A Review of In-Body Biotelemetry Devices: Implantables, Ingestibles, and Injectables

Asimina Kiourti, Member, IEEE, Konstantina S. Nikita, Senior Member, IEEE

Abstract—Objective: We present a review of wireless medical devices that are placed inside the human body to realize many and different sensing and/or stimulating functionalities. Methods: A critical literature review analysis is conducted focusing on three types of in-body medical devices, i.e., a) devices that are implanted inside the human body (implantables), b) devices that are ingested like regular pills (ingestibles), and c) devices that are injected into the human body via needles (injectables). Design considerations, current status and future directions related to the aforementioned in-body devices are discussed. Results: A number of design challenges are associated with in-body devices, including selection of operation frequency, antenna design, powering, and biocompatibility. Nevertheless, in-body devices are opening up new opportunities for medical prevention, prognosis, and treatment that quickly outweigh any design challenges and/or concerns on their invasive nature. Conclusion: In-body devices are already in use for several medical applications, ranging from pacemakers and capsule endoscopes to injectable micro-stimulators. As technology continues to evolve, in-body devices are promising several new and hitherto unexplored opportunities in healthcare. Significance: Unobtrusive in-body devices are envisioned to collect a multitude of physiological data from the early years of each individual. This big-data approach aims to enable a shift from symptom-based medicine to a proactive healthcare model.

Index Terms—biotelemetry, implantables, ingestibles, injectables, in-body devices, wireless telemetry

I. INTRODUCTION

WIRELESS medical devices used to sense physiological parameters (sensors) and/or stimulate the nervous system (stimulators) are becoming increasingly popular nowadays [1]-[5]. A comprehensive overview of related technologies, systems, application areas and research challenges is presented in [6]. In fact, statistics show that 27% of Americans already use some sort of wearable device, such as a smart watch that records heart rate and number of steps, or smart socks that track speed, calories, altitude, and distance [7]. Nevertheless, wearable devices are limited to monitoring only specific types of physiological parameters that are readily accessible from outside the human body. Along these lines, wireless in-body medical devices that are placed directly inside the human body are promising an entire new realm of applications [8]-[10].

As shown in Fig. 1, wireless in-body medical devices are divided into three categories based on the way of insertion into the human body, i.e., implantables, ingestibles, and injectables. Herewith, the term ‘wireless’ refers to in-body devices that communicate wirelessly with exterior monitoring/control equipment (e.g., a smart phone) without the need for wires that would otherwise penetrate through the tissues to ensure a connection. Specifically, implantable devices are placed inside the human body by means of a surgical operation, and entail the most traditional type of in-body devices [11]. Over the years, they have evolved from bulky pacemakers to miniature deep brain implants [12]. Ingestible devices are capsule-looking devices that are ingested and swallowed like regular pills [10]. The most traditional ingestible device is the wireless endoscope that was first discovered in year 2000 [13]. Today, wireless ingestible capsules are integrated with advanced capabilities that can even monitor reactions to pharmaceuticals [14]. Finally, injectable devices are micro-devices that are injected into the human body by means of needles. They have been reported very recently for both sensing and neuro-stimulation applications [15]. As technology continues to evolve, in-body devices are becoming more powerful and concurrently more unobtrusive. In doing so, new resources are opening up for medical prevention, prognosis, and treatment that quickly outweigh any concerns about their invasive nature.

In the past, we presented an overview of implantable and ingestible devices, focusing on the challenges related to design and fabrication of the corresponding in-body antennas [16].
In this paper, we take a step forward, and discuss in-body devices from an application point of view, addressing design challenges related to communication, powering, and biocompatibility. Beyond implantables and ingestibles, the recently introduced area of injectable devices is also included in this review. Section II will address design considerations related to wireless in-body devices. Section III will discuss research and commercial applications of in-body devices, providing the current status and indicating future directions.

II. DESIGN CONSIDERATIONS FOR IN-BODY DEVICES

Design of in-body devices is typically performed using analytical models of the human body and advanced electromagnetics (EM) simulation software. Experimental validation is further performed in-vitro using phantoms that emulate the electrical properties of biological tissues, and/or in-vivo using animals (rats, pigs, etc.) and potentially human subjects. Detailed overviews of numerical simulation and experimental validation concepts used to accurately emulate real-life scenarios for in-body devices are provided in [11], [17], [18]. Herewith, we will focus on specific challenges associated with the design of in-body devices, and specifically: selection of operation frequency, wireless interface design, powering, and biocompatibility. These considerations are discussed next, and are applicable to all types of in-body devices, including implantables, ingestibles, and injectables.

A. Operation Frequency

As shown in Table I, several frequency bands have been employed for in-body devices [19]-[45], with the most commonly used ones being the Medical Device Radio Communication Service (MedRadio) band of 403.5 MHz, and the Industrial, Scientific and Medical (ISM) band of 2.4 GHz. In general, selection of operation frequency involves several trade-offs. Specifically, low frequencies tend to be more attractive as they are associated with lower loss through the biological tissues. As an example, high frequencies in the order of 3-5 GHz imply attenuation as high as 20-30 dB for every 2 cm of biological tissue [10]. On the other hand, low frequencies limit the communication speed and imply large antennas and circuit components, which, in turn, increase the size of the in-body device. In fact, ingestible devices typically employ high-frequency telemetry links to achieve high data rates, better image resolution, and device miniaturization.

B. Wireless Interface: from Inductive Links to Antennas

Integration of wireless capabilities into the in-body device is highly critical as it enables unobtrusive and ubiquitous communication with the exterior monitoring/control equipment. Today, such equipment may be a smart phone, a smart watch, or another type of smart wearable garment. Data can further be wirelessly transmitted to remote physicians, family members, etc.

The first wireless implants integrated inductive coupling technology at a frequency of 20 MHz or lower. This technology employed inductors within the implant and exterior device that were brought in close proximity to realize wireless communication via coupling between the two. However, inductive coupling has typically been associated with several limitations, including slow data rates and high sensitivity to misalignments between the inductors. As such, inductive coupling has recently given its place to wireless antenna communication. In-body antennas alleviate the aforementioned issues, and are becoming increasingly popular nowadays. Their design entails several challenges that are mainly related to miniaturization while achieving wide operation bandwidth, and have been extensively addressed in [16]-[18]. Antenna designs for in-body devices reported to date are summarized in Table II [19]-[45], and are further illustrated in Fig. 2. As seen: a) Planar Inverted-F Antennas (PIFAs) are typically employed for implantable devices as they provide several degrees of freedom for miniaturization, b) helical antennas are typically employed for ingestible devices as they provide circular polarization, omnidirectional radiation pattern, and consistent bandwidth across a range of tissues surround the device, and c) loop or dipole antennas are employed for injectable devices depending on the size and shape of the device.

C. Powering

In-body devices have been traditionally powered via batteries [46]. Drawbacks in this case are that batteries increase the size of the in-body device, raise patient safety and biocompatibility concerns, and require frequent replacement and/or recharging. In fact, despite recent advances in...
of superstrates to cover the exposed metal parts [56], etc. For in-body devices, including use of biocompatible materials techniques have been explored to achieve biocompatibility for body won’t react with the surrounding tissues. A number of [55], coating with thin biocompatible polymers [23], addition demodulated by the exterior interrogator to retrieve the sensed signal (f_s).

physiological parameter (f_s) and immediately backscatters the device, in turn, mixes the carrier signal with the sensed that is wirelessly received by the in-body device. The in-body device, as is the case with existing pacemakers.

III. APPLICATIONS OF WIRELESS IN-BODY DEVICES: CURRENT STATUS AND FUTURE DIRECTIONS

A. Implantable Medical Devices

Implantable medical devices are typically placed inside the human body by means of a surgical operation, and may serve all sorts of sensing and stimulating functionalities. Example applications for wireless implantable medical devices reported to date are summarized in Table III. Some of the most representative implantable applications are further discussed below.

1) Pacemakers: One of the most popular implantable medical devices is the pacemaker, a miniature device placed inside the chest or abdomen to help control cardiac arrhythmias [58]. The first pacemaker was implanted in 1958, and, since then, advances in electronics, electromagnetics, and wireless communications have significantly improved the pacemakers’ physical size and performance. In fact, most modern pacemakers do not exceed 1.2” in size, and some may additionally communicate critical diagnostic information about the patient and themselves (device status) to exterior devices. As an example, the world’s smallest pacemaker, the Medtronic Micra [59] (see Fig. 4(a)), is about the size of a large vitamin and can actually be implanted inside the heart. This pacemaker delivers an estimated average 12-year battery longevity, and can be safely scanned using either a 1.5T or 3T full-body Magnetic Resonance Imaging (MRI).

2) Intra-Cranial Pressure (ICP) monitors: Elevated ICP is typically a result of cerebral edema, cerebrospinal fluid disorder, head injury, and/or localized intracranial mass lesion. In turn, elevated ICP increases the risk of severe brain damage and may cause disabilities or even death. With these in mind, a number of unobtrusive implantable solutions have been reported for measuring the IOP. For example, in [60], [61], a MEMS pressure sensor was reported to detect changes in ICP and wirelessly transmit them to an exterior device (see Fig. 4(b)). The system’s operation frequency was set to 2.45GHz, and indicated a maximum pressure error of only 0.8mmHg. In [62], an RF oscillator was employed that was designed to detect changes in the ICP based on changes in its oscillation frequency. This device operated at 2.4GHz and was demonstrated to accurately identify pressures in the 10-70mmHg range. Both of the aforementioned sensors were battery-powered, which, in turn, increased the overall size of the implant and required frequent replacement and/or recharging. To avoid batteries, [63], [64] introduced a passive capacitive MEMS ICP sensor that was powered via inductive RF coupling. The sensor formed an LC tank with a coil placed on the skull, and the tank’s resonance frequency changed as a function of changes in the ICP. The latter was eventually
detected by an exterior reader device. In-vitro measurement results proved the capability of these sensors to detect ICP variations ranging from 0 to 70mmHg at 2.5mmHg intervals.

3) CardioVascular Pressure Monitors: Chronic blood pressure monitoring is of utmost importance for continual assessment of various conditions of the cardiovascular system (e.g., restenosis, hypertension, heart failure), as well as for tracking the progress of surgical interventions (e.g., monitoring repaired aneurysms) [65]. However, the traditional gold standards of blood pressure measurement, such as external pressure cuffs or intra-arterial catheter-based systems, exhibit several drawbacks. Examples include lack of patient comfort, infrequent measurement, possible occlusion of blood flow, and long-term complications (trauma and infection). As such, fully implantable devices are becoming quite popular for long-term monitoring of blood pressure. The latter allow for continuous monitoring without hindering the individual’s daily activities, and have no associated risks of infection as would typically be the case for catheters or wires. Rapid progress in microfabrication technologies has enabled the production of low cost, highly accurate sensors that may be safely implanted into patients for chronic pressure monitoring. Implantable blood pressure monitors based on MEMS capacitive sensors [66], a Surface Acoustic Wave (SAW) resonator [67], and Pulse Transit Time (PTT) measured by using an accelerometer [68] have been proposed. Recent industry developments include a pressure sensor fabricated by Boston Scientific for measurement of pressures within an aneurysm sac following endovascular aneurysm repair (EVAR) [69], as well as the first FDA approved implantable blood pressure device from CardioMEMS for detection of heart failure within the pulmonary artery [70]. Moreover, the potential of a device, originally developed for energy harvesting from arterial motion, to monitor cardiovascular system parameters has been demonstrated [71].

4) Neurosensors: Deep brain neurosensors have recently attracted significant interest for several applications, including epilepsy, Parkinson’s, Alzheimer’s, addictions, etc. In one case [48] RFID-inspired neural tags were considered for wireless brain-machine interfaces. Batteries were avoided, and power storage was performed via RF energy harvesting techniques. In another case [72], a wireless neurosensor was presented for recording neural signals from the cortex of monkeys. The sensor in employed a head-mounted device with a ‘screw-on’ interconnect to the implant, and integrated a head-mounted battery. Recently, wireless fully-passive implanted neurosensors have been reported (see Fig. 4(c)) [12], [73]-[75]. These devices operate without internal power supply elements and exhibit a highly simplified implant circuit topology. Also, no intra-cranial wires or cables are used. As an example, one of the latest fully-passive brain neurosensors occupies a footprint of 10 mm × 8.7 mm, and can read emulated neuropotentials as low as 20 μVpp [75]. This is a 25 times improvement in sensitivity compared to previously reported fully-passive configurations [73].

5) Neurostimulators: Several implantable neurostimulators have been reported to stimulate the nervous system and recover functionality for Parkinson’s, dystonia, depression, stroke, artificial limbs, spasticity, Alzheimer’s, sleep apnea, chronic pain, obesity, epilepsy, hypertension, heart failure, incontinence, auditory and visual impairments, etc. For example, retinal neurostimulators may restore vision [76] [77] (see Fig. 4(d)), cochlear implants may improve hearing [78], stimulators in the subthalamic nucleus may manage Parkinson’s disease [79], brain-computer interfaces may develop robotic hands/arms/legs that can be controlled by thoughts [80], and stimulators in the grey matter may inhibit chronic pain [81].

A number of future applications are envisioned for implantable devices that will take advantage of breakthroughs in electronics, materials, power harvesting, etc. Examples include heart stents capable of wirelessly transmitting the health of an artery, implants that can detect performance-enhancing drugs, closed-loop glucose meters and insulin pumps that monitor and correct blood sugar levels, and implants capable of detecting the presence of oral cancers.

B. Ingestible Medical Devices

Ingestible medical devices are miniature capsule-looking devices, and are taken through the mouth like regular pills [10], [13]. While traveling through the gastrointestinal tract and digestive system, ingestible medical devices may collect images, transmit real-time video, sense several physiological parameters, deliver drugs, etc. Collected data are eventually transmitted to a nearby monitoring/control device for display and further post-processing. Example applications for wireless ingestible medical devices reported to date are summarized in Table III. Some of the most representative ingestible applications are further discussed below.

1) Imaging Capsules: Smart endoscopy capsules used for imaging the gastrointestinal tract and digestive system are the most well-known form of ingestible medical devices. For example, Given Imaging provides pill-sized disposable capsules that can visualize the small bowel, esophagus, and colon without sedation or invasive endoscopic procedures [82] (see Fig. 5(a)). To date, prototyping systems with data rates as high as 2 Mbps have been reported for wireless capsule endoscopy that employ advanced compression techniques to achieve up to 15-20 frames per sec [83]. To obtain clearer
1) *Implantable* Devices: This class of applications refers to devices that are surgically implanted inside the body to monitor or treat various health conditions. Examples include pacemakers, defibrillators, and cochlear implants.

2) *Ingestible* Devices: These devices are taken orally and can track physiological parameters inside the body. Examples include ingestible sensors that monitor pH of the stomach, blood glucose levels, and gastrointestinal motility.

3) *Injectable* Devices: These are micro-sensors injected into the body through a needle or catheter. Examples include glucose sensors, neurostimulators, and pressure monitors.

**TABLE III. Example Reported Applications of Implantable, Ingestible, and Injectable Wireless Medical Devices.**

<table>
<thead>
<tr>
<th>Implantable Devices</th>
<th>Ingestible Devices</th>
<th>Injectable Devices</th>
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<tr>
<td>Pacemakers [58], [59]</td>
<td>Imaging of the digestive system [82]-[84]</td>
<td>Neurostimulators [15]</td>
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<tr>
<td>Intracranial pressure monitors [8], [25], [60]-[64]</td>
<td>Heart failure detection [85]</td>
<td>Oxygen sensing sensors [89]</td>
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<tr>
<td>Deep brain neurosensors [12], [32], [48], [72]-[75]</td>
<td>Drug delivery capsule [87], [88]</td>
<td>Athletes’ muscle performance trackers [89]</td>
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<tr>
<td>Retinal stimulators [76], [77]</td>
<td>pH sensing of the esophagus [16]</td>
<td>Shoulder subluxation rehabilitation [90]</td>
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<tr>
<td>Cochlear implants [16], [78]</td>
<td>Pressure/temperature sensing of the gastrointestinal tract [16]</td>
<td>Knee osteoarthrosis rehabilitation [90]</td>
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<td>Brain computer interfaces for prosthetic limbs [80]</td>
<td>Gastric stimulators [9]</td>
<td>Ucers treatment [93]</td>
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<td>Drug infusion systems [16]</td>
<td>Gastric stimulators [9]</td>
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<tr>
<td>Identity verification chips [16]</td>
<td>Gastric stimulators [9]</td>
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Images, fluorescence-based ingestible capsules have also been reported [84]. These systems typically include three sub-modules, namely optical imaging, electronics control and image acquisition, and information processing and transmission.

2) *Ingestible Sensors*: Ingestible capsules are often used to sense physiological parameters inside the body as a means to diagnose a number of conditions. For example, an ingestible-sensor scheme developed by Proteus Digital Health has already been FDA approved, and is being rolled out for heart-failure related drugs [85]. In another case [14], a sensor was presented for detecting the ingestion of a pharmaceutical tablet or capsule (see Fig. 5(b)). Clinical trials in 412 subjects demonstrated 99.1% detection accuracy and 0% false positives. The system further allowed direct correlation between drug ingestion, health-related behaviors (e.g., physical activity), and critical metrics of physiological response (e.g., heart rate, sleep quality, and blood pressure). More recently, custom-made ingestible capsules were demonstrated that can measure the concentration of different gases during digestion in the gut [86]. It is noted that changes in production of certain gases in the human gut have been linked to gastrointestinal disorders including painful constipation, irritable bowel syndrome, and colon cancer.

3) *Drug Delivery Capsules*: This class of applications refers to electronic pills that are used to precisely deliver a certain drug along the gastrointestinal tract. In one case, a micropositioning mechanism was reported that can be easily integrated into a capsule, and deliver 1 ml of targeted medication [87]. The micropositioning mechanism allows a capsule to be positioned within a 22.5° segment of a cylindrical capsule and be extendible by up to 1.5 mm outside the capsule body. In another case, a smart pill was designed to release powdered medication just before reaching the ileocecal valve, where the small and large intestine meet (see Fig. 5(c)) [88]. Once activated through a magnetic proximity fuse, the capsule opens up and releases its powdered payload.

A number of future applications are envisioned for ingestible devices. Examples include: personalized drug delivery capsules to treat digestive disorders and diseases, higher-bandwidth data transmission to enable better diagnosis, ingestible sensors that are taken along with regular pills to affirm that a patient has taken the correct dosage, electronic capsules that monitor physiological reactions to the dose, capsules that activate and sense in specific parts of the gastrointestinal tract and digestive system, devices that can track electrical activity at the gastrointestinal tract while also measuring transit times, and smart capsules that release specialized drug profiles at specific target locations or when they detect a certain sensing event.

C. *Injectable Medical Devices*

Given their minimally invasive nature and smart capabilities, injectables are seen by many as the next generation of medical devices. Example applications for wireless injectable medical devices reported to date are summarized in Table III. Specifically, the term ‘injectable’ may refer to two classes of devices, as outlined below:

1) *Micro-sensors injected into the human body by means of a needle*. Very recently, Profusa demonstrated an injectable sensor, namely the Lumee Oxygen sensor, that can monitor oxygen levels in the surrounding tissues (see Fig. 6(a)) [89]. The sensor has the thickness of a few human hairs and the
IV. Conclusion

A review was presented for in-body wireless medical devices (implantables, ingestibles, injectables), addressing the state-of-the-art technology, and discussing future opportunities. Overall, design of in-body devices is highly challenging, and needs to concurrently address concerns related to operation frequency selection, antenna design, powering, and biocompatibility. Currently, extensive research efforts are pursued to address such technological concerns, along with developing novel sensing methods, materials, and, eventually, new clinical applications for in-body devices. Overall, in-body devices are opening up new opportunities for medical prevention, prognosis, and treatment that quickly outweigh any design challenges and/or concerns on their invasive nature.

In the future, unobtrusive in-body devices are envisioned to collect a multitude of physiologic data from the early years of each individual. Babies, children, and young healthy people would employ such unobtrusive devices to monitor heart rate, physical activity, nutritional status, calories burned, sleep duration, organ function, breathing rate, etc. Eventually, in the case of medical need, healthcare data collected over the years would enable personalized and, thus, much more efficient and cost-effective intervention. This big-data approach aims to enable a shift from reactive and symptom-based medicine to a proactive healthcare model. Applications are numerous, ranging from elderly monitoring to monitoring individuals in developing countries or individuals in the military, space, and sports arenas.

REFERENCES


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