

An overview of emerging smart capsules using other-than-light technologies for colonic disease detection

Gohar Jalayeri Nia , Ola Selnes, Pablo Cortegoso Valdivia and Anastasios Koulaouzidis

Abstract: Wireless capsule endoscopy (CE) has revolutionized gastrointestinal diagnostics, offering a non-invasive means to visualize and monitor the GI tract. This review traces the evolution of CE technology. Addressing the limitations of traditional white light (WL) CE, the paper explores non-WL technologies, integrating diverse sensing modalities and novel biomarkers to enhance diagnostic capabilities. Concluding with an assessment of Technology Readiness Levels, the paper emphasizes the transformative impact of non-WL colon CE devices on GI diagnostics, promising more precise, patient-centric, and accessible healthcare for GI disorders.

Keywords: Atmo Gas Capsule, biomarkers; C-scan system, e-Celsius®, gastrointestinal diagnostics, non-WL technologies, PillCam® system, SmartPill™, Technology Readiness Level, wireless capsule endoscopy

Received: 25 December 2023; revised manuscript accepted: 26 April 2024.

Introduction

The advent of wireless capsule endoscopy (CE) has marked a revolutionary milestone in gastrointestinal (GI) endoscopy, leading to a transformative era for diagnosing and monitoring GI disorders. At its core, this innovation owes its existence to the visionary insights of Dr. Paul Swain, whose inspiration drew from miniature imaging technologies initially designed for space exploration. Prof. Swain's groundbreaking vision centered around encapsulating a highly miniaturized camera within a pill-sized capsule, a technological marvel enabling the non-invasive visualization of the entire GI tract.^{1,2} The realization of this audacious endeavor came to fruition through a collaborative effort with Given Imaging (Yokneam Illit, Israel). The developmental phase was characterized by formidable engineering challenges, which necessitated the miniaturization of the camera, the design of a protective capsule shell, and the integration of a wireless transmission system. The result was nothing short of remarkable – a capsule of diminutive proportions, ingestible by patients yet equipped with the

extraordinary capacity to capture high-resolution images while traversing the complex landscape of the digestive system.

After rigorous clinical trials and regulatory approvals, the PillCam® capsule endoscopy system emerged as the first commercially available CE technology.³ Its impact has been profound, introducing a minimally invasive and patient-centric approach to diagnosing and monitoring GI conditions, particularly those elusive to traditional diagnostic methods, such as those affecting the small intestine. In 2006, Given Imaging Ltd. further expanded the capabilities of CE by introducing the inaugural generation of a colon exploration capsule, marking a significant stride in the evolution of this transformative technology. This development is built upon the existing small bowel and esophageal capsules, broadening diagnostic possibilities within the GI tract. Known as CCE-1 or the PillCam COLON, this pioneering capsule measured 11 mm × 31.5 mm. It was equipped with two cameras featuring a remarkable 156° angle of view on both sides, enhancing

Ther Adv Gastroenterol

2024, Vol. 17: 1–13

DOI: 10.1177/
17562848241255298

© The Author(s), 2024.
Article reuse guidelines:
sagepub.com/journals-permissions

Correspondence to:

Gohar Jalayeri Nia
Department of
Gastroenterology Queen
Elizabeth Hospital and
University Hospital
Birmingham NHS
Foundation Trust,
Mindelsohn Way
Edgbaston Birmingham,
B15 2GW, UK
Gohar.JalayeriNia@uhb.nhs.uk
doctornia@yahoo.com

Ola Selnes
Surgical Research
Unit, Odense University
Hospital, Svendborg,
Denmark

Pablo Cortegoso Valdivia
Gastroenterology and
Endoscopy Unit, University
Hospital of Parma,
University of Parma,
Parma, Italy

Anastasios Koulaouzidis
Department of Surgery,
SATC-C, OUH Svendborg
Sygehus, Svendborg,
Denmark

Department of Clinical
Research, University of
Southern Denmark (SDU),
Odense, Denmark

Department of Social
Medicine and Public
Health, Pomeranian
Medical University,
Szczecin, Poland

its ability to capture comprehensive images of the colon.⁴ Subsequently, the domain of colon capsule endoscopy (CCE) continued to advance with the introduction of CCE-2, the second-generation system known as the PillCam COLON2. This updated capsule represented a significant leap forward in specifications and technical capabilities. Albeit with the exact dimensions, it boasted an expanded angle of view of 172° for both imagers, effectively covering nearly 360° of the colon. During motion, the CCE-2 captured images at 35 frames per second (fps), adjusting to 4 fps while stationary to conserve battery power without compromising image quality.

Furthermore, the CCE-2 featured an extended operating duration of approximately 10h. It incorporated a power-saving ‘sleep’ mode activated upon ingestion to enhance energy efficiency, ensuring that battery life would be conserved until the capsule reached the colon.^{5,6} In recent years, multiple other manufacturers have also entered the market, offering double-domed capsules for colon examination. This expansion of industry players underscores the field’s ongoing advancements, progress, and clinical interest. The following is a compilation of commercially available capsules for the study of the colon (Table 1):

Table 1. Available types of colon capsule endoscopes and operating characteristics.

Capsule device	Pillcam COLON2 ⁷	Capso Cam plus ⁸	OMOM CCE ⁹	NAVICAM colon capsule ¹⁰
Company	Medtronic	Capsovision	Jinshan	AnX Robotica
Country	USA	USA	China	USA
Dimensions	32.3 × 11.6	31 × 11	31.5 × 11.6	31 × 11.6
Weight (g)	2.9 + 0.1	4	3	3
Frame rate, (fps)	4–35	20 max	4–35	0.5–17, 2–38
Battery life (h)	10	15	15	10
Cameras	2	4	2	2
Field of view	344	360	344	160
Real-time imager	Y	Y	Y	
FDA approval	Y	Y	N	N

As exciting as these advancements are, it’s essential to acknowledge the limitations of conventional white light (WL) CE. While CE has played a pivotal role in visualizing the digestive tract, offering valuable insights into mucosal inspection, it has often encountered challenges in providing the detailed and specific information necessary for early disease detection and the precise characterization of anomalies.¹¹ The introduction of WL imaging CE has sparked extensive research to enhance its diagnostic capabilities by integrating other sensing modalities. These developments can address the limitations of WL imaging by improving the detection of subtle mucosal

microlesions and submucosal or transmural pathology, thereby opening novel diagnostic possibilities.¹² Additionally, researchers are exploring incorporating various sensors to measure physiological parameters and discover new biomarkers, aiming to enhance sensitivity, specificity, and overall clinical utility in CE.¹³

This review paper endeavors to shed light on non-WL colon CE technologies, examining the advancements in diagnostics within the field. These innovations can revolutionize how we diagnose and manage GI conditions, particularly those affecting the colon. The integration of various sensing

modalities and the exploration of novel biomarkers exemplify the proactive steps taken by the medical community to enhance the capabilities of CE. As we delve deeper into this evolving landscape, it becomes increasingly evident that the future of CCE holds promise in terms of diagnosis.

SmartPill

GI motility (GIM) is crucial in efficiently transiting contents through the digestive system. In many patients with GI symptoms, dysmotility can significantly contribute to discomfort. GIM disorders can dramatically impact a patient's quality of life and contribute to a substantial socioeconomic burden.¹⁴ These disorders often manifest with symptoms such as abdominal pain, bloating, constipation, or diarrhea. In some cases, conventional medical therapy may not yield satisfactory results.¹⁵ Therefore, there is a clinical need for motility testing, especially in patients who do not respond well to empirical treatments. To investigate GIM disorders effectively, it is essential to have a diagnostic method providing precise measurements of motor activity that is standardized, reproducible, and acceptable to patients regarding invasiveness.¹² SmartPill™ (Medtronic, Minneapolis, MN, USA) motility testing system offers a comprehensive solution to these challenges.^{16,17}

Traditionally, motility testing has been focused on the specific region of the GI tract where the abnormality is suspected to reside. However, evidence suggests that GIM disorders may not always be confined to one segment of the GI tract.¹⁸ For instance, some patients with slow transit constipation exhibit delayed gastric and/or small bowel emptying rather than isolated colonic dysmotility.¹⁹ This realization highlights the importance of comprehensive GIM assessment to guide more accurate diagnoses and tailored treatment decisions. The SmartPill system comprises a 26.8 mm × 11.7 mm ingestible single-use wireless motility capsule (WMC) designed to measure several critical parameters as it traverses the entire GI tract.^{20,21} These parameters include (Figure 1):

- Pressure: The WMC measures pressure ranging from 0 to 350 mm Hg, capturing data every 0.5 s for the first 24 h and every

second after that. It offers an accuracy of ± 5 mm Hg below 100 mm Hg and $\pm 10\%$ above 100 mm Hg.

- pH: Intraluminal pH is monitored every 5 s for the first 24 h, every 10 s from 24 to 48 h, and every 2.5 min after 48 h, with an accuracy of ± 0.5 pH units.
- Transit Time (TT) measurement: The system records transit times through different regions of the GI tract, including gastric, small bowel, and colonic TT.
- Temperature: The capsule tracks temperature variations from 25°C to 49°C every 20 s for the first 24 h and every 40 s afterward, with an accuracy of $\pm 1^\circ\text{C}$.

This device is primarily used for the functional assessment of the GI system. It is recommended by both the American and European Neurogastroenterology & Motility Societies for assessing conditions like gastroparesis, small bowel dysmotility, and colonic TT in chronic constipation.^{16,22}

Data collected by the WMC is transmitted wirelessly to a motility receiver. At the end of the examination, the data is uploaded and analyzed using MotiliGI™ Software, which provides a comprehensive report with graphical and statistical analyses, including parameters like gastric emptying time, pressure patterns in the antrum and duodenum, small bowel and colonic TT, and whole gut TT.²³

One of the significant advantages of the SmartPill™ system is its ability to provide a minimally invasive assessment of GI motility without the need for radiation exposure. Traditional motility testing methods, such as gastric emptying scintigraphy (GES), whole gut scintigraphy (WGS), or the use of radio-opaque markers (ROM), often involve exposing patients to radiation, which can be a concern for both patients and healthcare providers (Table 2).

Measuring various parameters simultaneously and providing data on pressure, pH, and TT, allows for a more holistic understanding of GI motility. This multi-dimensional approach enables healthcare professionals to make more informed diagnoses and tailor treatment plans

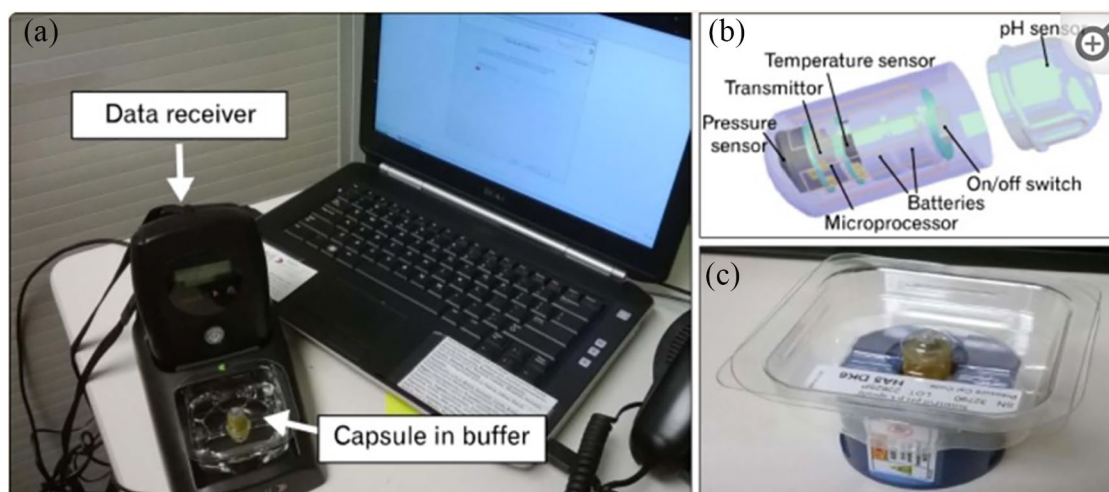


Figure 1. Equipment used for the SmartPill test. (a) The data receiver and laptop with the MotiliGI software are shown. The SmartPill capsule in the buffer is also shown. (b) The inside of a SmartPill capsule. (c) Activation of SmartPill capsule with a magnetic fixture.²³

Table 2. Current methods used for assessment of colon function.²⁴

Technique	GI tract region	Invasiveness	Radiation	Easiness of interpretation
SmartPill™	Whole GI tract	Low	No	Easy
Radio-opaque markers	Colon	Invasive	Yes	Easy
Colonic manometry	Colon	Invasive	No	Difficult

to each patient's specific needs.²⁵ Several studies have explored the validity and clinical utility of the SmartPill™ system in assessing GI motility.^{23,26} The SmartPill™ system has been validated to measure colonic TT in patients with chronic constipation. In one study by Rao and the team,²⁷ SmartPill™ testing was compared to traditional 2-day and 5-day radiopaque marker (ROM) studies to assess colonic TT in 78 adults with functional constipation. SmartPill™ exhibited a strong correlation with ROM results on Day 2 and Day 5, with correlation coefficients of 0.78 and 0.59, respectively. When using a 59-h colonic TT cutoff, SmartPill™ identified delayed transit in 46% of patients, compared to 37% with the 5-day ROM study. This suggests that SmartPill™ may be a sensitive and valuable diagnostic tool for (Colon Transit Time) CTT assessment in constipated individuals. Furthermore, using the SmartPill™

eliminated the need for more complex and invasive tests, such as GES or WGS, in many cases. This reduces the healthcare costs associated with these tests and minimizes patient discomfort and radiation exposure.

The SmartPill™ system offers valuable insights into pressure patterns throughout the GI tract. Pressure measurements are particularly relevant in assessing gastroparesis and chronic constipation conditions. The SmartPill™ system has shown promise in differentiating between constipation subtypes based on pressure patterns. The most comprehensive assessment of colonic pressure profiles in individuals characterized by Whole Gut Transit (WGT) was conducted by Hasler *et al.*²⁸ in a study comparing 53 healthy subjects with 36 individuals with constipation. The findings indicated a clear distal-to-proximal gradient in colonic pressure

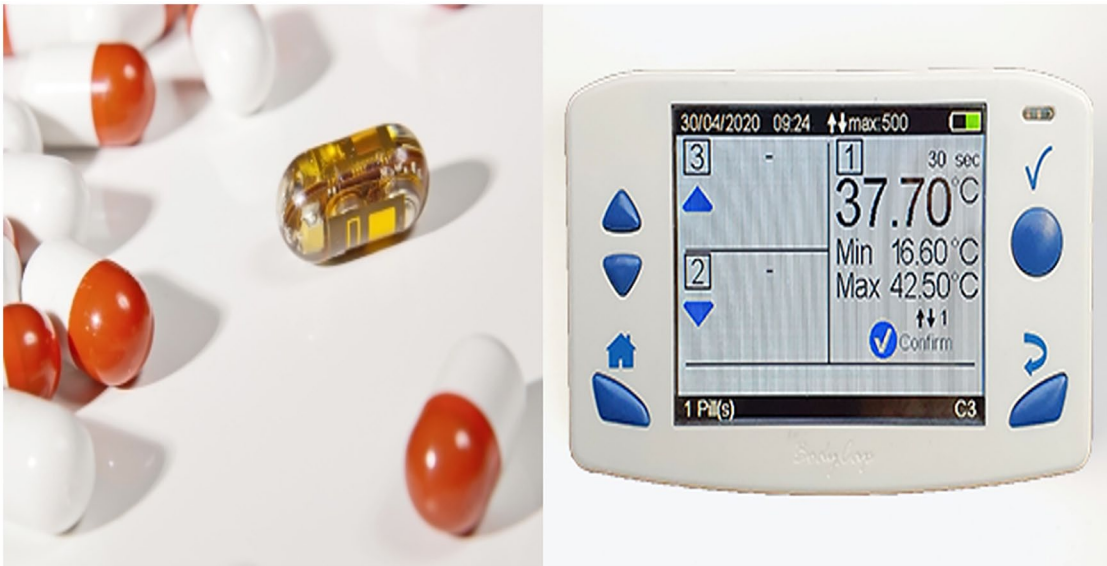


Figure 2. e-Celsius Medical capsule characteristic.³³ (a) e-Celsius Medical capsule and (b) eViewer Medical monitor.

Source: Image courtesy of Sébastien Moussay, BodyCap, France

activity, with a progressive increase in contractions from the first to the fourth quartiles in healthy individuals.

‘In conclusion’ The SmartPill™ WMC represents a significant advancement in assessing GI motility, potentially reducing the need for more invasive and cumbersome tests. While the system has shown great promise, there are still further research and refinement areas. Some discrepancies with conventional testing methods exist, highlighting the need for individualized interpretation and continued investigation to establish the SmartPill™ as a leading diagnostic tool for functional gut disorders. The SmartPill motility testing system’s maturity has led to challenges in finding alternative suppliers for the specialized components necessary to produce the SmartPill capsules and recorders. As a result, the manufacturer, Medtronic, has faced the tough choice of discontinuing worldwide sales starting in June 2023.²⁹

Continuous core temperature monitoring system

Maintaining a stable core temperature of around 37°C is crucial for overall health, supporting optimal metabolic and enzymatic functions. Traditional measurement methods like oral,

axillary, and rectal measurements have limitations, prompting a shift toward innovative approaches.

Ingestible telemetric capsules with temperature sensors offer a groundbreaking solution for continuous core temperature monitoring. These capsules, with miniature sensors and electronic circuits, provide accurate temperature measurements, particularly in the GI tract. The constant monitoring capability is invaluable in prolonged exercise, extreme environmental conditions, and surgical settings.

Using ingestible temperature measurement systems has gained traction in sports and occupational settings, benefiting professionals like deep-sea saturation divers, distance runners, and soldiers undergoing intense military training exercises.³⁰

Various sites have been used to measure temperature, including esophageal, vesical (bladder), and rectal locations. These sites have demonstrated an excellent approximation to pulmonary artery temperature measurement, considered the gold standard but highly invasive.³¹ In contrast, ingestible systems offer a less invasive alternative with continuous monitoring capabilities. Recent advancements have yielded the e-Celsius® system, a groundbreaking solution for

core temperature monitoring. This ingestible GI telemetric device introduces several unique features, significantly advancing the field of temperature monitoring. The e-Celsius® system (BodyCap, Hérouville Saint Clair, France; Figures 2 and 3), developed to measure temperature with a transmission distance of up to 5 m, incorporates self-memory capabilities to mitigate potential transmission impairments.³² This innovative system comprises an ingestible capsule designed to measure GI temperature, which is then connected to a Bluetooth monitor. The e-Celsius® capsule boasts 17.6 mm in length, 8.6 mm in diameter, and a weight of 1.2 grams, with a maximum sampling time of 30 s.³² The sampling frequency can be customized to desired intervals, providing adaptability throughout the examination process. Upon ingestion, the e-Celsius® pill is activated using an external activation box. Subsequently, it transmits data to a dedicated wristband or monitors *via* 433 Hz radiofrequency.³³

VitalSense (Table 3) is a telemetric physiological monitoring system that offers continuous monitoring of core body temperature, dermal temperature, heart rate, and respiration rate wirelessly and without probes. Its ingestible temperature capsule, the VitalSense Core Temperature Capsule developed by Phillips, also known as the Jonah Capsule, provides faster, more effective, and accurate measurements compared to traditional methods like ear or rectal probes. The information collected by the VitalSense Core Temperature Capsule is transmitted to an Equivital (EQ02) Life Monitor, securely strapped to the chest of the individual under monitoring. From there, the EQ02 monitor sends the data to a computer, where it can be conveniently collected and analyzed. This comprehensive monitoring system ensures precise and reliable data collection, enabling informed decision-making for a wide range of applications, from healthcare to sports performance analysis and beyond.³⁴

Monitoring can occur retrospectively or in real-time, offering flexibility and convenience for healthcare providers and patients. The e-Celsius® system has underscored its versatility and effectiveness in diverse fields such as chronobiology, sleep research, oncology, infectiology, and drug/vaccine development. Recent trials involving febrile patients have showcased the

device's accuracy and reproducibility, indicating a superior intraclass correlation with axillary temperature compared to other non-contact techniques.³⁸ Furthermore, the e-Celsius® system has undergone testing in sports medicine,^{39,40} circadian rhythm monitoring,⁴¹ metabolic monitoring,⁴² and prevention of hypo/hyperthermia.⁴³ In a validation study led by Koumar and colleagues,⁴⁴ 23 healthy volunteers were monitored for 24 h in a hospital while ingesting both e-Celsius® and Jonah capsules. The e-Celsius® device recorded slightly lower temperatures than VitalSense® and rectal probes but higher temperatures than esophageal probes. The study also compared missing data rates, concluding that the e-Celsius® system is a reliable option for continuous internal temperature monitoring, showing favorable characteristics compared to VitalSense® devices. Further research is needed to explore its accuracy and performance in clinical settings.

However, continuous research and development efforts are imperative to refine these ingestible temperature monitoring systems, address potential systematic biases, and further enhance their accuracy. In conclusion, as technology continues to advance, ingestible temperature measurement systems are poised to become more widespread, solidifying their pivotal role as crucial components of modern healthcare and scientific research.

The C-scan® system

The C-scan® system (Check-Cap, Isfiya, Israel; Figure 4) is a 34 mm × 11.6 mm smart pill powered by Tungsten 181 radioisotope designed to utilize low-dose X-ray imaging to produce transmural images of the colon.⁴⁵ The C-scan system is a revolutionary approach to colorectal cancer screening that has the potential to transform the way we detect and prevent this disease. This cutting-edge technology operates without requiring traditional bowel preparation: patients simply ingest an iodine-based contrast agent, typically during a meal. This allows the device to perform a radial scan of the colonic wall using three rotating X-ray beams.⁴⁶ The system comprises three key elements: the ingestible capsule (C-Scan® Cap), the recorder (C-Scan® Track), and the computer-based workstation (C-Scan® View).⁴⁷ The source emits X-ray photons through a rotating collimator, enabling the capsule to scan the

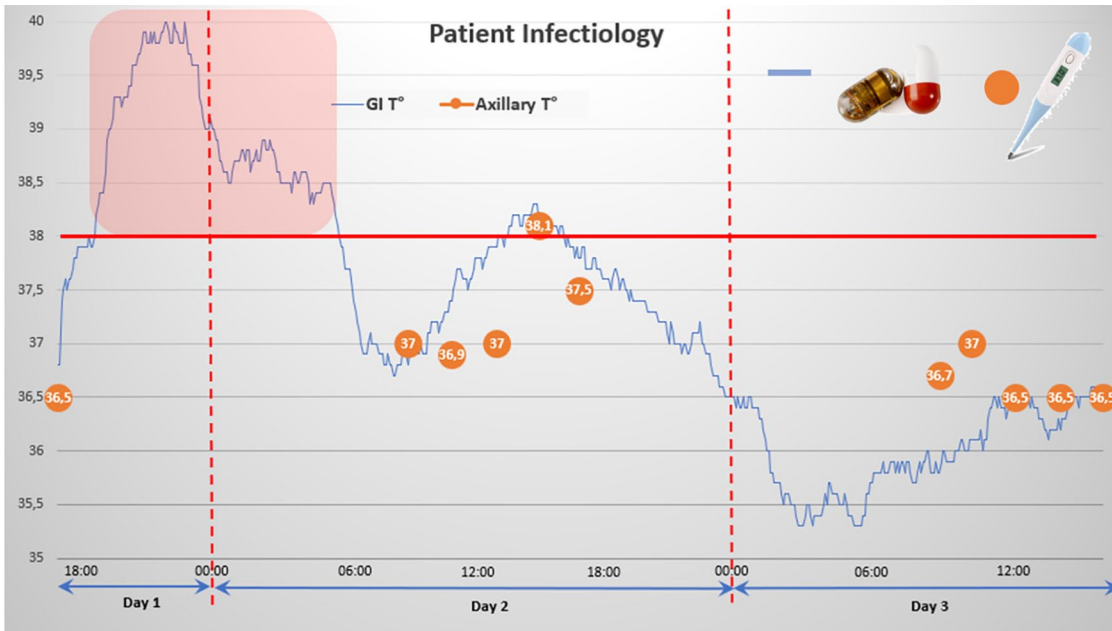


Figure 3. e-Celsius eViewer Medical monitor.
Source: Image courtesy of Sébastien Moussay, BodyCap, France.

Table 3. Commercially available devices to measure core body temperature.

Type	Manufacturer	size	weight	accuracy	Calibration range	Sampling period
eCelsius ³³ 	BodyCap France	17.7 mm × 8.9 mm	1.7 gr	0.2°C	25°C to 45°C	30 s
VitalSense ³⁵ 	Philips Respironics USA	120 mm × 90 mm × 25 mm	200 gr	±0.1°C	25°C to 50°C Capsule -20°C to 60°C Patch	15 s
CorTemp ³⁶ 	HQ, USA	10.9 mm × 22.4 mm	2.8 gr	±0.1°C	30°C to 45°C	10 s
MyTemp ³⁷ 	MyTemp The Netherlands	20 mm × 8 mm	1.3 gr	±0.01°C	30°C to 45°C	6 s

inner lining of the colon. The capsule is designed to initiate scanning once it reaches the cecum, propelled along the colon *via* peristalsis. The C-Scan® Track is a recorder unit securely fastened to the patient's lower back, through dermal patches. During the capsule's passage through the colon, data are transmitted to the recorder using radiofrequency communication. Additionally, the recorder includes an external capsule positioning system, collecting data about the capsule's real-time location as it travels through the colon through integrated sensors. The C-Scan® View is a computer-based workstation that facilitates the upload of procedure data from the recorder once the capsule is expelled. This workstation plays a crucial role in the analysis of the raw data, which encompasses various parameters such as the capsule's position in the colon, the distance of the capsule from the colon wall, X-ray fluorescence, Compton backscattering, pressure, and temperature. These data points are processed using a proprietary algorithm, resulting in the creation of a high-resolution 3D reconstruction model of the colon wall and lumen, enabling the detection of structural abnormalities. The output data from the C-Scan® View are subsequently reviewed, culminating in the generation of a report detailing the presence of polyps or masses.

Regarding the system's imaging resolution, the X-ray source within the capsule is carefully collimated and positioned in a tungsten shielding cylinder capable of rotation. This setup creates three beams that collectively scan a full slice of the colon in a 360° fashion every third of a rotation, as represented. During this rotation, the direction of the beams is well-known to the capsule's microprocessor, and all detected photons within each rotational sector are systematically recorded in the capsule's memory. The longitudinal and rotational impulse response of the capsule imaging system in a laboratory setting exhibits a line spread function with dimensions of approximately 2–3 mm in the longitudinal coordinate and 20°–25° in the rotational coordinate. This resolution is considered adequate for the detection of non-diminutive polyps measuring 6 mm and above. The average radiation dose is a mere 52 μ Sv, significantly lower than the radiation exposure from a single chest X-ray (0.1 mSv).⁴⁸ Scanning occurs exclusively during motion and switches to an idle mode when stationary. The WGT time of the capsule varies between 24 and 100 h, contingent

on colonic motility, and the capsule is naturally excreted. In a prospective pilot study⁴⁷ conducted at two tertiary care centers, patients scheduled for colonoscopies for colorectal cancer screening or surveillance were included. The study aimed to assess the safety and patient satisfaction of the colon-scan capsule in comparison to a colonoscopy. The study involved 40 participants, predominantly females with an average age of 52.9 years. There were no serious adverse events or capsule retention issues, with the most common complaint being mild, self-limiting abdominal cramping. More than 87% of patients completed satisfaction questionnaires, which revealed a significantly higher satisfaction score for the colon-scan capsule compared to colonoscopy. In the second study,⁴⁹ 66 capsules were ingested by 63 volunteers between the ages of 45 and 68 years (three individuals ingested the capsule on two separate occasions). Following capsule ingestion, each volunteer consumed 50–70 mL of an iodine-based contrast agent daily until the capsule was naturally expelled. Out of the 66 capsules ingested, 65 exhibited uneventful transit through the GI tract and were naturally excreted without any adverse effects. In a solitary instance, one capsule was retrieved from the cecum of an asymptomatic patient during a follow-up colonoscopy.

While the C-scan system shows great promise, it is essential to conduct further validation and comparative studies, particularly in the context of direct comparisons with optical colonoscopy. These studies will provide a more comprehensive understanding of the system's diagnostic performance and potential impact on colorectal cancer screening. The core of this pioneering technology is a disposable ingestible imaging capsule that accumulates radiological data to construct high-resolution 3D images of the colon, all without necessitating the usual cleansing regimen. This method could improve patient compliance by alleviating concerns and anxieties associated with the rigorous colon preparation requirements typically associated with colonoscopy.⁵⁰ Furthermore, adopting this self-contained imaging system has the added benefit of eliminating the need to schedule appointments at healthcare facilities, minimizing disruptions to daily activities, and mitigating the negative emotional and physical aspects often associated with colonoscopy. It's important to note that some patients may find the



Figure 4. ATMO gas capsule.

capsule's dimensions challenging to swallow, although these dimensions are like those of optical capsules already available in the U.S. market. In conclusion, the C-scan[®] system represents a groundbreaking advancement in colorectal cancer screening, offering the potential for improved patient experience and adherence. However, The diagnostic performance of this system in comparison to other established modalities, such as CE and traditional CT colonography (CTC), remains a subject of ongoing research.

Atmo gas capsule

The Atmo Gas Capsule system, offered by Atmo Biosciences, comprises a 28 mm × 11 mm pill, an external data receiver, and a smartphone application for cloud storage.⁵¹ The system utilizes temperature, gas concentrations, capsule orientation, and changes in the electromagnetic properties of the environment around the capsule to assess motility, segmental TT, and landmark detection (Figure 4). Atmo Biosciences advocates for patients with irritable bowel syndrome (IBS) as suitable candidates for gas capsule investigation due to the substantial number of patients, the complexity of the disease, and suspected GIM disorders.

The initial laboratory prototypes were introduced in 2011, and advantages have been made in the capsule's capabilities, culminating in an ongoing proof-of-concept study in the USA for capsule version 2.1. This study aims to recruit approximately 100 participants with functional GI symptoms and dysmotility to compare TT and gut motility with SmartPill.⁵² Previous trials have shown promising results in determining GI transit of metrics, albeit with healthy study participants.⁵³

Thwaites *et al.* compared the capsule's ability to determine landmarks with another FDA-approved wireless capsule and found no differences in TT or landmark determination.⁵³ Determining landmarks relies on identifying gases, temperature changes, and pH variations. For instance, the capsule's excretion is characterized by a sudden temperature drop. In contrast, the gastroduodenal junction is characterized by an abrupt shift in carbon dioxide, temperature fluctuations, capsule orientation, and electromagnetic properties of the surrounding environment. A previous proof-of-concept study was conducted using an outdated capsule version, highlighting the potential of gas analysis for specific components in the GI tract.⁵⁴ The latest capsule device measures gas concen-

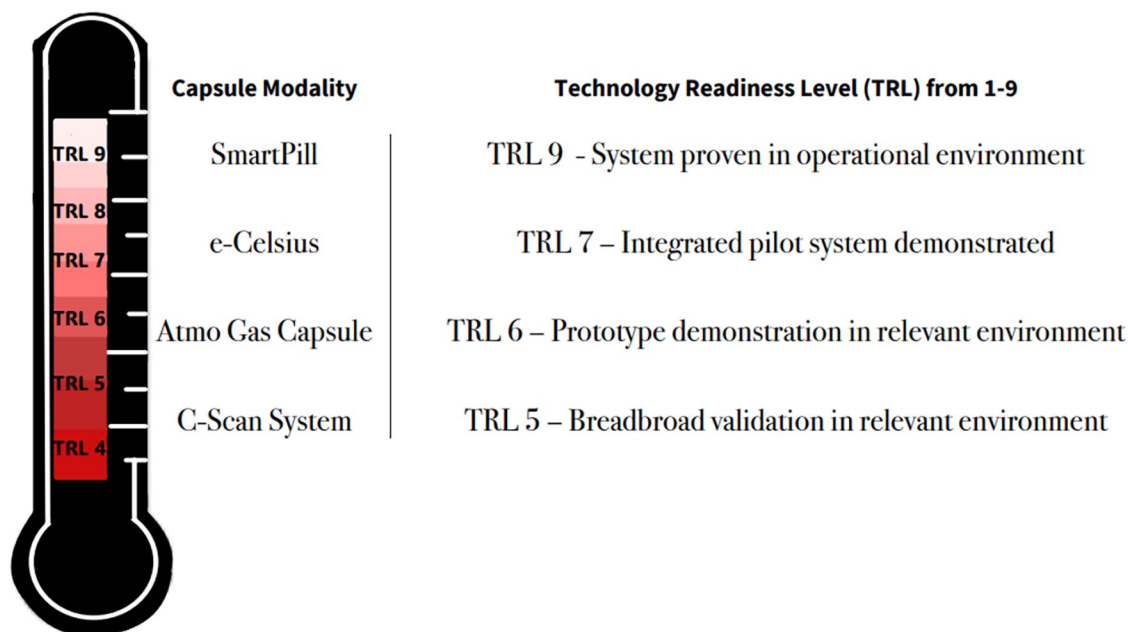


Figure 5. Technology readiness level of non-WL colon CE.

trations of hydrogen, carbon dioxide, and volatile organic compounds, enabling the evaluation of the environment as either aerobic or anaerobic.⁵³

In addition to the recent research on capsule-validated landmark detection, gas- and pH-sensing capsules have been employed to evaluate regional fermentation processes within the colon. The authors reported insights into the localization of colonic fermentation superior to conventional tools (no data available).⁵⁵ The clinical significance of gas-sensing capsules for fermentation has been discussed.⁵⁶

The potential impact of Atmo Gas Capsule on IBS patients requires further research and comprehensive testing. IBS patient groups are substantial and complex, making them potential candidates for gas capsule utilization. Future research should exercise caution and apply realistic medicine considerations when evaluating subsequent patient treatment following gas capsule investigation. In conclusion, the Atmo Gas Capsule system holds significant promise as a diagnostic tool for IBS and gastrointestinal motility disorders, but its clinical utility requires further validation and careful consideration in patient care pathways.

Where do we stand?

The Technology Readiness Level (TRL) serves as a summary scale to assess the readiness of a technology for adoption. Initially introduced by NASA in the 1980s to replace traditional research and development categories, TRL (Figure 5) offers an objective nine-stage assessment of a technology's advancement toward adoption. Scores range from 1, indicating the observation and reporting of fundamental principles, to 9, denoting proof of real-world successful use of the technology. This framework provides a structured approach for evaluating the developmental progress of emerging technologies. The below figure shows the TRL of commercially available non-WL colon CE devices.

In conclusion

GI diagnostics has witnessed a transformative evolution fueled by innovative technologies such as non-WL colon CE systems. From the visionary inception of wireless CE by Prof. Paul Swain to the continuous refinements seen in the PillCam® system and its successors, these advancements have significantly elevated our capacity for non-invasive exploration of the intricate GI landscape.

Challenges posed by traditional white light CE have catalyzed a new wave of research, aiming to augment diagnostic capabilities by integrating diverse sensing modalities and exploring novel biomarkers. These collective advancements signal a promising future for GI diagnostics, characterized by heightened precision, patient-centric methodologies, and a shift toward more efficient and accessible healthcare. As these technologies mature, their potential to redefine the diagnostic landscape of GI disorders remains a beacon of hope for improved patient outcomes and a more holistic approach to healthcare. However, acceptance and integration of these technologies into clinical practice are yet to be determined, necessitating further validation and adoption studies to realize their full potential.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Author contributions

Gohar Jalayeri Nia: Conceptualization; Visualization; Writing – original draft; Writing – review & editing.

Ola Selnes: Writing – review & editing.

Pablo Cortegoso Valdivia: Supervision; Visualization; Writing – review & editing.

Anastasios Koulaouzidis: Supervision; Visualization; Writing – review & editing.

Acknowledgement

None.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

Not applicable.

ORCID iD

Gohar Jalayeri Nia  <https://orcid.org/0009-0004-8668-899X>

References

1. Nakamura T and Terano A. Capsule endoscopy: past, present, and future. *J Gastroenterol* 2008;43:93–99.
2. Iddan G, Meron G, Glukhovskiy A, *et al.* Wireless capsule endoscopy. *Nature* 2000; 405: 417.
3. Pasha SF. Applications of colon capsule endoscopy. *Curr Gastroenterol Rep* 2018; 20: 22.
4. Eliakim R, Fireman Z, Gralnek I, *et al.* Evaluation of the PillCam Colon capsule in the detection of colonic pathology: results of the first multicenter, prospective, comparative study. *Endoscopy* 2006; 38: 963–970.
5. Eliakim R, Yassin K, Niv Y, *et al.* Prospective multicenter performance evaluation of the second-generation colon capsule compared with colonoscopy. *Endoscopy* 2009; 41:1026–1031.
6. Spada C, Pasha SF, Gross SA, *et al.* Accuracy of first- and second-generation colon capsules in endoscopic detection of colorectal polyps: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2016; 14: 1533–1543.e8.
7. Pillcam Colon Capsule system, <https://www.medtronic.com/covidien/en-us/products/capsule-endoscopy/pillcam-colon-2-system.html> (accessed 31 May 2024).
8. CapsoCamPlus, <https://capsovision.com/physician-resources/capsocam-plus-specifications/> (accessed 31 April 2023).
9. OMOM CC Colon Capsule Endoscopy System, <https://www.jinshangroup.com/solutions/omom-cc-colon-capsule-endoscopy-system/> (accessed 31 May 2024).
10. NAVICAM Colon System <https://www.anxrobotics.com/wp-content/uploads/2023/01/NaviCam-Colon-System-Brochure.pdf> (accessed 31 May 2024).
11. Cummins G, Cox BF, Ciuti G, *et al.* Gastrointestinal diagnosis using non-white light imaging capsule endoscopy. *Nat Rev Gastroenterol Hepatol* 2019; 16: 429–447.
12. Niwa H. *New challenges in gastrointestinal endoscopy*. Springer Science & Business Media; Japan, 2009.
13. Rehan M, Al-Bahadly I, Thomas DG, *et al.* Smart capsules for sensing and sampling the

- gut: status, challenges and prospects. *Gut*. 2023; gutjnl-2023-329614.
14. Lacy BE and Weiser K. Gastrointestinal motility disorders: an update. *Digestive Diseases*. 2006; 24: 228–242.
 15. Keller J, Bassotti G, Clarke J, *et al*. Advances in the diagnosis and classification of gastric and intestinal motility disorders. *Nat Rev Gastroenterol Hepatol* 2018; 15: 291–308.
 16. Rao SSC, Camilleri M, Hasler WL, *et al*. Evaluation of gastrointestinal transit in clinical practice: position paper of the American and European Neurogastroenterology and Motility Societies. *Neurogastroenterol Motil* 2011; 23: 8–23.
 17. Smartpill motility system, <https://www.medtronic.com/covidien/en-gb/products/motility-testing/smartpill-motility-testing-system.html#> (accessed 6 February 2023).
 18. Camilleri M, Hasler WL, Parkman HP, *et al*. Measurement of gastrointestinal motility in the GI laboratory. *Gastroenterology* 1998; 115: 747–762.
 19. Kuo B, Maneerattanaporn M, Lee AA, *et al*. Generalized transit delay on wireless motility capsule testing in patients with clinical suspicion of gastroparesis, small intestinal dysmotility, or slow transit constipation. *Dig Dis Sci* 2011; 56: 2928–2938.
 20. Farmer AD, Scott SM and Hobson AR. Gastrointestinal motility revisited: The wireless motility capsule. *United European Gastroenterol J* 2013; 1: 413–421.
 21. Saad RJ. The wireless motility capsule: a one-stop shop for the evaluation of GI motility disorders. *Curr Gastroenterol Rep* 2016; 18: 14.
 22. Maqbool S, Parkman HP and Friedenberg FK. Wireless capsule motility: comparison of the SmartPill® GI monitoring system with scintigraphy for measuring whole Gut transit. *Dig Dis Sci* 2009; 54: 2167–2174.
 23. Lee YY, Erdogan A and Rao SSC. How to assess regional and whole gut transit time with wireless motility capsule. *J Neurogastroenterol Motil* 2014; 20: 265–270.
 24. Kant R and Yadav P. Role of wireless motility capsule in diagnosing diabetic gut autonomic neuropathy: a narrative review. *J Diabetol* 2021; 12: 263.
 25. Saad RJ and Hasler WL. A technical review and clinical assessment of the wireless motility capsule. *Gastroenterol Hepatol (N Y)* 2011; 7: 795–804.
 26. Steiger C, Abramson A, Nadeau P, *et al*. Ingestible electronics for diagnostics and therapy. *Nat Rev Mater* 2018; 4: 83–98.
 27. Rao SSC, Kuo B, McCallum RW, *et al*. Investigation of colonic and whole-gut transit with wireless motility capsule and radiopaque markers in constipation. *Clin Gastroenterol Hepatol* 2009; 7: 537–544.
 28. Hasler WL, Saad RJ, Rao SS, *et al*. Heightened colon motor activity measured by a wireless capsule in patients with constipation: relation to colon transit and IBS. *Amn J Physiol Gastrointest Liver Physiol*. 2009; 297: G1107–G1114.
 29. Medtronic to discontinue SmartPill Capsule, <https://www.mdedge.com/gihepnews/article/263784/ibd-intestinal-disorders/medtronic-discontinue-smartpill-capsule> (accessed 31 May 2024).
 30. Byrne C and Lim CL. The ingestible telemetric body core temperature sensor: a review of validity and exercise applications. *Br J Sports Med* 2007; 41: 126–133.
 31. Lefrant JY, Muller L, de La Coussaye JE, *et al*. Temperature measurement in intensive care patients: comparison of urinary bladder, oesophageal, rectal, axillary, and inguinal methods versus pulmonary artery core method. *Intensive Care Med* 2003; 29: 414–448.
 32. Chapon PA, Gauthier A, Bulla J, *et al*. Calibration and performance assessment of a temperature sensor prototype using a 1-point calibration procedure. *Rev Scient Instrum* 2012; 83.
 33. e-celsius performance, <https://www.bodycap-medical.com/e-celsius-performance-body-temperature-monitoring-telemetric-pill/> (accessed 31 May 2024).
 34. Jonah: The body temperature monitoring pill, <https://community.element14.com/learn/publications/b/blog/posts/jonah-the-body-temperature-monitoring-pill> (accessed 31 May 2024).
 35. Philips motion biosensors, <http://www.actigraphy.respironics.com/solutions/equivalant/components> (accessed 31 May 2024).
 36. Wireless Temperature Sensing, <https://www.hqinc.net/cortemp/> (accessed 31 May 2024).
 37. Radboud umc, Human performance <https://www.radboudumc.nl/en/research/radboud-technology-centers/human-performance> (accessed 31 May 2024).

38. Huang Q, Komarzynski S, Bolborea M, *et al.* Telemonitored Human Circadian Temperature Dynamics During Daily Routine. *Front Physiol* 2021; 12: 1–13.
39. Drigny J, Rolland M, Pla R, *et al.* Risk Factors and Predictors of Hypothermia and Dropouts During Open-Water Swimming Competitions. *Int J Sports Physiol Perform* 2021; 16: 1692–1699.
40. Henderson MJ, Christmas BCR, Stevens CJ, *et al.* Limiting rise in heat load with an ice vest during elite female rugby sevens warm-ups. *Int J Sports Physiol Perform* 2021; 16: 1684–1691.
41. Webster WW and Smarr B. Using circadian rhythm patterns of continuous core body temperature to improve fertility and pregnancy planning. *J Circadian Rhythms* 2020; 18: 5.
42. Zuccarelli L, Sartorio A, De Micheli R, *et al.* Obese patients decrease work rate in order to keep a constant target heart rate. *Med Sci Sports Exerc* 2021; 53: 986–993.
43. Moussalem CK, Mneimneh F, Sarieedine R, *et al.* Effect of phase change material cooling vests on body thermoregulation and thermal comfort of patients with paraplegia: a human subject experimental study. *Global Spine J* 2023; 13: 1754–1764.
44. Koumar OC, Beaufile R, Chesneau C, *et al.* Validation of e-Celsius gastrointestinal telemetry system as measure of core temperature. *J Therm Biol* 2023; 112: 103471.
45. C-Scan, redefining Colorectal Cancer Screening <https://check-cap.com/> (accessed 31 May 2024).
46. Kimchy Y, Lifshitz R, Lewkowitz S, *et al.* Radiographic capsule-based system for non-cathartic colorectal cancer screening. *Abdominal Radiology* 2017; 42: 1291–1297.
47. Garcia Garcia de Paredes A, Gross SA, Hernandez-Lara AH, *et al.* Colorectal cancer and polyp detection using a new preparation-free, colon-scan capsule: a pilot study of safety and patient satisfaction. *Dig Dis Sci* 2022; 67: 4070–4077.
48. Lee RKL, Chu WCW, Graham CA, *et al.* Knowledge of radiation exposure in common radiological investigations: a comparison between radiologists and non-radiologists. *Emerg Med J* 2012; 29: 306–308.
49. Gluck N, Half EE, Bieber V, *et al.* Novel prepless X-ray imaging capsule for colon cancer screening: a feasibility study. *Gut* 2019; 68: 774–775.
50. Shamim S, Andresen YLM, Vind Thaysen H, *et al.* Experiences of patients undergoing bowel preparation and colonoscopy: a qualitative longitudinal study. *J Multidiscip Healthc* 2021; 14: 349–358.
51. The Atmo gas sensing capsule, <https://atmobiosciences.com/> (accessed 31 May 2024).
52. Comparison of the Atmo Motility Gas Capsule System to the Reference Standard, <https://classic.clinicaltrials.gov/ct2/show/NCT05718505> (accessed 31 May 2024).
53. Thwaites PA, Yao CK, Maggo J, *et al.* Comparison of gastrointestinal landmarks using the gas-sensing capsule and wireless motility capsule. *Aliment Pharmacol Ther* 2022; 56: 1337–1348.
54. Kalantar-zadeh K, Yao CK, Berean KJ, *et al.* Intestinal gas capsules: a proof-of-concept demonstration. *Gastroenterology*. 2016; 150: 37–39.
55. So D, Yao CK, Gill PA, *et al.* Detection of changes in regional colonic fermentation in response to supplementing a low FODMAP diet with dietary fibres by hydrogen concentrations, but not by luminal pH. *Aliment Pharmacol Ther* 2023; 58: 417–428.
56. So D, Thwaites PA and Gibson PR. Editorial: interaction between fibre and colonic fermentation assessed with a novel gas-sensing capsule—Authors' reply. *Aliment Pharmacol Ther* 2023; 58: 830–831.