Proceedings of 2019 IEEE
International Conference on Mechatronics and Automation
August 4 - 7, Tianjin, China

Design and Evaluation of A New Push-type Targeted Drug Delivery Capsule Robot

Jian Guo[1] and Zihong Bao[1]

[1]*Tianjin Key Laboratory for Control Theory & Applications in Complicated Systems and Biomedical Robot Laboratory*
Tianjin University of Technology
Binshui Xidao Extension 391, Tianjin,300384,China
jianguo@tjut.edu.cn; bzh5813@sina.cn

Shuxiang Guo[1,2*], Qiang Fu[1*]

[2]*Intelligent Mechanical Systems Engineering Department*
Faculty of Engineering
Kagawa University
Takamatsu, Kagawa, Japan
guo@eng.kagawa-u.ac.jp;fuqiang6369@hotmail.com

***Abstract* - Capsule endoscope robot is a new technology for the diagnosis and treatment of digestive tract diseases, which is painless and low invasive. However, the functions of capsule robots are mainly focused on diagnosis, and there are few studies on targeted drug delivery. This paper presents a new type of push-type capsule robot. The robot is 44mm long and has a diameter of 19mm. It is internally equipped with a piston, spring, drug compartment and magnetic lock. Through theoretical analysis of thrust and drug ejection speed, the drug can be sprayed to the uppermost end of the gastrointestinal wall in consideration of the drug resistance as its own gravity. When the external driving frequency is between 12 Hz and 14 Hz, the magnetic lock of the robot will be released, and the piston is squeezed out of the drug chamber by the combination of the spring force and the attraction of the magnet, and the drug is released to the lesion through the medicine outlet. The flexibility of this robot to deliver drugs has been proven in experiments and will soon be available for treatment.**

Index Terms - drug delivery, wireless capsule robot, ring-shaped magnet, Helmholtz coils, push structure

I. INTRODUCTION

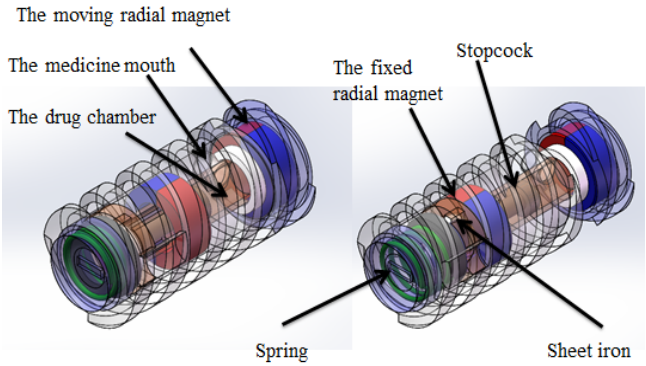
Gastrointestinal diseases are old problems that trouble people. As our daily diet must go through the gastrointestinal tract, it is necessary for us to pay attention to the health of the gastrointestinal tract. According to the data, the number of gastroenteritis patients in China is as high as 230 million, among which about 40% suffer from gastroenteropathy for a long time, and colorectal cancer patients are also on the rise [1-4]. The intestinal health of Chinese people is not optimistic. Early detection, early diagnosis and early treatment can significantly improve the cure rate and prolong the life of patients. With the development of micro electromechanical systems (MEMS) and capsule robots, there is a growing demand for targeted drug delivery capsule robots in drug therapy [5-8].

Given Imaging, a medical technology company from Israel, launched the world's first commercial capsule endoscope product called M2A capsule. But its movement depends on the physiological natural peristalsis of the digestive tract, which means it is passive [9-12]. In 2014, the Institute of Electrical Communication of Tohoku University of Japan proposed a capsule robot based on the magnetic characteristics and hybrid speed control method of a portable external drive device for a DC motor. In the same year, the agency proposed a robotic structure capable of autonomous movement and administration, but could not determine the lesion information and location [13-15]. In 2015, the Guo Lab team proposed a new magnetically driven hybrid micro-robot driven by an electromagnetic drive system. The drive source is provided by an external three-axis Helmholtz coil [24-25]. The robot can realize multi-degree-of-freedom movement, its mo vement form is more stable, the propulsive force is higher, and its environment adaptability is higher, and different movement modes are switched according to different environments.. Zhang et al. of Dalian University of Technology conducted continuous research on magnetic wireless capsule robots, and developed variable-diameter capsule robots and double hemisphere capsule robots based on multi-wedge effect. When the variable diameter robot rotates, the multi-wedge effect pushes the axial movement of the robot through the thrust generated by the wedge gap to realize the non-contact movement of the robot. Double hemisphere capsule robots can take active and passive flexible movements [14-17]. In 2017, the Chinese University of Hong Kong proposed a wireless airbag capsule robot that can achieve gastrointestinal hemostasis, with acid and alkali gas placed inside, inflated by acid-base endothermic reaction, when the balloon reaches a predetermined pressure level, internal acid The alkali reaction stops and the purpose of hemostasis is achieved by extrusion [17-20].

Although some achievements have been made in the research of wireless capsule robots in-pipe, the research in this field is still in the stage of continuous exploration and improvement for clinical application, and a series of key technical problems still need to be solved urgently. In this paper, our team designed a new robotic structure that can be used to administer drugs to certain fixed areas through the internal structure of the robot for drug delivery purposes,. as shown in Fig.1.

The structure of this paper is as follows. In the second part, we introduce the structural model and dimensions of the drug delivery robot. In the third section, we analyzed the structure of the robotic drug compartment. In the fourth part, we assembled the robot and tested its motion and application experiments to verify the feasibility of our model. Finally, our conclusions and future work.

978-1-7281-1697-6/19/$31.00 ©2019 IEEE



(a) Structure when drug is not released (b) Structure when drug is released

Fig1. 3D structural model of drug release robot

II. THE DESIGN OF THE PROPULSION DRUG - DELIVERY ROBOT

Previously, our team has proposed to rely on gravity to release drugs to achieve the drug delivery function, but the complete release of drugs cannot be achieved by relying on gravity alone. Therefore, in this paper, a kind of impelling-type dosing structure is proposed. The thrust has the elastic force of the spring and the magnetic attraction to the iron sheet. The release of a drug is by pushing.

A. The structure of the robot

The wireless spiral-capsule robot for drug delivery consists of a number of small components, as shown in Fig 2, including a moving housing, an internal cartridge, a thrust device, and a radial magnet driving the robot.

Fig 3 shows the size of the robot. Fig (a) shows the size of the robot when it is closed. The overall length is 44mm. Fig (b) shows the size of the robot when releasing the drug. The overall length is 48mm. Fig (c) shows the peripheral diameter of the robot is 19mm.

B. Fabrication of Robots

In the case of limiting the size and position of the robot, the two magnets inside the micro-robot are not easy to use conventional processing methods. Therefore, we divided the individual robot model into several parts, each of which was printed using ABS plastic 3D printer. The machining accuracy of the robot is 0.1mm, which is enough for the robot in this article.

C. Analysis of Robot torque

When the robot moves in the pipeline, two ring magnets inside the robot act as a driving source, and the external three-axis Helmholtz coil provides propulsion and torque to the robot. The robot rotates due to the magnetic torque T. The driving force F and torque T received by the robot can be obtained by equations. (1) and (2).

$$F = V\left(M \bullet \nabla\right) \times B \tag{1}$$

$$T = VM \times B \tag{2}$$

where, B is magnetic flux density, M is the magnetization of the magnet and V is the volume of the magnet[23].

When the frequency of the three-axis Helmholtz coil is between 12Hz and 14Hz, when the voltage rises to 15V, the moving magnet inside the robot will be rotated by the external influence, which is at the same end of the same magnetic pole, forcing the magnetic lock of the robot. Released, the drug store opened. When the frequency of the three-axis Helmholtz coil is between 12Hz and 14Hz, when the voltage rises to 15V, the moving magnet inside the robot will be rotated by the external influence, which is at the same end of the same magnetic pole, forcing the magnetic lock of the robot. Released, the drug store opened. The repulsive force between the two magnets is as shown in equation 3.

$$F1 = \frac{1.5}{1 + aL_q}\left(\frac{Bq}{4865}\right)^2 Aq \tag{3}$$

Where F1 is the attraction between magnets; a is the correction factor, usually a=3~5, taking the large value when the clearance is large, and the interval is small; Bq is magnetization of permanent magnet; Aq is the magnetic field area of permanent magnet; Lq is the gap between two permanent magnets[24].

III. DESIGN AND ANALYSIS OF MEDICINE BIN

The drug compartment is the most important part of the whole drug delivery robot. In order to ensure the accuracy of the drug delivery, it is necessary to have an accurate calculation of the thrust and the speed of drug ejection.

A. The design of the medicine bin

In this section, our team added a piston device inside the medicine bin. This device acts as a force transfer device, and the resultant force of the spring and the attraction between magnets is used as the thrust to transfer to the interface of the drug. The process and structure of the drug release are shown in Fig 4.

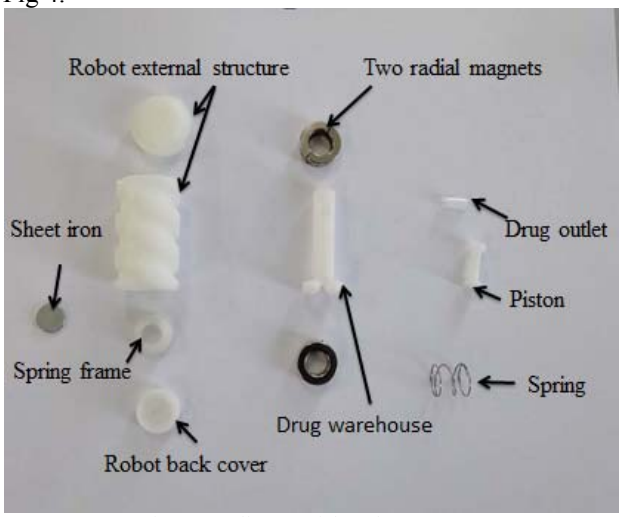
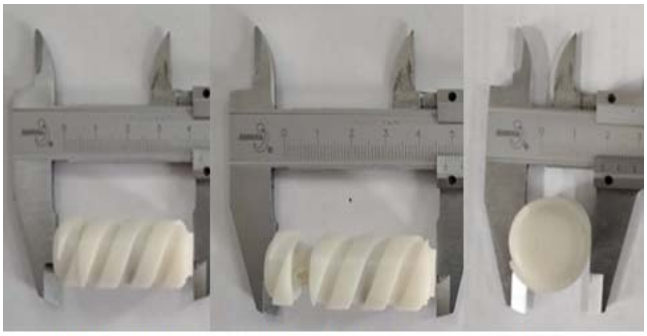


Fig. 2. Small parts of the robot structure



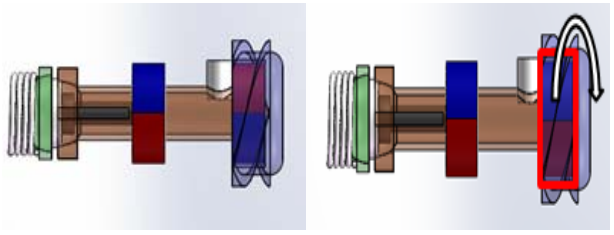
(a)The length of closed robot (b)The length of open robot (c)The diameter of robot

Fig.3. The size of the 3D printing robot model

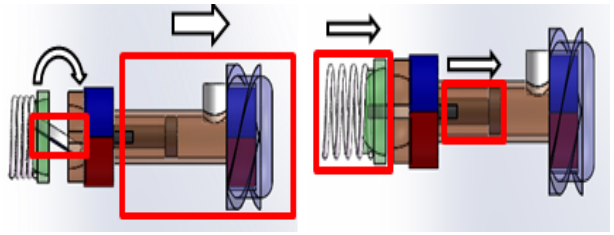
Fig3.(a) shows the initial state of the internal drug compartment of the robot. The drug is sealed in the capsule by a magnetic lock. At this point, the spring is in compression and locked. Fig.(b) shows the robot at an external magnetic field frequency of 13 Hz. The movable magnetic ring rotates and the magnetic lock is released. Fig.(c) shows the process of generating thrust during drug release. At the same time, the magnetic lock release is to push a part of the drug library to leave a space for the iron plate at the end of the drug store to rotate. Fig.(d) shows the internal state of the drug chamber after drug release. At the same time, the spring is in a fully released state, the iron plate is also close to the magnet, and the piston is at the bottom of the medicine box. Fig.(e) shows the thrust generated during the robot closing process.

B. Simulation analysis of the medicine bin

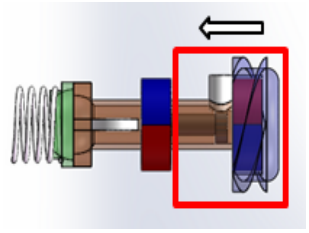
In order to better analyse the relationship between the force received by the drug and the speed of drug release, our team carried out fluid simulation analysis with FLUENT software in the medicine warehouse.



(a) The initial state of the drug store (b) The state of magnetic lock unlocked



(b) The state of iron piece rotated (d) The State of thrust generation



(e) The state of drug released completely

Fig. 4. The drug release process and structure

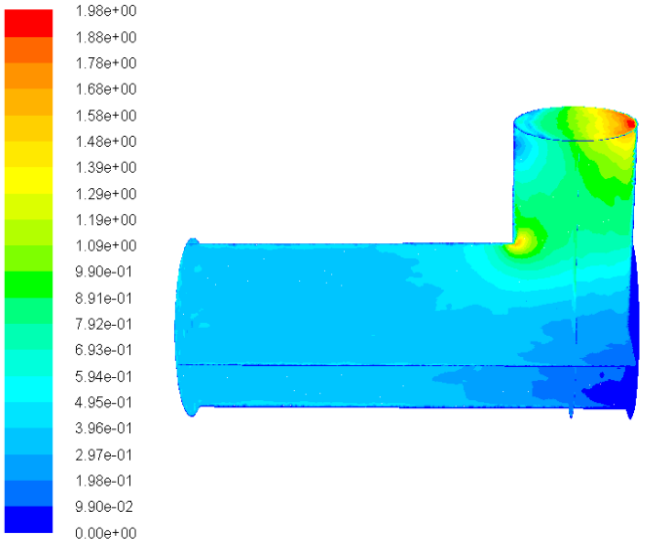


Fig.5. The model of drug spray speed

According to the elastic force equation (4) and the magnet attraction equation (3), the force acting on the piston surface of the charge can be calculated, and then the force can be converted into the applied pressure through the pressure according to equation (6).

$$F_2 = -kx \tag{4}$$

$$F_p = F_1 + F_2 \tag{5}$$

$$P = F_2 / S \tag{6}$$

Where F2 is the elastic force of the spring, k is the spring coefficient; Fp is the total thrust; S is the interface area of the hopper.

According to the pressure calculated by the formula shows above, and the actual measured pressure is 77.8 mm Hg in the experiment. We conducted a simulation on the part of the cartridge through Fluent, and carried out three-dimensional analysis. The results are shown in Fig.5.

As can be seen in Fig.5, the drug outlet has a maximum speed of 1.8m/s and an average speed of 0.9m/s. Assuming that the resistance to drug release is its own gravity, the robot can release the drug at that rate across the damaged section.

IV. Experiments and Results

Before this robot, our team made a capsule robot with a video transmission module. This experiment was carried out on the basis of a diagnostic module robot. The position of the lesion was determined by image acquisition, and the drug was released using this robot. As shown in Fig. 6, this is the process in which two robots work together. The robot for image acquisition starts to check until the lesion position is found, then controls the robot to move forward for a distance, and then changes the frequency to stop the robot. Since the speed of motion is known, this distance can be calculated based on the calculation. Next, the drug delivery robot enters and operates, and when it reaches the lesion site, the magnetic lock is opened for targeted local administration. The last two robots work together. In this article, we focus on targeted drug delivery robots, so there is only one robot in the experiment.

The experiment was carried out in acrylic tubes and did not completely mimic the internal environment of the intestinal tract. If we want to completely simulate the internal environment of the intestinal tract, we need to add peristaltic pump in the outside to simulate the peristalsis of the intestinal tract. In order to accurately realize the positioning, no peristalsis is added in the outside. In the future, peristalsis will be added for experiments. The experimental platform is shown in Fig.7.

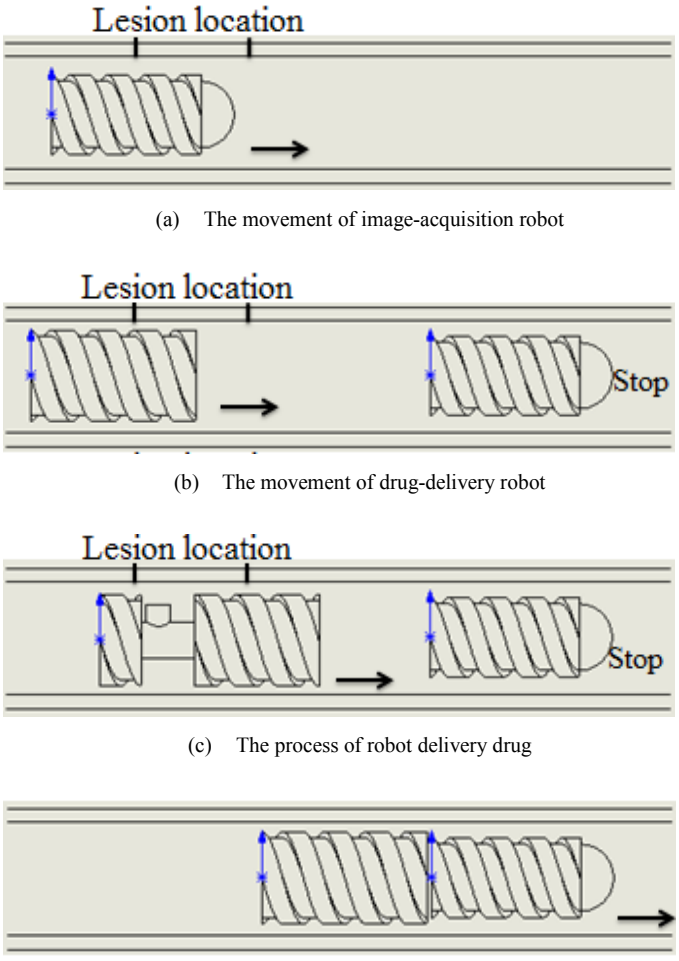
A. Movement Experiments

The experiment was performed outside the human body, and the robot was placed in a water-filled catheter that was driven in the catheter by a three-axis Helmholtz coil. Depending on the motion characteristics of the robot, the robot can be moved by supplying sinusoidal alternating current to the Helmholtz coils through the power supply. In this experiment, it is necessary to measure the relationship between the motion of the robot and the frequency. The movement speed of the robots was measured every 0.5 Hz from 0 Hz to 16 Hz of the frequency of currents. Fig.8 compares the experimental data of the robot moved forward and backward.

The experimental results are shown in Fig.7. The comparison experiments were carried out on the presence or absence of iron sheets inside the robot. It can be seen from the figure that the presence or absence of iron sheets has little effect on the motion of the robot. There is a partial speed drop between 12 Hz and 14 Hz because the magnetic lock is unlocked at this frequency and the robot is moving in the state of administration. In the low frequency range, the torque received by the magnet is too small to cancel the resistance; in the high frequency range, the frequency changes too fast and the robot cannot keep up. Therefore, robots cannot move in both low and high frequency bands.

B. Drug Release Experiment of Robots

Finally, this experiment proves the feasibility of this structure. In order to make the effect obviously, the experimental environment is placed in an environment without creep. During the experiment, blood powder will be simulated as a drug. The simulated blood powder will stain the red water as long as it encounters water. The experimental process is shown in Fig.9.



(a) The movement of image-acquisition robot

(b) The movement of drug-delivery robot

(c) The process of robot delivery drug

(d) The two robots combine and run

Fig.6 The schematic diagram of diagnostic robot and drug delivery robot

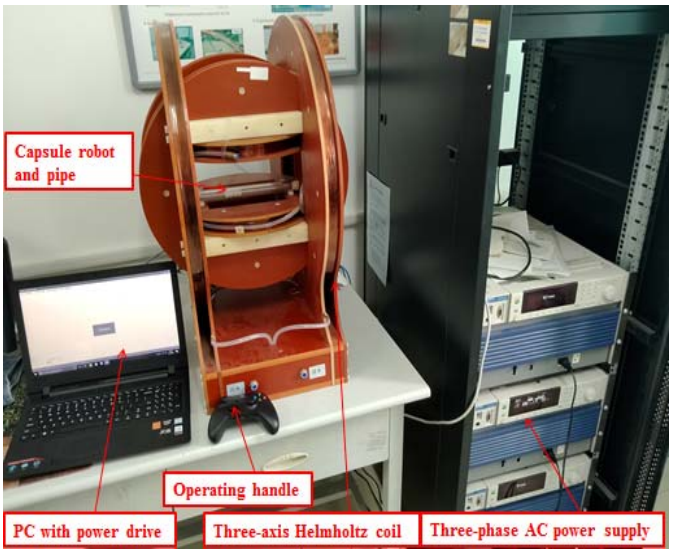
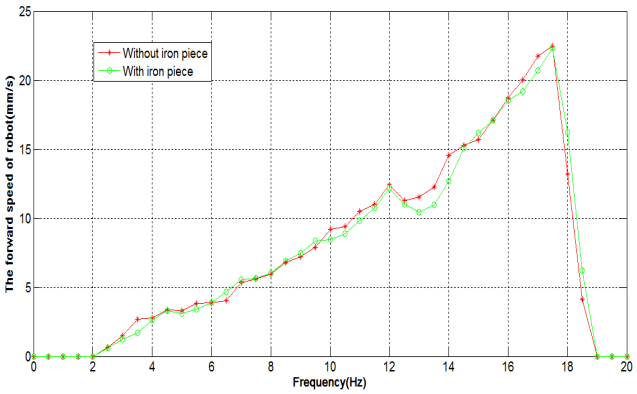
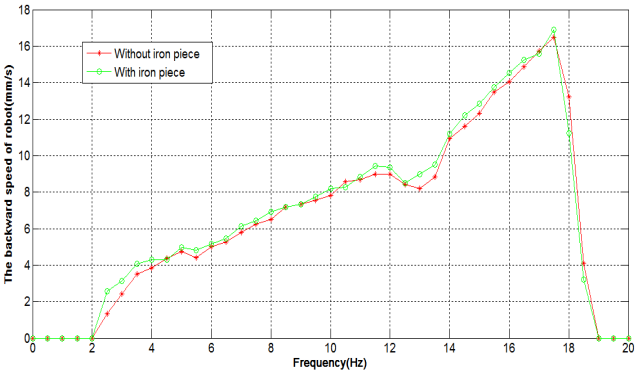


Fig.7. Experimental platform



(a) Experimental results when the robots moved forward



(b) Experimental results when the robots moved backward

Fig. 8. The speed of robots as a function of the

The robot starts moving in the first second, and the robot is still moving toward the lesion in the third second. Until the robot reaches the lesion position until the 5th second, the control handle changes the frequency of the power supply to unlock the magnetic lock, and the medicine in the robotic pharmacy is ejected, and the water turns red. In the next 10 seconds, the robot moves back and forth in the lesion area and continues to spray until the drug is sprayed. Starting from the 19th second, the power frequency is changed again, and the robot is closed and continues to move. At the 22nd second, the robot moved to the top and the experiment ended.

V. Conclusions

This paper proposed a robot with autonomous movement ability for drug delivery in the lesion area. The 3D Models were designed through the software—SolidWorks and fabricated by 3D printer. And then, through the analysis of Fluent, the relationship between the thrust and the speed of the drug ejected from the drug outlet is obtained, thereby obtaining the speed of the drug mouth.

Finally, the robot can realize autonomous motion under the driving of the three-axis Helmholtz coil, and the iron piece in the cabin has no effect on the robot motion were verified by experiments. The robot reached the fastest speed at 17.5Hz, the fastest forward speed is 22.32mm/s, and the fastest backward speed is 16.86mm/s. Since the robot head has a structure that reduces drag, this speed difference is within a reasonable range. The drug release experiment proved the rationality of this structure, and it was able to squeeze the drug to the outside by thrust.

In the future, we will carry out experiments “In Vivo” by using proposed capsule robot with drug delivery module.

Acknowledgmen

This research is supported by Natural Science Foundation of Tianjin (18JCYBJC43200) and Tianjin Key Laboratory for Control Theory and Application in Complicated Systems (TJKL-CTACS-201903) and Innovative Cooperation Project of Tianjin Scientific and Technological Support (18PTZWHZ00090).

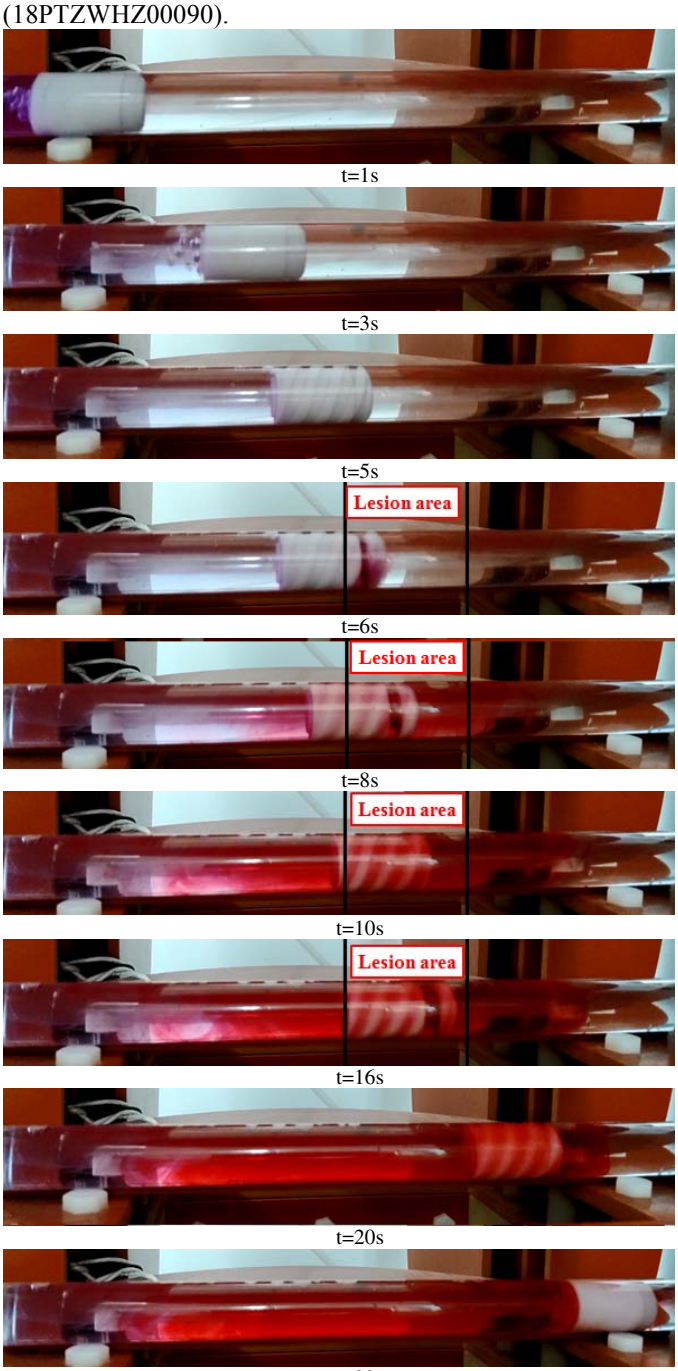


Fig. 9 The snapshots of the drug release process

REFERENCES

[1] Yu Marcia. M2ATM Capsule Endoscopy: A Breakthrough Diagnostic Tool for Small Intestine Imaging. Gastroenterology Nursing, vol. 25, no 1,:pp.24–27,2002

[2] Yim Sehyuk, Sitti Metin. Design and Rolling Locomotion of a Magnetically Actuated Soft Capsule Endoscope. IEEE Transactions on Robotics,, vol. 28, no 1, pp183–194,2012.

[3] Yim Sehyuk, Sitti Metin. Shape-Programmable Soft Capsule Robots for Semi-Implantable Drug Delivery. IEEE Transactions on Robotics, 28(5): 1198–1202,2012.

[4] Yim Sehyuk, Goyal Kartik, Sitti Metin. Magnetically Actuated Soft Capsule With the Multimodal Drug Release Function. IEEE/ASME Transactions on Mechatronics, vol 18, no 4, pp 1413–1418,2013.

[5] Chen Wenwen, Yan Guozheng, Wang Zhiwu, et al. A wireless capsule robot with spiral legs for human intestine. International Journal of Medical Robotics and Computer Assisted Surgery, vol. 10, no 2, pp147–161,2014

[6] He Shu, Yan Guozheng, Gao Jinyang, Frictional and Viscous Characteristics of an Expanding-Extending Robotic Endoscope in the Intestinal Environment. Tribology Letters, vol.58, no 3, pp36-40, 2015

[7] Zhang Yongshun, Jiang Shengyuan, Zhang Xuewen, A Variable-Diameter Capsule Robot Based on Multiple Wedge Effects. IEEE/ASME Transactions on Mechatronics, vol.16, no 2, pp 241–254, 2011

[8] Zhang Yongshun, Xie Huaying, Wang Na, et al. Design, analysis and experiments of a spatial universal rotating magnetic field system for capsule robot. 2012 IEEE International Conference on Mechatronics and Automation, vol.10, no 1, pp .998–1003, 2012

[9] Qiang Fu, Songyuan Zhang, Shuxiang Guo, Jian Guo, "Performance Evaluation of a Magnetically Actuated Capsule Microrobotic System for Medical Applications", Micromachines, vol.9, no.12,pp641, 2018

[10] Shuxiang Guo, Qiuxia Yang, Luchang Bai, Yan Zhao, "Development of Multiple Capsule Robots in Pipe", Micromachines, vol.9, no.6,pp259, 2018

[11] Zhang Yongshun, Bai Jianwei, Chi Minglu, et al. Optimal control of a universal rotating magnetic vector for petal-shaped capsule robot in curve environment. Chinese Journal of Mechanical Engineering, vol.27, no.2: pp.880–889,2014

[12] Fu Q, Guo S, Zhang S, et al. "Characteristic evaluation of a shrouded propeller mechanism for a magnetic actuated microrobot. Micromachines, vol 6,no 9,1272-1288, 2015

[13] Qiang Fu, Shuxiang Guo, Qiang Huang, Hideyuki Hirata, Hidenori Ishihara, " Development and Evaluation of a Novel Magnetic Actuated Microrobot with Spiral Motion using Electromagnetic Actuation System" Journal of Medical and Biological Engineering, Vol.36, No.4, pp.506–514, 2016

[14] Slawinski, K.L. Obstein, "Capsule endoscopy of the future: what's on the horizon? "World J. Gastroenterol. no21, pp.10528– 10541, 2015.

[15] J. Gao et al., "Design and Testing of a Motor-Based Capsule Robot Powered by Wireless Power Transmission," IEEE/ASME Transactions on Mechatronics, vol. 21, no. 2, pp. 683-693, 2016.

[16] Zixu Wang, Shuxiang Guo, Qiang Fu, Jian Guo, "Characteristic Evaluation of a Magnetic-actuated Microrobot in Pipe with Screw Jet Motion", Microsystem Technologies, Vol.24, No.7, pp.1272-1288, 2018

[17] Q. Fu, S. Guo, Y. Yamauchi, H. Hirata, and H. Ishihara, "A novel hybrid microrobot using rotational magnetic field for medical applications," Biomed Microdevices, vol. 17, no. 2, p. 31, 2015.

[18] H.A.E. Benson, "Vesicles for transdermal delivery of peptides and proteins, Percutaneous Penetration Enhanc". Chem. Methods Penetration Enhanc, Springer, Berlin, Heidelberg, pp.297-307, 2016.

[19] Siler-Marinkovic, "Liposomes as drug delivery systems in dermal and transdermal drug delivery", Percutaneous Penetration Enhanc. Chem. Methods Penetration Enhanc, Springer Berlin Heidelberg, Berlin, Heidelberg, pp.15-38, 2016.

[20] M. Beccani et al., "Component based design of a drug delivery capsule robot," Sensors and Actuators A: Physical, vol. 245, pp. 180-188, 2016.

[21] Qiang Fu, Shuxiang Guo, Yasuhiro Yamauchi, Hideyuki Hirata and Hidenori Ishihara "A Novel Hybrid Microrobot using Rotational Magnetic Field for Medical Applications" Biomedical Microdevices,vol.17 no.2, pp.1-12, 2015

[22] V. H. Le et al., "A soft-magnet-based drug-delivery module for active locomotive intestinal capsule endoscopy using an electromagnetic actuation system," Sensors and Actuators A: Physical, vol. 243, pp. 81-89, 2016.

[23] S. Yim, E. Gultepe, D. H. Gracias, and M. Sitti, "Biopsy using a Magnetic Capsule Endoscope Carrying, Releasing, and Retrieving Untethered Microgrippers," IEEE Transactions on Biomedical Engineering, vol. 61, no. 2, pp. 513-521, 2014.

[24] H. Zhou, G. Alici, and F. Munoz, "A magnetically actuated anchoring system for a wireless endoscopic capsule," Biomed Microdevices, vol. 18, no. 6, pp. 102, 2016.

[25] Peyer KE, Zhang L, Nelson BJ "Bio-inspired magnetic swimming microrobots for biomedical applications". Nanoscale, vol 5, no 4, pp1259–1272, 2013

[26] Kim S H, Ishiyama K. "Magnetic robot and manipulation for active-locomotion with targeted drug release". IEEE/ASME Transactions On Mechatronics, vol19,no5, pp1651–1659, 2013

[27] Guo J, Bao Z.H, Guo S X, et al. "Design of A Novel Drug-delivery Module for Active Locomotive Intestinal Capsule Endoscopy" 2018 IEEE International Conference on Mechatronics and Automation pp1633-1638,2018