Development and Thermal Distribution of An RF Capacitive Heating Device

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Hypertermia for the treatment of cancer has been introduced for a long time and the biological effect for the use of hyperthermia to treat malignant tumors has been well established and encouraging clinical results have been obserbed. Unfortunately, however, the engineering or technical aspects of hyperthermia for the deep seated tumors has not been satisfactory. We developed the radiofrequency capactive hyperthermia device (Greenytherm-GY8) in cooperation with Yonsei Cancer Center and Green Cross Medical Corporation. It was composed with 8~10 MHz RF generator, capacitive electrode, matching system, cooling system, temperature measuring system and control PC computer. The thermal profile was investigated in agar phantom, animals and in human tumors, heated with capactivie RF device. Deep and homogeneous heating could be achieved in a large phantom of 25 cm diameter and 19 cm thick when heated with a pair of 23 cm diameter electrodes, coupled to both bases of the phantom, when the size of the two electrodes was not the same, the region near the smaller electrode was preferentially heated. It was, therefore, possible to control the depth of heating by choosing proper size of electrodes. Therapeutic temperature (42℃~43℃) could be obtained in the living animal experiments. Indications are that deep heating of humn tumors might be achieved with the capacitive method, provided that subcutaenous fat layer is cooled by temperature controlled bolus and large size of electrodes.

Key Words: Hyperthermia, Capacitive heating, Radiofrequency, Greenytherm-GY8

INTRODUCTION

The biological effects for the use of hyperthermia used alone or in combination with radiotherapy or chemotherapy to treat malfignant tumors have been well established and encouraging clinical results have been observed.[1,5,7,15] Unfortunately, however, the engineerng or technical aspects of hyperthermia to raise the temperature of deep-seated tumors to a therapeutic range, 42~43℃, with acceptable side effects on the surrounding normal tissues has not been satisfactory.[3,8,20]

One of the possible non-invasive approaches to heat deep tumors is the use of radiofrequency (RF) applied capacitively through a pair of electrodes placed on the opposite side of the body or tumor.[10,12] LeVeen et al.[14] treated human tumors with three pairs of metal electrodes affixed on the surface of the body with an expectation that deep heating can be achieved by the crossfiring from the three pairs of electrodes. Unfortunately, the clinical results with the use of this approach were disappointing.[13] Despite these early disappointments, a theoretical calculation and experimental data by some investigators[4,16] indicated that deep and homogeneous heating may be achieved by

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capacitive application of RF if the size of the paired electrodes is larger than the thickness of the heating objects between the two electrodes. In addition, better depth heating may be achieved when the electrodes are connected to the RF generator by more than two wired pairs. It was also demostrated that placing a saline bolus between the metal electrodes and the body in the treatment of human tumors by the capacitive method improved the cooling and minimized the danger of skin burns at the edge of the metal plate. We have designed and manufactured an experimental hyperthermia unit (Greenytherm-GY8) in cooperation with Yonsei University and Green Cross Medical Corporation. It was fabricated to heat superficial as well as deep-seated tumors by capacitive application of 8 MHz RF current using various size of electrodes and a temperature controlled bolus. Studies conducted during the last two years indicate that it is possible to raise the temperature in many deep human tumors to therapeutic levels with the Greenytherm-GY8. We are reporting our investigation on the thermal distribution in agar phantoms and human tumors heated with this hyperthermia divice.

MATERIALS AND METHODS

1. Heating Device

A Greenytherm-GY8 unit is operated at 8~10 MHz RF and is comprised of 4 basic components, an RF generator and heat exchanger system enclosed in a steel cabinet; a gantry for a pair of electrodes, a treatment couch and a computerized control console (Fig. 1). The generator, which can provide up to 1,500 watts of 8~10 MHz RF current, impedence matching system and two heat exchangers for adjusting the temperature of saline bolus at 5~20℃ are housed in a partitioned steel enclosure. A pair of electrodes is connected to the pillars of the gantry and can be independently moved forward or backward about 20 cm. The surface of the metal plate of the electrodes is covered with a sheet of flexible vinyl, and the interior space between the vinyl sheet and the metal plate is filled with 0.4% NaCl solution which is circulated between the electrodes and the heat exchangers. The rate of circulation and temperature of the saline bolus for the two electrodes are independently controlled. The cooled, circulating saline suppresses the rise of skin temperature, particularly at the edge of the electrode metal plates. The bolus also improves the coupling of electrodes to the complex body contour. Three pairs of electrodes with diameters of 11, 17 and 23 cm are supplied with the hyperthermia unit. In the present study, the size of parallel electrodes used for the capacitive heating varied depending on the desired heating pattern, e. g. size and depth of tumor. The treatment couch can be moved horizontally and have electrode hole through which the lower electrode is protruded. Greenytherm-GY8 unit has a built-in thermometry system with two Tefloncoated probes of copper-constantan microthermocouple (Sensortek, Inc., Type 1T-18). An RF filtering circuit eliminates most of the RF current from the input signal through the thermocouple. For effectively elimiation of the RF signals, the temperature in tumor is repetitionally measured during 3 seconds after RF generating of 40 sec. The temperatures, monitored by the two

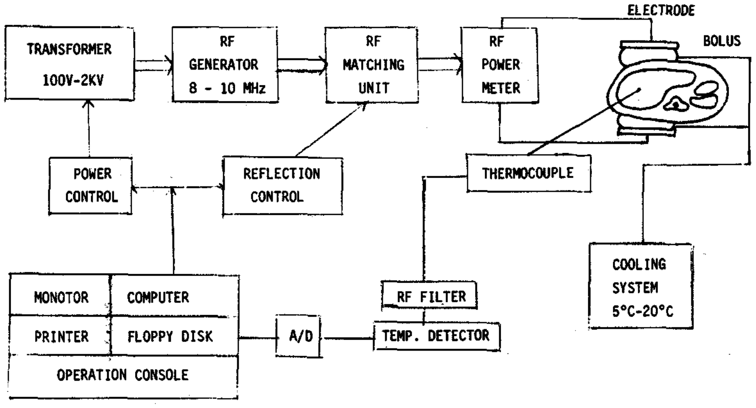

Fig. 1. Schematic diagram of RF hyperthermia device.

thermocouples, are graphically and numerically displayed on the computer screen, and the temperature profile and other informations are recorded in the computer of the control console.

2. Phantom Study

In order to reveal the factors in the capacitive heating, we investigated the thermal profile in static phantom during heating at various conditions. Body phantoms with thickness of 20 cm were made of 4% agar gel containing 0.2% NaC1 and 0.1% NaN3. Several 18-gauge catheter tubes were inserted into the phantoms from the side and the thermocuples were placed in the tubes. The phantoms were capacitively heated by concentrically coupling a pair of electrodes of various sizes to both bases of the phantom (Fig. 2). The temperature in the phantoms was monitored during heating with the two thermocouple probes placed at strategic

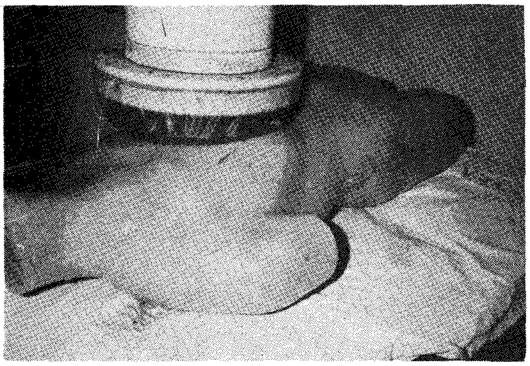

Fig. 2. An overview of heating a 20 cm thick body shaped agar phantom.

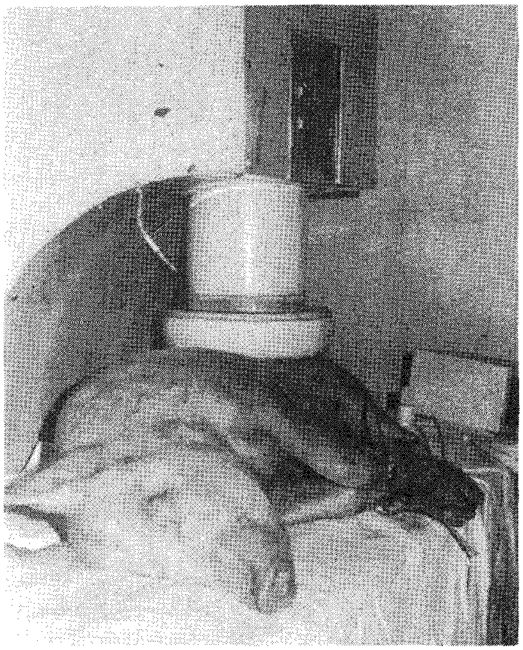

Fig. 3. Animal experiment of hyperthermia 40 kg male pig was heated under electrodes of 23 cm diameter.

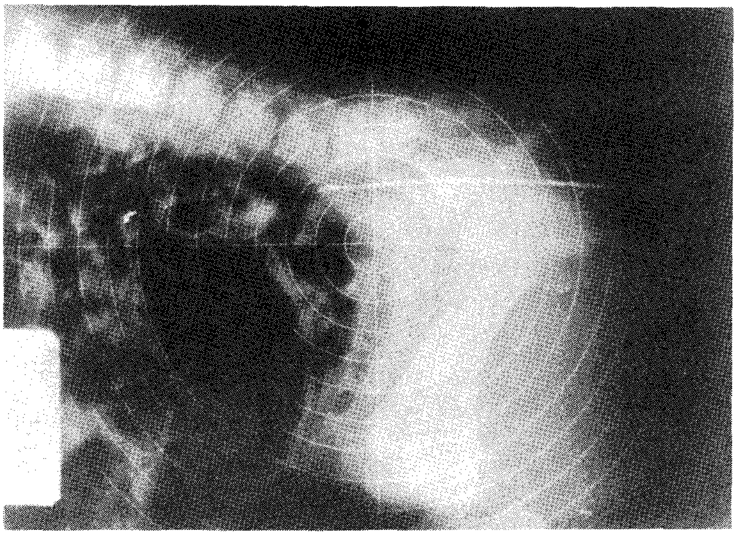

Fig. 4. Radiography of pig with the temperature senser in the rectum.

places. During and immediately after the heating, the temperature distributions in the phantoms were determined by moving the thermocouples through the catheters. The temperature readings with these probes were done with a digital thermometer after the RF power was turned off.

3. Animal Experiments

A 40 kg of male living pig with 20.4 cm of lateral pelvic dimension was used in this experiments. The anesthetized pig was placed recumbently on the table and four legs are immobilized A pair of electrodes was positioned on the lateral side of the pelvis (Fig. 3). A catheter was inserted into the rectum from the anus and the probe of the thermocouple was placed in the catheter at a depth of 4 cm in order to measure the temperature (Fig. 4).

4. Human Tumors

Advanced stage of malignancies with various size were heated with the Greenytherm-GY8. The heating was usually given twice a week within 30 ~60 min. after irradiation of the tumors. After local anesthesia with 1% lidocaine, 18-gauge angiocatheters were inserted to various depths of the tumors and then thermocouples were placed inside the catheters. A pair of electrodes of appropriate sizes were mounted on the gantry. Depending on the location of the tumors, the parallel opposed electrodes or right angled electrodes were placed on the body surface. The coupling of the electrodes was improved by the generous use of conductive jelly. The temperature of the saline bolus was maintained at 10~30℃, depending on the depth of the tumors under the subcutaneous tissues. The temperature in the tumors was monitored continuously during heating, and the temperature distribution was scanned by pulling the probes backward.

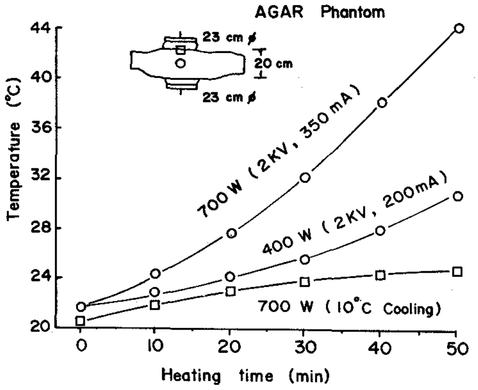

Fig. 5. The changes in temperature at center depth of agar phantom of 20 cm thickenss.

RESULTS

1. Thermal Profile in Phantom

The temperature was rised in a cylindrical pantom of 20 cm thick upon heating with a pair of electrodes of 23 cm diameter. The electrodes were concentrically coupled to both bases of the phantom with the use of 0.4% saline bolus maintained at 20℃. Angiocatheters (18-gauge) were inserted into the phantom from the side, placing the tip of the catheters at center and surface of the phantom. The rate of increase in temperature varied markedly depending on the distance from the two electrodes. The temperature at center of phantom increase as RF power and heating time increase. The temperature at center of phantom rose by

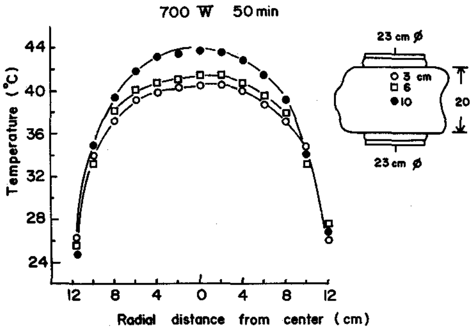

Fig. 6. Thermal profile in 20 cm thick agar phantom after heating with a pair of electrodes of 23 cm diameter.

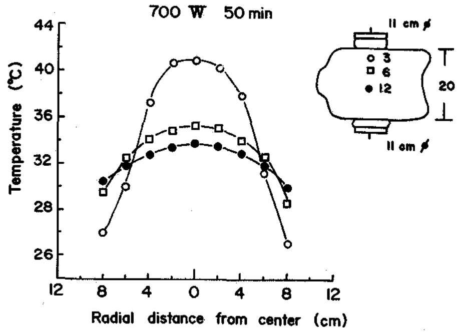

Fig. 7. Thermal profile in 20 cm thick agar phantom after heating with a pair of electrodes of 11 cm diameter.

approximately 22℃ and 9℃ on 700W and 400W RF power respectively, during 50 minutes heating (Fig. 5). The thermal profile in 20 cm thickness of body phantom after heating with two 23 cm diameter of electrodes is shown in Fig. 6. The tip of the catheters at different places along the central axis of the phantom. The temperature gradient became almost identical in the horizontal planes at differnet depths when the phantom was heated with pairs of electrodes of 23 cm of diameters. We noticed that the temperature in the midplane of the phantom usually rose slightly higher than that that in the other plane when the 20 cm thick phantom was heated with a pair of 23 cm diameter electrodes. It should also be noted that the diameter of the isothermal field within the horizontal planes was as large as 15 cm when the phantom was heated with the large electrodes.

The thermal profile in the 20 cm thick body phantom after heating with two 11 cm dameter electrodes is shown in Fig. 7. The temperatures at the midpoint of the plane at 3 cm depth from both bases were about 6℃ higher than the temperatures at the center of the midplane. The above results clearly demonstrated that relatively homogeneous heating can be achieved in both superficial and deep tumors.

The thermal profile in a body phantom of 20 cm thick after heating with a pair of electrodes of 23 cm and 11 cm diameter is shown in Fig. 8. The temperature at 3 cm and 6 cm depths along the central axis from the base coupled with the 11 cm

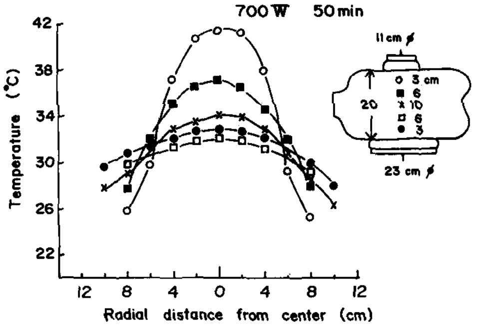

Fig. 8. Thermal profile in the phantom of 20 cm thick agar phantom after heating with a pair of electrodes or 11 cm and 23 cm diameters.

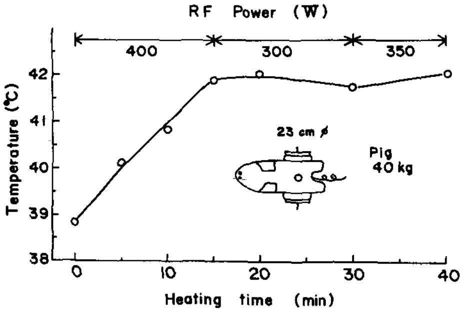

Fig. 9. Thermal profile in the rectum of pig during heating of 400 W with a pair of electrodes of 23 cm diameter.

Fig. 10. Photography of patient with buccal mass (Parotid Ca).

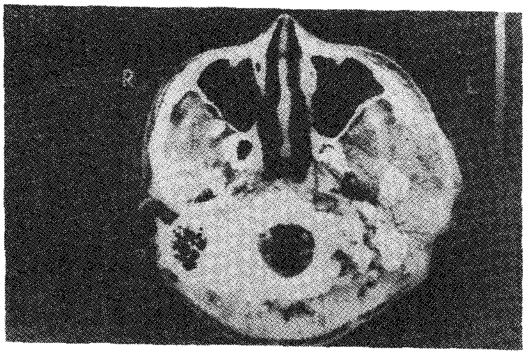

Fig. 11. CT image for tumor region of parotid cancer.

diameter electrode was by approximately 42℃ and 37℃, respectively, at the end of heating for 50 min. The temperature at the depth of 3 cm and 6 cm from the opposite base coupled with the large electrode of 23 cm diameter was by only approximately 33℃. The increase in temperature at the midpoint of axis, 10 cm from both bases, rose by about 34℃, which was less that that at a depth of 3 cm from the smaller electrode side.

For further analysis of the thermal profile in the phantom described above, the power was turned off after heating for 10 min., and the radial thermal distributions at the eifferent horizontal planes were determined by pulling the thermocouple probes outward at 2 cm intervals. A transverse thermal distribution was mapped by passing a probe through the horizontal midplane of the phantom. There was a temperature gradient along each horizontal plane with the highest temperature near the central axis of the phantom. For example, in the plane at the depth of 3 cm from the base coupled with the 11 cm diameter electrode, the temperature at the center of the plane was 42℃ and it fell off rather rapidlly with an increase in the distance from the center. The radial distance of the isothermal field with a temperature gradient of 1℃ was about 2 cm. As the distance between the plane and the smaller electrode increased, the temperature at the central part of the plane decreased, as described above, and the isothermal field size increased. For example, the temperature in the center of the midplane was 8℃ lower than that in the center of the plane at 3 cm depth from the base couple with the 11 cm electrode. The isothermal region with a 1℃ temperature gradient in the midplane had a radial distance of 5 cm from the center.

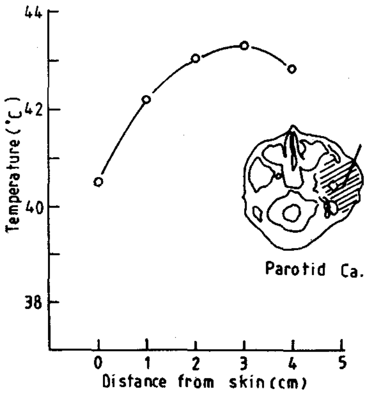

Fig. 12. Thermal distribution within the tumor mass of parotid cancer patient.

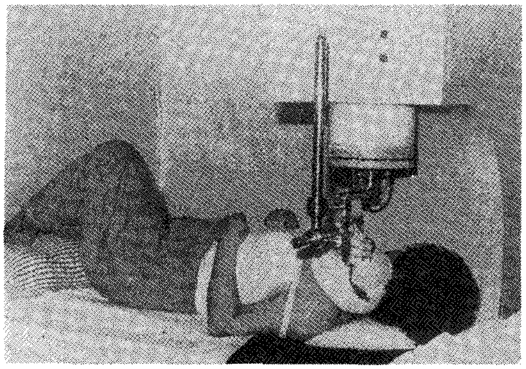

Fig. 13. Hyperthermia on neck mass with Greenytherm-GY8.

2. Thermal Dose Rate in Living Animals

Temperatures in the deep seated tissues of animal were measured with thermocouples before clinical trials. The thermal dose rate was 0.1℃ per minute in rectum of pig and rose to 42℃ in 15 minutes of 400W heating power with a pair of 23 cm ϕ electrodes and maintained at 42℃ with 300 ~350W heating power with the use of a feedback temperature control system (Fig. 9). When the heating power rose to 500W and the temperature rose above 43℃, the general condition of pig was very poor with rapid breathly and intermittent shock.

3. Thermal Profile in Human Tumor

The clinical trial of hyperthermia with the use of

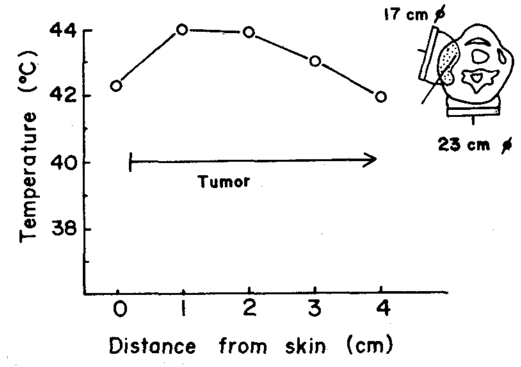

Fig. 14. Thermal distribution in the neck tumor during heating with 300 W with a pair of electrodes at right angle.

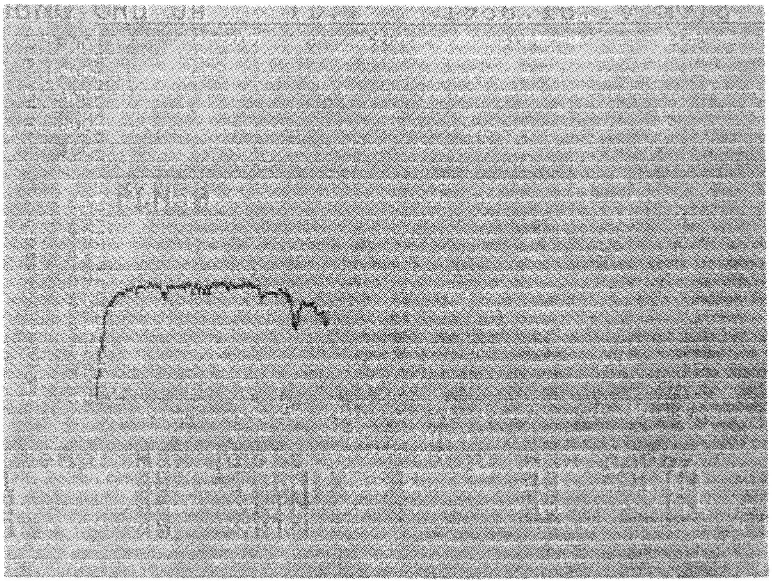

Fig. 15. A computer printout of changes on temperature in the recurrent cervical cancer.

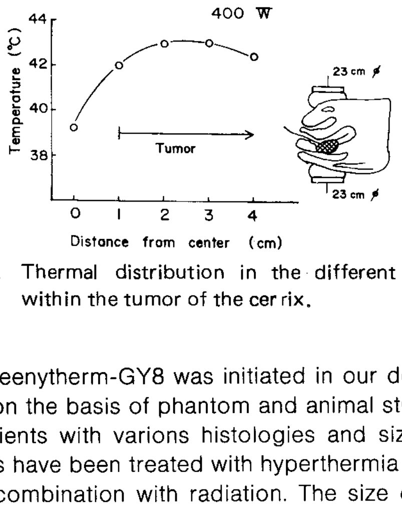

Fig. 16. Thermal distribution in the different depths within the tumor of the cer rix.

the Greenytherm-GY8 was initiated in our department on the basis of phantom and animal studies.

Patients with varions histologies and sizes of tumors have been treated with hyperthermia alone or in combination with radiation. The size of the tumors was 6×7×4 cm, in buccal region, 3×4×3 cm, in the neck and 5×4×5 cm, in the cernx. The size of the capacitor electordes to treat these tumors were selected depending on the size and depth of the tumors, the power needed to heat tumors varied from 300 to 500 Watt. The reflected power controlled as minimum to be an excellent impedance maching. The patient with large mass (6×7×4 cm) in left buccal region (Parotid Ca, Squamous Cell) was treated with hyperthermia (Fig. 10, Fig. 11). The tumor was heated capacitively by placing an electrode of 23 cm in diameter on the right side of neck and a smaller electrode of 17 cm in diameter on the left side. The temperature of the bolus of electrode of right side of neck was kept 15℃ and the lefx side with the tumor was not cooled. Fig. 12 shows the tumor temperature profile along the tumor center. We were able to raise the intratumor temperature above 42℃ for 50 minutes with 300 W of heating power. We tried to heat the tumor (cutaneous melanoma) on the left side of neck with electrodes arranged at right ansle (Fig. 13). We were able to raise the intratumor temperature above 42℃ in this patient with 300 W heating power even with is unusual selting of electrodes (Fig. 14). The tumor was heated with an electrode of 23 cm in diameter on the post neck, and a smaller electrode of 17 cm in diameter over ther tumor. The bolus of electrode on right neck was cooled and that on the tumor was not flowed blood but accumulation of heat. The other case was the recurrent cervical cancer which was treated of year ago. The tumor was heated with a pair of electrodes 23 cm in diameter coupled to the anterior and posterior walls of pelvis. The temperature of the saline bolus of the both electrodes was cooled to 15℃. The changes in temperature in side the tumor is shown in Fig. 15.

The tumor temperature rose to 42℃ in 12 minutes of heating and maintained at 43℃ in 300 ~400W heating power with the use of a feed-back tem-perature control system. Fig. 16 shows the thermal distribution in the tumor and 42~43℃ was recorded at the tip of the probe which was about 5 cm from the surface and 4 cm deep from the entrance of the probe.

DISCUSSION

An experimental studies on the capacitive heating with Greenytherm-GY8 revealed important information with regards to the implication of the electrode size on the heating pattern. These results. obtained in the phantom experiments demonstrated that capacitive application of RF current is potentially useful to heat small and large superficial malignant lesions. The fact that we were able to heat a consideraly deep region of rather bulky tumors suggested that heating of deep-seated tumors may also be possible with this approach.[17~19]

It should be pointed out that the capacitive heating of tumors is not a new method.[2,7,14] Unfortuantely, however, past attempts have been unsatisfactory in achieving therapeutic temperatures in tumors, particularly deep-seated tumors for a various of reasons. One of the causes for the past failure appears to be the lack of clear insight of the relationship between the electrode size and heating pattern. We were able to obtain almost perfect homogeneous heating in a 19 cm thick phantom by the use of a pair of electrodes of 23 cm in dianeter in the preseat study. This result is in agreement with the experimental observation reported by other investigators.[6,8,9] The thermla profiles in the phantoms heated with electrodes of different sizes demonstrated that one of the advantages of capacitive heating over other heating methods is the depth of heating can be controlled to a certain degree by changing the size of the paired capacitor electrodes.

The Greenytherm-GY8 is equipped with three pairs of electrodes with diametes of 11, 17 and 23 cm. We selected various combinations of the electrodes for the treatment of human tumors according to the diameter and depth of the tumors.

A limiting factor in the capacitive application of RF to heat tumors is believed to be the presence of subcutaneous fat layer, which is more resistive to RF current as compared with other tissues, and thus preferentially heated.[3,5] Furthermore, the dissipation of heat by blood perfusion is poor in fat. Indeed, the preferential heating of subcutaneous fat appeared to be the cause of the occasional difficulty we encountered in our attempt to raise the temperature above 42℃ in some of the tumors. Kato[11] reported that the temperature of 1.6 cm thick subcutaneous fat layer in a pig could be kept under 42℃, while the temperature in the inner muscle was raised to 42℃ when the skin was cooled at 10℃ for 20 min. prior to heating, In this study, it was also observed that the intratumor temperature could be raised higher than 42℃ of tumors when the fat layer under the skin was cooled during heating.

In the heating of tumors, it is highly desirable to obtain homogenous thermal distribution. Although the relatively homogeneous temperature distribution can be obtained in static phantoms when the size of the two capacitor electrodes are the same and larger than the thickness of the phantoms, as demonstrated in the present study, such a homogeneous heating would rarely occur in the tumors because of the variable physiological and electrophysical properties within the tumors and in the surrounding normal tissues. In homogeneous heat distribution in living tissues may be an inevitable fact in external electromagetic heating, including RF coapacitive heating.

In conclusion, our preliminary clinical results, indicate that RF capacitive heating is potentially useful for heating deep-seated tumors as well as superficial tumors, provided that the surface cooling can be achieved properly with our techrique as described above. However, the potential problem associated with the preferential heating of subcuteneous fat may limit the use of capacitive heating to treat obese patients. Investigations to reveal the effectiveness of RF capacitive heating to achieve a therapeutic temperature in deep-seated tumors will be undertaken in the near future.

CONCLUSION

The biological rationale for the use of hyperthermia to treat malignant tumors has been well studied and encouraging clinical results have been reported. However, the engineering and technical aspects of hyperthermia for the deep-seated tumors has not been satisfactory. We developed the RF capacitive hyperthermia device (Greenytherm-GY8) in cooperation with Yonsei

Cancer Center and Green Cross Medical Equipment Corporation. It was composed with 8~10 MHz RF generator, capacitive electrode, matching system, cooling system, temperature measuring thermocouples and control PC computer. We have measured the temperature and thermal distribution in agar phantom, animals and human tumors as follows.

1. The generating power could be varied from 200 to 1500 W.
2. The radio-frequency for capacitive heating could be produced to 8~10 MHz.
3. It was possible to cool the skin surface with the use of temperature regulating bolus and control the deepth of heating by choosing the proper size of electrodes.
4. Deep seated tumors (5~10 cm depth) could be heated to therapeutic temperature of 40~43℃.
5. Side effects and hot feeling on skin could be significantly reduced by cooling bolus and electric matching.

The RF hyperthermia device (Greenytherm-GY8) could be applied for the clinical trials as the results of this study. But futher investigation has been demanded for good matching, reduction of electric let-go currents and flaxible electrodes.

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= 국문초록 =

유전가열장치의 개발과 온열분포

연세대학교 의과대학 치료방사선과

추성실 · 서창옥 · 김귀언 · 노준규

연세 암센터

김 병 수

환부에 열을 가하여 종양을 치료할 수 있는 온열요법의 생물학적 효과는 상당히 고무적이며 새로운 암치료 수단으로 등장되었다. 그러나 체내 깊숙히 위치하고 있는 종양에 일정한 열을 계속 부여하면서 온도와 열의 분포를 정확히 측정하기가 어려웠다.

연세 암센터는 연세대학교 공과대학과 녹십자 의료 공업주식회사와 산학협동으로 라디오파 유전가열형 온열장치(가칭 Greenytherm-GY8)를 개발 제작하고 임상응용을 위해 기초 연구를 실시하였다. 개발된 온열장치는 8~10 MHz 라디오파 발생기와 유전가열 전극, 온도계측용 열정대, 냉각장치 및 제어용 개인 컴퓨터로 구성되었다. 온열장치의 성능을 시험하기 위하여 인체크기의 한천팬텀과 동물 및 인체의 악성종양에 대한 치료온도와 온열분포를 측정하였다.

라디오파 발생전력을 200~1,500W까지 조절할 수 있으며 유전가열을 위한 라디오파의 주파수는 8~10 MHz 범위를 얻을 수 있었다.

피부에 근접된 종양의 가열온도는 200~500W의 RF 전력으로 10분이내 치료가능온도(42.5℃) 이상으로 가열할 수 있었으며 정상조직 쪽의 전극은 5~10℃로 냉각시키므로서 피부손상을 방지할 수 있었다.

5~10 cm 깊이에 존재하는 종양의 가열온도는 치료 가능한 40~43℃까지 가열이 가능하였으며 냉각보러스와 정합회로에 의해 피부의 자극을 줄일 수 있었다.

이상과같은 실험결과로 유전가열형 온열장치는 임상응용에 적합하다고 판단되며 임상경험을 통하여 더 예민한 정합장치와 전기적 자극을 완전히 줄일 수 있는 방법 및 편리한 전극등의 개발이 가능한 기본자료가 될 수 있다.