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Wireless therapeutic endoscopic capsule: in vivo experiment

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Background and study aim: Capsule endoscopy is becoming well established as a diagnostic technique for the gastrointestinal tract. Nevertheless swallowable capsule devices that can effectively perform surgical and therapeutic interventions have not yet been developed. Such devices would also be a valuable support for natural orifice transluminal endoscopic surgery (NOTES). The objective of this study was to assess the feasibility of using a swallowable wireless capsule to deploy a surgical clip under remote control.
Materials and methods: A wireless endoscopic capsule, diameter 12.8 mm and length 33.5 mm, was developed. The device is equipped with four permanent magnets, thus enabling active external magnetic steering. A nitinol clip is loaded on the topside of the capsule, ready to be released when a control command is issued by an external operator. Repeated ex vivo trials were done to test the full functionality of the therapeutic capsule in terms of efficiency in releasing the clip and reliability of the remote control. An in vivo test was then carried out in a pig: the capsule was inserted transanally and steered by means of an external magnetic arm towards an iatrogenic bleeding lesion. The clip, mounted on the tip of the capsule, was released in response to a remote signal. The procedure was observed by means of a flexible endoscope.
Results: A wireless capsule clip-releasing mechanism was developed and tested. During ex vivo trials, the capsule was inserted into the sigmoid section of a phantom model and steered by means of the external magnet to a specific target, identified by a surgical suture at a distance of 3 cm before the left flexure. The capsule took 3 to 4 minutes to reach the desired location moving under external magnetic guidance, while positioning of the capsule directly on the target took 2 to 3 minutes. Successful in vivo clipping of an iatrogenic bleed by means of a wireless capsule was demonstrated.
Conclusions: This study reports the first successful in vivo surgical experiment using a wireless endoscopic capsule, paving the way to a new generation of capsule devices able to perform both diagnostic and therapeutic tasks.

Introduction

Endoscopic tools for diagnosis and treatment of the alimentary tract have evolved steadily over the past few decades. The introduction of new technologies for flexible endoscopy, such as optical fibres, digital optical sensors, new mechanical designs, and additional therapeutic features have allowed researchers to push the capabilities of endoscopic procedures towards new frontiers [1]. In addition to this, novel miniaturized devices for endoluminal robotic surgery have been developed, thanks to the technological achievements of recent years in the field of medical robotics [2]. Current technology allows the deployment of small, agile, remotely controlled machines with the ability to perform simple surgical tasks [3]. In particular, the platform presented by Lehman et al. [4] takes advantage of a set of miniature in vivo surgical robots that can be placed into the peritoneal cavity through an abdominal incision, or through a gastrotomy after entry into the stomach from the esophagus. However, although this approach may also show great promise for wireless applications, the size of the devices still prohibits scenarios where the patient can swallow the surgical robotic unit.
The rapid convergence of several technological advances, such as miniaturized actuators and mechanisms, reliable telemetric linking, batteries with high energy density, and "smart" solutions for steering and locomotion of biomedical devices, as applied in the revolutionary field of wireless capsule endoscopy (WCE), has enabled

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Fig. 1 **a** The clipping capsule loaded with the over-the-scope clip (OTSC). **b** The human-machine interface (HMI) is a personal computer. The USB transceiver (bottom left corner) allows wireless communication with the capsule.

the development of swallowable devices that can perform practical surgical procedures. In a previous work [5], the present authors demonstrated the feasibility of a "walking" robotic capsule for active WCE. This was made possible by developing miniaturization of both mechanisms and advanced actuators. By combining those features with a dedicated telemetric solution, specifically designed for data transmission from the gastrointestinal tract [6], and an external magnetic steering approach [7], we developed a wireless device able to deploy a surgical clip onto a selected gastrointestinal location under external guidance. This novel tool may be used to treat gastrointestinal hemorrhage in a completely noninvasive way [8].

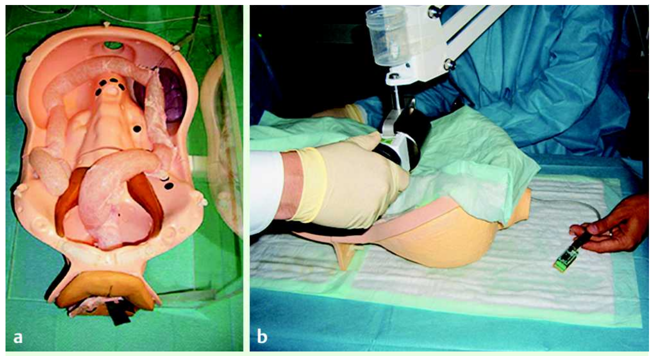

Fig. 2 **a** Lower gastrointestinal (LGI) tract phantom before the experiment. **b** LGI phantom during the experiment, with the external permanent magnet and the transceiver clearly visible.

Materials and methods

The proposed device (**Fig. 1 a**), has a cylindrical shape, with a diameter of 12.8 mm and a length of 33.5 mm, and incorporates an electromagnetic motor, a wireless bidirectional communication platform, and four permanent magnets arranged symmetrically on the external surface.

A purpose-developed mechanism, actuated by the onboard motor, releases a surgical clip on receiving the appropriate command from the external human–machine interface (HMI), running on a personal computer (**Fig. 1 b**). A dedicated transceiver, connected to a standard universal serial bus (USB) port on the computer, allows wireless communication with the robotic capsule.

The surgical clip [8,10] used here (over-the-scope clip [OTSC]), is made of nitinol, a biocompatible superelastic shape-memory alloy, and it is designed to be placed over the tip of a flexible endoscope without limiting the field of view of the imaging system. It is important to note that a slightly different design of the mechanism actuated by the motor would allow the deployment of different clips [11] or the accomplishment of a different surgical task, such as biopsy or controlled drug delivery, depending on the intended application.

Although the current capsule prototype does not include an imaging system, an appropriately sized space (about 300 mm^3) has been allocated in the capsule's front area, in between the jaws of the clip, for the future integration of a camera module having almost the same volume of that used in the Given Imaging SB1 [12]. This would not affect the final size of the device.

In the procedure as envisaged, first the clip will be loaded onto the capsule, then the device will be swallowed by the patient. Once it reaches the target area, the position of the capsule will be precisely adjusted vis-à-vis the treatment site by means of external magnetic steering. An external permanent magnet (Sintered NdFeBmagnets; B&W Technology & Trade GmbH, China) is currently used for this purpose. This is a cylinder with a diameter of 60 mm and a length of 70 mm placed on a passive hydraulic passive arm, and which is controlled manually by the medical operator, in the fashion of an ultrasound probe. The arm allows high precision rotations and tridimensional movements of the magnet in the space surrounding the patient's abdomen. With this kind of external navigation, the capsule can be maneuvered through the entire colon with high precision and good reliability.

The correct positioning of the capsule can be assessed using the onboard visualization system or by external imaging systems, such as fluoroscopy. Once the clipping capsule is correctly positioned with respect to the target, the releasing command can be issued by the HMI and wirelessly transmitted to the capsule, which immediately deploys the clip. As soon as this procedure is accomplished, the capsule can be magnetically navigated away from the operative area and left in the gastrointestinal tract for natural expulsion.

In an initial set of ex vivo trials using a phantom model, we assessed the functionality of the wireless therapeutic capsule and the steerability using the magnetic arm. We then validated the therapeutic capsule by means of an in vivo experiment.

Lower gastrointestinal phantom model

The lower gastrointestinal (LGI) tract model is a standard training phantom (**Fig. 2 a**).

It consists of an anatomical model of the abdominal, chest, and pelvic cavities with additional accessories for the simulation of organs (e.g. liver, spleen, and sphincters). In addition, the model has fixtures aligned in the shape of human mesenteries for the attachment of ex vivo animal intestine. In the present trials,

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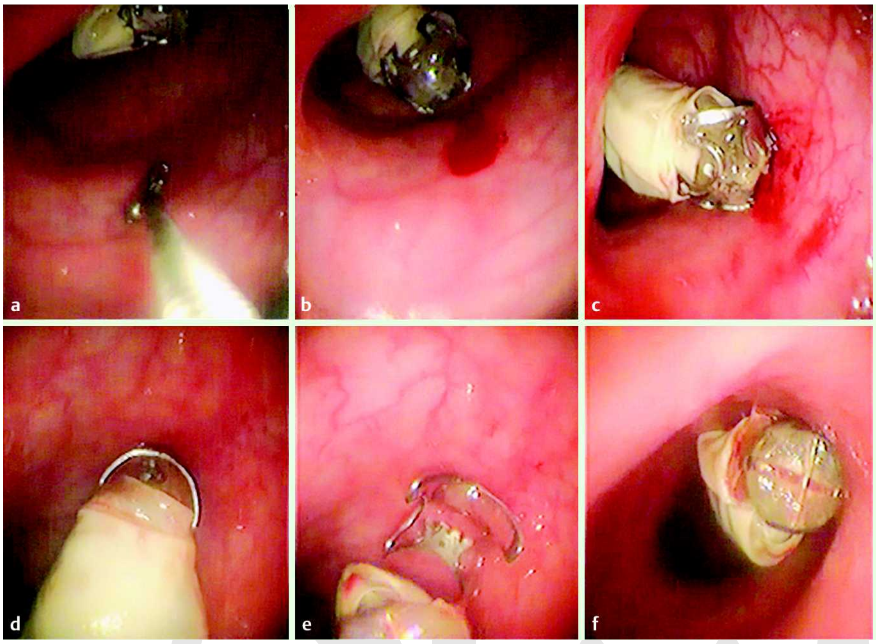

Fig. 3 **a** Biopsy grasper inducing a bleeding lesion in the colon wall; **b** the capsule approaching the target; **c** magnetic positioning of the capsule on the target; **d** capsule before release of the clip; **e** deployment of the clip; **f** capsule without the clip, moving away from the target.

fresh porcine colon was attached along the fixtures and set up to simulate typical anatomical characteristics such as the angles and alignment of the sigmoid curve and the acuteness of the left colonic flexure.

As mentioned above, the external magnet was fixed to the end of a massive metal arm-like framework (**Fig. 2b**). The purpose of the arm was to facilitate simple positioning of the magnet by the clinician.

The robotic capsule was prepared for introduction into the colon with a latex cover being used to secure waterproofing. The capsule was inserted into the sigmoid section of the LGI phantom and steered by means of the external magnet to a specific target, identified by a surgical suture at a distance of 3 cm before the left flexure. After the target had been approached, the capsule head was pushed upright into the colonic wall. The pushing maneuver was performed by reducing the distance between the external magnet and the capsule. The releasing signal was then issued through the HMI and the clip was deployed. For guidance and observation, a conventional flexible endoscope (Pentax, New Jersey, USA) was introduced into the colon and maneuvered to the suture knot.

In vivo animal model

After completion of the phantom trials, the capsule was assessed in an in vivo experimental session, with the aim of testing the effectiveness of approaching a bleed in the colon, finely positioning the capsule before releasing the clip, remotely controlling the deployment of the surgical clip, and finally, moving the wireless device away from the operative region.

The feasibility study was carried out a domestic female 50-kg pig. The experiments were done in an authorized laboratory, with the assistance and collaboration of a specially trained medical team, in accordance with all ethical considerations and the regulations related to animal experiments. The capsule was observed by using a flexible endoscope, which was kept at some distance from the operative location, in order not to affect the positioning and movement of the wireless capsule.

After intravenous sedation of the animal and preparation of the bowel by water enemas, the capsular device was inserted transanally up to 15 cm from the anus. A bleeding lesion was induced by using a biopsy grasper (**Fig. 3a**).

The capsule was moved towards the target by external magnetic locomotion (**Fig. 3b**). As soon as the capsule was correctly positioned (**Fig. 3c, d**), the releasing command was delivered, the clip was placed (**Fig. 3e**) and the capsule was moved away under magnetic control (**Fig. 3f**).

Results

LGI tract phantom model

The wireless therapeutic capsule was successfully assessed and showed that all functions were working correctly. The remotely controlled clip release and movement and positioning of the capsule were demonstrated in the experiment. The clip release occurred instantly, and moving of the capsule was effective and fast. The positioning of the capsule was precise and the designated target could be reached. It took from 3 to 4 minutes to reach the desired location, while the precise positioning of the capsule directly against the marker was accomplished in a time ranging from 2 to 3 minutes. Two sessions of five trials each were carried out, and all the clips were successfully released.

In vivo animal model

The locomotion and positioning of the capsule were as good as in the ex vivo experiment. The clip was released successfully onto the desired target. After release of the clip, the capsule was easily moved away by magnetic locomotion to the rectum. The clip was still in place at the end of the experiment. The amount of tissue grasped was satisfactory, even though it was less than the amount grasped when the standard endoscopic clip releaser is used [10].

A single in vivo trial was performed, since our main goal was to assess the feasibility of the proposed approach. Further in vivo tests will be carried out when an imaging system is incorporated in the capsule.

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Discussion

To the best of the authors' knowledge, this paper is the first presentation of a completely wireless therapeutic capsule for treatment of diseases in the gastrointestinal tract. In this particular application, wireless clip release was demonstrated; however the same technological platform can be easily adapted to other tasks by simple modification of the internal mechanism.

The current version of the capsule (cylindrical shape, diameter of 12.8 mm and length 33.5 mm) is not yet a swallowable size. However, because the design is fully scalable [8], the next prototype will be almost half of the size, thus enabling oral ingestion. A visualization system has not been implemented in the current prototype, but the required volume has been allocated in the capsule to allow future integration without any significant increase in size.

The results reported in this paper look promising for a wireless treatment of bleeding in the gastrointestinal tract; however further investigation is needed to clarify whether the released clip will have an effective hemostatic capability in real situations.

The proposed device can also be used to mark suspect areas of the gastrointestinal tract for natural orifice transluminal endoscopic surgery (NOTES) procedures, or could be used for port closure. For this purpose the capsule would need to be equipped with a tissue manipulation tool in order to approximate the tissue within the jaws of the clip.

A possible scenario can be envisaged whereby preoperative images, acquired by magnetic resonance imaging or tomographic scanning, are exploited together with robotic steering by the external permanent magnet [13]. The patient would need only to swallow the surgical pill and then a fully automated procedure would be started, thus minimizing invasiveness and discomfort. This approach would have a revolutionary potential similar to that of WCE, since it would enable, for the first time, surgery by swallowable untethered devices.

Furthermore, the proposed approach would mean that the endoscopic capsule could be stitched or clipped to the wall of the stomach, so that prolonged examination of bleeding ulcers or varices would become possible. Long-term endoscopy with wireless endoscopes attached to the wall of the gut seems an obvious way to improve the management of gastrointestinal bleeding and other disorders, as envisaged by Swain [14].

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Competing interests: Marc O. Schurr is among the founders of Ovesco Endoscopy and holds shares in the company.

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