Published in final edited form as:

Neurogastroenterol Motil. 2015 April ; 27(4): 580–585. doi:10.1111/nmo.12515.

Multi-channel wireless mapping of gastrointestinal serosal slow wave propagation

Niranchan Paskaranandavadivel¹, Rui Wang², Shameer Sathar¹, Gregory O'Grady¹, Leo K Cheng^{1,3}, and Aydin Farajidavar²

¹Auckland Bioengineering Institute, University of Auckland, New Zealand ²School of Engineering and Computing Sciences, Department of Electrical and Computer Engineering, New York Institute of Technology, Old Westbury, New York, USA ³Department of Surgery, Vanderbilt University, Nashville, Tennessee, USA

Abstract

Background—High-resolution (HR) extracellular mapping allows accurate profiling of normal and dysrhythmic slow wave patterns. A current limitation is that cables traverse the abdominal wall or a natural orifice, risking discomfort, dislodgement or infection. Wireless approaches offer advantages, but a multi-channel system is required, capable of recording slow waves and mapping propagation with high fidelity.

Methods—A novel multi-channel (n=7) wireless mapping system was developed and compared to a wired commercial system. Slow wave signals were recorded from the porcine gastric and intestinal serosa *in-vivo*. Signals were simultaneously acquired using both systems, and were filtered and processed to map activation wavefronts. For validation, the frequency and amplitude of detected events were compared, together with the speed and direction of mapped wavefronts.

Key Results—The wireless device achieved comparable signal quality to the reference device, and slow wave frequencies were identical. Amplitudes of the acquired gastric and intestinal slow wave signals were consistent between the devices. During normal propagation, spatiotemporal mapping remained accurate in the wireless system, however, during ectopic dysrhythmic pacemaking, the lower sampling resolution of the wireless device led to reduced accuracy in spatiotemporal mapping.

Conclusions and Inferences—A novel multichannel wireless device is presented for mapping slow wave activity. The device achieved high quality signals, and has the potential to facilitate chronic monitoring studies and clinical translation of spatiotemporal mapping. The current

Corresponding Author, Name: Aydin Farajidavar, afarajid@nyit.edu, Address: New York Institute of Technology, P.O. 8000 Northern Blvd., Harry Schure Hall, Room 226B, Old Westbury, NY 11568, Phone: +1(516) 686-4014, Fax: +1(516) 686-7439.

Disclosures

The authors have no competing interests.

Author contributions

Device design and development: AF, RW, SS. Data acquisition: NP, AF, LKC, SS. Data analysis and interpretation: NP, AF, LKC, GOG. Manuscript drafting and approval: NP, RW, SS LKC, AF, GOG.

implementation may be applied to detect normal patterns and dysrhythmia onset, but HR mapping with finely spaced arrays currently remains necessary to accurately define dysrhythmic patterns.

Keywords

Gastric electrical activity; wireless signal acquisition; dysrhythmia

Introduction

Slow wave activity, which is generated and propagated by the interstitial cells of Cajal, contributes to the coordination of gastrointestinal (GI) motility (1, 2). In recent years, extracellular high-resolution (HR) spatiotemporal mapping has been advanced to visualize and quantify slow wave propagation patterns (3, 4). These studies have revealed complex spatial patterns of slow wave dysrhythmia that may contribute to GI motility disorders such as gastroparesis (5–7).

One of the limitations of the current implementation of HR mapping is the large number of cables required to connect the electrodes to the data acquisition system. This setup limits the clinical translation of slow wave HR mapping, and is unsuitable for chronic monitoring of GI slow wave activity in animal models in fasted and fed states. The passage of wires from the body wall may cause discomfort and infection, and is prone to displacement (8, 9). Wireless technology has been advocated as a solution to overcome these barriers (10). Wireless approaches have successfully been employed for many years in other fields of electrophysiology such as in clinical cardiology (11) and neurology (12, 13), and have more recently been practiced to the GI field for capsule endoscopy (14) and wireless charging of gastric implantable stimulators (15).

Therefore, to expand and improve the potential clinical translation and experimental applications of slow wave monitoring techniques, a proof-of-concept wireless approach to record GI slow waves was recently proposed (16). In this report, we now present a novel multi-channel wireless acquisition system for GI mapping, which now allows seven channels of simultaneous recording with improved technical specifications. The wireless system was validated against a reference wired commercial acquisition system, and signal quality and slow wave metrics were assessed to inform future clinical and experimental applications.

Material and Methods

Ethical approvals were granted by the University of Auckland Animal Ethics Committee. Experiments were performed in female weaner cross-breed pigs ($n=6$, 36.2 ± 4.7 kg), and anaesthesia, surgical access and monitoring were undertaken according to our previously published methods (17). In brief, the pigs were anaesthetized using Tiletamine HCl 50 mg mL^{-1} and Zolazepam HCl 50 mg mL^{-1} , and maintained with Isoflurane (2.5–5% with an oxygen flow of 400 mL), after which a mid-line laparotomy was performed, followed by slow wave recording for 5–16 minutes.

A 32 channel contact silver-wire electrode array was applied sequentially to the serosal surface of the stomach (mid-corpus to antrum) and the duodenum, and held in place using warm saline-soaked gauze. All 32 channels of unipolar recordings were acquired using the ActiveTwo System (Biosemi, Amsterdam, Netherlands) with a sampling frequency of 512 Hz.

From the HR contact electrode, the analog signals from seven of the 32 channels were divided and used as input to the wireless transmitter system located next to the animal (Fig. 1). The wireless device receives the signals from seven distinct analog inputs via the contact electrodes, conditions the signals, digitizes, and wirelessly transmits the digital signals to a receiver via a 2.4 GHz transceiver (Fig. 1). The receiver was in turn connected to a computer where the data was stored for offline analysis. During the conditioning, the analog signals were amplified with a gain of 66dB and band pass filtered (0.016-1.6 Hz). The wireless signals were sampled at 100 Hz per channel with the resolution of 8 bits. The transmitter measured 62×20×7 mm, weighed 16 g and can communicate up to 10 m in the open field. The power consumption of the wireless system was 26 mW and it can operate continuously for more than 50 hours, based on a 3V, 620mAh coin cell battery. Experiments were undertaken in 6 pigs, with a median recording time of 420 seconds for gastric and intestinal recordings (gastric recording range: 300-960 seconds, intestinal recording range: 240-540 seconds).

The raw slow wave signals acquired from both system were downsampled to 30 Hz and filtered using a 20-second moving median to eliminate baseline wander and Savitzky-Golay filter (polynomial order: 9, window size: 1.7s) to eliminate high-frequency noise (18, 19). Slow wave events were marked and grouped into their associated wavefronts using the GEMS software (20). Velocity vectors (speed and angle) for the activation wavefront were computed via a polynomial estimate fit to the activation time wavefront:

$$T(x, y) = a \cdot xy + b \cdot x + c \cdot y + d, \quad \text{Eq 1}$$

where $T(x, y)$ represents the activation time of the wavefront at the contact electrode array at x and y coordinates and a, b, c and d are the coefficients of the second order equation, which were determined through a least squares fit (21, 22). The amplitudes of the slow wave events were determined by taking the difference between the maximum and minimum of the slow wave deflection event, determined by calculating the derivative of the signal using a 3 second window around the marked activation time (18). The results are reported as the mean of the means $\pm$ standard error. Student's t-test was performed to test differences in several metrics (frequency, amplitude, velocity) between the two systems.

Results

The signal traces from both systems showed clear agreement in terms of frequency and amplitude (Table 1). Fig. 2(A, B) shows gastric and intestinal slow wave signals, taken simultaneously from the both system, to illustrate signal fidelity. Overall, the slow wave signal amplitude, morphology and timing were statistically consistent across the two systems for normal and arrhythmic activity. There was no significant difference in slow

wave amplitude between both systems (mean difference: 0.01mV for gastric recordings and 0.004mV for intestinal recordings, Table 1).

Slow wave activation time profiles were also determined from the wireless and wired signals, from which velocity vectors were computed for the propagation pattern as shown in Fig. 2(C,D). The propagation profile in Fig. 2(C) demonstrates normal gastric antegrade propagation from the mid-corpus towards the antrum. During normal propagation, the calculated velocity between both systems was closely correlated, showing a minimal speed difference of 0.3 mm/s and a vector angle difference of 3° for gastric propagation and a speed difference of 0.3 mm/s and a vector angle difference of 0.3° for intestinal propagation.

Ectopic gastric slow wave activity was recorded during 50% of the recording time (150/300 seconds) in one study, without surgical or drug intervention as described in this model (23), providing the opportunity to also compare arrhythmic signals. Fig. 2(D) shows an example of ectopic propagation that occurred across five cycles, where there are three dominant directions; antegrade and retrograde at lower speed, and circumferentially at a higher speed (24). The velocity vectors from the wireless acquisition matched with those of the dominant propagation direction (red arrows; Fig. 2(C,D) (Table 1). During dysrhythmic propagation, however, the decreased spatial sampling of the wireless device (7 vs 32 electrodes) led to an increased relative velocity vector difference (Table 1), as illustrated by the speed difference of 5 mm/s and a vector angle difference of 27° for the data in Fig 2D.

Discussion

HR electrical mapping provides significant insights into patterns of GI slow wave activity (6, 25, 26). We developed and validated a wireless multi-channel acquisition system for mapping GI slow wave propagation. Slow wave activity from the serosal surface of the stomach and intestine was recorded using the wireless system, with the frequency and amplitude being consistent, along with reliable velocity estimates for normal propagation patterns. Gastric dysrhythmic patterns were also recorded which registered analogous speeds, but not directionality due to the low spatial resolution. It is plausible that surgery, anaesthesia, and gastric handling may have contributed to the spontaneous dysrhythmias seen in this pig model (23). As the data for this technical note were obtained from an acute anaesthetized weaner pig, further work is required to extrapolate the significance of gastric slow wave spatial dysrhythmias to chronic gastroparesis patients with ICC deficiency, without the influence of surgery and anaesthesia. Nonetheless, these slow wave patterns provide an excellent opportunity to measure complex spatial dysrhythmias, similar to what has been observed in gastroparesis patients with reduced ICC numbers (6). Changes in frequency, amplitude and speed alone are a useful guide to dysrhythmic onset (24), but a HR electrode array with fine spacing was still shown to be needed to accurately define dysrhythmic patterns. If this issue is found to be limiting in future applications, then more wireless channels can be added, and future studies can be performed to help define the optimal electrode spacing and distribution for pattern detection using a lower-density array (5). In this study, the wireless transmitter was limited to 7 channels, in part due to size constraints. Currently, each of the 7 channels has a dedicated analog conditioning module. In future designs we will incorporate multiplexers which allows a single conditioning

module to digitize multiple input channels, hence decreasing the size and allowing for increased channel count.

In comparison to our previous proof-of-principle prototype (16), this new system features a greater number of input channels, a higher sampling frequency, an improved signal quality with wider pass-band conditioning, a wider communication band-width, and the ability to map the direction of propagation. The increase in sampling frequency from 8 Hz in the initial prototype to 100 Hz also provides the opportunity for GI spike activity mapping, which may be useful in chronic fed-state studies (9). In addition, this is the first study to record wireless intestinal slow wave signals. This system eliminates the need for bulky electrode cables that traverse the abdominal wall, oral or nasal cavity, which may cause discomfort, dislodgement or infection. This technology will therefore facilitate HR mapping in chronic animal models and awake patients, for example, to achieve clinicopathological correlation studies and to investigate novel therapies (6).

Currently the wireless system can record and transmit data continuously for 50 hours. This duration could be readily increased for long-term studies by recording and transmitting intermittently or logging data at pre-defined intervals. Hermetic sealing, sterilization and biocompatibility studies of the wireless system will allow for chronic implantation. Further development of the wireless system may include increasing the channel count and improving the power efficiency. Wireless charging technology, similar to that used in a recently developed gastric stimulator, will also be investigated (15).

In conclusion, a novel multi-channel wireless system has been developed and the use of the wireless spatiotemporal mapping of slow wave activity has been validated. The strengths and shortcomings of the system and methodologies revealed the future directions towards clinical translation in chronic animal models and awake patients.

Acknowledgements

We thank Lynley Nisbet, Timothy R. Angeli, Peng Du and Rachel Berry for assisting with data collection.

Funding

This work was funded, in part, by grants from the National Science Foundation (ECCS 1337965), the New York Institute of Technology Institutional Support for Research and Creativity fund and the Health Research Council of New Zealand, NIH (R01 DK64775).

References

1. Huizinga JD, Lammers WJ. Gut peristalsis is governed by a multitude of cooperating mechanisms. *Am J Physiol Gastrointest Liver Physiol*. 2009; 296(1):G1–G8. [PubMed: 18988693]
2. O'Grady G, Du P, Cheng LK, Egbuji JU, Lammers WJ, Windsor JA, Pullan AJ. Origin and propagation of human gastric slow-wave activity defined by high-resolution mapping. *Am J Physiol Gastrointest Liver Physiol*. 2010; 299(3):G585–G592. [PubMed: 20595620]
3. Cheng LK, Du P, O'Grady G. Mapping and modeling gastrointestinal bioelectricity: from engineering bench to bedside. *Physiology*. 2013; 28(5):310–317. [PubMed: 23997190]
4. Lammers WJ, al-Kais A, Singh S, Arafat K, el-Sharkawy TY. Multielectrode mapping of slow-wave activity in the isolated rabbit duodenum. *J Appl Physiol*. 1993; 74(3):1454–1461. [PubMed: 8482690]

5. Paskaranandavadivel N, Gao J, Du P, O'Grady G, Cheng LK. Automated classification and identification of slow wave propagation patterns in gastric dysrhythmia. *Ann Biomed Eng.* 2014; 42(1):177–192. [PubMed: 24048711]
6. O'Grady G, Angeli TR, Du P, Lahr C, Lammers WJ, Windsor JA, Abell TL, Farrugia G, et al. Abnormal initiation and conduction of slow wave activity in gastroparesis defined by high-resolution electrical mapping. *Gastroenterology.* 2012; 143(3):589–598. e3. [PubMed: 22643349]
7. Lammers WJEP, Ver Donck L, Stephen B, Smets D, Schuurkes JAJ. Focal activities and re-entrant propagations as mechanisms of gastric tachyarrhythmias. *Gastroenterology.* 2008; 135(5):1601–1611. [PubMed: 18713627]
8. Albert NM, Hancock K, Murray T, Karafa M, Runner JC, Fowler SB, Nadeau CA, Rice KL, et al. Cleaned, ready-to-use, reusable electrocardiographic lead wires as a source of pathogenic microorganisms. *Am J Crit Care.* 2010; 19(6):e73–e80. [PubMed: 21041188]
9. Ver Donck L, Lammers WJ, Moreaux B, Smets D, Voeten J, Vekemans J, Schuurkes J, Coulie B. Mapping slow waves and spikes in chronically instrumented conscious dogs: implantation techniques and recordings. *Med Biol Eng Comput.* 2006; 44(3):170–178. [PubMed: 16937158]
10. Farajidavar A, Seifert JL, Bell JE, Seo Y-S, Delgado MR, Sparagana S, Romero MI, Chiao J-C. A wireless system for monitoring transcranial motor evoked potentials. *Ann Biomed Eng.* 2011; 39(1):517–523. [PubMed: 20824343]
11. Hindricks G, Pokushalov E, Urban L, Taborsky M, Kuck K-H, Lebedev D, Rieger G, Pürerfellner H. Performance of a new leadless implantable cardiac monitor in detecting and quantifying atrial fibrillation results of the XPECT trial. *Circ Arrhythm Electrophysiol.* 2010; 3(2):141–147. [PubMed: 20160169]
12. Borton DA, Yin M, Aceros J, Nurmikko A. An implantable wireless neural interface for recording cortical circuit dynamics in moving primates. *J Neural Eng.* 2013; 10(2):026010. [PubMed: 23428937]
13. Farajidavar A, Hagains CE, Peng YB, Chiao J. A closed loop feedback system for automatic detection and inhibition of mechano-nociceptive neural activity. *IEEE Trans Neural Syst Rehabil Eng.* 2012; 20(4):478–487. [PubMed: 22692935]
14. McCaffrey C, Chevalerias O, O'Mathuna C, Twomey K. Swallowable-capsule technology. *IEEE Pervasive Comput.* 2008; 7(1):23–29.
15. Deb S, Tang S-J, Abell TL, Rao S, Huang W-D, To SDF, Lahr C, Chiao J-C. An endoscopic wireless gastrostimulator (with video). *Gastrointest Endosc.* 2012; 75(2):411–415.e1. [PubMed: 22248609]
16. Farajidavar A, O'Grady G MN, Rao SK, Cheng L, Abell T, Chiao J-C. A miniature bidirectional telemetry system for in vivo gastric slow wave recordings. *Physiol Meas.* 2012; 33(6):N29. [PubMed: 22635054]
17. Egbuji JU, O'Grady G, Du P, Cheng LK, Lammers WJ, Windsor JA, Pullan AJ. Origin, propagation and regional characteristics of porcine gastric slow wave activity determined by high-resolution mapping. *Neurogastroenterol Motil.* 2010; 22(10):e292–e300. [PubMed: 20618830]
18. Paskaranandavadivel N, Cheng LK, Du P, O'Grady G, Pullan AJ. Improved signal processing techniques for the analysis of high resolution serosal slow wave activity in the stomach. *Conf Proc IEEE Eng Med Biol Soc.* 2011; 2011:1737–1740. [PubMed: 22254662]
19. Angeli TR, O'Grady G, Paskaranandavadivel N, Erickson JC, Du P, Pullan AJ, Bissett IP, Cheng LK. Experimental and automated analysis techniques for high-resolution electrical mapping of small intestine slow wave activity. *J Neurogastroenterol Motil.* 2013; 19(2):179–191. [PubMed: 23667749]
20. Yassi R, O'Grady G, Paskaranandavadivel N, Du P, Angeli TR, Pullan AJ, Cheng LK, Erickson JC. The gastrointestinal electrical mapping suite (GEMS): software for analyzing and visualizing high-resolution (multi-electrode) recordings in spatiotemporal detail. *BMC Gastroenterol.* 2012; 12:60. [PubMed: 22672254]
21. Bayly PV, KenKnight BH, Rogers JM, Hillsley RE, Ideker RE, Smith WM. Estimation of conduction velocity vector fields from epicardial mapping data. *IEEE Trans Biomed Eng.* 1998; 45(5):563–571. [PubMed: 9581054]

22. Fitzgerald TN, Rhee EK, Brooks DH, Triedman JK. Estimation of cardiac conduction velocities using small data sets. *Ann Biomed Eng.* 2003; 31(3):250–261. [PubMed: 12680723]
23. O'Grady G, Egbuji JU, Du P, Lammers WJ, Cheng LK, Windsor JA, Pullan AJ. High-resolution spatial analysis of slow wave initiation and conduction in porcine gastric dysrhythmia. *Neurogastroenterol Motil.* 2011; 23(9):e345–e355. [PubMed: 21714831]
24. O'Grady G, Du P, Paskaranandavadivel N, Angeli TR, Lammers WJ, Asirvatham SJ, Windsor JA, Farrugia G, et al. Rapid high-amplitude circumferential slow wave propagation during normal gastric pacemaking and dysrhythmias. *Neurogastroenterol Motil.* 2012; 24(7):e299–e312. [PubMed: 22709238]
25. Angeli TR, O'Grady G, Du P, Paskaranandavadivel N, Pullan AJ, Bissett IP, Cheng LK. Circumferential and functional re-entry of in vivo slow-wave activity in the porcine small intestine. *Neurogastroenterol Motil.* 2013; 25(5):e304–e314. [PubMed: 23489929]
26. Lammers WJ, Stephen B, Karam SM. Functional reentry and circus movement arrhythmias in the small intestine of normal and diabetic rats. *Am J Physiol Gastrointest Liver Physiol.* 2012; 302(7):G684–G689. [PubMed: 22207580]

Figure 1.

Schematic of the simultaneous wired and wireless mapping of gastric and intestinal slow wave propagation. (A) A multi-electrode array was placed on the serosal surface of the stomach or intestine and was connected to the ActiveTwo System. From the same electrode array, seven analog signals were divided and were also sent to the wireless transmitter as shown in (B); signals were then conditioned and digitized before wirelessly transmitted to the receiver.

Figure 2.

Simultaneous acquisition of slow wave signals by the wired and wireless system are illustrated in blue and red traces respectively. (A) and (B) shows the fidelity of the gastric and intestine slow waves recorded by the wireless system compared to the wired system. (C) and (D) show a normal antegrade and ectopic pattern of gastric slow wave propagation in terms of an isochronal map respectively.

Table 1

Quantitative metric comparisons. Average frequency, amplitude and propagation characteristics in terms of speed and angle of gastric and intestinal slow wave activity between the wired and wireless system. For amplitude and frequency, *n* is the number of slow wave events, while for velocity (speed and angle), *n* is the number of spatiotemporal maps that were analysed.

		Gastric			Intestine		
		Wired	Wireless	p value	n	Wired	Wireless
	Frequency (cpm)	3.0±0.2	3.0±0.2	---	130	16.21±0.3	16.21±0.3
	Amplitude (mV)	0.60±0.1	0.59±0.1	p>0.05	83	0.20±0.01	0.20±0.01
	Speed (mm/s)	7.4±1.0	7.7±1.3	p>0.05	26	19.0±0.9	19.3±1.0
Normal	Angle (°)	184±32	187±32	p>0.05	26	194±3	191±4
Ectopic	Speed (mm/s)	14.6±1.2	9.7±4.8	p>0.05	5	---	---
	Angle (°)	177±6	204±14	0.005*	5	---	---

A p value < 0.05 (shown as *) represents a difference across the data sets. The accuracy of the wireless mapping system was reduced during ectopic propagation due to the lower spatial sampling.