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Noninvasive Diagnosis of Mesenteric Ischemia Using a SQUID Magnetometer

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Objective

The authors assessed the ability of a Superconducting Quantum Interference Device (SQUID) magnetometer to noninvasively detect mesenteric ischemia in a rabbit model.

Summary Background Data

Superconducting Quantum Interference Device magnetometers have been used to detect magnetic fields created by the basic electrical rhythm (BER) and to detect changes in BER of exteriorized bowel of anesthetized rabbits during mesenteric ischemia.

Methods

The BER of rabbit ileum was noninvasively measured transabdominally using a SQUID magnetometer and compared with the electrical activity recorded with surgically implanted serosal electrodes before, during, and after snare occlusion of the superior mesenteric artery.

Results

Transabdominal SQUID recording of BER frequency was highly correlated to the measurements obtained with electrodes ($R = 0.91$). Basic electrical rhythm frequency decreased from 16.4 ± 0.8 to 8.3 ± 0.3 cpm ($p < 0.001$) after 25 minutes of ischemia. Reperfusion of ischemic bowel resulted in recovery of BER frequency to 14.3 ± 0.4 cpm 10 minutes after blood flow was restored.

Conclusions

A SQUID magnetometer is capable of noninvasively detecting mesenteric ischemia reliably and at an early stage by detecting a significant drop in BER frequency. These positive findings have encouraged the authors to continue development of clinically useful, noninvasive, detection of intestinal magnetic fields using SQUID magnetometers.

Acute mesenteric arterial occlusion is a devastating condition associated with a poor prognosis,[1,2] largely because diagnosis is not made until irreversible pathologic damage has taken place. Diagnosis of mesenteric ischemia at an earlier reversible phase could result in salvage of ischemic bowel with prompt therapeutic intervention.[2] Currently, there are very few useful diagnostic tools available to the surgeon that assist in the diagnosis of mesenteric ischemia and none that can do so noninvasively during the early phase of ischemia, before necrosis of the smooth muscle has occurred. Ideally, a diagnostic tool for the detection of mesenteric ischemia would be noninvasive, fast, sensitive, and specific in the detection of ischemic smooth muscle.

A number of investigators have demonstrated that the frequency of the small bowel basic electrical rhythm (BER) decreases with arterial ischemia.[3–5] In addition, studies in rabbits have shown that this decrease in the BER frequency of the small bowel occurs before the occurrence of irreversible pathologic changes.[6]

Superconducting Quantum Interference Device (SQUID) magnetometers are capable of detecting the magnetic fields generated by the electrical current of the smooth muscle of the small intestine.[7,8] Although electrodes must have contact with the tissue to measure the electrical currents, SQUID magnetometers are able to detect the magnetic fields in a noncontact manner, as shown in Figure 1.

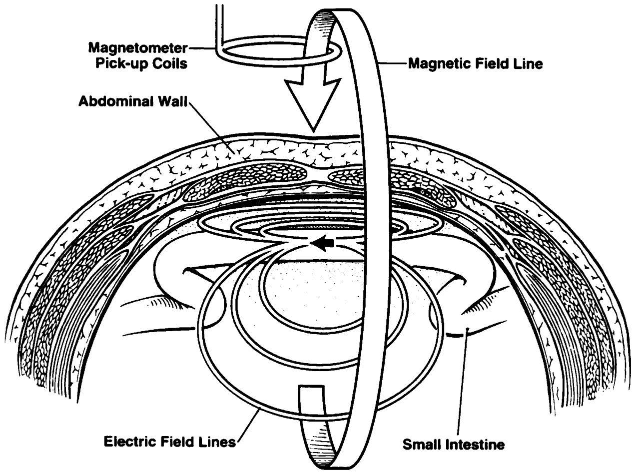

Figure 1. Cross-section of an abdomen illustrating why magnetic fields of the small intestine can be recorded noninvasively in animal and human subjects. The SQUID magnetometers detect the magnetic field generated by the electrical current of the smooth muscle of the small intestine. The magnetic field is relatively insensitive to the alternating layers of insulators present within the abdominal wall (i.e., the peritoneum, preperitoneal fat, fascia, muscles, subcutaneous fat, and skin). The electric field generated by this current flow are, however, greatly attenuated by the alternating layers of insulators present in the abdominal wall. Thus, the electric fields measured by cutaneous electrodes have an extremely low signal-to-noise ratio. Because the magnetic fields are not attenuated as much by the insulators of the abdominal wall, the signal-to-noise ratio is much higher than it is for cutaneous electrode recordings.

Earlier studies from our laboratory have demonstrated that SQUID magnetometers can detect decreases in BER frequency associated with intestinal ischemia in the exteriorized small intestine of anesthetized rabbits.[9] Although these data clearly demonstrate SQUID magnometers' ability to measure the BER of small intestine in normal and pathologic conditions, the clinical usefulness of such a device for the diagnosis of bowel ischemia can only be achieved if these measurements of BER frequency can be detected noninvasively through the intact abdominal wall.

This experiment determined the ability of the SQUID magnetometer to noninvasively detect the BER frequency of the small bowel in normal and ischemic conditions and correlate these recording to those taken with standard electrodes. These experiments are based on the hypothesis that a SQUID can noninvasively detect the changes in the BER magnetic fields during acute ischemia.

MATERIALS AND METHODS

The high resolution SQUID magnetometer (known as microSQUID) used in these experiments contains an array of four superconducting niobium pickup coils arranged at the corners of a 4.4-mm square.[10,11] The coils and SQUIDs are housed within the vacuum space of a liquid helium-filled Dewar that allows cooling of the coils to 9 K. This arrangement permits the detection of magnetic fields as small as one billionth of the earth's magnetic field. In each experiment, the microSQUID and the animal to be studied were placed in a magnetically shielded room (Vacuumschmelze, Hanaul, Germany). The room uses layers of aluminum and mumetal to reduce the earth's magnetic field and magnetic noise to less than 0.15 fT. The magnetic signals from each animal's ileum were measured at a frequency of 50 Hz from three channels of the SQUID magnetometer using a MP-100 analog to digital convertor (Biopac, Goleta, CA) connected to a Macintosh computer (Apple, Cupertino, CA) using Acknowledge strip chart recorder software (Biopac, Goleta, CA).

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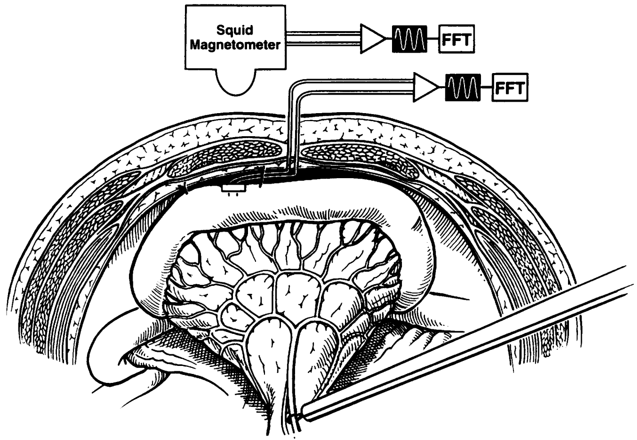

Figure 2. Diagram of setup for experiment 1. Through a midline laparotomy, a loop of ileum is isolated and the segmental mesenteric artery is dissected and encircled with a monofilament snare that is exteriorized. Bipolar electrodes are sutured onto the serosal surface of the bowel, and the bowel itself is sutured to the abdominal wall to ensure the same loop of intestine is measured by the SQUID magnetometer. After closing the abdomen with sutures, the SQUID magnetometer is brought down to, but does not touch, the abdominal wall of the anesthetized animal. The eight rabbits included in experiment 1 were studied for a 15-minute baseline period, with continuous recordings of BER from the serosal electrodes and SQUID magnetometer. The segmental mesenteric artery was then occluded for 15 minutes while continuous recordings of BER were taken from the electrodes and SQUID magnetometer.

Preparation of Experimental Animals

Two types of experiments were performed. The first experiment was performed to assess the ability of transabdominal SQUID recordings to detect changes in the ileum after snare occlusion of a segmental artery, thus inducing partial ischemia because the bowel was partially perfused through collaterals through the bowel wall.[12] The second study was performed to assess the ability to noninvasively identify a significant drop in BER frequency in the small intestine after snare occlusion of the main superior mesenteric artery, thus inducing total ischemia of the entire small intestine. The basic experimental setup for both is shown in Figure 2. The experiments were performed on male New Zealand rabbits that weighed between 3 and 5 kg. After an overnight fast, the animals were anesthetized using intramuscular injections of ketamine (30 mg/kg) and acepromazine (1 mg/kg). Maintenance anesthesia was obtained using intravenous injections of ketamine hydrochloride (20–40 mg). Body temperature was maintained using a water-perfused heating pad, and an intravenous line was established in an ear vein to maintain adequate hydration. All animal manipulations in this study were performed in accordance with guidelines established by the animal care and use committee at Vanderbilt University.

Recordings of Electrical and Biomagnetic Waves

After a midline laparotomy, a segmental branch of the superior mesenteric artery of each rabbit was dissected and a monofilament nylon line was passed around it to act as a snare. To obtain electrical recordings, a loop of terminal ileum was selected to which four pairs of silver electrodes on a silastic platform were attached using silk sutures. The entire platform with the attached bowel was then sutured to the inside of the anterior abdominal wall. This allowed simultaneous recording of the same loop of bowel by the SQUID (which was positioned outside the abdomen of the animal) and the serosal electrodes. The silver electrodes used are nonmagnetic and thus, did not interfere in the SQUID recording of magnetic fields. Control of the arterial blood flow was checked using a laser Doppler probe (Periflux PF3 Laser Doppler Perfusion Monitor, Perimed, Stockholm, Sweden). The laparotomy wound was closed, and the electrical wires were brought out through the wound. These wires were connected to an R-612 Beckman Chart recorder (Beckman, Fullerton, CA), the signals amplified and recorded onto the computerized strip chart recorder described previously.

To obtain biomagnetic recordings, the animal was placed under MicroSQUID in the shielded room. Continuous recordings of electrical and magnetic fields were obtained from the SQUID and the serosal electrodes. After baseline recordings were taken for 15 minutes, ischemia was induced in the loop of small bowel by tightening the snare around the segmental branch of the superior mesenteric artery. The animals ($n = 8$) were studied for 60 minutes after occlusion of the segmental artery. The animal preparation for the second experiment was identical except for encircling the main trunk of the superior mesenteric artery at the root of the mesentery which, when occluded, induced ischemia in the entire bowel. In experiment 2, simultaneous electrical and magnetic baseline recordings ($n = 10$) were obtained for 15 minutes, and the superior mesenteric artery was occluded for 30 minutes; then the snare was released and recordings continued for 20 minutes after reperfusion.

Data Analysis

Basic electrical rhythm or slow waves recorded by the SQUID magnetometer are referred to as magnetic slow waves to distinguish them from slow waves recorded by the electrodes. The BER frequencies were calculated for each 5-minute interval using the fast-Fourier transformation (Hamming window, mean and trend were removed). Because recordings from the electrodes and the SQUID were continuous and the fast-Fourier transformation calculation of BER frequency was for a 5-minute period, the time point referred to in the manuscript is the beginning of each 5-minute period. Thus, T 5 refers to the frequency of the BER recorded between 5 to 10 minutes during the experiment and does not refer to the instantaneous time point at 5 minutes. Basic electrical rhythm frequency is dynamic during ischemia and reperfusion, and the fast-Fourier transformation calculates the dominant frequency during that 5-minute segment. All fast-Fourier transformation calculations were performed on a Macintosh computer using Acknowledge software (Biopac, Goleta, CA). The mean frequencies for both electrical and magnetic recordings were calculated during the preischemic, ischemic, and postischemic periods for each animal. The results were expressed as mean ± standard error of the mean. The paired Student's t test was used to compare preischemic and ischemic frequencies in experiment 1. One way analysis of variance was used to compare baseline, ischemic, and postischemic BER frequencies in experiment 2. All statistical analysis was performed on a MacIntosh computer (Apple, Cupertino, CA) using Statview (Abacus Concepts, Berkley, CA) and Data Desk software (Data Descriptions, Inc., Ithaca, NY). Significance was accepted at $p < 0.05$.

Sensitivity of detection of ischemic bowel was calculated for the second experiment by the following formula: sensitivity = true positives/{true positives + false negatives} × 100. Specificity of detection of ischemic bowel was calculated by the following formula: specificity = true negatives/{true negatives + false positives} × 100. The positive predictive value of the test was calculated using the following formula: predictive value = true positives/{true positives + false positives} × 100. A positive test for ischemic intestine was defined as a drop in mean BER frequency greater than two standard deviations from mean of normal {16.4 ± 2.5} 16.4 − 5 = 11.4, i.e., <11.4 cpm.

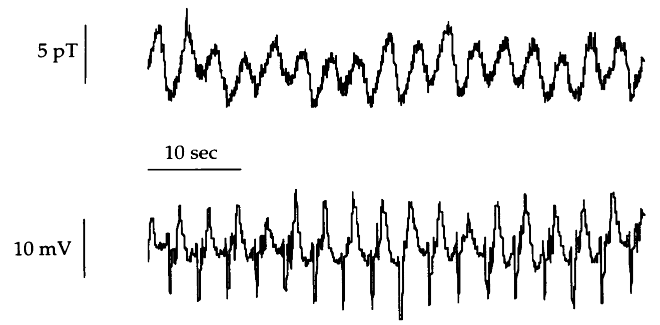

Figure 3. Baseline magnetic field recordings taken from the transabdominal SQUID recordings compared with simultaneous recordings taken from the bipolar electrodes. Fast-Fourier transformation was used on 5-minute segments of electrical and magnetic recordings to determine the BER frequency. The electrical and magnetic recordings taken from the same section of intestine have a nearly identical BER frequency.

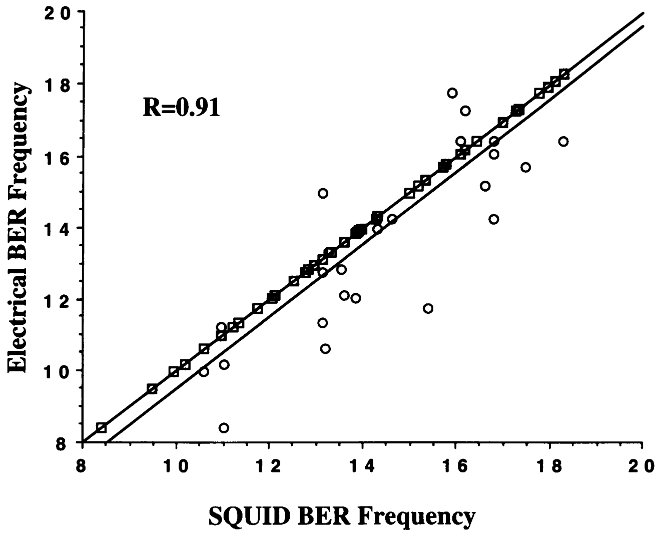

Figure 4. The frequency of the BER with the frequency determined by fast-Fourier transformation recorded by the electrode is plotted on the abscissa. The magnetic field BER frequencies obtained at the same time are plotted on the ordinant axis. There was a high level of correlation between the simultaneous recordings during experiment 1 (r = 0.91).

RESULTS

Experiment 1

The recordings taken from the transabdominal SQUID magnetometer were visually similar to the recordings taken from the serosal electrodes, as shown in Figure 3. The BER frequency as measured by the serosal electrodes was highly correlated (R = 0.91) to the measurements obtained from the transabdominal SQUID recordings (Fig. 4). During the baseline period, BER frequency determined using both methods was constant (14.9 ± 0.8 cpm). Fifteen minutes after occlusion of the segmental artery supplying the loop of intestine, the BER frequency fell from 14.9 ± 0.8 to 12.4 ± 0.6 cpm ($p = 0.03$, Students paired t test), as shown in Figure 5. A second set of experiments was undertaken to assess the ability of transabdominal SQUID magnetic field measurements to detect ischemic bowel and to detect changes in BER frequency after reperfusion.

Experiment 2

The BER of the loop of ileum was recorded using SQUID and serosal electrodes simultaneously. The BER decreased from a mean baseline value of 16.4 ± 0.8 cpm to 8.3 ± 0.3 cpm after 20 minutes of ischemia, as shown in Figure 6 ($p < 0.001$). On reperfusion, the BER re-

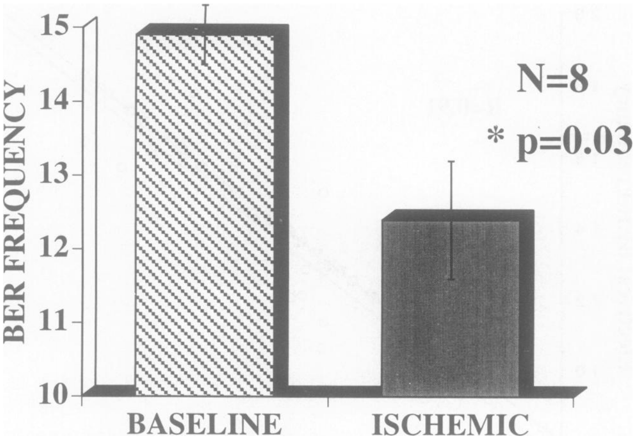

Figure 5. Graph of BER frequency recorded noninvasively by the SQUID magnetometer in eight rabbits before and after occlusion of the mesenteric artery in experiment 1. There is a significant decrease in BER frequency 15 minutes after snare occlusion of the segmental artery.

Table 1. BASIC ELECTRICAL RHYTHM RECORDINGS OF RABBIT SMALL INTESTINES USING THE SQUID AND SEROSAL ELECTRODES

	Experiment 2 (10 Animals)	
Perfusion State	Mean SQUID Recordings (cycles per minute)	Mean Electrical Recordings (cycles per minute)
Preischemia	16.4 ± 0.8†	16.5 ± 0.5†
Ischemia	8.3 ± 0.3†,‡	8.7 ± 0.3*
Postischemia	14.3 ± 0.4‡	14.2 ± 0.3‡

* $P < 0.05$.
Values are based on comparisons between preischemia and ischemia recordings,† and ischemia and postischemia recordings.‡

turned to a mean value of 14.3 ± 0.4 cpm ($p < 0.001$ between ischemic and reperfused bowel) (Table 1). In all of the studies, there was a drop of 40% to 50% on BER within the first 30 minutes of ischemia, with a return to normal range within 15 minutes of reperfusion (Fig. 7).

The correlation coefficient (r) of BER frequency determined by the transabdominal SQUID and the serosal electrodes was 0.92, confirming the results in experiment 1. Sensitivity of the SQUID magnetometer to detect ischemic bowel (defined as a drop in BER frequency <11.4 cpm) was calculated from the BER frequency detected 15 minutes after occluding the main superior mesenteric artery with the snare. All ten animals had positive findings, with no false-negative or false-positive studies, making the sensitivity of the test 100%. Specificity was determined from the 15 minutes of baseline recording. The SQUID measurement of BER frequency during baseline was always greater than 12 cpm; thus, specificity also was 100%. The positive predictive value was calculated to be 100%, as shown in Table 2.

During experiment 2, three animals had severe magnetic contamination present in their gastrointestinal tract, which precluded any further study. Investigation of this phenomenon showed that the rabbit chow (Purina rabbit chow, complete blend) that they were eating was highly magnetic. The SQUID magnetometer could not detect the magnetic fields from the small intestine through the abdominal wall because of the strong magnetic field emanating from the previously ingested meal. Subsequently, we fed the last two animals a diet of fresh vegetables, which were nonmagnetic, to rectify this problem.

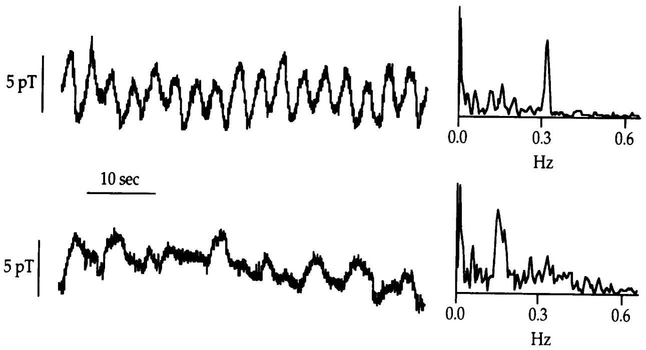

Figure 6. The SQUID magnetometer recordings of intestinal magnetic fields during baseline and then after 20 minutes of superior mesenteric artery occlusion. There is a dramatic shift to lower frequencies in the dominant frequency of the BER as determined by fast-Fourier transformation.

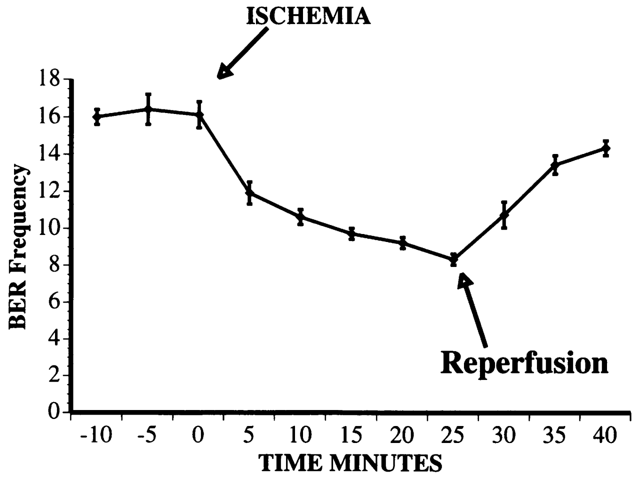

Figure 7. Basic electrical rhythm frequency determined with the SQUID magnetometer in ten animals before, during, and after snare occlusion of the main superior mesenteric artery. In experiment 2, there was a significant decrease in frequency 5 minutes after occlusion of the superior mesenteric artery. On reperfusion, BER frequency rises to near baseline values 15 minutes after start of reperfusion.

Table 2. SENSITIVITY AND SPECIFICITY OF NONINVASIVE DETECTION OF ISCHEMIA USING A SQUID MAGNETOMETER

	Ischemia Present	No Ischemia
+ Test	10	0
− Test	0	10

Sensitivity: 10/10 = 100%; specificity: 10/10 = 100%; predictive value: 10/10 = 100%.
The sensitivity and specificity of the SQUID magnetometer to detect ischemic bowel was determined by evaluating the BER frequency before and at 25 minutes after occlusion of the main SMA in experiment 2. A positive test was defined as a drop in BER frequency (greater than the normal mean—2 standard deviations [16.4 ± 2.5] 16.4 − 5 = 11.4) as detected by the SQUID magnetometer. Sensitivity of the SQUID to detect this drop in BER frequency at 25 minutes after SMA occlusion was 100%. The specificity of the test to detect normal bowel was 100%. The positive predicted value was 100%.

DISCUSSION

Small bowel ischemia is an acute surgical emergency that is associated with mortality rates of 70% to 90%.[1,2] Over the past 2 decades, it has become clear that the best patient outcomes could be achieved if prompt intervention could be started before widespread necrosis occurred.[13] However, the principal problem with this approach is the lack of a noninvasive, sensitive, diagnostic test that can detect acute ischemia before the development of smooth-muscle necrosis. The most useful diagnostic test has been mesenteric angiography, which is both invasive and time consuming. Another disadvantage of angiography is that it measures blood flow, not the viability of the intestine. Less invasive options, such as leukocytosis and metabolic acidosis, are present in almost all major abdominal surgical emergencies.[13] Elevations in alkaline phosphatase, lactic dehydrogenase, creatinine phosphokinase, and liver transaminases have been described; however, these changes occur late in the course of disease which, unfortunately, indicates that necrosis of intestinal cells already has taken place, thus limiting their usefulness for early detection.[14] Intraperitoneal radioisotope xenon scanning was useful in animal experiments, but has not proved useful in clinical practice.[15] Several other diagnostic studies, including duplex scanning[16] and magnetic resonance imaging,[17] are somewhat promising, although none has yet been established for clinical use. The major problem with the ultrasound study is that it measures blood flow, and not the viability of the bowel itself. Moreover, this test relies on visualizing the major vessels and thus, is limited to evaluation of large vessel disease. Finally, this test can be obscured by the overlying bowel gas that occurs frequently with ischemia. Magnetic resonance imaging scanning relies on visualizing the accumulation of intracellular and extracellular fluid caused by arterial occlusion. Because many other disease processes also induce bowel edema, a false-positive study may commonly be seen in clinical practice. Finally, these magnetic resonance imaging changes only occur after pathologic changes, and thus, they would not detect the early phase of ischemia while the ischemic changes are still reversible.

Several investigators have reported the effects of ischemia on small bowel electrical activity.[3-5] These effects include a reduction in frequency and amplitude of the BER that are normal after reperfusion.[3-5] If the ischemia continues long enough for the smooth-muscle fibers to die, the BER is lost altogether. The decreases in BER frequency occur within minutes after acute arterial occlusion and thus, can be identified long before pathologic changes.[6] These changes in the electromagnetic wave forms were noticed within 5 to 10 minutes of ischemia; in contrast, the earliest evidence of histopathologic changes in the muscle could not be detected until 60 minutes after onset of ischemia.[6] The SQUID biomagnetic recording of human gastrointestinal activity will have other important advantages over existing technology. The SQUID recordings are noninvasive and do not deliver any radiation to the patient and thus, would be particularly useful with pediatric patients and pregnant women.

Since 1991, when we first described measurement of prairie dog small bowel magnetic fields *in vitro,*[7] we have undertaken a systematic study of measurement of alimentary tract smooth-muscle magnetic fields in animals[8,18] and humans.[19] Magnetic field recordings have many advantages over cutaneous electrode recordings of current flow. Most significant is the relative insensitivity of magnetic fields to the electrically insulating layers of fat in the abdominal wall, which allows SQUID magnetometer measurement of small bowel BER, as demonstrated in this study. Cutaneous electrodes measure the potential difference that results from the flow of electrical current between the two points. Because cutaneous electrodes are located quite some distance from the bioelectric current source, the current flow must travel through the smooth muscle of the small bowel, the omentum, peritoneal surfaces, abdominal wall musculature, abdominal wall fat, and skin.[20] These many layers of insulators attenuate the wave forms recorded by cutaneous electrodes and markedly reduce the signal-to-noise ratio,[21] thereby making determination of the frequency spectra highly problematic. This study establishes that there is a good correlation between the BER frequency determined by serosal electrodes and those recorded by the SQUID magnetometer, demonstrating that the fundamental basis of using SQUID magnetometers to noninvasively record intestinal BER is sound.

This and previous studies demonstrate that intestinal ischemia may be detected noninvasively at an early stage using biomagnetic wave form measurements.[9] The importance of this finding is that the decrease in BER below two standard deviations of normal BER frequency was detected in all the animals at 15 minutes, well before irreversible changes, the earliest of which occurs at end of 1 hour of ischemia.[19] This increases the potential of the technique for early diagnosis of mesenteric ischemia.

The specificity of this technique to diagnose ischemia was 100% and thus, also may be useful in excluding patients with suspected ischemic bowel from undergoing unnecessary laparotomies or even invasive angiography. Further studies will be necessary to determine the amount of ischemic bowel that can be detected noninvasively with SQUID magnetometers, and the degree of specificity that can be obtained in a patient population. However, the extremely high specificity obtained in this study suggests that it may be possible to rule out many patients with suspected mesenteric ischemia.

One of the important qualities of the ideal test for mesenteric ischemia is the ability to repeat the study as interventions are carried out. All of the results reported in this study are derived from continuous measurement of BER frequency by the SQUID magnetometer. This aspect of SQUID measurement of BER frequency is an extremely important characteristic for the ideal test. Measurement of BER frequency during the operative procedure or using the SQUID magnetometer to monitor BER frequency noninvasively after the abdomen is closed might be extremely helpful to the surgeons caring for a patient after revascularization, resection, or intervention using pharmacologic means. After reperfusion, the BER returned to the normal preischemic range within 15 minutes. Not only could the viability of suspicious loops of ischemic bowel be assessed; a return to normal BER may denote successful revascularization. Other investigators[12,22] have developed techniques to assess the viability of the intestine intraoperatively using the muscle contraction response to electrical stimulation as a gauge of viability. This technique, pioneered by Brolin[12,22] and the fluorescent study of intestinal viability,[23] cannot be performed in a serial manner to determine response to therapy. One major advantage of SQUID monitoring of BER frequency is that it can be continued after closure of the abdomen.

By using a SQUID array with a large number of independent channels for simultaneous recording, the spontaneous activity of the entire gastrointestinal tract could be observed simultaneously. Unlike surface electrodes, which measure all the electrical activity between the two electrodes, SQUID magnetometers are able to detect and differentiate magnetic signals from different areas of the bowel. Such data would be well suited for mathematical imaging of abdominal current distributions. Our investigations in human volunteers have identified BER patterns of the stomach (f = 3.2 cpm) and of the small intestine (f = 8–10 cpm) in the same individual.[19] These studies have shown the capability of SQUID magnetometers to identify different electrical patterns within the abdominal cavity. This ability of SQUID magnetometers to spatially identify BER activity of the stomach and different parts of the small intestine may be critical in determining a small section of bowel that is ischemic.

Our studies in human subjects show that gastric and small bowel magnetic fields are of high enough amplitude to allow them to be recorded without requiring a shielded room. At least one group has measured gastric magnetic BER without a shielded room[24]; thus, advances in technology may make SQUIDs capable of detecting intestinal BER outside the confines of a shielded room. These advances might allow bedside diagnosis of critically ill patients.

There are two conditions that would interfere with interpretation of this decreased BER frequency—both hypothermia[25] and hypothyroidism[26] are known to cause a reduction in BER frequency. It would be unusual for either of these conditions to occur at the same time as mesenteric ischemia.

One problem encountered in three animals during this study was magnetic contamination in the food the rabbits were fed. This food, rich in iron and other metals, was highly magnetic and interfered with the electromagnetic recordings obtained by the SQUID. Subsequently, all animals were fed fresh vegetables, which were nonmagnetic, to improve the recording. This report includes data for experiment 2 from only three animals that ate the nonmagnetic diet. All other animals were studied while on the standard rabbit chow that was subsequently found to be magnetic. It is doubtful that standard human diets would contain enough magnetic contamination to interfere significantly in studies of this type. In addition, we have been able to record small bowel magnetic fields in every one of our human volunteers (n = 21) to date without manipulation of the diets before study (W. O. Richards, A. Bradshaw, L. Garrard, 1995 unpublished data).[27] Another alternative would be to degauss the subject before study, which is easily performed with an inexpensive hand-held videotape eraser. Nevertheless, difficulties in applying SQUID magnetometers may be encountered when we try to measure patients on iron supplements or who have magnetic materials within their body, such as shrapnel. Iron deposits in the liver of patients with hemochromatosis will produce magnetic fields only in the presence of strong external fields because iron is stored in a paramagnetic state that does not produce a remnant magnetic field. The staples found in stapling devices currently available are constructed from nonmagnetic materials—titanium or polyglycolic acid—thus, these types of devices will not interfere with noninvasive SQUID magnetometer recordings.

A potential problem for SQUID magnetometer recording of human electrical activity and diagnosis of ischemia is the relatively high cost of SQUIDs currently, both from the standpoints of purchase and maintenance. Superconducting technology generally is not cheap, and the SQUID must be operated in liquid helium for them to function. However, there is an increasing number of multichannel SQUIDs being used for noninvasive brain and cardiac studies across the country. As the technology of high-temperature superconductors develops, we anticipate the introduction of more portable, cheaper, high-temperature SQUIDS that will enable widespread use of these devices.

SUMMARY

Identification of decreases in BER frequency using SQUID magnetometers may be an extremely useful test for acute mesenteric ischemia. In this animal study, we demonstrated that this test possesses almost all the characteristics of the ideal test. It is noninvasive, 100% sensitive, 100% specific, can be used serially, and identifies ischemic bowel before irreversible changes. Because the study can be performed on a continuous basis, intraoperative and postoperative recordings may assist in determining the efficacy of the therapeutic interventions. These positive findings have encouraged us to continue development of clinically useful SQUID magnetometers for the noninvasive detection of mesenteric ischemia.

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Discussion

DR. GREGORY B. BULKLEY (Baltimore, Maryland): Dr. Jurkiewicz, Fellows, and Guests. In 1994, there remains no useful diagnostic clinical sign or laboratory test to noninvasively recognize intestinal ischemia. For example, in cases of small bowel obstruction, there is no clinical sign, physical finding or laboratory test that is accurate to discriminate strangulation from simple obstruction, and the reason is really quite simple: because all of the tests that we use depend upon the body's inflammatory response to irreversible tissue changes; for example: acidosis, leukocytosis, peritonitis, etc. And by definition, most of these things appear after the die has been cast, after the bowel is no longer viable.

For this reason, this study is really quite interesting because it addresses directly this problem by looking at very early changes in the small bowel. Actually they appear within minutes and, obviously, at this point the bowel is still viable. Moreover, if you think about it, the electrical rhythm, which is reflected by the changes in the magnetic field, is reflecting the activity in the muscularis propria itself. And, indeed, in studies that we have done many years ago, we found that this is really the layer which will determine the ultimate viability of the bowel. So it certainly makes sense to focus here.

In this study that was presented here by Dr. Richards for which I had the opportunity to see the manuscript and also to hear this preliminary report at the forum.

I have three reservations in terms of trying to apply this to our patients. And each of these three reservations generates a question.

First, how much ischemia do you need to have to be able to detect it? In your first experiment, you had a short segment of small intestine, but you tacked the loop up to the anterior bowel wall so that the magnetometer could sort it out from the others. But, of course, our patients do not come so conveniently arranged. And you have already pointed out that there is normally heterogeneity in the rhythm aborally. So how, in the case of segmental (e.g., strangulation obstruction) ischemia will the magnetometer be able to sort out the loop you are interested in from all the others? In your second experiment, you had a global ischemia, and it seemed to work under those circumstances.

Second, in your experiment, you used each animal as its own control, and this produced a very elegant comparison. But on the other hand, your patients will not give you this opportunity. Everyone had hoped that the B-mode Doppler was going to be very useful for measuring mesenteric blood flow, but it turned out to not work very well. In a given patient, you could see a nice flow increase with eating or something, with an error of about 10%. But, unfortunately, when you went from one patient acting as his own control, to one patient compared with others, studied by different operators, discriminant diagnostic capability disappeared.

Finally, patients with intestinal ischemia do not need to be distinguished clinically from normal people, but from other patients with abdominal pain, nausea and vomiting, and these things could easily affect the electrical rhythm. So how do you sort this out in the setting of patients who have concurring diseases, particularly the disease that is causing you to look at them in the first place?

Let me make one constructive suggestion. If you do address this in a clinical trial, you address this in patients who have small-bowel obstruction, attempting to discriminate thsoe who do from those who do not have strangulation. This will provide a built-in control.

In summary, I think that this is an interesting new approach. My own bias is that probably some more sophisticated but noninvasive measurement of blood flow will actually be the answer. I urge you to study it first in animals that more realistically simulate a clinical situation before going on to clinical trials.

Thank you all for the privilege of the floor.

DR. BRUCE SCHIRMER (Charlottesville, Virginia): Dr. Jurkiewicz, Dr. Copeland, Members, and Guests. I rise to congratulate Dr. Richards and his colleagues on some exciting work in the area of noninvasive measurement of gastrointestinal myoelectrical activity.

Currently, the only technique that is being used at all in this area is that of the electrogastrogram where cutaneous electrodes are placed on the skin in an attempt to measure the BER of the stomach.

Having been a collaborator on studies of that technology at our institution over the past decade, I can attest to its limitations in terms of signal attenuation that occurs with various layers of the body wall, as Dr. Richards told you in his presentation.

The SQUID magnetometer clearly seems to have overcome these limitations, and this technology should, I believe, continue to be explored for its great promise, a clinical application of which Dr. Richards and his colleagues have clearly shown us today.

I have several questions for Dr. Richards.

First, can the SQUID magnetometer differentiate between the BER of the stomach, small intestine and colon, since, as we know, the BER of the stomach and small intestine are markedly different, but the BER of the colon can have a varying range? Have you looked at trying to differentiate these different organs in your animal model and the ability of the SQUID to detect the differences between them?

Secondly, does spatial orientation of the organ itself attenuate or minimize the ability of the SQUID to detect its signal? In other words, if one bowel loop is 90 degrees to another, would you be able to detect the signal from the second loop?

Finally, this technology seems to have three major obstacles in terms of potentially keeping it from practical clinical use. They are its size, its requirement for shielding, and its cost. I'd like Dr. Richards particularly to comment on the potential for overcoming these three problems.

I'd like to thank the authors for the privilege of seeing the manuscript well ahead of the meeting and to congratulate them again on an excellent presentation and thank the Association for the privilege of the floor.

DR. WILLIAM O. RICHARDS (Closing Discussion): I'd like to thank the discussants for their kind reviews and their helpful comments.