P2-B13

Lymph-Node detection system using a high Tc SQUID and ultra-small particles

S. Tanaka, T.Mizoguchi , H. Ota and Y. Kondo
Toyohashi University of Technology, 1-1 Tempaku-cho Toyohashi Aichi 441-8580, Japan

Abstract---Lymph-node detection system using a high Tc SQUID and ultra-small particles was proposed. Pseudo lymph nodes containing small ion particles were made and the magnetic signal was measured. The SQUID signal was proportional to the weight of the iron in the fluid. At the distance of 20 mm, the detectable minimum weight of the iron was 40 μg. We demonstrated that the system could be applied to the human body.

I. Introduction

We have been proposing the application of a high-T_c superconducting quantum interference device (SQUID) for a sentinel node biopsy, which has been a newly developed surgical technology. Axillary lymph-node dissection is an important procedure in the surgical treatment of breast cancer. However, in the early diagnosis stage, the number of dissections in which axillary nodes are free of disease is apt to be increased. These treatments lead to some problems such as a lymph edema and a sensory neuropathy in the patient. The sentinel node biopsy is a kind of test to investigate whether the sentinel node, which initially receives malignant cells from a breast carcinoma is disease-free or not. If the sentinel node is free of disease, you can leave the rest of the lymph-nodes because of no concern for progression. This biopsy is based on the hypothesis that if the first lymph node (sentinel node) is free of disease, the second and the rest of the nodes must be negative. Two methods which detect the sentinel node have been developed and reported to date [1]-[3]. One is a kind of radio guide, which uses a gamma detector and a radio isotope such as technetium labeled sulfur colloid. After injecting the isotope into a breast lesion, the sentinel lymph node will be identified by the gamma detector. Then the sentinel node is excised and examined. In this method the sentinel lymph-node is successfully identified with 94.4% accuracy [1]. Though the predictability of this method is extremely high, radiation exposure is inevitable for medical staff. The other method uses a blue dye; a surgeon identifies the sentinel lymph-node with his naked eye. With this method the predictability is still 70% accurate [2].

Therefore we propose a localization system combined with a high sensitivity superconducting quantum interference device (SQUID) magnetometer and ultra-small iron oxide particles. The particles are injected into the breast; and the high-T_c SQUID is used as a sensing detector for the particles. This method has some advantages: no radiation exposure and an accurate identification because of the visible color of the particles themselves. For this application, the SQUID magnetic sensor should identify the location of the small quantity of particles under the sensor at a distance of several centimeters. Even if the particles are made of iron oxide, if their size becomes too small, they show super-paramagnetic properties. Therefore, some magnetic field should be applied to the particles for detection because they have almost no permanent magnetic dipole at room temperature. Koetitz et.al. applied a pulse field to the particles and then measured the field decay from the particles in the range of ms [5]. Empuku et.al. measured the field from the particles under a DC magnetic field [6]. For the work described here, we measured the field from the particles under an AC magnetic field.

We have already reported the results of preliminary study using particle dispersed liquid in a tube [7]. In this paper, we describe the results of the signal detection using a pseudo-lymph node made of a small spherical balloon.

II. Experimental

The schematic diagram of the system is shown in Fig. 1. The SQUID is made of $Y_1Ba_2Cu_3O_{7-y}$ thin film. The junctions utilized in the SQUID are of the step-edge type. The washer size of the SQUID is about 2.5 x 2.5 mm^2 and the effective area is 0.11 mm^2. The SQUID was operated in a flux-locked loop with a flux modulation frequency of 100 kHz. The magnetic flux noise in the white noise region was about 30 $\mu\phi_0/Hz^{1/2}$.

The cryostat was specially designed for a SQUID microscope. The SQUID was located inside a vacuum and separated by a 50 μm thick quartz window. A more detailed description can be found elsewhere [8]. Two coils (Helmholtz type) were mounted just above the SQUID microscope [9], [10].

A balloon sample with a fine string was drawn by an induction motor. The sample was introduced into the coils. A sinusoidal AC current with a frequency of 100Hz was directed to the coils; the magnetic field generated from the coil was modulated by the frequency. The modulated signal associated with the particle motion was then demodulated by the lock-in-amplifier. The rolloff frequency of the filter, which sets the bandwidth was 3 Hz. Since the rolloff gives you sensitivity to noise only within 3 Hz of the desired signal, the signal/noise ratio is improved. The phase shifter was adjusted to give the maximum output signal.

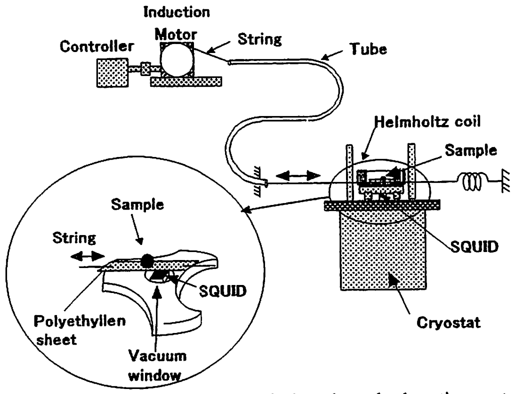

Fig. 1. Schematic diagram of pseudo lymph node detection system. Two identical 1000 turn wound coils (Helmholtz type) were mounted just above the SQUID microscope. A magnetic field generated from the coils was modulated by a 100Hz signal. A induction motor draws the spherical sample with string. The modulated signal associated with the particle motion was demodulated by the lock-in-amplifier.

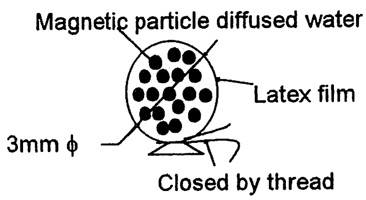

Fig. 2. Schematic drawing of a sample. Sample contains magnetic particles diluted with water. The outer dimension of the sample is 3mm in diameter. The sample was made as a pseudo lymph node.

We used ultra-small particles from Meito Sangyo Co., Ltd. Similar particles are used as a magnetic resonance imaging (MRI) contrast agent. The core of the particle is iron oxide Fe_3O_4 (magnetite) which is coated with an alkali-treated dextran. The average core diameter was 11nm. The particles had superparamagnetic properties. The particles were supplied in the form of an aqueous magnetic fluid. The original fluid contained 5.9 mg/ml of iron. If we suppose 5.2 g/cm^3 as the specific gravity of the core, we can estimate the weight of the mono-particle as 3.6×10^{-18}g and the total number of particles in the original solution as 1.5×10^{16}/ml. The original fluid was diluted with distilled water to have the desired concentrations. The diluted fluid was wrapped with a latex film as shown in Fig.2. Then the sample was moved with the scan speed of 0.33-1.1 mm/sec under an AC magnetic field of 9×10^{-5} to 7×10^{-4} T (peak to peak value).

III. Results and discussion

We investigated the detectable weights of the iron at the minimum distance of 1 mm and 20mm. As shown in Fig. 3, the SQUID signal was proportional to the weight of the iron in the fluid. At the distance of 20 mm, the detectable minimum weight of the iron was 40 μg.

If 10mg of Fe is injected into a human body, about 5% of the amount will be concentrated in the lymph node; i.e. Fe of 500 μg will exist at the lymph node. Therefore the detectable value of 40 μg is large enough to be used in mapping of a sentinel lymph node.

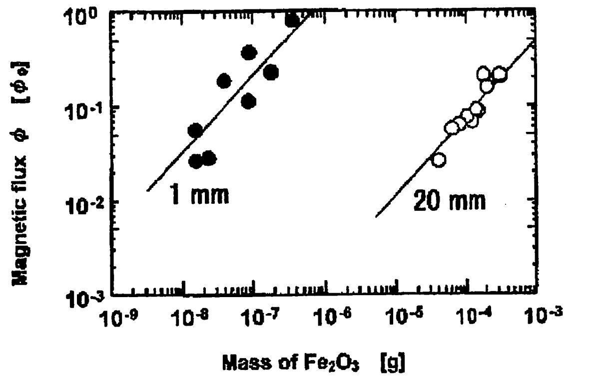

Fig. 3. Magnetic signal intensity from pseudo lymph node sample v.s. weight of Fe in particle. The SQUID signal was proportional to the weight of the iron in the fluid. The iron weight of 12ng and 40μg could be detected at the distance of 1mm and 20 mm, respectively.

Acknowledgment

This work was partially supported by a Grant –in-Aid for Science Research (B) and a Grant –in-Aid for Science Research in Priority Area (A) from the Ministry of Education, Culture, Sports, Science and Technology.

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