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State of the Art on Advancements in Wireless Capsule Endoscopy Telemetry: A Systematic Approach

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ABSTRACT In the last decades an innovative technique has emerged in clinical gastroenterology as a compelling alternative to the traditional wired endoscopy, known as Wireless Capsule Endoscopy (WCE). Such cutting-edge application is able to investigate the gastrointestinal (GI) tract through a miniaturized, swallowable and biocompatible capsule, equipped with electronic components. This allows for the non-invasive measurement of biological data, that is then sent to an external receiving unit through a wireless link. This systematic review prepared according to PRISMA guidelines focuses on the main technological advances of data transmission from the in-body ingestible capsule to an external receiver. A total of 142 studies were screened from a comprehensive literature search, performed in Scopus, Science Direct, and IEEE Xplore database. A final number of 47 met the inclusion criteria and were included in the review. The results highlight innovative technologies to optimize the wireless link efficacy and safety to an external receiver. High gain, wideband, omnidirectional radiation pattern, and low levels of specific absorption rate (SAR) are of crucial importance. Despite the capsule telemetry design being rather advanced, the bulk of the existing studies focus on the transmission unit design, rather than the receiving one. Moreover, comprehensive numerical studies on realistic human body models are lacking.

INDEX TERMS Biomedical telemetry systems, gastroenterology, ingestible, PRISMA review, wireless capsule endoscopy.

I. INTRODUCTION

WIRELESS Capsule Endoscopy is an innovative technology for research, treatment, and diagnosis of the gastro-intestinal (GI) tract diseases through an ingestible pill. The first capsule for endoscopy was presented in 1957 by Zworykin and Farrar and developed by engineers of the Radio Corporation of America in Camden, New Jersey [1]. In 2001 the capsule endoscopy obtained clearance by the Food and Drug Administration (FDA) and the Conformité Européenne (CE) mark certification. Since that moment, other pills for WCE were designed and commercialized by many companies around the world. Indeed, in the last decades, wireless technology gained momentum due to the unprecedented development of body-implantable and ingestible devices [2]. Specifically, ingestible capsules could be a worthwhile substitute for traditional wired endoscopy, which is a widely employed medical procedure for diagnosing various pathologies affecting the GI tract.

This examination involves the use of a thin and flexible tube equipped with optical fibers, inserted into the body through natural cavities.

Despite technological progress in conventional endoscopy, patients still encounter some discomfort during the procedure since, due to its invasive nature, anesthesia induction is necessary. Therefore, WCE is increasingly capturing interest within the scientific community due to its revolutionary nature. The current clinically approved capsules are miniaturized, with an average size of 26 mm × 11 mm for easy swallowing, smooth and without edges to avoid gastric wall lesions, biocompatible, and resistant to acid environments [3]. Such capsules could be specifically designed to investigate different parts of the GI tract in a painless and well tolerated manner, such as colon [4] and esophagus [5], [6]. In particular Colon Capsule Endoscopy (CCE) has gained prominence in clinical practice, as a valuable alternative to optical colonoscopy (OC), a sensitive and accurate tool in diagnosing colorectal cancer. Nonetheless, OC requires highly specialized personnel, is a time-consuming procedure and increases resource utilization [7]. Importantly, COVID-19 pandemic fostered CCE use, with more than 10000 examinations, thanks to its advantages, including non-invasiveness, lower discomfort and anxiety for the patient, favorable safety profile and the administration at local centers healthcare or even patients' residences. However, CCE has high sensitivity in detecting flat adenomas, but it is less precise in estimating its size. Thus, patients' preferences tend to lean towards OC, driven by the desire for comprehensive results. Inducing a clear preference for CCE, implies addressing issues such as incomplete examinations and improving bowel cleanliness [7]. It is worth noting that, Esophageal Capsule Endoscopy (ECE) underwent significant improvements related to induction of rapid esophageal transit [6]. The patient drinks 100 mL of water while standing and ingests the capsule while lying down, the recording of biological parameters takes place as the patient gradually transitions from a supine to an upright position [5], [6]. ECE features a two-camera device with a high frame rate to enhance image capture and gives accurate information in emergency situations, guiding the need for intervention. Numerous investigations have established the efficacy of ECE, compared to the gold standard esophagogastroduodenoscopy (EGD). The majority of these studies focused on individuals suffering from Barrett's esophagus (BE) or esophageal varices. Despite the advantages, ECE would pose potential challenges in capturing sufficient mucosal images. Furthermore, the capsules can provide information on the whole small intestine, whereas the traditional wired endoscopy can cover only a portion [8]. Small Bowel Capsule Endoscopy (SMBE) provides real-time painless imaging, without requiring anaesthesia, and valuable information for physicians. Moreover, after swallowing the pill, the patient does not need any monitoring by medical staff. SMBE eliminates infection risks associated with multidrug-resistant germs; thus it is particularly beneficial for elderly patients prone to infections and complications, while traditional endoscopic procedures pose risks or contraindications [9]. Nevertheless, SMBE faces uncertainties in incomplete studies due to slow bowel transit, inadequate imaging causing risk of overlooking or missing pathologies, and the risk of capsule retention. Bowel cleansing is crucial for high diagnostic performance, and generally 2 l of Polyethylene glycol (PEG)-based laxative is recommended by the European Society of Gastrointestinal Endoscopy (ESGE) [10]. Moreover, ESGE recommends pre-procedure diet modification and anti-foaming agents [11].

Generally, commercial pills have integrated sensors, activated and regulated by a microprocessor unit, to measure various physiological and biological parameters, including pH, pressure, temperature, haemoglobin levels, and even intestinal gases. They are often equipped with one or more cameras and a LED, enabling them to capture an average of 50.000 frames of the entire GI tract in the first 8 hours of activity [12]. These components allow the non-invasive investigation and diagnosis of gastric disorders, such as reflux, chronic constipation, intestinal bleeding or pathologies like gastroparesis, polyps and tumors in the small intestine up to the identification of chronic disorders, such as celiac and Chron's disease [13]. Specifically, a study on 105 patients (45.7% women, median age 72) revealed a diagnostic yield of 58.1% for WCE [14]. Moreover, ESGE recommends employing WCE as the primary diagnostic method for suspected Crohn's disease, particularly following a negative ileocolonoscopic examination and in the absence of obstruction or stenosis symptoms [15]. Leighton and colleagues demonstrated that the PillCam Crohn's, from Medtronic, had an 83.3% diagnostic yield for active Crohn's disease, surpassing ileocolonoscopic (69.7%) [15]. Gastroesophageal reflux disease has been investigated by monitoring pH levels through WCE, which has been demonstrated to be viable, well tolerated and safe in 91 patients [16]. Furthermore, second generation colon capsules have a sensitivity of about 85% for detecting 6 mm and 10 mm polyps, which is considered clinically adequate for diagnosis, compared to computed tomography colonography [17]. A total of 18 commercial pills (Table 1) were found in [3], [13], [18] with their dimensions and main characteristics, e.g., measurements range of pH, temperature, pressure and images sampling rate with view angle. Heading into the specifics of Table 1, here are reported as following. Three capsules designed by the company Medtronic: the *SmartPill*, used to assess gastrointestinal motility disorders, thanks to the MotiliGI^{TM} software, which calculates transit and gastric emptying times from the received data; the *Bravo pill*, used for gastroesophageal reflux testing and the *PillCam SB3*, equipped with a camera to collect images of the GI tract. Moreover, the *Heidelberg pill* (designed by Heidelberg Medical) is used for digestive disorders,

TABLE 1. Commercial capsules reported in literature.

Company	Capsule	Dimension (mm)	Battery Duration (hours)	Main Measurements and Characteristics
Medtronic	SmartPill	26 x 13	120	pH: 1 ÷ 9. Pressure: 0 ÷350 mmHg. Temperature 20 ÷ 40°C.
	Bravo	26 x 6.3	96	pH: 1.7 ÷ 7.
	PillCam SB3	26.2 x 11.4	11-12	Images sampling rate: 2-6 frames/s
	PillCam ESO3 UGI	32.3 x 11.6	1.5	View Angle 172°. Images sampling rate: 35 frames/s for the first 10 minutes, 18 frames/s in the next 80 minutes.
	PillCam Chron’s	32.3 x 11.6	10	View Angle 168°. Images sampling rate: 4 ÷ 35 frames/s.
	PillCam COLON2	32.3 x 11.6	10	View Angle 172°. Images sampling rate: 4 ÷ 35 frames/s.
Heidelberg Medical	Heidelberg	20 x 7	8	pH: 1 ÷ 9.
HQ Inc	CorTemp	22.3 x 10.2	6	Temperature:10 ÷ 50 °C.
BodyCap	E-Celsius	17.7 x 8.9	20 days	Temperature: 0 ÷ 50 °C.
Medimetrics	IntelliCap	27 x 11	48	pH: 1.7 ÷ 4.7.
Equivital	VitalSense	23 x 8.6	20 days	Temperature: -32 ÷ 42 °C.
Atmo Biosciences	Atmo Gas Capsule	25 x 10	72	Oxygen concentration measurement for inflammation and intestinal irritability
Olympus	Endocapsule 10	26 x 11	12	View Angle 160°. Images sampling rate: 2 frames/s.
IntroMedic	MiroCam	24.5 x 10.8	11-12	Images sampling rate: 3 frames/s.
	MiroCam MC2400	30.1 x 10.8	1.5	View Angle 170°. Images sampling rate: 24 frames/s.
Jinshan Science and Technology	OMOM Capsule 2	27.9 x 13	6-8	View Angle 165°. Images sampling rate: 2-10 frames/s.
Capso-Vision	CapsoCam SV-1	31 x 11	15	View Angle 360°. Images sampling rate: 12-20 frames/s.
ANKON Technologies	ANKON NaviCam	27 x 11.8	8	View Angle 151°. Images sampling rate 2 frames/s.

such as abnormal or absent production of stomach acid, Dumping syndrome (or rapid emptying), pyloric insufficiency. Specifically, we can mention three commercial capsules for the temperature measurements: the *CorTemp capsule*, which measures internal body temperature, prevents risks associated with excessive temperature rise during motor activities; *E-Celsius capsule* (BodyCap), used for internal body temperature monitoring for non-medical applications; finally, the *IntelliCap* (Medimetrics), that can activate the controlled release of drugs, contained inside the capsule. Other capsules, specialized in capturing images are the *Endocapsule 10* (Olimpus), able to capture a range from 80000 to 140000 images, and it can be used in Omni Mode, to recognize similar images and reconstruct the continuity of the intestinal tract: the *OMOM Capsule 2*, equipped with software that can remove 90% of redundant images and suggests those in which there are possible abnormalities; moreover, the *CapsoCam SV-1* is able to capture high resolution images to identify Celiac Disease, ulcers, and bleeding. Furthermore, a huge interest is growing in the investigation of innovative capsules technologies able to capture images beyond the mucosa. Alternative techniques presented in literature propose the exploitation of auto fluorescent imaging [19], in which a light with wavelength λ in a range between 380 nm and 500 nm is used to excite natural cellular fluorophores. The lower emission capacity of malignant tissues allows them to be distinguished from benign ones. Furthermore, ultrasonography is under investigation as well, even though it is still in its early stages [20]. An ultrasound beam characterized by a frequency of 5 MHz or 10 MHz can be used for high penetration depths, to reach organs, whereas a beam with a frequency of 30 MHz is exploitable for lower penetration depth, to assess tissue composition. At present, studies have been undertaken to evaluate the quality of the acquired images and, subsequently, the transducers will be incorporated inside the capsule with the battery and the transmission unit. Finally, X-rays have been proposed, specifically though the use of the radioisotope 191Os and the ingestion of an iodine-based contrast agent [21]. The images are reconstructed by measuring the low-energy X-ray fluorescence produced by the interaction between the photons emitted by the radioisotope and the ingested contrast agent, with a resolution adequate for detecting polyps larger than 6 mm.

In the interest of completeness, as is well known, the capsule moves in the GI tract following passively the natural peristaltic contractions and it is expelled spontaneously within generally 72 hours. Therefore, several research groups are currently working on implementing active locomotion control [22], that can be mainly classified in: internal systems, in which an actuator is embedded inside the capsule, propelling it inside the patient's body; external systems, in which the magnetic field is applied as an external agent to control the capsule's movements. Nonetheless, the mentioned systems should have specific technological characteristics such as the speed value of about 15 cm/min, in order to avoid tissues' lesions, to guarantee a suitable transit time to collect accurate images and to limit power consumption [23]. Among the internal locomotion systems, Valdastri and co-authors [24] used a paddle/legged-based mechanism, through 12 paddles mounted on the capsule to push it along the GI tract. Other groups adopted the hydrodynamic force-based method, as the one proposed by Chen et al., [25] that combines the straight movement, through a DC motor, and the steering mode to force the rotation. More recently, Khan and colleagues published the first prototype P1 of small bowel soft robotic enteroscopy (SOFTIE) [26]. The locomotion is provided by vibrating silicon legs, controlled by linear resonant actuators. Nevertheless, the mentioned method is still under investigation, due to the high battery consumption, limited capsule volume and risk of tissue damage. For these reasons, the external locomotion systems gained attention. They are based on the use of rotating or static magnetic field, with one or more permanent magnets embedded inside the capsule [27]. Shamsudhin and colleagues [28] designed a capsule magnetically guided, which changes its trajectory with the rotating magnetic field plane. Whereas, Beg and co-authors designed a magnetically assisted capsule endoscopy system [29], MiroCam MC4000-M, NaviSystem: in this system, external magnets, placed inside an hand-held control at a distance of 15 cm, are used in order to perform the capsule rotation and translation. A pilot study has demonstrated the accuracy of this system as diagnostic tool. Despite the advantage to have a null power consumption, the integrated magnets presence could interfere with other components devoted to electronic control. Furthermore, the mentioned techniques are expensive and it's important to control the application time of the magnetic forces.

Whatever type of data is collected by the various types of capsules just mentioned, it is essential that they be sent through a wireless link to an external receiver, typically placed on the patient's body [30], and then downloaded on a workstation for post-processing analysis, as sketched in Figure 1. In 1957, Vladimir Zworykin announced its ingestible device referred as "radio pill". At that time, the fundamental structure of swallowable telemetry systems had already been described.

These systems include a miniaturized, ingestible transmitter, equipped with a transducer, a power source and an antenna. Whereas the external receiver module comprises a receiving antenna, a data-processing receiver and a data output or storage unit. Technological progress has brought about numerous advancements over time. Microelectronics and information technology have played a crucial role in accelerating the ingestible telemetry systems development. Nonetheless, technological advancements in the field of WCE, including advanced imaging and the incorporation of artificial intelligence, demand the capture and subsequent transmission of increased amount of data. Additionally, the techniques for actively localizing the pill, crucial for targeted drug administration and to know precisely the GI abnormalities location, at present remain rudimentary. To this regard, different WCE localization techniques have been studied in the last years. Among the most relevant researched, it's possible to mention radio frequency (RF) and magnetic methods [31]. Nonetheless, RF localization technique is the most common in commercial ingestible devices and it is based on the analysis of the received signal characteristics for capsule telemetry (such as intensity, phase, direction of arrival). Currently, the accuracy of the capsule location is low and the localization estimation is rough. For instance, a mean absolute error of 37.7 mm was measured from *in vivo* experiments for the PillCam by Medtronic system, through eight sensors positioned on the abdomen and chest [32]. Magnetic localization methods, which involves a magnet embedded inside the capsule and a wearable array of tridimensional sensors, demonstrated higher localization accuracy. In fact, the average errors are of the order of some mm. Nevertheless, the main limitation is the wearability of such localization systems, which require bulky and rigid sensors or coils structures that could cause discomfort for the patient. Anyway, the RF methods have the main advantage to save space inside the capsule and to limit battery consumption, since it works through the telemetry system already included for data transmission. Moreover, some miniaturized on-body antennas for general biomedical purposes, that uses textile materials for the

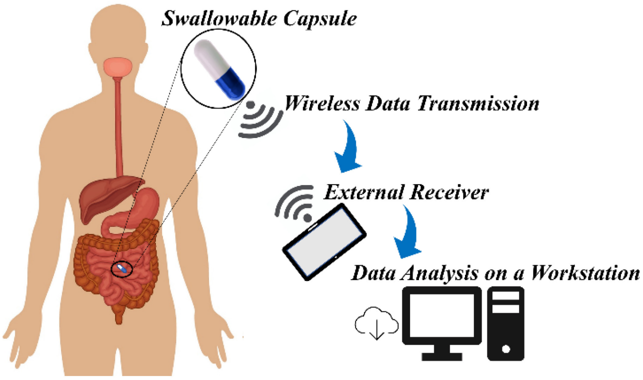

FIGURE 1. WCE main characteristics and operating flow: the ingestible pill travels in the GI tract, measuring biological parameters and collecting images. The data are transmitted wirelessly to an external receiver, placed on the patient's hips, and then downloaded on a workstation.

substrate, are proposed in literature and they could be exploited as more comfortable and wearable solutions [33], [34], [35]. Therefore, the optimization of the telemetry unit technology, as well as the main parameters in antenna design, is crucial to ensure efficient data transmission and to obtain precise capsule localization.

To this purpose, here we aim to perform an insightful systematic review of the literature to explore the significant advancements made in this field. Particular attention was given to the innovative methods employed for transmitting data from capsules located within the human body to a data recorder (i.e., a receiving antenna) placed externally. More specifically, this review is focused on the innovative design, in terms of antenna type (transmitter and receiver as well), miniaturization, biocompatibility, working bandwidth selection, and also on the SAR in the biological tissue, which must comply with the limitations provided by the regulatory framework. Furthermore, the review highlights the ingenious techniques developed to ensure seamless and efficient data transmission from within the body, while maintaining the utmost precision and accuracy. The analysis here described provides a comprehensive overview of the state-of-the-art technologies, emphasizing transmission methods strengths and limitations, and offering valuable insights to researchers, clinicians, and industry experts. This systematic review offers a deep understanding of the progress, facilitating the implementation of cutting-edge techniques in practical healthcare, and propelling advancements in capsule-based medical interventions. The future holds exciting possibilities as data transmission technologies continue to unlock new heights in the field.

II. MATERIALS AND METHODS

A. RESEARCH STRATEGY

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [36], created to report clearly the reasons behind conducting the systematic review and to present the research results. Indeed, to guarantee the review validity, authors need to furnish a transparent, comprehensive, and systematic description of their actions and the outcomes. Consequently, the choice to use for this study the PRISMA guidelines is exactly to facilitate a well-organized approach to the systematic review process and to ensure that no valuable information was omitted. The study flow diagram is reported in Fig. 2. A comprehensive literature search was performed to identify studies published starting from 2018 up to 2023 (both included). The research was performed using Scopus, Science Direct, and IEEE Xplore database using the following keywords: “Review Antenna for WCE”, “Antennas for WCE”, “Wireless capsule endoscopy telemetry”. Reference lists from the resulting publications and reviews were used to identify further relevant publications. Subsequently, each article was checked against the eligibility criteria.

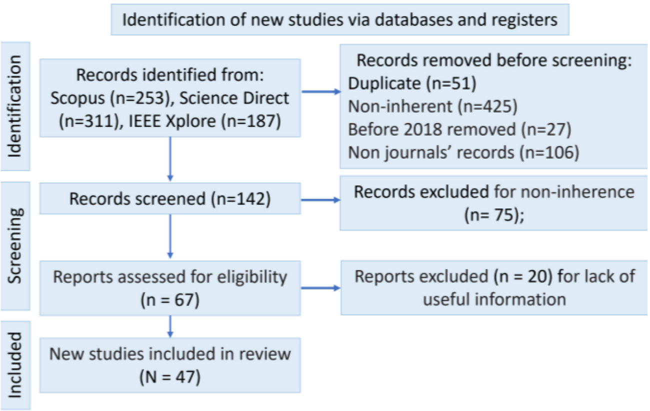

FIGURE 2. Study flow diagram. During the identification stage a research on three database, Scopus, Science Direct and IEEE Xplore, has been carried out using keywords, considering the last 5 years. After a preliminary records exclusion, the screening stage has been crucial to delve into the 142 papers in order to assess the final works to be included in the review.

B. SELECTION CRITERIA

The main focus of this review is to investigate the antenna design innovativeness in the most recent works. Afterward, we considered important that the selected papers were including certain key information, such as a description of the antenna design, operating frequency, and numerical validation of the antenna’s performances, thus excluding those not reporting such details. Finally, we also excluded the work without numerical SAR evaluation in the inner human tissues.

III. RESULTS

A. STUDIES INCLUSION

A total number of 751 studies were identified in the initial search. A number of 609 studies were excluded before the screening and a further 75 were excluded after the screening, because of their failure to meet the inclusion criteria. Sixty-seven studies were evaluated in full for eligibility, of these 47 studies were included in the review, because they were complete with all the interesting information mentioned in the Selection Criteria. Fig. 2 provides details regarding the selection process.

B. STUDIES CHARACTERISTICS

The studies included only one review paper [30], whereas the others are original articles that deal with the main characteristics of the proposed antenna following such workflow: geometry optimization at the frequency of interest, numerical validation of the antenna performances first in free space and then in simplified or realistic human phantoms; SAR and maximum input power computation, with a final ex vivo characterization. A thorough and detailed classification of the reviewed works included is presented in Table 2, organized into 5 sections: antenna design, operating frequency, numerical validation, presence of the receiving antenna, and other review papers. Within the design section, there is a breakdown of specific designs frequently investigated for WCE purposes, including conformal (further subdivided into loop, patch, microstrip, and helical), embedded, hybrid between conformal and embedded, MIMO, and others. The references for each design are listed in the last column. The frequency section refers to the MedRadio, ISMB bands, specifying the central frequencies of 433 Hz, 915 Hz, and 2.45 GHz, along with other bands and their respective references in the last column. Finally, in the numerical validation section, studies are categorized based on antenna modeling in air, the use of simplified human models, such as spheres, mono or multilayer cubes, or realistic models. Detailed information will be provided in the following sections.

C. GENERALITIES ABOUT WIRELESS LINK FOR WCE

The attention of the scientific community focuses on antenna design (in terms of antenna type, size, biocompatibility and patient safety), working bandwidth selection, electronics, powering innovations and modelling of the wireless channel. The in-body transmitting antennas for WCE can be classified into two main types: embedded antennas, integrated inside the capsule with the other components (battery, sensors, etc.), and conformal antennas shaping the outer or inner capsule surface. One of the biggest challenges is the miniaturization of the transmitting source, while maintaining high gain. Therefore, the conformal type allows to reserve more space inside the capsule for other components. In [30] some design considerations and miniaturization techniques have been provided. Wideband is another key requirement to guarantee high-resolution data transmission [37] and limit the detuning effect related to the different biological tissues, in which the capsule travels. Thus, the complexity of the human body and the highly dispersive and frequency dependent tissues dielectric properties could cause signal attenuation and reflection losses, an effect that has to be considered in assessing the antenna's performance. Finally, the radiation pattern is required to be possibly omnidirectional since the specific capsule position and orientation inside the GI tract could be random. In the best possible scenario, the antenna is miniaturized, with a high gain, low reflection coefficient S_{11} and SAR levels conformed to regulatory limits (IEEE C95.1-1999 [38], IEEE C95.1- 2005 [39]).

TABLE 2. Classification of the reviewed works.

TX – RX TECHNOLOGY			References
Design	Conformal	Loop	[40], [41], [42], [43], [44], [45], [46], [47], [48], [64], [65], [66], [67], [68], [69]
		Patch	[50], [51], [52], [53], [70], [71], [72], [73], [74], [75]
		Microstrip	[49], [55], [56], [54], [76]
		Helical	[57], [58]
	Embedded		[59], [60], [61], [62], [63], [77]
	Hybrid between conformal and embedded		[78]
	MIMO		[37], [79], [80], [81]
	Other		[82], [83], [54], [56]
Frequency	MedRadio and ISMB	433 MHz	[43], [48], [50], [53], [55], [54], [57], [82], [71], [67], [72], [68], [54], [56]
		915 MHz	[41], [42], [44], [47], [50], [61], [80], [66], [83], [71], [67], [73], [74], [77].
		2.45 GHz	[37], [41], [42], [45], [46], [50], [52], [49], [56], [60], [61], [62], [79], [81], [65], [66], [67], [72], [73], [76], [75], [69]
	Other		[40], [51], [58], [59], [63], [78], [64], [70]
Numerical Validation	Simplified Human Models		[37], [43], [44], [45], [46], [47], [48], [50], [51], [52], [53], [55], [54], [58], [60], [61], [62], [63], [78], [79], [81], [65], [66], [83], [71], [67], [72], [73], [68], [76], [74], [75], [77], [69], [54], [56]
	Realistic Human Models		[40], [41], [42], [44], [51], [49], [57], [61], [79], [80], [81], [64], [82], [70], [66], [83], [71], [74], [69]
	Air		[56], [59],
RX Antennas			[40], [57], [51], [58], [59], [63], [64]
Review Works			[30]

D. DESIGN AND TECHNOLOGIES

In recent years, several conformal antenna designs have been developed for WCE telemetry purposes. It is worth mentioning as examples: loop antennas [40], [41], [42], [43], [44], [45], [46], [47], [48] patch antennas [49], [50], [51], [52], [53] microstrip antennas [54], [55], [56], and helical antennas [57], [58]. The complete classification of the studies based on the antennas' design is reported in Table 2. Recently, Güreş and colleagues [48] proposed a circularly polarized meandered dual loop antenna, with a 1.3 λ perimeter and a rectangular shape, which they declared to have the widest axial ratio beamwidth reported in literature, a higher gain and a broader bandwidth, centred at 433 MHz. All antenna dimensions, length and widths of all meanders and gaps were determined to minimize the reflection coefficient S_{11} and maximize axial ratio beamwidth at the selected frequency. Nikolayev et al. [55] designed a cylindric conformal microstrip antenna, that features a ground plane shielding the antenna from the capsule. The electric field distribution is observed to be maximum at the cylinder extremities and zero in the middle of the antenna. Being generally attached to the pill surface, the conformal antennas have the advantage of saving space in the inner capsule environment. Nevertheless, the antenna can be affected by interferences with external factors, such as gastric juices. Moreover, conformal types suffer from the lack of a complete ground structure. Nonetheless, in recent years, also innovative embedded designs have been proposed, with very compact sizes in order to fit the small capsule [59], [60], [61], [62], [63]. Neebha and colleagues [59] fine-tuned an ultra-miniaturized monopole antenna, printed on a flexible polyimide material with a drastically reduced size of 4.6 mm × 7.6 mm × 0.15 mm, using an artificial magnetic conductor (AMC) unit cell. Such AMC materials, complementary to a perfect electric conductor (PEC), are high impedance layers, with zero-reflection characteristics and resonant behavior. These kinds of layers improve the gain, increasing the radiation efficacy and reduce SAR.

Wang et al. developed a miniaturized antenna sensor, with double layers of patches for radiation, three layers of dielectric substrate, and a ground plane, with a total small volume of 2.6 mm × 3 mm × 0.381 mm [60]. Thanks to its high gain and high sensitivity, this antenna is able to transmit images to an external receiver and to track the gastric juice changes, through the shift of the resonance frequency. Besides, the embedded structures occupy space inside the capsule, and it is not always so easy to reduce the antenna's dimension. For this reason, Ran and colleagues proposed a dual-band ultra-wideband antenna for WCE, that combines the conformal structure advantage of saving space and the presence of a complete planar ground substrate, typically used in the embedded types to avoid the interferences with the battery and other capsule's components [78]. Moreover, recently Multi-Input and Multi-Output (MIMO) technology is increasingly implemented [37], [79], [80], [81] to improve data transmission rate compared with single-input and single-output technology. As a final consideration, to the best of our knowledge, most of the works are focused on the transmitting unit design and optimization, whereas only a few articles mention the receiving one (or on-body antenna) [40], [51], [57], [58], [59], [63], [64]. Generally, some requirements for the on-body antenna, provide a planar design, to be easily attached on the body, with wideband to overcome the detuning effects and detect the capsule's data in different positions inside the GI tract. In [57] an innovative on-body wideband dual-polarized antenna is introduced to improve WCE link performances. The cross-bowtie structure with a compact feed achieves dual-polarized performance and high isolation. A loaded ring with stubs enhances bandwidth (381-990 MHz). Testing with homogeneous numerical phantom and ex vivo validates impedance matching. The proposed antenna demonstrates stability, enhanced transmission, and suitability for practical capsule endoscopy systems. Whereas, in [58] a Normal Mode Helical Antenna (NMHA) for WCE, working at 402 MHz, is introduced to carry out a thorough link budget analysis. The dimensions of the NMHA are 18 mm in height and 11 mm in diameter for the transmitter and 37 mm in height and 18 mm in diameter for the receiver. The transmitter incorporates an NMHA within a cylindrical phantom mimicking human stomach tissue, while the receiver employs an external NMHA. Furthermore, Fang and colleagues proposed models for in-body to on-body channels [63]. The planar elliptical ring in-body antenna covers the lower of a ultrawide band (UWB) frequency range, from 3.1 GHz to 5.1 GHz. A wideband semi-circle monopole antenna is proposed for on-body reception and fabricated on a RO3203 substrate, with relative permittivity of 3.02. The miniaturized, 40 mm × 40 mm dimension, and lightweight design is easily integrable with on-body electronic devices. Finally, Kissi and co-authors designed a planar dipole antenna, with a L-shape radiating element, printed on FR4 with dimension of 25 mm × 30.3 mm × 1.6 mm [64]. The antenna operates in a UWB range, from 3.75 GHz to 4.25 GHz.

E. WORKING FREQUENCY SELECTION

Finding the optimized bandwidth has been challenging, due to the trade-off between the degradation of the radiation efficacy and the limitation in the miniaturization at lower frequencies, and the fast attenuation at higher frequencies within lossy biological tissues. In literature, Medical Device Radiocommunications Service (MedRadio) and Industrial Scientific and Medical Bands (ISMB) have been chosen, mainly centered at frequencies of 433 MHz, 915 MHz, and 2.45 GHz (e.g., [37], [40], [65], [82]). A comprehensive identification of the operating frequency has been performed for each study and reported in Table 2. In particular, in [82] the standards recommended by the European Telecommunications Standards Institute (ETSI) to guarantee an ultra-low power WCE at 433 MHz are mentioned, in terms of minimum capsules length of 20 mm, minimum diameter of 10 mm, a bandwidth up to 10 MHz and an operational imaging rate up to 20 frames/sensor. Considering the works included in this review, most of them presented antennas with working frequencies above 2.45 GHz. Moreover, Ultra-Wide Band solutions, able to reach above 1 GHz bandwidth, are increasingly implemented [51], [52], [63], [70]. Finally, recently some multi-band antennas have been proposed to guarantee an efficient data transmission [61], [62], [66], [67], [71], [83].

F. NUMERICAL VALIDATION

The wireless link performances strongly depend on the electromagnetic (EM) properties of the surrounding environment. Whereas for implantable applications the device remains in a specific area of the body with defined EM behavior, ingestible capsules experience different dielectric properties varying with the working frequency and with the biological environment in which the capsule travels. The electric permittivity and conductivity of the human tissues have been reported by Gabriel et al., as a function of the frequency [84]. When considering an operating frequency of interest, the estimated range of EM properties should be considered, and the antenna should remain operable in the specified range. In [25] a low profile conformal microstrip antenna for ingestible application is presented, suitable to fit within an environment with higher EM properties and reach an acceptable match for tissues with lower EM properties. In this context, computational dosimetry is a powerful tool to validate the antenna performances in simplified or realistic 3D human body models, as well as in free space. This way the SAR could be quantified in a more real context, to define the maximum input power complying with the suggested limits. Human tissue phantoms with one or more layers are often employed [43], [44], [45], [46], [47], [50], [51], [52], [53], [55], [61], [62], [63], [66], [67], [68], [69], [72], [73], [74], [75], [76], [77], [79], [83], [85]. In [48] and [72] a homogenous cubic muscle phantom is considered. In [60] a three-layer model, divided into skin, fat and stomach, is fine-tuned, in which tissue properties at 2.45 GHz are assigned; [65] delves into separate examinations of human tissue models for the stomach, colon and small intestine. In [72], the importance of realistic anatomical models is discussed, as they play a crucial role in determining the radiation pattern, which is closely linked to the morphology and dielectric behaviour of the surrounding environment. Only few works use realistic human phantoms [40], [41], [42], [44], [51], [57], [61], [64], [66], [69], [70], [74], [79], [80], [82], [83], generally only to define the antenna maximum allowed input power starting from 1 g and 10 g averaged SAR evaluation (IEEE C95.1-1999 standard limits 1g-avg SAR to 1.6 W/Kg [38] and the IEEE C95.1-2005 standard limits 10g-avg SAR to 2 W/Kg [39]). All the studies included in this mini review have been further classified based on the human body models employed to carry out the antennas' numerical validation. For instance, Al-Hasan and colleagues simulated their antenna first inside a homogeneous skin model, then they evaluated the SAR distribution by placing the antenna inside the intestine and the head of a human model, at 0.91 GHz and 2.45 GHz considering a normalization with an input power of 1 W [73]. For compliance with the standard limits provided by IEEE for the SAR value, the authors evaluate an allowed input power of 3.32 mW for the proposed antenna. Moreover, Miah and colleagues modelled their device at 433 MHz, in the torso of the CST Gustav human model [68]. Only the torso, dimensions of 290 x 230 x 100 mm^3, was simulated to limit the computational cost, in which the antenna model was inserted in three different positions: inside the colon, the stomach and the small intestine, in which the capsule is about respectively 50 mm, 60 mm and 75 mm from the body surface. The simulations show that the capsule wireless link is safe, since the SAR levels are below the regulatory limits, and the authors define an input power interval for the three compartments considered: 7.2 ÷ 28 mW for the colon, 5 ÷ 24 mW for the small intestine, 7.2 ÷ 25 mW in the stomach over 1 g and 10 g averaged SAR. Just a few studies reported the analysis of the coupling strength between the endoscopy antenna inside the human body and an external receiving antenna. In [51] the coupling strength between the TX antenna, inside a cubic tissue phantom, and the RX coaxial-fed patch antenna at 3.3 GHz, has been analyzed. Results showed that the coupling link decreases with increasing distance between the TX antennas due to propagation loss. Evaluation at 3.3 GHz reveals closer coupling for stomach and colon compared to the small intestine. At 3.3 GHz, coupling strength is compared for stomach, colon, and small intestine, indicating better coupling in stomach and colon. Wang and colleagues positioned their RX antenna on the abdomen surface, simulated with a rectangular muscle equivalent phantom, maintaining a 1 mm gap [57]. Results showed a wide impedance bandwidth achieved, from 381 MHz to 990 MHz. Extensive link studies show a peak $|S_{21}|$ of −25.5 dB at a 60 mm in-body depth, guaranteeing stable data transmission. Finally, Kissi et al. used a female voxel model, Laura from CST Library, which is characterized by the presence of skin, visceral and subcutaneous fat, small intestine wall, and content layers. The RX antenna is a dipole printed on FR4 laminate and the radiating element has an inverted L-shape. The numerical simulations are performed with the RX antenna tested at 4 mm, to take into account the separation distance due to the clothes thickness, and 30 mm distance from the skin [64]. In this study, the antenna is tested in two established positions: perpendicular, i.e., vertically placed on the abdomen, and parallel, i.e., horizontally positioned on the abdomen. The numerical and experimental results are in line and highlight that the parallel position closely approximates the −10 dB impedance bandwidth observed in free-space conditions. Conversely, for the perpendicular position, significant degradation in reflection coefficients occurs at both distances, indicating poor impedance matching. Furthermore, the parallel position enhances also comfort for on-body applications, particularly for patient use. Nonetheless, a complete and detailed investigation of the communication link between the proposed on body antenna and the capsule in different positions is missing and the authors aim to pursue this as future work. Furthermore, in [42] abdominal implant communication utilizing a bio-matched mini-horn antenna is investigated. Through electromagnetic simulations with the same 3D anatomical voxel model, "Laura", the study evaluates signal coverage across ISM and UWB frequency bands, examining power flow and S-Parameters between a capsule endoscopy pill and an on-body receiver. The transmitting antenna is a double loop UWB, characterized by a working frequency range of 1 ÷ 6 GHz, embedded in a 11 mm × 25 mm capsule. The capsule is placed in two positions: in the nearest possible ("Location A") and in the furthest possible ("Location B") location inside the small intestine. The RX antenna is a directional bio-matched mini-horn antenna, featuring water-filled holes to mimic tissue properties, and designed for close contact with the skin surface. The S21 parameter at location B, measured at 915 MHz, stands at −62 dB, indicating a manageable level of channel attenuation for establishing wireless communication between the capsule and on-body antennas. Moreover, at location B, the power flow value registers at −65 dB, further affirming the feasibility of establishing the communication The power flow at 915 MHz reveals comprehensive coverage of the small intestine. Conversely, at 2.45 MHz, there's an anticipated increase in power flow loss, particularly noticeable at location B (−77 dB), indicating difficulties in maintaining communication reliability, necessitating a more sensitive receiver. Additionally, at higher frequencies such as 3.1 GHz and 5.8 GHz, significant signal loss occurs in the deepest regions of the intestine, despite employing a directional bio-matched antenna. As far as we know, a complete numerical analysis focused on different exposure scenarios, related to several capsule positions and orientations, inside a realistic human phantom is lacking.

IV. CLINICAL AND PRACTICAL APPLICATIONS

WCE has revolutionized GI diagnostics, offering a non-invasive and patient-friendly approach to visualizing the GI tract. This technology significantly enhances patient safety and comfort compared to traditional endoscopic procedures, as it eliminates the need for sedation and reduces the risk of complications such as perforation or infection [86]. This minimizes the risk of adverse events and eliminates the need for prolonged recovery periods, enhancing patient satisfaction and compliance. Moreover, WCE offers a more comfortable experience for patients, as it does not require the insertion of a conventional endoscope through the mouth or rectum, reducing discomfort and anxiety associated with invasive procedures. Furthermore, WCE enables comprehensive examination of the small intestine, a region often difficult to access using conventional endoscopes, thereby improving diagnostic accuracy and patient discomfort [87]. Clinical applications of WCE span various gastrointestinal conditions, including obscure gastrointestinal bleeding, Crohn's disease, and small bowel tumours. For instance, WCE has proven invaluable in identifying the source of obscure gastrointestinal bleeding, leading to timely intervention and improved patient management [88]. Moreover, in patients with suspected or established Crohn's disease, WCE aids in assessing disease activity, mucosal inflammation, and disease extent, guiding therapeutic strategies [89]. Additionally, WCE facilitates the detection and characterization of small bowel tumours, allowing for early diagnosis and treatment initiation [90]. In view of the above, it is of paramount importance to consider the cost-benefit analysis to evaluate the economic implications of implementing WCE in clinical practice. While the upfront costs of WCE equipment and consumables may be higher than those associated with traditional endoscopic procedures, such as esophagogastroduodenoscopy (EGD) or colonoscopy, the potential long-term benefits of WCE must be considered. As an example, in the case of the evaluation of obscure gastrointestinal bleeding, WCE can lead to earlier diagnosis, and could reduce healthcare burden (i.e., reduction of inpatient costs).

Despite its clinical benefits, several technical challenges limit the widespread adoption of WCE in clinical practice. These include the limited penetration ability of radio-frequency technology, which may compromise visualization of deeper gastrointestinal structures [91], particularly in obese patients or those with significant abdominal gas [92].

From a technological point of view, there are potential advances that should be made to improve the WCE application and enhance its clinical value. Indeed, the scientific community is exerting significant effort to surpass the existing technological constraints of WCE. Among the current limitations, the commercial capsules are not actively piloted, indeed they follow passively the natural peristaltic contractions and the force of gravity, despite several research groups proposed innovative internal or external, based on the magnetic field application, locomotion methods [22]. Furthermore, the design of advanced systems capable of continuously and precisely localize the pill is still a challenge, but it could be pivotal to correlate the data acquired through the capsule to its position inside the GI tract [31]. Additionally, many research groups are working on the implementation of classification method of the images acquired by the capsule, through machine learning algorithms, to both delete useless or low-quality frames, as well as identify those of interest to be screened [93], [94], [95]. Advancements in image processing and artificial intelligence have the potential to enhance the diagnostic accuracy of WCE and facilitate real-time interpretation of capsule images, further enhancing its clinical value. Furthermore, such procedure allows to reduce the time employed by the medical staff to analyze the data collected and it guarantees a faster and more reliable diagnosis [96]. With a future-oriented perspective on new capsule technologies implementation, envisioning even more advanced functionalities and a massive data transfer from the capsule, issues related to power supply pose significant challenges, as the transmitting and receiving antennas within the capsule require sufficient energy to ensure optimal functionality throughout the examination [97], [98]. Therefore, improving the battery duration is another key point that should be addressed, also to enhance the amount of data collected and to sustain additional advanced capsules' functions, such as the localization system and the telemetry system [99]. In this regard, the design of wireless power transfer to recharge the capsule remotely is increasingly investigated [44], [49], [100]. Moreover, advancements in microencapsulation technology are necessary to enhance the durability and functionality of the capsule within the harsh gastrointestinal environment, ensuring reliable performance and minimizing the risk of capsule retention or malfunction [92], [101]. Addressing these technical limitations is crucial for optimizing the clinical utility of WCE and further enhancing its role in gastrointestinal diagnostics. Future research efforts should focus on developing innovative solutions to improve capsule penetration, enhance power efficiency, and enhance capsule durability.

It is also important to mention that currently, the standard functionalities of the commercial capsules are the measurement of pH, pressure, temperature, intestinal gases, and hemoglobin levels [3]. Nonetheless, integrating additional diagnostic and therapeutic modalities, such as drug delivery techniques, can potentially enhance WCE technology, to overcome the limits of the classic endoscopic techniques or GI disorders treatments. Recently, Srinivasan and colleagues proposed a robotic capsule for drug delivery purposes, i.e., RoboCap, able to clear the intestinal mucus barrier in order to foster the absorption of Vancomycin and Insulin [102]. The drug is contained in a cargo hold and released in the small intestine, where the pH of the intestinal fluids activates a membrane, closing the onboard circuit to trigger the RoboCap. The widespread use of ingestible devices offers an appealing alternative for implantable devices that are still invasive and costly.

To conclude it is important to consider that also for the WCE medical application is of paramount importance to take into account: patient privacy for medical diagnoses, treatments, and personal information; sensitive data security. Regarding these ethical implications, numerous laws and regulations have been implemented and they are widely discussed also in the scientific literature [103]. Various regulations such as the Health Insurance Portability and Accountability Act (HIPAA) in the United States and the General Data Protection Regulation (GDPR) in Europe have been enacted. These regulations establish protocols for protecting personal health information and necessitate researchers and healthcare entities to acquire informed consent from patients before to gathering, storing, or utilizing their personal data for research or analytical purposes. Moreover, stringent security measures and data governance policies are often implemented by healthcare organizations to securely manage personal information. These regulations also dictate the utilization of data, fostering the creation of analytically prepared datasets. Mitigation strategies like de-identification and synthetic data generation help preserve patient privacy while still enabling valuable insights. Compliance with patient privacy protection laws, such as HIPAA and GDPR, is essential for healthcare organizations. Healthcare and data protection, considering also risk mitigation strategies, are provided with various methods, including internal evaluations and expert determinations. Additionally, techniques such as de-identification, anonymization, informed consent, and data security protocols are employed by healthcare organizations to safeguard patient information. These measures are vital for ensuring the secure collection, storage, and analysis of sensitive data. Furthermore, internal policies developed by privacy and security experts aid in organizational compliance.

V. DISCUSSIONS AND CONCLUSION

Wireless Capsule Endoscopy is an innovative and non-invasive technique for the diagnosis and the treatment of several GI disorders. Numerous strides have been achieved in the realm of WCE since receiving its initial FDA approval in 2001. Despite the potential advantages of using WCE, there are still many technological challenges to be faced. Moreover, the main drawbacks are: the expensiveness of the clinical exam; the possibility that the capsule may remain for a long time inside the body (up to 72 hours) and finally, the fact that the capsules are not actively driven. In particular, a big effort has been made to improve the efficacy and safety of the data transmission to the external receiver, which is assumed to be efficient and safe. Several studies indicate as common prerogatives for wireless link optimization: transmitting unit miniaturization, high gain, wideband, omnidirectional radiation pattern, and compliance with the suggested SAR limits. Importantly, studies [64], [104], [105] show that pills are typically quite safe, inducing SAR levels significantly below the limits. Nonetheless, a complete and accurate study on the interaction between the pill transmitting data and the surrounding biological tissues is needed, considering that capsules can take different positions and orientations inside a realistic human body model. Additionally, such kind of study could be fundamental to design the receiving antenna and optimize the wireless link with the in-body. There are still numerous untapped opportunities to develop enhanced and innovative capsules for endoscopy, with the aim of establishing WCE as a standard clinical practice.

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