

Noninvasive detection of ischemic bowel

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Purpose: Acute mesenteric arterial occlusion is an abdominal catastrophe that carries high morbidity and mortality rates. Current diagnostic methods, however, lack sensitivity and specificity and do not provide information about the viability of the affected bowel. Early diagnosis and intervention would improve patient outcomes and survival rates. The basic electrical rhythm (BER) is the omnipresent electrical slow wave of the gastrointestinal tract that characterizes the underlying electrical activity of the bowel. BER frequency is known to fall with ischemia. Superconducting quantum interference devices (SQUIDs) can detect BER by measuring the magnetic fields generated by the electrical activity of the smooth muscle of the small bowel. The purpose of this study was to determine the ability of a SQUID to detect mesenteric ischemia in a free-lying section of small bowel in an animal model of acute superior mesenteric artery occlusion.

Methods: Seven adult male rabbits (six experimental and one control) were studied with transabdominal SQUID and electrode recordings during baseline and after the induction of mesenteric ischemia with balloon occlusion of the superior mesenteric artery. Continuous recordings were taken for 120 minutes of ischemia and analyzed with autoregressive spectral analysis to determine the BER frequency during specific time points of the study. Two independent investigators blinded to the experimental preparation examined the results to determine whether there was decreased BER frequency and thus ischemia. The results are expressed as mean \pm SEM, and paired *t* tests were used to determine statistical significance.

Results: BER was detected in all seven animals and fell from 10.7 ± 0.5 cpm to 7.0 ± 1.8 cpm after 30 minutes of ischemia in the magnetic channels ($P < .05$, with *t* test). The fall in BER was detected by the SQUID in all six experimental animals. The blinded observers correctly identified healthy and ischemic magnetic data recording, with a sensitivity of 94% and specificity of 100%.

Conclusion: SQUIDs can noninvasively detect bowel ischemia early in a free-lying segment of small bowel in this animal model with a high degree of sensitivity and specificity. (J Vasc Surg 1999;30:309-19.)

Acute intestinal ischemia as the result of a sudden cessation of mesenteric arterial blood flow is an abdominal catastrophe that carries high morbidity and mortality rates.¹ Recent series still show a treatment mortality rate of almost 50%.² The poor outcomes of

this disease process are caused by the delay in initiating therapy because of difficulties in making an accurate and timely diagnosis. Current diagnostic methods are limited in their ability to noninvasively diagnose mesenteric ischemia, and none give information about the viability of the intestinal smooth muscle early in the course of ischemia before irreversible changes have occurred. Although techniques do exist to judge the viability of the bowel, these techniques lack sensitivity and specificity and are available only at laparotomy.³ The ideal test for mesenteric ischemia would be noninvasive, fast, reproducible (to follow changes over time), both sensitive and specific, and would provide information about the viability of the intestine.

The basic electrical rhythm (BER) is the omnipresent slow wave of the gastrointestinal tract that characterizes the underlying electrical activity of the bowel. Action potentials, which occur only during

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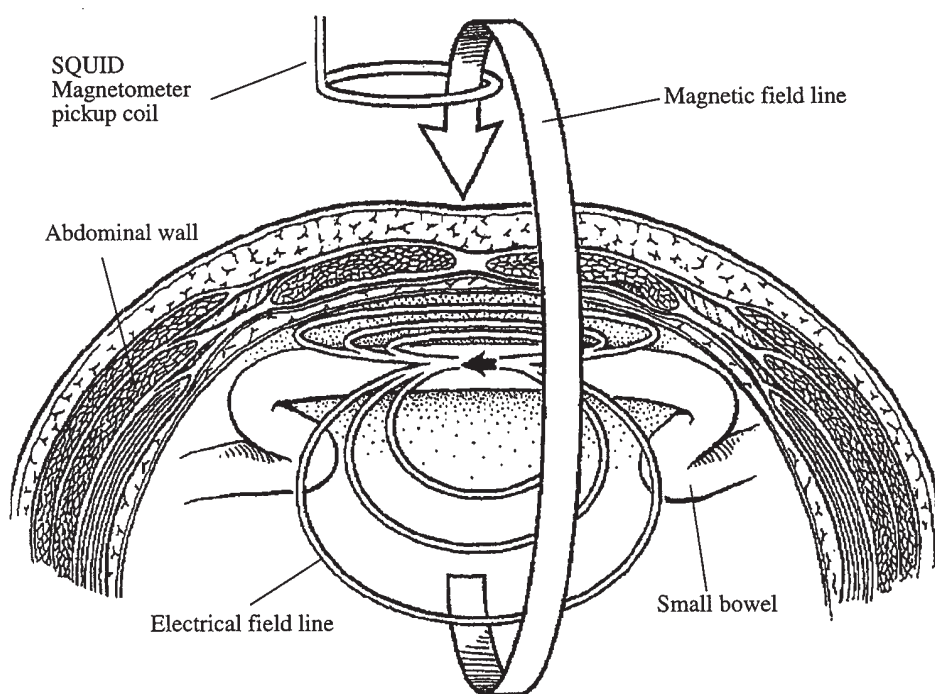


Fig 1. Graphic demonstration of SQUID pickup coils detecting magnetic field data from small bowel sources in abdominal cross section. Unlike magnetic fields, the electrical field is attenuated by intervening layers of muscle and fatty tissue. Thus, surface electrical recordings have low signal-to-noise ratio and those of the SQUID have high signal-to-noise ratio.

BER depolarization, cause contraction of the intestinal smooth muscle. As such, the BER is present even in the absence of peristalsis. Although bowel activity may be hyperactive early in ischemia (which reflects a greater number of action potentials), BER frequency is declining. Unlike other methods of assessing bowel viability, measurements of BER are passive and can yield useful information during short periods of analysis. In addition, there are only three known causes of decreased BER frequency: hypothermia,⁴ hypothyroidism,⁵ and hypoxia. The frequency and amplitude of small bowel BER have been shown to fall with arterial ischemia.⁶⁻⁸ This decrease has also been shown to occur before the onset of pathologic changes.⁹ Our laboratory has characterized the BER during both ischemia and reperfusion and correlated these changes with the histopathology of intestinal ischemia.¹⁰ BER is a highly sensitive measurement of bowel viability, and changes in BER during ischemia are present within 10 minutes after mesenteric occlusion, well before irreversible ischemic damage occurs.¹⁰

Superconducting quantum interference devices (SQUID) can detect the magnetic fields generated by the electrical activity of the smooth muscle of the small bowel.^{11,12} Fig 1 graphically illustrates the

concept of small bowel magnetic field detection. Whereas electrical signals are highly attenuated by the electrical insulators of the abdominal wall and thus have a low signal-to-noise ratio, the magnetic fields generated by the electrical fields are not attenuated and have a high signal-to-noise ratio.¹³ In addition, no contact between the SQUID instrument and the abdominal wall is necessary.

Previous studies in our laboratory have used SQUID measurements to detect not only normal BER but also ischemic BER frequencies in exteriorized small bowel segments of anesthetized rabbits.¹⁴ Further studies have shown the ability of the SQUID to detect an ischemic section of small bowel sewn to a known location of the abdominal wall.¹⁵

The purpose of this study was to determine the ability of a SQUID to detect mesenteric ischemia in a free-lying section of small bowel in an animal model of acute superior mesenteric artery (SMA) occlusion. Simultaneous electrode measurements were used for verification of the ischemic state. We hypothesized that SQUID measurements of the intestinal magnetic field activity can detect normal and ischemic BER frequencies and follow the BER change during ischemia.

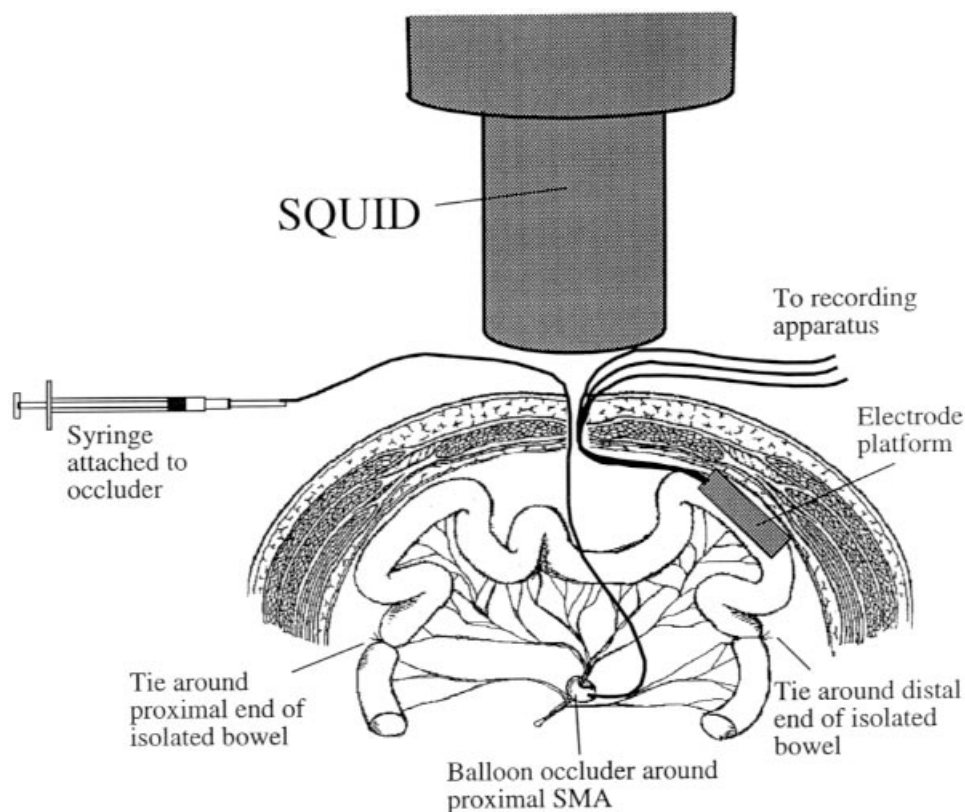


Fig 2. Abdominal cross section of experimental animal showing placement of vascular occluder, isolated bowel, electrode platform, and position of GutSQUID during the study.

MATERIALS AND METHODS

Animal preparation. Seven adult male New Zealand rabbits (six experimental and one control) weighing between 3 and 4 kg each were studied after a 3-day diet of nonmagnetic food followed by an overnight fast with free access to water. All animal care and manipulations during the course of this study complied with guidelines established by the animal care and use committee at Vanderbilt University and the Guide for the Care and Use of Laboratory Animals (Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council. Washington: National Academy Press, 1996). Induction of anesthesia was accomplished with intramuscular acepromazine maleate (0.5 mg/kg), xylazine hydrochloride (3 mg/kg), and ketamine hydrochloride (40 mg/kg). An intravenous catheter was placed in an ear vein for the administration of normal saline solution during the study and for the administration of subsequent doses of ketamine hydrochloride to maintain anesthesia. Body temperature was kept constant with a circulating fluid

warming blanket and was checked periodically with a rectal thermometer.

After a midline laparotomy, the small bowel was identified from the ligament of Treitz to the terminal ileum and isolated with its vascular supply intact. The SMA was identified and dissected free. A balloon vascular occluder (In Vivo Metric, Inc, Healdsburg, Calif) was positioned around the SMA at a level that rendered approximately 60% to 70% of the jejunum and ileum ischemic when the balloon was inflated with saline solution. Proper functioning of the occluder was verified with a Doppler scan flow probe (model ES-1000SPM, Koven Technology, Inc, St Louis, Mo). This resulted in a segment of approximately 120 cm of isolated small bowel that was then ligated at either end, but not transected, to prevent intramural blood flow (Fig 2). Ligation was used to ensure total vascular isolation when the balloon occluder was inflated because this study was designed to investigate a large segment of completely ischemic small bowel. In each animal, there remained approximately 30 to 40 cm of unaffected bowel proximal to and 30 to 40 cm distal

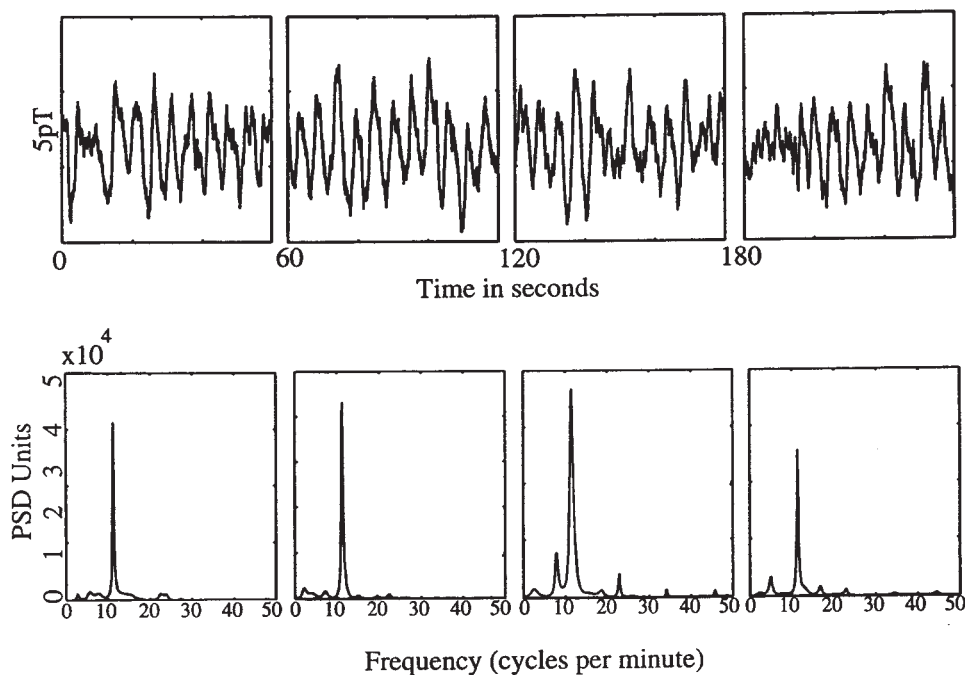


Fig 3. Raw data and autoregressive spectral analysis example. Shown are four 1-minute blocks of continuous magnetic data and corresponding PSD for each time period. Dominant frequency in each is approximately 11 cpm.

to the isolated segment. The electrode group consisted of a silastic platform containing three pairs of bipolar Ag-AgCl electrodes. The platform was sutured to this isolated segment near the distal end, and this segment then was wrapped with a nonconducting latex sheet (to prevent the recording of electrical activity from adjacent bowel loops) and replaced in the abdomen. The laparotomy was closed in two layers, with both the vascular occluder tubing and the electrode platform wires exiting through the inferior aspect of the incision. The bowel thus remained free lying in the abdomen. The control animal underwent laparotomy, dissection, electrode placement, and closure exactly as described previously, except the balloon occluder was sutured to the mesentery adjacent to the proximal SMA, not encircling it.

Data acquisition. GutSQUID, the device used in this study, has been especially designed for the detection of human gastrointestinal sources. Its superconducting pickup coils convert magnetic field data into voltage values that can be recorded and quantified. It is housed in a magnetically shielded room (Vacuumschmelze, Hanau, Germany) to minimize interference from nearby magnetic sources. Raw voltage data from GutSQUID was amplified with a SQUID amplifier (Conductus, Inc, San Diego, Calif),

and filtered from DC to 500 Hz. The data then were processed through a Beckman amplifier (model R612, Beckman Instruments, Inc, Palo Alto, Calif) that was connected to an analog-to-digital converter (model MP100, Biopac Systems, Cupertino, Calif) and an Apple Powerbook (Apple Computer, Inc, Goleta, Ga) with Acknowledge 3.1.2 data acquisition software (Biopac Systems). The magnetic signal was further filtered with the Beckman amplifier from 0.16 Hz to 30 Hz. The electrode platform also was connected to the Beckman amplifier and filtered from 0.16 Hz to 30 Hz; electrical data were acquired simultaneously with the SQUID recordings. All the experiments were performed in the magnetically shielded room to reduce background magnetic interference.

After the SQUID was positioned over the lower abdomen, BER signals (three channels of electrical data from the electrode platform and three channels of data from the three SQUID channels) were recorded for 1 hour of baseline BER determination. Ischemia was induced by filling the balloon with saline solution through the attached silicone tube. Filling the balloon did not induce ischemia in the control animal. Data were acquired for an additional 120 minutes. At the end of the period of ischemia,

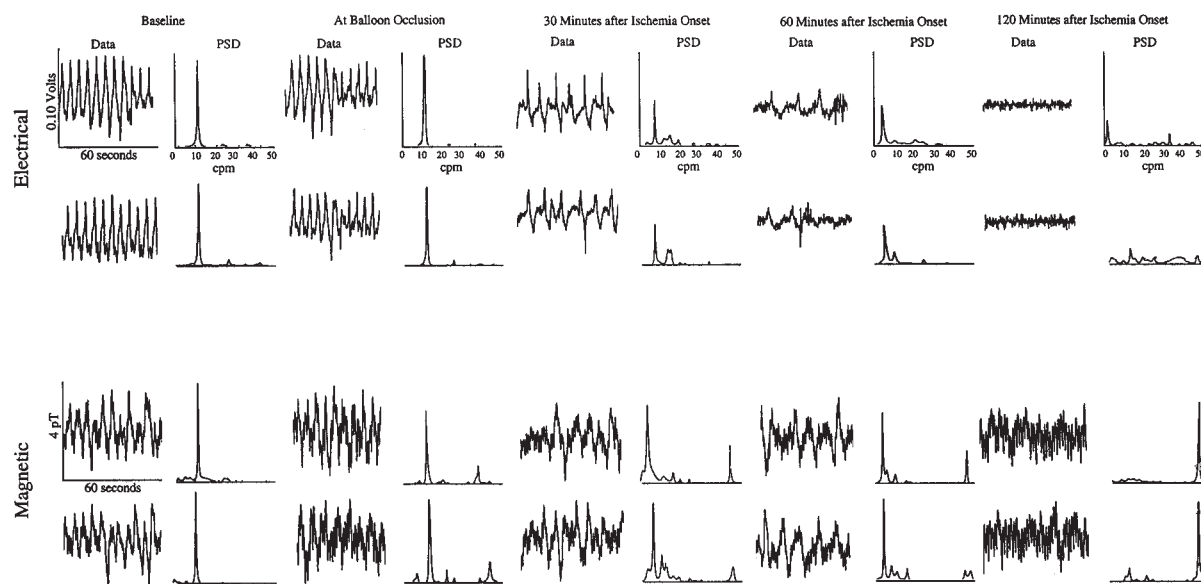


Fig 4. Comparison of electrical and magnetic data. Simultaneous 1-minute segments in electrode data and SQUID data are displayed with corresponding PSD graphs at various times during study for one animal. Decreasing BER frequency can be seen in both sets of data.

the animal was killed and the bowel was examined to visually confirm the presence of ischemia.

Data analysis. The BER signals were analyzed with autoregressive spectral analysis performed on a Macintosh computer (Apple Computer, Inc) running MATLAB software (The Mathworks, Inc, Natick, Mass). The autoregressive method examines electrical and magnetic signals over defined time periods and determines the dominant frequencies during that time displayed as power spectral density (PSD) estimate (Fig 3). It provides a rapid, objective way of assessing the BER frequency on a minute-to-minute basis, thus exposing the dynamic nature of the changes in the electrical activity of the bowel during ischemia.¹⁶ Unlike other methods of frequency analysis, such as Fast Fourier Transformation, autoregression does not necessitate long periods of stable signal, and, in this study, it was performed on successive 1-minute time periods. BER frequency is expressed as mean cpm \pm SEM. The two-tailed paired *t* test was used to determine significant BER frequency differences; significance was set at $P < .05$.

Determination of ischemia by blinded observers. Fifteen data segments of 5 consecutive minutes each were taken from the SQUID recordings during stable data periods at various timepoints during the study—six baseline and nine ischemic segments (all animals included). Two observers (W.O.R. and L.A.B.) blinded to the time points of the data

segments (ie, whether during baseline or during ischemia) were each given the 15 data segments in random order with the corresponding PSDs. Each was asked to indicate whether the data segments came from an animal without ischemia (baseline) or from an animal with ongoing ischemia by using the following criteria: *healthy*, defined as a single stable frequency peak of more than 10 and less than 20 cpm over the data period; and *ischemic*, defined as the absence of a single stable frequency peak in the previous range or the presence of multiple frequency peaks less than 10 cpm. After an indication on each sheet of the observer decisions, the data segments were organized by individual animals and the observers were given the opportunity to change their answer after viewing all time points from a given animal together. The sensitivity and specificity of analyzing the data in this way was determined from the following formulas: sensitivity = true positives / (true positives + false negatives) \times 100; specificity = true negatives / (true negatives + false positives) \times 100.

RESULTS

Baseline. Baseline BER frequency was detected in all six experimental animals in both the SQUID and electrical channels. The two forms of data—electrical and magnetic—were visually similar (Fig 4). In five of six cases, BER frequency could be appreciated from the raw magnetic data, and, in the

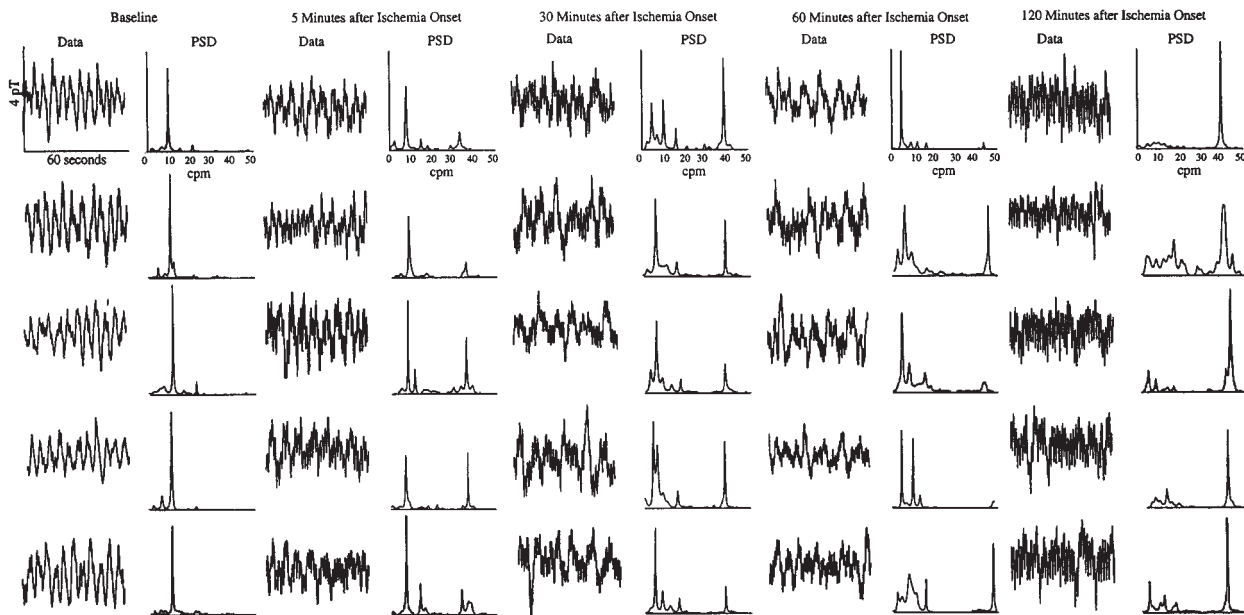


Fig 5. Raw magnetic signal data and corresponding autoregressive power spectra for consecutive 5-minute samples from single animal at baseline and at 5, 30, 60, and 120 minutes after induction of mesenteric ischemia with balloon occluder. BER frequency (11 cpm at baseline) decreases with increasing ischemia length. After 120 minutes of ischemia, BER peak is not present. These series of recordings also show multiple peaks seen at 0 to 10 cpm that are characteristic of ischemia. Animal's respiratory rate varied from 30 breaths per minute (bpm) to more than 50 bpm at various points in the study. When it was less than 50 bpm, it is seen as sharp peak in higher frequency range.

sixth animal, autoregressive spectral analysis was necessary to determine the presence of BER. There was no difference in the mean baseline BER frequency at each point in the study between the electrical and the magnetic channels, except at 90 minutes when the electrical BER signal was undetectable but the magnetic BER signal was still present. Table I lists the mean BER frequencies for each time point. A mean baseline BER frequency of 10.7 ± 0.5 cpm was evident in the electrical channels and was 11.0 ± 0.4 cpm in the SQUID channels.

Ischemia. A characteristic fall in BER frequency within several minutes after the induction of ischemia occurred in all six animals. By 90 minutes, BER was no longer detectable in the electrical channels in all animals. The magnetic BER signal was present longer than the electrode signals, disappearing in five of six animals by 120 minutes; one animal remained with a low 4 to 5 cpm dominant frequency at 120 minutes. Fig 5 shows the characteristic magnetic signal data and frequency profile for a single animal. Five continuous 1-minute data segments are shown at sequential time points during the study with the cor-

responding PSD. The animal's respiratory rate varied between 30 and 60 breaths per minute and appears on the PSD graph when less than 50 because this is the upper frequency value chosen for the autoregressive graphs (higher frequency determination is possible with autoregression but is not shown for clarity). Respiratory artifact may be easily filtered out, if desired. However, inclusion allows identification of this peak as the respiratory signal when correlated with the directly observed respiratory rate and thus excludes it as any other signal. It is important to note that at only 5 minutes of ischemia, the BER frequency had already begun to fall and was apparent from the magnetic field recordings (Fig 5). The control animal did not exhibit a fall in BER frequency after balloon inflation (which was sutured to the mesentery, not around the SMA, as described in the methods section) or during the subsequent 120-minute period. Fig 6 shows the fall in BER frequency for the SQUID channels and the electrical channels. By 30 minutes, the decrease in BER frequency was less than baseline in both sets of measurements ($P < .05$, with paired t test).

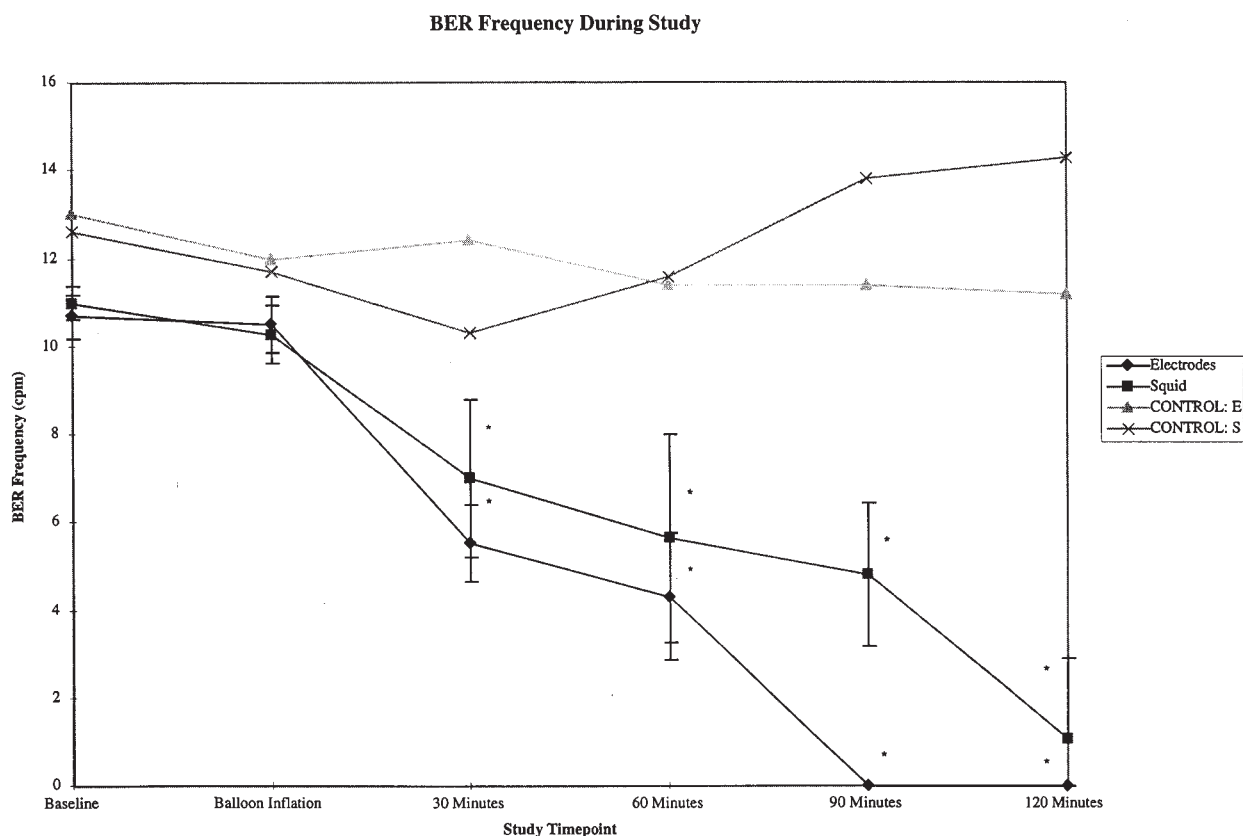


Fig 6. Mean magnetic and electrical BER frequency plotted together with control animal for each time period during study. Error bars correspond to \pm standard error of mean. Asterisks indicate ischemia values significantly different from baseline ($P < .05$, with paired t test). Control animal BER frequency did not decrease with time after inflation of occluder attached to mesentery.

Table I. Mean BER frequency for each group and control at specified time points during the study

	Baseline	Balloon filled	Ischemia			
			30 minutes	60 minutes	90 minutes	120 minutes
Experimental						
Electrical	10.7 \pm 0.5*	10.5 \pm 0.6*	5.5 \pm 0.9*	4.3 \pm 1.4*	0†	0*
Magnetic	11.0 \pm 0.4	10.3 \pm 0.7	7.0 \pm 1.8	5.6 \pm 2.4	4.8 \pm 0.6	1.1 \pm 1.8
Control animal						
Electrical	13.0	12.0	12.4	11.1	11.4	11.2
Magnetic	12.6	11.7	10.3	11.6	13.8	14.3

*Mean electrical values and magnetic BER values not statistically different when electrical and magnetic mean values are compared with paired t test for each point in the study ($P > .05$).

†Mean values statistically different with paired t test ($P < .05$).

Blinded observer determination of ischemia.

After viewing the data segments in random order, the observers independently identified nonischemic (baseline) segments correctly 12 of 12 times (100%). During ischemia, the observers labeled the data seg-

ments correctly as “ischemic” 17 of 18 times (94%). One observer labeled an ischemic time segment as “baseline or early ischemia” but correctly changed the designation to “ischemia” after viewing all the segments from this animal together. The segment

Table II. Sensitivity and specificity of the blinded observers' determination of ischemia

Observer choice	Study period	
	Baseline	Ischemia
Ischemia not present	12/12	0/0
Ischemia present	0/0	17/18*

*One observer scored an early ischemia time segment as "baseline or early ischemia." After reviewing all segments for this animal, the observer changed the designation to "ischemic."
Sensitivity, $17/18 \times 100 = 94\%$; specificity, $12/12 \times 100 = 100\%$.

was in fact early ischemia (30 minutes) in which there were not dramatic changes in the BER yet. The sensitivity (94%) and specificity (100%) of analysis of the data in this manner is given in Table II.

DISCUSSION

This is the first demonstration of noninvasive detection of ischemic bowel in an animal model in which the bowel is not localized by suturing to the abdominal wall. The basis of this technology to noninvasively detect ischemic bowel rests on the observation that electrical activity of the bowel is altered early after occlusion of the mesenteric blood supply. Szurszewski and Steggerda⁸ showed that the frequency of BER in unanesthetized dogs decreased in the ischemic segment of the small intestine but was unchanged in the adjacent, normally perfused bowel. In vitro studies showed that total anoxia significantly reduced the time occupied by migrating spike bursts and the BER frequency in the cat colon.¹⁷ The maximum change occurred 45 minutes after anoxia was induced and remained constant for as long as 3 hours. These changes were reversible within 15 minutes of restoring 95% oxygen.

To be a useful noninvasive tool for the detection of mesenteric ischemia, the electrical changes occurring during ischemia must occur before irreversible pathologic changes. Typically, microscopic changes occur first in the mucosa.¹⁸ Our laboratory showed in rabbits that the BER frequency decreased within minutes after the onset of ischemia but that pathologic changes were not detected until 60 minutes of ischemia with standard microscopic evaluation.⁹ Thus, significant changes in BER frequency occurred well before the onset of pathologic changes.

For noninvasive detection of smooth muscle electrical activity to be used to diagnose ischemic bowel, the BER parameters (for example, frequency and amplitude) would have to correlate to the

length of ischemia and accurately reflect the viability of the bowel. Our laboratory has performed studies in a rabbit model that indicate that BER amplitude, propagation velocity, and frequency accurately reflect bowel viability and that prolongation of an ischemic insult eventually causes the BER to fall to undetectable levels.¹⁰ Complete loss of BER during episodes of ischemia, however, does not preclude a subsequent recovery of BER during restoration of blood flow, in some cases to baseline levels. The likelihood that BER will return is highly correlated with the length of ischemia. Conversely, the recovery of BER during reperfusion does not necessarily preclude a subsequent loss of BER despite ongoing blood flow. In addition, the longer the ischemic episode, the lower the average BER frequency will be when it returns during reperfusion.¹⁰ These studies also indicate that there is a decrease in frequency, amplitude, and propagation velocity caused by reperfusion injury. Thus, the concept of noninvasive recordings of intestinal BER to diagnose mesenteric ischemia before pathologic changes is well founded in the pathophysiology of the disease process.

The first measurements of magnetic fields present in living tissue were made in the 1960s with room temperature coils.¹⁹ SQUIDS are used today because of their low intrinsic noise and wide frequency response. The concept of magnetic fields within living tissue is best understood by describing the electric currents and magnetic fields within a single nerve or fiber of muscle. Within a muscle, fiber electrical currents flow in a longitudinal axial direction. Separated from the intracellular space by the cell membrane, the extracellular space provides the path for the return current flow. The result of the intracellular current flow is the generation of a magnetic field. Study results of the examination of the magnetic fields generated from human nerve fibers have shown that fields of 50 femtotesla (nine orders of magnitude smaller than the Earth's magnetic field) are present.²⁰ SQUID biomagnetic field measurements are fundamentally different from those obtained with magnetic resonance imaging (MRI). Although MRI relies on the interaction between externally applied magnetic fields with the individual atomic nuclei, SQUIDS measure the magnetic field created by bioelectric current flow within the smooth muscle of the intestine. Thus, this measurement more closely resembles the electrocardiogram or the electroencephalogram than the MRI.

The use of cutaneous electrodes and SQUIDS are two different ways to record the same electromagnetic activity. Cutaneous electrodes measure the

potential difference that results from the flow of electrical current between two points. Thus, cutaneous electrodes record the electrical potentials through the smooth muscle of the small bowel and the omentum, peritoneal surfaces, abdominal wall musculature, abdominal wall fat, and skin.²¹ The wave forms and frequency spectra recorded with cutaneous electrodes are attenuated by the tissues that serve as electrical insulators between the electrodes and the source. Only by making assumptions about the nature of the source and the expected frequency of the source is it possible to make an estimate of the location and amplitude of the electric current measured.²² SQUID biomagnetic measurements are not attenuated as much by the intervening electrically insulating tissue.¹³ Another important concept regarding the advantages of noninvasive SQUID magnetometer measurement of BER over cutaneous electrodes is the concept of source separation. Because the insulating layers of the abdominal wall and omentum tend to smooth the signals emanating from the small intestine electrical potentials, the cutaneous electrode will tend to merge the two separate sources as coming from one location and the magnetic field measurements are able to distinguish that there are two sources.²³

Since our first recordings of smooth muscle BER *in vitro*, we have performed a series of magnetic field measurements in animals with several different SQUID systems.^{11,24} In these studies, we have demonstrated our ability to detect both BER and spiking activity and to identify *in vitro* the decreases in BER frequency in ischemic bowel after injection of thrombin into the supplying mesenteric artery and after injection of thrombin into the superior mesenteric vein, which causes venous ischemia.^{12,14,25,26}

Previous studies showed a high degree of correlation between magnetic field BER frequency obtained noninvasively and invasive serosal electrodes BER frequency.¹⁷ An important aspect of the current experimental model was that the ischemic segment was not sutured to the abdominal wall to localize it for the noninvasive SQUID measurements. These experiments therefore showed a lower correlation between the electrode measurements of BER frequency and the noninvasive SQUID measurements. This discrepancy can be related to the SQUID measuring slightly different segments of bowel, although the invasive serosal electrode data measured a single, constant small segment. In previous studies, we used Fast Fourier Transformation for both the serosal electrode and the SQUID recordings to determine the dominant frequency.¹⁷ The

disadvantages of this technique include the inability to use short time segments for measuring the dominant frequency. Thus, during ischemia, when we expect the BER frequency to be rapidly changing, the dominant frequency will have a lower power because of the instability of the signal.¹⁶ In this experiment, autoregressive spectral analysis was used to compare noninvasive SQUID recordings of BER frequency with invasive serosal electrode recordings. This technique allowed much shorter time periods to be used to determine the dominant frequency present. Autoregressive spectral analysis proved to be more successful in the determination of both the electrical and the magnetic field BER frequency during the time period of greatest signal change.¹⁶ Moreover, it would allow the use of short segment recordings in patients holding their breath. This has obvious advantages that would completely eliminate a significant source of biologic noise that contaminated the recordings taken in these animals. Other methods of signal analysis, such as the time-frequency method continuous wavelet transform, could also be used. Although autoregression does not necessitate long periods of stable signal, over the short signal period used (1 minute in our analysis), it does assume signal stationarity. In our data, however, we were most interested in the dominant frequency, and because the average frequency decrease during the greatest period of signal change during ischemia was 0.4 cpm, we believe autoregression accurately identified the signal frequency. In the application of this technology to human studies, we will investigate the use of continuous wavelet transform and other methods of time-frequency analysis to better characterize the changes in signal power during ischemia, as well.

The use of spectral analysis is an extremely important part of the signal analysis that allowed our observers to identify ischemic smooth muscle. In the healthy rabbit bowel, there is a single strong peak at 10 to 11 cpm and a smaller peak between 30 and 60 cpm that reflect respiration. As early as 5 minutes after the occlusion of the mesenteric vessels, there are dramatic changes in the BER recorded with the SQUID—not only is there a reduction in BER frequency, but multiple peaks are evident in the autoregressive PSD graph. This becomes even more prominent after 60 to 90 minutes of ischemia, and by 120 minutes of ischemia, there are no longer any peaks present in the lower frequencies, thus reflecting the loss of BER with prolonged ischemia. The human eye is unable to distinguish these multiple peaks seen during early ischemia that the autore-

gressive spectral analysis brings forth so clearly. We hypothesize that these multiple peaks seen with the SQUID are a reflection of smooth muscle decoupling with the emergence of multiple groups of smooth muscle cells entrained by a pacemaker at slightly different frequencies.¹⁰ This pattern would be similar to a "patchy" loss of viability. We believe that segments with different levels of ischemia will cycle at different frequencies. A completely healthy segment of intestine will cycle the BER at a normal frequency, and an ischemic piece of intestine will cycle at lower frequencies. Our studies with multiple electrodes show the same phenomenon, only to a lesser degree because the closely spaced bipolar electrode used in this study recorded a much smaller area of tissue and the SQUID recorded a larger segment of bowel containing segments of smooth muscle with their own intrinsic BER frequency.

There are significant hurdles to bringing SQUID technology to clinical use. The pickup coils must be superconducting: they are cooled with liquid helium to 9 K and need housing in a large insulating dewar. In addition, a magnetically shielded room is currently needed to minimize magnetic interference from outside sources (a metal stretcher moving close to the instrument, for example). Stretchers used for MRI applications can easily be adapted for use in a SQUID system, however. Advances in technology, though, are allowing the development of high temperature SQUIDs and smaller shields. Unshielded SQUID recordings are possible, as well.²⁷ Other questions that remain include how much ischemic bowel is necessary for detection and whether SQUIDs can detect ischemic bowel underneath healthy bowel. These recordings were performed with a single channel instrument: a multichannel instrument that provided coverage of the entire abdomen would allow simultaneous recordings of a much larger area and thus allow determination of BER signal from multiple intestinal sources within the abdomen simultaneously. A multichannel instrument would possibly allow detection of "patchy" areas of necrosis, as well. In addition, serial measurements could be used to follow the BER after operation for SMA occlusion or to obviate the need for second look laparotomy if no ischemic signals are detected. As these advances continue, we are hopeful that this technology can be used for clinical studies and perhaps even brought to the bedside.

CONCLUSION

Although biomagnetic signals have been recorded for 30 years and SQUID magnetometers have

been in use for more than 20 years, there have been surprisingly few applications of SQUIDs to the study of the physiology and pathology of the gastrointestinal system. Our previous research has shown that the pathologic biomagnetic signals from the gut are sufficiently large and of a temporal frequency that they can be recorded noninvasively with SQUIDs. This study shows the ability to diagnose ischemic bowel noninvasively with a SQUID and, importantly in a model in which the bowel is free lying within the abdomen, with a high degree of sensitivity and specificity. The use of SQUIDs to diagnose ischemic bowel has many of the characteristics of the ideal test: it is noninvasive, has high sensitivity and specificity, detects early ischemia before pathologic changes, can be used multiple times to follow therapy, and is fast in determination of viability. These results have encouraged us to continue in the development of this technology.

REFERENCES

1. Williams L. Mesenteric ischemia. In: Sawyers J, Williams L, editors. The acute abdomen. Philadelphia: W. B. Saunders; 1988. p. 331-53.
2. Levy PJ, Krausz MM, Manny J. Acute mesenteric ischemia: improved results—a retrospective analysis of ninety-two patients. *Surgery* 1990;107:372-80.
3. Ballard J, et al. A critical analysis of adjuvant techniques used to assess bowel viability in acute mesenteric ischemia. *Am Surg* 1993;59:309-11.
4. Daniel E, Wachter B, Honour A. The relationship between electrical and mechanical activity of the small intestine of dog and man. *Can J Biochem Physiol* 1960;38:777-801.
5. Duret R, Bastenie P. Intestinal disorders in hypothyroidism: clinical and manometry study. *Am J Dig Dis* 1971;16:723-7.
6. Cabot R, Kohatsu S. The effects of ischemia on the electrical and contractile activities of the canine small intestines. *Am J Surg* 1976;136:242-6.
7. Schamaun M. Electromyography to determine viability of injured small bowel segments: an experimental study with preliminary clinical observations. *Surgery* 1967;62:899-907.
8. Szurszewski J, Steggerda FR. The effect of hypoxia on the electrical slow wave of the canine small intestine. *Am J Dig Dis* 1968;13:168-77.
9. Garrard CL, Halter S, Richards WO. Correlation between pathology and electrical activity during acute intestinal ischemia. *Surg Forum* 1994;45:368-71.
10. Hegde SS, Seidel SA, Bradshaw LA, Ladipo JK, Richards WO. Effects of mesenteric ischemia and reperfusion on small bowel basic electrical rhythm. *J Surg Res* 1998;74:86-95.
11. Staton DJ, Soteriou MC, Friedman RN, Richards WO, Wikswo JP Jr. First magnetic measurements of smooth muscle in vitro using a high-resolution DC-SQUID magnetometer. In: Nagel JH, Smith WM, editors. New frontiers of biomedical engineering—innovations from nuclear to space technology. Proceedings of Annual International IEEE-EMBS Conference Proceedings; Orlando, Fla; 31 Oct–3 Nov 1991.
12. Staton D, Golzarian J, Wikswo JP Jr, Friedman RN, Richards WO. Measurements of small bowel basic electrical rhythm

- (BER) in vivo using a high resolution magnetometer. In: Baumgartner C, editor. Biomagnetism: fundamental research and clinical applications. Burke (VA): Elsevier; 1995. p. 748-52.
13. Bradshaw LA, Wikswow JP Jr, Richards WO. The effect of abdominal layers on electric and magnetic fields from gastrointestinal electrical activity: computer simulations. *Gastroenterology* 1996;110:A640.
 14. Golzarian J, Staton DJ, Wikswow JP Jr, Friedman RN, Richards WO. Diagnosing intestinal ischemia using a non-contact Superconducting QUantum Interference Device. *Am J Surg* 1994;167:586-92.
 15. Richards WO, Garrard CL, Allos SH, Bradshaw LA, Staton DJ, Wikswow JP Jr. Noninvasive diagnosis of mesenteric ischemia using a SQUID magnetometer. *Ann Surg* 1995;221:696-705.
 16. Bradshaw LA, Wikswow JP Jr. Autoregressive and eigenfrequency spectral analysis of magnetoenterographic signals. *Proceedings of the 17th Annual IEEE Conference in Medicine and Biology: CD ROM* 17; 1995.
 17. Sinn A, Chien SM, Christensen J. Metabolic dependence of the electromyogram of the cat colon. *Am J Physiol* 1980; 239:G173-6.
 18. Mitsudo S, Brandt L. Pathology of intestinal ischemia. In: Boley S, Brandt L, editors. *Intestinal ischemia*. Philadelphia: W. B. Saunders; 1992. p. 43-60.
 19. Baule G, McFee R. Detection of the magnetic field of the heart. *Am Heart J* 1963;65:95-6.
 20. Wikswow JP Jr, van Egeraat J. Cellular magnetic fields: fundamental and applied measurements on nerve axons, peripheral nerve bundles, and skeletal muscle. *J Clin Neurophysiol* 1991;8:170-88.
 21. Smout AJ, Van der Schee EJ, JL Grashuis. What is measured in electrogastrography? *Dig Dis Sci* 1980;25:179-87.
 22. Martin PM, Kingma YJ, Bowes KL. Different electrode configurations and active electrode surfaces yield different frequency spectra of gastric electrical signals. *Gastroenterology* 1993;104:A554.
 23. Bradshaw LA. Measurement and modeling of gastrointestinal bioelectric and biomagnetic fields [doctoral dissertation]. Nashville (TN): Vanderbilt Univ; 1995.
 24. Golzarian J, Staton DJ, Wikswow JP Jr, Friedman RN, Richards WO. First biomagnetic measurements of intestinal Basic Electrical Rhythms (BER) in vivo using a high-resolution magnetometer [abstract]. *Gastroenterology* 1992;103:1385.
 25. Allos SH, Bradshaw LA, Wikswow JP Jr, Richards WO. SQUID magnetometer diagnosis of mesenteric vein thrombosis. *Gastroenterology* 1995;108:A269.
 26. Allos SH, Bradshaw LA, Holter S, Richards WO. The use of the SQUID magnetometer for the diagnosis of ischemia caused by mesenteric venous thrombosis. *World J Surg* 1997;21:173-8.
 27. Zhuralev YE, Rassi D, Emery SJ. Clinical assessment of fetal magnetocardiography. In: Baumgartner C, editor. *Biomagnetism: fundamental research and clinical applications*. Burke (VA): Elsevier; 1995. p. 700-3.

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Please see the related commentary by Chaikof on pages 367-9.