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Emerging issues and future developments in capsule endoscopy

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ABSTRACT

Capsule endoscopy (CE) has transformed from a research venture into a widely used clinical tool and the primary means for diagnosing small bowel pathology. These orally administered capsules traverse passively through the gastrointestinal tract via peristalsis and are used in the esophagus, stomach, small bowel, and colon. The primary focus of CE research in recent years has been enabling active CE manipulation and extension of the technology to therapeutic functionality, thus, widening the scope of the procedure. This review outlines clinical standards of the technology as well as recent advances in CE research. Clinical capsule applications are discussed with respect to each portion of the gastrointestinal tract. Promising research efforts are presented with an emphasis on enabling active capsule locomotion. The presented studies suggest, in particular, that the most viable solution for active capsule manipulation is actuation of a capsule via exterior permanent magnet held by a robot. Developing capsule procedures adhering to current health care standards, such as enabling a tool channel or irrigation in a therapeutic device, is a vital phase in the adaptation of CE in the clinical setting.

1. Introduction

Since 1950, orally administered capsules with radiofrequency (RF) transmission capability have been prototyped with an aim to study the physiological parameters of the gastrointestinal (GI) tract. A dearth of miniaturized electronic technology such as semiconductors and integrated circuits prevented development of these capsules until the beginning of the 21st century [1]. Working independently, Gavriel Iddan (Israel) and Paul Swain (UK) introduced capsule endoscopy (CE) in 2000 as a means for providing patients with endoscopic imaging of the small bowel [2]. First CE human trials were presented in 2001 by Given Imaging Ltd. (Yoqneam, Israel), which was the first to commercialize the technology [1]. Given Imaging's first clinical CE, marketed as M2A (Mouth-to-Anus), was awarded approval from the Food And Drug Administration (FDA) in 2001. The second capsule to gain FDA approval was the M2A Plus, which was later remarketed under the now familiar name: PillCam. Since the first FDA CE approval, more than 2 million capsules have been ingested worldwide [3]. The PillCam series of capsules now encompasses approximately 95% of the CE market and has been used in more than 1.7 million procedures worldwide and in more than 1900 clinical studies (www.givenimaging.co). Today, leading CE companies include the following: Medtronic Inc (USA) (Given Imaging Ltd was acquired by Covidien Ltd, which was, in turn, acquired by Medtronic Inc in 2014), Olympus Corporation (Japan), Chongqing Jinshan Science & Technology Co Ltd, (China), IntroMedic Co Ltd, (South Korea), and CapsoVision Inc (USA). Originally developed for diagnostic use in the small bowel, CE application has spread to use in the esophagus, stomach, and colon. CE is still most widely used in the small bowel owing to a lack of a noninvasive alternative. This review examines current technology in clinical CE as well as the latest developments in image enhancement, investigation of active locomotion, and therapeutic possibilities.

2. Clinical capsule endoscopes

2.1. Esophageal CE

As opposed to the slow CE propagation through the small bowel, CE traversing the esophagus can reach speeds as high as

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20 cm/s, leading to difficulties in assessing for pathology [4]. Esophageal capsule primary indications include diagnosing reflux esophagitis, Barrett esophagus, and varices [5]. The most prevalent esophageal capsule, the PillCam ESO (Given Imaging Ltd), captures images at 7 frames per second (fps) from each of 2 cameras at its longitudinal ends, for a cumulative 14 fps. During a 2006 study of 42 patients with gastroesophageal reflux disease, a PillCam ESO capturing images at 4 fps was compared with one capturing at 14 fps. The higher image capture rate was observed to be superior in visualization of the entire esophagus (76% vs 12%, $P < 0.01$) making higher frame capture rate essential for esophageal CE [4]. The diagnostic sensitivity and specificity reported for the ESO were 85.8% and 80.5% for varices, 98% and 100% for gastroesophageal reflux disease, and 97% and 100% for Barrett esophagus [6]. Currently, the FDA-approved PillCam ESO3 captures images at 35 fps compared with the ESO's 14 fps, has a field of view of 169°, and an operating time of no more than 30 minutes. CEs in the esophagus are well tolerated but remain limited by poor visualization, passive motion, and lack of therapeutic ability, and thus have not replaced flexible endoscopy for esophageal evaluation [5].

2.2. Small bowel CE

CE is considered the gold standard for small bowel evaluation in patients with inflammatory bowel disease, suspected small bowel neoplastic lesions, and obscure GI tract bleeding [6-9]. The PillCam (Given Imaging Ltd) is the most widely used capsule worldwide, and the latest version, SB3 (FDA approved in 2013), acquires images at an adaptive rate of 2-6 fps.

The OMOM Smart Capsule (Chongqing Jinshan Science and Technology Co, Chongqing, China) is the first capsule to include 2-way data transmission via wearable RF sensors. This bidirectional communication allows for real-time adjustment of image capture rate and light intensity [10]. The MiroCam (IntroMedic Co, Ltd, South Korea) has similar parameters but is the only capsule to use electrical field propagation through the body—what is referred to as Human Body Communication (www.intromedic.com). The EndoCapsule (Olympus Corporation, Japan) operates similarly to the PillCam small bowel (SB) but uses high-resolution charge-coupled device technology for imaging rather than a complementary metal oxide semiconductor sensor (www.olympusamerica.com) [6].

CapsoCamSV-2 (CapsoVision Inc, Saratoga, CA) is the newest commercial CE and is the only one to employ onboard flash memory therefore requiring the patient to retrieve the capsule after passing it in their stool. Having undergone human trials [11], the CapsoCam takes a novel approach in providing a 360° panoramic view using 4 centralized cameras, each with >90° field of view. The CE has a battery life of 15 hours and captures images at 20 fps for the first 2 hours of operation and 12 fps for the duration of the procedure [12]. The CapsoVision system consists of the capsule, a stool retrieval tool: CapsoRetrieve, the CapsoAccess data retrieval system, and the CapsoView application for viewing the images. Head-to-head trials with the aforementioned small bowel capsules have suggested comparable diagnostic yield, image quality, and completion rate [3]. Various commercial capsules and related specifications are reported in the Table.

2.3. CE in the colon

Each year, colorectal cancer is the cause of nearly 608,000 deaths with approximately 14.5 million colonoscopies performed worldwide [13,14]. As reported by www.cancer.org, nearly 100,000 cases of colon cancer are being diagnosed annually in the US alone, and the number of occurrences is expected to increase by 62% by the year 2030 [15]. Introducing a less-invasive platform could prevent millions of patients from evading colonoscopy owing to fear of an invasive procedure, procedural discomfort, bowel

Table
GI capsules in clinical use today.

Capsule	Purpose	Company	FDA	FPS	Size (mm)	Software	Related devices
PillCam ESO 3	Esophageal imaging	Given Imaging Ltd (Israel)	Yes	35	26.0 × 11.0	RAPIDv8.0	PillCam recorder DR3, PillCam Express, Sensor Belt
PillCam SB 3	Small bowel (SB) imaging		Yes	2-6	26.0 × 11.0		
PillCam COLON 2	Colon imaging		Yes	4-35	31.5 × 11.6		
PillCam SmartPill	Sensory		Yes	No imaging	26.0 × 13.0	N/A	N/A
Bravo capsule	Sensory		Yes	No imaging	26.7 × 6.3 × 5.4	N/A	N/A
Agile patency capsule	Patency		Yes	No imaging	26.4 × 11.4	None. Dissolvable capsule	None
CapsoCam SV-2	SB Imaging	CapsoVision Inc (USA)	No	12-20	31.0 × 11.3	CapsoView	CapsoRetrieve, CapsoAccess CDAS2
MiroCamv2	SB imaging	IntroMedic Co, Ltd (South Korea)	Yes	3	24.5 × 10.8	MiroView v2	MiroCam Receiver
MiroCam Navi	SB Imaging and Navigation	IntroMedic Co, Ltd (South Korea)	N/A	3	24.0 × 11.0	MiroView v2	MiroCam Receiver
OMOM Smart Capsule	SB imaging	Chongqing Jinshan Science & Technology Co., Ltd (China)	Yes	2	27.9 × 13.0	OMOM workstation	OMOM image recorder
OMOM Controllable Capsule (Magnetic Control)	SB Imaging		N/A	N/A	N/A		OMOM image recorder, hand-held steering magnet
EndoCapsule	SB Imaging	Olympus Corporation (Japan)	Yes	2	26.0 × 11.0	Olympus VE-1 Real Time Viewer	EndoCapsule recorder set
IntelliCap	Sensory or drug delivery	Medimetrics, a Philips Company (Netherlands)	N/A	No imaging	26.7 × 11.0	N/A	N/A
Enterion capsule	Sensory or drug delivery	Quotient clinical (England)	N/A	No imaging	32.0 × 11.0	N/A	N/A

N/A, not applicable.