Mechatronics 36 (2016) 112–118

Contents lists available at ScienceDirect

Mechatronics

journal homepage: www.elsevier.com/locate/mechatronics

# Electromagnetic field intensity triggered micro-biopsy device for active locomotive capsule endoscope

Viet Ha Le, Zhen Jin, Hernando Leon-Rodriguez, Cheong Lee, Hyunchul Choi, Van Du Nguyen, Gwangjun Go, Seong-Young Ko, Jong-Oh Park, Sukho Park*

*School of Mechanical Engineering, Chonnam National University, Gwangju 500-757, Korea.*

ARTICLE INFO

*Article history:*
Received 14 October 2015
Revised 14 January 2016
Accepted 11 May 2016

*Keywords:*
Biopsy device
Capsule endoscope
Micro-reed switch
Electromagnetic actuation system

ABSTRACT

For an active and precise diagnosis, we developed an active locomotive intestinal capsule endoscope (ALICE), which can be wirelessly driven and controlled using an electromagnetic actuation (EMA) system. Since then, there has been a need to develop a biopsy device integrated into ALICE which can take a biopsy sample inside the gastrointestinal tract for a historical analysis of cancer disease. Toward this goal, this paper proposes a smart-triggered biopsy device for the ALICE using a micro-reed switch, where the integrated micro-reed switch is turned on using a strong magnetic field, and the biopsy device mechanism is activated by a micro-reed switch. To execute the biopsy process, first, the ALICE with the biopsy device is driven by an EMA system, where a moderate intensity magnetic field is used for driving the ALICE to reach a target region on the intestinal wall. After that, by increasing the magnetic field above a critical value, the ALICE is pushed hard against the target lesion, the micro-reed switch is turned on, and the biopsy device is triggered. The biopsy process, therefore, is totally wirelessly controlled by the external magnetic field of the EMA system, without an additional controller module. The prototype of the biopsy device, with dimensions of 12 mm in diameter and 5 mm in length, was integrated into the ALICE and the prototype of the ALICE, with the biopsy device having dimensions of 12 mm in diameter and 32 mm in length. The working principle and mechanism of the proposed biopsy device are introduced and the feasibility of ALICE with the biopsy device is demonstrated through in-vitro experiments.

© 2016 Elsevier Ltd. All rights reserved.

## 1. Introduction

Recently, the technology of the capsule endoscope (CE) has emerged as a spotlighted solution for investigating and diagnosing common diseases of the gastro-intestinal (GI) tract or celiac disease. There are several commercialized CEs, including the PillCam (Given-imaging, Israel), OMOM (Jinshan, China) [1], MIRO (Intromedic, Korea) [2], and Endo capsule (Olympus, Japan) [3]. They are untethered CEs the size of a pill, integrated with a high definition camera which can capture images of the gastrointestinal (GI) tract, and transfer them to a portable receiver device through the CE's telemetry module. They can be swallowed and moved passively by the peristaltic motion of the digestive system. Because of their passive locomotion, however, the diagnostic ranges of most CEs are limited to tubular organs, such as the esophagus and small intestine. In addition, valuable functions, such as pH sensing and biopsies for the diagnosis of the GI tract, could not be integrated into most CEs [4].

Therefore, to have an active and precise diagnosis, an ALICE system driven by EMA is developed [5]. The ALICE, containing a small permanent magnet, can be manipulated by the magnetic field of the EMA system, and can perform effective targeting movements in the patient's gut environment. Next, for the definitive diagnosis of digestive diseases, there is a need to develop various functional devices for sensing, drug delivery, and biopsy, which can be integrated into the ALICE.

In this paper, a biopsy function for the ALICE is presented. While recently, several research studies on biopsy modules have been reported. First, Kong et al.,et al., proposed a biopsy module using a spring rotational mechanism with a tissue-cutting razor triggered by a paraffin block [6]. The biopsy module can sequentially operate a quick rotation to extract the tissue, sealing and fixing the biopsy sample. Park et al., reported a micro-biopsy spike to extract the biopsy sample [7], which was triggered by a shape memory alloy (SMA) wire, and moved forward and backward using a slide-crank mechanism. The above two biopsy devices have small dimensions, and can be integrated into CEs; however, they could not generate a sufficient reaction force for an effective extraction process from their biopsy mechanisms acting on the tissue and

* Corresponding author.
*E-mail addresses:* jop@jnu.ac.kr (J.-O. Park), spark@jnu.ac.kr (S. Park).

http://dx.doi.org/10.1016/j.mechatronics.2016.05.001
0957-4158/© 2016 Elsevier Ltd. All rights reserved.

intestinal wall and also it is not clear whether they could collect sufficient volume of tissue for histological analysis. Kong et al., also proposed an anchoring biopsy module, which was introduced with complete visual guidance [8]. The anchoring biopsy module solved the restriction of the reaction force, but the challenge of its huge size of capsule endoscope (40 mm x 15 mm) and high power consumption remains. Furthermore, the above three biopsy modules need an additional controller module for their triggering signal via radio frequency. Because the biopsy modules were not integrated into CEs with locomotion function, it is very difficult for them to extract a biopsy sample from the target lesion.

Second, M. Simi et al., proposed a wireless biopsy capsule triggering system with an external permanent magnet, and solved the problem of the restriction of an additional controller module [9]. The capsule, with one concentric couple of fixed and freely rotating cylindrical permanent magnets inside, created a magnetic torsion spring to extract the biopsy sample. The biopsy module has advantage of using external permanent magnet therefore it does not consume internal power of capsule. However, there is a weak point that the size of the biopsy module (9 mm in diameter and 24 mm in length) is too large. The dimension is too large (more than 2/3 size of normal CE) to be integrated to capsule endoscope which has limited space due to storing others component: wireless module, battery and camera. In addition, the system of the fixed and freely rotating cylindrical magnet of the biopsy module could not maintain internal magnetized direction of the permanent magnet; therefore, the biopsy module could not be able to be integrated into ALICE to perform flexible motion in the external electro-magnetic field.

Finally, an SMA based biopsy device for ALICE was reported [10], in which an effective biopsy performance was demonstrated; however, the size of the permanent magnet inside the ALICE is still quite large, and it requires the modification of a telemetry module to make it possible to receive the radio frequency of the triggering signal. Therefore, in this paper another approach of executing biopsy tissue was studied and applied. The novel proposed biopsy device for ALICE with small dimension is triggered by a micro-reed switch and EMA system, without changing ALICE's initial telemetry module. Through in-vitro experimentation, the feasibility of the ALICE with the proposed biopsy device has been confirmed.

The remainder of this paper is organized as follows. In Section 2.1, the working principle and the main components of ALICE are provided. Section 2.2 describes the design specifications of the biopsy device which could be integrated into the capsule endoscope. Section 2.3 and 2.4 explain the mechanism and design of the biopsy device using the micro-reed switch. The fabrication results and the characteristics of the ALICE with the biopsy device are reported in Sections 3.1 and 3.2. Finally, through in-vitro tests, Section 3.3 verifies the feasibility of the ALICE with the biopsy device.

## 2. Materials and methods

### 2.1. Active Locomotive Intestinal Capsule Endoscope (ALICE)

As a powerful diagnostic tool for diseases of the stomach, esophagus, and duodenum, CEs have been widely used by clinical doctors. However, due to their passive locomotion which relies on the peristaltic motion of the digestive organs, CEs can only work effectively in small tubular digestive organs, such as the small intestine and esophagus, but ineffectively in larger organs like the stomach or colon. To solve the current problem, an ALICE with flexible targeting locomotion in the entire whole GI tracts was proposed in [5]. The ALICE is a capsule endoscope with a small permanent magnet, and is actuated by an EMA system. In addition, through various experiments, we demonstrated that the ALICE showed effective locomotion and flexible motion, with 5 degrees of freedom (DOFs), and could be a feasible tool for diagnoses in the GI tract.

The EMA system, as it was introduced in [11], consists of two parts: part 1 is three pairs of Helmholtz coils perpendicular to each other in the *x, y*, and *z*-axes, while part 2 is composed of three Maxwell coils that are also perpendicular to each other in three coincident directions. Each coil pair was controlled by a PCI controller with LabVIEW software (National Instruments) connected to an MX12 power supply (3EA) (California Instruments).

### 2.2. Design specifications of the biopsy device

Most CEs have a shape of a large pill, and consist of one tiny camera and a lighting system, integrated sensors, programmable electronics, wireless communication, and a power supply [12]. In this paper, a biopsy tool which could be integrated into the ALICE is proposed to help a physician take a biopsy sample in parallel with an endoscopic examination. Due to the unique characteristics of CEs, the following requirements for the biopsy device for the CEs must be satisfied. First, the biopsy device should be sufficiently small enough to be integrated into swallowable CEs. In this paper, the target dimension of the ALICE prototype with the biopsy device was a size similar to the PillCam COLON video capsule, with a diameter of 12 mm and a length of 32 mm, which has already been approved by the US Food and Drug Administration (FDA) [16]. Second, the CE should have a targeting locomotive mechanism to reach the target lesion during internal surgery. Third, the biopsy device should have wireless activation ability, and cutting capability with enough force or a cutting pressure of 20 MPa at the tool-tissue interface [13]. Fourth, the biopsy procedures should be executed with little energy consumption, and the CE with the biopsy device should remain in a stable position during the sampling process. Finally, the sampled tissue should have a sufficient volume ($1 \sim 5\,mm^3$) for the histological analysis [14,15].

### 2.3. Mechanism of the biopsy device triggered by a micro-reed switch

Fig. 1(a) shows the conceptual design of the ALICE with a biopsy tool. For the flexible targeting locomotion of the ALICE using the EMA system, two permanent magnets with different magnetization directions were included. Fig. 1(b) shows the schematic diagram of the EMA system for the ALICE, where the EMA system consists of three pairs of Helmholtz coils and three pairs of Maxwell coils arranged perpendicular to each other in the *x, y*, and *z*- axes. Fig. 2(a) depicts the schematic design of the proposed biopsy device, which consists of an elliptical hole in the body, a biopsy extracting razor connected to a spring, a smart triggering module with a micro-reed switch, a polymer string, and an SMA wire. Fig. 2(b) describes the operational mechanism of the biopsy device. In advance, the biopsy extracting razor connected to the torsional spring was fixed with a polymer string. After the micro-reed switch was triggered, the SMA wire was heated up and the polymer string was cut. Then, the biopsy extracting razor was rotated using the torsional spring.

Fig. 3 describes the entire biopsy procedure in sequence. First, the EMA system produced a magnetic field inside its region of interest (ROI), at a medium level, to move the ALICE to the target lesion. Second, the ALICE was driven to be attached to the target and intestinal wall. Third, the magnetic field intensity was raised to an excited level, which was greater than the pull-in value of the micro-reed switch. The higher magnetic field turned the micro-reed switch on, and gained the pushing force of the ALICE to the intestinal wall. Finally, based on the tissue sampling mechanism in Fig. 2(b), the cutting razor of the biopsy device in the ALICE could extract a biopsy sample.

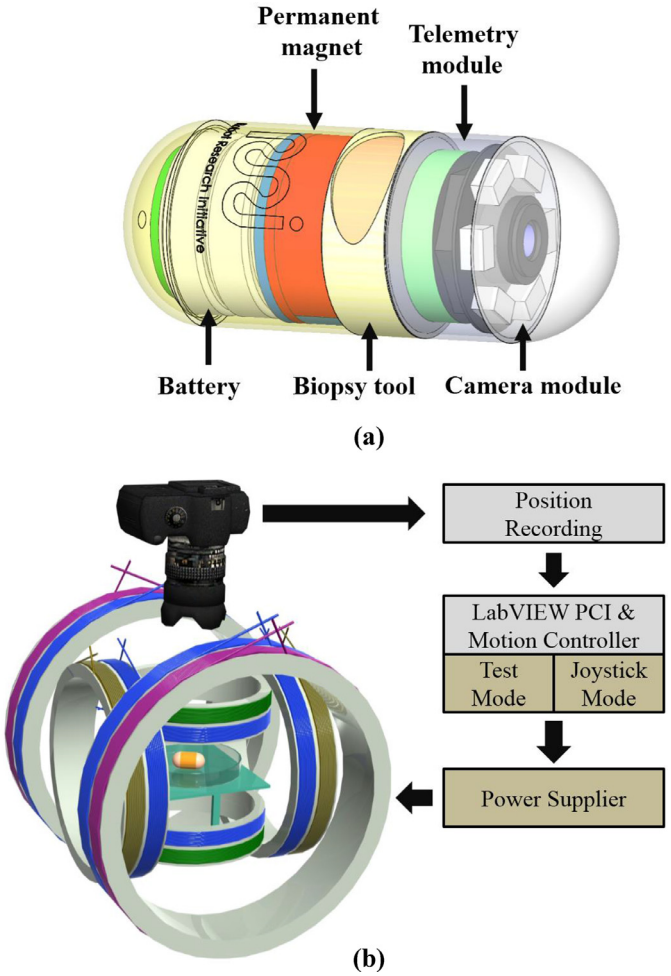


**Fig. 1.** (a) Conceptual design of the ALICE with a biopsy tool, and (b) Schematic diagram of the EMA for the ALICE.

The reed switch is an electrical switch operated by an applied magnetic field. This switch stays off in an environment with a small magnetic field, and on when the intensity of the magnetic field is increased to an excited level (the pull-in value of the reed switch). We adopted an RI-80 Series ultra-micro dry-reed switch (Shenzhen Fast Sensors Company), which is a single-pole, single-throw type of switch, with normally open contacts containing two magnetically actuated reeds with the dimensions of 1.8 mm in diameter and 5 mm in length. The original pull-in value of the reed switch that completes the circuit of the triggering system is 20 ampere-turns, which is almost equal to 2 mT. By using the Mu metal foil to cover the reed switch, we can adjust its pull-in value up to 600 ampere-turns (60 mT). Due to the limitations in the battery energy for the biopsy process, the SMA wire should have a low energy consumption. Therefore, we selected a nickel-titanium SMA with a small diameter of 0.08 mm and a length of 5 mm. The SMA wire needs a power of 19.57 Watts to be activated, and consumes about 12.5 ~ 18 mWh, which is about 4.0% of the energy of the CE's cell battery (3.0 V, 160 mAh, 475 mWh).

### *2.4. Design of the biopsy device triggered by a micro-reed switch*

Firstly, dimensions of the elliptical hole in the biopsy module is focused to determine the volume of the extracted biopsy sample. For a histological analysis, a biopsy volume of 1 to 5 $mm^3$ should be sufficient [14-15]. As shown in Fig. 4(a), several prototypes of the biopsy module body, with various dimensions of elliptical holes, were fabricated using rapid prototyping. The prototypes of the biopsy module body were used to execute a fundamental test for optimizing the dimensions of the biopsy hole, and the pushing force of the ALICE produced by the EMA system, as shown in Figs. 4(b) and 4(c). The biopsy holes have elliptical shapes in which the length of the major axis is fixed at 8 mm, and the length of the minor axis is varied. A load cell and a high definition camera were installed to measure the pushing force and the corresponding volume of the sampled tissue inside the biopsy hole, respectively. From the camera image, the shape and volume of the biopsy sample was determined by using image analysis software (ImageJ). The experimental results are summarized in Table 1 and we determined the dimension of the elliptical hole (5 mm minor axis and 8 mm major axis) and the necessary pushing force for the

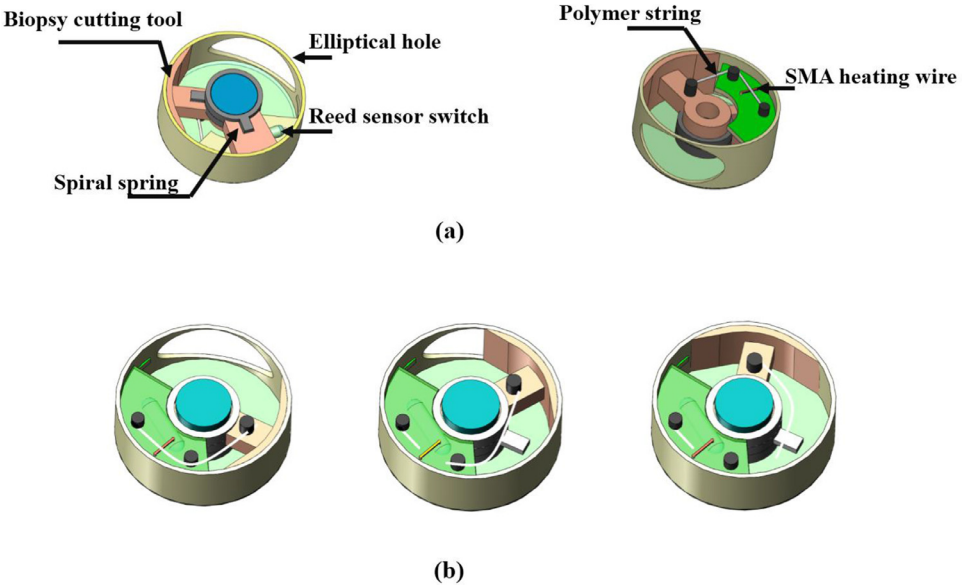


**Fig. 2.** (a) Schematic design of the biopsy device (top view and bottom view) and (b) Operational mechanism of the biopsy device (Micro-reed switch was triggered → SMA wire was heated up → Polymer string was cut → Biopsy cutting tool was rotated by torsional spring).

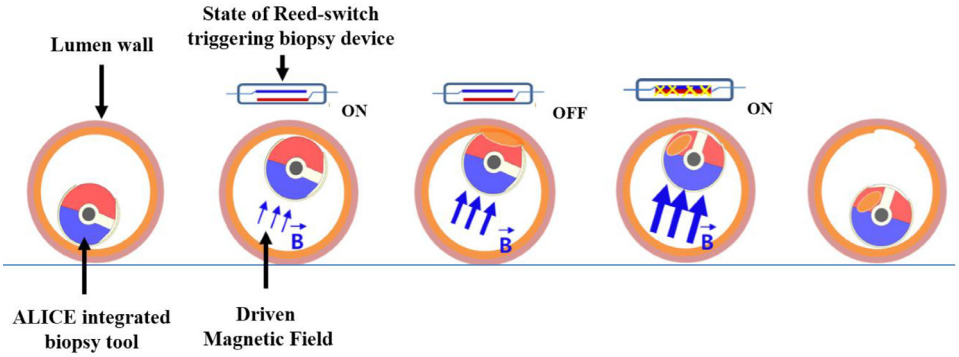


**Fig. 3.** Schematic diagram of the biopsy sampling procedure.

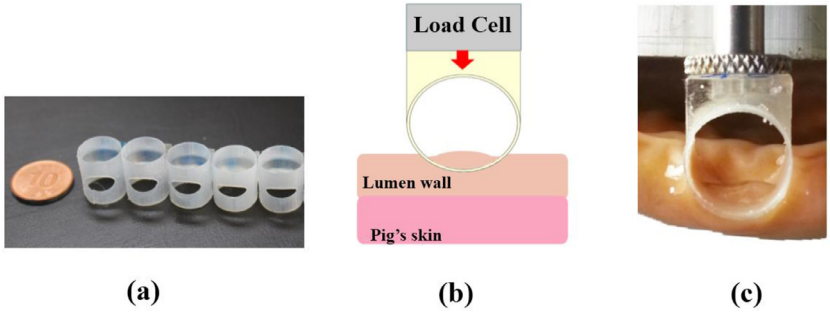


**Fig. 4.** (a) Prototype of capsule body with elliptical biopsy hole, (b) Schematic design of experimental setup to optimize the elliptical hole dimensions, and (c) Real experimental setup with pig intestine and load cell.

**Table 1**
Tissue volumes inside the hole for different dimensions and pushing forces.

| Force (N) | Minor axis (mm) | | | | |
|---|---|---|---|---|---|
| | 3.5 | 4 | 4.5 | 5 | 5.5 |
| 0.40 | 0.51 $mm^3$ | 0.74 $mm^3$ | 1.13 $mm^3$ | 2.45 $mm^3$ | 3.28 $mm^3$ |
| 0.60 | 0.63 $mm^3$ | 1.72 $mm^3$ | 3.50 $mm^3$ | 5.89 $mm^3$ | 7.64 $mm^3$ |
| 1.00 | 1.25 $mm^3$ | 2.24 $mm^3$ | 4.12 $mm^3$ | 7.97 $mm^3$ | 10.28 $mm^3$ |

biopsy process (about 0.6 N), where the expected biopsy tissue volume was about 5.89 $mm^3$.

Next, the pushing force of the ALICE using the EMA system was considered. The EMA system consists of three pairs of Helmholtz coils and three pairs of Maxwell coils arranged perpendicular to each other in the *x*, *y* and *z*-axes, as shown in Fig. 1(b). The propulsion force ($F_{propulsion}$) of the ALICE, as in [5,11], can be expressed by Eq. (3):

$$\mathbf{H}_{\mathrm{m}} = [-0.5 g_m x \ -0.5 g_m y \ g_m z]^T \tag{1}$$

$$g_m = 0.641 \frac{i_m \times n_m}{r_m^2} \tag{2}$$

$$F_{propulsion} = g_m \ \mu_0 MV cos\theta \tag{3}$$

where $V$ and $M$ are the volume and magnetization of the permanent magnet in the ALICE; $\mathbf{H}_{\mathrm{m}}$ and $g_m$ are the generated magnetic field and gradient of the magnetic field by each pair of Maxwell coils; $i_m$ is the current intensity and $r_m$ is the coil radius; $n_m$ is the number of turns of the Maxwell coils in each axis, $\theta$ denotes the angle between the magnetization direction and the magnetic field, and $\mu_0$ is the permeability of the vacuum.

As shown in Fig. 1, two cylindrical shaped NdFeB permanent magnets with a magnetization value of M = 2,700,000 A/m were adopted, where the pushing force for the biopsy process was determined by the magnet with the radial magnetization direction. Fig. 5 shows the simulation results of the pushing force according to the thickness and radius of the cylindrical permanent magnet. In Fig. 5, the three surfaces denote the pushing forces of the ALICE at three different applied currents (5, 7, and 10 Ampere). The maximum pushing force of the ALICE to the lumen wall was calculated by Eqs. (1) and (3) and plotted as shown in Fig. 5. From the simulation results, when a magnet which was magnetized in the radial direction (10 mm diameter and 3 mm height) is used, a pushing force of more than 0.6 N for the biopsy procedure can be produced. In addition, the volume of the permanent magnet was small enough to be integrated into the ALICE. Furthermore, for the flexible motion of the ALICE, another magnet with dimension of 10 mm diameter and 1 mm height, which was magnetized in the axial direction, was selected.

Finally, to extract the biopsy tissue, the razor tool should generate shear stress larger than the destructive stress of the tissue ($\tau_{\mathrm{des}} = 20$ MPa) [14]. The resulting shear stress ($\tau_{\mathrm{ex}}$) induced by the razor tool was calculated using the Eqs. (4) and (5):

$$\tau_{\mathrm{ex}} = \frac{\mathrm{F}}{\mathrm{t} \times \mathrm{s}} \geq \tau_{\mathrm{des}} = 20 \ \mathrm{Mpa} \tag{4}$$

$$\mathrm{F} \geq 20\mathrm{Mpa} \ \times \mathrm{t} \times \mathrm{s} \tag{5}$$

where F denotes the cutting force acting on the tissue, and $t$ and $s$ are the thickness and width of the razor, respectively. To reduce the cutting force, the values of $t$ and $s$ need to be minimized; in other words, a sharp razor with a small width should be designed and fabricated. In this research, the selected razor tool have a thickness of $t = 0.1$ mm, and the razor width $s = 5$ mm. Then, in the proposed tissue sampling mechanism Fig. 2(b), the torsional spring can generate at least 10 N of cutting force (F ≥ 20 Mpa × t × s = 10 N)

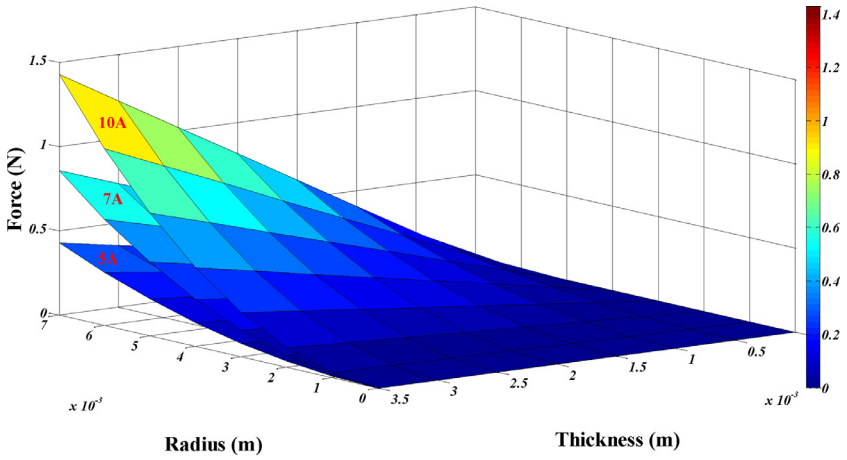


**Fig. 5.** Simulation result of the pushing force of the ALICE according to the thickness and radius of the cylindrical permanent magnet corresponding with various current supplied to EMA system.

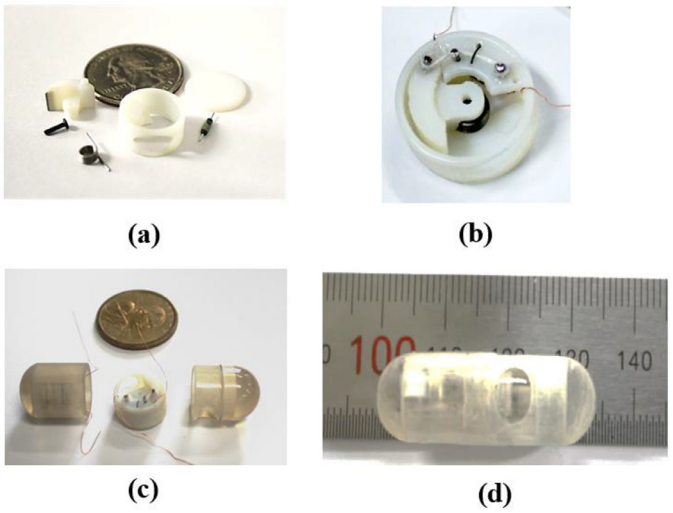


**Fig. 6.** (a) Components of the biopsy device, (b) the assembled biopsy device, (c) the bodies of ALICE prototype and the assembled biopsy device, and (d) ALICE prototype with the biopsy device.

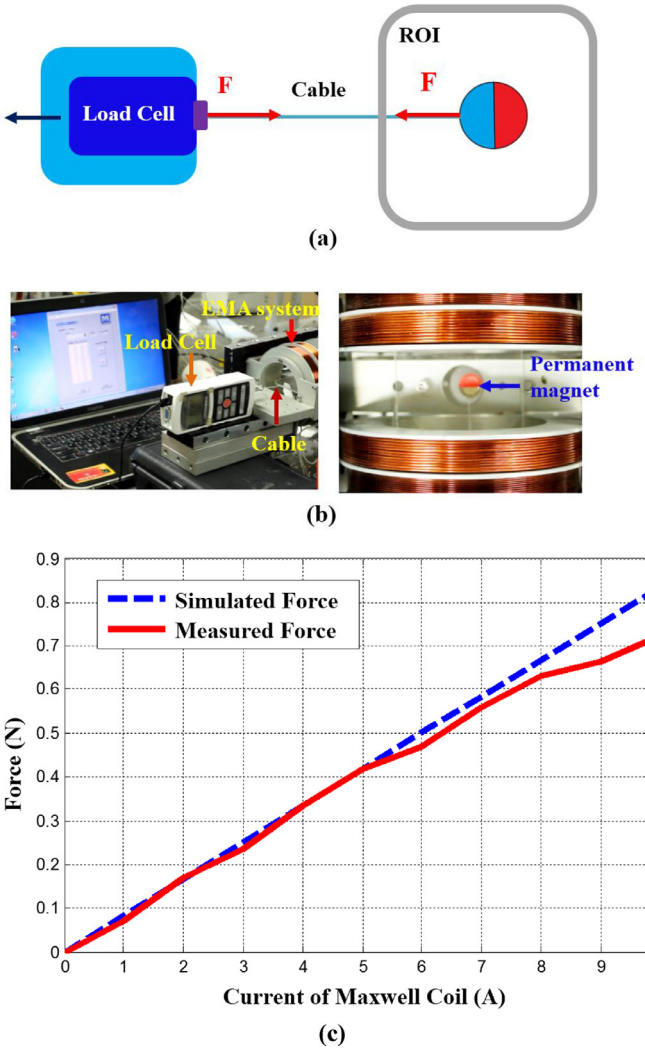


**Fig. 7.** (a) Schematic design of the experimental setup to measure the pushing force of the ALICE, (b) Real experimental set-up with an EMA system, and (c) Pushing force of the ALICE using an EMA system according to various applied currents.

## 3. Experiments

### *3.1. Fabrication results of the ALICE prototype with the biopsy device*

The prototype of the ALICE with the micro-biopsy device was fabricated using commercialized components through conventional methods. As shown in Fig. 6(a), the biopsy device consists of the biopsy tool with the sharp razor, the micro-reed switch, and the torsional spring. First, the chassis of ALICE and the body of the micro-biopsy device were fabricated through a rapid prototyping 3D printing machine (Objet 30 Pro, Stratasys Direct Manufacturing Ltd, USA) with the resins (VeroWhitePlus RGD835 and VeroClear RGD810). Second, the torsional spring and the biopsy razor were purchased from MISUMI Corporation (Japan), where the torsional spring has the wire diameter of 0.5 mm and the outer diameter of 3 mm, and generates the force of 12.15 N at 90 degree. In addition, the biopsy razor has the thickness of 0.1 mm. Finally, as a reed switch, we adopt an ultra-micro dry-reed switch (RI-80 series, Shenzhen Fast Sensors Company, China) and the permanent magnet (JL Magnet, Korea). Fig. 6(b) shows the assembled biopsy device and Fig. 6(c) presents the bodies of ALICE prototype and the assembled biopsy device. Finally, Fig. 6(d) shows the completed ALICE prototype with the biopsy device, where the ALICE prototype has the dimension of 12 mm in diameter and 32 mm in length.

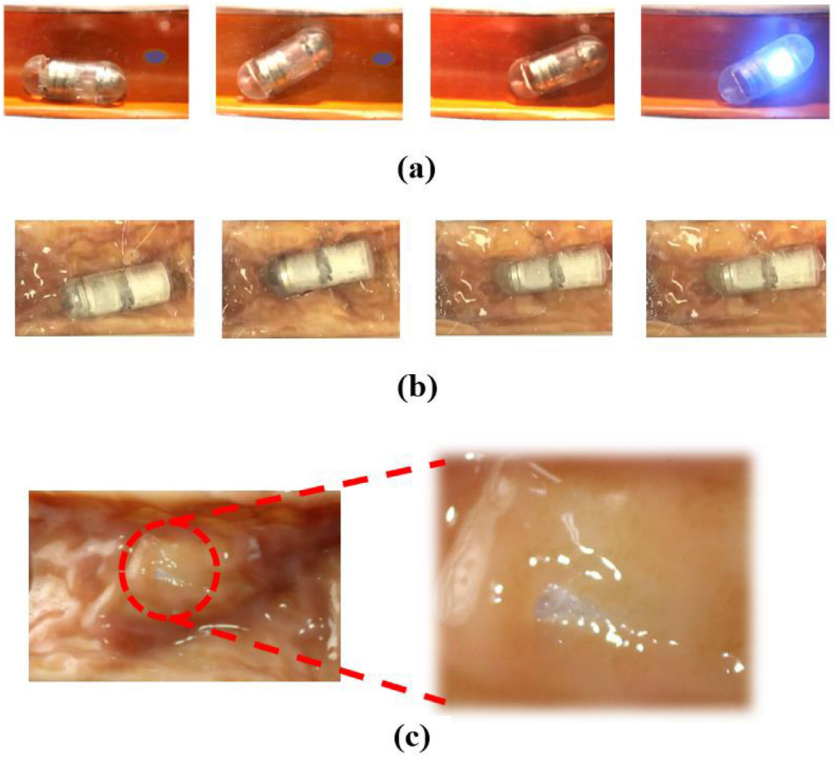


**Fig. 8.** In-vitro experimental results. (a) The targeting and triggering of the ALICE with the micro-reed switch and LED, (b) In-vitro biopsy procedure using the ALICE with the biopsy device, and (c) The surface of the target lesion after the biopsy procedure.

### 3.2. Pushing force of the ALICE with the biopsy device

Before the feasibility test of the ALICE prototype with the biopsy device, the pushing force of the ALICE prototype was measured. Fig. 7(a) and Fig. 7(b) show the schematic diagram and the experimental setup for the pushing force measurement of the ALICE prototype, respectively, in which we adopted a load cell (Advanced Digital Force Gauges Series 5, Mark-10). In addition, the pushing force can also be estimated using Eq. (3). Furthermore, Fig. 7(c) shows the pushing forces of the ALICE prototype according to the various applied currents of the Maxwell coils. When we applied 10 A to the Maxwell coil, the pushing force was measured at about 0.73 N, and was estimated at about 0.83 N. In addition, we confirmed that the micro-reed switch came to the excited level and triggered the proposed biopsy device. Because of the pushing force (0.73 N) with the 10 A current, the input of the Maxwell coil was larger than the required force of 0.6 N, and we expected that the proposed ALICE with the biopsy device could obtain a large enough biopsy sample in the biopsy module.

### 3.3. In-vitro tests of the ALICE prototype with the biopsy device

Since the activation process of EMA system to biopsy device is invisible from outside, there is a need to do excitation test for the biopsy device. In order to process the excitation test of the micro-reed switch and confirm the wireless activated of EMA system on the biopsy device of the ALICE prototype, we replaced the biopsy mechanism with an LED circuit in the ALICE prototype, where the LED was connected to a battery through a micro-reed switch. Then, we placed the ALICE prototype with the LED on the intestinal tract with a given target lesion. As shown in Fig. 8(a), through the control of the EMA system, the ALICE prototype could approach the target lesion with the off-state of LED circuit, which is corresponding to the non-activated state of the biopsy device. And, when the magnetic field of the EMA system was increased above 60 mT, the micro-reed switch was closed and the LED was turned on, which is corresponding to the activation of the biopsy device. Therefore, the feasibility of the smart triggering using the micro-reed switch for the biopsy device was confirmed.

Second, we executed an in-vitro biopsy test using the ALICE prototype with the proposed biopsy device. As shown in Fig. 8(b), the ALICE prototype was placed in a segment of a fresh pig's intestine in the ROI (region of interest) of the EMA system. Similar to the described procedure in Fig. 3, the ALICE prototype was attached to the target lesion on the intestinal wall. When the applied current on the Maxwell coil was increased, the micro-reed switch was excited, the SMA wire was heated, the heated SMA wire cut the polymer string, and the razor tool was rotated by the torsional spring. Then, the sampled tissue was extracted by the razor tool and stored inside the biopsy device. As shown in Fig. 8(c), we confirmed that the sampled tissue was extracted from the target lesion, and that the ALICE with the biopsy device successfully executed its biopsy function. After the biopsy process was finished, the biopsy device was disassembled from the ALICE and biopsy tissue was taken out.

Finally, the taken out biopsy tissue was stored in a centrifuge tube (Figs. 9(a) and 9(b). As shown in Fig. 9(c), the volume of the biopsy tissue sample was about 5 $mm^3$ (2.5 mm x 2 mm x 1 mm), which is a sufficient volume for a histological analysis of the biopsy sample. In addition, the biopsy function test of ALICE was executed for 12 times. The success rate of the biopsy sampling was 100% and the biopsy tissues obtained by the biopsy device has the average volume of about 4.55 $mm^3$. For additional histological analyses of the biopsy tissue sample, it was put into a tube of phosphate-buffered saline (PBS) and homogenized via ultra-sonication. After the sample tube was centrifuged, the supernatant was removed and the tissue sample was suspended in a solution of PBS and 4′,6-diamidino-2-phenylindole (DAPI) in a dark environment. We obtained a tissue pellet, and removed the remaining solution from

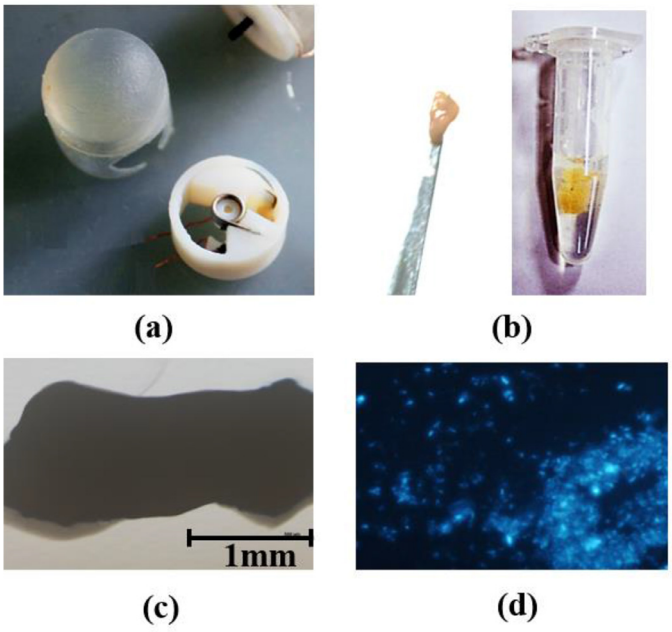


**Fig. 9.** Analysis of biopsy tissue. (a) Disassemble biopsy device after biopsy process, (b) Storing the biopsy tissue in a micro-centrifuge tube, (c) Microscopic image of the biopsy tissue, and (d) Fluorescent microscopic image of the biopsy tissue.

the tube. Then, the tissue pellet was suspended in PBS, and 1 mL of the tissue suspension was placed on a glass side with a cover slip, and investigated using a microscope. Fig. 9(d) shows the fluorescent microscopic image of the sampled tissue, and the blue color denotes the fresh animal cells in the sampled tissues. Consequently, the ALICE with the biopsy device can execute its biopsy function to collect tissue samples was confirmed.

## 4. Conclusion

In this paper, an ALICE with a magnetically triggered biopsy device using a micro-reed switch was proposed. The ALICE prototype was driven to do flexible investigation, and to approach the biopsy target lesion. The EMA system can both manipulate the flexible motion of the ALICE and trigger the biopsy module by adjusting the direction and intensity of the magnetic field. The biopsy module, with a small dimension of 5 mm in length, can effectively solve the restriction problem of the reaction force, without changing the ALICE capsule endoscope's telemetry module. Therefore, the proposed biopsy device has the potential to be integrated into ALICE and execute the biopsy process using the EMA system. In future, beside the biopsy device, we will develop and integrate several functions, such as tattooing and position recognition. The tattooing function may mark the exact positon of a target lesion and is necessary for an additional surgery. And, the position recognition function will be used for an exact diagnosis and treatment using ALICE. The additive functions including the proposed biopsy device hopefully could bring a bright future in the evolution of the next generation of active locomotive and multifunctional CEs. The proposed biopsy device hopefully could bring a bright future in the evolution of the next generation of active locomotive and multifunctional CEs.

## Acknowledgments

This research was supported by the Next-generation Medical Device Development Program for Newly-Created Market of the National Research Foundation (NRF) funded by the Korean government, MSIP (No. 2015M3D5A1065682).

## References

[1] Liao Z, Gao R, Li F, Xu C, Zhou Y, Wang JS, Li ZS. Fields of applications, diagnostic yields and findings of OMOM capsule endoscopy in 2400 Chinese patients. World J Gastroenterol 2010;16:2669–76.
[2] Bang S, Park JY, Jeong S, Kim YH, Shim HB, Kim TS, Lee DH, Song SY. First clinical trial of the "MiRo" capsule endoscope by using a novel transmission technology: electric-field propagation. Gastrointestin Endoscop 2009;69:253–9.
[3] Cave DR, Fleischer DE, Leighton JA, Faigel DO, Heigh RI, Sharma VK, Gostout CJ, Rajan E, Mergener K, Foley A, Lee M, Bhattacharya K. A multicenter randomized comparison of the Endocapsule and the Pillcam SB. Gastrointestin Endoscop 2008;68:487–94.
[4] Basar MR, Malek F, Juni KM, Idris MS, Saleh MIM. Ingestible wireless capsule technology: a review of development and future indication. Int J Antenna Propagat 2012:14 (2012).
[5] Cheong L, Hyunchul C, Gwangjun G, Semi J, Seong Young K, Jong-Oh P, Sukho P. Active Locomotive Intestinal Capsule Endoscope (ALICE) system: a prospective feasibility study, mechatronics. IEEE/ASME Trans 2015;20:2067–74.
[6] Kyoung-chul K, Jinhoon C, Doyoung J, Dong-il C. A rotational micro biopsy device for the capsule endoscope, Intelligent Robots and Systems. In: 2005. (IROS 2005). 2005 IEEE/RSJ International Conference on; 2005. p. 1839–43.
[7] Sunkil P, Kyo-in K, Seoung Min B, Jeong Youp P, Si Young S, Dongil 'Dan' C. A novel microactuator for microbiopsy in capsular endoscopes. Journal of Micromech Microeng 2008;18:025032.
[8] Kong K, Yim S, Choi S, Jeon D. A robotic biopsy device for capsule endoscopy. J Med Devices 2012;6 031004.
[9] Simi M, Gerboni G, Menciassi A, Valdastri P. Magnetic torsion spring mechanism for a wireless biopsy capsule. J Med Devices 2013;7 041009.
[10] Le VH, Hernando LR, Lee C, Choi H, Jin Z, Nguyen KT, Go G, Ko SY, Park JO, Park S. Shape memory alloy-based biopsy device for active locomotive intestinal capsule endoscope. In: Proceedings of the Institution of Mechanical Engineers. Part H, Journal of engineering in medicine, 229; 2015. p. 255–63.
[11] Yu C, Kim J, Choi H, Choi J, Jeong S, Cha K, Park J-o, Park S. Novel electromagnetic actuation system for three-dimensional locomotion and drilling of intravascular microrobot. Sens Actuat A 2010;161:297–304.
[12] Fireman Z, Glukhovsky A, Scapa E. Future of capsule endoscopy. Gastrointestin Endoscop Clinic North Am 2004;14:219–27.
[13] Egorov VI, Schastlivtsev IV, Prut EV, Baranov AO, Turusov RA. Mechanical properties of the human gastrointestinal tract. J Biomech 2002;35:1417–25.
[14] Hopper AD, Cross SS, Sanders DS. Patchy villous atrophy in adult patients with suspected gluten-sensitive enteropathy: is a multiple duodenal biopsy strategy appropriate? Endoscopy 2008;40:219–24.
[15] Catassi C, Fasano A. Celiac disease diagnosis: simple rules are better than complicated algorithms. Am J Med 2010;123:691–3.
[16] Given imaging receives FDA clearance for PillCam® COLON in patients following incomplete colonoscopy, http://www.givenimaging.com/en-us/Innovative-Solutions/Capsule-Endoscopy/pillcam-colon/Pages/COLON-Press-release.aspx#_ftnref1 (2013, accessed December 12, 2014).