LOW-INVASIVE HEATING AND TEMPERATURE MEASUREMENT METHOD FOR HYPERTHERMIA TREATMENT USING THE METAL COATED FERROMAGNETIC IMPLANT WITH LOW CURIE TEMPERATURE

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Abstract: Hyperthermia has been used for many years to treat various types of malignant tumor because tumor cells are more sensitive to temperature in the range of 42-45°C than are normal tissue cells. In this study, we aim to develop the local heating method and monitoring method for hyperthermia using the Ferromagnetic Implant with Low Curie Temperature (FILCT) under high frequency magnetic field. The heat generation inefficiency of FILCT causes a barrier in order to use this method as a bedside tool. In this research work, we coated the FILCT with a metal material in order to improve the heat generation efficiency. The magnetic permeability of FILCT decreased around the Curie temperature; therefore we can use FILCT as a thermal probe by measuring of the changing vector of the magnetic flux at the outside of human body noninvasively. In this paper, we describe about the experimental setup and in vitro experimental results.

1 INTRODUCTION

Hyperthermia has been used for many years to treat various types of malignant tumor because tumor cells are more sensitive to temperature in the range of 42-45°C than are normal tissue cells (Cavaliere, R., 1967 and Overgaard, K., 1972). There are a lot of heating methods for hyperthermia. The most commonly used method of heating in clinical settings is capacitive heating using a radiofrequency electrical field (Ishida, T., 1980, Abe, M., 1986 and Hiraoka, M., 1994). The great advantage of capacitive heating is that it is non-invasive. However, this method can cause excessive heating of the fat layer and is not suitable for site-specific hyperthermia because it is difficult to selectively heat only the local tumor region to the intended temperature without also damaging normal tissue. Moreover, this method needs an invasive thermometer to measure the temperature of tumor region. To overcome the disadvantages of capacitive heating for the treatment of tumors, attempts have been made to use inductive heating with magnetic implants (Jordan, A., 1993 and Shinkai, M., 1996). In 1982, Matsuki et al. developed a soft-heating method using the ferrite implant with low Curie point (Masaki, H., 1982). The merit of the soft-heating method is that it needn't measure the temperature as for the heat generation is automatically stopped up to Curie point of the implant. We previously described a system in which hyperthermia was induced using 'ferromagnetic implant with low Curie temperature (FILCT)' low enough to mediate automatic temperature control, and demonstrated its antitumor effect in a mouse melanoma model (Saito, H., 2008 and Ito, A. 2009). However, the improvement of the heating efficiency was necessary because much energy had been required to heat the target tumor.

In order to solve this problem, we have mixed the high conductivity metal material with FILCT. At the same time, we have used FILCT as a probe of thermometer. Thus a less invasive heating and temperature measurement system was developed based on this idea. A key advantage of this system is that it can distinguish whether the target temperature has reached the Curie temperature or not by non contact method. On the other hand, the infrared (IR) thermography, which is the most popular noncontact thermometer, can measure the skin temperature but not the internal body temperature. We have developed the experimental setup for the less

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invasive thermometry (Mitobe, K., 2008). In this paper, we have assessed the appropriateness of this system by the experiment of temperature dependence and heating efficiency using the 'Au coated FILCT'.

2 EXPERIMENTAL SETUP

Ferromagnetic material with high magnetic permeability attracts magnetic flux. If the temperature of ferromagnetic material increases over Curie temperature, then the magnetic permeability decreases immediately. As a result, the material can not attract magnetic flux. Figure 1 shows fundamental concept of non-invasive thermometry. The temperature of FILCT can be measured noninvasively by the shift of vector of magnetic flux. The Curie temperature of FILCT has been set at 43°C which is the target temperature in order to reduce the tumor cell.

Figure 2 shows the micrograph of FILCT' and 'Au coated FILCT'. FILCT was coated by Au in order to enhance heat divergence efficiency. Au coated FILCT was made using electroless gold plating technique without underlaying harmful metal such as Ni.

Figure 3 shows the block diagram of the experimental setup of this experiment. Magnetic flux was generated by the drive coil of 3 turns (External diameter of the drive coil was 80mm, internal diameter was 70mm). The frequency of the AC current for the drive coil was 190 kHz. AC current (500A) was generated by the power amplifier (Hotshot, AMERITHERM Inc.). The shift of vertical component of magnetic flux was measured as variation of the induced voltage of the pickup coil. The voltage of the pickup coil located orthogonally in the drive coil was measured as the synchronous signal of the voltage of the search coil by the lock-in amplifier (7265 DSP Lock-in amplifier, Signal Recovery). The number of turns, resistance, external and internal diameter of the pickup coil was 10 turns, 10Ω, 17mm and 10mm respectively. The temperature of FILCT was measured by an optical fiber thermometer (FL-2000, Anritsu-meter). In this experiment, we used Au coated FILCT (particle diameter was 40µm-150µm, total mass of powder was 1.0g) with 500µl of deionized water. The distance between the upper surface of the drive coil and a test tube of FILCT was 30mm, and the density of magnetic flux at the position of FILCT was 24.3mT.

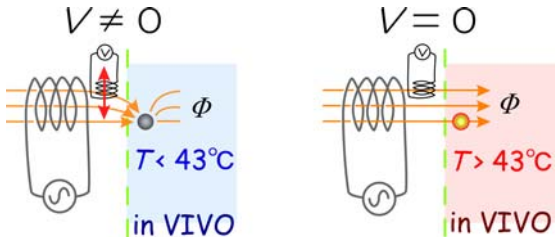
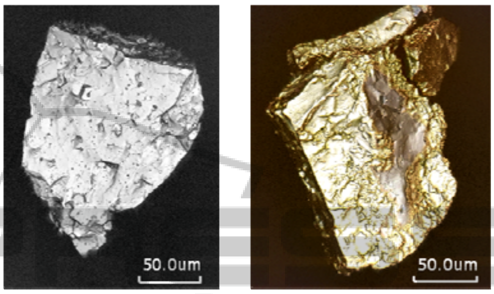


Figure 1: The fundamental concept of less invasive thermometry.



(a) FILCT (b) Au coated FILCT

Figure 2: Micrograph of a particle of the ferromagnetic implant with low Curie temperature.

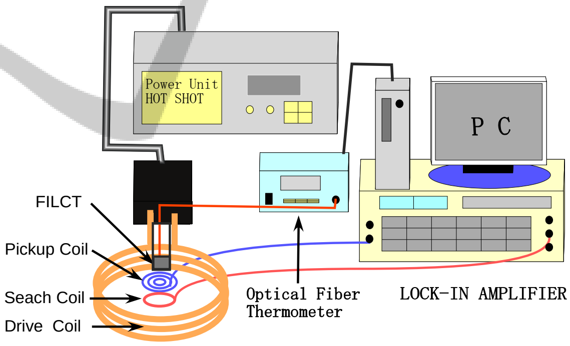


Figure 3: Block diagram of the experimental setup of the less-invasive heating and thermometry.

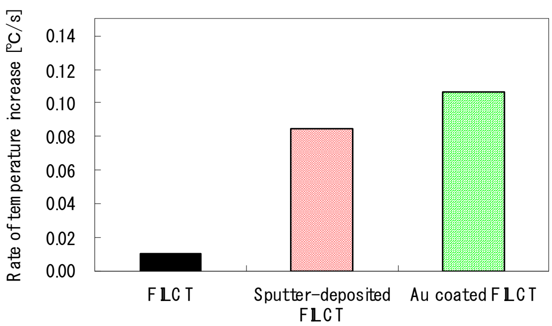


Figure 4: Rate of temperature increase.

3 RESULTS AND DISCUSSIONS

Figure 4 shows the rate of temperature increase of each implant. Applied density of magnetic flux was 7.85mT, the frequency was 190 kHz. The thickness of 'Au coated FILCT' was around 0.7µm. The rate of temperature increase of 'Au coated FILCT' was decuple compared with original FILCT.

We repeated induction heating over 50 times in order to evaluate the endurance of Au coating. Figure 5 shows the temperature rise curve of 'Au coated FILCT'. Here, horizontal axis shows time and vertical axis shows the average temperature of 50 times cycle test. As a result, the heat divergence profile was constant. We did not find any change in surface of Au coat FILCT such as a delamination or a crack after cycle tests by microscopic observation.

Figure 6 shows the change of the temperature of Au coated FILCT and the magnetic flux density at the pickup coil. Vertical axis shows the temperature of FILCT and the magnetic flux density at the pickup coil. The self-heating type FILCT produced heat of over 43 ˚C that was effective in the treatment temperature of malignancy. The temperature of FILCT rose to 43 ˚C within 30s. Rate of temperature increase changed around the Curie temperature. The magnetic flux density at the pickup coil was decreased in contradiction to the rising of temperature.

Figure 7 shows the relationship between the temperature of FILCT and the voltage of pickup coil. This graph was made from the data of figure 6 that was the result of cyclic test of heating. Here, horizontal axis shows the temperature and vertical axis shows the voltage of pickup coil. The profile of the voltage was almost same on each trial, and the voltage was decreased to 6mV. At the same time, the bias of voltage caused by the difference of position of FILCT appeared.

This approach can pave the way to heating and temperature measurements of tumor with no pain after injecting of FILCT to the tumor. However, long time measurements may be a burden to the subject persons as the body movements are restricted to minimize the noise for this method.

4 CONCLUSIONS

In this paper, we have described the concept for using 'ferromagnetic implant with low Curie temperature (FILCT)' as a probe for temperature. A key advantage of this system is that it can distinguish noninvasively whether the target

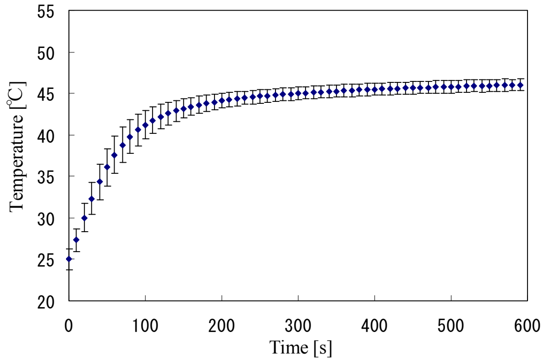


Figure 5: Temperature rise curve of 'Au coated FILCT'. (50 times cycle tests).

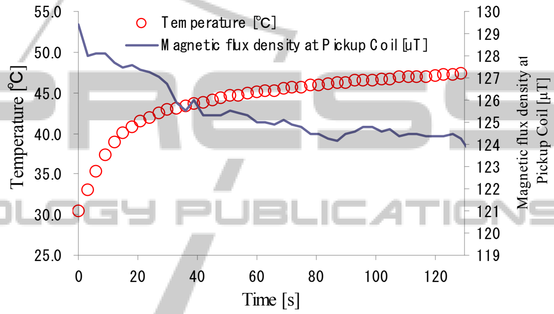


Figure 6: Change of the temperature of Au-coated FILCT and the voltage of pickup coil.

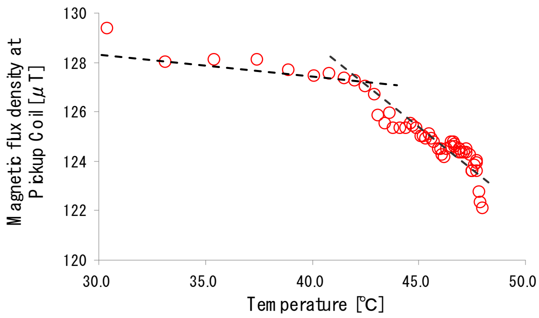


Figure 7: Relationship between temperature of FILCT and the voltage of the pickup coil.

temperature has reached the Curie temperature or not. Less invasive heating and temperature measurement system was evaluated using powder type of Au coated FILCT. As a result, it has become clear that we can heat up to 50mm of depth distance under thermal control. Furthermore, it is clear that we can use Au coated FILCT which have high heating efficiency for induction of heating. These results contribute to the less invasive heating and temperature measurement for a lot of types of hyperthermia.

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