A SYSTEM FOR PRODUCING LOCALIZED HYPERTHERMIA IN BRAIN TUMORS THROUGH MAGNETIC INDUCTION HEATING OF FERROMAGNETIC IMPLANTS.

[redacted]

Certain brain tumors, such as glioblastoma multiformate Grade IV which is universally fatal, have been identified as candidates for treatment with hyperthermia combined with ionizing radiation following the usual surgical debulking. This tumor contains radioresistant hypoxic cells which spread into normal brain tissue along microscopic tracts. In vitro data support the hypothesis that hypoxic cells may be particularly sensitive to the combination therapy. Thus, we are developing a magnetic induction system for producing localized hyperthermia in these intracranial tumors. Differential heating is achieved through use of small (1-2 mm diameter) ferromagnetic seeds which can be stereotactically imbedded in residual tumor at the time of craniotomy. The dependence of differential implant heating on the power source frequency has been characterized and indicates use of frequencies below 2MHz. Thermographic analysis of temperature distributions induced in phantom models has been performed for various implant materials, sizes, geometries and array configurations. The thermal conductivity and electrical properties of the phantom brain tissue were verified empirically and were used to construct simple mathematical models. Temperature distributions induced in single seed phantoms are consistent with the theoretically expected dependence on the inverse radial distance from the seed. In particular, Trial 16 showed a temperature differential greater than 4 ^{o}C out to five seed radii (1 cm) from the implant site with no significant direct heating of the phantom by the RF field. A description of the coil and system design is provided with special attention to the final impedance matching network. Trials on animals will be followed by application to humans as soon as confidence with the technique and apparatus can be established from these laboratory experiments.

Certain brain tumors would be excellent candidates for the use of adjuvant hyperthermia with x-irradiation which normally follows initial surgical debulking. In particular, glioblastoma multiforme grade IV contains radioresistant hypoxic cells which surround the necrotic core and spread into normal brain tissue along microscopic tracts. Previous in vitro data substantiates the sensitivity of hypoxic tumors to hyperthermic kill. Heat in conjunction with radiation may improve survival rates which are presently near zero. Thus a system is desired for producing a well controlled temperature field in soft brain tissue enclosed in bone.

A magnetic induction heating system is under development which achieves differential tumor heating through use of small (1-2 diameter) biocompatible ferromagnetic implants. These seeds can be stereotactically imbedded in residual tumor during the craniotomy or through small holes in the skull as described by Heath, John, and Fontana (1) et al. The apparatus consists of a helical induction coil with a double tuned coupling transformer. Variable capacitors on both the primary and secondary of the transformer permit matching into a wide range of load impedances. The coupling transformer and heating coil both are constructed from 3/8" tubing to permit water cooling. Phantom brain tissue similar to that developed by Guy (2) was mixed with in order to match the thermal and electrical conductivities to those of cat brain. An apparatus developed by Bowman and colleagues (3) was used for the thermal conductivity measurements. The electrical properties were verified using an impedance bridge and a probe similar to that described by Hahn and Stavros (4).

The dependence of seed heating on the power source frequency was studied for various implant materials and sizes. Results indicate use of frequencies below 2MHz in order to obtain substantial differential heating between the seeds and the brain tissue directly. Temperature distributions induced in phantom models containing various arrays of implant materials were analyzed with a thermographic camera. Heating patterns induced in single seed phantoms were found to be consistent with the theoretically expected dependence on the inverse radial distance from the seed. Thus a simple mathematical model of the brain used in calculations of power deposition into the brain via the implants. Although heating efficiency is low, large portions of 100 cm^3 phantoms placed in a 10 cm diameter heating coil have been elevated at least at 4 ^{o}C/min. using strong ferromagnetic implant materials with less than 100W. Work is now in progress with 1.5kW available power so that decreased implant size and full scale heating coils are possible. The thermographic studies of arrays of implants will be used to specify optimum spacing versus size requirements to achieve a uniform specific absorption rate over a specified volume of interest.

Future efforts include animal trials to be followed by clinical application to humans once confidence with the technique and apparatus is established.

In vivo studies may lead to the use of higher frequencies where moderate whole brain heating can be combined with a lesser degree of differential heating of the seeds. Extension of the technique to other anatomical sites and to tissue heating by direct induction will be pursued subject to clinical demands.

REFERENCES

1. Heath, R.G., John, S.B., Fontana, C.J.; "Stereotoxic Implantation of Electrodes in the Human Brain: A Method for Long Term Study and Treatment"; IEEE Trans. on Bio. Engr., Vol. BME 23 (4) July 76.

2. A.W. Guy, IEEE Trans. Microwave Theor. and Tech. MIT-19 205 (1971).

3. Balasubramaniam, T.A., Bowman, H.F.; "Thermal Conductivity and Thermal Differsity of Biomaterials: A Simultaneous Measurement Technique"

4. Hahn, G. and Stavros, P.; "Impedance Measurements of Pig Tissue in vivo", Private Communication, to be published.