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NOTE

A miniature bidirectional telemetry system for *in vivo* gastric slow wave recordings

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Abstract
Stomach contractions are initiated and coordinated by an underlying electrical activity (slow waves), and electrical dysrhythmias accompany motility diseases. Electrical recordings taken directly from the stomach provide the most valuable data, but face technical constraints. Serosal or mucosal electrodes have cables that traverse the abdominal wall, or a natural orifice, causing discomfort and possible infection, and restricting mobility. These problems motivated the development of a wireless system. The bidirectional telemetric system constitutes a front-end transponder, a back-end receiver and a graphical user interface. The front-end module conditions the analogue signals, then digitizes and loads the data into a radio for transmission. Data receipt at the back-end is acknowledged via a transceiver function. The system was validated in a bench-top study, then validated *in vivo* using serosal electrodes connected simultaneously to a commercial wired system. The front-end module was $35 \times 35 \times 27$ mm^3 and weighed 20 g. Bench-top tests demonstrated reliable communication within a distance range of 30 m, power consumption of 13.5 mW, and 124 h operation when utilizing a 560 mAh, 3 V battery. *In vivo*, slow wave frequencies were recorded identically with the wireless and wired reference systems (2.4 cycles min^{-1}), automated activation time detection was modestly better for the wireless system (5% versus 14% FP rate), and signal amplitudes were modestly higher via the wireless system (462 versus 386 μV; $p < 0.001$). This telemetric system for slow wave acquisition is reliable, power efficient, readily portable and potentially implantable. The device will

enable chronic monitoring and evaluation of slow wave patterns in animals and patients.

Keywords: wireless monitoring, gastric electrical activity, dysrhythmia, electrogastrography

(Some figures may appear in colour only in the online journal)

1. Introduction

Stomach contractions are initiated and coordinated by an underlying bioelectrical activity, termed slow waves. Slow waves are generated and propagated by a specialized cell type in the gastrointestinal (GI) tract wall, termed interstitial cells of Cajal (Huizinga and Lammers 2009). Aberrant slow wave patterns (dysrhythmias) have been associated with gastric dysmotility in several significant gastric disorders, notably gastroparesis and functional dyspepsia (Lin *et al* 2010, Leahy *et al* 1999).

Chronic studies in awake animals and patients, in fasted and fed states, are needed to better elucidate the pathophysiological significance of gut electrical abnormalities (Ver Donck *et al* 2006, O'Grady *et al* 2011a, Song *et al* 2011). Slow wave recordings taken directly from the stomach provide more reliable and descriptive data than cutaneous recordings (electrogastrography; EGG), however, are invasive and, therefore, face greater technical constraints. One important issue is that serosal or mucosal recording systems currently transmit signals through lead wires traversing either through the abdominal wall or a natural orifice (Du *et al* 2009, Lin *et al* 2011, Coleski and Hasler 2009). These wires can act as a conduit for infection, induce discomfort, and connect to bulky acquisition systems that restrict mobility (Ver Donck *et al* 2006, Albert *et al* 2010).

Wireless technology could eliminate the need for wired recording systems, offering a better solution for *in vivo* monitoring. Telemetric systems are established in other fields including electroencephalography, electromyography and electrocardiography (Farajidavar *et al* 2011, Joshi *et al* 2005). A capsule telemetry system was recently developed for acquiring recordings from the luminal surface of the small intestine, during transit through the GI tract (Woo and Cho 2010), and a telemetry system for cutaneous EGG has previously been presented (Haddab and Laghrouche 2009). However, to the best of our knowledge, no wireless system presently exists that is suitable for use in chronic invasive slow wave recordings, such as that could allow for the reliable identification and monitoring of gastric dysrhythmias.

An ideal wireless system should be small, portable, implantable and power efficient, while being reliable and dependable. To these ends, we have developed and validated a telemetric system prototype for recording gastric slow wave data.

2. Methods

2.1. System design

A bidirectional wireless system was developed constituting a front-end transponder, a back-end receiver and a custom-made graphical user interface (GUI). Figure 1(a) shows a block diagram of the system. The front-end module of the prototype was designed to acquire data from four channels, and consisted of an analogue board and a wireless system on-chip (nRF24Le1,

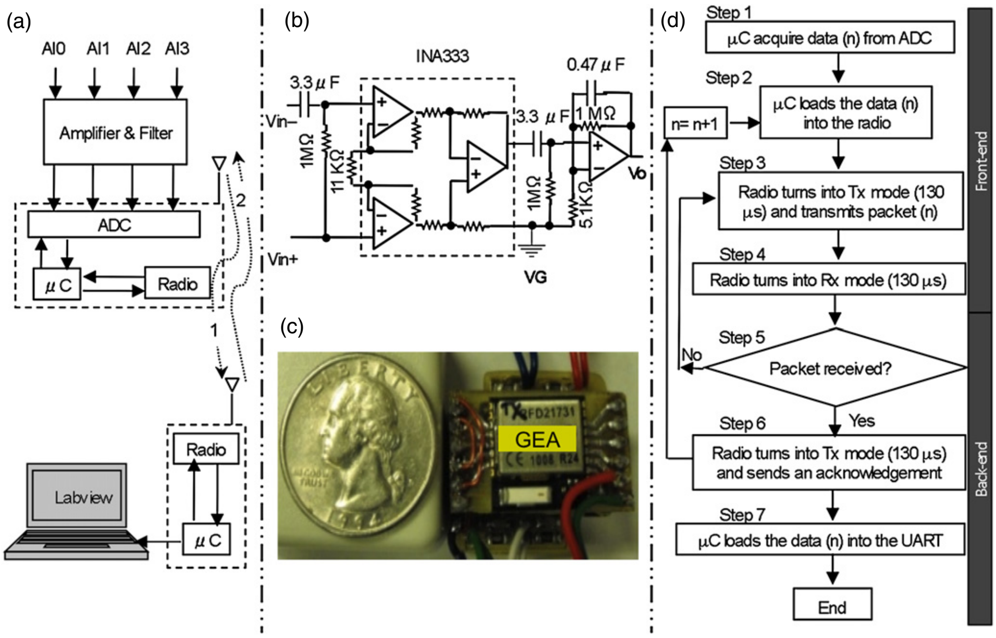

Figure 1. The new telemetric system. (a) Schematic block diagram of the system design. AI0–4: electrode channels; ADC: analogue-to-digital converter; μC: micro-controller. (b) Analogue front-end comprising filters and amplifiers. (c) The fabricated front-end in comparison to a US quarter. (d) Flowchart for bidirectional transmission.

Nordic Semiconductor), which includes an analogue-to-digital converter (ADC), a micro-controller (μC) and a 2.4 GHz transceiver. Signals passed through a high-pass filter (0.05 Hz) to an instrumentation amplifier (INA333; Texas Instruments) with a gain of 10, then to a second-order band-pass filter (0.05–0.3 Hz) with a gain of 196 (figure 1(b)).

The filtered signals were sampled at 8 Hz and digitized, then loaded into data packets and sent by the transceiver, which utilized Gaussian frequency-shift keying modulation. The fabricated front-end is shown in figure 1(c) compared to a US quarter. Packets were received in the back-end transceiver and the microcontroller unloaded the data and sent them to a computer via universal asynchronous receiver/transmitter (UART; 500 kBaud) communication, while transmitting a receipt acknowledgment packet back to the transmitter. A GUI was designed to process and display the signals in real time, and data was stored for off-line analysis.

To increase reliability, the microcontroller on both ends executed a series of commands shown in figure 1(d). After the microcontroller in the front-end acquired data from ADC (step 1), it loaded the data into the transceiver radio (step 2). It took 130 μs for the radio to turn into the transmitting mode and send the data packets wirelessly (step 3). The radio then returned back to the receiving mode, which took another 130 μs (step 4), while simultaneously the back-end radio looked for data packets (step 5). If the data packet was received, the device turned into the transmitting mode again and sent an acknowledgment to the front-end (step 6), while loading the packet onto the UART to be sent to the computer (step 7) as the microcontroller on the front-end prepared the next packet. If the packet was not received by the back-end, the microcontroller in the front-end loaded the same packet into the radio to be sent again (back to step 3) until attainment was confirmed. The retransmitting process mainly depended on the sampling rate in the front-end and the time for each packet to travel on-air (TOA), where TOA = (Packet length)/(Air data rate).

Each packet was composed of one preamble byte, 3–5 address bytes, payload of up to 32 bytes, and 1–2 bytes for cyclic redundancy check. The air data rate and the data packet length were chosen to be 1 Mbps and 4 bytes, respectively; hence, the TOA was 96 μs maximum, which is much shorter than the sampling period of 125 ms.

2.2. Validation methods

The system was first validated in a bench-top study, and then in a separate *in vivo* study in an anesthetized canine model. In the bench-top experiments, sinusoidal waveforms of known amplitudes and frequencies were fed into the transmitter and recorded at the receiver.

Ethical approval for the *in vivo* dog study was granted by the University of Mississippi Medical Center (UMMC) review committee. The canine model was chosen because canine gastric slow wave activity resembles human gastric electrical activity in pattern and morphology (Lammers *et al* 2009). A male hound dog of weight 23 kg was used. The surgical and anesthetic methods were the same as those recently described in detail in another recent study (Egbuji *et al* 2010). The anesthetic was administered after an overnight fast, and an upper midline laparotomy was performed. Vital signs were continuously monitored and temperature was maintained in the physiological range by the use of a heating pad and blankets. The animal was euthanized at the end of the study while still under anaesthesia.

Serosal slow wave data were acquired from the canine distal corpus using a flexible printed circuit board (PCB) array, with circular gold contacts with a 0.3 mm diameter and copper connection lines embedded in a polyimide ribbon base (Du *et al* 2009, O'Grady *et al* 2011b). The array was positioned flush with the serosa on the anterior stomach, midway between the curvatures, and just proximal to the corpus–antrum border (as defined by the nerves of Laterjet). The flexible PCB was attached to a ribbon cable, which was connected simultaneously to the novel wireless system and a commercial system (BioSemi, The Netherlands), through a signal splitter. After placement of the recording array, the wound edges were opposed and sutured closed, in order to evaluate for potential signal attenuation by absorption and scattering in the tissue layers surrounding the device.

Analysis was performed in the Gastrointestinal Electrical Mapping Suite (GEMS v1.4) (Yassi *et al* 2012). Wired data was down-sampled to 30 Hz and pre-processed with moving median and Savitzky–Golay filters to control drift and high-frequency noises (Paskaranandavadivel *et al* 2011). Individual slow wave events were automatically detected with the falling-edge variable threshold (FEVT) method, followed by manual review and correction (Erickson *et al* 2010). Slow wave events were marked at the point of maximal negative gradient (the activation time), which corresponds to the arrival of the wavefront directly under the electrode (O'Grady 2012). Outcomes from the wireless device and the commercial wired device were compared by frequency, FEVT false-positive (FP) detection rate, activation times and signal amplitudes, to provide information on the accuracy, reliability and quality of recordings. Slow wave frequencies were determined by fast-Fourier transform. Student's t-test was used to evaluate statistical difference (significance threshold $p < 0.05$).

3. Results

The encapsulated front-end module was $35 \times 35 \times 27$ mm^3 and weighed 20 g with a battery. Figure 1(c) shows the top view of the device.

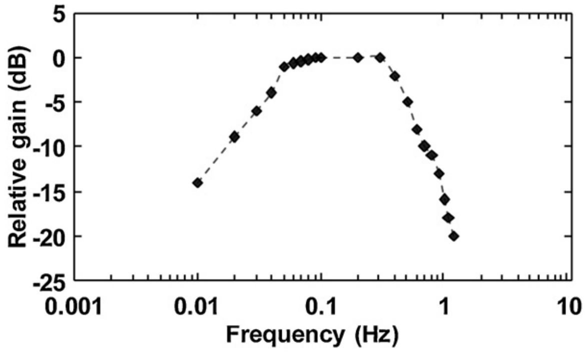

Figure 2. Bode plot of the wireless system response to sinusoidal waveforms generated at various frequencies.

3.1. Bench-top study outcomes

In the bench-top experiments, transmission and receipt of signals were successfully achieved at a distance up to 30 m. The device consumed 13.5 mW and functioned consistently for 124 h based on a 560 mAh, 3 V cell coin battery. Various sinusoidal waveforms were fed into the transmitter and recorded in the receiving station. Figure 2 shows the resultant system spectral response when the signal amplitude was chosen as 500 μV and the frequency was varied from 10 mHz–1 Hz. The system had an acceptable band-pass response in the range of 0.05–0.3 Hz, which matched the design.

3.2. In vivo study outcomes

The wireless and wired systems were used to acquire the slow wave signals side-by-side for 90 min. The results showed that the novel wireless system could record signals comparable to the commercial wired device. An overlay from a representative segment of 315 s in the signals recorded by both devices is shown in figure 3. The wirelessly recorded events showed a slightly steeper down-stroke than those recorded via the wired system, meaning that the FEVT algorithm consistently marked activation times slightly earlier than for the wired device data (mean absolute error = 0.57 s). Extracellular amplitudes were modestly higher for the wireless system (462 (SD 37) versus 386 (SD 47) μV; $p < 0.001$).

Across a continuous representative 600 s segment of *in vivo* data, the dominant slow wave frequency for the wired device, by fast-Fourier transform, was 0.04 Hz (2.4 cycles min^{-1}), which was identical to the frequency recorded by the wireless system (2.4 cycles min^{-1}; $p > 0.99$) (figure 4). The FEVT detection algorithm performance was higher for the wireless device because the designated sampling and filtering parameters effectively reduced competing noises (5% versus 14% FP rate).

4. Discussion

A bidirectional telemetry system has been developed and validated for monitoring gastric slow wave activity. This device is the first to enable slow wave recordings to be transmitted wirelessly through the tissues and skin from the stomach, with a sufficiently high signal quality for detecting individual slow wave activation times. The system was shown to be highly reliable and power efficient, and its small size makes it portable and suitable for implantation.

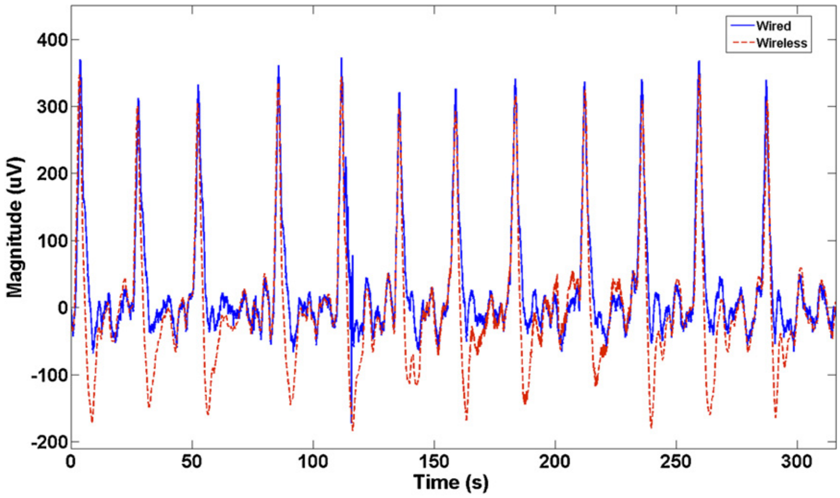

Figure 3. Wired (blue/solid line) and wireless (red/dashed line) *in vivo* signal overlay showing a very similar performance between the two devices.

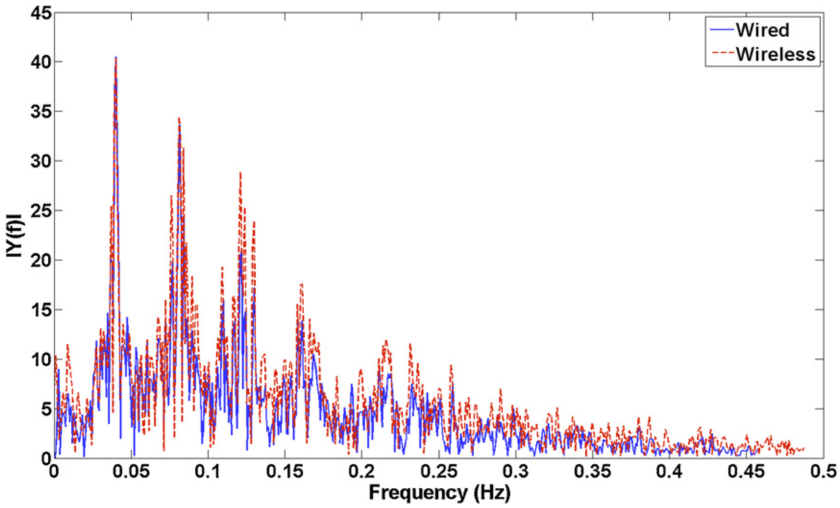

Figure 4. Fast-Fourier transform analysis of the *in vivo* wired (blue/solid line) and wireless (red/dashed line) data showing the dominant 0.04 Hz signal frequency (recorded identically between the two systems) and associated harmonics.

Importantly, the transmitted data closely matched the reference wired data, without signal distortion due to tissue absorption (Christ *et al* 2006). The signal integrity of the slow wave recordings was shown by validation to be of high quality, and reliability was ensured by the acknowledgment function in transmission. The low sampling rate provides a 125 ms quiet time for the transceiver operation, in which there was a 260 μs delay in the radio mode switching and a 96 μs period for TOA, meaning data could potentially be retransmitted up to 350 times before the next set of data appears to guarantee reception.

The first filter stage prevented saturation in the INA333 amplifier. The inbuilt low-pass filter setting of 0.3 Hz was found to be adequate for slow wave sampling, and automated slow wave detection was shown to be highly accurate. Another type of gastric electrical activity, termed 'spikes' also occurs in GI smooth muscles, being episodes of sharp Ca^{2+} influx associated with more vigorous contractions, particularly occurring in the fed state (Lammers *et al* 2009, Sanders 2008). The present device was not designed to evaluate spike potentials, because it is slow waves and not spikes that have been primarily associated with aberrant electrical activity in studies (Lammers *et al* 2008b, O'Grady *et al* 2011a). However, the low-pass filter could be tuned to allow spike detection or to detect a wider frequency band of slow wave data, if desirable in the future design. A higher sampling frequency may also be needed to effectively detect spikes (Lammers *et al* 2008a), which could be accommodated by reducing the number of retransmissions.

The focus of this study was on the technical development and validation of the wireless device, including its transmission capabilities and accuracy. A short *in vivo* testing period was therefore sufficient for the current work; however, in future, the front-end of the device will be hermetically sealed in order to conduct experiments in chronic preparations. In the current study, the recording included a period of bradygastric activity; 2.4 cycles min^{-1} being lower than the typical canine frequency of around 5 cycles min^{-1} (Lammers *et al* 2009). Stable bradygastric activity of this type is known to occur in dogs, and may be spontaneous or may reflect the experimental conditions (Qian *et al* 2003). Although tachygastria was not evaluated in this study, it is anticipated that the adjustability in frequency response of our system will also be well suited for detecting high-frequency slow wave activities (e.g. figure 2).

Invasive acquisition from the target organ provides a superior quantity and quality of data to cutaneous electrogastrography (O'Grady *et al* 2010, Lammers *et al* 2008b), and it is anticipated that this wireless system will be usefully applied in animal and clinical studies. Large animal recordings have previously been conducted using wires tunneled percutaneously and performed during periods when the animals were confined (e.g. (Ver Donck *et al* 2006, Xing *et al* 2003)). An implantable telemetry system will enable continuous monitoring in versatile conditions. The current battery life of 5 days could be extended by inductive recharging or a standby mode in the transceiver to facilitate more prolonged studies.

The greatest potential application that we perceive for this system is in patient diagnostic monitoring. Dysrhythmias have been associated with several motility disorders; however, their functional and symptomatic significance remains incompletely understood (Parkman *et al* 2003). Current investigations have been mainly limited to wired studies via oral, nasogastric, transcutaneous or PEG placement (Coleski and Hasler 2009, Lin *et al* 1998, Ayinala *et al* 2005). With further miniaturization, which is technically feasible, the device could be coupled to endoscopic recording electrodes (e.g. (Coleski and Hasler 2009, Ayinala *et al* 2005)), introduced into the patient's stomach via minimally invasive endoscopic intubation, and attached securely to the mucosa by endoclips (e.g. (Deb *et al* 2012)). In this way, the device could allow routine minimally invasive patient recordings for several days in both fasted and fed states.

Currently, the device is limited to four-channel recording, validated by individual channel recordings. Four-channel capacity is sufficient to provide useful localized information on slow wave frequency, amplitude and velocity, in the form of a 'miniature-activation map', so as to guide dysrhythmia identification in experimental and clinical studies (O'Grady *et al* 2009). However, recent work has shown that dysrhythmic slow wave patterns may be spatially complex, such that high-resolution (multi-electrode) analyses are most ideal for their proper characterization (Lammers *et al* 2008b, O'Grady *et al* 2011a). For this purpose, communication channels can be extended to 8 or 16 channels in the transceiver chip used in this prototype allowing multi-electrode signal transduction since there is sufficient bandwidth. Each transceiver can also be programmed with different individual identification; therefore, multiple modules can be implanted within the body for recording from 16, 32 and even 128 electrodes.

Acknowledgments

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