History and progress of biomagnetic measurement

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This review paper focuses on history and progress of biomagnetic measurement including SQUID system. There are two ways of generating magnetic field from human body. One is generated by ionic current with action potential in electrical excitation of neuron and cardiac cell etc., knowing as magnetoencephalography (MEG) and magnetocardiography (MCG). Other is generated by small magnets which is magnetized magnetic particles inhaling and accumulating in the lungs, knowing magnetopneumography (MPG).

Magnitudes of MEG and MCG are extremely so weak and ranges of a few femto-tesla (10^{-15}T) to pico-tesla(10^{-12}T) that are measured with SQUID magnetometer. MPG is in micro-tesla (10^{-6}T) and is measured by fluxgate magnetometer and/or SQUID magnetometer.

The first measurement of MCG was carried out by M.Baule and R.McFee in 1963 [1)] with induction coils wound two million turns. The first measurement of biomagnetic field with a SQUID magnetometer which is point-contact type was carried out by D. Cohen in 1970 [2)]. He became the first user of SQUID magnetometer in study of biomagnetic field from human body. It was the start of modern biomagnetic study not only development of SQUID devices but also signal processing technology at aiming for clinical use and brain study seeing the present.

This presentation, based on above historical measurement, will be composed as followings;

Firstly, an introduction of milestones of the beginnings of biomagnetic study, Secondly, progress of SQUID magnetometer and signal processing for source estimation, Thirdly, prospective of biomagnetic measurement including application for human adaptive mechatronics (HAM).

References

1) G.M.Baule, R. McFee, Am. Heart J., **55**, (1963) 95
2) D.Cohen, *et al.*,Appl. Phys. Letters, **16**, (1970) 278

Magnetocardiography predictors of premature ventricular contractions origin in LVOT vs. RVOT

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It is important to estimate premature ventricular contractions (PVC) origin in left or right outflow ventricular tract (LVOT or RVOT) in prior of catheter ablation. This study developed a Magnetocardiography (MCG) based method for discriminating LVOT from RVOT origin. MCG current arrow maps (CAMs) during QRS complex in 48 patients who were successfully ablated in RVOT (n = 30) or LVOT (n = 18) were analyzed. We focused on the PVC excitation propagation procedure captured by a 64-channel MCG system during QRS complex and found that rotation angle and displacement of maximum current arrow between two time-instants should be an effective way to discriminate LVOT from RVOT.

This study comprised 48 patients (14 men and 33 women; mean age 48 ± 18 years) who were successfully ablated for PVC origin in outflow tracts between April 2012 and October 2018. All patients had a normal ECG during sinus rhythm and no structural diseases found by physical examinations. We used a 64-channel MCG system (MC-6400, Hitachi High-Technologies Ltd., Tokyo, Japan) with highly sensitive superconducting quantum interference device (SQUID) sensors arranged in an 8×8 matrix with 2.5 cm pitch and 17.5×17.5 cm measurement area. MCG examination was carried in the resting supine position from the frontal planes in a magnetically shielded room. The MCG signals were acquired at a sampling frequency of 1 kHz and passed through band-pass (0.1 ~ 100 Hz) and power-line noise filters. To detect the PVC waveforms, we simultaneously measured the Lead II ECG signals.

To visualize the direction of excitation propagation during QRS complex, QRS duration was divided equally into 10 segments. Fig.1 shows the mean orientations of maximum current arrow of LVOT and RVOT origin estimated by averaging the selected time instants (0.1 ~ 0.9*QRS) from 48 patients. It can be found that LVOT and RVOT origin show clockwise and counterclockwise during QRS complex, respectively. Fig.2 shows the mean positions of maximum current arrow during QRS complex. The rotation angle and displacement are defineded as the orientation variation and position variation of maximum current arrow from a time instant to another, respectively. In this study, it is found that rotation angle from 0.1*QRS to 0.7*QRS has the best performance analyzed by area under the curve (AUC). Additionally, it is also found that the displacement of maximum current arrow from 0.1*QRS to 0.9*QRS is an effective way to discriminate LVOT from RVOT.

References
1) Yoko Ito *et al.*, Heart Rhythm 2014; **11**(9), 1605–1612.
2) Yoshida N *et al.*, Heart Rhythm. 2011; **8**(3): 349-56.

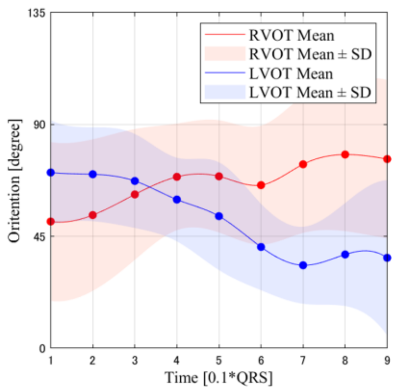

Fig.1 Mean orientations of maximum current arrows during QRS complex.

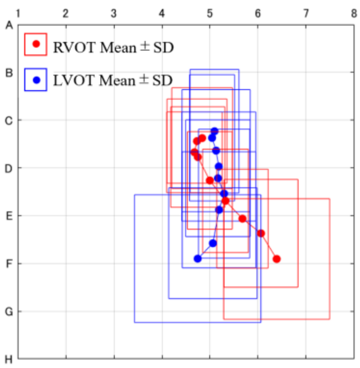

Fig.2 Mean positions of maximum current arrows during QRS complex.

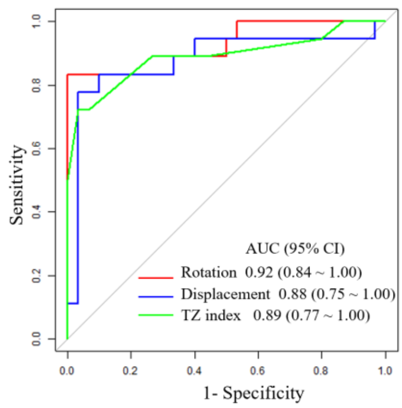

Fig.3 ROC curve of MCG parameters and TZ score of ECG.

Novel functional imaging methods by Magnetospinography and Magnetoneurography

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For the diagnosis of local conduction disturbances in nerves, it is useful to measure stimulation-induced nerve action potentials with electrodes attached to the body surface along with the nerve's travel. However, because the electric potential measurement method is strongly affected by the electrical resistance of the tissues surrounding the nerve, it could be effective only in the area where the nerve is close to the body surface. When we measure the action potential of the nerve located deep below the body surface, it is required to place electrodes adjacent to the nerve during surgery.

On the other hand, since the magnetic field generated by the electrical activity of nerves is not affected by biological tissues, the magnetoneurography (MNG) / magnetospinography (MSG) methods are considered to be innovative examination methods that enables the functional evaluation of nerves at depth, which has been difficult to evaluate noninvasively with conventional methods.

We are collaborating with Kanazawa Institute of Technology, Tokyo Medical and Dental University, and Kansai Medical University on the development and clinical research of MNG / MSG system[1)] (Fig. 1). Recent system development and clinical research have made it possible to visualize and evaluate the activity of the entire human spinal cord from the cervical to the lumbar spine (Fig. 2), as well as peripheral nerves.

In this lecture, we will introduce some of the technologies used in the system, as well as basic knowledge of methods for evaluating neural functions and the latest clinical research results with examples of clinical applications of the MSG / MSG system.

Reference

1) Adachi Y, et al. Recent advancements in the SQUID magnetospinogram system. Supercond Sci Technology. 2017;30(6):063001.

Fig. 1 Appearance of MNG system.

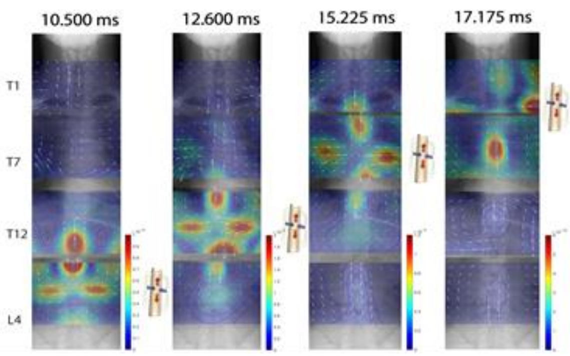

Fig. 2 Visualized nerve action current of entire spinal cord.

Usefulness and prospects of magnetic materials and magnetic probes in surgery of breast cancer.

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Sentinel lymph node biopsy (SLNB) is a standard surgical formula for breast cancer surgery. SLNB is important for determining treatment policies and position that greatly affects the patient's QOL. As a method, methods using radioactive isotopes are mainstream in Japan. SLNB using magnetic nanoparticles/magnetic probes without radioactive isotopes has been reported overseas using Sienna+® as magnetic nanoparticles and Sentimag® as magnetic probes, indicating its non-inferiority to RI method. As part of the Japan Agency for Medical Research and Development (AMED), the Medical Device and System R&D Project for Future Medicine, and the Minimally Invasive Cancer Treatment Equipment Research and Development Project (2015-2019), we conducted using a magnetic probe [1] and a SLNB using felcarbotran (risobist®), which is a magnetic particle that can be used in Japan, and compared with the conventional method (RI method).　210 cases were registered, and the identification rate of SLNB was 94.8% in the magnetic method (199/210 cases, 95% CI 91.6-98.0), and 98.1% in the RI method, and the identification rate of the magnetic method exceeded 90%, indicating non-inferiority compared to the conventional method.　[2]
By establishing these methods, it is expected that SLNB can be performed more reliably even in facilities without radioactive control areas, and that simple and safe SLNB can be performed without using radioactive isotopes.
In addition, as a development of the use of magnetic probes for SLNB, we developed the Wire guided localization method (WGL method), which is a method for resection of non-palpable lesions in the mammary gland.　As a marker, the guiding marker system ® is used to search for them with a magnetic probe and perform non-palpable lesion resection. By these, it is considered that the approach of the non-palpable lesion can be made more reliably and safely compared with the usual WGL method. With the progress of breast cancer screening and preoperational chemotherapy, non-palpable-detecting lesions of breast cancer are increasing, and this method is a very high-need method for breast surgeons, and it is expected to spread rapidly in the future.
It is expected that safe and effective technologies will be widely used in both these patients and those who use magnetic force, and that the usability will be improved, and the spread will spread further. In addition, we hope that we will continue to develop new medical devices using magnetism in cooperation with developers and surgeons to realize better medical care.

Reference

1.Sekino, M., et al., Handheld magnetic probe with permanent magnet and Hall sensor for identifying sentinel lymph nodes in breast cancer patients. Sci Rep, 2018. 8(1): p. 1195.

2.Taruno, K., et al., Multicenter clinical trial on sentinel lymph node biopsy using superparamagnetic iron oxide nanoparticles and a novel handheld magnetic probe. J Surg Oncol, 2019. 120(8): p. 1391-1396.

Hyperthermia using functional magnetic nanoparticles

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Magnetic nanoparticles including magnetite (Fe_3O_4) nanoparticles have unique features, and the development of a variety of medical applications has been possible.[1)] The most unique feature of magnetic nanoparticles is their reaction to a magnetic force, and magnetic labeling of target cells with magnetite nanoparticles enables the manipulation of cells and also the control of cell functions by applying an external magnetic field.[2)] On the other hand, because magnetite nanoparticles generate heat under an alternating magnetic field, magnetite nanoparticles have been used for cancer thermotherapy (hyperthermia)[3,4)]. We have developed a various type of functional magnetite nanoparticles, such as magnetite cationic liposomes and antibody-conjugated magnetoliposomes, by using techniques for drug delivery system (DDS). Magnetite nanoparticle-mediated hyperthermia has the potential to achieve tumor-targeted heating without serious side effects if magnetite nanoparticles can be accumulated only in the tumor tissue. The technique consists of targeting magnetite nanoparticles to the tumor tissue by DDS and then applying an external alternating magnetic field (AMF) to induce heat generation by the magnetite nanoparticles (Figure 1). The magnetite nanoparticle-mediated hyperthermia is also applicable to cancer diagnosis using magnetic resonance imaging (MRI), which enables theranostics for cancer patients. Recent years have seen the remarkable advances in magnetite nanoparticle-mediated hyperthermia; both functional magnetite nanoparticles and alternating magnetic field generators have been developed. Currently, some researchers are attempting to begin clinical trials, suggesting that time may have come for clinical applications.

References
1) A. Ito *et al*. J. Biosci. Bioeng., **100** (2005) 1.
2) A. Ito *et al*. J. Biosci. Bioeng., **128** (2019) 355.
3) A. Ito *et al*. Thermal. Med., **24** (2008) 113.
4) A. Ito *et al*. Nanomedicine (Lond), **8** (2013) 891.

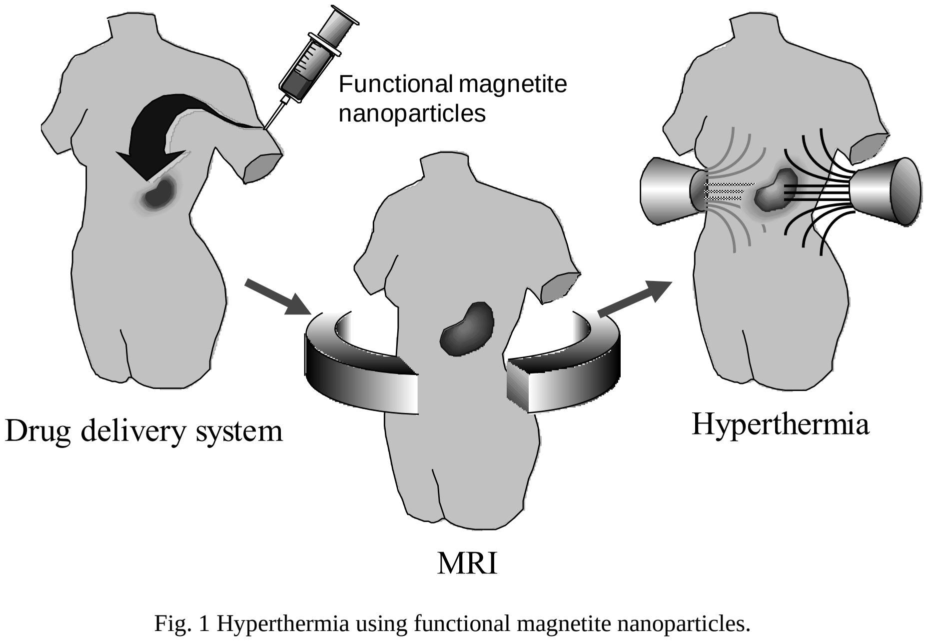

Fig. 1 Hyperthermia using functional magnetite nanoparticles.