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Interstitial Helical Coil Microwave Antenna for Experimental Brain Hyperthermia

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A helical coil 2450-MHz microwave antenna was used to induce interstitial hyperthermia in normal dog brain. The HCS-10(1)/11 antenna consisted of a miniature semirigid coaxial cable around which a fine wire coil with 10 turns per 1-cm length was wound. A single antenna and two or three temperature probes were implanted stereotactically, and the temperature distributions surrounding the antenna were measured and compared to those induced using a dipole antenna. The helical coil antenna produced well-localized temperature distributions at depths that were symmetrical around the coil and that extended to the antenna tip. There was minimal variation of the heating patterns with insertion depth using the HCS-10(1)/11 antenna and no excessive heating of extracerebral tissues. In contrast, 2450-MHz dipole antennas induced temperatures of 43 to 46°C at the brain surface and extracerebral tissues (skull, muscle, and scalp), with a relatively uniform but lower temperature in the targeted brain volume. One week after hyperthermia treatment, the thermal lesions induced by the helical coil antenna were visualized using computed tomography. The heating patterns correlated well with the location of the heat lesions and were reproducible among animals. The results indicated that the helical coil antenna could be used to induce localized hyperthermia at specific depths in normal brain without inducing unacceptable heating of the brain surface or extracerebral tissues. Consequently, this antenna seems to be suitable for studying the response of normal brain after a heat insult and may be effective in the application of interstitial microwave brain hyperthermia for malignant brain tumors. (*Neurosurgery* 23:564–569, 1988)

Key words: Brain tumor, Hyperthermia, Interstitial hyperthermia, Microwave antenna, Thermal dosimetry

INTRODUCTION

Recent laboratory and clinical results suggest that hyperthermia may have potential as an adjuvant therapy in the treatment of malignant tumors (16, 18, 22). Heat alone has a cytotoxic effect, but seems to be most effective when used in conjunction with ionizing radiation and chemotherapeutic drugs (5, 7). Malignant brain tumors, because of their localized nature and low incidence of metastasis, are promising candidates for interstitial hyperthermia, especially in combination with low dose rate brachytherapy (6, 8).

One of the most fundamental difficulties of heating in the brain is the physical means to deliver a sufficiently localized thermal field to a desired target volume. Invasive microwave radiators that can produce local heating at depth have been developed (13, 20–23, 28, 31). Commonly used dipole antennas have been characterized by variability of heating profiles with different insertion depths and a relatively cold area or "dead length" near the antenna tip (4, 23–25, 28). Certain therapeutic situations may require the use of alternative antennas that produce different heating profiles; the opportunity to select a given antenna whose specific heating pattern is optimal could be advantageous in the planning of hyperthermia treatment.

In the present study, a stereotactically implanted interstitial helical coil microwave antenna (24, 25) was used to produce a localized hyperthermic field in normal canine brain. The thermal profiles of single antennas were studied and compared to those obtained using 2450-MHz microwave dipole antennas. Comprehensive thermal dosimetry was compared with radiographically evident brain lesions 1 week after treatment.

MATERIALS AND METHODS

Antenna design

Helical coil antennas were designed to be operated at a frequency of 2450 MHz. Each antenna was fabricated from a .095-cm O.D. miniature semirigid coaxial cable (UT-34M; Uniform Tubes Inc., Collegeville, PA) as described previously (24, 25). An 11-mm-long section of outer conductor was stripped from the end of the coaxial cable, and a fine wire coil (0.032 cm O.D.) was formed over the bare dielectric insulator. The coil was soldered to the distal end of the inner conductor, leaving a 1-mm gap between the proximal end of the coil and the outer conductor. Because of the connection configuration of the helical coil to the feedline, these antennas were designated helical coil-separated (HCS) antennas (24) and, more specifically, the HCS-10(1)/11. The number of coil turns per bare insulated inner conductor length (mm) is indicated by the 10, followed by the gap width in parentheses and then the total bare length of the antenna (Fig. 1).

A single-gap dipole antenna with dimensions similar to those of the HCS-10(1)/11 was constructed as described by Samaras (23), with a 0.1-cm break (gap) in the coaxial cable outer conductor 1.0 to 1.1 cm from the tip. The remaining 1.0-cm-long distal portion of the outer conductor was then soldered to the inner conductor at the antenna tip (Dipole-11) (Fig. 1). The helical coil and dipole microwave antennas each fit inside a 16 gauge (0.122 cm I.D.) Teflon (E. I. du Pont de Nemours & Co., Wilmington, DE) catheter.

General experimental procedures

Anesthesia was required for all procedures including attachment of the stereotactic frame to the head, computed tomographic (CT) scanning, and all hyperthermia treatments. Premedication included atropine sulfate (0.01 mg/kg) and acepromazine maleate (0.13 mg/kg) administered intramuscularly 30 minutes before the induction of anesthesia. Anesthesia was induced using sodium thiamylal (4% to effect), and a surgical level of anesthesia was maintained using methoxyflurane and oxygen.

A CT scanning-compatible stereotactic frame was designed to facilitate the percutaneous implantation of catheters for

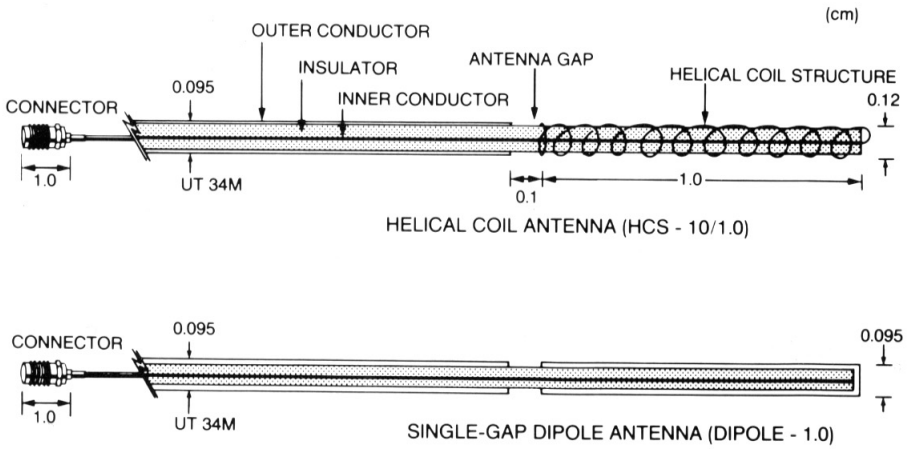

FIG. 1. Schematic drawings of the HCS-10(1)/11 (*top*) and the Dipole 11 (*bottom*) antennas, showing the dimensions and configurations of the two microwave radiators.

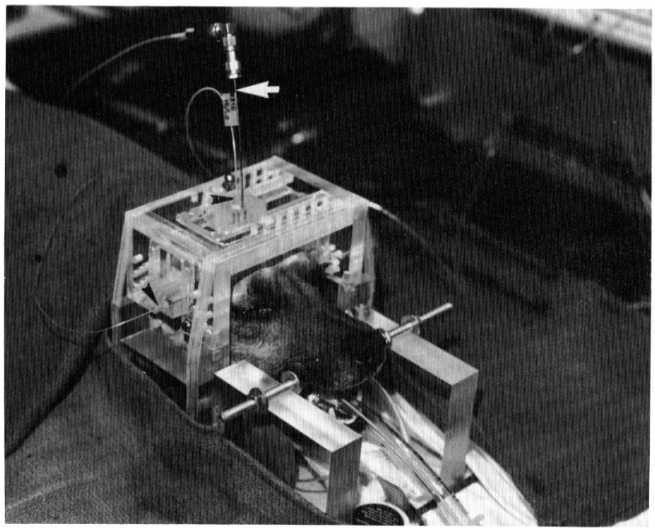

FIG. 2. Experimental set-up showing the stereotactic frame for percutaneous brain implantation of catheters for a single antenna (*arrow*) and two temperature-sensing probes. The frame is securely attached to the animal head by means of three metal screws.

the antenna and temperature-sensing probes (Fig. 2). Two 1.8-cm-thick Plexiglas (Rohm & Haas Co., Philadelphia, PA) templates, each with a square grid of 0.125-cm-diameter holes spaced 0.5 cm apart, were mounted into the frame at right angles. Template positions were adjustable with respect to the desired implant site in brain. The frame was attached securely to the head by means of three metal screws twisted through the skin directly into the zygomatic bones and the parietal region of the skull.

A series of contiguous 3-mm-thick coronal transverse CT scans (Model CT 9800; General Electric Medical Systems, Milwaukee, WI) were obtained with the stereotactic frame fixed in place. The desired implant site in the frontal white matter was determined, and stereotactic coordinates were calculated on the CT image for template positioning and catheter insertion into brain. Three 14 gauge (0.124 cm O.D.) stainless steel trocars were inserted via the templates through the scalp and muscle to the skull. Small drill holes were made in the skull using a high speed electric drill (Dremel Model 380-5; Emerson Electric Co., Racine, WI) inserted through the trocar guides. Steel stylets were used to insert closed, blunt end, 16 or 19 gauge Teflon catheters through the dura mater and into brain to the proper depth, as determined from the CT images. The trocars and stylets were then withdrawn.

A single antenna and one or more single- or multiple-sensor optical fiber thermometry probes (model TS-1200; Clini-Therm Corp., Dallas, TX) were placed into the catheters, which had previously been inserted into the frontal white matter at the level of the thalamus/caudate nucleus. In general, the antenna and at least one temperature-sensing probe were placed into the brain from a dorsal approach, while one temperature sensing probe entered laterally. The antenna was driven with a 2450-MHz continuous wave microwave power source (Model CA 2450; Cheung Laboratory Inc., Lanham-Seabrook, MD). Although both the Dipole-11 and the HCS-10(1)/11 antennas were adequately matched alone (typical return loss of about -8 dB or voltage standing wave ratio ≤ 2.3), precise and reproducible matching of the antennas to the generator and feedline was accomplished using a double stub tuner (Model 1729; Maury Microwave, Cucamonga, CA). All power and temperature information was recorded every 10 seconds by the data acquisition system (Model Mark-VI; Clini-Therm Corp.). The temperature distributions surrounding the antennas were recorded during steady state temperature conditions by mapping the temperature probes in 0.2-cm increments both axially (parallel to) and radially (perpendicular to) to the antenna axis.

Axial thermal profile studies

The axial thermal profiles from the HCS-10(1)/11 and Dipole-11 antennas were compared in six brain implant sites; three heat trials were performed with each antenna style. Animals were killed with an overdose of barbiturate immediately after a trial.

Single antennas were inserted to a depth of 1.35 cm from the brain surface to the antenna tip or 0.35 cm from the brain surface to the antenna gap. Including the extracerebral tissues, the total antenna length implanted in tissue was nominally 3.0 cm. A temperature-monitoring probe was inserted on each side of the antenna, 0.5 cm away from and parallel to the antenna ($r = 0.5$ cm). The probe on the medial side had multiple sensors for mapping temperatures from the skin surface to the antenna tip when a steady state temperature plateau was achieved. A stationary single-sensor probe was used on the lateral side for computerized feedback control of generator power. Control temperatures of 43.2 ± 0.1°C (mean $\pm$ standard error for three animals) and 42.8 ± 0.2°C ($n = 3$) for the HCS and Dipole antennas, respectively, were measured. These temperatures were obtained at a point 0.5 cm radially away from the antenna gap within 10 minutes of the initiation of microwave power and were maintained constant during the 10 to 15 minutes of temperature mapping. After euthanasia, the brain and extracerebral tissues were evaluated for gross abnormalities.

Survival studies

Single 30-minute hyperthermia treatments were performed in seven adult beagle dogs using the HCS-10(1)/11 microwave antenna. Two different antenna insertion depths were studied: 1.35 and 1.70 cm from the brain surface to the antenna tip. A multiple-sensor probe with four sensors spaced 1.0 cm apart was placed in a 16 gauge catheter located 0.5 cm away from and parallel to the antenna to measure the axial temperature profile.

A single-sensor probe was used to monitor the radial temperature distribution; this probe was inserted into a 19 gauge catheter that was perpendicular to the antenna axis at the level of the antenna gap. Power was manually adjusted to maintain approximately 43.0°C at the point of maximal temperature (control point) along the axial sensor probe. A steady-state temperature distribution was achieved within 10 minutes and was maintained during the 30-minute treatment period. Temperature mapping was done twice during the treatment, first along the radial probe using a temperature control point on the axial sensor and later along the axial sensing probe using a radial control point.

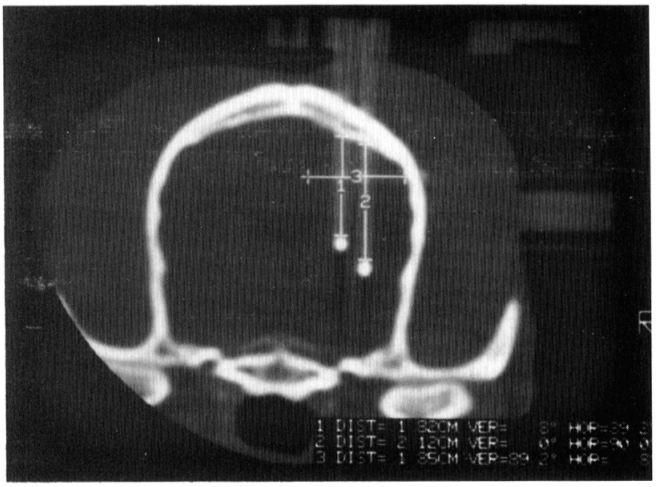

FIG. 3. Transverse CT image of the canine head obtained after hyperthermia treatment, confirming the correct catheter positioning of an antenna (*1*) and the axial (*2*) and radial (*3*) temperature probes.

Immediately after treatment, a series of contiguous 3-mm-thick coronal transverse CT scans was obtained with the frame and catheters in place to confirm correct catheter positioning in brain (Fig. 3). Contrast-enhanced CT scans were obtained 1 week after hyperthermia treatment to detect heat-induced changes in the brain.

RESULTS

Helical coil microwave antenna heating

In general, the HCS-10(1)/11 antenna produced a heating field surrounding the entire length of the coil element, including the antenna tip. The tissue temperature surrounding the antenna feedline tract in the extracerebral tissues did not exceed 40.2°C (Fig. 4). No evidence of swelling or edema was observed in the skin and scalp tissues immediately after or 1 week after treatment.

With a 1.35-cm antenna insertion depth, the axial (r = 0.5 cm) thermal profile had a maximal temperature of 43.2 ± 1.0°C (n = 3) 0.95 cm below the brain surface. Measured temperatures near the brain surface did not exceed 39.4 ±

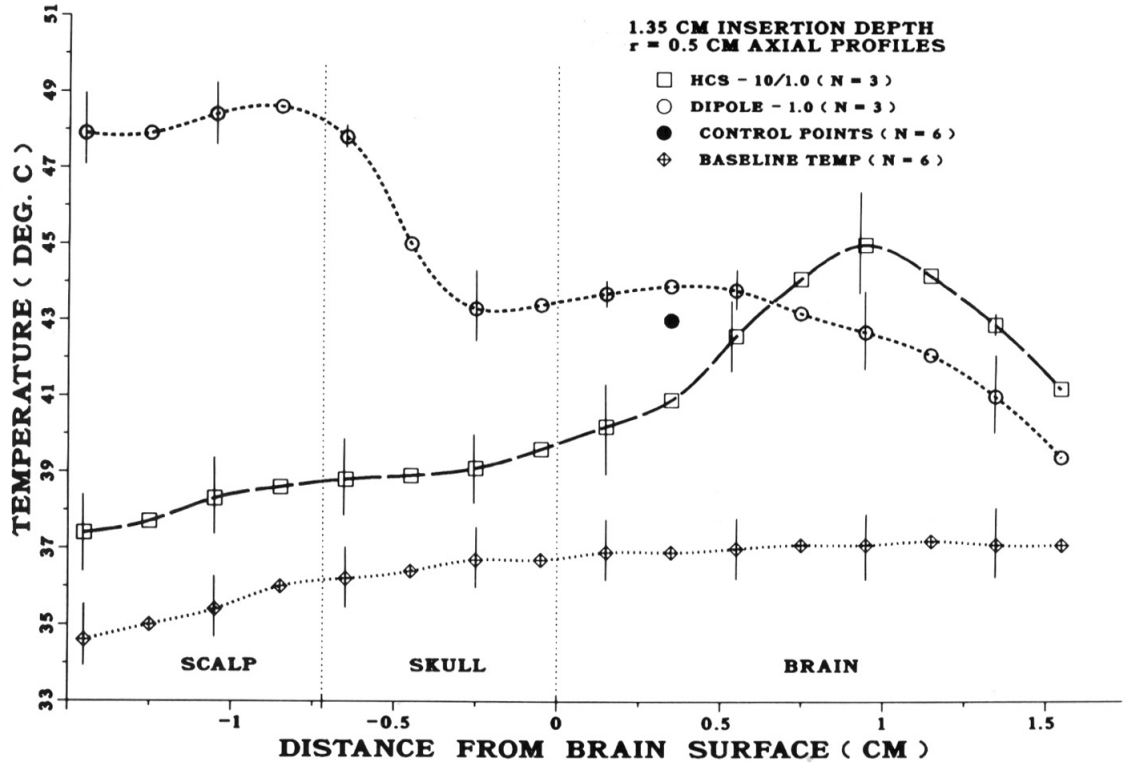

FIG. 4. Comparative axial (r = 0.5 cm) thermal profiles of HCS-10(1)/11 and Dipole-11 antennas in normal dog brain. Antennas were inserted 1.35 cm into brain by means of the percutaneous stereotactic brain implantation technique. The dipole antennas produced excessive heating in the skull, muscle, and scalp, whereas the HCS antenna heated only the region surrounding the 1-cm coil element. Means and standard error measurements are shown for the three animals in each group.

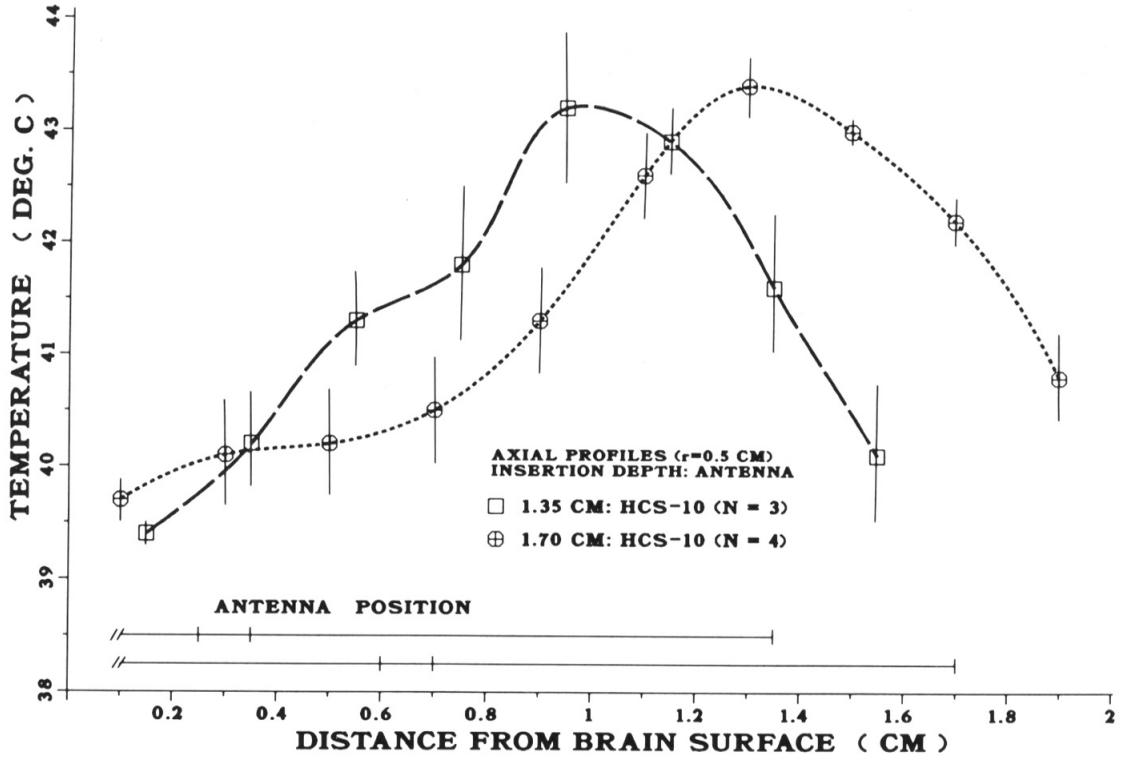

FIG. 5. The axial (r = 0.5 cm) thermal profiles of the HCS-10(1)/11 antennas obtained in canine brain as a function of insertion depth. Note the well-localized heating at depth, with the temperature peak of the profile located 0.95 and 1.3 cm below the surface for insertion depths of 1.35 and 1.70 cm, respectively. Means and standard errors are shown.

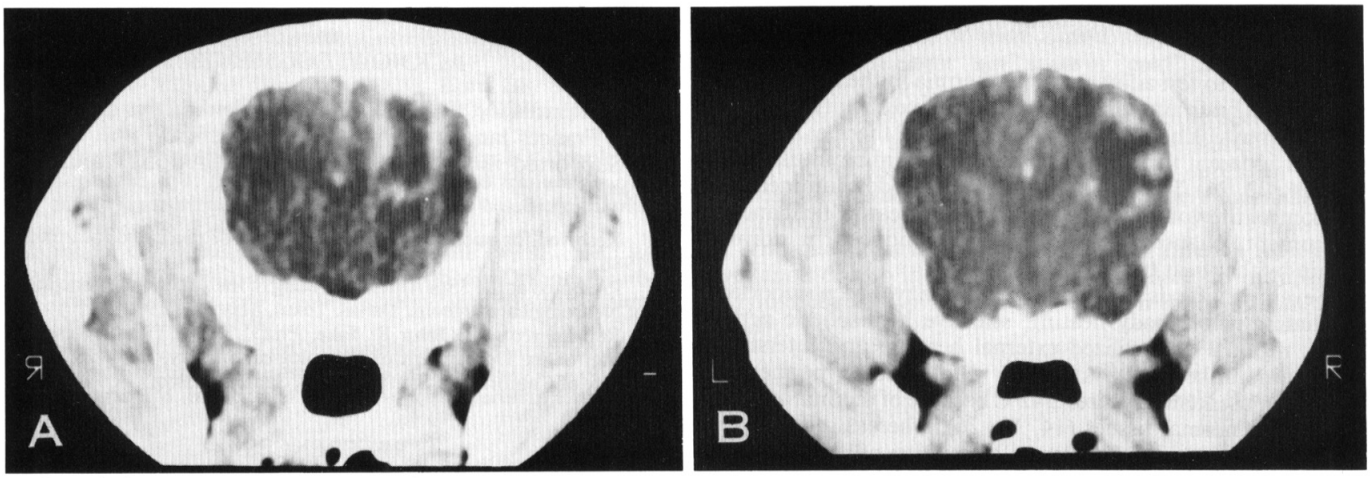

FIG. 6. Contrast-enhanced CT scans of two animals obtained 1 week after hyperthermia treatment (43.6°C × 30 minutes at r = 0.5 cm from the antenna gap) using a single HCS-10(1)/11 antenna with an insertion depth of 1.35 cm in *A* and 1.70 cm in *B*. Lesions consisted of a focal low density area in the white matter surrounded by a ring of contrast enhancement. In general, the location of the center of thermal lesions was deeper with a longer antenna insertion depth.

0.1°C (Fig. 5). When the antenna was inserted to a depth of 1.70 cm, the location of the profile peak moved correspondingly deeper, and a maximal temperature of 43.4 ± 0.3°C (n = 4) was measured 1.3 cm below the brain surface (Fig. 5). Temperature gradients in the radial direction away from the antenna were quite steep, decreasing about 1 to 2°C/mm.

Contrast-enhanced CT scans showed a well-demarcated cylindrical lesion in the white matter corresponding to the antenna implant site. The lesion consisted of a central low density necrotic area surrounded by a narrow ring of contrast enhancement or vascular permeability (Fig. 6), with no radiographically obvious edema or mass effect. The location of the focal lesion moved correspondingly deeper with increasing antenna insertion depth, which was in agreement with the thermal dosimetry results.

Dipole microwave antenna heating

An average peak temperature of 43.9 ± 0.2°C (n = 3) was measured in the axial (r = 0.5 cm) plane, 0.35 cm below the brain surface or at the level of the antenna gap (Fig. 4). The

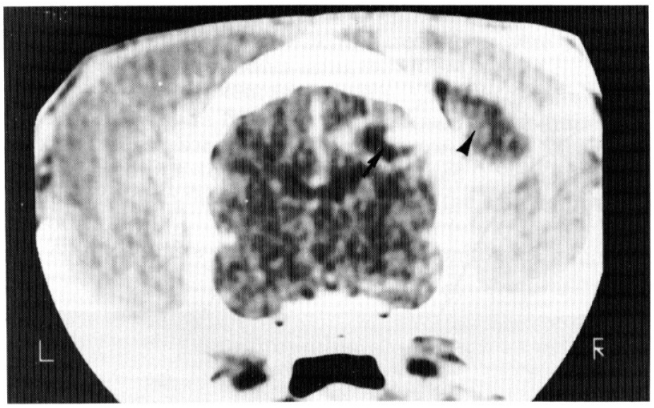

FIG. 7. Contrast-enhanced CT image obtained 1 week after hyperthermia treatment (44°C × 30 minutes at r = 0.5 cm from the antenna gap) with a single-gap dipole antenna implanted laterally 2.1 cm from the brain surface to the antenna tip or 1.0 to 1.1 cm from the brain surface to the antenna gap. An ellipsoidal thermal lesion (*arrow*) surrounded by a contrast-enhanced narrow ring was observed in brain. Note the additional low density area (*arrowhead*) surrounded by a thick region of enhancement in the temporalis muscle tissue along the tract of the antenna feed line.

temperature decreased distally along the antenna, resulting in temperatures ≤42°C near the antenna tip. Furthermore, temperatures 4 to 6°C higher than the maximal brain temperature were observed in extracerebral tissues along the antenna tract. At necropsy, significant edema, small hemorrhages, and tissue coagulation were macroscopically observed in the muscle and scalp tissues along the tract of the antenna feed line.

DISCUSSION

Attempts to test adjuvant hyperthermia in the treatment of malignant brain tumors are limited by the difficulty of inducing and physically characterizing a localized thermal field and by the apparent thermal sensitivity of normal brain tissue (2, 13, 21, 22, 26). It is essential, therefore, to develop methods to control the volume and location of the heating field and to document, quantitatively, the changes induced in normal brain by that heat treatment.

Several methods for heating brain have been reported, including whole body heating, selective hemispheric perfusion, regional or localized external heating, and interstitial intratumoral heating. Systemic or whole body hyperthermia generally uses temperatures ≤42°C because of thermal toxicity to critical normal tissues (14, 19, 26), whereas selective regional perfusion is limited by the dissipation of heat from the region of interest via collateral vessels or the circle of Willis (3, 9, 32). Regional or localized external heating can be applied noninvasively by means of an externally applied electromagnetic or ultrasound field (10, 12, 17, 27, 30); however, it is difficult to control the localization of heating and the temperature uniformity within a specific volume of brain tissue at depth. At present, interstitial approaches using radiofrequency-localized current field electrodes (1, 17), inductively heated ferromagnetic seeds (11, 15, 29), or implantable microwave radiators (13, 20–25, 28, 31) seem to offer the most promise in terms of the ability to deliver adequate and controllable tumor hyperthermia while sparing surrounding normal tissues. Another advantage of interstitial techniques is that the applicators can be inserted in the same catheters used for brachytherapy, thereby facilitating combined thermoradiotherapy.

Previously we used the single-gap dipole antenna design operated at 915 or 2450 MHz to produce localized heating in the normal canine brain (28). For those studies, the antenna was implanted laterally to a depth of one-half wavelength (6 to 8 cm for 915 MHz; 2 to 2.5 cm for 2450 MHz), which was considered optimal insertion for operation of the antenna as a symmetrical dipole (4, 13). Even with half-wavelength insertion from the brain surface to the antenna tip, however, unacceptable temperature increases (≥43°C) were observed in the extracerebral structures. This was manifest on CT scans as large cystic lesions in the temporalis muscle along the tract of the antenna (Fig. 7). In the present study, we tried to produce a focal heat lesion in the frontal white matter without inducing toxic temperatures in the muscle and scalp. To accomplish this, we used a dorsal approach and an antenna insertion depth of 1.35 cm (Fig. 4). With the dipole antenna, the temperature distribution over the region of interest ranged from 41–43.9°C at the antenna tip and from about 43–46°C in the extracerebral tissues.

Our results indicate that the helical coil microwave antenna (24, 25) may be more suitable for inducing a focal heat lesion in the normal canine brain without the accompanying superficial tissue heating observed with the dipole antenna. Heating patterns from the helical antenna were localized to the region immediately surrounding the entire coil length, and there was no "dead length" or region of relatively low temperature at the antenna tip. Furthermore, there was no significant heating of the extracerebral tissues or brain surface. The reproducibility of the heating patterns with variable antenna insertion depth should improve the delivery of a restricted heat field to a specific volume at depth and may be of critical importance in the brain, where overimplantation of antennas and/or temperature sensing probes into sensitive normal tissues may have serious consequences.

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COMMENT

Satoh et al. have made further efforts to create focal, uniform interstitial hyperthermia and have succeeded admirably in reducing extracerebral heating while delivering a preplanned thermal dosimetry effect. Temperatures sufficient to create cell death have been achieved. A tumor volume necessitating the use of more than a single antenna will, of necessity, create either "hot" spots or "cold" spots as perimeters of effect do or do not overlap.

No microscopic pathological findings are included to prove the contention that the tissue within the enhancing ring is "necrotic." I presume that this is a "gross" specimen observation only. Microscopic evaluation of the ring-enhancing area would be fascinating to view.

The interstitial helical coil microwave antenna represents yet another step in the quest to create localized intraparenchymal heating with ultimate adaptation to the human situation.

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