

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2022 June 27; 14(6): 528-631



MINIREVIEWS

- 528 Transarterial chemoembolization failure/refractoriness: A scientific concept or pseudo-proposition
Zhang S, Zhong BY, Zhang L, Wang WS, Ni CF
- 538 Indications for the surgical management of pancreatic trauma: An update
Pavlidis ET, Psarras K, Symeonidis NG, Geropoulos G, Pavlidis TE
- 544 Clinical application and research progress of extracellular slow wave recording in the gastrointestinal tract
Ding F, Guo R, Cui ZY, Hu H, Zhao G

ORIGINAL ARTICLE**Retrospective Cohort Study**

- 556 Predicting the outcome of closed-loop small bowel obstruction by preoperative characteristics
Toneman MK, de Kok BM, Zijta FM, Oei S, van Acker GJD, Westerterp M, van der Pool AEM
- 567 Transjugular intrahepatic portosystemic shunt with radioactive seed strand for main portal vein tumor thrombosis with cirrhotic portal hypertension
Yan XH, Yue ZD, Zhao HW, Wang L, Fan ZH, Wu YF, Meng MM, Zhang K, Jiang L, Ding HG, Zhang YN, Yang YP, Liu FQ

Retrospective Study

- 580 Prognostic significance of the preoperative hemoglobin to albumin ratio for the short-term survival of gastric cancer patients
Hu CG, Hu BE, Zhu JF, Zhu ZM, Huang C

META-ANALYSIS

- 594 Comparison between laparoscopic uncut Roux-en-Y and Billroth II with Braun anastomosis after distal gastrectomy: A meta-analysis
Jiao YJ, Lu TT, Liu DM, Xiang X, Wang LL, Ma SX, Wang YF, Chen YQ, Yang KH, Cai H

CASE REPORT

- 611 Intestinal perforation with abdominal abscess caused by extramedullary plasmacytoma of small intestine: A case report and literature review
Wang KW, Xiao N
- 621 Bowel intussusception caused by a percutaneously placed endoscopic gastrojejunostomy catheter: A case report
Winters MW, Kramer S, Mazairac AH, Jutte EH, van Putten PG

LETTER TO THE EDITOR

- 626** Important role of acute care surgery during pandemic time
Yang M, Zhang CY
- 629** Advances and effectiveness of the immunotherapy after liver transplantation
Vulasala SSR, Onteddu NK, Kumar SP, Lall C, Bhosale P, Virarkar MK

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Surgery*, Arun Prasad, FACS, FRCS (Ed), FRCS (Gen Surg), MBBS, Adjunct Professor, Doctor, Professor, Surgeon, Department of Minimal Access, Thoracoscopic, Bariatric and Robotic Surgery, Apollo Hospital, New Delhi 110044, India. surgerytimes@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS, World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc.*

INDEXING/ABSTRACTING

The *WJGS* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for *WJGS* as 2.505; IF without journal self cites: 2.473; 5-year IF: 3.099; Journal Citation Indicator: 0.49; Ranking: 104 among 211 journals in surgery; Quartile category: Q2; Ranking: 81 among 93 journals in gastroenterology and hepatology; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Rui-Rui Wu*; Production Department Director: *Xiang Li*; Editorial Office Director: *Ya-Juan Ma*.

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Peter Schemmer

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

PUBLICATION DATE

June 27, 2022

COPYRIGHT

© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Clinical application and research progress of extracellular slow wave recording in the gastrointestinal tract

Fan Ding, Run Guo, Zheng-Yu Cui, Hai Hu, Gang Zhao

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Jabbarpour Z, Iran; Perse M, Slovenia

Received: January 6, 2022

Peer-review started: January 6, 2022

First decision: March 12, 2022

Revised: March 21, 2022

Accepted: May 16, 2022

Article in press: May 16, 2022

Published online: June 27, 2022



Fan Ding, Hai Hu, Gang Zhao, Center of Gallbladder Disease, East Hospital of Tongji University, Shanghai 200120, China

Fan Ding, Hai Hu, Gang Zhao, Institute of Gallstone Disease, Tongji University School of Medicine, Shanghai 200331, China

Run Guo, Department of Ultrasonography, East Hospital of Tongji University, Shanghai 200120, China

Zheng-Yu Cui, Department of Internal Medicine of Traditional Chinese Medicine, East Hospital of Tongji University, Shanghai 200120, China

Corresponding author: Gang Zhao, PhD, Director, Center of Gallbladder Disease, East Hospital of Tongji University, No. 150 Jimo Road, Shanghai 200120, China. zhao_gang7@126.com

Abstract

The physiological function of the gastrointestinal (GI) tract is based on the slow wave generated and transmitted by the interstitial cells of Cajal. Extracellular myoelectric recording techniques are often used to record the characteristics and propagation of slow wave and analyze the models of slow wave transmission under physiological and pathological conditions to further explore the mechanism of GI dysfunction. This article reviews the application and research progress of electromyography, bioelectromagnetic technology, and high-resolution mapping in animal and clinical experiments, summarizes the clinical application of GI electrical stimulation therapy, and reviews the electrophysiological research in the biliary system.

Key Words: Gastrointestinal tract; Slow wave; Electromyography; High-resolution mapping; Bioelectromagnetic technology

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: The motility pattern of the gastrointestinal (GI) tract is fundamental in studying functional GI disorders. Extracellular recording has been used to characterize the generation and propagation of slow waves and abnormalities that may lead to GI motility disorders. This review focuses on the application and progress of extracellular recording techniques in the physiological and pathological state of the alimentary system.

Citation: Ding F, Guo R, Cui ZY, Hu H, Zhao G. Clinical application and research progress of extracellular slow wave recording in the gastrointestinal tract. *World J Gastrointest Surg* 2022; 14(6): 544-555

URL: <https://www.wjgnet.com/1948-9366/full/v14/i6/544.htm>

DOI: <https://dx.doi.org/10.4240/wjgs.v14.i6.544>

INTRODUCTION

The gastrointestinal (GI) tract is a complex organ that efficiently processes nutrients and waste. These tasks are facilitated by the phasic contractions resulting from a cyclical depolarization-repolarization cycle, known as electrical slow waves. The slow wave potential of the GI tract is generated by interstitial cells of Cajal (ICCs) distributed in the submucosa and smooth muscle layer of the GI wall and spreads to smooth muscle cells (SMCs), causing excitation-contraction coupling[1]. SMCs and ICCs are also electrically coupled with platelet-derived growth factor receptor alpha-positive (PDGFR α^+) cells, forming an integrated unit called the SMC-ICC-PDGFR α^+ cells (SIP) syncytium[2,3]. SIP cells provide pacemaker activity, propagation pathways for slow waves, transduction of inputs from motor neurons, and mechanosensitivity[4,5].

Alvarez *et al*[6] and Berkson *et al*[7] first recorded the extracellular slow wave potential of the stomach and small intestine, and proved the consistency between the frequency of slow wave and the rhythm of GI contraction. Over the past century, extracellular electrical recording technology has become one of the most critical methods to characterize the generation and propagation of slow wave and GI motility disorders[8]. The milestone research of GI extracellular slow wave recording is provided in Table 1. The limitation of electromyography (EMG) is the lack of temporal-spatial features of slow wave propagation, which has been proved to be an essential indicator of GI dysfunction[9]. In recent years, research on high-resolution (HR) mapping of GI mucosal slow wave using array matrix electrodes *in vivo* and a bioelectromagnetic technique for recording the magnetic field produced by GI electrical activity, has provided more accurate and reliable support for research on the role of GI dysrhythmia in digestive diseases.

This review explores the application and progress of extracellular recording techniques in the physiological and pathological states of the alimentary system.

GI ELECTROPHYSIOLOGY

In the GI tract, SMCs form gap junctions with two types of interstitial cells, ICCs and PDGFR α^+ cells, creating a highly integrated electrical SIP syncytium. Electrical coupling makes it very difficult to deduce the specific functions of one component in intact tissues, so the functions of SIP cells have benefitted from studies of particular cell types[10]. ICCs are organized into networks in the pacemaker regions of the GI tract[11]. Spontaneous electrical activity is generated by ICCs, which are electrically coupled to the SMCs[12,13]. Once a slow wave is generated, it regenerates and propagates actively through the ICC network. Depolarization of SMCs by slow wave enhances the open probability of L-type voltage-dependent calcium (Ca $^{2+}$) channels, resulting in the generation of Ca $^{2+}$ action potentials, which are superimposed upon the peaks of slow waves. Slow waves are actively propagated in GI muscle tissues, enabling the recruitment of thousands of SMCs to contract together or in sequence to generate segmental and peristaltic contractions. In normal condition, the PDGFR α^+ cells network runs parallel or even intercalates with that formed by the ICC network. PDGFR α^+ cells express small conductance calcium-activated potassium channel 3 (SK3) channels and P2Y1 receptors[14,15]. These proteins are essential for the purinergic inhibitory regulation of GI motility[5,16,17]. GI motility patterns are highly integrated behaviors requiring coordination between SMCs and utilizing regulatory inputs from interstitial cells (ICCs and PDGFR α^+ cells), neurons, and endocrine and immune cells[11,18].

Disorders of gastroduodenal function without an apparent organic cause, defined by the Rome IV criteria, are common, including functional dyspepsia, chronic nausea and vomiting, belching, and rumination disorders[19]. The resultant inefficiencies contribute to vast health and economic burden, considering societal prevalence rates of > 10% for functional dyspepsia and > 2% for chronic nausea and vomiting[20-22]. Diagnosing GI functional disorders remains challenging. Slow waves are omnipresent in GI organs, and motor activity is controlled, in part, by modulation of the frequency, amplitude, and

Table 1 Milestone research of extracellular gastrointestinal slow wave recording

Ref.	Year	Research type	Methods	Part of GI	Major advances
Alvarez <i>et al</i> [6]	1922	Rabbits	Monopolar electrode	Small intestine	First record the SW
Alvarez[32]	1922	Human	EKG	Abdominal wall	First electrogastrogram recording
Code and Marlett [89]	1974	Dogs	Multi-electrode	Stomach	First report gastric arrhythmia
Code <i>et al</i> [29]	1975	Dogs	Multi-electrode	Stomach and small intestine	Define the MMC
Hinder and Kell [54]	1977	Human	Multi-electrode	Stomach	First locate the gastric pacemaker
Di Luzio <i>et al</i> [90]	1989	Human	MGG	Stomach and small intestine	Noninvasively investigate the activity of the GI system
Miranda <i>et al</i> [91]	1992	Human	ACB	Stomach	Study stomach emptying model
Bradshaw <i>et al</i> [92]	2003	Rabbits	MGG	Stomach	Investigate gastric electrical activity under normal and vagotomized condition
Corá <i>et al</i> [76]	2005	Human	ACB	Stomach	Obtain a comprehensive knowledge of the behavior of pharmaceutical forms in the GI tract
Lammers <i>et al</i> [93]	2008	Dogs	HR mapping	Stomach	First observe the spatial origin and propagation patterns of SW arrhythmias
Bradshaw <i>et al</i> [68]	2009	Human	MGG	Stomach	Obtain spatiotemporal parameters of the gastric SW
Du <i>et al</i> [62]	2009	Pigs	HR mapping	Stomach	Design a new sterilized PCB electrode
O'Grady <i>et al</i> [66]	2009	Pigs and human	HR mapping	Stomach	Design a novel laparoscopic device for HR mapping
O'Grady <i>et al</i> [55]	2010	Human	HR mapping	Stomach	The most comprehensive study of the gastric conduction system
Farajidavar <i>et al</i> [52]	2012	Dogs	Multi-wireless modules	Stomach	Design a bidirectional wireless system for SW recording
Calabresi <i>et al</i> [72]	2015	Rats	ACB	Stomach	Assess gastric motility
Gharibans <i>et al</i> [94]	2017	Electrophysiology model	HR-EKG	Stomach	Address the spatial limitations of the EKG
Gharibans <i>et al</i> [95]	2019	Human	HR-EKG	Stomach	Achieve comprehensive spatial analytics of gastric far-field gastric potentials

ACB: Alternate current biosusceptometry; EKG: Electrocardiogram; GI: Gastrointestinal tract; HR: High-resolution; MGG: Magnetogastrogram; MMC: Migrating motor complex; PCB: Printed circuit board; SW: Slow wave.

duration of slow waves[23,24]. ICC loss and injury are now a significant research focus, as it is recognized as a hallmark of several functional GI motility disorders[25]. Hence, coupling between slow waves and contractions is vital in understanding GI motility and developing concepts about what might lead to motility disorders. It requires techniques to record and model the patterns of slow wave generation and propagation.

EMG

Since 1922, when Alvarez *et al*[6] first recorded the slow wave of an experimental animal using bioelectric recording devices, EMG has gradually developed into a technique for recording bioelectric signals produced by nerve-muscle activity, using electrical stimulation to detect nerve and muscle excitation conduction function, and has assisted in the diagnosis and treatment of diseases[26]. In the field of GI electrophysiology, the most commonly used electrodes are monopole electrodes and surface electrodes.

Monopolar electrode

The monopole electrode records the action potential (AP) of the muscle fiber adjacent to the electrode so that the signal of AP amplitude is reliable and prominent[27]. Szurszewski *et al*[28] investigated the

myoelectric activity of the small intestine in conscious healthy dogs by implanting a monopolar electrode in the muscular layer of the small intestine and found that the periodic AP activity spreads slowly from the duodenum to the end of the ileum. This regular electrical activity only occurs during fasting. In follow-up research, Code *et al*[29] divided the periodic GI myoelectric activity, namely, the migrating motor complex (MMC), into four typical stages (I-IV). Phase I is the quiescent phase with no contractions, phase II is characterized by random contractions, phase III has a sudden onset and ends with a burst of contractions with maximal amplitude and duration, and phase IV is characterized by the rapid decrease of contractions. The human GI tract also has regular MMCs, and is regulated by circadian rhythms, hormones, nerves, and other factors[24].

As monopolar electrode implantation is an invasive operation, the main complications are pain, bleeding, infection, and perforation[27,30,31]. Moreover, the reference electrode is routinely placed on the surface of the skin near the tested tissue or organ, so the recorded myoelectric signal has many interferences and poor baseline stability. Therefore, the monopolar electrode is rarely used in the clinical diagnosis and treatment of diseases of the digestive system.

Electrogastrography

Electrogastrography (EGG) is a non-invasive technique for recording GI myoelectric activity using a surface electrode placed on the abdominal wall[32]. Many early studies have shown a good correlation between EGG and EMG, which was recorded with a monopolar electrode[33,34]. Familonie *et al*[35] recorded the surface EGG and intragastric EMG of postoperative patients and healthy subjects, respectively. They found that EGG could not only detect normal slow wave and electrical rhythm but also successfully detected abnormal EGGs in patients with clinical GI symptoms.

EGG is currently regarded as an auxiliary diagnostic examination in the clinic, which is used to evaluate nausea, vomiting, and other GI rhythm disorders, eventually exploring the mechanism of functional GI disease[36,37]. Chen *et al*[38] found that approximately 75% of gastroparesis patients had preprandial or postprandial abnormal signal patterns following EGG examination of healthy subjects and gastroparesis patients. About 60% of patients with functional dyspepsia have an abnormal EGG, including delayed gastric emptying and slow wave reduction[39]. A prospective study that compared the EGG of mechanical, vascular, and paralytic intestinal obstruction, combined with inflammatory indices, indicated that EGG has a high sensitivity in evaluating vascular and paralytic intestinal obstruction, even though its specificity is low. However, the significant correlation between EGG and plasma levels of interleukin-6 and procalcitonin supports the role of inflammation in the pathogenesis of impaired gastric electrical activity in patients with intestinal obstruction[40].

EGG also shows potential in clinical pharmacological research, digestive system development, GI function evaluation, and treatment safety evaluation. A case-control study that studied the EGG changes in patients with esophageal variceal bleeding during treatment with octreotide found that octreotide could inhibit gastric electrical activity and was positively correlated with its hemostatic effect. Therefore, EGG can be used as a predictive index to evaluate the efficacy of octreotide in treating esophageal variceal bleeding[41]. Ortigoza *et al*[42] simultaneously used EGG, abdominal near-infrared spectroscopy, and intestinal tinnitus acoustics to monitor the development of the GI tract in premature infants, evaluate the safety of enteral feeding, and reduce the morbidity and mortality of premature infants.

Because the relative position of the electrode affixed to the body surface is easy to deviate from the stomach, it is difficult for the recording system to obtain stable and repeatable data. The main parameter of EGG analysis is the frequency of slow wave, which cannot fully reflect the function of the GI tract. Therefore, the value of EGG in clinical diagnosis is limited[43].

GI electrical stimulation

The GI myoelectric abnormalities observed in the models of gastroparesis, intractable nausea and vomiting, and intestinal obstruction provide a theoretical basis for the development of GI electrical stimulation (GIES) therapy[38,44]. According to the location of electrical stimulation, GIES can be divided into inhibitory electrical stimulation and excitatory electrical stimulation[45]. Inhibitory electrical stimulation can inhibit the contractile movement of the normal GI tract by placing the electrode near the tail end of the GI tract to send stimulation signals, forcing GI myoelectric activity and movement to reverse propagation[46,47]. Excitatory electrical stimulation, also known as "electrical pacing," promotes GI peristalsis by implanting electrodes into the area near the physiological pacemaker to send electrical stimulation signals[48,49].

Recently, many clinical studies have shown that GIES can improve the physiological function of the GI tract and relieve clinical symptoms by setting different parameters and electrical stimulation sites (Table 2). However, as a treatment modality, GIES is still in the exploratory stage. A meta-analysis based on case-control studies found that GIES had a significant "placebo effect" in the treatment of gastroparesis. Therefore, GIES therapy requires further clinical studies to prove its safety and efficacy and related animal models to explore the pathogenic mechanism[50]. Although GIES is still controversial, it has great potential to improve and treat GI motility disorders[51,52].

Table 2 Clinical research on gastrointestinal electrical stimulation

Ref.	Methods	Sample size	Indications	Location of GIES	Stimulation parameters	Duration	Results
Gastric electrical stimulation							
McCallum <i>et al</i> [96]	Multicenter, double-blind, RCT	32	Idiopathic gastroparesis	Stomach	14 Hz, 5 mA, 330 μ s	3 mo	Significant decrease in vomiting and days of hospitalization
Teich <i>et al</i> [97]	Prospective study	16 (children)	Chronic nausea and vomiting	Stomach	14 Hz, 5 V, 330 μ s	0.5-23 mo	Significant improvement in severity and frequency of vomiting, frequency, and severity of nausea
Morales-Conde <i>et al</i> [98]	Randomized, multicenter trial	47	Obesity	Stomach	/	24 mo	Limited weight regain with strong safety outcomes
Ducrotte <i>et al</i> [99]	RCT	172	Refractory vomiting	Stomach	14 Hz, 5 mA, 330 μ s	8 mo	Effectively reduced the frequency of refractory vomiting in patients with and without diabetes, although it did not accelerate gastric emptying or increase the quality of life
Intestinal electrical stimulation							
Norton <i>et al</i> [100]	RCT	90	Fecal incontinence	Anus	35 Hz, 300 ms	8 wk	Improved bowel control to a modest extent
Daram <i>et al</i> [101]	Case report	1	Roux stasis syndrome	Jejunum	14 Hz, 5 mA, 330 μ s	5 d	Effective relief of the symptom of stasis post-Roux-en-Y anastomosis
Cadeddu <i>et al</i> [102]	Randomized trial	81	Idiopathic constipation	Anus	2 Hz, 30-35V, 360-960 μ s	6 times	Continuous improvement of constipation symptoms and anorectal function
Nerve electrical stimulation							
Fassov <i>et al</i> [103]	RCT	20	IBS	Sacral nerve	14 Hz, 0.1-4.0 V, 210 μ s	3 wk	Reduced symptoms of diarrhea-predominant and mixed IBS
Stakenborg <i>et al</i> [104]	Pilot study	18	Post-colectomy surgery	Abdominal vagus nerve	5, 20 Hz, 2.5 mA, 0.5, 1, 2 ms	2 times (preparation, postoperation)	Inhibition of IL-6 and IL-8 induced by lipopolysaccharide to prevent postoperative intestinal obstruction
Zhang <i>et al</i> [105]	Pilot study	42	Major abdominal surgeries	Acupoints ST36 and PC6	25 Hz, 2-10 mA, 0.5 ms	3 d	Improved major postoperative symptoms
Teckentrup <i>et al</i> [106]	RCT	22	Healthy subjects	Vagus nerve	25 Hz, 0.3-0.9 mA	2 d	Reduced the frequency of gastric myoelectricity and did not affect resting energy consumption

GIES: Gastrointestinal electrical stimulation; IBS: Irritable bowel syndrome; IL: Interleukin; RCT: Randomized controlled trial.

HR MAPPING

In clinical practice, the myoelectric signal obtained directly from the surface of the GI tract is still the most reliable method for analyzing GI myoelectricity. However, both EMG and EGG are highly dependent on equipment hardware, filtering technology, and the size and material of recording electrodes. They could only obtain low-resolution GI myoelectric recordings, which have limited value for analyzing slow wave propagation mode and speed of the GI tract. By placing multiple arrays of electrodes on the serous surface of the GI tract to record GI myoelectric signals, HR mapping can accurately analyze GI myoelectric signals and electrical rhythm disorders under pathological conditions [53].

Gastric pacing region

Alvarez *et al*[6] first studied the pacing region of the human stomach and proposed the hypothesis that the "pacing region" may be located in the lesser curvature of the gastric cardia. Hinder *et al*[54] roughly located the "gastric pacing region" in the greater curvature of the middle gastric corpus by implanting multiple pairs of monopolar electrodes. Through HR mapping research of the stomach in patients with normal gastric function, O'Grady *et al*[55] found that the slow wave of the stomach originated from a "special region" in the middle and upper part of the great curvature of the stomach, which was consistent with the results of Hinder's work. They also found significant regional spread of slow waves from the pacing area to the distal gastric antrum. However, the pacing region lacked specialized

anatomical tissue or cellular structures and was labile in that if it was to be removed, a neighboring region would become the apparent site of initiation[56].

Gastric conduction system

HR mapping studies in humans and large animal healthy stomach models have shown that slow waves arise from the defined pacemaker region and are quickly propagated in a circular waveform from the pacing area to the antrum[55,57-59]. In the human stomach, the annular slow waves are propagated longitudinally at a velocity of 3 mm·s⁻¹ until the distal antrum is continuously moving at a higher velocity (almost > 7 mm·s⁻¹) at the greater *vs* lesser curvature and eventually terminate in the pylorus [55]. Interestingly, slow waves do not normally excite the gastric fundus[60].

HR mapping technology has apparent advantages in diagnosing and treating GI motility disorders. In an HR mapping study, O'Grady *et al*[61] found that approximately 50% of experimental pigs with abnormal gastric function had abnormal rhythms, including incomplete and complete conduction block, escape rhythm competing, ectopic pacemakers, and functional re-entry. Subsequently, Du *et al*[62] designed and optimized a flexible printed circuit board that can be sterilized repeatedly, which can be used for HR mapping of the slow wave of the GI tract in an experimental animal model and shows excellent spatiotemporal accuracy, thus providing a low cost and stable alternative for clinical GI myoelectric detection. A recent clinical study comparing EGG and HR mapping showed that gastric slow waves exhibit pacing and conduction abnormalities in patients with gastroparesis, but their frequency is not significantly abnormal, resulting in the missed detection of abnormal gastric myoelectricity on the EGG, indicating that earlier studies likely underestimated both the prevalence and complexity of gastric dysrhythmia[63]. Berry *et al*[64] found that ectopic pacing of the remnant stomach after laparoscopic sleeve gastrectomy is one of the possible mechanisms leading to postoperative chronic gastric dyskinesia. Mapping studies also revealed how anisotropic propagation, re-entry, and conduction block contribute to motility disruption during dysrhythmia[61,63,65]. These works have enabled several novel clinically relevant insights into the features and mechanisms of gastric arrhythmias.

However, due to the limitations of invasive examination, HR mapping is rarely applied in the clinic. A clinical study attempted to detect and analyze the rhythm and propagation pattern of gastric slow wave reliably through trocars in the limited area of the gastric mucosa (limited by the number of trocars, usually less than four) during laparoscopic surgery[66]. Implanting temporary electrodes in the GI mucosa through the endoscope may be the direction of its future development.

BIOELECTROMAGNETIC TECHNOLOGY

Compared with EMG and HR mapping technology, bioelectromagnetic technology has the advantages of non-invasiveness, non-ionizing radiation, and low risk, which provides a new direction for the research of GI tract dynamics. Until now, the bioelectromagnetic techniques used in GI research are mainly based on the alternate current biosusceptometry (ACB) of tracking the movement of magnetic tracers in the GI tract after ingestion and magnetogastrography (MGG) to detect the magnetic field produced by the electrical activity of GI smooth muscle[67,68].

ACB

ACB is a bioelectromagnetic technique that records the changes in the magnetic flux of magnetic tracers ingested *in vivo* with the movement of the GI tract by placing induction coils and reference coils *in vitro*. This technique has the advantages of simplicity, easy operation, and low cost in investigating gastric emptying time and dynamic activity of the GI tract in humans or experimental animals[69]. An animal experiment studying the effect of triple immunosuppressive therapy on GI function found that both ACB and EGG can accurately monitor the contraction frequency and amplitude of the GI tract. Américo *et al*[70] implanted magnetic markers and monopole electrodes under the serosa of the distal stomach and proximal ascending colon in beagle dogs. Compared with EMG, these works proved that ACB could safely and effectively record the contractile activity of GI smooth muscle *in vitro*. The ACB image could visualize intrasegmental tracer distribution and the automated scan of the GI motility segments [71-73]. In two animal experiments, analysis of the relationship between ACB and the strain-gauge signal amplitude showed that ACB may serve as an accurate and sensitive technique for GI motility research[74,75].

In the field of pharmacological research, Corá *et al*[76] obtained a magnetic image of the disintegration of drug tablets in the human stomach using ACB, which shows that the ACB has sufficient sensitivity and spatial resolution in evaluating drug dosage forms *in vivo*. It provides a new research method for comprehensively understanding the metabolic model of drug dosage forms in the human GI tract and developing a new drug delivery system to improve and control the bioavailability and effectiveness of drugs. Another study developed a biomagnetic cellulose gel composed of polymeric nanocapsules containing ferrite nanoparticles, which can be substantially retained in the stomach walls, and consequently has the potential to be used as a traceable drug delivery system for gastric diseases

[77].

However, the measurement of ACB is easily affected by the magnetic tracer, the shape and position of the coils, and the spatial position of the tracer relative to the coils. Bruno *et al*[78] combined ultrasound and ACB to overcome its overdependence on the position and distribution of magnetic tracers in magnetic inductors. Above all, ACB has apparent advantages in recording gastric emptying, which reflects the unique superiority of ACB in GI function evaluation[79].

MGG

MGG is a bioelectromagnetic technique based on a superconducting quantum interferometer to detect the extracellular magnetic field produced by the slow wave of the GI tract, which is highly related to EGG[69]. Several studies have shown that MGG is less affected by the difference in electrical conductivity of the tissue, so it is easier to reflect the physiological characteristics of slow waves in the GI tract[68,69,80]. Based on a study of the effect of erythromycin on gastric motility, Somarajan *et al*[81] compared the differences among MGG, EGG, and EMG, proving that MGG could objectively indicate gastric dysrhythmia and quantify the therapeutic effect in patients with functional gastropathy. In addition, MGG can reliably detect spatial parameters such as propagation velocity and mode of GI slow wave. Recently, Bradshaw *et al*[82] measured EGG and MGG in seven healthy subjects and seven patients with diabetic gastroparesis. The parameters such as dominant frequency, percentage of power distribution, and propagation characteristics were compared. They found that MGG could detect the pathological slow wave of gastroparesis. Above all, MGG shows unique advantages in detecting transmission speed and propagation mode, which provides a new method for studying the pathological myoelectric characteristics of digestive diseases.

ELECTROPHYSIOLOGICAL RESEARCH ON THE GALLBLADDER AND BILIARY TRACT

Early studies on MMC have shown that rhythmic myoelectric activity also exists in the biliary system, which is regulated by many factors such as cholecystokinin, cholinergic receptor agonists, and intestinal peristalsis[83]. Romański *et al*[84] found that the minute rhythm occurs regularly in the entire ovine small intestine and gallbladder, which is controlled by nicotinic receptors and muscarinic receptor subtypes. In benign gallbladder diseases, research on biliary dysfunction, especially smooth muscle in the biliary tract and the sphincter of Oddi, is from animal experiments. Abell *et al*[85] designed an annular electrode to detect Oddi sphincter EMG without damaging the Oddi sphincter wall, which has the advantages of less trauma, convenient placement, accurate location, and high repeatability. In the guinea pig lithogenic model, EMG was used to detect the myoelectric difference in the Oddi sphincter at different stages under a high cholesterol diet, indicating that Oddi sphincter dysfunction caused by a high cholesterol diet may be one of the pathogenic mechanisms of cholesterol gallstones[86]. Liu *et al*[87] also found Oddi sphincter dysfunction in rabbits with chronic cholangitis and proved that the intracellular calcium mobilization pathway was involved in the relaxation of the sphincter under pathological conditions.

To date, there is still little research on gallbladder myoelectricity. It may be because of the weak gallbladder myoelectricity or signal close to the heart or respiration, making it difficult for researchers to obtain stable myoelectric signals. Therefore, the gallbladder myoelectric activity detection method needs to be continuously optimized and improved. Recently, we detected gallbladder EMG in guinea pigs with acute acalculous cholecystitis (AAC) using a bipolar electrode, which showed that the slow wave frequency in the control group was 10.66 ± 0.51 cpm, in the AAC 12 h group was 7.13 ± 0.20 cpm (mean \pm standard deviation; $P < 0.001$), in the AAC 24 h group was 6.46 ± 0.16 cpm, and in the AAC 48 h group was 5.75 ± 0.43 cpm (unpublished data). There was no significant difference among the AAC 12 h, AAC 24 h, and AAC 48 h groups. This suggests that inflammation may first affect the function of gallbladder ICCs, then decrease gallbladder slow wave frequency, and eventually lead to a decline in gallbladder function.

With a deeper understanding of the electrophysiology of the biliary system, clinicians have begun to re-examine the necessity of gallbladder function evaluation for benign gallbladder diseases. Currently, the primary methods for evaluating gallbladder function are gallbladder angiography, three-dimensional ultrasonic detection, cholescintigraphy, and Oddi sphincter manometry, which indirectly evaluate gallbladder function through parameters such as gallbladder emptying and biliary pressure [88]. There is still a lack of direct methods to evaluate biliary function in the clinic. The advantages of EMG, bioelectromagnetic technology, and HR mapping in the study of the physiological function of the GI tract provide a new research direction for the evaluation of biliary system function, especially for gallbladder function. We believe that gallbladder EMG is the most concise, reliable, and direct method for evaluating gallbladder function. However, there is still a lack of research on gallbladder EMG under physiological and pathological conditions. Compared with EMG, HR mapping can directly detect the myoelectricity of the gallbladder and provide a spatiotemporal model of the origin and propagation pattern of gallbladder myoelectricity. This will enable a more comprehensive understanding of the origin and spread of myoelectric activity in gallbladder pathophysiology and may provide new

evaluation methods for the diagnosis and treatment of benign gallbladder diseases. Nevertheless, because EMG and HR mapping are invasive examinations, non-invasive low-risk bioelectromagnetic technology may be the best method for clinical gallbladder function evaluation in the future.

CONCLUSION

The rhythmic slow wave in the GI tract is the basis for the realization of the physiological function of the digestive system. EMG detects the GI electrical signals by placing electrodes on the GI serosa or mucosal surface and has been widely used to study the normal physiological rhythm of the GI tract and the mode of dyskinesia under pathological conditions. Because EMG is an invasive technique, which limits its application in clinical diagnosis and treatment, it is mainly used in clinical scientific research and electrical stimulation therapy. Therefore, non-invasive detection technologies such as EGG and bioelectromagnetic technology are gaining more and more attention from scientific researchers and clinical workers. EGG collects GI electrical signals through the surface electrode of the abdominal wall, but it is easily affected by the difference in tissue conductivity. ACB and MGG, which are based on bioelectromagnetic technology, could not only accurately record the frequency and distribution of GI slow wave, but also provide their time-space variation parameters. HR mapping is also an invasive technique for detecting GI myoelectric signals. Unlike EMG, HR mapping uses array electrodes to obtain the myoelectric signal of the GI serosa surface, which can accurately obtain the spatial propagation model. Given the lack of electrophysiological research on the gallbladder, it will be an important research direction in the field of GI electrophysiology in the future.

FOOTNOTES

Author contributions: Ding F and Cui ZY drafted the manuscript; Hu H and Zhao G conceived the review; Guo R provided critical feedback; all authors read and approved the final version to be submitted.

Conflict-of-interest statement: The authors have no conflicts of interest to declare.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Fan Ding 0000-0002-4624-3134; Run Guo 0000-0001-7036-0093; Zheng-Yu Cui 0000-0002-1041-5352; Hai Hu 0000-0001-6597-4375; Gang Zhao 0000-0003-4665-8492.

S-Editor: Gong ZM

L-Editor: Wang TQ

P-Editor: Gong ZM

REFERENCES

- 1 Sanders KM, Koh SD, Ward SM. Interstitial cells of cajal as pacemakers in the gastrointestinal tract. *Annu Rev Physiol* 2006; **68**: 307-343 [PMID: 16460275 DOI: 10.1146/annurev.physiol.68.040504.094718]
- 2 Sanders KM, Koh SD, Ro S, Ward SM. Regulation of gastrointestinal motility--insights from smooth muscle biology. *Nat Rev Gastroenterol Hepatol* 2012; **9**: 633-645 [PMID: 22965426 DOI: 10.1038/nrgastro.2012.168]
- 3 Sanders KM, Hwang SJ, Ward SM. Neuroeffector apparatus in gastrointestinal smooth muscle organs. *J Physiol* 2010; **588**: 4621-4639 [PMID: 20921202 DOI: 10.1113/jphysiol.2010.196030]
- 4 Sanders KM. Nerves, smooth muscle cells and interstitial cells in the GI tract: Molecular and cellular interactions. 2020
- 5 Kurahashi M, Zheng H, Dwyer L, Ward SM, Koh SD, Sanders KM. A functional role for the 'fibroblast-like cells' in gastrointestinal smooth muscles. *J Physiol* 2011; **589**: 697-710 [PMID: 21173079 DOI: 10.1113/jphysiol.2010.201129]
- 6 Alvarez WC. Action currents in stomach and intestine. *Am J Phys* 1922; **58**: 476-493 [DOI: 10.1152/ajplegacy.1922.58.3.476]
- 7 Berkson J, Baldes EJ, Alvarez WC. Electromyographic studies of the gastrointestinal tract. 1. The correlation between mechanical movement and changes in electrical potential during rhythmic contraction of the intestine. *Revista Brasileira De Coloproctologia* 1932; **27**: 423-431
- 8 Liu JYH, Du P, Chan WY, Rudd JA. Use of a microelectrode array to record extracellular pacemaker potentials from the gastrointestinal tracts of the ICR mouse and house musk shrew (*Suncus murinus*). *Cell Calcium* 2019; **80**: 175-188

- [PMID: 31125825 DOI: 10.1016/j.ceca.2019.05.002]
- 9 **O'Grady G**, Abell TL. Gastric arrhythmias in gastroparesis: low- and high-resolution mapping of gastric electrical activity. *Gastroenterol Clin North Am* 2015; **44**: 169-184 [PMID: 25667031 DOI: 10.1016/j.gtc.2014.11.013]
 - 10 **Sanders KM**, Ward SM, Koh SD. Interstitial cells: regulators of smooth muscle function. *Physiol Rev* 2014; **94**: 859-907 [PMID: 24987007 DOI: 10.1152/physrev.00037.2013]
 - 11 **Huizinga JD**, Zarate N, Farrugia G. Physiology, injury, and recovery of interstitial cells of Cajal: basic and clinical science. *Gastroenterology* 2009; **137**: 1548-1556 [PMID: 19778538 DOI: 10.1053/j.gastro.2009.09.023]
 - 12 **Huizinga JD**, Thuneberg L, Klüppel M, Malysz J, Mikkelsen HB, Bernstein A. W/kit gene required for interstitial cells of Cajal and for intestinal pacemaker activity. *Nature* 1995; **373**: 347-349 [PMID: 7530333 DOI: 10.1038/373347a0]
 - 13 **Langton P**, Ward SM, Carl A, Norell MA, Sanders KM. Spontaneous electrical activity of interstitial cells of Cajal isolated from canine proximal colon. *Proc Natl Acad Sci USA* 1989; **86**: 7280-7284 [PMID: 2550938 DOI: 10.1073/pnas.86.18.7280]
 - 14 **Iino S**, Nojyo Y. Immunohistochemical demonstration of c-Kit-negative fibroblast-like cells in murine gastrointestinal musculature. *Arch Histol Cytol* 2009; **72**: 107-115 [PMID: 20009347 DOI: 10.1679/aohc.72.107]
 - 15 **Iino S**, Horiguchi K, Horiguchi S, Nojyo Y. c-Kit-negative fibroblast-like cells express platelet-derived growth factor receptor alpha in the murine gastrointestinal musculature. *Histochem Cell Biol* 2009; **131**: 691-702 [PMID: 19280210 DOI: 10.1007/s00418-009-0580-6]
 - 16 **Hwang SJ**, Blair PJ, Durnin L, Mutafova-Yambolieva V, Sanders KM, Ward SM. P2Y1 purinoreceptors are fundamental to inhibitory motor control of murine colonic excitability and transit. *J Physiol* 2012; **590**: 1957-1972 [PMID: 22371476 DOI: 10.1113/jphysiol.2011.224634]
 - 17 **Gallego D**, Gil V, Martínez-Cutillas M, Mañé N, Martín MT, Jiménez M. Purinergic neuromuscular transmission is absent in the colon of P2Y(1) knocked out mice. *J Physiol* 2012; **590**: 1943-1956 [PMID: 22371472 DOI: 10.1113/jphysiol.2011.224345]
 - 18 **Maurer KJ**, Carey MC, Fox JG. Roles of infection, inflammation, and the immune system in cholesterol gallstone formation. *Gastroenterology* 2009; **136**: 425-440 [PMID: 19109959 DOI: 10.1053/j.gastro.2008.12.031]
 - 19 **Stanghellini V**, Chan FK, Hasler WL, Malagelada JR, Suzuki H, Tack J, Talley NJ. Gastrointestinal Disorders. *Gastroenterology* 2016; **150**: 1380-1392 [PMID: 27147122 DOI: 10.1053/j.gastro.2016.02.011]
 - 20 **Aziz I**, Palsson OS, Whitehead WE, Sperber AD, Simrén M, Törnblom H. Epidemiology, Clinical Characteristics, and Associations for Rome IV Functional Nausea and Vomiting Disorders in Adults. *Clin Gastroenterol Hepatol* 2019; **17**: 878-886 [PMID: 29857155 DOI: 10.1016/j.cgh.2018.05.020]
 - 21 **Lacy BE**, Weiser KT, Kennedy AT, Crowell MD, Talley NJ. Functional dyspepsia: the economic impact to patients. *Aliment Pharmacol Ther* 2013; **38**: 170-177 [PMID: 23725230 DOI: 10.1111/apt.12355]
 - 22 **Keller J**, Bassotti G, Clarke J, Dinning P, Fox M, Grover M, Hellström PM, Ke M, Layer P, Malagelada C, Parkman HP, Scott SM, Tack J, Simren M, Törnblom H, Camilleri M; International Working Group for Disorders of Gastrointestinal Motility and Function. Expert consensus document: Advances in the diagnosis and classification of gastric and intestinal motility disorders. *Nat Rev Gastroenterol Hepatol* 2018; **15**: 291-308 [PMID: 29622808 DOI: 10.1038/nrgastro.2018.7]
 - 23 **Szurszewski J**. Electrical basis of gastrointestinal motility. In: Johnson LR. *Physiology of the Gastrointestinal Tract* (2nd ed.). New York: Raven, 1987: 383-422
 - 24 **Deloese E**, Janssen P, Depoortere I, Tack J. The migrating motor complex: control mechanisms and its role in health and disease. *Nat Rev Gastroenterol Hepatol* 2012; **9**: 271-285 [PMID: 22450306 DOI: 10.1038/nrgastro.2012.57]
 - 25 **Pasternak A**, Szura M, Gil K, Matyja A. Interstitial cells of Cajal - systematic review. *Folia Morphol (Warsz)* 2016; **75**: 281-286 [PMID: 26806433 DOI: 10.5603/FM.a2016.0002]
 - 26 **Sanders KM**, Ward SM, Hennig GW. Problems with extracellular recording of electrical activity in gastrointestinal muscle. *Nat Rev Gastroenterol Hepatol* 2016; **13**: 731-741 [PMID: 27756919 DOI: 10.1038/nrgastro.2016.161]
 - 27 **Rubin DI**. Needle electromyography: Basic concepts. *Handb Clin Neurol* 2019; **160**: 243-256 [PMID: 31277852 DOI: 10.1016/B978-0-444-64032-1.00016-3]
 - 28 **Szurszewski JH**. A migrating electric complex of canine small intestine. *Am J Physiol* 1969; **217**: 1757-1763 [PMID: 5353053 DOI: 10.1152/ajplegacy.1969.217.6.1757]
 - 29 **Code CF**, Marlett JA. The interdigestive myo-electric complex of the stomach and small bowel of dogs. *J Physiol* 1975; **246**: 289-309 [PMID: 1142245 DOI: 10.1113/jphysiol.1975.sp010891]
 - 30 **Juel VC**. Single fiber electromyography. *Handb Clin Neurol* 2019; **160**: 303-310 [PMID: 31277856 DOI: 10.1016/B978-0-444-64032-1.00019-9]
 - 31 **Merletti R**, Farina D. Analysis of intramuscular electromyogram signals. *Philos Trans A Math Phys Eng Sci* 2009; **367**: 357-368 [PMID: 19008187 DOI: 10.1098/rsta.2008.0235]
 - 32 **Alvarez WC**. The electrogastrogram and what it shows. *JAMA* 1922; **78**: 1116-1119 [DOI: 10.1001/jama.1922.02640680020008]
 - 33 **Smout AJ**, van der Schee EJ, Grashuis JL. What is measured in electrogastrography? *Dig Dis Sci* 1980; **25**: 179-187 [PMID: 7371462 DOI: 10.1007/bf01308136]
 - 34 **Hamilton JW**, Bellahsene BE, Reichelderfer M, Webster JG, Bass P. Human electrogastrograms. Comparison of surface and mucosal recordings. *Dig Dis Sci* 1986; **31**: 33-39 [PMID: 2934238 DOI: 10.1007/bf01347907]
 - 35 **Familoni BO**, Kingma YJ, Bowes KL. Study of transcutaneous and intraluminal measurement of gastric electrical activity in humans. *Med Biol Eng Comput* 1987; **25**: 397-402 [PMID: 3450990 DOI: 10.1007/BF02443360]
 - 36 **Martinek R**, Ladrova M, Sidikova M, Jaros R, Behbehani K, Kahankova R, Kawala-Sterniuk A. Advanced Bioelectrical Signal Processing Methods: Past, Present, and Future Approach-Part III: Other Biosignals. *Sensors (Basel)* 2021; **21** [PMID: 34577270 DOI: 10.3390/s21186064]
 - 37 **Chang FY**. Electrogastrography: basic knowledge, recording, processing and its clinical applications. *J Gastroenterol Hepatol* 2005; **20**: 502-516 [PMID: 15836697 DOI: 10.1111/j.1440-1746.2004.03751.x]
 - 38 **Chen J**, McCallum RW. Gastric slow wave abnormalities in patients with gastroparesis. *Am J Gastroenterol* 1992; **87**:

- 477-482 [PMID: 1553934]
- 39 **Lin Z**, Eaker EY, Sarosiek I, McCallum RW. Gastric myoelectrical activity and gastric emptying in patients with functional dyspepsia. *Am J Gastroenterol* 1999; **94**: 2384-2389 [PMID: 10483996 DOI: 10.1111/j.1572-0241.1999.01362.x]
- 40 **Frasko R**, Maruna P, Gurlich R, Trca S. Transcutaneous electrogastrography in patients with ileus. Relations to interleukin-1beta, interleukin-6, procalcitonin and C-reactive protein. *Eur Surg Res* 2008; **41**: 197-202 [PMID: 18504369 DOI: 10.1159/000134918]
- 41 **Zhang Y**, Liu Z, Liu X, Han X, Zhou Y, Cao Y, Zhang X. Prediction of octreotide efficacy by electrogastrography in the treatment of patients with esophageal variceal hemorrhage. *Physiol Meas* 2013; **34**: 799-812 [PMID: 23780564 DOI: 10.1088/0967-3334/34/7/799]
- 42 **Ortigoza EB**, Cagle J, Chien JH, Oh S, Brown LS, Neu J. Electrogastrography, Near-infrared Spectroscopy, and Acoustics to Measure Gastrointestinal Development in Preterm Babies. *J Pediatr Gastroenterol Nutr* 2018; **66**: e146-e152 [PMID: 29287010 DOI: 10.1097/MPG.0000000000001867]
- 43 **Farajidavar A**. Bioelectronics for mapping gut activity. *Brain Res* 2018; **1693**: 169-173 [PMID: 29903619 DOI: 10.1016/j.brainres.2018.03.004]
- 44 **Sullivan MA**, Snape WJ Jr, Matarazzo SA, Petrokubi RJ, Jeffries G, Cohen S. Gastrointestinal myoelectrical activity in idiopathic intestinal pseudo-obstruction. *N Engl J Med* 1977; **297**: 233-238 [PMID: 876299 DOI: 10.1056/nejm197708042970501]
- 45 **Cheng LK**, Nagahawatte ND, Avci R, Du P, Liu Z, Paskaranandavivel N. Strategies to Refine Gastric Stimulation and Pacing Protocols: Experimental and Modeling Approaches. *Front Neurosci* 2021; **15**: 645472 [PMID: 33967679 DOI: 10.3389/fnins.2021.645472]
- 46 **Zhao X**, Yin J, Wang L, Chen JD. Diffused and sustained inhibitory effects of intestinal electrical stimulation on intestinal motility mediated via sympathetic pathway. *Neuromodulation* 2014; **17**: 373-79; discussion 380 [PMID: 23924055 DOI: 10.1111/ner.12099]
- 47 **Zaw TS**, Khin PP, Sohn UD. The signaling of amitriptyline-induced inhibitory effect on electrical field stimulation response in colon smooth muscle. *Naunyn Schmiedebergs Arch Pharmacol* 2016; **389**: 961-970 [PMID: 27234925 DOI: 10.1007/s00210-016-1259-x]
- 48 **Penfold JA**, Wells CI, Du P, Bissett IP, O'Grady G. Electrical Stimulation and Recovery of Gastrointestinal Function Following Surgery: A Systematic Review. *Neuromodulation* 2019; **22**: 669-679 [PMID: 30451336 DOI: 10.1111/ner.12878]
- 49 **McKenzie P**, Stocker A, Du P, Lahr C, Cheng LK, McElmurray L, Kedar A, Boatright B, Hassan H, Hughes M, Omer E, Bhandari B, Abell TL. The Effect of Gastric Electrical Stimulation on Small Bowel Motility in Patients With Gastroparesis and Concomitant Pancreatic and Small Bowel Dysfunction: From Animal Model to Human Application. *Neuromodulation* 2019; **22**: 723-729 [PMID: 30525253 DOI: 10.1111/ner.12888]
- 50 **Levinthal DJ**, Bielefeldt K. Systematic review and meta-analysis: Gastric electrical stimulation for gastroparesis. *Auton Neurosci* 2017; **202**: 45-55 [PMID: 27085627 DOI: 10.1016/j.autneu.2016.03.004]
- 51 **Deb S**, Tang SJ, Abell TL, McLawhorn T, Huang WD, Lahr C, To SD, Easter J, Chiao JC. Development of innovative techniques for the endoscopic implantation and securing of a novel, wireless, miniature gastrostimulator (with videos). *Gastrointest Endosc* 2012; **76**: 179-184 [PMID: 22726478 DOI: 10.1016/j.gie.2012.03.177]
- 52 **Farajidavar A**, O'Grady G, Rao SM, Cheng LK, Abell T, Chiao JC. A miniature bidirectional telemetry system for in vivo gastric slow wave recordings. *Physiol Meas* 2012; **33**: N29-N37 [PMID: 22635054 DOI: 10.1088/0967-3334/33/6/N29]
- 53 **Lammers WJ**, Ver Donck L, Schuurkes JA, Stephen B. Peripheral pacemakers and patterns of slow wave propagation in the canine small intestine in vivo. *Can J Physiol Pharmacol* 2005; **83**: 1031-1043 [PMID: 16391712 DOI: 10.1139/y05-084]
- 54 **Hinder RA**, Kelly KA. Human gastric pacesetter potential. Site of origin, spread, and response to gastric transection and proximal gastric vagotomy. *Am J Surg* 1977; **133**: 29-33 [PMID: 835775 DOI: 10.1016/0002-9610(77)90187-8]
- 55 **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**: G585-G592 [PMID: 20595620 DOI: 10.1152/ajpgi.00125.2010]
- 56 **O'Grady G**, Gharibans AA, Du P, Huizinga JD. The gastric conduction system in health and disease: a translational review. *Am J Physiol Gastrointest Liver Physiol* 2021; **321**: G527-G542 [PMID: 34549598 DOI: 10.1152/ajpgi.00065.2021]
- 57 **Du P**, Grady GO, Paskaranandavivel N, Tang SJ, Abell T, Cheng LK. High-resolution Mapping of Hyperglycemia-induced Gastric Slow Wave Dysrhythmias. *J Neurogastroenterol Motil* 2019; **25**: 276-285 [PMID: 30870879 DOI: 10.5056/jnm18192]
- 58 **Lammers WJ**, Ver Donck L, Stephen B, Smets D, Schuurkes JA. Origin and propagation of the slow wave in the canine stomach: the outlines of a gastric conduction system. *Am J Physiol Gastrointest Liver Physiol* 2009; **296**: G1200-G1210 [PMID: 19359425 DOI: 10.1152/ajpgi.90581.2008]
- 59 **Berry R**, Miyagawa T, Paskaranandavivel N, Du P, Angeli TR, Trew ML, Windsor JA, Imai Y, O'Grady G, Cheng LK. Functional physiology of the human terminal antrum defined by high-resolution electrical mapping and computational modeling. *Am J Physiol Gastrointest Liver Physiol* 2016; **311**: G895-G902 [PMID: 27659422 DOI: 10.1152/ajpgi.00255.2016]
- 60 **Rhee PL**, Lee JY, Son HJ, Kim JJ, Rhee JC, Kim S, Koh SD, Hwang SJ, Sanders KM, Ward SM. Analysis of pacemaker activity in the human stomach. *J Physiol* 2011; **589**: 6105-6118 [PMID: 22005683 DOI: 10.1113/jphysiol.2011.217497]
- 61 **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**: e345-e355 [PMID: 21714831 DOI: 10.1111/j.1365-2982.2011.01739.x]
- 62 **Du P**, O'Grady G, Egbuji JU, Lammers WJ, Budgett D, Nielsen P, Windsor JA, Pullan AJ, Cheng LK. High-resolution

- mapping of in vivo gastrointestinal slow wave activity using flexible printed circuit board electrodes: methodology and validation. *Ann Biomed Eng* 2009; **37**: 839-846 [PMID: 19224368 DOI: 10.1007/s10439-009-9654-9]
- 63 **O'Grady G**, Angeli TR, Du P, Lahr C, Lammers WJEP, Windsor JA, Abell TL, Farrugia G, Pullan AJ, Cheng LK. Abnormal initiation and conduction of slow-wave activity in gastroparesis, defined by high-resolution electrical mapping. *Gastroenterology* 2012; **143**: 589-598.e3 [PMID: 22643349 DOI: 10.1053/j.gastro.2012.05.036]
- 64 **Berry R**, Cheng LK, Du P, Paskaranandavivel N, Angeli TR, Mayne T, Beban G, O'Grady G. Patterns of Abnormal Gastric Pacemaking After Sleeve Gastrectomy Defined by Laparoscopic High-Resolution Electrical Mapping. *Obes Surg* 2017; **27**: 1929-1937 [PMID: 28213666 DOI: 10.1007/s11695-017-2597-6]
- 65 **Angeli TR**, Cheng LK, Du P, Wang TH, Bernard CE, Vannucchi MG, Faussone-Pellegrini MS, Lahr C, Vather R, Windsor JA, Farrugia G, Abell TL, O'Grady G. Loss of Interstitial Cells of Cajal and Patterns of Gastric Dysrhythmia in Patients With Chronic Unexplained Nausea and Vomiting. *Gastroenterology* 2015; **149**: 56-66.e5 [PMID: 25863217 DOI: 10.1053/j.gastro.2015.04.003]
- 66 **O'Grady G**, Du P, Egbuji JU, Lammers WJ, Wahab A, Pullan AJ, Cheng LK, Windsor JA. A novel laparoscopic device for measuring gastrointestinal slow-wave activity. *Surg Endosc* 2009; **23**: 2842-2848 [PMID: 19466491 DOI: 10.1007/s00464-009-0515-2]
- 67 **O'Mahony GD**, Gallucci MR, Córdova-Fraga T, Berch B, Richards WO, Bradshaw LA. Biomagnetic investigation of injury currents in rabbit intestinal smooth muscle during mesenteric ischemia and reperfusion. *Dig Dis Sci* 2007; **52**: 292-301 [PMID: 17160467 DOI: 10.1007/s10620-006-9559-5]
- 68 **Bradshaw LA**, Cheng LK, Richards WO, Pullan AJ. Surface current density mapping for identification of gastric slow wave propagation. *IEEE Trans Biomed Eng* 2009; **56**: 2131-2139 [PMID: 19403355 DOI: 10.1109/TBME.2009.2021576]
- 69 **Irimia A**, Cheng LK, Buist ML, Pullan AJ, Bradshaw LA. An integrative software package for gastrointestinal biomagnetic data acquisition and analysis using SQUID magnetometers. *Comput Methods Programs Biomed* 2006; **83**: 83-94 [PMID: 16857291 DOI: 10.1016/j.cmpb.2006.03.006]
- 70 **Américo MF**, Oliveira RB, Corá LA, Marques RG, Romeiro FG, Andreis U, Miranda JR. The ACB technique: a biomagnetic tool for monitoring gastrointestinal contraction directly from smooth muscle in dogs. *Physiol Meas* 2010; **31**: 159-169 [PMID: 20009185 DOI: 10.1088/0967-3334/31/2/003]
- 71 **Pinto L**, Soares G, Próspero A, Stoppa E, Biasotti G, Paixão F, Santos A, Oliveira R, Miranda J. An easy and low-cost biomagnetic methodology to study regional gastrointestinal transit in rats. *Biomed Tech (Berl)* 2021; **66**: 405-412 [PMID: 33544465 DOI: 10.1515/bmt-2020-0202]
- 72 **Calabresi MF**, Quini CC, Matos JF, Moretto GM, Americo MF, Graça JR, Santos AA, Oliveira RB, Pina DR, Miranda JR. Alternate current biosusceptometry for the assessment of gastric motility after proximal gastrectomy in rats: a feasibility study. *Neurogastroenterol Motil* 2015; **27**: 1613-1620 [PMID: 26303680 DOI: 10.1111/nmo.12660]
- 73 **Teixeira MC**, Magalhães I, Galvão PV, Souza GS, Miranda JR, Oliveira RB, Corá LA. Assessment of gastrointestinal motility in renal transplant recipients by alternate current biosusceptometry. *Transplant Proc* 2012; **44**: 2384-2387 [PMID: 23026600 DOI: 10.1016/j.transproceed.2012.07.048]
- 74 **Américo MF**, Marques RG, Zandoná EA, Andreis U, Stelzer M, Corá LA, Oliveira RB, Miranda JR. Validation of ACB in vitro and in vivo as a biomagnetic method for measuring stomach contraction. *Neurogastroenterol Motil* 2010; **22**: 1340-1344, e374 [PMID: 20874731 DOI: 10.1111/j.1365-2982.2010.01582.x]
- 75 **Agostinho M**, Américo MF, Marques RG, Zandoná EA, Stelzer M, Corá LA, Andreis U, Oliveira RB, Miranda JR. AC Biosusceptometry as a method for measuring gastric contraction. *Annu Int Conf IEEE Eng Med Biol Soc* 2010; **2010**: 5740-5743 [PMID: 21097331 DOI: 10.1109/IEMBS.2010.5627855]
- 76 **Corá LA**, Andreis U, Romeiro FG, Américo MF, Oliveira RB, Baffa O, Miranda JR. Magnetic images of the disintegration process of tablets in the human stomach by ac biosusceptometry. *Phys Med Biol* 2005; **50**: 5523-5534 [PMID: 16306649 DOI: 10.1088/0031-9155/50/23/007]
- 77 **Martins ML**, Calabresi MF, Quini C, Matos JF, Miranda JR, Saeki MJ, Bordallo HN. Enhancing the versatility of alternate current biosusceptometry (ACB) through the synthesis of a dextrose-modified tracer and a magnetic muco-adhesive cellulose gel. *Mater Sci Eng C Mater Biol Appl* 2015; **48**: 80-85 [PMID: 25579899 DOI: 10.1016/j.msec.2014.11.059]
- 78 **Bruno AC**, Pavan TZ, Baffa O, Carneiro AA. A hybrid transducer to magnetically and ultrasonically evaluate magnetic fluids. *IEEE Trans Ultrason Ferroelectr Freq Control* 2013; **60**: 2004-2012 [PMID: 24658731 DOI: 10.1109/TUFFC.2013.2785]
- 79 **Dallagnol DJR**, Corá LA, Gama LA, Caló RS, Miranda JRA, Américo MF. Gastrointestinal Side Effects of Triple Immunosuppressive Therapy Evaluated by AC Biosusceptometry and Electrogastrography in Rats. *Endocr Metab Immune Disord Drug Targets* 2020; **20**: 1494-1503 [PMID: 32368985 DOI: 10.2174/1871530320666200505111456]
- 80 **Somarajan S**, Cassilly S, Obioha C, Richards WO, Bradshaw LA. Effects of body mass index on gastric slow wave: a magnetogastrographic study. *Physiol Meas* 2014; **35**: 205-215 [PMID: 24398454 DOI: 10.1088/0967-3334/35/2/205]
- 81 **Somarajan S**, Muszynski ND, Hawrami D, Olson JD, Cheng LK, Bradshaw LA. Noninvasive Magnetogastrography Detects Erythromycin-Induced Effects on the Gastric Slow Wave. *IEEE Trans Biomed Eng* 2019; **66**: 327-334 [PMID: 29993499 DOI: 10.1109/TBME.2018.2837647]
- 82 **Bradshaw LA**, Cheng LK, Chung E, Obioha CB, Erickson JC, Gorman BL, Somarajan S, Richards WO. Diabetic gastroparesis alters the biomagnetic signature of the gastric slow wave. *Neurogastroenterol Motil* 2016; **28**: 837-848 [PMID: 26839980 DOI: 10.1111/nmo.12780]
- 83 **Pozo MJ**, Camello PJ, Mawe GM. Chemical mediators of gallbladder dysmotility. *Curr Med Chem* 2004; **11**: 1801-1812 [PMID: 15279583 DOI: 10.2174/0929867043364955]
- 84 **Romański KW**. Characteristics and cholinergic control of the 'minute rhythm' in ovine antrum, small bowel and gallbladder. *J Vet Med A Physiol Pathol Clin Med* 2002; **49**: 313-320 [PMID: 12227475 DOI: 10.1046/j.1439-0442.2002.00399.x]
- 85 **Abell TL**, Werkman RF, Familoni BO, Baggous W, Massie D, Vera S. Biliary, pancreatic, and sphincter of Oddi electrical and mechanical signals recorded during ERCP. *Dig Dis Sci* 1998; **43**: 540-546 [PMID: 9539649 DOI: 10.1007/s10620-006-9559-5]

- 10.1023/a:1018859007353]
- 86 **Rong ZH**, Chen HY, Wang XX, Wang ZY, Xian GZ, Ma BZ, Qin CK, Zhang ZH. Effects of sphincter of Oddi motility on the formation of cholesterol gallstones. *World J Gastroenterol* 2016; **22**: 5540-5547 [PMID: 27350732 DOI: 10.3748/wjg.v22.i24.5540]
- 87 **Liu YK**, Li ZH, Liu NZ, He Q, Lin H, Wang XJ, Li XW, Dong JH. Reduced myoelectric activity in the sphincter of Oddi in a new model of chronic cholangitis in rabbits: an in vivo and in vitro study. *Neurogastroenterol Motil* 2010; **22**: 927-934, e238 [PMID: 20426800 DOI: 10.1111/j.1365-2982.2010.01500.x]
- 88 **Fotos JS**, Tulchinsky M. Oral Cholecystagogue Cholescintigraphy: A Systematic Review of Fatty Meal Options. *Clin Nucl Med* 2015; **40**: 796-798 [PMID: 26222535 DOI: 10.1097/RLU.0000000000000913]
- 89 **Code CF**, Marlett JA. Canine tachygastria. *Mayo Clin Proc* 1974; **49**: 325-332 [PMID: 4829263]
- 90 **Di Luzio S**, Comani S, Romani GL, Basile M, Del Gratta C, Pizzella V. A biomagnetic method for studying gastrointestinal activity. *Nouv Cim D* 1989; **11**: 1853-1859 [DOI: 10.1007/BF02459126]
- 91 **Miranda JR**, Baffa O, de Oliveira RB, Matsuda NM. An AC biosusceptometer to study gastric emptying. *Med Phys* 1992; **19**: 445-448 [PMID: 1584144 DOI: 10.1118/1.596832]
- 92 **Bradshaw LA**, Myers AG, Redmond A, Wikswa JP, Richards WO. Biomagnetic detection of gastric electrical activity in normal and vagotomized rabbits. *Neurogastroenterol Motil* 2003; **15**: 475-482 [PMID: 14507349 DOI: 10.1046/j.1365-2982.2003.00432.x]
- 93 **Lammers WJ**, Ver Donck L, Stephen B, Smets D, Schuurkes JA. Focal activities and re-entrant propagations as mechanisms of gastric tachyarrhythmias. *Gastroenterology* 2008; **135**: 1601-1611 [PMID: 18713627 DOI: 10.1053/j.gastro.2008.07.020]
- 94 **Gharibans AA**, Kim S, Kunkel D, Coleman TP. High-Resolution Electrogastrogram: A Novel, Noninvasive Method for Determining Gastric Slow-Wave Direction and Speed. *IEEE Trans Biomed Eng* 2017; **64**: 807-815 [PMID: 27305668 DOI: 10.1109/tbme.2016.2579310]
- 95 **Gharibans AA**, Coleman TP, Mousa H, Kunkel DC. Spatial Patterns From High-Resolution Electrogastrography Correlate With Severity of Symptoms in Patients With Functional Dyspepsia and Gastroparesis. *Clin Gastroenterol Hepatol* 2019; **17**: 2668-2677 [PMID: 31009794 DOI: 10.1016/j.cgh.2019.04.039]
- 96 **McCallum RW**, Sarosiek I, Parkman HP, Snape W, Brody F, Wo J, Nowak T. Gastric electrical stimulation with Enterra therapy improves symptoms of idiopathic gastroparesis. *Neurogastroenterol Motil* 2013; **25**: 815-e636 [PMID: 23895180 DOI: 10.1111/nmo.12185]
- 97 **Teich S**, Mousa HM, Punati J, Di Lorenzo C. Efficacy of permanent gastric electrical stimulation for the treatment of gastroparesis and functional dyspepsia in children and adolescents. *J Pediatr Surg* 2013; **48**: 178-183 [PMID: 23331812 DOI: 10.1016/j.jpedsurg.2012.10.038]
- 98 **Morales-Conde S**, Alarcón Del Agua I, Busetto L, Favretti F, Anselmino M, Rovera GM, Socas-Macias M, Barranco-Moreno A, Province-Azalde R, Torres AJ. Implanted Closed-Loop Gastric Electrical Stimulation (CLGES) System with Sensor-Based Feedback Safely Limits Weight Regain at 24 Months. *Obes Surg* 2018; **28**: 1766-1774 [PMID: 29333595 DOI: 10.1007/s11695-017-3093-8]
- 99 **Ducrotte P**, Coffin B, Bonaz B, Fontaine S, Bruley Des Varannes S, Zerbib F, Caiazzo R, Grimaud JC, Mion F, Hadjadj S, Valensi PE, Vuitton L, Charpentier G, Ropert A, Altwegg R, Poudereux P, Dorval E, Dapoiny M, Duboc H, Benhamou PY, Schmidt A, Donnadiou N, Gourcerol G, Guerci B; ENTERRA Research Group. Gastric Electrical Stimulation Reduces Refractory Vomiting in a Randomized Crossover Trial. *Gastroenterology* 2020; **158**: 506-514.e2 [PMID: 31647902 DOI: 10.1053/j.gastro.2019.10.018]
- 100 **Norton C**, Gibbs A, Kamm MA. Randomized, controlled trial of anal electrical stimulation for fecal incontinence. *Dis Colon Rectum* 2006; **49**: 190-196 [PMID: 16362803 DOI: 10.1007/s10350-005-0251-1]
- 101 **Daram SR**, Tang SJ, Vick K, Aru G, Lahr C, Amin O, Taylor M, Sheehan JJ, Abell TL. Novel application of GI electrical stimulation in Roux stasis syndrome (with video). *Gastrointest Endosc* 2011; **74**: 683-686 [PMID: 21872718 DOI: 10.1016/j.gie.2011.05.023]
- 102 **Cadeddu F**, Salis F, De Luca E, Ciangola I, Milito G. Efficacy of biofeedback plus transanal stimulation in the management of pelvic floor dyssynergia: a randomized trial. *Tech Coloproctol* 2015; **19**: 333-338 [PMID: 25744688 DOI: 10.1007/s10151-015-1292-7]
- 103 **Fassov J**, Lundby L, Worsøe J, Buntzen S, Laurberg S, Krogh K. A randomised, controlled study of small intestinal motility in patients treated with sacral nerve stimulation for irritable bowel syndrome. *BMC Gastroenterol* 2014; **14**: 111 [PMID: 24965754 DOI: 10.1186/1471-230X-14-111]
- 104 **Stakenborg N**, Wolthuis AM, Gomez-Pinilla PJ, Farro G, Di Giovangiulio M, Bosmans G, Labeeuw E, Verhaegen M, Depoortere I, D'Hoore A, Matteoli G, Boeckxstaens GE. Abdominal vagus nerve stimulation as a new therapeutic approach to prevent postoperative ileus. *Neurogastroenterol Motil* 2017; **29** [PMID: 28429863 DOI: 10.1111/nmo.13075]
- 105 **Zhang B**, Xu F, Hu P, Zhang M, Tong K, Ma G, Xu Y, Zhu L, Chen JDZ. Needleless Transcutaneous Electrical Acustimulation: A Pilot Study Evaluating Improvement in Post-Operative Recovery. *Am J Gastroenterol* 2018; **113**: 1026-1035 [PMID: 29925916 DOI: 10.1038/s41395-018-0156-y]
- 106 **Teckentrup V**, Neubert S, Santiago JCP, Hallschmid M, Walter M, Kroemer NB. Non-invasive stimulation of vagal afferents reduces gastric frequency. *Brain Stimul* 2020; **13**: 470-473 [PMID: 31884186 DOI: 10.1016/j.brs.2019.12.018]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

