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MICROWAVE THERMOTHERAPY FOR THE TREATMENT OF HUMAN BRAIN CANCER

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Microwave apparatus for thermotherapy of human brain cancer is described. Key components of this apparatus are coaxial applicators that fit into 16-gauge tubes or needles (ID=1.32 mm) and can be inserted into the brain with minimum damage to healthy tissues. The case history of a patient treated with this apparatus is presented in some detail.

INTRODUCTION

Thermotherapy is used in a growing number of institutions around the world to treat solid malignant tumors. The therapy consists of heating the tumors until they reach a temperature several degrees centigrade above core temperature (hyperthermic temperatures) and maintaining the tumors at the elevated temperatures for certain lengths of time. The procedure is usually repeated several times. Thermotherapy is given either as a stand-alone therapy, or in combination with radiotherapy or chemotherapy, or prior to surgery.

Malignant human brain tumors are promising candidates for thermotherapy, since conventional cancer therapies often have limited therapeutic value in treating brain malignancies.[1] Attempts to treat human brain cancers with thermotherapy date back to at least 1971, when Sutton reported encouraging results using a combination of thermotherapy and chemotherapy.[2,3] Sutton produced hyperthermia in brain lesions using implanted resistive heaters; more recent investigators are using microwaves or ultrasound to achieve therapeutic temperatures in the brain.[4]

In the present paper we describe a microwave apparatus for producing hyperthermia in animal and human brains. Measurements of the temperature distribution produced by this apparatus in tissue phantoms and living dog brains are reported. This is followed by a report on our initial clinical results.

THE MICROWAVE APPARATUS

The microwave apparatus consists of a 2450 MHz signal generator followed by a travelling-wave tube amplifier, a directional coupler and a power meter to measure forward power, and a miniature coaxial applicator that is inserted into the brain.[1,5,6] Figure 1 is a photograph of the coaxial applicator. The applicator is fabricated from a 12-cm long piece of semi-rigid coaxial cable whose outside diameter is 0.86 mm. The radiating antenna is formed by removing a length of the outer conductor. A copper-constantan thermocouple using 0.08 mm Teflon-insulated wire is epoxied to the outer conductor at the antenna end. The shaft of the applicator is coated with epoxy to protect it from brain fluids and vice versa. The shaft fits into a 16-gauge tube.

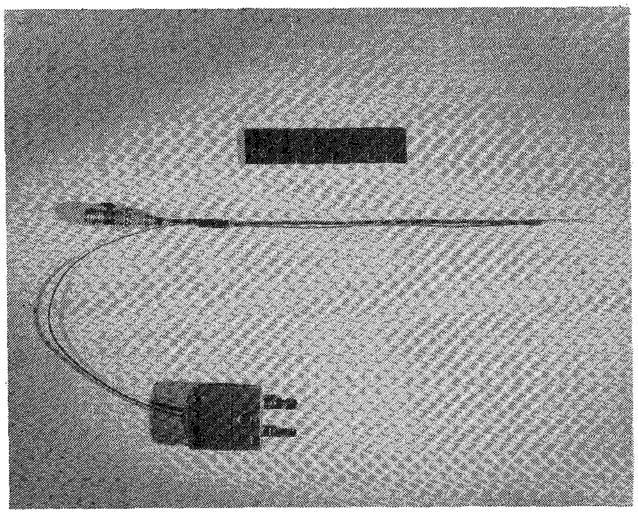


Fig. 1. Miniature coaxial applicator with integral thermocouple.

TEMPERATURE PROFILE IN PHANTOM

Several commercially available plastic catheters were used as implantable guides for the microwave applicator. These included a Fischer Ventricular Cannula,[+] a Field-Lee Biopsy Needle sheath,[++] , and a Holter Ventricular/Peritoneal Shunt.[+++] The axial and radial temperature profiles of an applicator inside a Fischer Ventricular Cannula that was implanted in a muscle-equivalent phantom material (69% H_2O, 30% gelatin, 1% NaCl) are shown in Figure 2. The temperatures were measured with small diameter thermocouples that were pulled through thin-wall Teflon tubes after the phantom had been heated with 2 watts of 2450 MHz power for 30 seconds. The tubes were positioned alongside and across the cannula. The measured temperature increases are shown in Figure 2(a) and an estimated therapeutic region is sketched in Figure 2(b). The therapeutic region is assumed to be the region bounded by the points of temperature increase that are one-half the increase at the center of the antenna. It was also noted that the temperature increase of the thermocouple that is epoxied onto the applicator was 2.6°C higher than the temperature just outside the cannula. This temperature difference

+ Heyer-Schulte del Caribe, Inc.,Anasco, PR 00610
++ American V. Mueller, Chicago, IL 60648
+++ Codman & Shurtless, Randolf, MA 02368

is primarily caused by the self-heating of the thin coaxial conductor due to the 2450 MHz power flowing through it.

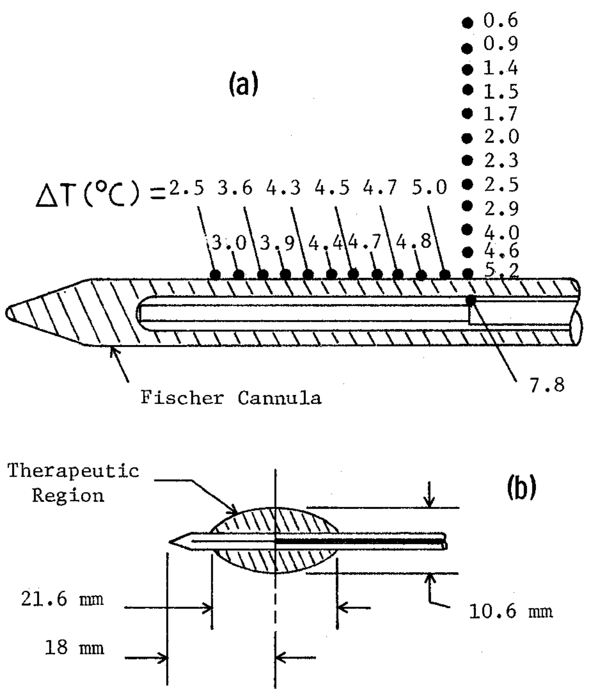


Fig. 2. (a) Measured axial and radial temperature profile of the miniature coaxial applicator in a Fischer ventricular cannula (O.D. = 2.8 mm) imbedded in a muscle-equivalent phantom material. (b) Therapeutic region of heating for the miniature coaxial applicator.

ANIMAL STUDIES

Two separate animal experiments were performed using anesthetized dogs. In each case the dogs were heated with an array of four applicators that were placed into one hemisphere of their brain through a burr hole in their skull. The applicators were inside Field-Lee Biopsy Needle sheaths located on the corners of a square, 2 cm on a side. An additional thermocouple was placed in the center of the array and another one was placed near the optic nerve, approximately 6 cm from the center of the array. The temperatures measured in the brain of the first dog are plotted in Figure 3. The readings of the thermocouples on the applicators were 1.5°C higher than the temperature just outside their sheaths. (The biopsy needle sheaths are thinner than the Fischer Cannulas used in the phantom experiments; this accounts for the smaller measured temperature difference). If the temperature curves for thermocouples 1-4 are corrected, i.e. reduced by 1.5°C, then curves 1-5 become nearly identical. Note that the corrected tissue temperatures in the intended treatment area (curves 1-5) reach hyperthermic temperatures (>42°C) within a few minutes after microwave power is applied. The temperature near the optic nerve remained below the hyperthermic range during the entire experiment.

A similar experiment was carried out with the second dog. In this case, however, the temperature of the thermocouples attached to the applicators was raised to 47°C.

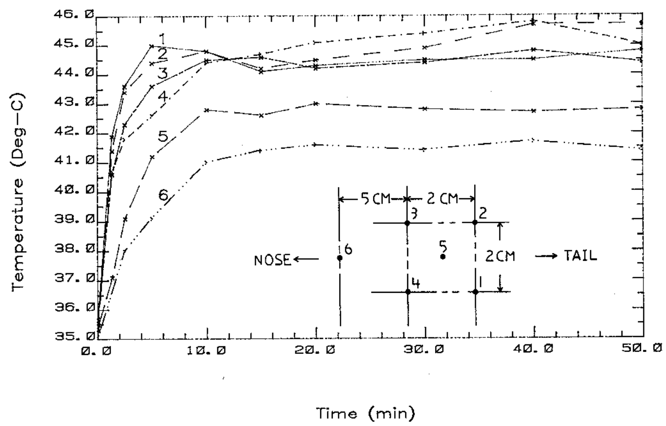


Fig. 3. Temperature measured in the dog brain as a function of time while heating with an array of four miniature coaxial applicators.

The brains of both dogs were sent to Rockefeller University for pathology. In both brains the hyperthermia produced an ellipsoidal lesion with edema around the area of thermalization.

CLINICAL TRIALS

Two patients with malignant brain tumors have so far been treated with the microwave apparatus described above. Both patients responded well to the microwave thermotherapy. The case history of the first patient who was treated is given below.

12/81	Onset of throbbing frontal headaches becoming progressively more severe, unremitting. Progressive loss of vision. Progressive weakness and inability to walk.
3/25/82	Frontal craniotomy. Removal of tumor (5 x 10 cm). Site: Dominant left hemisphere. Pathology: Angioblastic Meningioma. Post-operative: Mild weakness right leg for 3-4 days, general improvement.
4/15/82 - 5/28/82	5600 rad to tumor site.
11/82	Severe headaches, increased lethargy and confusion. CT scan shows tumor has regrown ≈ 5 cm in diameter.
1982-12/8, 12/10,12/16 1983-1/11,1/13	Microwave Thermotherapy sessions.

Each thermotherapy treatment used a single implanted applicator in a Fischer cannula positioned stereotactically to maximize the heat in the center of the tumor. The tumor was heated each time to 42.5°C (45°C indicated by the thermocouple attached to the antenna) for one hour. A typical plot of temperature and microwave power as a function of time is shown in Figure 4. Note that the microwave power required to maintain a constant tumor temperature decreased during this particular treatment session, indicating progressive damage to the tumor vascular system.

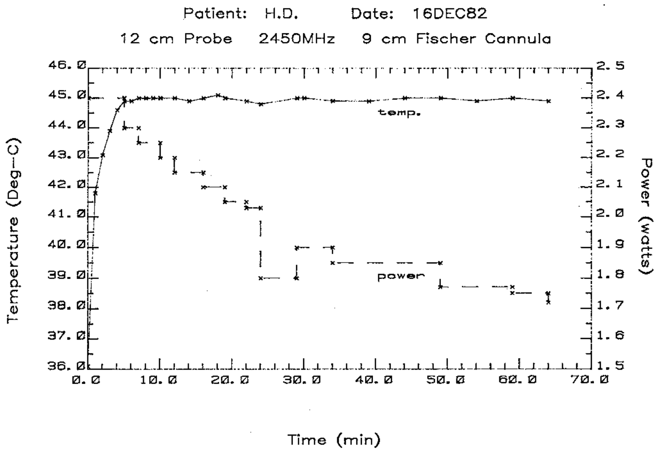


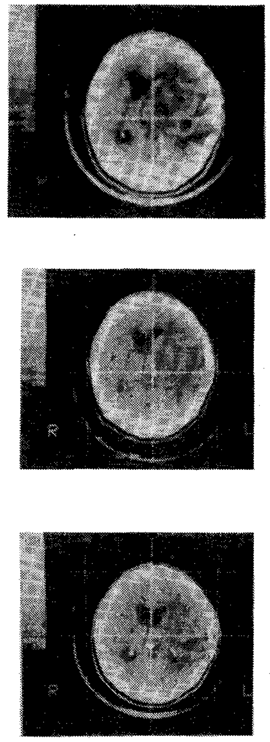
Fig. 4. Temperature response and drive power as a function of time for a miniature coaxial applicator in a Fischer ventricular cannula monitored during the treatment of a patient.

The patient's headaches started to remit almost immediately after the first thermotherapy session. He soon became ambulatory, with no headaches and no confusion.

Figure 5 shows three CT scans of the brain of this patient that were taken during the course of the thermotherapy. In these scans the nose is at the top, the plane shown is approximately at the level of the ears, and the bone flap from the original surgery can be seen on the right side of the scan. The bean-shaped black areas are portions of the left and right ventricles -- chambers in the brain that contain the cerebral-spinal fluid. The ventricles are normally symmetrical about the centerline between the two hemispheres of the brain and they should be approximately of the same size. The scan of Figure 5(a) was taken on 12/7/82, the day before the first thermotherapy session. Note that the left ventrical (shown on the right side of the scan) is almost completely occluded due to the pressure being exerted on it by the tumor, and the line of symmetry has been forced beyond the centerline of the brain. In Figure 5(b), 12/14/82, after two thermotherapy sessions, the left ventricle is opening and the line of symmetry is beginning to shift back. In Figure 5(c), 12/21/82, after three sessions, the ventricles are essentially back to normal. Biopsies taken at each time of treatment showed progressive change in the tumor cells

CONCLUSION

Microwave applicators that are small enough to fit into 16-gauge cannulas or needles can safely heat small volumes of brain tissues to therapeutic levels. Effective treatment volumes range from 1-2 cm^3 for single applicators, to several cubic centimeters for multiple applicators.



(a)

(b)

(c)

Fig. 5. CT Scans of a patient taken (a) prior to the first thermotherapy treatment; (b) after the second treatment; and (c) after the third treatment.

ACKNOWLEDGEMENT

The authors thank Dr. V. Bhardwaj of the Hospital Center at Orange for administering the anesthiesiology during the thermotherapy treatments, Dr. J. Walberg for the pathology on the dog brains, Dr. B. Orange of the Lexington Animal Hospital for supplying the dogs, and G. McDermott and F. Wozniak of the RCA Laboratories for their technical assistance in fabricating applicators.

REFERENCES

1. M. Salcman and G.M. Samaras, "Hyperthermia for Brain Tumors: Biophysical Rationale", Neurosurgery, Vol. 9, No. 3, Sept. 1981, pp 327-335.

2. C.H. Sutton, "Tumor Hyperthermia in the Treatment of Malignant Gliomas of the Brain", Trans. of Amer. Nuero. Assoc., 1971, Vol. 96, pp 195-199.

3. C.H. Sutton, "Use of Local Hyperthermia in Brain Tumor Therapy", Proc. Amer. Assoc. for Cancer Res., Denver, Colorado, 1977, p 200.

4. M. Salcman and G.M. Samaras, Private Communications.

5. J.W. Strohbehn, E.D. Bowers, J.E. Walsh, and E.B. Douple, "An Invasive Microwave Antenna for Locally-induced Hyperthermia for Cancer Therapy", J. Microwave Power, 14(4), 1979, pp 339-350.

6. L.S. Taylor, "Implantable Radiators for Cancer Therapy by Microwave Hyperthermia", Proc. IEEE, Vol. 68, No. 1, Jan., 1980, pp 142-149.