Review

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DOSIMETRIC CONCEPTS AND HEALTH RISK EVALUATION IN NONIONIZING ELECTROMAGNTIC RADIATION PROTECTION

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For publication in the Proceedings of the 6th International Congress of the International Radiation Protection Association, Berlin (West), May 7 - 12 , 1984

Chenik & Mays

This is very nice.

Please consider my comments & suggestions

Thanks

Suzy

Chenik

Very nice, but

I still a few rough

edges! Thanks

Suzy

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GENERAL CONSIDERATIONS

IRPA recently issued guidelines (1) on limits of exposure to electromagnetic fields (EMF) in the frequency range from 100 kHz to 300 GHz. A concept of basic and derived working limits was introduced for the frequency range from 10 MHz to 300 GHz. Basic limits are considered in terms of the specific absorption rate (SAR) expressed in W/kg of body weight. Working limits are derived using the frequency dependence of EMF energy absorption in the human body, and are specified in terms of incident unperturbed electric (E) and magnetic (H) field strengths or equivalent plane wave energy flux density (S) expressed respectively in V/m, A/m or W/m^2. Below 10 MHz no distinction between basic and derived limits was made, and the limits were specified only in terms of incident E and H field strengths. The need for refinement of guidelines was stressed. This requires further development of dosimetric concepts useful in health risk evaluation. The aim of this paper is to discuss possible approaches modelled after those used in ionizing radiation protection (2, 3).

The first step consists of identification of those parameters and quantities which characterize EMF and their interaction with living systems, and which can be meaningfully correlated with bioeffects. The quantities mentioned above (E and H field strengths, S, SAR) do not account fully for the complexity of exposure conditions and mechanisms of interaction. EMF can be generated as continuous (CW) or pulsed (PW) waves. A carrier wave may be amplitude (AM) or frequency (FM) modulated. EMF pulses may be of various shape, amplitude and duration (i.e. pulse width). The pulse repetition rate and on-off periods (duty factor) may vary. Simultaneous exposure to EMF generated by various sources and intermittent, repeated exposures (fractionated dose) variously spaced in time introduce additional complexity. Analysis of biological responses should include the considerations of : 1) the relationship between exposure conditions and the propagation, deposition and conversion of EMF energy within biological objects, or what may be termed the primary interaction, 2) the relationship between the primary interaction and bioeffects defined as changes in biological function and/or structure, 3) the distinction between direct bioeffects (i.e. direct interference of the primary interaction with biophysical and electrochemical phenomena in the living system), and indirect effects (i.e. changes mediated through chain reactions, feed-back loops and responses to direct effects). An indirect bioeffect may be many steps removed from the initial event, and may be detectable at sites different from that of the primary interaction (4).

SPECIFIC ABSORPTION RATE (SAR), SPECIFIC ABSORPTION (SA) AND THERMAL DOSAGE

Conversion of EMF energy into heat is the best understood mechanism of primary interaction. The SAR, defined as the time derivative of the incremental energy absorbed by, or dissipated in, a mass contained in a volume element of a given density (5), is convenient for considerations of bioeffects in terms of heat generation and dissipation rates. However, SAR is a "bulk" quantity dependent on macroscopic dielectric properties of tissues. SAR does not lend itself to considerations of mechanisms of interaction at the cellular or macromolecular level in biological systems, where many species of molecules with different properties coexist. SAR can be spatially and temporally averaged. EMF energy absorption in biological objects is typically nonuniform (5). A whole body average (WBA-SAR) or an average over 1 g of tissue is used (1). Spatial peak SAR may be an order of magnitude higher than the WBA-SAR(5). A peak instantaneous SAR associated with some modern PW sources may be many orders of magnitude higher than a corresponding time-averaged SAR. Once the SAR exceeds the capability of the system for heat dissipation, a temperature increase will occur. A predetermined temperature will be reached after a certain period of time, i.e. after a certain amount of energy is absorbed. The total amount of energy absorbed over a period of time is termed the specific absorption (SA) and is expressed in J/kg. SA can be, similarly to SAR, averaged over a mass (volume) of tissue. An inherent danger in using the SAR and

SA concepts lies in that that the use of any of those quantities may obscure the temporal and spatial variations of EMF energy absorption characteristics.

No systematic investigations of the relative significance of SAR vs SA in quantitating the dose rate or dose - bioeffect relationships were found in available literature. However, it should be noted that for rats and mice exposed under comparable environmental conditions to 2450 MHz CW radiation the lethal dose (WBA-SA) varied between 21 and 25 J/g (6, 7, 8). The SARs, exposure durations and body masses of exposed animals varied over one order of magnitude, from 10 to more than 100 W/kg, from 2 to 30 minutes, and from 30 to 450 g respectively. In other experiments (9), convulsions, which precede death, occurred in rats(400 g, 65 W/kg) and mice(30 g, 80 W/kg) at 24 or 25 J/g. However, an attempt to correlate literature data on effects on behavioral responses (9) with SAR or SA, did not demonstrate any clear advantage of using either the dose rate or dose to establish a quantitative relationship with effects. Assuming a thermal basis for disruption of operant behavior in rats, squirrel monkeys and rhesus monkeys, it was suggested (10) that this phenomenon occurs only if body temperature is raised by at least 1°C.

For a proper analysis a definition of thermal bioeffects is needed. Such bioeffects may be directly dependent on temperature increase, as eg. the passive increase in metabolic rate by 10% per °C. Indirect bioeffects consist in responses needed to maintain thermal homeostasis or in responses evoked by local thermally induced alteration in function of organs, which control functions of other parts

of the body, as eg. the thyroid gland. Such an example is also the decrease in core body temperature following EMF energy absorption in the hypothalamus (11). In this case, the thermal EMF bioeffect evoked by dielectric heating, leads to a net decrease in body temperature and may seem paradoxical, as long as the nonuniformity of EMF energy absorption is not taken into account. It should be added that SAR and SA do not account also for the work needed for activation and maintenance of thermoregulatory responses, i.e. the physiologic cost of thermoregulation.

Nonuniformity of EMF energy deposition leads to the induction of temperature gradients, which may be as large as 4 to 5°C and may persist for long periods of exposure (12). This phenomenon has proven to be most useful in clinical practice for hyperthermic EMF therapy of cancer. Experiences with clinical EMF hyperthermia demonstrated the usefullness of local thermal dosage. It was shown that cell killing depends on the minimum temperature and the duration (time) of heating at a particular location, i.e. within the tumor (13, 14). A concept of thermal dosage was developed (14). This is a function of time combined with a mathematical description of the time-temperature relationship. It was proposed to calculate an equivalent exposure time, which would correspond to "equivalent - minutes" at some reference temperature, chosen from an Arrhenius plot of cell killing rate at various temperatures. The reference temperature is chosen at the point of a break in the plot. For clinical hyperthermia in cancer therapy 43°C may be a convenient reference temperature, and equivalent "degree - minutes" can be calculated (14).

This approach could be used to analyse effects of nonuniform EMF energy deposition in various organs, and to establish temperature thresholds for changes in function. Equivalent degree-minutes can be used to correlate the effects with the time during which a particular organ is subjected to an elevated temperature. Such an approach would allow to establish firmly a thermal (defined as temperature dependent) nature of ~~an~~ a bioeffect. At present, many authors consider an effect as thermal if any increase in temperature has occurred, or even if such an increase may have had occurred. Such a speculative approach to thermal EMF bioeffects (eg. in 15) serves only to obscure the physiologic basis of EMF bioeffects and does not ~~allow~~ permit a scientific analysis of thermal vs nonthermal mechanisms of interaction.

In conclusion, further progress in analysis of EMF bioeffects and health risk evaluation may be achieved if ~~a~~ the concepts of local organ dose (SA) and dose rate (SAR) together with a thermal dose equivalent ~~will be~~ are introduced. Experiments should be designed to test the value of this approach. The design should allow to differentiate between the relative importance of SAR, SA and equivalent thermal dosage for the "threshold" for ~~a~~ any given biological response during exposure, and the time - course, as well as the severity of response, i.e. the tolerance limit. ~~Both~~ Theoretical considerations and the limited data available (eg. ref. 16) indicate that at the phase ~~shift~~ transition temperatures, the effects will not depend on SAR or SA, and ~~proper~~ some correction factors ~~will~~ may have to be introduced.

In the millimeter wave range, resonant frequency dependent effects were demonstrated (17). It was also shown that biologically important molecules (eg, DNA, see 18) may demonstrate resonant frequency absorption of EMF energy. Further refinement of analysis of such bioeffects requires the introduction of appropriate correction factors to account for frequency dependent phenomena, which necessitate interpretation in quantum mechanical terms. These do not lend themselves at present for dosimetric considerations, however, an attempt at developing correction factors for frequency dependent effects may provide an approach for accounting for such mechanisms in dosimetric considerations in future.

DOSIMETRIC CONCEPTS AT LOWER EMF FREQUENCIES

The incident E and H field strengths, proposed as limits for exposure at frequencies below 10 MHz (1), do not account for mechanisms of interaction, and can be considered as a preliminary approach. Available data (19) indicate that the cell membrane may be the site of the primary interaction at lower, particularly extremely low frequencies (19). Frequency and field strength windows for effects complicate the analysis of the dose effect relationship.

An analysis of such phenomena as calcium efflux, effects on cell membrane receptors and permeability (19), seem to indicate that induced current density and/or possibly peak induced E field strength may be the parameters, which may serve best to characterize the in-

teractions, and should be taken into account as quantities for dosimetric considerations, proper allowance being made for exposure durations, and pulse characteristics.

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Suggest listing these as 1. — 2. — 3. — 4. —

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