[CANCER RESEARCH 39, 2325-2327, June 1979]
0008-5472/79/0039-0000$02.00

Thermal Dosimetry and Temperature Measurements[1]

D. A. Christensen

Department of Bioengineering, University of Utah, Salt Lake City, Utah 84112

Abstract

A crucial ingredient of any hyperthermia procedure is the accurate measurement of achieved temperature. In this paper, we present some accuracy and resolution suggestions and address the problem of temperature measurements when electromagnetic energy is used as the mode of heating. In such cases, conventional metallic thermometers can cause severe errors due to reradiated fields, high internal heating, and electronic interference. To avoid these problems, several groups have developed either high-resistance lead thermometers or optical-fiber probes using a variety of sensors, including birefringent and semiconductor crystals. A new noninvasive approach uses ultrasound-computed tomography and relies upon the change in the speed of sound *versus* temperature to achieve maps of internal tissue temperature.

Introduction

The very term "hyperthermia" suggests that a critical component of any hyperthermia procedure is the temperature-monitoring system. There exists the requirement for an accurate and convenient means of measuring tissue temperature to assure, on the one hand, that the area under investigation has a sufficiently high temperature to be effective in its treatment (17) but, on the other hand, that this temperature is not so excessively high as to cause undesirable results. The general field of thermometry, including the usage, accuracy, and calibration of conventional temperature sensors, such as thermistor and thermocouple probes, is well documented in the literature (14, 15). Cetas (5) has published a comprehensive article covering the difficult aspects of calibration and accuracy in hyperthermia thermometry.

In this paper, we discuss the problems associated with temperature monitoring during one particular method of thermal delivery, namely, heating by electromagnetic radiation such as RF[2] and microwaves, and outline some possible temperature probes for use in the electromagnetic environment where conventional probes may lead to large measurement errors. We also discuss a novel idea for mapping internal body temperatures by using noninvasive ultrasound tomography.

Temperature Measurement in Electromagnetic Fields

Thermistors, thermocouples, and other traditional probes have numerous virtues for use in hyperthermia monitoring, including small size, accuracy, reliability, and low cost. Unfortunately, they all also possess the serious flaw of utilizing conductive metallic components, shields, and connecting wires in their design. These metallic parts are often the cause of gross temperature measurement errors when the probes are used to monitor tissue or phantom material in an electromagnetic environment. These measurements errors may be due to any one or a combination of the following factors.

Whenever a conducting material such as metal is immersed in electromagnetic radiation, the incident electric field induces a current flow on or near the surface of the metal. The boundary condition at the interface of the metal and the surrounding medium dictates that the tangential electric field vector be continuous across the boundary (16). Thus, for example, the incident tangential electric field will induce a tangential electric field E_t in the metal. This field causes a current flow in the metal of which the density is given by $i_t = \sigma E_t$, where σ is the conductivity of the metal. The current flow in turn reradiates an electromagnetic field (in other words, "scatters" the incident field) into the area surrounding the metal component, causing a perturbation of the field from the state that would exist if the metal were absent. Therefore, the very existence of a metal probe in tissue being heated by electromagnetic means will cause changes in the field patterns and may (depending upon the size and orientation of the probe) lead to sizable heating pattern modifications, such that the probe temperature is not a reliable indicator of mean tissue temperature (10).

The above problem can be alleviated somewhat by a judicious choice of the orientation of the major axis of a long, small-diameter probe. If the long axis is oriented to be perpendicular to the incident electric field (assuming a linearly polarized incident field), then the current flow will take the form of a very short dipole, and the reradiated perturbing field may be small enough to ignore. Unfortunately, it is often impossible to achieve the desired orientation, either because the true polarization of the incident electric field is unknown due to refraction and reflection in the intervening tissue between the applicator and the probe or because the field is not actually linearly polarized, as in the case of the near-field patterns of many antennae in which all 3 spatial components are present.

Incidently, even a nonconducting probe, such as one using a glass fiber bundle, will cause some scattered fields due to a mismatch in the dielectric constant (real) compared to that of tissue (complex), but the reflected energy will be sigificantly smaller than with metal interfaces.

The induced current density in the metal as mentioned above has another untoward temperature effect: it produces ohmic heating in the metal piece itself which is inconsistent with the amount of heating which would occur in the same volume of tissue as that displaced by the probe. This artifactual power density deposition rate, given by $P = i^2/\sigma$, will of course be produced in close proximity to the sensor itself, leading to possibly large errors.

Any probe (even a nonmetallic probe) introduced into the tissue site which does not have a conductivity (and dielectric constant) equivalent to that of the tissue displaced will therefore result in a temperature misreading. However, the conductivity and induced internal currents of metal are such that a nonme-

[1] Presented at the Conference on Hyperthermia in Cancer Treatment, September 15 and 16, 1978, San Diego, Calif.

[2] The abbreviations used are: RF, radiofrequency; LED, light-emitting diode.

tallic probe will cause significantly less volume heating error than a metallic probe when compared to tissue. In any case, the smaller the volume displaced by an implanted probe, the less the heating artifact.

Finally, the connecting wires of a metallic probe in which currents are induced by electric- or magnetic-field coupling to the incident radiation (often pulsed) will carry noise to the measuring electronics and will interfere with the signal from the sensor. By only enabling the measuring system between pulses or between bursts of pulses, one can avoid the interference, but this represents a measuring inconvenience.

The problems described above are of sufficient magnitude that several groups have pursued the development of nonperturbing temperature probes. The resolution and accuracy requirements of such candidate systems are discussed next.

Resolution and Accuracy Requirements

The resolution specifications of any temperature-monitoring system can be grouped into 3 categories: spatial, temporal, and thermometric. Our current understanding of the state of hyperthermia allows the approximate setting of some general guidelines for the resolution required in each category for a usable system.

Thermometric. Evidence gathered thus far seems to indicate that the cell survival rate is a fairly sensitive function of temperature in the region of 43°C (7). Experiments performed show that a difference of only 0.1–0.2°C can cause manyfold changes in the survival rate of exposed cells. Thus, the desired temperature accuracy, as well as temperature resolution, of a usable monitor should be near 0.1°C. It appears easier to provide that degree of resolution than that degree of accuracy, especially when considering long-term drift and instability. Occasional recalibration of the thermometer system may be necessary to have continued confidence in its accuracy.

Spatial. IR thermographic imaging of phantom models irradiated by microwave and RF heating has been performed by Guy (9) and by Cetas and Conner (5). In the latter work, in which RF heating was accomplished with implanted needle electrodes, thermographic views of unperfused models during initial rapid heating show that spatial temperature gradients on the order of 5–10°C/cm were common throughout the RF-heated region. To record such gradients to an accuracy of 0.1°C would require substantial spatial resolution of the monitoring system. However, these gradients became less severe as heating progressed, and steady-state conditions were reached with an accompanying reduction in applied power. Also, it is expected that, in physiologically perfused tissue and with the use of wider-field applicators rather than implanted needles (such as parallel plates or microwave antennae), the gradients would become much more gentle, perhaps ultimately defined by the physical boundaries between tissue regions of differing intrinsic power absorption. Thus, in realistic cases, a spatial resolution on the order of 1 cm would probably suffice. More *in vivo* experimentation with various applicators is certainly needed here to shed light on the question of how much resolution is needed to detect dangerous hot spots.

Temporal. Fortunately, precise temporal resolution (*i.e.*, fast time response of the system) is not needed in normal hyperthermia thermometry systems. Due to the large thermal mass of the heated regions, a time response of 1 sec or less appears to be more than adequate, and almost all current techniques are able to achieve this easily.

Examples of Nonperturbing Probes

The search for nonperturbing temperature probes has proceeded in 2 directions: probes which use conventional thermistor sensors in conjunction with very-high-resistance lead wires to reduce interaction and optical probes using plastic or glass fibers as the communicating link to the sensor. Some examples of certain promising probe designs are given below.

High-Resistance Leads. Bowman (3) and Larsen *et al.* (13) have taken the approach of reducing the interaction between the electrically conducting lead wires and the radiation fields while retaining the well-known advantages of the thermistor sensor by replacing the normal connecting wires with high-resistance leads. By the arguments presented in a previous section pertaining to the effects of conducting materials in electromagnetic fields, the high-resistance wires will have much smaller current densities induced in them so that both the scattered fields and the internal heating will be much lower. In fact, it is theoretically possible to match the conductivity (if not the dielectric constant) of the lead wires to that of typical tissue so that the heating pattern perturbation is minimal. These probes use carbon-impregnated plastic for the lead material. The advantage of such devices is that the thermistor sensor is relatively accurate, reproducible, and stable. Disadvantages are the need for highly sensitive electronics when using such high-resistance leads (several megohms), the limited length of the probe leads dictated by the requirement of keeping the total lead resistance manageable, and the relatively large diameter (about 1 to 2 mm) of the probe tip.

Optical-Fiber Probes. The earliest optical probe, which used plastic polymethylmethacrylate fibers, was the liquid-crystal sensor system developed by Rozzell and Johnson (11, 18). In this device, narrow-bandwidth light from a LED source is passed down a subset of fibers in the probe's bundle where it is reflected from a layer of cholesteric liquid-crystal material at the tip into receiving fibers for detection. The liquid crystals show a varying reflectance of the LED wavelength as a function of temperature. Principal drawbacks to this device are chemical instability of the sensor material (requiring frequent recalibration), hysteresis during temperature cycling, and the relatively large diameter of the tip (1.5 to 2.0 mm). Accuracy, if calibrated, is about 0.1°C.

Christensen (6) has reported the development of a small semiconductor sensor in conjunction with an optical-fiber probe. This particular technique is based upon the band-edge absorption of infrared light as it excites valence-band electrons across the forbidden energy gap into the conduction band upon transmission through the semiconductor sensor. The variation of band-gap energy with temperature provides a varying absorption of the narrow-band light from a LED as a function of sensor temperature. Presently, GaAs is used as the sensor material, giving a range from 20–50°C with a short-term accuracy of better than 0.1°C. Long-term electronic stability has yet to be determined. Advantages of the new device are its inherent sensor stability, range, and small tip diameter (presently 0.25 mm, unsheathed but coated), making it attractive for tissue implantation.

Cetas (4) has developed another type of optical sensor using a small birefringent crystal ($LiNbO_3$) in combination with a polarizing/analyzing film at the end of an optical fiber. The amount of rotation of the polarized optical vector upon passage through the crystal varies with the temperature of the crystal, and thus the intensity of the light transmitted back through the analyzing film is dependent upon temperature.

The electrooptical components of this device are influenced by the same instabilities as are common to other fiberoptic probes, so techniques for canceling source intensity variations are being instituted. Minimum tip diameter to date is about 1.0 mm.

All of the above point probes, of course, suffer from the necessity for implantation at the measurement site. A novel but still unproven technique to avoid this and to map temperature noninvasively is described next.

Noninvasive Ultrasound Temperature Tomography

S. A. Johnson and his colleagues at the Mayo Clinic have pioneered investigations using ultrasound as the energy source in computerized reconstruction tomography (12). Initial studies have successfully reconstructed both acoustic attenuation and acoustic index of refraction (inversely proportional to speed of sound) in several tissue types, including excised whole human breast tissue and temperature-controlled samples of muscle, fat, and connective tissue (1, 8).

The technique for mapping temperature is based upon the change in the speed of sound in tissue which accompanies a change in temperature. Initial studies using isolated samples of different tissues suspended in a temperature-controlled water-bath have shown that, although the absolute speed of sound is dependent upon specific tissue type, the slope of speed *versus* temperature (dv/dT) is nearly the same for all tissue types [with the exception of breast fat, which shows a discontinuity between 32 and 36°C, apparently due to a phase change (1)]. Thus, it is hoped that by reconstructing a tomographic map of acoustic velocity within a region of the body, both before heating and after heating, the common dv/dT term may be used to map information on temperature changes due to the heating.

Based upon experience collected thus far, it appears that the eventual temperature resolution of the technique may be about 0.1–0.3°C, with spatial resolution on the order of a few mm. Presently, the instruments for scanning the tissue regions are single transmitter/single receiver transducer designs, making the scanning times and resulting reconstruction times fairly long (5 to 10 min). But future plans call for multitransducer arrays in which the scanning will be achieved with all-electronic switching (or perhaps a minimum of mechanical movement), reducing scanning times considerably. Also, theoretical studies are addressing the question of reconstructions from reflected data in addition to through-transmission data, looking toward possible mapping of regions with significant bone or air pocket obstacles, such as the thorax and limbs.

Other workers, notably Sachs (19) and Bowen *et al.* (2), are also pursuing this technique. Although the remaining problems in the development of a clinically useful instrument are large, the promise of accurate, noninvasive temperature monitoring is appealing.

References

1. Balasubramanian, R., Greenleaf, J. F., Thomas, P. J., and Johnson, S. A. *In*: Temperature coefficients of acoustic speed in various human tissues. 2nd International Symposium on Ultrasonic Tissue Characterization, Gaithersburg, Maryland, June 1977.
2. Bowen, T., Conner, W. G., Nasoui, R. L., Pifer, A. E., and Sholes, R. R. *In*: Measurement of the Temperature Dependence of the Velocity of Ultrasound in Soft Tissues. 2nd International Symposium on Ultrasonic Tissue Characterization, Gaithersburg Maryland, June 1977. National Bureau of Standards, 1977.
3. Bowman, R. R. A probe for measuring temperature in radio frequency-heated material. IEEE Trans. Biomed. Eng., *MTT-24*: 43–45, 1976.
4. Cetas, T. C. A birefringent crystal optical thermometer for measurements in electromagnetically induced heating, *In*: C. C. Johnson and J. L. Shore, (eds.), Proceedings 1975 USNC/URSI Symposium (Bureau of Radiological Health, Rockville, Md., 1976).
5. Cetas, T. C., and Common, W. G. Thermometry considerations in localized hyperthermia. Med. Phys., *5*: 79–91, 1978.
6. Christensen, D. A. A new nonperturbing temperature probe using semiconductor band edge shift. J. Bioeng., *1*: 541–545, 1977.
7. Dewey, W. C., Hopwood, L. E., Separeto, S. A., and Gerveck, L. E. Cellular responses to combinations of hyperthermia and radiation. Radiology, *123*: 463–474, 1977.
8. Greenleaf, J. F., and Johnson, S. A. Algebraic reconstruction of spatial distributions of refractive index and attenuation in tissues from time-of-flight and amplitude profiles. *In*: Proceedings Symposium Ultrasonic Tissue Characterization, National Bureau of Standards Special Publication 453, 1976.
9. Guy, A. W. Analysis of electromagnetic fields induced in biological tissues by thermodynamic studies on equivalent phantom models. IEEE Trans. Biomed. Eng., *MTT-19*: 205–214, 1971.
10. Guy, A. W., Lehmann, J. F., and Stonebridge, J. B. Therapeutic applications of electromagnetic power. Proc. IEEE, *62*: 55–75, 1974.
11. Johnson, C. C., Gandhi, O. P., and Rozzell, T. C., A prototype liquid crystal fiberoptic probe for temperature and power measurements in RF fields. Microwave J., *18*: 55–59, 1975.
12. Johnson, S. A., Greenleaf, J. F., Samayoa, W. A., Duck, F. A., and Sjostand, J. *In*: Reconstruction of three-dimensional velocity fields and other parameters by acoustic ray tracing. 1975 Ultrasonics Symposium Proceedings. IEEE Catalog No. 75, CHO 994-45, 1975.
13. Larsen, L. E., Moore, R. A., and Acevedo, J. A microwave decoupled brain temperature transducer. IEEE Trans. Biomed. Eng., *MTT-22*: 438–444, 1974.
14. Plumb, H. H. (ed.). Temperature, Its Measurement and Control in Science and Industry. Pittsburgh: Instrument Society of America, 1972.
15. Quinn, T. J., and Compton, J. P. The foundations of thermometry. Prog. Physics. *38*: 151–239, 1975.
16. Ramo, S., and Whinnery, J. R. Fields, and Waves in Modern Radio. John Wiley and Sons, Inc., New York, N. Y., 1960.
17. Rossi-Fanelli, A., Cavaliere, R., Mondovi, B., and Moricca, G. (eds.), Selective Heat Sensitivity of Cancer Cells. Berlin: Springer Verlag, 1977.
18. Rozzell, T. C., Johnson, C. C., Durney, C. H., Lords, J. L., and Olsen, R. G. A Nonperturbing temperature sensor for measurements in electromagnetic fields. J. Microwave Power, *9*: 241–249, 1974.
19. Sachs, T. D., and Tanney, C. S. A two-beam acoustic system for tissue analysis. Phys. Med. Biol., *22*: 327–340, 1977.