Published in final edited form as:

J Pediatr Gastroenterol Nutr. 2018 June ; 66(6): e146–e152. doi:10.1097/MPG.0000000000001867.

Electrogastrography, near-infrared spectroscopy and acoustics to measure gastrointestinal development in preterm babies

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Abstract

Objectives—To obtain objective measures indicative of gastrointestinal maturity using three non-invasive technologies.

Methods—Electrogastrography (EGG), abdominal near-infrared spectroscopy (NIRS), and bowel sound/acoustics (AC) monitoring were used simultaneously to obtain physiologic measures

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Conflicts of Interest and Source of Funding: Neu, Oh, Chien, and Ortigoza have a patent application (WO2015117035 A1 Methods and systems for feeding readiness diagnosis) through the University of Florida Research Foundation, Inc. Neu received grant UF00100174 from Covidien that partially funded this study. He is also on the Scientific Advisory Boards for Medela, Infant Bacterial Therapeutics, and Nutricia. He also receives research funding from Medela and Infant Bacterial Therapeutics. For the remaining authors, none is declared.

of the gastrointestinal system of 18 preterm and 5 term neonates who were tolerating enteral feedings. Measures of EGG slow wave voltage (EGG dominant power) and AC signal amplitude (AC dominant power) were obtained after spectral density analysis. Mean abdominal regional saturations (A-rSO₂) were obtained directly from NIRS. The relationship of these three measures with postmenstrual age (PMA) was assessed.

Results—The results of the three methods differed depending on whether the measurements were pre-prandial or post-prandial. Post-prandial EGG dominant power increases with PMA ($r=0.67$, $p=0.003$), both pre- and post-prandial abdominal NIRS mean regional saturation increase with PMA ($r=0.73$, $p<0.001$ and $r=0.55$, $p=0.009$), and post-prandial AC dominant power (at 300–500Hz) increases with PMA ($r= -0.48$, $p=0.025$).

Conclusions—EGG, abdominal NIRS, and AC, when used simultaneously, can provide objective and synergistic measures that correlate with PMA. These findings may be helpful in the assessment of feeding readiness because they reveal quantitative measures suggestive of the developmental process of the gut.

Keywords

Bowel sounds; gastrointestinal maturity; feeding readiness; dominant power; spectral density

Introduction

Premature newborns who are fed enterally have decreased morbidity and mortality (1). However, gut immaturity makes feeding challenging because gut maturity is essential for feeding readiness and tolerance. There is also fear among neonatologists that too rapid advancement of feedings may lead to necrotizing enterocolitis. Objective measurements are not available for determining feeding readiness. Current clinical measures to assess feeding readiness such as abdominal circumference and color, gastric residuals, emesis, and stool patterns are subjective and poor indicators of gut maturity. In fact, they more likely contribute to slow advancement of feeds in babies who otherwise may tolerate a faster advancement. Because no objective measure of gut maturity exists, we depend on these subjective measures of feeding readiness that lead to prolonged intravenous nutrition that results in complications, such as cholestasis, infection, and increased hospital stay and costs. Thus, objective measures of gastrointestinal maturity are needed to help identify babies who are ready to feed and will benefit from a faster feeding advancement.

Electrogastrography (EGG), near-infrared spectroscopy (NIRS), and electronic bowel sound/acoustic (AC) monitoring are non-invasive technologies that measure gastric myoelectrical activity, mesenteric tissue oxygenation, and abdominal mechano-acoustic activity, respectively. EGG and NIRS parameters are known to correlate with postmenstrual age (PMA) (2–7). However, the addition of AC and the simultaneous application of these three technologies is novel and may provide objective measures of gastrointestinal maturity that will aid the assessment of feeding readiness. This may lead to faster and safer feeding advancements and decreased morbidity and mortality (8).

Methods

Participants

Thirty-three preterm babies from the neonatal intensive care unit (NICU) at UF Health Shands Children's Hospital and five term babies from Parkland Memorial Hospital NICU were enrolled in the study after parental consent. The Institutional Review Board at the University of Florida and at UT Southwestern Medical Center approved this study. Subjects were premature newborns less than 34 weeks of gestation, with birth weights less than 1500 grams and term newborns 37 weeks of gestation or greater. All babies were less than 4 weeks old. Babies were excluded if they had any congenital or chromosomal disorders, major skin abnormalities, and faults in skin integrity that preclude placement of skin sensors. Intubated newborns and those with questionable viability due to severe complications were also excluded.

Apparatus

EGG, NIRS, and AC were used simultaneously to obtain measurements of gastric myoelectrical activity, mesenteric tissue oxygenation, and abdominal mechano-acoustic activity, respectively.

Electrogastrography (EGG)—Neonatal electrocardiogram (ECG) electrodes were applied to the babies' abdominal skin as described and validated in Chen et al. 1999 and other studies (9–13). Because of the small abdominal size of our patient population, we limited our setup to 3 electrodes (Figure 1). The positive electrode was placed midway between the umbilicus and xyphoid process. The negative electrode was placed on the left upper quadrant, at the level of the mid-clavicular line, slightly above the level of the positive electrode. The ground electrode was placed below the left costal margin, at the mid-axillary line, horizontal to the positive electrode, forming an equidistant triangle with the positive and negative electrodes. The electrodes were connected to the BIOPAC® MP36 System data acquisition unit (BIOPAC® Systems, Inc., Goleta, CA).

Near-Infrared Spectroscopy (NIRS)—A neonatal INVOS™ Infant Regional Saturation Sensor (Covidien Ltd., Minneapolis, MN) was placed to the right of the umbilicus and another (control) on the baby's forehead. The sensors were connected to the INVOS System (Covidien Ltd., Minneapolis, MN) for processing. This system and the participants' cardiorespiratory monitor were interfaced with the Vital Sync™ 5000 System (Covidien, Ltd., Minneapolis, MN) for comparison on the same display and on the same time line.

Bowel Sound/Acoustic (AC) Monitoring—An electronic microphone, BIOPAC® SS17L (BIOPAC® Systems, Inc., Goleta, CA) was positioned to the left of the umbilicus and secured with 3M™ Double-Stick Disks (3M Company, Maplewood, MN). The electronic stethoscope was then connected to the data acquisition unit.

Procedure

Because most babies in the neonatal intensive care unit (NICU) are fed every 3 hours, measurements were obtained for 3 hours. For EGG and AC, measurements included the 30-

minute pre-prandial period and the entire 2.5-hour post-prandial period that followed the enteral feeding. The entire post-prandial period was included to ensure sufficient data after filtering, removal of motion artifacts, and spectral density analysis. NIRS measurements included the 30-minute pre-prandial period and the 30-minute post-prandial period (60–90 minutes post-feeding); consistent with other studies that observed peak A-rSO₂ 60 minutes after feeding (14). Enteral feeding management was left at the discretion of the on-service neonatologist.

No clinical decisions were made based on the results of the proposed technological measurement, because these have not been used previously for the purpose of evaluating gastrointestinal maturity and feeding readiness. In this study, we were anticipating to measure gastric emptying responses induced by gastrointestinal myoelectrical and mechano-acoustic activities (via EGG and AC respectively), and to measure oxygen balance in mesenteric tissues (via NIRS).

Outcome Measures

EGG—The raw data was pre-filtered using a 2nd order Butterworth bandpass filter from 0.016Hz to 0.25Hz (1 cpm to 15 cpm) to help eliminate motion artifacts (15). Welch's Power Spectral Density Analysis based on Fast Fourier transformation (FFT) was performed using Matlab® (MathWorks Inc., Natick, MA) environment to calculate EGG measures of dominant frequency, dominant power, percentage of normal gastric slow waves, and instability coefficient (16, 17). The dominant power is the voltage of the EGG slow gastric wave that has been shown in previous studies to increase with increased gastric contractile activity (18–20). This is the EGG measure of interest in the current study.

NIRS—Pre-prandial and post-prandial abdominal mean regional saturations (A-rSO₂) were calculated from the raw data.

AC—The raw data was pre-filtered using a 10th-order Butterworth high-pass filter with a cutoff frequency at 80 Hz to suppress signals of cardiovascular origin. Spectral Density Analysis using Fast Fourier transformation (FFT) was performed to calculate AC dominant frequency and dominant power. The AC dominant power is the amplitude of the dominant acoustic frequency within the 300–500 Hz spectrum. This is the AC measure of interest in the current study.

Statistical Analyses

A sample size determination was not done because this was an exploratory pilot study looking at the feasibility of obtaining simultaneous measures from EGG, NIRS, and AC in premature babies.

Outliers were removed from a distribution if the measurement was more than 1.5 times the interquartile range away from either the 25th or the 75th percentile. Such an outlier would indicate that the observation is contaminated and not from the same distribution as the other measurements. Spearman correlations were performed on EGG dominant power, NIRS mean abdominal regional saturation, and AC dominant power to check for potential

associations with PMA. Pearson and Spearman correlations were performed on the variables for EGG, NIRS and AC to check for associations between the three technologies. A paired t-test was used to compare pre-prandial and post-prandial means for EGG dominant power, NIRS A-rSO₂, and AC dominant power. P-values less than or equal to 0.05 were considered statistically significant.

Results

Thirty-eight patients were eligible for the study and parental consent was obtained in all patients. Fifteen subjects were excluded (5 were intubated and 10 had technical issues with poor EGG data quality). Twenty-three subjects were included in the study (18 preterm and 5 term). For NIRS, twenty-two subjects were included because of missing data from 1 additional subject. None of the subjects experienced skin complications from the placement of electrodes and sensors.

Baseline subject characteristics are presented in the Table, Supplemental Digital Content 1 and subject characteristics at the time of recording are presented in Table 1. Five outliers from the distribution of EGG dominant power and one from the distribution of AC dominant power were removed because these outliers were more than 1.5 times the interquartile range; therefore, they were not from the same distribution as the other measurements.

Using a Spearman correlation (Figure 2), pre-prandial EGG dominant power was not associated with PMA; post-prandial EGG dominant power was associated with PMA ($r=0.67$, $p=0.003$). Both pre- and post-prandial NIRS A-rSO₂ were associated with PMA ($r=0.73$, $p<0.001$ and $r=0.55$, $p=0.009$). The pre-prandial AC dominant power (between acoustic frequencies of 300–500 Hz) was not associated with PMA; post-prandial AC dominant power (between 300–500 Hz) was associated with PMA ($r=-0.48$, $p=0.025$). See Table, Supplemental Digital Content 2, which shows these associations. All other correlations were not significant. Pearson and Spearman correlations did not show an association between EGG, NIRS, and AC parameters when compared to each other.

A paired t-test was used to compare pre- and post-prandial means for EGG dominant power, NIRS A-rSO₂, and AC dominant power. See Table, Supplemental Digital Content 3, which demonstrates these comparisons. For preterm babies, results showed a significant decrease in the mean AC dominant power after feeding (pre-prandial: 0.12 ± 0.05 , post-prandial: 0.09 ± 0.02 , $p=0.02$). EGG dominant power and NIRS A-rSO₂ did not show a significant difference in response to feeding (Figure 3). For term babies, results showed a significant increase in the mean EGG dominant power after feeding (pre-prandial: 0.04 ± 0.02 , post-prandial: 0.17 ± 0.05 , $p=0.009$). NIRS A-rSO₂ and AC dominant power did not show a significant increase in response to feeding. See Figure, Supplemental Digital Content 4, which shows the percent change in NIRS A-rSO₂ after feeding for each subject.

Discussion

Gastric myoelectrical signals, mesenteric tissue oxygenation, and bowel mechano-acoustic activity related to motility can be measured by EGG, NIRS, and AC, respectively. Our results show that simultaneous use of these three technologies can provide objective and

synergistic measures that correlate with PMA. This may provide the ability to assess gut maturity from three different perspectives. This study does not provide measures indicative of feeding readiness. Normative values of gut maturity at different gestational ages will need to be established first. The ability to measure gut maturity will form the basis of future studies that will provide clinicians with reliable information to help advance enteral feeds safely. A faster feeding advancement may decrease the use of parenteral nutrition and central lines, thereby decreasing morbidity in premature babies.

EGG has been validated to measure gastric myoelectrical slow wave activities using electrodes on the abdominal skin (21, 22). In newborns, EGG has been used to study postnatal maturation effects on myoelectrical activities (3, 4, 6, 7, 21, 23, 24). One EGG measure (dominant power) increases with postnatal age (3). To our knowledge, the relationship between EGG dominant power and gestational age has not been established until the present study. Per our results, post-prandial EGG dominant power increases with PMA, suggesting that EGG dominant power is a potential marker of stomach myoelectrical maturity. Although EGG does not measure stomach contractions directly, the relative increase in EGG dominant power is associated with an increase in gastric contractile activity (19, 20, 25). Thus, our results suggest an increase in gastric contractile activity with increasing PMA.

NIRS measures regional tissue oxygenation. Our results show that pre- and post-prandial A-rSO₂ increases with PMA. This relationship is consistent with other studies, suggesting that NIRS may assess gastrointestinal maturity (5). Changes in A-rSO₂ may represent maturation of the control of oxygen delivery and utilization at the tissue level. Studies using NIRS have demonstrated a relationship between low A-rSO₂ with feeding readiness and intolerance, including necrotizing enterocolitis (26–28).

Bowel sounds result from vibration waves caused by contractions of the gut walls propelling intraluminal liquid and gas. Quantitative analysis of bowel sounds can provide objective interpretation of the acoustical activities of the intestine associated with motility. A relative scarcity of research exists in computerized bowel sound/acoustic (AC) analysis even though it is non-invasive and based on traditional abdominal auscultation, a component of routine physical examination. In adults, AC has been used to investigate intestinal obstruction, acute abdomen, irritable bowel syndrome, small-volume ascites, and delayed gastric emptying (29–34). To our knowledge, AC has not been used previously to study gastrointestinal development. Our results show that post-prandial AC dominant power increases with PMA, suggesting that dominant acoustic power between 300–500Hz may give us useful information about gut maturity.

Comparisons between the three technologies did not reveal an association. Although EGG, NIRS, and AC parameters are not associated with each other, they are each associated with PMA, suggesting that they may measure different aspects of the developmental process of the gut. This lack of association between the three technologies may be secondary to a small sample size.

In adults and older children, an expected response to feeding includes an increase in EGG power (amplitude) of the gastric slow waves (15, 17, 35, 36), an increase in NIRS A-rSO₂ (14), and an increase in intensity of bowel sounds. For term babies, we were able to show an increase in EGG dominant power after feeding; consistent with previous studies (Figure 3A). However, we were not able to show a significant change in NIRS or AC after feeding. This is probably secondary to a small sample of term babies (n=5). For preterm babies, our results did not show a significant change in neither EGG dominant power nor NIRS A-rSO₂ after a feeding bolus. Perhaps our sample size is small or this change may be difficult to detect in our cohort of babies who are more premature than those of most other studies. However, it is important to note that the variability of the pre-prandial NIRS data in preterm babies is larger than term babies. See Table, Supplemental Digital Content 3, which demonstrates this variability. A large standard deviation is noted for both pre- and post-prandial data in preterm babies. However, for term babies, the standard deviation only increases after feeding. The increased variability in the pre-prandial data of preterm babies may be secondary to immaturity or limitations of the technology itself. NIRS may need to be further customized for obtaining abdominal measurements in very small babies so that it can be more sensitive to postprandial changes in this population. For the tiniest babies, the depth of penetration may need to be shorter and algorithms for bone penetration may not be needed. See Figure, Supplemental Digital Content 4, which shows the percent change in A-rSO₂ for each subject as a result of feeding. Nonetheless, our results showed that AC dominant power decreased after a feeding bolus in preterm babies. This suggests that this bowel sound measure (between 300–500 Hz) is attenuated after feeding. Perhaps AC dominant power increases at frequencies outside of 300–500 Hz; this needs to be explored in future studies.

Current technologies used to evaluate the gastrointestinal tract are radiography, ultrasound, nuclear scans, and manometry. However, these are either suboptimal or not applicable for the evaluation of gastrointestinal maturity in preterm babies. Our results show that the simultaneous use of EGG, NIRS, and AC can provide quantitative, objective information suggestive of the developmental process of the gut. This may help identify babies who have a mature gastrointestinal system, ready and able to tolerate enteral feeds.

Because all three technologies are non-invasive and do not disturb ongoing physiologic activities, they are attractive for studying infant gastrointestinal electrophysiology, oxygenation, and motility in the neonatal intensive care environment. With additional refinement, the synergistic use of these technologies show promise in the assessment of feeding readiness and the management of enteral feedings.

Each technology has disadvantages and limitations. EGG requires additional set-up time for skin preparation and electrode-checking. It is also sensitive to motion artifacts that need to be removed. With NIRS, a strong signal may be difficult to capture during the first month after birth because newborns may experience significant basal changes in intestinal vascular resistance during that time (37). This phenomenon is seen by a significant increase in baseline A-rSO₂ as stable preterm babies mature, suggesting maturational changes of physiologic oxygen balance (5). AC is a very attractive way to monitor gut maturity because of its simple set-up and ease of use. However, noise-filtering can be a complex task to isolate individual bowel sounds. Denoising algorithms may need to be applied in future studies.

At present, no single tool can accurately measure gastrointestinal development. We have shown that simultaneous use of EGG, NIRS, and AC can circumvent their individual limitations and provide quantitative, objective information suggestive of the developmental process of the gut. This information may be essential in the assessment of feeding readiness. The ability to identify babies who can be fed safely and have their feedings advanced from those who cannot, will be a major breakthrough in neonatal medicine. With additional refinement, we should be able to utilize these technologies simultaneously to assess gastrointestinal maturity and feeding readiness from three different physiological perspectives so that we can safely initiate and advance feedings, thereby decreasing morbidity and mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work is supported in part by the NIH/NCATS Clinical and Translational Science Award to the University of Florida UL1 TR000064 and by a Covidien grant to Neu UF00100174.

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What is Known/What is New**What is known?**

- Feeding premature babies is challenging because “feeding readiness” depends on gut maturity.
- Current clinical measures to assess gut maturity and feeding readiness are subjective, contributing to slow advancement of enteral feeds and morbidity. Objective measures are needed to help advance feeds.
- Electrogastrography (EGG) and near-infrared spectroscopy (NIRS) parameters correlate with postmenstrual and postnatal age; however, these have not been evaluated together.
- Bowel sound/acoustics monitoring (AC) has not been used to assess gut maturity.

What is new?

- Simultaneous use of EGG, NIRS, and AC in preterm babies provide objective measures that correlate with postmenstrual age.
- These findings reveal objective measures suggestive of the developmental process of the gut.
- Synergistic use of EGG, NIRS, and AC may lead to safer and faster feeding advancements, thereby decreasing morbidity.

Figure 1. Study Setup showing the position of the EGG electrode leads, NIRS sensor, and AC microphone

Figure 2.

The relationship of three measures were assessed with postmenstrual age. Significant correlations include a coefficient and p-value. **A)** Post-prandial EGG dominant power correlates with postmenstrual age. **B)** Pre-prandial and Post-prandial NIRS abdominal mean regional saturation correlate with postmenstrual age. **C)** Post-prandial AC dominant power correlates with postmenstrual age. Outliers were removed from the distribution if measurement was more than 1.5 times the interquartile range away from either the 25th or 75th percentile, thus EGG (n=20), NIRS (n=22), and AC (n=22).

Figure 3.

Pre-prandial and post-prandial mean comparisons for EGG, NIRS, and AC (preterm and term babies). **A)** EGG power spectrum for preterm babies (left) showing no significant difference between pre- and post-prandial dominant power. For term babies (right), a significant difference can be seen between pre-prandial and post-prandial curves ($p=0.009$). The shaded-region represents the standard error at each frequency. The unit for frequency, c.p.m. = cycles per minute. **B)** Boxplot showing that NIRS pre- and post-prandial abdominal mean regional saturations (A-rSO₂) were not significantly different for preterm or term babies. **C)** AC power spectra heat maps (between 300–500 Hz) for preterm and term babies, showing the difference between pre-prandial and post-prandial AC dominant power. For preterm babies (left) a significant decrease in the AC dominant power after feeding is shown (post-prandial AC power colors are more blue and “colder”), $p=0.02$. For term babies (right),

the AC dominant power appears to increase at certain periods after feeding (post-prandial AC dominant power colors are “warmer”), but results show no statistically significant difference.

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Table 1**Characteristics at Time of Recording**

Descriptive data for demographic and medical variables for the entire sample (n=23) at the time of recording.

At time of the measurement	
Weight (g)	1628 ± 959
Postmenstrual age (weeks)	32 ± 4.2
Postnatal age (days)	11 ± 7.1
Total Enteral Volume (mL/Kg/day)	123 ± 47
Volume of each feed (mL/Kg)	15 ± 5.8
Type of feed, Breastmilk	20 (87)
Last hematocrit measurement	47 ± 7.3

Numbers are mean ± standard deviation

Numbers followed by a parenthesis are n (percent)