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Thermomagnetic Surgery for Cancer

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Abstract

Thermomagnetic Surgery is a unique technique that takes advantage of the phenomenon of hysteresis heating of a ferromagnetic material to produce intense but controlled temperatures within solid organs or tumors to cause coagulation necrosis. By controlling the power of the electromagnetic coil system, the degree of heating of the tumor can be controlled through temperature monitoring that allows limitation of the area of destruction to the disease process and avoids damage to surrounding structures. If the ferromagnetic material is delivered by the arterial route to the tumor or organ, there is an additional beneficial effect of ischemic necrosis of the tissue and in time more concentration of the ferromagnetic particles. This new technique is applicable to selected cases of human cancer because no ill effect has been shown to exposure of the electromagnetic field or the ferromagnetic material in experimental animals.

Index Entries: Thermomagnetic surgery, in cancer; hysteresis heating, in cancer surgery; hyperthermia, in cancer surgery; cancer, thermomagnetic surgery in; embolization, in thermomagnetic surgery.

Introduction

A technique has been developed to destroy cancerous tissue by intense focal hyperthermia. It is best described as Thermomagnetic Surgery because it uses a combination of the physical phenomenom of hysteresis heat loss of ferromagnetic

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materials and ischemic necrosis to produce cancer cell destruction. These materials are first placed within the target tissue in the anesthetized animal model that is then positioned in a low frequency alternating current coil system. The microferromagnetic particles can either be injected by transarterial catheter into the cancer, or they can be injected directly. After the needle shaped ferromagnetic particles are in place, the cancerous area is subjected to an alternating current low frequency magnetic field. With each cycle the ferromagnetic particles change their polarity to produce hysteresis heat loss, which is then conveyed by convection and contact to the surrounding cancerous tissue. The cancer is destroyed as the temperature rises beyond the point of survival of the intracellular protein systems and membranes, the membranes and intracellular protein systems having undergone coagulation necrosis and denaturation (Figs. 1 and 2).

The ferromagnetic particles have a length of 0.1–1 μm and when the transarterial route is employed they and the carrier fluid combine to cause occlusion, at the pre-capillary and capillary levels, of the selected vascular system of the organ or cancer. Ischemic necrosis and subsequently hysteresis coagulation are produced, permitting any cancerous tissue that may have escaped the initial ischemic necrosis to be destroyed by the coagulation necrosis. This is especially important since it is necessary to consider the interface between cancer and the normal tissue where the blood and lymphatic supply may exist to nourish residual cancer cells. The reason for using this combination of ischemic and hysteresis coagulation necrosis of cancer tissue is that an attempt is being made to totally destroy the primary origin of the cancer so that any subsequent surgical maneuver would have a mini-

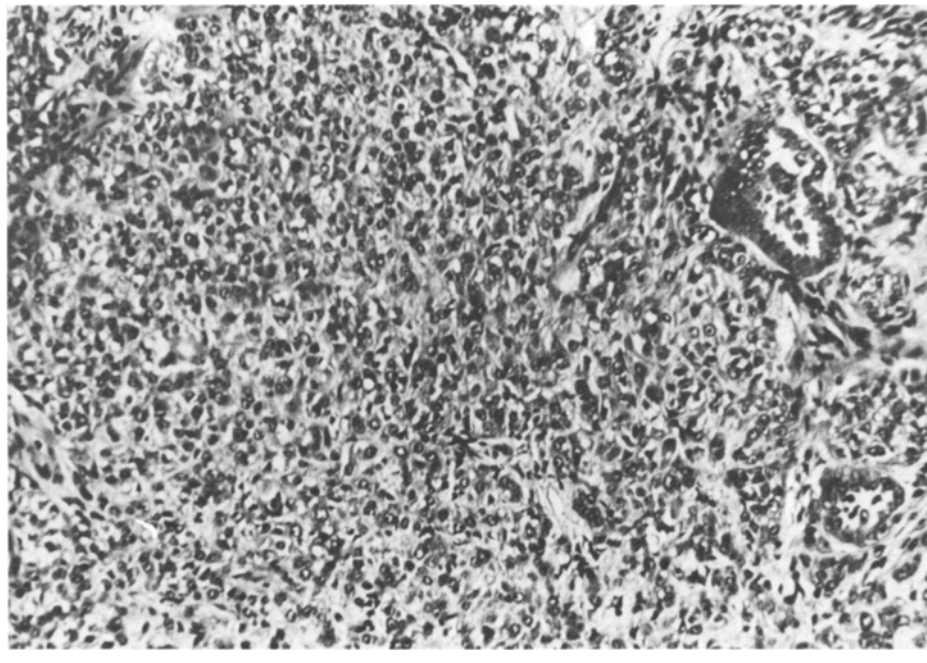

Fig. 1. Photomicrograph of a biopsy of a canine anaplastic carcinoma of the lung before Thermomagnetic Surgery.

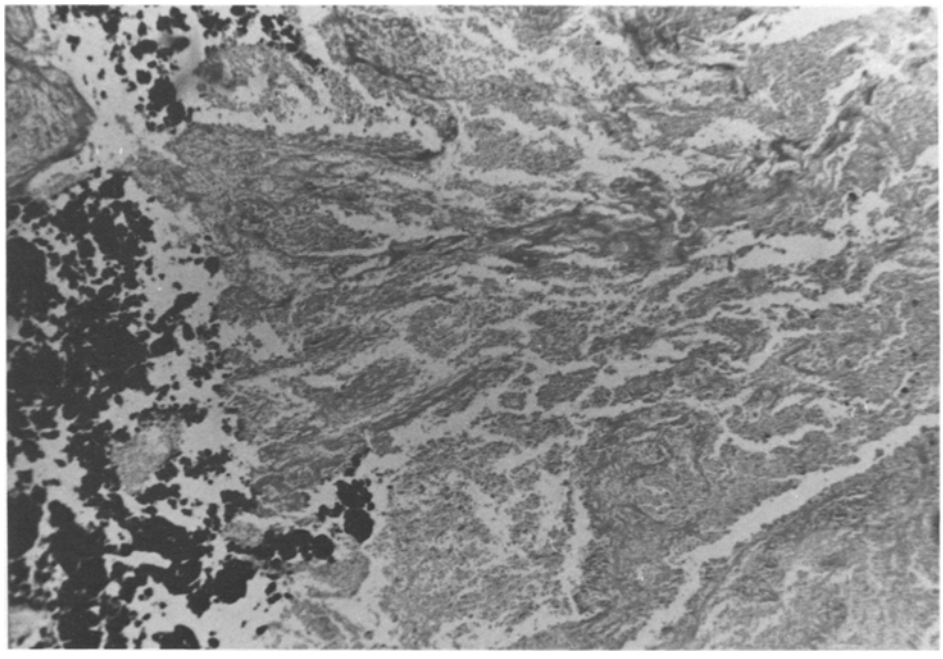

Fig. 2. Photomicrograph of the same anaplastic neoplasm adjacent to the ferrite compound placed within the tumor. This demonstrates coagulation necrosis by Thermomagnetic surgery after 5 min of hysteresis heating at 70°C. The tumor cells are seen as ghosts with areas of pyknotic nuclei consistent with cell death.

mal risk of causing spread of the cancer by metastasis; obviously, dead cancer cells do not metastasize.

Although this unique technique of Thermomagnetic Surgery is still in its experimental stage, it has been proven to be effective in totally destroying normal solid organs within experimental dog and rabbit models. This has been performed without producing any acute or chronic ill effects from the exposure to the powerful alternating current low frequency magnetic field (Figs. 3 and 4). These fields do, however, produce muscle spasm in varying degrees, depending on the orientation of the animal to the magnetic field during the treatment. Keeping the interface between the cancerous tissue and the surrounding normal tissue at 50°C or slightly less ensures minimal and reversible damage to the surrounding tissue. The central core is about 15°C higher than the periphery.

Methods of Procedure and Materials Used

This paper deals primarily with the investigators' experiments with 24 white New Zealand rabbits in which rabbit carcinoma (VX_2), extremely malignant, has been injected transarterially into the renal artery of the kidney on one side. Within 5 days this regularly produces obvious and active cancer, confirmed by histological examination and by the ability to transplant the cells to other rabbits.

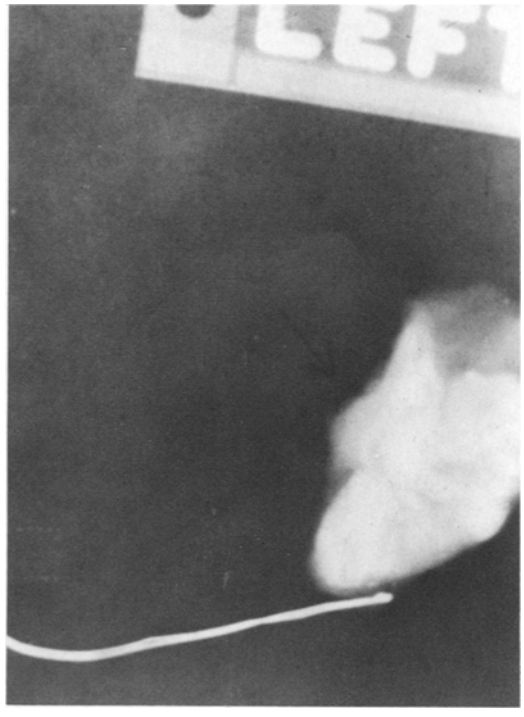

Fig. 3. Roentgenogram of the kidney of a dog removed at autopsy after Thermomagnetic Surgery. The controlled focal hysteresis hyperthermia produced the coagulation necrosis. A thermocouple was placed in the perirenal tissue to allow for temperature control during the Thermomagnetic Surgery at 50°C for 15 min.

After 10 days the neoplasm appears on the surface of the kidney. Metastasis to the peritoneum follows and a generalized spread to other organs can be observed. The control rabbits using this model (VX_2) type of cancer invariably have died.

To establish this VX_2 tumor model in the rabbit kidney a transfemoral catheter is placed into the renal artery under general anesthesia. With fluoroscopy an injection of 10^7 malignant VX_2 cells in 0.5–1.0 mL of carrier liquid is made. The rabbits are again anesthetized using Pentathol-type medications 5–10 days later and an abdominal laparotomy is made exposing the diseased kidney. Ligation of the renal artery and vein is then carried out and 2–3 mL of microferromagnetic material (Magnox Hi-EN555 FeO_2) suspended in 50% concentrations in sterile saline is placed into the pelvis of the kidney by direct injection. This fills up the renal calices and may to some degree extend into the ureter where it remains. Post-injection X-rays are then used to establish the location and distribution of this radio-opaque ferromagnetic material. Prior to closure of the wound, biologic adhesive is used to place fine thermocouples on the surface and within the cancerous kidney. The wire leads of these thermocouples are brought out through the abdominal incision, which is then closed with black silk.

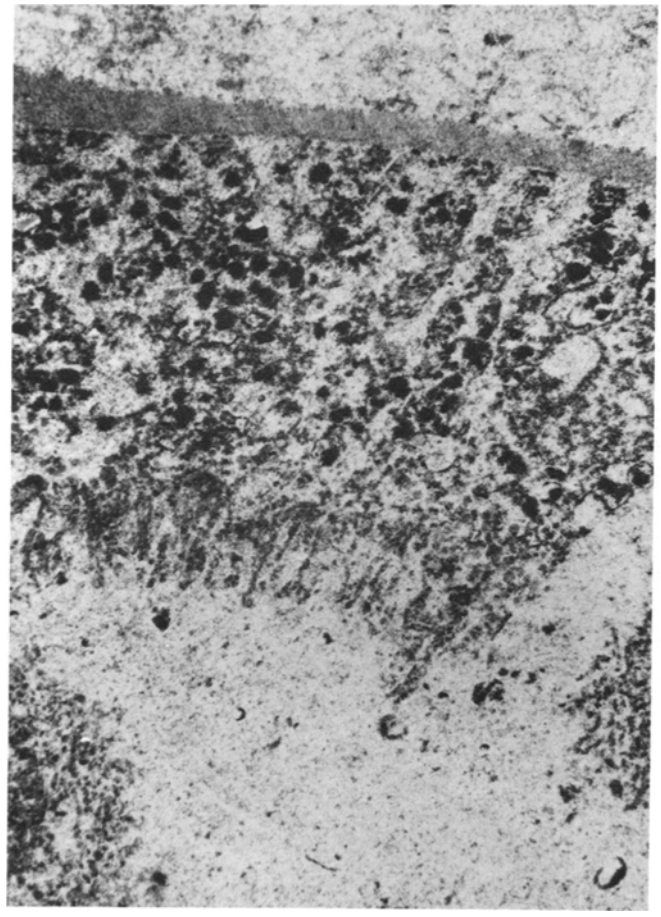

Fig. 4. Electronmicroscopy (EM) of canine renal cortex following Thermomagnetic Surgery showing destruction of the tubular components. The epithelium is totally degenerated and necrotic. (Plate mag., 3000; final mag., 10,000) with surface temperature at 50°C and parenchymal temperature of 95°C for 15 min.

Thus prepared, the XV_2 cancer model rabbits are placed in an alternating current low-frequency 2-KH_z coil that measures, internally, 12 inches high and 15 inches wide. A strong, alternating magnetic field of 0.1 Tesla (1000 Gauss or 1000 Aersted) rms amplitude at 2000 Hz is produced when the power is supplied to the coil and its capacitors, and this causes the phenomenon of the microferromagnetic particles being heated by hysteresis.

In an initial series of 12 rabbits with VX_2 carcinoma of the kidney, the temperature was permitted to go quickly to 55°C on the surface of the kidney as determined by the thermocouple reading. The power to the coil system was then cut off and there was cooling of the kidney for the next 5 min. The initial temperature of 55°C was reached in 1–2 min. Power was resupplied when the temperature was back to 43°C range, causing another sudden rise in temperature within the kidney. The cancer was thus exposed to 1, 2, or 3 episodes of hysteresis heating with this intermittent heating technique.

After the rabbits had recovered from anesthesia (24–72 h) and it was apparent that they had survived the surgery and the exposure to the magnetic field with no acute ill effects, they were sacrificed so that autopsy examinations could be carried out to allow careful study of the diseased and normal kidneys, as well as all other organs. The majority of the cancers within the kidneys was discovered to have been destroyed. However, some islands of carcinoma had remained in arteries and within the parenchyma, though surrounded by areas of total coagulation necrosis.

In the next series of six experiments, it was planned to raise the temperature of the surface of the kidney somewhat more gradually. Once the temperature reached 50°C, instead of completely turning off the power to the coil, it was reduced slowly in order to maintain a steady surface temperature. The power might be set at 75 A, for example, while bringing the temperature to 50°C on the kidney's surface, but once this temperature was achieved the power could gradually be reduced to a level of 60, and then 55 A, which would sustain the surface temperature of the cancerous kidney at 50°C for 5, 10, or 15 min in a particular rabbit.

This second series of experiments, using the longer exposure time of intense focal hyperthermia, achieved total destruction of the cancer within the kidney, thus preventing the possibility of metastases. It was therefore concluded that the successful results of total cancer destruction owed to the longer exposure of the cancer cells to intense controlled focal heat. All animals survived the Thermomagnetic Surgery and did not show evidence of metastases when sacrificed after 7–10 days and compared to control animals.

The current investigators have used this microferromagnetic material in the lungs and kidneys of dogs for a period of over 3 years without causing any clinically evident ill effects. The liver, kidney, and bone marrow functions have also remained unimpaired, as demonstrated by laboratory evaluation including a spectrum of blood chemistries and blood counts. In addition, dogs and rabbits that had been exposed to the magnetic field for up to 30 min have not shown ill effects after 3 and 1 years, respectively.

Discussion

The potential use of hysteresis heating of ferromagnetic particles within lymph nodes was first reported by Gilchrist (1, 2) in 1957 when he was attempting to destroy metastatic cancer from the gastrointestinal tract. A comparison was made, using extensive animal studies, between hysteresis hyperthermia and eddy current hyperthermia produced by microwave generators. These studies revealed not only the potential value of hysteresis hyperthermia in destroying cancerous tissue by intense focal heating, but also demonstrated that the magnetic field had no apparent adverse effects, not only on normal adult tissue by even on embryonic tissue. However, the work was never given a clinical trial and was discontinued.

At the beginning of this study in 1974, the current investigators were unaware of Gilchrist's and his associates' publications, but the development of the technique of Thermomagnetic Surgery was a natural outgrowth of prior research using ferrosilicone embolization to produce ischemic necrosis of organs and human can-

cer. It was found preferable to substitute materials such as ferrites, which show strong hysteresis heating characteristics, for the spherical carbonyl iron that has poor ferromagnetic properties. Many ferromagnetic materials were tested in vitro before finding the most desirable compound (3–5). It was first necessary to determine that these ferromagnetic needle-shaped particles would not interfere with vulcanization of the medical liquid silicone. Subsequently, small specially designed alternating current coils were used to subject them to strong electromagnetic fields. Since these in vitro experiments were highly successful, it was possible to inject these compounds into the vascular tree of normal tissue and organs. It was then clearly demonstrated that the combination of ischemic necrosis and coagulation necrosis secondary to hysteresis heating would produce total necrosis of the desired tissue, such as a kidney, for example (Figs. 3 and 4). The results of some of these earlier experiments were published in 1975 (*5, 6*).

Since that time, a satisfactory tumor model using the extremely malignant VX_2 rabbit carcinoma was developed. The current investigators decided to use the rabbit kidney as the target organ based on their 10 years experience of using ferrosilicone ischemic necrosis and hysteresis heating in various animals. The VX_2 rabbit carcinoma rarely has undergone spontaneous remission. It uniformly causes death of the rabbit within several months by metastasis to sites that depend upon where the tumor was initially placed.

These experiments demonstrated that a sustained constant heating of 50°C for longer periods of time, adjusting the power to the coil, was more effective in destroying renal cancer than periodic off-on heating to 55°C. It was further found that 50°C or slightly less, heated for 10 to 15 min, was the most satisfactory heating technique. It should be noted, however, that the temperature within the kidney is considerably higher, by at least 15°C.

A highly qualified pathologist made careful histologic examination of these model tumor specimens and found that they showed total necrosis of the kidney and the cancer within it both by light microscopy and electron microscopy.

All the animals survived the various operative procedures and exposure in the magnetic field without evidence of ill effects. Five dogs have been followed up to 3 years following 30 min of exposure to the magnetic fields with the ferromagnetic material in the lungs and kidneys. Based upon the life expectancy ratio, where 1 year in the dog is equivalent to 7 years in humans, the 3 years without evidence of ill effects from either the exposure to the magnetic field or the ferromagnetic material in the dogs would be equal to 21 years in man and therefore represents a definitive toxicology study.

The investigators believe that the Thermomagnetic Surgery using ferromagnetic materials is now ready for limited clinical application in selected patients with proven cancer using the ferromagnetic material suspended in medical grade silicone. This belief is based on the results of the 7-year in vitro and in vivo experiments in animals and man using nonmagnetic ferrosilicone. A patient with hypernephroma and metastasis could benefit first by the ischemic necrosis of the cancerous kidney alone, which in some cases may produce some immunologic phenomena to cause regression of the metastatic cancer. Several weeks after the ischemic necrosis, hysteresis hyperthermia could be carried out to assure more

complete destruction of any residual cancer in the kidney. We believe that this technique is particularly applicable also in uterine cancer and selected cancers of the liver and lung. The negative aspects of Thermomagnetic Surgery include potential damage to surrounding organs unless the temperature at the interface between normal and diseased organs is carefully controlled by temperature monitoring.

Conclusions

Thermomagnetic Surgery with ferromagnetic materials is an effective method of producing intense focal heating resulting in total necrosis and destruction of the cancer. This technique of Thermomagnetic Surgery is now a feasible and reasonable procedure for a clinical trial with selected human cancer patients.

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