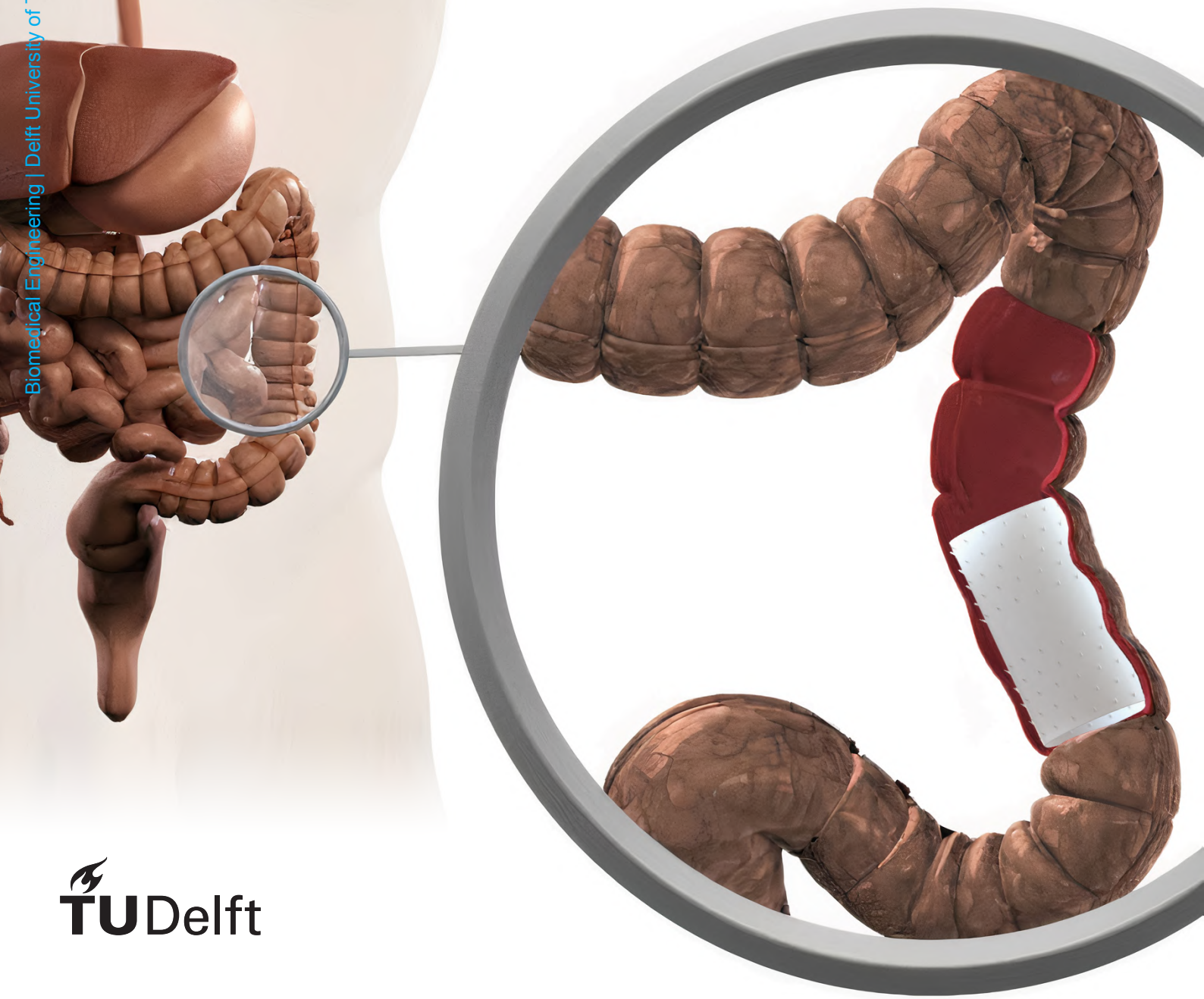
Biomedical Engineering | Delft University of Technology & Department of Surgery | Erasmus Medical Center

Preventing Anastomotic Leakage

An experimental approach to the redesign of a colorectal stent

Nout van Kuik



TU Delft

Preventing Anastomotic Leakage

An experimental approach to the redesign of a colorectal stent

by

Nout van Kuik

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This thesis is confidential and cannot be made public until December 8, 2024

TU Delft

Preface

This master thesis is about the redesign of a prototype for a colorectal stent to cover an anastomosis. The master thesis is an obligatory course for the Master of Science BioMedical Engineering at the TU Delft. The thesis assignment was proposed in collaboration with Prof. Dr. J.F. Lange, Prof. Dr. GJ. Kleinrensink from the department of Surgery and Dr. John Vlot from the department of Pediatric Surgery at the Erasmus Medical Center and was under supervision of Dr. John van den Dobbelsteen from the TU Delft.

Foremost, I would like to thank John Vlot for his guidance throughout this project. Thank you for always making time and for the fruitful discussions we had about the project. I would also like to thank all the other members from the REPAIR group at the Erasmus MC, especially Prof. Lange and Prof. Kleinrensink for making this project possible. Thanks to all the other colleagues in the basement for your help and company. At last, I would like to thank John van den Dobbelsteen for guiding me in this project from the TU Delft and Dimitra Dodou for taking place in the committee.

Nout van Kuik
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Abstract

The large intestines, or colon, is the last part of the digestive tract before the rectum. Colorectal cancer is one of the main reasons that patients need a colon resection. A colon resection is a surgery in which the malignant part of the colon is removed. After removal of the tumor, the two ends of the colon need to be reattached, also called anastomosed. This is usually done using sutures or staples. One of the most frequently occurring and major complications is that the anastomosis does not heal correctly. This can cause an anastomotic leakage, which means that fecal matter and fluids with bacteria can flow into the otherwise sterile abdominal cavity. This is a serious complication that can even result in death. Therefore, a solution can be to insert a stent to cover the anastomosis from the inside, preventing feces and fluids from entering the abdominal cavity. Such a stent was developed at the department of Surgery of the Erasmus MC.

This thesis focuses on the redesign of this stent to cover an anastomosis. Two main problems with the stent were stent migration due to insufficient friction between the stent and the colonic wall, and intestinal blockage due to the presence of the stent.

Preliminary research and a literature study showed that the addition of barbs to the stent could increase friction with the colonic wall. Optimal barb dimensions were researched on fresh colon specimens in an experimental setup. Ideal barb parameters were a height of 1.5 mm, diameter of 1.0 mm, an angle of 30°, with a distribution of 3 barbs per cm^2. In addition, the ideal stent diameter was explored in an experiment with fresh colon specimens. The stent should expand the colon with 50 - 60%. To safely insert and extract a stent with barbs in the colon, a patent search was executed to explore the possibilities of barb and colon protection. A stent with a reducible diameter and a tubular protection structure were identified as the most promising methods to safely insert a barbed stent. The second problem of intestinal blockage was analyzed and causes of intestinal blockage were identified. Minimizing the frontal contact surface at the proximal end of the stent was assumed to be the most important factor to reduce intestinal blockage. A minimal frontal contact surface also reduces the force that feces exerts on the stent, thus reducing the chance of stent migration.

The previously mentioned experiments and analysis formed the basis of a list of design requirements for a new prototype stent. The requirements were divided into five categories; fixation, dimensions, materials, delivery method and performance. After analyzing different manufacturing processes and available materials, two concepts were designed and produced. One concept was chosen after careful considerations of both options.

The final prototype consisted of a stent with barbs that was 3D printed. This design was validated on the set of requirements that were set up earlier. The material of the stent is both flexible and stiff. For insertion and extraction of the stent, the diameter can be reduced by longitudinal inward folding, while the stent forms a rigid tube while in a deployed state. The barbs are stiff and strong and can withstand the force that would move the stent. The frontal contact surface of the stent was reduced by more than 18 times compared to the old prototype, to reduce the influence on intestinal blockage. The stent is surrounded by a sheet to protect the barbs and prevent tissue damage during insertion. A validation experiment showed that the stent was improved in fixation compared to the old prototype. Therefore, based on the research executed in this thesis, the final prototype should theoretically migrate less and cause less blockage. However, an ex-vivo experiment should validate the fixation force of the new prototype, and in-vivo experiments on pigs should determine if the prototype actually does not migrate and actually does not cause intestinal blockage.

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Glossary

Abdominal cavity	Largest hollow space in the human body that contains most of the organs, such as the large intestines.
AL	Anastomotic leakage; leakage of fecal matter from the intestines into the abdominal cavity.
Anastomosis	A connection made surgically between two tubular parts of the body, such as the intestines.
Colon	The main part of the large intestines.
Colorectal	Referring to the colon and rectum of the human body.
Distal	Situated away from the center of the body or from the point of attachment.
Ex-vivo	Outside a living body.
Invasive profile	Profile with barbs.
In-vivo	In a living organism.
Noninvasive profile	Profiles made of soft polymer and without barbs.
Profile	A surface with a certain structure.
Proximal	Situated closer to the center of the body or the point of attachment.
Specimen	A sample of animal tissue.
Test plate	A plate on which a profile was added for experiments.

1

Introduction

The gastrointestinal tract is the tract that goes from the mouth to the rectum. It is further composed of the esophagus, stomach, small intestines and large intestines, the latter also called the colon. The tract digests food and transports the remains as feces to the rectum, before it is defecated. The main function of the colon is to extract water and remaining nutrients from the feces. A colon resection can be necessary for patients suffering from for example colorectal cancer. Colorectal cancer is the third most common type of cancer, with almost two million new cases worldwide per year [1]. The number of patients is also increasing for people aged under 50 years [2]. A colon resection is a procedure in which a part of the colon is removed. In the case of colorectal cancer, the malignant tissue is removed. After the resection, the two ends of the colon need to be reattached, also called anastomosed. See Fig. 1.1 for a schematic overview of this procedure. A colon resection was performed in 59.9% - 81.3% of patients diagnosed with colorectal cancer [3], and in the Netherlands alone, 10.000 of these procedures are performed each year [4]. These numbers underline the importance of good treatment options.

Currently, the most commonly used treatment option is reattaching the two ends using staples or sutures. Unfortunately, a major postoperative complication that can occur is anastomotic leakage. An anastomotic leakage implies that the anastomosis is not healed correctly or not reattached. This means that fecal matter and fluids can flow from the inside of the bowel into the otherwise sterile abdominal cavity. This is a serious complication that can cause severe damage to the patients' health, in some cases even resulting in death. Anastomotic leakage occurs in up to 11% of colonic anastomoses [5]. The mortality rate of patients with an anastomotic leakage ranged from 1.7% - 16.4% [6, 7]. These statistics underline the importance of preventing anastomotic leakage and ensuring a good and safe healing process.

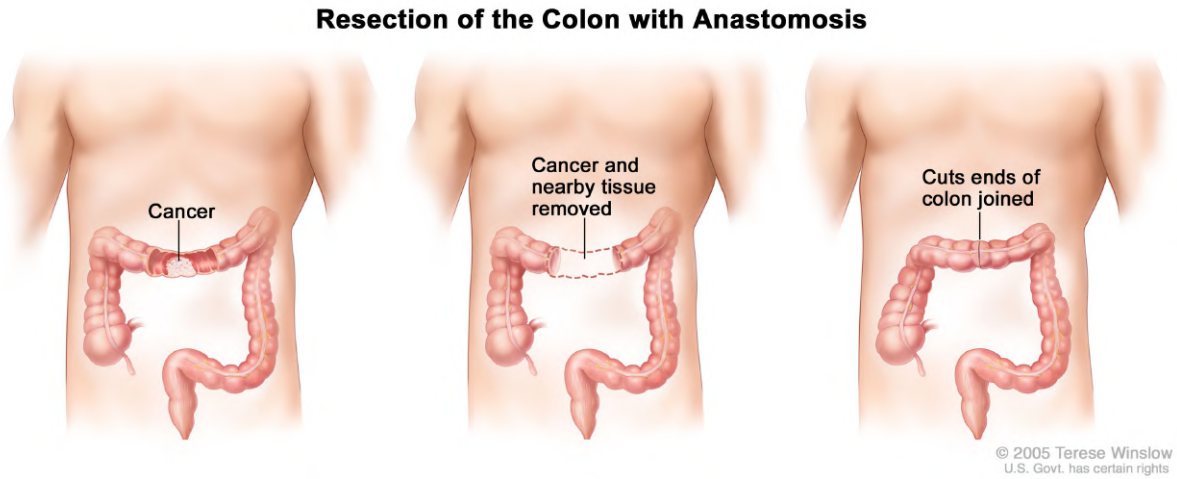


Figure 1.1: Resection of the colon with anastomosis, ©2005 Terese Winslow [8].

A possible solution to prevent intestinal fluids from entering the abdominal cavity is to place a stent or sheath to cover the anastomosis from inside. Colonic stenting is not a completely new technique for the adjuvant treatment of an anastomosis, and multiple designs of stents already exist [9]. However, for varying reasons none of these stents is currently used in clinical practice.

Therefore, the department of surgery of the Erasmus MC developed and patented a prototype to investigate the possibilities and feasibility of a new stent design [10]. This prototype design formed the starting point of this thesis. However, the scope of this thesis was not limited to the techniques used in the stent designed by the Erasmus MC. The design of this prototype is further elaborated in Chapter 2.

There are two advantages to this stent. First, the most important advantage is that it protects the abdominal cavity from contamination with fecal material in the case of a small leak in the anastomosis. Gut bacteria infecting the abdominal cavity, also called fecal peritonitis, as a result of an anastomotic leakage, is the most feared complication in colon resections. Second, the stent could support the anastomosis from undue external and internal forces that may disrupt the anastomosis. These advantages could lead to the prevention of unwanted complications from anastomotic leaks and thereby ensure faster recovery, decreased hospital stay and in the end decreased healthcare costs.

However, when this prototype was tested in an in-vivo experiment in a pig, two main problems were encountered, which are described in the next section on the problem definition. A more extended description and insights from the in-vivo experiment can be found in Chapter 2.

1.1. Problem definition

Two main problems were determined after the in-vivo experiments and before the start of this thesis:

1. Stent migration
2. Intestinal blockage

Firstly, stent migration was caused by the lack of friction between the colon and the outside of the stent. As in this experiment, stent migration is a known complication for colonic stents [11]. This complication could be solved by creating sufficient friction between colon and stent. Therefore, stent migration was determined as the first of two main problems to be tackled.

Secondly, intestinal blockage was observed during experiments. It was observed that fecal matter accumulated at the proximal end of the stent. It was assumed that this accumulation of feces in combination with peristalsis of the colon would 'push' the stent in the direction of the anus, and in the end expel the stent. This was seen as the driving force behind stent migration, thus intestinal blockage was considered as the second main problem. Together, these two problems were further researched.

1.2. Research question

The purpose of this thesis was to research stent fixation and intestinal blockage. This led to the following research question:

- *"How to improve the fixation and decrease the effect of intestinal blockage for a colorectal stent to cover an anastomosis?"*

Chapter 2 in this thesis describes necessary background information on the anatomy of the colon, the design of the prototype stent, previously executed experiments and insights from the literature study. This background information forms the basis for the research in this thesis. Chapter 3 describes three experiments in which different barb designs are tested on friction. Chapter 4 describes a patent search on safe deployment of barbs. Chapter 5 describes the intestinal blockage, its causes and a solution for this problem. Chapter 6 summarizes the previous three chapters in a list of design requirements. Chapter 7 describes the design considerations and presents the new prototype. Chapter 8 validates the new prototype on the basis of the design requirements. Chapter 9 discusses the thesis and describes the scientific relevance, limitations and future recommendations of this thesis. Chapter 10 presents the conclusion of the whole thesis.

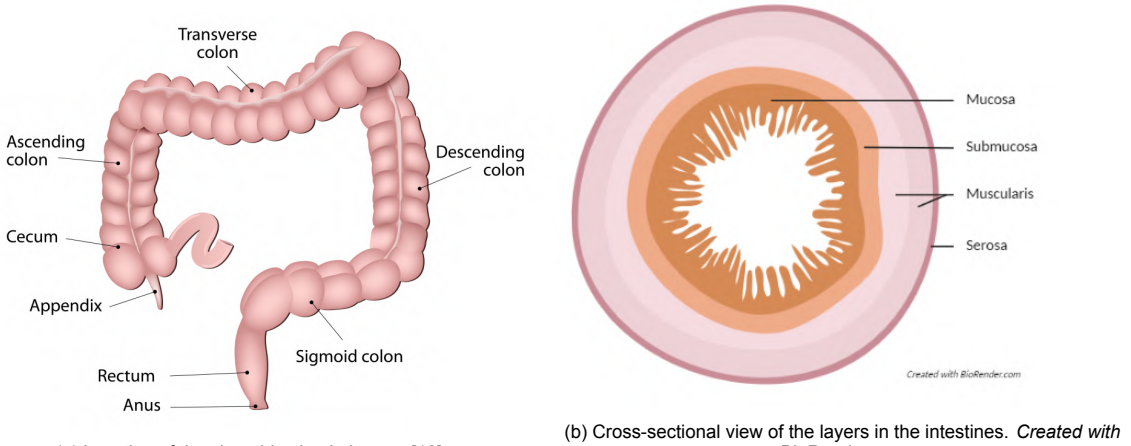
2

Background information

To answer the research question set in the introduction, new research was necessary. Before describing this new research, the functioning of the colon and previously executed research on this topic should be mentioned. Therefore, this chapter first gives an overview of the intestinal anatomy and the procedure of an anastomosis. Then the old stent design is analyzed and described. Furthermore, the previously executed experiments are summarized and the conclusion of the preliminary literature study is given.

2.1. Intestinal anatomy

The stent was designed for placement in the colon, and more specifically in the lower part, the sigmoid colon as presented in Fig. 2.1a. The colon is composed of four layers, as shown in Fig. 2.1b. It consists of the following from inside to outside: mucosa, submucosa, muscularis and serosa. The mucosal layer produces mucus, which is a thick and lubricious fluid. The mucosa is the most inner layer along which fecal matter passes. Mucus enhances the transport of fecal matter through the intestinal lumen, since it decreases friction. This property makes the fixation of stents more difficult. The second layer is the submucosa which contains blood vessels, lymphatics, and nerve fibers. The layer mostly consists of collagen fibers, which gives the colon the majority of its tensile strength. This layer plays an important role in the strength of an anastomosis. Direct opposition of the submucosal layers of the two ends, can minimize the risk of anastomotic leakage [5]. The muscularis or muscular layer consists of two smooth muscle layers: circular muscle and longitudinal muscle. Due to contractions and relaxations of these two layers, peristalsis takes place in the colon. Peristalsis is the movement of the colon to transport fecal matter through the colon. The last layer is the serosa and consists mostly of connective tissue.



(a) Location of the sigmoid colon in human [12].

(b) Cross-sectional view of the layers in the intestines. *Created with BioRender.com*

Figure 2.1: Location of sigmoid colon and colon layers.

These layers were of special interest for the research on barb design conducted in this thesis, as later explained in Chapter 3. The thickness of these layers was of importance. The mucosal layer of the colon consists of a firmly adhered mucus layer and a loosely adhered mucus layer. The first has a mean thickness of 116 μm and the latter 830 μm [13]. The submucosa has a mean thickness of 0.5 mm and the muscularis (circular and longitudinal muscles together) 0.8 mm [14].

Intestinal healing occurs in three phases: acute inflammatory phase, proliferative phase and a maturation phase. Bursting pressure, a property used to measure the anastomotic strength, reaches 60% by three to four days and 100% by the first week [5]. Thus, it is imperative that the stent should remain at the anastomotic site for at least a week. However, healing time could be longer for each individual patient, so ideally stent migration should be prevented for two weeks. Another important factor is that creating a tension-free anastomosis will improve the healing process of the colon [15].

2.2. Anastomosis procedure

Sutures and staples are currently the most used techniques to create an anastomosis. Sutures are used for side-to-side, end-to-side and end-to-end anastomoses [16]. Circular staplers are mostly used in low anterior resections for end-to-end anastomoses [5]. The stent is intended to be used with end-to-end anastomoses, because in this case the lumen will be more straight and continuous, therefore a better fit of the stent is expected in comparison to side-to-side or end-to-side anastomoses. A circular EEA stapler is preferred in recent years for end-to-end anastomoses. A stapler anvil is inserted in the proximal end of the colon, where a purse string keeps the anvil in place. Then the stapler is inserted through the rectum and attached to the anvil. Then the staples are fired by contracting the handle and the two colon parts are connected with staples. This procedure is shown in Fig. 2.2 from left to right.

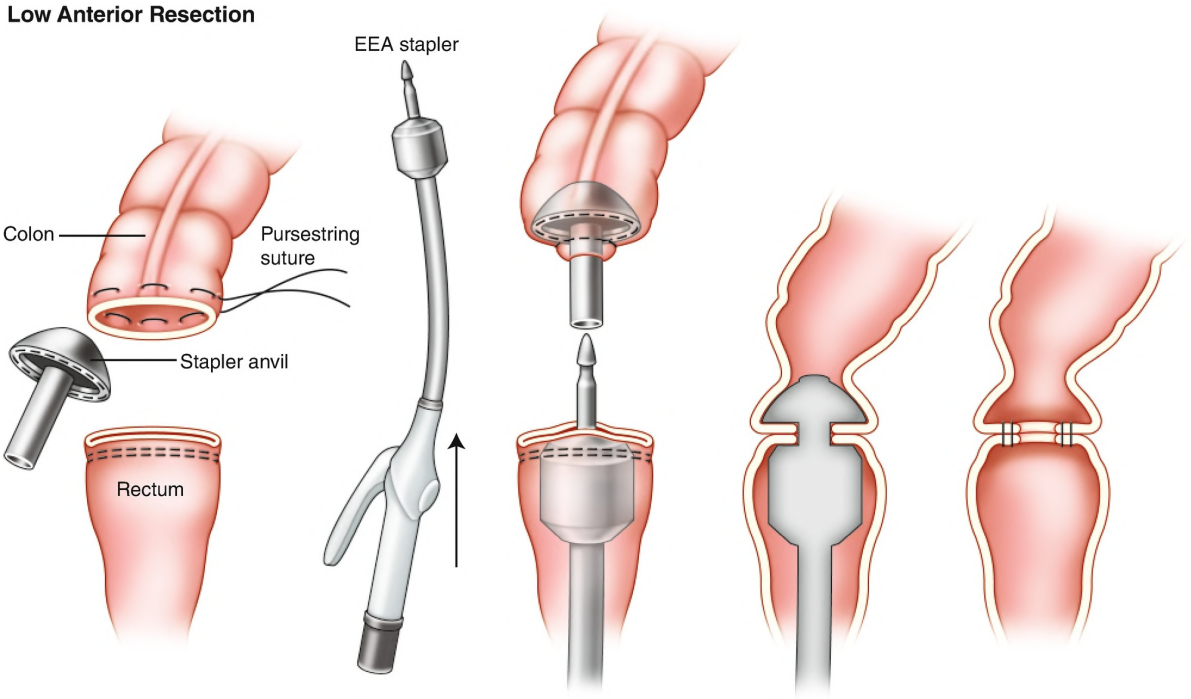


Figure 2.2: Procedure of creating a colorectal circular end-to-end anastomosis. Copied from: [17].

2.3. Old stent design

The stent design as proposed by the Erasmus MC formed the starting point of this thesis. To understand its working principle and moreover, why the stent was not working was of great importance. In addition, this stent design was already prototyped and tested ex-vivo and in-vivo. Therefore, data was available on how effective this design was in fixating in the colon and causing intestinal blockage. This data served as a point of reference to what extent a new design would improve fixation and blockage. The stent was patented by the Erasmus MC, so the schematic design of the stent was taken from this patent [10].

The current prototype stent consists of a hollow tube connected to two balloons, each at one end, around the tube. On the outside of the balloons, horizontal ridges were placed. In Fig. 2.3 a schematic cross-sectional view is shown of how the stent was designed and in Fig. 2.4 the approximate dimensions are given. The fixation of this stent was created by filling balloons with horizontal ridges on the outside. The prototype of the stent is presented in Fig. 2.5. The horizontal ridges can be seen on the outside of both balloons. The balloons are individually connected to plastic tubes (see Fig. 2.5b) that can be attached to a syringe, to fill the balloons.

The procedure of how the stent was intended to be used was as follows; First, an anastomosis is created by the surgeon with either staples or sutures, as described in the previous section. The stent is inserted either during the suturing of the anastomosis or afterwards retrograde from the rectum in case of a stapled anastomosis, thereby bridging the anastomosis. Then the balloons are filled with fluid to create sufficient friction between the colonic wall and the stent. The tubes to fill the balloons are cut off and closed with one or more clips. Once the stent is placed, fecal matter can pass through the stent while the colon heals on the outside of the stent. The stent can be seen as an extra means to reduce anastomotic leakage. The further clinical development of the stent was intended to be placed and removed transanally, to minimize the burden on patients. To remove the stent, the balloons could be punctured, decreasing the diameter of the stent for easier removal.

This stent design possessed several advantages and disadvantages, which are listed below.

Advantages

1. Diameter of the stent can be decreased and increased by means of filling the balloons. This ensures easier placement and removal.
2. Soft balloons were not harmful to the colonic tissue and caused no tissue damage or necrosis.
3. Good tissue healing in most in-vivo experiments.

Disadvantages

1. The balloons and ridges created insufficient friction with colonic wall.
2. Ridges on the balloons became flat when balloon was filled, further decreasing the effect on friction.
3. The inner diameter of the stent was small (24 mm) compared to the outer diameter (approx. 38 mm).
4. The stent caused intestinal blockage.

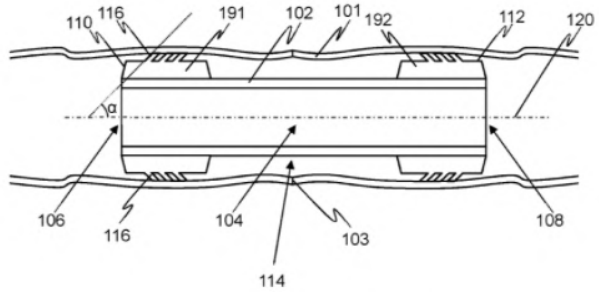


Figure 2.3: Schematic cross-sectional view of the current prototype stent, (102) tube, (191) & (192) balloons and (116) horizontal ridges [10].

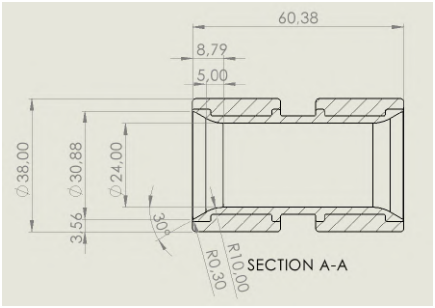
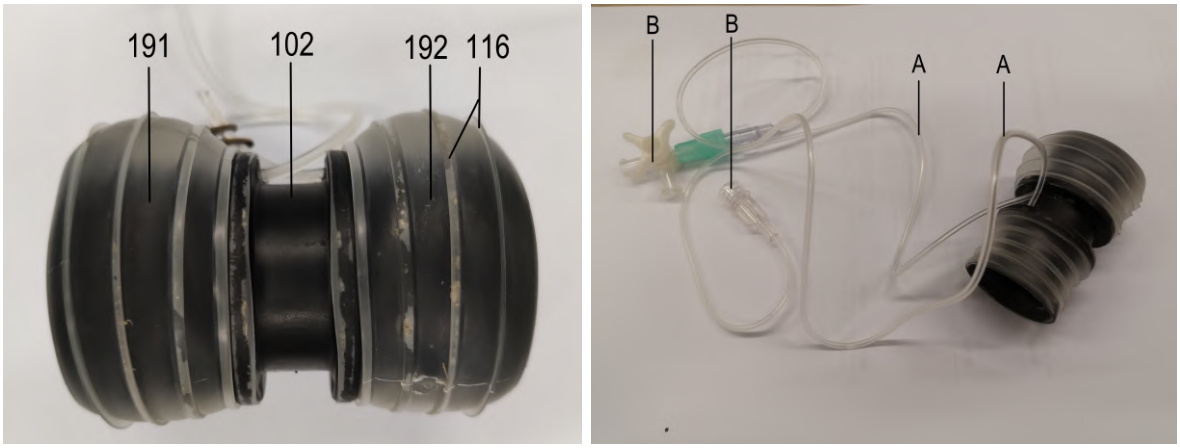


Figure 2.4: Dimensions of the old stent design.



(a) Close-up with (102) tube, (191) & (192) balloons and (116) horizontal ridges.

(b) Old prototype with (A) tubes and (B) syringe connections to fill balloons.

Figure 2.5: Old prototype stent.

2.4. Ex-vivo experiments

Certain choices made for the methods in this thesis, were influenced by a preliminary ex-vivo experiment executed by the work of previous researchers. A manuscript of these experiments was submitted for publication in the Journal of Investigative Surgery. The results of this article are presented in Appendix A. The experiment consisted of a linear stage connected to a weight and profile that was dragged over a stretched segment of cut-open pig-colon. A complete description of the setup and choices made, is given in the next chapter, since it was also used for this thesis. The goal was to measure the friction coefficient of different profiles made out of a flexible polymer material and compare these to the horizontal ridges profile of the old stent. Soft profiles were initially chosen as it was imagined to place the best performing profile on the balloons of the old stent design, thereby not causing any tissue damage. Besides the soft profiles, two more invasive profiles were tested, to compare with the non-invasive profiles from flexible polymer. The first one of the invasive profiles was designed as barbs based on the design of barbed suture thread, the other was a self gripping ProGrip mesh, used in abdominal wall surgeries. The most important results regarding attainable friction from this experiment are shown in Fig. 2.6, namely: 1) the old profile with horizontal ridges, 2) the best soft profile (horizontally spaced ridges), 3) barbs profile based on V-Loc sutures, and 4) the ProGrip mesh. It shows the test results and mean static friction coefficient.

This experiment gave two useful insights. First, profiles from soft materials could not improve the friction coefficient sufficiently, compared to the old design. Second, invasive profiles (barbs and ProGrip) increased the friction coefficient. This conclusion was used for further in-vivo experiments, which are described next.

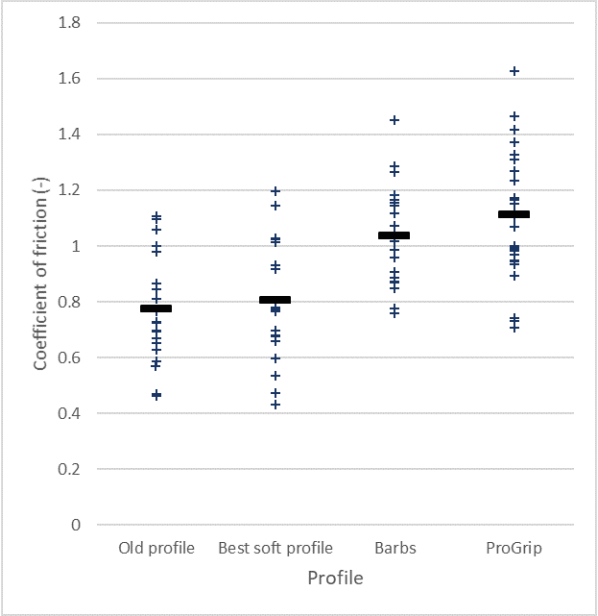
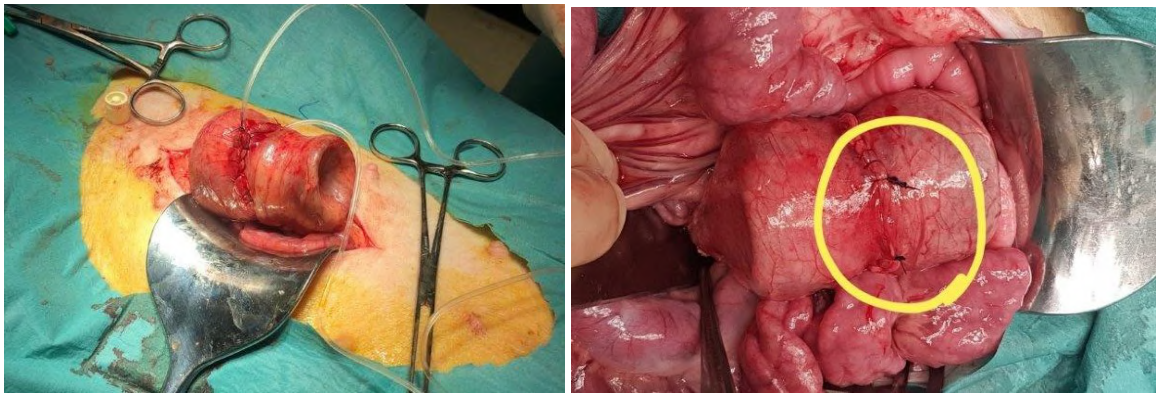


Figure 2.6: Results from preliminary ex-vivo experiment showing four different profiles and mean static friction coefficient in black.

2.5. In-vivo experiments

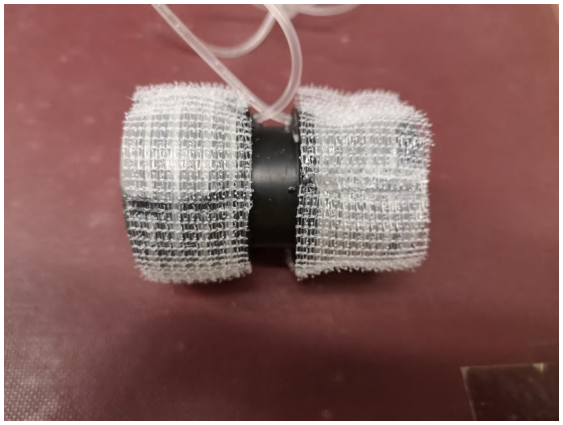
A total of nine in-vivo experiments were executed with the old stent design or with slight alterations to this design and in one experiment a 3D printed ring was inserted. One such experiment consisted of two surgeries. In the first surgery a stent was inserted under general anesthesia into the colon of a pig through an open surgery, as shown in Fig. 2.7. Afterwards all the wounds were closed and after recovery from anesthesia the pig was returned to the stables, fed and observed for two weeks. During the second surgery the abdomen was opened again, and the colon was inspected on healing, the presence of the stent (stent migration) and the state of the stent. In six out of eight experiments stent migration was observed. It should be noted that from the two experiments without migration, in one the stent was fixed to the colon with sutures and the other experiment was terminated after day two, due to illness resulting from bowel obstruction of the pig. In three out of eight experiments, stent failure occurred, most notably a leaking balloon. In some experiments, alterations to the design were made, as shown in Fig. 2.8. These alterations included: addition of ProGrip mesh (Fig. 2.8a and 2.8b), one half of the stent replaced with a polymer sleeve (Fig. 2.8c), a half stent (Fig. 2.8d) and a 3D printed ring (Fig. 2.8e). The stent with ProGrip was of greatest importance for this thesis and is explained in the next paragraph. The stent with a polymer sleeve was placed proximal to the anastomosis, such that the sleeve protected the anastomosis from leakage. This stent was sutured to the colon with four sutures and was expelled 11 days after implantation. During these 11 days the pig had a decreased stool, because feces was accumulated at the stent site. In another experiment a half stent was implanted and sutured to the colon. This stent was expelled after ten days. In another experiment a 3D printed ring was inserted and sutured to the colon, to test if the presence of a rigid tube obstructed the passage of fecal matter. Even though the ring was found flat in the colon after two weeks, it was assumed that the presence of a tube did not block fecal matter to pass through the lumen. To conclude, the experiments showed that the old stent design did not manage to achieve sufficient stent fixation.

The last in-vivo experiment was performed with an adjusted stent. The ex-vivo experiments concluded that of all tested profiles, a ProGrip mesh created the most friction with the colon. Therefore, a ProGrip mesh was mounted to the old stent design, as shown in Fig. 2.8a and 2.8b. Glue was added in longitudinal lines, so the possibility of inflating and deflating the balloons remained. Unfortunately, this experiment failed because the stent was not found fourteen days after implantation. Therefore, it was assumed that the ProGrip mesh did not create sufficient friction. Nevertheless, the cause of the failed experiment could have been related to other factors, for example balloon leakage or failure of the glue between the ProGrip and the balloons. A new fixation design should thus create more friction than the ProGrip mesh. This conclusion was later used in design requirements for a new design of the stent.

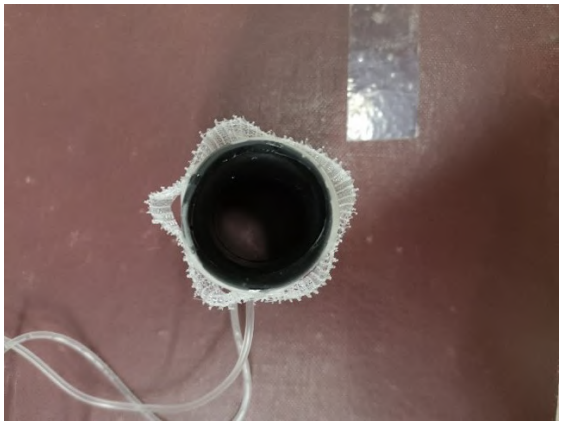


(a) (b)

Figure 2.7: Stent placed inside a pig colon during one of the in-vivo experiments at the Erasmus MC. In the circle a deliberate defect in the anastomosis is highlighted. The stent should prevent leakage at this location.



(a) Side view of stent with ProGrip mesh.



(b) Top view of stent with ProGrip mesh.

(c) Half stent with distal polymer sleeve.

(d) Old stent design cut in half.

(e) 3D printed ring to test intestinal blockage.

Figure 2.8: Stent variations of the old design, all tested in-vivo.

2.6. Literature study

Other preliminary work comprised a patent search and literature study on intestinal stent fixation. The patent search identified six different techniques to achieve intestinal stent fixation, each with multiple sub-techniques. The literature study concluded that partially covered stents, with uncovered flared ends and the addition of barbs could be an interesting fixation technique [18], see Appendix B for the complete conclusion. However, the literature review also stated that research was needed on tissue damage caused by barbs. Besides, safe insertion and removal of stents with outward pointing barbs should be investigated. This conclusion and considerations for further research were taken into account in this thesis.

3

Friction

The old stent design as described in the previous chapter proved to create insufficient friction with the colonic wall. Soft profiles were explored during ex-vivo experiments, but could not increase friction compared to the old profile design. However, more invasive designs such as the ProGrip mesh and one design with barbs that was based on V-Loc sutures, showed that it increased the friction. Besides, the preliminary executed literature study concluded that more research was needed on the effect of barbs on preventing stent migration. This was based on the fact that only three articles were found describing barbs for intestinal stent fixation. These researches reported stent migration in 0%, 0%, 0% and 25% of the cases, which showed the potential of barbs [19, 20, 21]. Therefore, the research in this thesis focused on increasing the friction with the colonic wall using barbs. It is important to notice that barbs could perforate the colonic tissue, and cause undesired mechanical damage to the colon. This could negatively influence anastomotic healing and should therefore be prevented.

The research consisted of three experiments to determine the most suitable barbed profile. The setup, methods, materials, and results of these experiments are described below. For these experiments with barbed profiles, a setup was used that was previously built to execute the previously described ex-vivo experiments. This setup was slightly adjusted to better fit the needs of these new experiments.

Information and results were already present from these earlier experiments. Results of new experiments could therefore be compared and improvement on friction could be quantified. In the most ideal case, a certain force or resistance would be present that indicated when a stent would move. No information on the forces that are exerted by the colon and feces on a stent was available from literature. Therefore, it was impossible to validate whether a certain profile or barb design would be suited based on the theoretical biomechanics. Most likely because such a value is hard to measure, since every colon, feces and dimensions of each individual are different. Therefore, the results of these experiments were compared to results from previous experiments done with the old stent design, as this was the only reference material.

3.1. Experiment 1

This experiment was executed to determine the ideal height, thickness and distribution of barbs.

3.1.1. Materials and methods

First, the used materials are described, most importantly the decisions made regarding the design of the barbs. Afterwards, the used setup and the followed protocol are given.

Barb design

For the design of the barbs several choices were made. First, the different parameters of a barb were identified, these included shape, height, thickness, distribution, and angle and increasing the normal force applied to the test plates. These last two were tested in Experiment 2, and will be described under that section. The parameters of height, thickness, and distribution were tested in this experiment. For

each parameter, two variants (small and large) were made and printed on a testplate of 30 mm by 30 mm. These were tested and the best results were further researched in later experiments.

Little research was found in literature on barb design or parameters, so some choices were arbitrary. First of all, the shape of the barbs was arbitrarily determined as a cylinder. Besides, to generate the most friction, the barbs needed to penetrate the mucosa and submucosa layer of the colon. The submucosa is responsible for most of the tensile strength of the colon, so penetrating this layer could ensure the most friction. Therefore, the barbs were designed with a sharp point, thus resulting in a conical shape. A previous Master Thesis by Lazarte at the TU Delft already conducted research on colonic stent fixation [22]. However, Lazarte's research focused on microhooks, whereas this thesis focused on hooks of macro-scale, as is explained later. Lazarte concluded that straight hooks were preferred over bend hooks. Therefore, straight hooks were chosen as a starting point for this research.

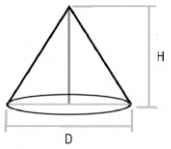
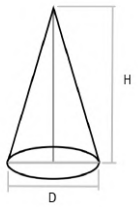
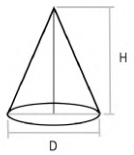
The first parameter was the height of the barbs. The hooks researched by Lazarte [22] were designed to deform the mucosal layer. The goal in this thesis was to penetrate the barbs into the submucosa, thus the barbs were made larger. As described in the background information, the mean thickness of the mucus layer and submucosa together ranged from approximately 0.6 mm up to 1.4 mm. There is also a certain force needed to penetrate into or through the colon [23], unfortunately this research tested for perforation through all the colonic layers and not for mucosa and submucosa only. Therefore, the height of the barbs was designed at 1.5 mm, 0.1 mm larger than the maximum thickness, so that the barb could penetrate the desired layers. To test the influence of changing this height, another barb was designed with a height of 3.0 mm. It was expected that not the whole barb length would penetrate the colon layers, therefore the two chosen heights were larger than the two layer thicknesses.

The second parameter of the barb was the diameter. It was expected that a smaller diameter would facilitate better tissue penetration. The diameters to test were set at 0.5 mm and 1.0 mm. However, the 3D printer was not capable of printing a diameter of 0.5 mm. More on the 3D printer will be discussed later. The barb with 1.0 mm diameter was printed correctly, therefore the diameters were set at 1.0 mm and 2.0 mm.

The third parameter was the distribution of barbs, in other words, the number of barbs per unit area. The barbs should penetrate into the layers of the colon to generate more friction. Therefore, fewer barbs per unit area was desired, because more force per barb would be exerted on the colon. On the other hand, more barbs could generate more friction, so an arbitrary choice of 3 barbs per square centimeter was made. To test the influence of distribution, another test plate was made with 9 barbs per square centimeter. All the barbs were spread evenly over each test plate with a constant distance in between.

To summarize, each of the parameters had two variants, namely small and large. The difference between these two variants was intentionally made large, to better see the difference in friction generated. To test the influence of each parameter, four different test plates (A-D) were produced. The dimensions of each plate are shown in Table 3.1. The barbs of Plate A had the smallest dimensions for diameter, height, and distribution. For Plate B the diameter was increased, for Plate C the height was increased and Plate D had an increased distribution of barbs. The test plates as used in the experiment are shown in Fig. 3.1.

Table 3.1: Dimension of the barbs for test plate A-D.

Profile	**Plate A**	**Plate B**	**Plate C**	**Plate D**
				
Diameter (D) (mm)	1.0	2.0	1.0	1.0
Height (H) (mm)	1.5	1.5	3.0	1.5
Distribution (barbs * cm^{-2})	3	3	3	9
Angle (A) (°)	90	90	90	90

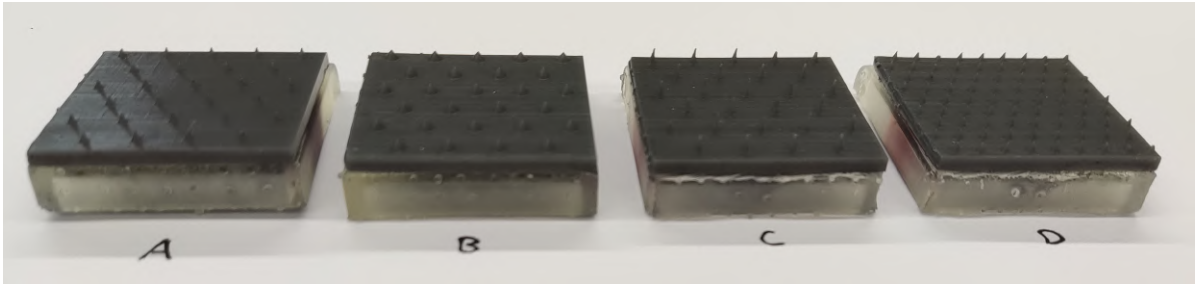


Figure 3.1: Test plates used in Experiment 1, f.l.t.r. A, B, C and D.

Profile fabrication
The profiles were 3D printed using a Form3 printer (Formlabs, Somerville, MA, USA). The easiest manufacturing process to make the profiles was 3D printing. It allowed for rapid prototyping and iterations on the design could be made. The Form3 printer is a resin printer and therefore allowed for high printing resolution of 50 microns [24], of the printed barbs. High printing resolution was desired because a sharper barb could penetrate the colon better, thereby generating more friction. The material used was the rigid material Formlabs Tough2000 (Formlabs, Somerville, MA, USA). This material was chosen because the barbs were fragile and were prone to break, especially when 3D printed, since this caused layers of material that could break at these intersections. The direction of printing was with the back of the test plates attached to the print plate. The profile was glued on a plate that could be attached to the weight holder, which is further explained under the section setup.

Organ specimen
The colon specimens were obtained from a slaughterhouse from six different pigs of around 100 kg. Within 30 minutes after termination of the pig, the distal colon was harvested, cleaned, and preserved in a gelofusin fluid and cooled with ice until used for the experiment. This gelofusin fluid was used to prevent dehydration of the colon during transport. The colon was dissected at 60 cm until 10 cm proximal of the anal verge. All tests were performed within five hours after being harvested, which is within the limit of seven hours after which alterations of frictional properties of the colon occur [25].

Setup
Shown in Fig. 3.2 is the setup used in the experiment. This setup was obtained from previous researchers that executed force measurements on animal tissue. This setup was altered such that it was suitable for this research. The experimental setup consisted of a linear stage (EGSL-BS-45-200-3P,

Festo BV, Delft, The Netherlands) which could move vertically. An S-Beam Load Cell sensor (LSB200-FSH00104, FUTEK Advanced Sensor Technology Inc., Irvine, CA, USA) was placed on the linear stage. The sensor was capable of reading forces from 0.1 N to 44.5 N, which was expected to be a suitable range for this experiment. The force sensor and linear stage were connected to a computer. This computer controlled the setup using a Matlab interface. Attached to the force sensor was a hook that was connected to a nylon thread via a pulley to the weight holder. The resistance of the pulley was assumed to be negligible. The weight holder was 3D printed, made from ABS and weighed 9.0 grams and contained room for an additional weight. A container filled with 5% mass fraction gelatin was covered with a white filter paper, the colon was placed over the filter paper and locked with a clamp. The setup is shown in Fig. 3.4 with all the components indicated with letters. The gelatin bed served to simulate the surroundings of the abdomen in which the colon is located. An additional weight of 50 grams was placed inside the weight holder. Together with the weight holder this resulted in a normal force acting on each profile of 0.58 N.

This total weight was experimentally determined with an arterial pressure machine. One balloon of the old prototype was inserted in a porcine colon. The plastic tube to fill the balloon was connected to the arterial pressure machine. In the first measurement the balloon was empty and the measured pressure was 48 mmHg. For the second measurement the balloon was filled with 12 ml fluid. The measured pressure for this case was 52 mmHg. This the resulting pressure difference between an empty and filled balloon was 4.0 mmHg. The weight necessary for experiment 1 was calculated with the following formula:

$$weight = P \cdot b \cdot A \tag{3.1}$$

with P the pressure difference between an empty and filled balloon, b the conversion factor for mmHg to g/cm^2, which was 1.0 gram equalled 1.359510026 mmHg, and A the area of the test plate used in experiment 1 which was 9.0 mm^2. This resulted in a weight necessary for experiment 1 of 48.9 grams. As weights of 50 grams each were available, the weight was determined as 50 grams.

Important to notice is that this weight was determined before this thesis was started. By then, the idea was still to add a new profile on the outside of the balloons. The results of this experiment will be compared to the results of the ex-vivo experiment (as described under background information). Therefore, this weight was kept constant to reduce the influence this could have on the results. Note that in experiment 2 the influence of this weight was tested.

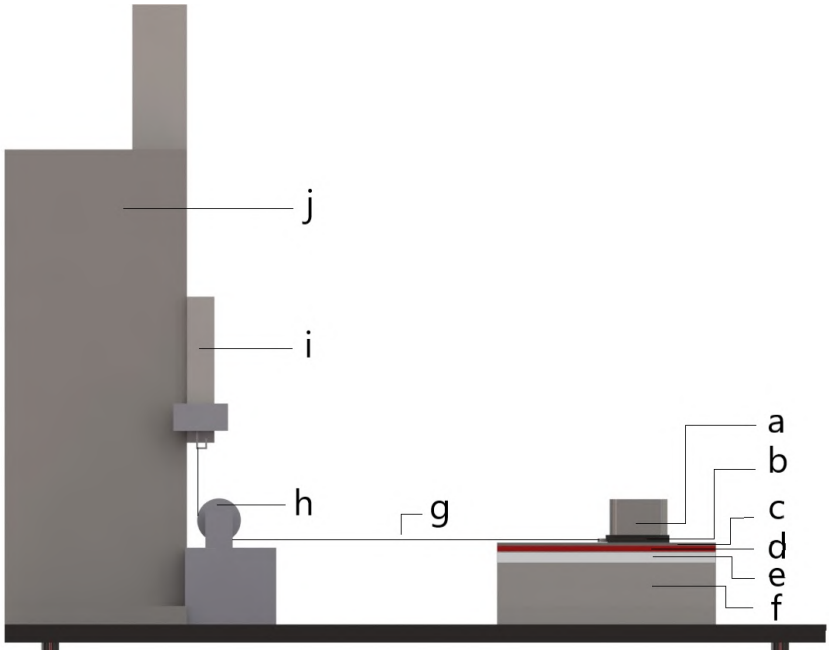


Figure 3.2: Schematic overview of the setup used for the experiment, with a) weight holder with weight, b) profile, c) clamp, d) colon, e) filter paper, f) container with gelatin, g) nylon wire, h) pulley, i) force sensor, and j) linear stage.

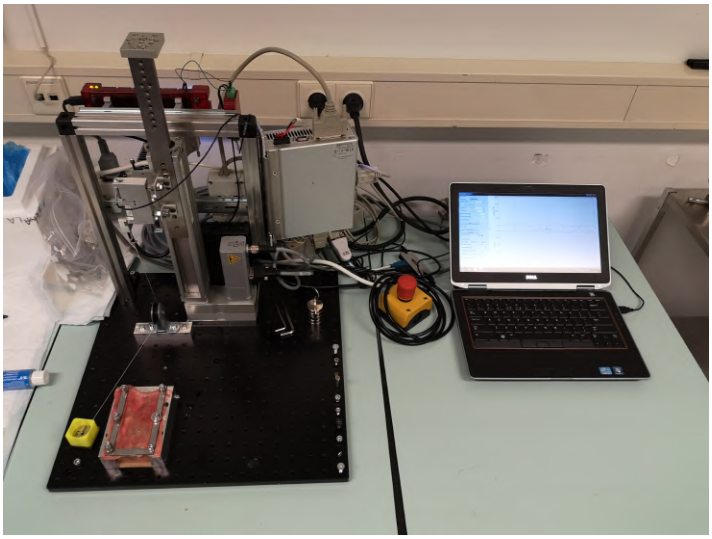


Figure 3.3: Experimental setup used in the experiment including the controlling computer.

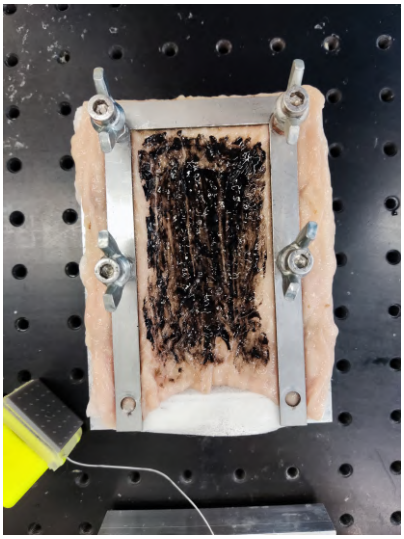


Figure 3.4: Colon on gelatin with black ink.

Protocol

For the experiments, a standardized protocol was followed. A colon part of approximately 10 cm was taken and incised longitudinally. Then it was stretched 50%, to be placed over the gelatin bed and locked using a clamp and bolts. Black ink was mixed with K-Y® Sterile Lubricating Jelly (Reckitt Benckiser Healthcare Ltd., Hull, UK) and placed onto the colonic specimen, and a white filter paper was placed between the gelatin and colonic tissue. The jelly served to prevent dehydration of the tissue when removed from the gelofusin fluid. If the filter paper contained ink after a test, perforation of the intestinal wall had occurred. The effectiveness of this method was verified beforehand by deliberately creating holes into a colonic tissue and applying the ink on top.

One test consisted of a profile with barbs being pulled over the colon once. Before each test the profile was cleaned and the colon was lubricated using around 0.15 grams of the jelly mixture. During this test, the force sensor measured the voltage needed over time to pull this profile. Displacement of the linear stage was set at 25 mm and the velocity at which the profile was pulled was set at 5 mm/s. Displacement was set at 25 mm since the static friction coefficient needed to be measured and not a dynamic friction coefficient, thus a short displacement was sufficient. The velocity was kept constant to the previous tests with non-invasive profiles, which was based on previous research that used the same speed [25, 26].

Data processing

For each test data were saved and processed using Matlab. The data obtained from each test were Volts measured over time. A Matlab code that was written converted these result into a graph which displayed Newtons over time. In order to convert the Volts to Newtons, the force sensor was calibrated using different weights of 50 grams each. Seven tests were performed, starting with 0 grams and adding 50 gram weights in each consecutive test. The voltage was plotted against the amount of Newtons of the weights, as shown in Fig. 3.5. A linear fit was then performed to extract the following formula to convert Volts to Newtons:

$$N = 8.2157 \cdot V + 36.766 \tag{3.2}$$

with N the force in Newtons, and V the measured Voltage. This calibration test was executed directly prior to the experiments. The experiment was executed on two days, so each day this calibration was performed.

The results of each test were plotted in individual graphs, which displayed the force in Newton over time. A typical result had to produce a graphic as shown in Fig. 3.6. Point A in Fig. 3.6 shows the static friction point and identified the force needed to move the profile. This point had to be identified to calculate the static friction coefficient. If such a point was not present, the test would be excluded for further analysis. For example, a test where a line was still increasing when the test stopped, had not yet reached its static friction point. This was done for each result individually.

The static friction coefficient was calculated by using the following formula:

$$\mu = Fmax/N \tag{3.3}$$

in which μ is the static friction coefficient, Fmax is the maximum initial force and N is the normal force acting on the profile. The results for each profile were combined and the mean was calculated.

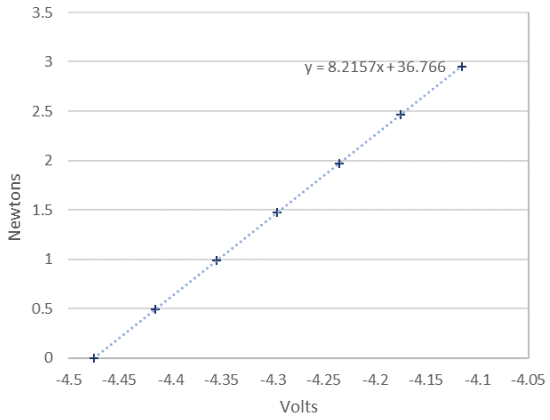


Figure 3.5: Graph with linear fit to convert Volts to Newtons.

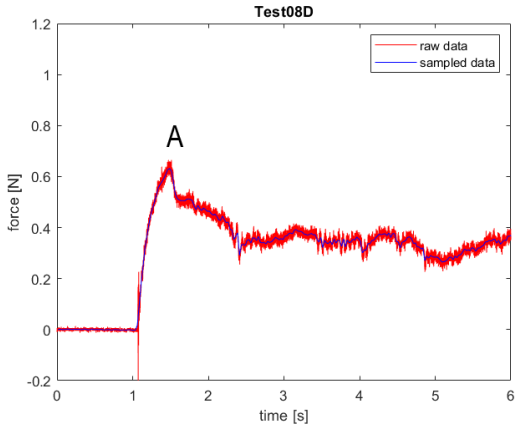


Figure 3.6: Example of a measurement result, with A) indicating the static friction point.

The example graph in Fig. 3.6 shows a typical pattern that was encountered in all results. The load cell measured the force at a rate of 2 kHz, so 2.000 times per second. This caused a lot of variability in the results as can be seen by the red line in Fig. 3.6. Since the maximum initial force was needed, taking the absolute maximum value could give an incorrect measured force. Therefore, all data was sampled. The average value was taken for 50 data points. All average values were inserted in the graph and a plot was made. The maximum force was taken from this sampled data. This sampled data line is presented as the blue line in Fig. 3.6. This was assumed to give better and more accurate results.

Another issue that was encountered in the result graphs was the initial second of the test. During this first second, the linear stage did not move, so the measured force should be zero. However, this was not the case for all tests. Therefore, all data points of a test were corrected with the difference between the measured force and zero for the first second.

3.1.2. Results

A total of 20 tests was performed with 5 tests per profile. Experiments were performed using colon specimens from 6 different pigs. Primary outcomes included the influence of changing diameter, height, and distribution of barbs on the friction coefficient. The results are given in Fig. 3.7. All test results represented by individual markers and the mean is represented by the black line. Secondary outcome included whether total perforation of the colonic tissue occurred.

Profile A had the highest mean coefficient of friction (μ = 1.16), followed by profile C (μ = 0.923), profile D (μ = 0.917) and the least mean friction was created by profile B (μ = 0.804). During all tests, no ink was observed on the filter papers placed under the colon specimens.

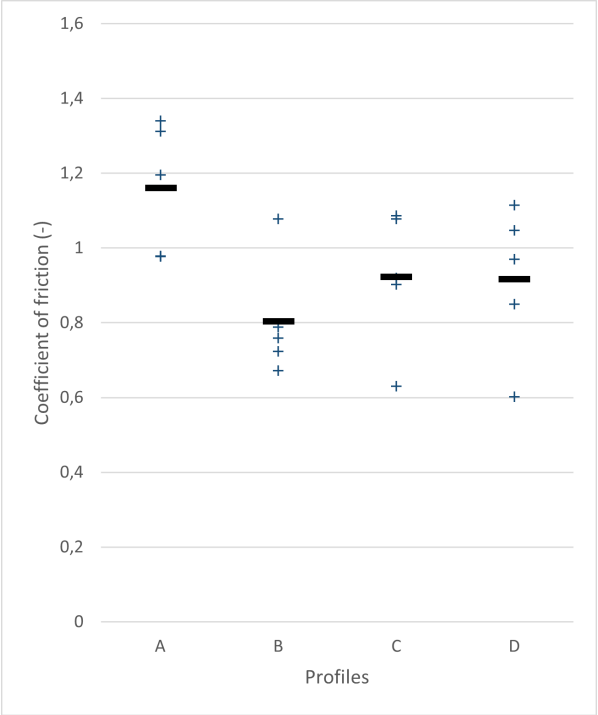


Figure 3.7: Results of Experiment 1 with different barb designs as coefficient of friction, with the mean as a black line.

3.1.3. Discussion

The experiment showed interesting results on the different design parameters of the barbs. Plate A with the smallest diameter, height, and distribution gave the largest mean coefficient of friction. With an increased diameter (Plate B), the mean coefficient of friction decreased. A reason could be that smaller diameter barbs penetrate the colon layers deeper, therefore anchoring themselves better and causing a higher coefficient of friction compared to larger diameter barbs. Increasing barb height (Plate C) also decreased the mean coefficient of friction compared to Plate A, with a smaller height. An increased barb height could penetrate the colon layers deeper and create more friction. However, this hypothesis was falsified with this experiment, when only the mean coefficient of friction was considered. Some reasons for this could be that the barbs did not penetrate any colon layer at all regardless of the barb height, the normal force exerted by the weight of 50 grams may not have been sufficient to enable tissue penetration or the 3D printed barbs were not pointed sharply enough to ensure penetration of the tissue. Corroborating this is the fact that no ink was observed on the filter paper, indicating no total perforation of the tissue. However, this only accounted for total perforation, and nothing could be concluded on partial tissue penetration. Furthermore, the colon had contact with the test plate in between the barbs, which created friction. Increased barb height could have caused a reduction or elimination of this contact, thus decreasing the friction created by test plate C. The main reason that increasing barb height did not increase friction could not be identified. Increasing the number of barbs (Plate D) did not increase the coefficient of friction either, based on the mean of the results. One reason could be that less force was exerted on each barb compared to Plate A, less tissue penetration occurred and therefore less friction. Alternatively, similar to increased height, an increased number of barbs decreased the contact between the base of the test plate and the colon, therefore decreasing the friction.

In preliminary work the profile that created the most friction was a ProGrip mesh (μ = 1.11). The results of this experiment showed that Plate A caused almost the same mean coefficient of friction (μ = 1.16). As it was concluded that the ProGrip mesh did not work in-vivo, the barb designs should be improved. Therefore, another experiment was conducted, described under Experiment 2.

As mentioned before, no ink was observed on the filter paper, indicating no total perforations caused by the barbs. This result showed that a stent with barbs could be a safe option for stent fixation, since surrounding tissue and organs would not be harmed. However, nothing could be said about necrosis caused by the barbs in this experiment.

The results showed a large variation per test plate, therefore conclusions should be made with care. One reason that could have caused this variability, was the morphology of the colon. The morphology differs for each specimen used in the experiment and also differs for specimens taken from the distal part compared to more proximal parts. This variation was minimized by only using colon parts that were dissected 10 cm until 60 cm proximal to the anal verge. Furthermore, colon specimens from six pigs were used, which also caused different tissue morphologies present. These variations between specimens and experiments was already encountered during preliminary experiments, but was difficult to eliminate as this is something that was inherent with colonic tissue [27].

Limitations

This experiment had several limitations that need to be mentioned. Firstly, the number of tests executed per test plate was limited to five tests, due to the availability of colon specimens that could be retrieved from the slaughterhouse. Secondly, each parameter was tested on only two values, small and large. This gave a limited view on the influence of the parameter on friction. Thirdly, the parameters were not tested on interdependent factors because this would have increased the number of tests. Again, this was limited due to the availability of colon specimens. Furthermore, the velocity of the test setup could have been lower. If the main factor of stent migration was assumed as feces pushing the stent outward, a lower velocity would be closer to reality, because fecal matter moves at a much slower velocity than 5 mm/s. This velocity was assumed and calculated slower than 1 mm/s, based on 1 kg feces excreted by a 50 kg pig on one day, which was measured by the animal facilities in the Erasmus MC. However, the velocity of 5 mm/s was maintained, so that the results could be compared to that of the previous experiment and would not be influenced by another factor. Finally, the printer used for the barbs had a high printing resolution. However, printing errors or inaccuracies were inherent to 3D printing. Thus, small inaccuracies could have occurred, but were minimized by visually checking the printed barbs.

3.1.4. Conclusion

The results of Experiment 1 showed that barbs with 1.0 mm diameter, 1.5 mm height and 3 barbs per cm^2 created the most friction on colonic tissue. However, a better barb design should be created in order to facilitate stent fixation. Besides, the barbs did not cause total perforation of the colonic wall and could thus be a safe option for stent fixation.

3.2. Experiment 2

The goal of the second experiment was to measure the influence of placing the barbs under an angle and increasing the normal force exerted on top of the profiles with barbs. Increased normal force should simulate the effect an increased stent diameter could have on the friction coefficient. So, the experiment can be seen as a 2D representation of a larger diameter stent. Although, it was noted that this was a simplification of the real situation.

3.2.1. Materials and methods

For the second experiment the same setup was used. Therefore, only the differences compared to the first experiment are mentioned.

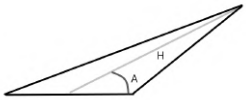
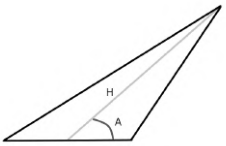
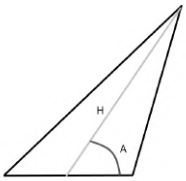
Materials

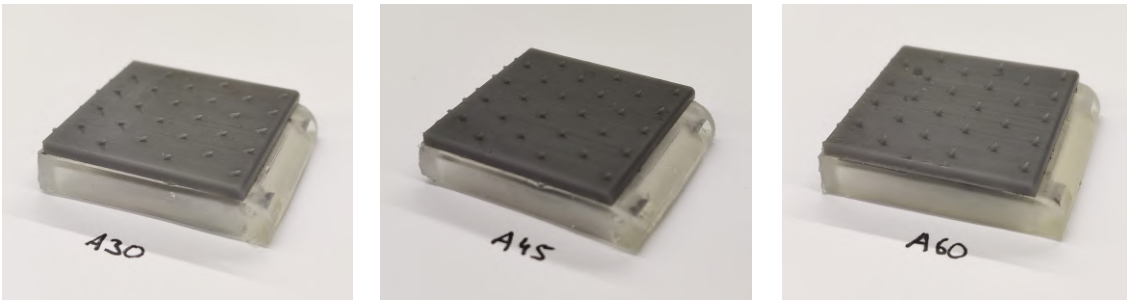
The first experiment concluded that Profile A created the highest mean static friction coefficient. Therefore, this barb design was further researched regarding the influence of increased normal force. Barbs that penetrated the colon further were assumed to create more friction, so the following choices were made. The hypothesis was that a smaller diameter barb would facilitate deeper penetration of the colonic tissue. Furthermore, fewer barbs (distribution) could achieve the same, since the force per barb is larger. These reasons also favored profile A over B and D. In addition to profile A from the first series of experiments, the barb dimensions of profile C, with increased height was chosen to further investigate, because such a barb could penetrate the tissue deeper. Consequently, these dimensions could increase the effect of the higher normal force on the friction coefficient.

For the influence of barb angle, profile A was further investigated. The hypothesis was that a smaller angle should increase friction, since the barbs are pointed more in the direction opposite to motion. On the other hand, decreasing the angle too much could cause the barbs to not penetrate the submucosa

layer, thus decreasing friction. This trade-off was therefore researched in this experiment. For the barb design, angles of 30, 45 and 60 degrees were chosen, and these were named A30, A45 and A60. These angles were measured from the midline of the barb, as shown in Table 3.2. The length of this midline (gray line marked with H in the figure) was kept constant at 1.5 mm, similar to the height of Profile A in Experiment 1. The angle of test plate A in the first experiment is considered as 90 degrees. All profiles were produced in the same way as Experiment 1.

Table 3.2: Dimensions of the barb designs with different angles in Experiment 2.

Profile	**Plate A30**	**Plate A45**	**Plate A60**
			
Diameter (D) (mm)	1.0	1.0	1.0
Height (H) (mm)	1.5	1.5	1.5
Distribution (barbs * cm^{-2})	3	3	3
Angle (A) (°)	30	45	60



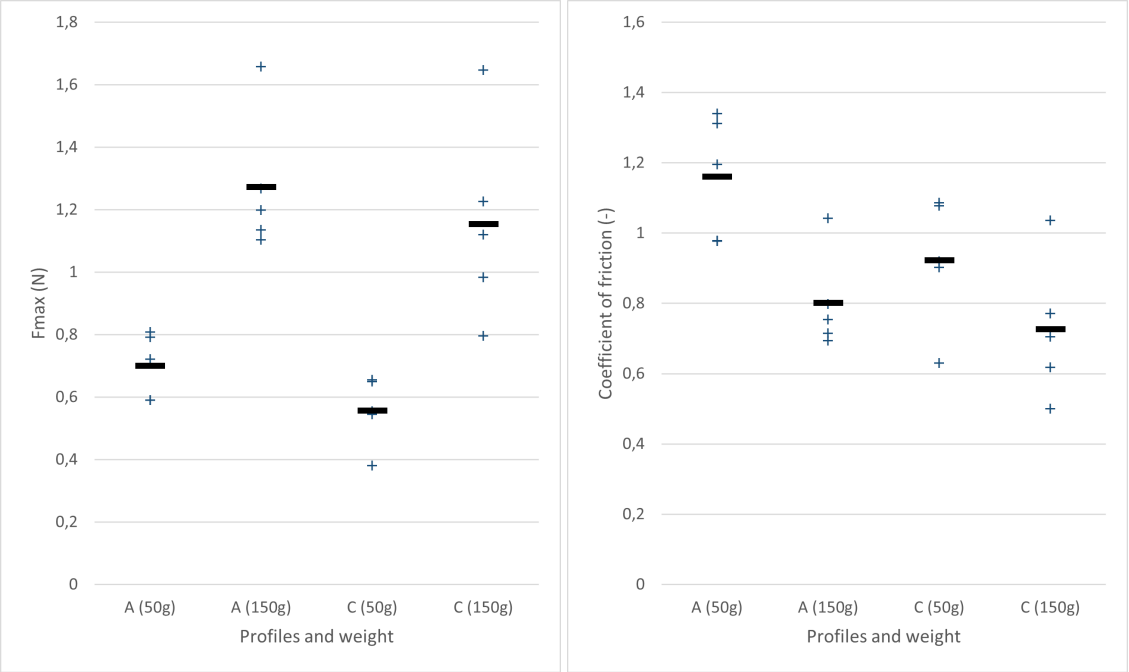
(a) Plate A30. (b) Plate A45. (c) Plate A60.

Figure 3.8: Test plates with angled barbs

Methods
The methods used for this experiment were the same as in Experiment 1. The increased weight that was used equalled 150 grams. These results were compared to the results for Plate A and C from Experiment 1, in which 50 grams was used, to test the influence of increased normal force. The results of Plate A from Experiment 1 were compared with the results of the angled barb plates.

3.2.2. Results

A total of 25 tests was performed with 5 tests per profile. Experiments were performed using colon specimens from 6 different pigs. The results of the normal force influence are given in Fig. 3.9 and the results of the angled barbs in Fig. 3.10. The results are given in coefficient of friction for both parameters and additionally in maximum force for the normal force influence. Primary outcomes included the influence of normal force on the resistant force and on friction, and the influence of barb angle on friction. Secondary outcome included if total perforation of the colonic tissue occurred.



(a) Results of the experiment in Newtons for different weights and profiles, with the mean as a black line.

(b) Results of the experiment as coefficient of friction for different weights and profiles, with the mean as a black line.

Figure 3.9: Results Experiment 2 for normal force influence.

The maximum force needed to overcome the static friction point increased with increased normal force. For Plate A the mean force increased from 0.700 N for 50 grams to 1.27 N for 150 grams. For Plate C the mean force increased from 0.557 N for 50 grams to 1.15 for 150 grams. The coefficient of friction decreased with increased normal force. For Plate A the mean coefficient of friction decreased from 1.16 for 50 grams to 0.801 for 150 grams. For Plate C the mean coefficient of decreased from 0.923 for 50 grams to 0.726 for 150 grams. In none of the tests total penetration of the colon occurred.

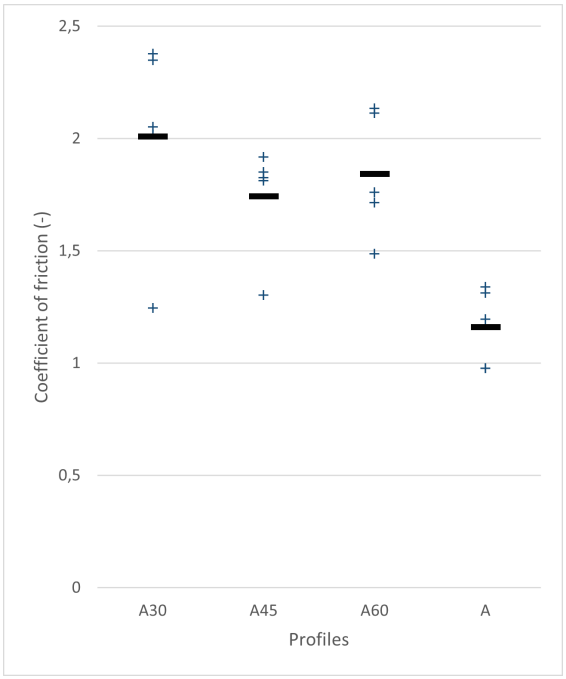


Figure 3.10: Results of Experiment 2 for barb angle with the mean as a black line.

The coefficient of friction increased for all three profiles with barbs at an angle compared to Plate A (μ = 1.16) with straight barbs. The mean coefficient of friction for barbs at a 30° angle was 2.01, for barbs at a 45° angle 1.74 and for barbs at a 60° angle 1.84. No total penetration of the colon was observed in the tests.

3.2.3. Discussion

This experiment showed interesting results regarding friction. First, increased normal force decreased the coefficient of friction, when looked at the mean of all tests. However, the force necessary to move the plates increased, which was an obvious result. The force did not increase with the same magnitude as the weight increased. A clear explanation could not be found or thought up for this. The increased force, could indicate that an increased diameter of the stent, would improve fixation. However, no relationship could be drawn on the magnitude of diameter expansion, as this experiment had some simplifications, as described under limitations.

Second, the results of the angled barb designs were promising. Changing the barb angle increased the coefficient of friction for all test plates. Regarding the means of all barb angles, a 30° angle should be favored over 45°, 60° and 90° angles. This could be explained by the fact that the smaller angle was directed more against the direction of motion. On the other hand, the height of the 30° angle barbs was smaller, and could thus penetrate the colon less, resulting in less friction. This trade off between angle and height of the barbs, could not necessarily be observed in the results, regarding the means of the tests. However, a decreasing trend in terms of coefficient of friction could be observed, when the angle was increased from 30° to 90°.

In general, again large variations in the results were observed. The same as in Experiment 1, this could partially be explained by the variability in morphology of the colonic tissue. The tests with angled barbs showed some outliers, especially for 30° and 45° angles. A cause could be that the barbs did not 'hook' into the colon, thereby losing the effect barbs had on friction. However, this could happen when a stent with such barbs was placed in a patient, therefore these results should be incorporated. If more tests were executed, a better and more convincing conclusion could have been made. Another remark was that the tests were compared to test results from Experiment 1. These experiments were not conducted on the same day and this could have influenced results. However, the same protocol was followed during these experiments, indicating that this should not have been the case.

Limitations

This experiment had several limitations. Firstly, regarding the increased normal force, which is a bold simplification of increased stent diameter. The contractile forces an intact colon would exert on a circular stent, were neglected in this 2D representation. Besides, an increased stent diameter would stretch the colon more, which was not incorporated in this experiment. A more stretched colon would become thinner [28], therefore the chance of perforation of the colon would increase. Consequently, this could have influenced the results on total perforation. Furthermore, there could have been printing inaccuracies while printing the barbs. Despite limitations and simplifications, some conclusions were drawn that were used later for a redesign of the stent.

3.2.4. Conclusion

Increasing the diameter of the stent should increase the force needed to expel it. Barbs with an angle of 30° created the most friction with the colonic wall. Therefore, a stent with this barb design should be further researched and used as a basis for a redesign of the stent.

3.3. Experiment 3

Experiment 3 was performed to evaluate the best diameter for the stent. In this experiment, the barbs were tested in an intact colon instead of on a flat colon surface. Contractile forces exerted by the colon could improve fixation of the stent. Therefore, this experiment could give a more realistic result regarding the influence of increased diameter on stent fixation, compared to experiment 2.

3.3.1. Materials and methods

For the third experiment the same setup for measuring friction forces was used as in the first two experiments, however with some adjustments which are described later.

Materials

Experiment 2 concluded that barbs at a 30° angle generated the most friction with the colon. Therefore, this barb design was used in this experiment. These barbs were placed on tubes, each with a different diameter. The diameters that were tested ranged from 28 mm to 36 mm. The old stent design's outer diameter in the middle part was 28 mm. This facilitated good tissue healing, therefore this diameter was chosen as the smallest value. The largest diameter was set at 36 mm because in one in-vivo experiment a ring was placed with a diameter of 40 mm. This turned out to be too big to fit in the colon and around one third of the ring was cut off before it fitted. The old stent design would reach an outer diameter of approximately 38 mm, but this was achieved by filling the balloons once placed inside the colon. This simplified insertion of the stent. These test stents were manufactured from a rigid material, therefore the diameter could not be decreased. Thus, the diameter was set at 36 mm to ensure that the diameter could be inserted into the colon, without rupturing it. The diameters in between were chosen with a step count of 2 mm.

The stents were designed with half of the length of the old stent design, so 30 mm. This ensured that less colon per test was needed, and more tests could be performed in total. A loop was placed in the middle of the stents for attachment of a suture thread that connected to the force sensor. The stents are presented in Fig. 3.11.

The stents were printed from the same material as the test plates in Experiment 1 and 2, namely Tough2000 (Formlabs, Somerville, MA, USA) and printed with the same 3D printer and settings.

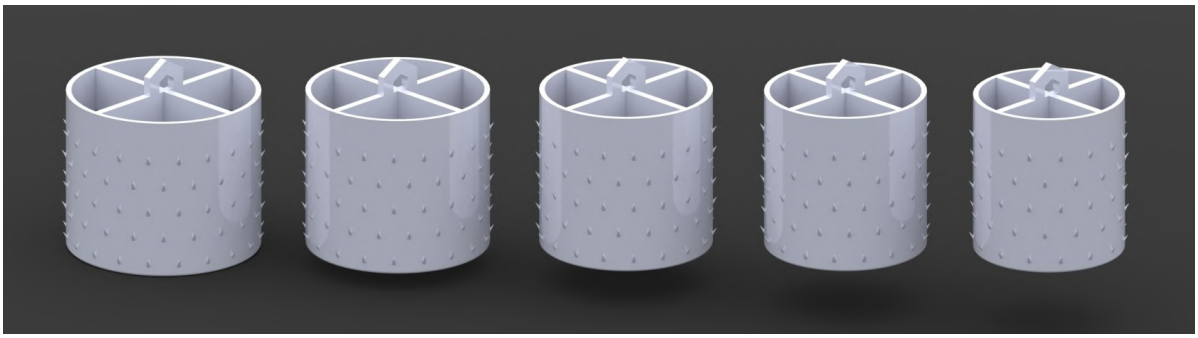


Figure 3.11: Render of half stents used in Experiment 3.

Setup

The setup for this experiment was the same linear stage as used for the previous experiments. The gelatin bed and pulley were removed and replaced with a clamp with horizontal ridges, as shown in Fig. 3.12. A colon specimen was placed in the clamp and the horizontal ridges provided extra grip to fix the colon. A test stent was placed retrograde in the colon with the barbs facing the direction of travel. The stent was connected via a suture thread to the hook on the force sensor.

Figure 3.12: Setup of Experiment 3, with on the right side A) clamp and B) colon with one test stent inside.

Protocol

A standardized protocol was followed during this experiment. One test consisted of the following steps. A colon segment of around 12 cm length was taken and put on a flat surface, without being stretched. The inner length of the colon was measured, and multiplied by two to get the circumference. Then the colon was inserted in the clamp and the clamp was closed. Next, the test stent was inserted into the colon and the thread was attached to the hook of the force sensor. The height of the linear stage was adjusted such that the colon was put under minimum tension before the test started. Same as in the previous experiments, the maximum initial force to move the stent was sought. Therefore, the moment the stent started moving inside the colon was noted, so that the peak in the graph at that moment was taken as maximum force. For each test a new colon specimen was used.

Because of the elasticity of the colon, it would stretch in the first part of the test. Therefore, the displacement of the linear stage was set at 50 mm, to ensure that the stent would move inside the colon. The velocity was set at 1 mm/s, so slower than the previous experiments. As discussed previously, this speed was closer to the velocity of feces moving through the colon. Therefore, this would represent the real situation more accurately.

For each test the outcome was the maximum force needed to initially move the stent inside the colon. This was compared to the expansion of the colon caused by the stent. First, the circumference of the colon was converted to diameter. The expansion of the colon would then be calculated by the following formula:

$$Expansion = (D1 - D0)/D0 \cdot 100\% \tag{3.4}$$

where D0 is the diameter of the colon and D1 is the diameter of the stent. The expansion was taken instead of stent diameter, because the pigs from the slaughterhouse were 100 kg, whereas the pigs used in the in-vivo experiments weighted approximately 50 kg. The colon of a pig grows in terms of total length and weight when a pig grows from 50 to 100 kg [29, 30]. However, the increase in diameter was not mentioned in these articles. Therefore, the expansion should give the best indication for the ideal stent diameter in terms of fixation force.

The colon was visually checked for damage on three occasions: before insertion of the stent, after insertion of the stent and after a test was completed.

3.3.2. Results

A total of 20 tests was performed with 4 tests per stent diameter. Experiments were performed using colon specimens from 5 different pigs. For each test stent, one colon of the same pig was used, so each stent was tested with distally and proximally located colon. The results are given in Fig. 3.13.

The maximum force needed for initial movement of the stent was plotted against the expansion of the colon caused by the stent.

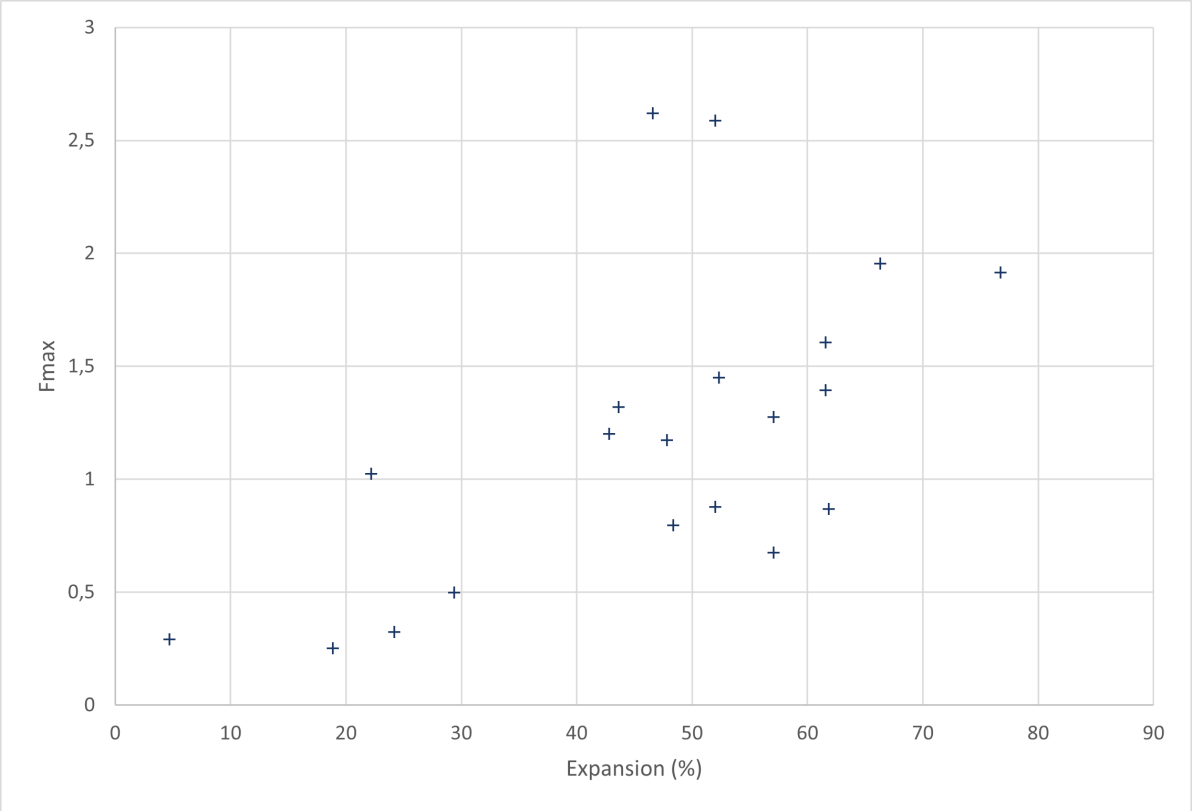


Figure 3.13: Results of Experiment 3, with expansion of colon diameter and maximum extraction force.

The graph shows the results of the experiment. The lowest expansion measured was 4.72%, and the largest 76.7%. The expansion of the colon was determined by what was available from the slaughterhouse, thus for some expansion rates, no tests were performed. An example was the expansion between 30 and 42%, where no tests were performed. The minimal extraction force measured was 0.251 N and the maximum extraction force 2.62 N. The results showed an increased extraction force with increased expansion. However, a clear trend line could not be drawn. Therefore, the maximum extraction force was also plotted against the initial colon diameter and the stent diameter. This gave no new insights in the individual influence of respectively initial colon diameter and stent diameter on the maximum extraction force.

In one test colon damage was observed. This occurred after insertion of the stent with a diameter of 32 mm and an expansion of 57.1%. The test result was still included because the location of the damaged colon was at the top of the segment. During the test, the stent did not pass this damaged segment during the extraction.

3.3.3. Discussion

As mentioned above, the experiment produced only indicative results. Once more indicating the complex and varied structure of the colon. The goal of this experiment was to measure the best expansion of the colon in terms of maximum extraction force. The tests showed an increased extraction force with increased expansion. The contraction forces exerted by the colon should increase with increased expansion. This could indicate that the maximum extraction force was not reached in this experiment, and that tests with a larger expansion should be performed. However, given the time management of this thesis and the minimal availability of colon specimens, extra tests were not performed. This could have been prevented with the addition of larger diameter stents, or by measuring all colon diameters beforehand to test larger expansion rates. The diameters used were chosen based on the colon diameter of 50 kg pigs, instead of 100 kg, since the difference in colon diameter was unknown between

these pigs. Besides, as mentioned earlier, increased tension on an anastomosis negatively influenced the healing process [15]. Therefore, larger expansions would physiologically not be relevant because the anastomosis might not heal correctly when stretched out too much.

The increasing force with increased expansion would indicate that an optimal expansion was not yet reached. It should be noted that there is a maximum expansion of the colon, before it would rupture. Therefore, the maximum expansion would be limited to a certain value where colon damage starts. In one test the colon ruptured at an expansion of 57.1%, so this could be the maximum. However, at larger expansion rates no damage occurred, thus disproving this maximum expansion. Besides, the flexibility of the colon was observed by surgeons from the EMC during in-vivo experiments, where diameters of up to 10 cm were observed. This could indicate that the expansion should be increased, but for a conclusion only this experiment was considered.

During this experiment an optimal expansion was not yet found. However, based on the results of this experiment, expansions of 42% up to 76% resulted in the largest extraction force. As an increased trend was observed, the largest expansion of around 76% could be chosen. However, this would increase the chance of disturbing the healing process due to the tension on the anastomosis. Therefore, after several discussions with an expert surgeon and considerations, the recommended optimal expansion should be 50 - 60%.

Limitations

This experiment had several limitations. First, the measurements of the inner diameter of the colon were done by hand. The colon was put on a flat surface to minimize influence of other factors. However, other factors that could have influenced these measurements e.g., the temperature of the colon and the fluid in which it was preserved, the different sized colon of each individual pig and the presence of surrounding tissue or fat on the colon. Secondly, the insertion of the stent into the colon was difficult, due to the inability to reduce the stent diameter. This could disturb the possibility to test larger expansions in future research. Thirdly, initial movement of the stent was noted by observation, so that the maximum extraction force was taken from that point in the graph where the force dropped. This may have caused an undue influence from inaccuracies by the observer on the results. At last, the printing errors and inaccuracies due to 3D printing could have influenced the barb dimensions. However, this was a limitation that occurred in all these experiments with 3D printed barbs.

3.3.4. Conclusion

For optimal friction, the expansion of the colon caused by the stent, should be between 50 - 60%.

3.4. Summary of the experiments

The summarized results of the experiments are given in Table 3.3. These results served as the basis for the design requirements in Chapter 6.

Table 3.3: Summary of the experiments.

Experiment 1	Barb height	1.5 mm
	Barb diameter	1.0 mm
	Barb distribution	3 barbs per cm^2
Experiment 2	Barb angle	30°
	Normal force	Increased normal force should increase fixation
Experiment 3	Colon expansion	50 - 60%

4

Deployment methods

The experiments described in Chapter 3 concluded that barbs improved the friction. However, inserting a stent with barbs in a patient carries the disadvantage of tissue damage. So, if a stent with barbs was to be designed, safe insertion of the stent should be investigated. Therefore, this chapter aims to discover different techniques for safely deploying barbs into a patient.

4.1. Patent search

The goal was to give an overview of currently described methods or techniques to introduce sharp devices or stents into a patient. This information was used as inspiration to define the insertion method of the stent. Hence, a patent search was executed to give a state-of-the-art impression.

The total search consisted of three independent classification searches on `worldwide.espacenet.com` and was executed in August 2022. These searches were composed with the help of an expert from the medical library from the Erasmus MC. The first search was focused on devices, instruments and stents inside the gastrointestinal tract that used fixation methods such as barbs. The second search focused on devices, instruments, and techniques for placement or removal of stents that used some sort of fixation method. The third search included techniques for deploying anchors or barbs of a stent specifically inside the intestines and colon. The full searches are given in Appendix G.

The searches resulted in 449 patents. In total, 158 duplicates were removed and from the 291 remaining patents, the title, abstract, and figures were scanned on interesting techniques and methods to safely insert stents with barbs. Hereafter, 27 patents were included that contained a method to deploy barbs or to insert a stent safely. These were then categorized into different techniques and are presented below in the results section. The PRISMA diagram of the patent search is shown in Fig. 4.1. The list of all included patents is given in Appendix H.

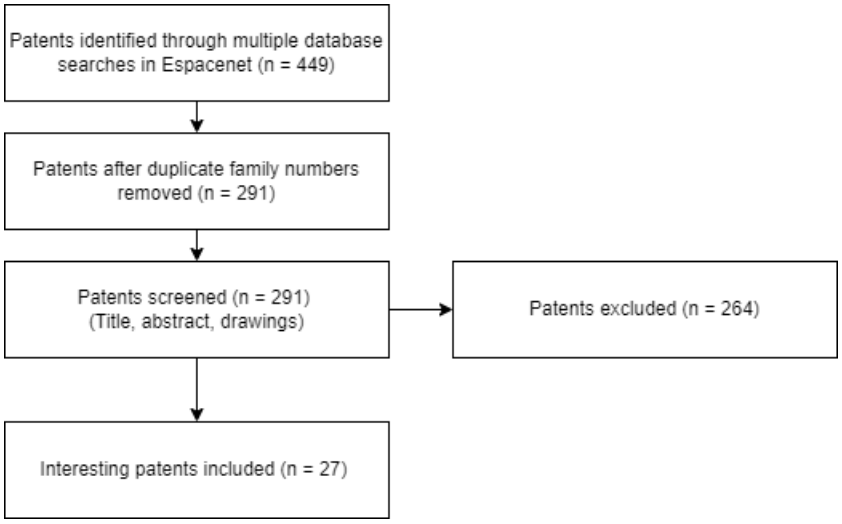


Figure 4.1: PRISMA diagram of the patent search.

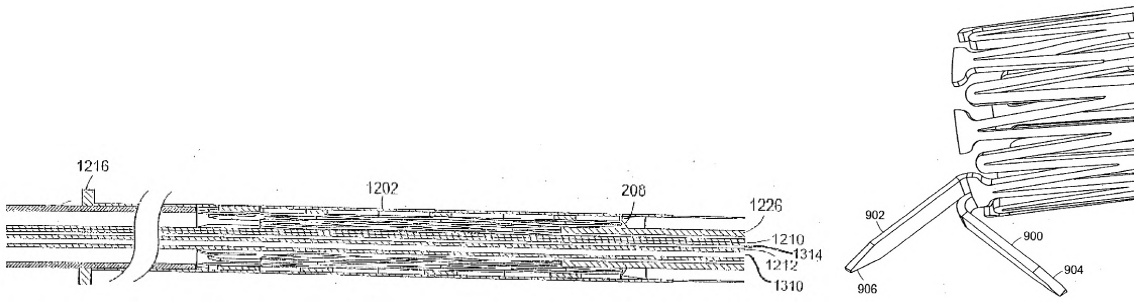
4.2. Results

The 27 included patents were categorized in six main categories and twelve subcategories on how to safely insert barbed stents. These categories were defined by the author and based on own knowledge and interpretation. Hereafter, each category and its subcategories are described and explained. Each category is accompanied by a figure displaying a typical example.

4.2.1. Catheter

The first category used catheters to insert or remove stents. This is a commonly used method to insert colonic stents in today's practice [31]. A metal stent is placed over a guide wire and inserted through a catheter. In most cases these stents are made from a shape memory alloy (SMA), such as Nitinol. If such a stent was made with barbs, the barbs would be protected by the catheter and could not cause any tissue damage, therefore ensuring safe insertion of a barbed stent. An example found in patents is given in Fig. 4.2a, where the stent is in a compressed state, as it would be inside a catheter [32]. This stent made from an SMA, contained barbs on the ends, as shown in Fig. 4.2b, where the left barb is still deploying and the right is already fully deployed.

Insertion via a catheter could be an interesting option, if a covered SMA stent would be designed. It carries the advantages that this insertion method is already widely used in practice and the colon will be protected from any damage. One of the challenges concerns the manufacturing of the barbs on a covered stent because a lot of barbs should be added. However, such stent designs have already been manufactured from stainless steel, so manufacturing could be possible in the near future [33].



(a) Stent and barbs compressed. (b) Barbs deployed.

Figure 4.2: Barb deployment with catheter [32].

4.2.2. Constraints

The second category concerned barbs that are deployed by releasing a physical constraint. These constraints were either nonabsorbable or absorbable. The constraints ensured that the barbs stayed in an undeployed state, thereby protecting the surrounding tissue from any harm or damage.

Nonabsorbable

Nonabsorbable constraints had a sort of mechanism to release barbs. One such example is given in Fig. 4.3 and shows a deployed coiled barb with a constraint indicated by (562) [34]. This constraint was a small rope that would deploy barbs when removed or loosened. The patents in this category only described deploying barbs individually. Therefore, such a method would be a difficult solution with the current barb design as described in Chapter 3, since this would require too many individual barbs.

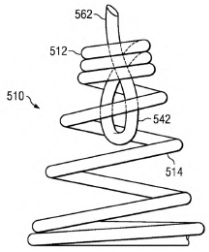
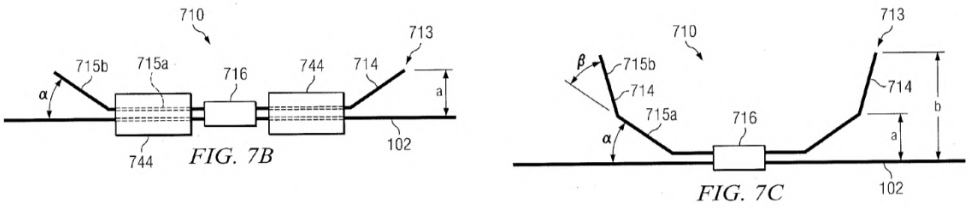


Figure 4.3: Nonabsorbable constraint [34].

Absorbable

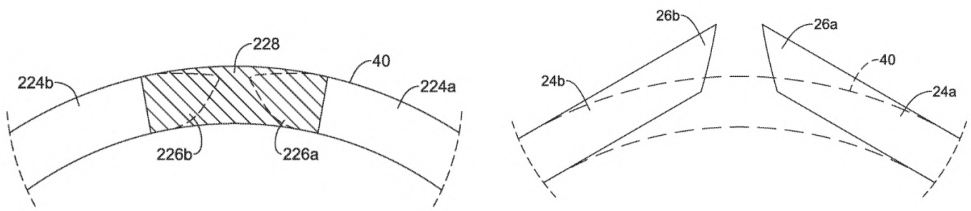
Different absorbable constraints were described in multiple patents. One example is given in Fig. 4.4, where the barbs were partially covered in an absorbable material [35]. Only the base of each barb was covered and the tip uncovered. When this was placed in an in-vivo environment, the material would dissolve and deploy the tip of the barbs. Another example is given in Fig. 4.5, where barbs were pre-bent and the tip of the barbs was covered in an absorbable material [36]. Here, the barb ends were covered and therefore could cause no harm to the colonic tissue.

Covering barbs in an absorbable material would be an interesting technique to safely insert a barbed stent, since it would protect both the barbs and colon from getting damaged. However, removal of the stent with barbs would remain another challenge with this technique.



(a) (b)

Figure 4.4: Absorbable constraint at base of barb [32].



(a) (b)

Figure 4.5: Absorbable constraint at tip of barb [36].

4.2.3. Forced through

The next category describes techniques that forced barbs outward in three different manners, namely using a balloon, multiple components and a retraction device.

Balloon

The first subcategory was described in one patent and used a balloon to force barbs through the outside of the stent [37]. In a non deployed state, the barbs were inside the stent and could cause no harm to the colonic tissue, as shown in Fig. 4.6. The barbs are indicated by (118), the outside of the stent by (11) and the balloon by (120). When the stent was placed in a correct position, the balloon was inflated, thereby pushing the barbs outward as indicated by the two arrows, and through the outside of the stent.

Such a technique could be interesting to use for safe insertion of the stent. However, perforating the outer layer of the stent could cause leakage of fecal matter through the stent. This could happen in such a design and is therefore a disadvantage of this technique for the use-case in this thesis.

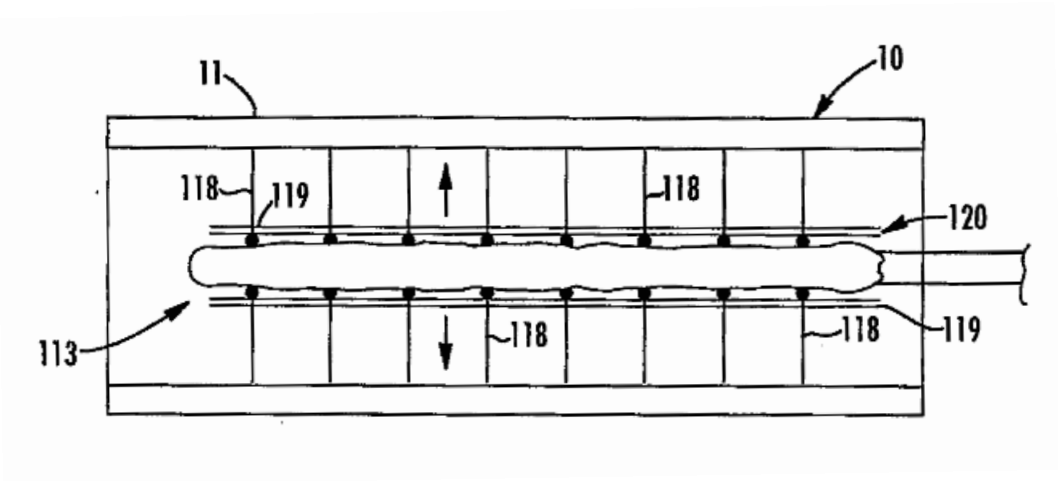


Figure 4.6: Barbs forced through stent by a balloon [37].

Multiple components

Another patent described a stent that was composed of two different components [38]. First, a metal stent with a certain pattern would be inserted into the desired position. Afterwards, a rigid tube with bulges pointing outward, would be inserted inside this metal wired stent. The bulged tube is indicated by (10), the bulges by (65) and the metal stent by (20), see Fig. 4.7a. As a result, the bulges caused outward pointing barbs because they forced the metal wire stent outwards in these locations. These barbs are indicated by (30) in Fig. 4.7b.

A stent made from two components could be interesting, however, it could cause the contact surface to increase. This could have negative influence on the intestinal blockage, as explained in Chapter 5.

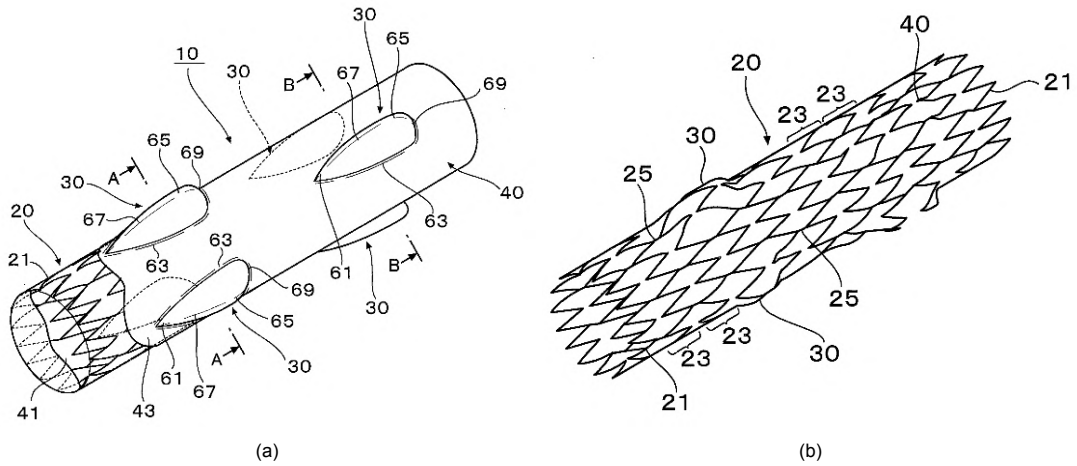


Figure 4.7: Barb deployment with multiple components stent [38].

Retraction

Barbs forced through the stent by a retraction device was based on the patent describing a stapler [39]. Barbs were inside the stent, so protected from causing damage to the colon. Fig. 4.8 shows the deployment of the barbs. A retraction device (246) containing an angled block could force the barbs (240) through the stent (232) and into the colonic tissue.

This mechanism would cause the same disadvantage as described with the balloon, namely that it perforated the stent, which could create a route for leakage of fecal matter through the covered part of the stent into the abdominal cavity.

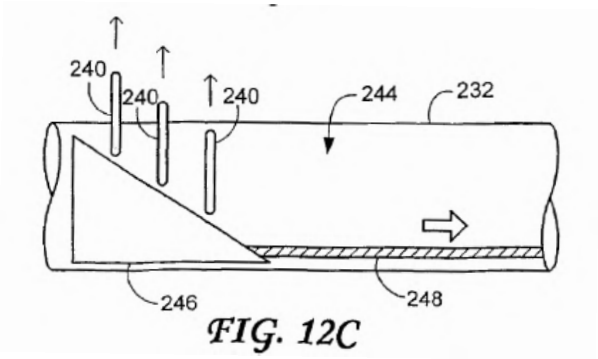


Figure 4.8: Barb deployment by a retraction device [39].

4.2.4. Radially foldable

The following techniques all contained structures that could fold radially. These were divided into three subcategories and are described below.

Helical

One patent described a stent where a metal wire was attached to a helical folded surface [40] and is shown in Fig. 4.9. The metal wire contained barbs indicated by (22r) and loops at the ends indicated by (26). This technique was focused on safely removing the stent. A hook would be attached to one loop. By retracting the hook, the stent could be removed as the helical surface would loosen up. This could then be retracted via a catheter if desired, as shown in the figure.

This technique looked interesting for retraction of the stent. However, safe insertion of the stent and making the helical surface leak-proof would remain challenges.

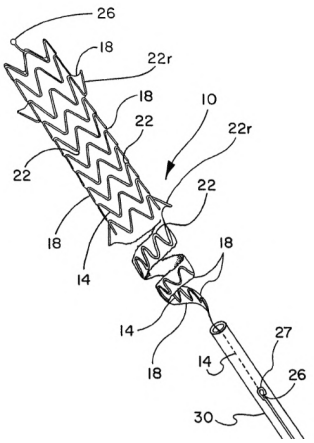


Figure 4.9: Removal of helical shaped stent [40].

Spiral

One patent described a method to decrease the diameter of the stent for insertion [41]. This would be achieved by folding the complete stent as a spiral, as shown on the left in Fig. 4.10. When the stent would be released in place, the spiral would fold outward and form a cylinder, as shown on the right in the figure. A decreased diameter could decrease the chance of damage to the colon. However, this technique did not fully protect the barbs and colon from any damage. Besides, in a deployed state, the stent could lack radial force, since it is not a rigid cylinder because it is not a continuous plate, as marked by point (A) in Fig. 4.10. This would also not ensure a leak-proof stent.

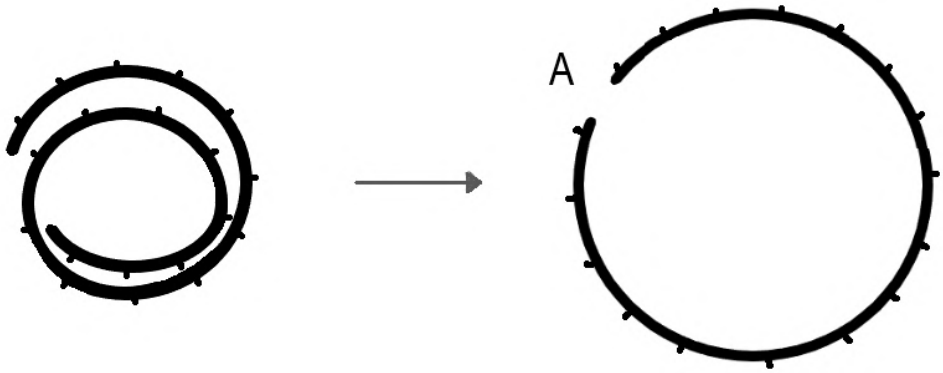
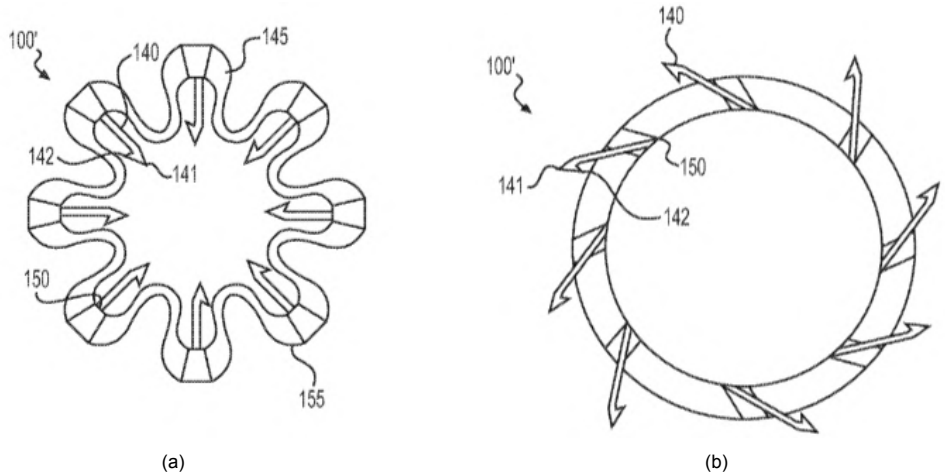


Figure 4.10: Top view of spiral stent in folded (left) and deployed (right) state.

Compressed inwards

This subcategory was described in one patent in which the whole stent could be compressed inwards [42]. During insertion, the stent would be compressed due to the presence of flexible parts, which is presented in Fig. 4.11a. The barbs would in this situation point inwards, thereby not causing any tissue damage. The stent would expand when placed on the right location and the barbs would turn and point outwards, see Fig. 4.11b. For the barbs to rotate and point outwards, holes next to the base of each barb were present in the stent.

Although this technique required holes in the stent that cause leakage, the idea seemed interesting to use. It could decrease the diameter and thereby reduce tissue damage, same as the spiral.



(a) (b)

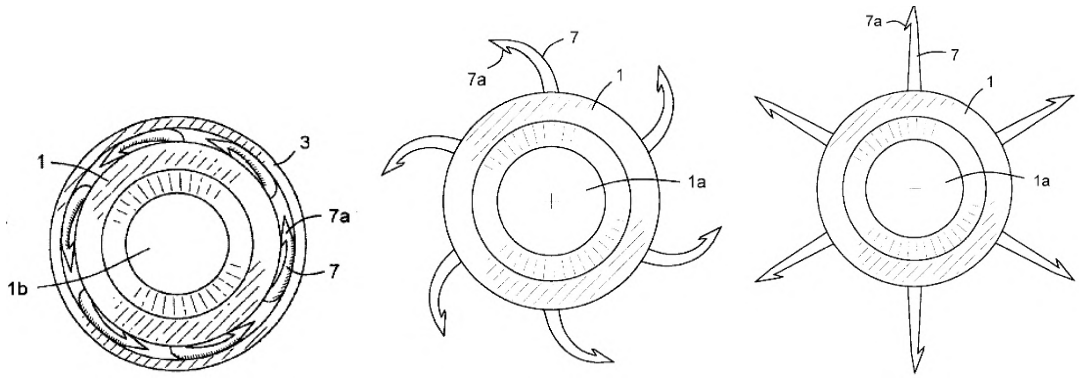
Figure 4.11: Inwards compressed stent with barbs [42].

4.2.5. Folded barbs

Stents including barbs that could move or fold were divided into three categories and are described below.

(Semi-)Flexible barbs

Barbs made from flexible or semi-flexible materials were described. One example is shown in Fig. 4.12 and shows the three stages of the barb deployment [43]. In Fig. 4.12a the barbs were in a non deployed state and protected by a removable tube indicated by (3). When this tube was removed, the semi-flexible barbs would deploy until straight, as in Fig. 4.12b and 4.12c. This technique could only be achieved by materials that could resist flexion, but still be rigid. Besides, no reduction in diameter to ease insertion and retraction of a stent was achieved with this technique.



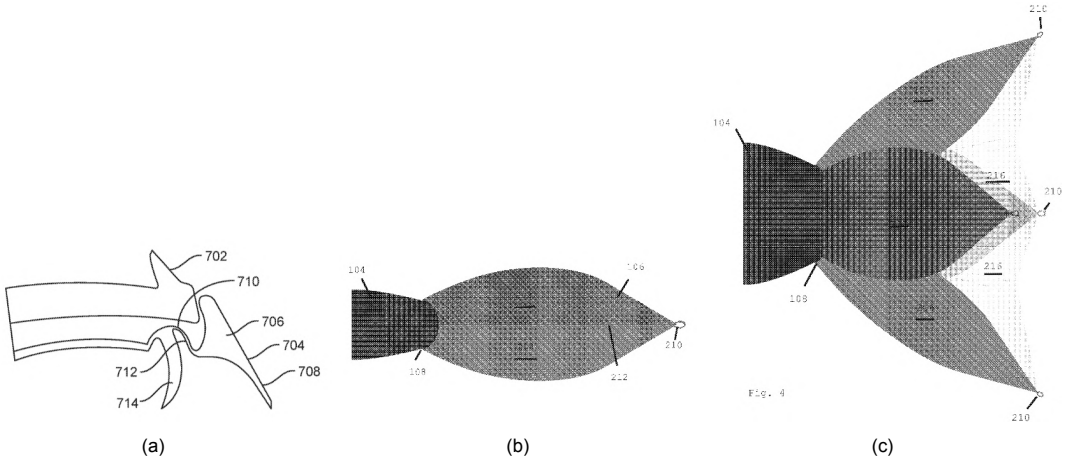
(a) (b) (c)

Figure 4.12: Flexible barbs on a stent [43].

Foldable barb

This technique concerned rigid barbs that could rotate to be deployed. One example could be rotated at the base indicated by (712) in Fig. 4.13a [44]. Therefore, the barb would not damage tissue during insertion. Another example described a system that contained four plate-like barbs [45]. These barbs were kept under tension when in a non deployed state, as in Fig. 4.13b. When the tension was released, the barbs would point outwards, which is shown in Fig. 4.13c.

Folding barbs could be an interesting option. However, with the current small barbs, this would face a lot of challenges to make all the barbs foldable.

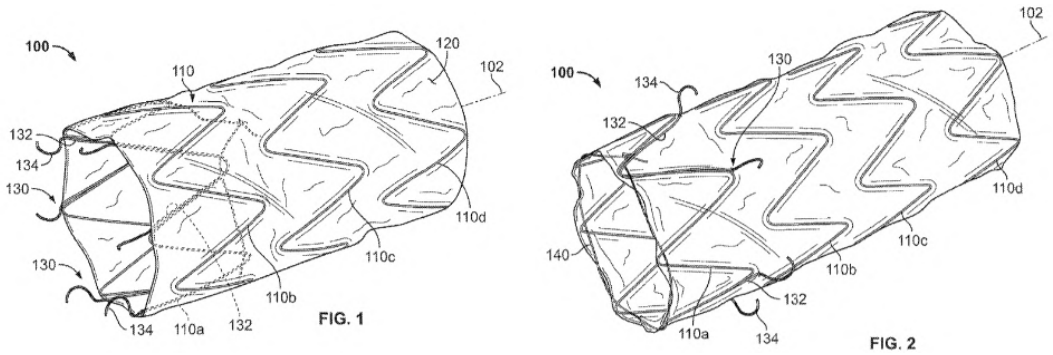


(a) (b) (c)

Figure 4.13: Examples of foldable barbs [44][45].

Foldable stent

This subcategory was encountered in one patent, where the proximal end of the stent could be folded entirely [46]. The barbs were half-circled, indicated by (134), and attached to a metal wire structure of the stent, as shown in Fig. 4.14. In a non deployed state, the barb ends would point outward, and the proximal end was on the inside of the stent, see Fig. 4.14a. The barbs would be deployed by folding the end of the stent outwards. This caused the barbs to be deployed circularly. The barbs could therefore penetrate the colon and would end up facing towards the outside of the stent, as in Fig. 4.14b. However, this technique to deploy barbs seemed not feasible for the current barb designs as described in Chapter 3.



(a) (b)

Figure 4.14: Stent with a foldable end [46].

4.2.6. Grasper

The last category was regarding barbs that could be deployed with a grasper [47]. This stent had multiple barbs that could be forced outwards in-situ with a grasper, as used in minimal invasive surgery. This category was deemed less relevant because the current barb designs would require a lot of barbs to be deployed, which would not be practical in clinical use.

4.3. Discussion

A patent search was executed and six categories were identified on different techniques to safely deploy barbs or barbed stents into the colon: catheter, constraints, forced through, radially foldable, folded barbs and grasper. These techniques all had their own advantages and disadvantages. In the light of the prototype that would be designed later in this thesis, the most promising results were discussed. Firstly, a catheter to insert and extract a barbed stent would be a good deployment method. However, such a stent would have to be manufactured from a shape memory alloy. This might be out of the

scope for the prototype, but could be considered in future research. On the other hand, covering the barbs of a stent in a tube, essentially the method a catheter uses, could be a solution for the prototype. Secondly, the addition of an absorbable material to cover the barbs of a stent during insertion, should be considered. It would be an easy strategy to protect the colon from damage. Nevertheless, this deployment technique would not decrease the diameter of the stent, which complicates the insertion and retraction. On the other hand, a combination of an absorbable material with a technique to decrease the diameter, could facilitate insertion. Thirdly, forced barbs through a stent would be an innovative way to safely deploy barbs. However, as described earlier, this could cause anastomotic leakage through these holes or alongside these barbs. Therefore, this technique should not be used in a prototype, since the goal of the stent is to decrease anastomotic leakage. At last, barbed stents that could be compressed inwards, thereby reducing the diameter and covering the barbs, should be considered for a prototype. However, this could reduce the radial strength of the stent. Another method could be to use a spiral shaped stent, but a solution should then be sought for the reduced radial strength and the opening this leaves in the stent.

This patent search discovered multiple techniques that could be used to deploy barbs in the prototype stent. Even though all relevant patents were sought with a dedicated search strategy, some techniques could be missed by the used methodology.

4.4. Conclusion

Interesting techniques found in patents included the use of a catheter, absorbable constraints and compressible stents. A conclusion on which technique would fit the prototype best was made later during the design phase of the stent. The most feasible techniques were the use of a catheter or tube to protect the colon and barbs from damage and a compressible stent for insertion and retraction.

5

Intestinal blockage

The two previous chapters looked into the improvement of stent fixation inside the colon. The other main problem was intestinal blockage caused by the stent, as described in the introduction and Chapter 2. Therefore, this chapter addresses this second problem. The in-vivo experiments concluded that the old stent design with balloons facilitated insufficient passage of fecal matter. Decreased stool observed during an experiment and an accumulation of fecal matter around the stent observed during termination of the pigs, indicated the presence of intestinal blockage. Therefore, the causes behind intestinal blockage and possible solutions needed further research. These causes, solution and reasoning are described in this short chapter.

5.1. Causes of intestinal blockage

Several causes for intestinal blockage were identified. These were mostly based on the in-vivo experiments performed in pigs. It should be noted already that most of these causes were assumptions, because the only available information was from visual inspection after termination of the pigs in these experiments.

First, the design of the old stent was analyzed. The first disadvantage concerned the large frontal surface of the outer diameter, compared to the surface of the lumen of the stent. The outer diameter of the stent with filled balloons was approximately 38 mm, whereas the inlet diameter of the stent was 30 mm, and the internal diameter in the middle part of the stent was 24 mm. Such a small lumen at the proximal end of the stent would form an obstacle for feces to be transported in the direction of the rectum. Feces could accumulate at the proximal end and 'push' against the stent's frontal surface, thereby causing stent migration. This was visualized in Fig. 5.1, where a simple cylinder resembled a stent. This large contact surface of the old stent is presented in red in Fig. 5.2a, with the forces of the feces presented as black arrows. Fig. 5.2b resembles a smaller difference between internal and external diameter of the stent, which could decrease the force exerted by feces on the stent. In addition, this larger frontal contact surface was more prone to accumulation of feces in front of the stent, causing obstruction and increasing the force exerted by the feces on the stent. Adding to this was the property of the colon to absorb all fluid from the blocked fecal matter, further hindering passage through the

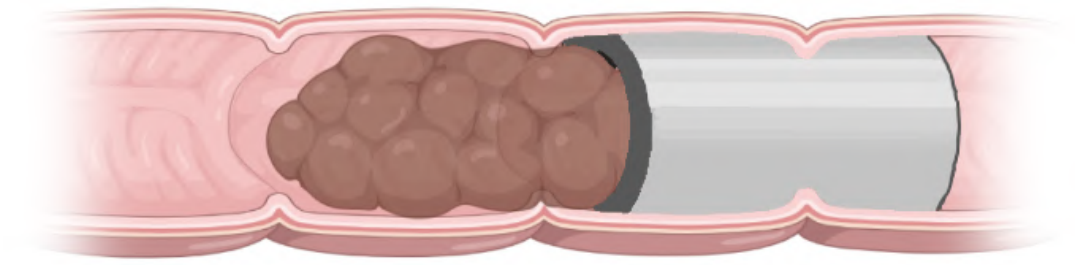
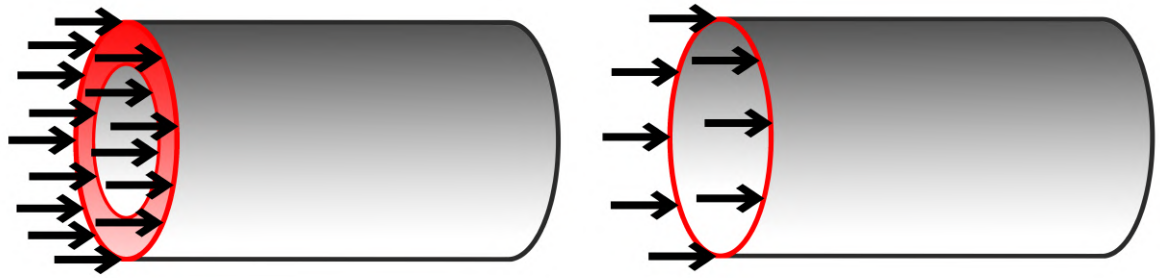


Figure 5.1: Schematic presentation of fecal matter accumulation. *Created with BioRender.com*



(a) Large contact surface old stent. (b) Decreased contact surface.

Figure 5.2: Influence of decreased contact surface.

small lumen. This large frontal contact area could mainly be attributed to the presence of the balloons. The idea was that expanding balloons, in combination with a certain profile, should increase the fixation of the stent. However, the balloons were reconsidered, as it caused a major disadvantage regarding intestinal blockage. The preliminary literature study described that currently researched intestinal stents with balloons, all used an extra means of fixation, mostly a strap around the outside of the colon [18]. Such a strap was undesired for this stent because this should be removed with a second surgery. A second surgery poses a burden for the patient and was therefore undesired. This led to the decision to omit the balloons as a means of fixation. This enabled a smaller contact surface, as in Fig. 5.2b, so that intestinal blockage could be minimized. Further supporting this design-decision were the results from the experiments in Chapter 3 that showed that a larger coefficient of friction was achieved with barbs, compared to the old stent designs with horizontal ridges and ProGrip. Thus, implicating that fixation could be improved and the balloon could be omitted as means of fixation.

In addition, placement of a stent or tubular structure in the colon influenced the peristaltic movements. Assumed was that the peristaltic movements had no effect on the transport of feces through the lumen of the stent. In other words, the peristaltic wave would not deform the stent and therefore not promote transport of feces to the distal part of the stent. Accumulation of feces at the proximal end of the stent would be a result of this, with the same negative effects on stent migration as described earlier. This could be solved with the use of a flexible tube. However, this was not researched during this thesis, so no conclusion could be given on this topic.

Thirdly, the length of the stent had an influence on intestinal blockage. As described in the previous paragraph, peristaltic movements of the colon would not be passed on through the stent. A larger length stent would cause the peristaltic movement to be blocked over a longer part of the colon. This could decrease the amount of feces that was transported across the length of the stent. Furthermore, an increased length would increase the surface inside the stent where feces flowed past. Shear between the fecal matter and the stent would also increase the force exerted on the stent that could increase the chances of stent migration. However, the length of the old stent prototype enabled a good healing of all the anastomoses during in-vivo experiments. Therefore, it was assumed that the length of the stent was sufficient to cover the anastomosis. However, the influence of a decreased length was not researched in this thesis. Consequently, the length of the stent should not be increased, to keep this parameter constant.

5.2. Model

Initially, the plan was to investigate and improve intestinal blockage by the means of a biomechanical model, which is further described in Appendix I. A stent with a colon placed around it, was measured and these dimensions were used to create a model in SolidWorks. Using SolidWorks Flow Simulation, a certain amount of feces would be moved from one end to the other end of the colon. The goal was to optimize the proximal end design of the stent. First, the old stent design would be tested and a pressure difference between the proximal and distal end would be measured. Then, multiple redesigns of a proximal end would be tested and the design which created the least pressure difference, would be further taken into account for a redesign of the stent. A smaller pressure difference would indicate that less force was exerted by feces on the stent, which was the desired outcome. However, this

model was not further used because the balloons of the stent were already deemed ineffective and not necessary for fixation of the stent. Therefore, by leaving out the balloon at the proximal and distal end, the thickness of the stent could be decreased to a minimum. This would make the intended optimization of the proximal end of less importance and influence on intestinal blockage.

5.3. Conclusion

To conclude, minimizing intestinal blockage was analyzed. Minimizing frontal contact surface was assumed to be the most responsible factor for this. Therefore, a minimal contact surface, achieved by removing balloons and reducing the stent thickness were further used in this thesis.

6

Design requirements

The research in the previous three chapters formed the basis for the design requirements for the improved stent. The redesign should ideally fulfil all these design requirements. First, the design requirements are elaborated and explained. A summary of these design requirements is given in Table 6.1, at the end of this chapter.

6.1. Elaboration of the requirements

The design requirements were divided into five different categories: fixation, dimensions, materials, delivery method and performance. Important to note is that these design requirements were set for a redesign that could be implanted during an in-vivo experiment on pigs. Therefore, only requirements relevant for this experiment were included. Consequently, no requirements for use in clinical practice were included.

6.1.1. Fixation

Barbs are needed to counter stent migration. The dimensions of the barbs and the friction coefficient generated by the barbs are mentioned in the following requirements.

Fixation method

The stent should have barbs for fixation in the colon. Preliminary experiments determined that profiles from soft materials did not create sufficient friction, and barbs were necessary. Besides, balloons filled with liquid, as used in the old design, were not needed. Such balloons created a large contact surface at the proximal end of the stent, which increased intestinal blockage. Therefore, barbs were the preferred method of fixation.

Barb parameters

This paragraph captures the five requirements from Table 6.1 regarding the dimensions of the barbs. The parameters of the barbs which provided the highest static friction were tested in Experiment 1 and 2. In these experiments conic shaped barbs were tested and the parameters that created the highest friction were the following: a barb height of 1.5 mm, measured from the center of the cone to the tip. Diameter at the base of 1.0 mm. The number of barbs should be 3 barbs per cm^2. The angle of the barbs should be 30°, measured from the centerline of the cone to the surface of the stent. The direction of these barbs should be in the opposite direction of motion, in other words, the barbs should point distally. The barbs should point in this direction on both sides of the anastomosis, to increase the resistance against stent migration.

Friction coefficient

The friction coefficient that is created by the barbs should exceed the friction coefficient of a ProGrip mesh, which proved to insufficiently fix the stent in an in-vivo experiment. A ProGrip mesh was previously tested and the friction coefficient was determined at 1.11. Therefore, the friction coefficient of the barbs should be higher than 1.11.

6.1.2. Dimensions

The general shape, diameter, thickness, and length of the stent are mentioned in the following requirements.

General design
The general design of the stent should be a tubular structure, to fit the colon and because of its structural stiffness. The stent should be closed over the whole length, as the purpose of the stent is to prevent spillage of fecal matter into the abdominal cavity in case of anastomotic disruption.

Diameter
The diameter of the stent was tested in Experiment 3. An expansion of 50 - 60% of the colon was considered as the best diameter. This experiment did not consider the influence of diameter on the flow of feces through the stent to reduce intestinal blockage.

Thickness
The thickness of the tube should be as small as possible. This causes a decreased contact surface and should decrease the force exerted by fecal matter on the stent. Besides, it should decrease obstruction and stasis at the proximal end of the stent.

Length
The old stent design had a length of 60 mm. During previously performed in-vivo experiments, this length or shorter lengths were tested. However, no conclusion was drawn on whether changing this length would improve fixation. Besides, no research was executed in this thesis on the influence of changing this length. Therefore, the length of the stent was kept constant at 60 mm, so this parameter would not influence results of a new in-vivo experiment.

6.1.3. Materials

The stent operates in a living environment, which means that the material should possess certain properties. The properties necessary for the tube and barbs are described below.

Barbs
The material used for the barbs should be manufactured with the same resolution as in Experiment 1 to 3. The print resolution in these experiments was 50 μm. This was necessary as the tip of the barbs should penetrate the colonic wall. Furthermore, the material for the barbs should be strong enough to not break when placed in a colon. When the stent is moved inside the colon, the barbs should withstand the force exerted.

Tube
The body of the stent should be made of a flexible material. Flexibility was desired as it would facilitate the possibilities to decrease the diameter of the stent for insertion and extraction, and ideally also allow for conveying some propulsive pressure from peristaltic movement. However, the material should be stiff when placed in-situ, so the proximal and distal end are opened to facilitate the passage of fecal matter. Besides, a rigid tube would increase the radial force of the tube, thus increasing the force on the barbs that fix the stent in the colon. This could in turn increase the tissue penetration, and consequently the fixation force of the barbs.

Safety
The materials used for the tube and barbs should not cause a foreign body reaction in a pig's colon, thereby influencing the healing process. This would increase the chance of inflammation, which increases the chance of anastomotic leakage [48]. Besides, the materials used should last for at least fourteen days inside the colonic environment. The material properties in terms of strength and stiffness should not change substantially in this period.

Temperature
The normal body temperature inside pigs measured via the rectum can reach up to 39.6° C in non-fevered pigs and up to 42.8° C in fevered pigs [49]. Therefore, all materials used in the stent should resist at least 43° C and should not weaken or break with this temperature.

6.1.4. Delivery method

The technique to insert and extract the stent, to prevent tissue damage, and to protect barbs are described in the following requirements.

Insertion and extraction method
The desired method to insert and extract the stent, was transanally. However, this was the intended method in clinical practice. The in-vivo experiments with the stent were performed as open surgeries. Therefore, no special method to insert and extract the stent transanally was needed. On the other hand, inserting the stent should be facilitated with a stent that could decrease in diameter. Besides, this decreased diameter should simplify the extraction of the stent.

Tissue damage
Colonic and surrounding tissue should not be damaged or harmed during insertion and extraction of the stent.

Barbs protection
The barbs of the stent should not be damaged during insertion or extraction. Therefore, the barbs should be protected with a tubular structure. This protection should also decrease the collateral tissue damage that barbs could cause. Furthermore, this protection should not cause an inflammatory reaction with the pig's colon.

6.1.5. Performance

The new prototype stent should succeed in decreasing stent migration and intestinal blockage. The stent should also have a life span of fourteen days, not influence tissue healing and in the end cause a decreased anastomotic leakage rate.

Stent migration
The redesign of the stent should not migrate in the colon. In an in-vivo experiment in pigs the occurrence of migration should be prevented compared to the experiments with the old stent design. In these experiments, the old stent design migrated in six out of eight occasions, so the new prototype should migrate less, and ideally not at all.

Intestinal blockage
The redesign of the stent should not cause obstruction of the colon. Fecal matter should pass through the lumen of the stent. This could in turn decrease the force the feces exerts on the stent, thus decreasing the chance of stent migration.

Life span in-vivo
The in-vivo experiments with pigs had a duration of fourteen days, based on the time it takes for an anastomosis to heal completely. Therefore, the stent should not migrate within fourteen days after implantation. Besides, the stent should not degrade during this period.

Tissue healing
The stent should not disturb the healing process of the colonic tissue. First, the tension on the anastomosis should be kept as low as possible, since a higher tension increased the chance of an anastomotic leakage [15]. This was mostly influenced by the diameter of the stent, but should also be achieved by not placing barbs around the anastomosis, so in the middle of the stent. Besides, removing barbs at the location of the anastomotic line should reduce the chance of local necrosis.

Anastomotic leakage
The most important requirement of the redesign was that it should decrease or even eliminate the occurrence of anastomotic leakage, when compared to a control group where no stent would be placed.

6.2. Summary of the requirements

A short summary of the design requirements is presented in Table 6.1.

Table 6.1: Summary of the design requirements.

Fixation	Fixation method	Barbs
	Barb height	1.5 mm
	Barb diameter	1 mm
	Barb distribution	3 barbs per cm^2
	Barb angle	30 degrees
	Barb direction	Opposite to direction of movement
	Friction coefficient	Larger than 1.11
Dimensions	General design	Circular and closed tube
	Diameter	Expansion of colon = 50 - 60%
	Wall thickness tube	Smallest possible
	Length	60 mm
Material	Barbs	Rigid material
	Tube	Flexible material
	Safety	Not influence tissue healing
	Temperature	Resist 43° C
Delivery method	Insertion and extraction method	Reduced diameter
	Tissue damage	No tissue damage during insertion and retraction
	Barbs protection	No damage during insertion and extraction
Performance	Stent migration	No stent migration
	Intestinal blockage	Decreased intestinal blockage
	Life span in-vivo	At least 14 days
	Tissue healing	Not hinder tissue healing
	Anastomotic leakage	Cause less anastomotic leakage vs. no stent

7

Stent design prototype

The goal of this chapter was to explore new stent designs that could be used during an in-vivo experiment. The design requirements set in the previous chapter served as a basis for the design choices. First, the design requirements were analyzed and the most important factors identified. Then the manufacturing and materials were discussed, and prototype designs were produced. Afterwards, a design choice was made and the final design is presented.

7.1. Analysis of the design requirements

An analysis of the design requirements was performed to identify the most important ones that served as a starting point. The first requirements regarding the fixation of the stent, all concerned the barb design. These barbs needed to be small and accurately manufactured. Therefore, the requirements regarding fixation were mostly dependent on the manufacturing technique. The requirements regarding the dimensions of the stent could be achieved in multiple ways, and were not necessarily dependent on another factor. However, the thickness of the stent was dependent on the manufacturing technique used and the material. The third category of requirements were regarding the materials used for the stent. In the category of delivery method requirements, folding the stent to reduce the diameter should be possible, which depended on the flexibility of the material. The barb protection and tissue damage should be achieved in some manner. At last, the performance requirements concerned factors that should still be tested in the in-vivo experiment.

This led to the conclusion that most requirements depended on the manufacturing technique and the materials. Therefore, these two factors were first researched for the redesign of the stent and are described in the next two sections.

7.2. Manufacturing

Multiple options for the manufacturing process were considered. Rapid prototyping of the redesign enabled to iterate the design and produce a cost-efficient design process. Three main prototyping processes included 3D printing, CNC machining and injection molding [50]. The advantages and disadvantages of these manufacturing processes for the redesign of the stent were researched. These are described in the next paragraphs.

7.2.1. 3D printing

Additive manufacturing or 3D printing is a manufacturing process used in healthcare for multiple applications [51]. Within the process of additive manufacturing multiple techniques could be used. The most common is Fused Deposition Modeling (FDM) where molten material is extruded and built layer on layer. Another is Stereolithography (SLA), which cures a bed of photopolymer resin with UV light. This technique was already used to print the test plates and stents in Experiment 1 to 3. SLA could be a viable option to produce the prototype stent due to the printing resolution. The pros and cons of this process are given in Table 7.1.

The advantages of SLA included the high print resolution and excellent surface finish to print the

barbs. Besides, the availability of a resin 3D printer, low costs of production and the fast delivery time were favorable for using this technique. The disdvantages concerned mostly the material properties of the available materials for this technique, such as the degradation, strength, and heat resistance.

Table 7.1: Pros and cons of 3D printing for a prototype stent.

Pros	**Cons**
Print resolution	Degradation to humidity
Excellent surface finish	Decreased strength
Fast delivery time	Heat resistance
Availability of printer	Limited materials available
Cheap production costs	

7.2.2. Injection molding

Injection molding is the process in which molten material is injected under high pressure into a mold. It is widely used for mass production of polymer parts. The advantages and disadvantages of this technique are mentioned in Table 7.2.

The pros of injection molding included the excellent surface finish of the products and a wide range of (strong) materials was available. The main disadvantages were the high initial costs to produce a mold and the long production time of such a mold. Besides, the angled barbs would be difficult to produce, considering the complex mold that would be necessary.

Table 7.2: Pros and cons of injection molding for a prototype stent.

Pros	**Cons**
Excellent surface finish	High initial costs
Wide range of materials available	Difficult to produce barbs
	Longer delivery time
	Availability of process

7.2.3. CNC machining

Subtractive manufacturing is the overarching term for Computer Numerically Controlled (CNC) machining. It is a technique where material is removed with tools such as mills and lathes, until the desired part is created. An overview of the pros and cons of this technique is provided in Table 7.3.

The advantages of CNC machining included the smooth surface finish, a wide range of materials to choose from, the strength of the produced part and the fast delivery time. Disadvantages included that a complex machine with multiple degrees of freedom was necessary for the barbs due to the angled barbs that created undercuts, which are difficult to machine [52]. Besides, machining was more expensive than 3D printing.

Table 7.3: Pros and cons of CNC machining for a prototype stent.

Pros	**Cons**
Good surface finish	More expensive than 3D printing
Wide range of materials available	Angled barbs difficult to machine
Strength of produced part	Complex CNC machine necessary
Fast delivery time	

7.2.4. Conclusion

3D printing seemed the most favorable manufacturing process. The test stents for Experiment 3 showed that stents could be produced with sufficient accuracy and this technique was easily accessible at the facilities of the TU Delft. From the different 3D printing methods, SLA seemed the most feasible option to produce the redesigned stent.

7.3. Materials

Two main challenges were present for the material choice. The first was that the barbs should be strong and stiff, whereas the tube should be flexible. Secondly, the material properties correlated to photopolymers that could be used with SLA should be looked into, regarding influence on tissue healing and temperature resistance.

The available printer at the TU Delft was the Form3 resin printer (Formlabs, Somerville, MA, USA). Multiple materials were available for this printer at the facilities. The material properties as given by the manufacturers were gathered. The properties of stiff materials for the barbs are summarized in Table 7.4 and flexible materials for the tube in Table 7.5. It should be noted that for parts created with SLA, the material properties could differ significantly based on printer settings, direction and part dimensions.

Table 7.4: Overview of considered materials for barbs.

Material	**Ultimate tensile strength**	**Tensile modulus**	**Elongation at break**	**Heat deflection temperature @0.45 MPa**	**Reference**
Tough2000	46 MPa	2.2 GPa	48%	63° C	[53]
Tough1500	33 MPa	1.5 GPa	51%	52° C	[54]
Grey	65 MPa	2.8 GPa	6,3%	73.1° C	[55]
Clear V4	65 MPa	2.8 GPa	6,3%	73.1° C	[55]
Rigid 4000	69 MPa	4.1 GPa	5,3%	77° C	[56]

Table 7.5: Overview of considered materials for tube.

Material	**Ultimate tensile strength**	**Elongation at break**	**Glass transition temperature**	**Reference**
Elastic 50A	3.23 MPa	160%		[57]
Flexible 80A	8.9 MPa	120%	27° C	[58]
Flexible V2	7.7 - 8.5 MPa	75 - 85%		[59]

Multiple interesting outcomes were encountered in the available materials. Firstly, regarding the stiff materials for the barbs. Five materials were available, from which the Tough2000 and Tough1500 differed from the other three on flexibility. The elongation at failure was respectively 48% and 51%. Besides, the Tough1500 was a material designed for both flexible and stiff parts [54]. The tensile modulus of Tough1500 was also slightly lower than the Tough2000. The other three materials were comparable regarding ultimate tensile strength and elongation at failure. Rigid4000 was the stiffest material among all.

Secondly, regarding the flexible materials for the tube. Elastic 50A was the most flexible material, but not the strongest. Flexible 80A was the only material for which a glass transition temperature was given, in this case 27° C. This material would therefore not be suitable, as temperatures in a pig's colon are higher. Flexible V2 was the least flexible of the three materials.

Furthermore, for most of the materials no glass transition temperature, the temperature at which the polymer starts softening, was given. Therefore, the design requirement of the minimal resistance to temperature could not be checked, except for Flexible 80A. For most of the materials the heat deflection temperature gave some insight in the resistance against temperature. However, this gives a temperature for an arbitrary deflection, so not a conclusion was drawn from this property. Besides, biocompatibility was not assured for all the materials. This was largely caused by the manufacturing process itself. However, after consulting the animal facilities in the EMC, it was assured that experimental 3D printed parts were allowed for experiments with animal subjects. The influence of the materials on tissue healing could not be identified at this stage.

Conclusion

Based on the available materials and their properties, two concepts were designed. First, a combination of stiff material for the barbs and a flexible material for the tube were combined in one concept.

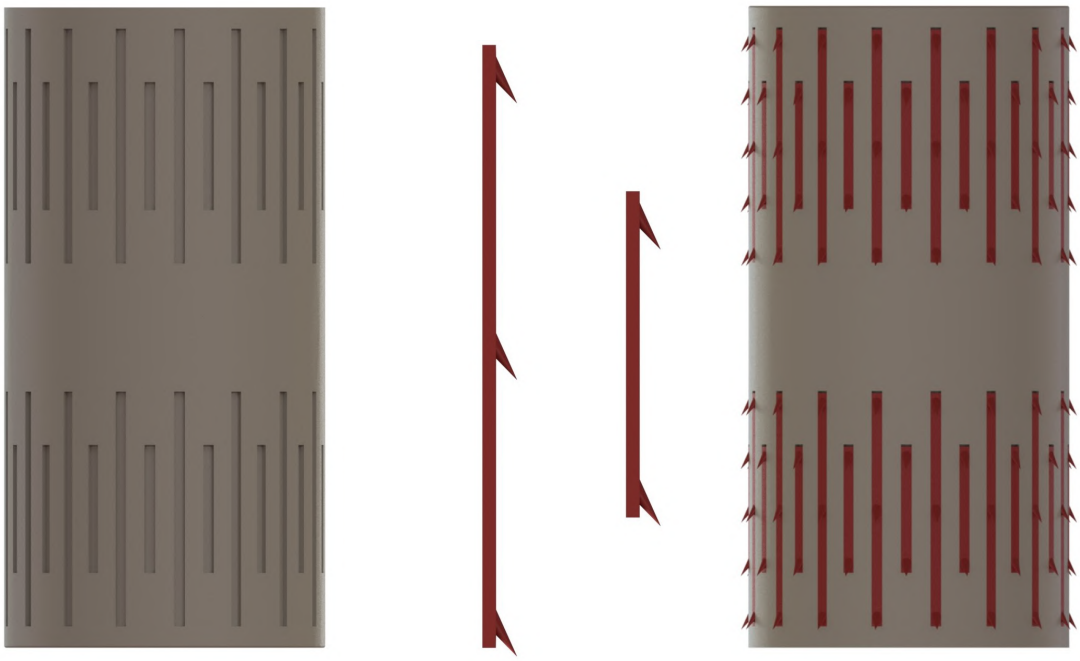
Secondly, the special stiff and flexible property of Tough1500, led to another concept made completely out of this material. The concepts and materials are described in the next section. It should be noted that the designs did not include a tubular structure to protect the barbs and colon from damage during insertion. Such protection was later designed and discussed.

7.4. Prototypes

Two prototypes were designed and produced. The first design had a flexible body and barbs made from rigid material. The second design was entirely made from Tough1500. The designs of these concepts are described in the next sections.

7.4.1. Concept A

The first concept had barbs and tube made from different materials. Assembly of these two parts was therefore needed. A tube with grooves as on the left in Fig. 7.1a was made of flexible material. The barbs were printed in strips of two or three barbs, shown enlarged in Fig. 7.1b, and assembled in these grooves, as shown on the right in Fig. 7.1c. The first reason was that this enabled easy mounting of the barbs at the right location. Secondly, the barbs would be positioned in exactly the right direction, compared to mounting each barb individually. Thirdly, this reduced the assembly time and due to the larger interaction surface between barbs and tube, the bonding would be stronger. The barbs were mounted in horizontal lines to enable tube compression, which was necessary for insertion and retraction of the stent. The tube had a thickness of 1.0 mm and the strips underneath the barbs had a thickness of 0.5 mm. The grooves in the tube had the same depth as the thickness of the strips holding the barbs. The grooves were designed 10% larger in width and length, compared to the strips under the barbs. This was done to correct for potential print errors of the tube that could cause the barbs to not fit correctly.



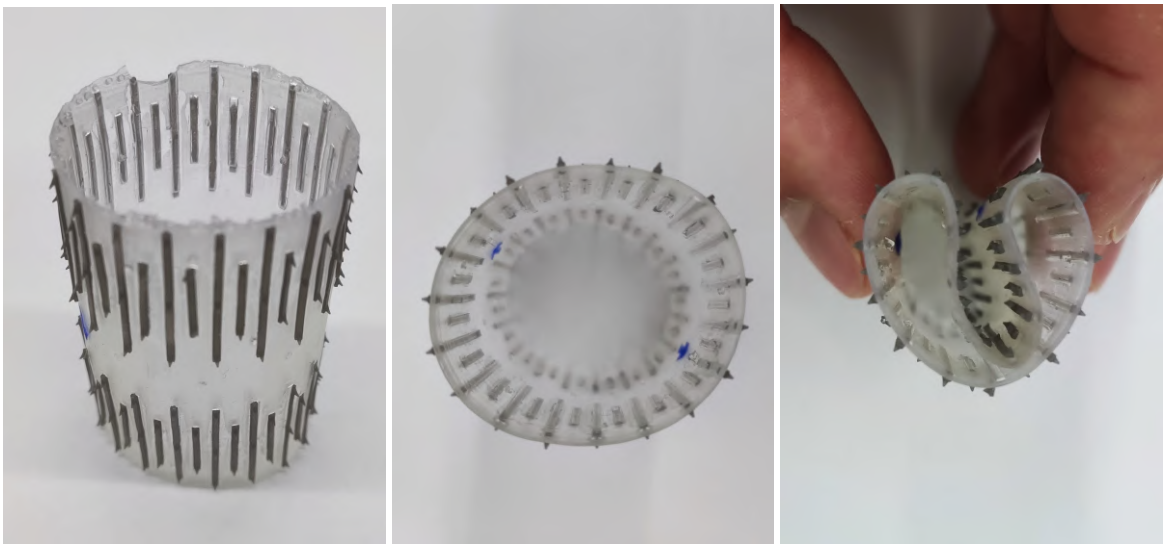
(a) Tube with grooves. (b) Strips with barbs. (c) Assembly Concept A.

Figure 7.1: Concept A design.

For the flexible tube, Elastic 50A was chosen as the material. With this material the flexibility of the tube to reduce the diameter for insertion and retraction was assured. The strips of barbs were glued to the flexible tube and it was expected that the glue would decrease the flexibility of the tube. Therefore, the most flexible material was preferred for this concept. The material for the barbs was Tough2000. This material had already showed its sufficient strength and stiffness during the experi-

ments from Chapter 3. Besides, the barbs were printed as strips, so a little flexibility was desired when the diameter of the stent was to be decreased for insertion. Tough2000 was therefore chosen over the three other stiff materials, because of its elongation at failure. It was also preferred over Tough1500, as this material had not proved its strength and stiffness yet.

The design was printed at the TU Delft with the Formlabs Form3 printer. The printed prototype is presented in Fig. 7.2 in an expanded state and with decreased diameter. The assembly of the barbs and tube was executed with Industrial Grade Superglue HV (EverBuild), a brush to apply the glue and tweezers to hold the strips of barbs. The printed prototype gave interesting insights on the concept. Foremost, the assembly of the stripes of barbs onto the tube was extremely difficult. The strips of barbs were tiny and difficult to put in place with sufficient and correctly placed glue. This was a huge disadvantage of this concept. Besides, the stiffness of the tube seemed insufficient to keep the lumen of the colon in an opened state, and provide a radial expansion force to aid in fixation. This could be improved by using another material from Table 7.5, such as Flexible V2. However, this would not solve the difficulty of the assembly of the stent. Other disadvantages included that the barbs could easily loosen from the tube, difficult removal of the support structures, unknown degradability and heat resistance and a larger thickness of the stent compared to concept B. These advantages and disadvantages of this concept are given in Table 7.6.



(a) Isometric view. (b) Top view expanded. (c) Decreased diameter.

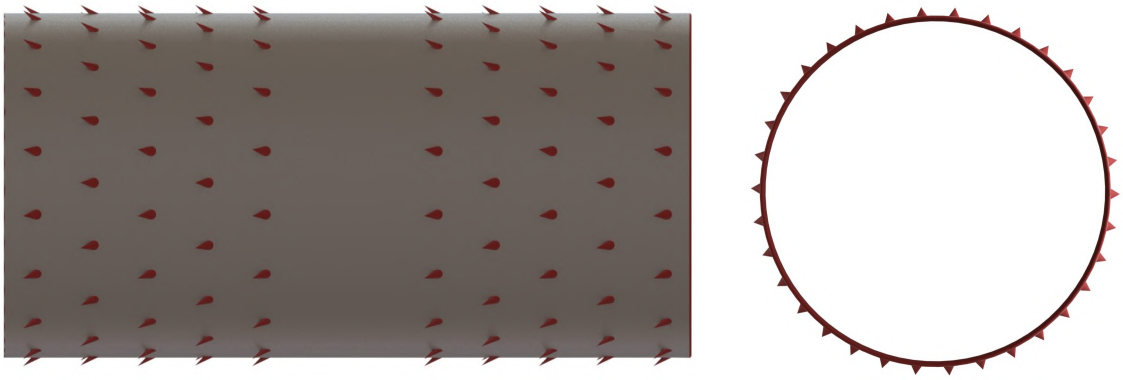
Figure 7.2: Printed and assembled design of Concept A.

Table 7.6: Pros and cons of Concept A.

Pros	**Cons**
Flexible tube enabling easy decreases in diameter for insertion	Difficult assembly of barbs and tube
Stiffness of barbs assured	Insufficient stiffness of tube
	Barbs could loosen from tube
	Difficult removal of support structures
	Degradability unknown
	Heat resistance unknown
	Increased wall-thickness of stent body

7.4.2. Concept B

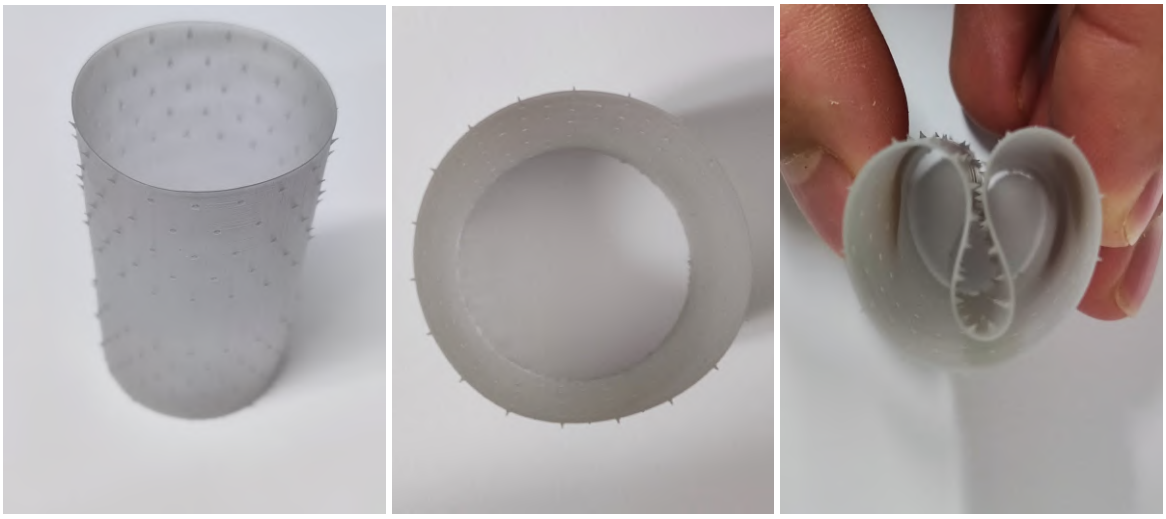
The second concept was a printed stent with barbs and tube made solely from Tough1500, as shown in Fig. 7.3. The barbs are made red for clarity only. The dimensions of this concept were equal to Concept A, except for the wall-thickness of the stent. The thickness was set at 0.3 and 0.5 mm. It was unknown which thickness was sufficient to enable enough flexibility of the tube to reduce the diameter for insertion and retain its stiffness when deployed. These thicknesses were empirically determined after consultation with the employee of the print facilities.



(a) Side view. (b) Top view.

Figure 7.3: Concept B design.

The design was printed at the TU Delft with the Formlabs printer. The concept is presented in Fig. 7.4, in expanded state and with a decreased diameter for insertion. The most important outcome of the print was that the material was flexible enough to decrease the diameter, as can be seen in Fig. 7.4c. This was the case for both printed thicknesses, but for the 0.5 mm thick stent the necessary force was quite large. Besides, the stent seemed to form a stiff tube when in an expanded shape. This concept needed no assembly, which was a great advantage compared to concept A. The disadvantages included that the degradability and heat resistance were unknown, the same as for concept A. The stiffness of the barbs seemed equal to the barbs from concept A, but it was still uncertain. Nevertheless, looking at the strength and stiffness given in Table 7.4 of Tough1500 compared to Tough2000, the barbs should be strong and stiff enough to sustain the forces in the colon. These advantages and disadvantages of this concept are given in Table 7.7.



(a) Isometric view. (b) Top view expanded. (c) Decreased diameter.

Figure 7.4: Printed design of Concept B.

Table 7.7: Pros and cons of Concept B.

Pros	Cons
Stiff and flexible tube	Degradability unknown
Minimal thickness possible	Heat resistance unknown
No assembly needed	Stiffness of barbs uncertain
Strong adhesion between barbs and tube	Removal of support structures

7.4.3. Design choice

The advantages and disadvantages of both concepts were summarized in Table 7.6 and 7.7. In general, concept B showed more promising results than concept A. Both concepts were able to decrease the diameter for insertion and extraction. The biggest disadvantage of concept A was the difficulty and inaccuracy of the assembly of barbs and tube. Even though this was executed with care, the adhesion between the barbs and the tube remained a problem. Furthermore, the stiffness of the tube in expanded state was assumed to be insufficient to keep the lumen of the colon fully opened to enable fecal transport. On the contrary, concept B formed a rigid tube in an expanded state. Therefore, regarding the assembly and stiffness of the stent, concept B was the favored design. The disadvantages of this concept were later validated in the next chapter. Some minor changes were made to the concept, which are described in the next section.

7.5. Final design

Minor changes and additions were made to the prototype stent. These additions were made based on observations of the printed versions of concept B. The three additions are listed below.

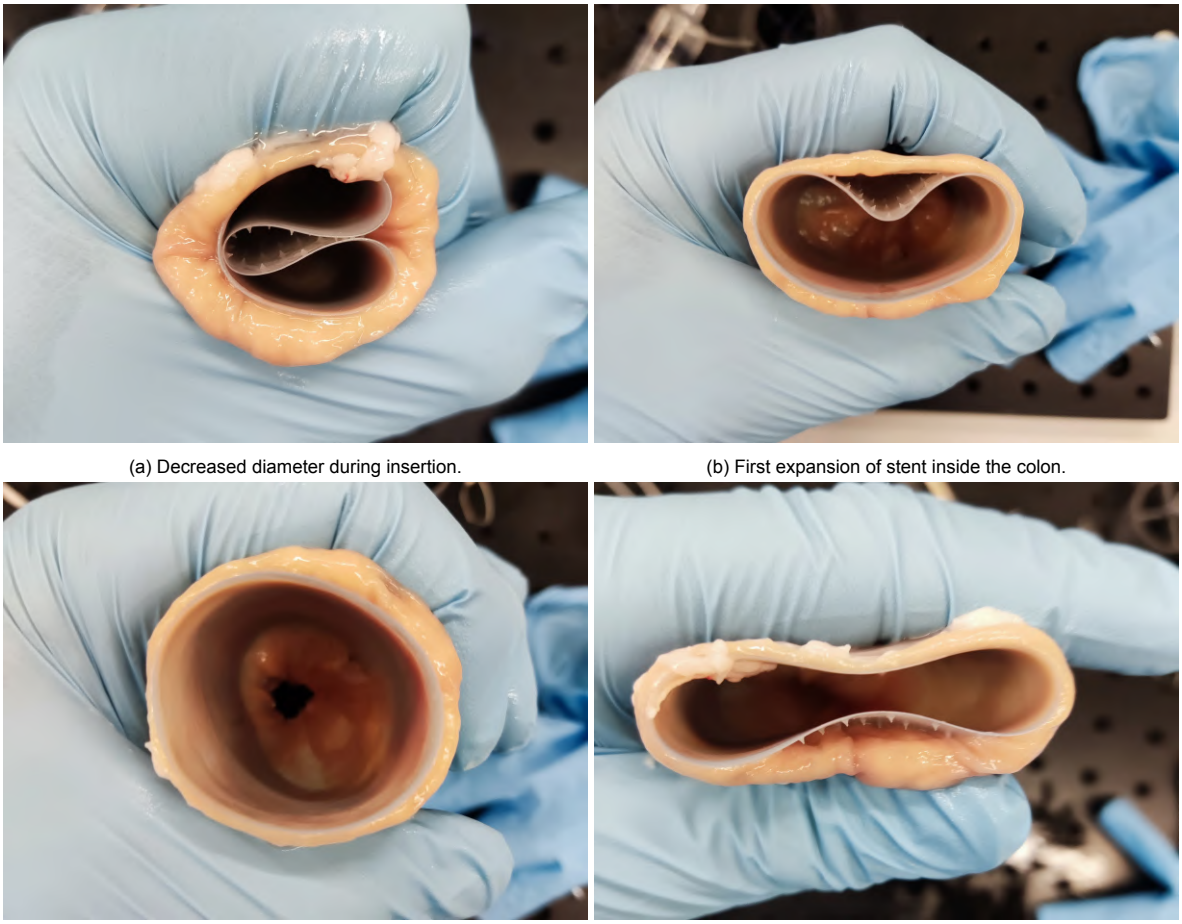
1. Thickness of 0.3 (mm).
2. Fillet at the proximal end.
3. Print direction with support structure at distal end.

A thickness of 0.3 (mm) was chosen. This thickness had more flexibility than the 0.5 (mm) thick stent. This would enable easier insertion and extraction of the prototype stent inside the colon. The stiffness of the tube seemed sufficient to keep the lumen fully opened. This was tested ex-vivo with a segment of a pig's colon that was kept frozen after the last experiments from Chapter 3. The test is shown in Fig. 7.5, in which (a) the stent was inserted by hand with a decreased diameter, (b) the stent was slowly expanded, (c) the stent fully expanded, and (d) the flexibility of the stent was shown by forcing the stent almost flat. This test also showed the capability of the stent to fully expand when inserted in the colon.

The next addition was a small fillet at the proximal end of the stent. As the thickness of the stent was only 0.3 (mm), this would have minimal effect on blockage at the proximal end, but it was still added. Furthermore, the stent should be printed with the distal end attached to the baseplate of the printer. This ensured that the support structures adhered to the distal end. Therefore, no inaccuracies due to the support structures would be present at the proximal end. The proximal end should be as smooth as possible to counter intestinal blockage.

Furthermore, a tubular structure to protect the barbs and the colon during insertion and retraction was added. During the last in-vivo experiment in which the old prototype with ProGrip mesh was inserted, the stent was covered in a PTFE sheet for insertion. This proved to be an effective, easy and cheap manner to achieve both barb protection and prevent collateral tissue damage. Therefore, this was advised for the new prototype. Such a protection sheet is visualized with a simple paper sheet in Fig. 7.6. The stent with protected sheet as in (b) could be inserted in one end of the colon, after which the sheet could be retracted.

To achieve the desired expansion (50 - 60%) of the colon to maximize the fixation, stents with multiple diameters should be present during a surgery. The initial diameter of the colon should be measured as in Experiment 3, then the diameter closest to the desired expansion should be calculated. This stent should then be inserted into the test subject.



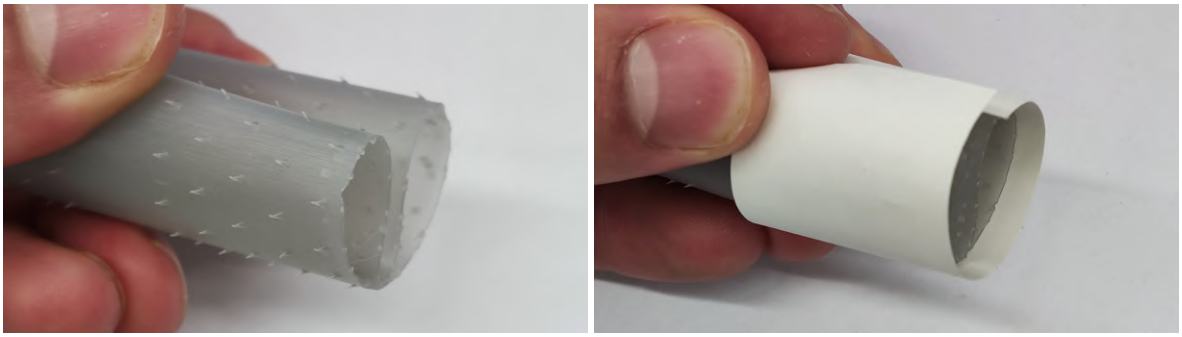
(a) Decreased diameter during insertion.

(b) First expansion of stent inside the colon.

(c) Fully expanded stent in a colon.

(d) Stent forced flat to show flexibility of the stent inside a colon.

Figure 7.5: Final design tested inside a colon.



(a)

(b)

Figure 7.6: Barb protection for insertion of the stent.

8

Validation

The new prototype stent should fulfil the design requirements as set in Chapter 6. Therefore, this chapter describes how and if the requirements were met.

8.1. Validation of design requirements

Table 8.1 gives the design requirements for the new prototype stent, and if the requirement was met or not. Green indicates that the requirement was met and yellow indicates that the requirement was not yet met or more research should be performed.

Table 8.1: Validation of the design requirements, green is met, yellow is not yet fully met.

Fixation	Fixation method	Barbs	
	Barb height	1.5 mm	
	Barb diameter	1 mm	
	Barb distribution	3 barbs per cm^2	
	Barb angle	30 degrees	
	Barb direction	Opposite to direction of movement	
	Friction coefficient	Larger than 1.11	
Dimensions	General design	Circular and closed tube	
	Diameter	Expansion of colon = 50 - 60%	
	Wall-thickness	Smallest possible	
	Length	60 mm	
Material	Barbs	Strong material	
	Tube	Flexible material	
	Safety	Not influence tissue healing	
	Temperature	Resist 43° C	
Delivery method	Insertion and extraction method	Reduced diameter	
	Tissue damage	No tissue damage during insertion and retraction	
	Barbs protection	No damage during insertion and extraction	
Performance	Stent migration	No stent migration	
	Intestinal blockage	Decreased intestinal blockage	
	Life span in-vivo	At least 14 days	
	Tissue healing	Not hinder tissue healing	
	Anastomotic leakage	Cause less anastomotic leakage vs. no stent	

8.2. Elaboration on the validation

Each of the design requirements is further elaborated in this section. It mentions if and how each requirement was met per category, or what should still be researched to meet the requirement.

8.2.1. Fixation

Fixation method

The prototype stent used outward pointing barbs as fixation method. Therefore, the design requirement was met.

Barb parameters

The dimensions of the barbs on the prototype fulfilled the requirements of the barb dimensions. The requirements regarding the height, diameter, distribution, angle, and direction of the barbs were all met.

Friction coefficient

The friction coefficient of the prototype stent was tested during experiments in Chapter 3. The measured mean friction coefficient was 2.01, which was larger than the 1.11 of the ProGrip, and larger than the 0.775 of the old prototype. Therefore, this design requirement was met.

8.2.2. Dimensions

General design

The prototype had a tubular structure in an expanded state and forms a rigid body to keep the colon opened. The prototype formed a closed structure without holes. Therefore, this design requirement was met.

Diameter

An expansion of the colon with 50 - 60% caused by the stent, was advised based on experiments performed in Chapter 3. To accomplish this requirement, multiple stents with different diameters should be present during a surgery. Just as in the experiment, the surgeon should measure the initial diameter of the colon, calculate the stent diameter necessary to accomplish 50 - 60% expansion, and choose that particular diameter. Using this method, the design requirement would be met.

Wall-thickness

The prototype stent had a thickness of 0.3 mm, as opposed to 12 mm with the old stent design with balloons. This meant that the frontal contact surface was reduced from approximately 682 mm^2 for the old prototype to 37.4 mm^2 for the new prototype with a 40 mm diameter, which was a reduction of more than 18 times. A fillet was added, thus an even smaller contact surface was achieved. This should decrease the chance of intestinal blockage. Therefore, this design requirement was met.

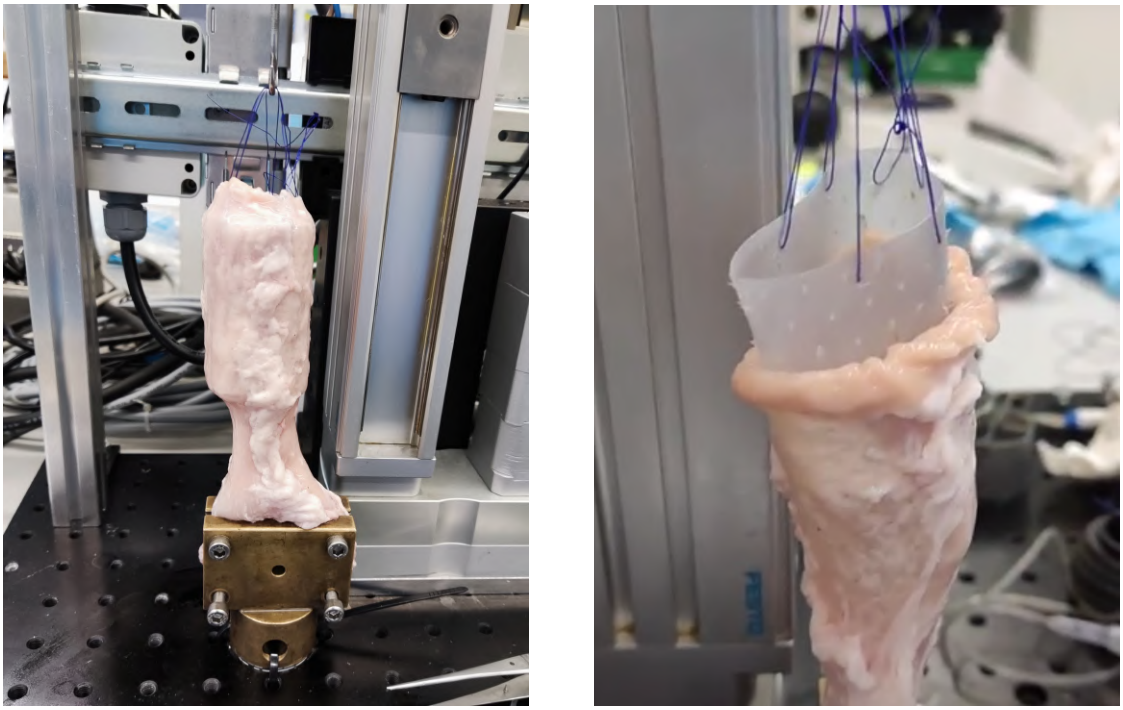
Length

The length of the prototype was kept constant at 60 mm, so the design requirement was met.

8.2.3. Materials

Barbs

The print resolution of the material used was the same as in the barbs printed in Chapter 3. This should have enabled barbs with equally sharp tips. Furthermore, the material of the prototype stent should create barbs strong enough to not break when forced out of a colon. To prove this, two tests were executed with colon specimens to test the stiffness of the stent in expanded state. The test setup was the same as used for Experiment 3 as described in Section 3.3 and is shown in Fig. 8.1. The colon was clamped and the stent was inserted inside the colon. At the top of the stent, suture thread was stitched to the stent and connected to the hook of the linear stage. The test in which the stent was pulled out of the colon by the motor in the linear stage was started. After the test, the barbs of the stent were visually checked for damage. No damage was observed after this test, so it was concluded that the barbs were strong enough and would not fail inside the colon. Therefore, this design requirement was met. It should be noted that the suture thread cut through the stent and left a crack. This did however not influence the results to test barb strength.



(a) Begin of the test.

(b) End of test with stent outside of the colon.

Figure 8.1: Experiment to test barb strength.

Tube
The stent was flexible to decrease the diameter for insertion and extraction. A prototype print, with a diameter of 34 mm in expanded state, could be decreased to a diameter of 22 mm. This meant a reduction in diameter of 35.3%. On the other hand, in an expanded state, the stent was stiff to keep the lumen of the colon opened to facilitate passage of fecal matter, as tested in Section 7.5. Therefore, this design requirement was met.

Safety
Biocompatibility of the material used for the stent was not ensured. However, it was ensured that for animal subjects 3D printed parts were allowed. Besides, colonic 3D printed stent have been tested in the past [60]. To test the influence on tissue healing and toxicity of the material used for the prototype, a cell culture assay could be performed, in addition to other more holistic methods.

Temperature
The material of the stent should withstand a temperature of 43° C without changing significantly in terms of strength and stiffness. A tensile test was performed with parts of the stent at room temperature and with heated parts. This was performed with an adjusted setup as used in the experiments described in Chapter 3. Unfortunately, the test results were not useful because the stent parts would cool down while being clamped in the experimental setup. Therefore, more research is needed on the performance of the used material under heated conditions.

8.2.4. Delivery method

Insertion and extraction method
Insertion and extraction was achieved by decreasing the diameter of the stent. As described earlier, a diameter reduction of 35.3% can be achieved. The stent could be decreased in diameter again when inside a colon, thus facilitating removal of the stent. Therefore, this design requirement was met.

Tissue damage
No tissue damage should occur during insertion of the stent. The reduced diameter should enable that the colon does not have to be expanded too much. A protective sheet should be used during the

insertion to protect the barbs from causing damage. Such a silicon sheet was successfully used in a previous in-vivo experiment, therefore this requirement should be met with this method.

Barbs protection
The silicon sheet should also protect the barbs from any collateral damage during insertion. The barbs of the stent will not be damaged by the silicon sheet, thus the requirement was met.

8.2.5. Performance

Stent migration
No in-vivo experiment with the redesigned stent could be performed at the end of this thesis. Therefore, this requirement unfortunately was not met. However, if new in-vivo experiments were to be executed, the stent should migrate in less than 75% of the cases. This very low number would mean an improvement compared to the old stent design, but obviously a migration rate close to 0% should be achieved to achieve a proof of principle for the stent. It should be noted that the stent design presented in this thesis improved friction, when looking at the friction coefficients of the old prototype and new prototype with barbs. Besides, the frontal contact surface at the proximal end was minimized and an optimal diameter was determined. These three improvements should in theory cause less stent migration, but no evidence could be given at this point.

Validation experiment
To quantify the improvement in stent fixation force that was made compared to the old prototype, an experiment was set up. In this experiment the old and new prototype would be placed in a colon specimen and pulled out, as described in section 8.2.3 and shown in Fig. 8.1. The maximum force needed to move the old and new prototype out of the colon was measured. However, the new prototype failed after two tests due to the suture thread that caused the stent to break. Therefore, the new prototype stent was not usable anymore, and the results should be interpreted with care. The old stent design that was used, was a half stent that was left over from an old in-vivo experiment. Therefore, the maximum force needed to extract the old prototypes were doubled. In total, six tests were performed, four with the old prototype and two with the new prototype. The results of this experiment are shown in Fig. 8.2.

The results showed that more force was needed to move the new prototype compared to the old prototype. The mean force for the old stent was 2.93 N and 14.0 N for the new prototype. The expansion rates of the colon for the old prototype were 92.5% (two tests), 49.2% and 38.8%, and for the new prototype 52.6% and 57.1%.

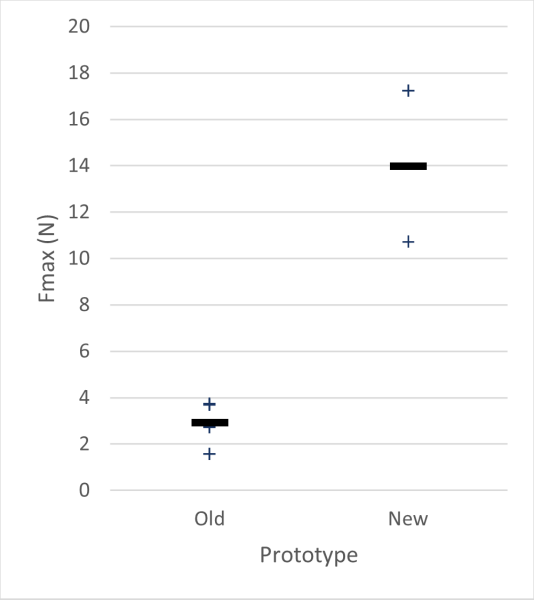


Figure 8.2: Results of validation tests, with black line representing the mean.

The tests clearly showed that the new prototype generated more friction with the colon than the old prototype. However, the number of tests were very limited, especially for the new prototype with only two tests. The old prototype was tested with a half stent, which influenced the results. During the tests with the new prototype, the suture thread ruptured the stent, which influenced the results and caused variability in the force measurements. Although, it was probable that the maximum force to move the stent was not influenced, it might have given inaccuracies in the results. To conclude, these results clearly showed the potential of the new prototype in terms of stent fixation compared to the old prototype.

As a result of the inaccuracies and the limited number of tests, new tests should be executed. A new prototype stent was designed that was suitable for this experiment. As in Experiment 3, a loop was added to two crossbars inside the stent, see Fig. 8.3. The downside of these crossbars was that it could complicate diameter reduction for easy insertion of the stent. Compared to Experiment 3, two stents with larger diameters of 38 mm and 40 mm were added. This was to ensure that for every colon segment tested, an optimal expansion of 50 - 60% could be achieved. For the old prototype, a whole stent should be used, instead of a half stent in the partially failed tests. The old prototype should be connected to the force sensor of the experimental setup via suture thread. The previous tests confirmed that the tube of the old prototype would not rupture due to the suture thread. The outcome of this experiment would be the maximum force necessary to extract the new prototype stent out of the colon versus the old prototype.

It should be noted that this experiment did not incorporate the effect that the minimal contact surface had on intestinal blockage, and thus on stent migration. Furthermore, in this experiment the stent was pulled out of the colon, whereas in an in-vivo environment, the forces would push the stent outwards. This was therefore a simplification of the real situation.

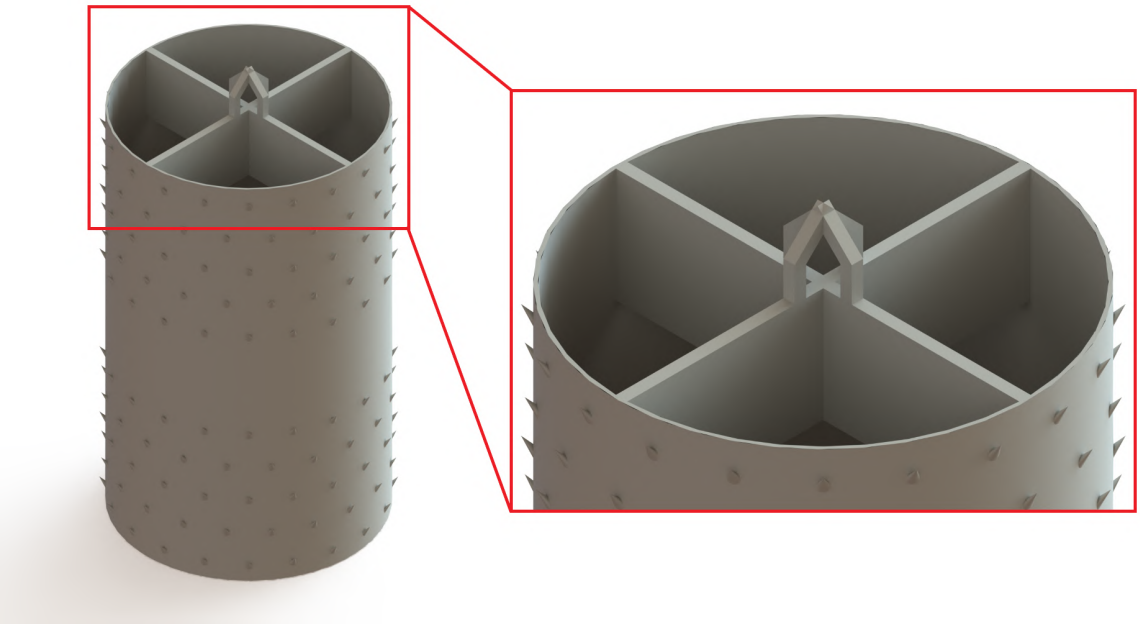


Figure 8.3: New prototype stent with a loop for new experiment.

Intestinal blockage

New in-vivo experiments should determine if the new prototype will cause less intestinal blockage. Passage of stool should be closely watched during the experiment and the presence of feces around the stent could be observed after termination of the pig. The reduction of the frontal contact surface of more than 18 times should in theory cause less intestinal blockage.

Life span in-vivo
The life span of the new prototype should be determined during new in-vivo experiments. Another method would be to mimic the environment of the pig's colon, and test if the material degrades within fourteen days.

Tissue healing
No barbs were placed in the middle of the prototype, to reduce the negative influence on the healing process. On the other hand, a higher tension on an anastomosis increased the chance of anastomotic leakage [15]. The new prototype did not include a decreased diameter in the middle of the stent, like the old design. This would increase the tension on the anastomosis, thus increasing the chance of anastomotic leakage. However, the expansion was advised to be limited to 50 - 60%, to keep the tension at an acceptable level. In-vivo experiments should determine if the new prototype influences the tissue healing.

Anastomotic leakage
Anastomotic leakage should be determined in new in-vivo experiments. When the prototype is inserted, no anastomotic leakage should occur.

9 Discussion

Anastomotic leakage remains one of the most feared complications after a colon resection. To prevent this complication from occurring after a surgery, a novel design of a colorectal stent to cover an anastomosis was presented. Such a stent should prevent fecal matter from flowing into the abdominal cavity at the anastomotic site in case of disruption of the anastomosis. Stent migration and intestinal blockage proved to be the two main problems of a previously designed stent at the department of Surgery at the Erasmus MC. Therefore, this thesis focused on improving fixation and decreasing the occurrence of intestinal blockage. Based on literature and previous experiments, the possibility to fixate a stent with barbs was explored. Three experiments were executed in order to find the optimal barb design and diameter of the stent. Barbs with a height of 1.5 mm, 1.0 mm diameter and angle of 30° that were distributed at 3 barbs per cm^2 proved to generate the most friction with colonic tissue. The last experiment concluded that the diameter of the stent should expand the colon with 50 - 60%, to create the most friction, whilst still facilitating healing of the anastomosis by putting limited tension on the anastomosis. To decrease intestinal blockage, the contact surface of the stent should be minimized. This minimizes the force that feces exerts on the stent and facilitates passage of fecal matter through the lumen of the stent. Techniques to safely insert a stent with barbs were discovered by means of a patent search. Decreasing the diameter of the stent and covering the barbs with a tubular structure were found as the best options. All these takeaways led to a list of requirements for a new stent prototype. This prototype was designed, 3D printed and validated concerning the requirements.

9.1. Scientific relevance

The Literature Study that was executed preliminary to this thesis concluded that intestinal stent fixation by means of barbs should be investigated. Only three articles were found that described the use of barbs to prevent stent migration, in which migration rates of 0% and 25% were reported [19, 20, 21]. Two of these studies were executed with stents with only two barbs and one was a rat esophagus model. This showed the potential of barbs for stent fixation in the colon, which was not found in literature. Therefore, one of the topics this thesis researched concerned colorectal stent fixation with barbs. This was researched in a scientific, structured manner using a relevant model.

This thesis is only a first step in order to come to a device that can protect colorectal anastomoses. As mentioned earlier, colon resections are mostly performed on patients suffering from colorectal cancer. Worldwide, up to two million new cases of colorectal cancer are reported [1]. An anastomotic leakage occurred in up to 11% of colon resections [5]. The mortality rate of patients with an anastomotic leakage ranged from 1.7% - 16.4% [6, 7]. If such a stent could reduce the occurrence of anastomotic leaks, the number of patients that would benefit are enormous. Reducing these anastomotic leakages could in the end cause shorter hospital stay, faster recovery and reduced healthcare costs. Therefore, there is room for improvement, which could be accomplished by covering anastomoses with a stent.

In this thesis, a prototype stent was designed and printed. The stent showed the potential of preventing stent migration and reducing intestinal blockage. The produced stent could serve as evidence to show the potential of stents to prevent complications after colorectal resections.

9.2. Limitations

Several limitations on the research in this thesis and about the new stent design should be mentioned. Firstly, regarding the experiments executed to test the friction of barbs. These experiments were executed with colon specimens obtained from the slaughterhouse. These specimens remain different from living tissue, although the tests were executed shortly after termination of the animals. The complex structure of the colon and the variability between the different colon specimens remained difficult factors to account for. Furthermore, the experiments were executed with colon specimens on a flat surface, which was a simplification of the real environment a colorectal stent would be situated in.

Secondly, the research regarding intestinal blockage was limited and partially based on assumptions. It was assumed that intestinal blockage was mainly caused by fecal matter accumulating at the proximal end of the stent. However, other factors could play a role in this. The length of the stent was not altered relative to the old design. A longer stent would have more outside contact surface, which could increase the force needed to expel the stent. However, this also means more contact surface on the inside, where the movement of feces creates a bigger expulsion force. The promotion of peristaltic movements inside the stent could help decrease intestinal blockage. This could be achieved by a flexible stent that moves with the peristaltic movements. However, this would be complicated to incorporate in the stent, as a rigid tube was desired to increase the radial force and keep the lumen of the colon fully opened.

Thirdly, the ex-vivo experiment to test the force necessary to move the new prototype out of a colon segment had inaccuracies. This could have validated the new prototype based on fixation force, compared to the old prototype. The results gave very promising results, which implicated that an improvement in fixation compared to the old prototype was achieved. In this experiment, the new prototype was tested in an intact colon segment, instead of on a flat surface. This incorporated the elasticity of the colon that would increase the fixation due to the barbs. Due to the inaccuracies and the fact that a half stent was used for the old prototype, no conclusion can be drawn on the quantitative improvement of the fixation of the stent. The results from a new and final ex-vivo experiment should be incorporated in the design process and updates for potential further clinical developments of the stent, in accordance with the Medical Device Regulation.

At last, the absence of in-vivo experiments meant that several requirements were not yet validated. Foremost, if stent migration and intestinal blockage would occur was not tested. Besides, the life span of the stent inside a pig's colon and the influence the barbs would have on the healing process were not validated. A small migration of the stent would cause the barbs to exert a force on the anastomotic line, thereby increasing the tension on the anastomosis. This could interfere with the healing process and in the end increase the chance of anastomotic leakage. Possible local damage at the site of the anastomosis caused by barbs were disadvantages of the use of barbs in general. It should however be noted that no total perforation of the colon was observed during the experiments. Furthermore, in-vivo tests could verify if feces would accumulate around the outside of the stent, as was seen during in-vivo tests with the old prototype. Additionally, the material used for the stent could be tested for influencing the healing process of the anastomosis.

9.3. Future research and recommendations

A new ex-vivo experiment to test the fixation force of the new prototype compared to the old prototype should be performed to validate the anti-migration properties of the new prototype. However, this experiment would not incorporate several factors that occur in an in-vivo environment.

Therefore, future research on the stent should involve in-vivo experiments in pigs. First, it should be validated if the friction caused by the barbs is sufficient to reduce or eliminate stent migration. Secondly, intestinal blockage should be reduced, such that feces does not accumulate at the proximal end of the stent. Thirdly, the healing process should not be disturbed by the presence of the stent and its barbs. This includes verifying if perforation or mechanical damage to the colon occurred. At last, it should be verified if no feces accumulated around the outside of the stent, as this occurred with the old prototype.

If the prototype stent shows promising results, the research should continue on improving the stent and making it feasible towards clinical use of the stent. Other aspects that could improve the stent are for example the length of the stent and other materials or printers to manufacture the stent.

On the other hand, if the results of in-vivo experiments show no improvements regarding stent migration and intestinal blockage, placement of a stent in the colon should be reconsidered. This could imply that covering an anastomosis with a stent is not a viable option and other ways should be sought to reduce anastomotic leakage in the colon.

10

Conclusion

The goal of this thesis was to create an improved colorectal stent to cover an anastomosis. This stent should reduce the chance of anastomotic leakage, which remains one of the major complications associated with colon resections. A first step in the design of such a stent was to ensure fixation of the stent in the colon. A non-migrating stent was not yet accomplished in previous experiments. Therefore, this thesis focused on the design of a fixation method with barbs without causing intestinal blockage.

This novel stent with barbs substantially increased friction with the colonic wall by a factor of more than two compared to the former prototype. The new stent should have a decreased effect on intestinal blockage due to a more than 18 times smaller frontal contact surface. The new stent can be folded inwards and the barbs can be covered with a protective sheet, to ensure safe insertion and retraction during surgery. The stent shows promising results, but new ex-vivo experiments should validate the fixation of the stent, and in-vivo experiments in pigs should verify if the stent does not migrate, does not cause intestinal blockade and most importantly protects the patient from the effects of anastomotic leakage.

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Appendix

A. Results noninvasive profiles

Shown here are the profiles tested preliminary to this thesis and the results.

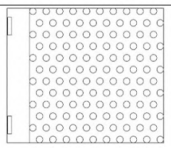
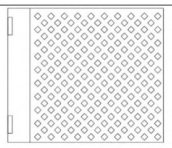
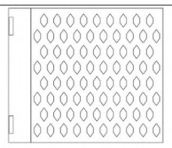
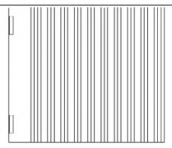
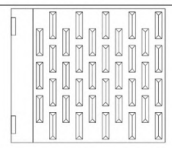
Small profiles	Cilinder	Diamond	Hexagon	Triangle	Triangle spaced
					
Code	Ci1	Di1	Hx1	Tg1	Tr1
Height [mm]	1	1	1	1	1
Length [mm]	1.5	1.5	3	30	3
Width [mm]	1.5	1.5	1.5	1.5	1.5
Spacing [mm]	1.5	1.5	1.5	1.5	1.5
Contact surface [mm^2]	212	204	228		

Figure A.1: Noninvasive small profiles.

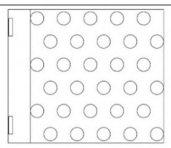
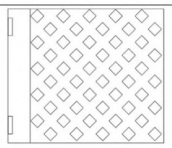
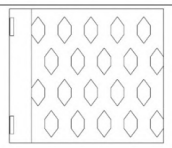
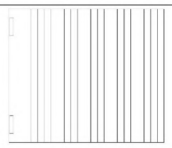
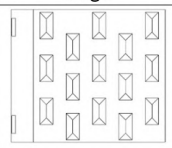
Large profiles	Cilinder large	Diamond large	Hexagon large	Triangle large	Triangle spaced large
					
Code	Ci2	Di2	Hx2	Tg2	Tr2
Height [mm]	2	2	2	2	2
Length [mm]	3	3	6	30	6
Width [mm]	3	3	3	3	3
Spacing [mm]	3	3	3	3	3
Contact surface [mm^2]	212	225	240	-	-

Figure A.2: Noninvasive large profiles.

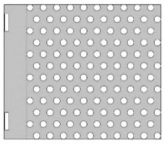
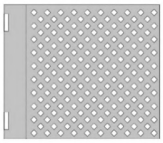
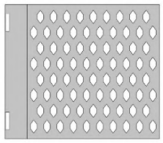
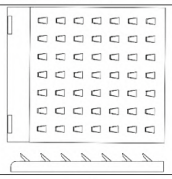
Other profiles	Control	Cilinder reversed	Diamond reversed	Hexagon reversed	Barbs
					
Code	Ctr	CiR	DiR	HxR	Brb
Height [mm]	-	1	1	1	1
Length [mm]	-	1.5	1.5	1.5	-
Width [mm]	-	1.5	1.5	1.5	-
Spacing [mm]	-	1.5	1.5	1.5	2
Contact surface [mm^2]	900	688	696	672	-

Figure A.3: Noninvasive other profiles.

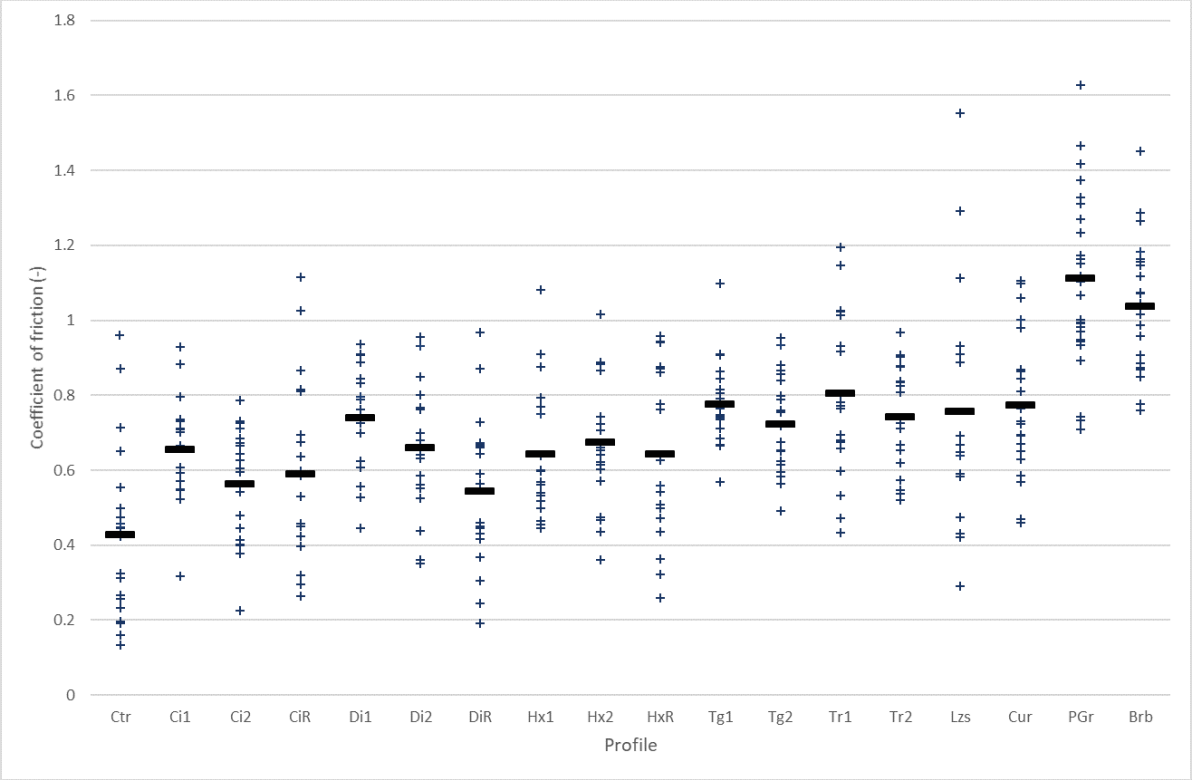


Figure A.4: Coefficient of friction results from prior experiments with noninvasive profiles, as shown in Fig. A.1, A.2, and A.3.

B. Literature study conclusion

This chapter is copied from the literature study executed in preparation for this thesis [18].

This chapter aims to answer the research question, *"How to fixate a stent inside the intestines to prevent stent migration?"*. Table B.1 provides an overview of the discussed migration rates of different techniques. Directly comparing the migration rates to answer what technique is most suitable would however be too short sighted and simplified. Therefore, conclusions on each technique are made with care and described after the table.

Main technique	Sub technique	Migration rate	Comments
Radial force	SMA	9% [61] 5.5% [11] 21.3% [11]	Covered and uncovered SEMSs Uncovered SEMSs Covered SEMSs
Expansion	Balloon	46% [62] 0% [63] 0% [64]	Most fixation by band Most fixation by band Most fixation by ring
	Flared ends	0% [65] 5.9%-6.2% [66] 11.1% [67]	Metal stent with uncovered flared ends Metal stents with bent-end and flared-end design Metal stent with uncovered flared end
	Bulges	-	-
Longitudinal force	Barbs	0% [19] 0% [20] 25% [21]	Uncovered metal stent with two barbs Rat esophagus model with stent with two barbs Half circle-shaped anchors
	Clamping	100% [68] 8% [69]	More about creating an anastomosis More about creating an anastomosis
	Pins	-	-
Air tightening	Vacuum	7,1% [70] 20% [71] 9,1% [72] 0% [73]	Colovac device, metal stent with vacuum chamber Colovac device Colovac+ device CG-100 device, for use in the esophagus. Maximum implantation of 18 days reported
(Biological) agents	Adhesives	-	Can be used as complementary technique to fixate stents
Tissue in-growth	-	-	Tissue in-growth reduces stent migration, larger sized cells and uncovered stents increase in-growth

Table B.1: Techniques and migration rates

Stents exerting a radial force, such as SEMSs, are extensively researched, but are still prone to stent migration, especially fully covered stents. However, partially covered stents with uncovered ends show promising results. Adding uncovered flared ends to metal stents has shown good results and could therefore be a good option for fixation of stents. For expandable stents with balloons no conclusion can be drawn, since it is assumed that most fixation of these stents described in literature is achieved by an external fixation ring or band. Such a ring or band is not an option if the stent is to be removed transanally after the colon has healed. This would require an extra surgery which is an extra burden to the patient. The addition of barbs in two small studies showed that this can increase the fixation of stents compared to no barbs. However, adding barbs can induce necrosis and damage to the intestines, so this should be further investigated. No examples of stents clamping two intestinal ends together were found in literature, even though compression anastomosis devices were described. This technique is not frequently used in clinical practice, therefore clamping is not considered to be a feasible technique. Stents that are secured in place by vacuum chambers are not used in practice yet and migration rates

show no superiority over other techniques. Besides, the suction tube and drain cause an unnecessary burden to the patient that should ideally be avoided. Biological agents such as adhesives and sealants can be used as an addition to other techniques to fixate stents, but the added value should also still be investigated. Tissue in-growth could help fixate stents, but an implantation time shorter than four weeks is assumed to be too short for this to happen.

In conclusion, partially covered metal stents with uncovered flared ends and the addition of barbs, could be an interesting fixation technique. This conclusion should however be interpreted with care. Besides, a combination with other techniques should not be omitted at this stage.

Research on intestinal damage caused by barbs is needed. Furthermore, the design of such a stent comprises many challenges and possibilities that need further research. One of such design challenges comprises insertion and removal of stents with outward pointing barbs, because of possible tissue damage. Especially removal of barbed stents is considered a challenge. Further research is needed to investigate the influence of design and dimensions on fixation strength. All in all, intestinal stent fixation is an interesting and complex subject with many challenges ahead.

C. Results Experiment 1

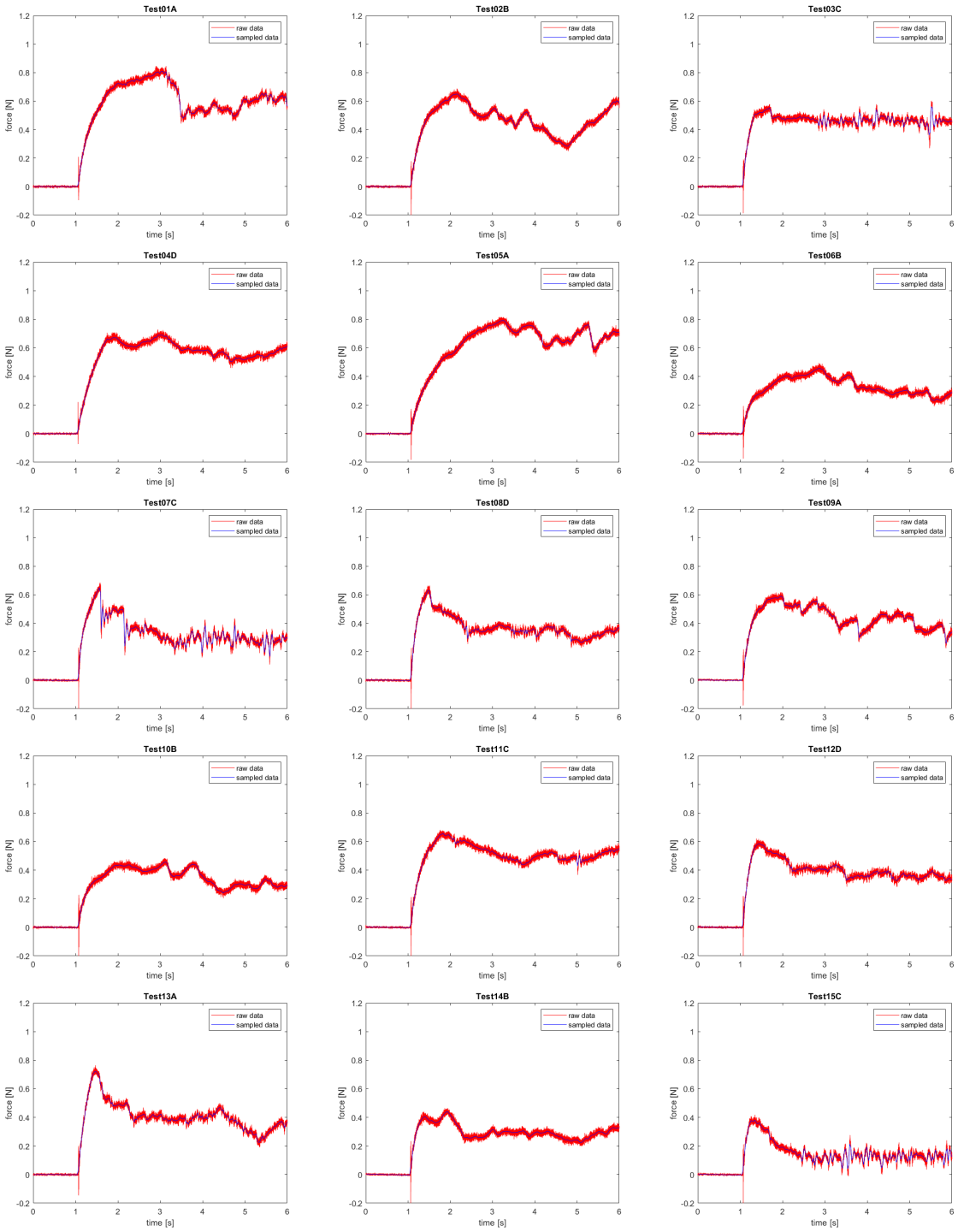


Figure C.5: Result graphs from Experiment 1: effect of orthogonal barb dimension and spacing.

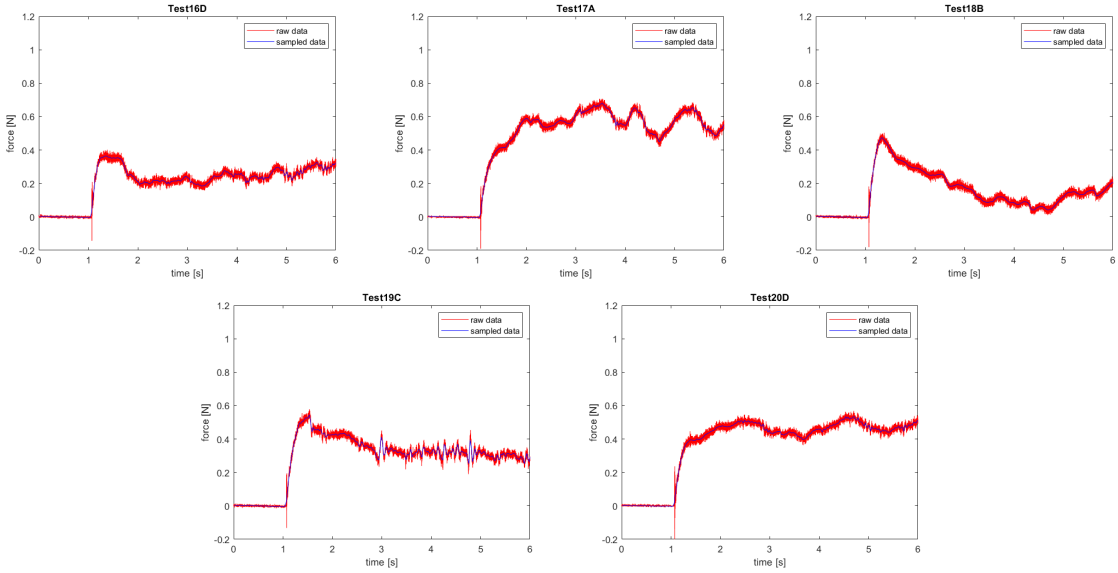


Figure C.5: Result graphs from Experiment 1 (cont.).

D. Results Experiment 2

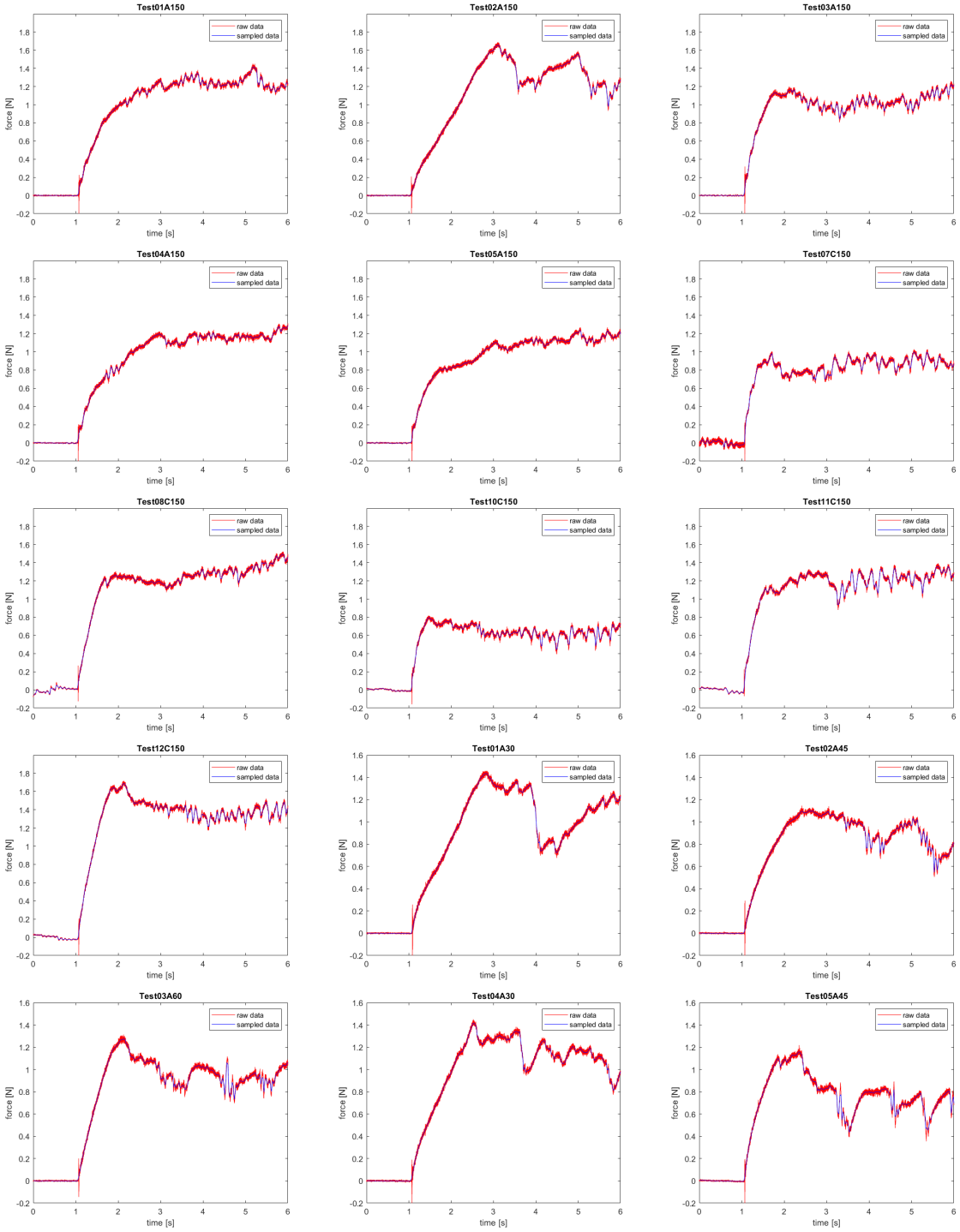


Figure D.6: Result graphs from Experiment 2: effect of barb angle and normal force.

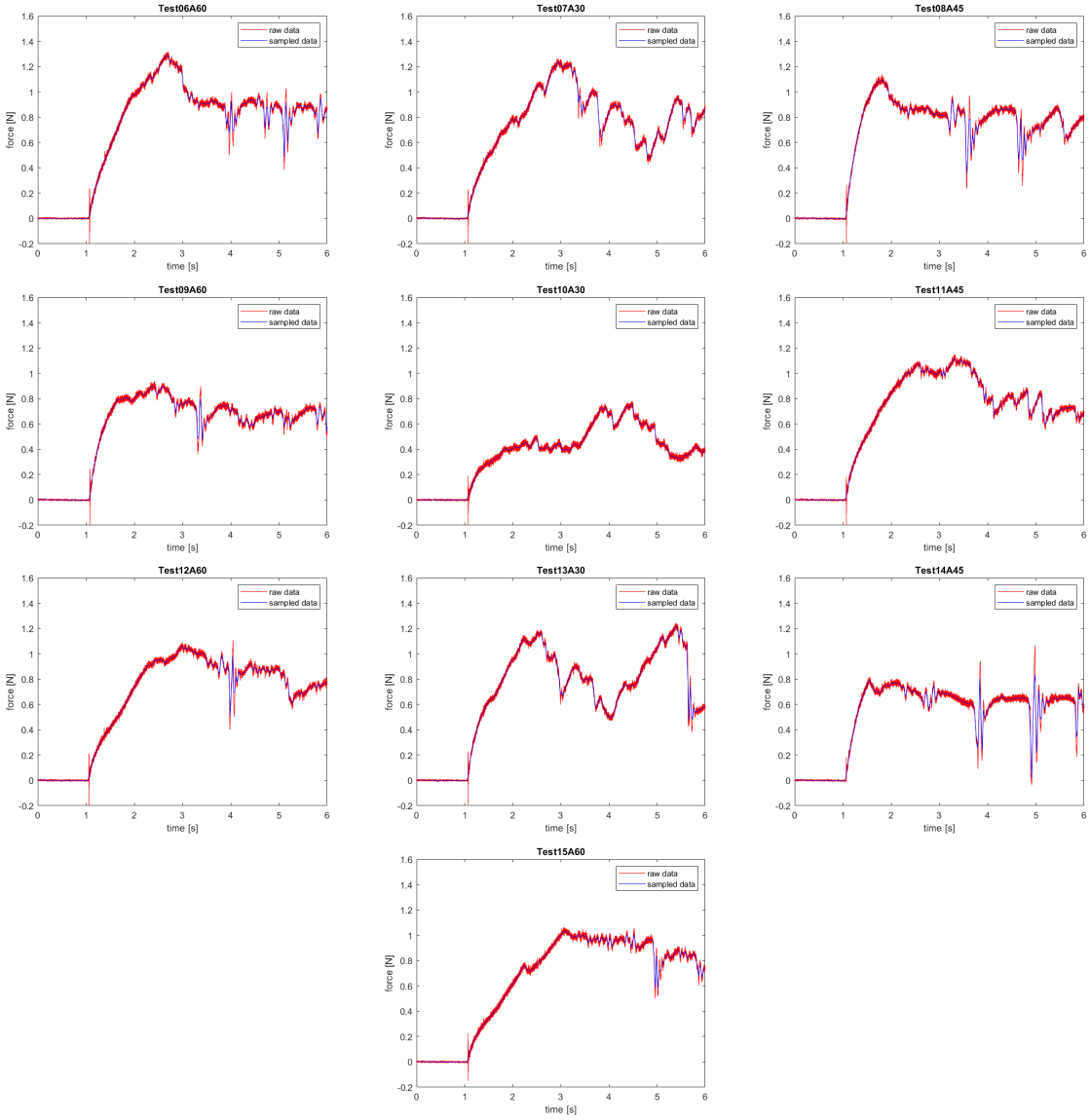


Figure D.6: Result graphs from Experiment 2 (cont.).

E. Results Experiment 3

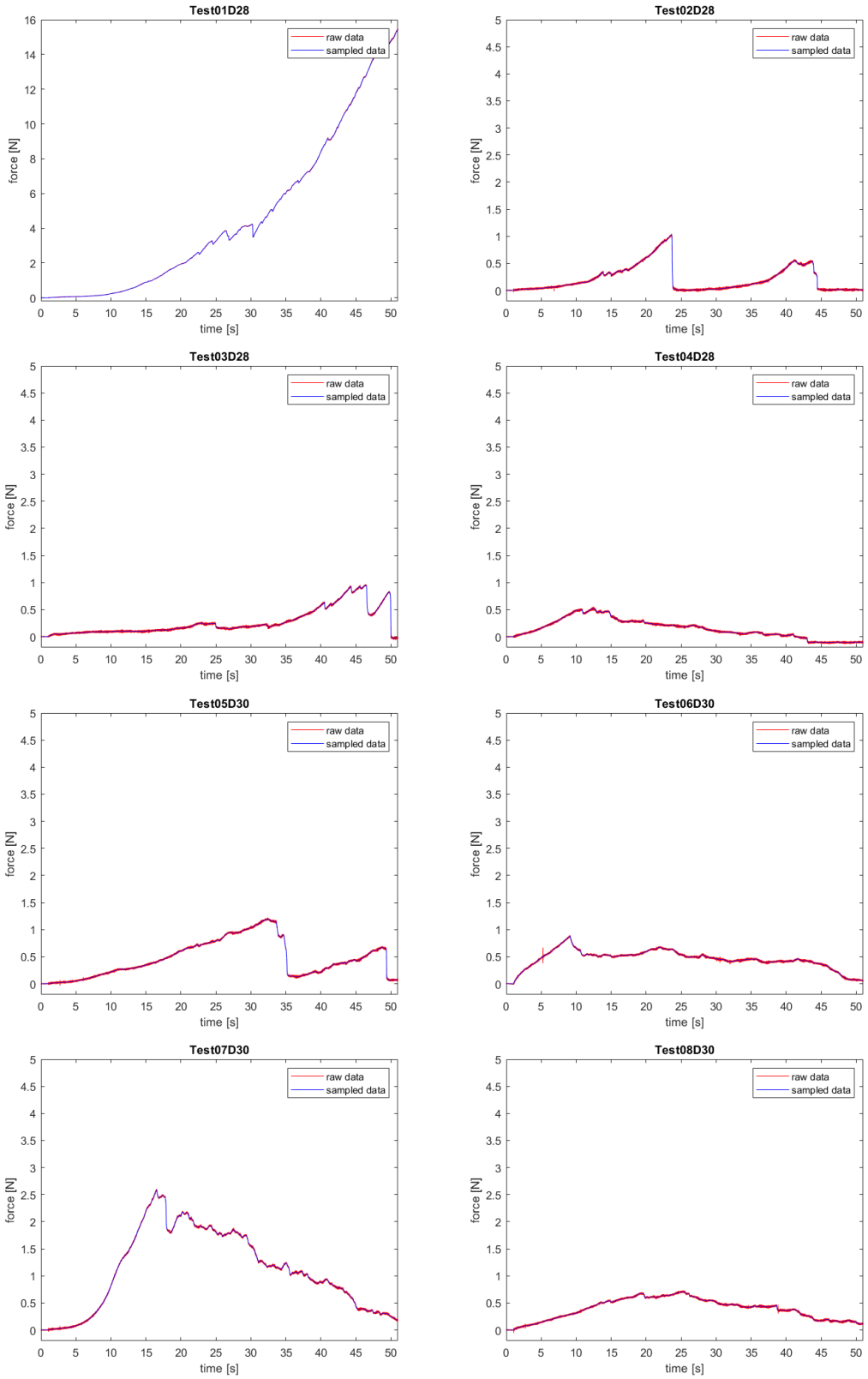


Figure E.7: Result graphs from Experiment 3: barbed short 3D stent in circular colon.

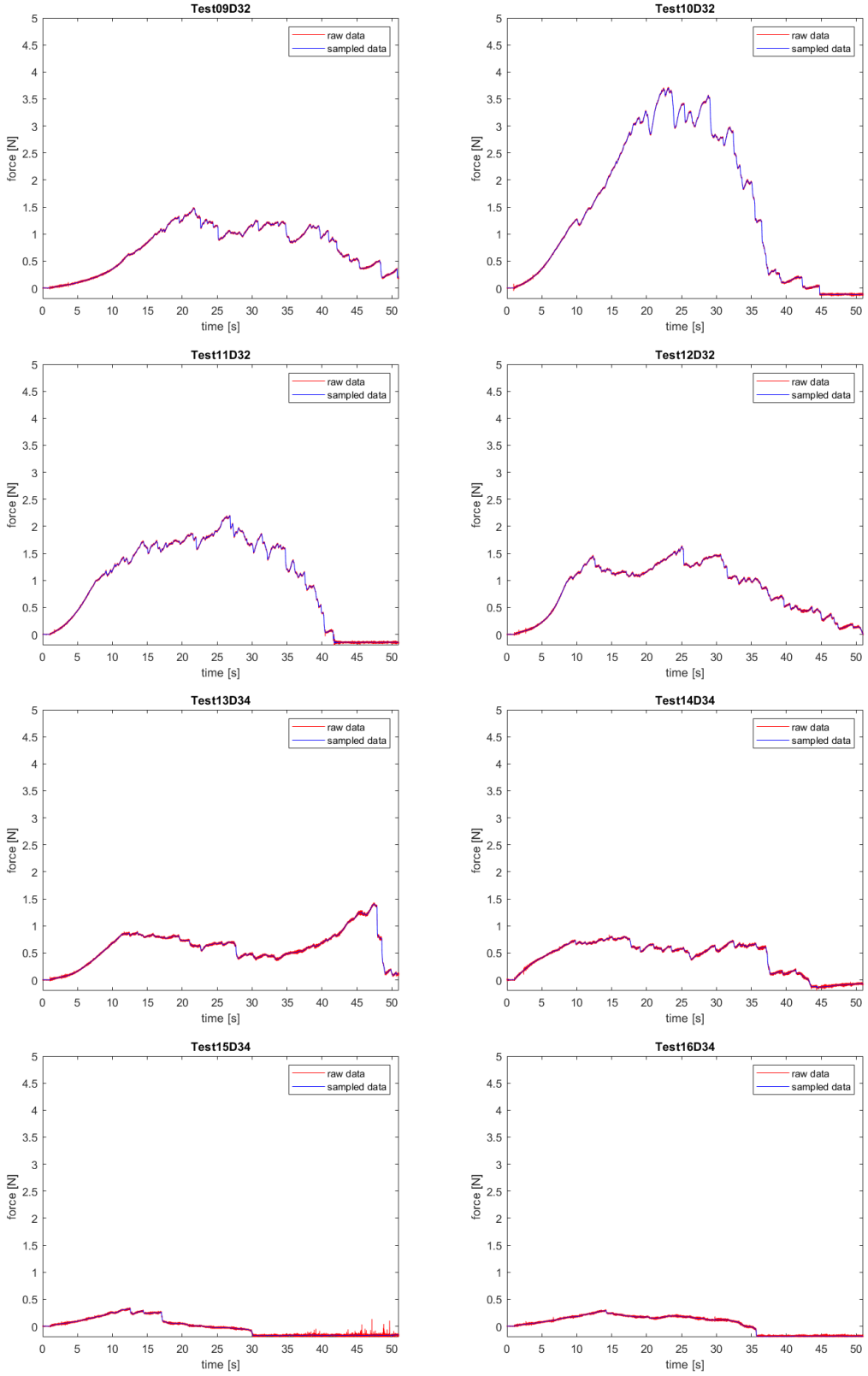


Figure E.7: Result graphs from Experiment 3 (cont.).

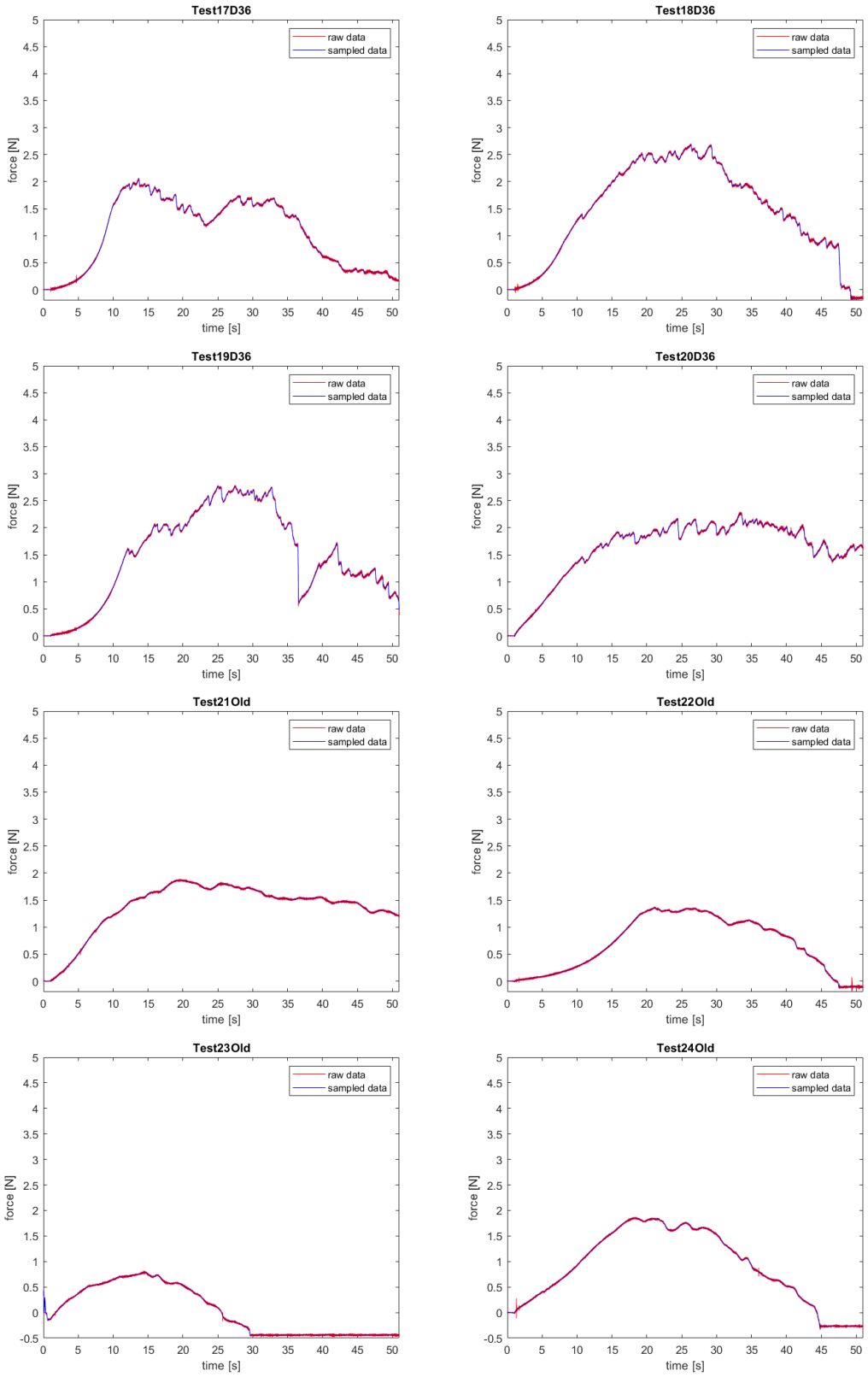


Figure E.7: Result graphs from Experiment 3 (cont.).

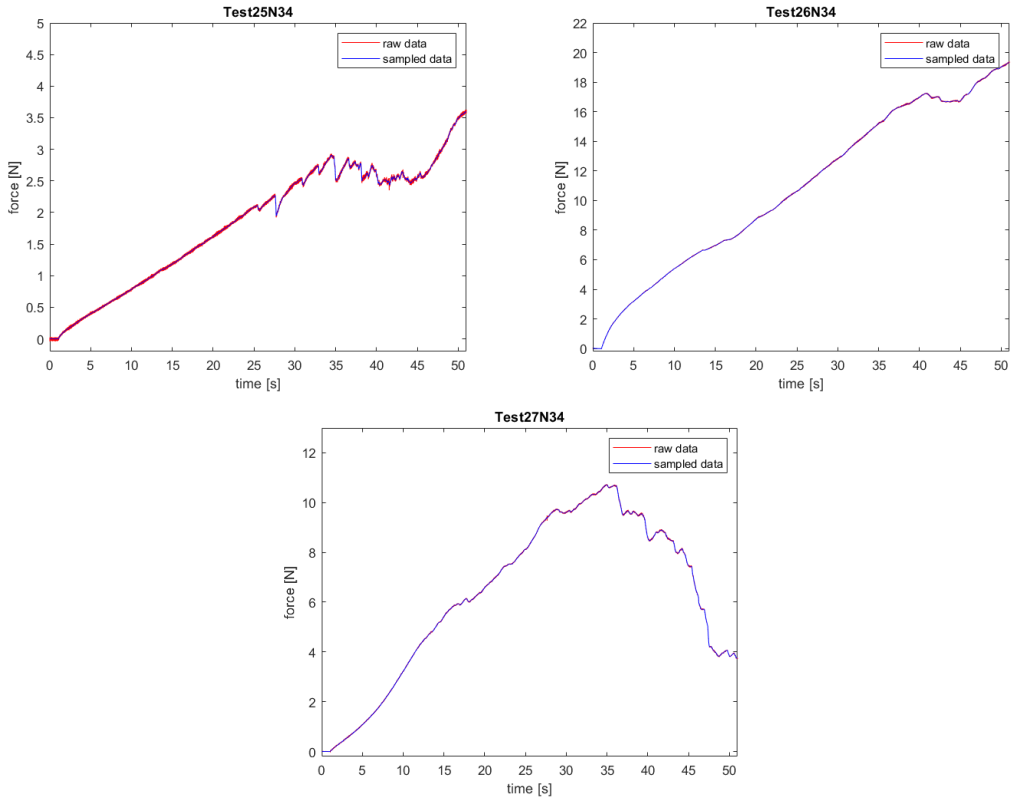


Figure E.7: Result graphs from Experiment 3 (cont.).

F. Results validation experiment

Full-size prototype new stent in circular colon.

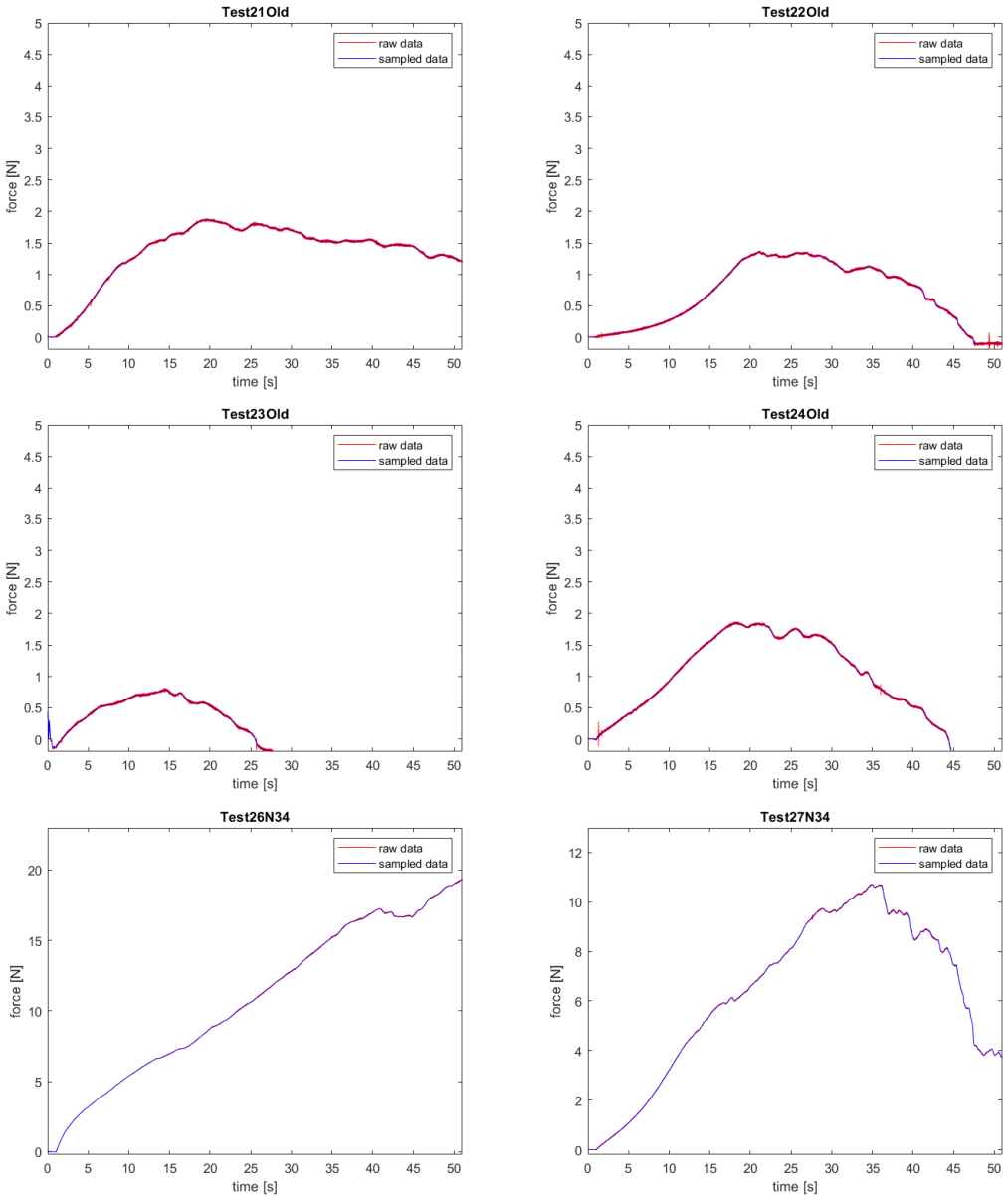


Figure F.8: Result graphs from the validation experiment.

G. Patent searches

Search 1:

(cl = ”A61B17/1114/low” OR cl = ”A61F2002/045/low”) AND cl = ”A61F2/82/low” AND (cl = ”A61F2220/-0016/low” OR cl = ”A61F2/848/low” OR cl = ”F16B13/08/low” OR ctxt = ”anchor*” OR ctxt = ”barb*” OR ctxt = ”spike*” OR ctxt = ”pin” OR ctxt = ”pins”)

Search 2:

(cl = ”A61B17/1114/low” OR cl = ”A61F2002/045/low”) AND (cl = ”A61F2220/0016/low” OR cl = ”A61F2/-848/low” OR cl = ”F16B13/08/low” OR ctxt = ”anchor*” OR ctxt = ”barb*” OR ctxt = ”spike*” OR ctxt = ”pin” OR ctxt = ”pins”) AND (cl = ”A61F2/95/low” OR cl = ”A61F2/82/low” OR ctxt = ”deploy*”)

Search 3:

cl = ”A61F2/04/low” AND (ctxt = ”INTESTIN*” OR ctxt = ”colon*”) AND ctxt = ”anchor*” AND ctxt = ”deploy*”

H. List of included patents

Table H.2: All patents included in the results of the patent search.

No	Title	Publication No	Category	Reference
1	Anastomosis device and method	WO0197695A1	1	[74]
2	Obesity treatment tools and methods	CA2448961A1	3	[39]
3	Surgical coupler for joining tubular and hollow organs	US6666873B1	4, 5	[43]
4	Methods of treatment using a bariatric sleeve	US2008103604A1	1	[32]
5	Removable stent-graft	US2010069916A1	3	[40]
6	Devices and methods for endolumenal gastrointestinal bypass	US2007198074A1	6	[47]
7	Method and apparatus for anchoring implants	US2006069400A1	1	[75]
8	A medical device suitable for treating reflux from a stomach to an oesophagus	CA2853623A1	3	[76]
9	Gastro-intestinal therapeutic device and method	WO2007059490A2	3	[37]
10	Fastening Device	US2009048665A1	1, 3	[77]
11	Medical apparatus and method of making the same	WO2008127552A2	1	[78]
12	Anchors with open heads	US2012179086A1	2	[34]
13	Anchors with Biodegradable Constraints	US2011276091A1	2	[35]
14	The system for introducing and positioning of a stent, in particular an intestinal stent, and a stent, in particular an intestinal stent	EP2620129A2	1	[79]
15	Stent	WO2014010679A1	3	[38]
16	Microanchors for anchoring devices to body tissues	JP2017047230A	1	[80]
17	Fistula treatment devices and methods	US2017020499A1	5	[44]
18	Devices and methods for delivering an anchored device	US2014207159A1	5	[81]
19	Intestinal barrier sleeve with expandable anchor section	EP3673867A1	5	[45]
20	Intralumenal Stent Graft Fixation	US10111741B2	5	[46]
21	Stents and stent deployment devices	US10420661B2	4	[82]
22	Degradable intestinal anchor	US2018333249A1	5	[41]
23	Stents for placement in an anatomical passageway and methods	US2017172767A1	1	[83]
24	Systems and related methods for tissue treatment	US2020000489A1	4	[42]
25	Stent including anti-migration capabilities	US2020197196A1	2	[36]
26	Anchor instrument	WO2020196336A1	1	[84]
27	Kirigami-inspired stents for sustained local delivery of therapeutics	US2021393422A1	5	[85]

Table H.3: Abbreviations of categories used in Table H.2.

Category No	Category
1	Catheter
2	Constraints
3	Forced through
4	Radially foldable
5	Folded barbs
6	Grasper

I. Intestinal blockage model

This is an overview of what was prepared for a model to simulate intestinal blockage and to improve a proximal end design of the stent.

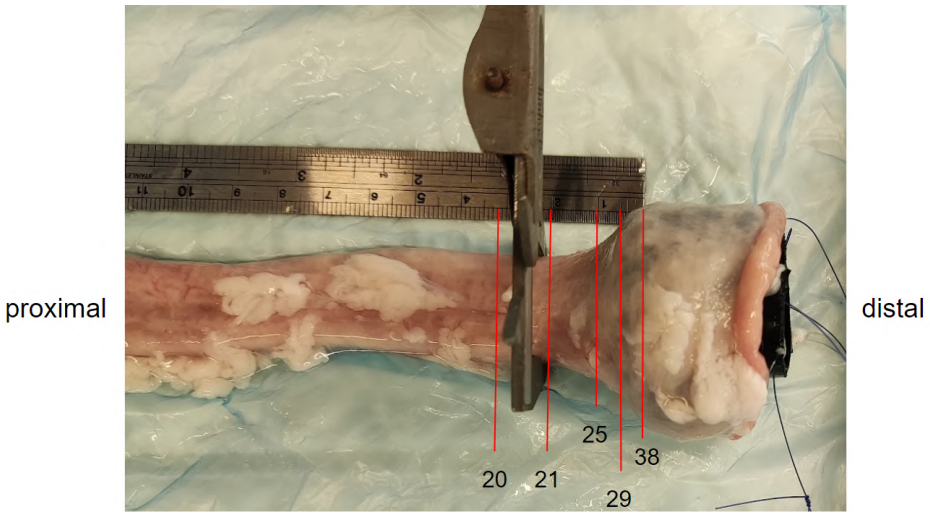


Figure I.9: Measurements of a stent in the colon.

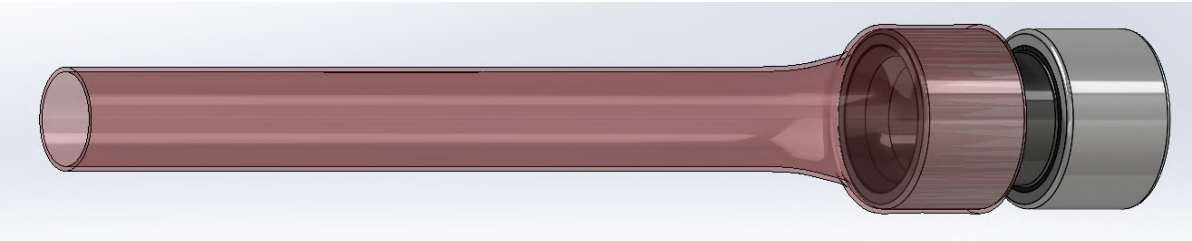


Figure I.10: Side view of the model designed in SolidWorks.

The following data would be used for the modelling of the feces:

- Viscosity: 0.50 Pa*s [86]
- Density: 886 - 1130 kg/m3 [87] [88]
- Quantity: 1000 g/day, (measured by animal facilities of the EMC for pig weighing 50kg)
- Velocity: 0,0263 mm/s
  - Velocity of passage through stent, calculation:
  - pi*r^2 = pi*12^2 = 452 mm^2 (24 mm diameter of stent)
  - 1.0 dm^3 = 1.000.000 mm^3 (feces quantity per day)
  - 1.000.000 mm^3 / 452 mm^2 = 2222 mm
  - 2222 mm / (24*60*60) s = 0.0263 mm/s