Development of Magnetic Nanoparticle Imaging Using Gradient Magnetic Field and Electric Scanning of Field Free Point

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（傾斜磁場とゼロ磁場点の電気スキャンを用いた磁気ナノ粒子イメージングシステムの開発）

区　　分　：甲

論 文 内 容 の 要 旨

Magnetic marker is a type of particles consisted of a magnetic core and specific biocompatible polymer coatings. The magnetic core is made of one or multi magnetic nanoparticles (MNPs) which are nanometer-scaled ferro- or ferrimagnetic materials. The magnetic markers are widely used in biomedical field, such as the separation of protein, magnetic immunoassay, drug delivery, and hyperthermia. Furthermore, a type of magnetic markers, carboxyl-dextran-coated iron oxide, has been used as contrast agents of the magnetic resonance imaging (MRI) for *in-vivo* diagnosis.

Magnetic nanoparticle imaging (MPI) is another technique for *in-vivo* diagnosis utilizing magnetic markers, and is expected as a next generation imaging method. The principle of MPI was first proposed by B. Gleichr et. al. in 2005. In MPI, an excitation field is applied to generate nonlinear magnetization of MNPs, and a pickup coil is used to detect the harmonic signals from magnetized makers. In addition, a DC gradient field is used to improve the spatial resolution. Compared with other *in-vivo* imaging techniques, such as MRI and x-ray CT, MPI is expected to provide high sensitivity and high spatial resolution in bio-diagnosis. The excitation field is small, and the contrast agents used in MPI are relatively safe in toxicity. Furthermore, a real-time detection is also feasible in MPI since the magnetization signals from the magnetic markers are directly detected.

Many types of MPI systems have been developed based on the different design principles in worldwide. They have been classified into three types: harmonic-space MPI, *x*-space MPI, and narrowband MPI. In the case of narrowband MPI, a particular harmonic signal is sensitively detected using a resonant circuit. Therefore, a small excitation field can be used without degrading the sensitivity for MNP detection. In this thesis, I will describe the development of a narrow band MPI system based on the third harmonic detection.

Chapter one introduces the background and purpose of the research. Basic characteristics of the MNPs, such as nonlinear magnetization, Brownian and Neel relaxations, are explained. Then, application of MPI for the detection of a sentinel lymph node (SLN) is described, which is used for sentinel lymph node biopsy (SLNB) in breast cancer. I also give the thesis outlines in the end of this chapter.

In Chapter two, we study the properties of the harmonic signals when both AC and DC fields are applied in order to design the most suitable MPI system with an additional gradient field. First, we clarify the dependence of the harmonic signal on the direction of the DC field with respect to the AC excitation field. The third harmonic signal detection with an orthogonal gradient field is found to be most suitable for the narrow band MPI system. Then, the detailed characteristics of the third harmonic signal, such as the dependence on the strength and frequency of the AC excitation field, are clarified. The experimental results agree well with the analytical ones based on the Langevin function. An equation expressing the effect of an orthogonal DC field on the third harmonic signal is also given based on the Gauss function, which is useful in processing the MNPs imaging.

In Chapter three, the development of the narrow band MPI system based on the third harmonic signal is described. The system consists of four coils; AC excitation coil, detection coil, gradient coil, and shift coil. First, the excitation coil is designed to generate the AC field of 1 mT at the depth of 35 mm or more, with which the third harmonic signal is generated from the MNPs. Next, the gradiometer pickup coil is used for the detection of the third harmonic signal. The coil parameters and detection circuit are optimized to realize high signal to noise ratio. Third, the planar gradient coil consisting of four pieces of square coils is developed to produce a field free point (FFP). The field gradient more than 0.4 T/m can be obtained with the coil. Finally, the shift coil consists of four rectangular coils, which are wound around the gradient coils. By supplying the current to the shift coil, the FFP can be electrically scanned. In the present system, we can image the area of 32×32 mm^2 with the electrical scanning. It must be noted that electrical scanning of the FFP, in which the sample remains fixed, is important to build a more practical system, which is much more kind to patients.

Chapter four gives the imaging results using the developed MPI system. We successfully demonstrate the detection of one or multiple MNP samples. It is shown that the electrical scanning of the FFP gives better image of the signal field, compared to that obtained with the conventional mechanical scanning of the MNP sample. We also clarify the relationship between the strength of the gradient field and the spatial resolution in MPI. Then, in order to improve the spatial resolution in MPI, the measured contour map of the signal field is analyzed. The mathematical technique called singular value decomposition (SVD) is used to reconstruct the MNPs distribution from the measured contour map. In applying the SVD, two types of system function, i.e., model based and experimental-value based function, are used. Better resolution is obtained for the case of the experimental-value based system function. We can identify two MNP samples,100 μg of Fe in each sample spaced with 5 mm apart located at 50 mm below the pickup coil, with a high spatial resolution of 4 mm.

At last, Chapter five concludes the important achievements in this thesis, and proposes some possible future works based on this study.