COMPARATIVE ASPECTS OF RADIOFREQUENCY AND MICROWAVE BIOMEDICAL RESEARCH*

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Abstract

Physical "scaling" and comparative biomedical aspects of size, metabolism, and thermal tolerance are discussed as criteria for selecting experimental animals to assess biologic effects and potential hazards to man from exposure to microwaves.

A careful review and critical analysis of the literature on biologic effects of rf and microwaves indicates the dilemma in trying to assess the real or imaginary, actual or potential hazard to man from exposure to these energies. Part of this dilemma is a reflection of lack of appreciation of past scientific achievements as well as lack of conceptual approaches to future research in this field. It is helpful to delineate the information into several categories such as a) Biophysical (primary events - absorption, reflection, scattering, heat sources, molecular and cellular biology), b) Biomedical (biochemical and pathophysiologic manifestations in experimental animals), and c) Clinical Response of Man.

The biophysical approach in essence deals with fundamental concepts usually in relation to a component rather than a major biological system or the entire organism. It utilizes whatever knowledge exists or has to be gained by corresponding research on the constituent parts of the tissues, i.e., membranes, proteins, amino acid properties, etc., and attempts by synthesis to predict what happens to the complex system as exemplified by the whole organism such as man with his integrative and homeokinetic control mechanisms. At the systems level, biophysicists make extensive use of models of a mathematical nature or of experimental design (such as layers of tissues, spherical or cylindrical or real shape simulations of man). The biophysical approach has great strength in providing principles of understanding and planning. Its weakness lies in the debatable simplicity of its models no matter how good the knowledge of the principle properties of the constituent part.

At the other end of the scale, the "clinical" or "black box" approach is predicated on recording the effects of actual exposure. This approach has its strength in providing a hoped for definitive answer to a definite investigation of a most complex system. An essential ingredient of this approach is that the experiment is well-conceived, appropriately conducted, and an intelligent relationship of exposure to an appropriate biological endpoint is established. The weakness of this approach stems from the difficulty of extrapolation to larger animals or man from small laboratory animals with differences in methods and capacities of thermal regulation, different absorption cross section, body size and surface area as well as metabolic rates. These differences impose great difficulty in establishing cause and effect relationships unequivocally in the face of considerable statistical problems.

From the aspect of biophysics, the electrical properties of tissues observed at microwave frequencies have been very well investigated, and the electrical properties of practically all tissues are known. The measured values are understood in terms of structure and function of the tissues.[1] In addition, field force effects have been extensively studied by Schwan and his associates.[2,3]

Using a "model" approach, Schwan and his associates[3,4,5] were able to establish the frequency dependence of the depth of penetration values using plane slabs. They were able to point out the reflection at the fat muscle interface and consequent possible heat load on fatty tissue; they were also able to show that low microwave frequencies produce heat in the deep tissues primarily, and that high microwave frequencies are absorbed in the skin.

A considerable body of relative absorption cross section data has been accumulated. It is based on theoretical and experimental studies on spherical and cylindrical phantoms of the human body. In using phantom models of man, Schwan and his associates[5] were able to determine whether the absorption cross section differs much from unity in order to see if measurable external flux and total absorbed energy can be interrelated. This had to be done since otherwise all externally measured values are entirely meaningless. The agreement of simple shapes, mathematically and experimentally studied, with complex forms approaching man instills confidence in the applicability of the model approach to man. From such studies, it has become apparent that the concept of "scaling" among different animal species and from animal to man has to be invoked in a more realistic and precise manner.

More recently the distribution of heat sources induced by microwaves in the body and particularly the brain has been of interest to various investigators. Again a model approach was chosen and the results compared favorably with experimental data.[6-9]

The experimental work of Lehmann and associates[10,11] has essentially demonstrated that the model approach of Schwan and his associates[5] agrees qualitatively and

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semi-quantitatively with measured temperature values. As a byproduct of these studies, doubt is cast on the value of experiments with small animals, since the absolute cross section of small animals is so small as to make it impossible to relate pertinent findings to man.

It is suggested by some investigators that microwaves may have a "specific" biologic effect at the "systems" level. In considering the known biophysical principles and properties of membranes and biopolymers, it is most unlikely that they will respond to microwave fields at 10 mW/cm^2 or less. It appears necessary, therefore, to perform very carefully controlled biomedical studies with respect to physical exposure and biological design by an interdisciplinary group of physical and biological scientists, to test the validity of this point.

Observations in the living animal indicate some of the variables and physiologic controls that yield results which may differ from calculated theoretical estimates. They do not, however, refute the theoretical work, but emphasize the differences between a static system such as a phantom or model on which calculations are based and a living dynamic system with multiple integrative functions, feedback mechanisms, and a fair amount of redundancy which the individual relies upon for homeokinesis.

One of the problems in studying biologic effects of microwaves, as in all biomedical investigations, is the selection of the most appropriate animal specie for study. Animals are quite often selected only on the basis of convenience, economy or familiarity and without regard to their suitability to the problem under study. Because of the lack of awareness and concern in the selection of the experimental animal, many investigations have no inherent value insofar as extrapolation to man is concerned and, in some cases, have led to incorrect interpretations necessitating expensive, time-consuming attempts at confirmation or logical application of the data.

The concept of biological unity implies that comparison between man and other animals will reveal the existence of fundamental mechanisms common to all species. The universality which governs biologic properties in animals should be explored and recognized. This can best be done by developing a comparative approach to the problem of acquisition and analysis of information applicable to man.

The comparative approach includes the use of animals that have anatomic, physiologic or biochemical characteristics and their integrative or coordinating mechansims that are well understood and provide a basis for extrapolation to man. The use of a living model for the study of biological interactions has the unique advantage of making a system available with a homeostatic capability which is the functional integration of the various organs and organ systems.

Many animal studies on the response to rf or microwave exposure have been done with small rodents. Results from experiments on this type of animal are not applicable to human beings, since these animals have high coefficients of heat absorption, small body surfaces, and relatively poor thermal regulatory mechanisms in contrast to man who has one of the best thermal regulatory mechanisms. Animals used in such studies should a) have biological characteristics similar to those of man, b) be of adequate size for meaningful energy absorption and distribution patterns for relating experimental results with that which might occur in man, c) be chosen whose dimensions are larger than depth of penetration values, (if the size of the animal becomes much smaller than the depth of penetration, the test animal is almost completely transparent for the incident energy, i.e. cannot be expected to respond even though exposed to large values of energy flux.) d) efficiency of physiologic thermal regulation should be relatively comparable to that of man, e) the animals should be docile, healthy and easy to handle and house.

Since extensive discussion of the principles of animal selection in biomedical investigations is beyond the scope of this paper, only a few examples will be indicated. Morphologic and functional characteristics of several species of animals are available which can be used to select the most appropriate specie or range of species to permit more valid extrapolation of observed results to anticipated response of man. Such information as surface area, temperature characteristics, cardiopulmonary anatomy and function for general homeokinetic and metabolic relationships as well as ocular dimensions for assessment of cataractogenesis are criteria that should be considered.

Homeotherms (warm-blooded animals) have a highly developed internal temperature controlling mechanism and, within an optimum temperature range, can adjust to temperature changes by controlling blood flow rate and distribution. Outside this region of "thermoneutrality," other mechanisms come into play in warm-blooded animals to provide adaptation. At low temperatures, the metabolic rate increases to provide extra heat, and at high temperatures sweating and panting provide evaporative cooling. The obvious physical analog of this temperature regulation process in homeotherms is that of a regulatory mechanism consisting of a temperature sensor, a controller, and heating and cooling devices.[12] The maintenance of a certain temperature is of vital importance to the organism because all biologic processes are conditioned by temperature. In mammals the central nervous system ceases to function at 44 to 45°C and the heart stops beating at 48°C. A rise in temperature of 5°C causes a twofold to threefold increase in pulse rate, oxygen consumption etc.

All animals have an optimal temperature range within which they can most successfully carry on their activities,and whenever the environmental temperature varies from this optimum range, the organism becomes progressively handicapped. At extremes of temperature, life is not possible. The temperature range at which organisms remain active is somewhat less than that at which life is possible. The optimum temperature range varies from one specie of organism to another, and temperatures that would be fatal for one organism are well within the optimum range for another. These differences undoubtedly arise by adaptation. However, rapid change of environmental temperature might be fatal to an organism, while gradual changes might not.[12]

In general, there is little doubt that biomedical study of several species is required to provide the most reliable extrapolation to man. Ideally, one should choose taxonomically unrelated species to bring out generalizations, with the realization, however, that simply to study multiple species alone will not advance understanding. The main contribution of comparative biology is not to record the same phenomenon in as many different animals as possible, but rather to select intelligently some that can serve for meaningful comparisons. From a spectrum of species, basic information on the comparative reaction of biologic systems can be acquired which in turn can be used to elucidate mechanisms of action. For the study of physiologic function, a common parameter such as metabolic rate, body weight or body surface area could be utilized to provide an index of extrapolation among species.[13] In comparing results of experiments performed in the same or different laboratories, standardization of conditions is mandatory. Studies of experimental animal models should be complemented by retrospective and prospective studies in man himself.

A combination of biomedical parameters should permit assessment of changes in basic physiological functions, differentiation of normal and pathophysiological states, differentiation of specific and nonspecific reactions, and differentiation of defensive-adaptational or compensatory changes, which show self-regulatory properties, from pathological manifestations. The most sensitive criteria for judging the state of regualtory systems are the variability of physiological indices, rather than their absolute values.

Conclusion

A comparative approach with appropriate "scaling" is basic to the elucidation of the nature of vital processes among animals and to place man in his proper biological perspective; it relates the different ways in which various species maintain homeostasis, characterizes animals particularly suitable for demonstrating specific parameters, integrates and coordinates anatomic, physiologic, biochemical, and pathologic similarities of various groups of animals. From a comparative approach we can learn what biologic attributes are unique or common among different animals, study interrelations with environmental stresses and find animals that are most suitable for study of important functions to provide a basis for biological generalization. It behooves the investigator to become aware of the attributes of various animals to obtain the most meaningful results for studying the effects of rf or microwave exposure so that reliable and relevant extrapolation to man can be made.

References

1. H.P. Schwan. Interaction of microwave and radio frequency radiation with biological systems. IEEE Trans. Microwave Theory and Techniques 19: 146, 1971.

2. M. Saito, H.P. Schwan, and G. Schwarz. Response of non-spherical biological particles to alternating electric fields. Biophysical J. 6: 313, 1966.

3. H.P. Schwan. Electrical properties of tissue and cell suspension, In: Advances in Biological and Medical Physics. vol. 5, J.H. Lawrence and C.A. Tobias (eds.), New York: Academic, 1957, p. 147.

4. H.P. Schwan and K. Li. The mechanism of absorption of ultrahigh frequency electromagnetic energy in tissues as related to the problem of tolerance dosage. IRE Trans. Med. Electr. 4: 45, 1956.

5. H.P. Schwan and G.M. Piersol. The absorption of electromagnetic energy in body tissues, a review and critical analysis. Part I. Biophysical aspects. Am. J. Phys. Med. 33: 371, 1954.

6. A.W. Guy. Analyses of electromagnetic fields induced in biological tissues by thermographic studies on equivalent phantom models. IEEE Trans. Microwave Theory and Techniques 19: 205, 1971.

7. C.C. Johnson and A.W. Guy. Non-ionizing electromagnetic wave effects in biological materials and systems. Proc. IEEE 60: 692, 1972.

8. H.N. Kritikos and H.P. Schwan. Hot spots generated in conducting spheres by electromagnetic waves and biological implications. IEEE Trans. Biomed. Engin. 19: 53, 1972.

9. A.R. Shapiro, R.F. Lutomirski, and H.T. Yura. Induced fields and heating within a cranial structure irradiated by an electromagnetic plane wave. IEEE Trans. Microwave Theory and Techniques 19: 187, 1971.

10. J.F. Lehmann, V.C. Johnston, J.A. McMillan, D.R. Silverman, G.D. Brunner, and L.A. Rathbun. Comparison of deep heating by microwaves at frequencies of 2456 and 900 megacycles. Arch. Phys. Med. 46: 307, 1965.

11. J.F. Lehmann, J.A. McMillan, G.D. Brunner, and A.W. Guy. A comparative evaluation of temperature distributions produced by microwaves at 2456 and 900 megacycles in geometrically complex specimens. Arch. Phys. Med. 43: 502, 1962.

12. L.O. Gilstrap, Jr., J.S. McNeil, L.P. Greenberg, and R.B. Spodak. A Compilation of Biological Laws, Effects, and Phenomena, with Associated Physical Analogs. Wright-Patterson Air Force Base, Ohio, 1964.

13. T. McMahon. Size and shape in biology. Science 179: 1201, 1973.