Development of a novel **steerable embolization microcatheter**

for endovascular tumor treatment

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Development of a novel steerable embolization microcatheter
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Master thesis in partial fulfilment of the requirements for the degree of

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MENCIUS
||||||||MEDICAL

spark

P R E F A C E

**On the cover: The Mayn River flows through the far northeas-
tern corner of Siberia, a USGS sattelite image.**
A river making its way across the earth to nourish its surrounding
land is captured in this image, depicting nature in its pure form.
Although not always recognized, rivers are one of the fundamentals
keeping the world alive. They carry water and nutrients across the
world, act as drainage channels for surface water, and provide an
excellent transportation system between destinations all over the
world.

Nature has its way to express itself in recognizable patterns. Just like
a river bed, blood vessels spread out their branches through the
human body, providing channels for nutrient delivery and flushing
away waste material. Like a fishing boat making its way through the
Mayn River in Siberia, minimally invasive instruments use blood ves-
sels as pathways to diseased areas in the body. This technique only
requires one small incision in the groin or radial area, minimizing
trauma to the patient. Therefore, it has become the main approach
to a variety of treatments and diagnosis procedures in the past
decade. Consequently, it demands its own set of minimally invasive
tools. This thesis contributes to the innovation of these instruments.
It takes the reader through the design process of the Easysteer, a
novel microcatheter with a mechanically actuated steerable tip for
minimally invasive tumor treatment purposes. The design process
includes clinical research, development of the working mechanism,
prototyping, testing and a recommendation clinical validation of the
product. The application of a user-centered design approach ena-
bles a fast, efficient and promising evolution of the product.

This thesis is a result of my graduation project to obtain a Master's
degree in Biomedical Engineering at Delft University of Technology.
The project is commisioned by Mencius Medical BV and executed in
the form of a graduation internship at Spark Design & Innovation.
Inspired by the endless possibilities of innovation in the medical
world and driven by the opportunity to contribute to it as a designer,
I aspire to reinforce the bridge between clinicians and engineers.
This thesis serves as a representation of this goal, combining my
skills obtained at Industrial Design Engineering (BSc) and Biomedical
Engineering (MSc).

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C.V.Blankensteijn

</div>

ACKNOWLEDGEMENTS

READING GUIDE

New chapters will start with a light blue page. Each chapter represents a pillar in the design process. These pillars are arranged in an order that is primarily logical and not chronological. This way, the reader is taken through all phases of the development of the Easysteer steerable microcatheter, validating all the design choices that are made along the way.

The report first provides background information on the subject, followed by a clinical research which is translated into design requirements. The report ends with a final concept and reccomendations for the necessary steps to take in the future towards market introduction.

Conclusions of each chapter will be presented in orange. These conclusions are mainly design considerations and insights that are translated to product resquirements, and need to be kept in mind for further development of the product. This way, they represent the common thread of important decisions and iterations in the design process.

The component of the guidewire mechanism refered to as the "bellow" is always visualized in green. It requires an in depth technical study for theoretical proof of principle. This technical study is attached in the form of a scientific paper (*Appendix 12*), and includes a mechanical test and Finite Element Analysis.

EXECUTIVE
SUMMARY

The Easysteer is a novel steerable microcatheter for interventional radiology, more specifically for embolization of distal tumors. It is designed to have a steerable tip to facilitate navigation to distal targets.

Interventional radiologists have confirmed and practise has shown that the human vascular anatomy can present complex pathways towards a tumor. A steerable tip is expected to decrease operation time and radiation, as difficult turns can be made faster and more controlled.

The design is based on existing microcatheters to give the inteventionalist a tool that he or she is used to. Unlike other steerable microcatheters, the mechanism of the Easysteer is based on using the guidewire (which is an instrument that always accompanies a catheter) to activate a tip deflection.This feature potentially allows the interventionalist to take the entire route through the vascular roadmap with one device, eliminating a trial and error process and the need for exchanging multiple instruments during the procedure.

This thesis report focuses on the theoretical substantiation of the designed distal mechanism, that is developed based on an existing patent. It covers part of the design process, documenting the development from patent to working prototype. All covered parts of the design process that led to this are summarized below.

The first phase of the design process includes a medical research and allows for thorough understanding of the clinical need. Observations in the operating theatre and specialist interviews gave an insights in the variety of interventions that would benefit from steerable instruments. These include liver tumor embolizations, prostate embolizations, distal aneurysm coiling and reopening of arteries in the iliac region. The possible applications of the Easysteer technology are broad, as every minimally invasive procedure involves navigation. The confirmation of the clinical need by interventional radiologists encouraged to continue the development of the Easysteer. The medical need is described as: gaining access to small diameter tubular structures and hard to reach confined spaces, fast and with high precision.

To be able to establish design specifications, a target intervention was chosen to tailor the product to. Once the functionality of the product is proven for this specific intervention, more customized versions of the product can be developed to fit other interventions in various specializations. Regular specialist feedback enabled the product to be simplified to its core functionality, and it resulted in fast and efficient convergence of design choices.

This simplification led to the definition of a more specific design goal, dividing the concept into three components: the catheter, the guidewire mechanism, and the control device. These components each had their own requirements and could therefore be designed fairly separately, to be eventually combined in the final prototype. This thesis covers part of the development and prototyping of the catheter and guidewire mechanism. Different mechanism oncepts are evaluated on their technical feasibility, producibility, and functionality. The resulting product consists of a laser modification to a catheter, combined with a guidewire assembly including a rubber bellow that can be expanded under axial compression. This expanded bellow is used to apply tension in the catheter tip to make it deflect in the direction of the catheter modification.

The final catheter prototype is realized by an iterative process of the necessary manufacturing techniques, and both the catheter and bellow component are individually prepared to be tested in a suitable test setup for proof of principle. Catheter prototypes are evaluated in a user test by a specialist. The catheter is steered through a specially designed phantom model representing a generalized liver vasculature, in which worst case navigation can be mimicked. This resulted in a proof of principle for the catheter design. The bellow mechanism is evaluated according to a Finite Element Analysis, for which mechanical tests of the chosen rubber are required. This provided a theoretical proof of principle of the design, which is later validated by testing the assembly in a simplified test setup.

A recommendation is done for further in-vivo validation of the concept, to result in a proof of concept of the final prototype. The product is expected to significantly improve navigation speed during endovascular tumor treatment interventions, as well as reducing frustration, vessel trauma, equipment waste, and lastly, increasing the accessability of more distally located tumors.

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01 Introduction

1.1 Interventional radiology

Endovascular microcatheters are used for diagnosis and treatment of various diseases in and via the human vasculature. Due to the minimization of trauma to the patient, this minimally invasive procedure has become the main approach for treatment of blood vessel obstructions and malformations. Due to changing demographics (aging) and unhealthy lifestyle, the reopening of narrowed or calcified blood vessels, medically referred to as atherosclerosis, is a procedure that is dealt with on a daily basis by interventional radiologists. Blood vessel malformations mostly include aneurysms, that have to be closed to prevent a potentially fatal rupture. Furthermore, more and more benign or cancerous tumors are treated endovascularly.

The first step of a catheter-based procedure is puncturing the femoral or radial artery with a hollow needle, creating a gateway for instruments to enter the vasculature. Various catheters and guidewires can be navigated towards the diseased area. Once the destination is reached, the appropriate catheter is used to perform the desired treatment. For example, a catheter with an inflatable balloon at the tip can be advanced over the guidewire, to reopen the blood vessel lumen, or chemoembolization particles can be injected locally into tumor supplying arteries.

1.2 The navigation challenge

A downside of the minimally invasive approach is the absence of direct visual feedback. Imaging techniques are used to be able to navigate through the vascular network (Figure 1). Unfortunately, the patient's vascular anatomy does not always allow endovascular treatment. Due to tortuosity, complex geometry of bifurcations and small diameter of blood vessels, some target areas remain difficult or impossible to reach. Especially older patients show increased blood vessel tortuosity due to smoking or unhealthy lifestyle. On the other hand, even in healthy vasculature precise vessel selection can be challenging in distal locations. Complex vascular roadmaps affect the ease of the operation, and a trial and error process slows down the procedure. The navigation challenges and trial and error process require a great deal of skill and patience of the interventionalist. For this reason, microcatheters with a steerable tip have been designed and are continuously being improved in terms of steerability and in-tuitiveness, to increase ease and speed of endovascular procedures and consequently decrease radiation time.

Recognizing the clinical need for more steerability of interventional radiology instruments, **Mencius Medical** has initiated the Easysteer project, in collaboration with the product designers at Spark Design & Innovation and several medical specialists. The goal of this project is to design & validate a unique mechanically actuated steering mechanism in the tip of a novel steerable microcatheter for interventional radiology.

1.3 Project approach

The design process followed in this thesis project is the Double Diamond structure (Figure 2). It is a design model created by the British Design Council in 2005, and provides a structured overview of the different phases of a design process, and guides the designer towards decision making. The first diamond represents the "research space". It starts with a problem statement explaining the navigation problem

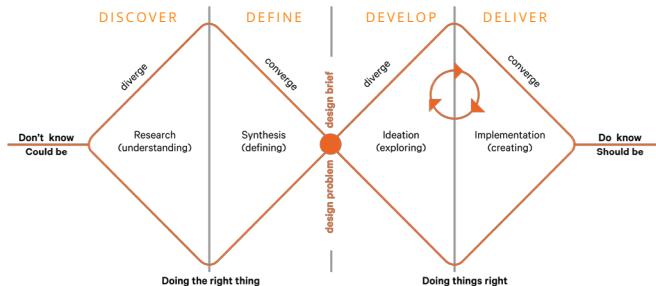Figure 1. Interventional radiologists in the OR. Image source: https://www.itnonline. com/article/defining-value-interventional-radiology

Figure 2. Double diamond design structure by the Design Council (UK). Source: https://www.designcouncil.org.ui/news-opinion/design-process-what-dou-

and unmet needs of current devices. A focus application is hypothesized to be targeted (chemo)embolization of distally located tumors. The goal of the research phase is to confirm this problem statement and focus application in close collaboration with specialists. Furthermore, the goal is to specify the desired functionality of a steerable device in terms of bending radius, pushability and flexibility. These outcomes are combined into a concept in the "design space" which is represented by the second diamond. Both diamonds consist of smaller iterative diamonds representing multiple diverging and converging processes that are needed to come to design considerations. [Design Council UK, 2005]

DISCOVER
In the DISCOVER phase, research is conducted to understand the problem, getting to know the user and explore existing devices and possible applications. This phase is **divergent**, as it is all about gathering data and insights, to identify the clinical demands. For example, the literature study preceding this thesis project covered a thorough understanding of the medical application of microcatheters and procedural challenges that are encountered (summarized in section 2.5). Furthermore, user interviews, stakeholder analyses, existing product analyses and competitor identifications are usually done in this phase.

DEFINE
The next step is to **converge** all this information, defining the key aspects for the design. This leads to a more specific design goal or *design brief*, located in the connection point between the research and design diamond. This is where the focus application of (chemo)embolization of tumors and specific requirements for the product are defined. Improving steerability was confirmed most important design challenge, of which operative precision and speed are expected to be the biggest gains.

DEVELOP
The particular focus application and design requirements that are concluded from the field study mark the beginning of the develop phase, which is **divergent** again. It includes an ideation phase with brainstorm sessions and usability testing, an iterative design process that can be repeated as often as necessary. Various distal mechanisms are explored for realization of steerability of the catheter tip.

DELIVER
Following an in-depth analysis of the concepts, the process **converges** again to a final concept. A final prototype is developed and used to perform a user validation test. The output of this phase is a Minimum Viable Product, and a technical and clinical validation of the concept is the end goal of this thesis project.

1.4 Innovation in healthcare

Medical device innovation is all about fulfilling an observed clinical demand with new technology. Introducing a new medical device to the market is however challenging compared to the consumer sector. A fundamental reason for this is the broad network of stakeholders involved in the development, approval and implementation of a novel medical device and - more specifically - the tradeoff between different interests of all these stakeholders. [Greer, 1987] Patients have the interest of receiving better care, however without increase of medical costs. Engineers want to facilitate better patient care with new technology, and sell this new technology to hospitals or hospital supplying firms. From a business perspective, the introduction of new technology to the medical field is influenced, and sometimes retained, based on corporate (intellectual property) and commercial interests of large companies.

Figure 3 visualizes the Healthcare Innovation Cycle [Parrish et al. 2015], including all the phases a novel medical device has to go through along it's journey to the operating table. Each milestone in this figure has to be reached in four different domains: Clinical, Tech-
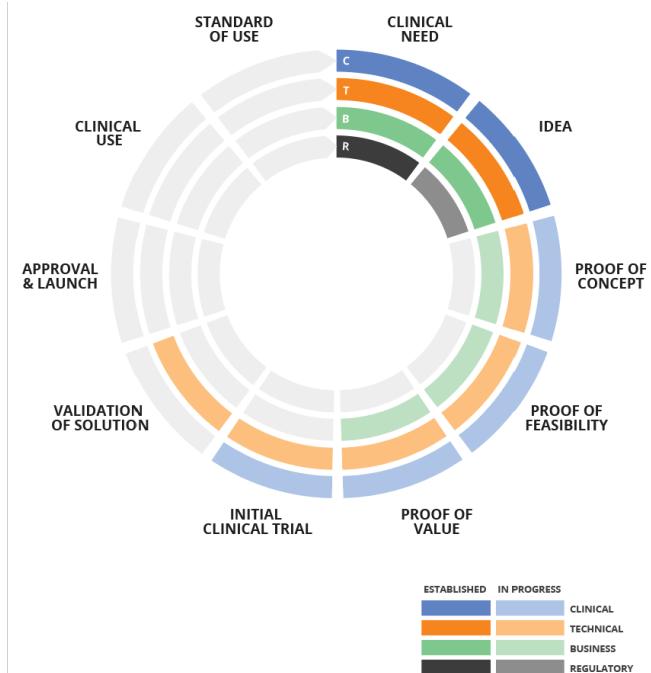

Figure 3. Chart representing a medical device innovation process, in relation to this project. Based on CIMIT's "Healthcare Innovation Cycle" & [Collins, 2019]

nical, Business and Regulatory. Keeping the project interdisciplinary will allow for efficient product development. In the figure, all milestones that have been reached for the Easysteer are colored, and the faded blocks represent the parts of the design process that are in progress and will be discussed in this report.

APPROVAL

A new medical device's first barrier is its approval by the Food and Drug Administration (USA) or the Conformité Européenne (CE) certification (Europe). These regulatory systems provide guidelines to assure safe implementation of the new product, and a certificate is provided when the product meets all the requirements. Many different products are considered a medical device, and are classified in three classes based on their invasiveness. In general, the higher the class, the more technological and clinical testing is required for the product to be introduced to clinical environment. Microcatheters being of class II, this process will include assessment based on clinical trials, and a proof that the device is equivalent to an existing approved device (according to the Pre-Market notification/501[k] by the FDA [US Food & Drug Administration]. It can take years and years of risk assessment studies for a new technology or procedure to be widely accepted by the industry, therefore slowing down the global innovation in the medical industry. [Yazdi et al., 2013] The estimated time and costs are, depending on the class of the product, up to 10 years and over $100 million from concept to market introduction. Due to this delay and investment, MedTech engineers must stay ahead of competitors and strategic choices have to be made. Nowadays, most healthcare innovation comes from start-ups backed by venture capital rather than academic medical centers.

ACCEPTANCE

Once approved, the device is only just one of thousands of medical devices that are on the market, waiting to be recognized by specialists as useful. It is considered 'useful' when the product improves a current procedure and patient outcomes, without risks for the patient and physician. As opposed to consumer goods, medical products require a specific level of proven potency in order to be purchased and used. Rogers [Rogers et al., 2003] established five factors that influence a person's decision to adopt or reject a new idea or product (figure 4).

Figure 4. Rogers' five factors that influence a decision to adopt a new product.

All hospitals have their designated product selectors, implementers and users, who all have their individual perception of Roger's five factors about the product. A hospital can only offer a limited selection of devices to its employees. Medical specialists are known to have busy agenda's, in which their day-to-day patient care often has priority over adopting new products that disrupt their routine. They have acquired a great amount of skill and experience over the years, and might all have their own tools of preference. The 'acceptance' is

therefore considered the second large barrier for a medical product to be recognized and implemented.

It is important to realize that cooperation between clinicians and engineers is crucial for the development of useful medical devices. [Yazdi et al., 2013] Therefore, a lot of programs have been set up throughout the world to facilitate this bridge between clinicians and engineers, for example the MSc Biomedical Engineering that has resulted in this thesis. During this project a focus is therefore put on actively involving the user. The initiators of the Easysteer being interdisciplinary is also a good foundation for this goal.

1.5 User centered design

Due to these extensive approval and acceptance processes, it is key to assure the added value of the product. This is achieved by actively involving experts in the design process, fundamentally focusing on offering the user what he or she considers useful. This is the only way for engineers to fully understand the medical need, and only then a novel medical device is worth going through the intensive approval and acceptance process. It should also be kept in mind that not only one, but multiple experts should be involved to avoid biases.

The user-centered design approach will accelerate the acceptance of the product. A factor that helps convince the user of the product's additional value is that there is not too much change in the user ritual required. Considering the **Easysteer** design, the activation of the steerable tip might ask for an extra user action. Therefore, the additional value must be enough to compensate for this extra action. Regular feedback sessions with the user are therefore done to keep evaluating the added value of the product compared to existing instruments, and whether the user would be willing to use it. Specialist interviews and a clinical study is set up to establish a thorough understanding of the user's needs.

It is not proven that steerability is directly related to improved clinical results. However, as [Rajappan et al., 2009] describes in a study in which steerability is evaluated during navigation to and inside the heart, steerability allegedly increases operating speed. It is therefore expected that this product is beneficial to the interventional radiologist in terms of making navigation during procedures easier, decreasing operating time and factors that induce frustration. The good thing about engineering products for clinicians is the indirect benefit that is experienced by the patient, which in this case is a shorter operating time and therefore reduction of exposure to radiation. It is not ruled out that steerability will cause improved clinical results, next to reducing operating time: if the product enables more selective artery access during tumor embolization, the risk for non-targeted embolization is reduced, potentially increasing clinical success rates.

This design report and the technical report embody a hybrid thesis project that combines the design of the product with regular user feedback. A sandwich strategy is applied to the project: It starts with studying the clinical user using current technology. Subsequently, this knowledge is implemented in the design of the product. Finally, the new product is validated by the clinical user again.
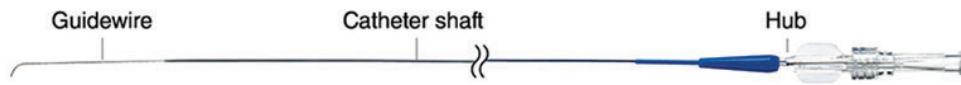
02 Background

Figure 5. Progreat 2.4/2.7/2.8 Fr microcatheter system (coaxial type with catheter and guidewire) Source: https://www.terumoeurope.com/en-emea/products/progreat%C2%AE-micro-catheter-system

2.1 Microcatheters

The word catheter is often associated with urine draining, which was originally the main purpose. Nowadays, catheters are generally tubular structures that exist in various diameters and can be used to reach diseased areas in the body. Minimally invasive (as opposed to an open surgical approach) means guiding the instrument through anatomical structures, for example the intestines [Art Photonics, 2018], the bronchi [Kontogianni, 2019], the urinary or vascular system. The scope of the project can theoretically include all minimally invasive instruments, including endoscopes, bronchoscopes, forceps, and other instruments that would benefit from a steerable tip. However, this project focuses on endovascular microcatheters in particular. The main reason for this is that the project initiators saw that a lack of steerability especially in smallest diameter endovascular instruments. This is not surprising, seen that decreasing the diameter of an instrument limits the options for implementing a steering mechanism. The specific shortcomings of current devices will be further investigated in Chapter 3.

The beginning of the development of endovascular instruments goes back to 1929. Werner Forssmann, a German post graduate of medical school, inserted a urinary catheter into the basilic vein of his own left arm. [Beheshti, 2011] He quickly went to the imaging room to make an X-ray that showed that the catheter tip had reached his heart. With this slightly irresponsible experiment, he was the first to discover an endovascular approach for reaching diseased areas in the body. Microcatheters were introduced to clinical environment in the 1950's. Since then, the challenges of endovascular procedures and the limitations of available equipment have sparked a continuous drive for innovation. As microcatheters became more versatile in functionality (think of balloon angioplasty, stent delivery, etc.), innovation was driven by two clear design objectives: increase navigation control and decrease diameter.

A company that joined the race for designing the next workhorse of steerable microcatheters is Mencius Medical BV. It is a joint venture with Spark Design & Innovation, and is established for the purpose of developing the Easysteer steerable microcatheter. The initial problem was identified by Dr. Vrancken Peeters, a vascular surgeon with an eye for innovation. These parties worked in close collaboration towards realization of the Easysteer concept.

2.2 Technical Background

The modern microcatheter is a hollow tube and comes with a guidewire. These two can be used together for advancement towards the diseased area: the guidewire being pushed through the vascular network and the catheter following. Both can be individually pushed, pulled or torqued at the hub (figure 5). The catheter often contains the treatment function, for example an inflatable balloon or stent, depending on the procedure. Guidewires are indicated in inches (0.014" or 0.018" mostly) and often have an atraumatic J-shaped tip [Perler et al. 2015]. Catheters are classified in French (F), which is the unit for the external circumference of the catheter. 2F means a circumference of 2/pi and a diameter of about 2/3 mm. Catheters that are 2F-3F, which will mostly be discussed in this report, are considered microcatheters. Design considerations for catheter and guidewire are reduced friction, hydrophilic coatings, and strong though flexible material properties.

The navigation during endovascular procedures can be a time consuming and frustrating aspect of endovascular procedures, as recognized by many specialists (Chapter 3). More and more novel technologies are being developed to reduce time, radiation and complications, and might even enable access to new locations in the body. Examples of current navigation solutions in the microcatheter range are:

- Catheters and guidewires with pre-bent shapes enable the specialist to make predictive turns. [Boston Scientific, 2019] When combining two pre-bent instruments, 3D shapes can be realized. A downside of this technique is the need for frequent exchanging of instruments during an operation, which is a factor that needs to be minimized in order to reduce operative time and trauma to the arteries.
- Shapeable tips: these tips are made of special material and can be bent in the desired shape when needed using the heat of steam. [Kiyosue, 2005] Downside is the same as for the pre-bent option. When the tip is shaped in a fixed curve, the catheter is not able to go straight when needed.
- Swiftninja™ is currently the most advanced microcatheter with a steerable tip. [Raina, 2019] It is however still not widely used by the interventionalists involved in this project, just like comparable steerable solutions, and the reasons for this are mainly costs or remaining technical limitations.

- Other steerability techniques, including mechanic, hydraulic, thermal, electric and magnetic actuation, are explored and being developed, as described in the preliminary literature study, but are not on the market yet. [Xiaohua

2.3 Starting point

The starting point of the Easysteer thesis project is a published patent for the general working mechanism. This idea was initiated by a medical specialist and together with the designers at Spark a unique and clever concept for the steerable microcatheter was developed.
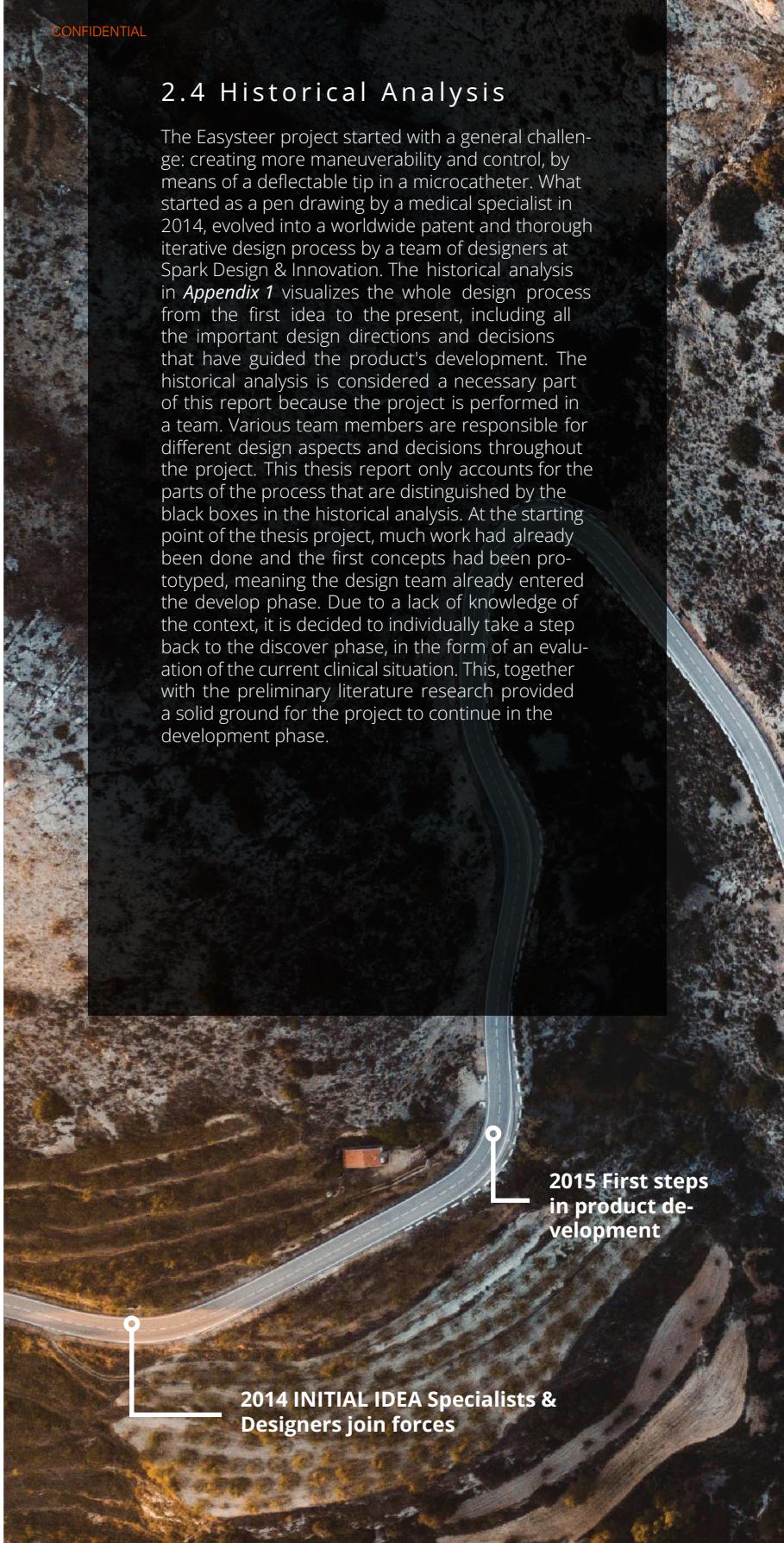
The concept is based on an asymmetric flexibility in the tip of the catheter. A mechanism in the guidewire tip can be activated to create tension in the catheter tip causing a bending motion in the direction of the least resistance. This functionality enables the user to control the activation and bending intensity of the tip deflection. A summary of the worldwide patent which was published in 2018 is visible in the blue box. The key aspects of the design that make it a worthy competitor to existing devices are:

- The mechanism does not use eccentric wires in the catheter wall, as opposed to existing steerable technologies.
- Therefore, catheters with thinner walls and smaller (outer) diameter can be made, and the amount of used material and complexity can be minimized.
- This way, the product accounts for less waste when thrown away.
- The product is based on modification of existing microcatheters which accounts for fast prototyping, fast acceptance, flexible application, and economical feasibility.
- The manufacturing costs are therefore also minimized, resulting in a lower product price.

This project's goal is to further engineer the guidewire mechanism and catheter tip into a working prototype, solving the technical challenges that are presented along the way.

2.4 Historical Analysis

The Easysteer project started with a general challenge: creating more maneuverability and control, by means of a deflectable tip in a microcatheter. What started as a pen drawing by a medical specialist in 2014, evolved into a worldwide patent and thorough iterative design process by a team of designers at Spark Design & Innovation. The historical analysis in *Appendix 1* visualizes the whole design process from the first idea to the present, including all the important design directions and decisions that have guided the product's development. The historical analysis is considered a necessary part of this report because the project is performed in a team. Various team members are responsible for different design aspects and decisions throughout the project. This thesis report only accounts for the parts of the process that are distinguished by the black boxes in the historical analysis. At the starting point of the thesis project, much work had already been done and the first concepts had been prototyped, meaning the design team already entered the develop phase. Due to a lack of knowledge of the context, it is decided to individually take a step back to the discover phase, in the form of an evaluation of the current clinical situation. This, together with the preliminary literature research provided a solid ground for the project to continue in the development phase.

2015 First steps in product development

2014 INITIAL IDEA Specialists & Designers join forces

CONFIDENTIAL

STILL A LONG ROAD AHEAD...

2020 Specialist Support:
further development,
technical & clinical testing

2019 1:1 Prototypes
& Testing

2018 Prototyping :
Scalemodels

2017 Easysteer Concept
established: USP's

2018 Patent Published by
Mencius Medical BV (Summary)
[Havik, S.M., Vrancken Peeters, M.P.F.M., (2018)]

Catheter
Multiflex technology: catheter walls have variations in
stiffness in specific areas near the catheter tip.

Guidewire
Guidewire consists of movable core guide wire inside
'mantle' (hollow coil). The core can be activated indepen-
dently to slide through the mantle. The displacement
between the two activates a bulge or bellow at the tip.

Assembly
When the bellow is deployed and is locked either at
the distal end of the catheter or inside the catheter, it
can apply axial compression, forcing the catheter to
bend in accordance with the path of least resistance. This
functionality enables our assembly to take on predictable
shapes.

Rotable part
The bendable part closest to the tip of the catheter can
rotate independently about a longitudinal axis of the
catheter with respect to the second bendable part and
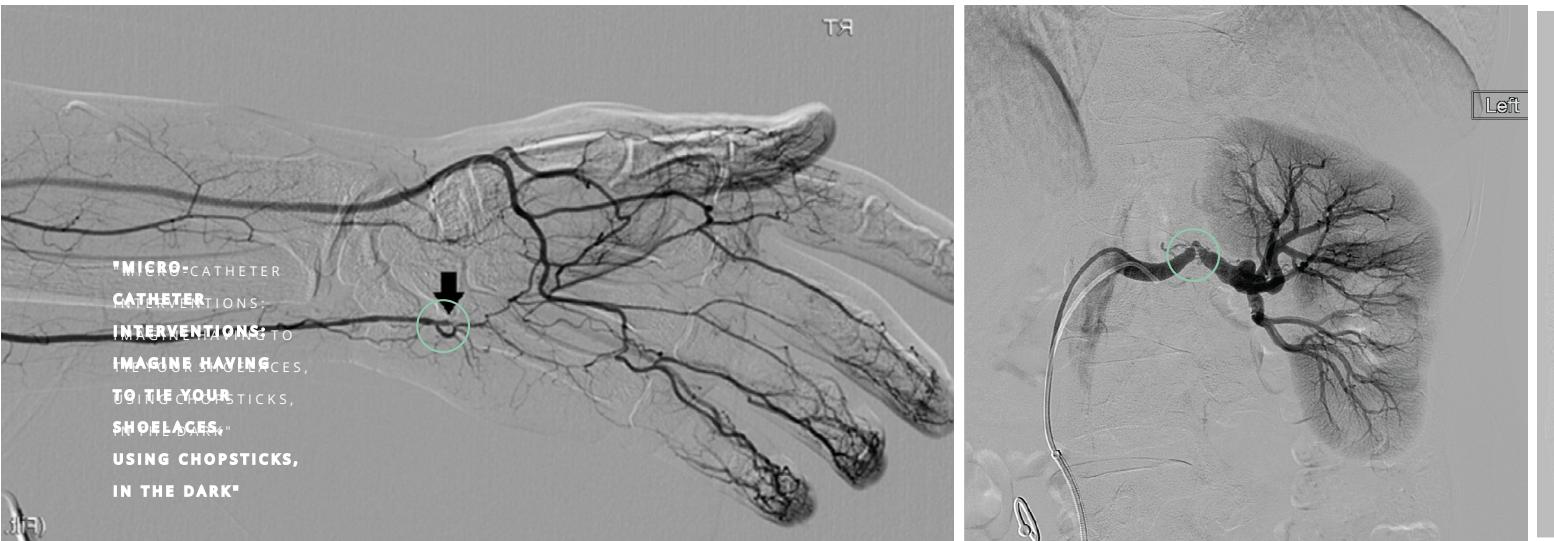the remainder of the catheter. (3D shapes)

"MICRO-CATHETER INTERVENTIONS: IMAGINE HAVING TO TIE YOUR SHOELACES, USING CHOPSTICKS, IN THE DARK"

Figure 6. Digital Substraction Angiography. A) Malformation in ulnar artery, Source: https://www.researchgate.net/publication/327378462_Firearm-related_hypothenar_hammer_syndrome_in_a_police_officer

B) Stenosis in renal (kidney) artery, Source: http://rfs.sirweb.org/ medical-student-section/introduction-to-ir/renal-artery-stenosiscase/

## 2.5 Medical Background (Literature Study)

To understand the clinical demand and scope of the problem, a preliminary literature research was conducted, in the months before this thesis project, about the various application possibilities of a steerable microcatheter. Relevant findings are summarized in this

The goal of a catheter/guidewire combination is in essence to reach certain places in the human body. When the desired location is reached, the necessary treatment can be performed, depending on the procedure. For example, the guidewire can be retracted to make place for radioactive or chemo particles to be injected through for the embolization of a tumor. For other procedures, the catheter can be retracted and a special catheter that is needed for the intervention (for example a balloon catheter) can be guided over the guidewire that is still in place. Catheter based diagnosis is done by injecting radio-opaque contrast material that is used in combination with X-ray or fluoroscopy imaging to visualize the vascular anatomy that precedes the catheter tip. This technique is called angiography. Digital subtraction angiography (DSA) is technique in which the surrounding anatomy (for example the bones) are substracted from the image, so that only the blood vessels (dark from the contrast material) become visible. This results in images that look like figure 6. These images show how malformations (Figure 6A), occlusions (Figure 6B), aneurysms (Figure 6C) or tumors (Figure 6D) are spotted, and how it can be used to map out a route while travelling towards a target area. [Perler, 2015] In figure 6B and 6D, the catheter tip is visible as a white tube.

There is a variety of diseases, most of them being diagnosed by angiography, that allow for endovascular treatment. The three main underlying factors of diseases are shown on the right. First of all, rea-

sons for hospitalization are stroke, heart failure, internal bleedings or organ dysfunction. Some of these are caused by a narrowing or occlusion of the blood vessel, or a stenosis, accounting for a large part of endovascular interventions. These can be reopened by specially designed catheters carrying an inflatable balloon or stent (balloon angioplasty, stenting). Another catheter type includes cutting blades to remove the plaque (atherectomy). Secondly, aneurysms are blood vessel malformations, or local enlargements of the blood vessel wall. The aneurysm sac, with walls that have become weak due to the stretching, has to be excluded from the bloodstream to prevent rupture. This is done by selectively placing the microcatheter head in the opening of the aneurysm and injecting coiling material through the catheter tube. The deliberate closing of a (part of a) bloodvessel is called embolization. This technique is also applied to a third and very important section of microcatheter interventions: oncology. The endovascular treatment of benign or malignant tumors is a safe and effective alternative or preliminary procedure to tumor removal. This type of intervention is especially interesting for the Easysteer project since it often requires complex and distal navigation paths towards hidden tumors: think of prostate or liver tumors. Regarding the upcoming radioembolization techniques, which is the injection of radio-active particles to irradiate a tumor from the inside, this is an interesting area of innovation.

These treatment options may sound straightforward but come with a lot of challenges and trial and error. The treatment being minimally invasive is greatly beneficial to both the patient and the specialist in terms of trauma and recovery. [Westebring-van der Putten, 2008] But no good things come without downsides. The big challenge of minimally invasive approach, as opposed to open surgery, is that the specialist does not have direct access to the diseased area anymore, minimizing haptic and visual feedback [Hu et al. 2018]. A level of expertise and craftmanship is needed in order to perform these treatments, the navigation to the target area being the most
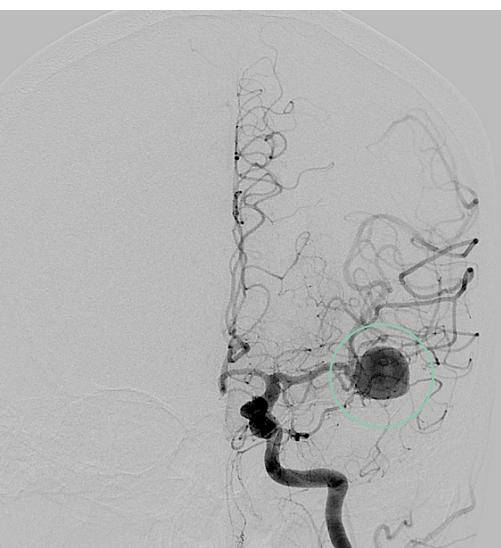
C) Brain aneurysm, Source: http://www.angio–calc. com/ed_sample_case.php
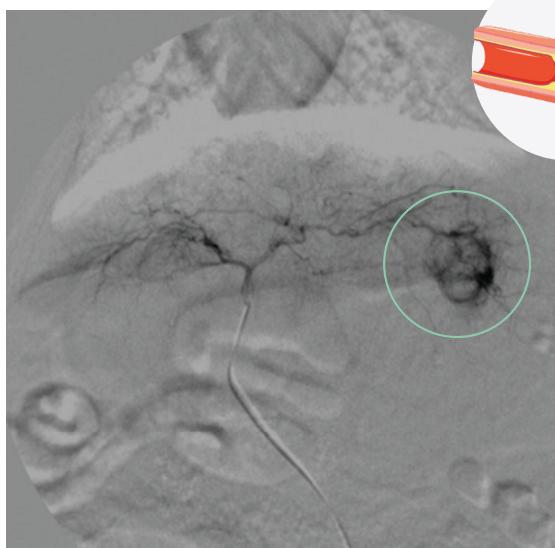
D) Tumor blush in left lobe of rabbit liver, Source: https://www.researchgate.net/figure/Hepatic–artery–digital–subtraction–angio–graphy–in–arabbit–a–Digital–subtraction_fig1_23221999

part. Small diameter, complex anatomy, sharp corners and tortuosity of vasculature [Han et al, 2012] make maneuvering towards the target area difficult. This is especially the case in cerebral arteries in the brain [Lylyk et al. 2002], coronary arteries in the heart [Shanmugam et al, 2015] and other low profile blood vessels in our organs. These problems are magnified in older patients, who are also more prone to these diseases, creating a vicious circle.

The more controllable and steerable microcatheters become, the more difficult and distal target areas can be accessed. To take steps in the design process, a strategic choice is made to choose one "killer" application, which is the specific intervention that will benefit most from a novel steerable device. When a proof of concept exists for this specialism, the product could be customized and spread out to other specialisms. With the information gathered during the literature research in mind, a field study is done to converge to the focus application and to understand the demands and wishes of the user.

Design Considerations

- A catheter is a hollow tube through which a guidwire can be advanced. This catheter/guidewire combination is crucial for some interventions to succeed.
- The catheter must be 6F (2mm) or smaller, to be considered a microcatheter, the focus of this project will be to design a microcatheter of 2.1-2.8F.
- The catheter is a Class II medical device and should obey all designated safety considerations in order to get CE certification, including sterilizability.
- The designed product must offer similar or better medical results compared to existing equipment for a specific (to be determined) intervention.
- The product must be visible with conventional imaging techniques.
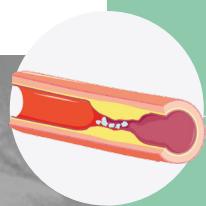
STENOSIS

Stenosis is a narrowing of the blood vessel hindering the blood supply. Atherosclerosis is a disease related to the formation of plaque in the blood vessels. This plaque consists of lipids, fibrous connective tissue and inflammatory cells, and builds up in the intima layer of a blood vessel. They can be soft to dense and calcified. The formation of such a lesion goes slowly, but it becomes life-threatening when it obstructs certain blood flows, which leads to a myocardial infarction, stroke or limb ischemia.

ANEURYSM

Aneurysms occur when blood vessels stretch over time.The blood vessel wall deforms and becomes weak, and prone to rupture. By closing (and, if needed, bypassing) aneurysms, internal bleedings can be prevented.

TUMOR

Tumors are malignant (cancerous) or benign (non-cancerous) accumulations of cells. Tumor supplying arteries can be blocked by embolization. Radioembolization is a procedure that combines embolization and radiation, killing the tumor from inside.

03 User/Context

3.1 Specialists interviews

With the importance of user-centered design in biomedical enginee-ring in mind (as described in chapter 1.5), in the discover phase of this project, interviews and an initial clinical evaluation have been conducted to get to know the interventional radiologist and his or her preferences for equipment. Based on a selection of presu-med applications, five interventional radiologists with different areas of interest invited to participate in the project. Furthermore, one pulmonologist is involved to explore one non-vascular application. Multiple interviews were conducted during different phases of the project, each time guiding the design of the Easysteer more in the right direction. This was done to pinpoint the optimal functionality, meeting the user's demands and wishes as much as possible. The first interviews were done at the beginning of the project to get an idea of the general opinion of the user, the context and the current products on the market. To substantiate the choice of the "killer" application, the oncology, cardiology, neurology and pulmonary areas were explored. Clinicians were interviewed with the followng speci-alisms: lung, neuro, cardio, and tumor treatment. Tumor treatment interventions are often done by general interventional radiologists who also perform other (often abdominal) procedures. The con-clusions per area are summarized below. From this knowledge, the first product specifications can be established.

ONCOLOGY

For this purpose, it is important that the catheterization is done as selective as possible. This is mainly because the blood vessels surrounding, but not supplying the tumor, should be excluded from embolization treatment, to keep as much healthy parts alive as possi-ble. With the current equipment, reaching distal tumors is a challenge. Dr. M. estimates around 100-150 really challenging radioemboliza-tions per year in the Erasmus MC, of which he performs a large percentage. Dr. vd. V. from the Franciscus Gasthuis & Vlietland, is amongst other procedures specialized in the treatment of Benign Prostate Hypertrophy (PBH), which he considers a procedure that often suffers from a lack of controllability and steerability of the used equipment. It is an intervention in which the catheter is guided from the iliac artery to the prostate arteries, to treat an enlarged prostate. This is done by injecting embolization particles in the prostate supplying arteries. This will stop the blood flow to the prostate which will cause it to shrink again. Along the route to the

present sharp angled turns. Smaller blood vessels branch off with 90 degree turns that are often hard to catheterize with conventional catheters. Currently, he manages to get in every desired location with conventional devices, but it sometimes is extremely time-consuming and frustrating due to the limited range of motion. Fibroids in the uterus are also part of his specialism, but he mentions that they are generally easier to reach through larger blood vessel diameters. Dr. P., an experienced interventional radiologist with generally the same expertise, shares this opinion. When comparing cardio, neuro and oncology interventions, he considers tumor embolization inter-ventions to be the most challenging in the field of navigation. In his experience, reaching distal tumors can be a very challenging task, sometimes even resulting in a failed procedure, which is less the case for PCI (cardio) or AVM (neuro). To illustrate, he explains the route a catheter has to follow before reaching a liver tumor (see figure 7). Up until the point where the hepatica communis (liver artery) splits up in the left and right liver arteries, the intervention is doable with a conventional catheter. After this point, the navigation becomes tricky. In these situations, it is chosen to use pre-shaped guidewires or shapeable guidewires. The latter is often done with much trial and error, and this would be an aspect he would love to
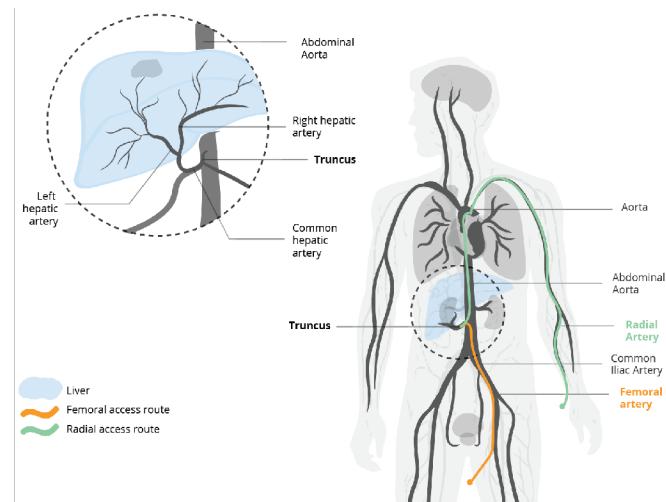

Figure 7: Route from radial access point to liver tumor: Aorta – abdominal aorta – truncus – common hepatic artery – left & right hepatic artery – further branching into the liver. Femoral access encounteres a slightly sharper turn at Truncus than radial.

CARDIOLOGY

In this field of specialization, the application of a steerable microcatheter would mainly involve PCI (Percutaneous Coronary Intervention), because of the tortuosity of coronary arteries (on the heart). Another interesting field to mention is child cardiology. According to Dr. M., in this specialism the SwiftNINJA™ is sometimes used to navigate through a child's fragile coronary arteries. Structural heart interventions are not really a microcatheter application. It involves difficult tasks inside the heart but those challenges are not often related to navigating through small and angled blood vessels.

PULMONOLOGY

Bronchoscopes are used for imaging during a lung intervention, and the smallest available are 2.8mm in diameter. According to Dr. C., taking biopsies in the distal bronchi presents some challenges: current bronchoscopes can reach the lobar bronchi easily, but the periphery of the lungs is difficult to reach from the inside. They are therefore often reached by puncturing from the outside. This technique gives a lot of complications (over 30% ends up with a pneumothorax, a collapsed lung). If innovation would be focused on enabling access to the tumor through the bronchi, this would be a suitable application. However, Dr. C. explains that the limitations of imaging techniques used during lung interventions are a larger obstacle than the complexity of the lung anatomy. In an endovascular intervention, the route is visible with angiography, but the challenges are presented by complex anatomy. In the lungs, this is the other way around: the curves are difficult to identify in the first place (very minimal in the pre-operative CT). In his experience, bifurcations of the bronchi re never sharper than 90 degrees. In the future, the Easysteer could be combined with a bronchoscope, but for now lung interventions are not a logical application to focus on.

NEUROLOGY

In the neurointerventional radiology, a demand for more steerability of devices is certainly there, according to Dr. vd. S. She works in the UMC Utrecht and her day-to-day operations are mainly treating acute strokes, aneurysm coiling, AVM embolizations (malformation of artery and vein) and cerebral or spinal dural fistulas (abnormal connections between an artery and a vein). Sometimes she also treats brain-tumors with radio-embolization. The brain-tissue is very fragile, and although the route to the brain is not very long, it is fraught with many complex turns. Interventions to the brain are high risk procedures, as even small damage to the brain can be fatal. Dr. vd. S. does not use steerable instruments, but she explains that there are certainly interventions that would benefit from a steerable device. For example, coiling of aneurysms of the brain often requires steerability. Furthermore, it would be a useful addition to treatment of AVM's, but they require an even larger amount of flexibility and small diameter than for coiling interventions. Dr. vd. S. emphasizes that for distal embolizations, the device would also require a lot of flexibility, because often multiple turns have to be made. Unfortunately, current steerable solutions are not yet available in small enough sizes. Neurointervention would be an interesting application if the design of the Easysteer could be downsized to these dimensions (±1.7F).

DEVICE SPECIFICATIONS

After presenting the initial concept of the Easysteer, each specialist was asked which design considerations would be most important for a new device in their practice. About the working mechanism, the following remarks were made: according to Dr. M., a novel product should focus on getting the farthest tip of the catheter steerable, in preferably varying bending radii. The mechanism should therefore be placed at the distal end of the catheter tip for optimal functioning. The mechanism itself should also be of minimal length, as it will be a straight addition to the deflected tip. The catheter should be at least 110cm long, according to Dr. P., but preferably longer for distal tumor embolizations. It is also desirable that the guidewire can be retracted advanced individually, because this is a technique that most specialists are used to during navigation.

In terms of safety, the interviewed specialists advised the following: chemoembolization involves particles that can be 7-800μm, however the ones that are most frequently used are 30μm or larger. Furthermore, the tip of the catheter should be atraumatic in all cases. When the mechanism sticks out in front of the catheter, attention should be paid to avoiding sharp elements or opening & closing elements. Some of the interviewed specialists agree that stiffness in the device is sometimes needed to push a catheter through tortuous blood vessels, however, it is emphasized that the tip should not be too stiff. This could cause trauma to the vasculature, for example when a curved tip relaxes and penetrates the blood vessel wall.

Finally, insights were gathered about what existing catheter the Easysteer design should be inspired on. Every specialist is asked what type and size catheter they often work with. Three of them mentioned the Progreat™ as a "workhorse" for (non-neuro) interventional radiology procedures. This catheter is flexible, but also has an integrated Tungsten coil to add stability and torqueability. Dr. vd. S., the neurosurgeon, uses 1.7F microcatheters. According to Dr. M., a size of 2.1/2.4F is a good starting point to focus on for the prototypes. For a novel catheter with a larger diameter, there would be less demand, because these ones are simpler, cheaper and less in need for steerability. Boston Scientific's Renegade™, which is identical to the Terumo Progreat™, is Dr. P.'s favorite microcatheter to operate

CONCLUSION

The information gathered from the interviews and the general opinion from specialists is extremely valuable for the design of the Easysteer. In the next section, the design directions concluded from the interviews will be confirmed by observations in the operating room. It is chosen to not focus on neuro interventions as they require smaller tools than the Easysteer is intended to be. Cardio-interventions are also left out of the focus area, because according to the interviewed specialists, PCI would not be the intervention that needs steerability the most, because the route to the heart is relatively short and without many navigation challenges. As discussed, for lung interventions, steerability is not considered the main focus area for innovation. Therefore, this specialism is also left out of the field research. All other catheter-based interventions, including stenosis, aneurysm and tumor treatments are investigated in the

Neuro

Cardio

Lung

Tumor

General

USER

THE INTERVENTIONAL
RADIOLOGIST

3.2 Observations in the Operating theatre

Six interventions were attended in the field of general interventional radiology, including tumor treatment. The goal of this research is to understand the context, current working methods, and challenges of different interventions. During each intervention, attention was paid to:

· The steps of the procedure and their duration
· Specific difficulties that were encountered
· The specialist's considerations and choices
· The handling of the tools by interventionalist & assistants
· The tools used

GENERAL PROCEDURE

1. Before the intervention starts, the operating table is prepared by the assistants. The operating theatre set up looks like figure 8. Preoperative scans have been made for the interventionalist to assess what needs to be done. This is when the choice is made between radial or femoral access, based on the intervention and preference of the interventionalist.
2. Everybody in the operating room wears lead aprons for radiation protection, and a face mask. Two assistants are present to prepare, hand over, clean and put away the instruments. The patient is awake, to enable asking the patient to hold his breath during imaging, or to indicate when he feels pain. The time-out procedure (TOP) is done, which is an indicator for the inspection (IGJ) for quality measurement: the team discussed the procedure with the patient, makes sure the patient is aware of potential risks, and the equipment is checked.
3. Local anesthesia is applied to the access area, and heparin is injected to dilute the blood and slow down the blood flow. Ultrasound helps the interventionalist locate the optimal penetration spot, after which the Seldinger technique [Seldinger, 1953] is used to penetrate into the access artery: a hollow needle punctures the skin through which a guidewire can be inserted. Then a sheath (a valved short tube) is placed to maintain vascular access through that access point during the procedure.

4. The guidewire is advanced first, and can be observed with imaging techniques while traveling to the target. A first catheter is guided over the wire and used for injecting contrast fluid to map out the working space for the interventional radiologist. This is done by a diagnostic (or "angiographic") catheter. Generally, a subtraction technique is applied: while injecting contrast, a new fluoroscopy is subtracted from the previous image which makes it possible to only visualize the difference between the two images. This results in a gray image with only the contrast-filled arteries visible. This image is translated to a negative image representing a roadmap that is used as an overlay on the real-time imaging in which the catheter moves. The images are controlled by the interventionalists feet and by joysticks on the operating table, and are watched closely during advancement of instruments. **5.** Now, various types of catheters, therapeutic ones, can be inserted over the wire, their function and design depending on the intervention. The instruments are manipulated with one hand at the access location, and the other hand holds a syringe or other equipment that is needed for the intervention. Sometimes it is necessary to exchange catheters multiple times during an intervention, diagnostic for therapeutic catheters, between different tip shapes, or conventional for steerable ones.
6. Whenever needed, the interventionalist can make a 3D image with contrast to check the current status of the intervention, for example whether all the targeted arteries are embolized. This enables him to assess whether the intervention is successful or more actions are required. While this image is made, everybody steps out of the operating room to the control room, from which the operating room is still visible through a large window. To create a still image without artifacts, the patient is asked to hold his breath for a few seconds.
7. When the intended goal of the operation is accomplished (for example: when there is no longer blood flow visible inside a tumor or aneurysm, or blood flow of stenotic arteries is restored), the instruments are retracted and the access point is closed. This is sometimes done with an Angioseal, an instrument helping with keeping hemostasis during closure. After a short evaluation, the patient is transferred to a recovery room, and the OR is cleaned, including the disposal of all instruments used.

Additional remarks of the user concerned the vulnerability of the tools used: instruments and guidewires are prepared and put away by the assistants, and are available for reuse during the remains of the operation. Used catheters and guidewires are loosely rolled up and put down gently, but fast. During this action, kinking of the instruments might be an issue when not done with care.
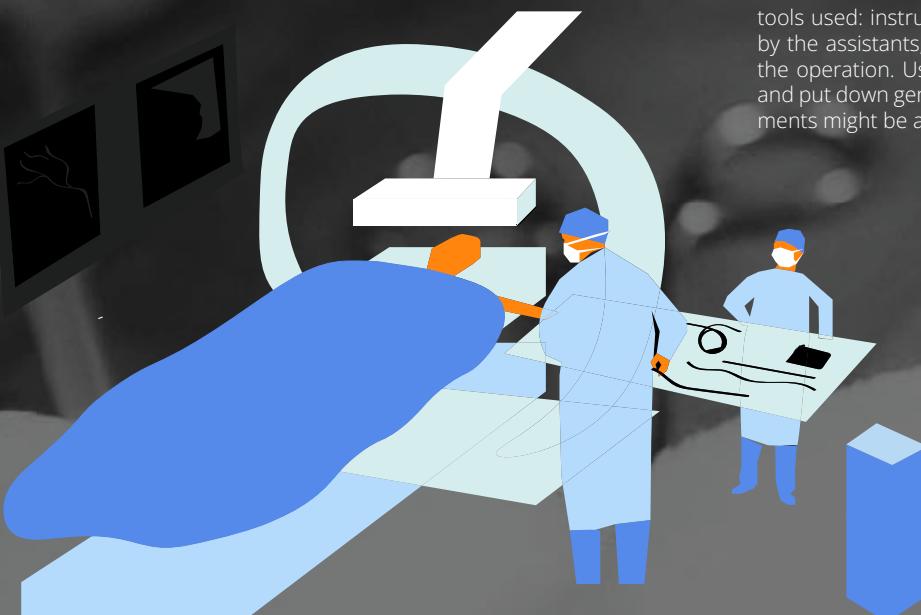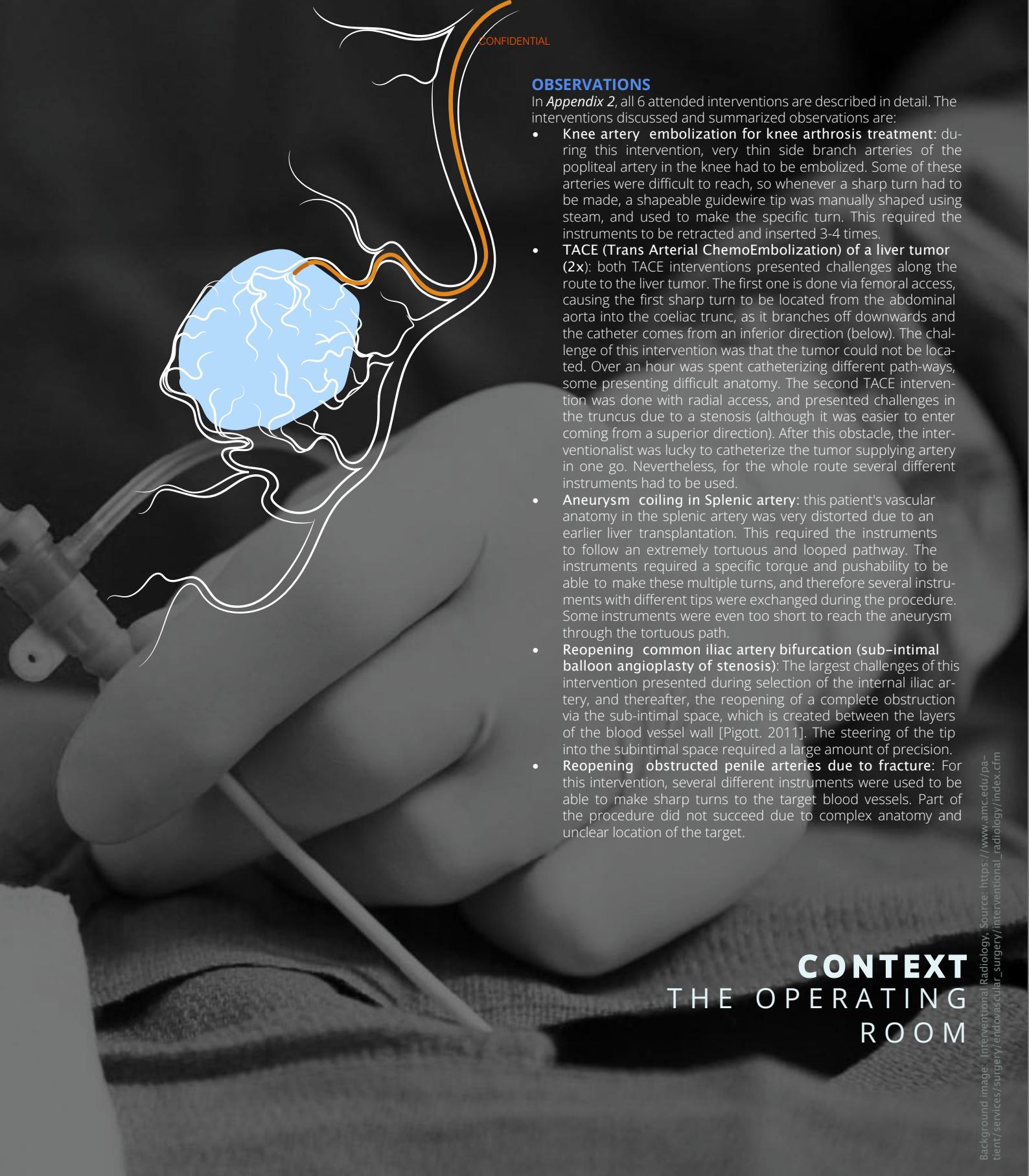

Figure 8: Operating room setup for radial access intervention, based on observations

OBSERVATIONS

In *Appendix 2*, all 6 attended interventions are described in detail. The interventions discussed and summarized observations are:

- **Knee artery embolization for knee arthrosis treatment**: during this intervention, very thin side branch arteries of the popliteal artery in the knee had to be embolized. Some of these arteries were difficult to reach, so whenever a sharp turn had to be made, a shapeable guidewire tip was manually shaped using steam, and used to make the specific turn. This required the instruments to be retracted and inserted 3-4 times.

- **TACE (Trans Arterial ChemoEmbolization) of a liver tumor (2x)**: both TACE interventions presented challenges along the route to the liver tumor. The first one is done via femoral access, causing the first sharp turn to be located from the abdominal aorta into the coeliac trunc, as it branches off downwards and the catheter comes from an inferior direction (below). The challenge of this intervention was that the tumor could not be located. Over an hour was spent catheterizing different path-ways, some presenting difficult anatomy. The second TACE intervention was done with radial access, and presented challenges in the truncus due to a stenosis (although it was easier to enter coming from a superior direction). After this obstacle, the interventionalist was lucky to catheterize the tumor supplying artery in one go. Nevertheless, for the whole route several different instruments had to be used.

- **Aneurysm coiling in Splenic artery**: this patient's vascular anatomy in the splenic artery was very distorted due to an earlier liver transplantation. This required the instruments to follow an extremely tortuous and looped pathway. The instruments required a specific torque and pushability to be able to make these multiple turns, and therefore several instruments with different tips were exchanged during the procedure. Some instruments were even too short to reach the aneurysm through the tortuous path.

- **Reopening common iliac artery bifurcation (sub-intimal balloon angioplasty of stenosis)**: The largest challenges of this intervention presented during selection of the internal iliac artery, and thereafter, the reopening of a complete obstruction via the sub-intimal space, which is created between the layers of the blood vessel wall [Pigott. 2011]. The steering of the tip into the subintimal space required a large amount of precision.

- **Reopening obstructed penile arteries due to fracture**: For this intervention, several different instruments were used to be able to make sharp turns to the target blood vessels. Part of the procedure did not succeed due to complex anatomy and unclear location of the target.

CONTEXT
THE OPERATING
ROOM

PROBLEM DEFINITION

The observed interventions were challenged by different factors. First, pre-operative planning is limited. Before the operation, CT scans are evaluated to make expectations about the patient's anatomy and the steps of the intervention. However, many unexpected difficulties are encountered in every intervention. Innovation based on improving phantom models of patient specific anatomy would avoid these surprises. Second, the intervention is limited by currently available imaging techniques: 2D images often do not clearly depict the vascular pathway, and 3D images still contain many artifacts. Innovations like Philips' FORS (Fiber Optic RealShape) technology (including real-time 3D imaging of the anatomy and the devices used) would increase efficiency of the intervention. Apart from these two fields of innovation, this project is only focused on limitations of the instruments. *The most prominent limitations of conventional instruments are: limited range of motion in general, and limited control of the tip.* Difficulties during interventions are caused by anatomical variations, sharp bifurcations, tortuous arteries, and repositioning of catheter during embolization. A pre-bent tip can only be moved by axial twisting: movement in multiple planes is not possible. To change the deflection angle, the instruments have to be reshaped, asking for frequent retraction and insertion of instruments. This is the main aspect that can be minimalized by using a device with an articulating tip. Other limitations have to do with device intuitiveness (haptic feedback), stiffness and torqueability.

CONCLUSION

It difficult to pinpoint the intervention that is most often affected by navigation problems. Complexity of vascular anatomy varies per patient, and is not related to the anatomical location. However, it becomes clear from the observations that tumor embolizations are a suitable focus area that is within the scope of the Easysteer project, due to distal tumor locations and the importance of selective artery catheterization.

According to the specialists consulted, steerability in the most distal tip of the catheter would be the most valuable functionality compared to conventional instruments. It will avoid having to exchange instruments for every navigational challenge, which increased the operation time of all the observed interventions. According to Dr. M., difficult bifurcations can be up to 120 degrees. The bending radius is difficult to generalize, but 0.5 is a realistic starting point. In order to be able to start the Develop phase, these insights are translated into design requirements for the Easysteer steerable microcatheter. Steerability is chosen as the main design direction, ideally accomplished with a simple mechanism that permits downscaling, while maintaining general catheter requirements including stiffness, torqueability and lubricity.

Design Considerations

- The functionality of the Easysteer must focus only on the navigation towards the target.
- The required bending radius is to be determined (0.5mm as starting point).
- A starting point of the catheter tip size is 2.1F/ 2.4 F. It should be taken into account that catheter diameter often influences stiffness.
- The catheter must be at least 110 long, preferably longer for reaching the most distal tumors.
- The guidewire is preferred to be individually advanceable.
- Existing instruments (microcatheters and guidewires) should be used for the prototypes. This way, many functionality requirements of the catheter in terms of flexibility of the tip (needed for making turns), and stiffness of the rest of the catheter (for pushability) can be accomplished, while avoiding a large part of the CE certification process.

The following design considerations eliminate some specifications of the established patent:
- Steerability must be focused in the most distal tip of the catheter (last 15mm as starting point). Therefore, multiple expansion of the bellow in different locations in the tip might not be necessary because only the most distal deflection is demanded by the user, and no special shaped deflections (S-shape) are necessary. This means that the mechanism can be placed at the end.
- Steerability in two directions is not necessary. Specialists have suggested the preference to torque the catheter in order to make curves in other directions. The rotatable parts (independently rotating the tip axially to create 3D shapes) are therefore left out of the design focus.

3.3 Product requirements

As discussed, there are general catheter requirements that should be preserved. These are pictured in the blue box on the right. All design considerations that conclude the previous chapters are combined and summarized in the following list of requirements for the Easysteer.

FUNCTIONALITY / USE

1. The instrument must not significantly change the original workflow of the intervention, which means that no special preparation or more than one extra action is needed for use. Two actions that can be performed: 1) activating the locking mechanism, and 2) control the deflection.
2. The instrument is compatible with existing (conventional) instruments and can be exchanged with other guidewires & catheters
3. The deflection of the catheter tip is controllable by one operator, via a proximal handheld control device.
4. The control device is intuitive and learning to use the device must take less than 10 minutes.

5. The distal tip (max. 20mm) of the catheter must be able to deflect in at least one degree of freedom. The precise required curve can be investigated in further research as it strongly depends on the application of the device. It should at least deflect 120 degrees.
6. The guidewire must be independently advanceable or removable from the catheter: this enables the user to insert other guidewires or embolization particles/coils. Various guidewires must be removed or inserted in the control device in one quick movement (under 3 seconds)
7. The tip of the catheter is visible/radiopaque on MR images without creating artifacts. This means that the radiopaque marker (that all catheters have) should be unaffected by the catheter modification.
8. Actuation of the mechanism does not cost more than 10N force of the user's hand.
9. The force of the catheter on to the vessel wall must be less than 5N.
10. The deflection of the turn must happen within 1 second after proximal actuation.

DESIGN
1. The dimensions of the catheter tip must be between 2.1 and 2.8F
2. The design must include a catheter and guidewire
3. The mechanism that activates deflection must not add more than 2mm to the end of the catheter tip, otherwise this would add as a straight part to the deflected tip and this way limit the sharpness of the curve made.
4. Manufacturing of the catheter must include the adaptation of an existing microcatheter
5. Manufacturing of the mechanism must allow for series production with general machining or laser machining, and allow for production with a maximum of 1% tolerance

SAFETY
1. In the application of chemoembolization, particles of >30µm must not pass the catheter wall. The particles must also not be obstructed by a steering mechanism in the tip. Other injectibles such as coils must only come out of the distal orifice of the catheter.
2. Tip must be atraumatic in all cases (in terms of stiffness and sharp corners) This means that the mechanism must either flush well with the catheter, or not stick out, or contain sharp edges.
3. The instrument can be safely operated in MRI environment (material: polymer, non-magnetic metals).
4. The material used needs to be chemical resistant (especially medicine and cancer treatment chemicals)
5. The material used needs to be heat resistant (for sterilization)
6. No parts must come loose from the product during use.
7. Stiffness of the device must not be higher than stiffness of conventional microcatheters (Boston Scientific Direxion 2.4F as benchmark catheter) that are not support catheters.

Costs and manufacturing requirements are not yet established as this is not required for the scope and design phase of this project.


Flexibility of the catheter is an important feature allowing the device to follow small and multiple turns in the vascular anatomy. It also contributes to avoiding trauma to the vessel walls.
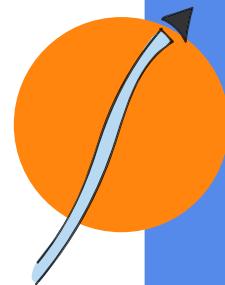
Pushability is the ability to push the catheter through small or lightly obstructed pathways. It is correlated with the stiffness of the material. The right combination of pushability and flexibility has to be realized, but is difficult to quantify.
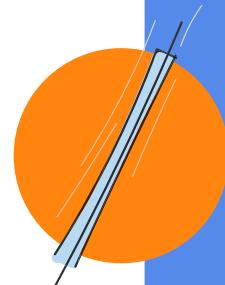
Trackability of the catheter means the ability to follow blood vessels without too much friction, but also applies to the way other devices or the guidewire slide over each other. This has to do with friction, lubricity andhydrophobic coatings.
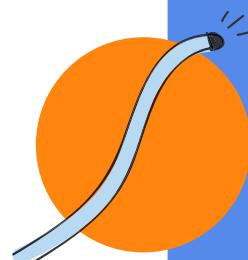
Atraumatic means that the tip is free of sharp edges, opening and closing elements, stiff materials, and other properties that might cause damage to the blood vessel it is advanced through.

Embolization is a function of the catheter that must be preserved, and asks for a catheter lumen through which embolization particles or coils can be injected. The only way out of the catheter is through the tip, to avoid untargeted embolization.

04 Concept

The list of design requirements, concluded from the initial clinical validation mark the end of the converging Define phase. Together with the already established patent, they can be reformulated into a threefold specific design challenge:
- Apply material strength variations in catheter wall
- Realize expandable guidewire mechanism on 2.4F scale
- Bring functionalities together in a single-handed intuitive control device

This challenge is the starting point of the "Develop" phase in which design methods will be applied to create a concept meeting all the requirements. This conceptualization starts with the basic idea, consisting of three parts, logically:
- The Catheter, of which the tip is modified asymmetrically to enable a pre-defined tip deflection.
- The Bellow, which is an expandable mechanism at the tip of the guidewire.
- Control device, providing intuitive control of the mechanism and device functionality.

In this project, the three components of the concept are each developed individually and are put together for the last prototype. The three design processes are parallel, but are also dependent on each other. The progress of each component is visible in figure 9. The solid colors represent to what extent the component is worked out by the designers at Spark, of which the results will be shortly addressed in this thesis. The faded colors represent what parts of the design process of each component will be part of this thesis and discussed elaborately. For example, when the thesis project started, a few first prototypes were made for the catheter. This thesis takes the design process from there and development of novel catheter designs and prototypes is discussed in this report. In the following sections, the design process of each of the components is discussed separately.
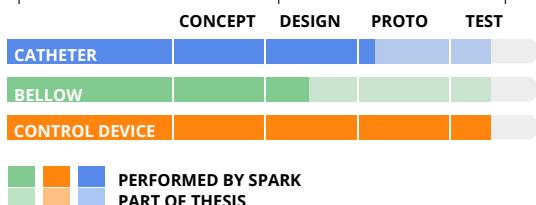
Figure 9: Progress of each component of the design

4.1 Catheter: conceptualization

The technical challenge of the catheter component to achieve the functionality of the device, is:
- *How can the catheter tip be modified, in order to achieve asymmetric material strength?*
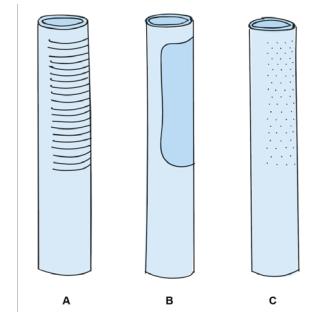
Figure 10: Different ways to achieve asymmetric material properties in the cahteter tip. A) Grooves, B) Combine two materials, C) Micro–holes

The concepts in figure 10 are evaluated on their feasibility, using expert opinion from a material machining company to which the modification will be outsourced. Applying a strength backbone to the tip will make the tip stiffer than the original catheter, and this is not allowed according to Safety requirement no. 7. Applying a variation in material properties requires secure attachment of the two materials to each other which is not feasible. The risk of the materials to detach from each other is too high. The application of micro-holes or grooves in the material of the catheter tip is feasible with micro-lasering, and therefore explored as main solution. Attention must be paid to the size of the grooves or holes so that no embolization particles can pass. The groove modification is decided to be the most promising modification to realize the deflection, because it allows for straight-forward reasoning of the amount and size of the grooves.

4.2 Catheter: Design details

In order for the microcatheter to make a curve, the catheter wall needs to be modified on one side. The microcatheter contains some
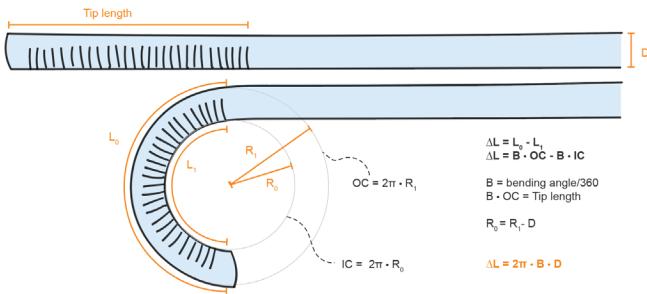
Figure 11: Derivation of the formula for required material reduction (ΔL), expressed in relation to B (bending angle/360) and D (catheter diameter)

flexibility which enables making curves, however, for the function of the concept, the curve needs to be concentrated at the tip and onedirectional. Therefore, material is removed from one side of the catheter tip in the form of grooves. Laser cutting is the only method to achieve this modification on such small scale.

Factors that contribute to the behavior of the modified tip, are:
- The amount of removed material and size of the grooves: this depends on the type of curve that is desired. The larger the (amount of) grooves, the sharper the deflection (small bending radius). Assumed that the catheter material is incompressible, the required material reduction is related to the bending angle and the catheter diameter according to the formula in figure 11. According to this calculation, the optimal groove designs can be made for each catheter.
- The material properties, which are fixed. These contribute to the amount of flexibility that the catheter has without modification, and the force that is needed for deflection.
- The depth of the grooves, which can be optimized. The deeper the grooves, the less force is needed for the desired deflection. This is because in general, when bending a tube, there are internal compression and tension forces [Karthikeyan et al., 2019] (visible in Figure 12, top), that try to resist the bending motion. To minimize these forces, the grooves should be at least as deep as the neutral axis (figure 12, bottom). The material removed from one side of the catheter reduces compression forces, since the grooves provide extra space in the compressed material.

The influence of the depth of the grooves can also be explained with the moment of inertia theory. Similar to mass influencing an force needed for a certain acceleration, the moment of inertia (I) accounts for the torque needed for a specific angular acceleration about a rotational axis, according to: Moment (vector) = I * angular acceleration (vector) . If the grooves are generalized as a weak section in the catheter tip, the rest of the catheter tip can be seen as a half cylindrical tube. Just like celery, this C-profile has a large moment of inertia, increasing the forces needed to bend the profile. The moment of inertia will decrease when the grooves become deeper, because the profile will start to look like a straight profile rather than a C-profile (See figure 13) causing the geometry to be easier to bend.

4.3 Bellow: conceptualization

The tension in the catheter tip responsible for its deflection, is transmitted from the guidewire tip on to the catheter wall. This can be done by pulling a bellow component at the end of the guidewire that is larger in diameter than the inner lumen of the catheter. The tension pulls the catheter tip in the direction of the least resistance (the grooves). Functionality requirement 6, which concerns the retraction of the guidewire out of the catheter during use, demands the bellow to also have an inactivated state, in which it can be freely moved through the catheter (requiring shrinking of the bellow). Therefore, the following technical challenge is presented:

- *How can a geometry at the tip of the guidewire be activated/deactivated, making it increase and decrease in diameter?*

A brainstorm has been carried out to develop 6 mechanical concepts (figure 14) that can expand as result to a simple movement that is applied via (part of) the guidewire. More elaboration on the development of these concepts can be found in *Appendix 5.*

Concepts A, C, D, E, and F in Figure 14 are all based on a concentric movement of a guidewire and a hollow wire that is placed around it. Concept G is based on a torque
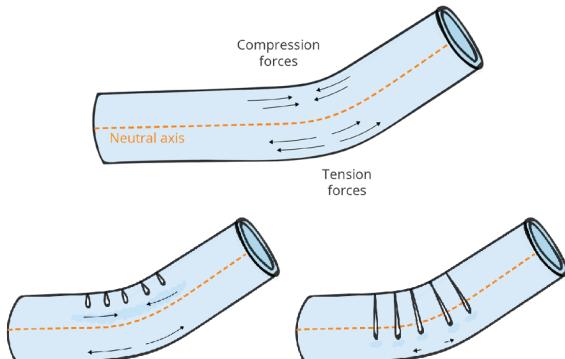

Figure 12: Internal tension and compression forces as a result of bending a tube (top), difference between small grooves (bottom left) and deep grooves (bottom right). Deeper grooves decrease internal compression and tension forces.
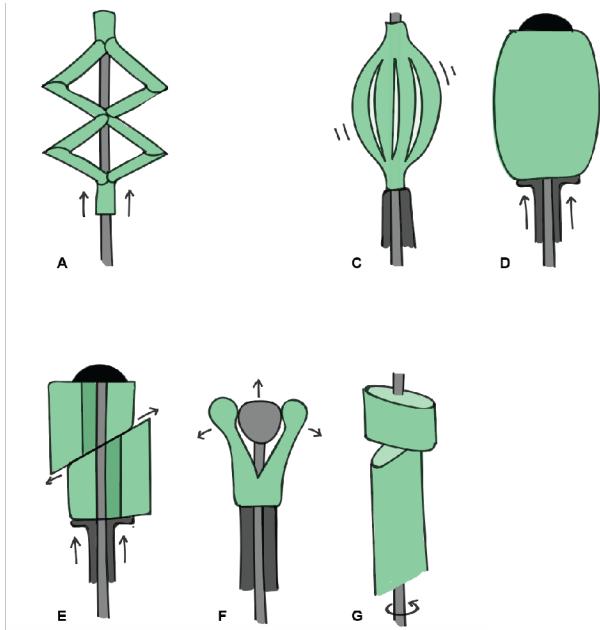
Figure 14: Bellow concepts. A) Hinge, C) Spider, D) Expansion, E) Wedges, F) Thicknut, G) Turning lock

movement of the guidewire, and for this an additional modification of the catheter tip is required to be able to lock the turning mechanism in front of the catheter tip. All concepts could theoretically be made out of metals or soft/hard polymers. The intended material for concept D has to be soft/deformable in order for it to work. Concept C and F also require some deformation but this could also be realized with harder polymers or even metals.
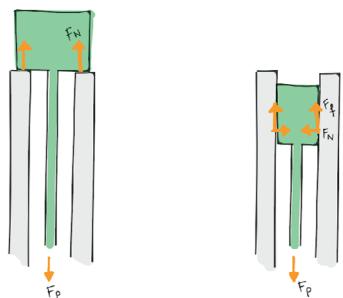

Figure 15: Bellow front of (left) VS inside the catheter (right)

There are two ways in which the developed guidewire concepts can interact with the catheter tip.
  · When the mechanism is activated **inside** the distal end of the catheter tip, the tension in the tip fully depends on the friction between the expanded bellow and the inside of the catheter. The friction must be high enough to prevent the expanded bellow to move inside the catheter. This is visualized in figure 15, where $Ff = \mu * Fn$, in which μ is the friction coefficient. Using this technique, all parts of the mechanism are kept inside the catheter wall, which is advantageous for the atraumaticity of the catheter. It also allows the bellow to

be expanded in different locations of the tip, enabling varying tip shapes.
  · When the bellow is expanded **in front of** the distal end of the catheter tip, and energy is stored due to stressing the object, which causes a firm expansion. When pulled back, tension is created by direct forces of the pre-stressed bellow on the catheter wall in opposite direction to the pull force. It depends on the geometry of the expanded bellow, rather than only on friction between bellow and catheter. The pulling force will now be counteracted by a normal force from the catheter on the bellow (Fn in figure 15, left). In this case, extra attention has to be paid to making the bellow atraumatic, as it sticks out of the catheter. Also, it must be made sure that the bellow does not expand much more than the outer diameter of the catheter,

A result of the specialist interviews (3.1) was that the functionality of expanding the bellow in different locations in the catheter tip is not desired. Therefore, it is chosen to develop a bellow that can be expanded in front of the catheter. This technique also gives more confidence and technical feasibility for the working mechanism as it is not solely dependent on the friction coefficient (which is often intentionaly low on the inside of catheters). The most important design requirements that are relevant for the design of the bellow are listed below:

• **Atraumatic**: since the mechanism sticks out in front of the catheter, it is of high importance that the shape does not include sharp edges or opening/closing elements that can cause harm to the vasculature.
• **Trackability**: The shape and material of the bellow in relaxed state must not interact with any friction with the catheter wall for an as smooth as possible guidewire advancement.
• **Producibility**: The extreme small scale of the device limits the design to a large extent. Springs, hinges, complex constructions are all not viable for manufacturing on this scale. Therefore, the mechanism needs to follow the motto; and production techniques must be generally thought through.
• **Deformation control**: The control of movements and forces is transferred over a distance (between the operator and the mechanism) and must therefore not require too specific or complex movements.

FIGHT COMPLEXITY WITH SIMPLICITY

• **Dimensions**: The mechanism needs to be as short as possible to allow a sharp turn.
• **Deactivation**: Deactivation of the bellow must be possible with a simple movement, but preferably happens automatically when tension is relieved from the mechanism.

In order to choose the most viable bellow design, a Harris Profile is established (figure 16). This is a concept comparison method in which the related requirements are listed based on their priority, and each concept is scored a -2, -1, +1 or +2 for that specific property. The concepts that score highest on all of the requirements is concept D. Concept D relies on

	CONCEPT A	CONCEPT C	CONCEPT D	CONCEPT E	CONCEPT F	CONCEPT G
Atraumatic	▨	▨	▧	▨	▧	▧
Trackability	▨	▧		▨	▧	▨
Producibility	▨	▨	▧	▧		▧
Deformation control	▧	▧	▨		▨	▨
Dimensions			▧	▨		▧
Deactivation	▧	▧		▨	▨	▨

Figure 16: Harris profile evaluating different Bellow concepts on the design requirements

the flexibility and elasticity of the material the bellow is made of, and expansion is accomplished through axial compression. Therefore, concept D has been chosen as most promising concept that is producible, very atraumatic, and uses its own elasticity to deactivate. Based on the established requirements and the envisioned functionality of the product, the elastic bellow (concept D) is considered feasible, however, a lot of quesitons arise about the suitable material properties to achieve the functionality: will it be possible to find an elastic material that expands enough and can also hold all the applied forces without breaking? How can this optimal material be prototyped into a 0.55 mm bellow? These questions will be evaluated thoroughly with a mechanical and computational analysis, in the next section.

4.4 Bellow: design details

The catheter modification is quite simple as it can be applied to existing catheters and tested with a static bellow (for example a drop of glue at the end of a guidewire). The bellow concept is however more complex to prototype and test due to the small dimensions (Outer diameter of 0.55mm based on the geometry of a Boston Scientific Direxion™ 2.8F microcatheter) and specific assembly requirements. It is valuable to theoretically prove the material choice and intended functionality beforehand. Therefore, a technical analysis is done, in which the concept is thoroughly evaluated based on the displacements acting on the bellow in the context of use and resulting material's behavior.

MATERIAL CHOICE

For the bellow, choosing the right material is of great importance because the working mechanism depends on it. Especially in these small dimensions, the bellow must be able to resist all the applied forces during use. First, a material study is done to select the most suitable material for the expandable bellow. A list of important requirements for the bellow to work properly is the starting point of this study, followed by a CES material search, hands-on rubber experience, including scale models and tensile tests with rubber samples, and an exploration of manufacturing techniques. Based on this study, PU rubber with a shore value of A60 as most suitable material, as it is elastic, castable, and expected to be not too soft and not too hard to prototype in the appropriate dimensions. Polyurethane rubbers are known to have great abrasion resistance and high tensile and tear properties. Biocompatibility, processability as well as its chemistry make polyurethane a good candidate for medical applications in general, of which one is already extruded

profiles for catheters, according to [Gent et al. 2012]. Biocompatibility, haemocompatibility, and other mechanical properties can be achieved by the proper selection of composition. The reader is referred to *Appendix 6* for an elaborate description the material study, and the other decisions that led to the choice for PU rubber. The chosen material will be the starting point for further evaluation of the theoretical proof of concept.

THEORETICAL VALIDATION

The next step is to theoretically prove the working mechanism in context of use. This will help predict the functionality and define boundary conditions for the design. Because of the non-linear behavior of the material, the technical problem can not be easily analyzed by hand. Therefore, the assembly including the bellow iis simulated using a Finite Element Analysis. This is a tool to evaluate deformation and reaction forces in a computated model, without having to prototype. In order get realistic results out of this analysis, accuracy of the material input is crucial. The material properties of the chosen material therefore first have to be identified using mechanical tests, splitting the analysis in two parts:

1. **Mechanical test**: Rubber properties strongly vary per rubber type, and depend on their composition and manufacturing process. A compression test is performed with a sample of the PU A60 rubber, a method to get the most accurate material properties. A force sensor measures the reaction forces during a constant compression of the sample. The output of this test can be translated in a stress-strain curve describing the material's elastic properties. The PU rubber is a hyper-elastic material, which means that this curve is non-linear, and can be evaluated according to a hyper-elastic material model.

2. **Computational analysis**: a Finite Element Analysis is performed. ABAQUS CAE is a powerful FEA software that allows the user to precisely define all the parameters (the geometry, displacements, forces and interaction properties) of the system. The material properties can be accurately described by the stress-strain values from the compression test. Figure 17 shows the used FEA model. First, a downward displacement is applied to only the top plate, causing a compression of the bellow. Thereafter, a downward displacement is applied to both the top and bottom plate, representing the bellow being pulled to create tension in the catheter wall. This way an accurate representation is created of the behavior of the bellow in context of use, if it were made from PU A60 rubber. The reaction force in the bottom plate is evaluated during the compression step, identifying the compression force. The reaction force in the catheter wall is

evaluated during the pull step, identifying the force that the bellow exerts on the catheter wall to create tension. For more elaborate description of both the mechanical and the computational analysis of the bellow, see *Appendix 12.* It is a scientific article describing both the compression test and the FEA in detail. It also elaborates more on the theory of the used methods, and on the study's assumptions, choices, discussion points and limitations.

RESULTS

The conclusion of this study is that a PU rubber of Shore value A60 is a suitable material for this design. The resulting reaction force graphs (See *Appendix 12*) suggest that the required forces are within realistic boundaries. The force needed for deflection has been set on 2N, based on testing the catheter prototypes with the static bellow (which is 0.5N, and a safety factor of 4 is applied). A compression of 4N or 0.4mm results in an expansion of the bellow that is enough to apply the required tension in catheter tip. This tension in the catheter tip is expressed as reaction force in the catheter tip in opposite direction of the pulling force, exceeding 2N. This means that a deflection can be successfully achieved, before the bellow breaks, or is pulled inside the catheter.

The simulation is limited by some assumptions and choices made. The analysis does not provide for a full proof of concept, however, it provides a promising indication for further development of the bellow. The theoretical analysis is a first indication of a proof of principle, and practical testing is required for validation of the FEA results and for final proof of principle. The next step is therefore to prototype the bellow with the A60 PU rubber, assemble it with the required components, and to test its behavior in a test setup explained in Chapter 6.
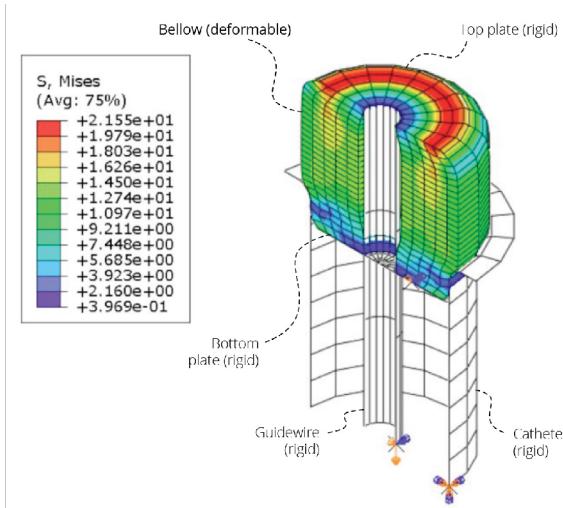

Figure 17: VIsualization of the bellow FEA, including all the modeled components. Rigid components are white and the bellow shows the Von Mises stresses at the moment is is pulled inside the catheter in expanded form.

4.5 The Control device

The FEA contains very specific boundary conditions as a foundation for the successful simulation of the mechanism. These boundary conditions contributed to producing positive results, and the-

refore it is crucial that these exact movements and forces can be realized in the prototype. The control device must be designed to translate an activation movement by a user at the proximal end to the required displacements in the distal mechanism. Because these movements and forces happen on such a small scale, the control device must be able to provide certain precision. The Easysteer working mechanism requires two activities; 1) activation of the bellow by moving the guidewire and mantle in respect to each other, and 2) activation of the deflection by pulling both the guidewire and mantle in locked position in proximal direction. Therefore, the control device consists of two separate mechanisms. It is desired that at least two control devices are developed to compare during the final test. One device will include an axial rotation wheel and the other one a lateral rotation thumb wheel (visualized on the next page) to actuate tip deflection. Following the feedback from specialists during the interviews and the user test described in *Appendix 8*, further development of the control device is necessary. A function that must be looked into in the future is the unlocking of the guidewire. This enables the guidewire to be used independently from the catheter, and suggests a third variation of the control device. Furthermore, the actuation mechanism of the bellow is yet to be designed.

It is chosen to not elaborate further on the design process of the control device since it is not part of the thesis project. At this point in the project, the control device is at a lower priority than the first proof of principle of the working mechanism. Naturally, the required displacements in the tip mechanism must be communicated and translated to design specifications to base the design of the control device on.

Design Considerations

- Grooves are the most feasible way to apply local material weakening. The larger the grooves, the sharper the allowed curve without compressing the material.
- For a 180 degree turn, the removed material on one side of the catheter must be π * catheter diameter
- The deeper the grooves, the smaller the required force for deflection. However, this also makes the tip more fragile, which is why a depth of 2/3 diameter is chosen.
- The catheter must be modified based on its dimensions, to be able to make a 180 degree turn, limiting the groove sizes to <30 μm
- This modification facilitates but does not limit the deflection: a modification for a 180 degree turn might result in an even larger deflection due to flexibility of the material It is important to limit the control device so that over-deflection or material damage is avoided.

- The rubber bellow concept is chosen to be the most feasible in terms of atraumaticity, trackability, producibility, deformation control, dimensions and deactivation.
- The bellow functionality is easier to accomplish when it is expanded in front of the catheter tip rather than inside the catheter tip considering the reaction forces in the system.
- An in depth mechanical and computational analysis suggests a theoretical proof of principle of the bellow in context of use, made of PU Rubber A60. It serves as a first step towards PoP and suggests prototyping specifications.

05 Prototyping

5.1 The Catheter

The catheters that are available for prototyping are listed in Table 1. The Rubicon™ catheter was first prototyped, due to its earlier availability. This catheter is a support catheter, meaning it is deliberately stiff compared to conventional embolization microcatheters. However, it created an opportunity to try out different groove patterns to see what the microlasering company could deliver. Grooves of 150 µm, 50 µm, and 30 µm were lasered into the catheter tip, according to the groove design discussed in the previous chapter, with a tolerance of 0.05 mm in dimensions of 0-6mm. A groove depth of 2/3 of the diameter is chosen to minimize the required deflection force, without compromising the catheter tip too much in its strength.

During the user test with the modified Rubicon™ catheters, it became clear quickly that the stiffness of this catheter is quite different from a regular embolization catheter (See *Appendix 3.1*). However, it did provide a step towards a proof of principle of the catheter modification causing the catheter tip to deflect upon the application of tension. Other catheters were modified to verify this Proof of principle for more flexible embolization catheters that are candidates for being used in the final design.

	Terumo - Progreat™	Boston Scientific - Direxion™		Boston Scientific - Renegade™	Boston Scientific - Rubicon™	
French	2.7F	2.4F	2.8F	2.8F	2.1F	2.4F
Outer diameter (mm)	0.9	0.8	0.93-0.95	0.93-0.95	0.70	0.8
Guidewire compatibility	0.021"	0.021"	0.027"	0.027"	0.014"	0.018"
Inner lumen	0.62-0.65mm	0.5-0.53	0.65-0.69	0.65-0.69	±0.41	±0.51

Table 1: Available catheters for prototyping and their dimensions

The Terumo Progreat™, Boston Scientific Direxion™ 2.4F and 2.8F, Boston Scientific Renegade™ (used catheters or display models) were collected from specialists and from Boston Scientific who were so kind to share these devices for this project. The discussed calculations were applied to each catheter to determine the optimal modification design in the most distal 15-20mm, for a required deflection of 180 degrees. Safety requirement 1 is temporarily neglected for the Renegade™ and Progreat™ with 50 µm grooves, and is validated as this first prototype is only for technical proof of principle (and not yet medical). The new catheters were modified according to *Appendix 4.* The Progreat™ catheter, which is Dr. M.'s favorite to work with, turned out to behave in a different way than expected. The most distal 20cm

Catheter: Progreat™ 2.7F
Guidewire: Progreat™ 0.021"
Modification: 50 µm grooves
Deflection force: 0.5N Deflection displacement: 0.6mm Bending radius: 3D spiral

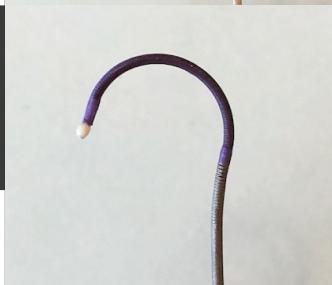Figure 18: Terumo Progreat™ modified with 50 µm grooves

Catheter: Renegade™ 2.8F
Guidewire: Fathom™ 0.016"
Modification: 50 µm grooves
Deflection force: 0.5N Deflection displacement: 0.7mm Bending radius: 6 mm

Figure 19: Boston Scientific Renegade™ modified with 50 µm grooves

Catheter: Direxion™ 2.4F
Guidewire: Transend™ 0.014"
Modification: 30 µm grooves
Deflection force: 0.5N Deflection displacement: 0.65mm Bending radius: 5 mm

Figure 20: Boston Scientific Direxion™ 2.4F modified with 30 µm grooves

Catheter: Direxion™ 2.8F
Guidewire: Fathom™ 0.016"
Modification: 30 µm grooves
Deflection force: 0.5N Deflection displacement: 0.7 Bending radius: 5,5 mm

Figure 21: Boston Scientific Direxion™ 2.8F modified with 30 µm grooves
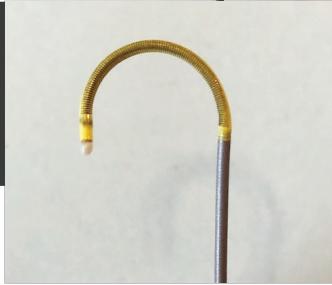
of the catheter was very flexible, making it difficult to concentrate the deflection in the tip. Therefore, the flexible part was cut off and the new tip was modified again. The deflection was now concentrated at the tip, however it was a spiraled shape curve (see figure 18). It was suggested that this is due to the tungsten coil that is incorporated in the catheter wall. Despite the 3D deflection, this prototype was still evaluated in the user test, because the tip might deflect differently in a confined space and still be useful. If this prototype were to be implemented in clinical use, the visibility should be reconsidered, because the marker at the tip of the catheter is cut off. Using a Progreat™ guidewire however would solve this problem as this has a radio-opaque tip. The favorability of the Progreat™ should also be re-evaluated by specialists, as cutting off the flexible end might influence the favorable characteristics of the catheter. The other three catheter prototypes deflected as expected after modification (figure 19, 20, 21). The tension was applied with a fitting guidewire that was provided with a permanent "bellow" made of a drop of 2-component glue, and this assembly can be used for testing the catheter principle as described in Chapter 6.

5.2 The Bellow

Following the theoretical substantiation of the rubber bellow working principle in *Appendix 12,* a translation was made to a usable prototype. In this step, not only the bellow was prototyped, but is assembled with all components of the guidewire system. The main parts of the assembly are the guidewire, the mantle and the bellow.

DIMENSIONS
The bellow in the FEA was modeled with an inner diameter of 0.15 mm (fitting the 0.15mm guidewire), and an outer diameter of 0.55. This outer diameter was based on the inner diameter of the catheter that was planned to be used in the prototype, which is 0.65 mm. The bellow must be thin enough to be advanced smoothly through the catheter (when not expanded) , and it was expected that a bellow expansion from 0.55 to >0.65 would be feasible. Other parts of the assembly were a hollow RVS mantle with an inner diameter of >0.15 mm (fitting the guidewire), and an outer diameter of 0.34 mm (< bellow diameter).

BELLOW
Different prototyping techniques were explored for the bellow. The first prototyping method was outsourced to a laser machining company. Different samples of rubber were collected and laser cut into bellows of 0.45 outer diameter (before the dimensions of the bellow were set to 0.55), and 0.15 inner diameter. Unfortunately, as explained in the *Appendix 6*, this production technique was only successful for the rubbers with a Shore value of <A45. Another disadvantage of this method was that assembling the bellow over the guidewire was very challenging manually. Therefore, another production technique was developed using castable rubber, in which the chosen PU rubber was available. A mold was designed and machined in-house out of brass, which is relatively soft material allowing the drilling of holes of the required dimensions. The design of the mold is visible in figure 22 and included several holes representing casting chambers for the bellow in 3 different diameters: 0.5, 0.55 and 0.6mm. Through the channels, the guidewire could be positioned, which allowed for the bellow to be cast around the guidewire, eliminating one assembly step. The material could be injected into the chamber with an injecti-
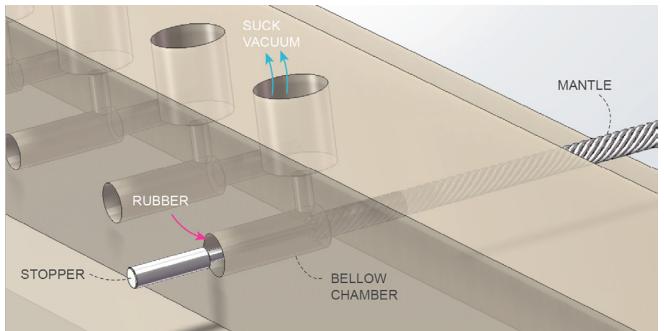

Figure 22: schematic drawing of mold for rubber casting. Guidewire with stopper and mantle are inserted into the "rubber chamber" for the rubber to be cast around
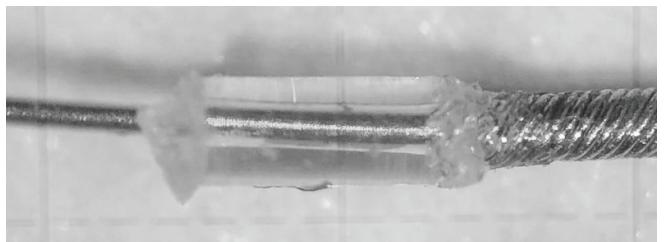

Figure 23: Cast bellow on 0.15mm guidewire, with mantle for reference (right)

on needle. Perpendicular to the bellow chambers were holes through which the chamber could be sucked vacuum, also with an injection needle. *Appendix 6* further evaluates this prototyping method and in *Appendix 7* a technical drawing for the mold can be found.
The resulting bellow, cast around the modified guidewire is shown in figure 23. The mantle guided over the wire (Figure 23, right) helped pushing the bellow out of the mold when set.

ASSEMBLY
Now that the bellow was produced, attention was paid to translating the specific applied conditions of the Finite Element model into the assembly of the prototype. The most important condition is the uniform compression of the bellow. When this is not correctly realized, the expansion of the bellow might not be enough for the mechanism to work. The top and bottom surface of the bellow should therefore be enclosed between two plates, with the same diameter as the bellow. When these diameters do not align, there is a risk of the bellow escaping in unwanted directions, due to the tension it is put under. For example, the bellow can slide over the mantle during compression. Similar effects can also be caused by a potentially lower friction in the system than simulated in the FEA, causing the bellow to slide. To rule out these effects, the following modifications were designed for the guidewire and mantle. Figure 24A shows the ideal situation, in which the bellow was clamped at the top and bottom, allowing only expansion of the middle part of the bellow, while holding it in its place. Figure 24B shows a version of this that was adjusted to be producible on this scale, by punching two rings in a conical shape, after which they were welded to the guidewire and mantle. The welding also allows for all the parts to flush together, increasing atraumaticity and trackability of the assembly when advanced through the catheter or blood vessel. The production of this assembly is outsourced to a third party specialized in micro-machining.

FINAL TEST MODEL

Due to the small dimensions of the assembly, the welding could not be done. This would influence the trackability of the system, but the assembly would still be suitable to test the proof of principle. The rings were successfully machined into a conical shape (figure 25), and all the parts were assembled on a 0.15mm guidewire with a welded "stopper" geometry at the end. This assembly was considered as close as currently possible to the FEA model, and therefore appropriate for an accurate test setup for technical proof of principle (see figure 26, right).
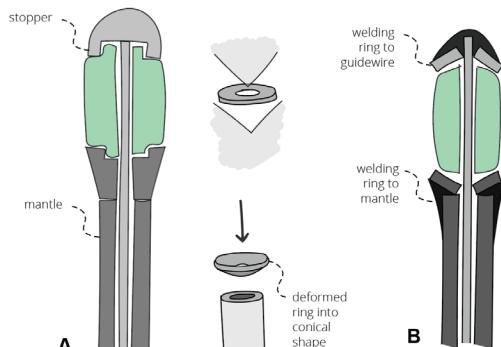

Figure 24: Modifications to the catheter and guidewire to enclose the bellow, limiting its freedom to move in unwanted directions during use.
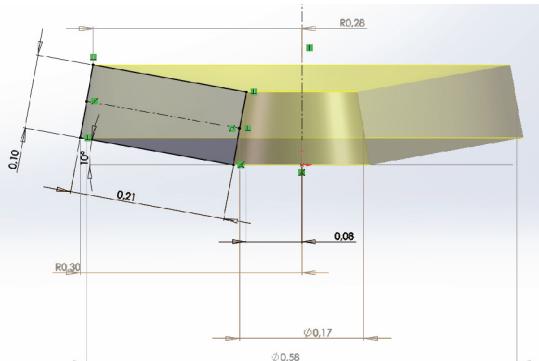

Figure 25: Machining the rings that enclose the bellow into a conical shape
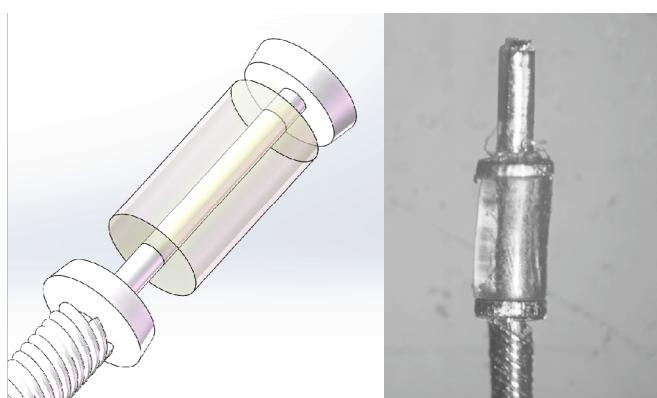

Figure 26: Simplified version of figure 24B (left), Final assembly of the guide-wirebellow system to be tested (right)
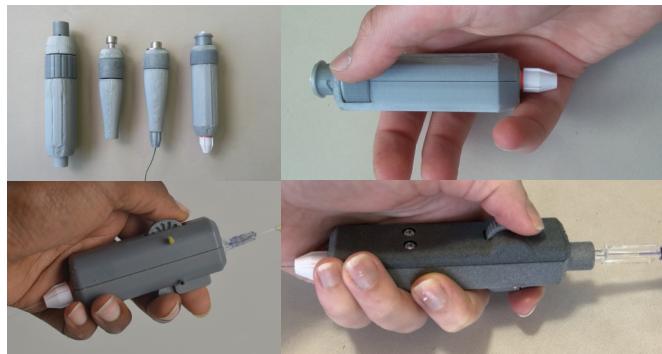

Figure 27: Pictures of the axially actuated control device (top) and the laterally actuated control device (bottom)
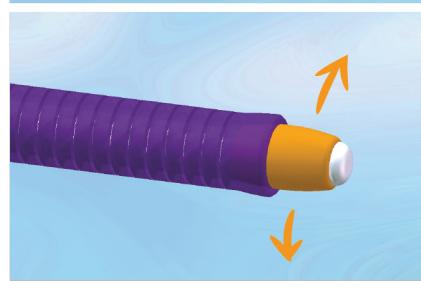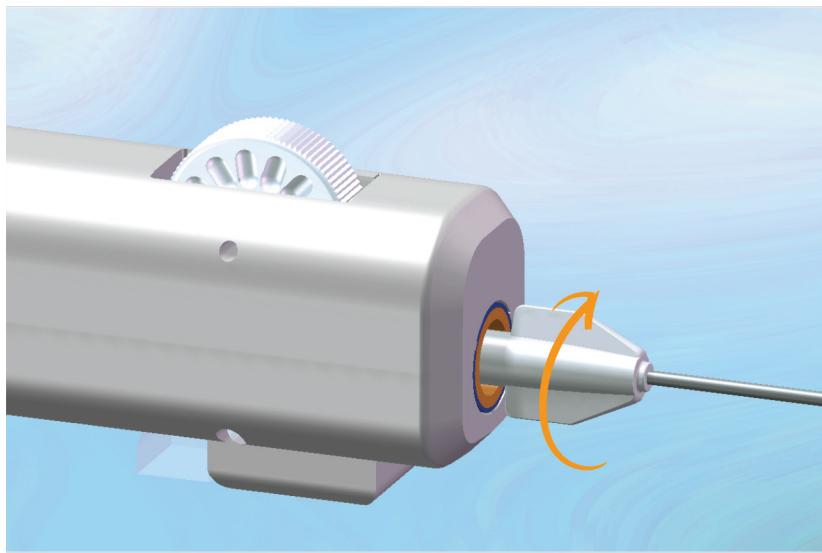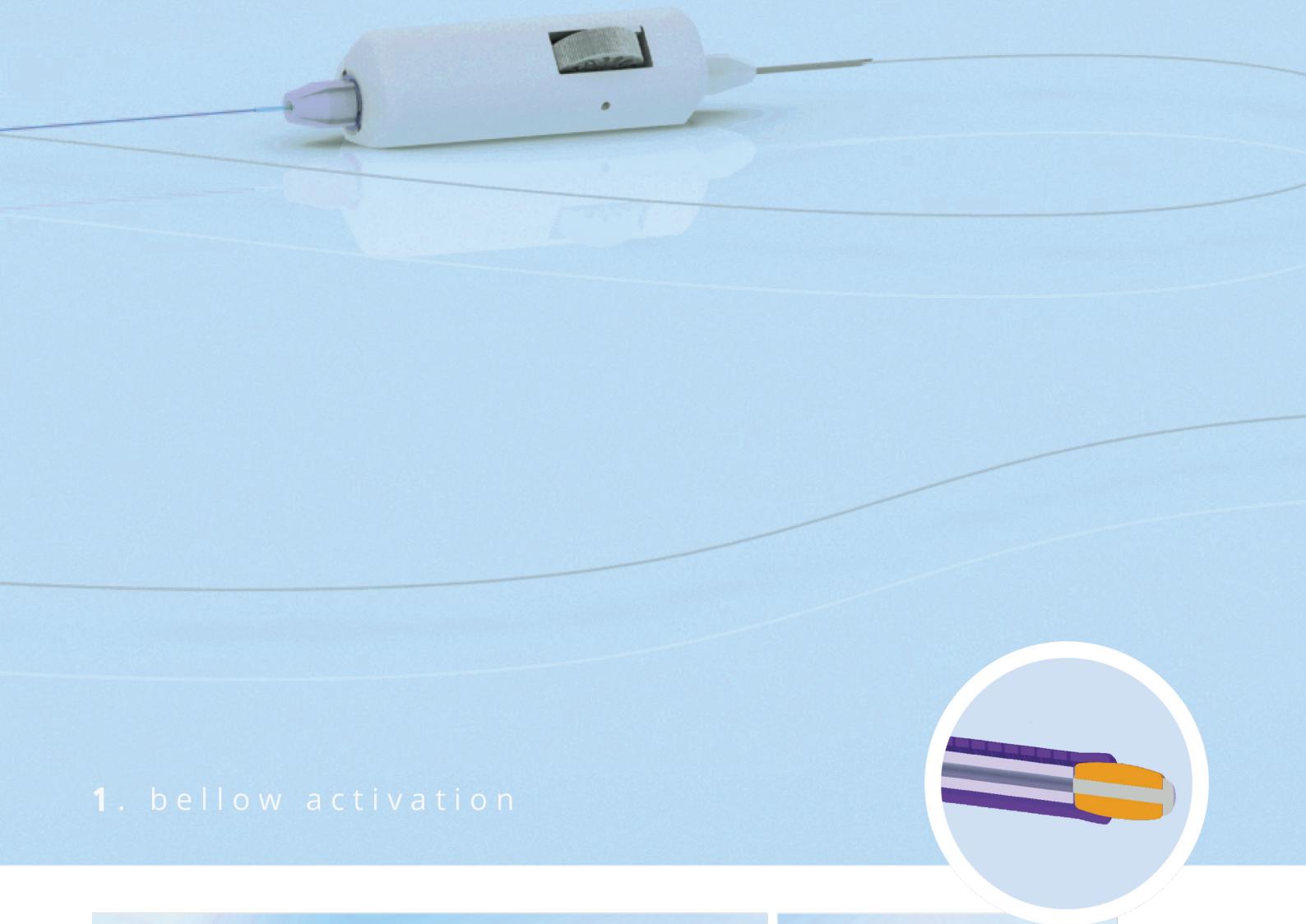
5.2 The Control Device

The development of the control device, was not part of this thesis project. The 3D prints are however shown in figure 27 as one of these will be part of the final prototype. The combination of all components will allow for a proof of principle for the complete design during the user test. The final prototype is visualized on the next page. The prototyped catheters showed a deflection at a pulling force of ±0.5N. The deflection can also be measured in displacement of the guidewire in respect to the catheter, which is realized by a mechanism in the control device. This required distance was translated to limits inside the control device, to prevent overloading the system.

NOTE: the control devices in figure 27 were only made for the actuation of the deflecting of the catheter tip. For the expansion of the bellow, an additional control mechanism must be developed. For the proof of principle of the mechanism, the bellow could be activated manually.

Design Considerations

- The catheters successfully demonstrating the intended deflection functionality after prototyping were the Renegade™, Direxion™ 2.4F and Direxion™ 2.8F. It must be evaluated in the user tests whether this bending angle and radius is appropriate to the context of use.
- The Progreat™ resulted in a spiraling deflection. It should be tested whether this influences the functionality when used in the confined space of arteries.
- A feasible production method for the bellow is casting it around the guidewire in a mold. This production method is quite specific and requires patience and precision but allows for customized inhouse bellow prototyping.
- This method has its limitations considering to the tolerances in the geometry and manual preparation of the guidewire in the bellow chamber. Nevertheless, it enables prototyping a final guidewire assembly that is sufficient for testing proof of principle.

WORKING MECHANISM
and user interaction

This is a representation of what the final prototype will look like. The control device (with lateral turning wheel chosen for this image) is easy to operate and has two controls: The first one is for the bellow activation (the user interaction for this functionality is still to be determined, but is visualized as a quick motion on the bottom left), for which the guidewire and mantle are manipulated in opposite directions.

The thumb wheel controls tip deflection, for which the guidewire system (guidewire, bellow and mantle) are pulled backwards to exert tension in the catheter tip. While controling this with one hand, the other hand can be used for torquing the catheter in order to steer the deflection in other directions. According to the tip modification, the tip can make turns up to 180 degrees, which can be controlled with the thumb wheel. With the displayed catheter and modification, the radius of the curve is 0.75mm. This will vary for each catheter and its modification.

2. tip deflection

up to 180°
Ø11.5 mm
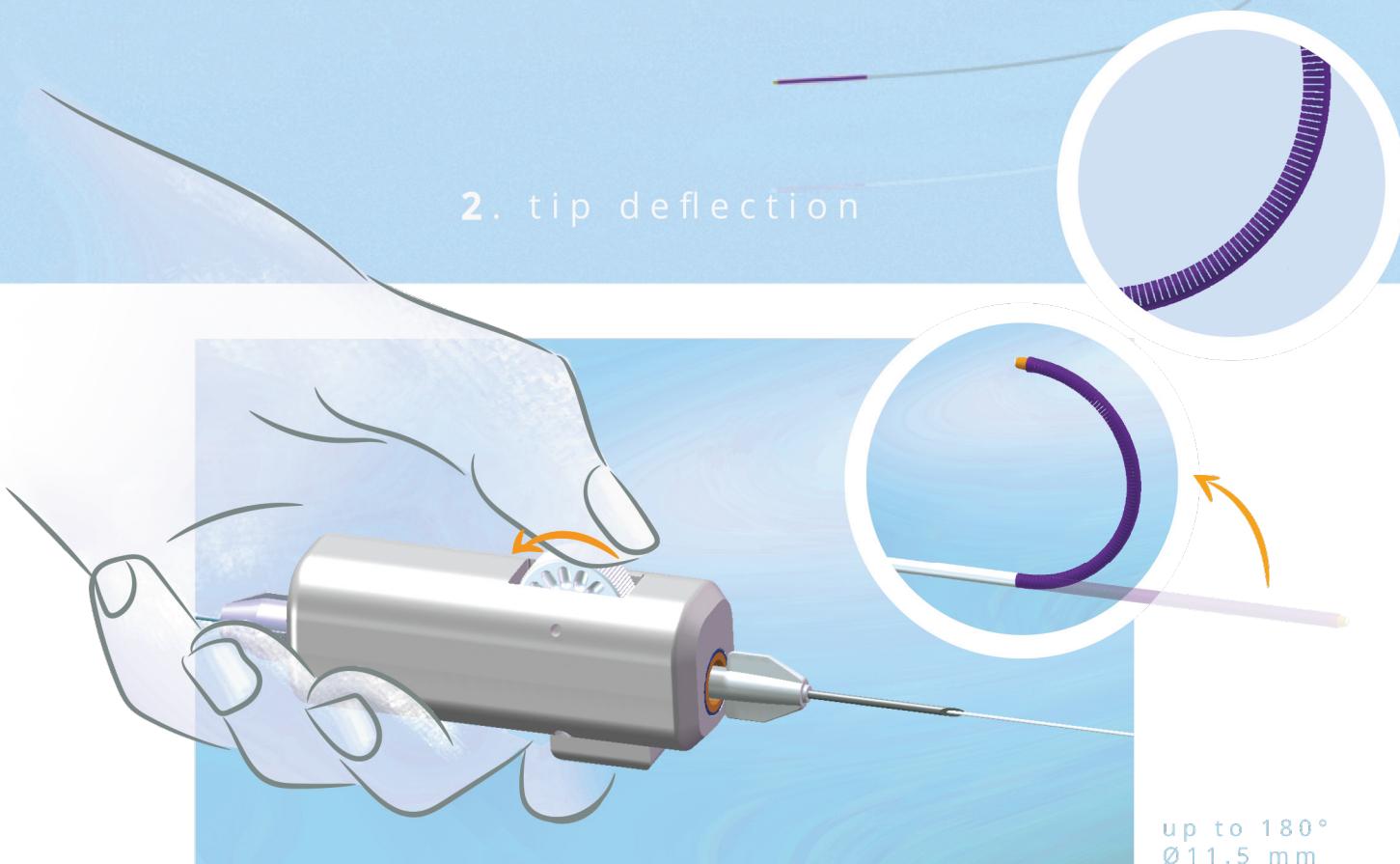
06 Testing

For the medical industry and other stakeholders to recognize the functionality of the Easysteer, and for taking steps towards CE-certification, a proof of principle is needed of the design. The proof of principle was first established for the catheter and the bellow separately, before combining the two in one prototype. This was done because the catheter prototype was developed to an extent that it could be tested already by the user, without a dynamic bellow. The bellow has its own requirements and could therefore be developed independently and incorporated in the modified catheter later. The final design was expected to be more promising after having established proof of principle for both catheter and bellow.

6.1 Catheter technical validation

The catheter tip functionality can be tested separately from the bellow mechanism, because the bellow can be mimicked in static form using a drop of glue or other geometry at the end of the guidewire that can exert tension in the catheter tip. This prototype can be tested by specialists, and their confirmation of the catheter principle is of great value for further development of the device.

LIVER VASCULATURE PHANTOM MODEL (SLA)
In order to establish this proof of principle for the catheter, a systematic test has to be done in the context of use. There are different ways to mimic the context of use, depending on how accurate it has to be done. The most accurate representation of the context of use would be a real operation in a human vasculature. However, for the first proof of principle it is more viable (in terms of safety and costs) to use a phantom model representing a generalized anatomy of the working area. Anatomical phantoms that mimic human anatomy, blood flow and tissue properties exist but are complex and expensive. Considering the scope of the research, of which the primary goal is to evaluate the technical performance of the catheter in respect to the geometry of bifurcations, a non-anthropomorphic (simplified) phantom model of the vasculature of interest was created. This model was inspired by a vascular model made by Helene Clogenson [Clogenson, 2014], except in her model, the smaller arteries were deliberately left out from her model, because the research was on navigating capabilities of the standard (macro) instruments in the main branches of the peripheral anatomy. The model for this test therefore included smaller vessel diameters of the more distal branches, where macrocatheters are generally ex-

changed for micro-catheters. The phantom model enabled systematic testing of various routes, including different bending angles and vessel diameters. This way, a "worst case" route could be attempted, and limits of the device could be identified precisely. The design of the model could also be specified into the vasculature of the focus intervention for this project, which is deep tumor embolization.

After consulting the specialists at DEMO (TU Delft), stereolithography (SLA) was considered the most suitable manufacturing technique for the phantom model. It is a 3D printing technique in which UV-sensitive liquid resins are used to create channels in the geometry. This, as opposed to other production techniques, allows for the channels to be transparent (which is crucial for the test), and can accurately print a CAD model in a relatively fast way. It was also considered less expensive and less complex than milling, especially for the small channels (<2mm). The SLA printer can print limited geometries, on which the design of the phantom model was adjusted.

First, a 60 x 100 x 10 mm test model was printed, to explore printing possibilities and accuracy. Figure 28a shows that channels of 1mm were too thin (as the top left channel failed). The channels were sufficiently transparent. The material used was E-Shell 600, which is a rigid and translucent 3D printing material. The channels in this model had diameters of 1-8mm, representing the diameters of liver vasculature based on the peripheral vessel diameter chart by Boston Scientific [Boston Scientific, 2015].

This phantom test model was already suitable for prototype testing. The catheter tip could be assessed on its manipulation ability through vessel diameters of 2 mm, 3mm and 4mm, and bifurcation angles of 30, 60 and 90 degrees (based on the generalization of angles in Clogenson's model). It was concluded that this model is a suitable model for the technical validation of all modified catheters. However, some optimization steps were suggested after evaluating the test model in a first user test, which is elaborated on in *Appendix 8*. The insights gained from this test, resulted in a more complex design allowing to test worst case routes with smaller diameters and sharper angles, and as such allowing for more precise identification of the device's limits. Therefore, the phantom model was optimized to the design in figure 28b. The geometry was based on different bifurcations in the human liver, distally from the common hepatic artery, assuming that this location is reached with conventional (macro)catheters. Further elaboration on the design of the model can be found in *Appendix 9*.

There are some limitations to this test model, making it deviate from a real liver vasculature. First of all, due to the STL limitations, the model is only 60 by 100 mm. A real liver is slightly larger than this: 14.5 cm for males and 13.5 cm for females [Kratzer]. Despite this, if the model is regarded as part of the liver in which the challenges of a tumor embolization procedure are concentrated, the dimensions are actually quite representative (see figure 29). A factor that however is very divergent from reality is the hardness of the material. The polymer of which the model is printed does not represent the flexibility, softness and lubricity of human vasculature. During the user test it can be attempted to inject a lubricant into the model to improve this factor. An important challenge in real interventions is caused by the limitations of the imaging techniques used. Efforts can be made to simulate this situation with camera's, mimicking conventional x-ray images by adjusting resolution, pixel or color, during the user test. Furthermore, the pathway covered by the catheter between the operator and the liver must be provided in the test setup.
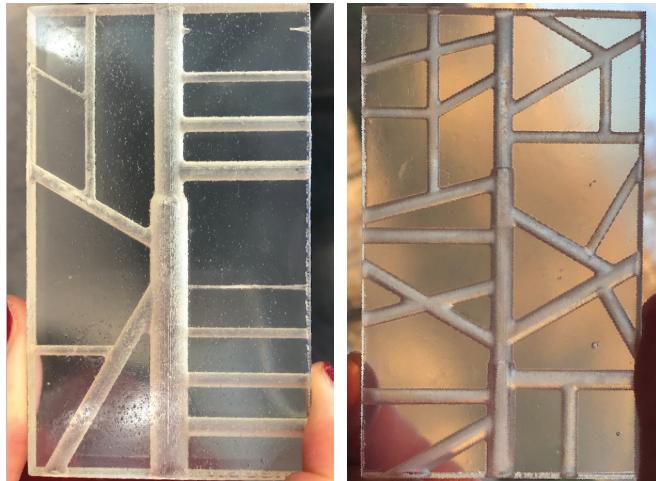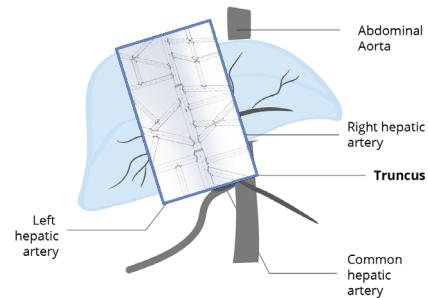

Figure 29: Phantom model compared to size of the liver. Common hepatic artery oriented at the model's starting point. Complexity of the arteries increase

Figure28:a)Phantommodel1.SLATestmodel(left),b)Redesignedphantommodelfortechnical validation (right)

USER TEST

A thorax model was created to represent the patient. This model allowed the catheter to be inserted in the radial area, beyond which touching of the catheter was not allowed (just like in a clinical situation). The specialist guided the catheter to the phantom model attached at the location of the liver inside the thorax model. In this model, different routes could be followed by the user and assessed. This was considered an adequate test setup to evaluate the technical functionality of the catheter by the user, and is visualized in figure 30. Using the static bellow, this test evaluated the catheter functionality only. Elaboration on the test set up, protocol and results of this experiment can be found in *Appendix 10*. When proof of principle of both the catheter and bellow are established separately, the test can also be performed with a working dynamic bellow.

RESULTS

The specialist is given the freedom to take randomized routes. Therefore, the conclusions of this test are mainly based on the specialist's opinion on his experience with trying all the catheters in the test setup, rather than quantified results from timing each curve taken,

documented in *Appendix 10*. In summary, the Renegade™, Direxion™ 2.4F and Direxion™ 2.8F all allowed negotiation of bifurcations of 120 degrees in under 5 seconds. All single turns taken up to 120 degrees were successful. Only some secondary sharp turns did not succeed. The Progreat™ catheter appeared not to be useful because of it's unpredictable spiraling curve. At one point, as described in *Appendix 10*, the Direxion 2.8 F catheter tip showed a weakening in the modified tip. Furthermore, Dr. M. preferred to work without the control device, and manually activate the deflection. These results gave important insights on the design:

- The main reason for difficult advancement through bifurcations this is the hardness of the phantom model. In a real vasculature, the catheterized vessels tend to deform to the shape of the catheter path, which facilitates making secondary/tertiary turns.
- It is suggested to optimize the catheter modification to avoid peek loads that weaken the catheter tip in certain areas.
- A user ritual must be realized that is as close to the current user ritual for catheters. This provides challenges for incorporating an extra user action for the bellow activation. Furthermore, the catheter must be axially totatable without having to rotate the device causing the turning wheel to be on the other side. The axial turning wheel would therefore be suitable.
- Dr. M. is very positive about the product as he expects that this device will significantly reduce time and frustration during an intervention. Live adjustment of the curve, and relaxing the tip when it needs to be straight, avoids having to retract, reshape and replace the currently used shapeable equipment.
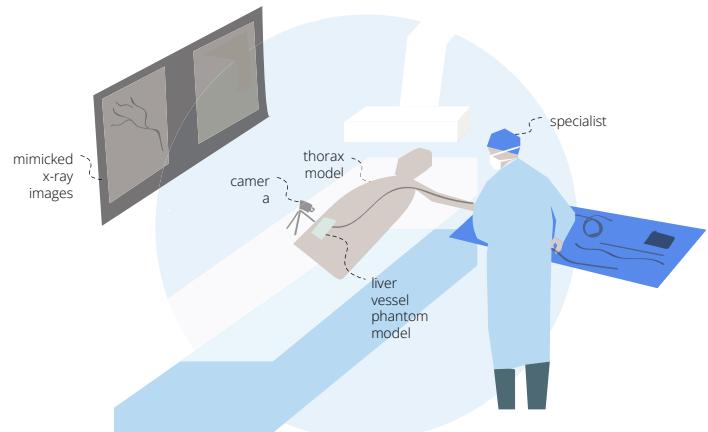

Figure 30: Test setup including the phantom liver model for user test

6.2 Bellow technical validation

The first technical test only served to validate the FEA results of *Appendix 12,* and included the evaluation of the bellow's expansion under axial compression. The expansion must be observed closely with a microscope. Once the bellow was expanded to the required extent, a technical validation of the bellow exerting force on a catheter tip could be done.

TEST SETUP
This was done in a small test setup (10cm), with a focus on the expansion of the bellow to allow force on the tip of a catheter by pulling the guidewire. The detailed test setup and bellow assembly is discussed in *Appendix 11*. Force gauges were used to monitor the forces applied. When the pulling force exceeded 0.5 N (which is the force needed for deflection of the catheter tip), the bellow-catheter combination worked satisfactory.
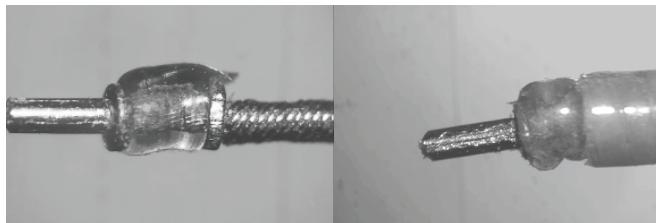

Figure 32: Proof of principle of the bellow mechanism, expansion (left) and applying tension to the catheter tip (right)

RESULT
FIgure 32 shows the main results from a technical proof of principle of the bellow. The assembly in figure 32 was as close to the FEA properties as possible with the used prototyping techniques. Upon axial compression, the bellow expanded quite uniformly from a diameter of 0.55 to 0.71mm, which is 129% (figure 32, left) Thereafter, the expanded bellow could hold a pulling force of 0.5N. So, proof of principle was established with this test.

6.3 Suggestion for invivo validation

Although the user test provided proof of principle of the catheter, the setup used showed some limitations. The liver phantom model represented the geometry of the vasculature but it was not fully reliable in terms of the characteristics of human vasculature. To be able to fully assess the prototype, an in vivo porcine expermiment was drafted for this project. It is expected to provide insight into the use of the catheter in "wet" environment (inside real vasculature), the ability to make multiple turns, and the visibility of the catheter tip using representative imaging techniques. This animal experiment will also provide feedback on how the user ritual is being altered. Unfortunately, due to the current Covid-19 pandemic, the in-vivo test had been postponed to a date beyond the timeframe of this project. Therefore, no results can presented in this thesis. The setup discussed is a recommendation for the clinical validation of the prototype as soon as the situation allows it.

ANIMAL FOR EXPERIMENT
The Erasmus MC agreed to supply a pig for this project, after it being used for a medical seminar. The pig will be prepared at the operation table in the Skills Lab of the Erasmus MC, and an interventional radiologist will perform an endovascular intervention.

OPERATING ROOM AND ANESTHESIA
The operation room will be prepared as usual. Imaging techniques that are similar to those at the interventional radiology department will be set up. The pig will be under general anesthesia.

MATERIALS
Prior to the intervention, it will be determined whether the bellow is safe enough to be used in the catheter prototype. For safety reasons this first animal test will be performed with the catheter and a static bellow at the guidewire tip, just like the user test described in 6.1. It is assumed that proving the catheter principle with a static bellow will almost be as valuable as with working bellow, because the context of use will especially influence the deflection and movement of the catheter tip through the vasculature.

PROCEDURE
An angiogram is made with the angiographic catheter tip in the common hepatic artery. From this angiograph, the routes can be planned out. The interventionalist is asked to follow four different routes, with increasing difficulty levels. For example:
• *Route 1: radial access to the common hepatic artery*
• *Route 2: radial access to a side branch of the right/left hepatic*
• *artery*
• *Route 3: radial access to a secondary side branch of the right/*
• *left hepatic artery*
• *Route 4: radial access to a tertiary side branch of the right/*
• *left hepatic artery, selecting a worst case turn based on the*
  angiogram

The same routes can be performed with conventional instruments, and the navigation time will be recorded. Meanwhile, the interventionalist is asked to identify procedural difficulties. It is made sure that all laws and regulation on animal experiments will be fully complied to. A risk assessment will be necessary of the prototype in terms of fragility and potential disintegration of the mechanism's components.

Design Considerations

• To be able to test in a realistic environment, more advanced phantom models or if possible in-vivo animal testing must be used for further evaluation.A proof of principle for the catheter is confirmed by Dr. M, and suggestions for modifications of the user ritual are made for further development of the control device.
• Proof of principle of the bellow is confirmed. The next step is to combine bellow and catheter in the final prototype.

07 Discussion

7.1 Final product evaluation

The Easysteer steerable microcatheter design is unique compared to existing instruments, as its guidewire is used for the actuation of the tip deflection in stead of cables in the catheter wall. Therefore, it's design is simple and can be implemeted in smaller catheter diameters than existing steerables. The designed mechanism allows for controlled steering of the tip, and the user can activate the deflection anytime and in any required bending angle. This controllable tip minimizes the exchanging and re-shaping of multiple instruments during a procedure. The unique mechanism also allows for retraction of the guidewire and therefore the individual use of the guidewire and catheter, a functionality that interventionalists are used to. The design is focused on tumor (radio-/chemo-) embolization in the liver, kidneys and prostate, but can eventually be customized to many different catheter sizes and types, and spread out to more specialisms.

The modification of existing catheters for this product is a simple way to realize prototypes and saves a large part of the CE certification process, and design steps, and can ideally be realized when cooperation with a catheter company is established. All design requirements that are established in Chapter 3, based on initial clinical evaluation have been realized in the design. The catheter principle is proven by the user and is ready to be tested in a clinical environment. The bellow mechanism has a technical proof of principle, and must be further optimized slightly and tested before implementation in the final combined prototype. To evaluate the potential of the final device, it has been assessed on Rogers' five factors influencing a decision to adopt a new product.

- The **relative advantage** of the Easysteer is the controlled steerability. This should be demonstrated and communicated with the final users, so that this additional value is recognized. Recognized advantages must also be communicated with all stakeholders influencing the decision of purchase or implementation of the product. The specialists involved in this project already recognized the main advantage being the adjustability of the catheter tip deflection, while keeping it inside the vasculature, as opposed to having to retract, reshape and reinsert instruments for each difficult turn. Specialists involved expected this feature to enable the entire navigation to a distal tumor possible with only this device. Consequently, reduction can be achieved of procedure time, subsequent radiation

exposure (to both the interventionalist and the patient), frustration of the interventionalist and trauma to the patient's blood vessels due to trial and error and repeated exchange of instruments. Furthermore, the use of only one device reduces instrumental waste. Faster and easier procedures also allows for more interventions to be done per day. In addition to the ease and decreased procedural time, the Easysteer might enable reaching locations in the body not reachable before, which could improve the medical outcome of some procedures also. Consequently, the hospital can realize more and better healthcare.

- The **compatibility** of the Easysteer is comparable to the other materials and equipment used for endovascular interventions, and requires similar handling and sterilization procedures. The Easysteer is compatible with other endovascular instruments, because the prototype is based on an existing catheter. The Easysteer can be used for the entire navigation part of the procedure. When the target is reached, the special Easysteer guidewire can be retracted to make space for a conventional guidewire when needed or injectables for embolization. Furthermore, the device has a regular microcatheter size (2.4-2.8F) which is compatible to any conventional microcatheter or sheath. Further development of the control device must facilitate fast detachment of the guidewire and catheter and exchanging of other guidewires in the system.

- The perceived **complexity** is generally the actual complexity multiplied by the perceived risks. The actual complexity of use is slightly increased because an extra action is required for bellow expansion. The actual complexity can be reduced by making the control device as simple to understand as possible, including clear use cues about how to (or how not to) operate the device. This way, the required change in the user ritual is minimized. A way to do this is including user known elements and interactions (similar to other devices they work with). The added complexity is expected to outweigh a great deal of avoided complexities arising when using a non-steerable device. Perceived risks are minimized in a risk assessment study (which is recommended to be done in next steps of the design process) of which the user should be aware. It should be noted that although the design can piggyback on the already established CE certification of the modified catheters, the risk assessment of the original catheter is not representative anymore after the groove modification.

- **Trialability** of the product gives the user confidence, according to a "first see, then believe" objective. The main advantage

of the Easysteer is not focused on changing the outcome or success of an intervention, but only to incease speed and ease of one specific part of the intervention: the navigation part. A clinical trial can be performed to confirm this advantage, and to show the effectiveness of the solution in different procedures, without affecting other parts of the procedure.

- **Observability** of the advantages of the product is enabled by performing identical or similar procedures with both the Easysteer and with conventional (non-steerable) equipment, and evaluate and compare both procedures on operational speed and success. These observations might lead to more insights for further iteration of the product, and will be of great value for further development of the control device and user interaction.

7.2 Design process evaluation

This project has successfully followed the double diamond design process and covered a significant part of the development of the Easysteer steerable microcatheter. Following the double diamond structure has helped in forcing some decisions to be made, which speeded up the process. The goal of applying a user-centered approach to the development of the device is achieved. The user has been involved constantly in all phases of the project, guiding the design towards the most useful innovation with optimal functionality, while keeping it within the scope of the project. This collaboration allowed for fast decision making in the convergent phases. Furthermore, it provided opportunities for the engineers to identify unmet needs and clinical demands with their own eyes in the operating room, and a valuable resource of prototyping materials such as used catheters. As a result, it was possible to transform a patented basic idea into a working prototype in only six months, while already being confirmed useful by specialists. This provides a promising starting point for the products journey to CE certification, and eventually to the operating table. The user centered approach is therefore highly recommended for any biomedical engineering project.

The approach to split up the design in the catheter, bellow and control device from the conceptualization phase on, is done or a reason. The three components can be developed and tested for proof of principle individually. This allows for giving each component the required attention it still needs. For example, the catheter development had a faster pace, as the design was simple and prototypes were easier to be made and tested. Meanwhile, the bellow concept still required thorough technical analysis, before having enough confidence that the bellow could be prototyped. During this evaluation, the catheter could already be tested by the user, so that small steps were continuously made throughout the project.

7.3 Limitations of the study

The design methodology followed resulted in the promising current design for the Easysteer. However, it is important to remain critical towards the approach of the project, the results achieved and the real added value of the product. For example, this thesis project covered a significant part of the development of the Easysteer, however, thorough evaluation is only done for one bellow concept. Due to the Covid-19 pandemic, the final prototype could not be tested in an in-vivo animal environment, leaving some questions about the current proof of principle unanswered.

RESEARCH
When involving medical specialists in a design process, it is important to pay attention, but also remain critical towards their opinion. Although the clinical demand is confirmed by multiple (6) users from different specializations, the working mechanism and functionality is only evaluated by one specialist. This is done to protect the intellectual property of the invention. Especially in the medical world, a specialist's opinion is extremely valuable, but with significant individual variation.

BELLOW DESIGN
While the catheter concept was established and prototypes were being made, the development of the bellow principle required thorough technical evaluation, using a mechanical and computational analysis. An approach is chosen to thoroughly evaluate one material in stead of comparing multiple materials. The preliminary material study created a rough selection of suitable elastomers. After that, the material was selected based on its availability in castable form, so prototyping could be done when the results of the analysis are positive. Also, to get accurate results from the computational analysis, a compression test with the chosen material was required. Due to the timeframe of this project, only one material could tested mechanically and evaluated using Finite Element Analysis (FEA). The analysis confirmed the suitability of the chosen material. If necessary, the process can be repeated for another material. Some people have suggested using a silicone rubber, as it is high temperature resistant, biocompatible and therefore often used for medical purposes, such as implants and prostheses, but also for gaskets, seals and o-rings. [Gent et al., 2012] For this project, silicon rubber is not evaluated due to unavailability in the required Shore Hardness, but repeating this project's approach with this material might be interesting for future research.

FEA requires several assumptions, limiting the results. These assumptions and limitations are thoroughly discussed in *Appendix 12.* The most important criticism is FEA merely being a computer model processing the input provided. As this input is based on several simplifications, results cannot be held fully accountable for the prediction of the material's behavior. Prototyping and testing is always required for validating results. Therefore, for this project, it is used as a first indication towards proof of principle, and to identify new design considerations. For example, the FEA's assembly and boundary conditions need to be mimicked precisely to achieve the same positive results in reality.

Furthermore, the definition of material properties for the FEA is based on a mechanical test that has its own limitations. For example, the available equipment allowed only a uniaxial compression test. An additional biaxial and planar test would allow the material properties to be defined more accurately. Furthermore, a force sensor is used with a capacity of 111N. This limits the amount of values to base the materials stress-strain curve on, which makes the curve more linear than a hyper-elastic material would generally be defined with. The reason for this is that tension and compression stress-strain performance can be assumed fairly linear up to 30% strain [Gent et al.

pression of the material sample, enabling more accurate definition of the hyper-elasticity of the material. This could also be accomplished with a tensile (instead of compression) test. However, the limited stress-strain curve is not considered to fundamentally change the result, as the compression in the bellow is 30-40% during use. The established stress-strain curve will therefore define the material with sufficient accuracy.

PROOF OF PRINCIPLE
After this theoretical proof of principle of the design, tests were performed with support from interventional radiologists' opinion to establish clinical proof of principle. It was chosen to first test the proof of principle of the bellow and catheter separately. It must be discussed whether it is valid to assume that adding together both components with individual proof of principle, will automatically result in a total proof of principler. If it can be proven that the bellow is capable of applying the same tension in the catheter tip as the static bellow, the catheter and bellow combination will yield the intended functionality. It is however still possible that the bellow behaves differently in the context of the deflecting catheter than in the context of a static test setup.

ALTERNATIVE BELLOW SOLUTIONS
When this is the case, the bellow must be redesigned. In the case that the bellow design is challenged by uncontrollable forces during use, other materials can be evaluated. In a worst-case scenario, when the bellow is rejected after the user tests, novel concepts can be evaluated. Spark Design & Innovation limited this project to mechanical solutions; however, novel concepts do not have to be mechanically actuated. For example, electropolymer material can be deformed by applying a small electrical current to it. Of course, making this shift in the design causes all requirements and safety assessments to be reconsidered.

When the actuation of the bellow presents too much challenges, other alternatives of the design can be reconsidered. For example, the dynamic function of the bellow could be eliminated. This means that the deflection is provided by a static bellow, and the guidewire must therefore always stay inside the catheter. It could be evaluated whether the lumen is still large enough for embolization material to be injected along the guidewire, after slightly advancing the guidewire out of the catheter tip. Another alternative would be to shift the focus of the product to solely the guidewire. If implemented the right way, the simplified version of the design (with static bellow) could become the core function of a steerable guidewire that can be guided to the target, over which conventional guidewires can be advanced.

The prototypes used for testing the proof of principle are limited by the available parts. The guidewires and mantles used are high quality parts, but they tend to stretch during use, affecting the controllability of the bellow expansion and tip deflection. Also, prototyping techniques are limited to the small dimensions of the design. This makes accurate machining, welding, and complex mechanisms challenging to realize. Boston Scientific has greatly contributed to the prototyping, by providing a few of their catheters. The prototype is therefore based on only these catheters, but other catheters might suit this design better. For example, a catheter with a stronger tip could prevent it from becoming fragile due to the required modification.

TESTING
An important limitation of the project is the extent to which both the catheter and the bellow are tested. The in-vivo porcine assessment, which was planned but postponed due to Covid-19 pandemic, is considered crucial for final validation of the product. When the bellow is tested more thoroughly and ready to be implemented in the catheter (after optimization the production of the bellow and safety evaluations), tests can be performed with the final prototype. It is expected that at the time the animal test is allowed, the final prototype is ready. The in-vivo testing will give insights on the following aspects:

- By performing a technical test and user test with the catheter, it is proven to deflect in the desired shape according to the applied modification, which is neatly done and can also be applied in batch mode. In the technical validation setup, the catheter is carefully manipulated. However, in context of use, it could be the case that the interventionalist handles the device with less care, which might cause the catheter to tear due to the increased fragiligy after modification. It might be useful to look into the visibility of the whole tip, to indicate in which direction and how much the catheter deflects.
- It should be assessed whether enough pushability is retained in the catheter after modifification. As the catheter tip turns significantly more flexible than before, this might influence the catheters ability to push through slightly stenotic blood vessels
- The bloody ("wet") environment might also influence the trackability of the guidewire inside the catheter. The guidewire assembly should be sufficiently atraumatic, for it to be able to slide through the catheter without too much resistance when the bellow is inactivated. The guidewire assembly can be reconsidered and optimized to realize this.
- Final testing of the bellow mechanism inside the catheter prototype will give insights on the transfer of displacements to the distal mechanism over the entire length of the catheter. The bellow behavior is currently tested in a 30cm test set up. The final assembly will however be influenced by stretch properties of the cable/mantle, which might influence the functionality and required boundary conditions for the use of the product.
- Assessment is required on whether the bellow behavior is affected by real vascular environment. The flowing blood might influence the friction between the bellow and the inside of the catheter. The friction in the system is one of the most questionable parts of the technical analysis, and should therefore be submitted to ini-vivo testing.
- The most important risk assessment that needs to be done is putting the bellow under some extreme forces. The applied forces to the bellow can be limited by the control device to a certain extent, but the pushing and pulling of the bellow against blood vessel walls adds extra forces to the bellow. In all cases, the bellow needs to stay in the assembly, which is why the enclosing components of the assembly are so important.

In conclusion, the most important discussion points will be analyzed with more elaborate testing, in extreme situations, and preferably in an in-vivo setting. It should then be reflected by multiple users whether the product is really useful, and whether the extra features and costs of the product outweigh its benefits, as compared to conventional techniques. But to be able to assess this, the final prototype should be optimized first.

7.4 Future perspective

RECOMMENDATIONS

After this thesis project, a sufficiently solid proof of principle is established for both the catheter modification and the bellow mechanism. The most important challenges and steps required to translate this into a clinically validated product that can be applied for CE certification, are listed below:

- Bellow and catheter must be combined in one protoype. The assembly must be optimized, and it can be explored whether the mantle/guidewire/catheter parts must be replaced by ones that are more suitable for the design in terms of stiffness, elasticity, traumaticity, steralizability and batch producibility.
- Further testing, preferably in clinical environment is necessary for final confirmation of the product's added value. A suggestion is done for testing the prototype in an in-vivo environment with a porcine experiment.
- A safety assessment must be done to assess the potential and risks of catheter breakage due to the groove modification, or detachment of the bellow or other parts from the system in extreme working conditions.
- Efforts are required for the design of the control device. Additional user actions must be minimized, and the actuation mechanisms must be adjusted to the limits of the bellow mechanism and the steerable tip. For this development, cooperation with specialists is valuable. The controllability of the bellow activation is a challenging aspect.
- If in-vivo tests or combined prototype suggest that another material is preferable for the bellow, the mechanical test and FEA approach used in this thesis can be repeated for that material. If the equipment is available, efforts could be made to make the mechanical tests and FEA more accurate.
- Other design considerations based on requirements that are not yet confirmed to be met, are: Independent use of the guidewire (while being stiff atraumatic enough), visibility of the guidewire tip and the deflected catheter tip, optimizing manufacturing techniques for series production with a maximum of 1% tolerance, and sterilization assessment of the product.

Because the user test is now done with one very experienced specialist, it might be interesting to generalize the use of the product, and make instructions for use, so that even unexperienced physicians can use the product. It would also be interesting to set up a comparative study, to quantify the actual benefits of the Easysteer compared to conventional instruments.

FUTURE OPPORTUNITIES

Clinical validation of the concept is not far away, and a in-vivo proof of concept will be an important step towards development of the product. It can be presented to potential investors or venture capital institutions. Accompanying this, a plan for production, assembly, market introduction and implementation should be established. Due to its unique design, the Easysteer has the potential to become the next workhorse of interventional radiology. It is a simple, mechanical solution to a problem that is very prominent during the majority of minimally invasive interventions: complex navigation. Specialists expect that the entire navigation part can be done with only this device. This will provide a great improvement in sustainability and costs. Even

if the Easysteer becomes more expensive (for example €400) than conventional instruments (around €100), it can reduce the costs of an intervention compared to using 4 or 5 lower cost instruments, as well as in terms of operating time. Existing catheters with a small diameter can be customized into steerable devices according to the Easysteer design, which has not been done before. When the benefits are recognized by some specialists, they can recommend the product to other specialists, for example during congresses or seminars, and this way the awareness of the novel technology will spread.

Especially the tumor treatment interventions will benefit greatly from better navigation, as tumor supplying arteries can be selected more precisely, and less untargeted arteries are affected by the embolization. It might also enable more tumors to be treated endovascularly, because possibly more distal or difficult to reach locations can be reached with the Easysteer. This must be confirmed by the clinical assessment, but it could cause a slight shift in the approach of cancer treatment.

For market introduction, it is recommended that the product becomes not too expensive. This is of course influenced by the production costs. But it is indicated by the consulted specialists that certain catheters are not being used because they are too expensive. It may also be necessary to better explain the benefits of this device. The most important step after clinical validation of the product, is to sell the patent or the license to a large medical device company. This company will have the resources to initiate automated production and has enough capacity to take all the necessary steps for the CE certification process. This company will then take over the marketing and strategic management of the product. Companies often wait to buy a patent until it is evolved to a certain level. Therefore, a few more milestones must be reached such as clinical validation. Until then, the intellectual property must be protected, while contact with medical device companies is encouraged. With these resources, sophisticated production methods can be explored such as 3D printing steel parts, automated assembly techniques and new methods for casting the bellow. Cooperation with companies that supply the required parts (catheters, guidewires) is valuable for this step.

When used successfully by some specialists in tumor treatment interventions, it is the moment to scale up the application of the product to more specializations, for example reconsidering endoscopy, lung nodule treatment, child cardiology, or even very specific applications such as fetal surgery. In the long term, opportunities lie in seeking cooperation between the Easysteer and imaging technology companies, to take endovascular navigation to the next level. For example, the FORS technology by Philips is an impressive new technology for real-time 3D visualization of minimally invasive instruments in the patient specific anatomical environment. If this technology can be realized in 2.4F devices and combined with a steerable microcatheter like the Easysteer, it would greatly impact the future of minimally invasive navigation through small vasculature. The steerability of the device and the sophisticated imaging technique have great synergetic potential for augmenting controllability of the catheter tip. These combined technologies will significantly increase the procedural

08

Conclusion

This thesis project started as a patent, that presented an idea for a novel steerable instrument. This patent did not elaborate on the fulfillment of the envisioned working mechanism, and was not specified on a medical application yet. This thesis project combined a double diamond design methodology with a user-centered approach, to be able to efficiently bring this initial idea to life, in the form of a proof of principle that is recognized as useful by the user. An initial clinical evaluation enabled the convergence to endovascular tumor embolization as killer application. After this, the mechanical solution was realized by conceptualizing, a mechanical and computational analysis for theoretical validation, and prototyping for final proof of principle. The catheter and bellow were both designed, prototyped and tested individually to a certain extent, but require further optimization and clinical assessment. However, the specialists involved in this project were already convinced of the added value of the product: they consider the Easysteer to have great potential, because it is exceeds conventional instruments in terms of navigation control. The main benefits are: reduced procedure time, reduced frustration, minimization of vascular trauma, and access to more complex and distal locations. The close cooperation with the user has been unique and crucial to achieve this level of success in only 6 months.

GLOSSARY

ANESTHESIA	Controlled, temporary loss of sensation or awareness that is induced for medical procedures
ANEURYSM	An excessive localized enlargement of an artery caused by a weakening of the artery wall
ANGIOGRAPHY	Examination by X-ray of blood or lymph vessels, carried out after introduction of a radiopaque substance.
ATRAUMATIC	Causing minimal tissue injury (during medical or surgical procedure)
AVM (ARTERIOVENOUS MALFORMATION)	A tangle of abnormal blood vessels connecting arteries and veins in the brain.
BALLOON ANGIOPLASTY	Surgical widening of a blocked or narrowed blood vessel, especially a coronary artery, by means of a balloon catheter.
BASILIC VEIN	A large superficial vein of the arm
BENIGN PROSTATE HYPERTROPHY	(BPH) A noncancerous increase in size of the prostate gland.
BENIGN	Noncancerous
BIOCOMPATIBLE	Capability of coexistence with living tissues or organisms without causing harm
BIOPSIES	An examination of tissue removed from a living body to discover the presence, cause, or extent of a disease.
BRONCHOSCOPE	A fiber-optic cable that is passed into the windpipe in order to view the bronchi.
CARDIOLOGY	Medical branch that deals with diseases and abnormalities of the heart.
CATHETERIZATION	The action or process of inserting a catheter into a body cavity, in the case of microcatheters, in blood vessels
CEREBRAL	Of the brain
CHEMOEMBOLIZATION	Injection of small embolic particles coated with chemotherapeutic drugs into tumor supplying arteries
COILING	Procedure to treat an aneurysm by filling it with material that closes off the sac and reduces the risk of bleeding.
COMMON HEPATIC ARTERY	Short blood vessel that supplies oxygenated blood to the liver, stomach pylorus, duodenum, pancreas, and gallbladder.
CT (COMPUTED TOMOGRAPHY)	Medical imaging technique that uses computer-processed combinations of multiple X-rays
DIAGNOSIS	The identification of the nature of an illness or other problem by examination of the symptoms.
DISTAL	Situated away from the point of origin or attachment, as of a limb, bone. For instruments, away from the user
EMBOLIZATION	The artificial or natural formation or development of an embolus, for example for closing tumor supplying arteries.
ENDOSCOPE	An instrument which can be introduced into the body to give a view of its internal parts.
ENDOVASCULAR	Medical procedure performed in or through the blood vessel system
FIBROIDS	a benign tumor of muscular and fibrous tissues, typically developing in the wall of the uterus.
FISTULA	An abnormal or surgically made passage between a hollow or tubular organ and the body surface
FLUOROSCOPY	Medical imaging technique that uses X-rays to obtain real-time moving images of anatomy or blood vessels
FORCEPS	Medical handheld, hinged instrument used for grasping and holding objects.
INTERVENTIONAL RADIOLOGIST	Medical specialisation that involves diagnosis and treatment based on a variety of medical imaging techniques
LOBAR BRONCHI	Subdivision of the main bronchi (= a passage or airway in the respiratory system that conducts air into the lungs)
MALIGNANT	Cancerous
MINIMALLY INVASIVE	Surgical techniques that limit the size of incisions needed, reducing recovery time, associated pain and risk of infection.
NEUROLOGY	Medical branch that deals with the anatomy, functions, and organic disorders of nerves and the nervous system.
ONCOLOGY	Medical branch that deals with the study and treatment of tumors
ORGAN DYSFUNCTION	Abnormality or impairment in the function of a specified bodily organ or system.
PERCUTANEOUS CORONARY INTERVENTION	(PCI) Catheter-based procedure that uses a balloon or stent to open up stenotic blood vessels in the heart
PORCINE	Of, affecting, or resembling a pig or pigs.
PROXIMAL	Situated nearer to the centre of the body or point of attachment. For instruments, near to the user
PULMONOLOGY	Medical branch that focuses specifically on diagnosing and treating disorders of the respiratory system.
RADIATION	Emission of energy as electromagnetic waves or as moving subatomic particles, harmful effect of imaging techniques.
RADIO-OPAQUE	Exhibiting relative opacity to, or impenetrability by, x-rays or any other form of radiation.
STENOSIS	Abnormal narrowing in a blood vessel or other tubular organ or structure, atherosclerosis characteristic
STENTING	Placement of stent (metal or plastic tube) in the lumen of an anatomic vessel or duct to keep the passageway open
STROKE	Medical condition in which poor blood flow to the brain causes cell death

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00 Appendices

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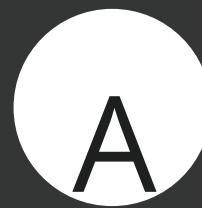
APPENDIX I

Historical Analysis visualizing the design process from the beginning, based on the Double Diamond structure.

DISCOVER CONFIDENTIAL DEFINE DEVELOP

PROJECT INITIATION	USER & STAKEHOLDER DRIVEN DESIGN RESEARCH	USER EMPATHY INTERVIEWS & OBSERVATIONS	GAIN INSIGHTS & DEFINE PROBLEM	DEVELOP POSSIBLE SOLUTIONS THROUGH ITERATION
CONTEXT	COMPETITOR ANALYSIS TECHNOLOGY RESEARCH		CHALLENGE DEFINITION	IDEA GENERATION
INSPIRATION				

2014

Initial idea by a vascular surgeon, who saw potential in steerability and improved controllability of microcatheters. Together with Spark Design & Innovation he initiated the project.

Start of the double diamond structure design process: the current medical procedures and available products were analyzed, to identify competitors and opportunities to penetrate the market.

A research was conducted into the clinical application, to find benchmark procedures and current shortcomings.

The product should:
Get feedwire into position..
· through the right route
· covering as least as many procedures as existing devices
· as least as deep (smaller diameter)
· in a better way than normal (speed/reliability)
· with no additional steps

2017 First patent application

Mencius Medical BV (joint venture between Spark & Never Odd or Even BV.) founded for development of this product.

2018 Patent filed by Mencius Medical B.V.

Publication (WO2018174712A1)

Patent and business model is presented to different parties / potential investors, as additional resources & funds are needed to take the product development to the next level.

CRITICAL TO SUCCESS
· **Functionality**
  speed, reliability, patient safety & comfort
· **Patent**
  type (device, production method), new & inventive, claim of added value
· **Cost**
  production, sterilization & quality, packaging, tooling & dev.
· **Technical credibility**
  scalable, Proof of Principle, prototypes (larger scale)

What exact functionality is the specialist looking for?

Conclusions:
· Different procedures require different entry points, diameters, maneuverability, bend types (U-turn, Y-Junction, 90, 180 degrees, S-turn).
· Current procedures take too much time (= radiation to the patient and specialist)
· Too much exchange of different catheters/ guidewires
· Limited navigation control
· Current steerable microcatheters are either too large in diameter or too expensive.

Additional research:
· Literature study application exploration
· Interviews neuro, lung, oncology
· Witnessing operation theatre procedures

Explore bronchoscope application: lung model printed 10:1

THESIS PROJECT

Reconsider focus application:
· Converge application to tumor embolization
· Confirm Proof of potential benefits
· S-turn not desired for most embolization interventions, focus on making a small turn in confined space
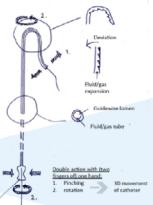
Take one step back to the Discover and Define phase for convergence of the application to focus on for the final design, and more exploration to the desired functionality of the product.

Design considerations:
· Simplify to 1 sharp turn in stead of S-turn for Proof of principle
· Bellow only at distal end
· Catheter grooves must be <30μm
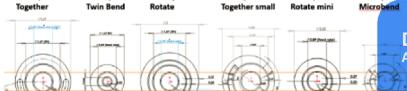· Required deflection up to 180°

SPECIALIST NEEDS
Access to small diameter tubular structures and hard to reach confined spaces, fast and with high precision

SPECIFIC CHALLENGE
· Single handed intuitive **control device**
· Apply material strength variations in **catheter** wall
· Realize expandable guidewire **lock mechanism** on small scale

By this time, the context was focused on endovascular procedures, but the potential was recognized to expand into multiple other medical disciplines in which minimally invasive devices are used (like endoscopes, brachitherapy devices) in the future.

diverge **converge**

CONTEXT

GENERAL CHALLENGE
A flexible, steerable endovascular catheter, increasing operation speed & enabling more difficult procedures

Convergence into a new design focus. This was the most theoretically patentable concept and would enable steerability in the smallest catheters:

Interventional Catheter Revolution

DESIGN FOCUS
Variations catheter stiffness and using core wire geometry to actuate the turn.

Pen-like handheld control device is developed, based on specialists preferences, to present to third parties.
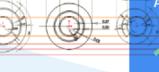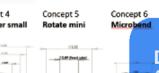
competitor: SwiftNINJA by Merit Medical

The first catheter concepts were explored to present to parties that might invest or contribute to the project. These were based on an idea of coincentrically extendable wires, decreasing in diameter. These concepts focused on making a double turn.

The initial idea had to do with a hydraulically actuated mechanism. However, the designers at Spark decided to explore more mechanical solutions.

Inspiration was acquired for the design about production methods, materials, and related technologies.

| Concept 1 Together | Concept 2 Twin Bend | Concept 3 Rotate | Concept 4 Together small | Concept 5 Rotate mini | Concept 6 Microbend |

Identify main design characteristics & Divide design into 3 parts (3 design challenges):

CONTROL DEVICE
CATHETER
BELLOW

The catheter is designed to make an S-turn, which means that the material weaker at 2 sides. Material studies and scalemodels (next page) are included in the exploration of this feature.

Catheter prototypes made by Veldlaser BV - explore different patterns

Prototype on 1:1 scale (Rubicon, cellebrity)

Specialists liked the idea but wanted an even smaller diameter. To realize this, the mechanism had to be placed on the smallest most inner guidewire, and then work from inside out.

DESIGN CHARACTERISTICS /patent
AS STARTING POINT FOR FURTHER DESIGN

1 The catheter wall has variations in stiffness in specific areas near the catheter tip.

2 Movable guidewire consists of core wire and mantle (hollow wire) When the core slides through the mantle, the displacement between the two activates a bulge or bellow at the tip.

3 When the bellow is deployed at the distal end of the catheter, axial compression creates tension in the catheter tip, causing it to bend predictable shapes (the path of least resistance).

4 The bendable part closest to the tip of the catheter can rotate independently about a longitudinal axis of the catheter.

· The tension in the catheter is caused by the core wire using friction.
· All functionality must take place inside the catheter.

First scale models and bellow ideas established + partial feasibility study

Exploration of different bellow concepts with feasibility study (See Appendix 5)

Choice made for most feasible concept to work out: rubber bellow

Additional exploration:
· flexible joints study
· lasered links for wire flexibility

rubber bellow concept

DELIVER

CONFIDENTIAL

**PROTOTYPING
USER TESTING**

IMPROVE AND OPTIMIZE FINAL PRODUCT

**TESTING
USER OBSERVATIONS & INTERVIEWS**

IMPLEMENT

2021

Serious interest from intervention radiology specialists

Support from third parties (Boston Scientific), new source of microcatheters to make prototypes from

Liver intervention phantom model

Future suggestions:
- more application possibilities
- towards whitepaper & CE certificaiton

THESIS PROJECT

strategic

How many times does the bellow need to be expanded?

Which microcatheter is preferred?

What type of deflection is required?

More collaboration with specialists gave new insights on the design:
- Use specialist's catheters of preference
- Proof of principle can be confirmed for the bellow and catheter separately

Design liver vasculature phantom model for technical validation of the catheter

- **Technical validation** of catheter (in phantom model) and bellow separately

- **Pig operation:** Test final prototype in clinical environment (catheter principle seperately with static bellow & catheter bellow combination)

Postponed to January 2021 due to Covid-19

(gives more time to optimize prototype & combine catheter and bellow PoP in one device)

USP
• Precise & fast navigation through vasculature
• Does not use wires in catheter wall
• Based on existing catheters (fast acceptance)
• Reduces frustration, trauma, and time
• Scalable product (+specializations)

SPECIFIC SOLUTION
Easysteer deflectable embolization microcatheter
• Laser modification on one side of the tip
• expandable rubber bellow at the distal end of the guidewire assembly
• intuitive control device with thumb wheel to deflect tip up to 180 degrees.

diverge

iterate

converge

control

Development of:
• A telescope mechanism (for movement guidewire without kinking)
• Control device (exploring different concepts)

Translate required movements in the mechanism to limits in the device

Future suggestions:
- Minimize tool
- Combine bellow expansion and catheter deflection in one device
- Allow for guidewire unlocking

THESIS PROJECT

Collect catheters from specialists and Boston Scientific to make prototypes from
· Catheter properties & dimensions influence modification design and bellow dimensions.

Prototype on 1:1 scale (Progreat, Direxion, Renegade)

Validation of catheter principle by specialist, with permanent "stopper" in stead of dynamic bellow.

Finalize prototype:
- predetermined curve, operator can vary between 0 to 180 degrees
- only the tip (15mm) bends
- application: embolization catheter
- choice of 3 modified catheters: Progreat (Terumo), Direxion 2.4F, Direxion 2.8F and Renegade (Boston Scientific)

by user confirmed

PoP

Future suggestions:
- Batch production of the most promising catheter
- Optimize curve design

catheter

Only a **single turn** in the distal end is required

• Functionality of the bellow can take place **in front of** to the catheter opening

scale models

Dynamic Rubber Bellow concept:
· Material study: to choose most suitable elastic material
· Feasibility study: FEA in ABAQUS to evaluate reaction forces and deformation during use
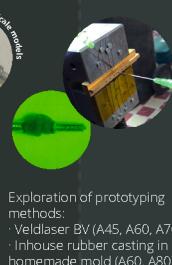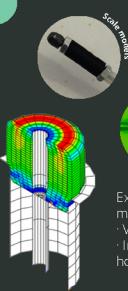
Mechanical test with the A60 material to get material properties for the FEA

Use bellow prototypes to validate FEA results

Finalize prototype:
· Optimize other components of assembly after positive ABAQUS results.
· In new prototype: boundary conditions similar to FEA
· Manual activation of the bellow for testing in a 10 cm setup

technical

PoP

Future suggestions:
- further design iterations following clinical test
- optimize production of the bellow
- Enable controlled expansion of the bellow in the device

Exploration of prototyping methods:
· Veldlaser BV (A45, A60, A70)
· Inhouse rubber casting in homemade mold (A60, A80)

bellow

development

A

APPENDIX 2

Clinical observations in the
operating theatre

A2.1 Knee artery embolization for knee arthrosis treatment

The first intervention that was attended in the Erasmus MC, concerned a knee arthrosis treatment. In this case, the intervention was part of a medical research in which placebo effects of different knee arthrosis treatments were studied. This means that a group of patients receives a real treatment, and the other group receives a fake treatment in which not even the skin is punctured. The real treatment involves the embolization of various side branches of the Popliteal artery in the knee. Patients do not know which group they are in and results of the treatments are compared. The patient observed received a real treatment, in which through a **sheath & microcatheter,** a **Terumo Progreat™** was advanced to the Poplitea artery in the knee (see figure A).
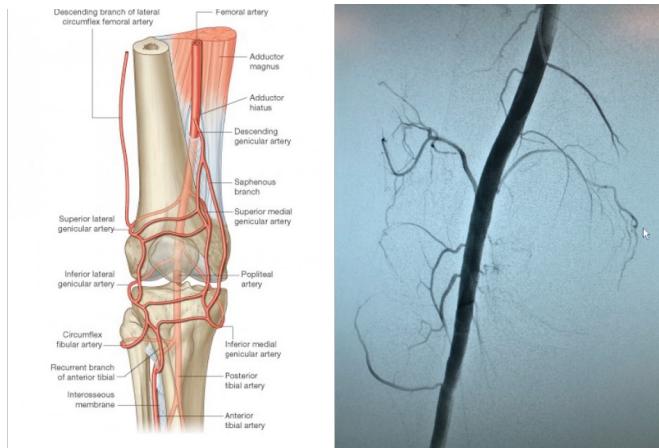
Figure A: Knee vascular anatomy (left), angiograph of poplietal artery with side branches (right).

The blood vessels in the knee are so thin, that a **1.8F microcatheter** was guided through the Progreat™. Multiple branches have to be selected in order for the catheter tip to reach vessels that have to be embolized. 75 μm particles are injected slowly to embolize. This has to be repeated a few times to be able to embolize all the intended blood vessels, only a few blood vessels are very difficult to reach or are extremely tortuous (figure B and C). Whenever a sharp turn has to be made, a **shapeable core wire** is used. Steam is used to soften the tip, and like curling a ribbon on a present, an injection needle is used to curl the wire tip. It is advanced through the catheter to try and make the turn. This has to be done 5 times. A 3D image shows that all the targeted blood vessels are embolized. Total time of operation was **1.5 hours**. More steerability of the instruments would have avoided the need for repeated manual tip shaping, reducing operation time.
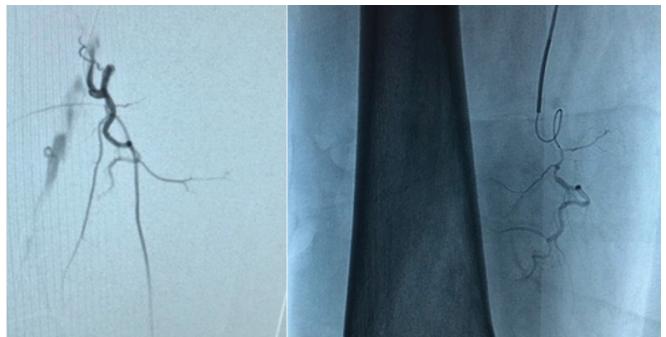
Figure B: highly tortuous side branches of the Poplitea artery.
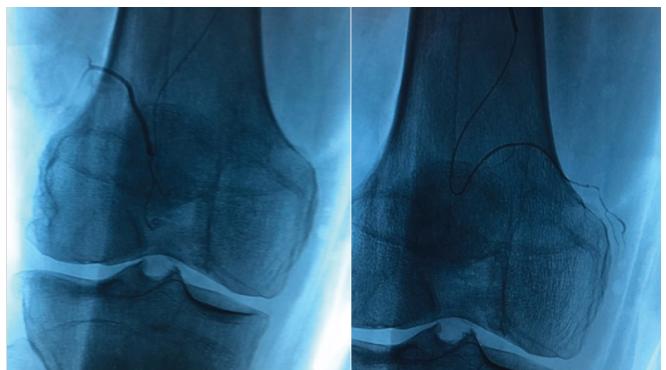
Figure C: Left and right acute angled side branches of Poplitea artery are both selected and embolized.

A2.2 TACE of a liver tumor

TACE stands for TransArterial Chemo-Embolization. The right femoral artery is accessed, through which a **Cordis 4F C2 angio catheter** is advanced. Through this catheter, a hydrophilic **Terumo guidewire** is advanced, which is a standard guidewire with a 45 degrees bent tip. The first sharp turn is when the celiac trunk branches off from the abdominal aorta (see Figure D, right). This artery goes slightly downwards, which causes the turn to be especially sharp when entering from the groin. If access were to be made from the wrist, the catheter would be advanced from above. Despite the sharp turn, it takes the interventionalist only 10 minutes to reach the truncus. At this point, an angiography is made to plan the route towards the tumor (Figure D, left). The trifurcation after the truncus causes the interventionalist to choose a path and the hepatic artery is first selected. A switch is made to a **Terumo Progreat™ 2.7F** which is advanced through the Cordis macrocatheter. When placed in the hepatic artery, the angiography shows a quite difficult route.

Figure D: Vascular anatomy towards liver, Source (right): Boston Scientific: Peripheral Vasculature, average vessel diameter chart (2015)
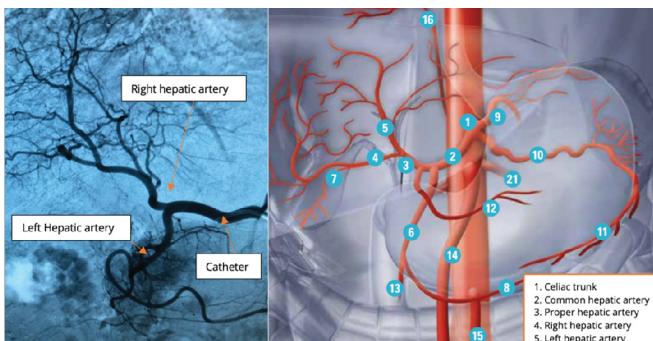
It is not yet visible where the tumor is exactly located. Therefore, various pathways are taken to explore which arteries lead to the tumor. The first side branch of the right hepatic artery is very difficult to enter, and the trial and error process takes over half an hour. When finally succeeded, a new angiograph shows more side branches which could all lead to the tumor. A 3D image is made to see more clearly from which artery the tumor can be reached. Even the gastric artery could provide access to the tumor. The process of finding the tumor supplying arteries almost takes an hour, in which different branches are catheterized and images are made from different angles. The patient's anatomy is slightly divergent from normal, and includes a 180 degree turn after which a complex bifurcation is located (figure E). A **PT graphix shapeable guidewire** is used to make the 180 degree turn in one of the blood vessels. Each time a different artery is selected, an angiography is made to see if the tumor is visible, however it is still not visible. This suggests that the tumor is not very vascular, and the interventionalist worries that the tumor can not be reached more closely than it is at that moment. After a quick consultation, it is decided to start embolizing from the location the catheter is placed now. This way, the tumor will most definitely be targeted, and the surrounding liver tissue that will also be embolized is small enough to be missed. Due to the complex route and unclear location of the tumor, the operation took **2:45 hours**.
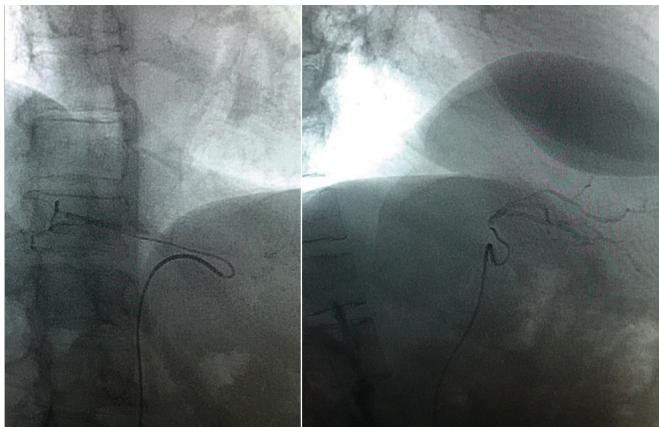
Figure E: 180 degree turn in the route towards tumor, from different angles of the 3D image.

A2.3 TACE of liver tumor 2

The pre-operative scan of this procedure showed that the hepatocarcinoma (liver tumor) can be reached from either the left or the right hepatic artery. In the truncus, there is a stenosis visible, so it is expected that this part of the route is difficult. Ultrasound is used to find the radial artery, and it is assessed whether it can be used as access point. Reasons for choosing radial access are preference of the interventionalist and it is considered favorable for the patient's recovery. Access is gained and the first **Terumo guidewire** is quickly advanced. Two different **catheters (4F/5F)** are used with pre-shaped tip, for the advancement through the aorta. Along the route to the liver, a few unclear obstacles are present. The guidewire has limited torque to get past some of the obstacles. It takes a few minutes to reach the liver (figure F).

Figure F: Angiographs visualizing the route in truncus (left) and in before the bifurcation of the left and right hepatic artery (right)

The guidewire is advanced a bit more and an angiograph is made to check whether it is the liver and not the kidney that is catheterized. It appears that the right hepatic artery is catheterized and the tumor of 44mm is visible on the images (Figure G). The catheter is advanced as close as possible, each time an angiograph is made to check whether they are still on the right route. The tumor supplying arteries are then embolized with a cocktail of chemoembolization (**Terumo Lifepearl 75 drug eluting microspheres)** particles, water and contrast agent.

Figure G: Tumor (left upper corner) visible on angiograph.

The cocktail is slowly injected and the tip of the catheter is watched closely to spot backflow of the embolization material. The embolization of the entire tumor goes in very controlled pulses, and takes about 15 minutes. When the flow starts to slow down and there is a backflow, it means that the tumor is filled, visible as a dark sphere in figure H (left).

Finally, the left hepatic artery is catheterized to check whether it supplies the tumor from this side as well. The tumor is however not visible in the angiograph (Figure H, right), which means that no extra embolization is needed. The entire procedure took **1:45 hours.**

In this intervention, the route towards the tumor was not very tortuous, and the guidewire could be successfully advanced through bifurcations. The only part in which the instruments were exchanced several times was in the in the beginning of the route, when some obstacles were encountered (presumably a light form of stenosis). The interventionalist got lucky and unintendedly catheterized the right artery, only using a few different guidewires with different tips. The interventionalist indicated that a lot of time could be saved if the entire route to the tumor could have been done with one all-round instrument.

Figure H: Tumor visible with contrast material (left), angiograph of left hepatic artery not visualizing the tumor (right).

A2.4 Aneurysm coiling Arteria Lienalis

Due to an earlier liver transplantation, this patient had a large aneurysm in the arterio lienalis (splenic artery). Due to the transplantation, the blood vessels in this area were fragile and slightly deformed. This aneurysm had a very tortuous shape and must be fully embolized for the blood supply to the spleen to be restored. The aneurysm is so large that the patient will lose part of her spleen.
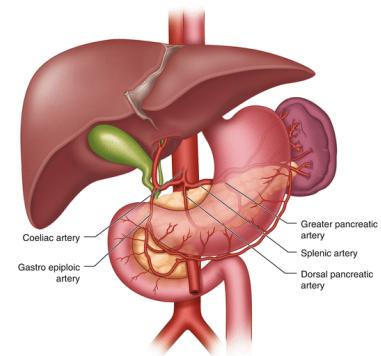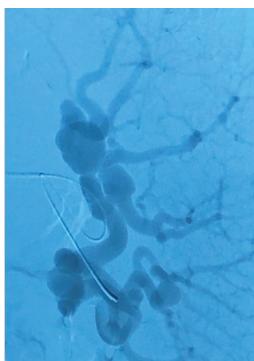
Figure I: Angiograph of large aneurysm (left), anatomical location of V. lienalis. Source: Varghese K., Adhyapak S. (2017) Splenic Artery Embolization for Non–surgical Splenectomy. In: Therapeutic Embolization. Springer, Cham. https://doi. org/10.1007/978–3–319–42494–1_5

Access is gained through the radial artery, and it takes about 20 seconds to place the sheath. This was painful for the patient, and some extra painkillers are injected in 40 seconds. A T**erumo guidewire with flexible tip** is advanced through a **4F catheter,** finds its way to the heart and descends through the abdominal aorta. A **new hydrophilic catheter** is advanced. In the lienalis, the guidewire has to make several extremely sharp turns and loops (see Figure I, left). The **Terumo guidewire** sometimes flips around due to all the turns made, and a **stiff variant of the Terumo guidewire** is required. When the guidewire finally reaches the aneurysm, a **microcatheter** is advanced over the guidewire for the coiling of the aneurysm. This one is 130cm long but is too short to reach the aneurysm due to all the turns that have to be made. Therefore, a **150cm 1.5F EV3 Marathon flow microcatheter** is suggested to be used, however, the coils will not fit through the 1.5F lumen. Therefore, the distal tip of the catheter (which is tapered to 1.5F) is cut off, so that the coils fit through the lumen. This took about 5 minutes. A **Cook Medical Tornado embolical microcoils** of 10mm/5mm are used, these are €100 each and 15 are needed to fill the aneurysm. These are injected into the catheter, and automatically curl up when they come out of the catheter tip. They are coated with Dacron which will cause the blood to clot and fill the space. There are no more Tornado coils, so the remaining part of the aneurysm is filled with **20mm detachable coils**. Steam from a water cooker is used to make them softer, which will result that they deploy in the aneurysm just like the other coils. An electric device is needed for them to detach. These are €400 each and 3 are used.

An angiogram is used to see if the aneurysm is completely filled (figure J, right). There is still contrast material flowing through
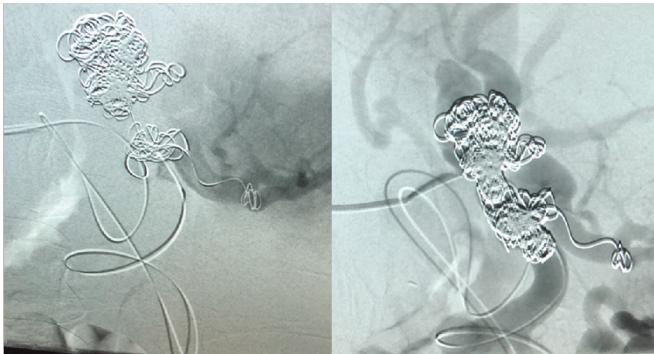
Figure J: Coils and catheter through tortuous route towards aneurysm are visible on angiograph (left), contrast material shows tha t aneurysm is not yet excluded from blood stream (right).

the aneurysm although slower than before, which means that a large part of the aneurysm is filled, but additional embolization is required. It is estimated that if the whole aneurysm is going to be embolized, at least half of the spleen is going to die down. When the whole spleen becomes inactive, this would be troubling for the patient's immune system. Furthermore, dying of the spleen can be very painful. A choice is made to embolize a little bit more, but not too much. For this embolization step medical glue is used. First, the **catheter (150mm Progreat™)** is pre-loaded with glucose (as this won't react with the glue), after which the glue is injected. When this glue is combined with blood, it immediately solidifies. It is important that the catheter tip is immediately retracted to avoid it getting stuck to the glue.
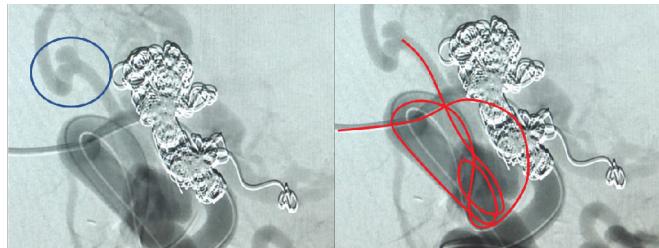
Figure K: Last part of the aneurysm that should be embolized (left) and the micro-catheter pathway to reach it (right).

After checking the embolization with an angiograph, the interventionalist notes that there is a small part of the aneurysm that is not yet embolized (Figure K, left). The route to this location is extremely complex (See figure K, right), and takes about 20 minutes using different CT overlay roadmaps. Around 10 coils are needed (smaller size than used previously), and the procedure is finished. A third of the spleen is spared and the angiograph (Figure L) shows successful exclusion of the aneurysm from the blood stream. The whole operation took **2:20 hours.**

This intervention did not present difficult bifurcations, but an extremely tortuous pathway. For this type of challenge, a steerable micro-catheter would be useful that has a lot of torque and pushability to make several consecutive turns. The interventionalist suggests that it would be a useful function if the catheter tip could be locked in a

certain position, to avoid flipping around in complex turns.
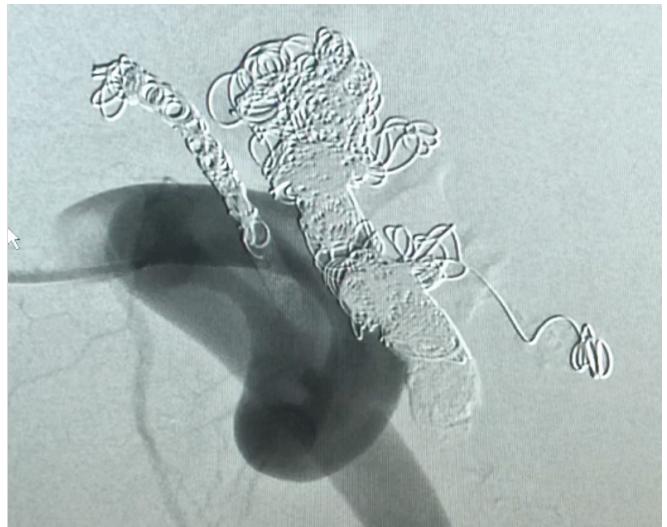
Figure L: Aneurysm is excluded from the bloodstream in the Arteria

A2.5 Reopening common iliac artery bifurcation

The patient had erection problems and pain in his left bottom. This suggests that the blood supply is hindered in that area.

For *part 1* of the intervention, A **Boston Scientific Imager II angiographic 6F catheter** with a 180 degrees bent tip is inserted in the right groin and a sheath is placed. This takes 10 seconds. The 180 degree turn in the catheter tip causes the contrast material to be injected in the opposite direction. This is needed because the catheter (with guidewire) is guided via the right iliac artery to the abdominal aorta, and an angiograph is then made from the iliac arteries (see figure M). A narrowing of the artery is visible at the bifurcation of the right iliac artery to the internal iliac (left in the image), and the left internal iliac seems totally obstructed (right in the image).

Figure M: Angiograph of iliac arteries

A choice is made to creat a new access point in the left groin. From this direction, it is easier to access the right internal iliac, because less sharp turns have to be made. A **Cordis 4F UF catheter** is used. The angiograph suggests that the left side might be beyond salvation. Therefore, the right iliac artery is first treated with a dottering technique. This will presumably relief the complaints in the left bottom of the patient. The first challenge that is encountered during this procedure is when the catheter tip needs to be turned into the iliac artery. The guidewire succeeds but the catheter tip is not stiff enough. A switch is made to another catheter, and the combination of concentrically used equipment now consists of a **6F guiding catheter (Cobra, Boston scientific, 90 degrees bent tip), a 4F catheter, a 2F micro-catheter, a 0.014" guidewire.** After trying for a few minutes, the tip of the microcatheter finally enters the iliac artery. This is achieved by putting the bent tip of the catheter against the blood vessel wall, and slowly pulling it back until it automatically finds its way into the orifice of the iliac artery. A roadmap overlay is now used to guide towards the internal iliac artery. A **PtCA NC emerge monorail balloon catheter (5mm x 15mm)** is used (a monorail means that the guidewire enters the catheter halfway, which makes switching tools easier) to dilate the stenosis in the bifurcation. This is visible in Figure N.

Figure N: Balloon (left), guided to the stenosis at the bifurcation of the internal iliac artery (right)

A vessel analysis (figure O) is performed which calculates the required dilation of the stenosis to restore original anatomical dimensions. The balloon successfully dilates the stenosis from 4 to 6mm.
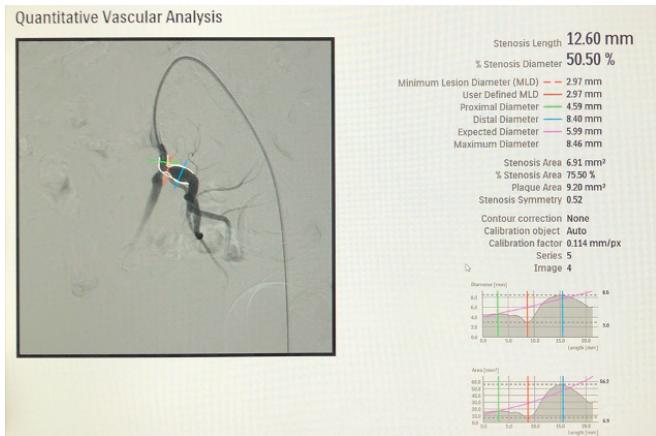
Figure O: Quantative vascular analysis used to calculate required dilation of the stenosis.

Part 2: The interventionalist decides to make an attempt to also restore the left iliac artery. This is expected to be difficult, because the left internal iliac artery is completely obstructed. The human body can close off such a side branch of a blood vessel completely so that the closed orifice flushes with the vessel wall of the parent vessel. This makes it a challenge to find the orifice, but it does show a small dent, called a "cul de sac". Via the sheath in the right groin that was placed initially, a catheter is guided to the obstruction, and placed in this cul de sac, (see Figure P)

Figure P: Catheter tip placed in "cul de sac" indicating the orifice of stenotic artery.

Puncturing the obstruction is difficult, therefore the guidewire must be guided subintimally across the lesion. This means that it punctures the blood vessel wall, creates a lumen inside the wall through which it can pass the obstruction, after which it can enter the blood vessel lumen again. The interventionalist notes that this action can also benefit from a steerable tip, for steering the tip in and out of the vessel wall. A **0.014" stiff guidewire** is advanced through the new lumen, and a **thin balloon (20mm long, 2mm diameter) catheter** is advanced through the **Cobra catheter** and used to dilate the lumen. To support this thin catheter, an extra **"support catheter"** is added to the assembly of equipment. The balloon catheter has trouble following the guidewire's path through the subintimal space. After trying for 10 minutes, an extra **0.014" guidewire** is inserted and the "buddy-wire" technique is applied to the situation. The new guidewire is placed next to the other guidewire in the subintimal space. The first balloon catheter is retracted, and a new **balloon catheter (Boston Scientific, 2mm diameter, 2.4F distal tip, monorail)** is advanced over the buddy wire. The balloon finally crosses the obstruction and is able to dilate it, pushing the stenosis out of the way. Caused by this action, a small rupture of the blood vessel happens (visible in figure Q, left). The patient does not feel pain from which can be concluded that the small bleeding is not dangerous.

After dilating the vessel, there is still 50% stenosis, which is dilated with a **longer balloon (4mm diameter)** on a **80cm sterling catheter.** In image Q (right), the balloon is made visible with contrast material. Attention must be paid to not further tear the small rupture during this dilation, and a catheter that is generally used to stop these kinds of ruptures is prepared for use when needed. The stenosis is successfully reopened, beyond all expectations of the team! The whole operation took **2 hours.**
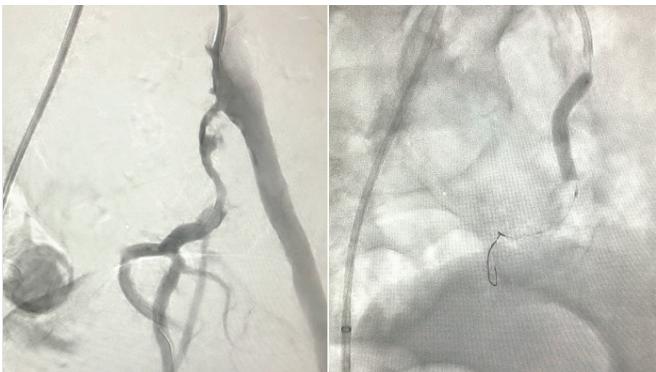
Figure Q: Small rupture visible as small bubble right after the bifurcation, caused by the first balloon dilation (left), and further dilation with larger balloon (right).

A2.6 Reopening obstructed penis arteries due to fracture

The patient has had erection problems since a penis fracture. This means that penis arteries can be obstructed to hinder blood flow. Under local anaesthesia, the right femoral artery is accessed and a sheath is placed. A **5F angiographic catheter** with a bent tip is used and guided to the abdominal aorta (just like in intervention 5). The angiograph shows two steep iliac arteries, which is common for young patients.
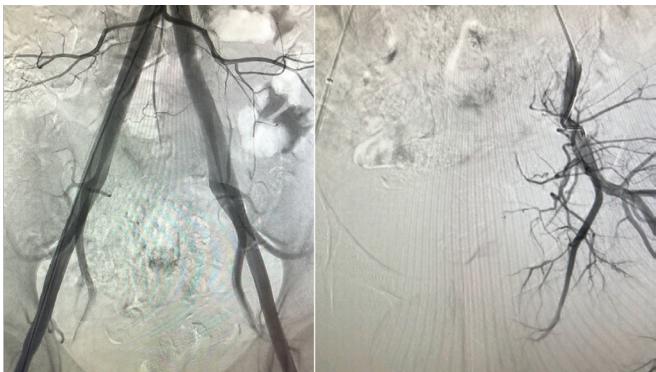
Figure R: Iliac arteries, catheter advanced trough right iliac artery (left side on image) (left), Catheter advanced from the right iliac artery into the left internal iliac artery, angiograph showing route to penis arteries.

This makes catheterization more difficult than in anatomy of older patients. A **4F catheter** is inserted towards the left internal iliac artery. A switch is made to a **stiffer catheter** to make the sharp turn to the pudendal artery. This stiff catheter has a bent tip, which is favorable for making the sharp turn. When access is gained (after half an hour into the intervention), a switch is made to a **Terumo Progreat™ microcatheter**. New angiographic images show the way to the penis arteries. A **pilot 50 guidewire** is used to penetrate the occluded parts of the dorsalis penis artery. This pushing of the guidewire was enough to revascularize the vessel (See figure S, left). The

other obstructed arteries (not sure which) are attempted to revascularize with the Progreat™ catheter. It is however not clear which route has to be taken to reach the obstructed artery. Different routes are followed, but the obstructed artery cannot be accessed. This process takes about half an hour.
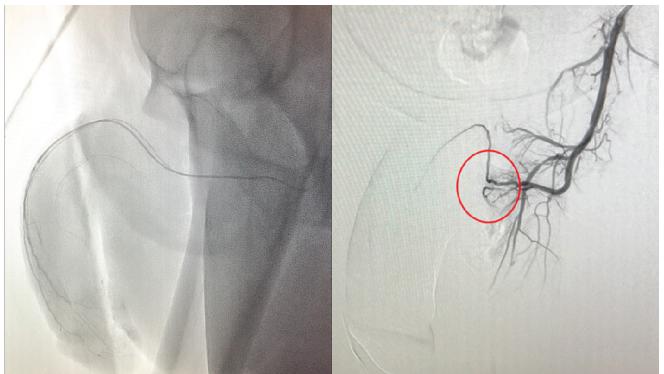
Figure S: Revascularization of dorsal penis artery (left), strange anatomy of other penis arteries (right)

The anatomy also shows a strange turn (see figure S, right). Added to this, because the bloodflow is very slow during the intervention, it is not clear where the contrast material goes. The interventionalist decides to leave this obstruction as it is. Because the right side is completely reopened, it is expected that everything will recover to normal. When blood flow is increased again in the penis, this will presumably also reopen the other vessels. The entire intervention took **1,5 hours**, cost 2mGY of radiation and 25 fluororadiation minutes.

A

APPENDIX 3

Rubicon™ catheter modification
& user test with Dr. M.

A3.1 Rubicon™ modification & test

For this user test, a Rubicon™ catheter (2.4F) with grooves of 30 μm (modified according to figure D & E(left) is tested by specialist Dr. M. Since only the proof of principle of the catheter modification is tested (and not yet the bellow mechanism) a guidewire is used with a permanent knot in the distal end as bellow solution for this test.

OBSERVATIONS
- The bending radius of the deflection looked large when observed in the air, however, when placed in a tubular structure (representing a blood vessel), the deflected tip was shaped by the surrounding structure into a smaller and more realistic bending radius.
- Using this assembly in a mimiced bifurcation of 110 degrees, the catheter tip succeeded in making the turn (see figure A).
- The bending angle was increased step by step, and the tip experienced difficulties in catheterizing the 120 degree turn (figure B). This was caused by a part of the guidewire that was sticking out distal to the knot, which was adding a straight geometry to the deflected tip.
- After cutting off this straight geometry from the guidewire, the 120 degree turn succeeded (figure C)

INSIGHTS
- The design requirement of minimizing the material distal to the working mechanism of the bellow is confirmed by this test.
- Dr. M. emphasizes that the static bellow is not atraumatic enough in this assembly.
- A functionality is discussed that allows the tip to bend in two directions: by locking the bellow mechanism in the distal cahteter tip, and pushing the guidewire in stead of pulling it, the tip will be pushed in the opposite direction of the grooves. This is however considered not a necessary attribute. Dr. M. feels more confidence in axially turning the catheter when deflections in other directions are required. Another consideration to reject this functionality is that the grooves will be stretched out and particles might pass through. This insight stimulates reconsideration of the bellow design.
- In general, the 30 μm grooves seem small enough, especially because most used chemoembolization particles are around 75 μm. It is also expected that the particles will not get a chance to escape through the grooves because of the speed in which they are injected.
- This is a first step towards PoP of the catheter (figure F, G), however more flexible catheters must be prototyped and tested.
- A suitable test environment should be developed in order to test different bifurcation angles.

A3.2 The control device

The control device used for this test was the one with an axial rotation wheel. Dr. M.'s opinions on the control device are listed below:
- Dr. M. likes the axial wheel, but would like to compare this with other actuation movements. For the next user tests, multiple control devices are required to be able to assess what works best.
- Size is not too large and bulky, not too small.
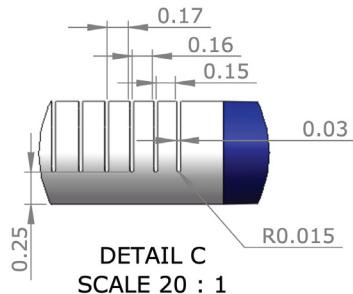
DETAIL C
SCALE 20 : 1

Figure D: Detail drawing of laser modification (30 μm)

Figure E: Microscope images of the modified catheter tip with 30 μm (left), 50 μm (middle) and 150 μm (right) grooves.
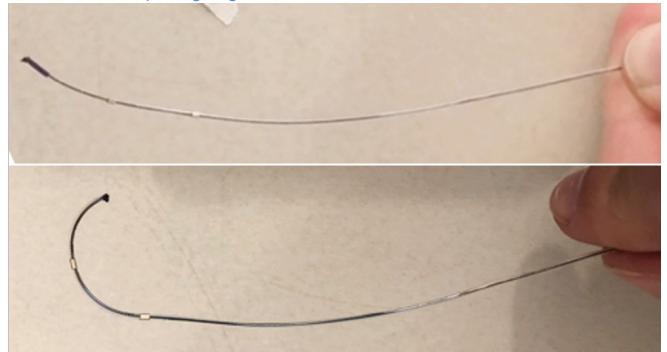
Figure F: Proof of principle for modified Rubicon™ tip, applying tension (with stiff guidewire with permanent bellow) and comparing deflection in unmodified tip (top) vs modified tip (bottom)
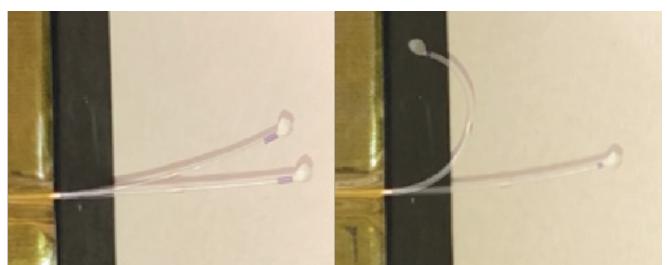
Figure G: Same test comparing deflection in unmodified tip (left) vs modified tip (right), but with guidewire with lower stiffness (Asahi 0.015 wire), to see whether this influences the deflection. Pulling force 5N.

Figure A: 90 degree turn not succeeded due to knot sticking out distally

Figure B: ±110 degree turn succeeded after cutting off part that was "sticking out"

Figure C: Left and right acute angled side branches of Poplitea artery are both selected and embolized.

A
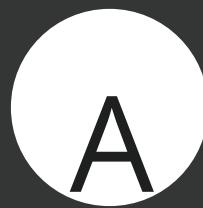
APPENDIX 4

Modification of the Terumo
Progreat™, Boston Scientific
Direxion™ 2.4F and 2.8F, Boston
Scientific Renegade™

A4.1 Progreat™ modification

The Progreat™ microcatheter is known amongst a lot of interventionalradiologists as "workhorse", being used in most of the procedures. It is also one of Dr. M's devices of preference, and with the user testing in mind, it would be best to use this catheter to make the prototypes from. It offers flexibility in the tip, but is also sufficiently torqueable due to a Tungsten coil that is incorporated in the catheter wall along the entire length of the catheter. This is visible in figure A. Its compatible guidewire has a bent tip with a radiopaque gold coil in it.

Figure C: Progreat™ catheter in relaxed state (left) vs. under tension (middle), showing resulting deformation of the flexible part of the catheter, rather than only the modified tip. Progreat™ under tension in tubular structure (right)
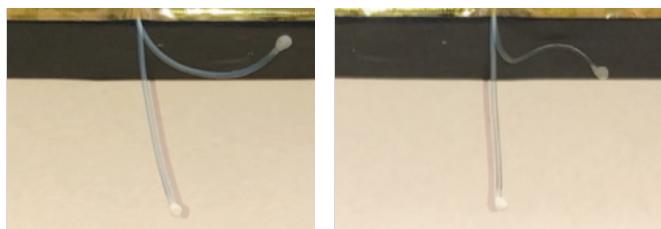
Figure D: Unmodified Progreat™ vs modified Progreat™ tip under 0.5N tension

Figure A: Progreat™ design with Tungsten coil and curved tip guidewire.

Unfortunately, testing the modified Progreat™ catheter showed unexpected results. The distal 20cm of the catheter have more flexibility than the rest of the catheter. Under tension, this whole flexible end tends to deform, rather than only the modified tip (Figure C). This has consequences during use as the deformed shape will touch the blood vessel walls in various places and exert force on it (figure C, right). It is also visible from figure D that the catheter already allows a deflection of 120 degrees when only the last 25mm is allowed to deflect. The modified tip (right) shows that the modification does not increase the curve made. It rather results in a 3D spiral shaped curve, that is generally not what is desired. It is argued that the difference in stiffness between the tip and the rest of the catheter should be larger in order to concentrate the deflection in the tip only. There are two ways to accomplish this in the next prototypes:

· Cut the flexible 20cm off: This part of the Progreat™ might just have too much flexibility of its own, which accounts for the deflection of that whole section. Modification will have a larger im pact when the rest of the catheter is relatively stiff.

PROTOTYPE 1

The results of this prototype are visible in figure F. In the last 15mm of the catheter (that is cut off to the stiffer part) is modified.
The modification successfully concentrates the deflection in the tip of the catheter, however, the deflection is still a spiraling shape in 3D in stead of 2D (see figure F).

Figure F: new Progreat™ 1, flexible 20cm of the catheter cut off and modified. Resulting curve with 0.5N pulling force (right). Guidewire used is a compatible guidewire of 0.021", with a "permanent bellow" made of 2Component-glue.

PROTOTYPE 2

For this prototype, an extreme option is explored: in the last 15mm all the material between the coil in 3x 4mm is burnt away on one side. (up to half the diameter of the catheter). Figure G shows that this prototype is absolutely not workable, and proves that there is a limit to the amount of removed material in this catheter.
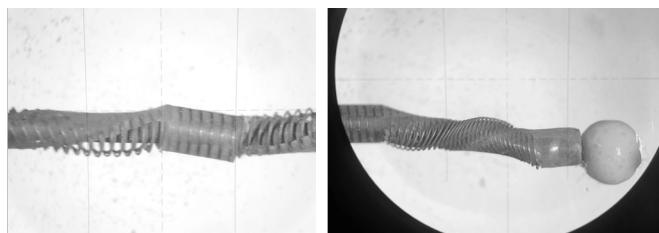

Figure G: new Progreat™ 2, 3x 4mm of removed material up to half of the diameter (left). 0.5N pulling force resulted in compression of the tip in stead of a curve. Guidewire used is a compatible guidewire of 0.021", with a "permanent bellow" made of 2Component–glue.

A4.2 Renegade™ modification

Boston Scientific's Renegade™ (figure H) is modified according to the calculated required material reduction to make a 180 degree deflection.
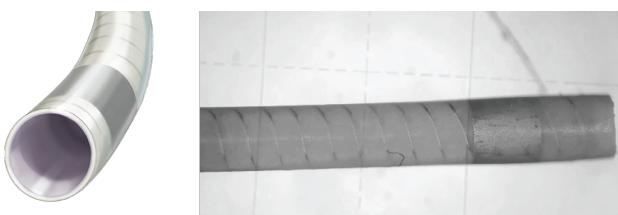
Figure H: Renegade™ with coil & marker.

A4.3 Direxion™ 2.4F modification

Boston Scientific's Direxion™ 2.4F (figure J) is modified in the last 18mm according to the calculated required material reduction to make a 180 degree deflection, resulting in 84 grooves of 30µm (chosen to not let particles pass through). Depth of the grooves is 2/3 diameter of the catheter.

Figure J: Direxion™ 2.4F with purple tip & itegrated marker (thickening, right).
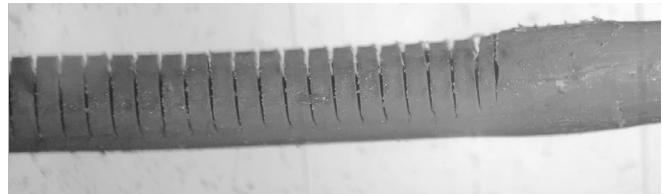
Figure K: Modified Direxion™ 2.4F with grooves up to marker

A4.4 Direxion™ 2.8F modification

Boston Scientific's Direxion™ 2.8F (figure L) is modified in the last 18mm according to the calculated required material reduction, which is 98 equally spaced grooves of 30µm for a 180 degree deflection. Groove depth is 2/3 diameter.

Figure L: Direxion™ 2.8F with yellow tip & itegrated marker (thickening, right).
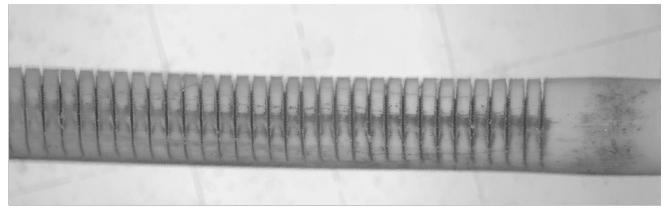
Figure M: Modified Direxion™ 2.8F with grooves up to marker.

A
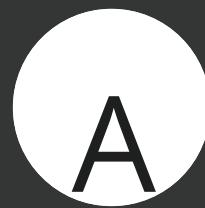
APPENDIX 5

Further explanation on different bellow concepts

A5.1 Bellow concepts elaboration

Concept A, which is the "hinge" concept, is quickly considered unfeasible, because the manufacturing of such small hinges is impossible on such a small scale (0.5mm diameter). A simplified alternative of this concept made of elastic material, resulted in a tube with a lateral hole in it, creating two thinner geometries that can bulge outward under compression. Concequently, concept C was born: an elastic tube with lateral slits, creating multiple thin geometries that can bulge outward (figure A). A conclusion was however drawn that this geometry will be atraumatic as it includes opening and closing parts. Concept C was therefore simplified into concept D, which is chosen as final concept in this report (figure B).
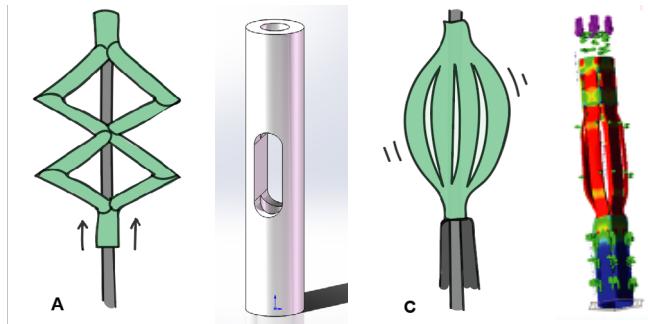
Figure A: development of concept A and C.
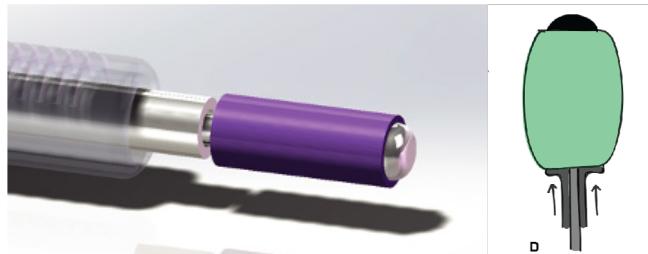
Figure B: Simplification of concept C resulted in concept D.

The feasibility of concept D was criticized because of its unknown required material properties to achieve enough expansion, and the possibility of not being able to control this expansion precisely enough.

The manufacturing of this shape out of rubber is however expected to be difficult on such a small scale.

Figure D: Concept G, Twisting lock (middle, source: https://nl.aliexpress.com/item/32357489032.html), twisting lock in tube (right, source: https://www.youtube.com/watch?v=yhztWHQiJeA)

Concept G was based on a twisting lock (figure D), however, this also requires extra modification of the catheter tip, which is the reason it is considered not optimal.

Figure E: Concept F, thicknut mechanism with multiple spikes (left, top), simplified version with only 2 spikes (left, bottom), SolidWorks model (middle)

Concept F, the thicknut mechanism, can be executed in different forms. One way is to pull a geometry into a "crown" shaped geometry, pushing the "spikes" of the crown outward (E, left). The other way is to push a geometry out of the "crown" to push out its spikes (E, right). To deactivate the expansion, the pushing/pulling motion should be reversed. This concept is not feasible due to difficult manufacturing and not being able to exert much pushing force with the thin inner cable.

Concept E is considered relatively easy to produce. A first prototype is therefore made and evaluated. It is made of diagonally cutting off injection needles and place them opposite of each other on the inner cable. Upon compression, the diagonal faces will make the two components (wedges) slide outward. This mechanism might even make it possible to be expanded inside the catheter wall. However, it is very traumatic due to the sharp corners and is therefore not developed further.
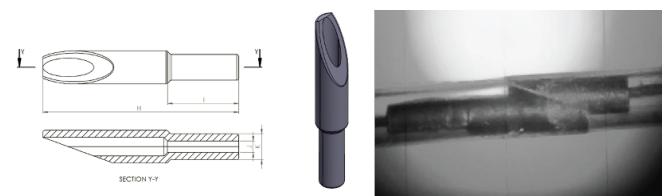

Figure F: Concept E prototype.

A

APPENDIX 6

Material study to choose most
suitable material for Bellow
component

A6.1 Introduction

This Material study describes the selection process of the most suitable material for the expandable bellow. A list of important requirements for the bellow to work properly is the starting point of this study.

REQUIREMENTS
- Material must allow radial expansion larger than catheter diameter, during axial compression with a compression force smaller than 12N (based on the limits of the assembly)
- Expanded/pre-stressed bellow must hold forces from the catheter wall up to 2N, and not be plastically deformed by this force.
- When compression is released, the bellow should return to original shape, meaning that there is no remaining plastic or elastic deformation visible
- The successful expanding and releasing of the bellow must be allowed by the material at least 5 times.
- The material should be resistant to chemotherapeutic agents.
- The material should be resistant to sterilization temperatures.

A6.2 Methods

1) CES EDUPACK MATERIAL EXPLORATION
The bellow is expected to return to the original shape when compressing forces are released. Any extra mechanisms for this inactivation are not desired, therefore the material needs to be elastic, and have a relatively low Young's modulus. Furthermore, based on the small diameter and proneness to relatively high forces (causing the bellow to break easily), the material needs to have a high tensile strength. But more importantly, the yield strength, the elastic limit, must be relatively high. Plotting the two important parameters Young's modulus and Yield strength against each other, a selection of materials emerges in the field of Rubbers. From these materials, predictions should be made about the usability and availability, and some materials can be eliminated due to additional selection criteria.

2) HANDS ON RUBBER EVALUATION - SCALEMODELS
Rubber is a variously adapted material, however also a complex one. Its behavior is not always easy to predict. This is due to the different types of rubber composites that exist. Rubber variations are mainly expressed by their Shore A hardness value ranging from 0 to 100. A rubber's hardness can be estimated by indenting the rubber sample with a barometer. For example, natural rubber has a shore value of A39, rubber bands have a shore of A20, harder rubbers, applied in shopping cart wheels (A95) or are often filled with solid fillers to improve hardness. These harder rubbers are also referred to with a Shore D value. (See image A) Given material properties like stiffness and compressive modulus for example are going to tell us more about the behavior of the material during use, but are highly specific for all rubbers. Therefore, some hands on rubber exploration is necessary. The material choice will affect the precise behavior of the bellow during compression. Softer materials will presumably roll up like a sleeve whereas stiffer elastic materials will bulge outward. Different shore values are therefore evaluated to find a correlation between the Shore value and the deformation under compression. The materials that remain from the CES selection are evaluated on

their hardness (Shore value). To achieve this, scalemodels are made of a few rubber variations ("soft", "medium" and "hard"). General insights are collected about the behavior, for example, which materials were too soft or hard, and what influence the shore value has on the type of deformation.
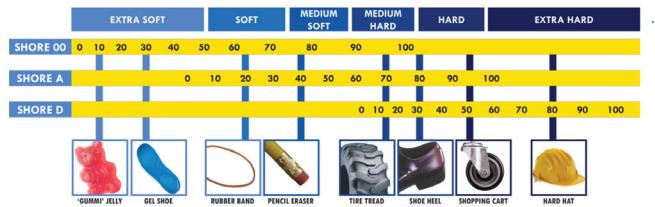
is taped right next to the sample. The sample is slowly extended, pulling the spring balance. At the exact moment the sample is extended to 1.5x its original size, the force on the spring balance is observed. With a simple calculation, the average Young's modulus can be calculated. This experiment ignores the fact that elastomers have a nonlinear stress-strain relationship, but it gives a useful indication of the elasticity of the material.

4) EVALUATION ON PRODUCIBILITY
The amount of variations of elastomer materials does not help choosing the most suitable one. Therefore, another property of the selected samples is explored: their machinability. For this application, it is of great importance that the material can be manufactured into a part with small dimensions. This experiment helps decide in which range of Shore values production of the bellow is viable. Two production method are explored: 1) Outsourced laser processing, in which samples with various Shore values are evaluated on their feasibility for laser processing into tiny bellows, and 2) Inhouse rubber casting, in which two shore values of rubber are cast into a homemade mold.

A6.3 Results

1) CES EDUPACK MATERIAL EXPLORATION
Regarding the requirements and the envisioned function of our bellow, a few parameters were used as selection criteria:
- Young's modulus: max. 50MPa
- Yield strength: min. 10Mpa

the following CES graph shows us that we are limited to the elastomer category, as expected since we need a particular amount of elasticity. 47 materials pass these criteria, mainly thermosets, but also thermoplastic elastomers. Even two polymers pass: flexible PVC shore A60 and shore A65.
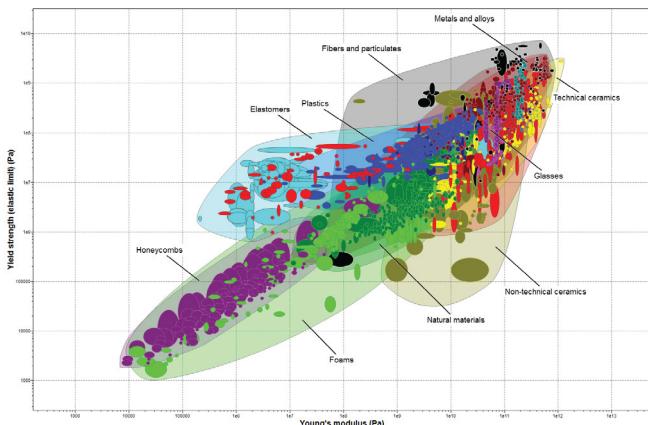
Figure B: CES graph, all materials, Young's modulus vs Yield strength. Source: CES Edupack

Further research on the selected materials support the choice for a rubber: Rubber materials are commonly experienced with a large elastic strain and deformation with small volume change. This means that the material is nearly incompressible. Compression will make the bellow deform in the direction of the open space instead, which is a suitable characteristic for our application. Furthermore, the production process of rubber includes a process called vulcanization, which gives them unique material properties. It creates strong crosslinks that account for the highly elastic behavior of rubbers.[Gent et al. 2012] These crosslinks mainly determine tensile, elongation and compression properties. Although rubbers can be very elastic and soft, they have high strength under shear and compressive deformation. All these properties make them suitable for many engineering applications, such as seals, damping components, shock absorbers and load bearing parts. It is also extensively used in the medical industry, due to its chemical and heat resistance. The amount of selected materials from CES is quite large and further selection is preferred.

2) HANDS ON RUBBER EVALUATION - SCALEMODELS

10:1 scalemodels were made with the available material to create an assembly with the dimension ratio's as close as possible to the concept. Bike gear cables were used as guidewire and mantle, the bellow was made out of hollow rubber tubes, and rubber cables. The latter were provided with a drilled hole to make it a hollow cylinder. The elastomer materials evaluated in these scalemodels were a "soft" (estimated around A40), two "medium" (estimated around A40-A60) and a "hard" (estimated around A60 - A80) rubber. The results are shown in figure C:

A simple system was created to apply the same axial compression to all the bellows, see figure D. The "guidewire" runs through two opposite holes in the arms of a clip. On one side (left in the figure), a stopper is screwed onto the wire. When opening the clamp, the two arms push this stopper and the mantle in opposite directions. This movement creates an axial compression in the bellow, the black part on the other end of the guidewire.

The difference between the "medium" rubber assemblies is their geometry. In figure C.b, there was space between the bellow and

the gui-dewire. This causes the bellow to use that open space to coil up. For the predictability of the movement of the bellow, it is preferred that this effect does not happen. The other three bellows' geometry are more in line with the concept's geometry, and expand more uniformly. The "hard" bellow in figure C.d does not show any deformation at all. Both "soft" and "medium 2" rubber show the desired deformation. Figure E shows the measurement of the expansion of the "soft" bellow under axial compression, which is from 4mm to 6mm in diameter.
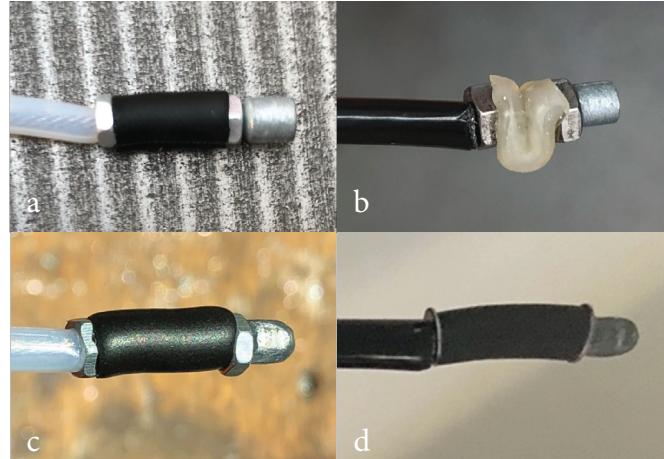

Figure C: a) "Soft" rubber compression, b) "Medium 1" rubber compression, c) "Medium 2" rubber compresson, d) "hard" rubber compression

3) TENSILE TEST WITH RUBBER SAMPLE SELECTION

To get a little bit more hands on feeling of the different rubber types that are available for prototyping, rubber samples are collected from different manufacturers. A selection was made to include a broad variety of Shore values (ranging from A35 - A70) and compositions (Foamrubber, Silicone rubber, Natural rubber, Nitril/NBR, EPDM, CR Neoprene, SBR). In Table I, there is a table in which the rubber samples are visible, their Shore value (provided or estimated with a durometer), E-modulus (an estimation based on the tensile test), Tensile strength (if provided) and remarks that led to the final selection of rubbers to try for prototyping.
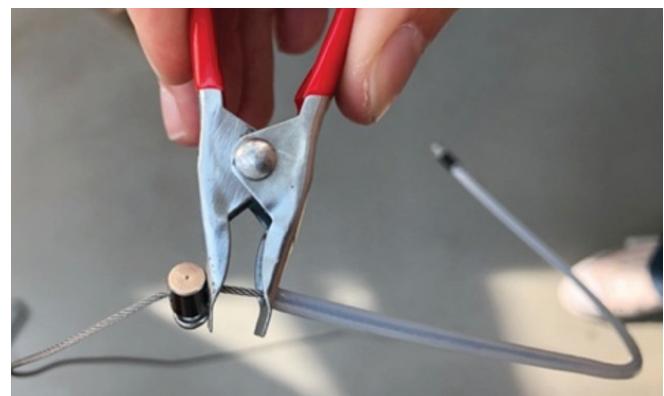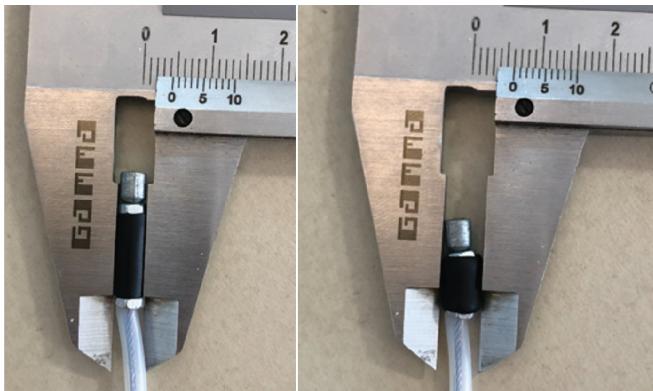

Figure D: Bellow Comression system for scale models

Figure E: Measurement of lateral expansion in result of axial compression of the "soft" rubber scalemodel

	Material (retrieved)	Shore A (estimated with durometer)	E-modulus (estimated average)	Tensile strength (if known)	Remarks
1	Foamrubber black (Unknown)	35	0.3018		Shore too low
2	Silicon Rubber anti vibration plug for PC fan black (Directkabels.nl)	±40	0.8564		Seems flexible & strong
3	Silicone rubber (Unknown)	45	1.2074		
4	Silicone rubber red (Snijlab.nl)	45	1.308		Soft silicone, 2mm thick
5	Para natural rubber brown (Rubbermagazijn.nl)	45	1.5696	20 Mpa	Soft silicone, 1mm thick
6	Silicone rubber black (Snijlab.nl)	±60	2.289		1 mm thick
7	Silicone rubber transparent (Snijlab.nl)	±60	1.962		1 mm thick
8	Nitril (NBR) white (Rubbermagazijn.nl)	60	2.0928	5 Mpa	Feels brittle
9	Silicone rubber red (Rubbermagazijn.nl)	60	3.924	6,5 Mpa	Feels strong and flexible
10	EPDM/SBR black (Rubbermagazijn.nl)	65	3.1065	5 MPa	Too hard
11	CR Neopreen black (Rubbermagazijn.nl)	65	3.7278	5 Mpa	Too hard
12	SBR black (Rubbermagazijn.nl)	70	6.54	5 MPa	Chosen to confirm hypothesis that hard rubber is not suitable

Table I: Evaluated Rubber samples and their known/estimated parameters

4) EVALUATION ON PRODUCIBILITY

I. Laser processing

Materials of different shore values are chosen to be tested on their producability. From table V, Material 2 (A40), 4 (A45), 5 (A45), 9 (A60) and 12 (A70) are prototyped. Only the softer materials (2, 4 and 5) turned out suitable for this production method. The higher shore values were too brittle and the result was a broken bellow (figure F.a) The results of the softer materials are shown in figures F.b, F.c, F.d, all assemblied with a guidewire with stopper and mantle. Furthermore, two steel rings are visible that are added for when the bellows are tested on compression/deformation. Nevertheless, the produced bellows are very fragile and do not allow any tolerance which causes challenges for the production. Another problem with this production method is that the bellows have to be stringed on the guidewire, which is a challenging job. Also, it allows for space between the bellow increasing the risk of rolling up and expand in random directions. Therefore, another production method is explored.
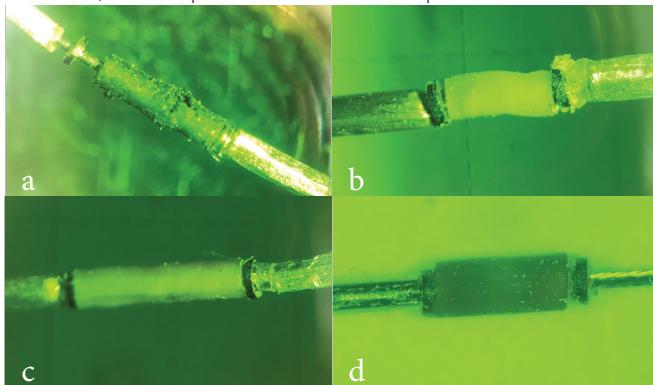
Figure F: a) lasered bellow from SBR A70, b) lasered bellow from natural rubber A4, c) lasered bellow from silicone rubber A45 d) lasered bellow from PC vent plug A40 (Directkabels.nl)

II. Rubber casting

Two castable rubbers are ordered to evaluate. A brass mold is designed and machined. See images G and H. The setup is quite tricky: The 0.15mm wires have to be perfectly aligned and positioned in the middle of the channels, as in figure I. The material can be injected

an injection needle and syringe into one side of the mold. Simultaneously, the chamber that is to be filled by the material can be sucked vacuum with a syringe through a side hole (figure J) Once the material starts to show inside the syringe, it is confirmed that the chamber is full and the bellow can be cured (in 48 hours). Before the bellows are pulled out, the mold is put in the freezer to let them shrink a little. The mold is designed to cast the rubber around the guidewire, minimizing challenges for the assembly. This also minimizes the space between the bellow and the guidewire, which positively influences the behavior and strength of the bellow. Therefore, this production method is preferred over laser processing. It also allows for more simultaneous bellow production, and in customized sizes. Figure K.a shows what comes out of the mold. The large piece of rubber has to be cut off and a bellow remains. The Polyurethane with a shore value of A60 turned out a very suitable material to cast bellows from in this mold (figure K.b), and the bellows were easily pushed out. The Polyurethane A80 was castable but very challenging to get out of the mold, which had damaged the part. (figure K.c). This material is considered too brittle and stiff, and difficult to cast.
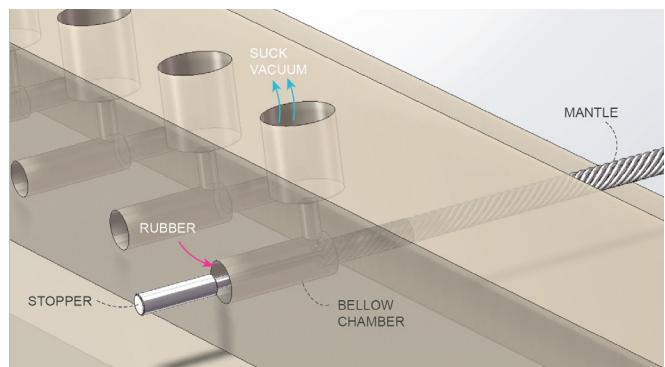

Figure G: Drawing of brass mold with guidewire assembly placed inside the chamber for Rubber casting
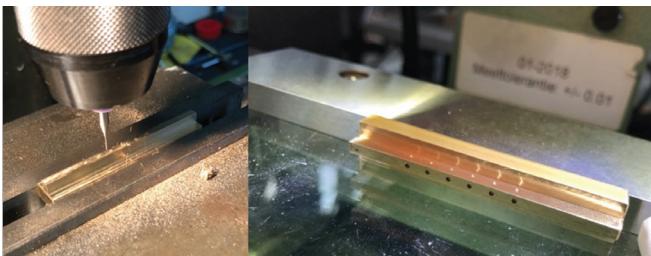
Figure H: Machining of the mold (milling and drilling small holes with diffe–rent diameters)

Figure I: Aligning the wires inside the chambers of the mold

Figure J: Injecting the chambers with rubber while sucking the chamber vacuum

6.4 Conclusion

A few conclusions can be drawn form this material exploration phase.
A) The CES Edupack material study validated the choice to focus on elastomers for the bellow, rubbers in particular, based on their known chemical and mechanical properties that are advantageous for this application.
B) The scalemodels gave insight into the deformation of different rubber Shore values. The diameter of the "soft" rubber increased uniformly, which is desired. Softer material will allow easier defor-mation but is also more prone to plastic deformation. Unfortunately, the "soft" bellow is made from a Computer air vent plug from China, of which the material properties are not known. Nevertheless, it is expected that this material will be too fragile for the envisioned use. This exploration suggests that a Shore value of at least A45 is rea-listic. Furthermore, what can be concluded from this test is that the space between the bellow and the guidewire needs to be minimized.
C) Tensile tests led to a smaller selection of materials, based on the need for a relatively low Young's modulus. Five materials were chosen to produce bellows from.
D)Rubber casting is a preferred production method over laser pro-
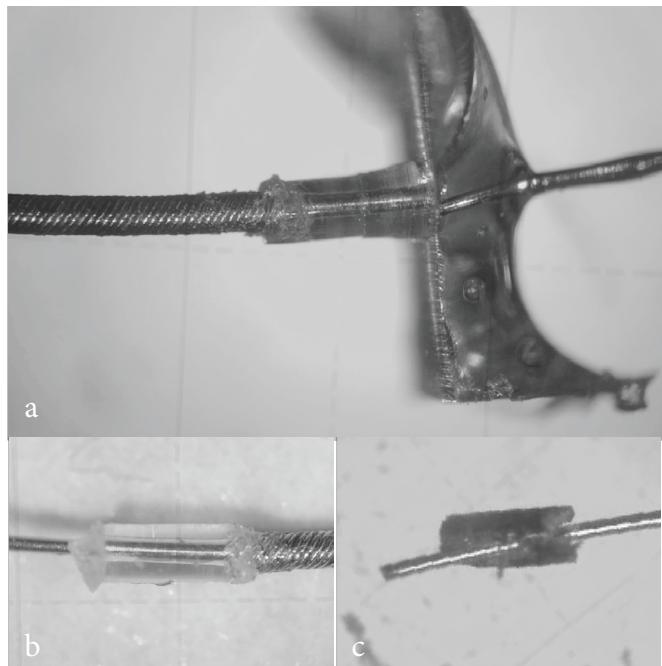
Figure K: a) Rubber bellow around guidewire when pushed out of the mold, b) Rubber A60 bellow, c) Rubber A80 bellow

cessing. It assures minimized space between bellow and guidewire, reduces assembly challenges and allows for accurate and custo-mized bellow production. PolyUrethane rubber A60 is chosen based on the knowledge that it is one of the rubber types that is widely used already in the medical field. Examples of this are implantable devices, which include PU rubbers due to their toughness, durability, biocompatibility and improved biostability. It is also chosen because it has a relatively high Shore value, that is not too high to deform or to prototype, and not too low to become fragile.

6.5 Discussion

This material study is limited by some factors. Only a certain collec-tion of rubber samples was available for the tensile test, and for the laser machining production. Another set of rubbers was available in castable form. Therefore not all the possible rubber types are tested. Furthermore, not all materials from the CES selection were evaluated, and some convergence decisions in the selection procedure were influenced by availability of material for further evaluation.
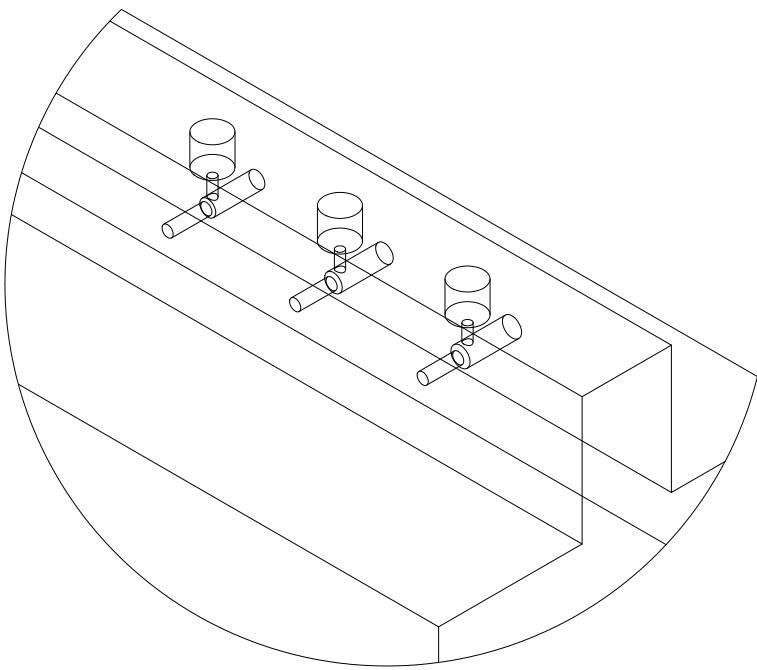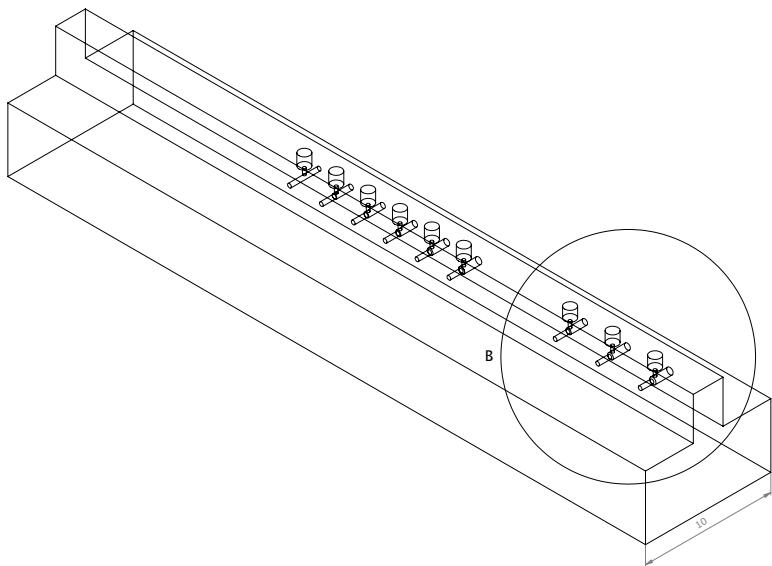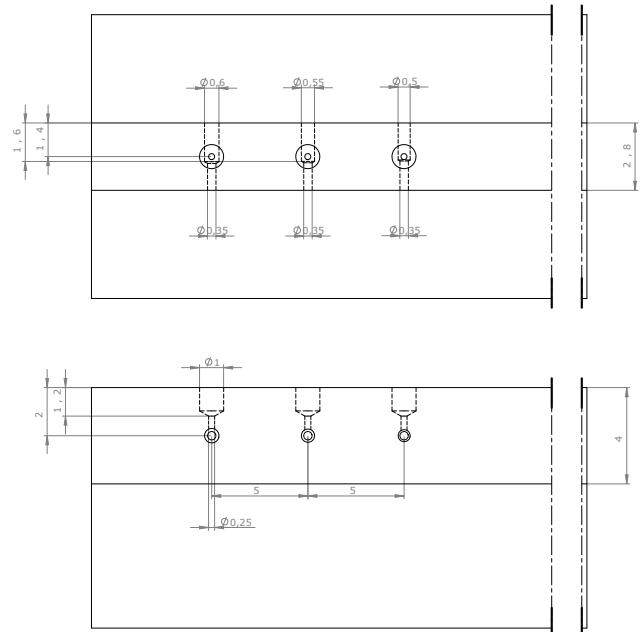
The scalemodels were used to demonstrate the compression, but they are not put under the amount of force that is proportional to the forces in a 1:1 scale prototype. Some materials might work on a large scale, but the foam rubber for example will definitely be too fragile in small dimensions.

Silicon rubber might also be a suitable material, due to its tempera-ture resistance and suitability for medical applications, but was not available to prototype with A60 hardness. Therefore it is not evalu-ated further, however this might be interesting for future research.

A

APPENDIX 7

Technical drawing mold for
bellow prototyping

10

B

DETAIL
B SCALE

Ø0,6   Ø0,55   Ø0,5

1,6
1,4

2,8

Ø0,35   Ø0,35   Ø0,35

Ø1

1,2
2

4

5   5

Ø0,25

A

APPENDIX 8

First evaluation of catheter
prototypes in test

A7.1 Test Setup

The first simplified validation model is tested with several catheters by Dr. M. The four successfully modified catheters were manipulated into various bending angles inside the artery phantom model. Also, the Rubicon catheter was tested as reference catheter with higher stiffness. This is done to see whether the stiffness of the catheter influences the navigation through difficult turns. The artery phantom model is positioned on a table, and can be rotated and presented to the user according to the desired entrance artery.
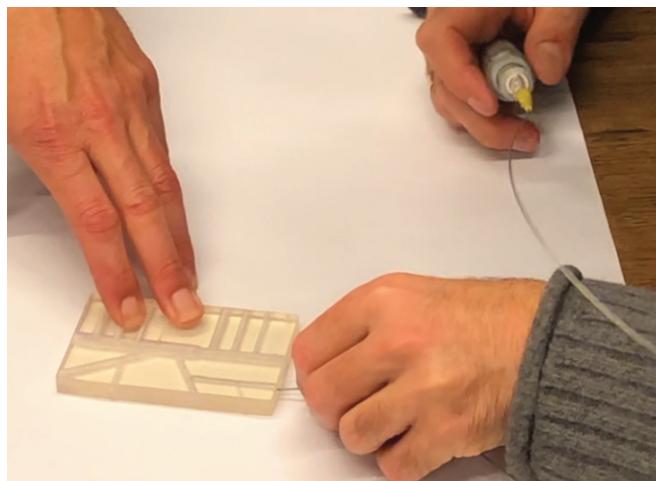
Figure A: Dr M. testing with the first phantom model

A7.2 Methods

The user holds the control device in one hand (for this test it does not matter which control device is used), and the catheter tip in the other hand. Various routes are followed with different catheters, the time is recorded and the user is asked to evaluate the ease of use, the amount of steerability and overall functionality of the catheter tip. On these factors, all catheters are compared and a catheter of preference is chosen.

A7.3 Results

Due to the limited time with Dr. M., and too many possibilities of routes, not all possible routes could be tested with each individual catheter. The acquired results of the test are displayed in Table 1 and 2. For each catheter the time was measured that was needed to complete the single turns (Table 1) and double turns (Table 2).
- Bifurcations of 150 degrees were impossible for all catheters, and 90 and 60 degree angles were "easy".
- Some navigation steps took longer than others. This is presumably caused by the friction in the model, and the hardness of the "artery" material.

Bending angle [degrees]	90			60		120		150
Vessel diameter [mm]	6→4	6→3	6→2	8→3	2→3	6→4	2→3	8→4
Progreat	0-5 s	0-5 s	10 s	0-5 s			x	x
Renegade	0.5 s	0-5 s	0-5 s	10 s		15 s		x
Direxion 2.4	0-5 s	0-5 s	10 s		30 s	0-5 s	x	x
Direxion 2.8	0-5 s	0-5 s	x	0-5 s			x	x
Rubicon		0-5 s	0-5 s	0-5 s		x	40 s	x

Table 1: Time measured of navigating through single turns.

Bending angle [degrees]	Route 1 30 + 90	Route 2 90 + 30	Route 3 60 + 60	Route 4 90 + 90	Route 5 120 + 60
Vessel diameter [mm]	4→8→6 →2	3→6→ 8→4	8→3 →2	2→6→ 4	6→4→ 3
Progreat		35 s	x		
Renegade					20 s
Direxion 2.4	40 s			10 s	x
Direxion 2.8					
Rubicon			80 s		

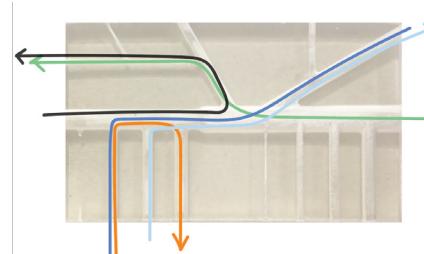Table 2: Time measured of navigating through double turns.

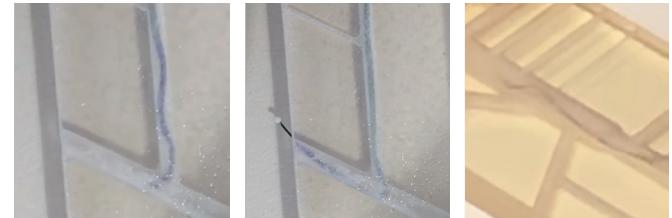Figure B: Routes measured, the colors corresponding with the route colors in table 2.

Figure C: Difficulties in trackability of Direxion™ inside sharp turn (left and middle), Spiral shaped Progreat™ inside too large diameter (right)

A7.4 Conclusions

- Difficult advancement of the catheter was often due to friction of the rough "arterys". Pushing the cahteter through sometimes causes the catheter shaft in the wrong direction, opposite of the turn (figure C, middle)
- When a sharp turn is not easily made, the catheter tip tends to spiral up inside the artery where it is coming from (Figure C, left).
- The spiral shaped deflection of the Progreat™ was a problem in the larger diameter "arteries"
- The "static bellow" is slightly larger than the catheter diameter, possibly responsible for the difficult navigation in small vessels.
- In this set up, the user holds and manipulates the catheter right in front of the validation model. In reality, there is of course a distance between the Common Hepatic artery and the radial or femoral access point of the intervention.
- These factors should be reevaluated for the next user test.

A

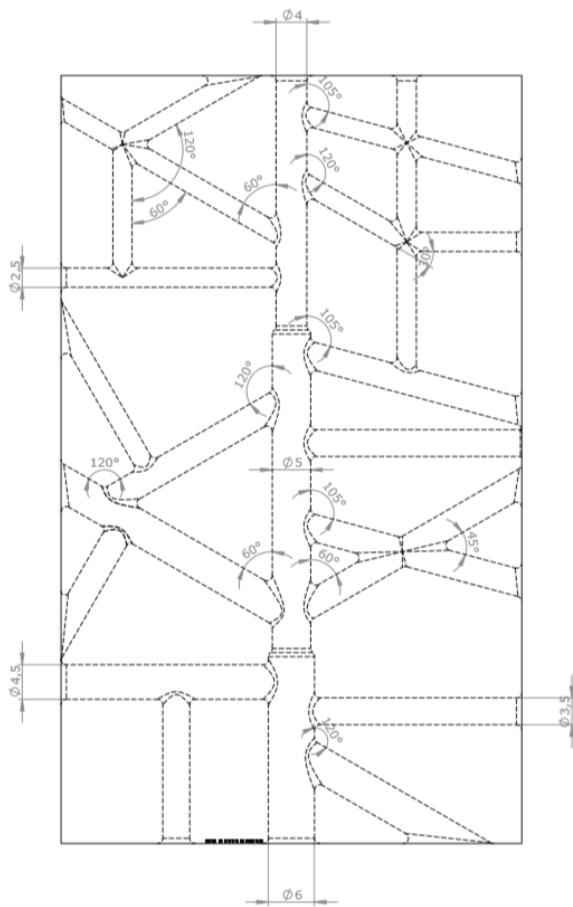# APPENDIX 9

Design of phantom model for
technical validation

Figure A: Geometry of phantom artery model.

Artery	Diameter	No. in figure
Celiac Trunk	6-8 mm	1
Common Hepatic Artery	5-7 mm	2
Proper Hepatic Artery	4-6 mm	3
Right Hepatic Artery	3-5 mm	4
Left Hepatic Artery	3-5 mm	5
Gastroduodenal Artery	4-6 mm	6
Cystic Artery	1-2 mm	7
Right Gastroepiploic Artery	2-4 mm	8
Left Gastric Artery	2-4 mm	9
Splenic Artery	5-8 mm	10
Left Gastroepiploic Artery	2-4 mm	11
Right Gastric Artery	2-4 mm	12
Superior Pancreaticoduodenal Artery	2-4 mm	13
Superior Mesenteric Artery	6-8 mm	14
Renal Artery	5-7 mm	21

Table 1: Artery diameters of the arteries in Hepatic, Gastro–Intestinal and Splenic vasculature [Source: Boston Scientific: Peripheral Vasculature, average artery diameter chart (2015)]
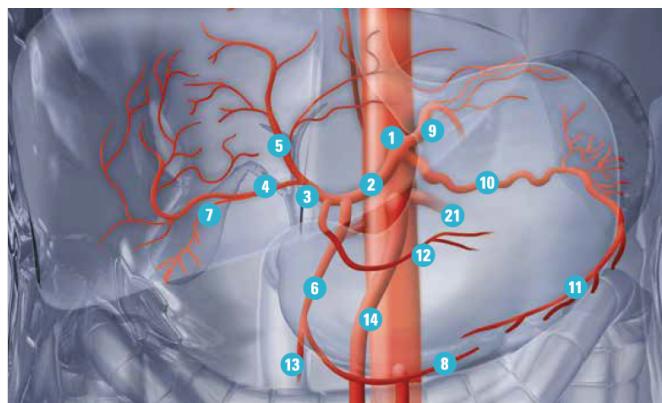

Figure B: Illustration supporting Table A1 [Source: Boston Scientific: Peripheral Vasculature, average artery diameter chart (2015)]

A7.1 Artery diameters

Based on the known artery diameters of the liver, this model is created to represent realistic, but also worst case scenario routes towards a potential liver tumor. In Table 1, the arteries involved in this segment are highlighted blue. Assuming that the Easysteer is especially required from the Common Hepatic Artery and further, the middle artery in the model represents the pathway from Common to Proper hepatic artery (therefore 6, 5 and 4 mm in diameter)

From there, the side branches generally become smaller, the more distally located. Therefore, the sidebranches in the model are generalized to three diameter sizes: 4.5 mm, 3.5 mm, and 2.5 mm.

A7.1 Bifurcation angles

It is difficult to generalize the angles of the artery bifurcations, as these are very patient specific, and each situation presents different challenges. One challenge might be a very sharp angle in a medium sized vessel, the other might be a sequence of bifurcations in different directions, the other might be due to a large difference in diameter of a side branch and its mother branch. During the specialist interviews, it was suggested that realistic bifurcations can ask for a turn of the catheter up to 120 degrees. This is therefore set as highest bifurcation angle. Four angles are chosen representing four levels of difficulty during catheterization: 90, 60, 105 and 120 degrees. To further increase the difficulty of the route for the user test, multiple turns with different angles and different diameters should be possible in the model. These requirements resulted in the geometry visualized in figure A. In the user test, the route for the catheter will always start at the mid bottom channel (the Common Hepatic Artery). Multiple routes can be followed identify the catheter's limitations. The higher up in the model, the smaller the diameters and the sharper the angles.

APPENDIX 10

User test final prototype
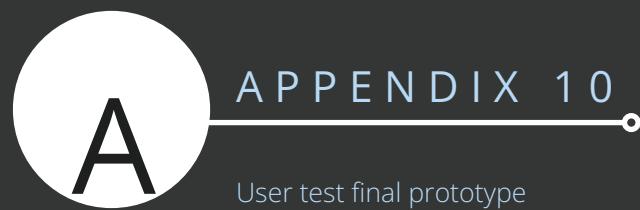
A10.1 Test setup

The goal of this experiment is to validate the working principle of the modified catheters (apart from the bellow). The experiment is performed by a skilled specialist in a set up that is similar to the real situation in the operating room.

This experiment's set up mimicks a liver intervention in a simplified form. A phantom model is made on a 1:1 scale of a 2D human torso, its arm stretched out, just like a patient is prepared for a radial access operation. The choice for radial access is made based on the specialist's preference. Furthermore, he and other specialists had indicated that more and more procedures are done via radial access. A simplified artery network of plastic tubes is attached to a wooden torso board, representing the radial artery, the abdominal aorta, and the truncus split-off to the hepatic artery. This hepatic artery ended in the orifice of the vascular phantom model from *Appendix 9*. This phantom model represents a liver, with generalized liver artery bifurcation angles and vessel diameters, and was placed at the location of the liver with Velcro.
A "macro-catheter", represented by another plastic tube, was prepared from the radial location to the hepatic artery, based on the knowledge that macro-catheters are always used for the first part of the navigation. A microcatheter is then guided through this macrocatheter to perform the rest of the navigation distal to the hepatic artery. Both the macro-catheter tube and the phantom model were pre-loaded with water, to stimulate smooth advancement of the catheters, and that the navigation of the instruments was not going to be hindered by potential friction inside the fake blood vessels. With this setup, the route towards the liver was prepared as close to reality as possible.

A10.2 Monitoring

As visible in figure A, monitoring of the experiment is done with multiple camera's. Camera 1 provided a live image of the liver phantom model, representing the image techniques used in the operating room. This assists the user to guide the instruments in the right direction (figure B). The other camera was pointed towards the user, to monitor the movements of his hands while operating the catheters (figure C). Both images are recorded post-experimental analysis.

10.3 Test Protocol

Dr. M. is asked to use each catheter prototype, including the guidewire with static bellow (made of a drop of 2-component glue). He is asked to treat the catheters as he would normally do, and to first guide them towards the liver. Once the catheter tip arrived in the liver, Dr. M. is asked to take several turns, making use of the deflecting functionality of the catheter tip. The liver phantom model provides many possibilities of combinations of bending angles and diameters. The goal is to try a few single turns, and some double or triple (consecutive) turns, and identify the limits of the device. Each turn taken is observed, documented and timed. Furthermore, the user is asked for his opinion on the operation of the device, and all control devices are evaluated and compared.
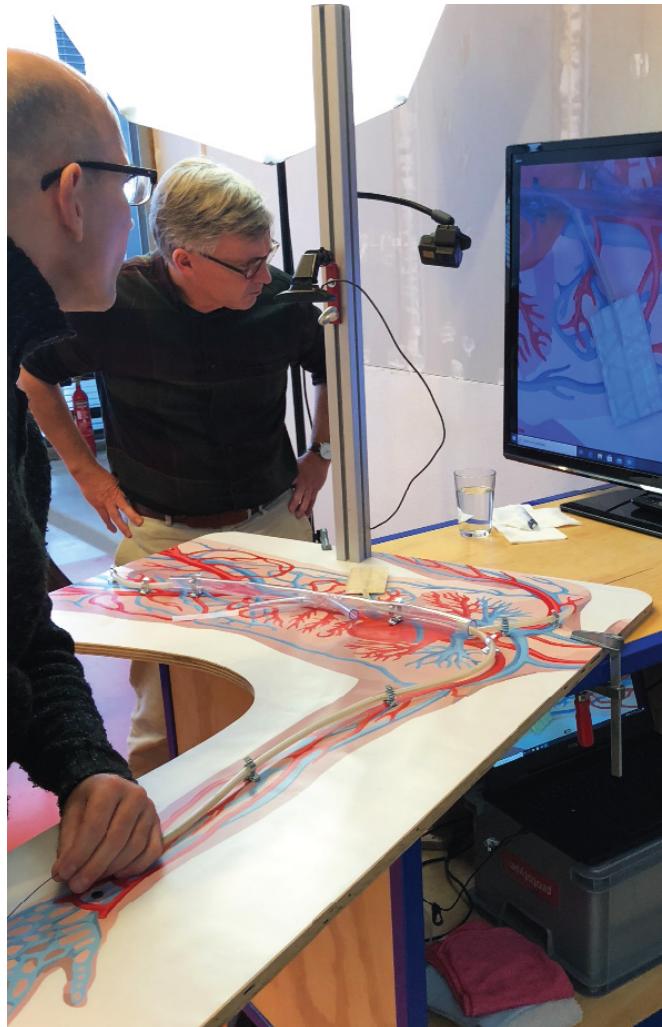

Figure A: Test setup, Dr. M inserting a catheter via the radial access point into the liver phantom model, while watching the live close up image on a screen.
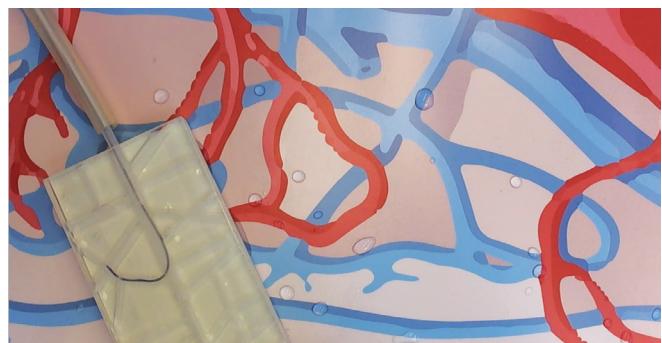

Figure B: Camera 1, live image on large screen, to mimick image techniques during the operation. Recorded for post–experimental analysis as well.
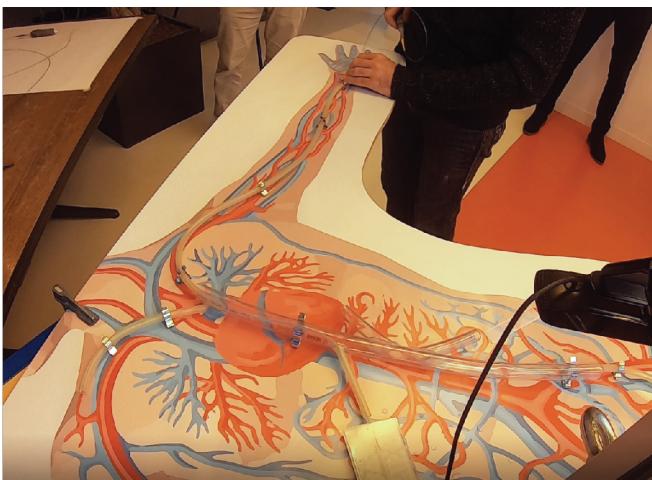
A10.3 Results

The documentation of the results is visible in Table 1. Because the specific routes taken are randomized, it is difficult to generalize the results. The opinion of Dr. M. is prioritized. For example, he did not like the use of the Progreat. Therefore more tests are done with the Direxion 2.8F. To emphasize the most impressive results, the times under 5 seconds are highlighted in green, the most sharp turns are highlighted in blue, and the turns that took longer than 10 seconds, or failed, are highlighted in red. The most important takeaways from this study are mainly based on the opinion of the user, to confirm the added value of the product comparing it to his experience. These results are presented in Chapter 6.

Table 1 (below): All the turns made in the vessel phantom model, per catheter, measuring the diameter of the vessel it comes from, the diameter of the vessel it is advanced in, the angle of required deflection, and the time it takes to take the turn.

Catheter	Units measured	Single #1	Single #2	Single #3	Double turn		Single #4	Single #5	Single #6	Remarks
Renegade	Øfrom [mm]	6	5	5	5	4,5	4	4	5	Dr. M. prefers using the catheter/guidewire without control device. He misses some torque in the catheter
	Øto [mm]	3,5	3,5	3,5	4,5	3,5	2,5	2,5	3,5	
	∠ [°]	60	90	120	60	120	120	105	120	
	T [min.sec]	0.07	0.07	0.13	0.06	0.08	0.03	0.03	0.06	

Catheter	Units measured	Single #1	Single #2	Triple turn			Remarks
Direxion 2.4F	Øfrom [mm]	6	6	5	3,5	6	At some point the phantom blood vessels feel a little rough, more water is injected in the system.
	Øto [mm]	4,5	3,5	3,5	4,5	3,5	
	∠ [°]	60	60	120	120	90	
	T [min.sec]	0.04	0.03	0.10	1.00	0.03	

Catheter	Units measured	Single #1	Single #2	Triple turn			Double turn		Double turn		Double turn		Remarks
Direxion 2.8F	Øfrom [mm]	5	6	5	3,5	4,5	6	3,5	4	2,5	4	2,5	The tip of the catheter seems slightly over-loaded / weakened after injecting water in the catheter to reduce friction in the system. After the last turn, the tip is damaged
	Øto [mm]	3,5	4,5	3,5	4,5	4,5	3,5	3,5	2,5	2,5	2,5	2,5	
	∠ [°]	120	60	120	120	120	60	135	120	60	120	120	
	T [min.sec]	0.04	0.03	0.03	0.03	0.06	0.03	X	0.03	0.08	0.03	X	

Catheter	Units measured	Single #1	Remarks
Progreat	Øfrom [mm]	5	After one successful turn, Dr. M quickly concludes that this catheter does not feel good and is not able to make the required turns due to the spiraled deflection.
	Øto [mm]	3,5	
	∠ [°]	120	
	T [min.sec]	0.04	

A
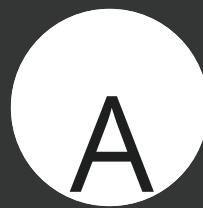
APPENDIX 11

Technical test bellow - Proof of principle

A11.1 Test setup

For the proof of principle for the bellow, a simplified test set up is created for the final bellow assembly to be tested. The goal of this experiment is to validate the results from the FEA, and proof the essence of the bellow concept. The test set up is chosen to be a simplified version, meaning it is only 10cm long and includes part of an unmodified catheter. The reason for this is that potential stretch of the guidewire and mantle used might influence the controllability of bellow compression. For the proof of principle it is not needed to test with a modified catheter, because it can be simply tested whether the tip can be put under the required tension. Force gauges are used to measure the compression force needed, and to increase the pulling force with which the expanded can be pulled against the catheter wall to 0.5N. This is the force required for deflection of the tip.

A11.2 Assembly

The assembly consisted of a 0.15 guidewire with a welded 0.30 stopper geometry at the end. Over the guidewire, the bellow was placed with the two conical rings enclosing it on both sides.
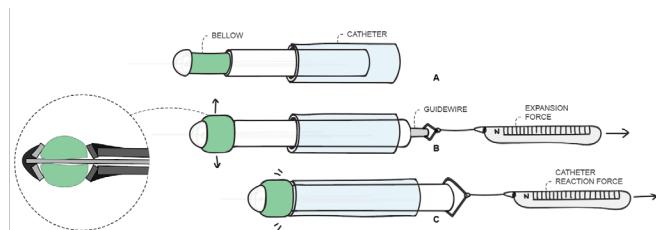
Figure A: 10cm Test setup for bellow proof of principle.

The production technique of the bellows is quite challenging. The guidewires have to be placed manually and the bellows must be pulled out of the mold with great care. The bellows of 0.55 mm diameter that came out of the mold most successfully, were compared in order to choose one bellow for the final assembly. The rings were produced in diameter sizes 0.56, 0.58, 0.6 and 0.62 mm, after which they were punched in a conical shape, a process that slightly reduced the diameter.

A11.3 Methods

The guidewire assembly (with un-expanded bellow) is first guided through a piece of catheter that fits the dimensions of the bellow, and it is evaluated whether it can be advanced smoothly without significant friction. This confirms that the dimensions of all the components are smaller than the catheter lumen.

The setup allowed for controlled compression of the bellow, by holding the mantle in place and pulling only the guidewire. After this, the bellow could be locked in expanded position with a locking tool.
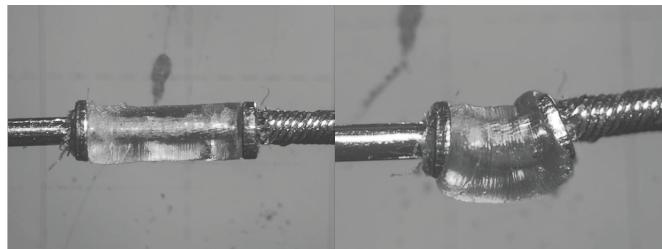

Figure B: 0.55 mm bellow assembly, off-centered expansion.

After successful expansion of the bellow, the guidewire assembly is guided through a piece of catheter again. This time, the bellow is expected to be large enough to resist being pulled inside the catheter tip. It is evaluated whether the bellow can hold a force of 0.5N (as reaction to the pull force) from the catheter wall.

A11.4 Results

Two assemblies were made:
The first bellow that was assembled was the 0.55 mm bellow and the 0.58 mm rings, visible in fiure B (left). When compressed, this bellow bulged out to one side (figure B, right). This indicated that the hole in the bellow was off center.
The other 0.55 mm diameter bellow was assembled with 0.56mm rings. When compressing, this bellow bulged out to a diagonal shape, visible in figure C (right). It is assumed that this was caused by the irregular ends of the bellow. They were carefully cut off as straight as possible with a surgical knife, resulting in the bellow in figure D.
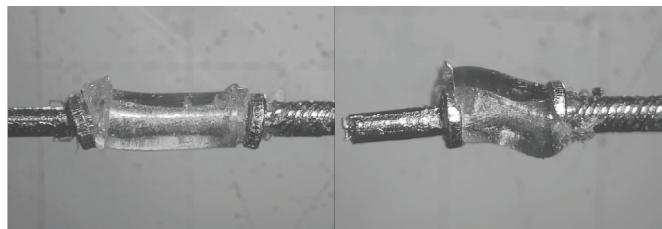

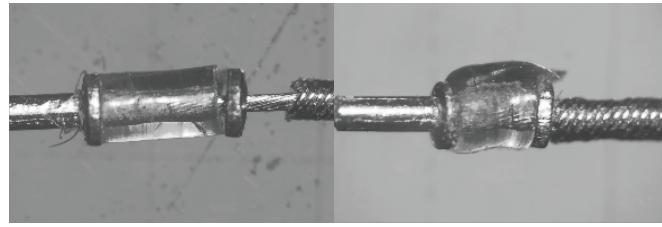Figure C: 0.55 bellow causing divergent expansion.

Figure D: Assembly 2 with modified bellow.

For testing the bellow assembly in the context of a catheter tip,, the Progreat™ is chosen because it suited the dimensions of the assembly the most. The expanded bellow is considered large enough to realize the working principle, because it expands up to a size larger than the inner diameter of the catheter (0.62-0.65mm). As visible in figure E, the bellow is advanced through the catheter tip smoothly when not expanded. No friction was experienced during this action. When the expanded bellow was pulled in proximal direction, it was not able to enter the catheter due to the enlarged diameter. A pulling force of 0.5 N was successfully exerted on the wire, without the bellow breaking or being pulled inside the catheter.

When compression forces were released, the bellow relaxed automatically, returning to the original 0.55 mm shape.

A11.5 Conclusion

The assembly in figure D is considered to be as close as currently possible to the assembly, dimensions, and accuracy of the FEA.
Upon axial compression, the bellow expanded quite uniformly from a diameter of 0.55 to 0.71mm, which is 129%.
The expanded bellow could hold a pulling force of 0.5N, which is the force needed for a deflection of the catheter tip. This means that a proof of principle is established with this test.

A11.6 Discussion

Limitations to the study are:
The bellow is handmade and can therefore be quite divergent from the intended dimensions. It became clear that the centered placement of the guidewire inside the bellow does not allow for much deviation. This suggests that the production technique of the bellow should be optimized. Especially the machining of the mold and the preparation of the guidewire inside the bellow chamber could be automated or perfectionated.
The fact that this test setup is 10cm in stead of 130cm (actual catheter size), should be taken into account while drawing conclusions.
The stretch in the guidewire and mantle will most definitely influence the controllability of compression. This factor is not focused on during this experiment because only the proof of principle is tested. When this appears to be a problem, investments should be made for using other guidewire and mantle parts. This will not affect the proof of principle concluded from this study.
Further testing can be done in full length and inside a modified catheter, to test the final (combined) functionality of the concept.
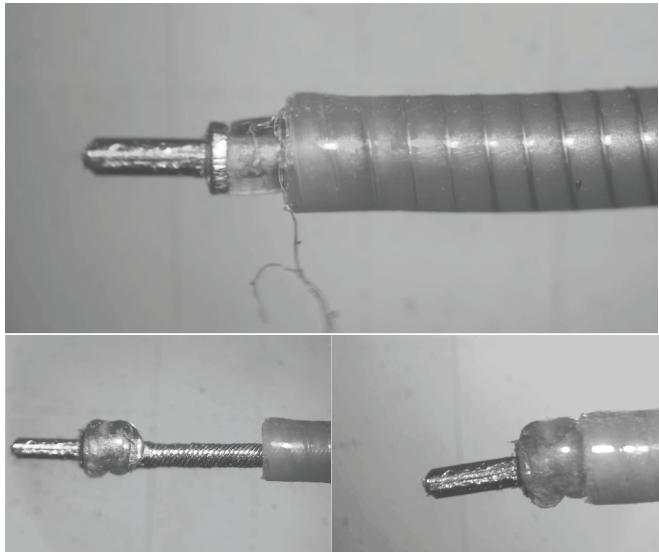

Figure E: Pulling non–expanded bellow through the Progreat™ catheter tip (top), and pulling the expanded bellow against the tip (bottom)

APPENDIX 12

Scientific report

Novel steerable microcatheter design: Mechanical test and FEA supporting theoretical validation of tip mechanism

Thesis - Scientific article

C.V. Blankensteijn, *4364732*, December 4, 2020

I. ABSTRACT

Background: In the field of interventional radiology, there is an increasing demand for more advanced instruments. More specifically, steerability of catheters and microcatheters would enable faster and easier navigation towards the target. Therefore, a novel steerable microcatheter concept is developed, based on a mechanism that can be activated to control a tip deflection. In order to realize a force transmission for this deflection, the mechanism involves an axial compression of a small elastic bellow, followed by a pull force. The theoretical feasibility of this concept is evaluated in this report, in combination with a validation for the material choice for the bellow. Based on a preliminary material study, PU rubber with a Shore value of A60 is chosen as most suitable material for this application. **Methods**: A mechanical compression test is done to get specific material properties of the chosen PU rubber, and a Finite Element Analysis is performed to simulate the bellow in the context of use, in order to evaluate the behavior and validate the material choice. **Results**: In the FEA, the acquired material properties from the mechanical test are used to provide an accurate representation of the stresses, deformations and reaction forces in the system. The compression of the bellow can be realized by applying a compression force of 0.4 N or a compression movement of 40% of the bellow. A pull force up to 2.0 N can be safely applied, resulting in tip deflection. **Conclusion**: The resulting stresses and strains in the system remain within the limits of the material. The material choice and working mechanism are therefore theoretically validated by the FEA results. The next step is physically test this bellow in the appropriate assembly.

II. INTRODUCTION

A. Background

Interventional radiology is a medical specialism that involves the diagnosis and treatment of various diseases in and via the vascular system. Minimally invasive instruments such as catheters are inserted in the femoral or radial artery, and navigated under image guidance through the vasculature to the diseased area. The advantage of this approach is that it minimizes trauma to the patient during procedures for vessel obstructions, aneurysms or tumors. The downside however is the procedural challenge of navigating through complex vascular pathways. Especially distal tumors can be difficult to reach due to vessel tortuosity, sharp bifurcations and small vessel diameter. The catheter-based treatment of tumors includes filling the tumor supplying arteries with embolization material, to stop the blood supply to the tumor. This procedure especially requires close access of the catheter tip to the tumor, to avoid non-targeted embolization of the surrounding arteries. Conventional instruments have a limited range of motion and tip control, which causes manipulating instruments through sharp bifurcations to be done with a trial and error process. Instruments with different tip shapes are often exchanged during this process, increasing procedural time and potential trauma to the vascular walls. Therefore, microcatheter innovation is focused on making the tip steerable, to enable easier and faster navigation towards a diseased area.

This report discusses a novel steerable microcatheter concept developed by Mencius Medical BV. It provides a theoretical validation of the concept, substantiated by a mechanical and computational analysis of the crucial part of the mechanism, which in this report is referred to as the "bellow". The bellow is basically an elastic (rubber) component of the mechanism that can be compressed for activation. This activation creates tension in the catheter tip that is needed for deflection. The working mechanism is further elaborated on in Section III.

B. Research question

For the envisioned working mechanism, choosing the right material for the bellow is crucial. Unfortunately, due to limitations of the study, not all materials that might be a suitable material can be thoroughly tested and evaluated. Therefore, a preliminary material study is set up to get insights about the behavior of different rubber types, and choose one to evaluate in this study. It includes a CES Edupack selection,

scale models, tensile tests and exploration of prototyping possibilities. This led to a hypothesis that PU Rubber with a Shore value of A60 is a suitable material to realize the bellow's functionality in the mechanism.

The purpose of this study is to confirm this hypothesis by thorough evaluation of this material in the context of the mechanism, testing its behavior in terms of stresses and strains during use. This way, the analysis will investigate the overall feasibility of the concept and suggest boundary conditions for the design. The research question is therefore specified to: *"Is Poly-PUR PS 161 a suitable material for the bellow based on its mechanical properties?"*

C. Relevance

The goal of this study is to provide theoretical proof of principle of the novel concept. This is an important step towards realization of the first ever microcatheter with this unique working mechanism. The product, or steerability of instruments in general, is a valuable addition to currently available equipment, as it is designed to allow easier navigation through complex vessel anatomy, increasing operation speed and success, and can be customized to various catheter sizes.

III. THE CONCEPT

Microcatheters are hollow tubes that are mostly used in combination with a guidewire running through it. Generally, during an interventional radiology procedure, the guidewire is navigated to the diseased area, over which the catheter can follow. The novel concept discussed and patented by Mencius Medical BV [1], is based on a mechanism on the guidewire tip, which can be activated to transfer tension to the catheter tip. Because the catheter material is weakened on one side of the tip, this tension causes a deflection in that direction (see figure 1A).

Activation of the mechanism expands the guidewire tip geometry (the bellow), so that it becomes larger than the catheter diameter. When the guidewire is pulled, the catheter tip deflects due to the tension created by the bellow. Expansion of the bellow is accomplished by axial compression. As the bellow is elastic, it returns to its original shape when this compression force is released. In this inactivated state, the guidewire can be advanced individually or pulled out of the catheter. The technical challenge of this study is making the bellow expandable, while being controlled from the proximal end of the microcatheter, which is often over a distance of around 130 cm. The assembly requires that the guidewire consists of a hollow wire, called the "mantle", that goes over the inner guidewire. This inner guidewire has a
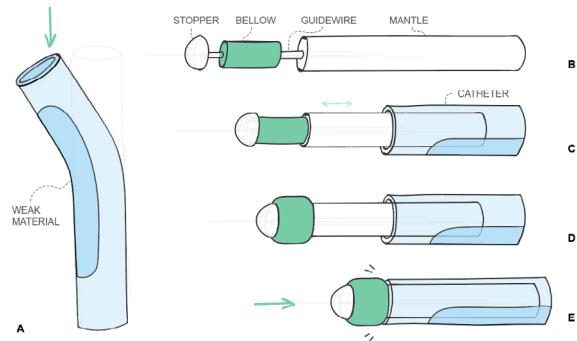
Fig. 1: Simplified representation of the novel steerable microcatheter concept: A) Asymmetric material properties of the catheter wall, B) Components of the guidewire assembly, C) Assembled system inside catheter, bellow relaxed, D) Axial compression of the bellow (green), E) Pulling the guidewire system to make turn.

"stopper" attached at the end. The bellow is positioned over the guidewire, and is compressed between the mantle and the stopper. The assembly is visible in figure (1, B). The guidewire and mantle are moved coincentrically, compressing the elastic bellow (1 C, D). When pulling the guidewire assembly from the proximal end, the compressed bellow is pulled against the catheter wall (1E), creating tension that deflects the tip.

IV. APPROACH

Results of this study must confirm or deny the intended functionality and material choice of the bellow. First of all, due to the small dimensions of the system (around 0.55mm in diameter), prototyping and testing possibilities are limited. Therefore, a theoretical approach is chosen to validate the design and a specific material before putting it into practice. The theoretical approach is divided in two parts.

A. FEA

Many technical problems of a design can be solved by equations. However, because of the specific non-linear material properties of the chosen hyperelastic material, and the specific boundary conditions the bellow is put under, the technical problem becomes complex. When trying to solve this problem with equations, required simplifications will make the results less trustworthy. A **Finite Element Analysis** (FEA) is therefore performed on the bellow using Computer Aided Engineering software, to simulate the bellow's behavior in context of use. The Finite Element Method discretizes the physical geometry of a structure into a collection of finite elements. All finite elements are connected with nodes, see

figure 2. The number of elements and nodes can be set by applying a mesh to the model. In a stress/strain analysis of such a model, the displacements of the nodes are calculated, and translated into stress/strain output per element. From this, conclusions can be drawn about the overall behavior and feasibility of a design. The software used for this research is ABAQUS. It is a powerful FEA software that can solve simple linear analyses, but also complex non-linear simulations. The user of this software can model any geometry, 2D or 3D, apply material properties and simulate movements and forces.
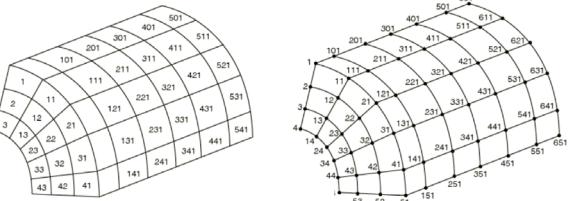
Fig. 2: Element numbers (left) and node numbers (right) [2]

The situation that is going to be simulated consists of two movements: 1) the lateral expansion due to axial compression of the bellow, and 2) pulling the expanded bellow inside the catheter, this movement being resisted by the catheter tube.

Non-linear deformation is expected due to possible high strains that the bellow experiences. Fortunately, ABAQUS has the power to evaluate non-linear models with reasonable accuracy provided that the input is correct. The output of the numerical simulation will define the reaction forces, stresses and strains in the system during use.

B. Mechanical test

Naturally, the FEA results are dependent on the material properties that are given as input. To get accurate results for the bellow made of the chosen PU Rubber, specific material properties are needed as input for the simulation. Unlike other engineering materials, material parameters of elastomers are not readily available or easy to determine, because these strongly depend on its particular composition and manufacturing process. Estimating these parameters using test data from literature is not valid for this study, because it cannot be trusted that it concerns the exact same material from the same manufacturer. The shore value of the material can be measured by indenting a sample with a durometer. However, to define the elastic properties, more elaborate testing is required. Therefore, **mechanical tests** with Poly-PUR PS 161 must be performed beforehand, of which the output can be

translated into an accurate "engineering stress-strain" curve for that specific material. Stresses in 3D solids are normally quite complex, but for this study, engineering stress can be simply defined by F/A. Strain is the response of the system to the applied stress. The engineering strain is defined as the amount of deformation in the direction of the applied force divided by the original length of the part in that direction. Monitoring the force needed for a certain deformation during a mechanical test, allows for accurate stress/strain definition.

A stress-strain curve is a useful tool to describe a material's elastic properties. The slope of this curve represents the Young's (elastic) modulus: the steeper the curve, the stiffer the material. Linear elastic materials follow Hooke's law, meaning that they have a constant Young's modulus and Poisson's ratio, and their stress-strain curve is linear. For elastomers, the stress strain relationship is however non-linear (visualized in figure 3), indicating that it is a hyperelastic material. From such a stress/strain curve, one can not derive a constant Young's modulus that can be used to describe the mechanical properties. The FEA therefore needs all of the stress/strain values to describe the material. In stead of following Hooke's law, hyper-elastic material models are based on several constitutive theories for larger elastic deformations following the strain energy density function W. ABAQUS is used to evaluate the stress/strain values, choose the hyper-elastic material model that fits these values best, and extract the required material constants.

These material constants, in combination with the right boundary conditions of the simulation, will make an as accurate as possible prediction of the behavior of the bellow, and the strains, stresses and reaction forces in the system. The mechanical test and FEA will both be described in the 'Materials & Methods', 'Results', 'Discussion' and 'Conclusion' sections.
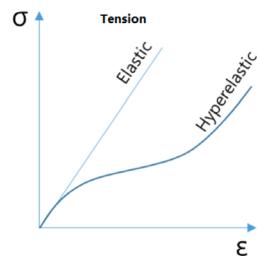
Fig. 3: General stress-strain curve of a hyper-elastic material [3]

V. Materials & Methods

A. *Mechanical test: experiment*

Mechanical tests that can be performed are: uniaxial test, biaxial test, planar test, or volumetric test (for compressible materials). Combining results of all these tests will give the most accurate material constants. However, considering the scope of this research and the limited available testing possibilities within the timeframe, only a uniaxial tensile or compression test is trusted to create a sufficiently reliable stress/strain curve of the chosen material. Based on the availability of testing equipment in the TU Delft MISIT (Minimally Invasive Surgery and Interventional Techniques) lab, it is chosen to perform a compression test.

1) Materials

Poly-PUR PS 161 is a flexible Polyurethane rubber that can be cast when two components are combined. It is produced by Polyservice B.V.[4], has a Shore value of A60 when hardened and is often used for making large molds and castings. A factor that supports this material choice is that PU (Polyurethane) rubbers are widely used in the medical field due to their biocompatibility, sterilizability and mechanical properties.[5]

The Poly-Pur PS 161 from Polyservice can be made by combining the A and B component in a 50/50 ratio. The resulting specimen hardens out in about 48 hours. Little cubes are cut out of the specimen, and a 20x20x20mm cube used for the test. Available material specifications provided by the manufacturer are shown in table I.

Shore A	60
Working time	10 minutes
Working temperature	18-25 degrees C.
Tensile strength	3.7 MPa
Strain until failure	450%
Tear strength	18 kN/m

TABLE I: Known material properties of Poly-Pur PS 161 [4]

2) Equipment

For this uniaxial compression test, equipment of the MISIT lab at TU Delft was used. A linear stage PRO-115 (Aerotech, USA/UK) was used to compress the sample and exert force on the material. A Force Sensor (LSB200, Futek, USA, serial number 10176-4) with a 111N capacity was attached to the moving head and used to measure the reaction force in Voltage. This force sensor is chosen because it is the force sensor with highest capacity that is currently available at the 3mE faculty (TU Delft).

Fig. 4: Poly-Pur PS 161 [4], 2 components
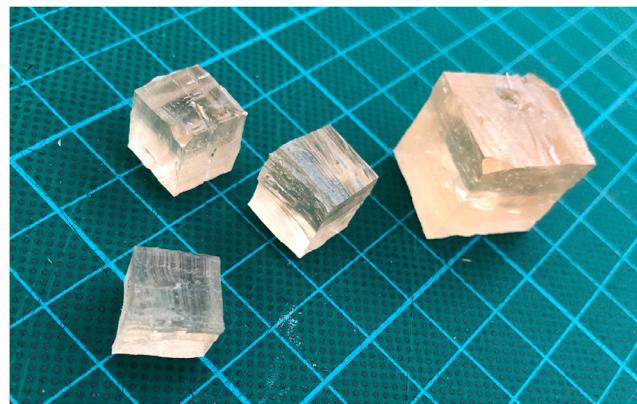

Fig. 5: Poly-Pur PS 161 [4] compounded

Fig. 6: Cubes of Poly-Pur PS 161

#### 3) Variables and constants

The dependent variables that are studied are the force and displacement while compressing the silicon rubber cube. These values depend on the elastic properties of the specimen. To evaluate any potential visco-elastic (time-dependent) behavior, the test is done with two different speeds: 1mm/s, and 2mm/s. The compression time is the only independent variable, therefore the condition matrix is quite simple (see table II).

The following constants were chosen for the experiments:

- Downwards movement of -5mm
- Number of iterations: 3
- Temperature: room temperature

Nuisance variables that could influence the outcome or cause noise are:

- Symmetry of the cube
- Surface curvature/unevenness of the cube
- Irregularities in the material (air bubbles, not homogeneous)
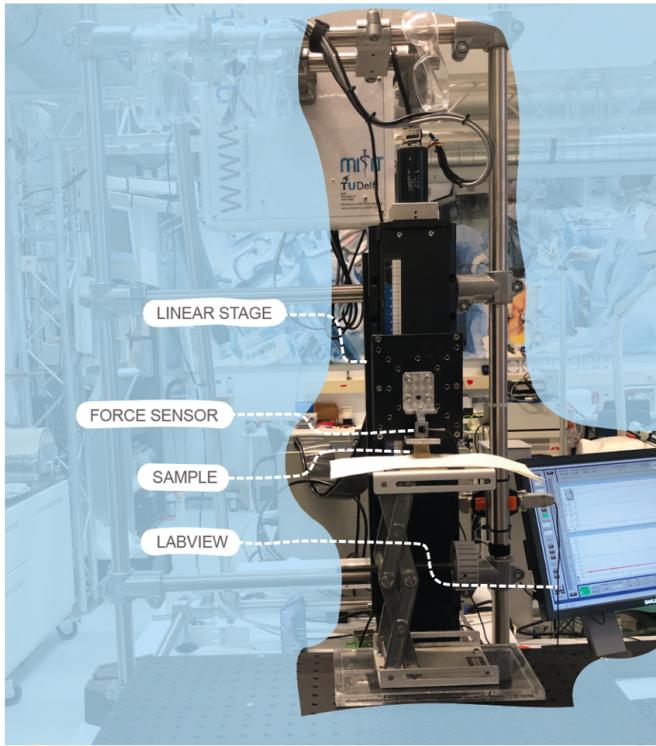
Fig. 7: Experimental setup for compression test

4) Experimental design

The goal of this test is to obtain a stress/strain curve of this specific material. Therefore, the sample is compressed, and three replications are done per sample. More replications are not necessary since the mechanical behavior of the rubber is not expected to change much while keeping the experimental conditions unchanged. As mentioned, the test is performed in two compression speeds to validate treating the material as hyper-elastic in stead of visco-elastic.

	Compression speed	
n = 3 (replications per EC)	**Low** (1 mm/s)	**High** (2 mm/s)
Poly-Pur A60 sample	EC$_1$	EC$_2$

TABLE II: Condition matrix of independent variables

5) Experimental protocol

The following experimental protocol is defined in a way that it permits replication of the study as accurate as possible.

1) Calibration: In order to translate the raw test data from Voltage to Newton, the setup first has to be calibrated. The force output of the sensor is monitored without the rubber sample in the setup. A set of zero-values is created by applying weight to the force sensor and monitoring the Voltage, in steps of 50 grams, until 300 grams is reached. Three measurements are made for each weight and the averages are taken. This method is considered to give sufficiently accurate calibration values. The applied masses in kg are translated to N (by multiplying it with 9,81), and the accompanying Voltage measurements, are used to plot a Voltage-Newton graph, from which a formula can be deducted. This formula can now be used to translate the measured voltage during compression to Newton.

2) A zero-pre-strain compression is applied to the silicon sample: The sample was placed directly under the force sensor plate, so that the top of the cube touches the plate but is not under compression yet. Measurements were performed with a strain rate of 2 mm/s, and the linear stage was programmed to go 5mm down, which is a strain of 25%. This strain is chosen based on the limits of the sensor's capacity.

3) The second set of three measurements was done with a strain rate of 1 mm/s and the same distance.

6) Data processing

The raw data from these tests was a measured output in Voltage representing the reaction force, and position of the linear stage representing the strain. Attention was paid to the domain of the useful results, so the exact time frame in which the compression was applied. In this time frame, it is expected that homogeneous stress states are achieved.

The useful results generally start after 1 second, giving the system some time to start the displacement. They end at the moment the final strain is reached. For the compression tests with a speed of 2 mm/s, it takes 2.5 seconds to reach a 5mm strain, so a domain of 1s - 3.5s is chosen. For the 1 mm/s compression, a domain of 1s - 6s is chosen. The Y-values in this domain are translated from Voltage to Newton using the calibration formula. Stress can be extracted using Stress (Pa) = F(N) / A, with A being the top surface of the cube in meters. Strain is calculated as the change in height of the cube divided by the initial height of the cube. The result is 3 stress-strain curves of both the fast and slow compression test, and these are averaged (with a moving average to eliminate noise) and projected in one graph.

7) Data analysis

The average stress strain curve is plotted for both the slow and the fast compression, in order to observe the difference between the two. Based on this evaluation, one of the two curves is chosen as accurate representation of the material,

and these values can be used as input for the Finite Element Model. When performing an in depth stress/strain study of a material, the *engineering* stress and strain normally has to be translated to *true* stress and strain. This is because engineering stresses and strains are calculated based on a fixed cross sectional area of the solid, and true stress and strain take into account changes in this cross-section during testing. For this study it is however not necessary as ABAQUS specifically asks for nominal (engineering) stress and strain values.

The Matlab code used to process the compression test data can be found in Appendix VII.

B. FEA: Pre-processing

FEA is the most accurate and versatile method for numerical problem solving, and it helps designers to estimate the behavior of the design during use. A pitfall however of using FEA is that its results will only be accurate if the input is correct. Therefore, attention must be paid to the steps taken for modelling the problem.

Expectation management is important when using FEA software. The situation has to be simplified where possible, without it causing the results to become unrealistic. FEA problems that are expected to give non-linear deformation results, require a refined model, and attention must be paid to providing the right input. When the input is not defined correctly, ABAQUS experiences difficulties in terms of converging to a solution. Converging problems can show in different ways: for example, errors in the boundary conditions, too large load/time steps, or severe distortion of elements. Due to the large strains and non-linear nature of a model, extreme deformations or snap-through buckling can be a result. It is generally explained as when the load-displacement response stiffness is negative, and in order to reach equilibrium, the structure has to release strain energy. This can cause the whole model to fail, which is often the case with complex rubber problems. Reasons for convergence problems can be examined in the field output with trial and error, and some factors of the model (boundary conditions, contact surfaces, mesh) have to be adjusted to fix the model. A lot of choices and assumptions are made to get this model to give the most accurate results, and considerations are taken to avoid buckling. A Static-Riks approach is chosen, which is a setting in ABAQUS and an appropriate method for solving models that are prone to buckling. It simply helps to to fix unstable non-linear situations [6]. This section elaborates on all other assumptions and choices made for accurate modelling of the situation.
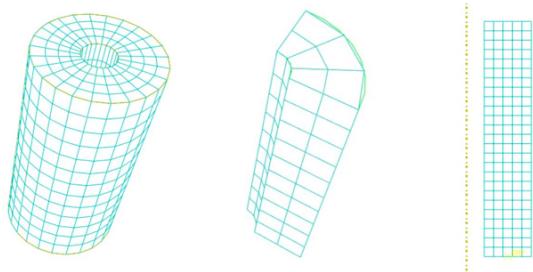

**Fig. 8:** 3D model VS quarter of a 3D model VS 2D plane model

1) Geometry

The geometry of the bellow is based on the bellow design that is compatible to a Terumo Progreat microcatheter or Boston Scientific Direxion 2.8F microcatheter with an inner diameter of 0.6-0.65 mm. These are both widely used, according to consulted specialists, and are used for the concept's prototype. The inner diameter of the bellow aligns with the guidewire with a diameter of 0.15. The outer diameter of the bellow is set at 0.55, so that it can move freely through the catheter in inactivated state, and only a 20-30% (minimum) expansion is required when activated.

The bellow can be modeled in a few ways, see figure 8. Because the bellow is a symmetric cylinder, not the whole 3D model has to be modeled. Taking advantage of the axis of symmetry, the model is simplified to a 2D plane, so that each element represents a complete 360 degrees ring. This saves nodes and allows for a more accurate simulation. Later on, the geometry can be visualized as a 3D shape in the Output Field using the function "Sweep", which is how most of the results are presented in this article. The rubber bellow is modeled as axisymmetric deformable part, and the catheter wall and guidewire (including "stopper" geometry) are modeled as axysymmetric rigid bodies. The assembly with dimensions are shown in figure 9.

2) Material model

It is assumed that the effects of internal viscosity, time dependency and delay of reaching equilibrium can be neglected. This is because at normal temperatures the response is usually very fast for rubbers. Therefore, the material is evaluated with a hyper-elastic material model. This is also validated by comparing the results of two compression speeds in the mechanical test. As adressed in the IV, a stress-strain relationship of a hyperelastic material model is derived from the strain energy density function. There is a variety of these hyperelastic models. Simple examples are Mooney-Rivlin, Reduced polynomial, Ogden, Yeoh or Neo-Hookean models. These models all require their own coefficients. [7] Each
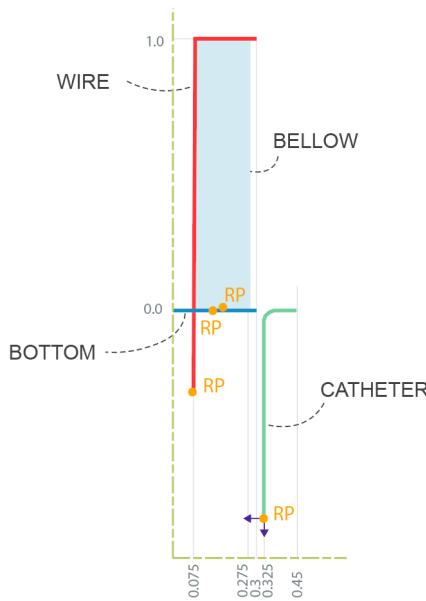
**Fig. 9:** 2D Geometry and dimensions of the assembly modeled in ABAQUS

model can be described for a specific order (N-value). The order N=1 means that test data of only one mechanical test is available. N=2 means that for example, both a uniaxial and a biaxial test are done, and N=3 means that a planar test is performed as well. In this case, only a uniaxial test is performed, and it is expected that this will give a sufficiently accurate material description. ABAQUS can be used to choose the material model that best describes the chosen PU rubber. The test data (nominal stress and nominal strain values) is inserted in ABAQUS, and the software compares these values to all the available material models using curve fitting. It indicates which model fits the stress-strain curve best, and creates the required coefficients.

Note: incompressibility can generally be assumed for rubber materials [7]. This means that the material will not change in volume when compressed or stretched, and D should be set to 0. This corresponds to a Poisson's ratio of 0.5. Because the ratio of the bulk to the shear modulus goes to infinity when Poisson's ratio is 0.5, and this will lead to instability problems of the model, Poisson's ratio for elastomers is assumed 0.4995+ and D should be written as almost zero (1e-7), for the model to run.

3) Meshing

To get adequate results out of a model that is prone to non-linearity issues like this model, it is important to apply a sufficiently refined mesh. A too coarse mesh (figure 10) will create inaccurate results, and the more refined the mesh is, the more specific the numerical outcome will be. Unfortunately, highly refined models (figure 11) require a lot of computer power, and sometimes the geometry can become 'over-defined', which induces buckling or other strange artifacts in the results. Therefore, the minimum amount of elements has to be chosen, that still gives an accurate result. In general, parametric studies can be performed to define unknown parameters. In this case, a mesh convergence test is performed evaluating the same model with different meshes. Each time, a more refined mesh is applied and results are compared. When further refinement does not significantly influence the results anymore, the right mesh density is reached. The reader is referenced to appendix IV for the mesh convergence test, resulting in an optimal mesh of 125 elements. The mesh of the catheter, wire and bottom are less influential to the results, because they are rigid. The amount of elements for these parts are set to 11, 4 and 10 respectively.[8]
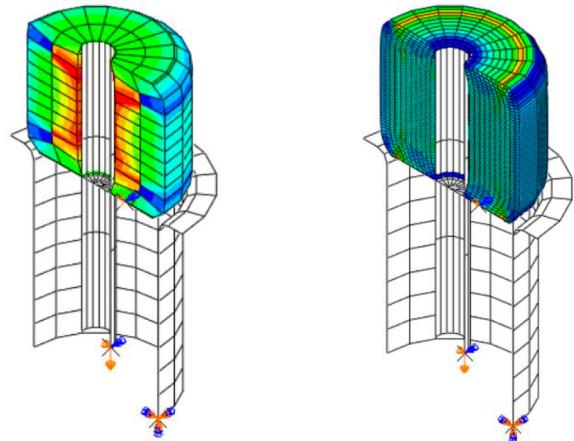
Fig. 10: Mesh with 22 elements, visualizing Von Mises stresses at the end of compression step

Fig. 11: Mesh with 500 elements, visualizing Von Mises stresses at the end of compression step

4) Interactions

In the assembly, a few "surface-to-surface" interactions, listed in table III have to be identified in ABAQUS.

Furthermore, the "self-contacts" that apply when the bellow touches itself when curled up, are listed below:

- Bellow (inner surface)
- Bellow (outer surface)
- Bellow (bottom surface)

Master Surface	Slave Surface
Bottom (top surface)	Bellow (bottom surface)
Catheter (inner surface)	Bellow (bottom surface)
Catheter (inner surface)	Bellow (outer surface)
Wire-vertical (outer surface)	Bellow (inner surface)
Wire-top (bottom surface)	Bellow (top surface)
Wire-top (bottom surface)	Bellow (outer surface)

TABLE III: Surface-to-surface contacts

For these interactions, the friction property is another unknown parameter. For example, the friction between the bellow and the stopper and bottom plate is not expected to be 0, since that will result in an unrealistic expansion visible in figure 12 (left). The friction coefficient of rubber ranges
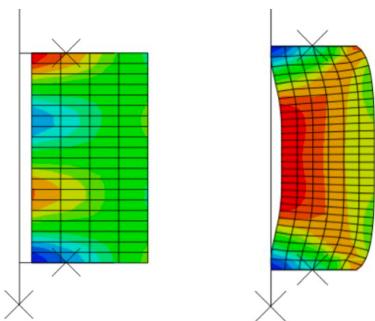
Fig. 12: No friction (left) VS friction (right) between bellow and stopper and bottom plate

from 0.001 to 10.[9] Friction coefficients between the rubber bellow and the catheter tube and other parts of the assembly, can be estimated as rather high (0.5), as rubber generally has a high friction coefficient. To validate the chosen friction coefficient of 0.5, a parametric study is done. Frictions 0.1, 0.2, 0.3, 0.4, 0.5 and 0.6 are applied to test whether the resulting reaction forces in the system are friction-dependent. These resulting plots are shown in Appendix V. The lower the friction coefficient, the more irregularities showed in the field output and in the reaction force plots after the compression of the bellow. The graphs that were assumed most accurate were those of the 0.5 and 0.6 friction coefficient, validating the choice for a 0.5 friction coefficient. The friction between all the different parts is generalized to one value, because the parametric study would otherwise become too complex.

5) Loads & Boundary conditions
The simulation has two steps:

- Step "compression": First, the bellow is (assumed uniformly) axially compressed. For these kind of models, it is preferred to work with displacements rather than forces, as it is less sensitive to inaccuracies. Therefore,

a downward movement is applied to the wire, pulling the top of the bellow 0.4 mm downwards. This is done while applying a movement of 0.0mm the bottom of the bellow, representing the mantle. This results in an axial compression of the rubber bellow. What can be read from this action's output is the amount of outward displacement of the bellow and the reaction force in the bottom plate, representing the required compression force.

- Step 2: The expanded bellow is pulled into the catheter. During this second step it is important that the boundary conditions from the first step remain the same (so that the bellow stays expanded, or "pre-stressed"). Therefore, a downward displacement of 0.4mm + 0.5mm has to be applied to the wire/stopper, and a 0.5mm downward displacement is applied to the bottom plate. The bellow will start sliding into the catheter and as it does this, the outer surface of the expanded bellow will be pushed against the catheter wall. During this sliding motion, it is important that the catheter wall does not have a too sharp corner, to avoid failure of the simulation.

6) Analysis step
The force that is needed to create enough tension in the catheter tip for it to make a 180 degree turn is only 0.5N, based on tests with modified catheters that will be used for the prototype. Therefore, while pulling the guidewire with a force up to 2N (safety factor x4), it must be guaranteed that the expanded bellow holds its place in front of the catheter tip, and stresses in the bellow do not exceed the material's limits (causing it to fail).

Rubber components are generally evaluated based on their strain energy, rather than stress levels (which would be the main output to look at for metal models). Visualizing the internal strains, and the elastic and plastic deformation in the field output, will provide conclusions about whether the functionality of the bellow is within the limits of the material.

Once the model is correctly set up, it must be defined what information form the FEA can be useful for the design. The input consists of material properties, surface interaction properties and displacements in the system, and the output will mainly present deformations and reaction forces to displacements in the system. The reaction force on the bottom plate (extracting values from the Reference Point in the bottom plate) will reveal the required compression force. The reaction force on the catheter wall (Reference Point) represents the pulling force applied to the guidewire. When these reaction forces are within the defined limits of the system, a theoretical proof of principle can be concluded.

VI. RESULTS

A. *Mechanical Test: Stress strain curve*

1) Raw data

The raw data from the force sensor during compression (Voltage in relation to time) from the three slow and three fast compression tests are visualized in figure 13.
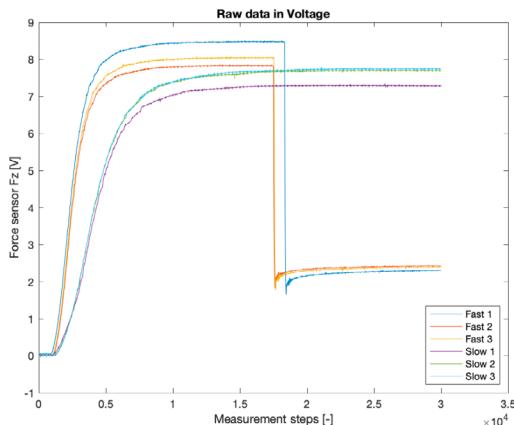

Fig. 13: Raw data of compression tests in Voltage

2) Processed data

A calibration is done of the experimental setup (see Appendix I), resulting in the following calibration formula:

$$y = 15,236x - 0,0574 \tag{1}$$

Using this formula, the acquired Voltage values are translated into Newton and plotted against time. Converted Force (N) – Time (s) graphs from all measurements are visible in Appendix II. From these raw data graphs a domain is chosen in which the compression took place. The averaged Force (N) - Time (s) graphs, within the useful domain and smoothed out are visible in Appendix III. The resulting graphs of the fast runs are scattered out more than the slow runs, and one of the "fast" graphs starts at a higher value than 0. This is the potential cause for the average fast stress-strain curve to be of higher value than that of the slow one, in figure 14. It is therefore concluded that the stress-strian curve from the slow compression test can be regarded as most accurate representation of the material properties of Poly-PUR PS 161. These stress-strain values are extracted from Matlab to use as material input in ABAQUS.
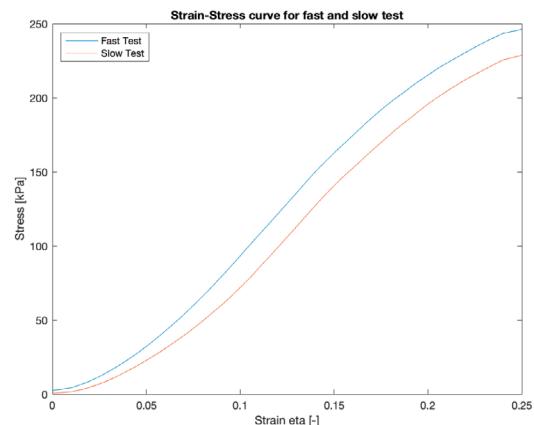
Fig. 14: Final stress strain curve of the fast and slow compression test for Poly-PUR PS 161
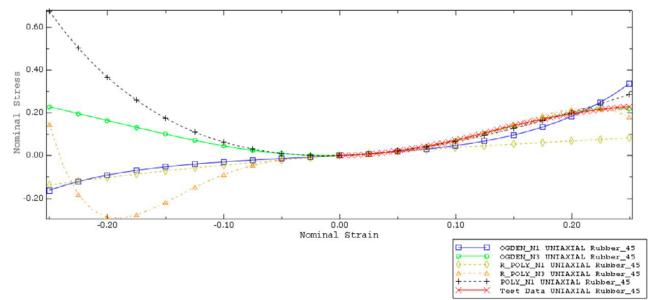
Fig. 15: ABAQUS curve fitting of stress strain curve to different hyperelastic material models

B. *Finite Element Analysis: Post-processing*

1) Material model

Hyperelastic material models that are available in ABAQUS can all be curve fitted to the stress strain curve. It is plotted against the following material model graphs: Mooney-Rivlin, Ogden N=1, Ogden N=3, Neo-Hookean, Reduced Polynomial N=1, and Yeoh (Reduced Polynomial N=3), as shown in figure 15. It is indicated that the Ogden N=1 and Neo Hookean (Reduced Polynomial N=1) model only give stable results, as shown in figure 16. In moderate strains, hyperelastic material can often be accurately described with Neo-Hookean model, which is the most simple hyperelastic model. Because in the performed compression test, the rubber is under only 25% strain, the resulting stress strain graph can be curvefitted to the Neo-hookean graph. However, to be able to identify higher strains in the ABAQUS model, a more sophisticated material model is chosen. The Ogden model is considered to give very accurate results in large strain

```
HYPERELASTICITY - OGDEN STRAIN ENERGY FUNCTION WITH N =   1

         I          MU_I         ALPHA_I          D_I

         1       0.100502249     15.6898892     0.00000000


            STABILITY LIMIT INFORMATION

   UNIAXIAL TENSION:        STABLE FOR ALL STRAINS
   UNIAXIAL COMPRESSION:    STABLE FOR ALL STRAINS
   BIAXIAL TENSION:         STABLE FOR ALL STRAINS
   BIAXIAL COMPRESSION:     STABLE FOR ALL STRAINS
   PLANAR TENSION:          STABLE FOR ALL STRAINS
   PLANAR COMPRESSION:      STABLE FOR ALL STRAINS
   VOLUMETRIC TENSION:      STABLE FOR ALL VOLUME RATIOS
   VOLUMETRIC COMPRESSION:  STABLE FOR ALL VOLUME RATIOS
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Fig. 16: ABAQUS evaluation of constants for the Ogden (N=1) model

Fig. 17: Reaction force plots of the upwards Reaction force in the bottom plate (pink) and in the catheter wall (brown)

ranges [10], as opposed to the Neo-Hookean or Mooney-Rivlin model, which are both two commonly used. The Ogden model is therefore chosen as most sophisticated and accurate for high strains.

The Ogden first order (N=1) material model is proven to be very good for fitting Hyperelastic data with just two parameters. Unlike other material models, The Ogden model directly uses the principle stretches as independent variable for the strain energy function W, in stead of using multiple independent strain invariants [11]. This approach is proven simple but trustworthy for mechanical evaluation of hyperelastic materials such as rubber.

The model is expressed in terms of the principal stretches λ_j, j=1,2,3 as equation 2, where N is the order of the model (usually 1-3, in this study N=1), μ_p is a material constant with unit pressure, and α_p is a unitless material constant.

$$W(\lambda_1, \lambda_2, \lambda_3) = \sum_{p=1}^{N} \frac{\mu_p}{\alpha_p} \left(\lambda_1^{\alpha_p} + \lambda_2^{\alpha_p} + \lambda_3^{\alpha_p} - 3 \right) \quad (2)$$
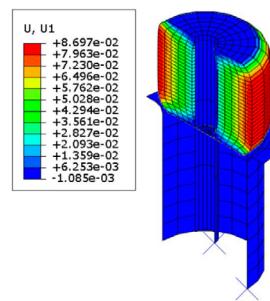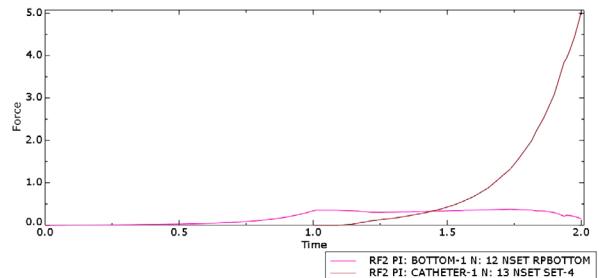
Under the assumption of an incompressible rubber, one can rewrite as:

$$W(\lambda_1, \lambda_2) = \sum_{p=1}^{N} \frac{\mu_p}{\alpha_p} \left(\lambda_1^{\alpha_p} + \lambda_2^{\alpha_p} + \lambda_1^{-\alpha_p} \lambda_2^{-\alpha_p} - 3 \right) \quad (3)$$

The scope of this report does not include further research into the theory of this material model, because ABAQUS will be able to extract the material coefficients. For a more thorough explanation, the reader is referred to Ogden's book "Large Deformation Isotropic Elasticity – On the Correlation of Theory and Experiment for Incompressible Rubberlike Solids" [11]. As can be seen in figure16, the results of the FEA based on the Ogden model are expected to be stable for all strains. It also presents the required constants generated by ABAQUS.

Fig. 18: Field Output of maximum bellow expansion (principle displacement) after compression step

2) History Output

With the right material constants defined, ABAQUS can now generate the useful output from data at specific points in a model. The output that is analyzed from this study is:

- The reaction force in the bottom plate, using the bottom plate reference point as measuring point. This will indicate the compressive forces that are needed to compress the bellow.
- The reaction force in the catheter wall (using catheter reference point) measures the tension that the catheter tip experiences by pulling the expanded bellow in.

In figure 17, these reaction forces are plotted. Time frame 0.0-1.0 represents the compression step, 1.0-2.0 represents the pulling step. At the beginning of this study, the tension was defined that is required to make the tip deflect 180 degrees. This was 0.5N. In this analysis, a safety factor of 4 is taken, which means that the reaction force in the catheter wall must reach at least 2.0N. The time value of this graph is observed at a reaction force of 2.0N, which is time step 1.81. This time step is considered the "crucial moment" in which it is theoretically guaranteed that the expanded bellow causes a deflection of the tip.

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Fig. 17: Reaction force plots of the upwards Reaction force in the bottom plate (pink) and in the catheter wall (brown)

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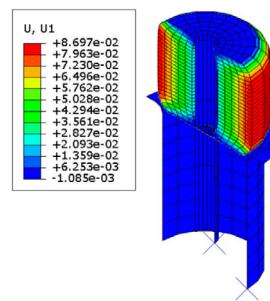
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$$W(\lambda_1, \lambda_2) = \sum_{p=1}^{N} \frac{\mu_p}{\alpha_p} \left(\lambda_1^{\alpha_p} + \lambda_2^{\alpha_p} + \lambda_1^{-\alpha_p} \lambda_2^{-\alpha_p} - 3 \right) \quad (3)$$

The scope of this report does not include further research into the theory of this material model, because ABAQUS will be able to extract the material coefficients. For a more thorough explanation, the reader is referred to Ogden's book "Large Deformation Isotropic Elasticity – On the Correlation of Theory and Experiment for Incompressible Rubberlike Solids" [11]. As can be seen in figure16, the results of the FEA based on the Ogden model are expected to be stable for all strains. It also presents the required constants generated by ABAQUS.
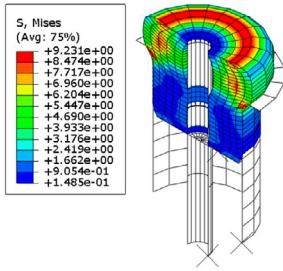

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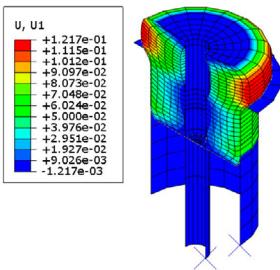
Fig. 19: Final Output of the bellow at crucial moment, Von Mises stress
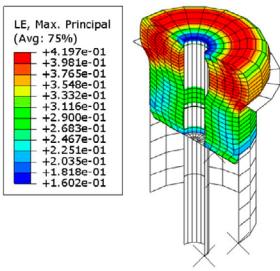
Fig. 20: Final Output of the bellow at crucial moment, principle strain
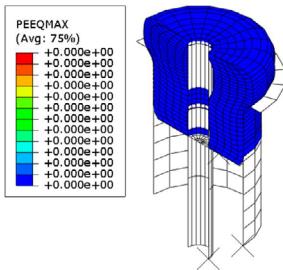
Fig. 21: Final Output of the bellow at crucial moment, PEEQ = 0

Fig. 22: Final Output of the bellow at crucial moment, principle displacement

3) Field Output

In figure 18, the field output is shown at time step 1.0, so at the maximum compression, pressing the top plate 0.4 mm down. The outward displacement of the bellow outer surface is at this point 0.087 mm, making the bellow in maximum expansion 0.724 mm. This is 132% of the original bellow size. The minimum compression force needed for this expansion is 0.4 N.

In figures 19, 20, 21 and 22, this moment is visualized for the modeled axisymmetric plane, swept a 180 degrees. Von Mises stresses, Maximum principle strains, maximum PEEQ (which is the plastic deformation experienced by the bellow) and displacement in the principle direction are indicated respectively. Figure 21 shows that the plastic deformation is 0 for the entire bellow, so the material's limits are not reached during use. Lastly, the lateral expansion of the bellow that causes the bellow to exert tension in the catheter tip is caused by axial compression. The maximum displacement of the outer surface of the bellow increases to 0.093 mm. This makes the bellow diameter increase to 0.736 mm which is almost 134% of its original size.

VII. DISCUSSION

The initial material choice is done based on various small tests with a variety of rubbers. In this study, it is not proven that the chosen PolyUrethane is the most suitable material out of all existing materials, only that its material properties are sufficient to realize the concept's functionality. It is a general limitation that only this one material is thoroughly evaluated. However, this approach provides results that allow for a next step in the design process, as prototypes can now be validly made of this material.

A. Mechanical test

1) Interpretation

Looking at both graphs in figure 14, the graphs are quite similar, only the fast compression curve is slightly higher (less than 10%)than the slow compression curve. This can be caused by the scattering of the individual measurements in figure 31 in Appendix III. The blue line deflects slightly from the other two graphs which shifts the average graph up. It also starts at a higher value than 0, which suggests that this might be an incorrect test run. This result is therefore considered slightly invalid and the final stress-strain curve of the slow compression test is chosen as most accurate result of the experiment.

2) Limitations of the experiment

Some limitations that might have influenced the validity of generalization of the results are listed below:

- The sample: For this test, it is chosen to compress one sample of the specimen. The amount of samples tested could influence the results, since the rubber might adapt slightly after multiple runs, although this is not expected. Furthermore, the Poly-PUR rubber is first cast into a random shape, then cut into cubes with a knife. The cutting with a knife causes the surface to not be 100% flat and horizontal, which could influence the uniformity of the compression. This technique might also have accounted for non-homogeneous material or small air bubbles inside the cube. This would be a reason for multiple material samples to be tested in future research. The sample would also be more accurate when cast into a cube shaped mold.

- Amount of runs: Only three runs per compression speed were used to determine the results. It is possible that for example one of these runs was disturbed by a small movement on the table or system, even though it is tried to keep this as constant as possible. This might have caused noise and using only three runs, any outcomes deviating from reality strongly influence the final result.

This is what probably happened in one of the fast runs, which is why these results are left out of the final plot.

- Experiment: The choice to perform only a uniaxial compression test was based on equipment availability and priorities of the design project. This gives a sufficiently accurate material description, however, the prediction of biaxial or planar behavior of the material is difficult when it is only based on uniaxial test data. [12]. Although not expected, it is possible that the bellow is subject to a biaxial compression during use (for example, the axial compression forces and lateral forces from the catheter on the bellow). In this case, the analysis of the bellow would be more reliable, when the material properties were defined more accurately. If additional biaxial and planar mechanical test data were available, this would increase the accuracy of the material coefficients. Nevertheless, for this study, as the prediction of the bellow behavior will be only an indication whether the concept will work, using only compression test data will give a sufficiently accurate representation. Additional practical tests are still to be done for final proof of principle.

- Friction: The described method to define the mechanical parameters of the material is ideally done based on homogeneous stress strain curves. To achieve this, compression tests require a fully frictionless setup. The pitfall of a compression test is that there is friction between the compression plates and the specimen. This friction can cause inhomogeneous stress states and is almost impossible to avoid in compression tests [13]. In a next experiment, it can be attempted by applying a lubricant between these interfaces. It is however not expected that this factor influences the stress/strain curve to an extent that it will change the outcome of the FEA.

- Limits of the equipment: In the performed compression test, yield and tensile strengths are not reached, as there is no plastic deformation during the compression test. In this case, the tensile strength is more accurately described as compression strength. It is the stress that is needed to destroy the sample by crushing it, and is not always easy to define for elastomers. The point of failure is not reached during the compression test because the force sensor is limited to a compression force of 111N. This was the sensor with highest capacity available at the time of the experiment. The domain of the strains measured during this compression test is limited by this sensors capacity, which therefore only represents for a part of the stress/strain curve of the material, representing 25% compression. Nevertheless, there are

a sufficient amount of values to describe the material behavior with for this simulation. For future research, it should be noted that according to [7], the tension or compression stress-strain relationship of rubbers can be assumed fairly linear up to 30% strain. The compression test does not reach 30% strain, which is why the results of this experiment are within the fairly linear section of the material's behavior. The resulting stress strain curve from this study also shows only a slight non-linearity. During use and in the ABAQUS analysis, the bellow is however compressed with 40%, and this is why a tensile test, or compression test with a stronger sensor would be a valuable addition to the completeness of the mechanical definition of the material.

B. Finite Element Analysis

1) Interpretation

Figure 19 indicates a maximum internal stress of 9.23 MPa, which realistically should not be possible since the material's limits are known to be lower (Tensile strength of 3.7 MPa). This result is caused by the way ABAQUS translates the model's data into a stress contour plot (Like figure 19, showing the occurring stresses in different parts of the model). A so-called 'contouring algorithm' is used that is based on all the measured data at the nodes. However, ABAQUS Standard calculates data at the integration points between the nodes in stead of at the nodes themselves. ABAQUS/CAE then calculates nodal values by translating this data at the integration points into data per element. This requires extrapolating of the stress components at the integration points to nodal locations within each element. Consequently, this causes extrapolated nodal stresses become higher than the values at the integration points [8]. This process can therefore result in Von Mises stress values exceeding the elastic limit.[14] Therefore, PEEQ is a more reliable factor to analyze to see if the material limits are reached.

The reaction force plots of the FEA show a realistic result. The bellow is compressed, after which it is large enough in diameter and strong enough to provide the required tension in the catheter wall. The forces of pulling the guidewire are almost fully transferred to a reaction force the catheter wall. In the preliminary tests with the catheter, it is experienced that only small forces are needed to make the tip deflect. This is advantageous for the design of the bellow since it is only subject to low forces. It is visible from the reaction force plots in figure 17 that the reaction force in the catheter rapidly increases. This graph suggests that even when a pulling force of 5N is applied, the bellow still provides tension and is not pulled inside catheter completely, because the measured

reaction force (in the direction opposite to the pull direction) would decrease when the bellow is pulled all the way through the catheter. This gives confidence about the bellow being able to hold the relatively low forces that are needed for realization of the working mechanism.

To achieve this required tension, it is specifically important to realize sufficient bellow expansion. The boundary condition for the compression step is set at a compression of 0.4mm (40% of the bellow). It is valuable to know that this compression, for which only 0.4N is needed, gives successful outcomes. However, it can be useful to evaluate if a smaller compression is also sufficient for the bellow to work. In Appendix VI, a compression of -0.3 mm, -0.35 mm, -0.4 mm, -0.45, and -0.5 are compared to see the differences the compression causes for the reaction forces in the system. It becomes clear that the less the bellow is expanded, the less reaction forces are present in the catheter wall. For the working mechanism it is important to create high reaction forces in the catheter wall, because then the tip deflection is easier accomplished. Added to this, it is expected that the catheter wall will deform slightly, so it is not afforded to take the risk of having a too small expansion for the mechanism to work. This validates the compression of -0.40 mm as minimally required. Since the -0.45 mm compression only costs 0.8N, it is even recommended to aim for this compression for easier tip deflection and optimal working of the mechanism.

2) Assumptions & Limitations

FEA is a powerful tool to simulate a material's behavior. However, to be able to use this tool for creating realistic and useful results, some assumptions have to be made:

- The rubber is assumed homogeneous, isotropic, and incompressible. This is favorable for the material choice since it makes the material model slightly simpler.
- The material is assumed to be hyperelastic and to show non-linear geometric effects in the FEA.
- The friction between all components is assumed the same for it to be generalized in the parametric study.
- The geometry of the bellow assembly is assumed as a perfectly shaped cylinder, that is under a uniform compression, placed precisely in the middle of the catheter when pulled.
- It is assumed that the guidewire, stopper, bottom plate (representing the mantle) and the catheter are rigid parts.
- It is assumed that the 2D plane model will give the same results as a 3D model of the whole bellow, and that the bellow behaves axisymmetrically. It is however proven that the deformation of the bellow in its circumference is
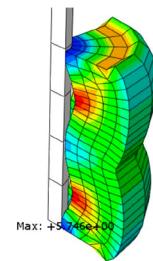
Fig. 23: 1.5 mm bellow, visualization of double bulge effect

uniform in reality. A 3D model would be able to simulate this more accurately, but due to the limited amount of elements of the available software, the axisymmetric method is applied.

- The length of the bellow is assumed to be optimal at 1mm, however this should be validated. Further FEA can be performed to test different lengths of the bellow, although a longer bellow might result in a double bulge in stead of a larger expansion (see figure 23. The length of the bellow should also be minimized, as it adds as a straight geometry to the deflected tip. Therefore it is valid to take a length of 1mm as starting point.
- It is assumed that failure, or fatigue models for cyclic loading are not necessary due to the fact that the bellow is only compressed 3-5 times during use.

The FEA is based on a variety of choices to make the model run smoothly. This is at the same time a limitation of FEA, as each choice limits the results of the model in some way. The most important choices are explained below:

First of all, the mesh is chosen based on a parametric study. The chosen mesh shows stable results, but What could be looked into is an adaptive mesh. This means that the areas where the most internal strains happen (for example at the corners), are more finely meshed than the other parts. This could take the accuracy of the results to another level.

The choice for the friction coefficient is also based on a parametric study evaluating the difference in reaction force outcomes. It is observed that the lower friction coefficient values give irregularities in the reaction force graphs in the form of a peak at the end of compression. This indicates buckling, and therefore validates the choice for a friction coefficient of 0.4 or higher. Nevertheless, it is still possible that the friction coefficient between all interfaces deviate from this value in reality. This is another reason for doing a validation test with a real bellow prototype, preferably in clinical working environment. The clinical environment consists of blood and fluids that might act as lubricant, and this can significantly influence the friction between the parts.

It might mean that in a wet environment, the forces to expand the bellow are different than the FEA suggests.

The choice for the Ogden material model is based on the curve fitting method, as well as the fact that this model is known for giving a reliable outcome for hyperelastic problems. The N=1 variant of the Ogden model is a logic choice because the material properties are only based on one mechanical test. Producing more parameters by doing more different mechanical test would allow the choice for more complex material models and for fitting experimental errors.[15] In a future study with more mechanical tests, other material models than the Ogden model could be explored and results could be compared.

It is chosen not to give the catheter, guidewire and bottom plate material properties, as it is known that when both elastomer and metal parts are connected in a model, the interfaces between the two will often create non-valid results.[7]. It should however be taken into account that there can be some non-rigid behavior of these components in reality. In the next section, the assumption of a rigid catheter tip is validated.

For the scope of this project, an ABAQUS/Standard FEA is done, because it is proven to give accurate results for a quasi-static simulation. A suggestion that can be done for an additional research would be to try an ABAQUS/Explicit FEA. This uses another numerical approach to solve problems. In ABAQUS/Standard, the equations are solved for each time step, making it more susceptible to also capturing non-linearities (buckling), whereas in Explicit the solution for a particular time step is based on the outcome of the previous step. This would be appropriate for extreme non-linear deformation problems or dynamic models, and could therefore also avoid buckling problems. This complex analysis however is not required and does not necessarily fit the scope of this project.

3) Validation

In the process of choosing unknown parameters, it is a pitfall to base the choice on which ones would improve the simulation, rather than which are most realistic. It should be evaluated whether the set FEA conditions are realistic and reproducible in the prototype.

FEA methods, when used correctly produce results that one can trust but should definitely verify. As formulated by [7], the results are approximate rather than exact: this means that a global indication of the material's response is given, and that it can not be fully held responsible as predictive tool for the engineering problem. To validate the results of the simulation, an assembly is set up to test the deformation of the rubber bellow. A bellow of 0.55 mm diameter is made

of the specific PU rubber in a special mold. The assembly consisted of a 0.15 guidewire with a welded 0.30 stopper geometry at the end. Over the guidewire, the bellow was placed with the two stainless steel (0.56 mm diameter, 0,1 mm thick and 10 degrees conical) rings enclosing it on both sides. Holding the mantle in place and pulling the guidewire resulted in an axial compression of the bellow. The force with which the guidewire was pulled was observed and expansion of the bellow was measured.
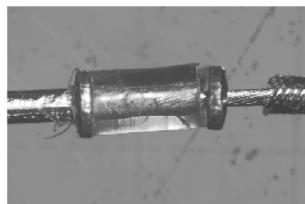
Fig. 24: Poly-Pur PS 161 bellow in validation assembly, non-expanded

Fig. 25: Poly-Pur PS 161 bellow in validation assembly, expanded with 0.5 N

Figure 24 and 25 show the results of 0.0 N and 0.5 N compression force respectively. This assembly is considered to be as close as possible with the current production techniques to the FEA model and its dimensions, properties and boundary conditions. Upon axial compression, the bellow expands quite uniformly from a diameter of 0.55 to 0.71mm, which is 129%.

This expansion is almost as much as the resulting expansion from the FEA at 0.4 N compression force. It concludes that an equally small amount of force is needed for the required expansion for realization of the working principle. This provides a promising step towards proof of principle of the product.


Fig. 26: Expanded bellow (left) before pulled into the catheter (right)

Fig. 27: Expanded bellow pulled into the catheter with a force of 0.5N

The expanded bellow is now pulled inside a Progreat catheter with a 0.65 inner diameter. The expanded bellow is considered large enough to create tension in the catheter wall, because it expands up to a size larger than the inner diameter of the catheter. Figure 26 and 27 show the expanded bellow on the guidewire that is pulled into the catheter. The
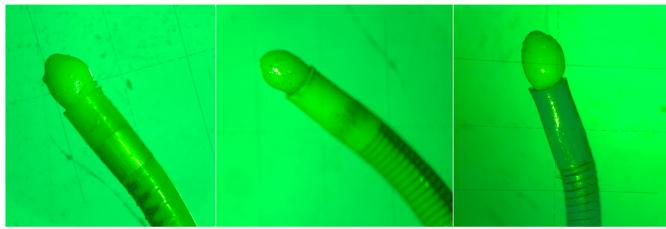
Fig. 28: Catheter tip deformation validation, from left to right: Boston Scientific Renegade 2.7F, Boston Scientific Direxion 2.8F, Boston Scientific Direxion 2.4F

expanded bellow is not able to go inside the catheter tip and pulling forces of ¡0.5 can be applied. This is a proof of principle and also confirms that the FEA results were representative with the theoretical prediction this proof of principle.

The catheter does not seem to deform significantly when the bellow is pulled against it with a force of 0.5N. The other catheters are also tested on the same effect, only with a permanent bellow (made of 2component glue) because the rubber bellows are not available yet in all catheter sizes.

From this evaluation it can be concluded that the deformation in the catheter tip during use can be neglected, so considering the catheter wall as a rigid part is validated for the FEA. This also decreases the risk of the bellow sliding into the catheter in a "wet" clinical environment, because the catheter wall will not deform significantly.

VIII. CONCLUSION

A. Mechanical test

The compression test with the 1 mm/s compression speed yielded an accurate stress-strain curve for the Poly-Pur PS 161 rubber. The stress-strain curve is based on a small compression domain due to limitations of the test equipment, however, it gives sufficient data to define accurate material properties in ABAQUS using the curve fitting method. In order to take the accuracy of the material properties to a next level, a next study would benefit from an additional biaxial and planar mechanical test, or a tensile test that gives results up to material failure.

B. Finite Element Analysis

The main takeaways from this study in terms of the design are: Based on the FEA results, Poly-PUR PS 161 is approved to be a suitable material for the envisioned bellow functionality, as long as the displacements/forces and geometries in the system can be precisely mimicked and controlled. A force of 0.4 N or even 0.8 N (respectively causing a

40% and 45% compression of the bellow) is required for sufficient expansion of the bellow. A pulling force of 2.0N (that guarantees deflection of the catheter tip) is successfully achieved, without the bellow reaching its material limits.

These values are within realistic boundaries for the physical prototype and are validated by prototyping the assembly as accurate as possible with the current production techniques. The results from this validation test are promising for the further development of this mechanism, as they are in line with the computational assessment of the concept by the FEA. Both the theoretical study and practical test conclude to a proof of principle for the bellow design.

C. Future outlook

For future research, the assumptions made can be reconsidered and a more elaborate FEA can be performed. Different material models can be compared (based on more accurate material properties), and a non-symmetric simulation can be evaluated with a more complex 3D model. Nevertheless, this study with validated assumptions and simplifications gives an accurate representation of the behavior of the rubber bellow during use.

As stated before, a proof of principle can not solely be based on an FEA, but physical testing is required to validate the results. That is why the next step of the design process is to make more bellows from the Poly-PUR PS 161 and translate the boundary conditions of the FEA to the mechanism in the prototype. Efforts should be made to recreate the mechanism as in the FEA as precisely as possible:

- Assembly: Achieving the level of precision in geometry might be a challenge for manufacturing. Non-centrical placement might cause a different deformation of the bellow when pulled. Therefore, the components of the system must be modified to precisely align with each other.
- Friction: When the friction between the bellow and the other components is low, the bellow might slide over the other parts when compressed. To eliminate this, the stopper and mantle could both be glued to the top and bottom of the bellow, which would eliminate the influence of friction (or actually, create a maximum friction) in those interfaces. This is beneficial to the assembly as the bellow is held in place. Other solutions can be developed to hold the bellow in place in the assembly.
- Use: For expansion of the bellow, a specific displacement must be applied to the mechanism from a distance of 1.30 - 1.50 m (length of the catheter). It will be a challenge to apply these boundary conditions in such

level of precision in reality, considering stretch in the cables. The control device must be precisely calibrated to apply the right amount of boundary conditions in the mechanism. The control device must also include a mechanism to deflect the catheter tip after the bellow is activated.

With this prototype, the team can start testing the bellow in combination with a modified catheter. Technical validation of the concept can be done measuring the turns that can be made and the required forces. After that, the test is preferably performed by specialists in clinical environment representing the real "wet" working conditions (in a phantom model or real vasculature), for a final proof of concept.

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APPENDIX I
CONVERT VOLTAGE TO NEWTON

The measured values in Voltage have to be recalculated to values in Newton to show how the dependent variable is extracted from the raw data. By putting small weights (50 gr, 100 gr, 150 gr, 200 gr, 250 gr, 300 gr) on the linear stage to create a correlation between weight, and thereby Newton, and the measured voltage. The graphs of the measurements showed after three seconds, when the weight was stabilised, a value of the voltage that corresponded with the weight. The average of the voltage was calculated in the period of the graph where the value was close to stable. The corresponding value in Newton was calculated with the following formula:

$$F = m \cdot g \qquad (4)$$

with F is the force [N], m is the mass [kg] and g is the gravity with an approximate value of 9.81 m/s^2. This has been done for all six weights which resulted in a straight line which are the measured values in voltage and the corresponding values in Newton. See Figure 29.
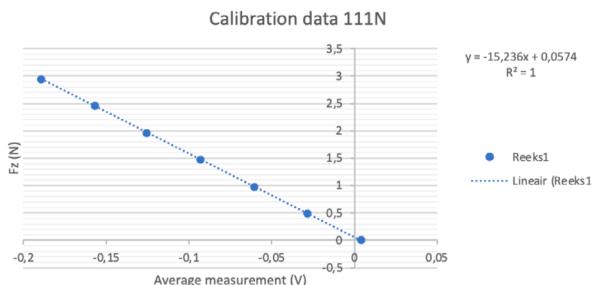
Fig. 29: Correlation between applied force and voltage output of the sensor

Fig. 30: Raw data of all measurements in N
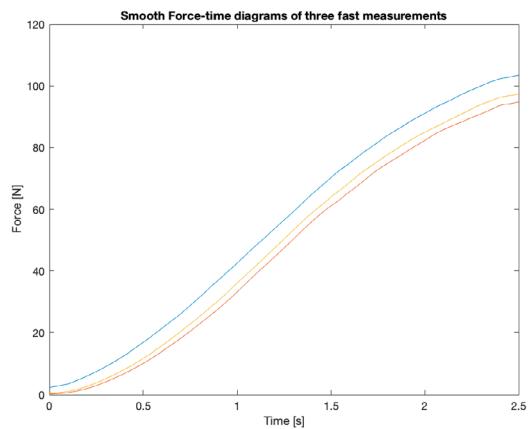
Fig. 31: Fast compression test 3 resulting Force-time graphs

APPENDIX II
RAW DATA PLOTS

In figure 30, the raw data in V is converted to N, and limited to only the useful domain in which the compression took place. Logically, it is visible that the graphs of the slow compression test have a twice as large domain as the fast compression test.

APPENDIX III
PROCESSED DATA PLOTS

Figure 31 shows the 3 Force (N) – Time (s) graphs of the fast compression tests (smoothened out and in the right domain). This method was repeated for the slow compression test and the Force (N) – Time (s) graphs of the slow compression tests are visible in figure 32.

APPENDIX IV
MESH CONVERGENCE TEST

The Mesh Convergence test is performed for the FEA model evaluated with Ogden material model, to evaluate what mesh is most suitable. By decreasing the mesh element size, the amount of elements increases. Each time a larger amount of elements is applied, the simulation is run and the results are observed. The reaction force in the bottom plate at the end of the compression step is plotted against element size in figure 33. The graph has the recognizable shape of a mesh convergence graph. The first coarse meshes show a strong increase, and as soon as the mesh becomes refined enough, the graph flattens out. From this graph, it can be concluded that a mesh of 125 elements will give sufficiently accurate results.
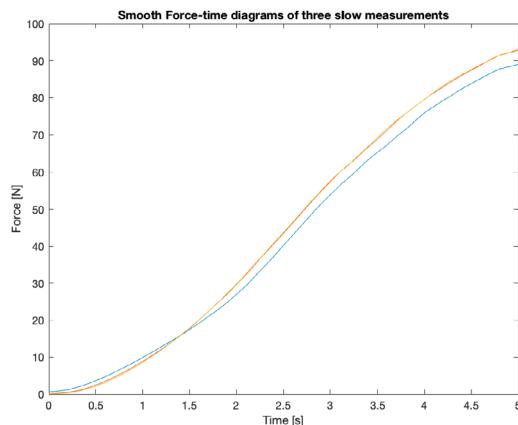
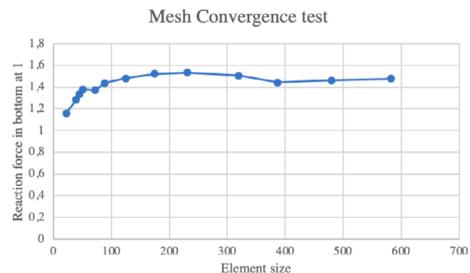**Fig. 32:** Slow compression test 3 resulting Force-time graphs

Fig. 34: Reaction force in the bottom plate, of all different meshes in one graph

Fig. 33: Ogden Mesh convergence graph, amount of elements VS reaction force in the bottom plate at the end of compression step

The results of the parametric study first of all show that friction coefficients of 0 to 0.3 give buckling results in the Field Output, as visible in figure 35. The elements at the edges show extreme distortion: the outer parts of the bellow material are folding over the edges of the stopper and bottom plate. This strongly influences the validity of the reaction force results. These invalid results show as a large peak in the reaction force plot of the bottom plate at time 1.0, as in figure 36, 37 and 38. These friction coefficient values are therefore not considered to do the simulation any good.
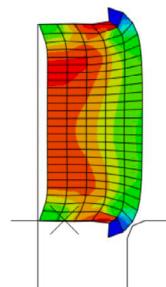
Another way to validate this mesh, is to plot the reaction force graphs of all different meshes, as shown in figure 34. The meshes of 22, 39, 45, 51, 72, 88 elements, the reaction force in the bottom plate increases in a linear way. From the 174 mesh and higher, the graph is not linear anymore which suggests some irregular movements in the model. This effect is also visible in the field output (the corners of the bellow fold over the edges, which causes the reaction force to become unrealistic). A mesh of 125 will provide enough detail, as well as a linear reaction force graph.

Fig. 35: output 0.2 friction buckling that causes peak in reaction force graph

APPENDIX V
FRICTION PARAMETRIC STUDY

For the most appropriate friction coefficient, a parametric study is done in which the friction is increased in steps, and the resulting reaction force graphs are compared. Since rubber is known to have a large friction coefficient, the hypothesis is that the higher friction coefficients are most likely to give accurate results.

The reaction force plots resulting from applying a higher friction coefficient can now be compared to choose the value that is most likely to give accurate results. In figure 39, the reaction force in the bottom plate shows a small peak at time 1.0, after which it flattens out to 0. It is not realistic that the reaction force in the bottom plate is 0, and therefore friction coefficients of 0.5 or 0.6 are considered to be reliable. Both 40 and 41 show an approximately constant reaction force after compression. A choice is made
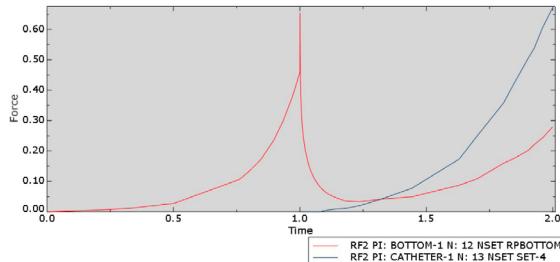
Fig. 36: Reaction forces in catheter and bottom plate, friction coefficient f=0.1
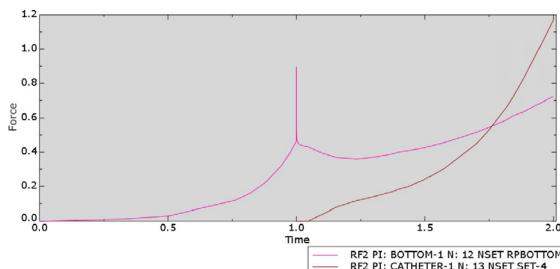
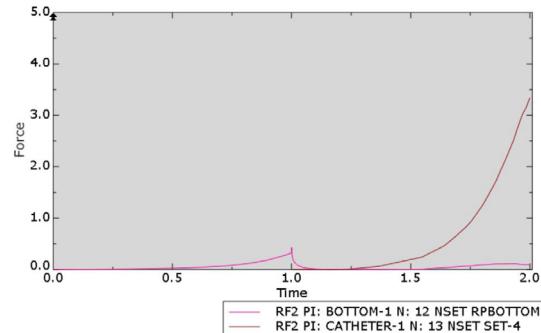**Fig. 37:** Reaction forces in catheter and bottom plate, friction coefficient f=0.2
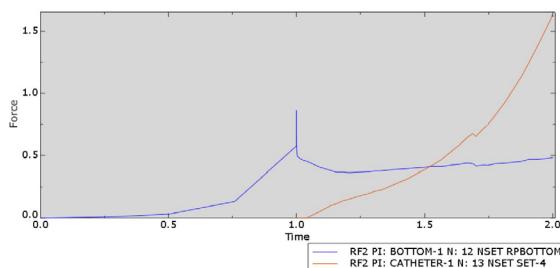
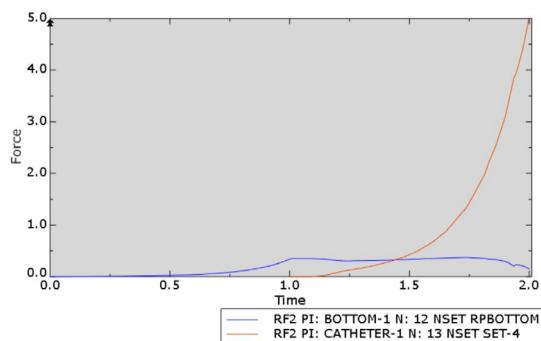**Fig. 38:** Reaction forces in catheter and bottom plate, friction coefficient f=0.3

to use the friction coefficient of 0.5, because it is assumed that this value will be more realistic than 0.6 in this assembly.

Appendix VI
### Lower compression force trial

After analyzing the result of the FEA, it is put to the discussion whether a smaller compression of the bellow would also be sufficient to achieve the mechanism's functionality. A compression (expressed as downward movement of the top plate) of -0.3 mm until -0.5 mm is applied, increasing in steps of -0.05 mm. All results are based on a system in which a friction coefficient of 0.5 is

Fig. 39: Reaction forces in catheter and bottom plate, friction coefficient f=0.4
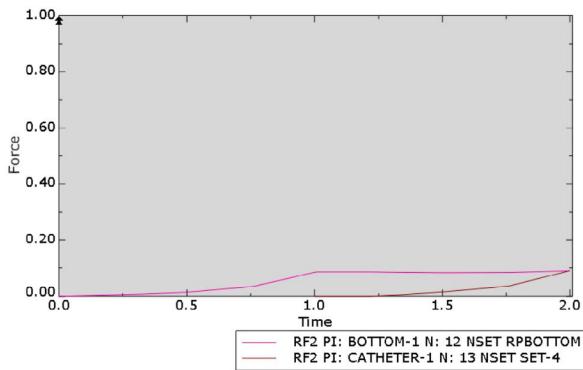

Fig. 40: Reaction forces in catheter and bottom plate, friction coefficient f=0.5
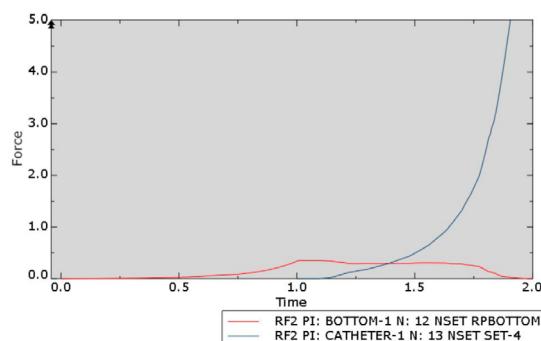
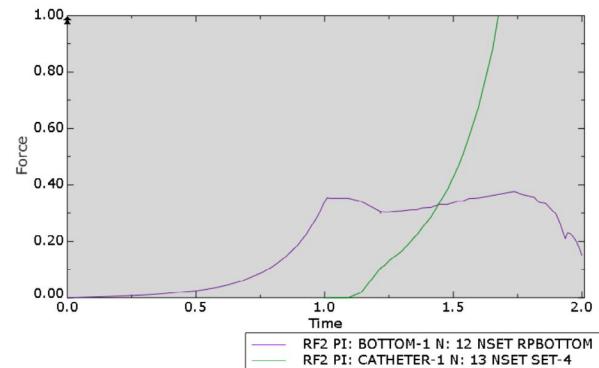

Fig. 41: Reaction forces in catheter and bottom plate, friction coefficient f=0.6

applied on all the interactions. Figure 42 shows that the intended reaction force of 0.5 N in the catheter wall is not reached. This indicates that a compression of -0.3 mm is not enough. Figure 43 shows the desired resulting reaction force graphs. Only 0.2 N is needed for the compression, and the reaction force in the catheter of 0.5 N is reached

at time ±1.8. However, as it is expected that the catheter might also deform slightly (although this is only the slightest amount), this result does not give enough confidence for validating the working mechanism. Also, the 2 N (the required reaction force multiplied by the safety factor of 4) is never reached. Figure 44, 45 and 46 show an increasing irregularity in the reaction force graph of the bottom plate, and the compression of -0.5 mm gives a strong peak at time 1.0. Both the compression forces of -0.4 mm or -0.45 mm are considered realistic (the 2 N reaction force in the catheter is also reached before time step 2.0), and since a -0.45 mm compression only costs 0.8N, it is even recommended to aim for this compression for optimal working of the mechanism.
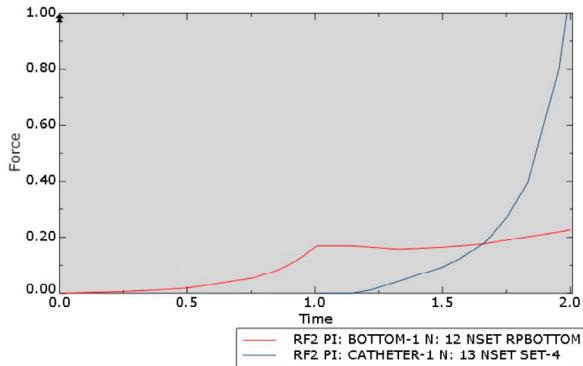
Fig. 44: Reaction forces in catheter and bottom plate, compression of -0.4 mm

Fig. 42: Reaction forces in catheter and bottom plate, compression of -0.3 mm
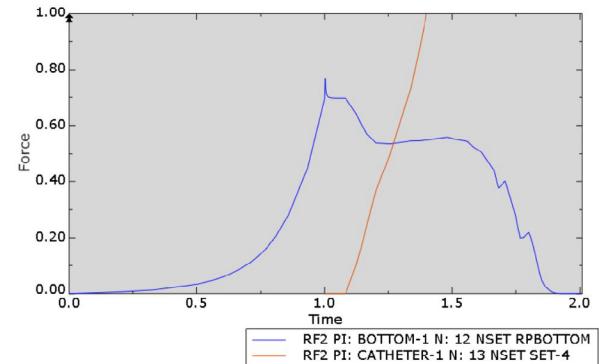
Fig. 45: Reaction forces in catheter and bottom plate, compression of -0.45
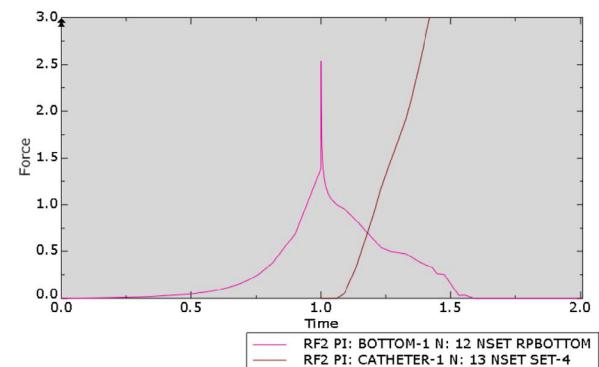
Fig. 43: Reaction forces in catheter and bottom plate, compression of -0.35 mm

Fig. 46: Reaction forces in catheter and bottom plate, compression of -0.5 mm

Appendix VII
Matlab Code

```matlab
1   clear all
2   clc
3
4   %% Constants
5   h0 = 20;                        %height sample in mm
6   speedslow = 1;                  % mm/s
7   speedfast = 2;                  % mm/s
8   A = 0.0004;                     %area in m2
9
10  %% Load data from .mat files directory
11  DataFastRaw1 = load('nieuw2a');
12  DataFastRaw2 = load('nieuw2b');
13  DataFastRaw3 = load('nieuw2c');
14  DataSlowRaw1 = load('nieuw1a');
15  DataSlowRaw2 = load('nieuw1b');
16  DataSlowRaw3 = load('nieuw1c');
17
18  % Define needed voltage file from raw data
19  DataFastVoltage1 = DataFastRaw1.nieuw2a.Y(1).Data;
20  DataFastVoltage2 = DataFastRaw2.nieuw2b.Y(1).Data;
21  DataFastVoltage3 = DataFastRaw3.nieuw2c.Y(1).Data;
22  DataSlowVoltage1 = DataSlowRaw1.nieuw1a.Y(1).Data;
23  DataSlowVoltage2 = DataSlowRaw2.nieuw1b.Y(1).Data;
24  DataSlowVoltage3 = DataSlowRaw3.nieuw1c.Y(1).Data;
25
26  %% Voltage to Newton via calibration test
27  NewtonFast11 = ((15.236*DataFastVoltage1) - 0.0574);
28  NewtonFast22 = ((15.236*DataFastVoltage2) - 0.0574);
29  NewtonFast33 = ((15.236*DataFastVoltage3) - 0.0574);
30  NewtonSlow11 = ((15.236*DataSlowVoltage1) - 0.0574);
31  NewtonSlow22 = ((15.236*DataSlowVoltage2) - 0.0574);
32  NewtonSlow33 = ((15.236*DataSlowVoltage3) - 0.0574);
33
34  %% Selecting correct domain for the hyperelastic material (1s to 6s for slow, 1s to 3.5s for fast)
35  NewtonFast1 = NewtonFast11(1001:3501);
36  NewtonFast2 = NewtonFast22(1001:3501);
37  NewtonFast3 = NewtonFast33(1001:3501);
38  NewtonSlow1 = NewtonSlow11(1001:6001);
39  NewtonSlow2 = NewtonSlow22(1001:6001);
40  NewtonSlow3 = NewtonSlow33(1001:6001);
41
42  %% Smoothing signal using movmean
43  KFast = 201;                    %Period value over which vector is averaged
44  NFast1 = movmean(NewtonFast1,KFast);
45  NFast2 = movmean(NewtonFast2,KFast);
46  NFast3 = movmean(NewtonFast3,KFast);
47  KSlow = 402;                    %Period value over which vector is averaged
48  NSlow1 = movmean(NewtonSlow1,KSlow);
49  NSlow2 = movmean(NewtonSlow2,KSlow);
50  NSlow3 = movmean(NewtonSlow3,KSlow);
51
52  %% Averaging signals to get most reliable curve
53  AverageFast = (NFast1+NFast2+NFast3)/3;
54  AverageSlow = (NSlow1+NSlow2+NSlow3)/3;
55
56  %% Making time vectors
57  TFast = [0:0.001:2.5];          %time vector fast 0 to 2.5s, Hz= 1/0.001 = 1000Hz
58  TSlow = [0:0.001:5];            %time vector slow 0 to 5.0s, Hz= 1/0.001 = 1000Hz
59
60  %% Displacement using the fact that compression is constant delta_h = V*T
61  DeltaHFast = TFast*speedfast;
62  DeltaHSlow = TSlow*speedslow;
63
64  %% Strain Calculation (delta_h)/h1
65  StrainFast = DeltaHFast/h0;
66  StrainSlow = DeltaHSlow/h0;
67
68  %% Stress Calculation sigma = F/A
69  StressFast = AverageFast/(1000*A);          %Stress in kPa
70  StressSlow = AverageSlow/(1000*A);          %Stress in kPa
```

```matlab
71
72   %% Figures
73   figure
74   plot(DataFastVoltage1)
75   hold on
76   plot(DataFastVoltage2)
77   plot(DataFastVoltage3)
78   plot(DataSlowVoltage1)
79   plot(DataSlowVoltage2)
80   plot(DataSlowVoltage3)
81   title('Raw data in Voltage')
82   ylabel('Force sensor Fz [V]')
83   xlabel('Measurement steps [-]')
84   legend('Fast 1','Fast 2','Fast 3', 'Slow 1', 'Slow 2', 'Slow 3', 'location','southeast')
85
86   figure
87   plot(NewtonFast1)
88   hold on
89   plot(NewtonFast2)
90   plot(NewtonFast3)
91   plot(NewtonSlow1)
92   plot(NewtonSlow2)
93   plot(NewtonSlow3)
94   title('Raw data in Newton')
95   ylabel('Force sensor Fz [N]')
96   xlabel('Measurement steps [-]')
97   legend('Fast 1','Fast 2','Fast 3', 'Slow 1', 'Slow 2', 'Slow 3', 'location','southeast')
98
99   figure
100  plot(TFast, NFast1)
101  hold on
102  plot(TFast, NFast2)
103  plot(TFast, NFast3)
104  title('Smooth Force-time diagrams of three fast measurements')
105  ylabel('Force [N]')
106  xlabel('Time [s]')
107
108  figure
109  plot(TSlow, NSlow1)
110  hold on
111  plot(TSlow, NSlow2)
112  plot(TSlow, NSlow3)
113  title('Smooth Force-time diagrams of three slow measurements')
114  ylabel('Force [N]')
115  xlabel('Time [s]')
116
117  figure
118  plot(StrainFast, StressFast)
119  hold on
120  plot(StrainSlow,StressSlow)
121  title('Strain-Stress curve for fast and slow test')
122  ylabel('Stress [kPa]')
123  xlabel('Strain eta [-]')
124  legend('Fast Test','Slow Test', 'location','northwest')
125
126  %% Extract data points (n<100) to export to ABAQUS
127  ValueStrainSlow = StrainSlow(:);
128  ValueStressSlow = StressSlow(:);
129  DataNewStrain = ValueStrainSlow(1:52:end);
130  DataNewStress = ValueStressSlow(1:52:end);
```