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ORIGINAL ARTICLE

Validation of an Acoustic Gastrointestinal Surveillance Biosensor for Postoperative Ileus

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Abstract

Background Postoperative ileus (POI) can worsen outcomes, increase cost, and prolong hospitalization. An objective marker could help identify POI patients who should not be prematurely fed. We developed a disposable, non-invasive acoustic gastrointestinal surveillance (AGIS) biosensor. We tested whether AGIS can distinguish healthy controls from patients recovering from abdominal surgery.

Study Design AGIS is a disposable plastic device embedded with a microphone that adheres to the abdominal wall and connects to a computer that measures acoustic event rates. We compared intestinal rates of healthy subjects using AGIS for 60 min after a standardized meal to recordings of two postoperative groups: (1) patients tolerating standardized feeding and (2) POI patients. We compared intestinal rates among groups using ANOVA and *t* tests.

Results There were 8 healthy controls, 7 patients tolerating feeding, and 25 with POI; mean intestinal rates were 0.14, 0.03, and 0.016 events per second, respectively (ANOVA $p<0.001$). AGIS separated patients from controls with 100 % sensitivity and 97 % specificity. Among patients, rates were higher in fed versus POI subjects ($p=0.017$).

Conclusion Non-invasive, abdominal acoustic monitoring distinguishes POI from non-POI subjects. Future research will test whether AGIS can identify patients at risk for development of POI and assist with postoperative feeding decisions.

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Introduction

Despite advances in surgical techniques, most patients develop temporary bowel paralysis following abdominal surgery.[1–3] There is general consensus that some degree of ileus is a normal physiologic consequence of abdominal surgery, although the mechanisms remain incompletely understood.[1–3] When prolonged or complicated, postoperative ileus (POI) can worsen patient outcomes, increase resource utilization and cost, and extend hospital length of stay by 30 %.[4,5] Delays in oral feeding can lead to poor wound healing, increased infection, or the need for parenteral nutrition.[1] Because of the high prevalence and impact of POI, the condition costs over $1.75 billion annually in the USA.[4,5]

To help reduce length of stay, many hospitals now use enhanced recovery (aka "fast track") pathways that expeditiously advance postoperative feeding.[6–9] Although enhanced recovery pathways are generally safe and reduce length of stay, between 4 and 25 % of patients cannot tolerate feeding and require nasogastric tube decompression or bowel rest,[10–14] which can delay discharge and increase risk of complications. If there were an objective marker to help surgeons and nurses identify patients intolerant of fast-track feeding, then it would help ensure that rapid feeding is applied judiciously—i.e., to expedite feeding in patients ready to eat, yet hold feeding in those likely to experience further complications.

Because many factors conspire to undermine bowel function after abdominal surgery, it is difficult to predict which patients will develop POI and which will not. In addition, monitoring for the development of POI is generally imprecise and subjective. Clinical assessments rely on observation, intermittent physical examination, assessments for flatus or stool passage, and use of a stethoscope to monitor bowel sounds.

Bowel sounds, in particular, are generally considered unhelpful as they are only assessed for short periods, are measured in an unstandardized manner, and are analyzed using gestalt rather than objective parameters. Although some research indicates that bowel sounds are useful to guide postoperative management,[15] other studies suggest that bowel sounds do not correlate well with clinical status.[16] Moreover, a brief abdominal examination and assessment of bowel sounds only provide data about the immediate moment in time.

However, data reveal that continuous audio recordings of bowel sounds strongly correlate with true intestinal motility, as measured using the gold standard of antroduodenal manometry.[17] But until recently, there has been no way to perform routine acoustic monitoring in a clinically feasible, cost-effective, point-of-care manner. To address this shortcoming, our multidisciplinary team of colorectal surgeons, gastroenterologists, and electrical engineers used advances in low-cost sensor technologies and computer-aided analysis to develop a disposable, non-invasive, acoustic gastro-intestinal surveillance (AGIS) biosensor. The AGIS sensor allows continuous and automated analysis of bowel sounds across the acoustic spectrum—including hertz ranges below the threshold detected by the human ear. Here, we report a proof-of-concept study to test whether AGIS monitoring can distinguish healthy controls from patients recovering from abdominal surgery who are tolerating standardized feeding as well as patients with POI.

Materials and Methods

Study Overview

We performed a cross-sectional analysis to measure AGIS-derived intestinal motility rates in postoperative patients with POI and to compare their rates to postoperative patients without POI and to normal healthy subjects. Additionally, we developed a graphical user interface to display bedside AGIS scores to caretakers. We hypothesized that AGIS could use computer-analyzed bowel sounds to accurately separate patients with POI versus those tolerating oral feeding and could further separate postoperative patients versus healthy controls. In the sections that follow, we describe the AGIS device and its engineering, the subjects enrolled in this trial, and the analyses employed to evaluate the accuracy of AGIS measurements.

Device Description

The AGIS system is a compact, rapidly deployable unit that is designed to be unobtrusive and convenient in application. The AGIS sensor includes a standard microelectronic microphone that measures abdominal vibration and acoustic signals. Figure 1 shows the AGIS sensor applied to the abdomen of a subject and also demonstrates the device with its Tegaderm adhesive. The sensor includes flexible cables that connect to a small bedside computer that calculates motility scores and visually presents the results to a provider.

AGIS GI Motility Signal Processing

AGIS sensor signals are acquired and appear as in Fig. 2, which shows both motility events as well as a propulsive event called a migrating myoelectric complex (MMC).[17] The AGIS algorithm uses a signal search engine, developed by the University of California, Los Angeles (UCLA), Wireless Health Institute and used in other biosensor applications,[18–20] to recognize and classify these GI signals. Typical acoustic motility

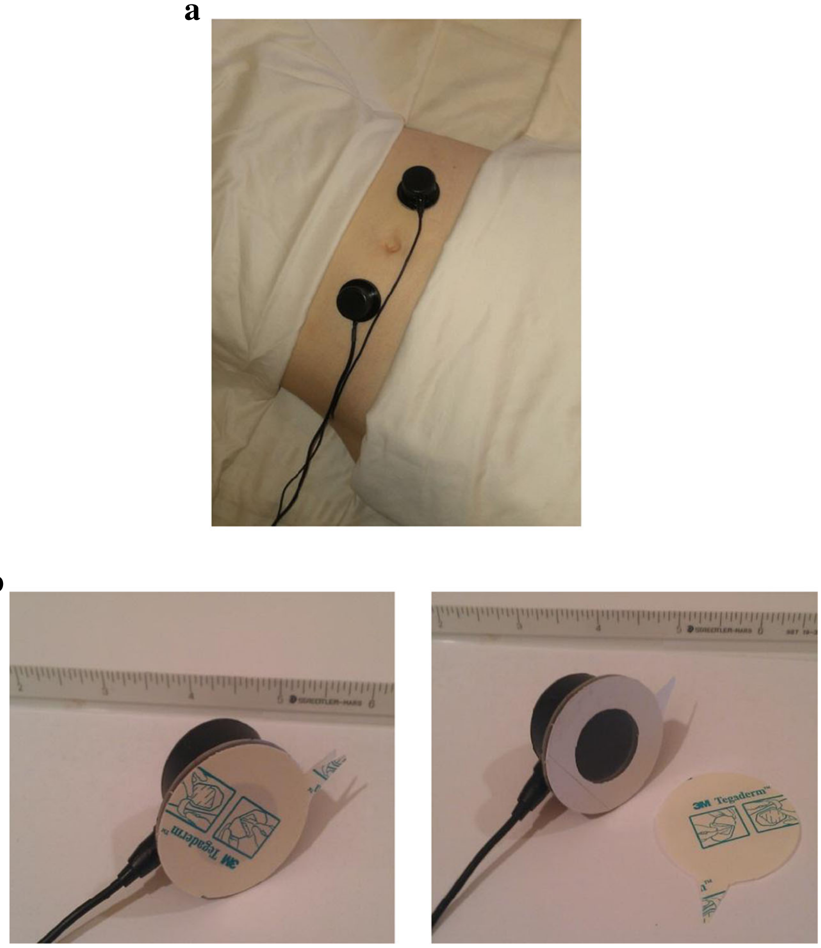

Fig. 1 AGIS sensors. **a** AGIS disposable sensors applied to the abdominal wall of a patient. **b** AGIS sensor with Tegaderm bandage. The *right image* in **b** shows the sensor ready for application and the *left image* shows the sensor with the adhesive covered

signals appear in all healthy subjects and are characterized as a short time duration pulse bearing a characteristic unlike other signals generated internally or external to the system (e.g., ambient noise). Motility events are recognized, counted, and time-averaged to determine an "intestinal rate" based on the acoustic event frequency.

Subjects and Setting

We recruited inpatients from the West Los Angeles Veteran Administration (VA) Medical Center, a University-affiliated teaching hospital. Patients were 18 years of age or older, able to provide informed consent, and recovering from abdominal surgery. For each patient, we recorded demographic characteristics, type of surgery, and body mass index (BMI). All patients received a standardized feeding protocol as part of usual care, including ice chips on postoperative day (POD) zero, sips of clear liquids on POD#1 (not to exceed 60 cc per hour), clear liquid diet on POD#2, and advancement to regular diet on POD#3. Patients intolerant of the feeding protocol, including nausea or vomiting precluding advancement, or those that developed significant abdominal distension fell off the feeding protocol.

We classified patients into those with POI versus without POI and purposefully oversampled POI patients in this non-consecutive series. Although POI has many definitions in the literature, we applied a pragmatic definition of POI including the presence of one or more of the following: (1) postoperative nausea that precluded advancement of diet beyond sips on POD#1 or later, (2) postoperative vomiting that precluded any oral intake, and (3) need for nasogastric tube decompression. As this was a cross-sectional pragmatic trial—not a longitudinal surveillance design—we recruited patients across PODs. Patients wore the AGIS device for 60 min to measure motility signals averaged over the recording period. We then correlated those signals with concurrent clinical status, as described in the "Analysis" section below.

In addition to patients recovering from surgery, we recruited a convenience sample of normal healthy subjects, aged 18 years or older, through local advertising. Subjects were all fed a standardized breakfast of two eggs, a slice of buttered toast, and choice of a non-caffeinated beverage. We measured AGIS-derived motility signals for 60 min following the meal and calculated a time-averaged AGIS-derived intestinal rate for the recording period.

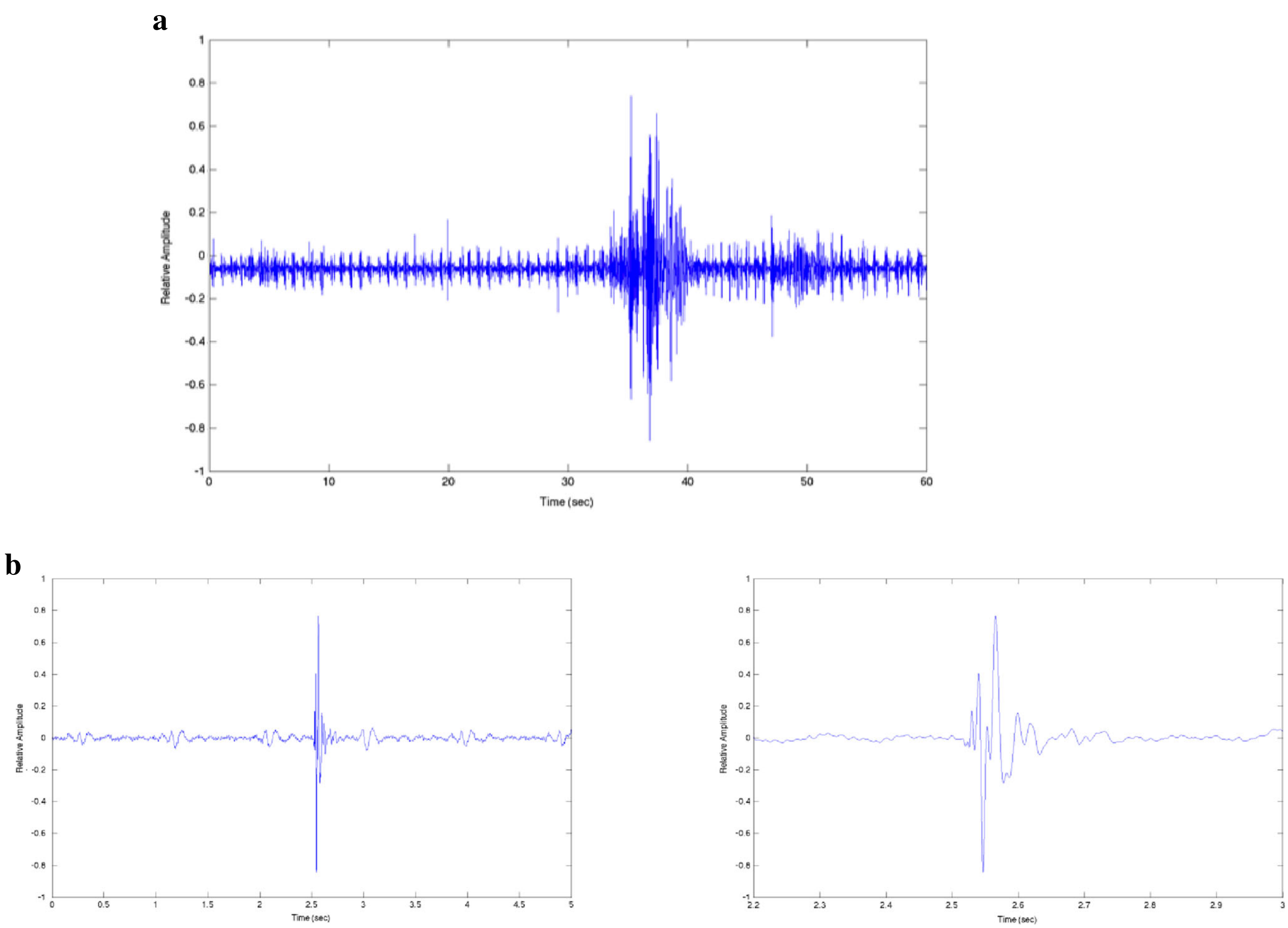

Fig. 2 Example AGIS signals. **a** AGIS signal example showing migrating motor complex (MMC) event at time index between 35 and 40 s. Small amplitude signals are due to the acoustic signals emanating from abdominal blood circulation. **b** AGIS motility event shown over a 5-s and 800-ms time span. At this time scale, more details emerge, allowing the computer to characterize signals with greater precision

Analysis

The AGIS-derived acoustic data were calculated as intestinal motility events per second averaged over the 60-min recording period. We compared AGIS intestinal rates across all three groups (POI patients, fed patients, and healthy controls) using ANOVA. We then used *t* tests to compare rates between patients versus controls and between POI patients versus fed patients. Using receiver operator characteristic (ROC) curve analysis, we identified an intestinal rate threshold that maximized discrimination between patients versus healthy controls. We used the ROC-defined threshold to calculate the sensitivity, specificity, and accuracy of AGIS in distinguishing between groups. In addition, because high BMI might affect the ability of the AGIS sensor to detect intestinal acoustics, we performed a linear regression analysis to evaluate the impact of BMI on the detected intestinal rate. Finally, we converted raw intestinal event rates to a more clinically interpretable scale ranging from zero (no motility) to ten (highest measured intestinal rate in normal healthy subjects). We report the relative difference in intestinal rates among groups on the simplified zero to ten scale. All analyses were conducted using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). The West Los Angeles Veterans Administration Institutional Review Board approved this study, which was conducted in accordance with the ethical standards of the Helsinki Declaration (VA IRB # CC 2013–040489).

Developing AGIS Motility Tracker Dashboard

In order to enhance the future clinical utility of AGIS monitoring, we developed a graphical user interface to portray intestinal rates to clinicians using a bedside interface. We collaborated with colorectal surgeons (M.M.R. and A.L.), a graphical designer (M.W.R.), and psychometricians (B.S. and M.W.R.) to design an interface that displays AGIS data in a clinically interpretable manner.

Results

Participant Characteristics

We enrolled eight healthy controls (mean age=35.5±16.5; five men), seven postoperative patients tolerating the fast-track feeding protocol (age=65.4±4.6; all men), and 25 patients with evidence of POI (age=64.3±10.6; all men). Table 1 displays characteristics of the participants. Among patients, the most common surgery was partial colectomy with primary anastomosis (*N*=24), and the primary indication for surgery was colorectal cancer or endoscopically unresectable polyp (*N*=27). The average BMI was 29.9, with a range from 24.3 to 61.8.

We evaluated the medications that patients were taking at the time of the study that could have an effect on gastrointestinal motility. In both postoperative groups, all patients were taking narcotic medications. Five of 25 (20 %) patients in the POI group were taking anticholinergics versus none in the feeding group. Three of 25 (12 %) patients in the POI group were on antibiotics versus none in the feeding group. No patients in either group were on a medication with prokinetic properties such as alvimopan or metoclopramide at the time of their AGIS reading.

Comparison of AGIS Intestinal Rates Among Groups

Figure 3 demonstrates the mean AGIS intestinal rates in each of the three comparison groups. The mean (standard deviation) intestinal rates were 0.14 (0.03), 0.03 (0.05), and 0.016 (0.01) events per second for healthy controls, patients tolerating feeding, and patients with POI, respectively. Using ANOVA, the difference in AGIS intestinal rates among the three groups was significantly different ($p<0.001$). When excluding healthy controls from the analysis and focusing exclusively on postoperative patients, AGIS intestinal rates were significantly higher in patients tolerating fast-track feeding versus those with POI ($p=0.017$).

Figure 4 demonstrates a representative "GI telemetry" tracing of patients with severe POI compared to a subject tolerating postoperative feeding; the figure shows a near "flat line" of AGIS signals over ten consecutive minutes of monitoring in the POI patients and frequent motility events in the fed patient.

Sensitivity and Specificity of AGIS

Using an AGIS intestinal rate threshold of 0.1 events per second to distinguish healthy controls from patients, the area under the ROC curve was 0.995. The 0.1 event per second threshold separated controls from patients with 100 % sensitivity, 97 % specificity, and with an overall accuracy of 97 %.

Impact of BMI on AGIS Signals

In linear regression analysis, BMI was not a significant predictor of AGIS intestinal rate and did not alter the relationship between patient group and intestinal rate

Table 1 Patient characteristics

	Post-operative ileus (*n*=25)	Tolerating oral feeding (*n*=7)	Healthy control (*n*=8)
Age—mean (SD)	64.3 (10.6)	65.4 (4.6)	35.5 (16.4)
Male gender—*N* (%)	25 (100)	7 (100)	5 (62.5)
Race—*N* (%)			
White	16 (64)	4 (57)	5 (62.5)
Black	9 (36)	3 (43)	0
Asian	0	0	3 (37.5)
BMI—mean (SD)	30.1 (7.1)	28.9 (3.7)	23.8 (3.7)
Type of surgery—*N* (%)			–
Partial colectomy with anastomosis	18 (72)	6 (86)	
Exploratory laparotomy[a]	6 (24)	1 (14)	
Partial colectomy with anastomosis and diverting loop ileostomy	1 (4)	0	
Indication for surgery—*N* (%)			–
Colorectal cancer or endoscopically unresectable polyp	21 (84)	6 (86)	
Small bowel obstruction	2 (8)	1 (14)	
Diverticulitis	1 (4)	0	
Perforated duodenal ulcer	1 (4)	0	
Incisional hernia	1 (4)	0	

[a] Procedures performed during exploratory laparotomy include lysis of adhesions, colostomy ?reversal, incisional hernia repair, and repair of perforated duodenal ulcer

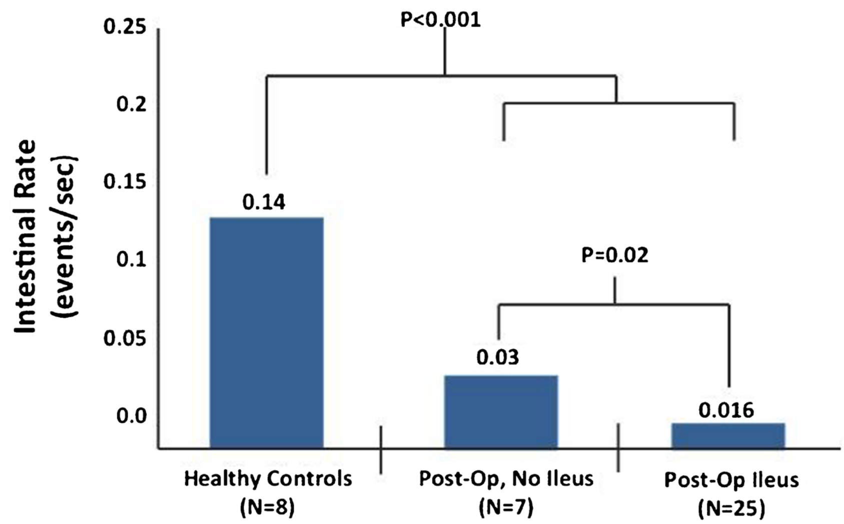

Fig. 3 AGIS-derived intestinal motility rates among study groups. Healthy controls demonstrated statistically higher motility rates than postoperative patients. Among patients, those with evidence of postoperative ileus had significantly lower AGIS signals than subjects without ileus tolerating the fast-track feeding protocol

(adjusted $\beta=-0.0004$, SE=0.0006, $p=0.55$). Signals captured from the patient in this series with the highest BMI (61.8) were accurately amplified and processed by the software and did not differ from those captured from patients with lower BMIs.

AGIS Data Display

Figure 5 shows a graphical user interface for AGIS signals, rendered in a "heat map" dashboard to demonstrate intestinal rates transformed onto a zero to ten scale for easy clinical

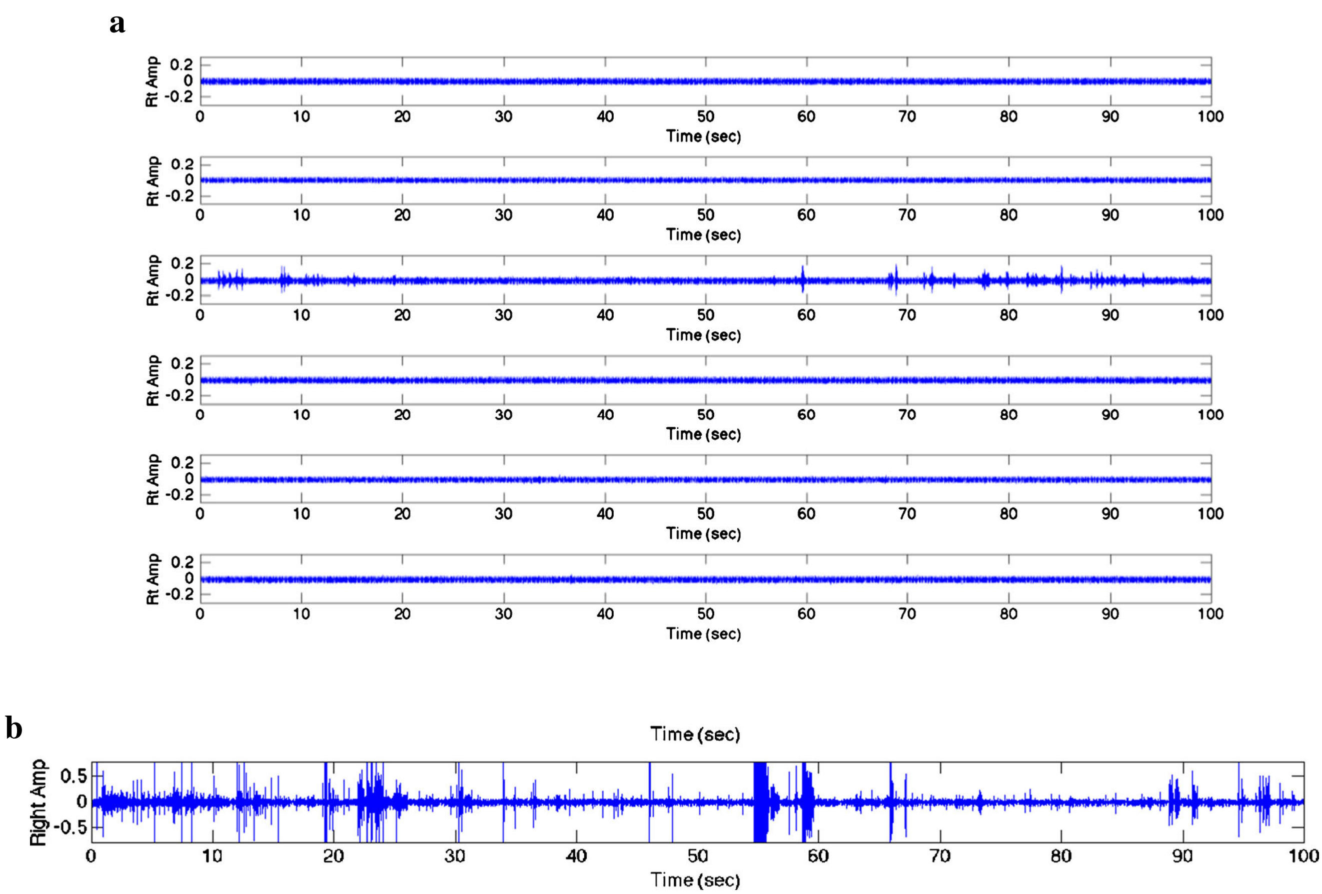

Fig. 4 Example GI telemetry. **a** Representative "GI telemetry" tracing in a patient with severe ileus. For 600 consecutive seconds, AGIS detected a "flat line" for all but fleeting moments in this subject with nausea and vomiting. **b** Representative tracing of a patient tolerating the standardized feeding protocol. In contrast to the patient with ileus, this patient demonstrates evidence of ongoing GI motility

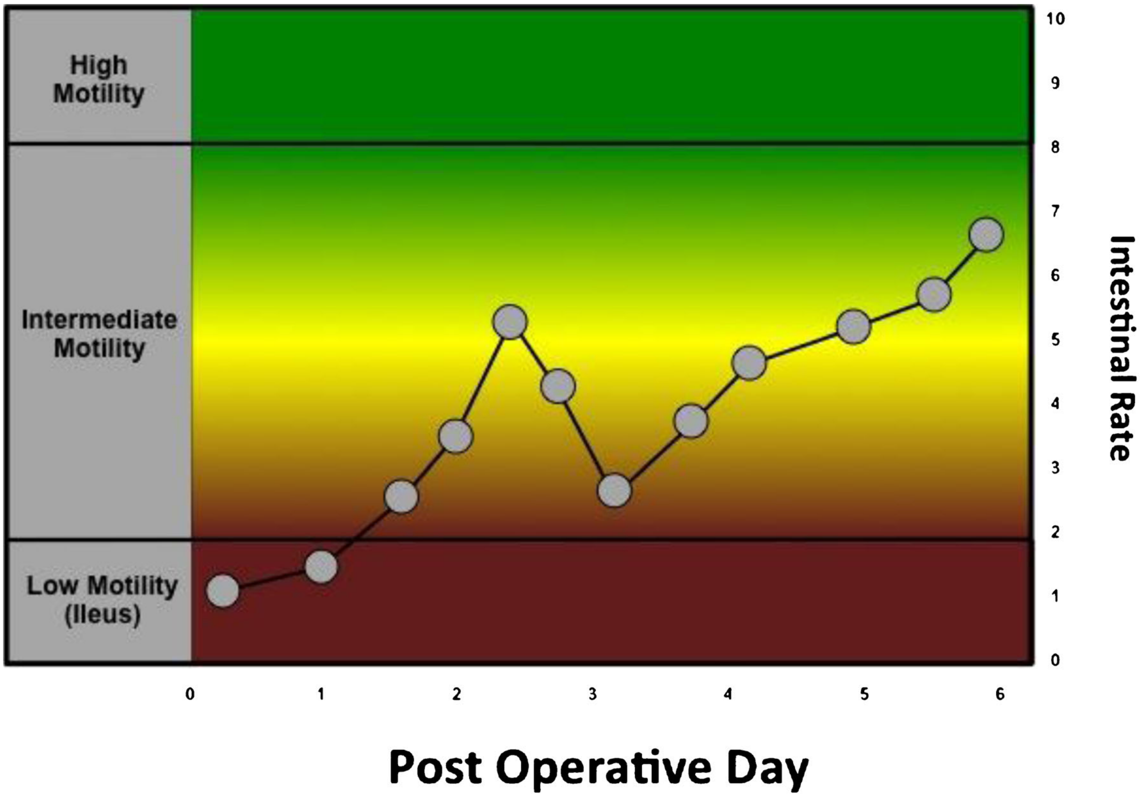

Fig. 5 AGIS intestinal motility tracker. Each AGIS measurement is presented on a motility score "heat map" along a 10-point scale. Scores below 2 indicate markedly low motility, consistent with POI, and suggest that oral feeding should be withheld. Scores above 2 are not consistent with POI and can be used to track intestinal recovery using serial measurements. Scores above 8 are consistent with healthy control subjects for purposes of comparison

interpretability. Scores below 2 are consistent with POI patients who cannot tolerate feeds (corresponding to an average rate of 0.01 intestinal events per second or lower), scores between 2 and 8 indicate intermediate motility, and scores above 8 indicate high motility consistent with healthy subjects. The "red zone" in the AGIS motility tracker indicates POI and suggests that oral feeding should be withheld until the score improves. Scores outside of the red zone are not consistent with POI in this data display. Notably, in this case series, we did not observe measurements in the high-motility zone, indicating that even among POI patients tolerating feeds, the underlying motility is often below that of healthy subjects and may not fully respond until well after discharge.

Discussion

In this study, we report a technique of monitoring bowel sounds in postoperative patients using a computer-aided, non-invasive AGIS biosensor. We found that AGIS-derived intestinal rates are significantly lower in patients with POI versus patients tolerating a standardized feeding protocol. We also found that patients recovering from abdominal surgery have markedly lower AGIS intestinal rates compared to healthy controls. Finally, we found that the biosensor could detect signals even in patients with a large body habitus.

The AGIS sensor may provide an incremental value over a stethoscope because it allows long-term acoustic monitoring, captures sounds below the threshold of human detection, and employs computer-aided analysis to quantify intestinal motility objectively. The sensor may help to address postoperative digestion monitoring by performing continuous analysis of GI signals, conducting automated data processing, and offering immediate reporting of the patient's progress to caretakers. As there is currently no standard approach to postoperative monitoring of intestinal motility, AGIS represents a clinically accessible approach to non-invasively track recovery of bowel function.

Although there is controversy about the clinical utility of bowel sounds in the postoperative setting,[15,16] there is less debate about whether bowel sounds have physiologic meaning. The ultimate proof that bowel sounds matter comes from carefully conducted manometric studies linking abdominal acoustics with catheter-based invasive measurements of GI motility.[17–21] In a study of healthy fasting subjects, Tomomasa and colleagues performed a computer-aided analysis of bowel sounds using microphones attached to the upper and lower abdominal walls and compared the results to readings obtained from an invasively positioned antroduodenal catheter. The investigators found that GI acoustics accurately performed tracking with propulsive MMC events and intestinal transit compared to the manometric gold standard. Because the appearance of propagating MMCs is the tipping point for bowel recovery in POI,[21] and since surface acoustics can reliably identify MMCs,[17] there is a strong physiologic rationale to monitor GI acoustics in the postoperative setting; this represents a more objective and quantifiable approach than relying exclusively on subjective parameters.

An advantage of modern microcomputing in health care is the ability to rapidly deliver automated, point-of-care results to caretakers. In postoperative diet management, a device like the AGIS sensor can provide "GI telemetry" and offer a new vital sign to complement traditionally measured parameters. Whereas caretakers routinely monitor a wide variety of cardiovascular, pulmonary, and neurocognitive parameters in abdominal surgery patients, there is still no routine objective marker for the abdomen, itself, yet abdominal physiology is vital to understand and perform tracking in the postoperative setting. The AGIS approach, coupled with a bedside computer, offers the potential for real-time intestinal motility tracking.

Although the AGIS-derived heat map (Fig. 5) should not provide the sole determination of whether and how to feed a postoperative patient, it may complement clinical gestalt by offering an additional, objective parameter to integrate with clinical decision making. It also provides patients with a direct visualization of their own GI motility, potentially offering a form of "biofeedback" using real-time data; the information might empower some patients to minimize narcotic usage or increase ambulation, where appropriate, to promote faster return of bowel function. AGIS monitoring also offers nurses monitoring and assurance opportunities; this might enhance discussions with patients and provide an objective marker to direct conversations with surgeons. Finally, although not tested in this study, AGIS could provide outpatient data to help surgeons evaluate the clinical importance of the development of nausea, vomiting, or feeding intolerance among patients at home who were recently discharged from the hospital.

This study has important limitations. First, we did not employ antroduodenal manometry as a gold standard to validate the AGIS signals. Therefore, we cannot know with certainty which signals are truly propulsive and which simply indicate uncoordinated intestinal activity. Nonetheless, previous work has shown that GI acoustics accurately correlate with meaningful motility events, such as the MMC.[17] Moreover, the most relevant standard in this study is actual clinical status—in this case, the presence or absence of POI. Our data indicate that there is a relationship between AGIS-derived intestinal rate and clinical status. Second, although there is separation between groups using AGIS, there remains an overlap in intestinal rates among the groups, especially between the POI and non-POI patient groups. Therefore, other than for very low AGIS scores, the signals cannot be used to definitely rule in, or rule out, ileus. Nonetheless, very low scores strongly indicate inadequate motility and sound a note of caution; that alone may be of important clinical value for patients where decision making is difficult. In addition, whereas *absolute* scores may not provide immediate value, *changes* in scores over time could be of even greater use. For example, a patient achieving a score of "6" on POD#1 may do well with fast-track feeding but later regress to a score of "3" on POD#2, indicating slowing of bowel motility, possibly because of concurrent use of narcotic pain medicine. This dynamic information might help surgeons, nurses, and patients make real-time decisions not only about how quickly to advance diet but also about whether and how to titrate narcotic exposure. A third limitation of this study is its overwhelmingly male population, which may not be generalizable. A final limitation is that this study is only cross sectional—not longitudinal. AGIS can physiologically distinguish among known groups, but it remains unknown if the method can proactively determine POI. For future applications, we will explore using AGIS as a diagnostic test to predict which patients will develop POI following abdominal surgery. If AGIS could proactively predict which patients will safely tolerate feeding, and which will not, then AGIS monitoring could be further used to direct individual patient feeding decisions in the vulnerable postoperative period rather than empiric use of an enhanced recovery pathway. In the meantime, this pilot study provides proof-of-principle evidence that AGIS distinguishes among clinically different groups and provides rationale to study the approach further in prospective predictive studies.

Conclusion

In conclusion, a computer-aided, acoustic, gastrointestinal surveillance biosensor can accurately distinguish between healthy controls and postoperative patients and further distinguish patients with POI versus those tolerating fast-track diet advancement. The AGIS sensor may offer a new abdominal vital sign—an "intestinal rate" in contrast to heart rate or respiratory rate—that delivers physiologic data to complement important yet subjective clinical gestalt. Future research will evaluate whether longitudinal AGIS monitoring can impact outcomes in postoperative management, including length of stay and feeding-related complications.

Conflict of Interest This study was conducted with funding from the Principal Investigators (B.S. and W.K.). The technology described in this study was developed by B.S. and W.K. and is managed by the UCLA Office of Intellectual Property (OIP). At the time of this study, UCLA submitted a patent application and was evaluating university in-licensing options. The authors did not receive outside funding to conduct this study. The opinions and assertions contained herein are the sole views of the authors and are not to be construed as official or as reflecting the views of the Department of Veteran Affairs.

References

1. Doorly MG, Senagore AJ. Pathogenesis and clinical and economic consequences of postoperative ileus. Surg Clin North Am 2012;92: 259–72, viii.
2. Lubawski J, Saclarides T. Postoperative ileus: strategies for reduction. Ther Clin Risk Manag 2008;4:913–7.
3. Kehlet H, Holte K. Review of postoperative ileus. Am J Surg 2001;182:3S-10S.
4. Asgeirsson T. Postoperative ileus: it costs more than you expect. J Am Coll Surg 2010;210:228–31.
5. Prasad M, Matthews JB. Deflating postoperative ileus. Gastroenterology 1999;117:489–92.
6. Lewis SJ, Egger M, Sylvester PA, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. BMJ 2001;323:773–6.
7. Andersen HK, Lewis SJ, Thomas S. Early enteral nutrition within 24h of colorectal surgery versus later commencement of feeding for postoperative complications. Cochrane Database Syst Rev 2006: CD004080.
8. Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24h of intestinal surgery versus later commencement of feeding: a systematic review and meta-analysis. J Gastrointest Surg 2009;13:569–75.
9. Warren J, Bhalla V, Cresci G. Postoperative diet advancement: surgical dogma vs evidence-based medicine. Nutr Clin Pract 2011;26: 115–25.
10. Wolff BG, Viscusi ER, Delaney CP, Senagore AJ, Fort JG, Du W, Techner L, Wallin B. Patterns of gastrointestinal recovery after bowel resection and total abdominal hysterectomy: pooled results from the placebo arms of alvimopan phase III North American clinical trials. J Am Coll Surg 2007;205:43–51.
11. Iyer S, Saunders WB, Stemkowski S. Economic burden of postoperative ileus associated with colectomy in the United States. J Manag Care Pharm 2009;15:485–94.
12. Asgeirsson T, El-Badawi KI, Mahmood A, Barletta J, Luchtefeld M, Senagore AJ. Postoperative ileus: it costs more than you expect. J Am Coll Surg 2010;210:228–31.
13. Barletta JF, Senagore AJ. Reducing the Burden of Postoperative ileus: Evaluating and Implementing an Evidence-based Strategy. World J Surg 2014.
14. Muller S, Zalunardo MP, Hubner M, Clavien PA, Demartines N. A fast-track program reduces complications and length of hospital stay after open colonic surgery. Gastroenterology 2009;136: 842–7.
15. Gu Y, Lim HJ, Moser MA. How useful are bowel sounds in assessing the abdomen? Dig Surg 2010;27:422–6.
16. Massey RL. Return of bowel sounds indicating an end of postoperative ileus: is it time to cease this long-standing nursing tradition? Medsurg Nurs 2012;21:146–50.
17. Tomomasa T, Morikawa A, Sandler RH, Mansy HA, Koneko H, Masahiko T, Hyman PE, Itoh Z. Gastrointestinal sounds and migrating motor complex in fasted humans. Am J Gastroenterol 1999;94: 374–81.
18. Dobkin BH, Xu X, Batalin M, Thomas S, Kaiser W. Reliability and validity of bilateral ankle accelerometer algorithms for activity recognition and walking speed after stroke. Stroke 2011;42:2246–50.
19. Au LK, Batalin MA, Stathopoulos T, Bui AA, Kaiser WJ. Episodic sampling: towards energy-efficient patient monitoring with wearable sensors. Conf Proc IEEE Eng Med Biol Soc 2009;2009:6901–5.
20. Xu JY, Chang HI, Chien C, Kaiser WJ, Pottie GJ. Context-driven, Prescription based Personal Activity Classification: Methodology, Architecture and End-to-End Implementation. IEEE J Biomed Health Inform 2013.
21. Shibata Y, Toyoda S, Nimura Y, Miyati M. Patterns of intestinal motility recovery during the early stage following abdominal surgery: clinical and manometric study. World J Surg 1997;21:806–9; discussion 809–10.