Physical Basis of RF Hyperthermia for Cancer Therapy (1)

Measurement for Distribution in Absorbed Power from
Radiofrequency Exposure in Agar Phantom

TETSUYA ISHIDA,1) HIROKAZU KATO,1) JUNJI MIYAKOSHI,2)
MASAYO FURUKAWA,2) SUSUMU OHSAKI3)
and EICHI KANO4)

1)Department of Radiology, Shimane Medical University, Izumo, 693; 2)Department of
Radiation Biology, Kyoto College of Pharmacy, Kyoto, 607; 3)Department of
Chemistry, Faculty of Science, Kyushu University, Hakozaki, Fukuoka, 812; 4)Department of Experimental Radiology and Health Physics,
Fukui Medical University School of Medicine, Fukui, 910-11
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In order to utilize RF hyperthermia for the clinical cancer therapy, the development in
dosimetry of the RF absorbed power in situ is considered to be necessary. In the present ex-
periments, it was clarified that RF absorbed power distribution in agar-physiological salt solution
phantom can be estimated from time variation of temperature which is measured by a fine
thermocouple introduced to the phantom after heating process.

I. INTRODUCTION

Since A. D'Arsonval reported human body could be successfully heated by radio-
frequency (RF), RF had been utilized as diathermy for the human deep heating. RF
hyperthermia had been undertaken as one of the independent methodology in
the field of cancer therapy, since E. Pflomm reported. Combined effect of RF with radia-
tion had been recognized. Since blood flow through tumor was less than 15% of
that through the adjacent normal tissue, remarkable differential heating could be
performed. Resultantly temperature of tumor tissue was 10°C higher than that of
the adjacent normal tissue.

Distribution of the absorbed power and the simultaneous measurement at the
heating seems to be of importance. Temperature profile in deep seated tissues were
determined by the absorbed power profile, heat conductivity and cooling blood flow.
In the present work, temperature distribution by RF heating was measured in agar phantom, from which distribution of RF absorbed power could be estimated.

II. MATERIALS AND METHODS

The block diagram of the device was shown in Fig. 1.

1) Heating device:
RF generator (#1 in Fig. 1), laboratory trial instrument, at frequency of 40.46 MHz was utilized.

2) Thermometric devices:
0.1 mmφ C-C enameled thermocouple (#2 in Fig. 1) of ASAHI INDUSTRY Co. Ltd. was used as temperature detector and Model 612-2P of CHINO MANUFACTURE Co. Ltd. as reference thermocouple (#3 in Fig. 1) at 0°C. Recording was performed by a flat bed pen-recorder (#4 in Fig. 1), Type 3044-22, of YOKOGAWA ELECTRIC Co. Ltd.

3) Calibration of thermocouples:
The calibration was carried out by digital multimeter, 177, of KEITHLEY INSTRUMENTS Inc., water bath, BT-22, of YAMATO SCIENTIFIC Inc. and columnar standard thermometer, Type-1, of JAPAN METRIC INDUSTRY Co. Ltd. One of a pair of thermocouples was attached to the standard thermometer and the pair was immersed into the water bath at standard condition. Electromotive force of the thermocouples at variety of the temperatures were measured by the digital multimeter.

4) Response time of the thermometric system:
C-C thermocouple, 0.1 mm in diameter, was utilized as a probe, the temperature was recorded by the pen-recorder and characteristics of the response time was measured. The time required for 90% of the saturation amplitude was adopted as the response time of the present thermometric system.

![Fig. 1. Block diagram of RF generator and thermometry systems. 1: RF generator, 2: thermocouple, 3: reference thermocouple device (0°C), 4: pen-recorder, 5: agar, 6: earthed electrode, 7: un-earthed electrode, 8: cotton thread was drawn in the direction (arrow), 9: junction of thermocouple.](image-url)
5) Agar phantom:
Two w/v % agar, containing 0.85 w/v % NaCl, was prepared for phantom (#5 in Fig. 1) which could be solidified at 37°C in contrast to liquid phantom. Solid phantom was used to prevent convection. Electric conductivity could be varied by NaCl concentrations.

6) Measurement for temperature distribution in the agar phantom:
Two aluminum electrodes of 5.0 cm in the diameter and 16 μm in the thickness (#6 and 7 in Fig. 1) were patched on the opposite faces of the agar in cubic shape of 10×10×10 cm³. The prepared cubic agar was contained in foaming polystyrol container. RF heating was provided for 10 seconds, where the plate current in RF generator was 120 mA. Immediately after the heating, the cotton thread of No. 80 count cotton yarn (#8 in Fig. 1) was drawn at a speed of 2 cm a second to record the temperature profiles along the central axis of the cubic agar phantom. The junction of the thermocouple (#9 in Fig. 1) was set in motion from the center of the earthed electrode and moved along the central axis towards the opposit un-earthed electrode. The RF heating for 10 seconds followed by immediated measurement of the temperature profile was done once in 30 seconds and repeated 20 times. The sequential measurements of the temperature profile along the central axis were thus performed.

III. THEORETICAL CONSIDERATIONS

1) Absorbed power:
Assume that two minute agars A and B, that have volume of V cm³, density of ρ g/cm³ and specific heat of S cal/g·deg, are in contact with each other and heated by RF. The temperatures of the agars satisfy differential equations given below.

\[
\frac{dT_A}{dt} = \frac{Q_A}{J\rho S} - \frac{h}{V\rho S} (T_A - T_B) \quad (1)
\]

\[
\frac{dT_B}{dt} = \frac{Q_B}{J\rho S} - \frac{h}{V\rho S} (T_B - T_A) \quad (2)
\]

where, \(Q_A\) and \(Q_B\) (W/cm³) are the absorbed powers by the minute agars A and B, \(T_A\) and \(T_B\) (°C) the temperatures of agars A and B after t seconds of RF heating, h (cal/s·deg) the heat conductivity of agars, and J is the mechanical equivalent of heat (4.1855 J/cal). These simultaneous differential equations were solved under the initial conditions of \(T_A=T_B=T_0\) at \(t=0\) and the roots are in the following

\[
T_A = T_0 + \frac{V(Q_A - Q_B)}{4hJ} (1 - e^{-\frac{3hJ}{V\rho S} t}) + \frac{Q_A + Q_B}{2J\rho S} t \quad (3)
\]

\[
T_B = T_0 - \frac{V(Q_A - Q_B)}{4hJ} (1 - e^{-\frac{3hJ}{V\rho S} t}) + \frac{Q_A + Q_B}{2J\rho S} t \quad (4)
\]

The calculated temperatures of the agars are shown in Fig. 2, where the factors in
equations (3) and (4) are $Q_A/J=1$, $Q_B/J=0.1$, $\rho=1$, $S=1$, $V=1$ and $h=0.1$. $T_A$ and $T_B$ increased linearly after 4 seconds' heating. The tangents of the two curves at $t=0$ are given by differentiating equation (3) and (4), i.e.:

$$\frac{dT_A}{dt} \bigg|_{t=0} = \frac{Q_A}{J\rho S} \quad (5)$$

$$\frac{dT_B}{dt} \bigg|_{t=0} = \frac{Q_B}{J\rho S} \quad (6)$$

Therefore, the tangents at $t=0$ gives absorbed powers. After a certain period of RF heating, the temperatures $T_A$ and $T_B$ show parallel increments, whereas the absorbed powers are different. Differentiation of equations, where $t$ is infinite,

$$\frac{dT_A}{dt} \bigg|_{t=\infty} = \frac{Q_A+Q_B}{2J\rho S} \quad (7)$$

$$\frac{dT_B}{dt} \bigg|_{t=\infty} = \frac{Q_A+Q_B}{2J\rho S} \quad (8)$$
Equation (7) and (8) show that the temperature of either agar rises in proportion to mean absorbed power. Although the real temperature distribution in the agar phantom must be calculated on the three dimensional continuum model, above simple calculation on isolated system seems to reveal some principal features of the present experiment.

IV. RESULTS

1) Electromotive force of C-C thermocouple:

The electromotive force of C-C thermocouple increases linearly with temperature between 18°C and 51°C. The temperature T in Celsius is given by an empirical equation

\[ T = 24.00 V + 1.600 \]  \hspace{1cm} (9),

where, V is the electromotive force of the thermocouple in mV. Error was within 0.2°C in the above range of temperature and within 0.1°C in the range of temperature

![Graph showing temperature over time after immersion](image)

**Fig. 3.** Response time of thermometric system. Relationship between the time after the immersion and the temperature of the thermocouple were shown. Heating time required for the temperature increment as much as 90% of the differential temperature, \( t_R \), was 170 msec.
between 20°C and 45°C.

2) Response characteristics of the thermocouple:

The thermocouple at room temperature of 22.4°C was immersed into water bath at 41.0°C and the response was observed by the pen-recorder, as shown in Fig. 3. 170 msec was required till the pen-recorder showed increment of temperature as much as 90% of the difference between the two temperatures.

3) Temperature profile:

Temperature profiles along the central axis of the agar phantom after the variety of heating time are shown in Fig. 4. Temperature increment near the electrodes was more remarkable than that in between the electrodes. Sequential changes of temperature at three positions are shown in Fig. 5. Those positions were the centers of the earthed (at position 0 cm) and un-earthed (at position 10 cm) electrodes and a point at 5.9 cm from the earthed electrode, where the measured temperatures were lowest among those at the positions. The increment of temperature at the centers of both

![Temperature profile diagram](image_url)

**Fig. 4.** Temperature profiles along the central axis of the agar normal to electrodes. RF heating for 10 sec in 120 mA plate current was repeated with the interval times of 20 sec. The number n's represent the repeated heating cycle. Position "0 cm" represents that of earthed electrode, while "10 cm" un-earthed electrode.
electrodes were linear within 4 min of heating time, followed by a downward swerving from the linearity.

V. DISCUSSION

In the agar phantom utilized, temperature gradient was produced due to the heterogeneous RF absorbed power which resulted in heat diffusion proportional to the temperature gradient. The absorbed power can be obtained from temperature increment of small specimen thermally insulated. Another alternative is to use initial
increment ratio of the temperature in the phantom which is not thermally insulated. The temperature increment ratio in early stage of heating, as is shown by equations (5) and (6), is not influenced by heat diffusion. RF absorbed power was estimated from measured temperature increment ratio at t=0. In the successive stage of RF heating, temperature gradient increases and dissipated heat by conduction become significant compared with absorbed power as shown in equations (7) and (8). Gradient of the temperature increases until the conduction mediates the heterogeneity of absorbed power. Consequently constant temperature gradient distribution is constituted within the medium.

The electromotive force of the C-C thermocouple increased linearly at the range of temperatures from 18°C to 51°C. The relationship between electromotive force of the thermocouple and temperature is expressed, in general, as a quadratic equation. In the present experiment, the relationship in the range of temperature from 18°C to 51°C could be approximated by a linear equation with moderate error. The errors were within 0.1°C and 0.2°C in the ranges of temperatures from 20°C to 45°C and from 18°C to 51°C respectively.

The response time of the present thermometric system was 170 msec. For the precise monitoring of the temperature profile, heat capacity of the thermocouple and the time constant of the recorder should be minimized to shorten the response time.

Temperature profiles of RF heated agar phantom were assayed. Heating temperature relationships of the phantom were measured. The absorbed RF power was obtained by transforming the equation (5), as shown below:

\[ Q = J \rho S \frac{dT}{dt} \]  

Where, \( \frac{dT}{dt} \) is temperature increment ratio, which is constant only when increment in temperature is linearly related to the heating time. Therefore, only the data obtained within the first 4 minutes of heating can be used for calculation of absorbed power profile.

The cause of deviation from linear relationship between absorbed power profile and the temperature increment ratio would be enumerated as follows:

i) Finite spatial resolution in thermometry due to finite response time resulting from heat capacity of thermometer and the time constant of the recorder.

ii) Altered temperature profile due to heat transfers within or out of phantom.

iii) Concomitant alteration of electro-conductivity of the phantom with the temperature increment. When the temperature raises 1°C, electro-conductivity of an electrolyte increases about 2.5%, but on the other hand the electric constant decreases about 0.5%.

The enumerated phenomena influence one another.

Since the above enumerated causes appear negligible when the linear temperature increment holds, absorbed power profile would be the same as a profile of the increment ratio of temperature under the condition. The above linear temperature increment
holds when the difference of temperature along the central axis of the phantom was less than 3°C and less than 4 minutes of heating time, and when temperature gradient in the phantom was less than 3.2°C/cm.

VI. SUMMARY

(1) RF absorbed power could be measured using agar-physiological salt solution phantom.

(2) Temperatures in variety of positions of the phantom increased linearly with heating time, under the conditions of: less than 4 minutes RF heating, less than 3°C of the temperature difference along the central axis of the phantom and less than 3.2°C/cm of the gradient in temperature profile.

(3) Profile of RF absorbed power can be expressed by the temperature profile under the above condition.

(4) C-C thermocouple of 0.1 mm in diameter was available in measurement of temperature profile of the phantom due to its small heat capacity.

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REFERENCES

1. Arch. D' Arsonval (1893) Action physiologique des courants alterantifs a grande fréquence. Arch. Physiol. Norm. et Path., 25: 401-408.
2. F. K. Storm, D. L. Morton, R. S. Elliott and W. H. Harrison (1979) Radio frequency hyperthermia of advanced human sarcomas. Presented at the annual meeting of the society of surgical oncology, Atlanta, Georgia.
3. S. Sugaar and H. H. LeVeen (1979) A histopathologic study on the effects of radiofrequency, thermotherapy on malignant tumors of the lung. Cancer, 43: 767-783.
4. E. Pfloorn (1930) Kurzwellenbestrahlung des Rattensarkoms. Münch. med Wschr., 77: 1854-1856.
5. J. A. G. Holt (1975) The use of V.H.F. radiowaves in cancer therapy. Australasian Radiol., 12: 222-241.
6. F. Dietzel, D. Gericke, L. Schumacher and G. Linhart (1978) Combination of radiology, microwave hyperthermia and clostridial oncolysis on experimental mouse tumors. In Cancer Therapy by Hyperthermia and Radiation. Urban and Schwarzenberg, Baltimore/Munich, 233-235.
7. A. J. Delario (1935) Methods of enhancing roentgen-ray action. Radiol., 25: 617-627.
8. M. Mikawa (1937) Effect of heat and ultra-short wave rays on Radiosensitivity. Jap. J. Obstet. Gynec., 20: 515-535.
9. R. J. Traub, R. J. Vetter and G. A. Stoetzel (1977) Microwave hyperthermia, chemotherapy, and Co-60 radiation in the treatment of hamster melanoma. J. Microwave power, 12: 40.
10. G. L. Rohdenburg and F. Prime (1921) The effect of combined radiation and heat on neoplasms. Arch. Surg., 2: 116-122.
11. H. H. LeVeen, S. Wapnick, V. Piccone, G. Falk and N. Ahmed (1976) Tumor eradication by radiofrequency therapy. JAMA, 235: 2198-2200.
12. J.A. Dickson and S.A. Shah (1977) Technology for the hyperthermic treatment of large solid tumours at 50°C. Clinical Oncology, 3: 301-318.

13. S.J. Allen (1975) Measurements of power absorption by human phantoms immersed in radio-frequency fields. Ann. N.Y. Acad. Sci., 247: 494-498.

14. C.C. Johnson and A.W. Guy (1972) Nonionizing electromagnetic wave effects in biological materials and systems. Proc. IEEE, 60: 692-718.