

TOPICAL REVIEW

Magnetically Actuated Capsule Robots: A Review

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ABSTRACT Capsule endoscopy is a procedure that uses a tiny wireless camera inside a capsule endoscope to capture pictures of the patient's gastrointestinal tract for diagnosis. Gastrointestinal examination has been revolutionized by capsule endoscope owing to its simplicity and non-invasiveness. However, at this stage, the capsule endoscope has a weak controllable locomotion capability and does not have extended functions such as biopsy, localization, and therapeutics, which has become the main obstacle to expanding its application. The use of an external magnetic field to actuate the capsule endoscope has the advantages of simple response structure inside the capsule and remote energy supply, which can expand the above-mentioned functions of the capsule endoscope and develop into a multifunctional capsule robot. This paper analyzes two types of magnetic actuation systems for magnetically actuated capsule robots, discusses research on the functions of magnetically actuated capsule robots in active locomotion, anchoring, biopsy, localization, therapeutics, wireless power supply, and multi-capsule robot collaboration, and points out the existing problems and future development directions of magnetically actuated capsule robots.

INDEX TERMS Gastrointestinal tract, magnetically actuated, capsule endoscopy, capsule robot.

I. INTRODUCTION

Gastrointestinal (GI) diseases, such as GI inflammation, ulcers, bleeding, infection and cancer, are among the most common clinical diseases with high morbidity and mortality [1]. It is estimated that there are approximately 40 million clinic visits annually for GI diseases in the United States [2]. Among all cancers in 2020, GI cancer deaths account for 32% of all cancer deaths [3]. Moreover, survival rates for GI cancers can vary based on several factors, particularly stage. For instance, the 5-year survival rate for early diagnosis of rectal cancer is 90%, whereas the 5-year survival rate for late diagnosis is reduced to 20% [4]. Therefore, early screening and diagnosis of GI diseases, especially cancers, are of great importance [5].

GI endoscopy is used for the diagnosis and treatment of GI diseases. A traditional invasive endoscope (rigid or flexible endoscope) needs to enter the GI tract from the patient's natural body orifice (mouth or anus), which causes discomfort and pain to the patient. Although the use of anesthesia can improve the comfort of the procedure, some patients will experience discomfort caused by anesthetics and even serious

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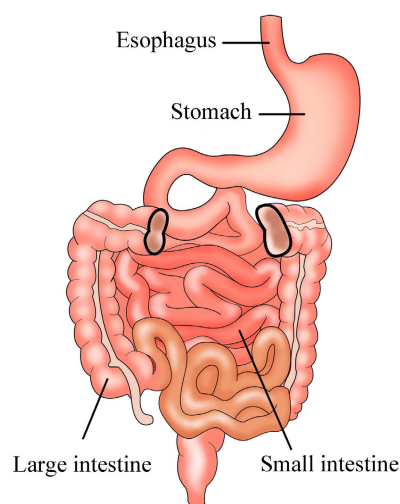


FIGURE 1. A Schematic of the GI tract.

complications after the procedure [6]. Moreover, well-trained physicians are required for GI endoscopy. In addition, it is difficult to perform GI endoscopy for the small intestine because the average length of the small intestine is 7 meters, which is far away from the natural body orifice [7], [8]. A schematic diagram of the human GI tract is shown in Fig. 1.

TABLE 1. Commercial capsule endoscope.

Capsule type	Company	Size(mm)	Weight (g)	Locomotion	Frames per second	Number of camera	Angle of view	Depth of view(mm)	Battery life
PillCam SB3 [12]	Medtronic	Ø11.4×26.2	3.0	Passive	2~6	1	156°	-	8h
PillCam Colon2 [38]	Medtronic	Ø11.6×32.3	2.9	Passive	4~35	2	172°	0.1-30	10h
PillCam UGI [39]	Medtronic	Ø11.6×32.3	2.9	Passive	18~38	2	172°	0.1-30	90min
EndoCapsule 10 [40]	Olympus	Ø11×26	3.3	Passive	2	1	160°	0-20	12h
NaviCam [41], [42]	Ankon	Ø11.6×26.8	4.8	GMR	2	1	151°	0-30	8h
OMOM-HD [43]	Jinshan	Ø11×25.4	3	Passive	2~10	1	172°	0-50	12h
OMOM-RC22 [44]	Jinshan	Ø11.5×30	5	GMR	2~10	1	172°	0-50	12h
CapsoCam Plus [15]	CapsoVision	Ø11×31	4	Passive	20	4	360°	0-18	15h
MiroCam Navi [42], [45]	IntroMedic	Ø11×24	4.2	HM	6	1	170°	0-30	8h
SMCE [46]	JIFU Medical	Ø12×27	2.7	GMR	4	1	136°	0-50	-

GMR = Guidance magnet robot; HM = Handheld magnet; “-” = The data have not been provided.

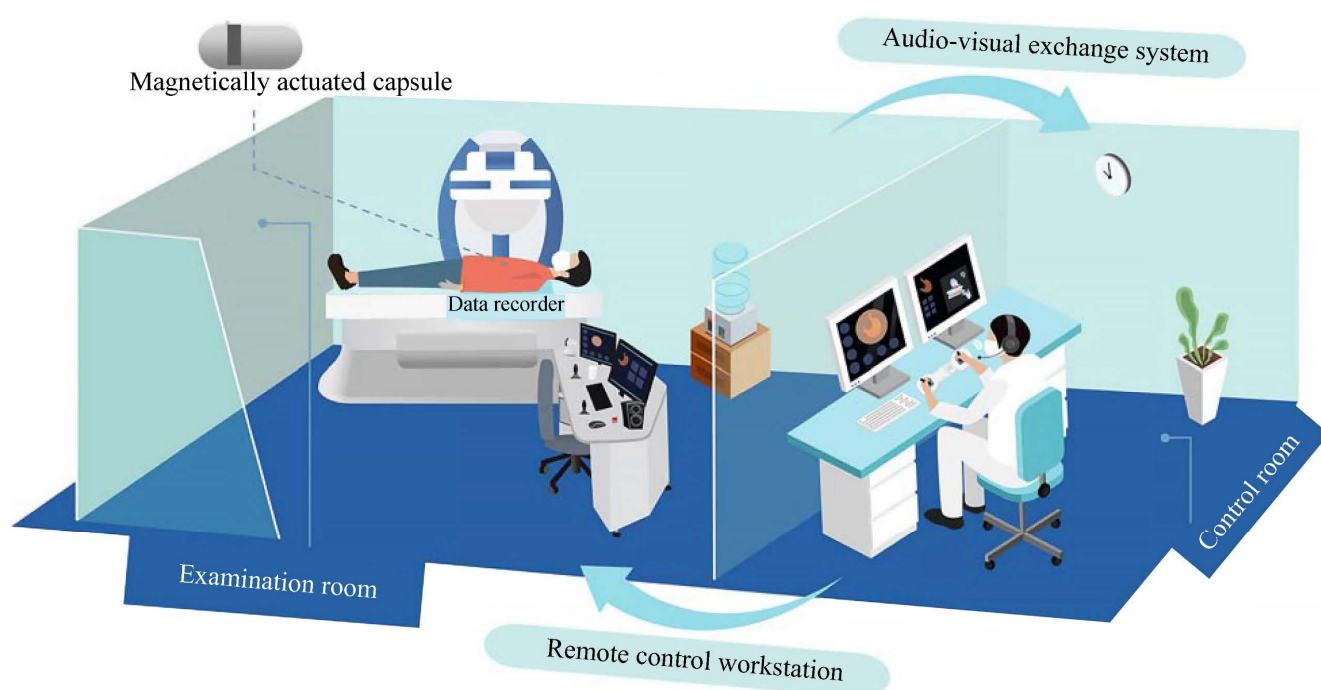


FIGURE 2. Noncontact magnetically actuated capsule endoscopy system. The system consists of a magnetic actuation system, a capsule endoscope, an audiovisual exchange system, and a remote-control workstation [24].

Capsule endoscopes (CE) can inspect the GI tract and avoid discomfort and pain to the patients. Swain *et al.* [9] first proposed the prototype of a CE in 1995, which is a capsule-like device that is small enough to be swallowed by a patient and can locomote in the human GI tract. This prototype was composed of a camera, flash, battery, signal transmitter, and housing. It can transmit images captured in the GI tract of a patient to an external receiver without connecting cables, thereby realizing wireless GI tract diagnosis. In 2000, the Royal London Hospital successfully used the capsule endoscope to conduct clinical trials in humans for the first time

and achieved painless endoscopic imaging of the small intestine [10]. In 2001, Given Imaging produced the world’s first commercial capsule endoscope called M2A (later renamed PillCam SB), which can be used for small intestine inspection and has been updated to SB3 with improved image depth, sharpness, resolution, and real-time observation of the captured images [11], [12]. Other capsule endoscope manufacturers have also subsequently entered the market. Olympus released the EndoCapsule capsule endoscope and Jinshan Technology released the OMOM capsule endoscope both in 2005 [13], [14]. CapsoVision has greatly improved the field

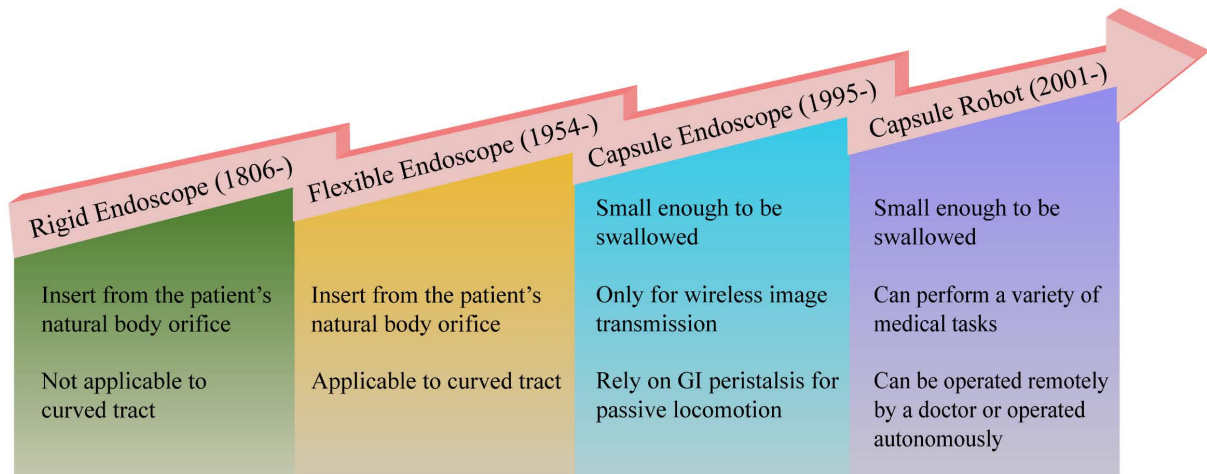


FIGURE 3. The evolution of GI endoscopes [9], [29], [47], [48].

of view by releasing the CapsoCam Plus capsule endoscope, which has four cameras distributed around the circumference, capturing images at a rate of 20 frames per second and using stitching algorithms to provide 360-degree panoramic views for small intestine inspection [15]. Commercial capsule endoscopes that are commonly used clinically are listed in Table 1.

Because of painless and non-invasive, CE has been widely used in the evaluation and diagnosis of GI bleeding, small bowel tumors, Crohn's disease, polyp syndrome and malabsorption syndrome [16], [17], [18]. CE has become the first choice for small bowel endoscopy in children [19], [20], [21]. Moreover, single-use CE can effectively prevent cross-infection between patients owing to the repeated use of endoscopes compared with traditional endoscopy [22], [23]. In addition, it can effectively prevent the spread of infectious diseases between patients and medical staff because CE can be operated remotely, as shown in Fig. 2 [23], [24].

Although various CEs have made encouraging progress in recent years, their clinical functions still have great limitations at this stage. Compared with conventional invasive endoscopes, current CEs have several shortcomings: lack of biopsy function, lack of lesion marking function, lack of therapeutic function, and weak active control function. Active research has been conducted to integrate CEs into robotics technology with the aim of transforming passively moving diagnostic devices into actively locomotive robots with extended capabilities (capsule robot, or CR), in order to achieve or even surpass the functions of current invasive endoscopes [25]. Fig. 3 shows the evolution of GI endoscopes.

In a variety of studies, many methods of actuating capsule robot have been proposed, such as electric motor actuation [26], [27], [28], electrical stimulation actuation [29], electrothermal actuation [30], [31], magnetic actuation [32], [33] and so on. Among them, magnetic actuation is considered to be the most promising method because of its simple response

structure in the capsule body and the advantages of external power supply [13], [34].

In the current review papers describing GI endoscopes, some introduce different types of endoscopes, and some introduce different types of capsule endoscopes [35], [36], [37]. Different from previous researches, in this paper, the implementation of different functions of capsule robots by means of magnetic actuation is critically introduced. The research fields of magnetically actuated capsule robots are illustrated in Fig. 4. First, various magnetic actuation systems and their characteristics are summarized in Section II. Then, various locomotion and anchoring methods are analyzed and compared for basic locomotive functions of the capsule robot in Section III. Afterward, more extended functions based on the capsule robot are discussed in Section IV. Finally, the existing problems and future development directions of magnetically actuated capsule robots are discussed in Section V followed by conclusion.

II. MAGNETIC ACTUATION SYSTEMS

In this section, the principle of magnetic actuation of capsule robots is introduced, and two common magnetic actuation systems are reviewed, namely movable external magnet systems and electromagnetic coil systems.

A. PRINCIPLE OF MAGNETIC ACTUATION

The magnetic actuation system generates an external magnetic field that applies forces and torques to the internal permanent magnet (IPM) or internal electromagnet of the capsule robot [49], [50]. During the magnetic actuation of the capsule robot, the quasi-static magnetic field can be described by Maxwell's equation as [51]

$$\nabla \cdot \mathbf{B} = 0 \quad (1)$$

$$\nabla \times \mathbf{B} = 0 \quad (2)$$

where \mathbf{B} is the external magnetic vector field and ∇ is the gradient operator.

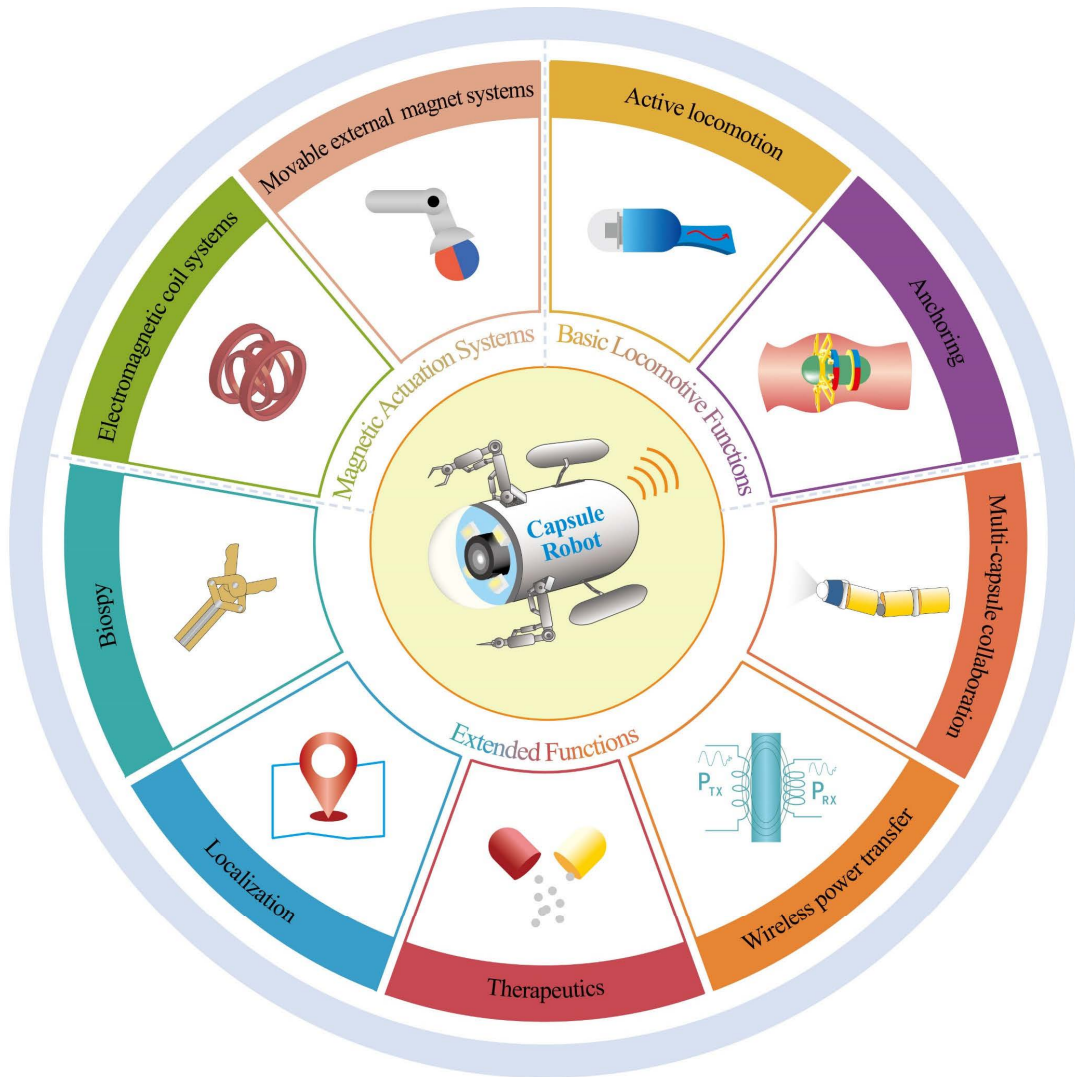


FIGURE 4. The research fields of magnetically actuated capsule robots.

When the magnetic moment of a magnetic object \mathbf{m} misaligns with the direction of the external magnetic field \mathbf{B} (Fig. 5a), a magnetic torque τ acts on the magnetic object \mathbf{m} as [51]

$$\tau = \mathbf{m} \times \mathbf{B} \quad (3)$$

When the magnetic object \mathbf{m} is in a nonuniform magnetic field (Fig. 5b), a magnetic force \mathbf{F} acts on the magnetic object \mathbf{m} as [51]

$$\mathbf{F} = (\mathbf{m} \cdot \nabla)\mathbf{B} \quad (4)$$

During the magnetic actuation process, the magnetic torque and magnetic force can act on the capsule robot separately or simultaneously. Except for some special magnetization cases [52], [53], general magnetically actuated capsule robots cannot rotate around their own magnetization axis and usually have five degrees of freedom, that is two degrees

of freedom for rotation and three degrees of freedom for translation.

The disadvantage of the magnetic field generated by a single external magnet is that the direction of the magnetic field gradient in the working area is not uniform. There are external magnetic field gradients in both the axial and radial directions of the capsule robot, so that when the capsule robot moves, it is often accompanied by pressure on the intestinal wall in the direction of the connection between the capsule robot and the external magnet (Fig. 6a). Therefore, in order to reduce or avoid the pressure on the intestinal wall, it is necessary to track the precise position of the capsule robot to control the distance between the external magnet and the capsule robot during its actuation, otherwise it will increase the friction force during its movement and the risk of GI injury [55]. Recently, some researchers have proposed that under the actuation of a single external magnet, capsule robot levitation control can be realized based on the gravity

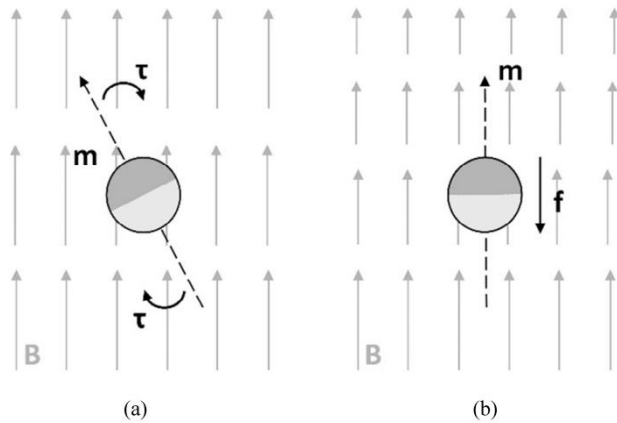


FIGURE 5. Diagram of magnetic actuation [54] (a) In a uniform magnetic field, magnetic torque actuation when the magnetic moment of a magnetic object misaligns with the direction of the external magnetic field. (b) In a nonuniform magnetic field, magnetic force actuation when the magnetic moment of a magnetic object aligns with the direction of the external magnetic field.

compensation method, but this method reduces the maximum locomotion speed of the capsule robot to a certain extent [56], [57], [58]. The magnetic sources of electromagnetic coil systems are symmetrically distributed in space, and the generated magnetic field can be uniform in the working area. By controlling the direction of the external magnetic field to be consistent with the direction of the GI tract, there will be no or little radial pressure on the GI tract when the capsule robot is moving, except for the gravity of the capsule robot. Fig. 6b shows a schematic diagram of magnetic actuation with electromagnetic coil systems in an ideal state. In addition, electromagnetic coil systems can not only generate a gradient magnetic field, but can also generate a uniform magnetic field, which is conducive to the pure magnetic torque actuation of the capsule robot.

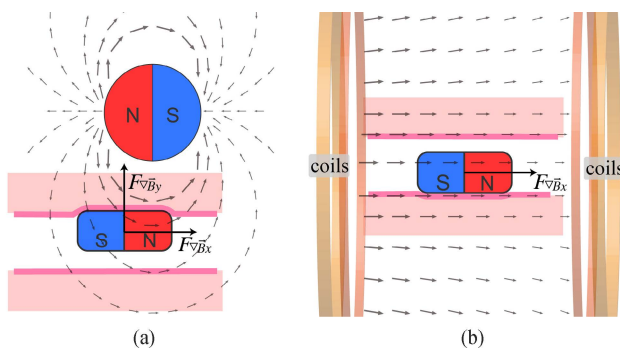


FIGURE 6. Diagram of actuate magnetic capsule robot. The influence of the magnet in the capsule robot on the external magnetic field is ignored in the figure. (a) Actuation with a single external magnet. (b) Actuation with electromagnetic coil system.

B. MOVABLE EXTERNAL MAGNET SYSTEMS

By moving or rotating the external Nd-Fe-B magnet with hand or an external mechanism, the movable external magnet

system can apply a magnetic force or torque to the IPM to realize its movement in the body. The use of a movable external magnet system has the advantages of small size, light weight, low power consumption, low cost, and low or no heat generation.

In Yokoi et al. [59] proposed the use of an external magnetic field to control a capsule endoscope for controllable movement. In 2010, Swain et al. reported the first clinical application of magnetic actuation for capsule endoscopy [60]. The capsule used in the experiment was modified from a Given Imaging’s colon capsule endoscope with Nd-Fe-B magnets. An external magnetic field was generated by using two small handheld magnetic plates. In the clinical experiment, an invasive endoscope was inserted into the stomach of an examinee to observe and verify the movement of the magnetically actuated capsule. In the following year, Keller et al. [61] from the same research team optimized the original equipment (Fig. 7a) and conducted gastric observation tests in ten volunteers, of which seven cases were highly visualized (75%-90%) and the remaining three cases were moderately visualized (50%-60%), preliminarily proving the safety and feasibility of magnetic actuation.

The magnetic capsule guidance system, launched by Ankon Technologies Co., Ltd. (Wuhan, China), uses a single spherical permanent magnet to provide an external magnetic field, and its movement is controlled by a five-degree-of-freedom C-shaped robotic arm (Fig. 7b) [62], [63]. The system obtained CFDA certification in 2013 and has been used clinically in many medical institutions. The standing-type magnetic capsule endoscope system developed by JIFU Medical Co., Ltd. (Shenzhen, China), as shown in Fig. 7c, adopts a fully enclosed structure to avoid collision with the patient’s body during movement of the mechanism [46], [64]. Lucarini et al. [65] proposed the use of electromagnets to replace permanent magnets, so that the movable external magnet system has the advantage that the electromagnet can turn off the magnetic field at any time and the flexibility of the robot’s multi-degree-of-freedom operation. Owing to the physical constraints of the robot manipulator (singularities and joint constraints), its ability to drive a capsule robot through tortuous paths is limited. Wright et al. proposed a spherical-actuator-magnet manipulator (Fig. 7d), which can achieve any instantaneous magnet rotation axis by using three linearly independent omniwheels to drive a spherical magnet at the end of the robot, avoiding the kinematic singularity of the robot manipulator [66].

The Niobe magnetic navigation system (Fig. 7e) developed by Stereotaxis Inc. (St. Louis, America) is currently used to guide magnetic catheters in the treatment of cardiovascular diseases. In this system, two magnets are distributed on both sides of the bed to generate a nearly uniform magnetic field in the working area [67]. Each magnet can rotate in its pedestal to drive the magnetic catheter to complete pitch and yaw rotations. Carpi et al. [67], [68] successfully applied this system to actuate a capsule endoscope. However, unlike magnetic catheters, which can exert axial force by pushing

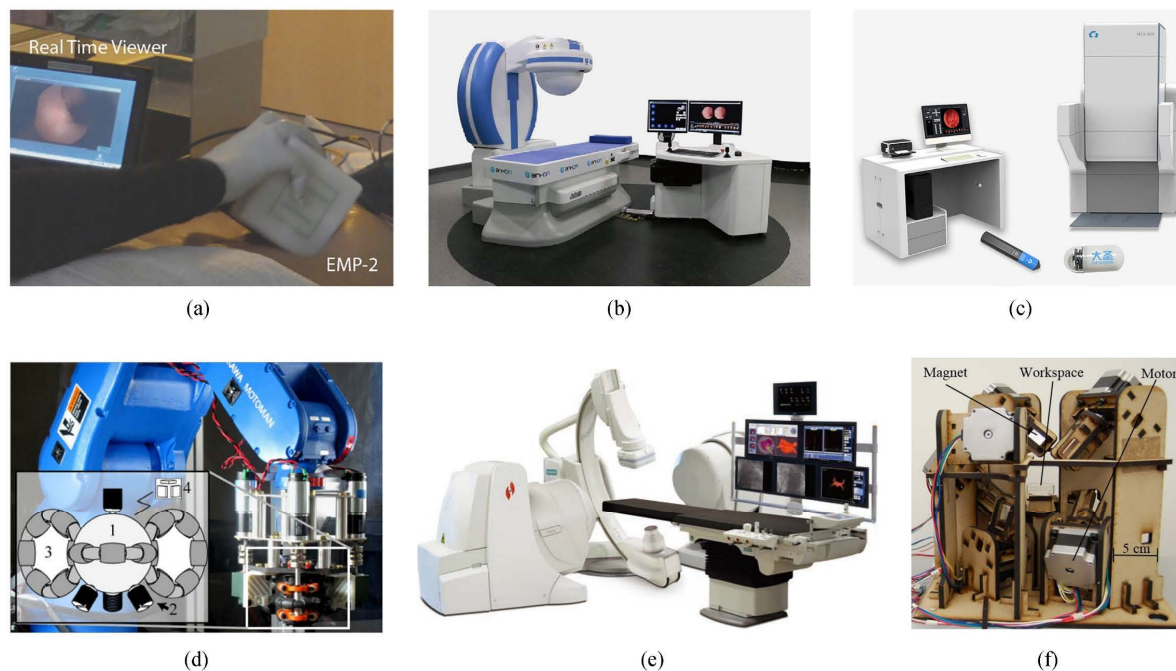


FIGURE 7. Movable external magnet systems. (a) The handheld magnet [61]. (b) The Ankon magnetic capsule endoscope guidance system [62]. (c) The JIFU standing-type magnetic capsule endoscope guidance system [46]. (d) The spherical-actuator-magnet manipulator [66]. (e) The Niobe magnetic navigation system [67]. (f) The multiple rotating magnets system [70].

the external catheter, conventional magnetically actuated capsules cannot generate a magnetic force to drive translation in a uniform magnetic field, and its translation needs to be controlled by moving the patient's body. Gao *et al.* [69] presented a dual-magnet navigation system composing a magnetic source mechanism and a movable bed. The magnetic source mechanism includes a rotatable C-shaped arm and permanent magnet sliding tables installed at both ends of the C-shaped arm. By rotating the C-shaped arm and translating the permanent magnet sliding tables, the axis direction of two symmetrically placed Nd-Fe-B magnets can be adjusted to realize attitude control of the capsule. The movable bed can be translated in the XY direction so that the working area of the magnetic source mechanism can be translated relative to the bed, thereby realizing the displacement control of the capsule.

A magnetic field superposition scheme that uses multiple permanent magnets to rotate independently, as shown in Fig. 7f, was introduced by Ryan *et al.* [70], [71]. The prototype uses eight permanent magnets, each of which is driven by an independent motor and can rotate around its own fixed axis. These magnets can be used to generate a uniform magnetic field or a gradient magnetic field in any direction. Because the system does not contain a translation unit, the potential danger of collision between the external magnet and patient can be avoided.

In order to increase the external magnetic field intensity, Munoz *et al.* [49] proposed the use of multiple permanent magnets to form a rotatable annular permanent magnet array based on the principle of magnetic field superposition to

generate a high-intensity rotating magnetic field. Compared with the rotating magnetic field generated by a single rotating external magnet, the IPM can maintain a relatively constant torque in this manner, which is beneficial for improving the smoothness of the action. However, the proposed design had only one fixed rotational axis. To realize the motion control of three rotation degrees of freedom simultaneously, a spherical pair of motion mechanism is required.

C. ELECTROMAGNETIC COIL SYSTEMS

Electromagnetic coil systems are composed of multiple electromagnetic coils. By controlling the current applied to each coil, the intensity and direction of the generated magnetic field can be controlled. Compared with moving permanent magnets by mechanism, this method is more convenient and controllable, and can generate a complex magnetic field distribution for advanced motion control. In addition, because electromagnetic coil systems are stationary in position, there is no potential risk of collision with the human body, as with movable external magnet systems.

The catheter guidance control and imaging (CGCI) system developed by Magnetecs Inc. (Los Angeles, America) is composed of eight cored electromagnets [72]. Four electromagnets are arranged in a hemispherical shape above the working area and the other four are arranged symmetrically below the working area (Fig. 8a). By controlling the current of each coil, a uniform or gradient magnetic field can be generated in the working area, so as to drive the target for translation

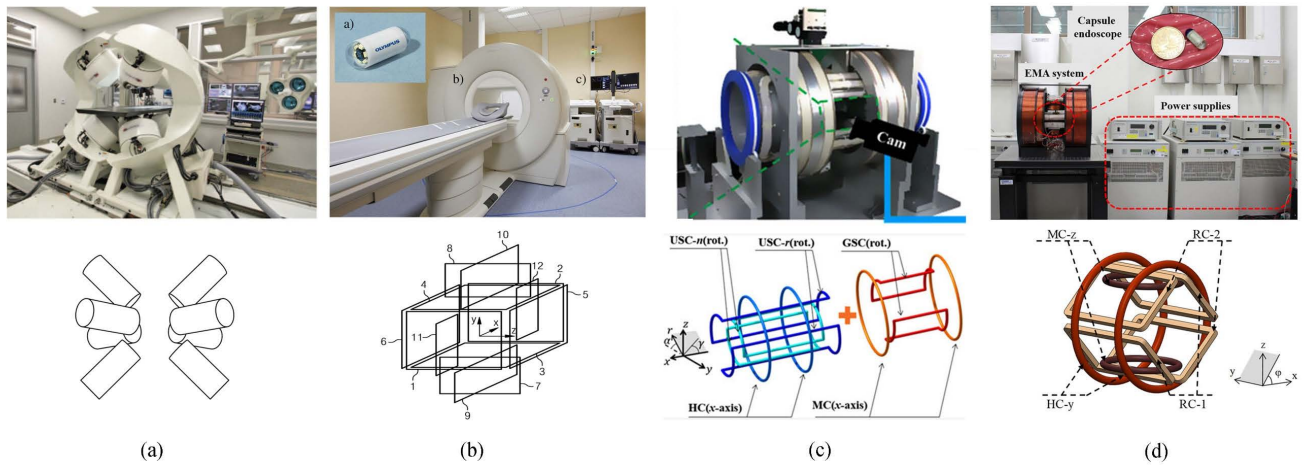


FIGURE 8. The Electromagnetic coil systems. In each subfigure, the upper part is the physical system diagram, and the lower part is the coils layout diagram. (a) The CGCI system [72]. (b) The MGCE system [76]. (c) The ALICE system [77]. (d) The MACE system [80].

and rotation. The system is mainly used for magnetic catheter operations in cardiac ablation surgery, but has not yet been used in magnetically actuated capsule endoscopy. A modular and reconfigurable electromagnet system was developed by the University of Utah [73], [74]. A spherical ferromagnetic core and three orthogonal solenoids were used to form an Omnimagnets. This system can be easily reconfigured with different numbers of Omnimagnets for different application tasks.

The Magnetically Guided Capsule Endoscopy (MGCE) system was developed jointly by Olympus Medical System Corporation (Tokyo, Japan) and Siemens Healthineers (Erlangen, Germany) [75], [76]. The system consists of six pairs of electromagnetic coils, which can generate a gradient or rotating magnetic field (Fig. 8b). The generated magnetic field can be controlled by the doctor through two joysticks, so as to realize five-degree-of-freedom motion of the capsule.

Lee et al. [77], [78] proposed the active locomotive intestinal capsule endoscope (ALICE) system for controlling a capsule robot with five degree of freedom. The system consists of one pair of Helmholtz coils, one pair of Maxwell coils and three pairs of saddle coils (Fig. 8c). The rotating and gradient magnetic fields generated by this system can be used to adjust the attitude of the capsule and push it to move along the gradient direction, respectively. In addition, the system can generate magnetic field gradients in the axial and radial directions of the capsule simultaneously, actuating the capsule robot to perform helical motion, namely, rotating and propelling simultaneously.

In the gradient magnetic field generated by previous electromagnetic coil systems, the magnetic force applied to the capsule robot is in the same direction as the magnetic field, so the magnetic moment direction of the capsule robot needs to be aligned with the propulsion direction to perform the head-and-go (HAG) motion. Zhang et al. [79] presented an electromagnetic coil system that can perform the

orientation-independent-driving (OID) control of a capsule robot. The system is composed of a pair of Helmholtz coils and Maxwell coils in each XYZ triaxial direction. The system can effectively compensate for the gravity of the capsule robot, perform horizontal or nearly horizontal motion of the capsule robot, and enable rectangular motion of the capsule robot in the three-dimensional region while keeping the capsule’s attitude unchanged. In addition, Hoang et al. [80] proposed the magnetically actuated capsule endoscope (MACE) system consisting of a pair of Helmholtz coils, a pair of Maxwell coils, and four rectangular coils on the basis of the ALICE system (Fig. 8d). By adopting new type of coil structure and independent control of each coil, the system also realizes the OID control of the capsule robot by using fewer coils.

III. BASIC LOCOMOTION FUNCTIONS

A. ACTIVE LOCOMOTION

Traditional capsule endoscopes rely on GI peristalsis for passive locomotion. In the absence of active motion control, doctors cannot control the capsule to stay or return for further analysis and treatment of suspected lesions, and the slow motion of the capsule leads to a prolonged examination process [11], [81]. In addition, compared with the small intestine (lumen diameter is 2.5-3.0 cm) and the large intestine (lumen diameter is 2.5-7.5 cm), the stomach has a larger cavity (approximately 30 cm height and 15 cm wide). Due to the limitations of capsule position, posture, angle of view, and depth of field, it is difficult for a passively moving capsule endoscope to perform complete examination of the stomach [13]. In order to overcome these shortcomings, a variety of active capsule robots have been developed in recent years.

A typical magnetically actuated capsule robot is equipped with a circular or cylindrical IPM [45], [82]. By applying gradient and rotating magnetic fields to the permanent magnet, the capsule robot could achieve translation and rotation.

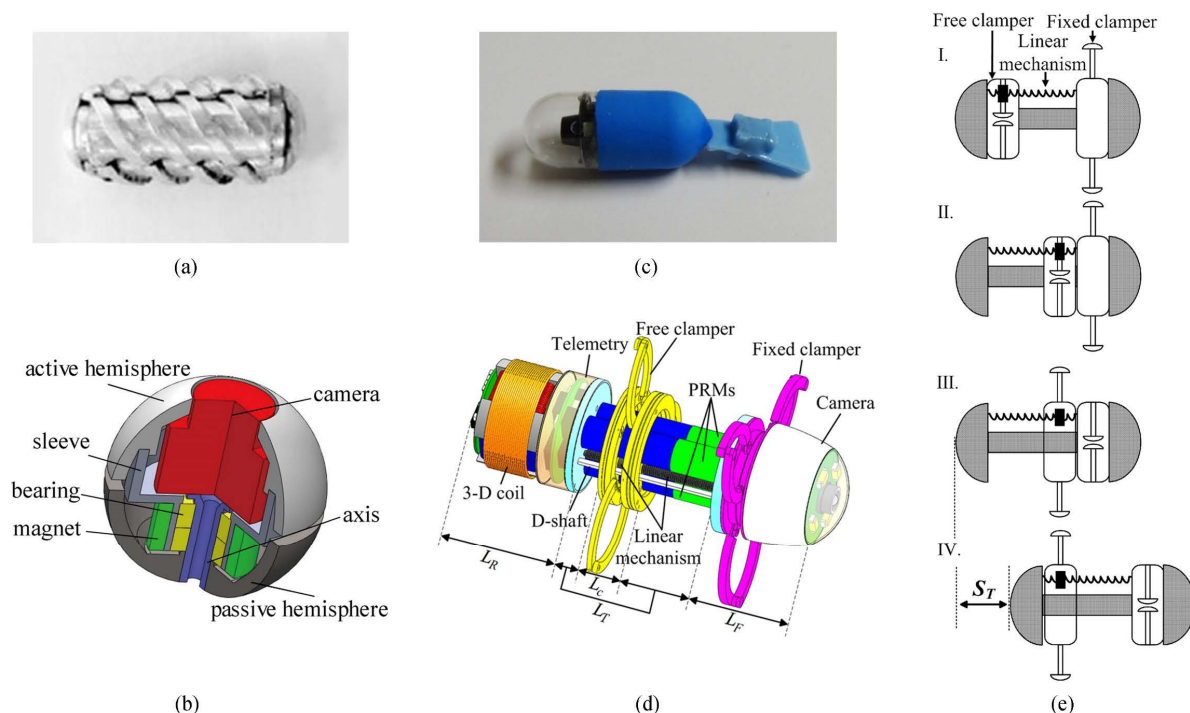


FIGURE 9. Active locomotion capsule robots. (a) The spiral structure capsule robot [88]. (b) The double hemispherical capsule robot [92]. (c) The fish-like capsule robot [93]. (d) The clamper-based capsule robot [96]. (e) The action steps of clamper-based capsule robot [96].

Since the intestine is unstructured and highly deformable, a capsule robot is easily prevented from locomoting in areas of intestinal collapse. A capsule robot with an internal motor driving a leg mechanism that can change the outer contour of the capsule was proposed [83]. It used a hybrid solution that combined external magnetic drive and space creation by the legs on the capsule, giving the capsule robot a good ability to pass through the collapsed area of the intestine.

When the rotating magnetic field has a gradient in the working area, the capsule robot is simultaneously subjected to a magnetic force and torque. Due to the strong coupling between translation and rotation, the flexibility of the attitude adjustment of the capsule robot is poor, and the capsule robot is prone to drift (or unwanted translation) during rotation [84]. Erin *et al.* [85] introduced a capsule robot with a spherical IPM, which has a certain clearance between the IPM and the magnet cavity, so that the spherical magnet can rotate freely in the magnet cavity. This structure allows the IPM to transmit magnetic force to the capsule, whereas the magnetic torque is not transmitted, and the capsule robot can obtain various rotation directions using only the magnetic force. By adjusting the duty cycle of the external gradient magnetic field, the capsule robot can be driven to perform yaw and pitch rotations at different angles, and the drift of the capsule robot can be effectively minimized.

Because the magnetic field gradient decays quickly in space, there are high requirements for the magnetic actuation system to generate a well-controlled gradient magnetic field with sufficient magnetic field gradient intensity to cover

the human body to actuate the capsule robot. The use of a magnetic torque drive is one way to avoid this problem. Researchers have proposed the use of a single rotating magnet [33], [86] or a group of Helmholtz coils [87], [88], [89] to generate a rotating magnetic field to drive a spiral capsule robot. As shown in Fig. 9a, the outer wall of the spiral capsule robot is equipped with spiral ribs, and the robot is equipped with a radially magnetized IPM. Under an external rotating uniform magnetic field, the robot can be driven to rotate in the circumferential direction. Similar to spiral enteroscopes [90], [91], it can generate an axial propulsion force through circumferential rotation to propel itself forward. By changing the rotation axis of the external rotating magnetic field, the capsule robot can be driven to achieve yaw and pitch rotation. Based on models of fluid membrane thickness and hydrodynamic pressure, Zhang *et al.* [87] proposed that if a patient takes a large amount of fluid to fill their intestines before the examination, the capsule robot would realize self-centering characteristics when it locomotes through the intestines, but this method has not been clinically verified. In addition, the camera is in a rotating state when the capsule robot is locomoting, which is not conducive to image processing and requires post-processing technology to create a stable motion video. Then the research team designed a double hemispherical capsule robot with active and passive dual modes (Fig. 9b) [92]. In the passive mode, the passive hemisphere of the capsule robot is in contact with the intestinal wall and remains stationary. The active hemisphere idles relative to the passive hemisphere under the action of an external rotating

magnetic field, which can realize fixed-point hovering and attitude transformation. In the active mode, the capsule robot rolls on the intestinal wall as a whole to realize displacement control. The robot has strong stability in fixed-point attitude adjustment, and the rolling friction between the robot and the intestinal tract causes little damage to the intestinal tract. However, the camera is in a rolling state when the robot is locomoting, making image processing difficult.

A fish-like capsule robot was reported by Ota *et al.* [93], [94]. As shown in Fig. 9c, the capsule robot was fabricated by attaching a silicone fish tail fin with a micromagnet to the PillCam COLON2 capsule endoscope. The length and width of the whole robot were 50 mm and 11 mm respectively. When placed in an alternating magnetic field, the fin swings and generates a propulsion force in water, thereby realizing the movement of the capsule robot. The capsule robot has been tested in humans, and none of the capsules damaged the GI mucosa of the patients. However, compared with locomotion in the gastric cavity, this driving method has a poor effect on locomotion in the intestinal tract. In the experiment, the fin could be stuck or even broken between the bends and folds of the intestine. In addition, the patient needs to drink a large amount of fluid to fill the gastrointestinal tract before the examination, which causes discomfort to the patient.

The intestinal tract has a certain degree of viscoelasticity, and single- and double-balloon enteroscopes have been widely used in clinical practice to locomote and anchor in the intestinal tract by extending the diameter of intestine [95]. Gao *et al.* [96], [97] proposed a clasper-based capsule robot, as shown in Fig. 9d. The locomotion unit of the capsule robot consists of a fixed clasper, a free clasper, and a linear mechanism, and each sub-component is independently driven by a planetary gear motor. The clasper could achieve a wide expansion range of 14-31 mm, anchoring the capsule robot in the intestine. The expansion force of the clasper could be adjusted by setting the upper current limit of the motor to avoid damage to the intestine. The free clasper can be driven by a linear mechanism to move back and forth in the axial direction of the capsule robot, and the capsule robot can move in the intestinal tract according to the action steps shown in Fig. 9e. In addition, the capsule robot was equipped with a 3-D coil at the rear, which could realize wireless energy transmission. The capsule robot has good anchoring and locomotion functions, but it has only one degree of freedom of movement (axial displacement), which is not suitable for stomach examination and limits the possibility of future development as a multifunctional robot.

B. ANCHORING

Under the action of gastrointestinal peristalsis, the capsule robot is difficult to be fixed in a certain position for a long time, which causes difficulties in accurate biopsy, marking and treatment [98]. The researchers proposed adding an anchoring mechanism to the capsule robot to overcome the

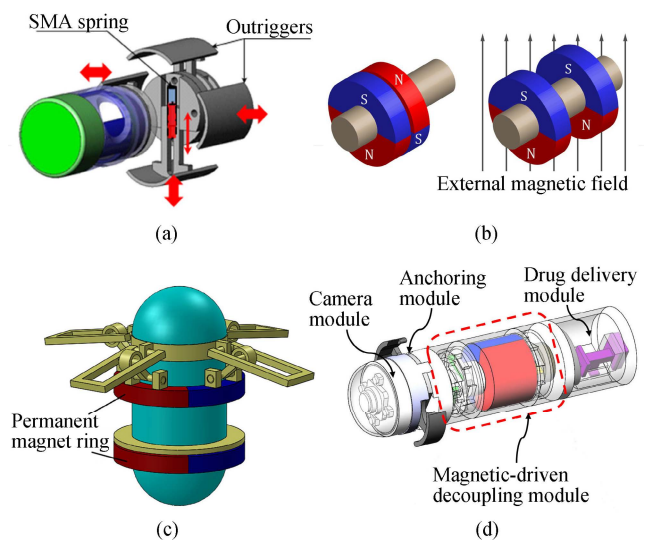


FIGURE 10. Anchoring. (a) The memory metal-electrothermal driven anchoring capsule robot [31]. (b) Schematic diagram of magnetic spring. (c) The umbrella-type anchoring capsule robot [100]. (d) The anchoring and drug release capsule robot with self-locking function [101].

peristaltic force of the gastrointestinal tract and enable the capsule robot to stay at the designated position.

A memory alloy-electrothermal driven anchoring capsule robot was introduced by Kong *et al.* [31] (Fig. 10a). The mechanism uses electricity to heat the shape memory alloy (SMA) to make it shrink, thereby pulling the outriggers to expand outward along the linear guide rails for anchoring action. Each outrigger was connected to a rubber band, and the outriggers could be reset by the pulling force of the rubber bands in the non-anchoring state.

A magnetic torsion spring (MTS), consisting of two radially magnetized rings placed in a coaxial position, is a magnetically driven mechanical structure that provides circumferential torque and axial propulsion [7]. In general, two magnetic rings are attracted to lie close to each other, and their magnetic moment directions are opposite. When a sufficiently strong external magnetic field is applied to the MTS, the attractive force of the external magnetic field on the magnetic ring is greater than the mutual attractive force between the magnetic rings, driving the two magnetic rings to rotate until the magnetic moment direction is aligned with the direction of the external magnetic field (Fig. 10b). When the external magnetic field is removed or the intensity is reduced to a certain value, the two magnetic rings attract each other, the torsional and linear elastic energy are released, and the MTS returns to the initial state. Zhou *et al.* [99] proposed a claw-type anchoring capsule robot using the circumferential rotation force of MTS. The rotation of the MTS in the capsule robot drives the four-bar linkage mechanism to clamp, so that the arc claw expands outward for anchoring action. In addition, the team proposed an umbrella-shaped anchoring capsule robot, as shown in Fig. 10c, using the axial propulsion of the MTS [100]. The MTS in the capsule robot

can drive the slider to move axially, opening the umbrella ribs for anchoring action.

Compared with previous anchoring designs, which require a continuous power supply or continuous external magnetic field to drive, Wang *et al.* [101] proposed an anchoring capsule robot with a self-locking function. Both ends of the capsule robot have an axially magnetized permanent magnet arranged in the same direction, and the two magnets are connected by four elastic rubber legs. Using external permanent magnets, the magnets at both ends of the capsule robot can be attracted to the middle of the capsule, making them approach and squeeze the rubber legs to bend and expand outward to realize the anchoring function. When the magnets at both ends are close to a certain distance, their mutual attractive force is greater than the thrust force of the elastic rubber legs, and the capsule is still in an anchored state after removing the external permanent magnet. Similarly, the two magnets of the capsule robot can also be separated by using an external permanent magnet to release the capsule robot from anchoring. This anchoring method does not require a continuous external energy supply and is flexible to use, but its anchoring structure occupies a large space in the capsule robot. Song *et al.* [102], [103] proposed to use a magnetically driven ratchet mechanism and an eccentric cam mechanism to control anchoring outriggers, which can also achieve a self-locking function (Fig. 10d). In addition, this design consists of a magnetically actuated decoupling module, realizing the integration of anchoring into a functional capsule robot such as drug release and biopsy.

IV. EXTENDED FUNCTIONS

A. BIOPSY

In GI examinations, some diseases cannot be accurately diagnosed by image information, and further biopsy is needed for pathological diagnosis. However, the traditional capsule endoscope has only an image capture function and does not have a biopsy function. If suspicious lesions are found during the examination, additional biopsy procedures need to be performed on the patient with traditional invasive endoscopy; that is, a small piece of tissue is removed from the patient to achieve a pathological diagnosis [62], [104], [105]. This not only complicates the examination process, but also induces additional discomfort in patients.

A biopsy needle can be used to collect deep tissue samples and increase the detection rate of submucosal tumors [106]. As shown in Fig. 11a, Son *et al.* [105] introduced a soft capsule robot equipped with a biopsy needle. Driven by a gradient magnetic field, the capsule robot compressed itself axially and extended the needle for biopsy after approaching the target area. In order to prevent gastric peristalsis from accidentally compressing the capsule robot before reaching the destination area, it must be encapsulated with gelatin or ice before swallowing. After the biopsy was completed, the capsule robot was removed from the patient's body through a soft rope tied to its tail of the capsule robot. Compared with soft

capsules, capsule robots with hard shells can prevent accidental sticking of the biopsy needle and scratching of the patient. Hoang *et al.* [107] presented a capsule robot with a retractable biopsy needle using a threaded mechanism (Fig. 11b). The needle holder was connected to the capsule body by thread. Using a rotating external magnetic field, the biopsy needle could be stretched and retracted under the action of the thread. The capsule robot could then locomote axially and push the extended needle for biopsy. Ye *et al.* [108] proposed a capsule robot with a retractable biopsy needle using a spring mechanism (Fig. 11c). When performing biopsy, the permanent magnet inside the capsule can be actuated by an external magnetic field to compress the spring mechanism and push the biopsy needle out. Fig. 11g shows the action steps of the capsule robot.

Forceps biopsy is also a standard technique used to establish a preoperative diagnosis [106]. Le *et al.* [109] reported a capsule robot that used a gear set to drive forceps for biopsy (Fig. 11d). The IPM drives the gears connected to it to rotate under the action of the external rotating magnetic field. After the torque is increased through the gear set, the forceps can be driven to grip a target tissue. Ye *et al.* [110] proposed a capsule robot that uses a MTS to drive forceps for biopsy. The MTS of the capsule robot can push the forceps out axially to perform biopsy sampling operations. However, because the magnetic block of the MTS needs to move 9 mm to fully open the biopsy forceps, the MTS occupies a large space in the capsule robot. When an external magnetic field is used to control the movement and attitude of the capsule robot, the forceps may extend out and cause damage to GI tissues. Yim *et al.* [111] introduced a capsule robot that uses microgrippers for biopsy. After the capsule robot approached the target area, the transport bin on the capsule robot was opened by a magnetically controlled mechanism, and a large number of heat-sensitive microgrippers were released. After the microgrippers are released and their temperature rises to the human body temperature, they can shrink and grip GI tissues. Subsequently, the micro-column array on the front end of the capsule robot was used to adhere and collect the microgrippers. However, the collection rate of the microgrippers using this method was low (only 3%). In addition, the internal temperature of the capsule robot gradually converged with that of the human body in the process of locomotion to the target area in the GI tract. On the premise of ensuring the minimum effective temperature difference between the microgrippers and the human body, the effective working time of the capsule robot needs to be further verified.

A capsule robot that uses a rotating blade to perform biopsy was presented by Simi *et al.* [7] (Fig. 11e). A rotating blade was installed in the middle of the capsule robot, and its rotation axis coincided with the axis of the capsule robot. Two sets of MTS are distributed at both ends of the blade, which can drive it to rotate. As shown in Fig. 11f, when a strong external magnetic field is applied, the blade rotates so as to expose the lateral biopsy hole. When the external magnet is removed or the external magnetic field intensity

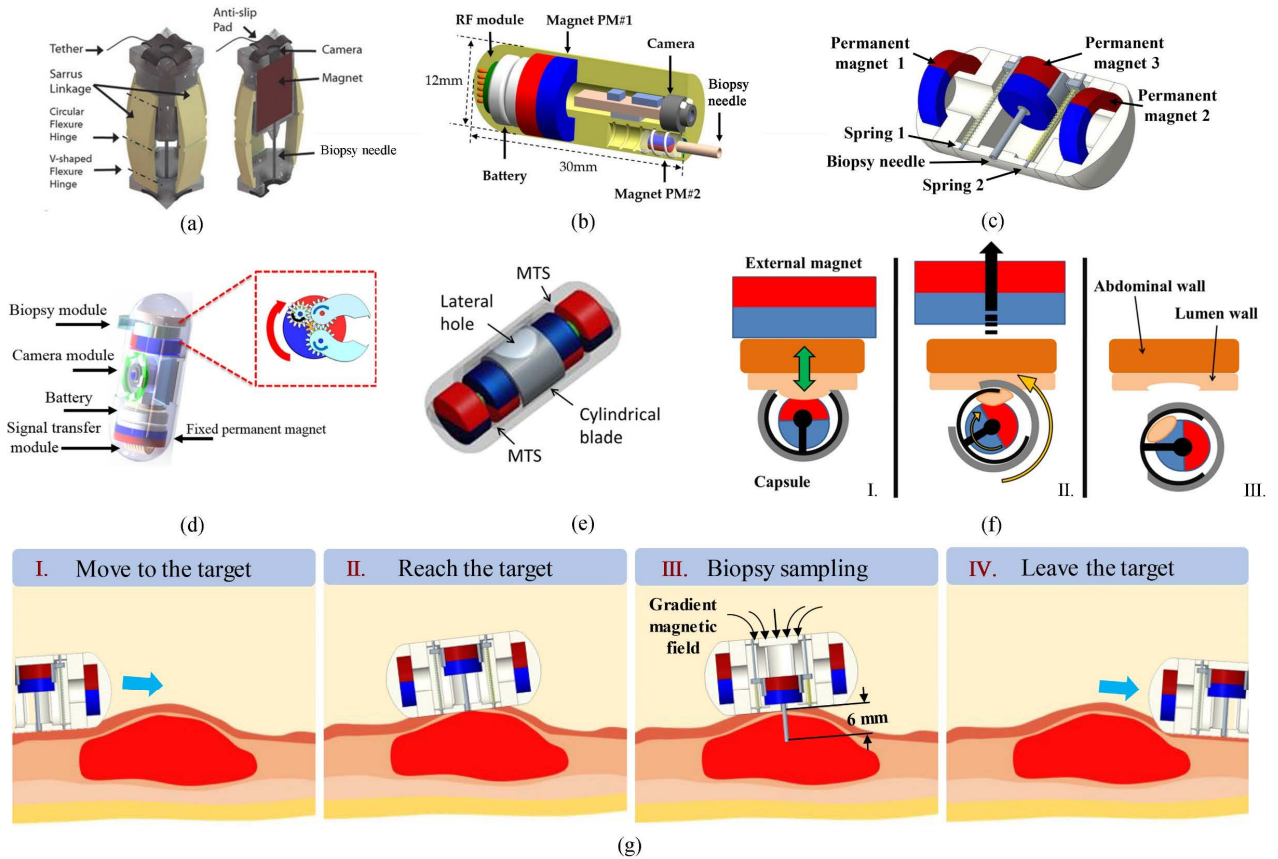


FIGURE 11. Biopsy. (a) The soft capsule robot equipped with a biopsy needle [105]. (b) The capsule robot using threaded retractable needle for biopsy [107]. (c) The internal structure of the capsule robot with a retractable biopsy needle using a spring mechanism [108]. (d) The capsule robot using a gear set to drive a gripper for biopsy [109]. (e) The capsule robot using a rotating blade for biopsy [7]. (f) The action steps of rotating blade for biopsy [7]. (g) The action steps of the capsule robot with a retractable biopsy needle.

drops to a certain value, the blade is reset and rotated to cut and store a GI tissue sample. However, this mechanism occupies a large space and is difficult to be integrated into the current commercial capsule endoscopes. Similarly, the MTS structure was used for sampling bacteria from the GI tract [112]. However, owing to the opposite magnetic moment directions of the two magnets of each MTS, the directions of the magnetic force or magnetic torque acting on the IPMs are inconsistent, which weakens the magnetic locomotion ability of the capsule robot. Hoang *et al.* [113] proposed another biopsy capsule robot based on this mechanism. The rotation axis of the biopsy blade was perpendicular to the axis of the capsule robot. By changing the structure of the MTS, the magnetic moment directions of the IPMs are consistent under normal conditions, so that the capsule robot has a better magnetic locomotion ability.

B. LOCALIZATION

The position and attitude information of the capsule robot are very important for its precise control in the body. In addition, learning the exact location of a patient’s lesions is essential for subsequent diagnosis and precise treatment, such as precise drug delivery, tumor monitoring, and preparation of surgical

incisions, and can reduce the operation time during clinical surgery [114].

The image information obtained by the camera in the capsule robot can be used to estimate the translation and rotation of the capsule robot between each frame, and the real-time position and attitude information of the capsule robot can be further calculated. This method does not require any additional hardware and is promising for localization. However, this requires finding sufficient data in the images of the GI tract and finding the corresponding points, regions, or features between frames to accurately calculate the basic matrix [115]. In addition, the capsule movement caused by gastrointestinal peristalsis and patient activity should be considered. This localization method still unable to achieve high accuracy at this stage (less than 25mm) [116], [117].

Capsule endoscopes are typically equipped with a radio frequency (RF) module to wirelessly transmit image data to external signal receivers. The RF signals received by two or more signal receivers can be used to calculate the three-dimensional position of the capsule using information such as time of arrival (TOA), time difference of arrival (TDOA), direction of arrival (DOA), and signal strength (RSS) [118], [119]. This is a commonly used localization

method for commercial capsule endoscopes [120]. However, owing to differences in the attenuation of RF signals in different tissue components of the human body, and differences in tissue components between patients, the positioning accuracy of this method is low, usually on the order of centimeters [117], [121], [122]. The advantages of this method are that the original RF module in the capsule robot is utilized, no extra space in the capsule is required for the new component, and the cost of additional parts required outside the body is low.

The magnetic localization technology has also been used to track capsule robots. Because the magnetic permeability of the human body is very close to that of air, it has little effect on static or low-frequency magnetic signals and can achieve high positioning accuracy [123]. Boroujeni *et al.* [124] used an external sensor array composed of 16 magnetic field sensors (Fig. 12a) to locate a capsule robot equipped with permanent magnets in real time. In this study, a capsule robot magnetic localization algorithm based on Kalman filter was proposed by combining the dynamic equation of the moving magnetic part with the measurement of an external magnetic sensor using model-assisted technology. It is verified by experiments that the average errors of the position and attitude estimations were less than 1 mm and 1° , respectively. Shao and Guo [125] proposed a hybrid system based on Helmholtz coils with wireless power transfer and capsule localization functions. The system generated a gradient magnetic field for capsule localization and a uniform magnetic field for wireless power transfer by changing the excitation current of the Helmholtz coils. In the experiment, the average position and attitude errors of the system positioning were 1.57 mm and 6.7° , respectively. In addition, calibrating the magnetic sensor array before using it for tracking a capsule robot is unavoidable [126], [127], [128].

It is worth considering that for a magnetically actuated capsule robot, it is necessary to use the external magnetic source to interact with the IPM to actuate the capsule robot. Obviously, the external magnetic field interferes with the magnetic localization system. Taddese *et al.* [129] presented a magnetic localization method for a magnetically actuated capsule robot. In this method, an axially magnetized permanent magnet, six magnetic field sensors, and an inertial measurement unit were installed in the capsule robot. An external permanent magnet and an electromagnetic coil were fixed on the end effector of the six-degree-of-freedom robot (Fig. 12b). The external permanent magnet provided a strong magnetic field to drive the capsule. The electromagnetic coil generates a time-varying weak magnetic field, and its magnetic moment is orthogonal to that of the external permanent magnet. The static magnetic field of the external permanent magnet and the time-varying magnetic field of the electromagnetic coil can be used simultaneously to estimate the six-degree-of-freedom pose of the capsule robot. It was verified by *in vitro* experiments that even when the capsule robot is located in the singular area of the magnetic field, the scheme still has strong robustness, and the average errors of its position and attitude estimation were less than 5 mm

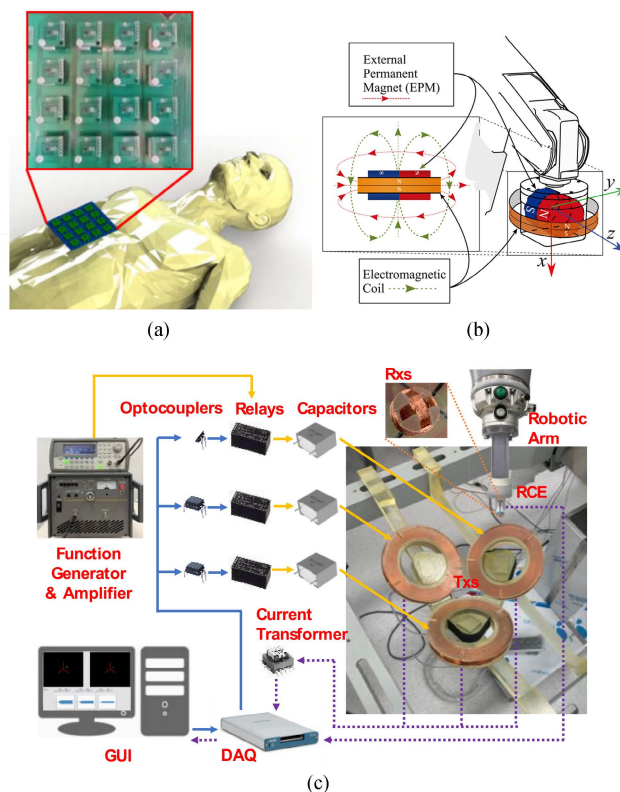


FIGURE 12. Localization. (a) The external sensor array composed of 16 magnetic sensors [124]. (b) An external permanent magnet and an electromagnetic coil fixed on the robot end-effector [129]. (c) The Six-Dimensional localization system using magnetoquasistatic field [132].

and 6° , respectively. Fu *et al.* [130] proposed a localization method for magnetically actuated capsule robots used in electromagnetic coil systems. In this method, a sensor array composed of 36 magnetic field sensors was used to measure the position of the capsule robot while it was driven by a triaxial Helmholtz coil. The actual position of the capsule robot was fitted by the least square method, and the average positioning accuracy was 2.25mm. Popek *et al.* [131] presented a simultaneous localization and propulsion strategy for a magnetic capsule robot that use a single rotating magnet. It can achieve an average locomotion velocity of 2.2 m/s in a curved small intestine model, and the average error of its position and attitude estimation is 8.5 mm and 7.1° , respectively. As shown in Fig. 12c, Liu *et al.* [132] used three transmitting coils fixed under the foundation bed to generate a magnetoquasistatic field acting on the three orthogonal receiving coils in the capsule robot for magnetic localization. The attitude and position information of the capsule robot can be obtained by solving the nonlinear net magnetic field model and the rotation matrix. The Experimental results show that the average errors of position and attitude estimation were 1.68 mm and 1.74° , respectively.

The magnetic localization system mentioned above can only be used for static positioning devices. For passive capsule endoscopy, a GI examination takes a long time

(usually more than 8 hours), and the patient usually completes the examination at home [133]. During the examination, the patient will inevitably ambulate, and changes in the geomagnetic field will significantly interfere with magnetic localization. Shao *et al.* [134] introduced a wearable capsule robot localization system with geomagnetic noise cancellation. In addition to the 16 magnetic sensors arranged around the patient's waist, two geo-noise cancellation sensors were added to the system, which were arranged on the patient's upper chest and upper abdomen. Because of the long distance between the noise cancellation sensors and the capsule robot, the system ignores the influence of the IPM on the noise cancellation sensors, and the data measured by the noise cancellation sensors are regarded as geomagnetic noise. The system used a variance-based algorithm for calculation, and the average errors of position and attitude estimations were 10 mm and 12° respectively. Song *et al.* [135] proposed a magnetically actuated capsule robot localization method based on differential signals. This method is based on the assumption that the geomagnetic signals between adjacent sensors are almost equal. The four adjacent sensors are divided into a differential signal unit, and the signals collected by the 16 magnetic field sensors were calculated to obtain the position and attitude information of the capsule without additional compensation sensors. In the experimental motion range of 2 m × 6 m, the average errors of position and attitude estimation obtained by this method were 7.5 mm and 13.8°, respectively.

In contrast to three-dimensional coordinate positioning, the use of *in-vivo* marker positioning can enable surgeons to find the location of lesions more intuitively and quickly. Chandrappan *et al.* [136] presented a capsule robot that could eject micro-tags. The capsule robot was equipped with four micro-tags ejection mechanisms. The spring latch can be disconnected by activating the thermal igniter, and the micro-tags can be ejected through the actuator. The micro-tags can be embedded in the GI mucosa as a location marker. The location of the micro-tags can be visualized using common medical imaging techniques such as X-rays or magnetic resonance imaging (MRI). In addition, during open surgery, doctors can quickly locate the lesions based on the tactile perception of their hands. However, with the development and popularization of laparoscopic surgery, compared with open surgery, doctors cannot tactilely find markers to locate lesions during surgery and need to rely on visual feedback from laparoscopy [137]. Injecting dye under the GI mucosa enables doctors to directly observe the location of the lesion during the operation, and the injection of Indian ink for preoperative marking has become a common means of preparation for laparoscopic surgery [138], [139]. Hoang *et al.* [140] proposed a capsule robot for ink injection. The injection needle in the capsule robot was connected to the capsule with a threaded structure. The injection needle can be driven to rotate by using an external rotating magnetic field, and extension and retraction of the injection needle can be realized under the action of the thread. The internal reed switch can

be controlled using an external magnetic field. When the reed switch is turned on, the metal wire is heated and fused so that the water bag is pushed to the metal needle below by the spring, and the water bag is crushed. The water reacts with the chemical dry powder in the capsule robot to produce carbon dioxide gas, which pushes the ink chamber to compress for ink injection.

C. THERAPEUTICS

Due to the influence of digestive enzymes and the acidic pH of stomach, some drugs, especially macromolecule drugs, will reduce efficacy or even be ineffective [141]. Traditionally, drugs are released in specific areas of the GI tract based on the specific chemical properties of the drug coating or substrate [142]. However, there are differences in gastric emptying time and gastrointestinal physicochemical properties in different patients or different physical states of the same patient, making it difficult for traditional methods to achieve highly predictable and accurate drug dose delivery to specific parts of the gastrointestinal tract [141], [142]. Achieving precise drug delivery can effectively improve drug efficacy at the target site and reduce unnecessary systemic effects. Compared with pH responsive capsule robots [143], [144], magnetically actuated capsule robots have higher controllability and accuracy for drug delivery.

A drug delivery capsule robot with controllable detachment of the capsule body was introduced by Le *et al.* [145] (Fig. 13a). Two axially distributed soft magnets (pure iron) are installed in the middle of the robot. By controlling the direction of an external magnetic field, the soft magnets can be magnetized axially or radially. When the soft magnets are magnetized axially, the two soft magnets attract each other, which can further control the movement and attitude of the capsule robot by the external magnetic field; When the soft magnet is magnetized radially, the two soft magnets repel each other, so that the middle part of the capsule robot is unfolded and the drug is released. However, because the magnetization of pure iron is related to the intensity of the external magnetic field and is always less than that of a Nd-Fe-B magnet, the soft magnet capsule generates less magnetic force and has weak movement ability under the same conditions. Yim *et al.* [146] proposed a capsule robot that directly squeezes an elastic drug bin to achieve drug release by controlling two magnetic blocks distributed on both sides of the bin. The capsule robot has two drug delivery modes: continuous drug delivery mode driven by a pulsed weak magnetic field, and the drug release rate can be adjusted by the frequency of the external magnetic pulse; and rapid drug delivery mode driven by a strong magnetic field, and the magnet squeezes and destroys the elastic structure of the drug bin to realize the full release of the drug. Munoz *et al.* [49] presented a capsule robot that used a crank slider mechanism to propel drug release. Under the action of an external rotating magnetic field, the magnetic crank in the capsule robot rotates to drive the slider to push the drug bin and can control the release amount and release rate of the drug.

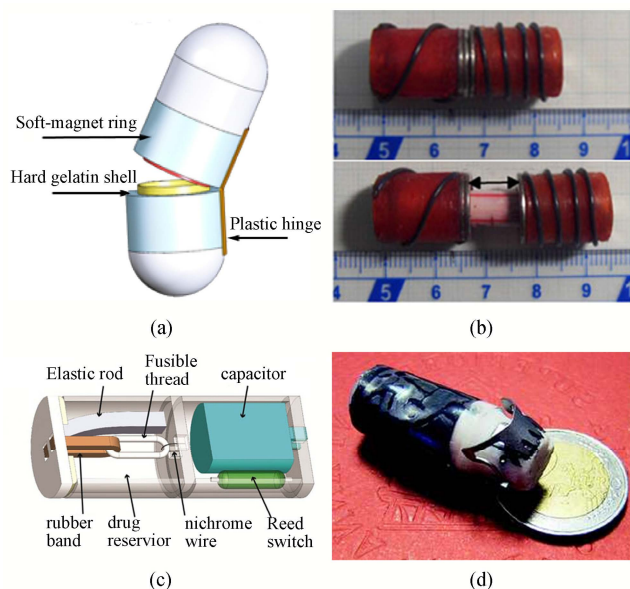


FIGURE 13. Therapeutics. (a) The capsule robot with controllable detachment of capsule body [145]. (b) The drug-releasing capsule robot driven by two spiral bodies with opposite spiral directions [147]. (c) profile schematic of the capsule robot that uses a reed switch to control drug release [148]. (d) The capsule robot that could release a Nitinol clip [152].

A drug-releasing capsule robot driven by two spiral bodies with opposite spiral directions was introduced by Kim *et al.* [147] (Fig. 13b). A small axially magnetized permanent magnet was connected to each adjacent end face of the two spiral bodies. In general, the two spirals are close to each other under the magnetic attractive force of the axially magnetized permanent magnet, and the drug bin is in a closed state. The capsule robot could be driven to rotate by using an external rotating magnetic field. The counterclockwise rotation of the capsule robot could generate a force that separates the two spiral bodies outward. When the force was greater than the magnetic attractive force of the axially magnetized permanent magnet, the two spiral bodies were separated, the drug bin was opened, and the drug was released. The clockwise rotation of the capsule robot could be used to drive the capsule robot to locomote, but the total propulsion force is the difference between the propulsion forces generated by the two spiral bodies, and the overall efficiency is low.

Yu *et al.* [148] proposed a capsule robot that uses a reed switch to control the drug release (Fig. 13c). The capsule robot can remotely turn on the reed switch by using an external magnetic field, so that the nickel-chromium alloy wire can be heated by electricity and fuses the nylon wire, limiting the release of the spring drug bin to release the drug from the drug bin. The requirement for an external magnetic field to turn on the reed switch is low, and does not require a complex magnetic actuation system. Patients can use small permanent magnets implanted in the epidermal body or portable permanent magnets. Zhang *et al.* [149] presented a capsule robot that could release magnetically responsive

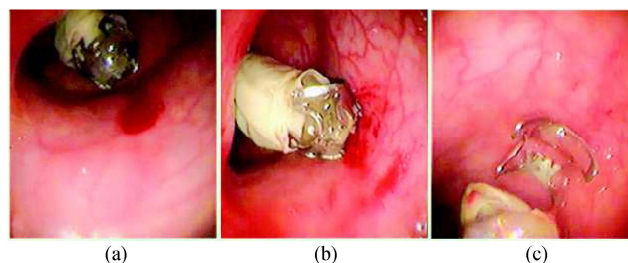


FIGURE 14. In-vivo animal experimental of the capsule robot releasing a Nitinol clip [152]. (a) The capsule robot approaching a bleeding lesion. (b) Magnetic positioning of the capsule robot. (c) Deployment of the clip.

drug-loaded microneedles. The capsule robot has an enteric coating, and when it reaches the intestine, it can release the microneedles inside. The microneedles deliver drugs to the intestine guided by a magnetic field generated by a magnetic belt worn by the patient. The above two capsule robots can be used by patients daily at home, and are very suitable for treatment situations that do not require high accuracy of the drug delivery location and require repeated administration.

In addition to drug delivery, other therapeutic functions have been proposed. Tortora *et al.* [150] proposed a capsule robot capable of performing photodynamic therapy. The capsule robot was equipped with eight LED lights, which could emit light of a specific wavelength to kill *Helicobacter pylori*. The magnetic switch in the capsule robot is controlled by an external magnetic field, and the LED lights could be turned on or off remotely. However, the light intensity of the capsule robot prototype was insufficient, and at least three capsule robots were required to achieve the target dose of killing *Helicobacter pylori* in the stomach.

In clinical endoscopic surgery, clipping devices are often used for GI hemostasis, tissue defect closure, and preoperative marking [151]. Valdastrì *et al.* [152] reported a capsule robot that could release a Nitinol clip (Fig. 13d). As shown in Fig. 14, the capsule robot can move to the target position under the action of an external magnetic field, and a Nitinol clip preinstalled on the topside of the capsule robot can be triggered to be released through a wireless control signal. The capsule robot has been successfully tested on pigs, but further clinical verification is required. Lee *et al.* [153] proposed a capsule robot that could release drug-loaded microneedle blocks. The capsule robot can be actuated by an external magnetic field for locomotion, and the three drug-loaded microneedle blocks in the capsule robot can be released to three target lesion sites in the GI tract. At present, this capsule robot lacks a mechanism to isolate microneedle blocks from external GI fluid before releasing them.

Researchers have also proposed a variety of magnetically inflatable capsule robots for treatment. Leung *et al.* [154] introduced a capsule robot for intestinal hemostasis using the tamponade effect. The capsule robot produces carbon dioxide gas by injecting acetic acid into sodium bicarbonate powder to inflate a silicone balloon to stop intestinal bleeding.

After the treatment, the solenoid valve could be opened to vent the gas. The prototype was successfully tested on pigs. In addition, Thanh *et al.* [155] proposed the use of a magnetically actuated inflatable capsule robot to fill the stomach so that patients can increase their sense of satiety to achieve the effect of dieting and weight loss. It is worth mentioning that there are clinically poor endoscopic results due to GI folds, residual fluid, or stool [11]. Pasricha *et al.* [156] presented a capsule robot that used a chemical reaction to produce carbon dioxide gas to inflate the intestine. In this scheme, the capsule robot has two independent chambers separated by two magnetic valves. When the external permanent magnet is approached, the magnet valve can be opened, allowing acid to flow into another chamber to react with sodium bicarbonate, producing carbon dioxide gas and releasing it into the intestine. When the external permanent magnet was removed, the magnet valve was closed and the reaction was stopped. The capsule robot can produce approximately half a liter of gas. It has been successfully tested in pigs and proven to be effective in improving intestinal imaging.

D. WIRELESS POWER TRANSFER

In addition to directly actuating capsule robots, magnetic fields can be used for wireless power transfer (WPT), charging batteries in capsule robots, or supplying power to capsule robots directly.

Existing capsule robots mainly use built-in button batteries for power supply, causing them to be unable to keep working in the body for a long time owing to their limited capacity. In clinical practice, the completion rate of some passive capsule endoscopies is low because of slow GI peristalsis in some patients [18]. In particular, the capsule robot is developing towards higher frame rate, higher resolution image capturing, and multiple medical functions, which will put forward higher requirements on the power consumption of the capsule robot. However, limited by the size of the capsule robot, the battery capacity will not be able to meet new demands [150], [157], [158]. The development of batteries with higher energy densities is one solution. The other is to use the WPT technology, which uses magnetic fields as a medium to transmit power through human tissue to the capsule robot in the GI tract [159]. The application of wireless power transmission technology is expected to solve the problem of insufficient built-in energy in capsule robots and to avoid the harm of chemical batteries to the human body caused by accidental damage to the capsule.

Inductive coupling based on the principle of electromagnetic induction is a common WPT method used for medical implant devices [159]. Because the position and attitude of the capsule endoscope in the human body are not fixed, in order to improve the connection efficiency of WPT, Lenaerts and Puers [160] used geometrically orthogonal three-dimensional coils (Fig. 15a) as the power receiver to ensure full coupling with the transmitter in any direction. In this system, multiple receiving coils are placed inside the cylindrical transmitting coil. The operating frequency of the

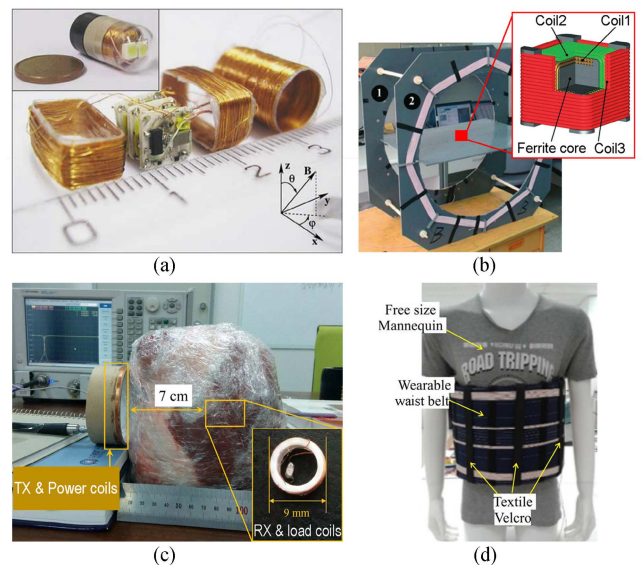


FIGURE 15. Wireless power transfer. (a) The geometrically orthogonal three-dimensional coils as power receivers [160]. (b) The Helmholtz coil and three-dimensional coils [161]. (c) Penetration experiment setting with pork chop [158]. (d) The transmitting coil installed in a wearable belt [163].

transmitting coil was 1 MHz, and the external dimensions of the multiple receiving coils were 10 mm in diameter and 13 mm in length. The output power of the system was 150 mW, power transfer efficiency (PTE) of the link was 1%, and specific absorption rate (SAR) was 0.4 W/kg. SAR refers to the electromagnetic power absorbed by human tissue per unit mass. If the SAR is too high, it can harm the human body [158]. Xin *et al.* [161] introduced a WPT system with a lower SAR for capsule robots. In this system (Fig. 15b), the power receiver is composed of three-dimensional coils that are geometrically orthogonal and wound on a ferrite core. The power transmitter was a Helmholtz coil that generated a uniform alternating magnetic field. The system operates at 400 kHz with an output power of 310 mW, link PTE of 1.2%, and SAR as low as 0.329 W/kg.

The non-radiative magnetic resonance coupling (NRMRC) technology was proposed in 2007 [162]. Conventional magnetic coupling is used for short range, whereas NRMRC has a better impedance matching ability and enables magnetic coupling to occur over longer distances. Na *et al.* [158] reported a wireless power transfer system for a capsule robot using the NRMRC technology with a four-coil based architecture. The system consists of a driving coil, a transmitting coil, a receiving coil, and a load coil. The system operates at 16.47 MHz, the receiver diameter is as small as 9 mm, the output power is 26 mW, the maximum PTE is 0.7%, and the SAR is 1.74 W/kg. In the experiment, the receiver was wrapped in pork tissue 7 cm away from the transmitter (Fig. 15c), and the measured attenuation was 0.39 dB. Basar *et al.* [163] reported a wireless power transfer system using the NRMRC technology with a three-coil based architecture for capsule robots. In this system, the transmitting coil installed

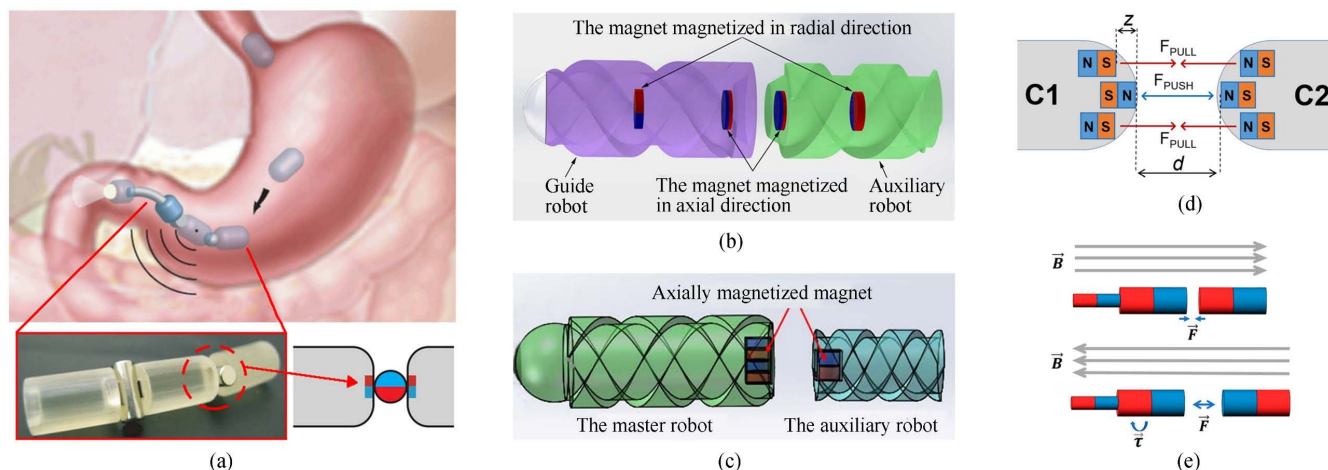


FIGURE 16. Multi-capsule collaboration. (a) The modular capsule robots with cylindrical magnetic joints [164]. (b) The modular capsule robots with opposite directions of spiral ribs [165]. (c) The modular capsule robots with different step-out frequencies [166]. (d) The noncontact modular capsule robots [167]. (e) The connection mode of soft magnet modular capsule robot [168].

in the wearable belt is the power transfer side (Fig. 15d), and the power receiving side is composed of a receiving coil and a load coil. The system has a high PTE and received power stability. The operating frequency is 250 kHz, received power stability is 79.2%, output power is 570 mW, and link PTE is 5.4%.

E. MULTI-CAPSULE COLLABORATION

The size of the capsule robot should be within the range in which humans can swallow normally. In the limited space of a capsule robot, it is very difficult to integrate all functions, such as image acquisition, active movement, biopsy, and treatment. In addition, the pre-integration of all functions required by different patient conditions on the disposable capsule robot will cause waste and greatly increase the manufacturing cost. Researchers have proposed using modular capsule robot strategies to increase the final overall function of the capsule robot. In other words, each single capsule robot realizes a unique function. During the examination, the capsule robot with an image capturing function is first used as the main functional module, and then, according to the actual needs of the patient, the capsule robot with the corresponding function is swallowed as an additional functional module. Multiple modules can be assembled *in-vivo* and can complete medical tasks together [32], [164].

To realize multi-capsule robot collaboration, the main problem that needs to be solved is the self-assembly of modular capsule robots in the human body. Nagy et al. [164] proposed adding specific magnets to the mating surface of capsule robots to achieve self-assembly via mutual attractive forces between the magnets. As shown in Fig. 16a, in order to enable the capsule robot to adapt to an irregular GI tract, the modules can slide on the surface of the cylindrical magnetic joints arranged between the modules, thereby allowing

a degree of freedom of rotation between the two modules. However, the module connection process in this method is uncontrollable and cannot be restored after a misaligned connection (the probability of occurrence in the experiment was 55%).

Guo et al. [165] presented a modular capsule robot with a controllable combination and separation functions based on spiral rib propulsion. As shown in Fig. 16b, the spiral ribs of the two modular capsule robots to be assembled had opposite spiral directions. Under the action of the same rotating magnetic field, the two capsule robots move in opposite directions, which allows them to approach or move away from each other. The matching surfaces of the capsule robots were equipped with axially magnetized permanent magnets. When they are sufficiently close, the magnetic force generated between the two magnets attracts the two capsule robots together. The two capsule robots combined using this method have spiral ribs in opposite directions, which limits their locomotive ability. Then the team designed modular capsule robots with different step-out frequencies by changing the geometric parameters and IPM dimensions (Fig. 16c) [166]. The ribs of each modular capsule robot are in the same spiral direction. In an external rotating magnetic field of a certain frequency, the capsule robot whose step-out frequency is less than the frequency of the external magnetic field will remain stationary or vibrate slightly in place, while the other capsule robots will continue to rotate and move, so that different modular capsule robots can approach and realize magnetic adsorption. On this basis, Zheng et al. [32] changed the magnetic adsorption between modules to a thread and claw mechanism connection. This method avoids the impact collision caused by magnetic adsorption and enables two degrees of freedom of rotation between the connected modules so that the capsule robots can work more easily in the curved intestine.

A noncontact connection method for modular capsule robots was proposed by Peker *et al.* [167]. In this method, a magnetic rod and magnetic ring were installed on the mating surface of each capsule robot. Both magnets were axially magnetized, and the distance between the rear ends after installation is z , as shown in Fig. 16d. The magnetic rods on the mating surface cause a repulsive force between the capsule robots, whereas the magnetic rings cause an attractive force. The equilibrium gap between the modules is d , at which the repulsive force is equal to the attractive force. The gap between the capsule robots reduces the risk of GI tissue being pinched when multiple capsule robots are connected within the body.

A connection method using soft magnets for modular capsule robots was reported by Li *et al.* [168]. As shown in Fig. 16e, a permanent magnet and a soft magnet were installed in the driving capsule robot, whereas only a soft magnet was installed in the functional capsule robot. The high permeability of the soft magnet in the driving capsule robot has a magnetic shielding effect, which significantly reduces the influence of the permanent magnet in the driving capsule robot on the soft magnet in the functional capsule robot, making the magnetization direction of the soft magnet in the functional capsule robot more susceptible to the influence of the external magnetic field. By changing the direction of the external magnetic field, the magnetization direction of the soft magnet in the functional capsule robot can be changed to generate an attractive or repulsive force between the capsule robots. This method can realize the controllable connection and separation of capsule robots in the body, but when multiple functional capsule robots need to be connected simultaneously, each functional capsule robot is not easily controlled independently because of the mutual influence between soft magnets.

V. FUTURE DIRECTIONS AND OPEN ISSUES

A. CLINICAL VALIDATION

Although researchers have proposed a variety of capsule robots with different functions, most experiments have only been carried out in tube models or *ex-vivo* GI tracts of swine, lacking *in-vivo* and clinical tests. The movement of the capsule robot in the human GI tract could not be directly observed, as in the phantom experiment. In addition, the unstructured, highly deformable, and peristaltic GI environment necessitates higher requirements for the control robustness of capsule robots. However, the research progress in this area has been slow.

B. MINIATURIZATION

It should be noted that compared with traditional invasive endoscopes, the functional integration of capsule robot prototypes is still very weak. Often, only one functional structure occupies a large amount of space in the capsule, and even affects the original image capturing structure or makes the capsule too large to be swallowed. However, to perform the

treatment or biopsy function in clinic, the capsule robot needs to have the functional structures of active locomotion, anchoring, and localization at the same time, so as to effectively perform the task in clinic. This is another obstacle to clinical research on capsule robots.

In future research, it will be necessary to reduce the size of functional structures of capsule robots. The components of magnetically actuated capsule robots can be classified into mechanical execution structures, electronic components and internal permanent magnets. The further development and application of micro electro mechanical system (MEMS) technology are expected to miniaturize the mechanical execution structure and electronic components of capsule robots.

The miniaturization of internal permanent magnets requires the development of magnetic materials with higher magnetic energy products or magnetic actuation systems that can generate a higher magnetic field intensity and gradient in the future. However, it should be noted that the magnetic field intensity must comply with the safety guidelines established by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) for human exposure to electromagnetic radiation [169].

C. INDEPENDENT CONTROL OF MULTI-CAPSULE ROBOT

Multi-capsule robot collaboration is another way to increase the capabilities of capsule robots, and the development of this technology is expected to expand the clinical functions of capsule robots without increasing unnecessary costs. However, because the magnetic field acts on all magnetic response devices in the working area, the key problem to be solved at present is how to achieve efficient independent control and collaborative task execution for each modular robot. We predict that functions such as image capturing, drug delivery, biopsy, and anchoring can be used to construct different modular capsule robots to meet different clinical needs.

D. SOFT-TETHERED CAPSULE ROBOT

Recently, magnetically actuated soft-tethered capsule robots have attracted the interest of researchers. This type of capsule robot uses a magnetically actuated front end to locomote, eliminating the need for propulsion and steering mechanisms in the endoscope's connecting tether, which can significantly reduce the diameter, weight, and bending stiffness of the tether. A soft and slender tether results in smaller GI deformations, which can reduce tissue damage and discomfort of patients, whereas preserving the therapeutic capabilities of traditional flexible endoscopes. It is an effective solution for the application of capsule robots in clinic [170], [171]. However, owing to the inevitable friction between the tether and GI tract, the comfort of the patient is still lower than that when using a wireless capsule robot. In addition, existing studies have focused on the upper GI trace and colon examination, and there is no report that this type of capsule robot has a sufficient driving force to drag the tether into the long and winding small intestine for examination.

E. TELEMEDICINE

Capsule robots are particularly beneficial to the development of telemedicine. GI tract examinations using capsule robots have the characteristics of noncontact operation, so the telemedicine platform can be easily built in a short time (it only needs to connect the workstation to the network), and it will not impose an additional economic burden on patients and medical institutions. This can concentrate resources of medical experts, thereby significantly reducing capital expenditure, and may be particularly effective in rural communities or in communities where there is little access to gastroenterologists [36], [172]. However, to date, the clinical application of telemedicine is still limited to monitoring disease activity or follow-up care of patients with chronic diseases, such as inflammatory bowel disease [173], [174].

F. COMPUTER AIDED DIAGNOSIS AND AUTONOMOUS DIAGNOSIS

In recent years, artificial intelligence technology has developed rapidly, and the combination of artificial intelligence and capsule robots will undoubtedly make diagnose more intelligent [175], [176], [177]. It was reported that more than 10% of upper GI cancers are missed by conventional endoscopy [178]. This may be caused by low professional level, fatigue, and inattention of endoscopic doctors. Computer aided diagnosis aims to minimize these missed lesions. An increasing number of studies have shown that computer-aided diagnostic systems can perform as well or even better than endoscopists in detecting single type of lesions, especially colon polyps [179], [180]. However, the training of the endoscope artificial intelligence system relies on a large amount of image data, which requires human observers to annotate the position and shape of lesions in existing images one by one. This is a very large and time-consuming task. Currently, there is no artificial intelligence system with multiple decision-makings abilities for various GI diseases [179].

Furthermore, with the development of simultaneous localization and mapping technology in the GI tract [181], [182], the capsule robot can model an unknown and complex GI environment in real time to provide guidance for driving the capsule robot. In the future, capsule robots are expected to develop from relying on doctors' judgments and operations to fully automatic intelligent locomotion, diagnosis, and treatment.

VI. CONCLUSION

In this review, we conducted a comprehensive survey on magnetically actuated capsule robots. Due to the advantages of simple internal response structure and external remote power supply, external magnetic field actuation is the mainstream direction of current research. This technology uses a magnetic actuation system to generate a controllable external magnetic field to actuate a capsule robot that can actively move in the GI tract and perform a series of medical tasks. However, the

development of this field is still immature, and many aspects need to be improved and further studied before capsule robots can meet the needs of clinical applications. We believe that future multifunctional wireless capsule robots will excite both gastroenterologists and patients as research progresses.

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