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Corresponding Author:

Ana Vidaurre, Centre for Biomaterials and Tissue Engineering (CBIT), Universitat Politècnica de València, Camino de Vera s/n, 46022, Valencia, Spain

Email: vidaurre@fis.upv.es

Article title: Analysis of the "Endoworm" prototype's ability to grip the bowel in in vitro and ex vivo models

Authors:

Javier Tobella[1], Vicente Pons-Beltrán[2], Alberto Santonja[3], Carlos Sánchez[4], Alberto J. Campillo-Fernández [1], Ana Vidaurre[1,5]

[1]Centre for Biomaterials and Tissue Engineering (CBIT), Universitat Politècnica de València, Camino de Vera s/n, 46022, Valencia, Spain

[2]Digestive Endoscopy Unit, Digestive Diseases Department, La Fe Polytechnic University Hospital, Valencia, Spain. Gastrointestinal Endoscopy Research Group, IIS Hospital La Fe, Valencia, Spain. Avda. Fernando Abril Martorell, n: 106, 46126 Valencia, Spain

[3]ETSID, Universitat Politècnica de València, Camino de Vera s/n, 46022, Valencia, Spain

[4]Department of Electronic Engineering, Universitat Politècnica de València, Camino de Vera s/n, 46022, Valencia, Spain

[5]Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Spain

Abstract.

Access to the small bowel by means an enteroscope is difficult, even using current devices as single balloon or double balloon enteroscopes. Exploration time and patient discomfort are the main drawbacks. The prototype "Endoworm" analyzed in this paper is based on a pneumatic translation system that, gripping the bowel, enables the endoscope to move forward while the bowel slides back over its most proximal part. The grip capacity is related to the pressure inside the balloon, which depends on the insufflate volume of air. Different materials were used as *in vitro* and *ex vivo* models: rigid polymethyl methacrylate (PMMA), flexible silicone, and polyester urethane (PU), and *ex vivo* pig small bowel. On measuring the pressure-volume relationship, we found that it depended on the elastic properties of the lumen and that the frictional force depended on the air pressure inside the balloons and the lumen's elastic properties. In the presence of a lubricant, the grip on the simulated intestinal lumens was drastically reduced, as was the influence of the lumen's properties. This paper focuses on the Endoworm's ability to grip the bowel, which is crucial to achieving effective endoscope forward advance and bowel folding.

Keywords

Enteroscopy, Small bowel, Medical control systems, Grip force measurement

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Introduction

There are more than 10 metres of digestive tract from the oesophagus to the rectum in which a multitude of different pathologies can occur. Bleeding, mucosal neoplastic lesions, and benign strictures of Crohn's disease in the small intestine, which currently require surgical treatment, are all good candidates for nonsurgical endoscopic therapies. Access to this gut in a minimally invasive way from the natural orifices (mouth and anus) has been the key to the diagnosis and treatment of this wide range of diseases, which were out of reach of push enteroscopy in the past.

The problems involved in exploring the small bowel were partially overcome by the introduction of capsule endoscopy in 2000,[1] and soon after by double balloon endoscopy.[2] Capsule endoscopy, used for diagnosis only, is a powerful tool in assessing the small bowel[3] and has the advantage of being non-aggressive to the patient.[4] Considerable efforts have been made to provide the endoscopic capsule with therapeutic capacity but so far none of the prototypes has gone beyond the clinical trials stage.

Besides, its detection yield is nearly equal to that that of other techniques, such as double-balloon endoscopy, which also offers therapeutic options.[5,6] These techniques are still being improved and new devices are now available such as single-balloon enteroscopy[7] and spiral enteroscopy,[8] which make diagnostic and therapeutic interventions possible.[9] According to recent publications in the literature, balloon-assisted devices and spiral enteroscopy techniques appear to have comparable diagnostic and therapeutic yield.[10,11,12] Small-bowel disorders can be managed non-surgically by these enteroscopic techniques, although each does have its own limitations: they either require considerable skill, long exploration times, anaesthetics, or involve a great deal of discomfort to the patient.

Different proposals have involved robotic locomotion systems,[13,14] some inspired by nature[15,16,17] and some by mechanical means.[18,19] Although some provide therapeutic capabilities, all are still at the experimental stage and have not been tested in clinical trials. From our point of view, they have the drawback of not allowing the doctor to get involved.

Considering the difficulties involved in gripping the bowel, the biggest challenge of mobile devices is to design an effective propelling mechanism. These difficulties include the bowel's viscoelastic properties[20,21,22] and its non-uniform diameter, but most of all its slippery surface due to the presence of intestinal mucosa.[23,19,24,25] De Simone and Luongo[26] studied a nonlinear model of a viscoelastic balloon compressed between two rigid plates concluding that, in the majority of the biomedical applications where the strain is not too high, the complex nonlinear constitutive models are unnecessary. Some work has been done on modelling the frictional force between the gastrointestinal tract and a capsule robot.[27, 28] Other researchers have focused on the influence of the capsule parameters on friction, such as its weight, shape, dimensions and surface area,[24] while the effects of the intestine's material properties have also been studied.[29,30] Woo et al. proposed a model which considered drag and friction forces using a thin-walled model and Stokes' drag equation.[31] Sliker and Rentschler developed an experimental platform to measure the performance of robotic wheels treads in a dynamic environment.[32]

In this context, our research group designed and developed a new device, known as the *Endoworm*, which enables the endoscope to advance through the intestinal lumen in a semi-automatic way, while folding the intestine over the most proximal part of the device during the exploration. The system can be fitted to a commercial enteroscope and consists of a pneumatic system controlled by an electronic device. It was conceived to combine robotic technology with the push-and-pull principle.[33,34] Although it was designed to achieve easier and faster explorations, certain problems related to its gripping capacity were found in its ability to advance. The aim of this work is to get a deeper knowledge of the different parameters that influence on this new prototype's gripping capacity. The influence of the different parameters was analyzed separately in a wide range of different situations during the evaluation of the prototype, carried out *in vitro* to avoid tests on live animals. The gripping power of the system was evaluated in different rigid and flexible simulated bowel cavities as well as in *ex vivo* bowel. The rigid cavity enabled us to evaluate its locomotive ability, while the flexible cavities represented more realistic models.

Materials and Methods

Endoworm's pneumatic translation system consists of two balloons and a bellows that automatically inflate and deflate. This locomotion concept is similar to that used in double balloon enteroscopy,[2] but in this case the movement is automatic. In a previous work,[34] it was described the prototype in detail. Briefly, an electronic microcontroller governs the pneumatic system. The cavities are inflated and deflated by means of a pressure pump, while a vacuum pump keeps a negative pressure, both connected to the cavities by a set of solenoid valves.
The cavity balloons were designed to grip the inner bowel wall and the bellows controls the advancing function (Figure 1a and 1b).
The materials for the cavities were selected to fulfil certain requirements; the balloons had to be able to expand radially, while the bellows had to be able to stretch axially by the action of the folds. Silicone was chosen as the cavity material due to its greater stretching capacity than polyurethane (elastic modulus ranging from 4 to 20 MPa; elongation 90%) and was considered the best alternative to the more allergenic latex. The selection of the materials was explained in detail in a previous work.[34] Briefly, the balloons were made of Silastic Q7-4720 (Dow Corning®, elastic modulus 0.4 MPa; elongation 1280%; data provided by the supplier, measured following ASTM D412 procedure) supplied in a two-component kit, equal parts of which must be thoroughly blended together prior to use. The elastomer was then thermally cured in a mould to obtain an uninflated balloon 25 mm in diameter with a 0.4 mm thick wall, and more than 40 mm when inflated (Figure 1 c). Following the same procedure, the less elastic silicone Silastic 7-4870 (elastic modulus 5.7 MPa; elongation 420%; data provided by the supplier, measured following ASTM D412 procedure) was used for the bellows. Both silicones are specially designed for use in medical devices, including those intended for implantation in humans for less than 30 days. The cavities and air pipes were mounted in rings designed to adapt the device to a conventional endoscope (Figure 1 b).

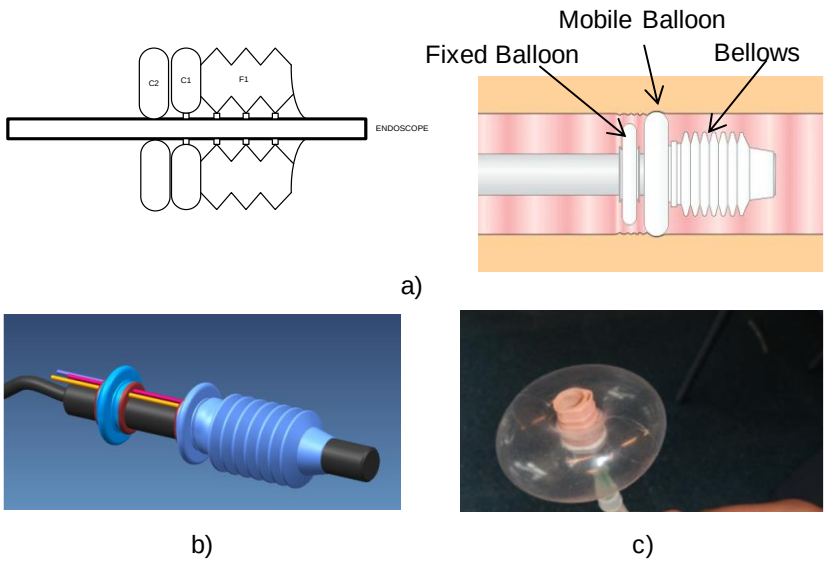

Figure 1. a) Scheme of bowel retraction during exploration; b) 3D image of the set of cavities adapted to a commercial endoscope; c) balloon cavity.

Pressure-volume measurement

Different air volumes were pumped manually into the balloons by means of a syringe. The pressure of the air inside the balloon was obtained under four conditions: with the balloon in air at atmospheric pressure, in a rigid poly methyl methacrylate PMMA tube (27.5 mm in diameter; 1 mm thick wall), inside a flexible silicone tube, (diameter 30 mm; 0.4 mm thick wall), flexible PU tube, (diameter 30 mm; 0.05 mm thick wall), and in *ex vivo* pig intestine (diameter 28 mm; 1 mm thick wall). The mechanical properties of the different type of tubes were as follows: PMMA, with a tensile modulus of 3000 MPa and strain at failure 4% (data provided by the supplier), with no significant deformation during the experiment. The Silastic Q7-4720 silicone tube (tensile modulus 0.4 MPa; strain at failure 1280%, as cited previously); the 0.4 mm thick wall suffer slight deformation during the experiment. The 30 mm diameter PU tube was adapted from CIV-Flex™ Transducer Cover from Ibersurgical S.L. (tensile modulus 13 MPa; 200% failure strain). *Ex vivo* pig intestine samples were kept hydrated during the whole test. The tensile modulus for axial specimens was 2.5 MPa while the transversal specimens had a lower tensile modulus of 0.9 MPa; failure strain was of the order of 30% for both, axial and transversal experiments. PU and ex vivo pig intestine mechanical properties were measured by means a Microtest tensile apparatus, maximum length 1000 mm, load cell 15 N, strain rate 1mm/min; n=5 replicates were measured for each experiment, and the average and the standard deviation were calculated.

Volumes of between 5 and 20 ml of air were measured and pumped into the balloons, by means of a syringe. The pressure in the cavities was measured by a 3-stage tailor-made system installed on the Endoworm control device: the first obtains and amplifies the analogue signal proportional to the air pressure; the second converts the analogue signal to a digital number, and the third gives the pressure value on the control system screen.

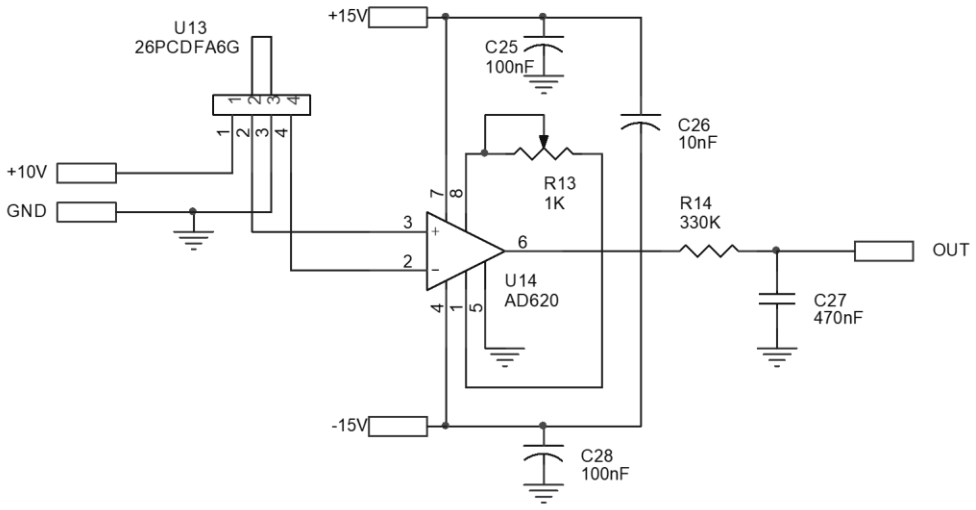

Figure 2. Scheme of the circuit used to measure pressure in the cavities.

The cavity was directly connected to a Honeywell 26PCDFA6G pressure sensor, which could measure a maximum pressure of 30 psi (206.84 kPa) with a sensitivity of 3.33 mV/psi (0.48 mV/kPa). The signal was amplified by means of an AD620 amplifier connected to the differential output. The gain of the amplifier was tuned to obtain an output voltage of 4 V for the maximum system pressure (150 kPa), which gave a gain of 55.55. The amplifier output was filtered by a first order passive low-pass filter (R = 330kOhm, C = 470nF), with a cut-off frequency of 1.026 Hz (Figure 2). The second stage was a PIC18F4550 8-bit microcontroller. Digitalization was by a 10-bit on-board analogue-to-digital converter. The reference voltage of the converter was 5 V for a resolution of 4.8 mV, which represents a pressure resolution of 0.18 kPa. The digital information (in kPa) is transmitted to the touch screen by the serial interface with an RS-232 serial protocol, which represents the third stage.

Grip Force

The grip force of the inflated balloon was evaluated by a tensile Adamel-Lhomargy DY34, maximum length 1000 mm, load cell 100N, and maximum velocity 1.67 mm/s. The four lumens described above were used to evaluate the grip force. Figure 3 shows the design of the experiment, in which the balloon was fixed to one of the clamps while the tube simulating the small bowel was fixed to the other clamp. An additional rigid conduit was needed to fix PU tube and the *ex vivo* small intestine. The experiment was performed with four different air volume values inside the balloon, ranging between 5 and 20 ml, measured by means of a syringe. In all cases the tensile force was applied to obtain a rate displacement of 0.83 mm/s. The force, time and displacement were recorded. The same experiment was conducted with and without Sulky® hydrosoluble lubricant (recommended by the medical team to simulate intestinal mucus). Five replicates were used for each test. The grip force depends on the friction between balloon and tube (or small intestine) and can be modelled assuming dry friction and therefore a proportional relationship between the normal force and the frictional force.[35] In general, three stages can be distinguished. When the pulley force is lower than the maximum friction force, the actual friction force equals the pulley force and the net force is null. The friction force reaches a maximum value just before the object starts to move; a static friction coefficient can be obtained as the pulley force divided by the frictional force at this point. Once the

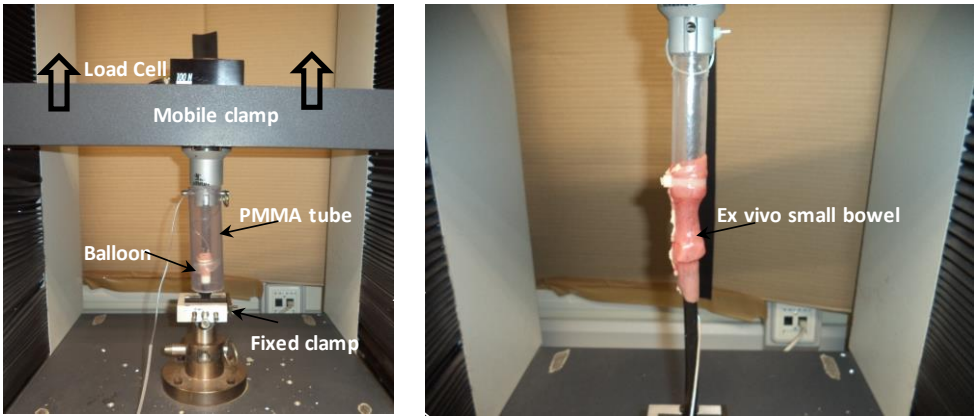

Figure 3. Experimental set-up used to measure the grip force when the balloon is inside a rigid tube (left) and *ex vivo* small intestine (right).

object moves, the frictional force diminishes and reaches a constant value; the kinetic friction coefficient can be obtained for this region.

Scanning Electron Microscopy (SEM)

To determine lumen surface roughness, SEM pictures of wall tubes were taken by JEOL JSM-6300 scanning electron microscope at 10 kV of acceleration voltage and 15 mm of working distance. The samples were previously sputter-coated with gold.

Results and Discussion

Pressure-volume measurements

The air volume pumped into the balloons is correlated with the pressure measurements, which in turn relates to the frictional force, which determines the gripping capacity of the system. It is worth noting that the frictional force is, in a first approximation, proportional to the normal force applied on the contact surface between the balloon and the intestine wall. This normal force depends on the air pressure inside the balloon and the contact surface area. In addition, these last depend on the air volume inside the balloon and also

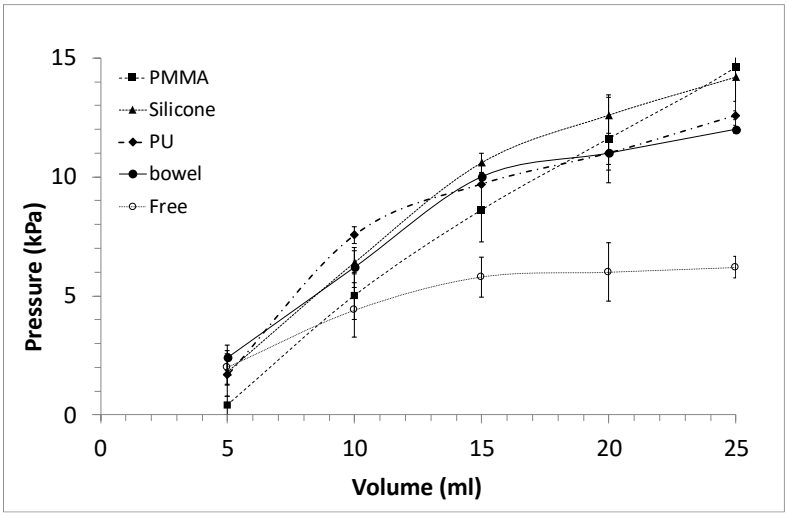

Figure 4. Pressure measured inside the balloon as a function of the volume of air in the balloon for different types of tube and "free in air". Lines have been drawn as a guide. The error bars represent the standard deviation (n = 5 replicates).

on the diameter of the intestine lumen and its elastic properties.
Figure 4, shows the pressure results as a function of the air volume in a balloon surrounded by air at atmospheric pressure (free in air) or in tubes. The maximum air pressure inside the balloon was 15 kPa, while in the current commercial double-balloon and single balloon endoscopes it is approximately 5.5 kPa. The balloon pump controllers have a safety mechanism that activates an alarm when the balloon pressure goes above 8.2 kPa for 5 s or longer.[36] It can be seen that a maximum value of around 6 kPa was obtained with the balloon in air at atmospheric pressure. Glozman *et al.*[37] and Müller *et al.*[38] observed similar behavior in spherical silicone balloons. However, when the balloon was inside a rigid PMMA tube the pressure-volume ratio was quite different. The balloon adapted its shape to the lumen and the pressure increased linearly due to the stiff tube wall. With less rigid tubes, as in the case of the artificial silicone or PU intestine, the curve initially rose linearly and then became less steep as pressure increased. The differences between the pressure inside the balloon when placed inside *ex vivo* pig intestine and when it was inside the PU tube were less than 10% for almost all the

volumes (except for 10 ml). It should be noted that the tendency of the *ex vivo* small bowel curve was quite similar to that of the balloon surrounded by air, which can be explained by the viscoelastic properties of the small bowel. This pressure-volume test is similar to that performed by De Simone and Luongo[26] who studied the behavior of cylindrical polymer balloons for biomedical applications squeezed between two rigid plates. They found that, if the material viscosity had a predominant effect, volume and the strain increased while pressure decreased. The higher pressure (due to the force exerted by the tube wall and rigid plates) is balanced by the increased volume of the part of the balloon not in contact with the tube wall. In the present study, a new variable was considered: the mechanical properties of the tube wall. Poon *et al.*,[17] in their design considerations, pointed out the strong influence of the mechanical characteristics of the wall on the pressure-volume relationship; they found similarities in the force sensor triggering time between the hard PVC tube and the stiffest areas of porcine intestines. Egorov *et al*.[21] performed a detailed study on the tensile properties of different human tissues; they paid special attention to the large bowel, measuring cadaveric and surgically removed specimens at different strain rates. They found that the curves obtained for specimens tested at different strain rates (from 0.04λ to 20λ, $\lambda=l/l_0$) were qualitatively and quantitatively very similar. In all cases, the stress strain curves of small bowel specimens showed an initial plateau stage after which there was a sharp increase in stress. In the mechanical testing of transversal specimens, these authors found that stress was very low

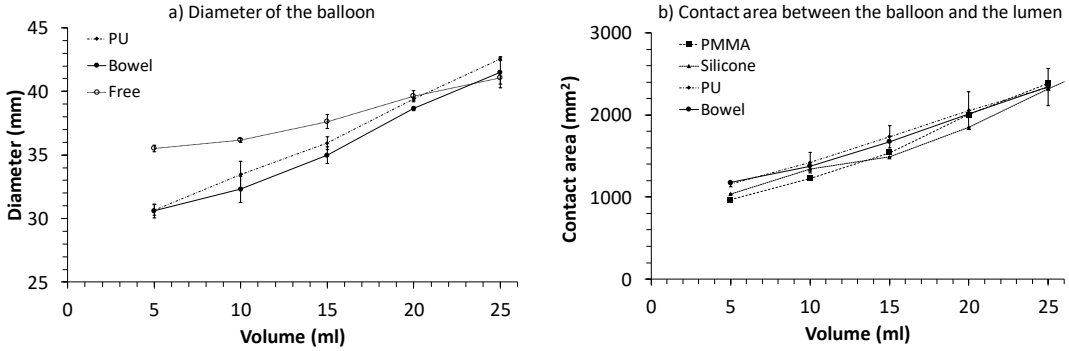

Figure 5. a) Diameter of the balloon, and b) Contact area between the balloon and the tube, as a function of the volume of air in the balloon for different types of tube. Lines have been drawn as a guide. The error bars represent the standard deviation (n = 5 replicates).

at a strain below 33%. As mentioned previously, we obtained a value of 0.9 MPa for the tensile modulus of transversal specimens of *ex vivo* pig intestine,

Figure 5 shows the diameter of the balloon and the contact area as a function of the volume of air. As the balloon volume increases, its diameter and the balloon/tube contact area also increase. The diameter of the PMMA and silicone tubes did not change significantly. As one would expect, the diameter of the unrestricted balloon was larger than the balloon restrained within the tubes. The diameter of the balloon free in air increased steadily as a function of the air volume, ranging from 37 to 41 mm between 15 and 25 ml. These diameter values are the most common maximum values in the human small bowel. The unrestricted balloon tends to the spherical and expanded in all

directions. When the balloon was inside the tube its diameter and contact area increased as shown in figure 5 b. In all cases there was a linear tendency. When the volume of air was 5 ml, the diameter of the balloon was slightly larger than the diameter of the tube and only a small part of the balloon was in contact with the tube. When the volume of air was 20 ml, the contact area was approximately two times greater, for any tube. When the tube was more rigid, the balloon expanded axially and increased the contact area without changes in its diameter. In the more flexible tubes, the balloon was able to deform them increasing its diameter while expanding axially. In the first case, the contact area was a flat cylindrical surface while in the second it had a barrel-shaped surface. Statistical differences between lumens were determined by a nonparametric Kruskal–Wallis test for each volume. The statistical analysis found no significant differences ($p > 0.05$) in the contact area for the different tubes at all air volumes.

Measuring the grip

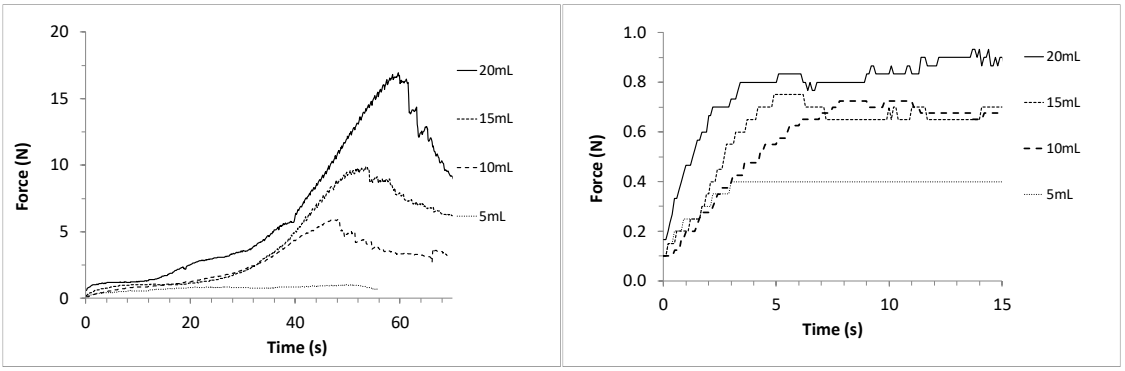

Figure 6. Grip force as a function of time measured for different volumes of air pumped into the balloon inside a PMMA tube without (left) and with (right) lubricant.

The grip capacity of the inflated balloon was evaluated by the procedure described in Material and Methods section. Five replicates were used for each volume of air and cavity, with and without lubricant. As mentioned previously, the volume of air, together with the wall's physical properties (elastic modulus, thickness), determine the pressure of the air inside the balloon which, in turn influences the friction force between the balloon and the lumen. The gripping capacity of the Endoworm system was thus measured as a function of the volume of air pumped into the balloons.
The measure of the applied force as a function of time for the PMMA tube is shown by way of example in Figure 6. The first part of the curve is the case in which the applied traction force is lower than the maximum static friction force. The friction force is thus equal to the applied force and the balloon is fixed to the sides of the tube. Once the maximum static friction force is reached, the balloon slides forward and the friction force decreases. An approximately constant value of the friction force was reached corresponding to the dynamic friction force. The value of the friction force and the difference between the static and dynamic friction forces depended largely on the lubrication of the tube. Figure 6 (left) shows the results of the friction force between

balloon and tube without lubrication, and Figure 6 (right) shows the friction values in the lubricated tube. It can be seen that the maximum friction force was reached much earlier in the lubricated than in the non-lubricated tube. When lubrication was used there was no significant difference between the static and dynamic friction forces.

The results of the average dynamic friction force (grip force) of the balloon with the different types of tube with and without lubricant are given in Figure 7; the *ex vivo* bowel has natural lubrication and it was maintained hydrated during the whole test by spraying a phosphate buffered saline solution. The numerical results of the grip force, as a function of the air pumped into the balloon, are shown in Table 1. As mentioned previously, the volume of air inside the tube influenced the pressure inside the balloon, and consequently also the force applied on the tube wall, due to the increased pressure (Figure 4) and balloon/tube contact area (Figure 5). The influence of the contact area has been discussed previously by Kim *et al.*[24], when studying the frictional force of a self-propelled capsule endoscope while being pulled on a porcine intestine specimen. They found that the friction coefficient did not change significantly with respect to the contact area between the capsule and the intestine. Besides, in a previous work of the same group, they found that when capsules had relatively sharp edges, the frictional force was much higher that when capsules had a smooth cylindrical shape (as is our case).[39] They concluded that when the capsule surface presented corrugations or sharp corners, the frictional force of the capsule increased with the contact area between the surface grooves and the intestine tissue. Kwon *et al.*[40] trying to enhance the frictional force between the endoscopic capsule and the intestinal wall proposed the addition of micro-pillars to the capsule surface. In the optimization study they obtained a frictional force about 58 mN, 3.5 times the corresponding to flat surface. It is worth noting that, even in our less favorable situation, small air volume and lubricated surface, we obtain frictional forces of 360 mN. The differences in the cited data can be explained by the differences in the experimental setup: they perform the experiments of the capsule moving on the intestine tissue while we perform the experiment inside the tube or intestine. The influence of having one, two, or three-surface contact on the locomotion of a capsule prototype has been studied elsewhere. [41] Kwon *et al.*[40] performed various intestine friction test with the optimum micro-patterned adhesive and found that the frictional force increased with the normal force. A similar result was found by Sliker and Rentschler when comparing traction force with normal force acting on wheels rotating on different artificial and biological substrates.[32]

Table1. Grip force as a function of the air pumped in the balloon inside different tubes without lubricant (sub index NL) and with lubricant (sub index L). Δ represents the difference in percentage of the lubrication effect.

V (ml)	PMMA			Silicone			PU			Bowel
	F_{NL}(N)	F_L(N)	Δ(%)	F_{NL}(N)	F_L(N)	Δ (%)	F_{NL}(N)	F_L(N)	Δ (%)	F_L(N)
5	1.06	0.46	-56.6	1.34	0.86	-35.8	0.83	0.36	-56.6	0.45
10	6.00	0.74	-87.7	3.18	1.58	-50.3	2.47	0.62	-75.0	0.56

15	10.84	0.86	-92.1	6.86	2.84	-58.6	6.47	0.74	-88.6	0.47
20	17.88	0.96	-94.6	9.88	3.98	-59.7	9.74	1.83	-81.2	0.48

The influence of lubrication on the grip force should be noted. The grip force variation reached 94.6% in the rigid PMMA tube, while its influence was lower in the more flexible silicone and PU tubes. Grip force was also influenced by the pressure on the tube walls due to the air pumped into the balloon and was more pronounced in the non-lubricated tubes. The grip force measured in the lubricated tubes was of the same order as that measured in the *ex vivo* bowel, with minor differences between the lumens. Whereas the dependence of the friction force with the volume of air pumped into the balloon was nearly linear in the non-lubricated tubes, the friction force increased nonlinearly in proportion to the air volume in the lubricated tubes and *ex vivo* bowel, (except for the silicone tube). It can be due to the microscale friction which is a function of material elasticity and viscous liquid layer shear.[40] Figure 8 shows representative SEM microphotographs of two of the tubes. Both present a rough surface with a more

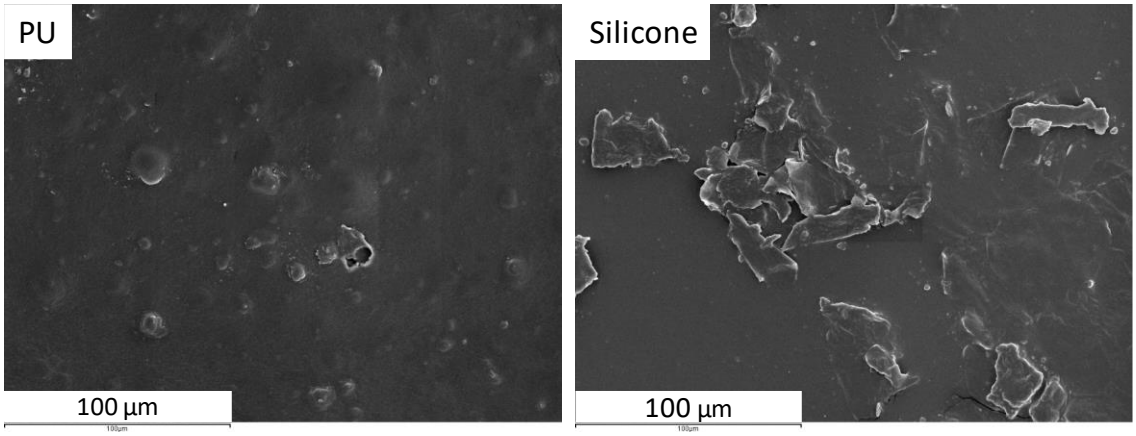

Figure 8. SEM images of two of the tubes wall: left, PU; right, silicone.

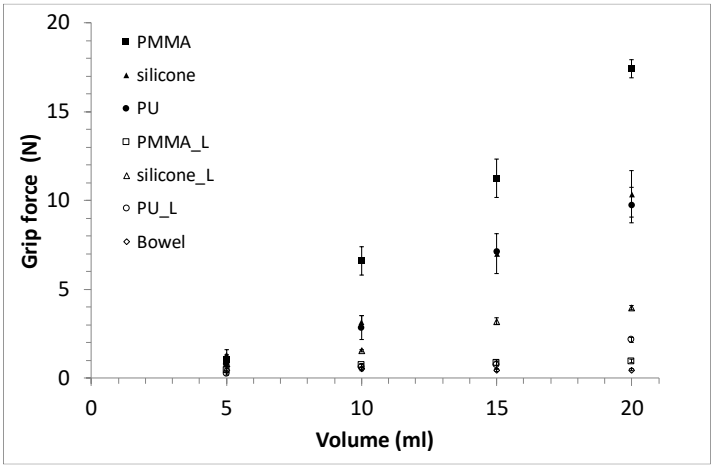

Figure 7. Grip force as a function of the air volume pumped into the balloon inside different types of tube with and without lubricant. Sub index L refers to lubricated tubes. The error bars represent the standard

pronounced relief in the case of silicone, which could explain the differences in the grip force.

With lubrication, the grip forces on the rigid PMMA were of the same order as that of PU lumen (except for the highest volume), while the highest grip forces were obtained in the silicone lumen. This result was possibly due to the greater surface roughness in this case (see Figure 8), whereas the rest of the lumens had smoother surfaces, similar to those of the intestine.

Conclusions

The aim of this study was to improve the performance of the prototype Endoworm. The proof of concept has shown that the prototype works as expected, although certain items, such as grip, could be improved. This paper describes the grip force capacity of the proposed Endoworm system in *in vitro* small bowel models. The grip depends on the normal force applied to the tube walls, which in turn depends on the pressure inside the balloons. The results have important implications for the optimal balloon design as regards allowing the system to advance while retracting the bowel, both, critically depend on the balloon's grip capacity. And this is a critical issue to any device intended to advance into the intestinal lumen, including current commercial devices. It was found that the amount of air pumped into the balloon in the *ex vivo* pig intestine showed a steady pressure region after an initial rise, the same as in the cases of the more flexible tubes, such as silicone and PU. The lowest differences were found between the *ex vivo* pig intestine and PU lumen. Therefore, increasing the air volume, which could burst the balloon, would not be enough to increase the grip force, other variables being more influential.

The results obtained in the different types of tube showed that the *ex vivo* pig intestine exerted the weakest grip force and that lubricating the walls of the lumen had a strong

influence. In lubricated tubes, besides the elastic properties of the lumen, the viscous liquid layer shear also plays an important role. As the lack of grip will clearly prevent the system from advancing in the in vivo intestine, it is a crucial parameter to be controlled. The in vitro models proposed in this paper serve the dual purpose of reducing the number of animal experiments and analyzing the variables individually. As this is a somewhat complex problem and many variables are involved, the experiment should aim to evaluate the influence of each parameter separately. In the rigid PMMA tube, only the forward movement of the prototype can be evaluated as the folding is not possible, while in the PU tube, both forward movement and folding are possible, and the lubrication effect can also be evaluated. As a consequence of this work, new balloon designs, are now being tested. More realistic bowel models are being developed, including the simulated curves and mesentery forces.

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