

# Effects of Electromagnetic Heating on Internal Viscera: \*

## A Preliminary to the Treatment of Human Tumors

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AS PREVIOUSLY reported,<sup>3</sup> metastases in lymph nodes not removed at operation for cancer of the colon involved only a small part of the node (Fig. 1). These missed lymph node metastases were just outside the field of resection and were found in about one half of those subjects who had involved nodes in the cleared specimen, but were never found if the surgical specimen was node free (Fig. 2). We have also shown<sup>2</sup> that particulate material 1 m $\mu$  or less in diameter could be injected (about a breast tumor) in living patients and that we could fill the normal part of the node even when the node was largely replaced by cancer (Fig. 3).

### Method and Materials

Our objective<sup>4</sup> is to pasteurize or kill these missed lymph node metastases by controlled, moderate, localized heating of the involved nodes. This is accomplished by hysteresis when magnetic material is heated in an alternating electromagnetic field. At present our target material is a ferrite magnetic form of  $Fe^{203}$  having a diameter of 0.5 to 0.10  $\mu$ . The target material will be injected in various ways about the tumor. The usual resection will remove the tumor and the surgically accessible nodes. If

pathologic examination of the specimen suggests that tumor may be present in the remaining nodes, hysteresis is produced. This electromagnetic heating eventually should afford at least a 15% increased cure rate in cancer of the rectum, breast and stomach.

At present, in animals, we use a 100 KW generator producing an electromagnetic field having a frequency of 55,000 cycles/second and a 500 oersted magnetic field or 15,000,000 volt-amperes.

Previously we described<sup>6</sup> the development of this generator and the use of the ceramic thermistors to record temperature in the intact animal during treatment from as many as ten different areas. The target material is innocuous even after a year and can be reheated for at least 4 months. Five mg. of target material will effect necrosis in 1 Gm. of living tissue. The only untoward reaction<sup>7</sup> was seen in rabbits. Full power for 7 to 15 minutes caused necrosis of the stomach or colon, but there was no heating if the stomach and colon were empty at the time of treatment. This heating was due to eddy currents and not to hysteresis. The dog's diet is such that eddy current heating of the food does not occur. Dogs develop tetanic contractions during treatment and must be anesthetized. However rabbits can be treated without anesthesia and seem to suffer no distress.

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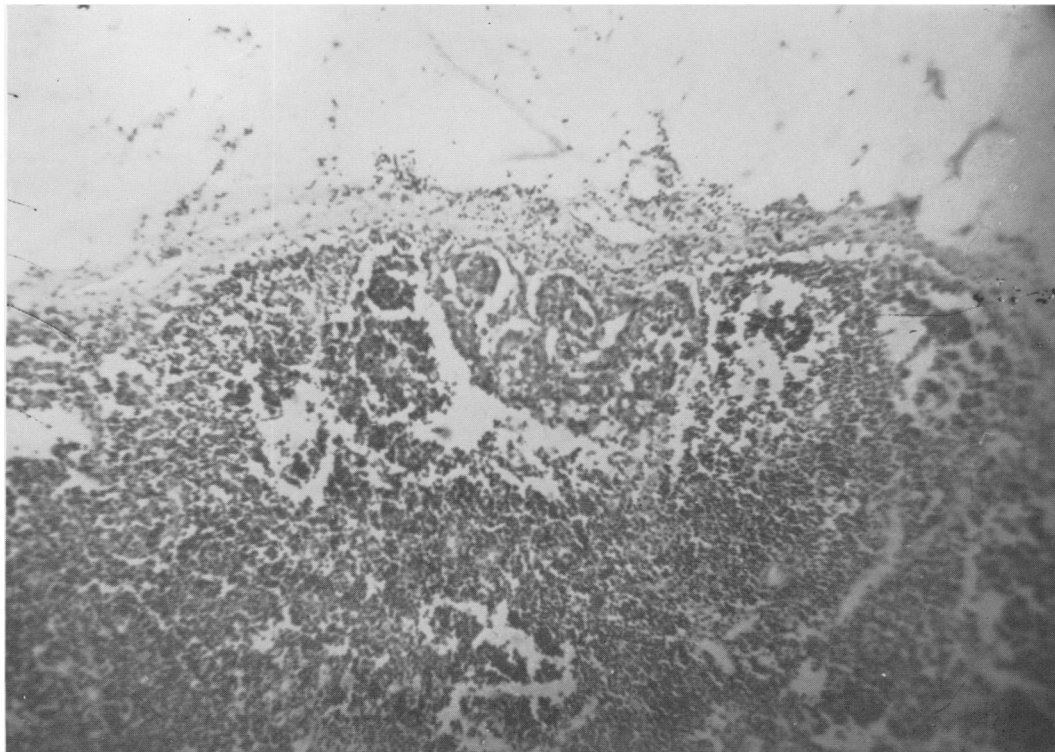
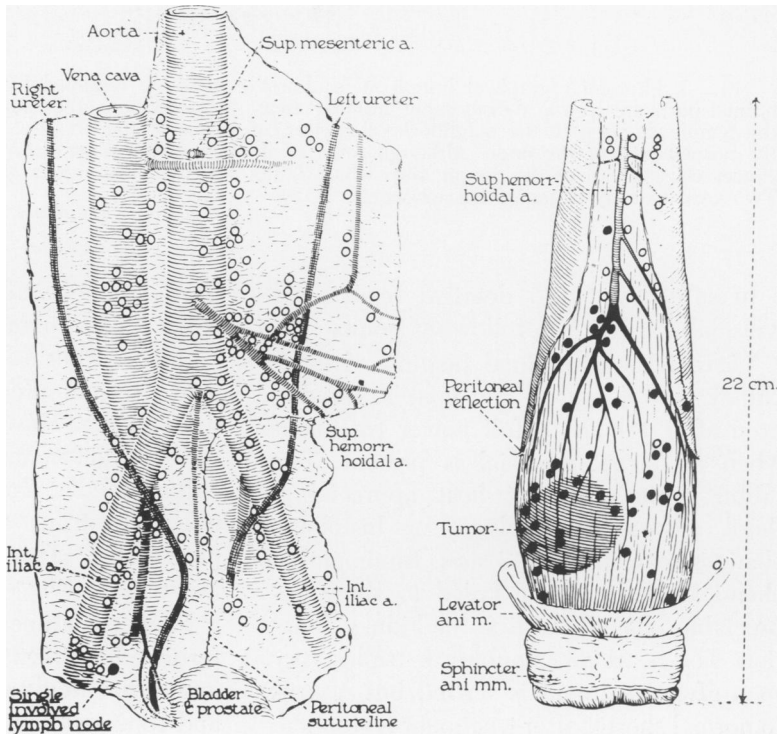


FIG. 1. Total amount of cancer in single involved node remaining in postmortem preparation.

FIG. 2. Operative specimen of carcinoma of the rectum known to be present 1 year, having 43 nodes (solid black dots) containing metastases. Postmortem showing one node containing cancer 1 cm. outside the field of resection. Only a very small part of this node contained cancer.



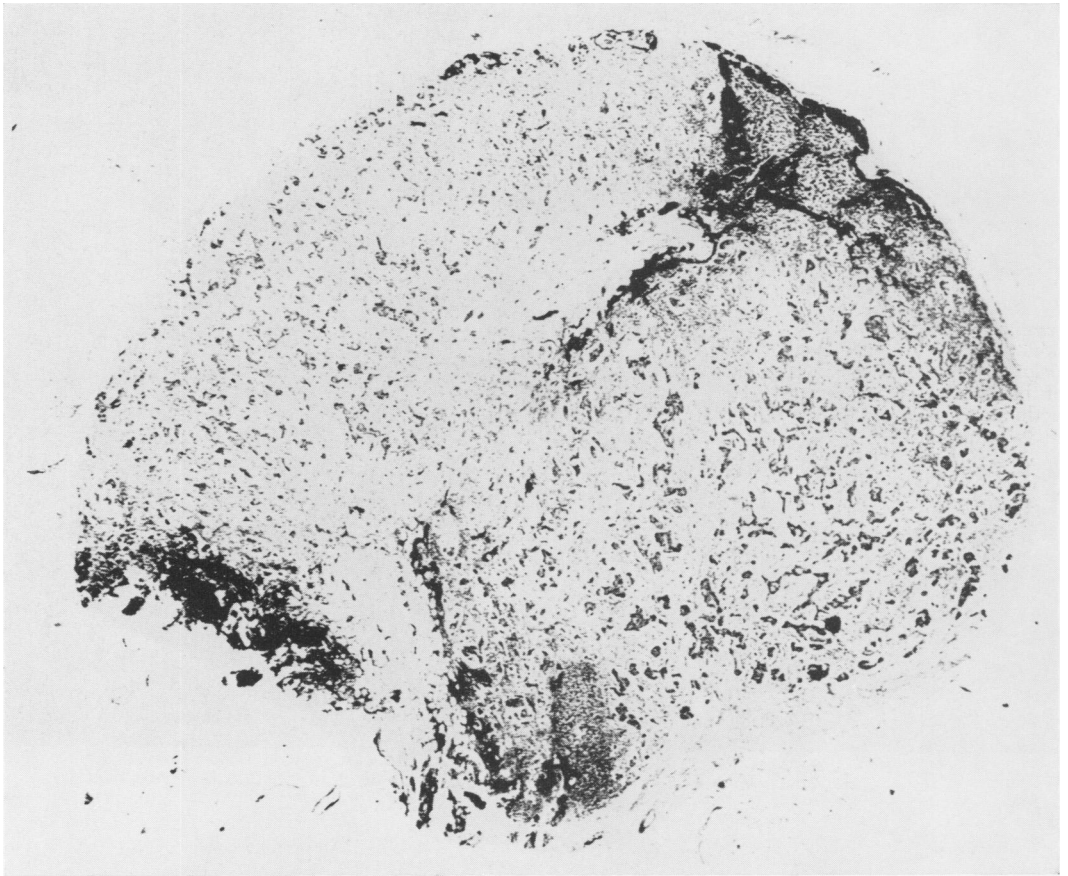


FIG. 3. Photomicrograph of lymph node almost completely replaced by carcinoma metastases. The normal parts are seen as dense, finely granular areas. A suspension of carbon particles was injected into the lymph channels in the neighborhood of the carcinoma of the breast. Most of the carbon is seen in the normal part of the node. Although some of it penetrates a short distance along spaces between the cancer cells, a part of the lymph sinus which is involved with carcinoma also contains carbon particles. Two areas of fatty degeneration are seen.

In subsequent and detailed reports we will elaborate on the following points.

There is only minimal heating of liver, kidney, bowel, muscle and bone in the dog even after 1 hour of full power treatment when no target material is present. The rabbit brain does not heat appreciably; there are no morphologic or histologic changes seen in these tissues. Innumerable chemical studies have failed to show appreciable changes in liver or kidney function. The heart rate doubles or triples very soon after treatment is started but returns to normal shortly after treatment is stopped.

EKG cannot be taken during treatment but when taken immediately afterward it is normal. Exposure to the electromagnetic field does not affect bacterial or human tissue cultures. However if a minute amount of the target material is added to the tissue culture media, Knock<sup>5</sup> has shown that the effect of drugs active against cancer is potentiated. This seems to be due to a minimal heating effect.

Many experiments show that progeny of fertilized chicken eggs, mice, rabbits, rats and some dogs are not affected by long and repeated exposure to the strong fields.

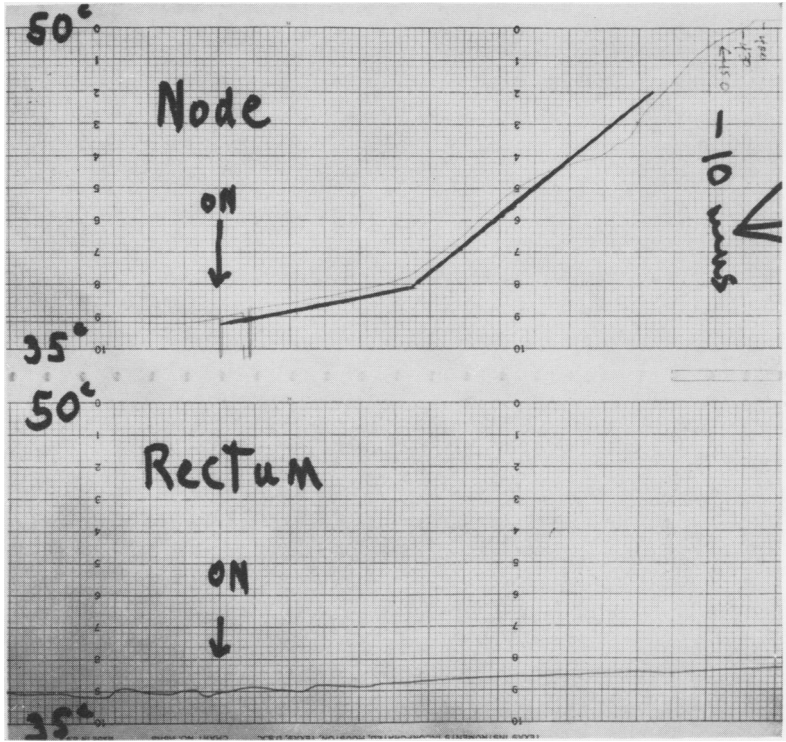


FIG. 4. Tracing of temperature recording in node above and rectum below. Note the two rates of heating in the lymph node and the slow rise in body temperature.

The offspring are normal and fertility is not affected.

As anticipated, the lymph node is peculiarly adapted for the production of localized heat.<sup>4</sup> It has a capsule and a single artery

and vein. There are two rates of heating in the node containing target material (Fig. 4). Heating produces edema which occludes venous drainage and the more rapid rise in heating is due to complete loss of

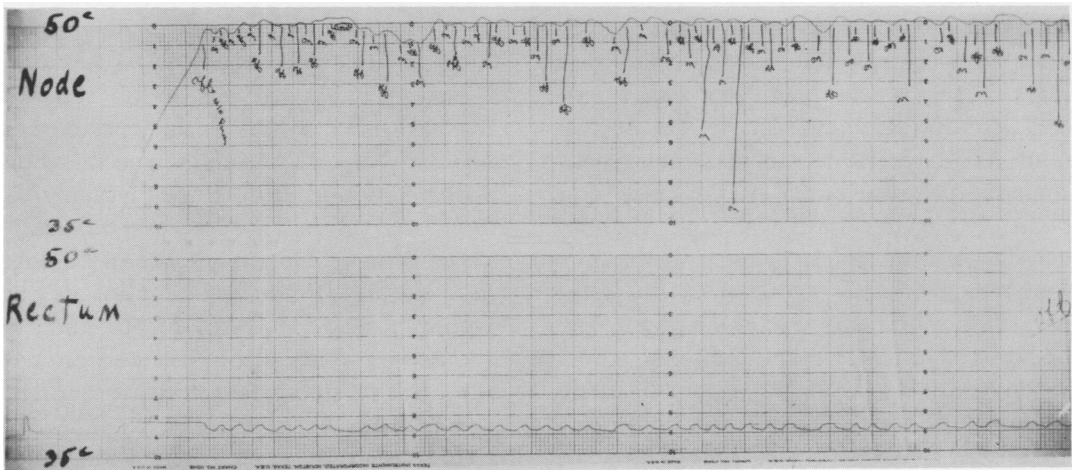


FIG. 5. Recording of temperature in lymph node and rectum over thirty minute period. Temperature maintained at 50° C. by means of pulsation of electromagnetic field.

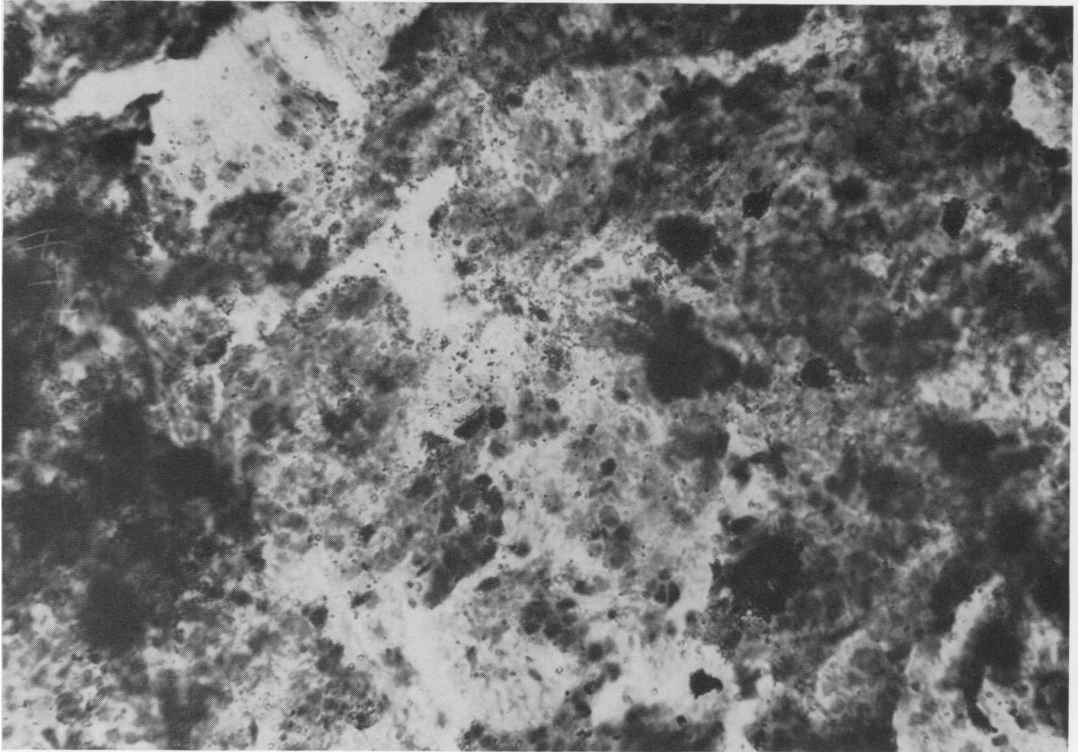


FIG. 6. Lymph nodes after 30 min. at 50° C. showing destruction of normal architecture (H & E).

the vascular cooling mechanism since the capsule does not expand.

### Results

We studied time-temperature factors which would produce necrosis in a lymph node without destruction of adjacent structures. Previous work indicates that tumor cells die if maintained at 49° C. for 20 min.<sup>1</sup> We have chosen to maintain a constant temperature of 50° C. in the lymph node. By varying the power input slightly, and in some instances by pulsing the current, we were able to maintain this temperature in the node (Fig. 5). The top line of the scale is 50° C. The pulses of power are indicated by the vertical lines. The node was maintained at 50° C. for 30 min. with an accuracy of  $\pm 0.5^\circ$  C. This degree of hyperthermia was studied at 15, 20, 25 and 30 min.

The production of necrosis in a lymph node incites an inflammatory reaction with infiltration of leukocytes including lymphocytes. To determine if all of the original lymphocytes had been killed, a method of enzyme staining was developed which could be carried out immediately after cessation of heating. This technic, to be reported elsewhere, shows that if the enzyme systems involving DNA, RNA, succinate dehydrogenase and DPNH are thermally destroyed the cell may be considered dead.

Using this technic in a series of 15 dogs, we were able to show that all cells survived exposure to 50° C. for 15 min.; 20 min. caused most cells to die, and after 30 min. there was complete destruction of the node (Fig. 6).

To evaluate the specific effect of an electromagnetic field in the heating of tissue, the liver was perfused with hot water

through a silver cannula. Temperatures of the water in the cannula and in the liver at 3 mm. intervals from the source of heat were recorded. Time-temperature factors leading to necrosis of liver tissue were essentially the same as in tissues which had been heated electromagnetically.

### Summary and Conclusions

Sixty per cent of patients having surgically removable tumors have node metastases and about one half of these have nodes containing small metastases just outside of the field of resection.

Particulate material can be floated into these involved nodes.

Magnetic particles can be heated by an alternating electromagnetic field.

Strong 55 kilocycle electromagnetic fields do not affect the function of vital organs nor raise the body temperature significantly in dogs.

Chick, rat and mouse embryos are not affected by treatment during gestation and their progeny are fertile.

We have not had a special target material made. We anticipate that much more finely divided target material can be made

and this will permit the normal parts of the involved nodes to be filled more easily.

When this material is available, these studies indicate that it will be possible to produce necrosis in nodes in man. If only half of the 30 per cent of those patients with surgically inaccessible involved nodes are helped, the cure rate of carcinoma of the breast, stomach and rectum will be increased by 15 per cent.

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### DISCUSSION

DR. WILLIAM W. SHINGLETON (Durham): I would like to congratulate Dr. Joe Gilchrist on his continued basic research on the effects of tissue heating, both in normal tissue and in tumor tissue. He has certainly pioneered in this field and he has done a tremendous amount of work in the past few years on this problem.

I have had the opportunity of reading his paper and herein he has defined more clearly the parameters of the possibility of the use of heat on the effective eradication of metastatic cancer in lymph nodes.

He stimulated us to try to measure the effects of local tissue heating, combined with cancer chemotherapy. We have used the same type of tissue heating, that is, electromagnetic induction heating, and have demonstrated in an experimental animal tumor, the rabbit VX-2 carcinoma, a definite increase in uptake of a cancer chemotherapeutic drug ( $C^{14}$  labeled HN<sub>2</sub>) in the presence of

increased local heat. A 5° C. rise in the tissue or tumor tissue caused an uptake of labeled nitrogen mustard of about twofold.

In addition to this, heat apparently potentiates the local effects of the cancer chemotherapy. We have applied this principle clinically, in which we have heated the perfusate in local perfusion of both melanoma and sarcoma of the extremity, and we have found that when heat is used along with the chemotherapeutic agent, one needs to reduce the dosage of the drug because of the side effects on local tissue.

Conversely, cooling tissue will protect normal tissues against the effects of these chemotherapeutic agents. We have used the combination, actually, of general body cooling with local hyperthermia in the area of the perfusion and we have been convinced that this approach has protected patients against the lethal or potentially lethal effects of the chemotherapeutic agent, and it appears that hyperthermia has greatly increased the