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Superconducting Quantum Interference Device Magnetometer for Diagnosis of Ischemia Caused by Mesenteric Venous Thrombosis

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Abstract. Although mesenteric venous thrombosis carries a better prognosis than arterial thrombosis, mortality and morbidity are still high. Previous studies have shown that the basic electrical rhythm (BER) of the bowel decreases early after induction of arterial ischemia. Furthermore, our studies have shown that these changes occur prior to pathologic changes and that they can be recorded noninvasively using a superconducting quantum interference device (SQUID). SQUIDs measure magnetic fields that are created by the electrical activity of the gastrointestinal smooth muscle and have been used to measure the BER of the small intestine in human volunteers. This study was conducted to determine if a SQUID could be used for early noninvasive detection of mesenteric venous ischemia in an animal model. Simultaneous recordings from serosal electrodes and a SQUID outside the abdomen were taken from anesthetized New Zealand rabbits. Recordings were made for 15 minutes before and 90 minutes after injection of thrombin into the superior mesenteric vein. The basic electrical rhythm of the small bowel dropped from 16.42 ± 0.69 to 8.80 ± 0.74 cycles per minute at 30 minutes and to 6.82 ± 0.72 after 90 minutes (p < 0.0001, paired t-test). The correlation coefficient between the SQUID and electrical recordings was 0.954 (p < 0.0001). These data suggest that the ischemia caused by mesenteric venous thrombosis results in changes in the bioelectrical activity, which can be noninvasively detected using a SQUID.

Acute mesenteric venous thrombosis (MVT) accounts for only 5% to 15% of cases of mesenteric ischemia [1, 2], but the mortality rate remains high, approaching 20% to 60% if the diagnosis is delayed until intestinal necrosis has occurred [3]. Since the mid-1970s major advances in the diagnosis of MVT have evolved, mainly utilizing duplex ultrasonography and contrast-enhanced computed tomography (CT) scanning. Such scans allow visualization of the thrombus within the superior mesenteric vein (SMV). The next step in confirming the diagnosis is either angiography or a laparotomy, although these procedures are not always necessary. Despite these advances, cases of acute MVT are still misdiagnosed and detected only at laparotomy. If these cases could be diagnosed earlier, anticoagulation therapy might suffice to prevent the propagation of thrombosis [4, 5].

Several investigators have used serosal electrodes to demonstrate that the basic electrical rhythm (BER) of the small bowel decreases with arterial ischemia [6–9]. We have previously shown that this decrease occurs early in arterial ischemia, before pathologic changes take place [10]. The decrease continues as long as the ischemia persists or until smooth muscle necrosis with loss of electrical activity occurs.

The superconducting quantum interference device (SQUID) magnetometer can detect the magnetic fields produced by the electrical current of the smooth muscle of the small intestine [11]. Furthermore, the SQUID can detect the magnetic fields through the layers of the abdominal wall without direct contact with the bowel serosa. The magnetic fields of the stomach [12] and small intestine [13] have been measured on human subjects noninvasively by a number of groups around the world. The advantages of magnetic field measurement over cutaneous electrode measurement of small intestinal electrical activity can be seen in Figure 1. Electrical activity is attenuated and filtered by the multiple layers of electrical insulators of the abdominal wall and omentum, whereas the magnetic fields are not attenuated nearly as much. Measurements from cutaneous electrodes have a much smaller signal-to-noise ratio than do measurements taken from a SQUID outside the abdominal wall in a rabbit [14].

We previously reported that the SQUID magnetometer could be used for early detection of acute arterial mesenteric ischemia in a rabbit model [6, 15]. We hypothesized that acute MVT causes enough ischemia in the small bowel of animals to produce changes in the BER that might be detected noninvasively by the SQUID. Specifically, we sought to determine (1) if the SQUID magnetometer can noninvasively detect the changes in BER associated with ischemia due to acute MVT in a rabbit model; (2) if these SQUID recordings correlate with direct serosal electrical recordings; and (3) if these changes occur before pathologic changes take place,
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., peritoneum, preperitoneal fat, fascia, muscles, subcutaneous fat, and skin). The electrical field generated by these insulators present in the abdominal wall. Thus the electrical fields measured by cutaneous electrodes have 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 recordings, enabling us to use this technology to aid in the early diagnosis of this condition.

Materials and Methods

A high resolution SQUID magnetometer (microSQUID) was used in these experiments. It contains four superconducting niobium pickup coils housed within a vacuum space of a liquid helium-filled Dewar to allow cooling to 9° Kelvin. All the studies were performed inside a magnetically shielded room (Vacuumschmelze, Berlin, Germany). This room reduces the earth’s magnetic field and magnetic noise to less than 0.15 femtotesla (fT).

A Beckman amplifier (model R612) with an analog-to-digital convertor (Biopac Systems, model MP100; Goleta, CA, USA) and an Apple Powerbook 170 running Acknowledge 3.1.2 software (Biopac Systems) were used to record the signals. The signals were bandpass-filtered from 0.16 to 30 Hz, and the magnetic signal was lowpass filtered at 30 Hz.

The study was performed on 10 white male New Zealand rabbits weighing 3 to 5 kg. All the animal manipulations in this study were performed in accordance with guidelines established by the Animal Care and Use Committee at Vanderbilt University and the Nashville Veterans Administration Medical Center. The rabbits were fed fresh vegetables for a minimum of 3 days to reduce the interference by magnetic contamination of the food. Anesthesia was induced by ketamine (30 mg/kg) and acepromazine (0.75 mg/kg) intramuscularly with maintenance doses of ketamine (10–15 mg boluses) by intravenous injection. An intravenous catheter was placed for administration of fluids and medication.

Table 1. Swerdlow and Antonioli grading scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No pathologic changes</td>
</tr>
<tr>
<td>1</td>
<td>Mucosal infarction: focal loss of surface epithelium</td>
</tr>
<tr>
<td>2</td>
<td>Mucosal infarction: extensive loss of surface epithelium and intact muscularis mucosa</td>
</tr>
<tr>
<td>3</td>
<td>Mural infarction: loss of muscularis mucosa</td>
</tr>
<tr>
<td>4</td>
<td>Mural infarction: complete necrosis of the mucosa and submucosa</td>
</tr>
<tr>
<td>5</td>
<td>Transmural infarction: complete necrosis of entire bowel wall</td>
</tr>
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This grading scale [16] was used by the pathologist (S.H.) to score the degree of pathologic injury. Following a midline laparotomy, four pairs of silver electrodes on a Silastic platform were attached to a loop of jejunum, which was fixed to the inside of the anterior abdominal wall (Fig. 2). The abdomen was closed, and simultaneous baseline recordings of both electrical and magnetic BER were performed for 15 minutes. The incision was then reopened, the SMV dissected, and 1000 units of thrombin injected into the main vein. The abdomen was then closed again and recordings continued; there was a delay of 10 to 15 minutes between injection of thrombin and recording. The recording was continued for 90 minutes, following which the animal was killed and the segment of small bowel resected and sent for histopathologic examination to determine the extent of ischemia. The physician (S.H.) reading the slides to determine pathologic grade was blinded to the identity of specimen. Histopathologic grading was based on a modification of the pathologic classification of Swerdlow and Antonioli [16] (Table 1).