

A soft-magnet-based drug-delivery module for active locomotive intestinal capsule endoscopy using an electromagnetic actuation system



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ABSTRACT

Nowadays, capsule endoscope (CE) technology is highly evaluated as a promising medical apparatus for minimally invasive diagnosis and therapy. Active locomotive capsule endoscopy (ALICE) using an electromagnetic actuation (EMA) system is one of the new state-of-the-art solutions that effectively increase the diagnostic ability of CE. Together with a locomotive CE, there are various requests for multifunctional modules that can deliver drugs or execute biopsy functions. This paper presents a drug delivery module for ALICE using EMA, where we adopt a soft magnet due to its special physical properties. The drug-delivery module consists of two ring-type soft magnets and a simple plastic hinge; it has a volume of 0.78 ml, which is approximately 26% the total volume of a conventional active CE. The drug-delivery module can be integrated with ALICE. First, the drug is encapsulated into the module by the attracting force between two axially magnetized soft-magnetic rings. Second, ALICE with the drug delivery module can be driven by a precisely controlled external magnetic field to investigate and situate correct drug delivery to a target lesion. Third, at the target lesion, the external magnetic field is turned off and the two axial magnetized soft-magnetic rings of the drug-delivery module are demagnetized. Fourth, when we apply a strong pulsating magnetic field in a radial direction, the drug-delivery module is opened by the repulsive force between the two radially magnetized soft-magnetic rings, and the encapsulated drug can be released. After the drug release, the drug-delivery module can be returned to its initial shape thanks to an integrated plastic hinge in the drug delivery module and the attracting force between two axially magnetized soft-magnetic rings. Finally, the active CE can continue to show its intrinsic diagnostic work. Consequently, we demonstrate the feasibility of the drug-delivery module which is integrated in ALICE.

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1. Introduction

To date, several types of capsule endoscopes (CEs) have been developed from the first generation of small intestinal capsules (M2A, Given Imaging, Israel) [1] to the improved esophageal and colonic capsules [2,3]. Recently, a later version of CE has been widely commercialized as PillCam (Given Imaging, Israel), EndoCapsule (Olympus, Japan), MiroCam (IntroMedic, Korea), and OMOM (Chongqing Jinshan Science and Technology Co., China). However, CEs have a common weak point in terms of their passive locomotion, where they rely on the peristaltic motions of the human digestive system. Due to their passive locomotion, the CEs

might miss some abnormal lesions. As a promising solution to this problem, an active locomotive intestinal capsule endoscope (ALICE) was previously reported, which was driven by an external electromagnetic actuation (EMA) system [4].

Besides the locomotive function of CEs, different functions have been requested by several physicians, including biopsy, pH sensing, and drug delivery. These functions can be used for the diagnosis and treatment of gastrointestinal (GI) diseases. In this paper, we present a prototype of a drug-delivery function module for ALICE that can deliver a therapeutic drug to a specific target region in the GI tract. We expect that the ALICE with the proposed drug delivery function module can be used for the treatment of the GI diseases. In addition, it can be also applied for the drug absorption research of a therapeutic drug in the GI tract, as the efficacy evaluation of the therapeutic drug is very important and often costs the pharmaceutical industry millions of dollars per year to carry out [5–7].

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There have been several reports on the CE drug-delivery function. First, a drug-delivery capsule using a small gas-producing cell was proposed, where the cell was activated by a high-frequency current induced from its oscillating circuit [8]. The activated gas-producing cell generates sufficient pressure to push the piston forward and release the drug from the reservoir. This system demonstrates the feasibility of controlled drug release. However, only 16% volume of the capsule was used for the drug loading and the activation time for releasing a dose takes an hour. Second, an active drug-delivery CE using a micro-thruster was reported [9]; this had a large volume for the drug loading (about 30% volume of the CE) and a relatively fast activation time. However, because the active drug-delivery CE does not have any locomotive function, it cannot be positioned to deliver to a specific target lesion in an intestinal tract. Third, Stephen et al. developed a CE comprising a holding or anchoring mechanism with a C-shaped tip legging mechanism [10]. However, because the CE was composed of complex and large mechanisms, it was very difficult to apply it to the intestinal tract. In addition, the CE does not also have any locomotive function. Finally, Yim et al. proposed a soft-capsule with two magnetic parts, where the two magnets were attracted to each other with an appropriate magnetic force to keep the drug encapsulated inside the capsule during its traveling through the GI tract. When the capsule reached the target position, an external magnetic field from the external permanent magnet was used to extract and release the drug [11]. We found that the drug delivery capsule includes a targeting mechanism, and at the same time, an active drug-releasing mechanism. Therefore, it is considered as a feasible method for a drug delivery CE. Nevertheless, the drug-releasing module can be integrated with only a soft-capsule endoscope and it is not compatible with the popular pill-shaped CEs or ALICE.

In this paper, a new platform for a drug-delivery function module for ALICE will be presented. The ALICE with the proposed soft-magnet-material-based drug-delivery module shows advanced features of positioning controllability and drug releasing performance due to the external magnetic field of an electromagnetic actuation (EMA) system. The new drug-delivery module for ALICE can be made compatible and integrated with other commercialized pill-shaped CEs. Through several fundamental experiments, we will evaluate the feasibility of the drug-delivery module integrated with ALICE.

2. Materials and methods

2.1. Active locomotive intestinal capsule endoscope (ALICE)

Considered a non-invasive procedure, conventional CEs have been used as an excellent and safe device for diagnosis in the small intestine and esophagus. However, because CEs locomotion is passive, relying on the peristalsis motion of digestive organs, they cannot give a sufficient diagnosis and may have many blind spots in other organs such as the stomach and colon. In our previous research, as a promising solution for this limitation of CEs, we proposed an active locomotive intestinal capsule endoscope (ALICE) that consists of CEs with an integrated small permanent magnet and an external electromagnetic actuation (EMA) system [4]. The ALICE exhibits 5-degree-of-freedom (DOF) motions through the control of the coil currents in the EMA system. As shown in Fig. 1, the EMA system consists of two parts. One comprises coils for the generation of a uniform magnetic field with a pair of Helmholtz coils and two pairs of uniform saddle coils. The other includes coils for the generation of a uniform gradient magnetic field with a pair of Maxwell coils and two pairs of uniform gradient saddle coils. Each coil pair is connected to an MX12 (3EA) power supply (California Instruments, USA) and the currents of the coils are controlled via a peripheral

component interconnect (PCI) controller with LabVIEW software (National Instruments, USA). Thanks to the controllable magnetic field of the EMA system, the movement, posture, and angle of ALICE inside the digestive system can be effectively driven with 5-DOF. In addition, for accurate diagnosis of the digestive organs, a biopsy module for ALICE has been developed as a functional module of CEs [12,13]. This paper will present the functional drug-delivery module for ALICE.

2.2. Design basic specifications of the drug delivery module for capsule endoscopy

CEs have the same shape as a large antibiotic pill and consist of a camera and lighting LEDs, programmable electronics and power batteries [14]. Therefore, the size of the functional modules for CEs should be suitable for integration into the existing swallowable CEs, which are 12 mm in diameter, 33 mm in length, or 3.0 cm³ [15]. The wireless remote actuation of a drug-releasing mechanism should consume a small amount of energy, as the available energy is limited in CEs. CEs should have an active drug-releasing function that is independent from environmental conditions, such as pH levels, different intestinal sizes, and disease condition. Moreover, the drug must be safely encapsulated without any leakage before the activation of the drug-release process. It is desirable for the drug reservoir to have a large volume ratio compared to the total volume of CEs. Finally, the drug delivery module should be easily activated and reliably controlled to ensure that the encapsulated drug will be released at the targeted position, which is an important role for the drug-delivery system required [8,16].

2.3. The drug-delivery module for the ALICE system

Fig. 1 shows a schematic diagram of the ALICE operating system. ALICE with a drug-delivery module was placed inside the EMA system and driven by the magnetic field generated from the EMA system. The EMA system consists of one Maxwell coil pair, one Helmholtz coil pair, two uniform saddle coil pairs, and two gradient saddle coil pairs arranged perpendicularly on the X-, Y-, and Z-axes; it can produce a uniform, gradient magnetic field inside the region of interest (ROI). Fig. 2 introduces the novel ALICE with the drug-delivery module. Fig. 2a presents the overall shape of ALICE with the drug-delivery module but seems to exhibit no differences from other CEs. The inside structure of ALICE is shown in Fig. 2b, where the upper part is the main part of ALICE—which is the same as a conventional CEs (camera, telemetry module, and batteries)—and the lower part is the drug delivery module using two axial magnetized soft-magnetic rings. The axially magnetized soft-magnetic rings pull toward each other to keep the encapsulated drug in ALICE. In addition, to improve the sealing of the encapsulated drug, a layer of hard gelatin shell was added, as shown in Fig. 2b. The axially magnetized soft-magnet rings help to control ALICE's movement through the external magnetic field created by EMA system. Fig. 2c describes the drug-releasing state of ALICE, where the plastic hinge on the system's shell helps the lower part connect with the main body during the drug-releasing process and assists ALICE to return to its original shape (Fig. 2a) after the drug release. Therefore, after the drug is released, ALICE can continue to diagnose the digestive organs. Since the drug-delivery module in ALICE was made with two soft magnets, the drug chamber has a greater volume and there is a higher ratio between the encapsulated drug and the ALICE capsule volume.

Fig. 3 illustrates the detaching and attaching procedures of the two soft magnets in the drug-delivery module. In step 1, the two ring-type soft magnets are magnetized in the axial direction, and the attraction force between the two soft-magnets is generated. The attraction force is sufficient to safely store the encapsulated

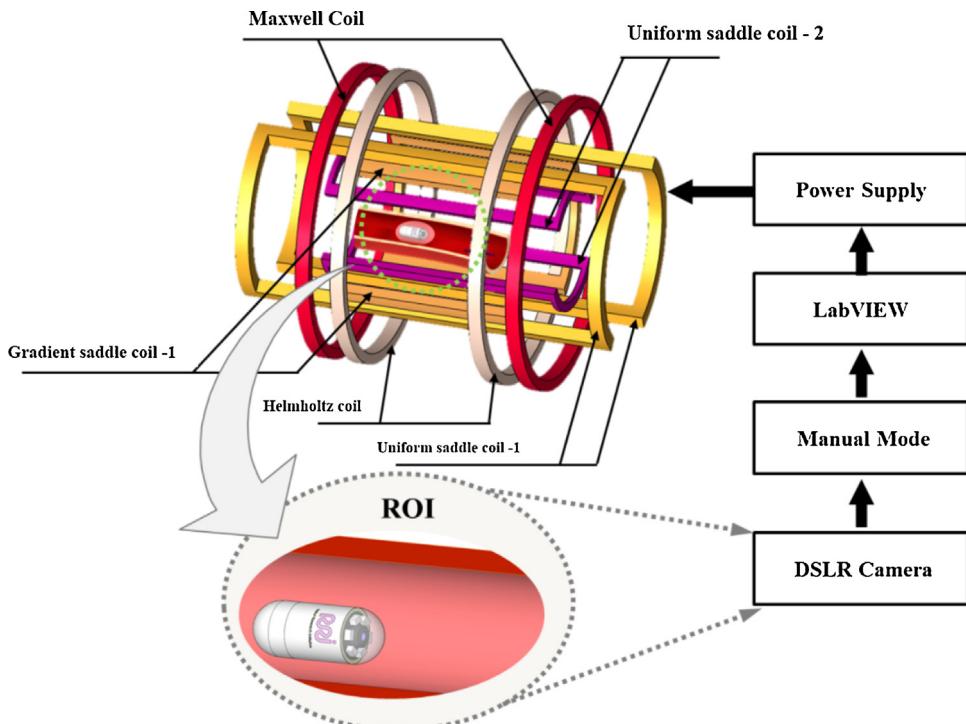


Fig. 1. Schematic of an active locomotive intestinal capsule endoscope with a drug-delivery function inside an electromagnetic actuation system.

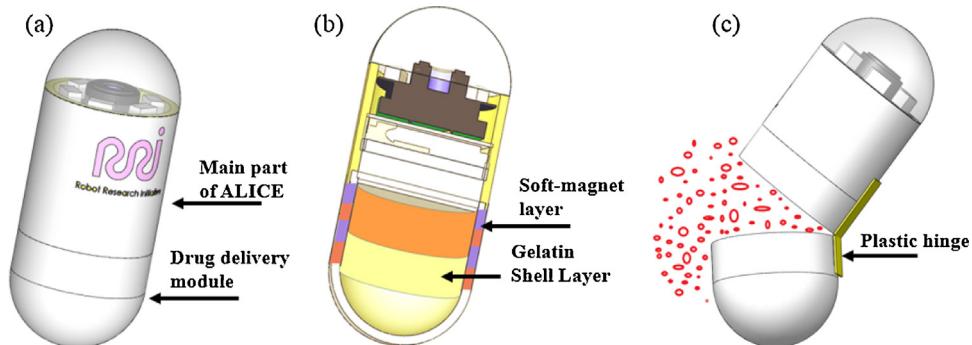


Fig. 2. (a) Normal state of ALICE, (b) Cross-sectional view of ALICE where the upper part is a normal capsule endoscope and the lower part is the drug-delivery module with hard gelatin shells and soft magnets, (c) Drug-releasing state of ALICE.

drug inside ALICE during the diagnosis and locomotion process. In step 2, after ALICE is situated at the target lesion position for the drug release through a precise controlled external EMA magnetic field, the soft magnets are demagnetized to eliminate the initial attraction force between them through an alternating magnetic field. To demagnetize the soft-magnet, we applied a cyclic magnetic field with a decreasing amplitude which repeatedly passes the hysteresis loop of the magnetic material in the proposed drug-delivery module. The applied magnetic field was firstly begun about 30 kA/m, and then was reduced an amount of 5 kA/m at each cycle until zero. In step 3 and step 4, the two soft magnets are detached. When the pulse of a strong magnetic field created by the EMA system with the Helmholtz coil and uniform saddle coil pairs is applied in the radial direction of the drug-delivery module, the two soft magnets are radially magnetized in step 3. Then, as shown in step 4, a repulsive force between the two soft magnets is generated, the drug delivery module is detached, and the encapsulated drug can be released. Finally, after the drug released, the two soft magnets are demagnetized and a suitable magnetic field is applied in the axial direction. Then, the attraction force between the two

soft magnets is generated and the drug delivery module is attached and re-assembled, as shown in step 5. Then, with the drug-delivery module, ALICE can continue the procedure of GI diagnosis.

2.4. Design of the active drug-delivery module integrating the capsule endoscope

Considering the power limitation of the battery in CEs, the drug-delivery module was designed to be actuated without any battery power consumption. Thanks to the magnetization and demagnetization of the soft-magnetic material, the proposed drug-delivery module can be activated without using any battery power. We adopted a pure iron made of more than 99.5% of iron and few impurities, such as phosphorous, sulfur, and carbon. The pure iron has a high magnetic stability, high permeability, high value of remanence (about 1.45 T) and high saturation magnetic induction with a low coercivity. The intrinsic properties of the pure iron facilitate its various uses, such as in aviation instrumentation, electronic tubes, electromagnetic valves, and magnetic separators. Therefore, we selected a soft magnet of pure iron as the main part of the drug-

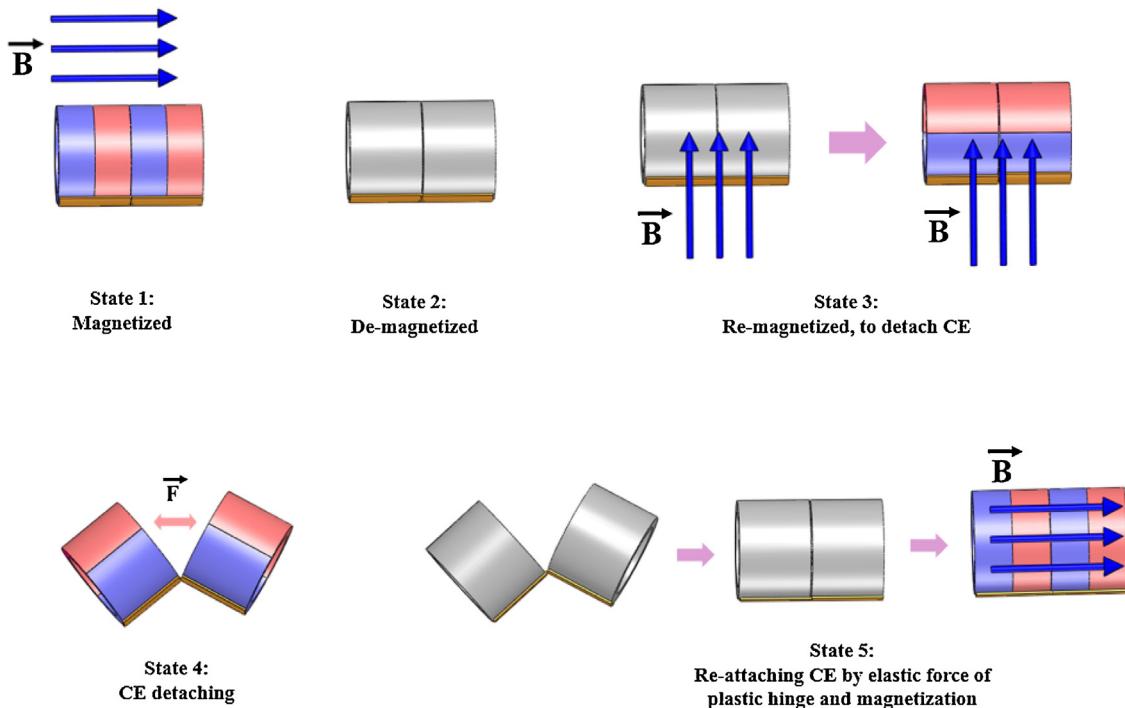


Fig. 3. Principle of active detachment of the capsule to release the drug through the external magnetic field.

delivery module. As shown in Fig. 2b, two ring-type soft magnets made of pure iron were used as the main magnets to generate the actuation force for the locomotion of ALICE and the attaching and detaching force for the drug-releasing mechanism.

To ensure that the active locomotion and diagnosis of ALICE using the two soft magnets were still effective, we considered the actuation force of ALICE with the drug-delivery module. As mentioned above, the EMA system consists of three pairs of magnetic coils for a uniform magnetic field and three pairs of magnetic coils for a uniform gradient magnetic field; ALICE's propulsion force ($F_{propulsion}$) can be expressed as follows [4,17]:

$$\mathbf{H}_m = [g_m x - 0.5 g_m y - 0.5 g_m z]^T \quad (1)$$

$$g_m = 0.641 \frac{\mathbf{i}_m \times \mathbf{n}_m}{r_m^2} \quad (2)$$

$$\mathbf{H}_g = [g_g x - 2.4398 g_g y 1.4398 g_g z]^T \quad (3)$$

$$g_g = 0.3286 \frac{\mathbf{i}_g \times \mathbf{n}_g}{r_g^2} \quad (4)$$

$$i_m = -1.1751 \left(\frac{r_m}{r_g} \right)^2 i_g \quad (5)$$

$$F_{propulsion} = \frac{0.3616 \mu_0 M V i_m}{r_m^2} (\cos \theta \mathbf{i} + \sin \theta \mathbf{j}) \quad (6)$$

where V and M are the volume and magnetization of the soft-magnets; \mathbf{H}_m and g_m are the magnetic field and gradient of magnetic field generated by each pair of Maxwell coils, respectively; \mathbf{H}_g and g_g are the magnetic field and gradient of magnetic field generated by each pair of gradient saddle coils; i_m and i_g represent the current intensity of the Maxwell and gradient saddle coils; r_m and r_g signify the coil radius of the Maxwell and gradient saddle coils; n_m and n_g are number of turns of Maxwell coils and gradient saddle coils; θ denotes the angle between the magnetization direction and the magnetic field; and μ_0 is the vacuum permeability, specifically $\mu_0 = 4\pi * 10^{-7} \frac{T \cdot m}{A}$.

The attraction force between the two soft magnets should be considered to ensure the safe loading of the encapsulated drug during other ALICE procedures. According to [18], to keep the drug inside the chamber without leakage out of the capsule body, the attraction force between the two magnets must be greater than 4N. The attraction force (F) between the nearby magnetized surfaces with the contact area A can be calculated as follows:

$$F = \frac{B^2 A}{2\mu_0} \quad (7)$$

where A is the area of each surface, B is the flux density, and μ_0 is the vacuum permeability. Through calculations obtained using MATLAB, the dimensions of the ring-type soft magnets were chosen as an outer diameter of 5.5 mm, inner diameter of 4.5 mm, and length of 4 mm.

As presented in Fig. 4, the final design of ALICE with the drug-delivery module was fabricated using a rapid prototype 3-D printer with the actual dimensions of a real CE. The prototype of ALICE with the drug-delivery module consists of the body back and forth, two ring-type soft magnets, the gelatin shell layer, and a plastic hinge, as shown in Fig. 4a. Fig. 4b shows the prototype of ALICE before assembling and Fig. 4c presents the complete prototype of ALICE with the drug-delivery module with a pill shape of 12 mm in diameter and 33 mm in length.

3. Experiment

3.1. Evaluation of attraction force for safe drug loading and propulsion force for active locomotion

The attraction force for the safe drug loading and the propulsion force for active locomotion in ALICE with the drug-delivery module were evaluated. The attraction and propulsion forces can be measured using the following experimental setup. First, Fig. 5a shows the schematics of the experimental setup for the measurement of the attraction force between the two soft magnets of the drug-delivery module in ALICE. ALICE was axially positioned and

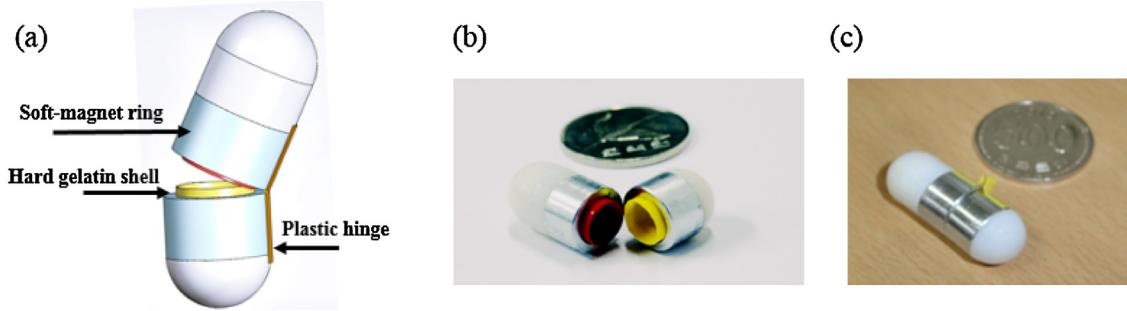


Fig. 4. (a) Designed prototype of ALICE with the drug-delivery function, (b) Prototype of ALICE before assembling, (c) Assembled ALICE prototype.

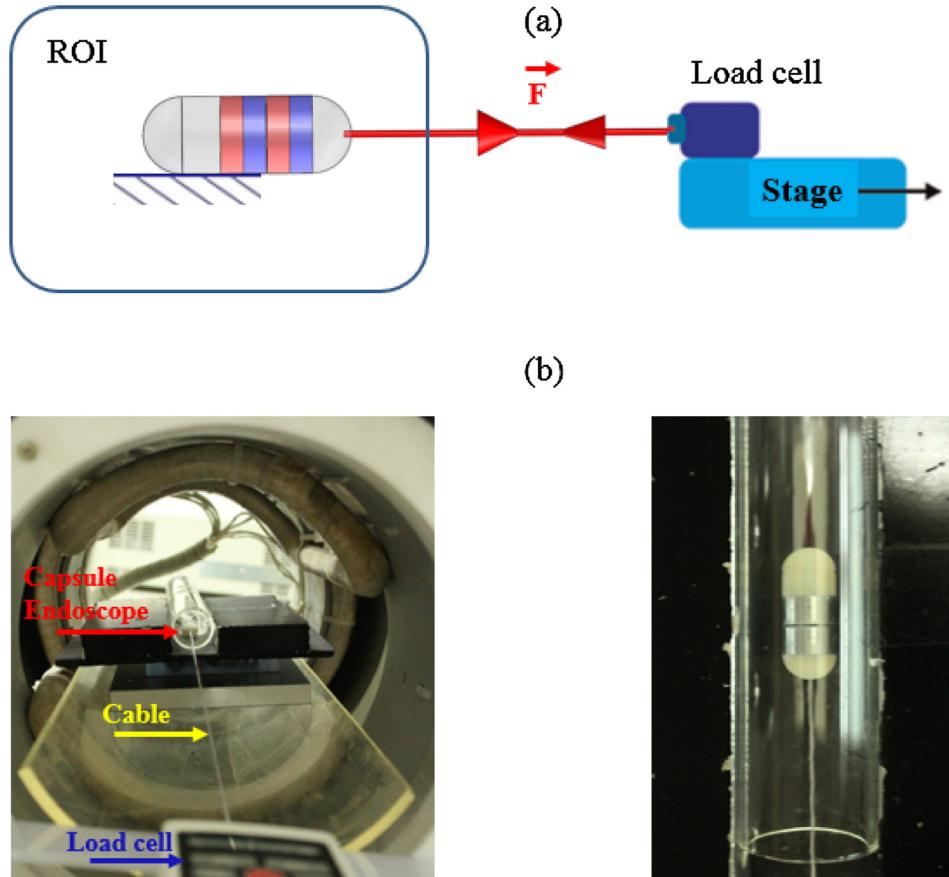


Fig. 5. Experiment testing the attracting force between the two parts of the drug-delivery module.

one main part was adhered to the ROI of the EMA. The other part was connected with a load cell on a linear stage. Fig. 5b shows the real experiment setup with the digital load cell (Advanced Digital Force Gauges Series 5, Mark-10, USA), where the attraction force between the two soft magnets in ALICE was measured and recorded. In addition, the attraction force between two soft magnets can be estimated by Eq. (7). Fig. 6a shows the estimated attraction force and measured attraction force of the two soft magnets in the drug-delivery module in ALICE. As the applied current in the Helmholtz coil pair increases, the uniform magnetic field for the magnetization of the two soft magnets in ALICE increases along with the attraction force between the two soft magnets. The small error between the calculated force and the measured force might have originated from the error of the magnetization value (M) of the soft magnets and the uncertainties of the EMA coil system. The minimum attraction force for safe drug loading in CE is about 4 N [5]. Therefore, when a current of 2A was applied to the Helmholtz

coils, we obtained an attraction force of 4.23N, which is greater than the minimum attraction force of 4N. Because we use a sufficient strong magnetic field (30 kA/m) in our EMA system, the magnetic flux density of the soft magnet reaches a saturation value and the attraction force between the two soft magnets can be considered as a constant (6.5N) which is independent from the applied currents. Consequently, it was verified that the proposed ALICE drug-delivery module has no risk of leakage of the encapsulated drug.

Second, the propulsion force for active locomotion in ALICE was measured using the experimental setup shown in Fig. 5. ALICE was axially positioned and connected with the digital load cell. Fig. 6b shows ALICE's estimated propulsion force and measured propulsion force. When we increase the applied current of the Maxwell coil pair, the uniform gradient magnetic field increased; the propulsion force of the ALICE also increased. With the applied current (15A) on the Maxwell coil pair, the maximum propulsion force (64mN) of ALICE was generated, which was sufficiently greater than

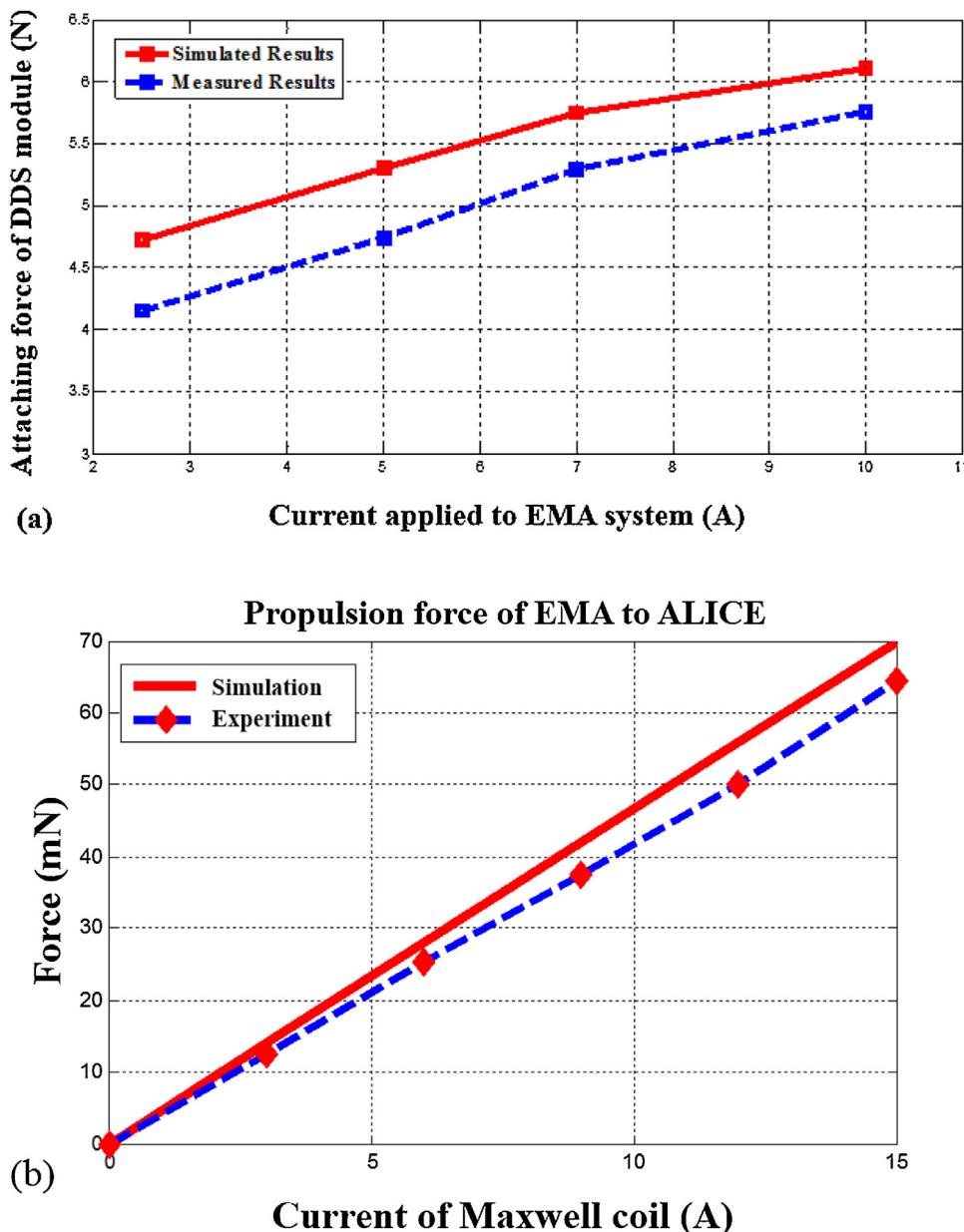


Fig. 6. (a) Force between two parts of the drug-delivery module with various currents applied to Helmholtz pair coils; (b) propulsion force produced by the EMA system on the active capsule endoscope.

the maximum force (50mN) needed to overcome the viscosity and friction force of the digestive system [19]. Therefore, we expected that the drug-delivery module with ALICE would exhibit effective locomotion inside the intestines.

For the evaluation of the drug encapsulation in the drug delivery module, we executed a leakage test, as shown in Fig. 7. We adopted Calcein (Sigma Aldrich, St. Louis, MO, USA) as a simulate drug which was filled the drug delivery module with the Calcein (Fig. 7(a)). First, the assembled ALICE with the drug delivery module was immersed in a bath of 50 ml pure water in EMA system with the magnetic field of 15 kA/m for 4 h (Fig. 7(b)). Then, the concentration of Calcein from the solution in the bath was measured by Varioskan Flash Spectral Scanning Multimode Reader (Thermo Scientific, Waltham, CA, USA). The experiment was executed 10 times and the concentration of Calcein was about 0.026%, which was correspond to about 1.80% of the filled drug in the drug delivery module. Second, the assembled ALICE with the drug delivery

module was also tested a PVC plastic tube (Fig. 7(c)). Similarly, after the locomotion of the ALICE with the drug delivery module in the PVC plastic tube, the drug leakage of the drug delivery module was measured about 1.83% of the filled drug. Based on the leakage tests, therefore, we could confirm the safe drug encapsulation for the ALICE with the drug delivery module.

3.2. Feasibility of ALICE with the drug-delivery module in a stomach phantom

The feasibility of the ALICE prototype was demonstrated through an in-vitro experiment with pig's stomach phantom. The pig's stomach phantom was fabricated using a pig's stomach and the plastic stomach phantom. Then, the pig's stomach phantom was placed into the region of interest (ROI) of EMA system and was filled with water, and the ALICE prototype was put in the pig's stomach phantom, as shown in Fig. 8a. In the in-vitro experiment using

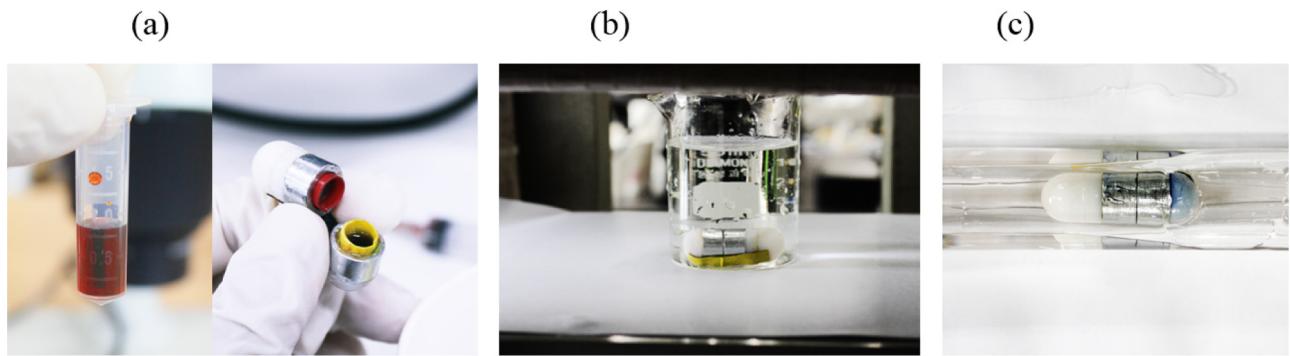


Fig. 7. Feasibility test of the safe drug encapsulation: (a) Drug-delivery module filled with Calcein, (b) ALICE prototype with drug-delivery module in a water bath inside the EMA system, and (c) ALICE prototype with drug-delivery module during locomotion in a water PVC tube inside the EMA system.

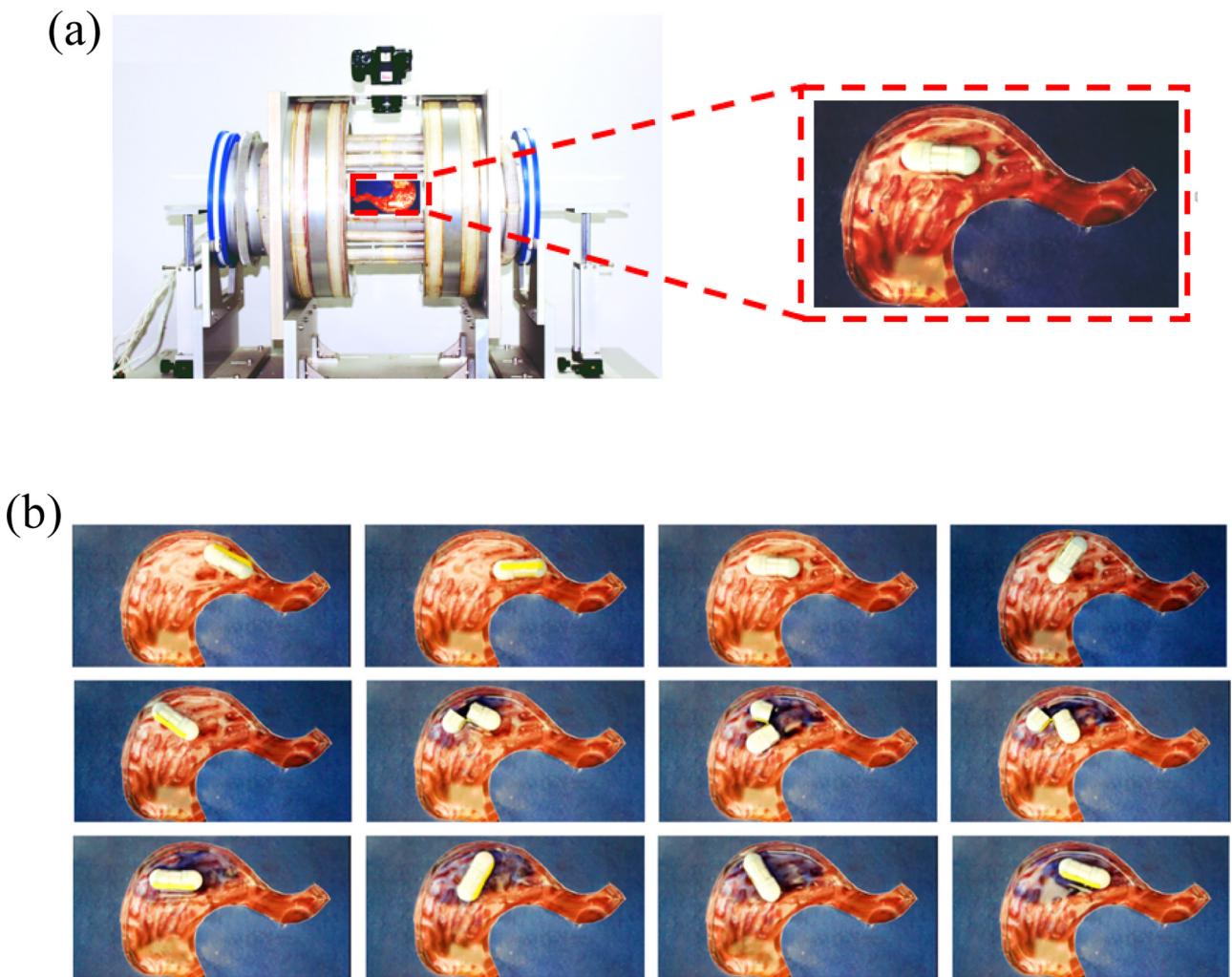


Fig. 8. In-vitro experiment of ALICE prototype using pig's stomach phantom. (a) Pig's stomach phantom and installation of in-vitro experiment of ALICE prototype, and (b) Feasibility tests of ALICE prototype, such as locomotion to a target lesion (first row), the drug-releasing (second row), and the reassembling (third row).

the pig's stomach phantom of the ALICE prototype, we demonstrated the locomotion to a target lesion, the drug-releasing, and the reassembling, as shown in Fig. 8b. Instead of a real drug, a dye was encapsulated in the drug-delivery module. During the locomotion of the ALICE prototype, we adopted the magnetic fields from 10 kA/m to 35 kA/m and the gradient magnetic fields from 0 to 350 kA/m². Consequently, the motion of the ALICE prototype was mainly dependent on the intensities of the magnetic fields and the gradient magnetic fields. In addition, for the open and close

motions of the ALICE prototype, we applied magnetic fields of about 30 kA/m. Fig. 8b shows the feasibility of the locomotion and drug release of the drug delivery module with ALICE. First, ALICE—driven by the magnetic field generated from the EMA system—can move from an initial position to a target lesion without any leakage of the dye in the drug-delivery module. Second, when ALICE is positioned at the target lesion, the drug-delivery module is activated and ALICE is detached into two parts through its detaching mechanism. Then, the encapsulated dye is released to the target lesion. Finally, after

the drug release is complete, the two parts of ALICE reattach and return to the initial state.

4. Conclusion

In this paper, we presented ALICE with an active drug-delivery function and active locomotion. ALICE's drug-delivery module was driven by the interaction between the two ring-type soft magnets and the generated magnetic field of the EMA system. The fabricated ALICE prototype had a diameter of 12 mm and a length of 33 mm. Through the feasibility test, it was shown that the drug-delivery module with ALICE could move to a targeting region and demonstrate the positioning to a target lesion. Therefore, ALICE with the drug-delivery module can provide a powerful tool for surgeons in the treatment of diseases of the digestive system. ALICE with the drug-delivery module allows a non-invasive operation and an easy and quick active-releasing mechanism. Therefore, it has the potential to bring about great benefits in pharmaceutical studies, where the evaluation of drug absorption is a fundamental component in the development of new medications.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.sna.2016.03.020>.

References

- [1] G. Iddan, G. Meron, A. Glukhovsky, P. Swain, Wireless capsule endoscopy, *Nature* 405 (2000) 417.
- [2] R. Eliakim, K. Yassin, I. Shlomi, A. Suissa, G.M. Eisen, A novel diagnostic tool for detecting oesophageal pathology: the PillCam oesophageal video capsule, *Aliment. Pharmacol. Ther.* 20 (2004) 1083–1089.
- [3] R. Eliakim, Z. Fireman, I.M. Gralnek, K. Yassin, M. Waterman, Y. Kopelman, et al., Evaluation of the PillCam Colon capsule in the detection of colonic pathology: results of the first multicenter, prospective, comparative study, *Endoscopy* 38 (2006) 963–970.
- [4] L. Cheong, C. Hyunchul, G. Gwangjun, J. Semi, K. Seong Young, P. Jong-Oh, et al., Active locomotive intestinal capsule endoscope (ALICE) system: a prospective feasibility study, mechatronics, *IEEE/ASME Trans. Mechatron.* 20 (2015) 2067–2074.
- [5] C.T. Dietzel, H. Richert, S. Abert, U. Merkel, M. Hippius, A. Stallmach, Magnetic Active Agent Release System (MAARS): evaluation of a new way for a reproducible, externally controlled drug release into the small intestine, *J. Control. Release* 161 (2012) 722–727.
- [6] A. Connor, Location, location, location: gastrointestinal delivery site and its impact on absorption, *Ther. Delivery* 3 (2012) 575–578.
- [7] C.S.R. cherukuri sowmya, neelaboina vishnu priya, redripalli sandhya, komaragiri keerthi, colon specific drug delivery systems: a review on pharmaceutical approaches with current trends, *Int. Res. J. Pharm.* 3 (2012) 45–55.
- [8] R. Groening, H. Bensmann, High frequency controlled capsules with integrated gas producing cells, *Eur. J. Pharm. Biopharm.* 72 (2009) 282–284.
- [9] X. Pi, Y. Lin, K. Wei, H. Liu, G. Wang, X. Zheng, et al., A novel micro-fabricated thruster for drug release in remote controlled capsule, *Sens. Actuators A* 159 (2010) 227–232.
- [10] S.P. Woods, T.G. Constantinou, Wireless capsule endoscope for targeted drug delivery: mechanics and design considerations, *IEEE Trans. Biomed. Eng.* 60 (2013) 945–953.
- [11] Y. Sehyuk, M. Sitti, Shape-Programmable soft capsule robots for semi-Implantable drug delivery, *IEEE Trans. Rob.* 28 (2012) 1198–1202.
- [12] V.H. Le, L.R. Hernando, C. Lee, H. Choi, Z. Jin, K.T. Nguyen, et al., Shape memory alloy-based biopsy device for active locomotive intestinal capsule endoscope, *Proceedings of the Institution of Mechanical Engineers Part H, J. Eng. Med.* 229 (2015) 255–263.
- [13] K. Kong, S. Yim, S. Choi, D. Jeon, A robotic biopsy device for capsule endoscopy, *J. Med. Devices* 6 (2012) 031004.
- [14] Z. Fireman, A. Glukhovsky, E. Scapa, Future of capsule endoscopy, *Gastrointest. Endosc. Clin. N. Am.* 14 (2004) 219–227.
- [15] P. Valdastri, R.J. Webster, C. Quaglia, M. Quirini, A. Menciassi, P. Dario, A new mechanism for mesoscale legged locomotion in compliant tubular environments, *IEEE Trans. Rob.* 25 (2009) 1047–1057.
- [16] P. Xitian, L. Hongying, W. Kang, L. Yulin, Z. Xiaolin, W. Zhiyu, A novel remote controlled capsule for site-specific drug delivery in human GI tract, *Int. J. Pharm.* 382 (2009) 160–164.
- [17] C. Yu, J. Kim, H. Choi, J. Choi, S. Jeong, K. Cha, et al., Novel electromagnetic actuation system for three-dimensional locomotion and drilling of intravascular microrobot, *Sens. Actuators A* 161 (2010) 297–304.
- [18] H. Richert, O. Surzhenko, S. Wangemann, J. Heinrich, P. Görner, Development of a magnetic capsule as a drug release system for future applications in the human GI tract, *J. Magn. Magn. Mater.* 293 (2005) 497–500.
- [19] J.S. Kim, I.H. Sung, Y.T. Kim, E.Y. Kwon, D.E. Kim, Y.H. Jang, Experimental investigation of frictional and viscoelastic properties of intestine for microendoscope application, *Tribol. Lett.* 22 (2006) 143–149.

Biographies



Viet Ha Le received his B.S. (2013) degree from the school of mechanical engineering at Hanoi University of Science and Technology, Vietnam. Currently, he is a Ph.D. candidate in Chonnam National University and a researcher in Robot Research Initiative (RRI). His research interests are microrobot, microactuator and medical robot.



Hernando Leon Rodriguez awarder his Ph.D. (2008) in Climbing Robot for none destructive testing in London South Bank University- England. Since 2008, he been working in as a lecture and research several macro robots projects sponsor by Nueva Granada Military University in Colombia in industrial application. In 2013, he begins to research in robot research initiative (RRI) of Chonnam National University in Korea, where he is now registering as Ph.D student at the School of Mechanical Engineering. His new research interests are micro robot development and micromanipulation for biomedical applications.



Cheong Lee received his B.S. (2012) and M.S. (2014) degree from the department of mechanical engineering at Chonnam National University, Korea. Currently, he is a Ph.D. candidate in Chonnam National University and researcher in Robot Research Initiative (RRI). His research interests are microrobot and medical robot.



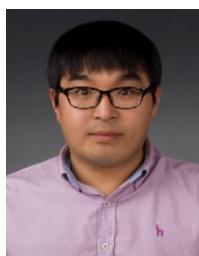
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Van Du Nguyen received his Master's degree of Science in Industrial & Systems Engineering from Korea Advanced Institute of Science and Technology (KAIST), Korea in 2009. In 2014, he joined the Robot Research Initiative, School of Mechanical Engineering, Chonnam National University, Korea as a Ph.D. student. His research interests include biomedical micro/nano robots, targeted drug delivery systems.



Hyunchul Choi received his B.S. (2008) and M.S. (2010) degrees from the Department of Mechanical Engineering at Chonnam National University, Korea. Currently, he is a Ph.D. candidate at Chonnam National University and a researcher in the Robot Research Initiative (RRI). His research interests are microactuators and microrobots.



Seong Young Ko obtained his Master's degree (2002) and Ph.D. (2008) both in Mechanical Engineering from Korea Advanced Institute of Science and Technology (KAIST), Korea. From 2009–2011, he was a Postdoctoral Research Associate at the Mechatronics in Medicine Laboratory, Department of Mechanical Engineering, Imperial College London, UK. In 2011, he joined School of Mechanical Engineering, Chonnam National University as an Associate Professor. His research interests include Medical Robotics, Human-Robot Interaction and Intelligent Control.



Jong-Oh Park received his Master's degree in Mechanical Engineering from Korea Advanced Institute of Science and Technology (KAIST), Korea in 1981 and Dr.-Ing in Robotics from Stuttgart University, Germany in 1987. From 1982 to 1987, he worked as a guest researcher Fraunhofer-Gesellschaft Institut für Produktionstechnik und Automatisierung (FhG IPA), Germany. He worked as a principal researcher in the Korea Institute of Science and Technology (KIST) from 1987 to 2005, and he was a director of the Microsystem Research Center in KIST from 1999 to 2005. In 2005, he moved to Chonnam National University, where he is now a full professor of the School of Mechanical Engineering and a director of the robot research initiative (RRI). His research interests are biomedical microrobot, medical robot and service robot.



Sukho Park earned his Master's degree (1995) and Ph.D. (2000) in Mechanical Engineering from Korea Advanced Institute of Science and Technology (KAIST), Korea. From 2000 to 2004, he worked as a senior research engineer at LG Electronics Production Research Center, Korea. From 2004 to 2006, he worked as a senior researcher of Microsystem Research Center in the Korea Institute of Science and Technology. In 2006, he moved to Chonnam National University, where he is now a professor of the School of Mechanical Engineering and a section head of the robot research initiative (RRI). His research interests are microactuator/robot and micromanipulation for biomedical instrumental applications.