Novel Active Locomotive Capsule Endoscope with Micro-Hydraulic Pump for Drug Delivery Function

Viet Ha Le, Hernando Leon-Rodriguez, Cheong Lee, Jin Zhen, Hyun Chul Choi, Gwangjun Ko, Van Du Nguyen, Seong Young Ko, Jong-Oh Park*, and Sukho Park*, Member, IEEE

Abstract— This paper presents a novel mechanism and design of capsule endoscope in order to perform an active locomotive capsule endoscope (ALICE) robot integrated with micro-hydraulic pump for drug delivery function. The proposed locomotive capsule endoscope can actively move and investigate in gastrointestinal tract, powered externally by an electro-magnetic actuation (EMA) system. To perform a drug pumping function, the rotating frequency of the active hydraulic pump can be adjusted by the EMA system. The novel capsule endoscope with the micro-hydraulic pump is focused on target drug delivery function. The capsule endoscope is able to target suspicious region and release controllable amount of drug. Through preliminary tests of the locomotive capsule endoscope with the micro-pump, the feasibility of the locomotion and the drug releasing of the novel capsule endoscope will be presented. The micro-hydraulic pump for a drug delivery function will be a potential component for a future capsule endoscope with active maneuverability, diagnostic and therapeutic functions.

***Index Terms*— Capsule endoscope, active locomotion, drug delivery, electromagnetic actuation, pump**

I. Introduction

Recently, to deal with gastrointestinal (GI) diseases medical doctors use endoscopy and capsule endoscope to investigate on upper or lower visual endoscopy examination. Since 2002, a later version of capsule endoscope was widely commercialized as PillCam (Given Imaging, Israel), EndoCapsule (Olympus, Japan), and MiroCam (Intromedic, Korea). However, the capsule endoscopes have a common weak point in terms of passive locomotion which is relying on peristaltic force of human digestive system. The passive locomotion will make the capsule endoscope miss some abnormal lesions due to the lack of orientation and speed control of capsule camera. One solution of the problem has been previously reported with an active locomotion capsule endoscope driven by external electromagnetic actuation system [1, 2]. Taking advantages of the novel technology, a multi-functional capsule endoscope should be developed to meet the crucial need of the doctors: treating gastrointestinal diseases, defining abnormal cell or discovery the absorbing ability of each area of the colon.

Concretely, there are need integrated function to capsule endoscope such as biopsy or pH concentration measurement and the function of drug delivery. In this paper, we present a module of capsule endoscope with drug delivery function at specific section of the gastrointestinal (GI) tract. The topic of drug delivery system is a very important field of research which can use for therapeutic treatment of intestinal diseases or for drug absorption studies which often cost millions of dollars per year to pharmaceutical industry [3].

Several research studies about drug delivery function for capsule endoscope have been reported since last several years. In 2009, the first idea for the capsule endoscope with active drug delivery function was reported in [4]. A capsule with small gas producing cell is activated by a high frequency signal induced current in an oscillating circuit. The pressure produced by the cell can push the piston forward to release drug from a reservoir. The platform can release drug with controlled releasing rate. However, only 16% volume of the capsule can be used for loading drug. In addition, the activation time for the drug releasing takes an hour, which makes it less attractive to doctors. Second, an active DDS using micro-thruster was reported in [5] and the above disadvantages of the low drug loading volume and the slow releasing time were solved. The capsule can load effective a large volume of drug (30% total volume of capsule endoscope). However, a common weak point in the both capsule endoscope with the drug delivery modules is the inability of anchoring and targeting to a specific lesion of the intestinal tract.

S. Yim et al. proposed a soft-capsule which made of two magnetic parts which attracted to each other with enough magnetic force to keep the capsule closed during its travel through the GI tract [6]. Once the capsule reached the target position, an external magnetic field was used to open the capsule and release drug. The DDS method therefore is more effective with an anchoring mechanism and active releasing method. Nevertheless, the volume for loading drug of the soft capsule endoscope is small; also, the module can only integrated with soft-capsule endoscope which is not yet full

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develop to commercialize as the pill-shaped capsule endoscope, and used popularly.

Stephen et al. developed a capsule endoscope comprising holding or anchoring mechanism with C shaped tip legging mechanism which is expanded by a micro-motor [7]. However, with only an on-board battery the actuation of micro-motor and the limitation of capsule endoscope size would lead to the complex fabrication of capsule endoscope. Another major challenge of the mechanism is that it could not work in the region with diameter larger than 40mm such as the stomach.

In this paper, a new platform of capsule endoscope will be presented. The novel capsule endoscope integrated with a micro-hydraulic pump powered by external magnetic field of electromagnetic actuation system is introduced. The new capsule endoscope can go to specific targeting lesion in the intestine and release a specific amount of drug. The new method of drug delivery can be compatible with pill-shaped capsule endoscope which is popular commercialized. Several experiments are conducted to show the feasibility of the proposed active locomotive capsule endoscope with a micro-hydraulic pump for a drug delivery function.

II. Capsule Endoscope Design Specification

The capsule endoscope should have the shape of a large pill-type, camera and lightning system, programmable electronics and a power supply [8]. The size of the modules also should be suitable to be integrated into the existing capsule endoscope which have the volume of 3.0cm3 or any device with similar dimension [9]. The wireless telemetry module is plugged with several electrode pads (array of sensors) placed on the patient abdomen, similar to long-term electrocardiogram techniques in order to collect wirelessly data from the capsule when it moves by the peristaltic motions in the digestion system. The vision module consists in one micro-camera with the highest quality images possible on this size which could around (320x 320 pixel); but, in order to optimize images quality, an automatic brightness control of 4 to 6 white led lights enables to get clear images. And the acquired images are transmitted in real time. The capsule endoscope is also required not only just to be able to take pictures and send them out from the body; but also requires several functions of localization, position control, carry and perform hopefully the function of drug delivery or biopsy [7]. The wireless remote actuation mechanism should consume small amount of energy which is limited available in battery of capsule endoscope. The magnetic field and radiation created by the external field system must be in safety range for human body as well as cause no risk of damaging human tissue, according to the standard requirement [12]. For drug delivery function of capsule endoscope, the active releasing mechanism of drug delivery module should have wireless active controlled function which could be used in any environmental conditions of various section of GI tract independently from pH level or diameter of the intestine as well as disease conditions and the aging factor. The drug reservoir is desirable to have the large ratio compare to the total volume of the capsule endoscope [10].

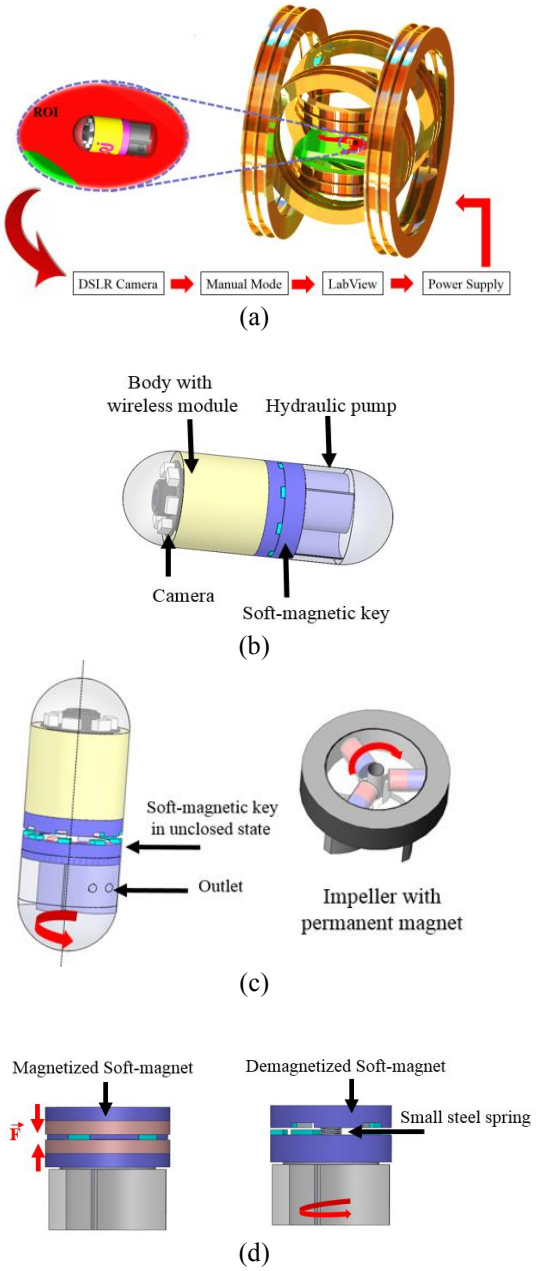


Figure 1. (a) Schematic of active locomotive intestinal capsule endoscope powered by electro-magnetic actuation system, (b) Schematic of conceptual capsule endoscope with micro hydraulic pump in locomotion state, (c) Capsule endoscope in the state of releasing drug with unclosed soft-magnetic key and the impeller structure, (d) working mechanism of soft magnetic key

III. Target Drug Delivery Mechanism

A. Principle Mechanism

Figure 1(a) shows the schematic diagram of overall active locomotive intestine capsule endoscope (ALICE) operating

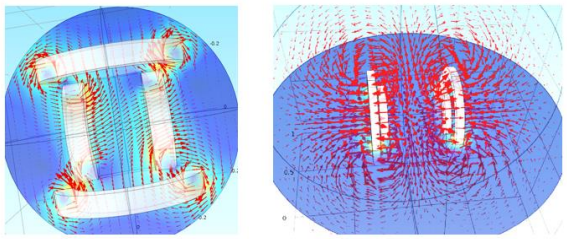
system. The ALICE with drug delivery module was put inside the electromagnetic actuation (EMA) system and driven by EMA system's external magnetic field. The EMA system, as it was introduced in [11], consists of two parts: part 1 is three pairs of Helmholtz coils perpendicular to each other in the x, 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). The system can provide various voltages to magnetic coil pairs with the limit of 160V and frequency up to 20Hz. The system creates safety amount of magnetic field intensity which is not harmful to human body.

Figure 1(b) introduces the novel ALICE with drug delivery module. The upper part of capsule endoscope is called as main part of ALICE having main components of the conventional capsule endoscopy with camera, telemetry module, batteries. The lower part of ALICE is the drug delivery module with magnetic system consisting of permanent magnet and 1 pair of soft-magnetic material. Under the interaction of the external magnet of EMA system, the magnet system can have perform in two states helping the ALICE perform the locomotion function and drug releasing function respectively. Firstly, as shown in figure 1(b) the ALICE is in the state of giving active locomotion. In this first state, the pair of soft magnetic keys made of pure-iron was magnetized in the axial direction of the ALICE. Due to physical properties of soft magnet which is easily magnetized as it was put in strong magnetic field, the soft-magnetic key pairs attach to each other and also fixed the propeller of the ALICE. Therefore, pair of permanent magnet in the propeller is fixed and together with the fixed soft-magnetic keys it create a fixed magnetic system with union magnetization direction. Under the interaction with uniform and gradient magnetic field of EMA system, the ALICE with fixed magnetic system can be driven and controlled to perform the investigation locomotion approaching the targeting lesion in the gastro-intestinal tract.

Secondly, figure 1(c) shows the ALICE and the magnetic system in the state of releasing drug after the ALICE approaching the targeting lesion. In this state, the soft-magnetic key is demagnetized detaching away from each other to unfix the pair of permanent magnet of the impeller. Then the rotation of magnetic field of both Helmholtz coil pairs and Maxwell coil pairs are applied to the ALICE. Un-fixed permanent magnets by their interaction with external magnetic field rotates the propeller and pump the drug to the outside of ALICE. Rotation magnetic field and gradient field created by EMA system help the permanent magnet pairs can rotate about the shaft coincident with ALICE's axis without changing ALICE position. Therefore, the drug can be exactly release at target position. By controlling the rotation frequency of the magnetic field the releasing rate of drug is controllable.

After the drug releasing, the magnetic field is applied in the axial direction of ALICE to magnetized soft-magnetic key. The magnetic system of the ALICE return to the state of giving active locomotion helping the ALICE continue its investigation function.

Figure 1(d) presents the structure of drug delivery module consisting of pair of soft-magnet ring made of pure iron, sandwiched in the middle an small spring. At the state of targeting lesion, the pure iron rings were magnetized to having magnetic direction in axial axis of ALICE. The two rings attach to each other prevents the rotation of hydraulic propeller. After approaching to targeting lesion, the pure-iron will be demagnetized and detach from each other helping the hydraulic propeller can be rotate by external rotation magnetic field.



(a) (b)

Figure 2. (a) Simulation of magnetic field created by Helmholtz coils, (b) Simulation of magnetic field created by pairs of Maxwell coils

B. Electro-magnetic actuation system (EMA)

With the demand of recent technology wireless magnetic robot powered by an electromagnetic coils at a specific arrange surged as the most reliable way for microrobot which does not have space to store battery or energy. The EMA system, as it was introduced in [11] can effectively solving the problem. Generally, the EMA system consists of the combination of 2D, 3D electromagnetic coils arranged at 90 degrees with one pair of Helmholtz and Maxwell coils. In other words, they are uniform or gradient coils which generates uniform and uniform gradient magnetic field in x-, y-, z-axes. Two identical circular magnetic coils are called as Helmholtz coils, where the radius of the coils is equal to the distance between them and the applied currents with the same intensity flow in the same direction. Through the simulation of Helmholtz coil, as shown in Figure 2(a), we found that the uniform magnetic field was generated. In addition, the Maxwell coil pair creates a gradient magnetic field in every direction to push a force forward or backward to the aligned object in Figure 2(b). With the combination of Maxwell coils pairs and Helmholtz coil pairs, we built an EMA system for the 3D locomotion of ALICE, as shown in Figure 3. The EMA system can perform function of align capsule endoscope in the given direction and control its direction of movement within the region of interest of EMA system. In addition, the three Helmholtz coil pairs can generate a rotational magnetic field and the rotational motion in the axial direction of the impeller can be produced. The torque (τ) produced by Helmholtz coil pairs to aligned magnet:

$$\tau = VMB \quad (1)$$

where V and M are the volume and magnetization of magnet and B is the magnetic flux.
The maximum magnetic field strength of our EMA system can create is about 0.05T which is much less than the harmful intensity which can be cause problem to human body 2T [12].

C. Drug releasing compeller design

The propeller with structure shown in Figure 1(c) has three permanent magnet. By using rotational magnetic field created by EMA system, the impeller is controlled by an operator. The angular speed ω of the propeller is directly proportional to the frequency which can be set for the Helmholtz coil pairs. When sine wave currents are applied to the Helmholtz coils, the rotating magnetic field is generated. Figure 6(a) presents capsule endoscope ALICE in space in arbitrary direction. Figure 6(b) shows the schematic diagram about principle of hydraulic pump propeller rotation motion, where P, $\boldsymbol{a}$ and φ are the center of rotation axis (magnetization direction), normal vector (on P-z plane) and angle with the x-y plane. θ denotes the angle between P-$\underline{a}$ plane and x-axis. The vector a and P coordinate can be expressed like as equation (2).

$$\begin{bmatrix} P \\ a \end{bmatrix} = \begin{bmatrix} cos\varphi \times cos\theta & cos\varphi \times sin\theta & sin\varphi \\ -sin\varphi \times cos\theta & -sin\varphi \times sin\theta & cos\varphi \end{bmatrix} \quad (2)$$

By using $\boldsymbol{\alpha_t} = 2\pi\omega t$ (the angle of rotation about the $\boldsymbol{a}$ axis), Eq. (3) can be calculated.

$$\begin{bmatrix} B_{x,t} \\ B_{y,t} \\ B_{z,t} \end{bmatrix} = \begin{bmatrix} -sin\varphi \times cos\theta \times cos2\pi\omega t + sin\theta \times sin2\pi\omega t \\ -sin\varphi \times sin\theta \times cos2\pi\omega t - cos\theta \times sin2\pi\omega t \\ cos\varphi \times cos2\pi\omega t \end{bmatrix} \quad (3)$$

where $B_{x,t}$, $B_{y,t}$, and $B_{z,t}$ mean the direction vectors of magnetic magnetization angle. The magnetization direction of magnetic and the direction of the movement can be driven by setting arbitrary desire direction. It is defined rotating magnetic field.

The gradient magnetic can be created by x-axis Maxwell coil pair with the same frequency with rotation magnetic field. The hydraulic propeller there force can rotate around the axis of ALICE.

The hydraulic pump has the flow rate of the liquid relates to the rate of rotation of the impeller as Eq. (4):

$$\boldsymbol{V_j} = V_r \left(\frac{r}{R}\right) \boldsymbol{j} \quad (4)$$

where V_r = rω is the speed of the liquid at the tip of the impeller (which should be identical to the tip speed of the impeller); r and R are the distance of liquid at the point of simulation, and the tip of propeller from the center of propeller; $\boldsymbol{j}$ is the orthogonal unit vectors in axial direction **P** of the capsule endoscope.

The liquid Q passing through the outlet of the capsule with the area A is expressed by Eq. (5):

$$Q = A\boldsymbol{V_j} \quad (5)$$

According to the Eq.(4) and Eq.(5), the simulation of the velocity of drug releasing out of ALICE with the circular shaped outlet of 1.2mm in diameter and various frequency of 0.33Hz, 0.67Hz and 1 Hz created by EMA system was estimated as in Figure 4. According to the simulation, the amount of drug releasing out ALICE is controllable by the adjustment of the frequency current applied to EMA system.

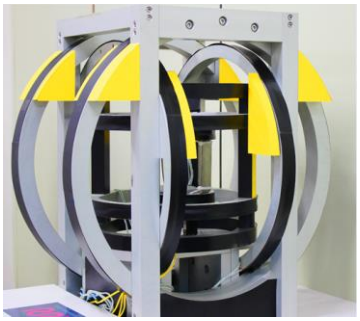


Figure 3. Electromagnetic actuation system

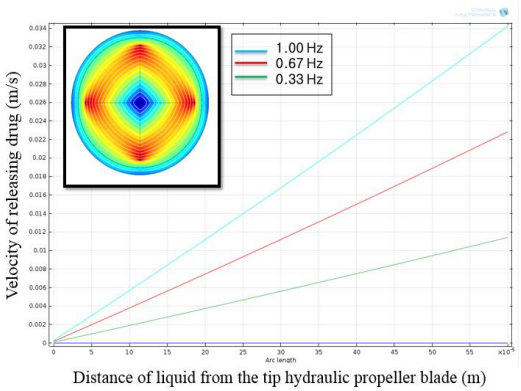


Figure 4. Simulation of drug releasing velocity

IV. Experiment

Firstly, the preliminary test to check the releasing rate of the drug with ALICE integrated hydraulic pump was processed. The ALICE prototype was assembled from the printed chassis by rapid prototype 3D printing machine and the soft-magnetic key and permanent magnet. Figure 5 shows the model of ALICE prototype on SolidWork computer aided design software and the real fabricated prototype of ALICE for the experiment. The fabricated ALICE has dimension of 32mm in length and 12mm in diameter, the outlet to releasing drug has circular shape with radius 0.6mm. The ALICE was put in the region of interest (ROI) in EMA system, as shown in the schematic diagram in Figure 1(a). Then we applied the current with various frequency to EMA system. The applied currents to EMA system can be seen in the Figure 6(b). Under the driven of alternating rotation magnetic field of Helmholtz

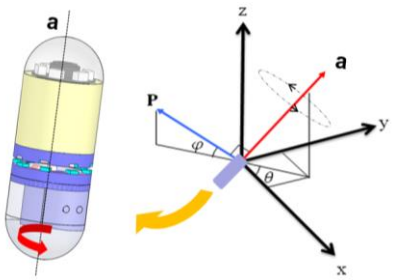
coil pair in x-axis and y-axis, the propeller in the ALICE was rotated and the loaded drug was released out, as shown in Figure 6(c). With the applied frequency of 0.33Hz, the ALICE with micro-hydraulic pumps can release total drug volume of 0.8ml inside within 22 second. The releasing rate is almost identical with the simulation results with the simulation in Figure 4.

Figure 5. SolidWorks model and real prototype of active drug delivery capsule endoscope

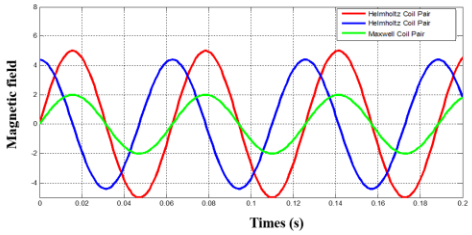
Next, an additional experiment was proceeded to demonstrate ALICE full function with ability of locomotion and drug releasing. Both the plastic phantom of human stomach and real fabricated prototype of ALICE with drug delivery module were put inside ROI of the EMA system, as the presented diagram shown in the schematic diagram of Figure 1(a). As shown in Figure 7, under the driven of EMA system, the capsule endoscope ALICE could perform active locomotion with it specific features such as: forward moving and rotating. At last, the ALICE with drug delivery module performed drug releasing function after the approaching the target lesion. The experiment confirmed the feasibility of the active locomotive capsule endoscope with drug delivery module working principle and proposed mechanism.

V. Conclusion

An active capsule endoscope with the drug delivery function has been proposed and presented in this paper. The ALICE with the dimension of a large pill integrated with micro-hydraulic pump can execute a locomotion to a target lesion and a drug releasing of the desired amount of drug. The design and mechanism of ALICE with the drug delivery function was presented and the feasibility of the model was verified through fundamental experiments. Consequently, it is expected that the proposed ALICE with the drug delivery function can be a powerful tool for a surgeon and can be used for the diagnosis and treatment of various digestive diseases. Because the proposed ALICE with the drug delivery function can be used for the development of new medication as well as the studies about the drug absorption inside human body, it can be also a potential to bring the great benefits of the pharmaceutical industry. In future, it is necessary to develop a real ALICE with biocompatible material which can really come into human gastrointestinal tract.



(a)



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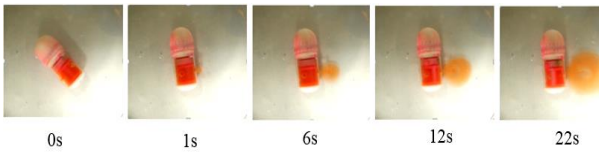

(c)

Figure 6.(a) free body diagram of ALICEE in space (b) Sinusoidal response of Helmholtz and Maxwell coils pairs to powered micro-hydraulic pumps for capsule endoscope. (c) Drug releasing of capsule endoscope

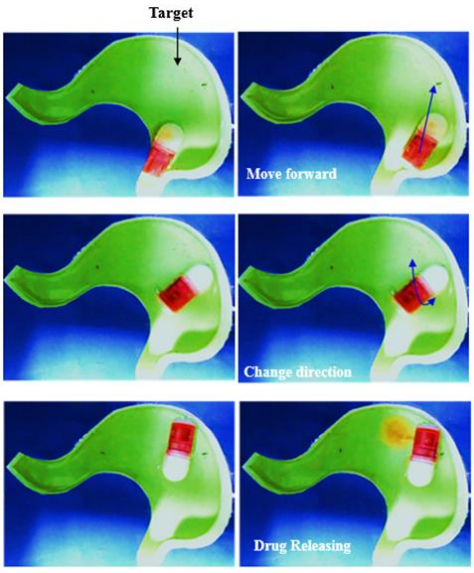

Figure 7. Test of active locomotive ability and target releasing drug of novel capsule endoscope

Acknowledgments

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