Wireless Robotic Capsule for Releasing Bioadhesive Patches in the Gastrointestinal Tract

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A novel, miniature wireless robotic capsule for releasing bioadhesive patches in the gastrointestinal (GI) tract was designed, fabricated, and preliminarily tested. In particular, the assembled prototype was successfully navigated in a GI phantom, up to a target site where the release mechanism was verified. Then, deployment of a bioadhesive patch onto ex vivo porcine tissue was accomplished, and patch adhesion strength was verified. The main application of the present system is the deployment of anchoring patches for miniature robotic modules to be operated in the targeted anatomical domain. Such an innovative application stems from the wise blend of robotics and bioadhesion. Obtained results, which are consistent with previous investigations by the group, confirm the viability of the adopted bioadhesives for the envisaged anchoring tasks. The present feasibility study complies with the spirit of minimally invasive, wireless diagnosis, and therapy, and provides a preliminary contribution for their advancement. [DOI: 10.1115/1.4025450]

1 Introduction

Current medical research is increasingly moving toward minimally invasive approaches for both diagnosis and therapy, and robotic capsule endoscopy is one of the medical technologies that best represents this trend. Starting from imaging and telemetry capsules, nowadays robotic capsule endoscopes possess active locomotion capabilities for reliable control and they can also perform some simple interventional tasks [1,2].

As regards locomotion, different methods have been proposed, essentially relying on characteristic features of the working district. Even if, for tubular geometries, legs [3] and paddle-type mechanisms [4] activated by on-board micromotors seem feasible, magnetic actuation has demonstrated to be more promising thanks to off-board powering [5]. For larger regions of the gastrointestinal (GI) tract such as the stomach, wall-to-wall locomotion in a liquid-filled environment has been recently proposed, either by using internal micropropellers [6] or magnetic actuation [7,8]. Moreover, continuous progress in microelectromechanical systems (MEMS) technologies has permitted us to integrate in the capsules many diagnostic tools, including sensors for *p*H [9,10], pressure and temperature [11], as well as for blood detection (see also [2]). Along this developmental stream, a further challenge for active capsule endoscopy is the integration of on-board interventional capabilities. In this regard, a few applications have already been identified and assessed, namely biopsy [12,13], suturing/clipping [14], and local drug delivery/medication [15,16].

Anchoring capabilities represent a valuable asset, not only for specific diagnostic systems (such as [9], where adhesion is achieved by suction), but also for minimally invasive interventional devices for natural orifice transluminal endoscopic surgery (NOTES) [17]. For instance, early attempts to achieve safe anchoring of miniature robotic modules onto the abdominal cavity wall by means of magnetic forces have been recently documented [18]. Nonetheless, chemical anchoring mechanisms, based on biocompatible materials, have been also developed, able to effectively and safely interact with GI tissues [19–21]. Hence, a wise integration between wireless capsule technology and such a bioadhesive means holds promise to be a winning blend for local release of enhanced anchoring approaches, especially for remote body districts.

In light of these points, we propose a preliminary investigation of a swallowable wireless robotic capsule for deployment of a bioadhesive patch in the GI tract. In more detail, the proposed capsule capitalizes on remote actuation (magnetic link is used for navigation [22] and for contact establishment prior to patch release), while RF signals trigger a purposely designed, SMA-based release mechanism. It is worth remarking that, contrarily to, e.g., [8,9] which deliver liquids or powders, a main asset of the present device is the effective deployment of a planar patchlike structure.

2 Capsule Overview

2.1 Main Design Issues. Main capsule requirements and desired features for bioadhesive films release in the GI tract were preliminarily identified as follows.

Capsule Size. The capsule must be small enough to be swallowed; a reference capsule diameter is around 15 mm [2]. However, since the proposed mechanism needs to be first demonstrated and in view of nontrivial fabrication steps, it seemed reasonable to address a slightly larger prototype having 19 mm diameter and 50 mm length. Scalable technologies were nonetheless adopted, so as to enable further miniaturization.

Bioadhesive Patch Deployment. Bioadhesive patches are planar, compliant structures to be adhered onto GI tissue [19–21]; hence a plate supporting such planar structures must be integrated into the capsule. Moreover, for effective adhesion to take place, a large enough patch surface must be available. More precisely, nearly 1 cm^2 is needed for the anchoring force to be on the order of 1 N [20]; such a force value can be conservatively assumed to be enough for anchoring the envisioned swallowable modules. By taking advantage of the actually fabricated, scaled up prototype, a 15×25 mm^2 patch supporting plate (PSP) was then designed. Additionally, patch exposure prior to application must be minimized in order to avoid degradation of bioadhesion characteristics. Hence, the PSP was fully encapsulated within capsule case, and a release mechanism was designed for its ejection, also exploiting two ejectable shells (ES). For preserving bioadhesive properties, the capsule needs not be watertight until the ES are opened: it suffices that the devised sealing of the ES (see the "closed" configuration in Fig. 1) contains potential bodily fluids leakages; thus avoiding detrimental patch swelling leading to hampered adhesion.

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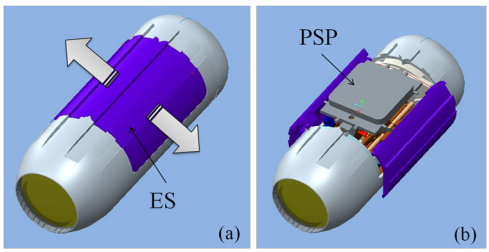

Fig. 1 (*a*) Schematic view of the capsule "closed" configuration adopted during locomotion: ejectable shells (ES) are aligned with capsule surface. (*b*) Schematic view at patch release: ES are ejected and patch supporting plate (PSP) is displaced for patch deployment.

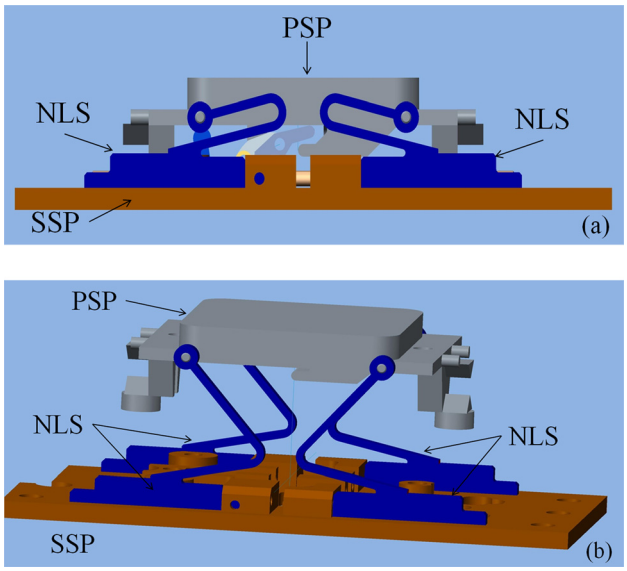

Fig. 2 PSP release: (*a*) starting from a preloaded configuration and (*b*) PSP is released by remotely activated triggering

Preliminary design considerations suggested aligning the PSP with a sagittal section of the capsule, so as to maximize PSP surface area. The associated release mechanism was therefore constrained to a working volume of around 4000 mm^3.

Enhanced Remote Operability. The capsule must be safely and accurately navigated to the target site. Magnetic locomotion appeared as a suitable option for the capsule system, for manifold reasons. Besides capitalizing on group expertise [22], magnetic locomotion allows for fast and accurate navigation to the target. Moreover, tissue scraping prior to patch release may represent a desired option in specific applications, namely in the presence of excessive liquid/mucosal layers potentially detrimental for adhesion. Hence, besides introducing suitable grooves on the ES, the magnetic link was designed so as to also enable a roll degree-of-freedom (DOF) devoted to tissue scraping (Fig. 1). Furthermore, the magnetic link is functional to the establishment of adhesion right after patch deployment. In particular, 2 cylindrical, diametrically magnetized N35 NdFeB permanent magnets (1.21 T magnetic flux density) with 13 mm diameter and 2.5 mm length were integrated at the ends of the capsule body (these sizes are compatible with a volume budget of around 1500 mm^3, as derived from preliminary design estimates). These internal magnets were coupled with an N35 NdFeB external permanent magnet (EPM). The chosen magnets were suitable for compensating capsule weight (assumed around 20 g) over a characteristic working distance of about 10 cm [23]. The EPM was manipulated through a

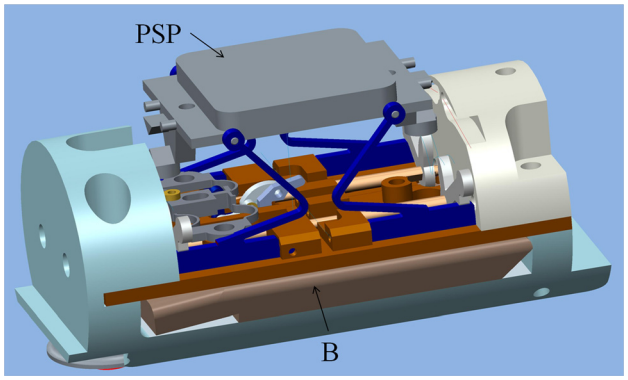

Fig. 3 Assembly of the patch release mechanism. On-board battery (B) is also sketched.

robotic arm (RV-3SB, Mitsubishi Electric, Japan), to improve accuracy/repeatability of capsule poses, and to implement closed-loop strategies for safe interaction with tissue.

On-Board Vision System. On-board vision systems for tissue inspection prior to patch release were foreseen. Incorporation of such a module was considered out of the scope at the present feasibility stage; nevertheless a relevant portion was left in the prototype volume budget (around 3000 mm^3), arranged in light of previous successful implementations carried out by the group (Vector European project, www.vector-project.com).

In light of the above considerations, the design of the PSP mechanism was addressed, together with its triggering strategy. This way, a working prototype was achieved, suitable for preliminary demonstration.

2.2 Patch Release Mechanism. A preloaded mechanism was adopted in order to contain power cost for patch release. In more detail: (i) an elastic preloading was designed for PSP holding prior to release (Fig. 2); (ii) PSP release was associated with a remotely activated triggering mechanism; and (iii) patch deployment onto tissue was achieved by synchronizing PSP lift with suitable displacement of the ES. With reference to Fig. 3, it should be noticed that part of the volume originally budgeted for PSP release mechanism (around 1200 mm^3) was actually devoted to battery hosting (see Sec. 2.3).

As regards elastic preload, 4 nonlinear springs (NLS) were mounted on a structural supporting plate (SSP), as in Fig. 2. The SSP serves as an accurate support for the whole release mechanism. Once adopted Nitinol as material and assuming a 0.4×0.5 mm^2 rectangular cross section, NLS shape was preliminarily defined so as to obtain volume packing in the preloaded configuration, while properly bearing bending stresses. In particular, the latter point was verified by accepting a maximum von Mises stress (as computed by the finite-element software Ansys, Canonsburg, Pennsylvania, USA), around 75% of the material yield limit.

As regards triggering of the plate release mechanism (Fig. 4), a shape memory alloy (SMA) wire 0.13 mm in diameter was considered; it has to be heated upon closure of the on-board circuit, by Joule effect. Corresponding SMA traction force was up to 2 N, as experimentally determined through an auxiliary test bench (not reported here for brevity). Such a traction force was used for releasing a securing hook (SH), which enforced the preloaded configuration by implementing an articulated quadrilateral (4-bars) constraint. Furthermore, SMA contraction implied the rotation of the left pulley (LP in Fig. 4(*a*)), engaging with a mediating spring (MS) through a connecting rod (CR) as in Fig. 4. A safety stop (SS in Fig. 4(*a*)) was introduced for containing pulley rotation, and the MS shape was defined based on fastening needs, while allowing for the necessary stroke to retract the SH. Moreover, SMA actuation was mainly chosen for the sake of

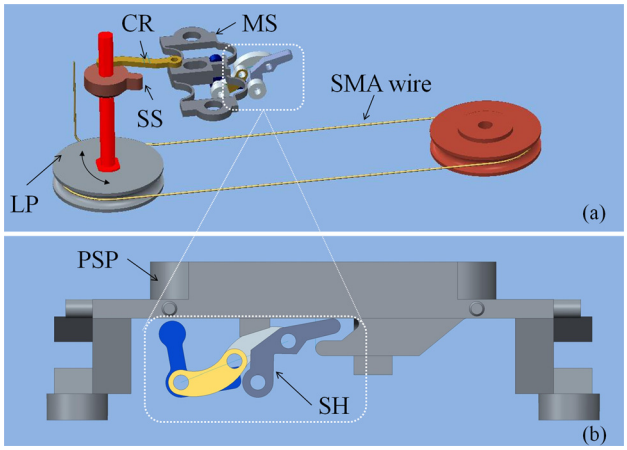

Fig. 4 (*a*) Triggering mechanism for PSP release. (*b*) Detail of PSP locking in the preloaded configuration.

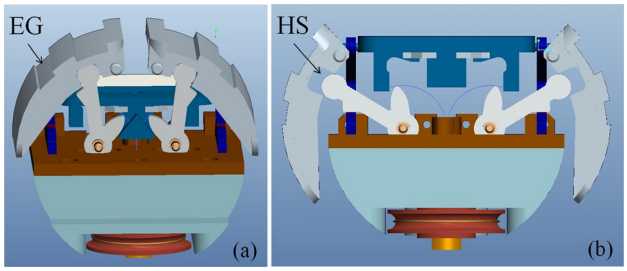

Fig. 5 Ejection mechanism of the ES. The external grooves (EG), for tissue scraping through capsule roll, are also labeled.

compactness (pulleys interaxis distance and radius were maximized in order to maximize wire contraction) and simplicity, also in view of the short actuation time (around 0.1 s, well below the characteristic time needed for patch adhesion, see Sec. 4).

Finally, as regards patch deployment, PSP lift was supported by two cylindrical pivot guides. Moreover, ejection of the ES was geometrically coupled to PSP lift by means of levers/pins engaging with corresponding hosting seats (HS in Fig. 5) on the internal portion of the ES.

2.3 On-Board Electronics. A circular electronic board (10.8 mm diameter, 2.3 mm thickness, 0.3 g mass), previously in-house developed and tested [24], was integrated in the rear of the capsule. It contains a wireless microcontroller (CC2430, Texas Instruments, Dallas, TX, USA) suitable for bidirectional communication to an external circuit. Upon receiving an RF signal (carrier frequency 2.4 GHz, Zig-Bee protocol) by means of a whip antenna embedded in the back part of the capsule, the microcontroller closes a circuit. The circuit is powered by a commercial lithium ion polymer battery (LP50 from Plantraco, Canada), which is compactly hosted close to the SMA wires (Fig. 3). The adopted battery ($22 \times 12 \times 4$ mm^3) is based on a 3.7 V LiPo cell with a nominal capacity of 50 mA h. Upon circuit closure, a peak value of 320 mA was achieved for the SMA heating. It is worth mentioning that LiPo batteries are being used for wireless capsule endoscopic applications [25], yet wireless power transmission can be a valuable alternative [26] in view of safety/biocompatibility issues. The adopted arrangement prevents from possible contacts between electronics and bodily fluids. Also battery and SMA wire are protected, since potential leakages might only occur at pulleys pins bushings, yet they are minimized by tight tolerances.

2.4 Bioadhesive Patches. The bioadhesive polymeric films proposed for biomedical robotics applications in [19–21] were considered for the anchoring strategy. For instance, the authors managed to successfully anchor surgical assistive tools to the gastric cavity through such mucoadhesive patches [20,21]. For the GI application here considered, bioadhesive patches were prepared according to the method described in [19].

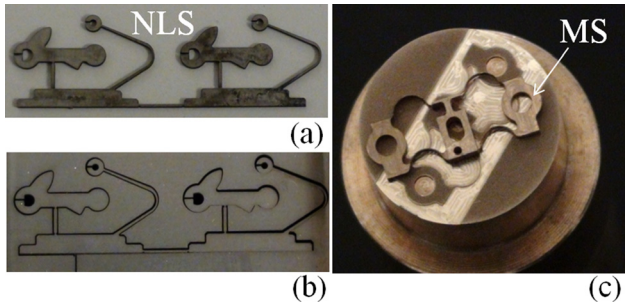

Fig. 6 (*a*) Nonlinear springs and (*b*) shaped in the Nitinol sheet. (*c*) Mediating spring, leaned on a dedicated fixturing tool.

3 Capsule Fabrication

Relevant capsule fabrication steps involve both conventional and precision micromachining processes. In particular, the SSP was machined in 7075 aluminum, for ease of machinability and by taking advantage of its lightness. Upon fixturing on the CNC 5 axis micromilling machine (HSPC, KERN, Germany) chuck, all relevant surfaces were machined on one side. The piece was then cut to the proper thickness by lathe (EMCOMAT 17D, EMCO, Austria), and refixtured on the KERN so as to machine the opposite side.

The NLS were manufactured by using the high-precision CNC wire EDM machine (AP 200 L, Sodick, Japan) (Fig. 6). A 100 μm diameter piano wire with brass coating was employed for cutting the NLS profile. Nitinol was chosen for its superelastic properties (approximately 8% recoverable strain) at both room and body temperature.

As regards triggering, both SH and CR were machined using wire EDM. AISI 316 stainless steel was chosen for parts subjected to non-negligible mechanical stresses to enhance device robustness and lifetime. Furthermore, the MS was fabricated using both the HSPC KERN and wire EDM. Brass was adopted for such spring, since it exhibits good machinability and resistance to wear.

Finally, levers and pins for ES ejection were fabricated in steel by means of the wire EDM machine, whereas cylindrical pivots guides were machined in brass on a traditional lathe. Furthermore, capsule case and ES were fabricated in UV photopolymerization resin, by using the 3Dsystems (Projet, HD3000, USA) high resolution rapid prototyping machine (layer thickness ≤ 30 μm).

4 Capsule Experimental Assessment

The obtained robotic capsule prototype is shown in Fig. 7, while Fig. 8 shows the assembly of the main components of the plate release mechanism. Assembly consisted of several steps: pulleys and SMA rod were first mounted on the capsule case; then SH and CR were separately assembled and inserted into the capsule; next, the NLS were mounted, followed by the PSP and the ES.

Main on-board electronic components are shown in Fig. 9, while the robotic arm used for moving the permanent magnet is shown in Fig. 10, together with the magnetoresponsive capsule. Finally, Fig. 11 shows the bioadhesive patch (about 0.5 mm thick) loaded on the capsule PSP.

We first addressed capsule navigation and PSP release (without bioadhesive patch) through a preliminary in vitro test session, by using the GI phantom shown in Fig. 12 (images were taken by

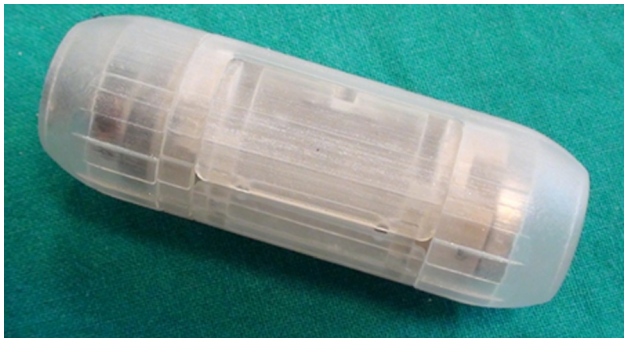

Fig. 7 Robotic capsule prototype (closed configuration)

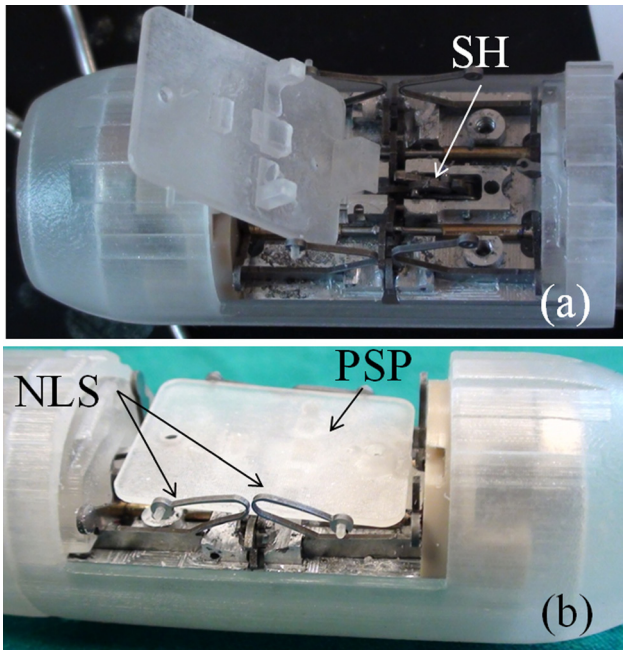

Fig. 8 Robotic capsule prototype: (*a*) subassembly of the plate release mechanism, with a partly mounted PSP (for ease of visualization); and (*b*) with the PSP in the preloaded configuration

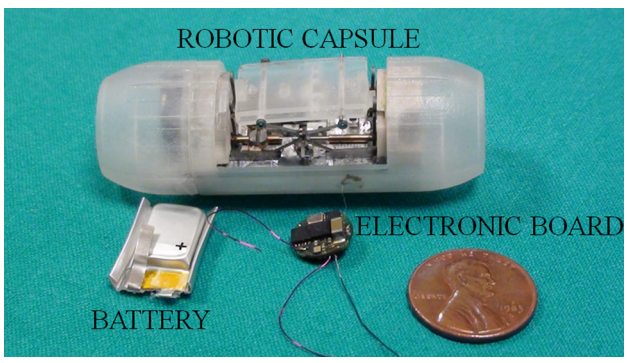

Fig. 9 Main on-board electronic components

means of a gastroscope). More precisely, the capsule was robotically navigated to a target site of the phantom, and tissue scraping was performed by driving capsule roll motion. Then, PSP release was successfully achieved; thus verifying the conceived release mechanism.

A subsequent test session involving ex vivo porcine GI tissue was carried out, aimed at assessing bioadhesive patch release. In particular, a custom-made phantom was preliminarily lined with a freshly excised porcine GI tissue, and the capsule was robotically navigated up to a target site. PSP release mechanism was then triggered, and magnetic link was enhanced (by decreasing the distance between capsule and external magnet) so as to tightly keep the capsule in contact with the GI tissue for nearly 3 min (time derived from [20]). We also verified that the patch was thin enough for adhering onto the PSP without slipping during navigation, while allowing for easy detachment from PSP once stamped onto tissue. Figure 13 shows some details of the successful patch deployment onto tissue. It can be noticed that adhesion effectively took place over a fraction of the patch area, also depending on tissue corrugation (this aspect is fully consistent with real application conditions). We nonetheless verified that the obtained adhesion was strong enough for tissue manipulation, through manual displacement tests. Quantitative assessment of adhesion strength is needed for characterizing the robotic device, yet it will be addressed in subsequent studies.

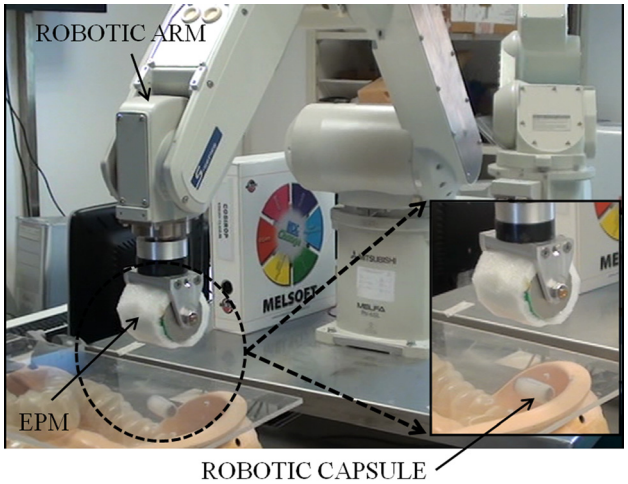

Fig. 10 Robotic arm moving the permanent magnet (EPM) used for capsule navigation and tissue scraping

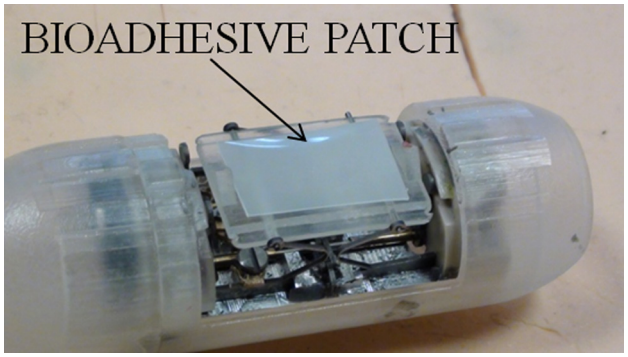

Fig. 11 Bioadhesive patch loaded on the robotic capsule PSP

5 Discussion and Concluding Remarks

A novel, miniature wireless robotic capsule for releasing bioadhesive patches in the GI tract was proposed and preliminary assessed. Having selected bioadhesive patches already demonstrated in literature, the main release mechanism for such planar and soft structures was conceived and effectively framed in a slightly up-scaled prototype. Indeed, full miniaturization was beyond the scope of the present feasibility study, yet it is fully enabled by the adopted scalable technologies. Moreover, magnetic capsule navigation was considered, despite not being implied by the proposed release mechanism per se, which also enabled tissue

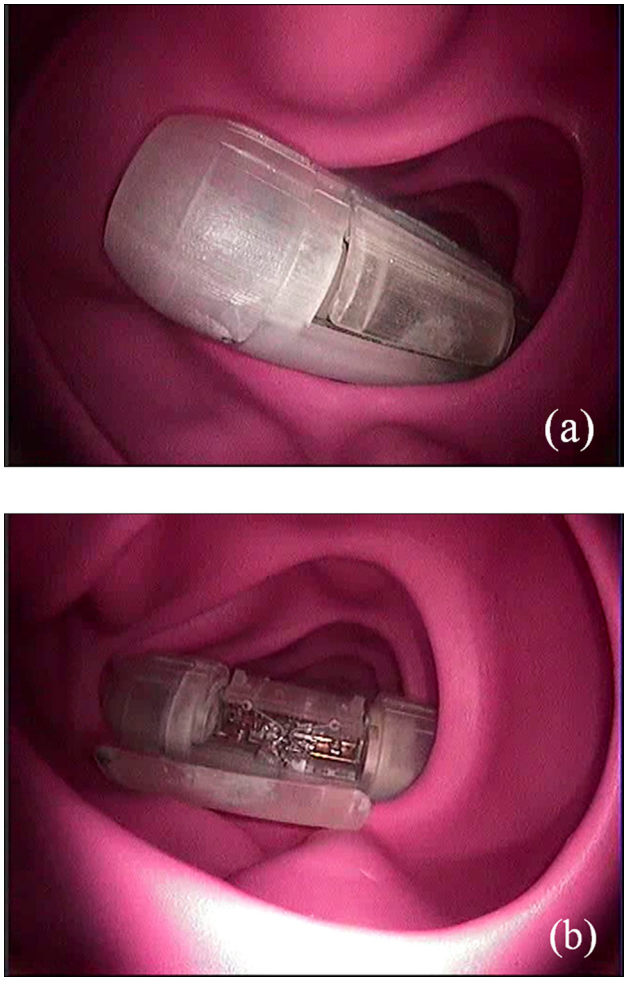

Fig. 12 PSP release test in GI phantom: robotic capsule, navigated to the target area, (*a*) prior to and (*b*) after PSP release

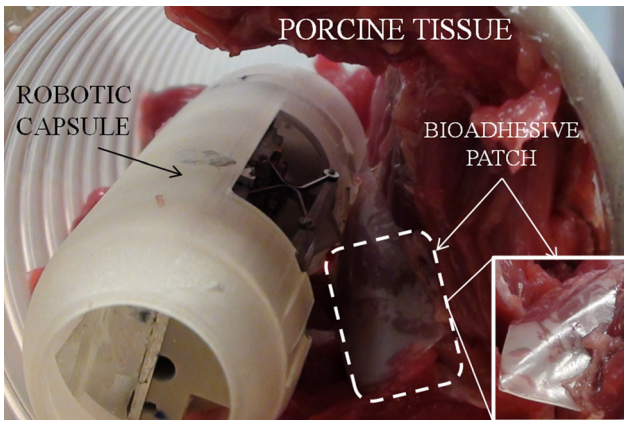

Fig. 13 Bioadhesive patch release test onto ex vivo porcine GI tissue. After patch deployment, capsule was slightly displaced and PSP was removed, for ease of visualization.

scraping prior to patch release to improve adhesion. Furthermore, the assembled prototype was successfully navigated in an in vitro GI phantom, up to a target site where PSP release was verified. Finally, deployment of a bioadhesive patch onto ex vivo porcine tissue was accomplished, and qualitative patch adhesion strength was verified.

Even if the most relevant critical issues were identified and tested through this study, further aspects need to be carefully addressed and improved. For instance, it may be convenient to foresee PSP detachment after patch release, so as to obtain a smoother and thus safer capsule profile in view of capsule expulsion. Furthermore, a more accurate assessment should be based on an enhanced prototype also encompassing a vision system. Moreover, the proposed capsule was preliminarily devised as a disposable device, yet reusability/disposability should be better addressed, based on a careful analysis of cost effectiveness. Finally, the single-shot release cannot be directly applied when the deployment of multiple patches is needed. Yet the proposed device could open up further perspectives, also from a therapeutic viewpoint, namely for those diseases which may take benefit from a topical, single-shot release [27].

Overall, the proposed system takes a leap towards enhanced diagnostic and therapeutic applications through the deployment of bioadhesive patches, for anchoring and, subsequently, therapeutic tasks.

Acknowledgment

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