PULSED RADIOFREQUENCY FIELD EFFECTS IN BIOLOGICAL SYSTEMS

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INTRODUCTION

The possibility that pulsed fields produce biological responses other than those elicited by continuous-wave field of the same average power has been conjectured since the early years of research into the biological effect of radiofrequency (RF) energy. However, because of the limited availability of experimental results, few protection guides and exposure standards promulgated by various private organizations or governmental agencies attempted to specify limits to guard against potential hazards of pulsed radiofrequency fields. Indeed, available results have led some to conclude that there is no compelling evidence that pulsed microwave, of the type produced by radar transmitters, cause biological effects not found following exposure under conditions of continuous-wave radiation at the same average power density (Postow and Swicord, 1986). Nevertheless, the accumulation of recent experimental evidence on the biological effects of pulsed and modulated RF field suggests a need to put such interactions in a more meaningful context and a closer examination of the mechanism(s) of such interactions.

That pulse modulated radiation may penetrate more deeply and therefore, be absorbed more strongly than continuous-wave radiation having the same carrier frequency arises from the fact that pulse modulation provides a series of harmonics whose fundamental components coincides with the modulation frequency. While higher order harmonics are strongly attenuated by biological tissues, harmonics whose frequencies are lower than the sinusoidal carrier frequency will generally penetrated deeper than continuous waves. Moreover, the frequency spectrum of a transient field of short duration may span a wide band from zero to a few GHz. Aside from the effects that are elicited exclusively by pulsed radiation, it is conceivable that the above mentioned difference in energy distribution may be sufficient to produce biological responses from whole organisms that are functions of modulation characteristics of the impinging RF radiation.

This paper will begin with the 1982 ANSI C95 recommendation for safety level of radiofrequency fields with respect to personnel and discuss pertinent findings of pulsed and modulated RF field interaction with single cells and whole-body structures. The objective is to provide a succinct introduction to a variety of peak power effects attending pulsed RF radiation. It should be noted that there is clear indication that the study of pulsed RF field effects in biological systems will continue and even accelerate.

ANSI SAFETY GUIDE

In 1974, the American National Standards Institute issued a standard concerning the safety level of electromagnetic radiation with respect to personnel. Major revisions of this standard were made in 1982 to take into account the significant expansion of scientific knowledge base. Changes include a wider frequency coverage, incorporation of dosimetry and frequency dependence resulting from whole body resonance absorption. This standards prescribes recommended radiation protection guides to prevent biological injury from exposure to RF electromagnetic radiation. Specifically, for human exposure to electromagnetic energy at radio frequencies from 300 KHz to 100 GHz, the protection guides in terms of squared electric field strengths and in term of the equivalent plane-wave, free-space power density, as a function of frequency, are given in Table 1. For both pulsed and non-pulsed fields, the permissible exposure levels are averaged over any 0.1 hour period and the time averaged values should not exceed the values given in Table 1.

The applicability of these safety quides to situations involving short pulsed of RF energy with low pulse repetition frequency is questionable (Lin 1978). The plane-wave, free-space power density allowed by the safety guide for a 0.1-microsecond to 6-minute pulse repeated at once every 0.1 hour is shown in Table 2. The dielectric breakdown field strength or power density of air is 3 X 10^6 V/m or 1.2 X 10^{10} W/m^2, respectively. It can be seen that permissible exposure levels for 0.1 microsecond pulse repeated once every 0.1 hour would exceed the breakdown field strength of air in all cases. Clearly, the safety standard needs to be refined to account for peak power and modulation to provide the protection promised by the standard.

Table 1. ANSI C95.1 - 1982 Radio Frequency Protection Guides

Frequency Range (MHz)	Electric Field Strength E^2 (V^2/m^2)	Magnetic Field Strength H^2 (A^2/m^2)	Power Density (mW/cm^2)
0.3 - 3	400,000	2.5	100
3 - 30	4,000 ($900/f^2$)	0.025 ($900/f^2$)	$900/f^2$
30 - 300	4,000	0.025	1.0
300 - 1500	4,000 (f/300)	0.025 (f/300)	f/300
1500 - 100,000	20,000	0.125	5.0

Note: f = frequency (MHz), 1 mW/cm^2 = 10 W/m^2

Table 2. Permissible Levels for Pulse Power According to ANSI C95.1 - 1982

Exposure Duration (Sec)	Power Density (W/m^2)			
360	10	50	100	10^3
60	60	300	600	6×10^3
1	3.6×10^3	1.8×10^4	3.6×10^4	3.6×10^5
0.1	3.6×10^4	1.8×10^5	3.6×10^5	3.6×10^6
0.01	3.6×10^5	1.8×10^6	3.6×10^6	3.6×10^7
10^{-3}	3.6×10^6	1.8×10^7	3.6×10^7	3.6×10^8
10^{-4}	3.6×10^7	1.8×10^8	3.6×10^8	3.6×10^9
10^{-5}	3.6×10^8	1.8×10^9	3.6×10^9	3.6×10^{10}
10^{-6}	3.6×10^9	1.8×10^{10}	3.6×10^{10}	3.6×10^{11}
10^{-7}	3.6×10^{10}	1.8×10^{11}	3.6×10^{11}	3.6×10^{12}

Note: Dielectric Strength of Air: 3×10^6 V/m, 1.2×10^{10} W/m^2.

PULSED RADIATION

This chapter is concerned mainly with pulse-modulated RF radiation. Figure 1 shows the waveform of rectangular pulses with a pulse width of t_o and a period of T. The pulse repetition frequency is given by 1/T. It is customary to characterize an RF pulse by its duty cycle, which is defined as the ratio of pulse width to the period, i.e. t_o/T. A duty cycle of 1.0 corresponds, therefore, to CW operation. The average power (averaged over a period) is given by the product of the peak power and the duty cycle. For short pulses with low pulse repetition frequency, the average power can therefore be very low, even though the peak power may be in the gigwatt (GW) region.

The peak power output from RF sources has grown by an order of magnitude every decade since 1940 (Florig, 1988). Current high-power laboratory sources range in pulse width from 10 nanoseconds to continuous wave; in frequency from 0.5 GHz to over 100 GHz; in pulse repetition frequency from single shot to thousands of pulses per second; and in power output from several megawatts for continuous wave to many gigawatts for single shot pulsed units (see Table 3). Pulsed power sources with these capabilities are in use today in particle acceleration, inertial-confinement fusion, electromagnetic pulse (EMP) simulation, and in experiments directed toward assessing troop and weapon vulnerability.

Electromagnetic pulses with electric field strength up to 500 kV/m or 663 MW/m^2 and with frequency spectra of 0-100 MHz are produced by nuclear

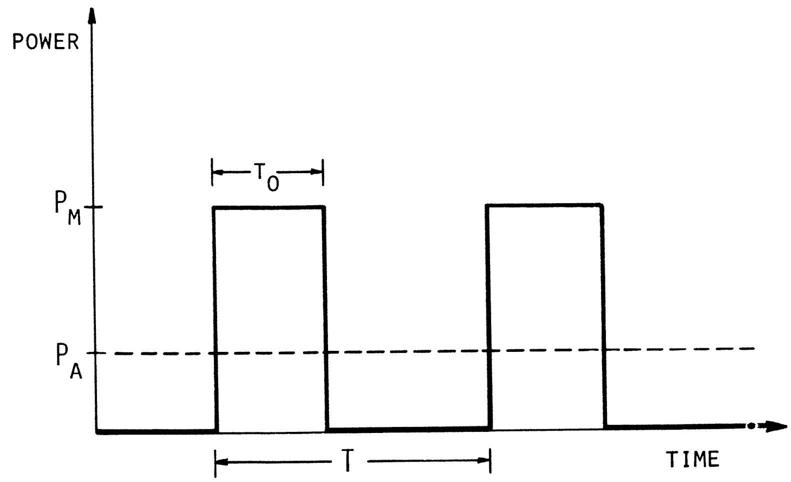

Fig. 1 Characteristics of a rectangular pulse waveform.

detonation and, of course, by EMP simulators. Indeed, some recent simulators have frequency contents that exceed one GHz. A typical EMP waveform can be characterized by a triple exponential time function (Lin,

Table 3. The Frontier of High Peak Microwave Power Generation

Frequency (GHz)	Peak Power (MW)	Generating Devices
1	20,000	Vircator
3	10,000	Magnetron
	5,000	Gyrotron
	200	Klystron
	100	Beam-Plasma Device
10	6,000	Magnetron
30	1,000	Free Electron Laser
100	800	Free Electron Laser

From Florig, 1988

et al., 1975). Indeed, the electric field waveform shown is Fig. 2 represents an average measured EMP time function which has already been exceeded by a significant amount in time (shorter) or in strength (higher).

SINGLE PULSE EFFECTS

A number of intriguing single-pulse exposure effects have been reported in recent years. A few of these are briefly described in the following paragraphs of this section.

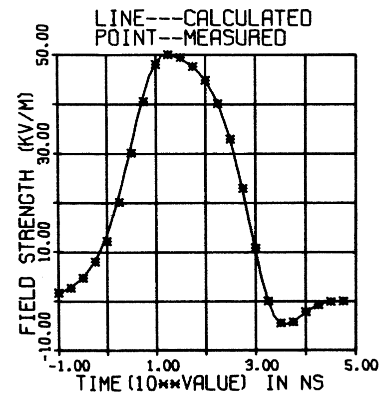

Fig. 2 A representative electric field waveform of EMP signal.

Short bursts (1 sec. or less) of high power microwave energy is used for rapid _in vivo_ inactivation of brain enzymes prior to analysis for neurochemicals. The technique is based on the principle that many neurochemicals are relatively heat-stable substances, while the enzymes that both produce and degrade them are heat labile and denature irreversibly at temperatures around 85^{o}C. In fact, at the present time the most accurate and most widely accepted measurement of many critical neurochemicals depends on the use of microwave to fix brain tissue within a fraction of a second with heat inactivation. The peak power and burst duration reported for mice and rats are given in Table 4. It can be seen that the peak power densities sufficient for sacrifice of laboratory animals in a 2450 MHz waveguide is less than 500 kW/m^2.

Exposure of heads of laboratory animals and human subjects to pulsed microwave radiation evoke auditory sensations in the exposed subject (Lin, 1978). The studies concerning microwave hearing phenomenon have emphasized demonstration of auditory responses and delineation of interactive mechanism. This is as it should be inasmuch as the effect is so very different from those associated with responses to CW radiation, so much so that it implied the possibility of direct modes of interaction that may be neurophysiologically significant. The accumulated results indicate that there is little likelihood that microwave hearing phenomenon arises from an interaction of microwave pulses directly with the cochlear nerve or neurons at higher structures along the auditory pathway, but rather the pulsed microwave energy initiates a thermoelastic wave of pressure in soft tissues that activates the inner ear receptors via bone conduction (Lin, 1980; 1981; Chou and Guy, 1982). A highly pertinent question that remains is: does microwave auditory phenomenon pose a risk to the health of an exposed individual, or under what condition does the effect become a hazard? It has been shown that the threshold of audibility of 2450 MHz microwave-induced sound in humans is about 400 mJ/m^2 per pulse for pulses shorter than 30 microsecond regardless of pulse width or peak power density (Guy, et al, 1975). There exists apparently an optimal pulse width for efficient sound pressure generation which varies according to the head size and frequency of the impinging microwaves (Lin, 1977).

Table 4. Animal Brain Fixation for Rapid Enzyme Inactivation

Exposure Duration (Sec)	Net Power (KW)	Incident Power* (W/m^2)	Brain Absorption (W/g)
Rats (Lenox, et al, 1977)			
2.80	3.5	2.1×10^5	20.5
Mice (Schneider, et al, 1982)			
1.40	2.5	1.5×10^5	145
0.50	6.3	3.7×10^5	400
0.35	6.3	3.7×10^5	575

*WR 430 Waveguide Cavity at 2450 MHz

The susceptibility of rodents to pulsed microwave-induced startle and convulsive responses have been reported nearly a decade ago (Guy and Chou, 1982). Animals exposed to a single pulse of 915 MHz microwave in the range of one microsecond to 360 milliseconds were shown to exhibit seizure reactions lasting for one minute after exposure, followed by a 5-minute unconscious state during which normal reflexes were displayed. These results indicate a threshold energy density of 28 kJ/kg in the head of a rodent for convulsion, regardless of pulse width. It should be noted that a maximum brain temperature of 46°C was recorded at the threshold exposure level. The animal began moving when brain temperature returned to within 1°C of normal. Histological examination revealed some demyelination of neurons one day after exposure and some microfocal glial nodules in the brain one month after exposure.

Although the potential biological effects of EMP pulses have been suggested for sometime (Milroy, et al., 1974, Lin, et al., 1975, 1976), its importance has been recognized only in recent years. While much remains to be learned about the biological effects of EMP, it is clear that the effects are very different from responses to CW radiation. So much so that it implies the possibility of significant neurophysiological interaction. For example, it has been shown (Bernardi, et al, 1984) using the Hodgkin and Hexley nonlinear membrane model that the current density induced in biological tissues by a Gaussian EMP pulse with a energy density equivalent to the maximum permissible under the 1982 ANSI guide would produce a large alteration in the resting potential of excitable cellular membranes. Indeed, action potentials could be generated for pulse widths of one millisecond or less. However, the physiological significance is obscure. The threshold of action potential excitation varies inversely with pulse width; i.e. the required incident electric field strength would be 400 and 2000 kV/m for 1 millisecond and 10 microsecond pulses, respectively (Bernardi and D'Inzeo, 1984).

MULTIPLE PULSE EFFECTS

The literature on biological effects of RF fields modulated with a train of brief rectangular pulses of high peak power and low repetition rate while scarce is becoming increasingly more abundant. Although such irradiation has been shown to produce responses alone or in combination with other stimulants that are dependent on the animal and tissue preparations, and on peak power and pulse width, effects have often been characterized in terms of average power or average specific absorption rate (SAR). It should be noted that for short pulses with low pulse repetition rate, the average power can be very low, even though the peak power may be in the megawatt (MW) or gigawatt (GW) region. Clearly, there is a need to specify explicitly the pertinent pulse power exposure parameters. Nevertheless, there exists a few studies which attempted to quantify the relationship between biological changes and peak power and pulse repetition rate.

A behavior study involving rhesus monkey exposed at near resonant and above resonant frequencies showed that the performance of an animal trained to press a lever for food (observing -response) was impaired at a threshold of 514 kW/m^2 of 1.3 GHz energy pulsed at 370 pps with a pulse width of 3-microsecond, and 1.06 MW/m^2 of 5.8 GHz energy pulsed at 662 pps with a pulse width of 2-microsecond (deLorge, 1984). In all cases, the front surface of the upright, seated rhesus monkey was irradiated by a horizontally propagated, vertically polarized plane wave. These exposure conditions were associated with reliable increases in colonic temperatures typically in the range of 1^oC above sham exposure levels.

That microwave pulses can serve as a discriminative cue in behavioral situations is supported by the works of several investigators (Frey and Feld, 1975; Johnson, et al, 1976; Hjeresen, et al, 1978). Food-deprived laboratory rats could be trained to make a specific response to obtain food during presentation of 150 kW/m^2 of 915 MHz energy pulsed at 10 pps with a pulse width of 10-microsecond (Johnson, et al, 1976). Similarly, rats tested in a two-compartment shuttlebox, where one compartment is exposed with 330 kW/m^2 of 2880 MHz microwave pulsed at 100 pps with a pulse width of 2.3-microsecond, and the other is shielded, spend a significantly higher percentage of time in the shielded side (Hjeresen, et al, 1978). Apparently, the rats found the microwave stimulus sufficiently aversive to exhibit an active avoidance response. It is interesting to note in both situations mentioned above, the animals showed continued ability to perform correctly when presented with conventional acoustic stimuli.

Pulsed microwaves have been shown to affect the action of a variety of psychoactive drugs. For example, 45 minutes of irradiation with 10 kW/cm^2 of 2450 MHz energy (SAR, 600 W/kg) pulsed at 500 pps with a pulse width of 2-microsecond enhanced apomorphine hypothermia and stereotypic behavior, morphine-induced catalepsy and lethality, but it attenuated amphetamine-induced hyperthermia (Lai, et al, 1983). Other specific and nonspecific effects of pulsed microwave on the actions of psychoactive drug and implications of the data regarding function of the nervous system can be found in a recent review (Lai, et al, 1987).

Using isolated rat lenses, a series of studies have found that irradiation in vitro with 918 MHz pulses of 10-microsecond width and 24 kW peak power delivered at different repetition rates produced histopathological damages at the lens equator (Stewart-DeHaan, et al., 1983, 1985; Creighton, et al., 1987). Although the threshold at which damage was observed in the lenses varied depending on the type of damage, the lowest SAR at which holes within the fiber cells in the equatorial region were observed occurred at 231 W/kg after 6 minutes of exposure. Moreover, the depth of damage was about 4.7 times as great as for unmodulated sinusoidal radiation. The actual ratio of damage from pulsed to CW radiation varies depending on total dose and decreases when either total dose is increased or peak power is decreased (Trevithick, J.R., 1988, private communication). It should be noted that extrapolation from in vitro to intact lens in the whole animal is speculative and difficult to substantiate. Nevertheless, these results suggest that high power pulsed microwave radiation is capable of causing lenticular damage that is not related to average temperature elevation.

MECHANISM OF INTERACTION

The mechanism(s) responsible for pulse-modulated RF interaction with biological systems is poorly understood. Several investigators have attempted to account for the responses from physical and physiological considerations (Adey, this volume; Lai, et al., 1987). While microwave-induced increase in thermal stress is clearly a contributing factor to some of the effects outlined above, a majority of the responses can not be easily related to average temperature elevation.

Absorption of high power pulsed microwave radiation can produce thermoelastic waves in biological tissues (Lin, 1978). Whether the microwave energy is delivered as a single pulse or a train of pulses, displacement and pressure are induced in target organs and propagate with a speed comparable to an acoustic wave in tissue (Lin, et al., 1988). The calculated peak displacement and pressure in a spherical model of animal or human head whose size varying from 20 to 70 mm irradiated with a 10-microsecond pulse of 918 or 2450 MHz energy at a peak SAR of 1 W/g are shown in Table 5. It can be seen that a peak power density of 5 MW/m^2 of short pulse width radiation produced by newly developed high-peak-power microwave sources could induce in the adult human head a pressure increase and tissue displacement of 170 N/m^2 and 10 nm, respectively. The quantity of increase in pressure and displacement could conceivably cause physical damage to cell membranes and cytoplasm. Indeed, isolated rat lens has been found to displace by 10 nm when irradiated with a 10-microsecond microwave pulse having an energy density of 300 J/m^2 (Brown and Wyeth, 1983). It has been suggested that thermoelastic expansion and the resulting pressure waves in the lens is the most likely mechanism by which high-power pulsed microwave produce histopathological damage to the ocular lens (Creighton, et al., 1987).

Table 5. Peak Pressure and Displacement in Sherical Head Models Irradiated with 10 us Rectangular Microwave Pulses at a Peak Absorption Rate of one W/g

Sphere Radius (mm)	Microwave Frequency (MHz)	Species	Pressure (N/m^2)	Displacement (10^{-4}nm)	Incident Power (W/m^2)
20	2450	guinea pig	0.408	2.16	4,450
30	2450	cat, monkey	0.369	1.51	5,890
50	918	human infant	0.961	9.34	12,820
70	918	human adult	0.682	3.97	21,830

As mentioned previously, the microwave pulse induced hearing in humans arises from an interaction of microwave pulses with soft tissues in the head to initiate a thermoelastic wave of pressure that activates the inner ear receptors via bone conduction. While there is very little data regarding the effect on the hearing apparatus of exposure to microwave pulses, many factors in addition to microwave frequency that possibly influence the response including pulse shape, duration, peak power and pulse repetition rate. It is clear that threshold microwave auditory response would have insignificant effect on the hearing apparatus. However, the known effects of sound exposure in addition to hearing include the nonauditory, general physiological and psychological reactions.

The nonauditory effects of sound exposure are quite subtle compared with responses of the hearing apparatus. The reactions are in many aspects similar to general stress responses that can be elicited by such stimuli as pain and motion stress. Some of the bodily functions which have been reported to be affected by excessive sound exposure include respiration, digestion, and circulation. However, the most widely reported nonauditory effect of sound exposure is annoyance. In fact, criteria for limiting community noise are often based on the presence of annoyance reactions among exposed population groups (Kryter, 1970; Krichagin, 1978; Ahrlin and Ohrstrom, 1978).

Annoyance is influenced by such factors as attitude, motivation, physical surroundings, temperature, and a host of others. It generally refers to a reaction which is present after prolonged sound exposure and has been defined as a feeling of displeasure or a general adverse attitude toward a factor in the environment which the subject knows or believes could adversely affect its health or well being (Borsky, 1972).

Although annoyance reaction to microwave pulses has not been explicitly evaluated in humans or animals, the studies described above show that laboratory rats find the microwave auditory effect sufficiently annoying or aversive so that they are motivated to actively avoid the exposure (Frey and Feld, 1975; Hjeresen, et al., 1978). In fact, it can be shown that for the microwave parameters used, i.e. 2.3-microsecond wide 2880 MHz microwave pulses at 450 kW/m^2, peak power density, microwave-induced peak pressure level inside the rat's head is about 120 db. A value that is well within the hearing range and comparable to that found to be very annoying to humans.

The effects on psychoactive drug actions observed after pulsed microwave exposure may also be caused by an annoyance reaction. The auditory system could be the afferent sensory pathway that causes changes in brain functions and alteration in psychoactive drug actions. However, the present knowledge is far from adequate to unequivocally explain the altered drug effects (Lai, et al., 1987). It should be noted that microwave radiation has been speculated as a generalized stressor (Lu, et al., 1980).

CONCLUSIONS

The question of whether high power pulsed microwave poses a risk to the health of an exposed individual or under what conditions do effects become health hazards is highly pertinent and deserves urgent attention. While a meaningful consensus on the benignity or peril of pulsed microwave exposure is yet to be achieved, it is clear that exposure of laboratory animals and human subjects to pulsed microwave radiation can evoke physiological and psychological responses in the exposed subject. Moreover, these effects can occur at incident power levels that are at or below the existing ANSI C95.1-1982 guidelines for safe human exposure (Tables 2 and 6). While there is very little likelihood that the microwave auditory effect at threshold incident power can constitute a hazard, exposures at levels that are significantly higher than threshold will undoubtedly be very harmful to cell membranes, cytoplasm and whole organisms. Inasmuch as auditory effect signifies an effect on sensory function and lens damage represents an influence on tissue pathology, and both appear to stem from pulsed microwave-induced thermoelastic expansion of tissue, it seems reasonable to

Table 6. Biological Responses to Pulsed RF Energy

Responses	Exposure Duration (sec)	Incident Power (W/m^2)	Peak SAR (W/g)
Auditory Sensation	10^{-6}	4×10^5	160
Membrane Excitation	10^{-3}	4×10^8	
	10^{-5}	8×10^9	
Unconsciousness	0.1		280
Lens Damage	360 (10 us)	5×10^6	
Drug Interaction	27×10^3 (2 us)	4.5×10^4	6×10^5
Behavior Response	3600 (2.3 us)	3.3×10^5	9.1×10^6
	30 (10 us)	1.5×10^5	1.5×10^6

regard these as lower and upper bounds for a consideration of permissible limits of pulsed microwave exposure. The thresholds for behavior modification and drug interaction are lower by about one to two order of magnitude.

For example, the threshold of audibility of microwave pulses to humans is about 400 mJ/m^2 per pulse for pulse widths shorter than 30-microsecond regardless of peak power. Moreover, deformation (10 nm) of lens has been found to occur when irradiated with a 10-microsecond pulse having an energy density of 300 J/m^2 per pulse; the calculated pressure increase was as high as 170 N/m^2. These presumably caused the observed lens histopathology. It should be noted that the threshold for excitation of excitable membranes would be several orders of magnitude greater than the above mentioned values for the pulse widths of interest. Moreover, the startle and unconciousness responses observed in rodents occurred only for long pulses and in all cases, there were substantial temperature elevation (2-8°C). Thus, a quantity based on absorbed energy derived from between the values of 400 mJ/m^2 and 300 J/m^2 per pulse for pulse widths of 1 ms or less may be sufficient for protection against inadvertant exposure to pulsed RF radiation except for the microwave auditory effect.

Obviously, the above consideration is based on theoretical treatment and limited experimental evidence. The kinds of studies that would be useful are behavioral investigations of pulsed microwave exposed animals including effects on learning and performance, and morphological examinations of the central nervous system and hearing apparatus of exposed animal subjects.

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