calculated estimates are still needed to confirm the viability of this concept.

Force transformation: Since the input force is rotational, it needs to be converted into an axial force. A threaded profile is used to achieve this. The force transformation is also used to create a mechanical advantage, so that less actuation force is needed. This is done by using a threaded profile with a small pitch (the distance between two 'ridges' of the profile) of 1mm. This means that 1 full rotation of the wheel results in a 1mm displacement, reducing the force needed. An added benefit of using a small pitch is that the ridges of the threaded profile become almost orthogonal to the orientation of the shaft. Additionally, the diameter of the threaded rod is made small, gaining even more mechanical advantage. This makes sure that any pressure on the Bowden cable (for example from the blood pressure in the shunt) does not result in a displacement.

Multiple states: Since the movement is continuous, this concept can output an unlimited amount of different states, assuming that the locking mechanism is sufficient to keep the actuator in a specific state over time.

Prevent accidental activation: The input force is generated through the use of magnets. This means no physical force from outside the body can actuate the mechanism. Accidental activation therefore, likely will not be a problem for this concept. Additionally, because of the mechanical advantage created, a reverse force coming from the valve or shunt needs to be very strong in order to change the position of the actuator.

Fixate: The actuator will be fixated due to the magnetic attraction in the rotating magnetic coupling. Additionally, the actuator can manually be held in place during operation to prevent rotation of the entire actuator due to friction in the mechanism.

Prevent ingrowth: Since there are no moving parts on the outside of the actuator, the entire actuator can be covered in a hard cover and be fully sealed.

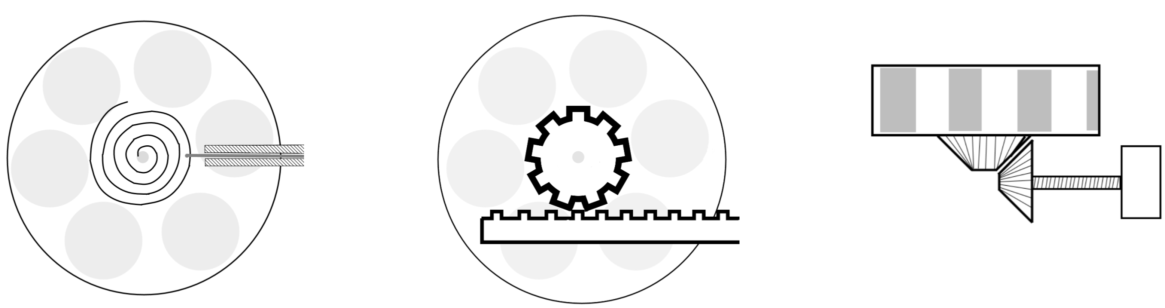
Gradual output: A threaded profile with a small pitch will be used. Besides lowering the amount of force needed to overcome the resistance in the system, this means a lot of revolutions of the rotating wheel (1) are needed for a small displacement of (3). This solves the gradual output requirement of the actuator.

7.2.1 Testing & validation

After the cadaver study (see section 8), it became apparent that the current orientation of the magnetic coupling was not optimal. Initially, this orientation was chosen because it resulted in a direction or rotation that was easy to convert into a translation using a screw mechanism. The cadaver study however, pointed out that the skin won't allow a good magnetic coupling using this orientation.
Because of this, the decision was made to alter this concept in such a way that the orientation of the magnetic coupling is normal to the skin. This way, a strong coupling can be achieved without the skin having to move around the cylinder.

7.2.2 Force transmission

This does mean however, that a different force transmission is needed: the direction needs to be changed by 90°, and it needs to be converted from a rotation to a translation.
There are multiple ways to achieve this, and a brainstorm session was held to identify the different options.



(a) Bottom view of transmission 1. (b) Bottom view of transmission 2. (c) Side view of transmission 3.

Figure 29: The different transmission types identified in the brainstorm session

Figure 29 shows the three different transmission options.

Transmission 1:
A narrow groove is made in the magnetic wheel. This groove is being tracked by a follower that is limited to only move in one direction. This results in axial displacement of the follower when the wheel is rotated.
+ Can be made small
+ Elegant design, least parts needed out of the three solutions
+ Easy to make

- Hard to get a very high transmission ratio. This is limited by how small you can make the grooves

Transmission 2:
A small pinion gear is attached to the bottom of the wheel. This gear is coupled to a geared rack that can move left and right. When the wheel is rotated, the pinion gear also rotates. This drives the rack left and right, resulting in axial displacement.
+ Easy to make
+ Transmission ratio can be increased by changing the size of the pinion gear
- Transmission ratio is limited by how small you can make the pinion gear, unless you're adding more gears
- Forces from the valve and blood vessel may cause the wheel to rotate when no locking mechanism is present

Transmission 3:
A bevel gear is attached to the bottom of the wheel and coupled to another bevel gear, changing the direction of the rotation by 90°. Then, a threaded profile attached to the second bevel gear and coupled to a cylinder that is limited to only move axially transforms the rotation into an axial translation.
+ Transmission ratio can be increased by changing the gear ratio of the bevel gears and by changing the threaded profile, resulting in a large possible transmission ratio.
- Harder to make, since all gears need to be stabilized in a case.

7.2.3 Torque measurements

The first step in identifying which of the above transmissions are most suitable in this scenario, is finding out which ones can supply enough force for the opening of the valve.
For all transmissions, the force generation is the same; a wheel that is magnetically coupled to another wheel. In between the wheels is a housing and a layer of skin. This distance between the individual magnets in the wheels is the most important parameter, limiting the magnetic attraction force between the two, and thus limiting the force (or torque) that can be generated.
In order to find out what the maximum torque is that can be achieved in the wheel, a prototype was built.

Determining the optimal magnet setup
Differently sized magnets, in different setups and amounts, can be used to fill the wheel. The goal of the setup is to create the highest magnetic attraction force (and thus torque) as possible.

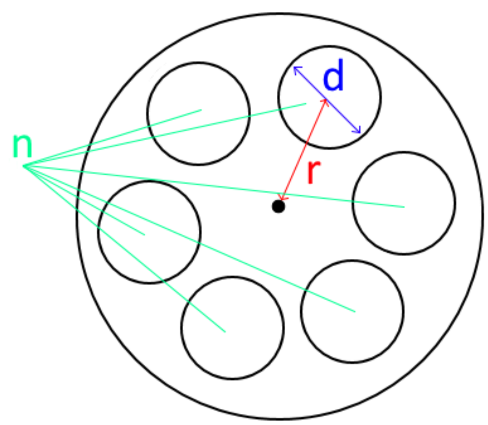


Figure 30: Graphical representation of the magnetic wheel and the parameters influencing the torque that can be generated

Figure 30 shows the different parameters determining the torque that can be generated, where:

d = the diameter of the magnet [mm].
r = the arm for calculating the torque [mm].
n = the number of magnets.

Unfortunately, not all sizes of magnets were available. The supplier (supermagnete.nl) had three different suitable sizes with a height of 5mm available. 5mm was picked as the maximum height of the magnets (at least for the initial test) due to the set dimensions. The three different diameters available were 5mm, 8mm and 10mm. For these sizes, the maximum even amount of magnets that fit into the circle were 10, 6 and 4 respectively. Only even amounts of magnets were used here, since the orientation of the magnets was being alternated (so N-S,S-N,N-S etc.). This anti-parallel configuration is energetically more stable than when the polarity of all magnets were to be aligned (Vokoun, Beleggia, Heller, & Šittner, 2009). Additionally, this alternating polarity would make slip more noticeable when rotating (when the wheel slips, it will have to move past a repelling magnet first, and then reattach to the next attracting magnet in the wheel), which will help when determining when the actuator has reached its beginning or end state later on, as this will probably be determined by registering this slip.

In order to generate the largest torque, the moment arm r should be as large as possible. This means the magnets are placed as far away from the center of rotation as possible. For larger magnets however, this means that the center of the magnet gets closer to the center of rotation, the larger the magnet gets, effectively reducing the length of the moment arm r. Torque τ is found using:

$$\tau = rFsin\theta \tag{1}$$

From this equation, we can see that torque is directly proportional to the moment arm r.

However, when the radius of the magnet increases, it also increases the magnetic attraction force between the magnets. This magnetic attraction force F (or rather, the shear coefficient of the attraction Force, which for the purchased magnets is about 15-25% of the attraction force), is also directly proportional to the torque. The relation between radius and magnetic attraction however, is not directly proportional, but squared or even larger, depending on the setup between the magnets (Vokoun et al., 2009). This means that magnets should never be made smaller in order to increase the moment arm r.

When the magnets get smaller however, we can place more of them in a ring in the wheel. The optimum number of magnets in a magnetic coupling is not easy to determine and the attraction force can even decrease when introducing more pole pairs (Lubin, Mezani, & Rezzoug, 2012), due to the individual magnets starting to repel each other. In the end, the choice was made to include six magnets (or three pole pairs), so that a large total surface area was achieved, but magnets weren't too close to each other.

Optimization of magnetic attraction

The current setup does not have an optimal magnetic attraction force. There are multiple ways in which the magnetic attraction force can still be increased. Even though it can still be increased, the choice was made to keep the setup as is (see **test setup**) and continue development without spending too much time on this topic. When magnetic attraction ends up being insufficient however, the optimization should be revisited.

Custom magnet shapes: in order to achieve a higher magnetic attraction force, each individual magnet should be as strong as possible. Due to the circular shape of the magnets being used now, a lot of surface area goes unused. An optimal magnet shape and setup would look something like what is shown in figure 31.

Halbach array: Halbach arrays use a certain array involving different orientations of the individual magnets to end up with a magnetic field that is much stronger on one side than on the other. For magnetic couplings this can result in a higher output torque (Liu, Choi, & Walmer, 2006). In order to do this well however, magnets with other shapes should be used, like square magnets or, even better, custom shaped magnets.

Optimization of number of pole pairs: intuition tells us that more magnets mean more attraction, but this is not the case for magnetic couplings. When too many pole pairs are present, they get too close too each other, and the magnets in the same orientation can start repelling each other. This results in a decrease in the magnetic attraction and thus torque (Liu et al., 2006)(Lubin et al., 2012). The optimal number of pairs however, is not the same for each coupling, and depends on the size and air gap between the magnets.

Iron back plate: iron back plates or yokes can be used on the sides of the magnets that do not need to be coupled. Because ferromagnetic materials can be regarded as having an infinite magnetic permeability (P»1), the back

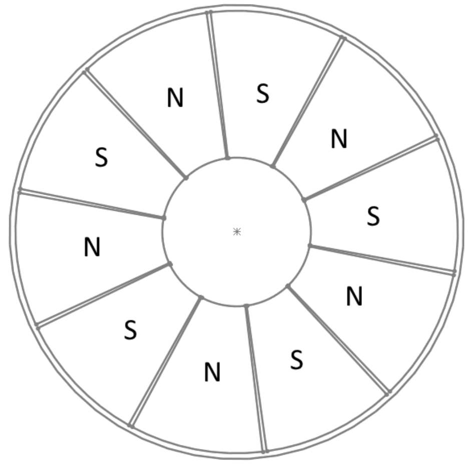


Figure 31: More optimal shapes for the magnetic setup

plate causes the magnetic force to cancel out on one side, and get stronger on the other side. The exact effect of this is hard to predict however, and due to space constraints, only the activator of the current prototype has an iron back plate right now.

More pure titanium: pure titanium is not ferromagnetic. However, this material is hard to work with, so most types of titanium that are used in a workshop have some iron in them, so that they are easier to work with. This does however, give them some ferromagnetic properties. For a prototype this is fine, but when magnetic attraction proves to be difficult, a more pure form of titanium (or another material) could be used.

Test setup

(a) The implantable actuator

(b) The remote activator

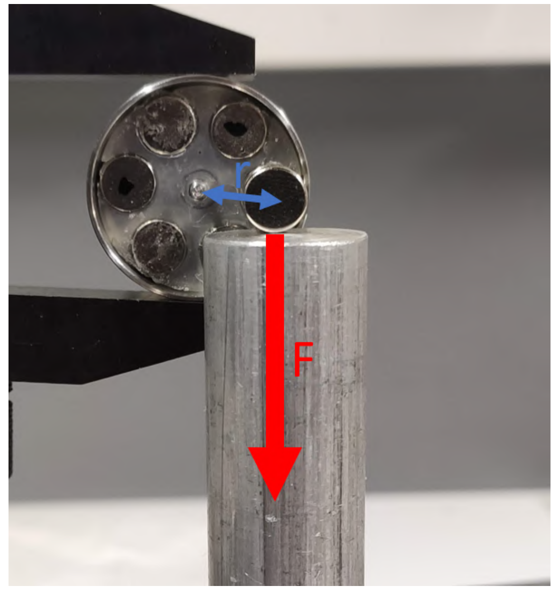
(c) Actuator and activator when coupled together.

Figure 32: The prototype actuator used to determine torque

Next, a prototype was developed, see figure 32. It consisted of a 3D-printed wheel made out of clear resin (Formlabs, Somerville, Massachusetts, United States) (see figure 32c), in which six magnets (2) were glued with alternating polarity. An outer casing (1) was constructed out of titanium. Titanium was chosen because it is not ferromagnetic, and thus not stopping the magnetic field lines, and because it is a highly biocompatible material, and could be suited for the end product as well. A lid (4) made out of transparent plexiglass was made to close the casing and still be able to see the rotation of the wheel. An axis (3) runs through the wheel, the casing and

the lid, supported by two ball bearings in order to keep friction low.
To make the actuator rotate, a plexiglass cylinder was made with an iron backplate (2) on top. On top of the iron backplate was a similar 3D printed wheel with magnets (1) in the same setup as in the actuator itself.

(a) Overview of the test setup



(b) Front-view of the test setup, showing the force and moment arm used to calculate the torque.

Figure 33: The test setup used to determine torque

Next, the actuator was placed in a test setup, as seen in figure 33. The actuator was clamped in place above a weighing scale. A cylinder was placed in the center of the weighing scale so that the actuator could push down on it and be suspended above the weighing scale. One of the magnets in the actuator was extended using three more magnets so that it could push down on the cylinder when rotated.

Different pieces of silicone were available to place between the actuator and the activator in order to increase the gap between the magnets. For each measurement, the actuator was rotated so that the direction of the force was perpendicular to the moment arm (so that $sin\theta = 1$). Then, the activator was rotated slowly until the magnetic coupling failed and it slipped. The maximum weight w (in grams) on the weighing scale was registered, and using this and the length of the moment arm r (9.71mm), the torque was calculated using the following formula:

$$\tau = w \times 0.00981 m/s^2 \times 0.00971 m \tag{2}$$

For each gap, five measurements were taken. The results can be seen in figure 34. As seen here, there is quite a bit of variance between the measurements. This is most likely because of the cylinder placed on top of the weighing scale. When this cylinder shifts out of the middle of the weighing scale a little bit, it can influence the outcome.

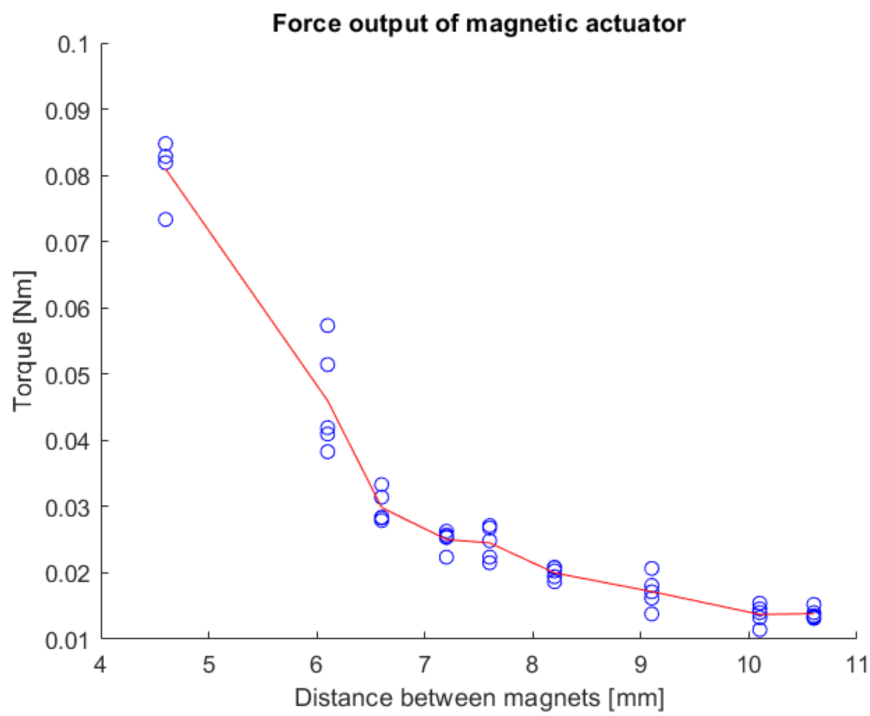


Figure 34: Results of the torque measurements. Each blue circle indicates a single measurement, and the red line connects the average values of the five measurements for each distance between the magnets.

7.2.4 Mechanical advantage

Transmission 3

The next step in identifying the optimal solution, is calculating the mechanical advantage of each transmission, starting with the third transmission. When looking at the screw movement, the elevating movement resulting from rotating the thread simply follows the principle of an incline plane. There are multiple forces acting on the interface between the 'bolt' and 'nut' of this transmission, all represented in figure 35.

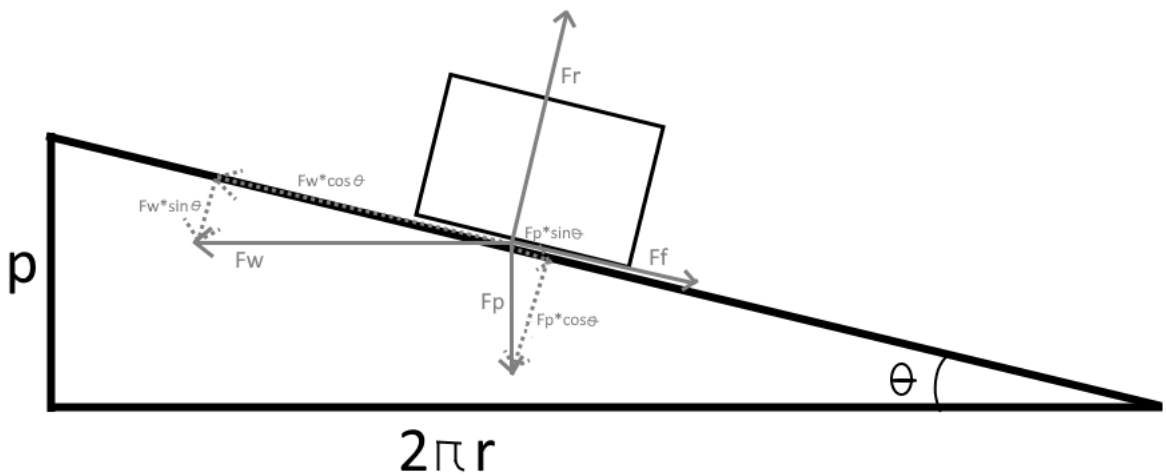


Figure 35: The incline plane used to represent the transmission and all the forces that act on it.

θ = Helix angle of the thread
p = Pitch of the screw (1mm)
r = Radius of the threaded profile (3mm)
F_w = The force applied by rotating the wheel.
F_p = The resistance force applied by the blood pressure in the valve and the resistance of the system (estimated to be 6.0N).
F_r = The reaction force acting perpendicular to the inclined surface.
F_f = The friction force resulting from the resistance force. This force is equal to:

$$F_f = \mu \times F_p \tag{3}$$

Where μ = the friction coefficient between the two surfaces (a value of 0.15 is taken here).

The value for θ can be found using:

$$\theta = tan^{-1}(\frac{p}{2\pi r}) \tag{4}$$

In an equilibrium condition, all forces parallel to the plane should equal 0, so:

$$F_w cos\theta = F_p sin\theta + \mu F_r \tag{5}$$

Additionally, all forces perpendicular to the plane should equal 0:

$$F_r = F_p cos\theta + F_w sin\theta \tag{6}$$

Substituting equation 6 into equation 5 gives:

$$\begin{gathered}
F_w cos\theta = F_p sin\theta + \mu(F_p cos\theta + F_w sin\theta) \\
= F_p sin\theta + \mu F_p cos\theta + \mu F_w sin\theta \\
F_w cos\theta - \mu F_w sin\theta = F_p sin\theta + \mu F_p cos\theta \\
F_w(cos\theta - \mu sin\theta) = F_p(sin\theta + \mu cos\theta) \\
F_w = \frac{F_p(sin\theta + \mu cos\theta)}{cos\theta - \mu sin\theta} \qquad (7)
\end{gathered}$$

A minimum force of $6.0N$ is needed to actuate the valve. A low friction coefficient of 0.15 (for a material like UHMWPE (Ultra-High Molecular Weight Polyethylene) is taken. Using equation 7, we can calculate a minimum force of $1.22N$ needed to open the valve. This corresponds to a torque of:

$$\tau = F_w \times r = 0.0037Nm$$

When a higher friction coefficient is taken, like 0.5, the torque is increased to $0.010Nm$. Looking at figure 34, we can conclude that this transmission, even with a high friction coefficient, can easily supply enough force even at a distance of 10mm between the magnets.

Transmission 1

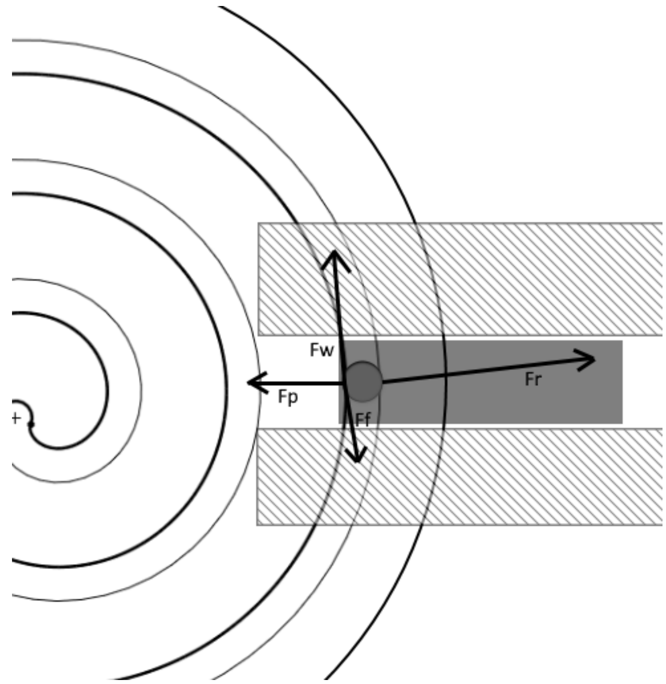


Figure 36: Schematic view of transmission 1, where the same forces as in transmission 3 apply.

Transmission 1 is very similar to transmission 3. The same principle of an incline plane is used, with the difference being that this time the part that is being moved moves in and out instead of up and down, see figure 36. This also means that the radius of the threaded profile is variable during the movement. This variable radius changes the angle θ, but also changes the torque that is needed. This means we get different amounts of torque needed at different positions. We use the same method of calculating the torque needed for transmission 1, but change some values.

$$r(n) = r_{max} - p \times n \tag{8}$$

The radius after n revolutions is now dependent on which revolution of the spiral the follower is on.
The pitch, p, is now the distance between two grooves of the spiral, which is estimated to be 2mm.

At the outside of the spiral, we now get a value of $1.3N$ for F_w (with a friction coefficient of 0.15), resulting in a needed torque of $0.011Nm$, which can easily be supplied by the magnetic coupling.
When the friction coefficient is increased to 0.50, the torque is increased to $0.032Nm$, which is still enough for a distance of 6-7mm between magnets.
On the inside of the spiral, after four revolutions, we get a value of $1.9N$ for F_w, which is higher than on the outside. Due to the smaller radius however, the resulting torque is only $0.0038Nm$, which is even less than on the outside. This means that the transmission can supply more torque at the end of its motion (so at the end of the pulling action on the Bowden cable.
With a friction coefficient of 0.50, this results in a torque of $0.0086Nm$.

Transmission 2

Transmission 2 works differently from transmission 1 and 3, so the same principle of an incline plane cannot be used.

In this transmission, the force is simply transmitted through the use of a pinion and a rack. Figure 37 gives a graphic representation of the transmission.

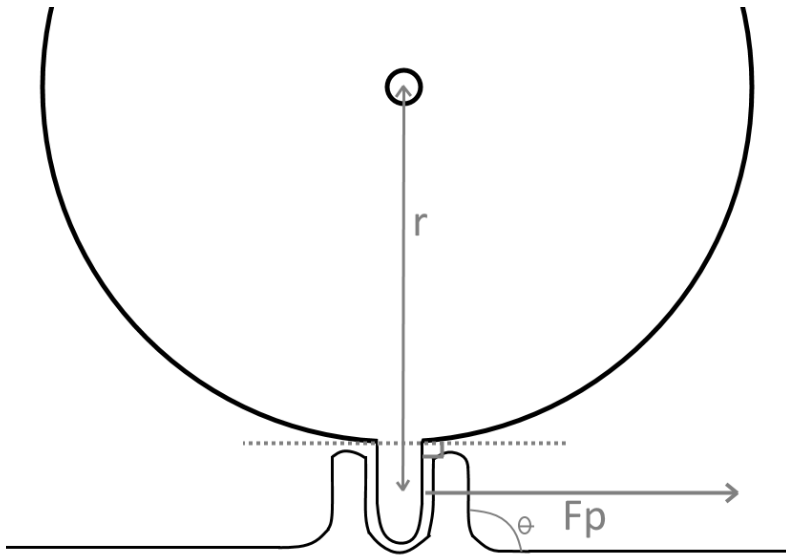


Figure 37: Schematic overview of the second transmission

The torque needed can be calculated using:

$$\tau = F_r r \tag{9}$$

Where:
τ = The torque needed in the pinion
F_r = The resistance force of the blood vessel and valve that need to be closed (estimated again at 6N)
r = The radius of the pinion
θ = The angle between the teeth and the pinion and the rack. Here considered to be 90°

For this transmission, the friction forces between the teeth are very small, so friction forces are left out for this calculation. For a pinion radius of 4mm, this gives a torque of $0.024Nm$. Looking at figure 34, this transmission gives enough torque on a distance up to 7-8mm.

Table 2 summarizes the results of the transmission calculations.

Table 2: Torque needed by each transmission to supply an output force of 6.0N

	$\mu = 0.15$	$\mu = 0.50$
Transmission 3	0.0037Nm	0.010Nm
Transmission 2	0.024Nm	0.024Nm
Transmission 1 (low n)	0.0065Nm	0.017Nm
Transmission 1 (high n)	0.0039Nm	0.0058Nm

7.2.5 Conclusion

From the above sections, it can be concluded that all transmission can be made viable. Looking at table 2, we can see that transmission 2 offers the least mechanical advantage, even without implementing friction in the

calculation. However, more gears could be implemented in order to lower the needed torque. This will however, add more parts and thus more complexity. Both transmission 1 and 3 offer great mechanical advantage, with very low torques being needed to supply a force of 6.0N.
Now that all transmissions are viable when looking at the force they can supply, the choice for the optimal transmission depends solely on the complexity, makeability and required size of the transmissions.
Considering that transmission 2 will most likely need an added gear for a good enough mechanical advantage, transmission 1 has the least individual parts. Looking at the required size, transmission 1 also scores best, since the spiral can be made on the magnetic wheel itself, keeping the height of the total actuator very low.
Judging makeability, transmission 1 also scores best, since transmission 1 and 2 both have rotating parts with axes that need to be stabilized.

In short, it can be concluded that transmission 1 is the most optimal transmission, supplying enough force, being the least complex, and easiest to make.

7.3 Morphological overview concepts 3 & 4

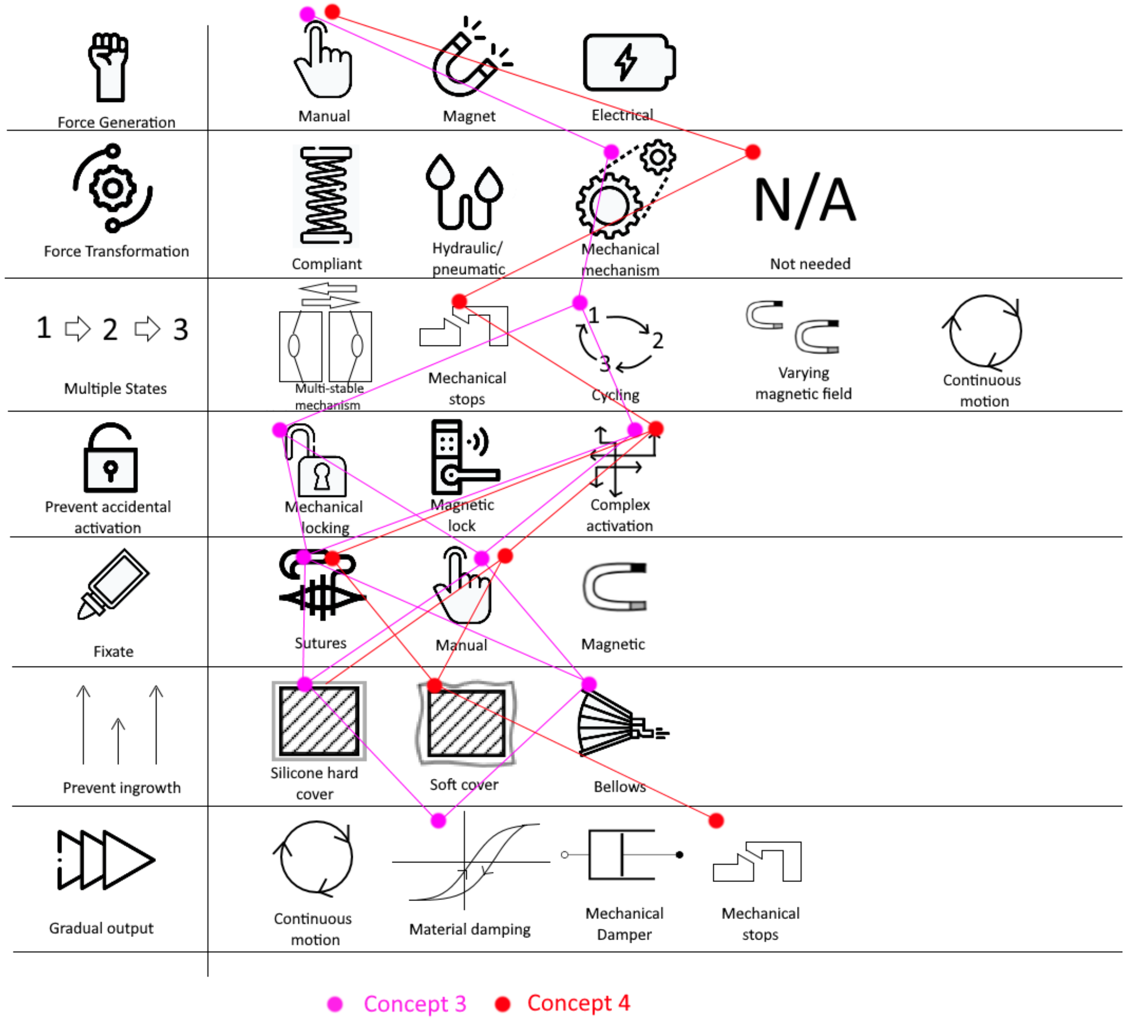


Figure 38: Morphological overview for the third and fourth designs

7.4 Concept 3 - Click pen - theme: *easy to operate*

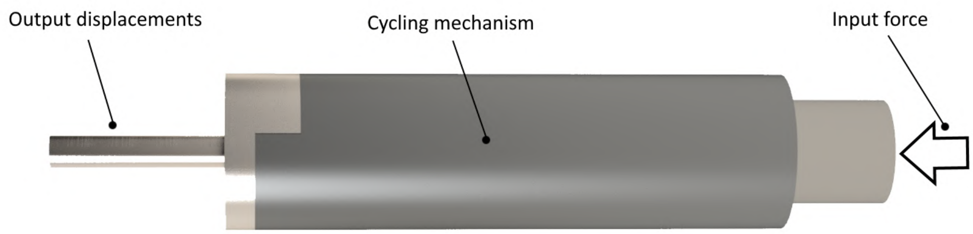


Figure 39: Concept 3 - version 1, using a click pen mechanism to cycle between states.

The aim of the third concept was to make an actuator that is as easy to operate as possible. This means that preferably only a single action is required to operate it.

For this concept, inspiration was taken from the click pen mechanism. Click pens have a mechanism that allows them to cycle between two different states using only one simple pushing motion. In click-pens, the cycling mechanism is rotational, however, the same design solutions can also be combined into a non-rotational, linear mechanism.

Version 1: rotational
The first version, that is similar to the mechanism found in common click-pens, is shown in figure 39 A better view of the cycling mechanism is given in figure 40.

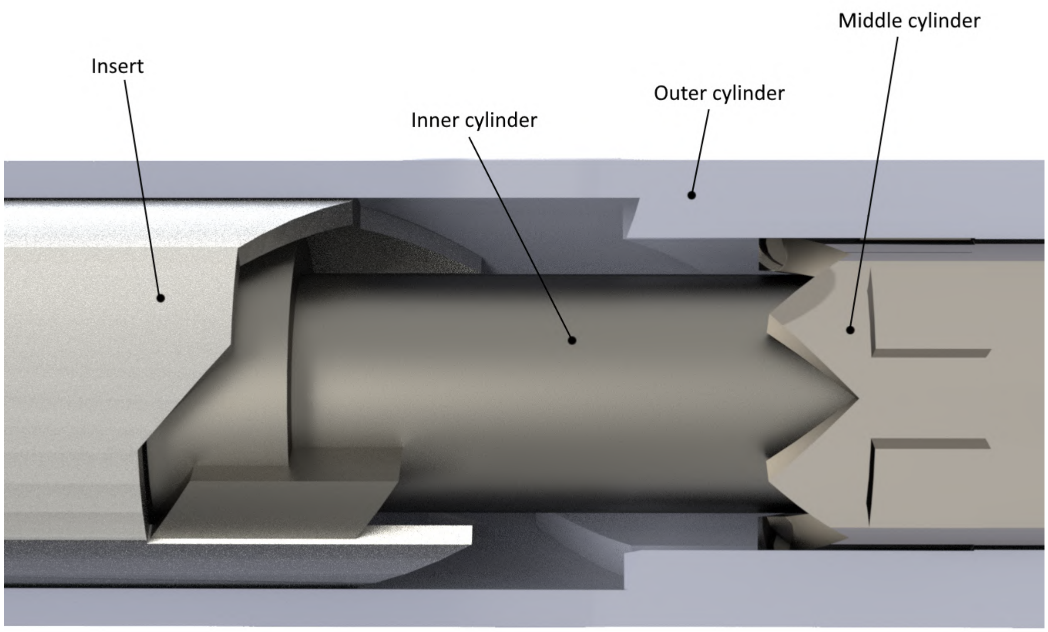


Figure 40: Close-up view of the cycling mechanism used in concept 3. The 'top' of the actuator is on the left, and the 'bottom' is on the right.

The mechanism from common click-pens was modified so that the mechanism can cycle between three different output states, needed for the actuator, and features three different cylinders sliding up and down and rotating. The middle cylinder is pushed up by the pushing force on the button, thereby latching on to the inner cylinder

and lifting it up with it. The inner cylinder is constrained to only move up and down by the ridges in the outer cylinder. When the inner cylinder moves past a certain point in the outer cylinder, it is no longer constrained, and the edge of the middle cylinder causes it to rotate. Next, a return spring pushes the cylinder back down between another ridge in the outer cylinder, this time with a different depth, resulting in a different output displacement of the actuator.
An insert is placed into the outer cylinder to limit the displacement output when pushing on the button and changing states.

Version 2: linear

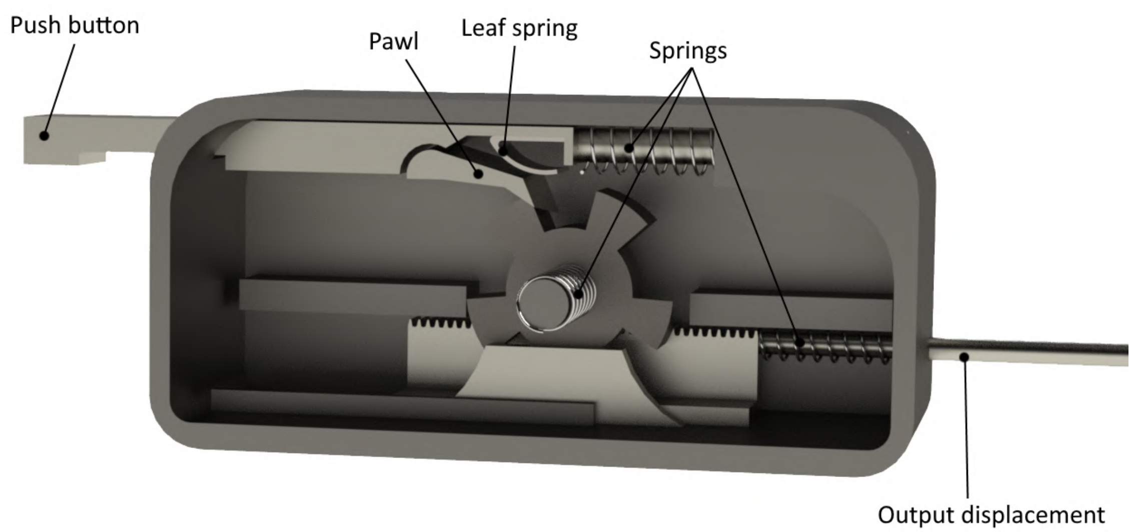


Figure 41: Overview of the second version of concept 3, featuring a linear cycling mechanism

The second version of concept 3 is shown in figure 41. As opposed to version 1, this version features a linear cycling mechanism. Similar to concept 1, a button is pushed repeatedly, changing the output displacement with each press until arriving back at the initial displacement.

When the push button is pressed, it moves to the right, forcing the wheel to rotate. A return spring then forces the button back into position without it rotating the wheel back due to the leaf spring and shape of the pawl. When the button is pressed four times, the sliding element connected to the output has moved all the way to the left due to the interface between the small teeth on the wheel (see figure 42) and the sliding element. At this point, the wheel is no longer constrained to move out by the sliding element. The next large tooth on the wheel is slanted, as can be seen better in figure 42, causing the large wheel to move out past the sliding element. The two elements are now no longer engaged, and a return spring can move the sliding element back to the right. When it has arrived all the way to the right, the wheel is again not constrained anymore by the sliding element, and another return spring connected to the wheel forces the wheel back into place, arriving again at the initial position.

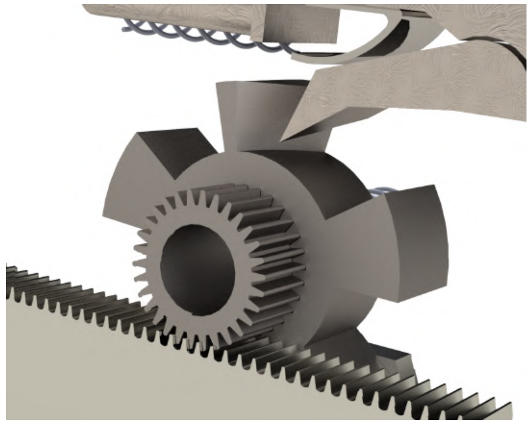


Figure 42: Better view of the ratchet interface between the wheel and the slider, and the slanted tooth.

Force generation: Force is generated by hand by pushing on the button on the end of the actuator.

Force transformation: Force transformation is not needed because the generated force is already an axial force in the right direction. Version 1 however, does transform the force into a rotation and then back into an axial displacement.

Multiple states: Multiple states are introduced through the cycling mechanism; each click of the button advances the system to the next state, resulting in a different output. When the last state is reached, another press of the button returns the system to its first state.

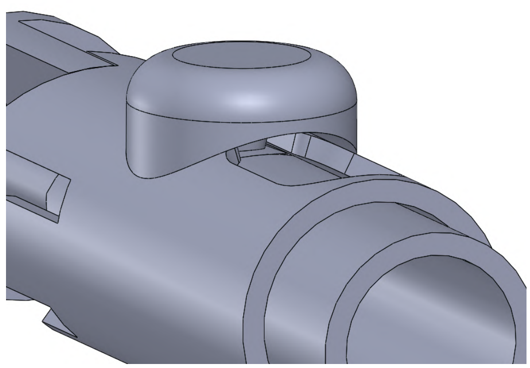


Figure 43: Close-up view of the button locking mechanism. Here, the button is depressed, allowing the inner cylinder to slide.

Prevent accidental activation: Further testing will have to point out whether accidental activation is a problem. Because of the direction of the input force (parallel to the upper arm), accidental activation is less likely than when the input force were to be tangent to the arm.
If however, accidental activation turns out to be a problem, a button locking mechanism can be implemented, see figure 43 for an example of a locking button for the first version. Now, the button needs to be pressed down wile providing the input force for the mechanism to cycle between its states.

Fixate: the actuator can be fixated by hand, or by using sutures. Fixation by sutures could be convenient, but may also make the actuator more prone to accidental activation. Additionally, resultant forces on the sutures could be too high.

Prevent ingrowth: Ingrowth can be prevented by using a hard cover around the non-moving parts of the actuator, and using a bellows-like structure around the moving part.

Gradual output: Three methods can be used for achieving a gradual output:

1. Using many states; by splitting the movement into many states, each button press changes the output displacement by only a small amount, effectively resulting in a gradual output.
2. Dampen the input; by introducing a mechanical damper, or a viscoelastic material, the input force can be damped. For the first version this damper could be placed inside the outer cylinder. For the second version it could be placed parallel to the push button.
3. Damp the output; by introducing a mechanical damper after the actuator, the output can be damped.

7.4.1 Deciding which version is best

Above, two different versions of the same generated concept have been explained. Now, a decision on which version is optimal needs to be made.

Complexity: although version 1 might seen complex, it is essentially relatively simple. Is basically consists out of some cylinders that are placed into each other and that can slide. Version 2 however is much more complex, featuring many springs and sliding and rotating elements mounted on axes. This version would be much harder to manufacture and assembly and would therefor also likely be less durable.

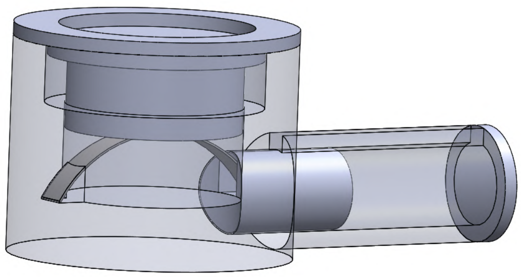
Shape and dimensions: version 1 has a shape that is similar to a cylinder, version 2 has a shape that is more similar to a box. The cylinder is more rounded and therefor would fit better in the anatomy of the arm. Dimensions of the two versions depend on how small the individual components can be made. We know that the click-pen mechanism can be made very small, as seen in common pens. Version 2 would be harder to make as small, due to the many individual components and axes that need to be placed.

Function: Function of the two versions are very similar, with the only difference being that the return mechanism in version 2 can not be made gradual; it will happen quickly. In version 1, multiple 'sub-steps' can be added in the return mechanism, causing it to slowly return to its initial state in multiple presses of the button. This most likely means that version 2 would need some kind of mechanical damper or material damping, while version 1 could introduce gradual output by simply introducing a lot of sub-steps.

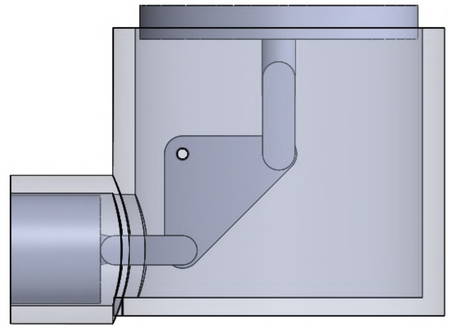
Conclusion: as seen from the above arguments, the first version would be more optimal due to being less complex, more fitting dimensions and having for options for gradual output.

7.4.2 Further development

Similar to concept 2, the cadaver study pointed out that the input direction of the force needs to be perpendicular to the skin. This means that a force transmission needs to be introduced. Two different transmission mechanisms were identified to do this. The first is a leaf spring, seen in figure 44a. When the button on top is pressed, the leaf spring elastically deforms, pushing the cylinder to the right. An added benefit of this transmission is that the leaf spring works like a spring, which is needed anyways in the actuator to return the push button to its initial position.
The second transmission is shown in figure 44b. This transmission features a cam mechanism that can rotate around an axis, changing the direction of the displacement that way.
The choice was made to utilise the first transmission system that uses the leaf spring. This version is the easiest to manufacture, since the other transmission relies on rotation and needs multiple axes to work. Additionally, the first version uses a compliant mechanism, namely the leaf spring, which is supposed to be more durable. Lastly, the first version has the added benefit of being a spring, meaning an additional spring in the actuator as a return spring may not be needed anymore.



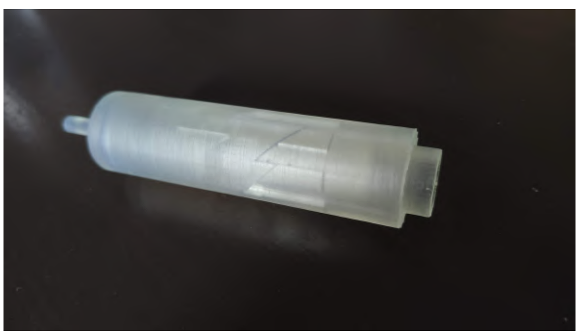
(a) 3D model of transmission system 1



(b) 3D model of transmission system 2

Figure 44: Overview of the two proposed transmission systems.

To validate the working principle of the concept, the click pen mechanism and transmission mechanism were 3D-printed individually at a larger scale to test their functions, see image 45. 3D-printing is not suitable for prototyping at the intended scale due to the limited resolution, but for proving a working principle printing at a larger scale was sufficient.
Now that both parts of the concept had been printed and it was confirmed that they functioned properly, enough information about this concept had been gathered to judge it against the other concepts.

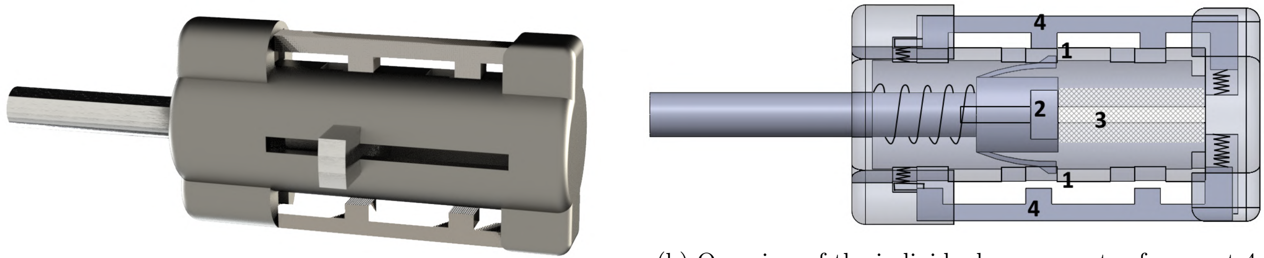


(a) 3D-printed version of the click-pen mechanism

(b) 3D-printed version of the transmission mechanism

Figure 45: 3D-printed mechanisms used to validate the working principle of this concept.

7.5 Concept 4 - Piston - theme: *split*



(a) 3D render of concept 4

(b) Overview of the individual components of concept 4

Figure 46: Concept 3, using a piston-like mechanism and mechanical stops.

The theme for this concept was *split*. The goal for this concept was to see whether it would be possible to split the operation for opening and closing of the valve into two different actions and therefor reducing the chance of erroneous operation.

The fourth concept uses a piston-like mechanism. A piston head, attached to the inner cable of a Bowden cable setup slides in a cylinder, providing actuation. A supplied force can move the piston head to the left in figure 46b, while a return spring can move it back to the right. In order to move the piston back, pawls (1) are depressed by pressing on the side-bars (4).

Force generation: Force is again generated manually through the skin. This can happen either by applying it on two handles, as depicted in figure 46b (2), or by applying it on a single button at the end of the cylinder, similar to concept three.

Force transformation: Since the input force is already in the right direction, it does not need transformation.

Multiple states: Multiple states are introduced using the mechanical stops in the cylinder and mechanical pawls (1) on the piston head. When the piston moves from right to left, the compliant pawls automatically get depressed when enough force is applied until they move into the next stop. During this motion the spring is being compressed. When the piston head wants to move from left to right, and the spring releases its force, the stops prevent the piston from doing so.
The piston can be allowed to move one stop further my compressing the side bars (4). This forces the compliant pawls down, allowing the spring to push the piston head one stop further to the right. Note that the piston head can only ever move 1 stop, and holding down the side bars doesn't cause it to move all the way to the right in one go.

Prevent accidental activation: Since the activation force is to be supplied parallel to the arm, accidental activation is not expected to be a problem. If it turns out to be however, the required force for activation can be increased by increasing the strength of the spring, reducing the chance of the activation happening accidentally.

Fixation: The actuator can be fixated manually, or by sutures. In practise (and showing from testing in the skin model), the actuator will probably need to be held while moving pulling on the handles to prevent resulting forces from pulling on the shunt too hard. To do this, the index and middle finger can be placed on the handles, while the thumb stabilizes the actuator near the Bowden cable.
Some sutures could also be used to keep the actuator in place in between operation.

Prevent ingrowth: A hard cover can be used for the non-moving parts of the actuator, while a soft cover needs to be used for the handles or button.

Gradual output: Gradual output can be achieved in two different ways:

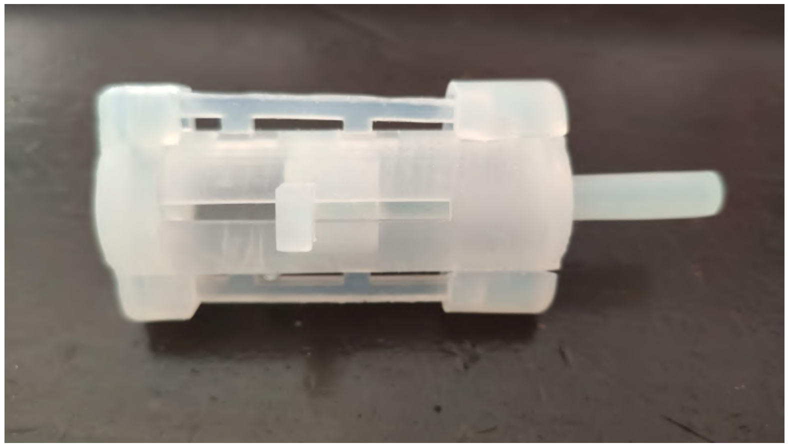


Figure 47: 3D-printed prototype of concept4

1. By increasing the amount of mechanical stops and splitting up the motion into multiple small increments.
2. By introducing a viscoelastic material or damper (3) in the cylinder, limiting the speed of the movement of the piston-head.

7.5.1 Further testing & validation

In order to validate this concept, a functioning 3D-printed prototype was created, see figure 47. This prototype was created at a larger scale, due to the accuracy and resolution of the printer. This functioning prototype was tested in the skin model, in which it was still operable.

8. ANATOMY STUDY

8.1 Introduction

In order to further check the viability of the generated concepts, an anatomy study was performed. This study consisted of two parts. The goal of the first part was to check the available space for the actuator. Due to the COVID-19 pandemic, a cadaver study could not be performed in the earlier stage of setting up design requirements. Therefore, in the design requirements, an initial set of dimensions was determined, mainly based on experience by a vascular surgeon and dimensions of other implantable devices. In this part, additionally, the choice for the location of the actuator was revisited.

The goal of the second part was to check the viability of the different concepts in terms of function; while the concepts in theory could be easy to operate (even in the skin model), in practise this could be very different. This is mainly due to the skin and subdermal fatty tissue that needs to be manipulated in order to operate the actuator.

8.2 Setup and anatomy

The cadaver study was performed in the anatomy lab of the Leiden University Medical Center. First, arms were studied that were already opened and cleaned up. Because these arms were being used repetitively and being preserved using formaldehyde and drained of blood, the mechanical properties of the tissues changed drastically, making them unsuitable for checking dimensions or operability. Therefore, these arms were only used for getting a better feeling for the anatomy of the arm.

Then, an arm was used that was still intact. The arm was of a person typical for a patient that could need kidney dialysis in terms of size and BMI. For this arm, the mechanical properties and 'feel' were still much more comparable to the properties of living tissues.
First an incision was made on the elbow joint, similar to when a shunt or anastomosis would be created. Then the vascular surgeon exposed all the relevant veins, arteries and nerves and showed us the possible locations for the shunt and valve, see figure 48. Using a piece of clay, the maximum allowed dimensions for the parallel project involving the valve were determined.
Then, the dorsal area in the forearm and the medial area in the upper arm were made accessible and the dimensions and operability of the actuator could be tested.

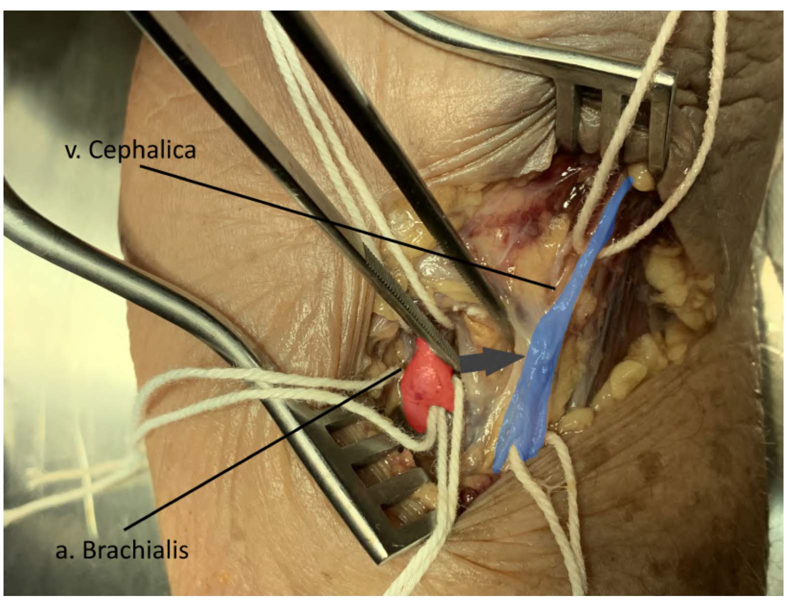


Figure 48: Incision in the cadaver arm in the medial side of the elbow, showing the v.cephalica (blue), the a. Brachialis (red) and the location for the shunt (arrow).

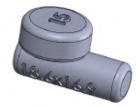
8.3 Part I: Dimensions & aesthetics

In the design requirements, an initial set of dimensions was determined to be 35mm x 25mm x 13mm. During this part of the cadaver study, objects of different shapes and sizes were placed in two locations to see what the maximum allowed dimensions are. 3D models of these shapes can be seen in figure 49

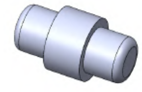
(a) Block with the maximum allowed dimensions determined for the design requirements

(b) The same block as in (a), but at 75% scale

(c) A shape similar to concept 2



(d) A shape similar to concept 2, but at 75% scale



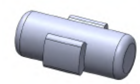
(e) A shape that could be used for concept 4

(f) A cylinder shape with the maximum allowed dimensions according to the design requirements

(g) A similar shape to (f), at 75% scale.

(h) A thick ring shape

(i) A thin ring shape



(j) A shape that could be used for concept 4

Figure 49: 3D models of the different shapes that were used to assess the maximum allowed dimensions for the actuator

For the two possible implantation sites, each test shape was inserted. When inserted, the skin was pulled back over the open incision. Now each case was judged on tension and aesthetics. For tension, the skin around the test shape was felt, and the amount of tension on the skin was judged to be either acceptable or not acceptable. For aesthetics, each shape was awarded a mark between 1 and 5, with 5 being 'barely visible', and 1 being 'obtrusive'. Table 3 shows the result of this part of the cadaver study.

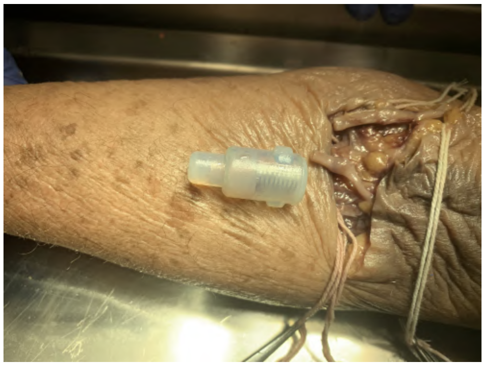
Table 3: Results of the first part of the cadaver study, judging allowed dimensions. The letters in brackets (x) behind the shapes correspond to the entries in figure 49

	Biceps		Forearm	
	Tension	Aesthetics	Tension	Aesthetics
Large block (a)	✓	4	✓	3
Small block (b)	✓	5	✓	4
Concept 2 large (c)	✓	3	✓	3
Concept 2 small (d)	✓	4	✓	3
Concept 4 round (e)	✓	5	✓	4
Cylinder large (f)	✓	4	✓	3
Cylinder small (g)	✓	5	✓	4
Ring thick (h)	✓	3	✓	3
Ring thin (i)	✓	4	✓	4
Concept 4 wings (j)	✓	4	✓	4

As can be seen in table 3, each shape fit into the two anatomical implantation sites with acceptable tension. Because everything fit so easily, some clay was used to expand on some of the shapes to arrive at the actual maximum dimensions. This was especially important for concept 2, which benefits the most from a large size, since it can then generate a stronger magnetic field. After some experimenting, the maximum allowed diameter for the wheel in concept 2 were determined to be 35mm.
Similarly, the maximum diameter for the cylinder shape was increased from 15mm to 20mm.

8.4 Part II: Function

In this second part, the function of the concepts was tested. The concepts rely on three different actuation methods; a button in line with the arm, a magnetic coupling, and a piston head that can slide in a piston housing. Unfortunately, the magnetic coupling could not yet be tested at the time of the cadaver study, since an adequate prototype needs to be developed first. The other two could easily be tested however with some dummy actuators. Four dummy actuators were constructed using 3D printed material and some springs, see figure 51. These dummy actuators were made in two sizes: large (35mm x 15mm) and small (25mm x 10mm). The dummy actuators were inserted into the two possible implantation sites, see image 50. Then, the skin was pulled back over the incision, and an attempt was made to fully activate the dummy actuators.

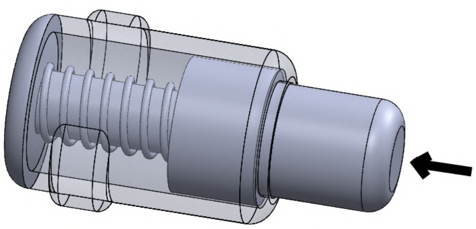


(a) Dummy actuator 1 (large) shown on the arm for a reference to the size.

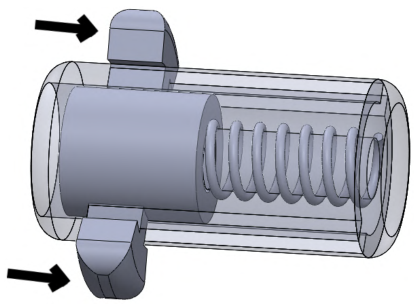
(b) Dummy 1 placed inside the arm (forearm implantation site). The bulge at the arrow shows where the actuator is placed.

Figure 50: One of the dummy actuators, first shown out of the body, and then inside the body under the skin.

Dummy 1 (small and large) was able to be activated through the skin. However, activation needed a lot of force. This meant that a very high force had to be exerted on the skin. Due to the orientation of the actuator, the skin needed to be pressed down around the actuator, forcing the fingernails to go into the skin, which would be very uncomfortable for the patient. Additionally, very little control over the actuator was possible, making designs that have to be pushed only halfway for different states for example, not viable. Dummy 2 (small and large) was even harder to activate. In neither the large or the small version full activation was possible to achieve without tearing the skin.
The ring shapes were also very hard to compress and operate, similar to the other dummy actuators. Another problem with the rings was that they could rotate while trying to compress them.



(a) Dummy 1: A simple push-button type of actuator.



(b) Dummy 2: A piston-like type of actuator, with two wings that can be pushed.

Figure 51: The two different types of dummy actuators that were used to assess the function. The arrows indicate the direction of the force needed to activate them.

8.5 Conclusion & implications

The cadaver study was very informative with regard to what can and can not be operated under the skin, and what dimensions are available for implantation.
All the dimensions that were set in the design requirements could be confirmed, and for some shapes, the maximum dimensions could even be increased, giving some more room for the design.
In retrospect, some more shapes could've been brought with dimensions a little larger than the pre-determined maximum dimensions. This would have made it easier to determine the new maximum allowed dimensions.

Looking at the function of the test actuators, the results were surprising. While these were able to be operated in the skin model, the dummy actuators could not be operated in the cadaver arm without damaging the skin. From the study it could be concluded that the only action that could be performed through the skin is a single pushing motion, where the direction of the pushing is normal to the skin. This means that two of the conceptual designs become non viable; concept 1 and 4.
For concept 2 and 3, it means that some changes need to be made: the direction of activation needs to be changed. For concept 2 that means that the magnetic activating element needs to be able to be placed normal to the skin, as opposed to in line with the arm. Similarly, for concept 3, it means that the pushing direction needs to be normal to the skin, so the direction of the force needs to be changed by 90°.

9. HARRIS PROFILE WINNING CONCEPT

Now that enough information has been gathered to judge all the concepts, a winning concept can be selected that is going to be developed further into a working prototype.
After the human anatomy study, two out of four concepts became non-viable, leaving two concepts; concept 2 and concept 3. In order to find out which concept scores best for this project, a Harris profile was made, judging the concepts on the before drafted design requirements. On each requirement, the concepts could score between -2 and +2 points, according to the following guidelines:

Table 4: Requirements for the values attributed to all the design requirements, used for the judging of concepts in the Harris profile.

Requirement	+2	+1	-1	-2
Dimensions	Does not exceed max dimensions & total volume <1250mm3	Does not exceed max dimensions & total volume 1250-2500mm3	Does not exceed max dimensions & total volume 2500-4000mm3	Does not exceed max dimensions & total volume >4000mm3
Force/energy	10+N & fail-safe	10+N	6-10N	<6N / power transmission needed
States	Continuous motion/ infinite states possible	3+	3	<3
Gradual output	Adjustable damping & continuous motion	15+ sec damping & continuous motion	5-15 sec damping & continuous motion OR stepping motion	0-5 sec damping & continuous motion
Durability	7000+ cycles	3500-7000 cycles	2000-3500 cycles	<2000 cycles
Reliability	<<1% failed activation rate	<<5% failed activation rate	<<10% failed activation rate	<<15% failed activation rate
Usability	Remote activation & <3 actions	1 action	2 actions	3+ actions
Costs	>75% margin	50-75% margin	25-50% margin	<25% margin
Biological safety	4/4: Biocompatible, no sharp edges, little room for ingrowth, modular	3/4: Biocompatible, no sharp edges, little room for ingrowth, modular	2/4: Biocompatible, no sharp edges, little room for ingrowth, modular	1/4: Biocompatible, no sharp edges, little room for ingrowth, modular
Makeability	<1/2 day prototype production time	1/2-1 day prototype production time	1-2 day prototype production time	2+ days prototype production time

Using the requirements from table 4, we can now fill in the Harris profile. For some requirements, the absolute values are known, like the dimensions or the force/energy, so the corresponding values for the Harris profile are easily found.
For some others, an estimation is done to find the most likely value. These requirements are explained below.

Gradual output: For concept 2, this value is known, since the control output can be adjusted by changing the rotational speed of the activator, scoring a +2. For concept 3, there are two different methods of introducing a gradual output; viscoelastic materials or stepping motion. Achieving a damping of >15 seconds with viscoelastic materials will be challenging, and stepping motion is assigned a -1, so overall, a -1 is assigned here for concept 3.

Durability: Since both concepts have not been fully developed yet, the exact durability can not yet be determined. Because of this, an estimation will be used. For concept 2, the thing that is most likely to break and stop the functioning of the device, is the interface between the spiral and the follower. Repeatedly trying to rotate the wheel past its stops could cause metal fatigue or breaking of the pin. However, when the pin is made large and strong enough this shouldn't be much of a problem. Additionally, because bearings can be used, friction in the system should be low. This all results in the estimation for the durability falling is the highest category, assigning +2 points.
For concept 3, we can take a look at click-pens we know and use to write. These pens can last for a long time, and the mechanism should last well over 7000 cycles. The other mechanism used in concept 2, the leaf spring, should also last a long time, as this is essentially a compliant mechanism. This concept therefor also receives +2 for durability.

Reliability: Since both actuators are of the 'independent' type, as explained in the design requirements, only the activation rate is used here for grading. For concept 2, actuation force is limited by the coupling between magnets and friction in the system. Because of the magnetic coupling, failed activation can only occur when slip happens between the magnets. This, in turn, can only happen when the coupling is near its max force. Overall, there is not a lot of room for failed activation, either by malfunctioning or wrong operation of the actuator. Therefore, a value of +2 is assigned.
For concept 3, an activation of the actuator will always result in the same amount of displacement, due to the design of the cyclic mechanism. As long as an adequate input force is supplied, the mechanism should always successfully output its displacement. This concept is a little bit more prone to failed activation on the side of the operator however, since the actuator needs to be fixated manually, and it could slip while operating it. Therefore, this concept will receive a score that is a little bit lower than its competitor; a +1.

Costs: At this point in the development, it is hard to estimate the exact costs of production of the concepts. Since concept 2 has a lower total volume than concept 2, material costs will be lower for concept 2. This is especially relevant if titanium is used, which can be quite costly. Also, the shapes used in concept 3 are more complex and difficult to manufacture. Exact values are hard to estimate here, but concept 3 will most likely be more expensive than concept 2. Therefore, concept 2 will be granted +1, and concept 3 -1.

Using the values mentioned above for the requirements that require an estimation, and filling in the other values, results of the Harris profile seen in figure 52. Following the results of the Harris profile, we can clearly see that concept 2 scores better than concept 3, with 17 and 3 points, respectively. Therefore, concept 2 will be developed further.

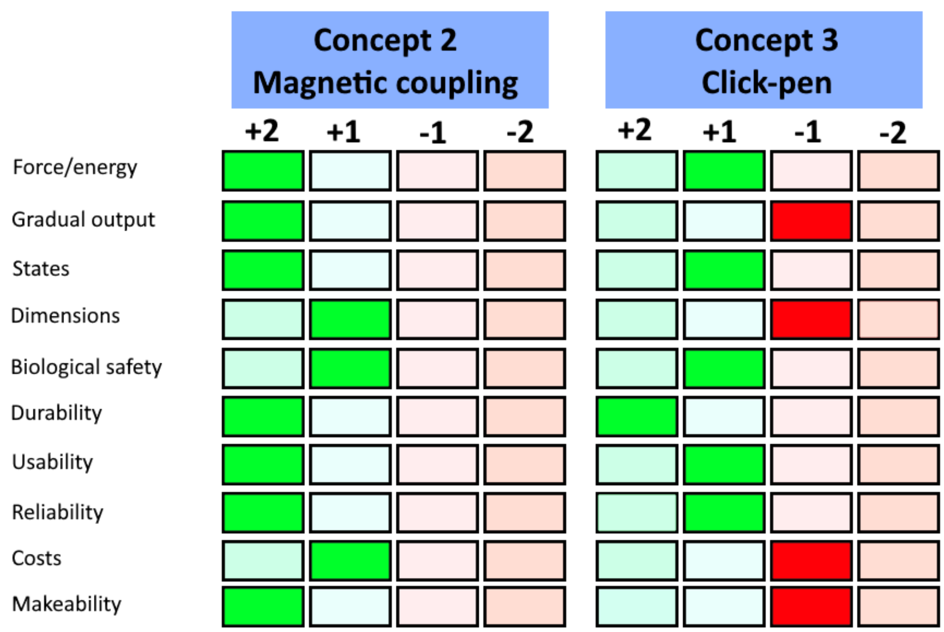


Figure 52: Harris profile of the two remaining viable concepts

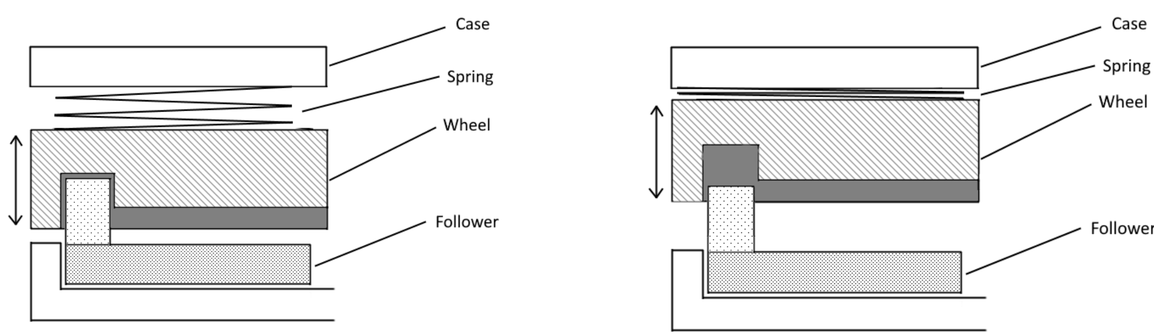
10. FURTHER DEVELOPMENT

Now that a winning concept has been chosen, the concept can be developed further. Most of the design requirements could already be validated based on previous testing, however to provide a good proof-of-concept all design requirements should be validated. The validation of these requirements requires testing in an experimental test setup with a proper prototype, which will be developed in this section. In this chapter, a locking mechanism will be selected, improvements to the friction profile will be made, the assembly of the actuator from its individual parts will be discussed, the material choices will be presented and the resulting physical prototype will be shown.

10.1 Locking mechanism

In order to make the wheel rotate by applying a pulling or pushing force on the Bowden cable, for example by the blood pressure in the piece of graft, a very large force is needed. This is due to the spiral mechanism and mechanical advantage that is used. It would not hurt however, to implement an additional locking mechanism. This is especially important for when the valve is closed. Here, it is important that the valve stays properly closed. When the valve were to slowly open over time, even only slightly, blood will be able to enter the piece of graft and start clotting there, which can be problematic. Because of this, a locking mechanism will be implemented that can at least lock the device in the fully open and fully closed position.

Option 1 - locking pin



(a) The locking mechanism in an engaged state.

(b) The locking mechanism in a disengaged state.

Figure 53: Schematic overview of the first option for the locking mechanism, inhibiting rotation of the wheel when the activator is removed at the end of the rotation.

This locking mechanism could be implemented using the pin that follows the spiral and is connected to the axially moving follower, and a spring, see figure 53. When the activator is coupled to the magnets in the wheel, the wheel is lifted and the spring between the case and the wheel is compressed, allowing the wheel to rotate (figure 53b). When the wheel is at the end of its rotation, and the activator is removed, the spring expands, pushing the wheel down. The pin will now fall into a small hole in the groove of the spiral. The spring will keep it here, locking any rotation (figure 53a). Implementing this mechanism will increase the distance between the magnets by the thickness of the material used for the skin. Testing with the eventual prototype will have to point out whether this is a problem, or whether enough force can still be generated.

Option 2 - locking magnet

The second locking mechanism features an additional magnet that is placed at the same height as the magnets in the wheel, see figure 54. When this magnet is coupled to one of the magnets in the wheel, a larger torque is needed to overcome the magnetic attraction between the magnets and start rotation of the wheel, effectively locking it. Another consequence of implementing this would be that passing each magnet with the same polarity would require a larger amount of force. It would also give some tactile feedback to confirm that the wheel is actually rotating. During manufacturing, it would have to be made sure that when the actuator is in its end

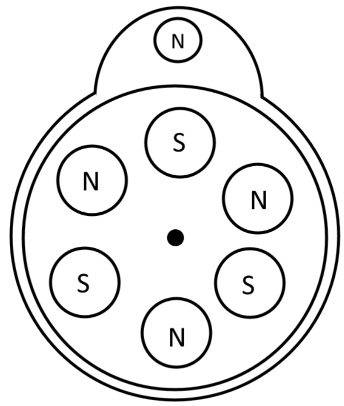


Figure 54: Schematic overview of the second option for the locking mechanism, using an additional magnet.

position, so when the valve is closed, a magnet with opposing polarity needs to be adjacent to the locking magnet, so that the actuator is locked in the right place.

Decision and further development

The pros of the second locking mechanism are that it is not prone to breaking, since the locking force that is generated is frictionless, that multiple locking positions are possible and that some additional tactile feedback is introduced. This mechanism does however increase the needed minimum actuation force for closing the valve. Also, the additional magnet could interfere with the magnetic field in the wheel, weakening it and mess with the coupling to the activator.
The first locking mechanism requires an additional spring to be added, which increased the distance between the magnets in the actuator and activator, although only slightly. It is very easy to implement.
The choice was made to include the first locking mechanism, due to the fact that it is easy to implement, requires less trial and error than the second one, and doesn't change the behavior of the actuator due to influencing the magnetic field. Also, the change in minimum force required for actuation is easier to predict using the previously used equations, and probably lower.

The first step in implementing the lock is finding a suitable spring. A spring needs to be used with a loaded height that is as small as possible, in order to keep the distance between the magnets as small as possible. The difference between the loaded height and the unloaded height should be small as well, so that the total height of the actuator can remain low, and magnetic attraction between the magnets is still possible when the spring is unloaded. Additionally, the spring shouldn't be too stiff, so that the magnetic attraction force is enough to compress the spring; the spring only has to overcome the gravity acting on the wheel.
Three different types of springs were ordered with a spring manufacturer (Amatec, Alphen aan den Rijn, Netherlands). After some testing and fitting with the prototype used for measuring the available torque, the spring represented in figure 55 was used, with a loaded height of 1.57mm.

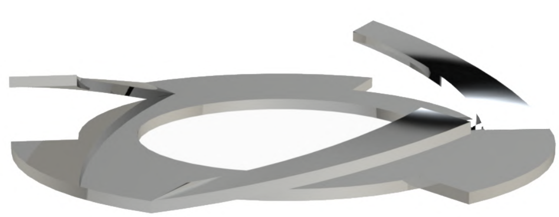


Figure 55: Spring used for the locking mechanism

One of the consequences of implementing this locking mechanism, is that the wheel now needs to be able to not only rotate, but also slide up and down. Because of this, ball bearings are no longer suitable. Instead, a sliding bearing will be used.

10.2 Reducing friction on the skin

The actuator up until this point was actuated using an activator that was a simple cylinder. This cylinder was coupled to the actuator and rotated directly on the skin. Initial testing on skin models pointed out that this rotation could cause twisting of the skin due to friction, which in turn caused twisting of the actuator while rotating. In order to reduce friction and thus twisting, a 'cup' was constructed that was placed on the skin. The activator was in turn placed into this cup, in which it could rotate.

10.3 Assembly

The actuator consists of 13 individual parts: 6 magnets, a case, a wheel, an iron backplate, a follower, a spring, 2 bearings. In order to be able to assemble it, the casing needs to be separated into two parts. Assembly of the actuator will look like this: (1) The wheel is placed on the iron backplate, and the magnets are inserted into the designated slots. Magnetic attraction between the magnets and the backplate will keep everything in place. (2) The bearings are placed in the wheel. (3) The spring is placed on top of the wheel. (4) The wheel + spring is placed on the axis inside the casing. (5) The cable attached to the follower is ran through the hole in the second part of the casing, and the follower is placed inside the designated slot in the casing. (6) The second part of the casing is placed, sealing the actuator.

Now that all the required mechanisms are known, a model was created in Solidworks, see figure 57 for an exploded view & figure 56 for an assembled view.

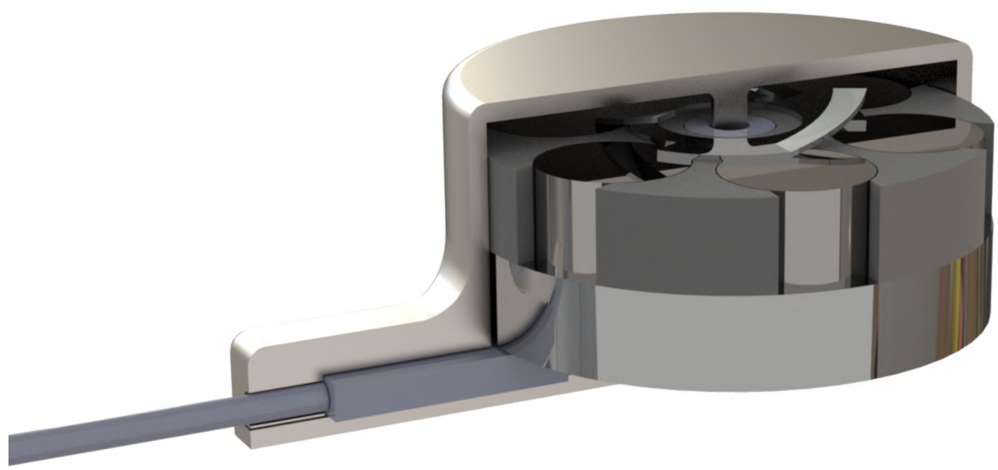


Figure 56: Assembled view of the actuator

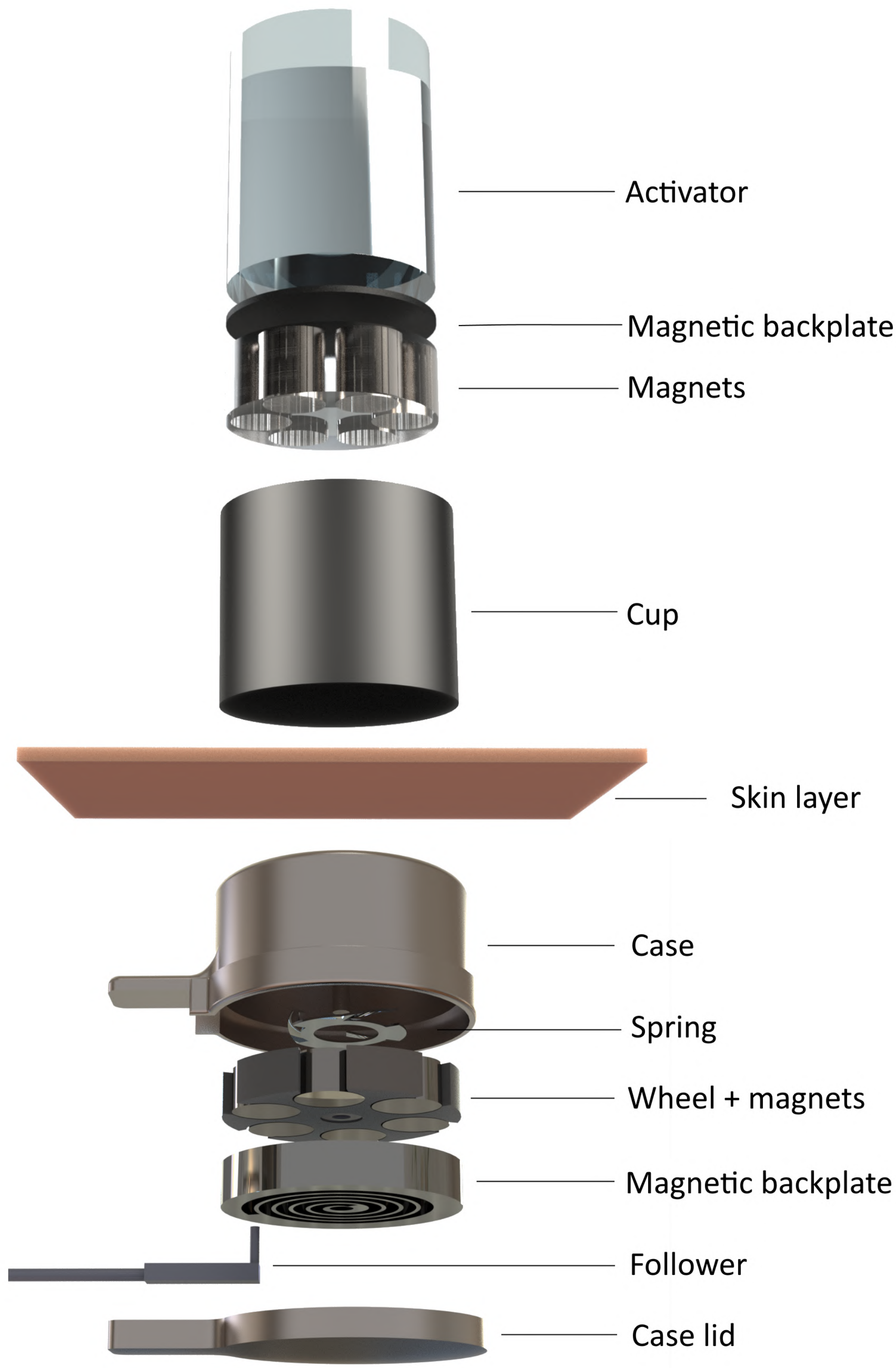


Figure 57: Exploded view of the actuator and activator, showing all the individual parts

10.4 Materials

Before a physical prototype can be constructed, suitable materials need to be chosen for each part.

Casing: for this first prototype, transparent plexiglass will be used. This is done in order to be able to see the functioning of the actuator while assembled. For the final product, titanium will most likely be used, because this can be made much thinner than plexiglass and it biocompatible.

Backplate: this needs to be made from a magnetic material. Iron is not optimal however, since it can oxidize and rust. Therefore, a ferritic type of stainless steel will be used.

Bearings: The bearings will be made out of PET-P, which has a low friction coefficient, and won't oxidize like some of the metals used for sliding bearings.

Follower: the follower will be made from stainless steel.

Wheel: The wheel will be made out of POM (PolyOxyMethylene), which is suitable because the shape can easily be made out of POM, and the mechanical requirements of this part are not very demanding.

Next to these materials, a lubricant was used on the interface between the follower and the spiral in order to prevent the wear and release of wear particles.

10.5 Physical prototype

Now that a model has been made, and a decision has been made for all the materials, a physical prototype can be constructed. This prototype was made by the development department of the LUMC, see figure 58.

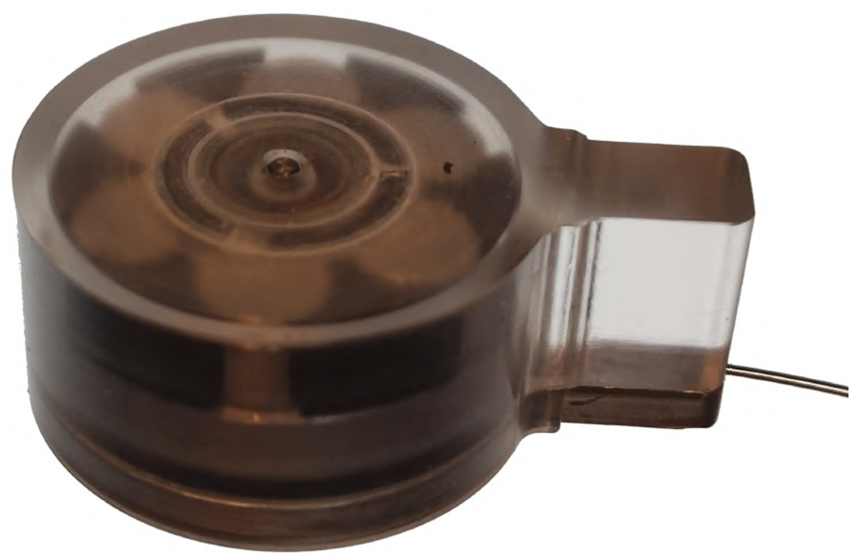


Figure 58: The physical prototype that was developed by the LUMC

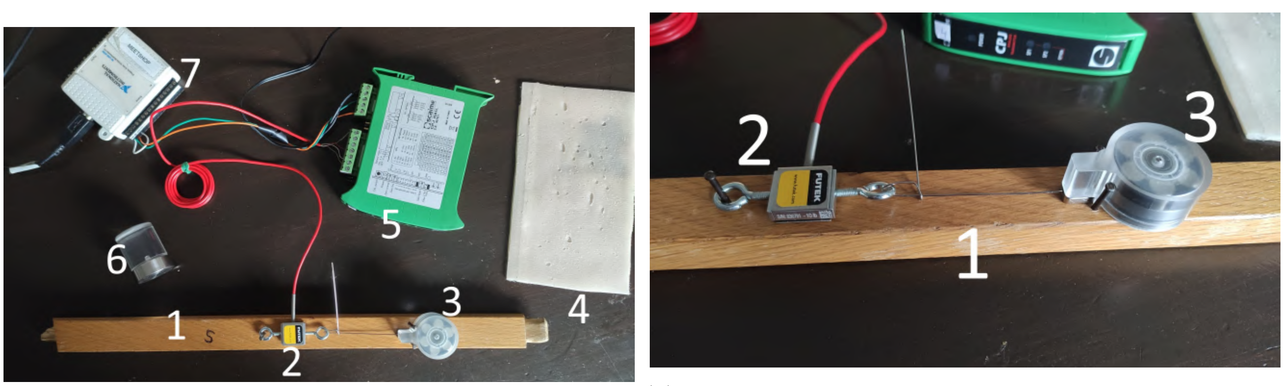
11. EXPERIMENTAL METHOD

In the previous section, the final design for the actuator was presented. The next step in this thesis project is the testing and validation of the developed device. The scores that were given in the Harris profile were based on testing on an earlier prototype, calculations, or estimations. Some design requirements however, could not yet be validated, and still need some testing in order to confirm that they are met.

The maximum force for different skin thicknesses will be measured in a test setup using a load cell. This same setup, with some alterations, will then be used to test the reliability and the durability of the device. Lastly, a functional test will be performed in a goat cadaver study.

11.1 Force validation

The first requirement that will be tested is the maximum force. This will be tested in an ex-vivo test setup using a load cell. There are two variables that can influence the maximum force of the actuator: (1) the distance between actuator and activator (thickness of the skin) and (2) the position of the follower in the spiral.
Maximum force tests will be done using three different distances between magnets; 3, 4 and 5mm, and two different follower positions: at the beginning (outside) of the spiral and at the end (inside) of the spiral. This will result in six different combinations of variables.
The test setup is shown in figure 59. Some nails were placed in a wooden board (1) to keep the actuator (3) and load cell (2) in place. A Futek miniature load cell (Futek, Irvine, California, USA) was used to measure voltages. The voltages generated by the load cell were fed into a data acquisition system (Scaime, Juvigny, France) (5) which was powered by a power supply (National Instruments, Austin, Texas, USA) (7). Two different wooden boards were used, with varying distances between load cell and actuator (one for the most outer position, and for the most inner position of the follower). For a measurement, the load cell and actuator were placed on the designated board, a piece of silicone fake skin (4) was placed on the actuator, and the activator (6) was coupled. Then, the activator was rotated, so that a pulling force was exerted through the transmission on the load cell until slip occurred in the coupling between activator and actuator.
The data was processed in LabView (National Instruments, Austin, Texas, USA).



(a) Overview of the entire test setup

(b) Close-up view of the wooden board, load cell and actuator in the test setup

Figure 59: The test setup used to measure the forces generated by the actuator.

Since the system output a voltage every 100ms, it still needed to be calibrated to output Newtons. This was done by using three different weights and determining the corresponding voltage. Using these three points, a line was fitted through. The slope of this line was used to multiply the voltage with to end up with a force. The LabView script that was used output an excel file with timestamps, voltages and corresponding forces. This excel file was in turn imported into Matlab, where the data was processed.
For each combination of variables, a total of at least 15 measurements were done. In Matlab, a script was written that automatically determined the peak forces for each measurement and gave the maximum measured force, and the average peak force over all measurements. For the script, see appendix III, section 18.

11.2 Reliability test

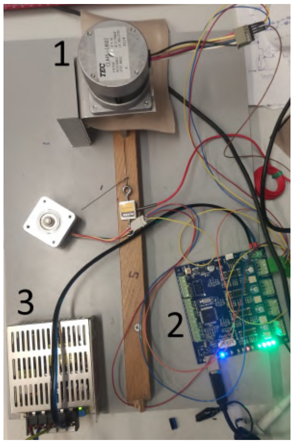
The second requirement that is tested is the reliability of the device. It will be tested in the same test setup described in the previous section. According to the reliability requirement, the failed activation rate cannot be below 5%. In order to test this, the device was activated and deactivated 450 times until slip occurred between magnets, and the failed activation attempts were counted. Activation attempts were counted as failed when either the actuator needed to be reattached, when the actuator did not reach 12N, or when the activator needed to be rotated back before reaching 12N for whatever reason.
Additionally, in order to give a first measure of durability, the actuator was activated until slip occurred for each measurement. This data will then be used for the durability validation in the next section.

11.3 Durability test

First, the data that was acquired during the reliability test will be used. The force data will be analyzed to see whether the average and maximum peak force decreased over time. Using the data, a line will be fitted through the peak force values. This line, when suitable, will be extrapolated to get an idea of the loss of force and built-up of wear in the device. Note that this testing is a worst-case scenario testing, since the actuator will have to work at its maximum force every time that it is activated, which is not something that will happen in actual usage (since only about 6-8N is needed to open the valve). Pushing the actuator past this threshold every time will most likely cause more wear.

11.4 Durability test part 2

From the data acquired from the first durability test (see section 12.4), it became clear that simply using this data and extrapolating was not a good representation of actual usage, because only 6N is probably needed for actuation of the valve. Because of this, a more representative test was performed. For this test, the actuator was to be activated and deactivated until the durability requirement of 3500 cycles was met, with a speed of 5 sec/rotation. Doing this by hand would require a lot of time and put a lot of unnecessary strain on the hand, so a test setup was built, see figure 60. The actuator and load cell were placed in the same test setup as the previous tests but this time a stepper motor (1) was connected to the activator and fixated in place, powered by a power supply (3). Using a TinyG CNC controller board (Adafruit, New York, United States) (2), a G-code file was sent to the stepper motor, which instructed it to rotate a fixed amount back and forth for 3000 times (only 3000 cycles were chosen as opposed to 3500 cycles because of all the previous testing that was already performed using the actuator). Similar to previous tests, the test data was collected and analyzed in LabView and Matlab. For the matlab script, see appendix III, section 18.



(a) Overview of the entire test setup

(b) Close-up view of the actuator and stepper motor in the test setup

Figure 60: The test setup used to measure the durability of the actuator

In order to confirm that the stepper motor still caused the same rotation at the end of the test, pictures of the activator were taken with a visual indicator before and after the test.

11.5 Goat cadaver study

Before the device can be implanted in humans for testing and validation, it will have to be tested in an animal model first. The animal that will be used for this study is the goat. The blood vessels in the neck of the goat are similar to blood vessels found in humans and thus the goat study will function as a first study to test function and long-term implantation viability of the device.
The anatomy of the neck of the goat is of course very different from the anatomy of the human arm. Therefore, the goal of this study was to identify the best implantation site for the upcoming goat study, identify the differences with the implantation in a human arm, and the possible adaptations that need to be made to the device in order for it to work in a goat.
The study was performed in collaboration with the GDL (Gemeenschappelijk DierenLaboratorium) of the University of Utrecht. One goat was used in this study, whose neck was opened up by the vascular surgeon, exposing all the blood vessels, nerves, muscles and tendons in the neck. Then, the possible implantation sites were explored, starting with finding a suitable place for the shunt between an artery and a vein.
Then, a suitable place for the actuator was searched for.
In the identified possible implantation locations, the actuator was placed, and the skin was placed back over the open wound and held in place. Next, the activator was coupled to the actuator and the function of the actuator was tested by rotating and seeing whether the transmission would move.
Additionally, the thickness of the skin of the goat was measured, since this thickness determines the distance between the sets of magnets, and thus the maximum force that can be generated.

12. RESULTS OF EXPERIMENTS

12.1 Force validation

A total of six measurements were done, with at least 15 sub-measurements per combination of variables. Figure 61 shows the output of all individual measurements. Note that some peaks were (incorrectly) identified. These weren't however counted towards the average value since there was a cutoff value for peaks that they need to meet in order to count toward the average.
From the resulting data, the average and maximum peak values were also extracted. These are represented in table 5.

Table 5: Table displaying the maximum and average peak force values for all measurements at different skin thicknesses

	Position 1		Position 2	
	Max peak value	Average peak value	Max peak value	Average peak value
3mm	53N	46N $\pm 3.7N$	74N	67N $\pm 3.7N$
4mm	45N	34N $\pm 3.1N$	70N	68N $\pm 3.4N$
5mm	17N	15N $\pm 1.2N$	23N	21N $\pm 1.2N$

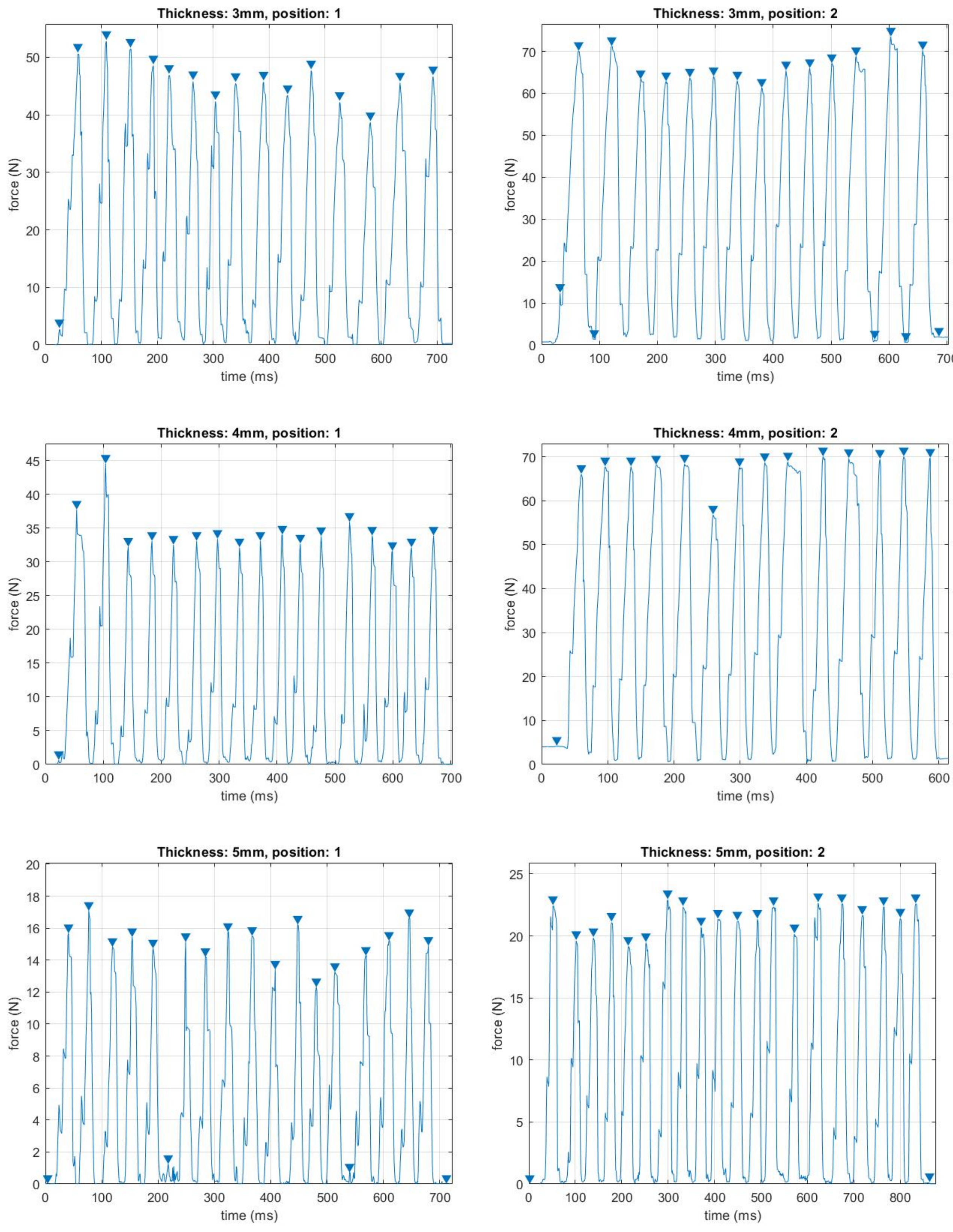


Figure 61: Results of the force measurements. Arrows indicate identified peaks.

12.2 Calculation validation

Now that experimental data has been collected, the calculations and equations that were used earlier can be validated. Since a lot of excess force is available, some changes can be made to the actuator that lower the generated force, but improve on the function in some other ways. When the used equations have been validated, these can later be used to calculate new values for proposed improvements to the device.
For the validation, the calculation and force testing with a distance of 5mm between magnets is taken, since this distance occurred in both. Note that the measurement of 5mm in the first test corresponds to a skin thickness of 4mm in the last test, since the spring adds another 1mm. Using equation 7, we can calculate the maximum force for both positions using the following variables:

p = 2mm
r = 9mm (position 1) & 4.25mm (position 2)
F_w = 8.3N (position 1) & 17.6N (position 2)

Using these values and a friction coefficient of 0.16 (toolbox, 2004), we arrive at a maximum force of 42.3N for position 1, and 74.0N for position 2. These calculated values are close to the experimentally found values at 4mm, see table 5, which were 34.1N and 67.8N respectively.

12.3 Reliability test

Over all the test measurements, 0 failed activation attempts were recorded, resulting in a failed activation rate of 0%.

12.4 Durability test

From the raw test data (see appendix II, section 17), the peak value of each individual measurement was taken, and a trend line was fitted through the data, see figure 62. From this data, the formula for the trend line was extracted using the basic linear fitting tool in Matlab:

$$y = -0.038 \times x + 74 \tag{10}$$

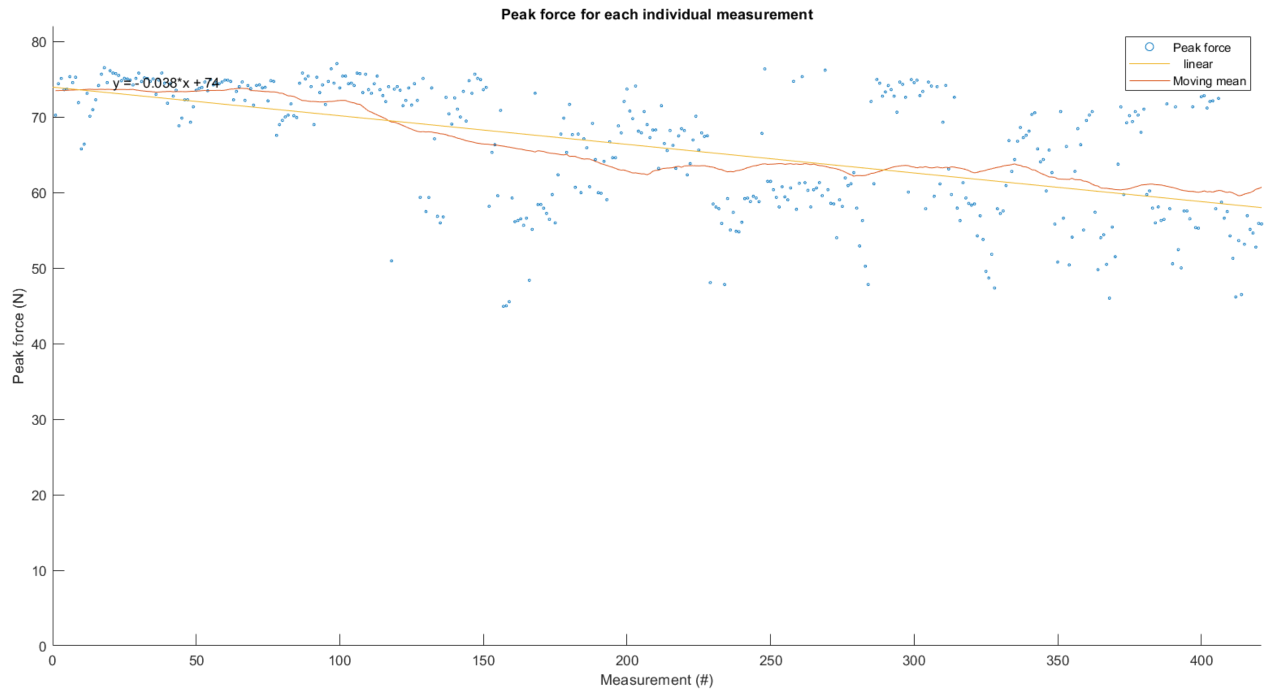


Figure 62: Plot of the peak values of the durability test. A linear trend line is fitted through the data. Additionally, the moving mean (100 samples) is plotted.

Using equation 10, we can obtain an estimate of the supplied force after 3500 cycles, by substituting x with 3500 and solving, arriving at a value below 0. This would mean that the force that can be supplied after 3500 cycles will not be sufficient. A large assumption here however, is that wear and deterioration of the max force will continue linearly. When taking the moving mean with a window of 100 measurements, the peaks are filtered out and the progression of the force data is easier to interpret. Looking at this moving mean, it becomes clear that the decrease isn't linear. Rather, the average peak value stays very consistent until measurement 100, where it makes quite a drop until measurement 200, after which it stabilizes again. This means that simply fitting a linear line through the data and extrapolating probably does not give a good estimate. Also, pushing the mechanism to around 70N every time is not a good representation of a real use case so additional testing is needed.

12.5 Durability test part 2

The actuator successfully completed all cycles in the test setup without breaking and was still functional after the test. According to the visual indicator, the stepper motor was still performing the same rotations as before the test, implying that no steps were skipped in the stepping motor. Results are shown in figure 63.

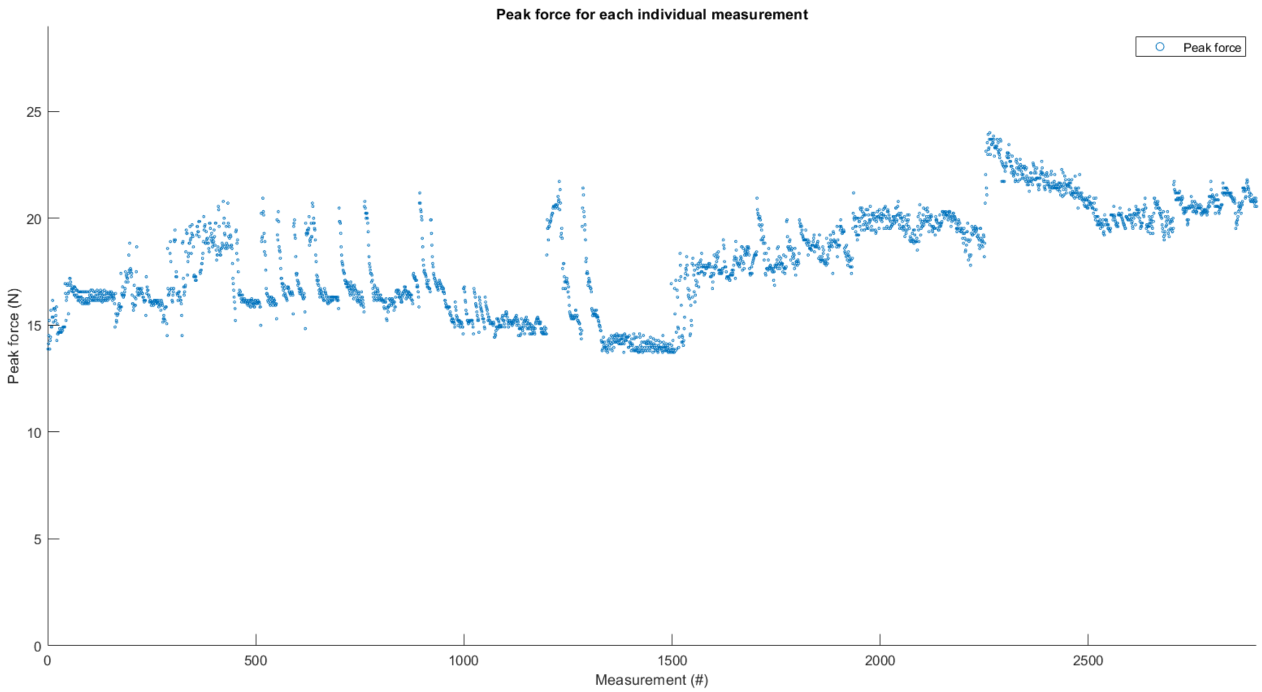
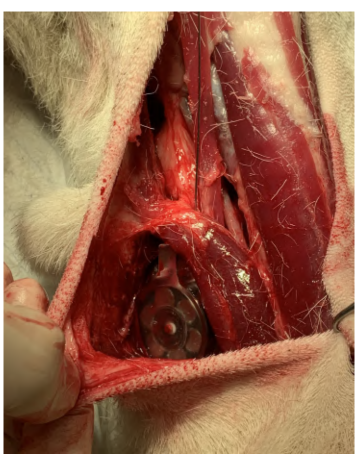


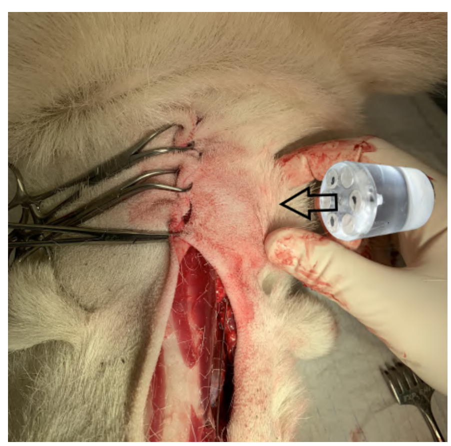
Figure 63: Results of the durability test. For each individual measurement, the peak force was taken.

12.6 Goat cadaver study

Following from the cadaver study, two possible implantation sites were identified for the valve. Following these locations, two possible implantation sites for the actuator were identified; one proximal, at the beginning of the neck, and one distal, at the end of the neck just before the jawbone. Figure 64 shows the actuator placed in one of the implantation sites. When coupled to the activator, the actuator could successfully be operated.
The thickness of the skin of the goat was measured to be between 4 and 5mm.



(a) The actuator placed in the proximal area of the neck



(b) The actuator in the proximal area of the neck, with the skin of the goat covering it. The actuator is located between the thumb and index finger of the hand in the picture.

Figure 64: The actuator placed in the goat in the proximal implantation site.

13. DISCUSSION

In this chapter, the entire process of this master thesis project will be discussed. First, a discussion on results of the experiments performed in the previous chapters will be given. Then, shortcomings and limitations of the entire process will be discussed. Lastly, recommendations will be given for the further development of this device.

13.1 Findings of experiments

The peak force tests at different skin thicknesses and follower positions showed that a more than adequate amount of force is being generated by the actuator. This surplus of available force could definitely come in handy, since this gives room for improvements to the actuator at the expense of generated force. For more on this, see section 15.1.

The reliability test suggests that the device is reliable, giving little room for error in usage, either on the side of the mechanism, or on the side of the operator.

Looking at the results of the durability test, see figure 63, the first thing that stands out is the fluctuations in the measured peak forces. Even though the stepper motor performed the same rotations for each measurement, the peak forces are not the same for every cycle. Additionally, the average peak force seems to increase over time. There are a couple possible explanations for this:

1. *Positional errors*: a transmission was taken that was pretty rigid, where only a small displacement took place of about 1.66mm, causing a force difference of 15N. This meant that when there was a small change in the displacement, or positional error, this could result in a rather large change in force. There were a couple places that could cause positional errors:
    (a) *The transmission rod.* Inconsistencies in the bending of the transmission rod could result in different output displacements.
    (b) *The interface between actuator and test setup.* When putting tension on the transmission, the actuator would rotate a little bit. Small variations here could change the total displacement.
    (c) *The interface between the transmission and the load cell.* The hook that connects the transmission to the load cell could introduce some variations in displacement.
2. *Distance between magnets:* due to the constant rotation and grinding of the spring against the (soft) plexiglass housing, wear caused the distance between magnets to decrease, which could explain the gradual increase in peak force.
3. *Wear in the device*: friction on the interfaces between follower and spiral and between the follower and the housing could introduce wear particles that can change the resulting peak forces. Although this would rather introduce a decrease in peak force than an increase, it could explain the small fluctuations in peak force.

Even though the fluctuations could possibly be decreased by improving on the test setup, the measurements still fulfilled their function; they showed that the actuator can still function and output an adequate force after at least 3500 cycles. Additionally, the peak force never degraded to under the threshold of 8N needed to operate the valve. Therefore, the durability requirement was met.

The goat cadaver study showed that the actuator in its current design could be implanted into the goat and be functional. This means that the same design can probably be used for the goat as for the following human trials. This is good news, since having to make changes in order to suit the device for implantation into the goat would decrease the representativeness of the goat study for the following human trials.
For the implantation site, the proximal site was determined to be preferable, since the distal site could cause trouble when the goat is chewing or moving its neck, since it was so close to the jaw bone.

13.2 Shortcomings & limitations

First of all, only the pulling force was tested. This was done partly because of the larger required force when pulling, due to having to compress the shunt and work against the blood pressure. But also because the pulling force was easier to test in a test setup. The test setup featured a load cell, which was connected to the actuator by an iron wire. No pushing forces could be propagated through this flexible iron wire. Adequate testing of the pushing forces would require a Bowden cable, which will (most likely) be used in the final device.

All the experiments that were performed for validation were performed ex-vivo or in a cadaver. Even though this is a good place to start for validating the device, especially looking at the functioning of the mechanism, multiple variables that can influence the durability, reliability and general functioning of the actuator exist that were not tested. During implantation, multiple physiological responses like foreign body responses and ingrowth of tissue can have an effect on the actuator, especially in the long term. Because the working principle of the mechanism relies on a certain distance between the sets of magnets, growth of new tissue between the magnets could be troublesome. Research into how likely this is to happen, and into possible coatings that can be used to prevent this is needed before long-term implantation.

The fixation method for keeping the actuator in place during handling deserves some more attention. During the goat study, some fixation by hand was needed in order to counteract the rotation caused by the friction in the device. Some further testing should be done to point out whether this counteraction is still needed when only a small force needs to be generated. Also, this test was done before the 'cup' was added that reduced twisting of the skin.
Even though this method of manual fixation did work, it is not the most elegant solution, and other options should also be considered, possibly introducing another magnet to counteract rotation, or some form of fixation to the skin or underlying tissue.

Resultant forces on the actuator can transfer to the valve through the transmission. When the actuator gets caught on something while implanted, a large pulling force could be propagated by the transmission to the valve, in turn pulling on the shunt and blood vessels. Introducing a bending angle in the Bowden cable and a fixation method for the actuator can prevent these forces, but not enough attention was given to this for this proof-of-concept project. Before implantation this should definitely be revisited and tested.

The current design of the actuator features some materials that are not biocompatible, like the magnets, spring and lubricant. Some more research should be done in order to either find suitable materials that are biocompatible, or to find out whether some non-biocompatible materials can be used when the device is sufficiently sealed. In this case, more attention should be given to how a full seal of the device can be ensured.

It is a known fact that magnets can lose their magnetism. Since the entire working principle of the current actuator relies on magnetism, a loss of magnetism could be a big problem.
There are five main ways for a magnet to lose its magnetism:

1. Heat: this shouldn't be much of a problem, since the maximum working temperature of neodymium magnets is 150°C.
2. Impact: large impact and chipping can damage a magnet and reduce its magnetism. This should not be a problem either since the magnets are shielded from impact by the arm, skin and casing.
3. Moisture: neodymium magnets are prone to corrosion. The magnets used in the current design are coated, however, this coating is not biocompatible. Proper sealing of the device could also keep fluids away.
4. Demagnetising fields: luckily, neodymium magnets are tough to demagnetize. In normal use, the magnets should never encounter these fields.
5. Age: magnets can simply lose their magnetism over time. This effect should, however, barely be noticeable during the lifetime of the device.

According to the above points, loss of magnetism should be a big worry, however, some cases are known where small implanted neodymium magnets in fingertips lose their magnetism over time (Robertson, 2017). It would be a good idea to look deeper into why these magnets lose their magnetism and whether this is something to expect to happen in the magnets in the actuator as well.

14. CONCLUSION

In this thesis project, a subdermal actuator to be used for opening and closing a valve has been developed and validated. Using a magnetic coupling, a device has been created that can supply enough force to open and close an implanted valve that can regulate the blood flow in a shunt.
The device was validated ex-vivo in a test-setup, as well as in a cadaver study. From this validation, it can be concluded that the prototype meets all the design requirements that were set for the device. Therefore, this study provided a proof-of-concept for an actuator that can be used to actuate a valve in a dynamic arteriovenous shunt system.

This study acts as the first promising step in a long development process for the DAS. Hopefully the current design can be implemented in the full shunt system and eventually be developed into a clinical device that can be used for dialysis patients. This way, dialysis patient could have control over the flow patterns in their shunt, allowing them to open their shunt for dialysis and close the shunt in between sessions. The reduction in flow in the shunt and adjacent vein when compared to current vascular access methods will hopefully result in improved patency and reintervention rates, as well as reduced burden on the heart. This way, the vulnerable group of dialysis patients could finally have a better alternative to the disappointing performance and complications of current vascular access methods.

15. RECOMMENDATIONS

Now that an initial prototype has been made, design requirements have been fulfilled, and the generated forces are known, improvements can be suggested for a next prototype.

15.1 Proposed improvements

Increased durability
One of the things that needs to be improved is the durability and stability of the pawl that follows the spiral. When high forces are exerted on the pawl, it is prone to bending, which already happened during testing.
In order to prevent this, three different measures can be taken:

1. Use a stronger material. Even though stainless steel already has quite a high Young's modulus of around 180GPa, using a type of steel with a higher Young's modulus could slightly improve durability.

2. Increase the thickness of the pawl. Increasing the thickness of the pawl is the most straightforward method of increasing its strength.

3. Decreasing the height of the iron backplate. When the height of the iron backplate is decreased, the pawl doesn't have to be as long. This will in turn decrease the moment arm acting on the pawl that causes the bending.

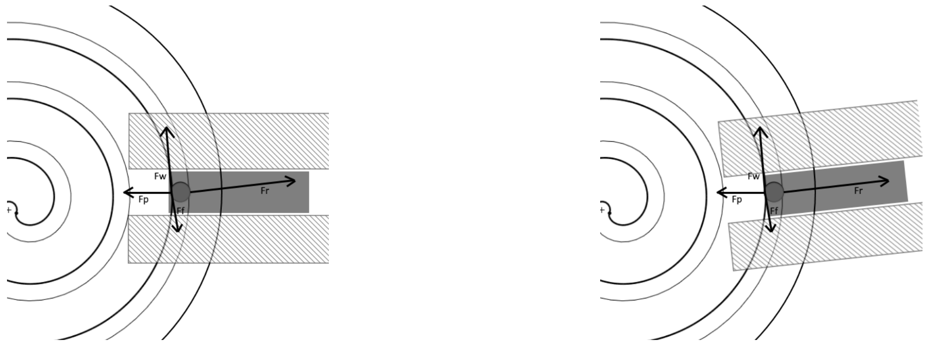
Locking mechanism
Even though the locking mechanism was functioning, there are a few things that could be improved. The locking mechanism at the outside of the spiral engaged reliably, but the one at the beginning of the movement did not. To make this more reliable, a slope could be added, through which the pawl is pushed into the recess in the spiral, see figure 65. This way, the wheel does not have to be in the exact right position when disengaging the activator for the locking mechanism to fall in to place.

(a) Schematic view of the current locking system (b) Schematic view of the proposed locking system

Figure 65: Overview of the proposed improvement for the locking mechanism

Reducing friction and wear
In the current design there is quite some wear happening. After the tests, wear could be observed on the interface between the pawl and the spiral, and between the follower and the case. Note though, that during the tests, the actuator was pushed to its limits every time it was activated, which was way above the forces it actually needs to deliver. This means that the wear in actual use will most likely be much lower. It is still a good idea however, to reduce wear and friction whenever possible.

Orientation of follower
Some friction can be reduced by changing the orientation of the follower with respect to the center of rotation, see figure 66. The off-angle can be calculated using equations 8 and 4. This way, the force pushing the follower out is in the same direction as the actual movement of the follower. As such, the friction between the follower and the case should be reduced. Note that, because of the changing radius in the spiral, and thus the changing angle of the force vector, it is not possible to keep the force in line with the displacement during the entire movement. An orientation can be picked that represents the average angle, or an orientation can be picked that is most beneficial when the forces in the actuator are highest.



(a) The current transmission

(b) The proposed improvement

Figure 66: Schematic overview of the improvement for the proposed improved follower transmission system

Bearing in follower
Most of the wear seems to happen on the interface between the follower pawl and the spiral. When the size of each individual groove can be made large enough, a bearing could be placed, which could greatly reduce wear. This does mean a large drop in the available force however.

Additional bearing
In the current design, there are two bearings acting between the axis and the wheel; one on the top of the wheel with the magnets, and one on the bottom. Because of the size of the opening in the iron back-plate, there was no room for an additional bearing. This can cause an imbalance when loading the wheel, causing it to tilt. Because of the excess of force available, the spiral could be moved out a bit, which reduces the available force, but gives room for an additional bearing.

Actuator size
Even though the actuator in its current state meets the dimension requirements, it still feels a little bit bulky. If, after implementing the previously mentioned changes, there still is a surplus of force available, the magnets can be made smaller. It would be best to decrease the height of the magnets, since that has the lowest impact on the magnetic attraction force. Also, the height of the actuator seems most troublesome, so decreasing this would be the first priority for decreasing its bulkiness.

Another potential improvement is producing custom-shaped magnets, as suggested earlier and seen in figure 31. This way, the magnets could be made even thinner, and the diameter of the wheel could potentially be decreased.

Addition of tabs (for goat study)
For implantation into a goat, the device needs a method to be fixated. One of the methods that is used more frequently in animal studies, is to suture the device percutaneously. This would require the addition of some tabs at the top of the device to run the sutures through. This fixation can keep the actuator in place in between use, can oppose the resulting force during operation, and can prevent some of the external forces on the actuator from transmitting to the shunt.

Calculations and values
Implementing the above changes would change the following values determining the maximum available force:

1. *Increasing thickness of the pawl:* increasing the thickness of the pawl will increase the diameter of the individual grooves in the spiral.
   Doubling the diameter of the pawl results in a doubling of the pitch of the spiral:
   $$p \rightarrow 4.0mm$$
2. *Placing an additional bearing:* placing an additional bearing in the wheel means that the spiral would have to move out a bit. This changes the maximum and minimum radius of the spiral:
   $$r_{max} \rightarrow 12.35mm$$

Calculating the maximum force at the beginning of the movement (outside of the spiral) now results in a value of 28.5N. This is still more than enough to close the valve. Note that the implementation of a bearing in the spiral is not accounted for here. When too much friction is still present after implementation of the other changes, this can be revisited.

Using 28.5N as a starting point now, we can look at decreasing the height of the magnets.
When this value of 28.5N is halved, about 14N is available, which is still enough to open the valve and have some room for decreasing of the force due to wear, tissue ingrowth over time, and loss of magnetization, as well as disparity between calculations and actual force values. This means that the magnetic attraction force between the magnets can be halved, since all relations between this attraction force and the eventual maximum force are directly proportional. Using an online magnetic attraction calculation tool (Supermagnete, 2020), we see that the magnetic attraction between two magnets with a diameter of 8mm is almost halved when going down from 5mm to 3mm in height (5mm = 2.413N, 3mm = 1.442N). The initial attraction of 2.413N is decreased by the following ratio:

$$1.4N/2.4N = 0.60$$

Applying this ratio to our experimental findings in figure 34, we now would have an available torque of:

$$0.075Nm \times 0.60 = 0.045Nm$$

Using this new torque, we can again calculate the maximum available force in the actuator, resulting in a value of **17N**. This means that the above improvements can be implemented and the height of the magnets (and thus actuator) can be decreased by 2mm. Note that this calculation is a simplification, since it uses the theoretical attraction between only two magnets and applies it to a larger magnetic field, which is amplified by an alternating magnetic field pattern and a magnetic backplate. This impact of the amplification could be different for the set of magnets than for the two theoretical magnets used in the calculator.

Next to the changes influencing the maximum force, decreasing the height of the magnetic backplate (and of the follower) has no effect on the maximum force. The height of the magnetic backplate can be decreased, decreasing the depth of the spiral and the length of the follower with it. Another benefit is that the bending moment arm of the follower pawl is decreased because of this. The height is decreased by 2mm.
The total height of the device should now be decreased by 4mm, which is about a 25% decrease total.

15.2 Next steps

Since this master thesis is only the proof-of-concept phase of a much larger project, a PhD project will continue the development of the actuator that was developed in this project. This section proposes some followup steps in the continuation of this project.

15.2.1 Version 2.0

One of the first upcoming steps that should be completed is the construction of a second version of the prototype, with all the proposed changes and improvements implemented. An important step here is the selection of materials. Biocompatible materials would preferably be used that can meet the mechanical requirements of the actuator. Most critical is the selection of materials for the interface between spiral and follower, where most friction occurs. The follower needs to be stiff enough to not bend or break, but the material should also not be prone to wear and the release of particles. Alternatively, more research should be done into sealing and possibly being able to use non-biocompatible materials when and adequate seal can be guaranteed.
Next, this version should be tested and compared to the first version. Most important here is that the locking mechanism has become more reliable, and that wear in the device is reduced. Possibly, some experimentation with the alternate locking mechanism could be performed.

15.2.2 Transmission selection

Another important step in the development of the device, is the selection of a transmission system. A preference for a Bowden cable has already been expressed, since it can propagate pushing and pulling forces and can be flexible, preventing sudden jerking movements to directly act on the shunt. An open mind should be kept however towards possible other transmission systems. A suitable material needs to be picked for the transmission system. This should be a biocompatible material that determines:

1. *Loss of force and displacement.* When using a Bowden cable for example, an inner cable slides inside an outer housing cable. Because of this sliding friction occurs. The material choice determines the friction coefficient and thus determines the loss of force. Additionally, when the cable is placed at an angle, the sliding will cause a loss of displacement. It is very important to know the values for force and displacement loss in order to be able to adjust the actuator properly.

2. *Bending angle.* An optimal bending angle should be found that finds a balance between loss of force and displacement (see above) and safety regarding forces acting on the shunt. The material choice can limit the maximum possible bending angle when a stiff material is chosen.

15.2.3 Integration into one device.

The next step should be the integration of the actuator, transmission and valve into one device. Important here is to think about how the transmission is connected to the valve and the actuator.
Preferably, a connection is used here that can still be broken. This would allow the device to be modular, allowing only part of the device to be replaced. This would reduce the burden and costs of reintervention surgeries in case something breaks and needs to be replaced.
When the individual components have successfully been integrated into one device, it should be tested. Force tests, reliability tests, durability tests and functional tests should be performed again, and improvements should be made accordingly.

15.2.4 Revisit patients and question end-users

At this point, it would be a good idea to revisit the end-user input. It has been a while since patients were questioned about the device and a lot has changed about it since then. It would be a good idea to interview patients and other end-users, like nurses, again to see what their opinion is on the device. It would also be a good idea to have some sort of functional model so that the end-users can test the device as a whole and give their opinion on how it is operated.

15.2.5 Goat study

When the device has been improved to a point where it is ready for implantation, a goat study will be performed as a first test of function and long-term implantability. A couple goats will be available for this study. These should be used in series, as opposed to parallel, so that each individual case can be assessed and improvements can be made before the next implantation.

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16. APPENDIX I - PATIENT INTERVIEWS

In the development of medical devices, which is already a complex gathering of multiple technical and medical disciplines, the patient is sometimes forgotten. This patient however, is one of the largest shareholders in these new technologies, and user needs often vary largely from develop needs (Cahill, 1994). Understanding these users' needs can determine the success or failure of a new medical innovation (Shaw, 1998). Cardiac Pacemakers Inc, which is a large manufacturer of pacemakers also finds involvement from end-users to be 'effective and efficient' (Wei-Tek, Mojdehbakhsh, & Rayadurgam, n.d.). Because of this, it was decided to start involving patients from an early point on.

To coordinate this patient involvement, a collaboration with the Nierpatient Vereniging Nederland (NVN) was set up. The NVN has a large pool of patients, or 'experience experts' who are currently undergoing treatment for kidney failure by means of kidney dialysis. Additionally, they have experience with coordinating these kinds of patient involvements for development of new therapies and technologies.

Initially, the plan was to gather information using a questionnaire. However, it was hard to cover everything this way, and left too little room for questions by the patients. Because of this, the choice was made to plan video interviews with small groups of patients. The NVN sent out an invitation to their patients, and two separate group interviews were planned, with 2 and 3 patients respectively.

The interviews lasted about 1-1.5 hours. First, an explanation on the device was given, and it was made sure that all patients fully understood the concept.
In the next section, the location for the actuator was discussed. First, the patients were given images of an arm, and were asked to point out what location they would prefer for the actuator. Then, a couple possible implantation sites were given that were already identified as 'viable' were shown, and the opinion of the participants on these locations was asked.

In the following section, the possible methods of activation for the actuator were discussed. Using visuals, five different methods of activation using manual force on the skin, and one method using magnets were shown to the participants, and their preference was asked.

16.1 Findings

Implantation site
Most patients agreed that an implantation in the upper arm is preferable to implantation in the lower arm, mainly due to aesthetics; when wearing short sleeve clothing, the upper arm is hidden while the lower arm is not. For the same reason, the inner (medial) side of the arm was preferred. Additionally, the participants expressed that they thought that it would probably be less likely to bump into stuff on the inner side of the arm.

Activation method
Most patients agreed that a magnetic activation would be preferably, since no interaction with the skin would be needed.
From all the methods involving manual force on the skin, pushing was preferred, followed by sliding and pinching. Twisting and spreading was not appreciated by the participants.

Other findings
Mainly, the participants had a lot of questions regarding the practicalities and changes in their day-to-day lives when they would be living with a DAS. They asked questions regarding other devices that they may have implanted in a similar locations, whether applying pressure after receiving dialysis would still be necessary, and if they could still get an MRI. While these questions kind of exceeded the scope and goal of the interviews in this early stage of development, the participants raised some interesting points.
It would definitely be interesting to stay in touch with the NVN and consult with their patients again later in the development stage when prototypes are ready to be tested, and in the implementation stage.

17. APPENDIX II - RAW DATA OF DURABILITY TEST

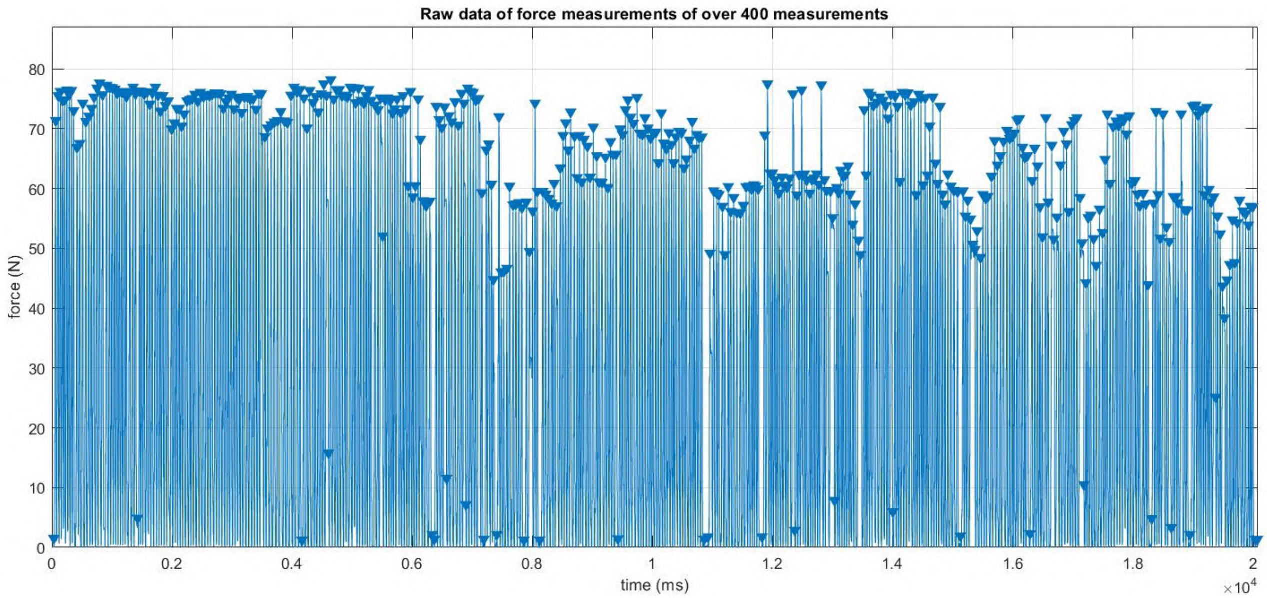

Figure 67: Raw data from the first durability test

18. APPENDIX III - MATLAB SCRIPTS

18.1 Script for extracting data from excel, plotting and identifying peaks

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% This script takes an excel file containing a time and       %
% voltage column, extracts the data and makes a graph         %
% showing identified peaks, and gives max and average peak    %
% values.                                                     %
% Author: Sander van der Kroft                                %
% Date: 01/12/2020                                            %
% Project: Master thesis                                      %
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

%%
clc
clear all
close all
%%
prompt = 'enter file name: ';                % Prompts given to the user
prompt2 = 'enter graph title: ';
%%
str = input(prompt,'s');                     % Reading the file name to be analyzed
A = xlsread(str);
A_t = (A(:,1));                              % Taking the time column out of the matrix
A_f = A(:,2);                                % Taking the voltage column out of the matrix
A_f = A_f.*15.372;                           % Multiplying the voltage column with the ...
    calibration factor to obtain Newtons
```

```
Cutoff=max(A_f)/1.75;                          % Calculating a cutoff value to eliminate ...
    misidentified peaks

name = input(prompt2,'s');                     % Getting the title for the graph

scatter(A_t,A_f,3)
findpeaks(A_f,'MinPeakDistance',25)            % Finding peaks with a minimum distance of 25 ...
    between them
peaks = findpeaks(A_f,'MinPeakDistance',25);   % Showing the peaks in the plotted graph
xlabel('time (ms)')                            % Setting axes, labels and title
ylabel('force (N)')
axis([0 length(A_t) 0 max(A_f)+3])
title(name)
peak_ind = peaks>Cutoff;                       % Finding indices of values above the cutoff value
peaks2 = peak_ind.*peaks;                      % Eliminating values below the cutoff
avg = sum(peaks2) / sum(peaks2>0)              % Calculating and displaying the average value
max = max(peaks2)                              % Calculating and displating the max value
peaks3 = peaks2(peaks2≠0);
S = std(peaks3)
```

18.2 Script for extracting data from excel sheet, plotting peaks and moving mean

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% This script takes an excel file containing a time and       %
% voltage column, extracts the data and makes a graph         %
% showing identified peaks, and gives max and average peak    %
% values.                                                     %
% Author: Sander van der Kroft                                %
% Date: 01/12/2020                                            %
% Project: Master thesis                                      %
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

clc
clear all
close all
%%
A = xlsread('durabilitytest1.xlsx');         % Importing data from excel sheet
A_t = 0.001.*A(:,1);
A_f = A(:,2).*15.372;
Cutoff=max(A_f)/1.75                         % Determining cut-off value for falsely identified ...
    peaks

stem(A_t,A_f);                               % Plotting raw data
findpeaks(A_f,'MinPeakDistance',30)          % Finding peaks
peaks = findpeaks(A_f,'MinPeakDistance',30);
title('Raw data of force measurements of over 400 measurements')
xlabel('time (ms)');
ylabel('force (N)');
axis([0 length(A_t) 0 max(A_f+10)])
peak_ind = peaks>Cutoff;
peaks2 = peak_ind.*peaks;                    % Extracting peak values
peaks3 = peaks2(peaks2≠0);
avg = sum(peaks2) / sum(peaks2>0)            % Calculating average value
%%
A_f2 = peaks3;
A_t2 = linspace(1,length(peaks3),length(peaks3))';
figure;
scatter(A_t2,A_f2,[3])                           % Plotting peak values
title('Peak force for each individual measurement')
xlabel('Measurement (#)')
ylabel('Peak force (N)')
axis([0 length(peaks3) 0 max(peaks3)+5])
movavg = movmean(A_f2,100);                      % Extracting moving mean
hold on;
plot(A_t2,movavg);                               % Plotting moving mean in existing plot
legend('Peak force','Moving mean')
```