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Interstitial Radiofrequency Hyperthermia for Brain Tumors

—Preliminary Laboratory Studies and Clinical Application—

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Abstract

An interstitial radiofrequency (RF) hyperthermia system for brain tumor was evaluated in cranial phantoms and cat brains. An intracranial RF applicator and thermocouple microprobes were emplaced in the brain and a headband-type flexible extracranial electrode fixed over the scalp. An 8 MHz RF capacitive-type heating machine provided power. The temperature distribution was measured by thermography. In phantom and animal studies, the RF power had good penetration into the tissue and generated uniform and easily controllable high-temperature fields within the intracranial cavity. There was little change in temperature near or in the cranium itself. Six cases of human malignant glioma were treated with this interstitial RF hyperthermia system, achieving therapeutic temperature without adverse effects.

Key words: hyperthermia, brain tumor, radiofrequency

Introduction

The prognosis for malignant glioma patients receiving only surgical treatment is usually discouraging. Conventional adjuvant therapies such as radiation therapy or chemotherapy achieve only a slight increase in median survival rates. Localized hyperthermia is a recent development used to treat solid malignant tumors. Hyperthermia treatment for the malignant brain tumors has a biophysical rationale,[6] but technology for delivering uniform and easily controllable high-temperature fields within the intracranial cavity is necessary.

Here, we report our ongoing laboratory studies of interstitial radiofrequency (RF) hyperthermia for brain tumors and present our initial clinical experience.

Materials and Methods

Our interstitial RF hyperthermia system uses an 8 MHz oscillating frequency generator (Yamamoto Vinytor Co., Ltd., Osaka). Figure 1 shows the block diagram of the RF apparatus. Energy is transmitted from the amplifier to an impedance-matching circuit and then to the electrode *via* two coaxial cables. The RF power is supplied to a pair of electrodes resulting in a current flow. Two RF power meters are provided for measuring the power from the generator and the reflected power. The automatic power control system achieves continuous heating of the target tissue at a predetermined temperature level based on the temperatures measured by the sensors. The intracranial electrode is made from a small brass rigid pipe coated with gold. The extracranial electrode consists of a headband-type flexible aluminum strip fixed to the cranium. The temperature profiles are monitored by tissue-implantable copper-constantan thermocouple microprobes (Type IT-18; Physitemp Instruments Inc., Clifton, N.J., U.S.A.) connected to a TH-54H thermometer (Internova Co., Ltd., Tokyo).

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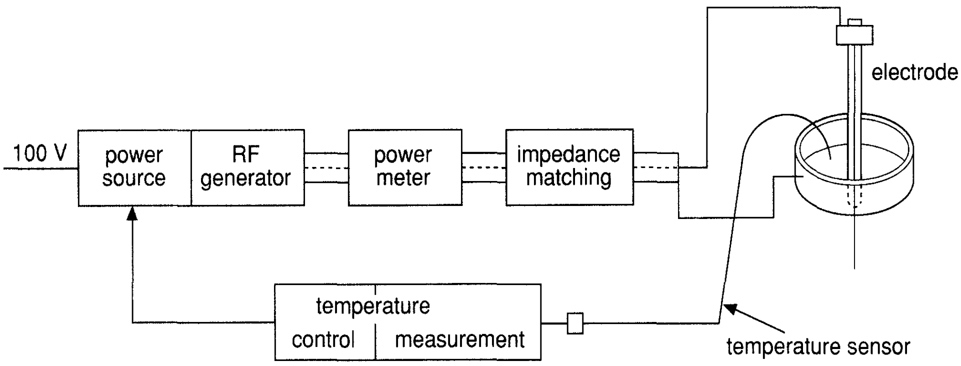

Fig. 1 Block diagram of the interstitial RF hyperthermia system, applying energy from an RF source to an external extracranial electrode and a small intracranial electrode.

The temperature distribution was also measured by infrared thermography in the phantom studies (Infraeye 160; Fujitsu Co., Ltd., Tokyo). The skull phantom consisted of a quadrasected human dry skull filled with agar gel with dielectric properties similar to living tissue. An intracranial electrode was inserted in the midportion of the phantom material at a depth of 4 cm. Thermocouple microprobes were positioned parallel to the applicator at 0.5-cm intervals and a depth of 4 cm. An extracranial electrode was placed around the entire cranium (Fig. 2). The skull phantom was heated for 15 minutes at 8 MHz with the RF apparatus. Immediately after heating, the dry skull sections were removed and the skull phantom bisected along the sagittal or horizontal plane. Thermograms of the plane were then obtained by infrared thermography.

Nine adult cats were used in experimental studies. The heads of the ether-anesthetized cats were fixed to a stereotactic frame. An internal electrode was inserted into one hemisphere of the brain through burr holes in the skull and a headband-type external electrode applied to the cranium. Thermocouple microprobes were also inserted using a manipulator parallel to the sagittal sinus in the ipsilateral hemisphere at 0.5-cm intervals from the internal electrode and a depth of 0.5 cm. The rectal temperature and systemic blood pressure were monitored.

Results

Temperature profiles along the sagittal plane of the phantom demonstrated a radially concentric distribution around the intracranial applicator. The thermal gradient showed a bell-like curve for the temperature distribution (Fig. 3). The temperature close to the skull did not rise.

A typical example of the heating pattern variation

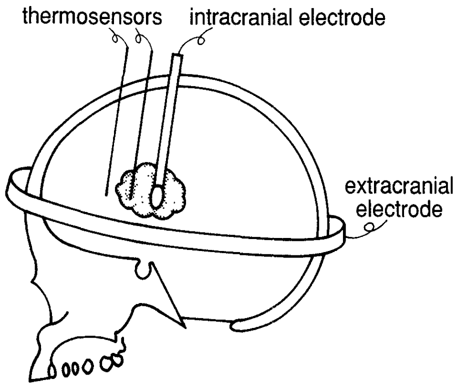

Fig. 2 Interstitial RF hyperthermia system for brain tumor. The intracranial electrode and thermocouple microprobes are implanted in the cranial cavity, and the extracranial electrode fixed over the cranium.

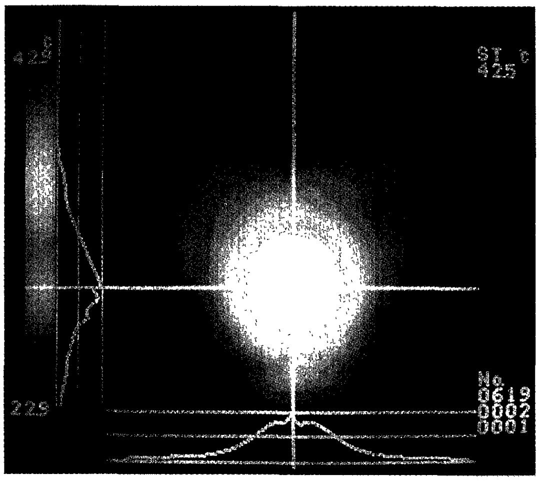

Fig. 3 Thermogram along the sagittal plane of a skull phantom after RF heating by an electrode placed at the center of the phantom. The bell-like curve (*bottom*) shows the temperature profile.

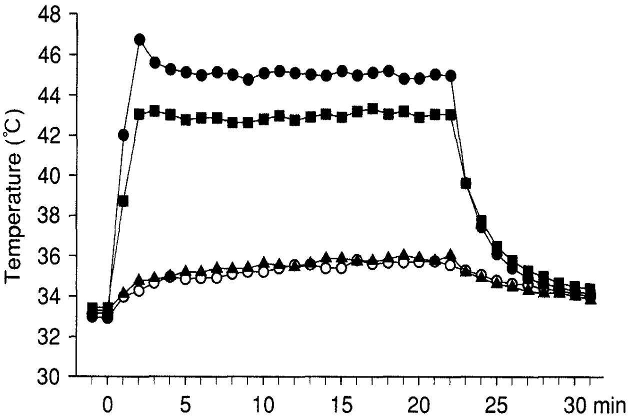

Fig. 4 Temperature profile in a cat brain during heating with an RF electrode. The thermocouple microprobe sensors 1 (●), 2 (■), 3 (▲), and 4 (○) are 5, 10, 15, and 20 mm from the RF probe, respectively.

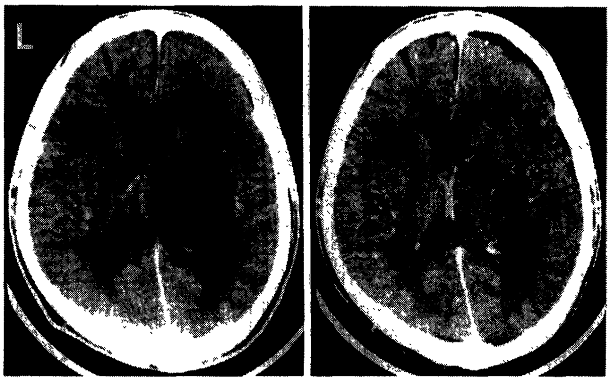

Fig. 5 Case 2. *left*: Postcontrast CT scan, demonstrating a low-density mass in the right thalamic region. *right*: Postcontrast CT scan after thermotherapy, radiation therapy, and chemotherapy, showing reduced tumor size. Note the low-density spot corresponding to the heating center.

with time around the implanted applicator in a normal cat brain is shown in Fig. 4. The thermocouple microprobe sensor 2 was positioned 1 cm from the applicator prior to treatment to maintain a control temperature of 43°C. After the power supply was turned on, this sensor showed a rapid rise in temperature and soon reached the temperature level set. When the automatic power control system generating the intermittent power supply for continuous heating of the target had stabilized, the temperature distribution in the horizontal plane correlated closely with the phantom studies. The microprobe sensors 3 and 4, located approximately 1.5 and 2 cm from the applicator, recorded only 36.0° and 35.8°C. These data suggest that our in-

Table 1 Summary of cases undergoing interstitial RF hyperthermia for malignant gliomas

Case No.	Age (yrs)	Sex	Location	Histology	Thermotherapy	
					Date	Maximum tumor temperature (°C)
1	55	F	lt frontal	recurrent malignant astrocytoma	7/ 8/86	44.3
					7/10/86	44.8
					7/12/86	44.3
2	22	M	rt thalamus	glioblastoma	3/ 2/88	42.9
					3/ 5/88	43.1
					3/ 8/88	42.9
3	43	M	lt frontal	recurrent malignant astrocytoma	5/18/88	43.4
					5/21/88	43.5
					5/24/88	43.7
4	72	M	rt thalamus	glioblastoma	6/16/88	43.9
					6/19/88	44.0
					6/22/88	44.1
5	62	M	rt parietal	glioblastoma	11/17/88	43.6
					11/20/88	46.5
					11/22/88	43.4
6	51	M	lt parietal	recurrent glioblastoma	12/14/88	43.3
					12/16/88	43.5
					12/19/88	43.7

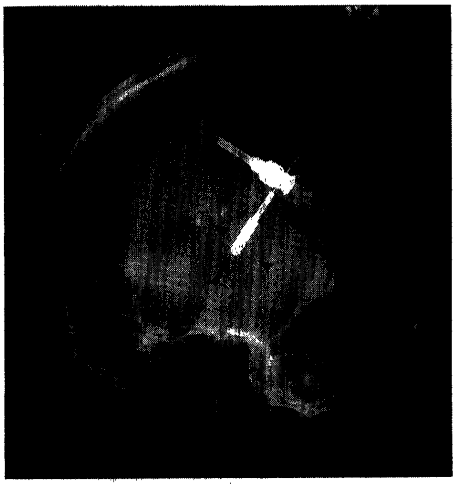

Fig. 6 Case 2. Lateral skull roentgenogram, showing the internal electrode (*arrow*) and the thermosensors (*arrowheads*).

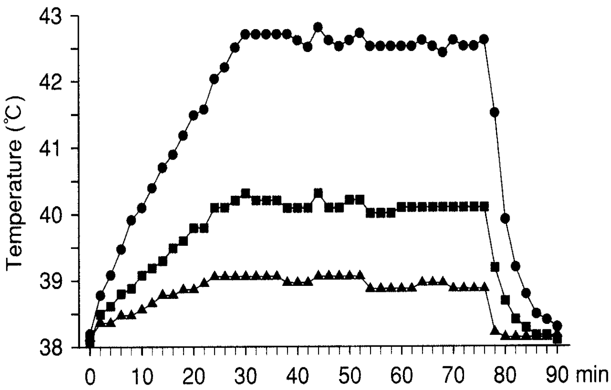

Fig. 7 Case 2. Temperature profile during the first hyperthermia treatment. Thermosensor 1 (●) shows the tumor temperature, sensor 2 (■) shows the surrounding tissue temperature, and sensor 3 (▲) shows the temperature in anterior horn of the left lateral ventricle.

terstitial RF heating system can be used to heat brain tumors without causing damage to the surrounding tissues.

Six patients with malignant glioma were treated using our interstitial RF hyperthermia apparatus. Table 1 summarizes the clinical case histories and thermotherapeutic data.

Case 2: A 22-year-old male presented with progressive left hemiparesis. Computed tomographic (CT) scans and magnetic resonance images revealed a right thalamic tumor (Fig. 5 *left*). A biopsy was performed using the transcallosal approach. The histological finding was glioblastoma. An intracranial electrode and thermocouple microprobes were implanted into the tumor cavity and surrounding brain tissue under ultrasonographic guidance (Fig. 6). A headband-type flexible extracranial electrode was fixed on the scalp while he was in the postoperative intensive care unit. The tumor site was heated three times a week with him under mild sedation. The RF power was adjusted to maintain the temperature in the tumor at just over 42.5°C for 60 minutes. The surrounding brain tissue temperature rose no higher than 42°C (Fig. 7). He did not complain of discomfort or any unpleasant sensation of excessive warmth. After thermotherapy, he received radiation therapy and chemotherapy. Serial CT scans showed a decrease in the tumor size (Fig. 5 *right*).

Discussion

Several types of localized hyperthermia treatment systems for brain tumor are under investigation: the regional hyperthermia system, the superficial applicator, and interstitial hyperthermia.[10)]

The electromagnetic method for inducing regional hyperthermia is a noninvasive system,[8)] but the temperature distribution depends upon the thermal absorption and conductivity of the anatomical structures and blood flow. The major problem is difficulty in delivering a uniform temperature distribution within the tumor volume using external electrodes. In addition, invasive thermometry probes are essential. Silberman *et al.*[9)] inserted thermocouple microprobes into the brain for conducting thermometry. Tanaka and Yamada[11)] investigated RF capacitive-type heating for regional hyperthermia, requiring bilateral craniotomies larger than the RF applicators to avoid the influence of the bone material on the RF distribution. Superficial applicators are designed to facilitate access to superficial tumors. The disadvantage of microwave applicators is that significant power cannot be delivered to any considerable depth below the surface without overheating the surrounding tissue. Ultrasound transducers have a smaller wavelength (in the frequency range of 0.5–5 MHz) and the beam is well collimated, combining excellent penetration into tissue and precise focusing.[3)] However, impedance mismatches between soft tissue and bone cause most of the energy to reflect at the interfaces, so craniotomy is necessary to allow the ultrasound beam to penetrate the brain.[2)]

The interstitial technique can achieve better control of the heat distribution within the tumor volume, and therefore spare the surrounding normal tissues. A number of groups have investigated the use of linear coaxial microwave antennas.[5,7,12,13] A single microwave antenna will radiate power into the surrounding tissue, but most of the energy will be absorbed quite close to the antenna. At a frequency of 2450 MHz, the microwave antenna radiates energy in an ellipsoidal field with an effective cross-sectional radius of less than 1 cm.[7] Therefore, an array of these antennas is necessary to generate therapeutic temperatures in large volumes.[4] In clinical studies, Winter *et al.*[13] implanted five cannulas with a diameter of 2.8 mm at distances of 5 mm for insertion of the microwave antenna probes. The total diameter of the effectively heated region using their system was probably not more than 3 cm, suggesting that the field delivered by an interstitial microwave antenna array is limited. Astrahan and Norman[1] described an RF needle electrode system using pairs of stainless steel needles implanted near the tumor boundary. Many needle electrodes were required and power supply control between the pairs of electrodes was difficult, preventing delivery of uniform high-temperature fields to the tumor volume. Therefore, this system is not suitable for application to brain tumors.

The simplest method of RF hyperthermia heats the tissue between or near two electrodes connected to the output of an RF generator. If the electrodes have different areas, tissues near the small electrode receive energy at a greater rate than those near the larger one.[3] Our interstitial RF hyperthermia system is quite different from RF needle electrode hyperthermia. A single small electrode is implanted into the brain and an extracranial electrode surrounds the cranium. The RF power is supplied to this pair of electrodes, resulting in currents between them. Since the extracranial electrode is much larger than the intracranial electrode, RF current converges on the area around the small electrode, and the impedance mismatch between brain and bone is no major problem. The RF energy has good penetration into the tissue and generates uniform and easily controllable high-temperature fields within the cranial cavity.

The relatively high temperatures induced in discrete brain volumes by our technically simple and efficient system are potentially valuable in the therapy of malignant brain tumor.

Acknowledgment

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