Magnetic induction hyperthermia for brain tumor using ferromagnetic implant with low Curie temperature

I. Experimental study

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Abstract

Experimental study was made on magnetic induction hyperthermia for brain tumor using ferromagnetic implant with low Curie temperature. Thermoseed (implant) was made of nickel-palladium alloy, which was confirmed to produce enough heat by eddy current and also to have low Curie point between 43 °C–58 °C. Using this implant heating system, the effect of hyperthermia on normal rat brain and intracutaneously inoculated rat gliosarcoma (T9) were studied. Heat conduction from seed was twice as much in tumor tissue as in normal brain. It was also found that the intradermal brain tumors were completely diminished within 4 weeks by single local hyperthermia at 45 °C for 60 min.

Introduction

Hyperthermia as a cancer treatment has recently been re-evaluated and highlighted with the development of new medico-engineering devices. Various approaches of hyperthermia have been tried and developed for the treatment of malignant brain tumors (1–8), because the results of all modalities of conventional therapy have been disappointing. However there exist intrinsic disadvantages in heating CNS malignancies compared to other organs. First of all, there exists technical limitation of localizing heat in the brain by such as electromagnetic waves through intact skull. Secondly, the heating area must be strictly limited to the tumor bulk but not surrounding brain because the heat tolerance of normal brain is not well established. This is extremely important for deep-seated tumors in basal ganglia, thalamus or brainstem where important vital centers are located. Finally, long-term placement of intra- and extracranial connection tubing for power supply or thermal control must be avoided for protection of CSF leakage or infection.

The implant heating seems to be promising, because it is possible to heat tumor selectively by the metal seeds, which are previously implanted in the tumor and heated by eddy current induced by high-frequency magnetic field through extracranially placed magnetic coil. It has also advantage of self-control of temperature of implant itself by Curie point, which can be settled at any degree suitable for hyperthermia.

This is to report the characteristic of heat production of newly developed nickel-palladium (Ni-Pd) alloys as a metal implant and in vivo experiments regarding the thermal effects in normal rat brain and intracutaneously implanted brain tumors (T9; gliosarcoma) using this system.

Material and method

Experimental system for induction hyperthermia of brain tumor has been developed. This is com-
posed of two compartments, ferromagnetic implant (thermo-seed) and induction coil with generator, which produce high-frequency magnetic field. Several induction coils of solenoid type were manufactured, one of which the inner diameter of 80 mm, width of 34 mm and of four turns was chosen for animal experiments using CDF rats. Water pipe was built-in for cooling the coil during hyperthermia (Fig. 1). High-frequency magnetic field were generated by a inverter circuit using Power MOS FET. Using this generator and induction coil, the frequency was set for 250 kHz and maximum magnetic field strength was 1 KA/m.

Ni-Pd alloy was used in this experiments, because enough heat production and low Curie points desirable for hyperthermia has been obtained (2). Ni-Pd alloy was conformed to cylindrical form and used as tumor implant with the diameter of 1 mm and the length of 10 mm. Composition ratio of nickel and palladium was changed to obtain different Curie temperature.

Calorimetric determination of Curie point with these implants was made using specially designed phantom which simulated to in vivo models. The phantom consists of two cylindrical chambers, of which the outside is tightly covered by styrene to shut out heat from outside and keeps the temperature inside constant. The most inner chamber is filled with hot water. The induction coil is placed outside of the phantom concentrically and an implant is placed in the center of inner chamber, of which the long axis is parallel to magnetic line of force (Fig. 2). The temperature of the water and implant was measured by thermocouples (Bailey Co. Ltd.) during induction heating.

CDF rats were used as experimental animal. Normal brain was implanted by a Ni-Pd seed and temperature gradient was measured during heating. Intracutaneous tumor was made by inoculation of T9 cells in the back of rat, which is cell line of gliosarcoma induced by methylnitrosourea. When the tumors become manifested and measured as large as 10×10 mm in 2 weeks, three metal seeds of Ni-Pd alloy were implanted in an array fashion. The