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Review article

Medical capsule robots: A renaissance for diagnostics, drug delivery and surgical treatment

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ABSTRACT

The advancements in electronics and the progress in nanotechnology have resulted in path breaking development that will transform the way diagnosis and treatment are carried out currently. This development is Medical Capsule Robots, which has emerged from the science fiction idea of robots travelling inside the body to diagnose and cure disorders. The first marketed capsule robot was a capsule endoscope developed to capture images of the gastrointestinal tract. Today, varieties of capsule endoscopes are available in the market. They are slightly larger than regular oral capsules, made up of a biocompatible case and have electronic circuitry and mechanisms to capture and transmit images. In addition, robots with diagnostic features such as *in vivo* body temperature detection and pH monitoring have also been launched in the market. However, a multi-functional unit that will diagnose and cure diseases inside the body has not yet been realized. A remote controlled capsule that will undertake drug delivery and surgical treatment has not been successfully launched in the market. High cost, inadequate power supply, lack of control over drug release, limited space for drug storage on the capsule, inadequate safety and no mechanisms for active locomotion and anchoring have prevented their entry in the market.

The capsule robots can revolutionize the current way of diagnosis and treatment. This paper discusses in detail the applications of medical capsule robots in diagnostics, drug delivery and surgical treatment. In diagnostics, detailed analysis has been presented on wireless capsule endoscopes, issues associated with the marketed versions and their corresponding solutions in literature. Moreover, an assessment has been made of the existing state of remote controlled capsules for targeted drug delivery and surgical treatment and their future impact is predicted. Besides the need for multi-functional capsule robots and the areas for further research have also been highlighted.

1. Introduction

In early 20th century, Paul Ehrlich had envisaged the concept of a magic bullet that can selectively target diseased part inside the body. Since then, scientists all over the world have tirelessly tried to make this dream a reality [1]. Newer breakthroughs like targeted drug delivery systems showed a considerable promise yet the science fiction idea of a mini-submarine of medication travelling inside the body and targeting desired areas eluded the realms of reality. The advancements in miniaturized electronics and sensors in the early 21st century has ushered in a new sense of confidence in scientists to make this dream a reality [2].

Richard Feynman mentioned in his famous address, “There's plenty of room at the bottom” in 1959 about swallowing small machines that can function as surgeons to treat disorders inside the body. That address also marked the beginning of nanotechnology [3]. In the last six decades, plethora of techniques have been devised to create nanosized materials and newer analytical techniques have been developed to characterize these materials. Electronics is one sector that has witnessed unprecedented transformation due to progress in nanotechnology [4–6]. As Gordon Moore described in his famous Moore's law in 1965, the number of transistors have doubled in an integrated circuit every two years. The size of these transistors has reduced from 10 µm then to less than 30 nm today [7]. This ability to develop

Abbreviations: GI, gastrointestinal; MEMS, microelectromechanical systems; WCE, wireless capsule endoscope; GERD, gastroesophageal reflux disease; LED, light emitting diode; CMOS, complementary metal oxide semiconductor; CCD, charge coupled device; ASIC, application specific integrated circuit; FI, fluorescent imaging; RF, radio frequency; SMA, shape memory alloy; DC, direct current; MRI, magnetic resonance imaging; CT, computer tomography; WPT, wireless power transmission; NSAID, non-steroidal anti-inflammatory drug; PDMS, polydimethylsiloxane; RCC, remote controlled capsule

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electronic circuits at nanoscale helped to develop capsule robots, which can travel inside body to diagnose disorders and provide treatment.

One of the first areas to receive application of these robots was endoscopy. Traditional endoscopy involves usage of a flexible endoscope, which is inserted into body cavities by a doctor for medical imaging of a concerned part inside the body. Physicians have been using these endoscopes for over two centuries since their invention. They have been successful in assisting doctors for viewing gastrointestinal tract, respiratory tract, urinary tract and other cavities in the human body. On the contrary, utilization of these endoscopes accompanies various problems like the risk of infection, perforation and tear. Besides, the most important drawback of them is that they are not user-friendly and endoscopy can be carried out only under the supervision of a medical practitioner [8]. These issues gave birth to the idea of wireless capsule endoscopes (WCE).

It was in the year 2001, when Given Imaging launched the first commercial capsule endoscope, PillCam, into the market. A simple, non-invasive swallowing of the pill and no anesthesia requirement provided an attractive alternative to traditional scope based endoscopy approach to visualize GI tract [9]. Subsequently, an array of capsule endoscopes flooded the market as shown in Fig. 1. Initially meant to investigate disorders in the small intestine, today, capsule endoscopes diagnose disorders in various parts of GI tract comprising oesophagus, stomach, small intestine and large intestine. However, various challenges like passive locomotion, telemetry, advanced vision and image sensing are yet to be overcomed in the marketed products. Still, over 1.5 million patients have experienced the benefits of PillCam capsule endoscopy which speak volumes of the success of capsule endoscopes [10].

non-mechanical systems. Microelectromechanical systems (MEMS) may or may not use anchoring systems to stay at the targeted area and use wireless signals to control the drug release. While, magnetic interactions between a permanent magnet located inside the capsule and an external magnet present outside the body generates anchoring mechanisms in non-mechanical systems [17]. A variety of capsule robots have been developed with an effort to enhance the controllability over capsule position [18] and to achieve remote actuation of drug releasing mechanism [17].

The purpose of this paper is to review the journey of capsule robots particularly the role of capsule endoscopes in transforming the diagnosis of GI disorders and the future of capsule robots for their specific treatment.

2. Diagnosis

2.1. Wireless capsule endoscopy

Apart from being non-user friendly, the traditional endoscopy has a limitation wherein imaging of a few areas in GI tract is not possible. With a view to overcome the drawbacks of traditional endoscopy, Given Imaging launched the first WCE in the market in 2001. The main challenges associated with these first generation WCEs were lack of control over capsule locomotion, inadequate battery life, poor quality of images, poor illumination and low frame rate per second. With the advancements in technology, next generation WCEs were developed with better features. The various capsule endoscopes present in the market are shown in Fig. 1. The global market for capsule endoscopes is expected to reach $485 million by 2020. The key players in the market

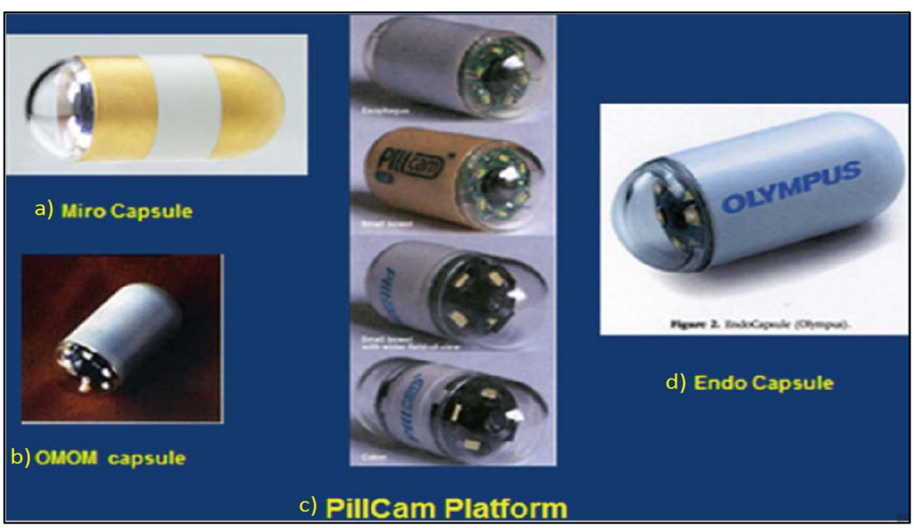

Fig. 1. Various types of capsule endoscopes present in the market: a) MiroCam® by IntroMedic Inc. b) OMOM® Capsule by Chongqing Jinshan Science and Technology (Group) Co. Ltd. c) PillCam® Capsule Endoscopes by Given Imaging Inc. d) EndoCapsule® by Olympus America. Figure reproduced from [8] with permission from Springer.

Even after the success of capsule endoscopes, the dream of targeted drug delivery using robots has not yet realized. Targeted drug delivery has been in practice using various drug carriers like vesicular drug delivery systems [11,12], particulate drug delivery systems [13], polymeric nanoparticles [14], carbon nanotubes [15] and quantum dots [16]. All these systems have a major drawback. There is little or no control over these systems after their intake inside the body. Besides, there are stability and safety issues, along with inadequate drug loading, which pose problems with the current form of these systems.

Taking inspiration from the success of WCEs, research work in developing smart capsule robots is rapidly increasing. Most of these capsule robots are broadly categorized in two domains – those incorporating microelectromechanical systems and those incorporating

include Given Imaging Ltd., Olympus Corporation, RF Co. Ltd., CapsoVision Inc., IntroMedic Co. Ltd., Check-Cap Ltd. and Chongqing Jinshan Science and Technology Co. Ltd. [19]. The following sections focus on special characteristics of WCEs, various components of WCEs and their fabrication.

2.1.1. Special characteristics of different WCEs

Today, WCEs are developed to diagnose disorders in various parts of GI tract comprising oesophagus, stomach, small intestine and large intestine. Depending upon the end usage, the design and fabrication of WCEs differ. The specific design characteristics of WCEs for observing a particular organ are mentioned in Table 1.