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Magnetic air capsule robotic system: proof of concept of a novel approach for painless colonoscopy

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Abstract
Background Despite being considered the most effective method for colorectal cancer diagnosis, colonoscopy take-up as a mass-screening procedure is limited mainly due to invasiveness, patient discomfort, fear of pain, and the need for sedation. In an effort to mitigate some of the disadvantages associated with colonoscopy, this work provides a preliminary assessment of a novel endoscopic device consisting in a softly tethered capsule for painless colonoscopy under robotic magnetic steering.
Methods The proposed platform consists of the endoscopic device, a robotic unit, and a control box. In contrast to the traditional insertion method (i.e., pushing from behind), a "front-wheel" propulsion approach is proposed. A compliant tether connecting the device to an external box is used to provide insufflation, passing a flexible operative tool, enabling lens cleaning, and operating the vision module. To assess the diagnostic and treatment ability of the platform, 12 users were asked to find and remove artificially implanted beads as polyp surrogates in an ex vivo model. In vivo testing consisted of a qualitative study of the platform in pigs, focusing on active locomotion, diagnostic and therapeutic capabilities, safety, and usability.
Results The mean percentage of beads identified by each user during ex vivo trials was 85 ± 11%. All the identified beads were removed successfully using the polypectomy loop. The mean completion time for accomplishing the entire procedure was 678 ± 179 s. No immediate mucosal damage, acute complications such as perforation, or delayed adverse consequences were observed following application of the proposed method in vivo.
Conclusions Use of the proposed platform in ex vivo and preliminary animal studies indicates that it is safe and operates effectively in a manner similar to a standard colonoscope. These studies served to demonstrate the platform's added advantages of reduced size, front-wheel drive strategy, and robotic control over locomotion and orientation.

Keywords Colonoscopy · Colorectal cancer · Robotic endoscopy · Wireless capsule endoscopy · Advanced colonoscopy · Self-propelling colonoscopy

Colorectal cancer (CRC) is third in terms of incidence rate among all cancers in high-income countries, accounting for 610,000 deaths worldwide in 2008 [1]. The survival rate of CRC patients can reach 90% in cases with early diagnosis [2]. For this reason, regular screening is highly recommended for patients older than 50 years or having family history of CRC [3]. Colonoscopy is considered to be the most effective method for CRC screening due to the

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possibility of visualizing the inner surface of the colon, acquiring biopsies, and treating lesions as soon as they are detected [4, 5]. However, take-up of screening colonoscopy is limited due to various factors including invasiveness, patient discomfort, fear of pain, and the need for sedation [6, 7]. The technology behind flexible endoscopy basically consists of a long (approximately from 130 up to 160 cm), semirigid tube with a steerable head (diameter from 12 up to 14 mm). Steering cables pass through the shaft, making it relatively stiff compared with the compliant nature of the colon. This relative stiffness allows a colonscope to push against, and deform, the colon wall, yet as was correctly observed in [8], it is still too compliant to fully avoid undesired bending and buckling effects. The common way to introduce the instrument consists of pushing it into the colon while steering the tip to follow the lumen. As a result of this "back-wheel drive" approach, the shaft pushes against the colonic wall until the lumen and its surroundings provide sufficient counterpressure to force the shaft to bend. This maneuver stretches the colon and often leads to loop formation, thus causing substantial pain and discomfort to the patient. In particular, looping occurs when the insertion tube continues to be advanced into the colon without corresponding progression of the distal tip, which displaces the colon from its native configuration and stretches mesentery muscles. Looping of the scope has been shown to be responsible for 90% of pain episodes in colonoscopy and increases the chance of tissue damage and perforation [9]. Some special maneuvers can be applied to minimize this effect, thus making colonoscopy an extremely difficult procedure to learn and master [10].

The perceived need for better colonoscopy performance and acceptance by potential asymptomatic screeners has pushed the frontier of research further on, as is demonstrated by the various alternative technologies proposed in recent years. Methods such as fecal occult blood testing [11], tomographic colonography [12], and magnetic resonance colonography [13] have been proposed as alternatives to screening and diagnostic colonoscopy. However, these procedures do not entirely replace flexible endoscopy because they miss all flat or sessile lesions, which account for about 30% of all lesions, and they lack the therapeutic means that colonoscopy provides; i.e., if abnormalities are diagnosed, flexible endoscopy is still required for biopsies or potential treatment. The same applies to diagnosis-only devices such as the Endotics (EraEndoscopy s.r.l., Peccioli, Italy) [14], the CathCam (Ethicon, Cincinnati, OH, USA) [15], the Aer-O-Scope (GI View Ltd., Ramat Gan, Israel) [16], and capsule endoscopes [17]. Despite the promise of painless colonoscopy, the lack of an operative channel prevents them from fully replacing colonoscopy. To fulfill this goal, future technology must provide diagnostic and therapeutic means similar to current flexible endoscopes while also providing clear steps forward in terms of patient acceptability and procedure ease [8].

Therapeutic colonoscopes with alternative propulsion mechanisms have also been reported in recent works. Devices such as the NeoGuide (Neoguide Systems Inc., Los Gatos, CA) [9], the Invendo SC20 (Invendo Medical GmbH, Kissing, Germany) [18, 19], the Colonosight (Stryker Corp., Kalamazoo, MI, USA) [20], and the EndoEase [21] aim to improve colonoscopy outcomes and reduce patient discomfort, however the size of the shaft (always larger than 10 mm) is a main concern in terms of patient acceptability.

Distal control of tip deflection by wires running through the length of the device imposes a lower bound on the outer diameter of the instrument. Having a "front-wheel" steering and propulsion method would enable a drastic reduction of shaft diameter down to the size of the operative channel plus the space needed for electrical connection to the vision module. Magnetic steering and control of endoscopic capsules has been reported by several groups worldwide [22–24], with authors always identifying the need for insufflation, and lack of instrumentation for tissue interaction, as main limitations. In this work, robotic magnetic control and steering, reported elsewhere for wireless capsule locomotion [25], is applied to an endoscopic device containing a frontal magnetic camera (diameter 11 mm, length 26 mm) connected to an external control box by a 5.4-mm-wide soft tether. This multilumen connection is used for providing insufflation, passing an operative flexible tool, enabling lens cleaning, and operating the vision module. A magnetic field sensor is also embedded in the device head to allow for real-time robotic control. This "front-wheel" magnetic propulsion was adopted to eliminate the need of pushing the shaft to advance the scope, thus preventing looping and the colonic "stretching" phenomena currently associated with colonoscopy. These advantageous characteristics are enhanced by a drastic reduction in both the bending stiffness of the shaft and the mass of the proposed device (from 1,240 g of a standard colonoscope down to 34 g for the current device, including the soft tether), while the therapeutic capabilities provided by a standard colonoscope are retained. Additionally, robotic control can drastically speed up the learning curve associated with training physicians thanks to motion scaling, enhanced repeatability, and precision of movement [26].

These features may make advancement along the tortuous path towards the cecum easier while reducing patient discomfort and enhancing the possibility of sedation-free screening.

Materials and methods

Platform description

The proposed platform, schematically represented in Fig. 1, consists of three main modules, i.e., the endoscopic device, the robotic unit, and the control box.

The endoscopic device, also referred to as the magnetic air capsule (MAC), is composed of a capsule-like frontal unit and a compliant multilumen tether. The frontal unit contains a vision module, a permanent magnet, a magnetic field sensor, and two channels, one for lens cleaning and the other for insufflation/suction/irrigation or insertion of an operative tool. The vision module consists of a 500×582 charge-coupled device (CCD) camera with 120° field of view (provided by Karl Storz GmbH, Tuttlingen, Germany), four high-efficiency white light-emitting diodes (LEDs) (NESW007BT; Nichia Corp., Tokushima, Japan), and a transparent flat glass cover. A custom-shaped NdFeB permanent magnet is included in the MAC to provide the magnetic link. This magnet has axial magnetization along the main dimension of the capsule, with residual magnetic flux density of 1.48 T. The magnetic field sensor is based on the Hall effect and has a full range of 2 T. The channel for lens rinsing is a polytetrafluoroethylene (PTFE) sheath with inner diameter of 0.8 mm and external diameter of 1.2 mm. At the distal end of the channel, a metallic deflector directs the water jet onto the glass cover of the vision module. A second PTFE sheath with inner diameter of 2.8 mm and external diameter of 3.2 mm allows gas insufflation, suction, irrigation, or access for standard endoscopic tools such as biopsy forceps, polypectomy snare, retrieval basket, grasper, etc. To achieve optimal performance of the system, the endoscopic tools must be inert to the magnetic field. A picture of standard biopsy forceps inserted into the operative channel of the MAC is shown in Fig. 2.

The frontal unit is 11 mm in diameter, 26 mm in length, and 10.5 g in mass. Its shape, size, and volume are comparable to a wireless capsule endoscope [27]. The multilumen tether has three channels, i.e., the two PTFE sheaths described above and a third lumen allowing electrical connection to the vision module and the magnetic field sensor. The overall external diameter of the tether is about 5.4 mm, while its length is 2 m. The total mass of the MAC is 34 g.

Magnetic coupling allows movement of a permanent magnet in a tridimensional volume external to the patient's body to affect the position and orientation of the robot inside the patient. This technique allows the endoscopic device to be advanced into the colon and oriented toward the lumen wall under direct guidance of the operator. The external magnet is made of NdFeB in a cylindrical shape (diameter 9 cm, length 8 cm), resulting in a residual flux density of 1.48 T; it is placed as the end-effector of a six-degree-of-freedom (DoF) anthropomorphic robotic arm (RV-6SL; Mitsubishi Electric, Tokyo, Japan). The user

Fig. 2 The MAC with standard biopsy forceps

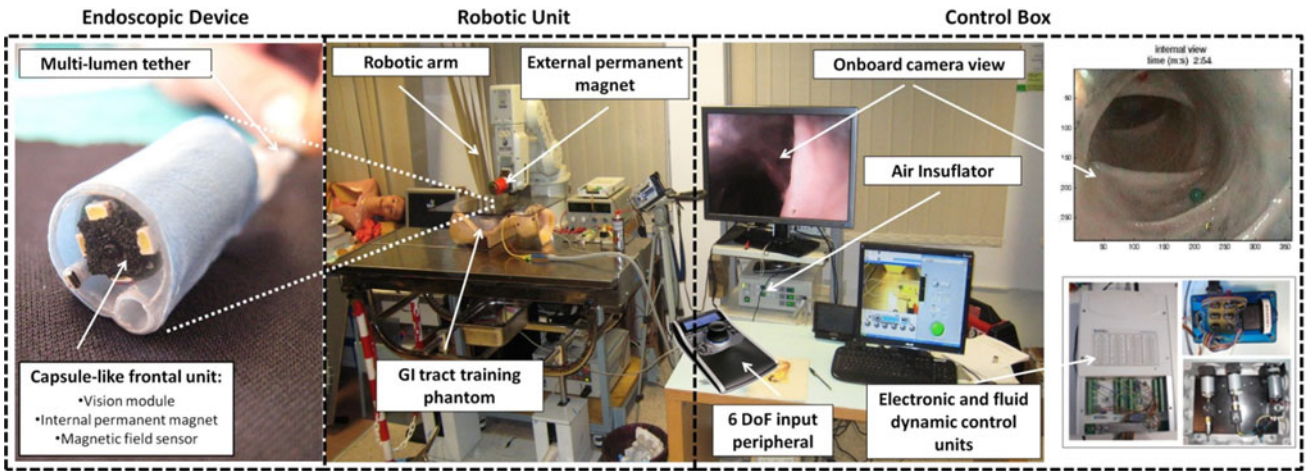

Fig. 1 View of the complete endoscopic platform, consisting of the endoscopic device (*left*), the robotic unit (*center*), and the control box (*right*)

controls the position of the external magnet in real time through use of a six-DoF input peripheral (3D SpacePilot; 3Dconnexion Inc., USA). The translational and rotational motion commands provided by the input device are processed by the robotic arm as incremental changes to be added to the current end-effector absolute position. The magnetic link, defined by the features of the two permanent magnets, is designed to properly drag and steer the MAC at maximum working distance of 150 mm between the external magnet and the endoscopic device. In the case of an obese patient, an external magnet with larger volume can be used to cope with the increased working distance. The magnetic field sensor embedded in the MAC provides feedback about the magnetic link strength, alerting the user if the field strength falls below the threshold required to properly control the endoscopic device. A close-up view of both the MAC and the external driving magnet is shown in Fig. 3.

The control box displays the image stream coming from the endoscopic camera and allows the user to trim illumination, set the insufflation level or apply suction, rinse the camera lens, and provide irrigation to clean the bowel. This box is composed by a set of electromechanical pumps and valves to maintain the user-selectable lumen pressure.

Experimental trials

This study was conducted to test both the diagnostic and treatment ability of the MAC platform using artificially implanted beads as polyp surrogates in an ex vivo model, and in a proof-of-concept study of the system in vivo. The ex vivo study methodology included blind assessment of simulated polyps by independent physicians. In vivo testing consisted of an observational study of the MAC in pigs.

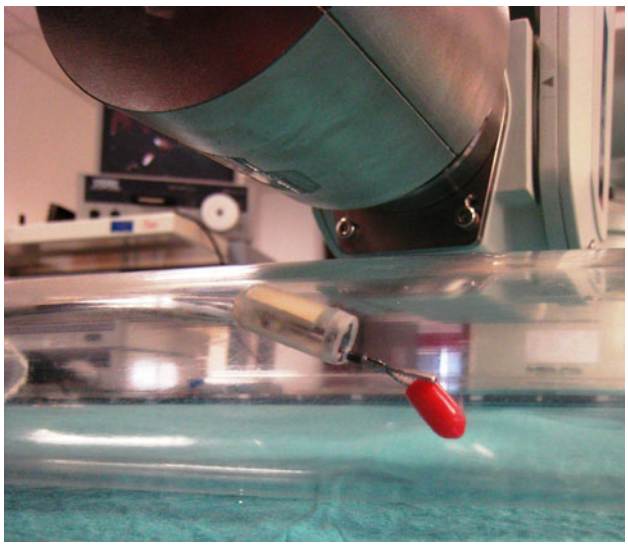

Fig. 3 View of the MAC inside a transparent plastic tube holding a red object with a standard endoscopic grasper. The MAC is magnetically linked to the external magnet mounted as end-effector of the robotic manipulator

Lower gastrointestinal phantom model

The proposed task consisted in exploring an ex vivo swine colon tract containing straight and curved paths within a human abdominal phantom (Limbs & Things Ltd., Bristol, UK) arranged in a manner mimicking human anatomical angles and alignments of the entire colon tract, from the rectum to the cecum (850 mm in total length), as represented in Fig. 4. Colon tissue was harvested from a 50-kg pig, and the anal sphincter was included in the preparation. A fixed constant endoluminal pressure of 1 mmHg was maintained by the MAC during locomotion. A reference pressure sensor was connected to the cecum with a rubber tube, to assess the precision of pressure regulation. Six to eight colored beads, measuring 5 mm in diameter, were placed along the internal surface of the colon, and their number and position were blind to the operator and randomly changed in each trial. During experiments, a single tester was asked to navigate the capsule through the colon, starting from the rectum and reaching the cecum, identifying and removing each target visualized by using a polypectomy loop. Once removed, the bead was dropped nearby, the instrument was retrieved, and inspection was resumed. An opaque plastic covering was placed on top of the phantom to prevent the user from localizing the device within the colon by making use of the light coming from the camera LEDs. To promote magnetic dragging, an assistant was placed in charge of providing more tether whenever requested by the operator. A total of 12 physicians participated in the study. All trials were observed by an assistant who recorded the completion time and the number of colored beads reached and removed. Physicians involved in the tests had no previous experience with the proposed platform. Each session was preceded by a theoretical briefing on the MAC platform and practical training of 5 min using the transparent plastic tube shown in Fig. 3. This allowed the operator to get a feel for the movements

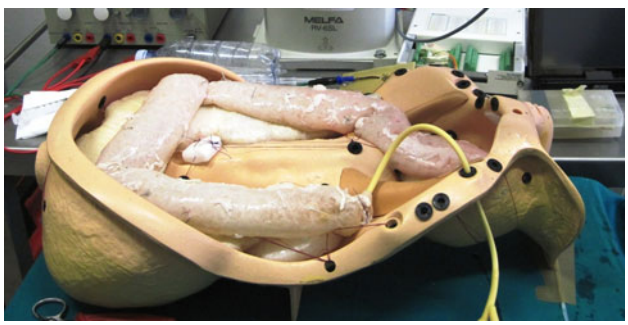

Fig. 4 Phantom setup for ex vivo trials

the MAC is able to perform. Since this is simply an initial feasibility study, extensive statistical analysis and rationale were not applicable. Descriptive statistics are specified as mean ± standard deviation and range of values of completion times and target percentages, as appropriate.

In vivo testing

To prove the proposed concept, the following qualitative outcomes were addressed during in vivo trials:

- Active locomotion, i.e., feasibility of navigation by magnetic dragging
- Diagnostic capabilities, i.e., user controllability of camera orientation
- Therapeutic capabilities, i.e., use of standard endoscopic tools (e.g., biopsy forceps, polypectomy snare, retrieval basket, grasper)
- Safety, i.e., absence of perforations on the lumen walls due to magnetic pinching
- Usability, i.e., impact of the robotic platform on the available space in the room

Distance traveled and time for insertion were the only two quantitative parameters acquired during the procedure. However, considering the difficulty associated with navigating a pig colon, because it is twice as long as the human colon and features a narrowing spiral, the relevance of these numbers may be questionable.

In vivo trials were performed on two domestic female pigs (average weight 30 kg). The experiments were executed in an authorized laboratory, with the assistance and collaboration of a medical team, in accordance with all ethical considerations and the regulatory issues related to animal experiments. After intravenous sedation of each animal and preparation of the bowel by water enemas, the experimental procedure was performed, maintaining 1 mmHg constant pressure inside the colon. Both animals were examined three times with the MAC, and different endoscopic tools were used to prove the feasibility of taking biopsies and interacting with lumen tissue. The endoscopist who controlled the robot in the two trials was already skilled with the platform, having taken part in the ex vivo trials. After the examinations, both animals were killed and the absence of perforations in the intestine was assessed by water filling (Fig. 5).

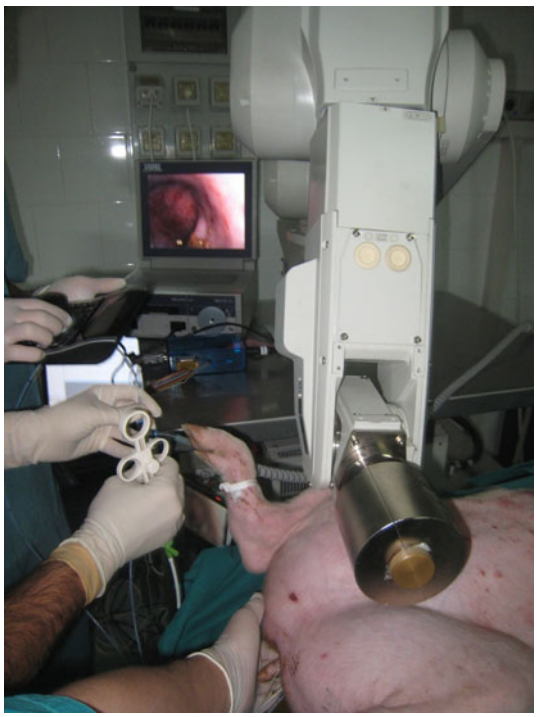

Fig. 5 Setup for in vivo trials. A first operator was controlling the MAC, while a second one was using the polypectomy loop

Results

Lower gastrointestinal phantom model

Performance of the endoscopic capsule was successfully assessed in terms of locomotion, steerability, and diagnostic capabilities. During the ex vivo robotic procedures, all system modules were found to work properly. For all procedures the operators successfully maneuvered the capsule to the end of the colon segment, removing each identified bead by using the polypectomy loop. The vision module enabled reliable feedback in inspecting the lumen and recognizing the beads. Good maneuverability of the capsule throughout the colon segment demonstrated the proper design of the multilumen tether and dimensioning of the magnetic link. In particular, friction of the tether on colon wall was not significant enough to hamper magnetic dragging, even in cases where the MAC was close to the cecum and several round bends were present along the length of the tether path. Pressure regulation error was always below 5% of the desired pressure.

The mean percentage of colored beads identified by each user with the MAC was 85 ± 11% (range 64–96%). All the identified beads were removed successfully using the polypectomy loop. A sequence of pictures during the removal of a bead is shown in Fig. 6. The magnetic link was always strong enough to hold the MAC in place during the removal procedure and during multiple insertions and retractions of the tool. The mean completion time for accomplishing the entire procedure, i.e., inspection and bead removal, was 678 ± 179 s (range 384–1,082 s). Bead removal required an average of 18 ± 3 s (range 11–25 s), including insertion and retrieval of the polypectomy loop.

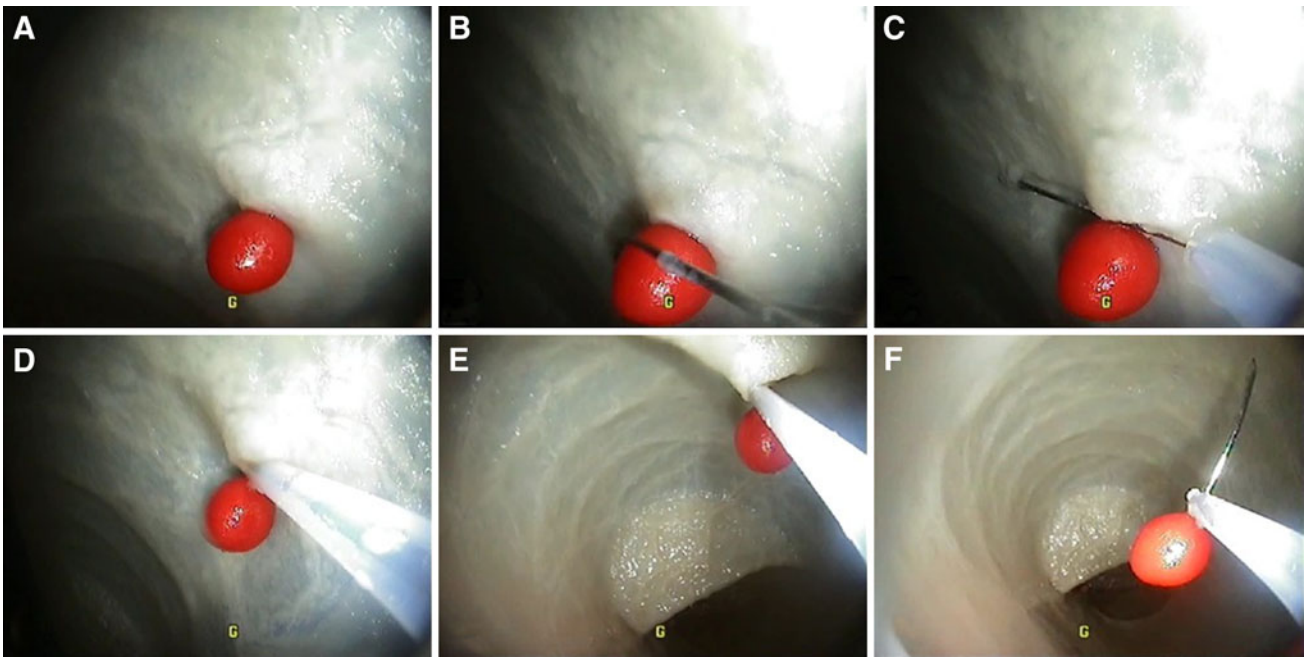

Fig. 6 Sequence from a bead removal process using the MAC and a standard polypectomy loop. First, the bead is localized (**A**), then the polypectomy loop is introduced in the operative channel and passed around the bead (**B**, **C**). Finally, the bead is pulled (**D**, **E**) until it comes out from the lumen wall (**F**)

In vivo testing

Concerning qualitative endpoints, magnetic dragging was effective and the operator was able to navigate the MAC in the pigs' intestines, successfully overcoming several bends (at least three) and folds. Steering of the camera's point of view was always reliable and easy to achieve. Thanks to the compact profile of the MAC, retroflection of the camera was easily achieved, as shown in Fig. 7A. All the tools were introduced and used successfully. A view of the MAC while introducing a retrieval basket is shown in Figs. 7B, and 8 shows a complete sequence for a biopsy. The magnetic link was always strong enough to hold the capsule during tool operation. The amount of tissue gathered during the biopsies exactly compares to what is usually collected when the procedure is performed with a traditional colonoscope. It is interesting to observe that, once the instrument is inserted in the channel, the MAC turns out to be more difficult to steer and control. This is mainly due to the increase in the stiffness of the tether. To cope with this, the instrument was introduced just before operation, so that the MAC was already facing the target. To improve controllability, the external magnet was placed closer to the pig's body. Introduction of an instrument once the MAC is retroflected was not possible, due to the sharp bending of the tether. The retrieval of the device at the end of the procedure was easy, smooth, and uninterrupted in all cases. No immediate mucosal damage, acute complications such as perforation, or delayed adverse consequences to the pigs were observed following application of the proposed method. Concerning usability, sometimes the profile of the external robotic manipulator conflicted with the body of the pig. Similarly to in traditional colonoscopy, the best use of this platform is achieved with the endoscopist controlling the robot through the user interface and an assistant operating the tool, as can be seen in Fig. 5. The average distance traveled was 800 ± 40 mm in an average time of 900 ± 195 s, including the time devoted to inserting the tool into the dedicated channel and operating the instrument.

Discussion

The first colonoscopy with a flexible instrument dates back 1963. The device was a modification of the gastroscope introduced by Hirschowitz a few years earlier [28]. Since that time, there have been substantial technological improvements, particularly in image resolution and video technology. However, the basic features of the colonoscope have progressed little [20]. In particular, the instrument is still advanced in the colon solely by pushing from behind. Often, the direction of the force used to advance the colonoscope is at a sharp angle to the desired direction of advancement of the tip, or in a completely opposite direction. The only way the colonoscope advances under these circumstances is by pushing on the colonic wall, thus creating wall tension and a counterforce that propels the

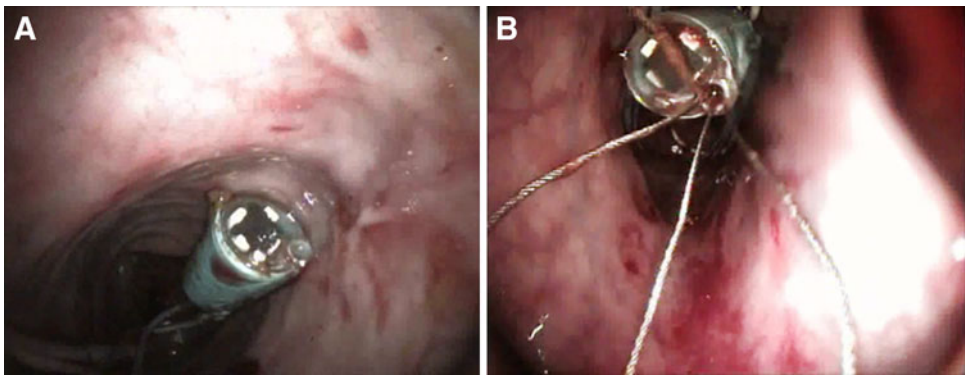

Fig. 7 Snapshots from in vivo test: (**A**) the MAC in a retrograde position, and (**B**) the MAC ejecting a standard endoscopic retrieval basket

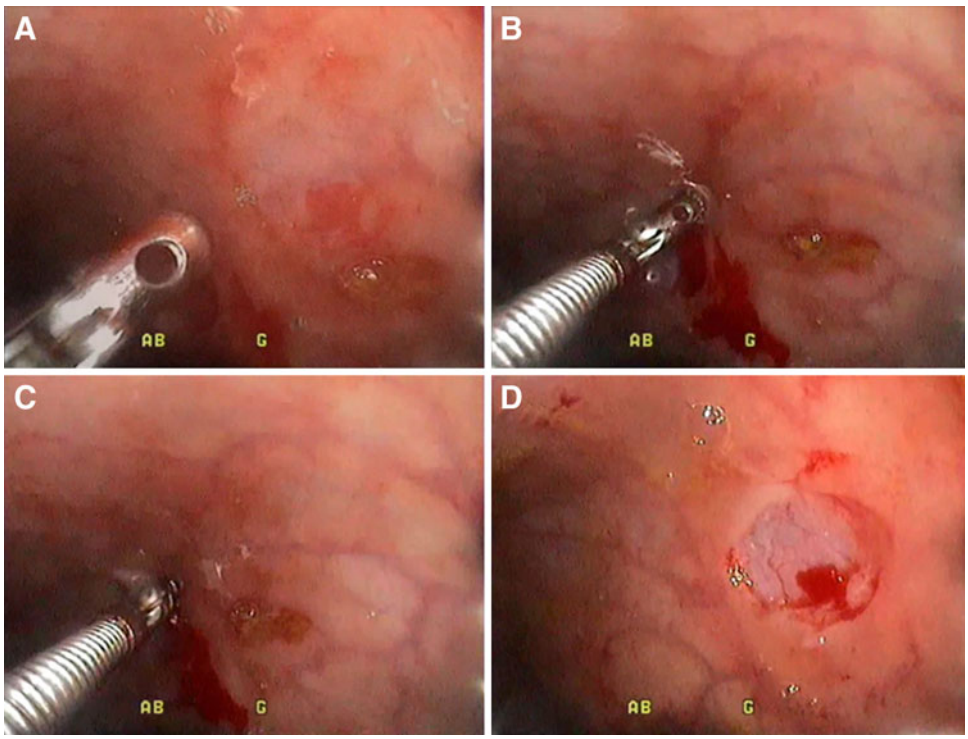

Fig. 8 Sequence from a biopsy. First, the site is localized (**A**), then the forceps are pushed towards the lumen wall (**B**), tissue is grasped in the jaws (**C**), and biopsy is performed. The site of the biopsy is then inspected (**D**)

colonoscope forward. This can lead to loop formation and to shearing tears of the colon wall by the shaft. As correctly stated in [29], the physical nature of the colonoscope needs to change if the procedure is to improve.

The novel approach proposed in this paper comes from authors' experience in magnetic locomotion and steering of wireless capsule endoscopes (WCE) [24, 25]. The main limit of this approach to WCE was related to the lack of tissue insufflation, which prevented effective magnetic control of the wireless device. However, by simply introducing a thin tether for insufflation and giving up the oral access in favor of the anal one, an effective platform for painless colonoscopy can be achieved. Moreover, the same channel can be used to introduce an endoscopic instrument, to irrigate the tissue, and to drain fluids. Having the possibility to gather biopsies and to remove polyps makes the proposed technology a potential alternative to colonoscopy.

Similarly to the Colonosight [20], the propelling force is exerted at the tip of the instrument (as in the case of a locomotive pulling a train from the front), and thus the vector of the propelling force is in the same direction as tip advancement. This feature facilitates locomotion and prevents loop formation, and, potentially, may reduce the risk of colon perforation. Thanks to the magnetic orientation of the camera, steering cables running inside the shaft are no longer required. This enables a dramatic reduction in the external diameter of the endoscopic device body down to 5.4 mm. The capsule-like frontal unit is the only part still having 11 mm external diameter. Such a relevant reduction in size allowed the MAC to also work in retroflected mode, which may be beneficial to explore human colon folds from an additional point of view.

Because of the variability of the colonic anatomy from patient to patient, colonoscopy may be technically difficult

to perform and teach, and lesions may be localized inaccurately by the endoscopist [9]. Thanks to the robotic approach, the proposed platform has the potential to make colonoscopy an intuitive procedure, replicating the paradigmatic shift introduced by robotic surgery [30]. Increased precision of movement, motion scaling, tremor compensation, intuitive user interface, and steepening of the learning curve [26] are just some of the improvements brought about by robotics, toward the futuristic vision of automated procedures where a single nurse will be enough to carry out several robotic examinations. It is also worth mentioning that the LED lighting source eliminates the need for fiber optics and a separate external light source.

The porcine experiments in this study were preliminary, and the end points were qualitative observations of diagnostic and therapeutic efficacy and mucosal damage due to magnetic pinching. Other limitations of the study are that the porcine anatomy does not simulate haustral folds and that it was a proof-of-concept study and not a comparative study. Despite these methodological limitations, the quality of control over the camera and the ability to operate standard flexible instruments were remarkable and established the proof of principle and basic safety for this device. Subsequent animal and human trials will require comparison with standard colonoscopy, to quantitatively assess the reduction in pain, the decrease in learning time, and the effectiveness of using endoscopic tools for therapeutic goals.

From a technological standpoint, a relevant, yet feasible, improvement would be to make the MAC completely disposable. Indeed, disinfection of endoscopes is a multistep, difficult process, being operator dependent and often inconsistent, making transmission of infections among patients after endoscopic procedures a relevant issue [20].

Finally, a torque-force feedback at each joint of the robotic arm would prevent any possible collision with the patient and the staff operating in the room, improving the safety of the platform.

Conclusions

Use of the MAC platform in ex vivo and preliminary animal studies, designed to determine the safety and effectiveness of the device, indicates that it is safe and operates effectively in a manner similar to a standard colonoscope. These studies served to demonstrate the platform's added advantages of reduced size, front-wheel drive strategy which reduces the risk of looping and perforations, robotic control over locomotion and orientation, and the potential to become a disposable instrument. Obviously, additional studies are mandatory to assess its efficacy in vivo, as well as head-to-head comparison with standard colonoscopy.

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Disclosures Authors P. Valdastri, G. Ciuti, A. Verbeni, A. Menciassi, P. Dario, A. Arezzo, and M. Morino have no conflicts of interest or financial ties to disclose.

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