8MHz RF Capacitive Heating on Rabbit Lung

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The usefulness of hyperthermia for cancer therapy has been established. The purpose of the present investigation was to access feasibility of heating normal lung and the temperature and power requirement were compared with that for liver as solid organ in rabbits by using radiofrequent heating machine. In this study, 20 rabbits were divided into 2 groups according to the heating site and the method of temperature measurement; in group I : lung heating and temperature measuring in skin, esophagus and lung parenchyme; in group II: liver heating and temperature measuring in skin and liver parenchyme. The results were as follows; 1) When the maximum temperature was almost same in lung heating group and liver heating group, the power for liver heating was lesser required than the power for lung heating ($p<0.05$). 2) The temperature of esophagus for the measurement of mediastinum temperature was $1.1\pm0.9°C$ higher than the temperature of lung parenchyme ($p<0.05$). Therefore the above findings suggest lung, air containing organ, is well heated as same as liver, solid organ. So more active trials of lung heating in the lung cancer must be likely considered. But when the lung is heated, the esophageal temperature is higher than lung parenchyme, so the mediastinum damage must be considered seriously.

Key Words: Hyperthermia, Radiofrequency, Lung

INTRODUCTION

Over the last decade, there has been a great interest in the use of hyperthermia as one modality in cancer treatment after Busch described a patient with sarcoma of the face who underwent a complete resolution of all his tumor following two episodes of erysipelas infection[1]. Many articles have been published demonstrating the remarkable effects of heat on tumor control when used in combination with radiation or some anticancer drug[2~5].

Various techniques have been developed for systemic and regional heating. Whereas several methods are effective in heating solid tumors, none is completely satisfactory for effectively raising temperature in thorax as an air containing organ. The difficulties in applying the biological promise of lung hyperthermia relate to the physical difficulties associated with the delivery of heat and the measurement of temperature. Recently systemic whole body hyperthermia and local hyperthermia have been applied to lung cancer. Whole body heating gets over some of the above problems but its use has been compromised by morbidity and mortality. Local hyperthemia using radiofrequency has a major problem of the preferential heating of superficial fat. This makes use of 8MHz radiofrequency capacitive heating device only suited to small, thin patients.

This study was designed to assess feasibility of hyperthermia for rabbit lung by radiofrequency heating device. Parameters were compared with those for hyperthermia of liver.

MATERIALS AND METHODS

Normal healthy rabbits, weghing 1.5-2 kg were used in this study. The heating device is Cancermia GHT-RF 8 (Green Cross Co. Korea), and schematically illustrated in Fig 1A.

The RF generator has a self excited oscillation circuit at 8 MHz and 1.5 kw maximum output power. GHT-RF 8 has a thermometry system with Teflon-coated probes of copper-constantin microthermocouple (Sensortek, Inc. U.S.A.). 20 rabbits were divided into 2 groups; lung heating group and liver heating group, which included 10 animals respectively. Each rabbit was anesthesized by intravenous Ketamine injection (25 mg/kg) and fixed in a fixing device. The hair on chest wall was cut and painted with Betadin solution. In liver heat-

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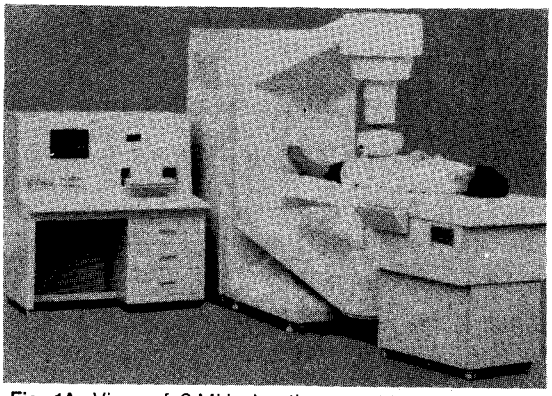

Fig. 1A. View of 8 MHz heating machine (Cancermia GHT-RF 8).

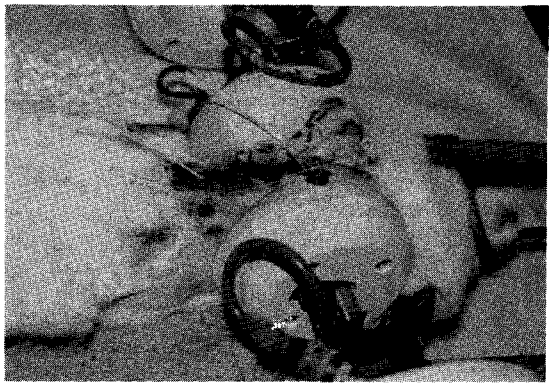

Fig. 1B. Photography showing temperature measurement in a rabbit with thermocouple (Sensortek, Inc. U.S.A.).

ing group, the abdomen of rabbit was incised in the midline, about 5 cm and the liver was exposed. The thermocouple for heat monitoring was inserted into the liver about 3 cm from right lateral chest wall. Then, skin was sutured. In the lung heating group, an 18 gage blind catheter was inserted into the anterior chest wall about 3 cm from lateral chest wall on the level of midaxillary line, and a guide wire was removed. The catheter was sutured to skin. At this time, the abdomen of rabbit was also incised in the midline, and stomach was exposed. Another catheter was inserted into the esophagus and a thermocouple was inserted into the catheter for mediastinal temperature monitoring. The tip of the thermocouple was placed in the subcarinal area (Fig. 1B).

After all of these procedures, we verified the position of thermocouples.

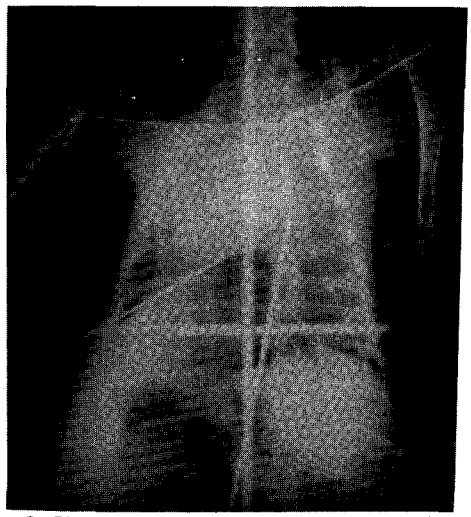

Fig. 1C. Photography of simulation showing appropriate sites of thermocouple for temperature measurement.

The electrodes, 10 cm in diameter, were placed bilaterally on the both flanks of rabbit. We heat the each rabbit for about 15 min and checked each temperature every 15 seconds. We didn't do surface cooling (Fig. 1C). The student t-test was used to determine statistical significance. P values of less than 0.05 were considered as significant.

RESULTS

In the lung heating group, the mean temperature was 41±1.7°C in esophagus, and 39.8±1.5°C on skin, respectively (Fig. 2A).

In the liver heating group, the mean temperature of liver was 42.1±1.6°C, and the mean temperature of skin was 39.5±1.4°C (Fig. 2B).

The time required to reach 42°C was 9.3±1.8 min in the lung heating group, and 5.7±0.7 min in the liver heating group, longer time is required in lung heating group than liver heating group.

The temperature increasing rate was 0.46±0.17 °C/min in the lung heating group, and 0.56±0.2°C/min in the liver heating group. The temperature increasing rate was more rapid in the liver heating group than the lung heating group.

The mean RF power required to reach 42-43°C was 48±20 W in the lung heating group, and 39±19 W in the liver heating group respectively, thus higher RF power was required in the lung heating than in the liver heating ($p<0.05$)(Fig. 3).

The mean temperature of esophagus was 1.1±0.

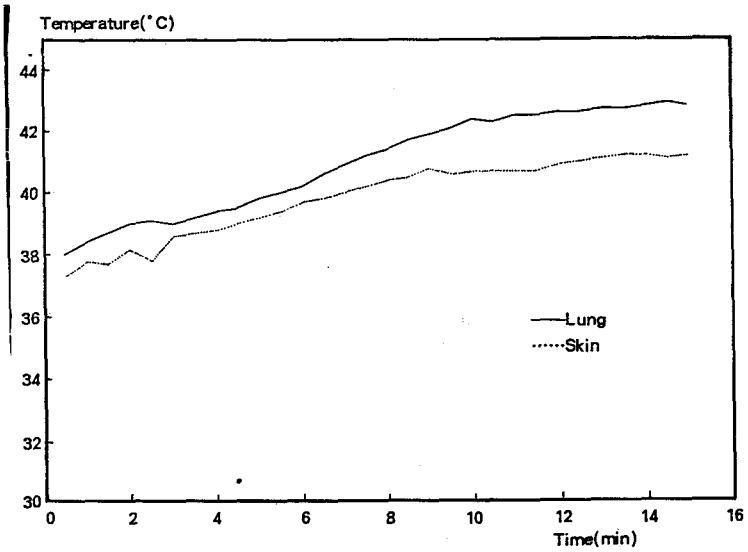

Fig. 2A. Graph showing mean temperature of skin and lung in the lung heating group.

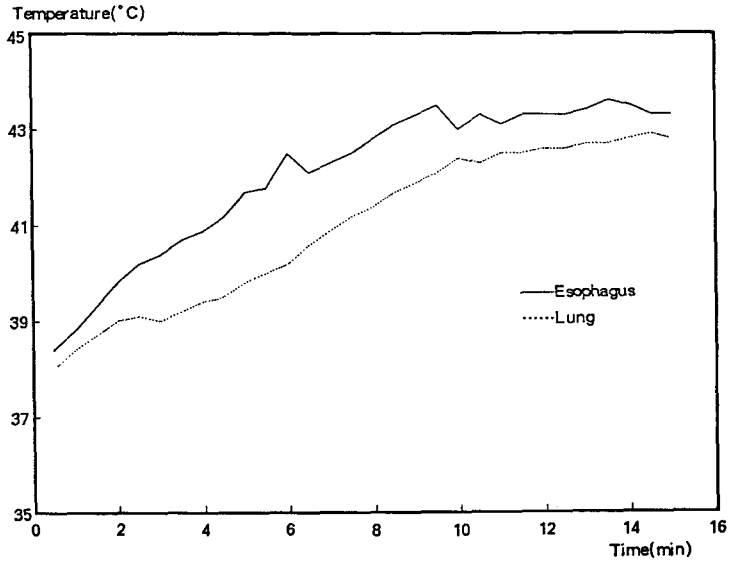

Fig. 2B. Graph showing mean temperature of skin and liver in the liver heating group.

9°C, higher than that of lung parenchyme ($p<0.05$) (Fig. 4).

DISCUSSION

The first report of a malignant tumor spontaneously regressing following a febrile illness appeared in medical literature in 1866. In this report, Busch described a patient with a sarcoma of the face who underwent a complete resolution of tumor following an episode of an erysipelas infection with high fever[1].

An orthopedic surgeon, Coley was the most widely known early physician to artificially induce systemic hyperthermia in cancer patients, although he was not the first[8]. Following the reports, experimental and clinical studies have been doing about the heat effect on the normal and malignant tissues[9~17].

In the clinic, the applications of hyperthemia to the treatment of cancer can be divided into two broad categories; whole body systemic hyperth-

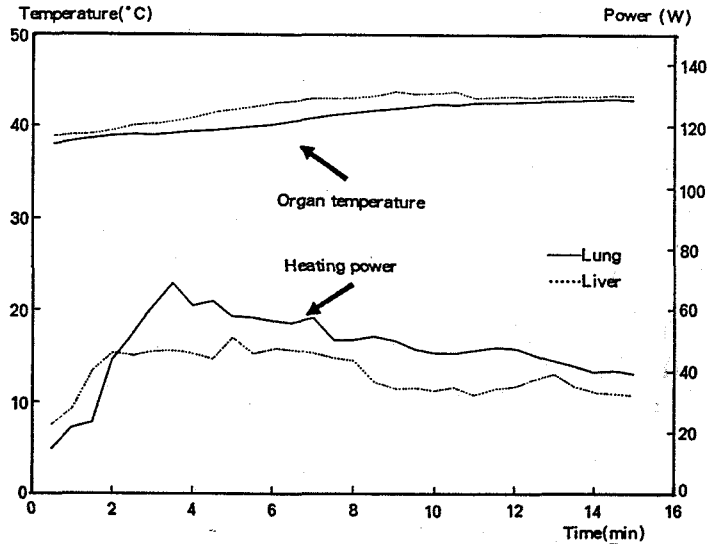

Fig. 3. Graph showing mean power of RF (watt) required in lung heating group vs liver heating group.
To reach the maximun temperature, higher RF power was required in the lung heating than in the liver heating ($p<0.05$).

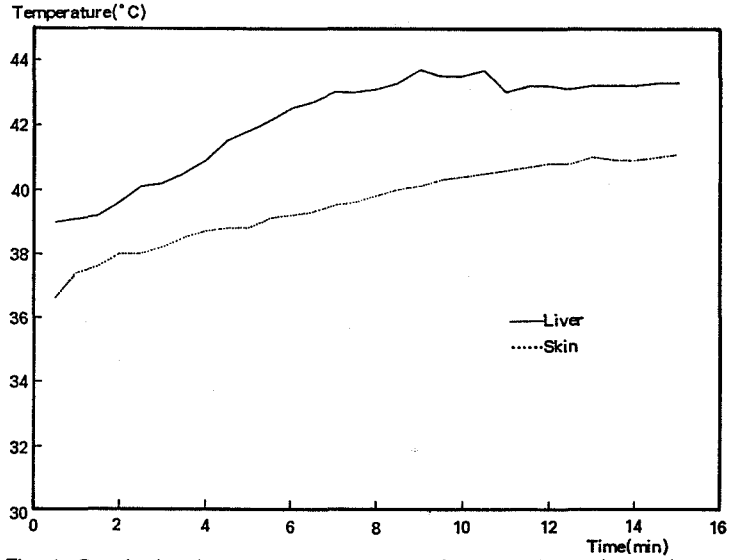

Fig. 4. Graph showing mean temperature of lung and esophagus in lung heating group; mean temperature of esophagus was 1.1± 0.9°C higher than that of lung parenchyme ($p<0.05$).

emia and localized hyperthermia. Whole body can be heated by infrared radiation or extracorporeal heat exchange. The control and measurement of temperature is relatively simple but its use has been compromised by morbidity and mortality. Localized heating is much more difficult to achieve with any degree of control. Methods of local heating are microwaves, ultrasounds and radiofrequency induced currents.

For clinical hyperthermia it is important to develop a heating machine that can heat tumors in various locations selectively and homogeneously up to desired temperature. In all cases, however, present methods of heating have a problem. None is completely satisfactory for effectively raising temperature in deep seated tumors or an air

containing organ, so there are few reports of its use in lung cancer.

Even so, some reports of good heating of lung tumors have been published. Bleehen reported 2 of 4 patients treated with the RF hyperthermia had achieved tumor temperature between 42~43°C[6]. These results also showed that lung as air containing organ is properly heated as well as liver, as described by our investigation. Robinson et al reported the results which 6 patients received a combination of hyperthermia and local radiotherapy[7]. A radiant heat system was used to deliver the 41.8°C whole body hyperthermia.

We used 8 MHz radiofrequency capacitive heating device to heat the lung and thorax. Temperature could be raised to around 42~43°C in both lung heating group and liver heating group. The mean RF power required to maintain above 42°C was significantly higher in the lung heating group than in the liver heating group ($p<0.05$). Thermal conduction rate of lung, air containing organ, is lower than liver, soild organ, and the ventilation of air by respiration induces heat loss. Additionally, after heating, blood flow increases in lung parenchyme. These may result in decreasing temperature in lung, and the higher RF power may be needed in the lung heating group. At this time, the mean temperature of esophagus was significantly higher than that of lung ($p<0.05$). The esophageal temperature may be higher than lung temperature because there is no ventilation effect in esophagus.

Therefore, it is suspected that lung is properly heated as well as liver even though the higher RF power is needed. And the mediastinum damage must be considered seriously because the esophageal temperature is higher than the lung.

CONCLUSION

It is difficult to heat tumors in the thorax. The difficulites in applying hyperthermia to the lung relate to the physical difficulties associated with the delivery of heat. We did this study to assess the heat on rabbit lung comparing with rabbit liver using RF capacitive heating machine (Cancermia, GHT RF-8, Green Cross. Co. Korea).

Obtained results are follows.

1) The time required to reach 42°C was 9.3 ± 1.8 min in lung heating group, and 5.7 ± 0.7 min in liver heating group. The temperature increasing rate was 0.46 ± 0.17°C/min in the lung heating group, and 0.56 ± 0.2°C/min in the liver heating group.

2) The mean RF power required to maintain 42~43°C was higher in the lung heating group than in the liver heating group ($p<0.05$).

3) The mean temperature of esophagus was 1.1 ± 0.9°C higher than that of lung parenchyme ($p<0.05$).

In summary, above mentioned analysis demonstrated that lung as an air containing organ can be properly heated as well as liver, though the higher RF power and longer time is required in the lung heating. Thus more active trials of lung heating in lung cancer must be likely considered. However, when the lung is heated, the mediastinum damage must be considered seriously because the esophageal temperature is higher than the lung parenchyme.

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= 국문초록 =

가토의 정상폐의 고주파 유전형 가온에 관한 연구

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장 홍 석·김 종 우

온열요법은 최근 10년간 암치료 요법의 한 방법으로 큰 관심을 끌어왔다. 그러나, 아직까지 폐종양에 대해서는 온열요법이 잘 시행되지 않고 있는 바, 이는 폐가 물리학적으로 공기를 함유한 비교적 가온하기 어려운 함기성기관이어서 이의 효과적인 가온에 대한 시도가 많지않았기 때문으로 생각된다.

저자들은 고주파 유전형 가온에 의한 폐의 가온효과를 평가하기 위하여 가온이 비교적 용이한 충실성기관(solid organ)인 가토의 정상간과, 가토의 정상폐의 가온정도를 비교하고자 하였다. 실험 동물들을 폐 가온군과 간 가온군으로 각각 10마리씩 2개의 군으로 나누었으며, 다음과 같은 결과를 얻었다.

1) 폐 가온군에서 15분간 가온한 폐의 평균 온도는 41±1.7°C이었고, 식도의 평균 온도는 42±1.7°C이었다.

2) 간 가온군에서 15분간 가온한 간의 평균 온도는 42.1±1.6°C이었고, 이때 피부의 평균 온도는 39.5±1.4°C이었다.

3) 42°C까지의 가온에 소요된 시간은 폐 가온군 에서는 9.3±1.8분 이었고, 간 가온군 에서는 5.7±0.7분 이었다.

4) 42°C까지의 분당 열 증가율은 폐 가온군 에서는 0.46±0.17°C/분 이었고, 간 가온군 에서는 0.56±0.2°C/분 이었다.

5) 가온 온도가 42°C-43°C 도달시까지, 폐 가온군 에서의 RF 총 평균 출력은 각각 48±20 W 및 39±19 W이었으며, 폐 가온군이 간 가온군 보다 높았다($p<0.05$).

6) 가온에의한 식도내 온도가 폐의 온도보다 1.1±0.9°C높았다($p<0.05$).

이상과같은 결과는 기낭성기관인 폐도 RF의 보다 높은 출력이 소요되기는 하나 온열요법을 시행하였을 때 충실성기관인 간과 마찬가지로 종양치료에 유효한 42°C-43°C까지 잘 가온될 수 있음을 입증하였다. 또한 폐의 온열요법시 종격동은 보다 높은 온도에 도달함으로 종격동의 열손상에 대한 고려가 필요함을 시사한다.