6-3

ENHANCING THE EFFICACY OF LOCALIZED THERMOTHERAPY BY MONITORING CHANGES IN TUMOR BLOOD FLOW

F. Sterzer* and R.W. Paglione*
A. Winter** and J. Laing**
E. Friedenthal,*** J. Mendecki,*** and C. Botstein***

RCA Laboratories, Princeton, NJ 08540
The Hospital Center at Orange, Orange, NJ 07051
Albert Einstein College of Medicine, Bronx, NY 10467

Abstract

Changes in the blood flow of tumors being heated with microwaves can be conveniently monitored by monitoring the applied heating power needed to maintain the tumors at given temperatures. Data obtained by this method are presented, and applications to clinical localized thermotherapy are discussed.

Introduction

The changes in tumor blood flow (TBF) caused by localized thermotherapy cannot be accurately predicted because tumors vary from one another in every detail including the organization of their vasculature and their response to hyperthermic temperatures. As will be shown, however, one can conveniently monitor changes in TBF during localized thermotherapy by monitoring the applied heating power needed to maintain the tumor at the temperatures of interest. (Changes in blood flow (BF)in heated normal tissues can also be monitored by the same method.) This ability to monitor changes in TBF during heating is of potentially great value in clinical thermotherapy.

Monitoring Blood Flow

Changes in BF due to microwave heating were monitored by monitoring the ratio of microwave heating power (P) to the increase in tissue temperature (ΔT) due to the microwave heating. For sufficiently large values of BF,

$$P/\Delta T = KBF \qquad (1)$$

where K is a constant.

The minimum value of BF for which equation (1) is valid can be estimated by solving the bioheat equation, a second order differential equation that relates tissue temperatures to microwave heating, blood flow, and various other tissue and environmental parameters. Figure 1 shows a set of solutions of the bioheat equation for plane-wave radiation at 2450 MHz that is incident on a thick slab of muscle. Tissue temperatures are measured 0.5 cm into the muscle slab. It can be seen from the figure that for values of BF greater than about 2.5 mℓ/100 gm/min, ($P/\Delta T$) at any given tissue temperature, is proportonal to BF. Solutions of the bioheat equation for radially propagating waves give similar results. Since the BF in most tumors and in the healthy tissues surrounding them is typically greater than 2.5 mℓ/100 gm/min,[1] equation 1 is applicable in most clinical situations.

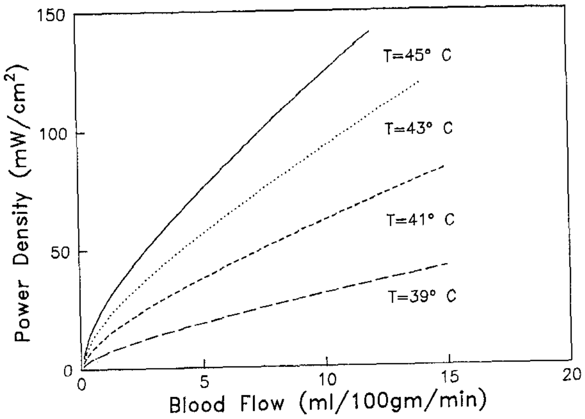

Fig. 1. Calculated values of power density versus blood flow for four temperatures. The model for these calculations consisted of a 10 cm thick slab of muscle type tissue (dielectric constant = 47) that was heated with plane-wave radiation at a frequency of 2450 MHz. The arterial blood temperature was assumed to be 37°C, and the ambient air temperature at the front and back of the slab was assumed to be 21°C. Tissue temperatures at a depth of 0.5 cm are plotted.

Figure 2 shows typical measured curves of equilibrium tissue temperatures versus microwave power. Curve A is for healthy tissues and curve B is for an angioblastic meningioma that had previously received a full course of radiation therapy.

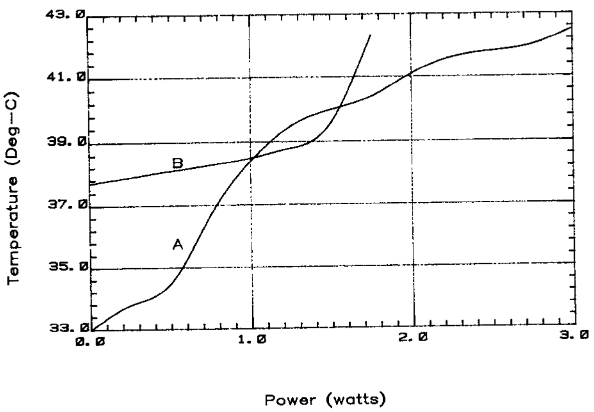

Fig. 2. Steady-state tissue temperature as a function of microwave power measured on (A) a healthy muscle of the right forearm, and (B) in an angioblastic meningioma.

Figure 3 shows a plot of tumor temperature and microwave power taken during a thermotherapy session of a patient with a glioma. Note that the power required to maintain the desired tumor temperature had to be steadily educed during the thermotherapy session.

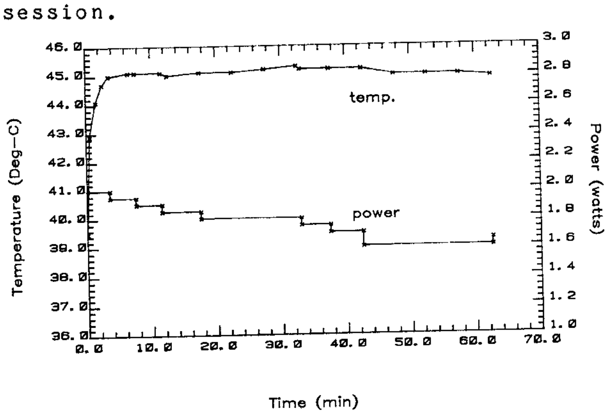

Fig. 3. Temperature and microwave power as a function of time measured during the thermotherapy sessions of a patient with a glioma. A miniature coaxial[1] applicator in a Fischer ventricular[2] cannula was used to heat the tissues. The temperature in the brain tissues immediately surrounding the cannula is about 2.6°C lower than the temperature plotted in the graphs.

Interpretation of Equilibrium Heating Curves

In the healthy tissues measured (Figure 2, Curve A), P/ΔT increased by about a factor of four at hyperthermic temperatures. According to equation 1, this fourfold increase in P can be attributed to an approximately fourfold increase in BF. Fourfold increases in BF in healthy muscle heated to hyperthermic temperatures with 2450 MHz radiations have also been measured by McNiver and Wyper using an Xe-137 clearance technique.[3]

In the equilibrium heating curve of the malignant tumor (Figure 2, Curve B), P/ΔT decreased at high temperatures, indicating that in this particular tumor TBF decreases at high temperatures. Reductions in TBF at high temperatures have also been observed in implanted animal tumors.[4]

Figure 3 illustrates instances where P/ΔT at constant tumor temperatures decreased during thermotherapy sessions. This decrease is most likely due to a reduction in TBF during the thermotherapy. Similar decreases in TBF during and after heating of tumors to hyperthermic temperatures have been observed in animals where heating tumors to 43°C produced petechiae, statis, occasional thrombosis, some endothelial degeneration and persistent hyperemia.[4]

Clinical Implications

With the method described above changes in TBF can be conveniently monitored with standard microwave thermotherapy equipment. This makes it possible to use thermotherapy protocols that are based on the measured response of TBF to heating. Examples of such protocols will be given.

Acknowledgement

The authors wish to thank Dr. M. Ettenberg for calculating Figure 1, Mr. M. Nowogrodzki for many helpful discussions, and Mr. F. Wozniak for building some of the applicators used in our work.

References

1. M.J. Mantyla, "Regional Blood Flow in Human Tumors", Cancer Research, vol. 39, pp 2304-2306, June 1979.
2. A. Winter, et al., "Microwave Thermotherapy for the Treatment of Human Brain Cancer," IEEE MTT-S Digest, pp 180-188, 1983.
3. D.R. McNiver & D.J. Wyper, "Microwave Therapy and Muscle Blood Flow in Man," J. of Microwave Power, vol. 11, pp 168-170, June 1976.
4. H.A. Eddy, "Alterations in Tumor Microvasculature During Hyperthermia", Radiology, vol. 137, pp 515-521, November 1980.