The authors present a novel magneto-mechanical elastic element that can be loaded remotely by varying the magnetic field surrounding it and that is able to store and release mechanical energy upon external triggering. The Magnetic Torsion Spring (MTS) is used as the core component of a self-contained miniaturized biopsy capsule (9 mm in diameter and 24 mm in length) for random tissue sampling in the small bowel. Thanks to the MTS concept, the biopsy mechanism can be loaded wirelessly by a magnetic field applied outside the body of the patient. At the same time, magnetic coupling guarantees stabilization against the small bowel tissue during sampling. Extreme miniaturization is possible with the proposed approach, since no electronics and no power supply are required onboard.

1. INTRODUCTION

The small intestine is home to a number of increasingly common human diseases. Celiac disease alone has a worldwide prevalence of 1% (i.e., 70,000,000 patients) [1] and its incidence has been doubling every 15 years since 1974 [2]. Early diagnosis of small intestine diseases is crucial to enable effective therapy and prevent complications such as severe anaemia or irreversible villous atrophy, especially in paediatric patients [3]. Unfortunately, the small intestine is the most difficult organ of the gastrointestinal (GI) tract to access due to its length (7 m in average) and distance from a natural body orifice [2]. Flexible endoscopy allows for reliable diagnosis – including collection of tissue samples under visual guidance – at the price of relevant patient discomfort and often requiring sedation [4]. Furthermore, this technique is not suitable for children younger than three years due to its invasiveness [5]. Wireless capsule endoscopy (WCE) has emerged as a promising technique for diagnosis of suspected diseases in the small bowel since its introduction in 2001 [4]. Thanks to its low invasiveness, WCE is also a well established diagnostic method for children [5], with the youngest child undergoing WCE reported so far being eight-months-old [6]. Although in some cases visual information provided by WCE are sufficient for identifying GI lesions [7-9], this technique lacks the ability of collecting biopsy samples, which is crucial for an effective and definitive diagnosis [10]. In particular, random biopsies of small bowel tissue are required to diagnose celiac disease, malabsorption syndromes, food sensitivity, autoimmune diseases, inflammatory small bowel disease, and small bowel infection [11].

The clinical need for a noninvasive technique to gather biopsy samples in the small intestine encouraged a relevant body of research in medical devices. The Crosby capsule, developed in 1957, was the first tethered device for GI tract biopsy collection [12]. Today, it is mainly used in children due to its small size (11 mm in diameter and 20 mm in length). Suction applied to the tube triggers an onboard mechanism which causes a spring-loaded knife to sweep across an aperture in the capsule, cutting away any mucosa protruding into the aperture and collecting the sample in a dedicated chamber. The presence of a tether – to assist with both biopsy collection and retrieval – and the need for X-ray to localize the capsule severely limited the impact of this device in terms of adoption. The first
example of a wireless biopsy capsule consists of a rotational tissue-cutting razor attached to a torsion spring and constrained by a paraffin block [13]. When the paraffin block melts by heating, the razor is released, thus collecting a tissue sample. The biopsy module alone is 10 mm in diameter and 2 mm in thickness, but it requires additional space for control electronics and power supply. Another compact solution with the same size, designed to be integrated in the MiRo endoscopic capsule (IntroMedic, Seoul, Korea), consists of a micro-biopsy spike with protruding barbs, a spring, and a mechanism actuated by shape memory alloy (SMA) [14]. The device is designed to operate sequentially so that tissue sampling, sealing and fixation are achieved in a single operation. However, it is not yet clear whether such a mechanism will be able to collect a sufficient number or volume of samples for accurate external histological analysis. In both of these solutions, system stabilization during tissue sampling remains as the main open issue (i.e., if the capsule is not anchored, the reaction force from the biopsy mechanism acting on the tissue may jeopardize tissue sampling effectiveness). This issue is addressed in [15], where a complete capsule device for tissue biopsy under visual guidance is proposed. This system is composed by a vision module, an anchoring module, and a SMA-based tissue sampling module. The three modules together were integrated into a 40 mm long by 15 mm in diameter capsule, which, however, does not include power supply. This highlights a significant limitation for all the proposed solutions, that is the need for onboard control electronics and power supply. Given the tight volume constraint for a swallowable device, the design of a biopsy mechanism that relies on an on-board power supply and wireless electronics for triggering and operation may not be a viable solution, particularly if the biopsy device is intended for paediatric patients.

In this paper, we introduce the novel concept of Magnetic Torsion Spring (MTS) and we leverage it to design a self-contained miniature biopsy capsule for random tissue sampling in the small bowel. Thanks to the MTS concept, the biopsy mechanism can be loaded wirelessly by a magnetic field applied from outside the body of the patient. At the same time, magnetic coupling guarantees stabilization against the small bowel tissue during sampling. Extreme miniaturization is possible with the proposed approach, since no electronics and no power supply are required onboard.

The remainder of this paper is organized as follows. The main design specifications are provided in Section II. Section III describes the principle of operation for both the MTS and the wireless biopsy capsule. The capsule design is described in Section IV, while fabrication and assembly are detailed in Section V. Experimental assessment is reported in Section VI, while Section VII outlines conclusions and future directions.

2. DESIGN SPECIFICATIONS

Design requirements to develop a miniature biopsy capsule for random tissue sampling in the small bowel are mainly determined by medical considerations and functionality constraints as follows:

- **Size.** The smaller the volume of the capsule, the larger will be the population able to swallow it, possibly including children. Although “swallowable” is somewhat challenging to define – because the maximum swallowable size varies from person to person – we can reasonably target state-of-the-art WCE devices. In particular, Given Imaging PillCam SB2 [4] – which is 11 mm in diameter and 26 mm in length – has been approved by Food and Drug Administration in 2001 for use in adults and in 2003 for use in children older than ten years [5].

- **Tissue sampling – Cutting pressure.** The biopsy mechanism must provide a sufficient force – or torque, depending on the mechanism design – to cut a tissue sample. An average value of 1 MPa at the tool-tissue interface is assumed as destructive stress for GI tract tissues, as reported for human cadaver trials [16].

- **Tissue sampling – Stabilization.** For an effective sampling, the capsule must firmly adhere to the tissue and balance the reaction force (or torque) while operating the biopsy mechanism.

- **Tissue sampling – Storage.** Typically, a small bowel biopsy test consists in 1 to 5 tissue samples approximately 1 mm³ in volume [10, 17-19]. Therefore, an ideal biopsy mechanism needs to collect and preserve multiple samples in a total storage volume larger than 5 mm³. Cross-contamination of tissue samples in the same reservoir does not alter the diagnostic value for diffuse GI diseases, such celiac disease. Concerning preservation, intestinal biopsy samples can be stored up to 24 hours on a gauze soaked with liquid solution, still preserving their diagnostic significance [20].

- **Safety.** The sampling mechanism design must be fail-safe, possibly avoiding parts protruding from the surface of the capsule and the risk of lumen perforation.

- **Localization.** Since we target random biopsies in the small intestine, the main purpose of localization for the proposed application is to detect when the capsule has reached the small intestine. Therefore, simultaneous localization and biopsy is not required. Localization methods based on ionizing radiation should be avoided for the sake of patient safety.

3. A NOVEL BIOPSY CAPSULE DESIGN BASED ON MAGNETIC TORSION SPRINGS

The standard approach in designing active medical devices builds upon mechatronics. Most of the miniature active capsules for GI applications reported to date integrate sensors, actuators, programmable electronics, wireless communication, and power supply [21]. Miniaturizing all these components to
fit a swallowable volume poses several challenges which severely limit the translational impact of novel designs. The solution we propose relies completely on passive components and leverages magnetic fields to remotely operate a mechanism that satisfies the above mentioned specifications.

3.a MAGNETIC TORSION SPRING - PRINCIPLE OF OPERATION

The core component of our design is the Magnetic Torsion Spring (MTS), a novel magneto-mechanical elastic element that can be loaded remotely by varying the magnetic field surrounding it and that is able to store and release mechanical energy upon external triggering.

A single MTS, represented in Fig. 1, is composed by two coaxial cylindrical diametrically-magnetized permanent magnets. One magnet is mounted on a shaft and is free to rotate, while the other one is constrained to the body of the device where the MTS is integrated.

**FIG.1 The basic components of a MTS.**

Defining $\theta$ as the relative displacement angle between the two magnets, the magnet free to rotate will orient itself so to zero under the effect of the local magnetic coupling. If an external magnetic field with opposite polarity of the MTS constrained magnet and strong enough to overcome local interaction between the two MTS magnets is applied, $\theta$ will reach $\pi$, storing elastic potential energy into the mechanism. Then, the sudden removal of the external magnetic field will trigger the release of the magnetic spring, which will zero $\theta$ again under the effect of the local magnetic coupling between the two MTS magnets. During this transition, all the elastic energy stored in the MTS is transformed to kinetic energy that can be used by the mechanism to perform its specific task.

3.b MAGNETIC TORSION SPRING - ANALYTICAL DESCRIPTION

Unlike a conventional torsion spring, the MTS has a nonlinear torque transfer function [22] that can be estimated as follows:

$$T_m(\theta) = T_p \cdot \sin \theta , \quad (1)$$

where $T_m$ represents the torque required to displace the magnet free to rotate of an angle $\theta$ from the $\theta=0$ position, while $T_p$ represents the peak torque, that is a function of MTS design (i.e., $T_p$ depends on the distance between the two MTS magnets and on the geometry and magnetization of each MTS magnet). The analytical model described in [23] or finite element analysis software (e.g., COMSOL MultiPhysics, Sweden) can be used to quantify $T_p$ by considering the MTS at $\theta=\pi/2$ (i.e., $T_m(\pi/2)=T_p$).

The elastic potential energy stored in the MTS can be expressed by calculating the work required to displace the rotating magnet of an angle $\theta$ from the $\theta=0$ position:

$$U(\theta) = -W(\theta) = - \int_0^\theta T_m(\varphi) \, d\varphi . \quad (2)$$

By substituting eq. (1) in eq. (2), we have:

$$U(\theta) = -T_p \int_0^\theta \sin \varphi \, d\varphi = T_p (1 - \cos \theta) . \quad (3)$$

where the result of the integration is expressed in rad.

Plots of $T_m(\theta)$ and $U(\theta)$ are represented in Fig. 2.a and 2.b, respectively. The plot of the potential energy shows that the MTS possesses stable equilibrium points for $\theta = \pm n 2\pi$, with $n=0, 1, 2, 3, \ldots$ and unstable equilibrium points for $\theta = \pi \pm n 2\pi$, with $n=0, 1, 2, 3, \ldots$ In order to remotely load the MTS to its unstable equilibrium position, the external magnetic field must provide a torque larger than $T_p$ at the MTS magnet that is free to rotate.

**FIG.2 The MTS torque versus angular displacement of the rotating magnet (a). The MTS potential energy as a function of the angular displacement of the rotating magnet (b).**
3.c WIRELESS BIOPSY CAPSULE - PRINCIPLE OF OPERATION

The proposed design for a wireless biopsy capsule is represented in Fig. 3 and takes advantage of two MTSs located at the two ends of the capsule. For each MTS, one cylindrical magnet is constrained to the body of the capsule, while the other one is mounted on a shaft together with a cylindrical razor blade. The external profile of the capsule has a lateral hole, which is closed by the blade for \( \theta = 0 \) (Fig. 3.a), while it is open to host tissue for \( \theta = \pm \pi \) (Fig. 3.b). Local coupling at the two MTSs maintains \( \theta = 0 \) in case no external magnetic field is present. In this configuration, the capsule can be swallowed by the patient. Transition from \( \theta = 0 \) to \( \theta = \pm \pi \) – thus opening the lateral hole and loading the MTSs – can be obtained by providing the appropriate external magnetic field as in Fig. 3.b, e.g., by placing a permanent magnet polarized outside the patient in the proximity of the biopsy capsule.

As represented in Fig. 4.a, the external magnetic field has also the function of attracting the biopsy capsule toward the lumen wall, thus promoting the superficial layer of the bowel to enter in the capsule lateral hole. By decreasing the intensity of the external magnetic field (e.g., by moving the external magnet away from the patient), the MTSs-blade assembly moves back to its original position, thus cutting the tissue inside the hole and storing it within the capsule (Fig. 4.b). Once the external magnetic field is completely removed, the capsule detaches from the lumen wall and is again free to move along the GI tract under the effect of peristalsis (Fig. 4.c).

The proposed approach addresses all the design specifications discussed in section 2. In particular, size is optimized by preventing the need for control electronics and onboard power supply. Adequate cutting pressure is provided by two MTSs – as better quantified in the rest of the paper. Stabilization is achieved by magnetic coupling between the capsule and the external permanent magnet. Reliable storage of the tissue sample is allowed by the cutting mechanism design. The absence of protruding parts enhances safety. As concern localization, the permanent magnets inside the capsule allow for real-time position tracking with commercial platforms (e.g., 3D-Magma, Matesy GmbH, Germany). Magnetic localization – outside the scope of this paper – must be performed at a different time than biopsy, since the external magnet will interfere with position tracking [24].

4. DESIGN FLOW

A stepwise approach has been adopted to address each design parameter in order to meet the specifications. The design flow started from the MTS permanent magnet selection and arrangement in order to maximize the available torque at the mechanism. Then, an external permanent magnet that was able to remotely load the mechanism and appropriately stabilize the capsule against the GI tissue was selected. The size of the lateral hole was defined by taking into account the attraction force between the external magnet and the capsule, while having in mind the desired sample volume. Finally, the blade geometrical features were selected considering the magnetic torque transmitted, the hole size, and the average pressure required to cut GI tissue.

A. MTS Design

The first step in the design flow consisted in selecting the permanent magnets for the MTS. Given the constraint in capsule diameter, we maximized the magnetic coupling by selecting permanent magnets with the strongest magnetization currently available for a doughnut-shaped magnet. Therefore, we selected off-the-shelf cylindrical diametrically-magnetized NdFeB permanent magnets, 6.3 mm in outer diameter, 1 mm in inner diameter, and 3.2 mm in thickness, with N52 magnetization (magnetic remanence of 1.48 T) (KJ Magnetics, Jamison PA).

The second design choice was to fix the distance \( (d_{mm}) \) between the two doughnut-shape magnets of the MTS. As previously mentioned, the maximum torque that a MTS can release (\( T_p \))
depends on MTS magnet features and their relative distance \((d_m)\). On the other hand, \(T_p\) is the torque that the external magnetic field must overcome in order to remotely load the MTS. In order to quantify \(T_p\) as a function of \(d_m\), finite element analysis software (COMSOL MultiPhysics, Sweden) was used and the results are represented in Fig. 5. In particular \(T_p\) was calculated fixing \(\theta = \pi/2\) and for \(d_m\) increasing in 0.25 mm steps from 0.5 mm to 3 mm neglecting any friction effect.

Given this configuration (two MTSs with \(d_m=1\) mm separated by \(d_s = 7\) mm), a dedicated finite element simulation was performed to obtain \(T_{m2}(\theta)\) – where subscript 2 is used for quantities related to two MTSs – for \(\theta\) ranging from 0 to \(\pi\). The angular displacement \(\pi\) was increased in steps of 0.0175 rad (equal to 1°) from 0 to \(\pi\). A screenshot from the simulation for \(\theta=0\) is represented in Fig. 6.a.

In order to validate the simulation results and to experimentally quantify \(T_{m2}(\theta)\) in the same range of \(\theta\), a dedicated bench test was set up. Two MTSs – spaced 7 mm apart – were embedded into a plastic chassis. The two magnets free to rotate were connected to a spool (diameter \(b=14\) mm) connected to a load cell (Nano 17-E, ATI Industrial Automation, USA) through an inextensible Dacron string, as sketched in Fig. 6.b. The load cell was mounted on a linear slider. Force was recorded while the slider was pulling the load cell away from the spool with a speed of 0.1 mm/s (i.e., quasi-static conditions). The range of motion of the slider was selected so to vary \(\theta\) from 0 to \(\pi\). This trial was repeated 10 times and the results were averaged.

A value of \(d=1\) mm, thus \(T_p = 5.3\) mNm, was selected as trade-off between MTS maximum torque and remote loading ability. However, if multiple MTSs are spaced far enough not to interact each other, the same magnetic field required to open a single MTS shall open all of them. This can be easily demonstrated by considering the superposition of effects, which holds true for magnetic fields when no other ferromagnetic materials are present in the environment. Therefore, we decided to use two MTSs mounted on the same shaft to double the total torque available at the tissue cutting mechanism, without increasing the requirements in terms of external magnetic field. To prevent cross coupling, the two MTSs were spaced as much as the design constraint on capsule length allowed, i.e. \(d_s = 7\) mm, and a finite element simulation was performed to confirm the absence of magnetic interaction. It is also worth mentioning that using two MTSs increases the attraction force toward the external permanent magnet, potentially improving anchoring while tissue is being cut. Furthermore, if the cutting mechanism is placed in between the two MTSs as in Fig. 3, design symmetry guarantees a uniform pressure of the sapling cavity onto the tissue.
mechanism is 10.7 mNm. This value is almost two times $T_{p2}$, thus confirming that no significant magnetic interaction was occurring between the two MTSs. The experimental value for $T_{p2}$ is 11 mNm. The 0.3 mNm deviation from the simulation results can be explained by considering the dynamic friction of the spool.

$$\text{FIG. 7 Simulated and experimental trends for } T_{\text{mt}}(\theta).$$

B. External magnetic field generation

The external magnetic field has the dual function of loading the MTSs to their unstable equilibrium condition and attracting the biopsy capsule towards the small intestine wall. A single MTS can be loaded if the external magnetic field is able to generate at least a torque of 5.3 mNm at the MTS magnet free to rotate. This corresponds to a magnetic flux density of 103.5 mT, as results from an additional purposely developed finite element simulation. As previously mentioned, if multiple MTSs are spaced enough not to interact each other, the same magnetic field required to open a single MTS shall open all of them. Therefore, the magnetic field source must be able to generate an uniform magnetic flux larger than 103.5 mT at the capsule from a distance outside the body of the patient. This value is far below the safety threshold of 2 T recommended for occupational exposure in [25]. The magnetic field also needs a gradient along the its main direction to guarantee a stable anchoring of the capsule against the intestine wall.

While there are precise constraints on the external magnetic field value, there are no stringent requirements for the size of the field generator, since it is located outside the patient’s body. Electromagnetic field generators [26, 27] are the best option to obtain a uniform magnetic field that can be controlled in intensity and gradient. We decided to use an off-the-shelf permanent magnet to prove the principle with the simplest and cheapest possible approach. This is particularly relevant for a potential translation of a novel medical device, since deployment costs are always one of the main barriers to adoption. We selected a disc-shape NdFeB permanent magnet (50 mm in diameter and 20 mm in thickness) with an N52 axial magnetization (Fig. 8). A finite element simulation was performed to evaluate the distance from the disc-shape magnet where the magnetic flux density is large enough to load the MTS, the uniformity of the flux density in that region, and the gradient of the field. Then, a second finite element simulation was performed by adding to the previous scenario the second MTS (features as detailed in the previous subsection) in the region where the magnetic flux density is large enough to load them. The aim of this second set of simulations was to estimate the torque induced by the external magnet on the two MTSs for $\theta=0$ to confirm that it corresponds to $T_{p2}$, thus strong enough to fully load the MTSs. Finally, a third simulation was performed varying the distance between the disc-shape magnet and the two MTSs while keeping the two boundary conditions – i.e., mechanism closed, $\theta=0$, and mechanism open, $\theta=\pi$ – to quantify the trend of the attraction force. For this simulation, the distance between the disc-shape magnet and the two MTSs was varied from 10.5 mm down to 0.5 mm in steps of 0.5 mm. This range is typically used for magnetic locomotion of capsule endoscopes [4, 28] and is valid for population with a body mass index (BMI) up to 30.

In order to assess the simulation results and to obtain the experimental trend of the attraction force within the two boundary conditions, which corresponds to the attraction force effectively available during cutting, while the mechanism goes from open to close, we set up the bench test sketched in Fig. 9. In particular, two MTSs were spaced 7 mm apart inside a plastic capsule (9 mm in diameter and 24 mm in length) and the two magnets free to rotate were glued on a plastic shaft mounted on synthetic ruby bushes. The capsule was connected to the load cell through an inextensible cable and the magnetic attraction force was acquired while incrementally positioning the load cell-capsule assembly toward the disc-shape permanent magnet with a slider. This setup allows for a quantification of the magnetic attraction force with the MTSs free to rotate under the action of the external magnetic field. Concerning simulation results, the selected disc-shaped magnet was able to provide a magnetic flux density of 103.5 mT at 27 mm from its circular surface, thus generating a torque at the two MTSs for $\theta=0$ of 10.7 mNm (a screenshot of this simulation is represented in Fig. 8). Assuming a two-MTS capsule with its center 27 mm away from the disc-shape magnet, the variation of magnetic flux density at the two MTSs is below 1%, while the gradient along the direction connecting the center of the external magnet and the center of the capsule is ~7.5 T/m. Attraction force along the same direction is plotted in Fig. 10 as a result from simulations and from experimental data. The experimental plot overlays the simulated trend except for the distance range related to the transition from $\theta=\pi$ to $\theta=0$, occurring for a magnet-capsule distance ($d_c$) ranging from 27 mm to 50 mm.
FIG. 8 Finite element simulation screenshot for estimating the torque exerted by the external permanent magnet on two MTSs located \( d_e = 27 \) mm away on the vertical axis. The two MTSs were spaced \( d_s = 7 \) mm each other and \( \theta = 0 \) was assumed. The mesh consisted approximately of 380,000 elements with a maximum element size set at 1/50 of the maximum geometric feature in the scenario.

FIG. 9 Sketch of the experimental setup to measure the magnetic attraction force between a capsule embedding two MTSs and the chosen external permanent magnet.

FIG. 10 Plot of the magnetic attraction force between the external permanent magnet and the biopsy capsule embedding two MTSs as a function of \( d_e \). Simulation results for \( \theta = 0 \) and \( \theta = \pi \) superimposed to experimental data.

C. Hole dimensioning

Once characterized the trend of the force attracting the capsule to the intestinal wall (Fig. 10), we focused on selecting the diameter of the lateral hole that would guarantee the penetration of at least 1 mm\(^3\) of tissue (typically 1 mm thick). Five capsule mock-ups (9 mm in diameter) with lateral hole diameters ranging from 3 mm to 7 mm in steps of 1 mm were fabricated by rapid prototyping. This range is centered on 5 mm, which is the diameter of the hole for the Crosby capsule [12]. Each capsule mock-up was connected to a load cell mounted on a vertical slider and pressed against the inside of a freshly-excised porcine small intestine sample. The tissue sample was fixed to a layer of artificial skin to mimic the compliance of abdominal organs. A high-definition camera was mounted on the side of the experimental setup to quantify the height of the tissue penetrating the hole. Image analysis software ImageJ v1.46 was used on each acquired image to extract the numeric values for the tissue height. For each capsule mock-up, penetration depths were acquired for two different values of compression force, i.e., the maximum (2 N) and the minimum (0.18 N) of the magnetic attraction force.

An approximation of the volume of the tissue inside the lateral hole as a spherical cap can be expressed as:

\[
V = \frac{\pi h}{6} \left( \frac{3}{4} (d/2)^2 + h^2 \right),
\]

where \( d \) is the diameter of the hole and \( h \) is the measured penetration height. Each measurement was repeated for 5 times and the results were averaged. A sketch of the setup is reported in Fig. 11.

Given the experimental results, reported in Tab. 1, a lateral hole of 4 mm in diameter is not able to guarantee enough tissue penetration to collect a tissue sample larger than 1 mm\(^3\) for the entire attraction force range. On the other hand, a lateral hole of 6 mm in diameter – or larger – may jeopardize safety by allowing the full thickness of the small intestine to enter into the cavity. Therefore, to meet the requirements in terms of
tissue sample volume and to prevent small intestine perforation at the time of tissue cutting, a lateral hole of 5 mm in diameter was adopted for the proposed design.

<table>
<thead>
<tr>
<th>Mock-up diameter</th>
<th>Tissue volume for 2 N of compression force</th>
<th>Tissue volume for 0.18 N of compression force</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mm</td>
<td>0.3 mm³ (σ = 35-10⁻²)</td>
<td>0.0 mm³ (σ = 13-10⁻²)</td>
</tr>
<tr>
<td>4 mm</td>
<td>1.3 mm³ (σ = 31-10⁻²)</td>
<td>0.7 mm³ (σ = 36-10⁻²)</td>
</tr>
<tr>
<td>5 mm</td>
<td>4.3 mm³ (σ = 33-10⁻²)</td>
<td>1.5 mm³ (σ = 35-10⁻²)</td>
</tr>
<tr>
<td>6 mm</td>
<td>8.5 mm³ (σ = 30-10⁻²)</td>
<td>4.0 mm³ (σ = 33-10⁻²)</td>
</tr>
<tr>
<td>7 mm</td>
<td>13.8 mm³ (σ = 25-10⁻²)</td>
<td>7.4 mm³ (σ = 29-10⁻²)</td>
</tr>
</tbody>
</table>

Table 1. Tissue volume penetrating inside the hole for different hole diameters and compression force.

**FIG.11** Sketch of the experimental setup to estimate the typical volume of the tissue penetrating the lateral hole as a function of the hole diameter (a). Image of a capsule mock-up, with a 5 mm hole, pressed against an excised porcine small intestine sample.

**D. Blade design**

In order to motivate the choices made for the dimensioning of the blade, an analytical description of the pressure that it exerts on the tissue as a function of θ is provided for θ ranging from ±π to 0. This formulation is then used to verify that the pressure exceeds the average destructive stress for GI tissues of 1 MPa [16] for the entire range of motion of the blade. Referring to Fig. 12b, we define the following parameters:

- $R_b$ as the cylindrical blade outer radius. In order to obtain the largest possible lever for $T_{in}$, this value must be minimized as much as fabrication and assembly constraints allow. On the other hand, this parameter must be close to the inner diameter of the capsule to guarantee an effective grip of the blade on the tissue penetrating the lateral hole. Since the inner diameter of the capsule body is 7.2 mm, we chose $R_b = 3.55$ mm to leave enough room for blade rotation. With this selection, a maximum force of 3.1 N can be applied to the tissue.

- $t$ as the thickness of the blade. This parameter must be minimized in order to increase the cutting pressure. It strictly depends upon the fabrication technology adopted for the blade. As better detailed in the following subsection, the blade was fabricated by micro-Electro-Discharge-Machining (µEDM). This technology allowed for $t = 30$ µm. This same thickness was adopted in [15] for the same application.

- $γ$ as the capsule lateral hole angular opening. This quantity is two times the arcsine of the ratio between the hole radius ($d/2$) and the capsule radius ($D/2$). From the previous steps of the design flow, we can assume $d = 5$ mm and $D = 9$ mm, thus resulting in $γ = 1.178$ rad (67.5°).

- $β$ as the blade angular opening. This is the main free design parameter for the blade and it affects the range of $θ$ where the blade starts to cut the tissue, as better detailed below.

Since $θ=±π$ is an unstable equilibrium condition – thus the blade can rotate either clockwise ($dθ/dt>0$) or counter clockwise ($dθ/dt<0$) when the mechanism is triggered – the blade must approach the tissue in the same way disregarding the direction of rotation. Therefore, symmetry constraints apply to the blade shape. In particular, the center of the blade opening for $θ=±π$ must coincide to the center of the lateral hole in the capsule and the blade must be symmetric along the vertical axis of Fig. 12b.

To better underline the role of $β$, it is possible to define the angles $±θ_1$ and $±θ_2$ where the blade starts and ends to cut the tissue, respectively. While the sign depends on the direction of rotation of the blade, the absolute values can be expressed as follows:

$$\theta_1 = π - \left(\frac{β}{2} - \frac{γ}{2}\right)$$

$$\theta_2 = π - \left(\frac{β}{2} + \frac{γ}{2}\right)$$

The pressure exerted by the blade on the tissue as a function of $θ$ can then be expressed as:

$$P(\theta) = \frac{(T_{p2} \sin \theta) / R_b}{S(\theta)}$$

for $θ_2 < |θ| < θ_1$  \(7a\)

where $S(θ)$ is blade surface in contact with the tissue as a function of $θ$. Referring to Fig. 12a, $S(θ)$ can be seen as the product of $t$ and $L(θ)$, defined as the lateral dimension of the blade that overlaps the lateral opening for a given $θ$. This quantity can be expressed as:

$$L(θ) = d \sin(α)$$

\(7b\)

where:

$$α = π - \frac{θ - θ_1}{γ}$$

\(7c\)

By substituting Eq.\(7c\) in Eq.\(7b\) and then in Eq.\(7a\), we have:

$$P(θ) = \frac{(T_{p2} \sin \theta) / R_b}{t d \sin[π(θ-θ_1)/γ]}$$

for $θ_2 < |θ| < θ_1$  \(8\)
In order to start cutting the tissue when the attraction force – thus the stabilization against the tissue – is maximum, we decided to fix $\beta$ so as to have $\theta_1 = \pi$, thus $\beta = \gamma = 67.5^\circ$ and $\theta_2 = 112.5^\circ$. The value of $P(\theta)$ for $\theta$ ranging from $\theta_1$ to $\theta_2$ is represented in Fig. 13 and it is always larger than 1 MPa. It is worth mentioning that, with the current design choices, the mechanism ends the cut before reaching the peak of torque ($T_{p2}$, that is achieved for $\theta = \pi/2$). This is mainly due to the selection of the lateral hole diameter, that directly affects $\gamma$.

All the permanent magnets were purchased off-the-shelf from the same supplier (KJ Magnetics, Jamison, PA, USA). The shaft and the cylindrical blade were fabricated in Ergal™ (i.e., 7075 aluminium alloy) in order to guarantee high stiffness to avoid magnetic interaction with the MTSs. As represented in Fig. 14.a, b, the shaft is 15 mm long and has 3 different diameters. The central part is 4 mm in diameter and hosts a T-shape groove in the profile to mate with the cylindrical blade (Fig. 14.d). The intermediate parts are 1 mm in diameter to fit in the central hole of the MTSs rotating magnets. The lateral parts of the shaft have a diameter of 0.8 mm to enable the connection with custom-made bushes in synthetic ruby (2.3 mm outer diameter and 0.8 mm in thickness, having a buffing surface to minimize friction) (Fig 14.e). A five-axis micro-Computer Numerical Control ($\mu$CNC) center (HSPC, KERN GmbH, Germany) was used to fabricate the shaft. Starting from 7.1 mm in diameter and 7 mm long Ergal™ cylinder, the blade was machined as shown in figure 14.c by $\mu$EDM (AP 200L, Sodick, Japan), and then fitted into the T-shape groove obtained in the shaft. The lateral profile of the blade guarantees a volume of $40 \text{ mm}^3$ as reservoir for tissue samples. This volume is larger than the $5 \text{ mm}^3$ that would be required to host five 1 mm$^3$ samples.

The capsule chassis is composed by two complementary shells fabricated in plastic by stereo-lithographic rapid prototyping (3-D Printer Invision Si2, 3D Systems Inc., US) (Fig 14.g).
The two MTSs rotating magnets were glued (Loctite 401) to the shaft so that their magnetization directions are parallel. Similarly, the two MTSs fixed magnets were glued to the chassis so that their magnetization directions are parallel. The assembly of the shaft, the blade, the rotating magnets, and the ruby bushes was mounted at the center of the capsule. In order to provide a sharp edge to the hole, thus promoting tissue cutting, a metallic layer was aligned with the chassis lateral hole and glued on the inner side of the shell. This metallic part – represented in Fig. 14.f – was fabricated in Ergal™ with a thickness of 0.5 mm, a length of 6 mm, a width of 5 mm, and outer and inner diameter of 8.10 mm and 7.10 mm, respectively, and with a 5 mm central hole.

Once all the components were embedded in the chassis, the two plastic shells were mated and glued together, obtaining a working prototype of the capsule which is 9 mm in diameter and 24 mm in length, with a 5 mm lateral hole along its profile (Fig 15). The weight of the capsule prototype is 4.2 g.

![Image](https://via.placeholder.com/150)

**FIG.15 Assembled biopsy capsule prototype laying on graph paper for reference.**

### 6. EXPERIMENTAL ASSESSMENT

A single test was performed on the capsule prototype before assessing tissue sampling through dedicated ex-vivo trials. The goal of the bench test was to assess the correct opening of the lateral hole of the capsule – thus the loading of the MTSs – with the external permanent magnet 27 mm away. The capsule was fixed to the bench, exposing the lateral hole on the top side. The external magnet was mounted on a vertical slider and made to approach the capsule ten times. For each trial, the complete opening of the lateral hole was observed when the external magnet was 27 mm away from the capsule, as expected.

Ex-vivo trials were performed by using freshly excised porcine intestine segments, placed on an artificial skin layer, and covered with half-liter plastic bags filled with water to simulate the organs surrounding the lumen. Each segment was 30 cm long and was replaced after 15 minutes of use to minimize the effect of tissue degradation. Three different sessions of ex-vivo trials were performed. The first aimed to observe the capsule behaviour during the mechanism actuation. Therefore, the capsule was introduced into the lumen followed by a paediatric gastroscope (Karl Storz Endoscopy, Tuttlingen, Germany). The external magnet was manually moved on the outside of the lumen by an operator – at approximately 3 cm of distance – until magnetic coupling with the capsule was observed through the gastroscope (Fig. 16.a). Then, the external magnet was moved out from the experimental setup and the capsule detached from the lumen, closing the mechanism, and cutting a layer of tissue (Fig. 16.b, c). The capsule was then taken out from the lumen, the lateral hole was opened by placing the capsule close to the external magnet, and the tissue sample was retrieved using surgical tweezers. A typical tissue sample is represented in Fig. 16.d. This procedure – repeated ten times – provided the opportunity to familiarize the operator with the tissue sampling process.

![Image](https://via.placeholder.com/150)

**FIG.16 Ex-vivo trials. The capsule is lifted against the tissue by magnetic interaction with the external magnet, while the MTSs are loaded (a). Removing the external magnet the MTSs turn the blade, cutting a sample (b). The lumen wall region where the sample has been removed (c). The biopsy sample retrieved from the capsule (d).**

The second session focused on blind operation of the biopsy capsule; therefore, the gastroscope was not used. The capsule was introduced randomly inside the lumen. The sampling mechanism was activated by slowly moving the external handheld magnet along the outside of the lumen, leveraging the experience gained during the previous session. The capsule was then removed from the lumen, the tissue sample was retrieved, and its volume was derived by measuring its weight. This procedure was repeated twenty times to achieve statistical relevance. The biopsy capsule was able to gather a tissue sample larger than 1 mm³ all the twenty times. The lumen wall was never perforated by the blade and the mechanism never got stuck while cutting.

The third ex-vivo session focused on multiple biopsy sampling. The same procedure of the previous session was followed moving the external magnet three times along the outside of the lumen, thus activating the mechanism for three times each trial. A total of five trials were performed and in all the cases the capsule was able to cut and safely store three different samples, each larger than 1 mm³.
Although we obtained very positive results, it is worth mentioning that tissue degradation of the ex-vivo intestinal tissue may favour tissue cutting. This effect is not present in-vivo, where tissue is continuously perfused. Therefore, an ultimate assessment of the proposed technology must be performed in-vivo. This is outside the scope of this paper and will be the subject of future studies.

7. CONCLUSIONS AND FUTURE DIRECTIONS

In this paper, a novel magneto-mechanical elastic element – the MTS – was introduced, analysed, and used as a remotely-triggered actuator in a miniature wireless capsule for random biopsy in the small intestine. This approach allowed for extreme miniaturization (i.e., the capsule prototype was 9 mm in diameter and 24 mm in length), since no batteries and no control electronics were required on board. Remote loading of the cutting mechanism – obtained by an external permanent magnet – provided stabilization, anchoring, and a sufficient torque to acquire intestinal biopsies. Storage of multiple samples larger than 1 mm³ was possible thanks to a large reservoir underneath the cylindrical rotating blade. The absence of parts protruding from the capsule profile guaranteed safety. The capsule position can be easily localized before biopsy by using commercial magnetic trackers [29], thanks to the onboard magnets.

The detailed description of the sequential design flow provided in this paper should pave the way for design variations. A different magnetic field source or a larger permanent magnet can be used to adapt the platform to patients with different BMI – thus requiring the capsule to be operated from a larger distance than 27 mm. To reduce the size of the capsule further, a single MTS can be used to operate the blade, provided that the pressure on the tissue is enough to cut.

Since the lack of miniature and efficient actuators is commonly identified as one of the main barriers to the design of capsule-size robots [4], the MTS has the potential to be an enabling component for a new generation of remotely-controllable medical devices.

Further future directions for this work include extensive in-vivo trials, the use of a soft sponge soaked in a weakly saline solution – to be included in the reservoir in order to promote biopsy preservation – and the study of a miniature sensing system to remotely detect the open and closed state of the mechanism.

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